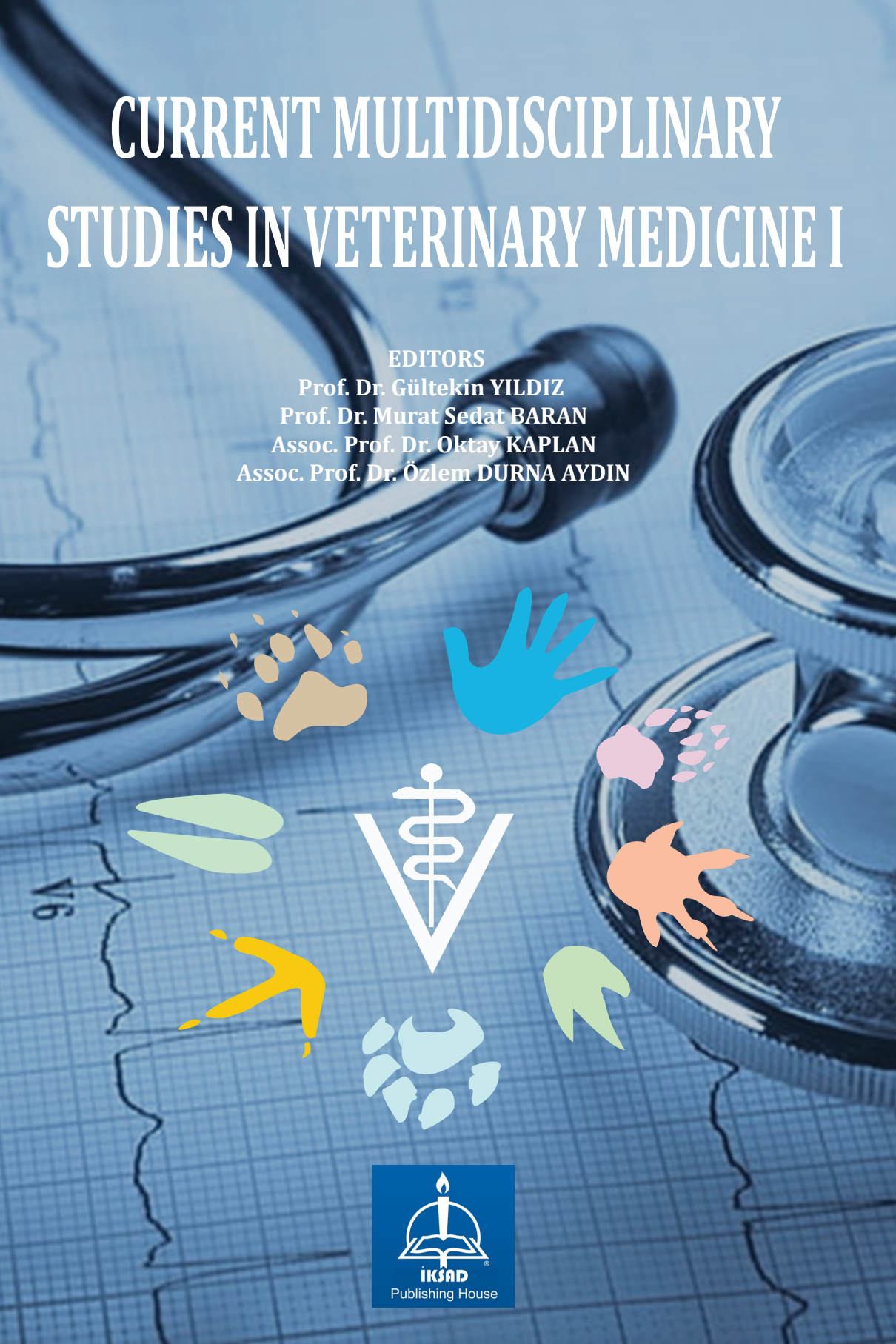
CURRENT MULTIDISCIPLINARY STUDIES IN VETERINARY MEDICINE I

EDITORS
Prof. Dr. Gültekin YILDIZ
Prof. Dr. Murat Sedat BARAN
Assoc. Prof. Dr. Oktay KAPLAN
Assoc. Prof. Dr. Özlem DURNA AYDIN



İKSAD
Publishing House

CURRENT MULTIDISCIPLINARY STUDIES IN VETERINARY MEDICINE I

EDITORS
Prof. Dr. Gültekin YILDIZ
Prof. Dr. Murat Sedat BARAN
Assoc. Prof. Dr. Oktay KAPLAN
Assoc. Prof. Dr. Özlem DURNA AYDIN

AUTHORS

Prof. Dr. Gültekin YILDIZ
Prof. Dr. Hüseyin NURSOY
Prof. Dr. Murat Sedat BARAN
Prof. Dr. Turgut KIRMIZIBAYRAK
Assoc. Prof. Dr. Duygu Neval SAYIN İPEK
Assoc. Prof. Dr. Kadir BOZUKLUHAN
Assoc. Prof. Dr. Kadir ONK
Assoc. Prof. Dr. Oğuz MERHAN
Assoc. Prof. Dr. Oktay KAPLAN
Assoc. Prof. Dr. Özlem DURNA AYDIN
Assoc. Prof. Dr. Tahir BAYRIL
Assist. Prof. Dr. Emine ÇATALKAYA
Assist. Prof. Dr. Polat İPEK

İKSAD
Publishing House

(The Licence Number of Publicator: 2014/31220)
TURKEY TR: +90 342 606 06 75
USA: +1 631 685 0 853
E mail: iksadyayinevi@gmail.com
www.iksadyayinevi.com

ISBN: 978-625-8323-21-4
Cover Design: İbrahim KAYA
July / 2022
Ankara / Turkey
Size = 16x24 cm

CONTENTS

PREFACE

Due to some reasons such as population growth, global warming, drought and globalization, human beings have the most basic right of "food security", in other words, "to always be able to provide food produced with appropriate production techniques and reliable and superior nutritional qualities in order to live a healthy, effective and productive life". is rapidly losing its potential. The increasing population, the ineffective use of existing natural resources, the decrease in the amount of food per person day by day are important problems that are expected to be solved. These problems show their effects with various crises around the world. Since the world food crisis affects the most basic need of human beings, nutrition, its impact is not as indirect as other crises. The high increases in food prices around the world have turned into a global crisis, and unfortunately, economic instability causes social unrest in all countries today.

Among the basic nutrients, those of animal origin occupy a very important place. This importance; It originates both from its qualities as a nutrient and from the production characteristics of animal products. In order to be able to talk about an adequate and balanced diet, a certain part of the daily protein requirement, at least 40-50%, must be provided from animal-derived nutrients. In the sufficient and economical production of animal foods, multidisciplinary knowledge, synthesis and studies are needed in many branches of veterinary medicine. In this book, information on Current Multidisciplinary Studies in Veterinary Medicine has been compiled.

We would like to thank our valuable academic friends for their contributions in the preparation of the book "Current Multidisciplinary Studies in Veterinary Medicine I", and we hope that this book, prepared with great effort and devotion, will be useful to students, Veterinarians, Agricultural Engineers, breeders and researchers.

EDITORS

Prof. Dr. Gültekin YILDIZ[1]

Prof. Dr. Murat Sedat BARAN[2]

Assoc. Prof. Dr. Oktay KAPLAN[3]

Assoc. Prof. Dr. Özlem DURNA AYDIN[4]

[1] Ankara University, Veterinary Faculty, Department of Animal Nutrition, and Nutritional Diseases, 06110, Ankara, TURKEY; ORCID: 0000-0002- 1003- 9254; E-mail: gyildiz@ankara.edu.tr

[2] Dicle University, Veterinary Faculty, Department of Animal Nutrition, and Nutritional Diseases, 21280, Diyarbakır,TURKEY; ORCID: 0000-0002-7297-8556;E-mail: msedatbaran@dicle.edu.tr

[3] Dicle University, Veterinary Faculty, Department of Animal Nutrition, and Nutritional Diseases, 21280, Diyarbakır,TURKEY; ORCID: 0000-0001-6143-8987; E-mail:okaplan61@gmail.com

[4] Kafkas University, Veterinary Faculty, Department of Animal Nutrition, and Nutritional Diseases, 36040, Kars, TURKEY; ORCID: 0000-0003-4532-6795; E-mail:odurna36@gmail.com

CHAPTER 1

ACUTE PHASE RESPONSE AND SOME ACUTE PHASE PROTEINS IN ANIMALS

Assoc. Prof. Dr. Oğuz MERHAN[1],
Assoc. Prof. Dr. Kadir BOZUKLUHAN[2]

[1] Kafkas University, Veterinary Faculty, Department of Biochemistry, 36100, Kars, TURKEY; ORCID: 0000-0002-3399-0667; Email: oguzmerhan@hotmail.com
[2] Kafkas University, Kars School of Higher Vocational Education, 36100, Kars, TURKEY; ORCID: 0000-0003-4929-5156; E-mail: kbozukluhan@hotmail.com

1. INTRODUCTION

Acute phase proteins (APP) are known as a group of proteins whose concentrations increase (positive APP) or decrease (negative APP) in the blood in inflammation, infection, tissue damage, neoplastic developments and some immunological diseases occurring in the organism (Gruys et al., 1994; Petersen et al., 2004).

During the disease, a physiological defense reaction occurs in the organism, which restores homeostasis and prevents microbial growth. In this reaction, which is called the acute phase response (APR), a local response occurs in the diseased body area and some mediators are released into the environment. Many different reactions such as fever, anorexia, leukocytosis, increased secretion of glucocorticoids, increased blood flow to the inflamed area, activation of the complement system, clot formation, decreased serum Ca, Zn, Fe, vitamin A levels, negative nitrogen balance, and changes in the concentration of some plasma proteins develop in these mediators by activating receptors on different cell (Whicher et al., 1991; Gruys et al., 1994; Gruys et al., 2005a). APP are species specific and although their diagnostic importance varies by animal species, while the serum level of positive APP (pAPP) such as haptoglobin, ceruloplasmin, and fibrinogen increases due to APR, the level of negative APP (nAPP) such as albumin, prealbumin and transferrin decreases (Murata et al., 2004; Gökçe and Bozukluhan, 2009).

2. ACUTE PHASE RESPONSE (APR)

The acute phase response is a nonspecific reaction shown by the organism to restore the homeostasis that is impaired as a result of inflammation, tissue damage, infection, and neoplastic growth (Gruys et al., 1994; Petersen et al., 2004; Gruys et al., 2005a; Gruys et al., 2005b). The task of APR is to protect organs from further injury, destroy infectious agents, clean harmful molecules and residues for the organism, and activate repair process necessary for the organism to return to its normal function and restore homeostasis as soon as possible (Gruys et al., 1994; Petersen et al., 2004; Gruys et al., 2005a).

Cytokines: The cytokines that act as intracellular and intercellular signaling molecules and are soluble biological mediators (Ramadori and Christ, 1999; Ceciliani et al., 2002) are in peptide or glycoprotein structure and their molecular weights vary between 20-30 kDa. While the cytokines generally stimulate APP synthesis, they regulate corticosteroids cytokine activity. Macrophages and neutrophils arriving at the inflammation site secrete pro-inflammatory cytokines (Interleukin 'IL'-6, IL-1β, tumor necrosis factor 'TNF'-α, interferon 'IFN'γ, IL-8 and macrophage inhibitor protein-1) together with endothelial cells. The pro-inflammatory cytokines, which cause systemic APR to occur and APP to be synthesized, provide to regulate the immune response by showing a wide variety of effects (Suffredini et al., 1999; Ceciliani et al., 2002). TNF-α, which has a polypeptide structure and a weight of 17 kDa, is a cytokine that plays a role in the inflammatory response and causes muscle catabolism, hyperglycemia

and amino acid uptake by the liver via glucocorticosteroids. IL-1, which is synthesized from mononuclear cells spread to various tissues (Ceciliani et al., 2002; Gruys et al., 2005a), provides more IL-1, IL-6 and chemokine synthesis by affecting macrophage and endothelial cells, while regulating local inflammatory reactions at low concentrations. As a result, neutrophils attach to the endothelium and pass into the inflamed tissue. When it reaches high concentrations, it causes an increase in body temperature, release of APP from the liver, and cachexia by entering into the bloodstream (Massart et al., 2020).

IL-6, which is secreted by monocytes, macrophages, lymphocytes, endothelial cells, fibroblasts, hepatocytes and many other cells (Ceciliani et al., 2002; Tizard, 2004; Gruys et al., 2005a), is a glycosylated protein with a molecular weight of 22-27 kDa (Tizard, 2004). IL-6 (Fattori et al., 1994), which is responsible for the production of fibrinogen and C-reactive protein (CRP), provides monocytes to come stabile condition by inhibiting cytokine secretion (Gruys et al., 1994).

The cytokines, which are related with inflammation, increase the production of cytokines corticotropin and cortisol by stimulating corticotropin-releasing hormone. Cortisol reduces pro-inflammatory cytokine release, capillary permeability and leukocyte activation, stabilizes lysosomal membranes, and suppresses immune system cells (Ceciliani et al., 2002). The stimulation of arginine-vasopressin production by IL-6 may explain the hyponatremia that occurs in some inflammatory diseases. The cytokines, which are related with

inflammation, are also induced nitric oxide synthase, Mn-superoxide dismutase, and microsomal heme oxygenase; thus, they can reduce tissue damage due to oxidants. IL-6 increases the production of metal-binding metallothionein and, accordingly, Zn binding. IL-1β and TNF-α decrease the response to growth hormone by reducing the synthesis of growth hormone receptors in liver cells and reduce plasma insulin-like growth factor I levels (Gabay and Kushner, 1999).

During APR, while ACTH, cortisol, adrenal catecholamines, glucagon, insulin, growth hormone, aldosterone, vasopressin and prolactin concentrations increase (Gabay ve Kushner, 1999), levels of renin, thyroxine and gonadal steroids decrease (Gruys et al., 1994). Protein catabolism and gluconeogenesis increase during APR. The degradation of muscle proteins increases due to hunger and negative energy balance that develops as a result of many diseases (Gabay and Kushner, 1999; Gruys et al., 1994; Petersen et al., 2004; Gruys et al., 2005a) and the released amino acids are used to synthesize APP, immunoglobulins, and collagen used for tissue repair. In addition, these amino acids are used in gluconeogenesis and energy production as well as lymphocyte and fibroblast production (Gruys et al., 1994; Petersen et al., 2004; Gruys et al., 2005a). APR causes a decrease in lymphocyte function, bactericidal effect of neutrophils and phagocytosis abilities of macrophages in animals with its suppressive effect on the immune system (Kushner, 1982).

3. ACUTE PHASE PROTEINS (APP)

Concentrations of acute phase proteins change in cases of infection and inflammation, and the level of response is accepted as a nonspecific indicator of damaged tissue status (Kent, 1992). APP provide killing pathogenic microorganisms, repairing tissue damage and making the body healthy again (Murata et al., 2004). In addition to informing the clinician about the formation of the inflammatory process and being a good marker in the diagnosis of the disease, the use of fast and sensitive measurement methods was made the measurement of APP popular (Whicher et al., 1991). Although classical APP such as albumin and fibrinogen are easier and cheaper to measure, they are less clinically relevant for diagnosis and monitoring of inflammation. For example, a low albumin/globulin ratio (A/G) is indicative of an acute phase reaction in infection or inflammation in dogs and cats. However, the sensitivity and specificity of the ratio is not as high as that of pAPP such as CRP in the diagnosis of clinical diseases. Similarly, the A/G ratio can sometimes be a valuable test to detect this infection in cats with feline infectious peritonitis, but α1-acid glycoprotein (α1-AGP) [orosomucoid, serosomucoid] from pAPP offers a much better diagnosis (Ceron et al., 2005). CRP and α1-AGP ceruloplasmin are important APP in dogs and cats (Jain et al., 2011), haptoglobin and SAA in ruminants and it was stated that serum or plasma concentrations increase following tissue damage in trauma, various infections and inflammatory conditions (Cray et al., 2009).

It was noted that important information can be obtained in the control or diagnosis of existing or subclinical diseases with the measurement of APP in herds (Karreman et al., 2000). Especially, it was noted that there may be an important relationship between the increase rate and duration of the pAPP concentration and the severity and prognosis of the disease (Petersen et al., 2004), but if the environment and stress forming factors are ignored during the evaluation of the measurements (Alsemgeest et al., 1995), false results may be obtained (Petersen et al., 2004).

APP are classified as those whose blood concentrations decrease during inflammation (prealbumin, albumin, transferrin) of nAPP and those whose blood concentration increases (CRP, serum amyloid A 'SAA', α1-antitrypsin 'AT', α1-AGP, ceruloplasmin, haptoglobin, fibrinogen) of pAPP (Skinner et al., 1991; Gruys et al.,1994; Petersen et al., 2004).

A) Positive Acute Phase Proteins (pAPP)

Haptoglobin: The molecular weight of haptoglobin, which consists of 2α and 2β chains linked by disulfide bonds, varies according to its monomeric and oligomeric structure and variations in the chains (Onat et al., 2002; Lipiski et al., 2013). One molecule of haptoglobin binds two molecules of free hemoglobin irreversibly (Naryzny and Legina, 2021). Although haptoglobin has many functions which binds hemoglobin released from fragmented erythrocytes, the main function of it is to form very stable complexes with free hemoglobin in the

blood and thus to prevent iron (Fe) loss (Petersen et al., 2004). As a result of haptoglobin binding to hemoglobin, HEM compounds that catalyze the oxidation of arachidonic acid by prostaglandin synthase are also removed from the environment. This effect is very important in terms of the anti-inflammatory property of haptoglobin (Gabay and Kushner, 1999). Haptoglobin naturally shows bacteriostatic effect by also preventing bacteria to use free Fe. For example, human haptoglobin inhibits the growth of *Streptococcus pyogenes*. In addition, haptoglobin hydrolyzes the peroxides released from neutrophils in the inflammation area by making them harmless. In cattle, haptoglobin plays a role in the regulation of lipid metabolism and in stimulating the immune system as an immunomodulator (Petersen et al., 2004).

The haptoglobin-hemoglobin complex is transported to the liver and metabolized by Kupffer cells by binding to CD163 (Murata et al., 2004), which is one of the special surface receptors of macrophages (Petersen et al., 2004). The HEM and globin are released with the breakdown of hemoglobin in the reticuloendothelial system (RES) and the HEM molecule is then broken down into Fe and bilirubin (Onat et al., 2002). Renal excretion of free hemoglobin does not occur until all circulating haptoglobins exceed their binding capacity. While the concentration of haptoglobin (Gruys et al., 1994), which is the most important APP in ruminants, in healthy animals is below detectable limits, it is stated that tissue damage increases in direct proportion to the severity of infection and inflammation (Skinner and Roberts,

1994). The haptoglobin concentration, which begins to increase within 24 hours of the onset of inflammation, makes peak on 3-5 days, then decreases on days 8-21 days, and it goes down to normal limits (Eckersall and Conner, 1988).

Although haptoglobin production is stimulated by inflammation, it is not found at high levels in the circulation because it binds hemoglobin and therefore, when the concentration of free hemoglobin in the serum increases, the amount of serum haptoglobin decreases. There is no circulating haptoglobin during acute hemolytic crisis due to babesiosis in cattle and in hematoma after surgical operation in horses and hyperhaptoglobinemia is seen in renal diseases and obstructive jaundice (Petersen et al., 2004). It is stated that the haptoglobin level of sheep is increased in diseases such as enteritis, meningoencephalitis, pyemia, bronchopneumonia, bacterial meningitis, pasteurella, septicemia, septic polyarthritis and Johne's disease, dystocia, and it may be used as a useful marker in the diagnosis of these diseases (Skinner and Roberts, 1994). In addition, Bayyit and Merhan (2020) reported that haptoglobin measurement in cows with dystocia may be useful in the diagnosis. After multivalent clostradial vaccination in newborn lambs (Eckersall et al., 2008), it is reported that there is an increase in SAA and haptoglobin values in small ruminant plague (Arslan et al., 2007). It was reported that plasma haptoglobin SAA and α1-AGP levels increase more in acute inflammations than in chronic ones (Heegaard et al., 2000). In a study conducted with turpentine, it was reported that the haptoglobin level

reached the maximum concentration depending on the dose (Conner et al., 1988). In addition, they determined that the haptoglobin level increased and decreased due to treatment in rabbits given diethylnitrosamine (Merhan et al., 2016). It was noted that the level of hypocalcemia and ketosis did not change (Skinner et al., 1991), but increased in fatty liver (Uchida et al., 1993).

Although some researchers report that its level does not increase in viral diseases (Skinner et al., 1991), it was noted that its level increased in experimentally induced infections with Herpes virus 1 and *Pasteurella haemolytica* serotype A1 in cattle, a relationship was found between this increase and the severity of clinical signs, duration of symptoms, and fever, and the level of antibiotics applied in cattle decreased in animals (Godson et al., 1996). Again, while its level increases in animals with metritis and mastitis, its level decreases after antibiotic treatment (Petersen et al., 2004).

In a study conducted by Tothova et al. (2008) in cattle, it was reported that serum haptoglobin and SAA increase after birth and that these proteins may be used in the diagnosis of postpartum inflammatory diseases. In another study conducted by Kuru et al. (2015), it was reported that short-term administration of PRID increases haptoglobin and ceruloplasmin levels, but decreases albumin levels.

Unlike the situation in cattle, haptoglobin levels increase in dogs and horses after surgery in natural or experimental diseases (Kent and Goodall, 1991), and in pregnancy and parturition in ruminants

(Merhan and Özcan, 2010; Varol et al., 2022). Measurement of acute phase protein levels gives more precise and clear results in the diagnosis of inflammatory diseases in ruminants compared to hematological findings. It was reported that it may be used as an auxiliary parameter in the diagnosis of parasitic diseases such as neonatal diarrhea (Merhan et al., 2016; Erkılıç et al., 2019), omphalitis (Bozukluhan et al., 2018; Kurt et al., 2019), pneumonia (Bozukluhan et al., 2021), *Toxocara vitulorum* (Bozukluhan et al., 2017) in calves with brucellosis (Bozukluhan et al., 2016), tuberculosis (Merhan et al., 2017), reticuloperitonitis traumatica (Bozukluhan and Gökçe, 2007; Akyüz and Aydın, 2022), endometritis (Kaya et al., 2016), hypodermosis (Merhan et al., 2017), foot and mouth disease (Merhan et al., 2017) in cattle and dogs infected with *Babesia canis* (Kırmızıgül et al., 2020).

Kırbaş et al. (2021) in a study they conducted in sheep naturally infected with *Streptococcus pluranimalium* reported that high haptoglobin and low albumin concentrations may be an indicator of acute phase response in infected animals, in addition to this, Kaya et al. (2021) in another study conducted in cattle with endometritis stated that serum haptoglobin and TNF-α levels decreased significantly after treatment compared to pre-treatment values.

Serum Amyloid A (SAA): The molecular weight of a single polypeptide chain SAA consisting of 104 amino acids, normally in complex with HDL, is approximately 180 kDa, and the molecular weight of the subunits that emerge after denaturation varies between

9-14 kDa (Yamada, 1999; Petersen et al., 2004). SAA is locally synthesized in hepatocytes (Yamada, 1999) and in the breast ('milk SAA', MAA) in bovine mastitis in response to SAA-stimulating factor similar to IL-1 molecule released from macrophages (Petersen et al., 2004). SAA, which can show increases in circulation exceeding 1000 times in inflammatory conditions, inhibits antibody formation by lymphocytes, and is chemotactic for neutrophils and monocytes and increases leukocyte adhesion to endothelial cells (Suffredini et al., 1999). In addition, it also inhibits endotoxin detoxification, lymphocyte and endothelial cell proliferation/inhibition, platelet aggregation and has functions such as inhibition of T lymphocytes adhesion (Murata et al., 2004; Petersen et al., 2004).

SAA, which rises within 2-5 hours after inflammatory stimulation and reaches a peak level within 24 hours, can be used for earlier diagnosis of acute cases. In addition, when evaluated together with haptoglobin, it is helpful in the diagnosis of inflammatory diseases, and it is stated that the determination of the haptoglobin/SAA value provides valuable information in the differential diagnosis of acute and chronic cases (Gruys et al., 1994).

Serum concentration of SAA (Gruys et al., 1994), which is one of the important APP in cattle, was noted to increase in foot and mouth diseases infected cattle (Merhan et al., 2017), in sheep infections such as poxvirus (Bozukluhan et al., 2018) and contagious ecthyma (Merhan et al., 2021), and increases in relation to the severity of

clinical symptoms in viral respiratory system diseases (Petersen et al., 2004).

Ceruloplasmin: Ceruloplasmin has a half-life of 5-7 days with a molecular weight of approximately 151 kDa. The sialic acid (SA) chains attached to the polypeptide chain of ceruloplasmin contain up to 10% of carbohydrates (Hellman and Gitlin, 2002; Ceron et al., 2005).

Ceruloplasmin, which was shown to have oxidase activity for many polyamine and polyphenol substrates and is named "copper oxidase", has an important role in APP as an oxido-reductase. Because it can neutralize free radicals, which have unpaired electrons derived from oxygen, participate in highly reactive reactions and cause tissue damage in this way. Ceruloplasmin and transferrin show an important part of the antioxidant activity, which is formed as a result of spontaneous oxidation of organic compounds with oxygen and found in plasma and tissues against cellular toxic compounds. It was also noted that it plays a role in the activity of ferroxidase, which is necessary for the oxidation of Fe^{+2} to Fe^{+3} (Hellman and Gitlin, 2002).

Ceruloplasmin, whose concentration increases within 4-10 days after the onset of inflammation or infection, is an APP of moderate importance in sheep (Kushner, 1982). Bozukluhan et al. (2020) reported that ceruloplasmin level increased but was statistically insignificant in a study they conducted in sheep with toxoplasmosis. In another study conducted by Merhan and Özcan (2004) in geese,

they reported that the determination of ceruloplasmin level can be used for early and accurate diagnosis of infectious/non-infectious diseases. In addition, it was reported that the serum ceruloplasmin concentration increased gradually in cattle infected *Salmonella dublin* until the 3rd day after infection, and reached 2 times its normal level in cows with mastitis (Eckersall and Conner, 1988). In addition, the level of ceruloplasmin increases in dogs following surgical trauma and is also used in the diagnosis of early pregnancy (Murata et al., 2004).

C Reactive Protein (CRP): CRP is a protein that consists of 5 subunits containing 206 amino acid residues of the same structure with a molecular weight of approximately 115 kDa of which each is 23 kDa with a molecular weight of approximately 115 kDa. The subunits are spherical structure and form a circular shape (pentraxin) by connecting to each other with noncovalent bonds (Pepys and Hirschfield 2003; Black et al., 2004). CRP, which is synthesized by the binding of Ca to the phosphoester ring in the liver, is also found in monocyte macrophages and adipose tissue. Cytokines, which are released from macrophages as a result of oxidative stress and inflammatory response in the vessel wall with infectious agents, stimulate CRP synthesis by binding to its receptors in the liver. The plasma half-life of CRP is short and is approximately 19 hours (Pasceri et al., 2000; Volanakis, 2001).

The biological activity of CRP is carried out by sugars such as phosphorus esters (especially phosphocholine), galactose and galactosamine by means of its ability to bind to various molecules

such as polycations, some lipids and lipoproteins (Hirschfield and Pepys, 2003; Pepys and Hirschfield 2003; Marnell et al., 2005).

C-reactive protein which plays a nonspecific role in various immunological events, activates the complement pathway by binding to the C polysaccharide found in the membrane of microorganisms and provides the formation of immunomodulatory tools. Two CRP molecules initiate chain complement reactions by holding a piece of C1. Reactions initiated by CRP can lead to cell death with the formation of the C5-9 membrane attack complex (Pepys and Hirschfield 2003; Black et al., 2004).

C-reactive protein whose concentration increases after the onset of inflammation or infection, has functions such as binding to the chromatin of damaged cells and disrupting the nuclear structure, complement activation, platelet aggregation and degranulation (Eckersall and Conner, 1988).

C-reactive protein whose level increases 1000 times or more after APR (Hirschfield and Pepys, 2003), reaches its highest level in 24 hours (Eckersall and Conner, 1988). Although it is understood by CRP analysis that diseases such as meningitis and pneumonia in human medicine are bacterial or viral, it is not used for this purpose due to the large individual differences in CRP production in other species (Petersen et al., 2004).

CRP serum concentration increases in laminitis, castration, arthritis, enteritis and pneumonia in horses with aseptic inflammation caused

by turpentine injection (Eckersall and Conner, 1988), which is used to induce experimental inflammation in animals and to initiate APR (Petersen et al., 2004).

It was reported that the determination of CRP level in serum and peritoneal fluid of cats with feline infectious peritonitis is a useful biomarker in the evaluation of T-lymphocyte-mediated immune response, inflammation and possible organ damage (Kahraman and Gökçe, 2020).

α1-Acid Glycoprotein (α1-AGP): α1-Acid glycoprotein is a very important sialoglycoprotein containing 5 types of N-linked complexes with oligosaccharide side chains (Ryden et al., 2002). α1-AGP, which is single-chain, contains 180 amino acids and has a molecular weight of 41 kDa, is 40% carbohydrate and 10-14% sialic acid (Albani, 2004).

α1-Acid glycoprotein which has functions such as neutrophil activation, drug binding and immunomodulation, is used to monitor the inflammatory process in cattle. Serum levels of α1-AGP increases with ceruloplasmin following surgical trauma in dogs, whose hepatitis and turpentine injection are made (Murata et al., 2004), with ceruloplasmin following surgical trauma (Eckersall and Conner, 1988). In addition, α1-AGP and haptoglobin provide information about whether dogs have clinical or subclinical diseases (Yuki et al., 2010). In a study conducted in dogs with *Ehrlichia canis*, it was noted that both α1-AGP and CRP levels increased (Rikihisa et al., 1994).

It is suggested that α1-AGP has diagnostic value when used together with haptoglobin and fibrinogen in ruminants and CRP in carnivores (Eckersall and Conner, 1988). Although α1-AGP level increased in cattle with reticulo peritonitis traumatic, it was reported that it can provide information about the prognosis as well as the treatment method when evaluated together with haptoglobin and fibrinogen (Bozukluhan and Gökçe, 2007).

Fibrinogen: Plasma fibrinogen, which is the most important coagulation protein, is a glycoprotein with a molecular weight of 340 kDa that is formed by connecting three pairs of polypeptides with disulfide bonds (Kamath and Lip, 2003). The task of fibrinogen synthesized in the liver is to provide tissue repair by forming fibrin and to form a matrix for the migration of inflammatory cells. It also delays antibody dependent cytotoxicity and apoptosis (Murata et al., 2004).

While hyperfibrinogenemia is observed in inflammation or tissue damage (Kamath and Lip, 2003), infectious, traumatic, pregnancy and neoplastic diseases (Vilar et al., 2020), hypofibrinogenemia are found cachexia, diffuse intravascular coagulation disorder and in liver failure (Kawasugi et al., 2021). Fibrinogen, which is an important APP used in the detection of inflammatory bacterial infection or surgical trauma in cattle and sheep (Murata et al., 2004), it is noted that it is safer to evaluate it together with haptoglobin and ceruloplasmin levels in the diagnosis of infectious and inflammatory diseases (Gruys et al., 1994).

B) Negative Acute Phase Proteins (nAPP)

Albumin: Albumin, which has different properties and functions, constitutes approximately 60% of the total protein amount in human plasma. In humans, it is a polypeptide chain consisting of 585 amino acids containing 17 disulfide bonds and has a molecular weight of about 66 kDa (Sugio et al., 1999). It consists of 607 amino acids, 18 peptide residues and 6 propeptides in sheep. Sheep serum albumin is 90% similar to bovine albumin (Brown et al., 1989).
It acts as a carrier for many organic and inorganic molecules (thyroxine, bilirubin, penicillin, cortisol, estrogen, free fatty acids, Ca, Mg and HEM) and also supports the protein synthesis activity of the liver by acting as an amino acid store (Onat et al., 2002; Don and Kaysen, 2004).

It causes hypoalbuminemia with urine in enteropathies with increase catabolism due to tissue damage or inflammation, decrease in amino acids required for synthesis due to nutritional and absorption disorders, with urine in cases of nephrotic syndrome, chronic glomerulonephritis, diabetes and systemic lupus erythematosus, with fecal excretion in enteropathies for protein loss as a result of inflammation or neoplastic diseases, and protein losses from the skin in burns (Onat et al., 2002).

Paraoxonase: Paraoxonase (PON) is an enzyme with a molecular weight of 43-45 kDa and a Ca^{+2} ion is required for the measurement of its stability and activity (Yılmaz and Dilek, 2019). In mammals, PON

enzymes are divided into three subfamilies, namely PON1, PON2 and PON3, which show wide similarities with each other because 60-70% of the amino acids they contain in their structures are common (Harel et al., 2004). PON1, whose molecular mass of approximately is 43 kDa, is a glycoprotein consisting of 354 amino acids (Mackness and Mackness, 2015). In the center of the enzyme, there is a tunnel with two Ca^{+2} ion, which is one for the enzyme's catalytic activity and the other for the stability of the enzyme (Harel et al., 2004). When looking at the general structure of paraoxonase, it is seen that it consists of 4 chains consisting of 6 beta-broken structures (Manco et al., 2021). PON1 enzyme is a glycoprotein closely related to HDL (Dullaart et al., 2014). It is reported that the antioxidant activity of PON1 secreted by the liver is due to the free sulfhydryl group on cysteine-284 (Jaouad et al., 2006).

The level of PON1, which is the negative acute phase protein, contributes to inflammatory and infectious diseases (Kulka, 2016). They reported that the concentration of paraoxonase decreased in aspiration pneumonia in calves (Akyüz et al., 2022), in sheep with babesiosis (Deveci et al., 2017), foot and mouth disease (Deveci et al., 2018), contagious ecthyma (Deveci et al., 2017) and clinical mastitis in cattle (Deveci et al., 2017).

4. CONCLUSION

Many functions and properties of acute phase proteins synthesized by the liver as a result of the acute phase response have been determined.

By determining the structure and functions of acute phase proteins, acute phase reactions that occur in response to infection and inflammation can be better understood. Therefore, the interest in the use of acute phase proteins in the veterinary field is increasing day by day and they are used in the diagnosis of diseases and in determining the prognosis.

5. REFERENCES

Akyüz, E., Merhan, O., Aydın, U., Sezer, M., Kuru, M., Karakurt, E., Yıldız, U., Bozukluhan, K., Batı, YU., Yıldız, A., Gökce, G. (2022). Neopterin, procalcitonin, total sialic acid, paraoxonase-1 and selected haematological indices in calves with aspiration pneumonia. *Acta Veterinaria Brno* 91: 115-124.

Akyüz, E., Aydın, U. (2022). Prognostic value of haptoglobin and ceruloplasmin levels determined in cows with adhesive and non-adhesive traumatic reticuloperitonitis. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi* 28(3): 337-344.

Albani, J.R. (2004). Tertiary structure of human α_1-acid glycoprotein (orosomucoid). Straightforward fluorescence experiments revealing the presence of a binding pocket. *Carbohydrate Research* 339: 607-612.

Alsemgeest, S.P.M., Lambooy, I.E., Wierenga, H.K., Dieleman, S.J., Meerkerk, B. van Ederen, A.M., Niewold, T.A. (1995). Influence of physical stress on the plasma concentration of serum amyloid-A (SAA) and haptoglobin (Hp) in calves. *Veterinary Quarterly* 17: 9-12.

Arslan, H.H., Cenesiz, S., Nisbet, C., Yazıcı, Z. (2007). Serum haptoglobin and amyloid a concentrations and clinical findings in sheep with peste des petits ruminants. *Bulletin of the Veterinary Institute in Puławy* 51(4): 471-474.

Bayyit, E., Merhan, O. (2020). Normal ve güç doğum yapan ineklerde bazı akut faz proteinlerinin ve oksidatif stres düzeyinin belirlenmesi. *Atatürk Üniversitesi Veteriner Bilimleri Dergisi* 15(2): 145-150.

Black, S., Kushner I., Samols, D. (2004). C-reactive protein. J. Biol. Chem., 279(47): 48487-48490.

Bozukluhan, K., Merhan, O., Büyük, F., Çelebi, Ö., Gökçe, G. (2016). Brusellozisli sığırlarda bazı akut faz proteinlerin düzeyinin saptanması. *Ankara Üniversitesi Veteriner Fakültesi Dergisi* 63: 13-16.

Bozukluhan, K., Merhan, O., Gökçe, Hİ., Öğün, M., Atakişi, E., Kızıltepe, Ş., Gökçe, G. (2018). Determination of some acute phase proteins, biochemical

parameters and oxidative stress in sheep with naturally infected sheeppox virus. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi* 24(3): 437-441.

Bozukluhan, K., Merhan, O., Kızıltepe, Ş., Harmankaya, A., Gökçe, G. (2020). Toksoplazmozisli koyunlarda oksidatif stres ve seruloplazmin düzeylerinin belirlenmesi. *Van Veterinary Journal* 31(2): 83-86.

Bozukluhan, K., Merhan, O., Kiziltepe, S., Ergin Egritag, H., Akyuz, E., Gokce, H.I. (2021). Determination of haptoglobin, some biochemical and oxidative stress parameters in calves with pneumonia. *Fresenius Environmental Bulletin* 30: 9485-9489.

Bozukluhan, K., Merhan, O., Ogun, M., Kurt, B., Cihan, M., Erkilic, E.E., Gokce, G., Aydin, U., Ozcan, A. (2018). Investigation of haptoglobin, serum amyloid A, and some biochemical parameters in calves with omphalitis. *Veterinary World* 11(8): 1055-1058.

Bozukluhan, K., Merhan, O., Özcan, A., Gökçe, H.İ., Gökçe, G. (2017). *Toxocara vitulorum* ile doğal enfekte buzağılarda serum haptoglobin düzeyi, oksidatif belirteçler ve bazı biyokimyasal parametrelerin düzeyinin belirlenmesi. *Ankara Üniversitesi Veteriner Fakültesi Dergisi* 64(2): 75-79.

Bozukluhan, K., Gökçe, H.İ. (2007). Retikuloperitonitis travmatika ve retikuloperikarditis travmatika'lı sığırlarda bazı akut faz proteinlerin araştırılması. *Erciyes Üniversitesi Veteriner Fakültesi Dergisi* 4(2): 107-113.

Brown, W.M., Dziegielewska, K.M., Foreman, R.C., Saunders, N.R. (1989). Nucleotide and deduced amino acid sequence of sheep serum albumin. *Nucleic Acids Research* 17(24): 10495.

Ceciliani, F., Giordano, A., Spagnolo, V. (2002). The systemic reaction during inflammation: the acute phase proteins. *Protein and Peptide Letters* 9(3): 211-223.

Ceron, J.J., Eckersall, P.D., Martinez-Subiela, S. (2005). Acute phase proteins in dogs and cats: current knowledge and future perspectives. *Veterinary Clinical Pathology* 34(2): 85-99.

Conner, J.G., Eckersall P.D., Wiseman, A., Aitchison, T.C., Douglas, T.A. (1988). Bovine acute phase response following turpentine injection. *Research in Veterinary Science* 44: 82-88.

Cray, C., Zaias, J., Altman, N.H. (2009). Acute phase response in animals: a review. *Comparative Medicine* 59(6): 517-526.

Deveci, H.A., Kükürt, A., Nur, G., Alpay, M., Merhan, O., Bozukluhan, K., Yilmaz, V., Karapehlivan, M. (2018). Serum paraoxonase activity and total sialic acid in sheep with foot and mouth disease. *Medycyna Weterynaryjna* 74(3): 199-202.

Deveci, H.A., Kükürt, A., Uzlu, E., Sözdutmaz, İ., Merhan, O., Aktaş, S., Alpay, M., Kaya, İ., Karapehlivan, M. (2017). Evaluation of paraoxonase activity, total sialic acid and oxidative stress in sheep with ecthyma contagiosa. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi* 23(3): 453-457.

Deveci, H.A., Kuru, M., Kükürt, A., Makav, M., Karapehlivan, M. (2017). Determination of serum paraoxonase activity, total sialic acid concentration, and oxidative status in cattle with clinical mastitis. *International Journal of Veterinary Science* 6(3): 136-140.

Deveci, H.A., Nur, G., Kukurt, A. (2017). Biochemical and histopathological changes of babesiosis in naturally infected sheep in Gaziantep region. *Fresenius Environmental Bulletin* 26: 4883-4889.

Don, B.R., Kaysen, G. (2004). Serum albumin: relationship to inflammation and nutrition. *Seminars in Dialysis* 17(6): 432-437.

Dullaart, R.P.F., Otvos J.D., James, R.W. (2014). Serum paraoxonase-1 activity is more closely related to HDL particle concentration and large HDL particles than to HDL cholesterol in Type 2 diabetic and non-diabetic subjects. *Clinical Biochemistry* 47: 1022-1027.

Eckersall, P.D., Conner J.G. (1988). Bovine and canine acute phase proteins. *Veterinary Research Communications* 12: 169-178.

Eckersall, P.D., Lawson, F.P., Kyle, C.E., Waterston, M., Bence, L., Stear, M.J., Rhind, S.M. (2008). Maternal undernutrition and the ovine acute phase response to vaccination. *BMC Veterinary Research* 4(1): 1-10.

Erkılıç, E.E., Merhan, O., Kırmızıgül, A.H., Öğün, M., Akyüz, E., Çitil, M. (2019). Salivary and serum levels of serum amyloid A, haptoglobin, ceruloplasmin and albumin in neonatal calves with diarrhoea. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi* 25(4): 583-586.

Fattori, E., Cappelletti, M., Costa, P., Sellitto, C., Cantoni, L., Carelli, M., Faggioni, R., Fantuzzi, G., Ghezzi, P., Poli, V. (1994). Defective inflammatory response in interleukin 6-deficient mice. *The Journal of Experimental Medicine* 180(4): 1243-1250.

Gabay, C., Kushner, I. (1999). Acute-phase proteins and other systemic responses to inflammation. *The New England journal of Medicine* 340(6): 448-454.

Godson, D.L., Campos, M., Attah-Poku, S.K., Redmond, M.J., Cordeiro, D.M., Sethi, M.S., Harland, R.J., Babiuk, L.A. (1996). Serum haptoglobin as an indicator of the acute phase response in bovine respiratory disease. *Veterinary Immunology and Immunopathology* 51: 292-299.

Gökçe, H.İ., Bozukluhan, K. (2009). Çiftlik hayvanlarında önemli akut faz proteinleri ve bunların veteriner hekimlik alanındaki kullanımı. *Dicle Üniversitesi Veteriner Fakültesi Dergisi* 1(1): 1-14.

Gruys, E., Obwolo, M.J., Toussaint, M.J.M. (1994). Diagnostic significance of the major acute phase proteins in veterinary clinical chemistry: a rewiev. *Veterinary Bulletin* 64(11): 1009-1018.

Gruys, E., Toussaint, M.J.M., Niewold, T.A., Koopmans, S.J. (2005a). Acute phase reactant and acute phase proteins. *Journal of Zhejiang University Science B* 6(11): 1045-1056.

Gruys, E., Toussaint, M.J.M., Upragarin, N., van Ederen, A.M., Adewuyi, A.A., Candiani, D., Nguyen, T.K.A., Sabeckiene (Balciute), J. (2005b). Acute phase reactants, challenge in the near future of animal production and veterinary medicine. *Journal of Zhejiang University Science B* 6(10): 941-947.

Harel, M., Aharoni, A., Gaidukov, L., Brumshtein, B., Khersonsky, O., Meged, R., Dvir, H., Ravelli, R.B.G., McCarthy, A., Toker, L., Silman, I., Sussman, J.L., Tawfik, D.S. (2004). Structure and evolution of the serum paraoxonase

family of detoxifying and anti-atherosclerotic enzymes. *Nature Structural & Molecular Biology* 11: 412-419.

Heegaard, P.M.H., Godson, D.L., Toussaint, M.J.M., Tjornehoj, K., Larsen, L.E., Viuff, B., Ronsholt, L. (2000). The acute phase response of haptoglobin and serum amyloid A (SAA) in cattle undergoing experimental infection with bovine respiratory syncytial virus. *Veterinary Immunology and Immunopathology* 77: 151-159.

Hellman, N.E., Gitlin, J.D. (2002). Ceruloplasmin metabolism and function. *Annual Review of Nutrition* 22: 439-458.

Hirschfield, G.M., Pepys, M.B. (2003). C-reactive protein and cardiovascular disease: new insights from an old molecule. *QJM: Monthly Journal of the Association of Physicians* 96: 793-807.

Jain, S., Gautam, V., Naseem, S. (2011). Acute-phase proteins: As diagnostic tool. *Journal of Pharmacy and Bioallied Sciences* 3(1): 118-127.

Jaouad, L., de Guise, C., Berrougui, H., Cloutier, M., Isabelle, M., Fulop, T., Payette, H., Khalil, A. (2006). Age-related decrease in high-density lipoproteins antioxidant activity is due to an alteration in the PON1's free sulfhydyl groups. *Atherosclerosis* 185: 191-200.

Kahraman, M.A., Gökçe, H.İ. (2020). Investigations of adenosine deaminase and c-reactive protein in cats with feline infectious peritonitis. *Mehmet Akif Ersoy University Journal of Health Sciences Institute* 8(3): 98-107.

Kamath, S., Lip, G.Y.H. (2003). Fibrinogen: biochemistry, epidemiology and determinants. *QJM: Monthly Journal of the Association of Physicians* 96: 711-729.

Karreman, H.J., Wentink, G.H., Wensing, T. (2000). Using serum amyloid A to screen dairy cows for subclinical inflammation. *Veterinary Quarterly* 22: 175-178.

Kawasugi, K., Wada, H., Honda, G., Kawano, N., Uchiyama, T., Madoiwa, S., Takezako, N., Suzuki, K., Seki, Y., Ikezoe, T., Iba, T., Okamoto, K. (2021). Hypofibrinogenemia is associated with a high degree of risk in infectious diseases: a post-hoc analysis of post-marketing surveillance of patients with

disseminated intravascular coagulation treated with thrombomodulin alfa. *Thrombosis Journal* 19(1): 12.

Kaya, S., Kaçar, C., Merhan, O., Demir, M.C., Arı, U.Ç., Zonturlu, A.K. (2021). Klinik endometritisli ineklerde intrauterin kekik esansiyel yağı ile birlikte dimetil sülfoksit uygulamasının klinik iyileşme üzerine ve serum haptoglobin, tümör nekrozis faktör ve nitrik oksit düzeylerine etkisi. *Kocatepe Veteriner Dergisi* 14(1): 45-50.

Kaya, S., Merhan, O., Kacar, C., Colak, A., Bozukluhan, K. (2016). Determination of ceruloplasmin, some other acute phase proteins, and biochemical parameters in cows with endometritis. *Veterinary World* 9(10): 1056-1062.

Kent, J.E. (1992). Acute phase proteins: their use in veterinary diagnosis. *The British Veterinary Journal* 148(4): 279-282.

Kent, J.E., Goodall, J. (1991). Assessment of an immunoturbidimetric method for measuring equine serum haptoglobin concentrations. *Equine Veterinary Journal* 23(1): 59-66.

Kırbaş, A., Kaman, R., Merhan, O., Bozukluhan, K., Değirmençay, S., Eroğlu, M.S. (2021). Evaluation of acute phase response and oxidative damage in sheep naturally infected with *streptococcus pluranimalium* using haptoglobin, nitric oxide, and malondialdehyde levels. *Fırat Üniversitesi Sağlık Bilimleri Veteriner Dergisi* 35(3): 145-150.

Kırmızıgül, A.H., Erkılıç, E.E., Merhan, O., Öğün, M., Ölmez, N., Taşçı, G.T., Vatansever, Z. (2020). *Babesia canis* ile enfekte köpeklerde serum amiloid-A, haptoglobin, seruloplazmin ve albumin seviyeleri. *Kocatepe Veteriner Dergisi* 13(2): 219-223.

Kulka, M. (2016). A review of paraoxonase 1 properties and diagnostic applications. Polish Journal of Veterinary Sciences 19(1): 225-232.

Kurt, B., Erkilic, E.E., Merhan, O., Aydin, U., Akyuz, E., Sezer, M., Kirmizigul, A.H., Ogun, M. (2019). The determination of levels of acute-phase proteins, inducible nitric oxide synthase and endothelial nitric oxide synthase in calves with omphalophlebitis. *Fresenius Environmental Bulletin* 28: 8601-8605.

Kuru, M., Merhan, O., Kaya, S., Oral, H., Kükürt, S. (2015). The effect of short term progesterone-releasing intravaginal device treatment on acute inflamation markers for Holstein heifers. *Revue de Medecine Veterinaire* 166: 336-340.

Kushner, I. (1982). The phenomenom of the acute phase response. *Annals of the New York Academy of Sciences* 389: 39-48.

Lipiski, M., Deuel, J.W., Baek, J.H., Engelsberger, W.R., Buehler, P.W., Schaer, D.J. (2013). Human Hp1-1 and Hp2-2 phenotype-specific haptoglobin therapeutics are both effective in vitro and in guinea pigs to attenuate hemoglobin toxicity. *Antioxidants&Redox Signaling* 19(14): 1619-1633.

Mackness, M., Mackness, B. (2015). Human paraoxonase-1 (PON1) gene structure and expression, promiscuous activities and multiple physiological roles. *Gene* 567(1): 12-21.

Manco, G., Porzio, E., Carusone, T.M. (2021). Human paraoxonase-2 (PON2): protein functions and modulation. *Antioxidants* 10: 256.

Marnell, L., Mold, C., Du Clos, T.W. (2005). C-reactive protein: ligands, receptors and role in inflammation. *Clinical Immunology* 117(2): 104-111.

Massart, I.S., Paulissen, G., Loumaye, A., Lause, P., Pötgens, S.A., Thibaut, M.M., Balan, E., Deldicque, L., Atfi, A., Louis, E., Gruson, D., Bindels, L.B., Meuwis, M.A., Thissen, J.P. (2020). Marked increased production of acute phase reactants by skeletal muscle during cancer cachexia. *Cancers (Basel)* 12(11): 3221.

Merhan, O., Bozukluhan, K., Çelebi, Ö., Öğün, M., Atakişi, E., Büyük, F. (2017). Levels of acute phase protein and some biochemical parameter in cattle infected with *Mycobacterium bovis*. *Erciyes Üniversitesi Veteriner Fakültesi Dergisi* 14(2): 101-105.

Merhan, O., Bozukluhan, K., Gokce, H.I. (2017). Acute phase proteins and biochemical and oxidative stress parameters in *Hypoderma spp.* infested cattle. *Journal of the Hellenic Veterinary Medical Society* 68(4): 535-540.

Merhan, O., Bozukluhan, K., Gökçe, G., Yılmaz, O. (2016). İshalli buzağılarda haptoglobin, seruloplazmin ve bazı biyokimyasal parametre düzeylerinin

araştırılması. *Fırat Üniversitesi Sağlık Bilimleri Veteriner Dergisi* 30(3): 195-198.

Merhan, O., Bozukluhan, K., Kiziltepe, S., Gokce, H.I. (2017). Investigation of levels of haptoglobin, serum amyloid A, ceruloplasmin and albumin in cattle with foot-and-mouth disease. *Israel Journal of Veterinary Medicine* 72(4): 14-17.

Merhan, O., Erkılıç, E.E., Bozukluhan, K., Öğün, M., Kırmızıgül, A.H. (2021). Bulaşıcı ektimalı koyunlarda haptoglobin, serum amiloid A ve seruloplazmin düzeylerinin araştırılması. *Fırat Üniversitesi Sağlık Bilimleri Veteriner Dergisi* 35(2): 77-80.

Merhan, O., Ozcan, A., Atakisi, E., Ogun, M., Kükürt, A. (2016). The effect of β-carotene on acute phase response in diethylnitrosamine given rabbits. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi* 22(4): 533-537.

Merhan, O., Özcan, A. (2004). Kazlarda serum seruloplazmin ve total sialik asit düzeylerinin araştırılması. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi* 10(2): 139-142.

Merhan, O., Özcan, A. (2010). Peripartum dönemdeki koyunlarda seruloplazmin, haptoglobin, fibrinojen, albümin ve transferrin düzeylerinin araştırılması. *Erciyes Üniversitesi Veteriner Fakültesi Dergisi* 7(1): 13-20.

Murata, H., Shimada, N., Yoshioka, M. (2004). Current research on acute phase proteins in veterinary diagnosis: an overview. *The Veterinary Journal* 168: 28-40.

Naryzhny, S.N., Legina, O.K. (2021). Haptoglobin as a biomarker. *Biochemistry (Moscow), Supplement Series B: Biomedical Chemistry* 15(3): 184-198.

Onat, T., Emerk, K., Sözmen, E.Y. (2002). İnsan Biyokimyası. Palme Yayıncılık, Ankara.

Pasceri, V., Willerson, J.T., Yeh, E.T.H. (2000). Direct proinflammatory effect of C-reactive protein on human endothelial cells. *Circulation* 102(18): 2165-2168.

Pepys, M.B., Hirschfield, G.M. (2003). C-reactive protein: a critical update. *The Journal of Clinical Investigation* 111(12): 1805-1812.

Petersen, H.H., Nielsen, J.P., Heegaard, P.M.H. (2004). Application of acute phase protein measurements in veterinary clinical chemistry. *Veterinary Research* 35: 163-187.

Ramadori, G., Christ, B. (1999). Cytokines and the hepatic acute-phase response. *Seminars in Liver Disease* 19(2): 141-155.

Rikihisa, Y., Yamamoto, S., Kwak, I., Iqbal, Z., Kociba, G., Mott, J., Chichanasiriwithaya, W. (1994). C-reactive protein and α1-acid glycoprotein levels in dogs infected with *Ehrlichia canis*. *Journal of Clinical Microbiology* 32: 912-917.

Ryden, I., Pahlsson, P., Lundblad, A., Skogh, T. (2002). Fucosylation of α1-acid glycoprotein (orosomucoid) compared with traditional biochemical markers of inflammation in recent onset rheumatoid arthritis. *Clinica Chimica Acta* 317: 221-229.

Skinner, J.G., Brown, R.A., Roberts, L. (1991). Bovine haptoglobin response in clinically defined field conditions. *The Veterinary Record* 128:147-149.

Skinner, J.G., Roberts, L. (1994). Haptoglobin as an indicatör of infection in sheep. *The Veterinary Record* 134: 33-36.

Suffredini, A.F., Fantuzzi, G., Badolato, R., Oppenheim, J.J., O'Grady, N.P. (1999). New insights into the biology of the acute phase response. *Journal of Clinical Immunology* 19(4): 203-214.

Sugio, S., Kashima, A., Mochizuki, S., Noda, M., Kobayashi, K. (1999). Crystal structure of human serum albumin at 2.5 Å resolution. *Protein Engineering* 12(6): 439-446.

Tizard, I.R. (2004). Veterinary Immunology: An Introduction. W. B. Saunders Company, Philadelphia.

Tothova, C.S., Nagy, O., Seidel, H., Konvicna, J., Farkasova, Z., Kovac, G. (2008). Acute phase proteins and variables of protein metabolism in dairy cows during the pre- and postpartal period. *Acta Veterinaria Brno* 77: 51-57.

Uchida, E., Katoh, N., Takahashi, K. (1993). Appearance of haptoglobin in serum from cows at parturition. *The Journal of Veterinary Medical Science* 55(5): 893-894.

Varol, K., Ergin Eğritağ, H., Merhan, O., Bozukluhan, K. (2022). Evaluation of acute phase response in blood and milk samples of healthy Holstein breed cattle in the postpartum period. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi* 28(1): 59-65.

Vilar, R., Fish, R.J., Casini, A., Neerman-Arbez, M. (2020). Fibrin(ogen) in human disease: both friend and foe. *Haematologica* 105(2): 284-296.

Volanakis, J.E. (2001). Human C-reactive protein: expression, structure, and function. *Molecular Immunology* 38(2–3): 189-197.

Whicher, T., Bienvenu, J., Price, C.P. (1991). Molecular biology, measurement and clinical utility of the acute phase proteins. *Pure and Applied Chemistry* 63(8): 1111-1116.

Yamada, T. (1999). Serum amyloid A (SAA): a concise review of biology, assay methods and clinical usefulness. *Clinical Chemistry and Laboratory Medicine* 37(4): 381-388.

Yılmaz, A., Dilek, E. (2019). Antibiotics used in patients after surgery and effects of human serum paraoxonase-I (PON1) enzyme activity. *Protein&Peptide Letters* 26: 215-220.

Yuki, M., Itoh, H., Takase, K. (2010). Serum alpha-1-acid glycoprotein concentration in clinically healthy puppies and adult dogs and in dogs with various diseases. *Veterinary Clinical Pathology* 39(1): 65-71.

CHAPTER 2

CLINICAL AND PERFORMANCE EFFECTS OF BETA GLUCANS

Prof. Dr. Gültekin YILDIZ[1]

[1] Ankara University, Veterinary Faculty, Animal Nutrition and Nutritional Diseases, 06110, Altındağ, Ankara, Türkiye. ORCID: 0000-0002-1003-9254;
E-mail:gyildiz@ankara.edu.tr

1. INTRODUCTION

In recent years, feed additives such as probiotics and prebiotics have found wide use as an alternative to antibiotics. When the use of antibiotics as growth factors in animal feeds was completely banned on 21.01.2006, probiotics became candidate feed additives to close this gap.

Probiotics; They are live bacterial, yeast, or fungal organisms that can improve the gut bacteria balance and positively impact the host animal. *Lactobacillus, Bifidobacterium, Enterococcus* lactic acid-producing bacteria, Bacillus, yeasts, with the lactic, acetic, and formic acids they secrete in the digestive system environment, reduce the pH of the environment and prevent the proliferation of pathogenic microorganisms. These microorganisms are plastered to the intestinal villi like a layer, preventing pathogenic organisms from forming colonies. They contribute to digestion with the digestive enzymes they secrete, create an anaerobic environment, and strengthen the immune system (Yıldız and Akan, 2004; Ergün et al., 2019). Unlike pathogenic bacteria such as E.coli, probiotic bacteria are Gram (+) and facultative anaerobes and are not pathogenic. Lactobacillus, Leuconostoc, Pediococcus, and Streptococcus are lactic acid-producing bacteria (Yıldız and Akan, 2004).

Prebiotics; At first, they were considered power-digestible carbohydrates (Drochner et al., 1993). These substances, which cannot be broken down by the digestive enzymes synthesized in the animal

organism but can be fermented by the microorganisms living in the large intestines, stimulate the growth of beneficial Gram-positive bacteria such as *Bifidobacteria and Lactobacilli.* These substances include fructooligosaccharides (FOS), galactooligosaccharides (GOS), inulin, mannanoligosaccharides (MOS), lactulose, lactitol, lactose, pectin, sorbitol, and xylitol. Prebiotics are cellulosic and αreduce the activity of the 7-hydroxylase enzyme responsible for forming bile acids, causing a decrease in the pH value of the intestinal content due to fermentation. Oligosaccharides are resistant to intestinal enzymes and cannot be metabolized by the animal. By reaching the colon, they help reduce the number of undesirable bacteria such as clostridia, eubacteria, enterobacteria, and coliforms while serving as a growth substrate for nonpathogenic microorganisms such as bifidobacteria, lactobacilli, and Bacteroides species. Mannose-type sugars can prevent bacteria from adhering to the digestive tract through their receptors and thus reduce the colonization of pathogens. FOS is a complex sugar found in nature, consisting of 2-10 glucose and fructose monosaccharide micromolecules. They are cellulose-like compounds in the group of carbohydrates. It cannot be digested by normal digestive enzymes, day-old chicks, or enteropathogens likely to settle in immature digestive systems. These complex sugars, Lactobacillus spp., are used as an energy source. Prebiotics are used by the intestinal flora as a source of C and increase the bacterial mass. Increasing probiotic bacteria use N and S in the digestive system and prevent the formation of irritating substances such as H_2S, indole, and ammonia in the intestine. FOS is

effective in reducing odor intensity and/or improving odor quality (Yıldız and Dikicioğlu, 1999; Yıldız, 2002).

Prebiotics are used as nutrients by the beneficial bacteria in the large intestine. The lactic, acetic, propionic, and butyric acids they produce reduce the environment's pH and prevent Gram-negative microorganisms' growth. Stadermann et al. (1992), in their study on laying hens, did not show much change in the dry matter content of the cecum in the high level (6%) consumption of highly digestible carbohydrates (lactose, pectin, inulin from nutmeg) from different sources. Values were determined as 6.3-6.5 and 7.1, respectively. A decrease in fecal pH indicates fermentation intensity in the segments of the digestive tract. With the addition of pectin to laying hens, feces pH values were determined as 7.3 and 6.7 in the control and experimental groups, respectively.

The addition of fructooligosaccharide increases fecal density and regulates intestinal flow. This complex sugar promotes the proliferation of acid-producing bacteria in the caecum, preventing enteropathogens such as Salmonella and E. coli from colonizing this region. This way, the colonization of pathogens is prevented, and the immune system is strengthened. Effects of fructooligosaccharides;

1. Increasing the number of bifidobacterium in the back of the digestive tract
2. Increasing acid formation in the cecum
3. Increasing ileal digestion

4. Blocking carcinogenic agents by reducing proteolytic activity in the colon
5. Reducing clostridial colonization
6. strengthen the immune system
7. increasing the absorption of magnesium and calcium from feed (Yıldız, 2002).

Besides probiotics and prebiotics, beta-glucans are among the important feed additives alternative to antibiotics. The use of beta-glucan, considered an antinutritional factor found in significant amounts in cereals, is of great importance both in keeping the immune system ready for possible diseases and in eliminating the resulting immune suppression.

2. BETA-GLUCAN

Beta-glucan (ß-glucan) is a polysaccharide formed by bonding many glucose molecules in various ways. Beta-glucans are non-starchy polysaccharides in grain feeds. It is a cell wall component of grain feeds such as barley, oats, and rye.

Oat bran has 15% beta-glucan. Barley and oats have the most β-glucan per 100 g dry weight: 20 and 8 g. Sorghum (6.2 g), rye (2.7 g), maize (1.7 g), triticale (1.2 g), wheat (1.0 g), durum (0.6 g) and rice (0.13 g) also contain β-glucans (Bacic et al., 2009). *Saccharomyces cerevisiae*, *Maitake* and *Shiitake fungi,* and *Laminaria sp.* are other sources of β-glucans (Teas, 1983); (Wasser and Weis, 1999). Table 1 lists the main β -glucans, their structures, and sources of clinical importance.

Table 1. The Structure and Sources of Common Bioactive B -Glucans (Bashir and Choi, 2017).

β-Glucan	Abbreviation	Source	Structure
Fungal β-Glucan			
β-glucan	MFL-glucan	*Monilinia fructicola*	Branched (1,3;1,6) β-glucan
β-glucan	MFN-glucan	*Monilinia fructigena*	Branched (1,3;1,6) β-glucan
β-glucan	AM-ASN	*Amanita muscaria*	Branched (1,3;1,6) β-glucan
β-glucan	AAG	*Auricularia auricular*-judae	Branched (1,3;1,6) β-glucan
Polysaccharide-glucan	PS-G	*Ganoderma lucidum*	Branched (1,3;1,6) β-glucan
β-glucan	HEP3	*Hericium erinaceus*	Branched (1,3;1,6) β-glucan
β-glucan	SBG	Sparassis crispa	Branched (1,3;1,6) β-glucan
Yeast β-Glucan			
Betafectin/TH-glucan	PGG	*Saccharomyces cerevisiae*	Branched (1,3;1,6) β-glucan
β-glucan	MG	*Saccharomyces cerevisiae*	Linear (1,3) β-glucan
Bacterial β-Glucan			
β-glucan	DMJ-E	*Agrobacterium* sp. *R259*	Linear (1,3) β-glucan

β-Glucan	Abbreviation	Source	Structure
Seaweed/Algal β-Glucan			
Phycarine	-	*Laminaria digitata*	Linear (1,3) β-glucan
Cereal β-Glucan			
Barley β-glucan	-	*Hordeum vulgare* L.	Linear (1,3;1,4) β-glucan
Oat β-glucan	-	*Avena sativa* L.	Linear (1,3;1,4) β-glucan
Wheat β-glucan	-	*Triticum vulgare*	Linear (1,3;1,4) β-glucan

Pneumocystis carinii, Cryptococcus neoformans, Histoplasma capsulatum, Candida albicans from bacteria such as A*spergillus fumigatus, Lentinus edodes, Grifola frondosa, Schizophillum commune and from fungi such as Sclerotinia sclerotiorum and* Saccharomyces cerevisiae *It can be* obtained from yeasts such as (Akramiene et al. 2007). Beta-glucans from yeast and fungi differ structurally from those from cereals (barley and oats). The cell wall component of yeast and fungi contains glucopyranosyl to which the glucans ß-1,3 D-glucose ß-1,6 chain is attached (Manners et al., 1973). Beta-glucan in the oat and barley endosperm cell wall is a polysaccharide-protein polymer complex with a molecular weight of approximately $2x10^6$ linked to ß-1,3 and ß-1,4 (Bhatty, 1993).

2.1. MECHANISM OF ACTION AND EFFECTS OF BETA-GLUCAN

It has been extensively proven that fibers and polysaccharides from fungi, yeasts, and grains have anticancer, antibacterial, anti-allergic, and cardiovascular disease risk-reducing properties in addition to immunomodulatory effects. It is often credited to its bioactive constituents, β -glucans. β -glucans are deemed safe to use and are natural bioactive substances that can be taken orally as a dietary supplement or as part of a regular diet. Polysaccharide glucans delay the pace of lipid and carbohydrate absorption, which eventually changes the way that food affects hormone and lipid responses. Clinical use of unprocessed extracts or purified β -glucans have been made to treat cancer and other infectious illnesses. As the first food to decrease cholesterol, oat bran (3 g β-glucan/day dosage) was approved by the US Food and Drug Administration in 1997.

β-glucans have strong anti-osteoporotic and immunomodulatory properties that have been shown in vitro and animal and human clinical studies. The anti-diabetic and/or anti-obesity properties of β-glucans have not been documented in vitro investigations but have been widely explored in animal and human-based clinical trials. The benefits of beta-glucans on decreasing blood pressure and/or cholesterol have been widely investigated in human clinical trials, but in vitro or in vivo investigations using animals have seldom been published. In vitro and in vivo investigations on animals have been used extensively to study the anticancer, antigenotoxic, antimutagenic, and/or antioxidative

properties of β-glucans; however, human clinical trials are seldom documented. There are few systematic studies on the medical efficacy, clinical, and physiological significance of β-glucans as an antimicrobial and anticancer (Bashir and Choi, 2017).

Over the last 20 years, β-glucans have been the subject of substantial research. Many nations, including the United States, Canada, Finland, Sweden, China, Japan, and Korea (Kim et al., 2006), authorize β-glucans as strong immunological activators. β-glucans are employed as an anti-disease agent and an anti-inflammatory or cancer treatment component. The most popular soluble fibre immunomodulator with significant anticancer, anti-insulin resistance, anti-hypertension, and anti-obesity properties is β-glucans. To combat infectious illnesses such as bacterial, viral, fungal, and parasite disorders, β-glucans are thought to boost the immune system and alter humoral and cellular immunity (Mantovani et al., 2008; Ina et al., 2013; Chen, 2013; Vetvicka et al., 2014).

Beta-glucans can activate leukocytes, stimulate phagocytic activity, and stimulate the production of reactive oxygen mediators, inflammatory mediators, cytokines such as TNF-a (tumor necrosis factor-a), and are recognized by the innate immune system (Akramiene et al. 2007).

It has been reported that glucan stimulates the immune system in various animals such as fish, chickens, mice, rabbits, sheep, pigs, horses, and humans (Vetvicka, 2001). Beta-glucans with different molecular sizes and structures obtained from different sources increase the host's defense mechanisms against microorganisms and parasitic infestations (Yun et al., 2003).

After the first avian flu in South Korea in 2003, beta-glucans have been used as an immunostimulant in many countries. Beta-glucan binds to specific receptors on various cell types in the first step of the defense reaction. In this way, glucans play a role in macrophage stimulation.

A study conducted on humans (Brown and Gordon, 2001), it was revealed that the dectin-1 receptor on leukocytes is stimulated by beta-glucan. Vetvicka et al. (2002), in the case of oral administration of yeast beta-glucan at a dose of 2-20 mg/kg to mice, an anti- anthrax effect and a slowdown in the proliferation of cancerous cells in vivo were detected.

Hetland and Sandev (2002) reported that beta-glucan inhibits the proliferation of Mycobacterium tuberculosis in vitro by increasing cellular stimulation and/or uptake of bacteria by macrophages in the host cell. It has been determined that beta-glucan reduces the total cholesterol level and tolerates the HDL cholesterol (high-density cholesterol) level well (Nicolosi et al., 1999). In addition to the antitumor effect of beta-glucan, there are also reports that it reduces the release of cytokines during sepsis (Yun et al., 2003).

β -glucans have been shown to have the ability to maintain body weight while decreasing blood total cholesterol and blood lipid profiles (Liatis et al., 2009). In addition to demonstrating the significant inhibitory action of β-glucans on lipid peroxidation, Kogan et al. (2008) also showed the synergistic effects of β-glucans as an antioxidant, antigenotoxic, and antimutagenic activities. By stimulating macrophages and raising immunoglobulin levels, Daou and Zhang

(2012) showed that oat β-glucans had immunostimulatory action. The immunomodulatory effects of β-glucans and their advantages in treating cancer and infectious disorders were reviewed by Murphy et al. (2010https://www.mdpi.com/1422-0067/18/9/1906/htm - B30-ijms-18-01906https://www.mdpi.com/1422-0067/18/9/1906/htm - B30-ijms-18-01906). The association between the immunomodulatory and anticancer effects of fungi-derived -glucans and their structure and antitumor actions, was studied by Ooi and Liu (2000). East Asian nations, especially Japan and Korea, have significant markets for antitumor fungal polysaccharides such as lentinan, schizophylan, and krestin (Ooi and Liu, 2000).

Jesenak et al. (2014) reviewed the impact of beta-glucans on the management and prevention of respiratory infections (Jesenak et al, 2017) as well as the treatment of allergic diseases (Jesenak et al, 2014). Khoury et al. (2012) reviewed the potential of β -glucans in food applications and their efficacy in treating and preventing metabolic syndrome. By regulating blood sugar levels and blood pressure, β -glucans can mediate diabetes, according to Chen and Raymond's (2008) research. β-glucans may help with diabetes management by lowering risk factors connected to diabetes mellitus. Additionally, β-glucans may lessen ischemic heart damage and hasten the healing of wounds. A β-glucan test is a helpful screening tool with good sensitivity and specificity to discriminate between patients with and without invasive fungal illnesses, according to Hou et al. (2015)'s evaluation of the effects of β-glucans on invasive fungal diseases.

Consuming β -glucans, mostly found in oats or barley, has not been linked to any negative consequences in people (Hallfrisch and Behall, 2003). As antibacterial, anticancer, anti-diabetic, and anti-hypercholesterolemic polysaccharides, β-glucans have been shown to have medicinal importance and effectiveness (Kim et al., 2006; Daou and Zhang, 2012; Chen and Seviour, 2007).

Children with chronic respiratory illnesses who were administered -glucan (glucan #300) showed enhanced salivary production of IgM, IgA, and IgG as well as significantly activated immunity, according to Vetvicka et al. (2013).

Children aged 6 to 12 with mild to moderate asthma were evaluated by Sarinho et al. (2009) to determine the immunomodulatory effects of yeast-derived β -glucans against asthma and other allergic illnesses. Children who received β-glucans showed a substantial rise in blood IL-10 levels and a reduction in asthmatic reactions. This research has shown that β -glucans may be utilized to understand and treat inflammatory and allergy illnesses.

In normal healthy male and female volunteers, Juvonen et al. investigated the effects of a modified oat bran beverage containing β-glucans on satiety-related gastrointestinal hormone responses (Juvonen et al., 2009). Satiety, plasma glucose, cholecystokinin, insulin, and glucagons like peptide 1 and peptide YY all increased more after meals, whereas postprandial ghrelin decreased more. The oat bran beverage's varying viscosities significantly impacted the short-term gut hormone responses and the physiology associated with fullness. In both male and

female participants, Carpenter et al. (2013) examined the post-exercise immunosuppressive response of yeast-derived whole glucan particles (WGP). Supplementing with WGP-glucans significantly increased the production of CD14+ and CD14+/CD16+, LPS-stimulated interferon, IL-2, IL-4, and IL-5. According to the study, WGP β-glucan has immune-protective properties after exercise.

Children with respiratory tract infections were shown to benefit from β-glucans' immunomodulatory action, according to Grau et al. (2015). The mean number and risk of respiratory tract infection episodes and respiratory illnesses like the common cold, otitis, laryngitis, pharyngitis, and bronchitis were significantly decreased.

2.2. ANTITUMOR EFFECTS OF BETA-GLUCANS

Human dendritic cells' reactions to isolated glucans and the immunological effects of β-glucans from barley and mushrooms were compared by Chan et al. (2007). Different β-glucans have been found to affect human immune cells, including dendritic cells, differently and to have varying immune potentials. The dectin-1 pathway is used by yeast-derived particulate β-glucan (p β-glucan) to activate macrophages and dendritic cells (Qi et al., 2011).

Muted S. cerevisiae significantly reduced lung metastasis in CDF1 mice, IS-2, B16-BL6 melanoma, and colon 26-M3.1 carcinoma cells. When the tumor was given a two-day pretreatment with IS-2 before inoculation, the survival of mice with tumors increased. During an in vitro cytotoxicity assay, IS-2 increased splenocyte proliferation activity

and produced a number of cytokines, including IL-12, IFN-, and IL-1. Additionally, IS-2 promoted natural killer cell cytotoxicity against Yac-1 tumor cells and incited peritoneal macrophage antitumor activity against colon 26-M3.1 cell. By stimulating natural killer cells and macrophages, IS-2 β-glucan prevented tumor metastasis (Yoon et al., 2008).

Insoluble β-glucans derived from yeast and fungi have been shown to have antitumor properties. Oats' low molecular weight -glucan was not toxic to normal cells but significantly decreased the viability of cancer cells. This study (Choromanska et al., 2015) showed the low molecular weight -of glucan from oats' potent antitumor potential while demonstrating its non-toxicity to normal cells.

Monoclonal antibodies (mAbs) against tumors are well-known for their use in treating tumors. By covering the tumors in inactive C3b, the mAb binds to the tumor and activates the components (iC3b). In C3- or CR3-deficient mice, Hong et al. investigated the effects of yeast β-glucan as an adjuvant for antitumor mAb therapy (Hong et al., 2004). In the bone marrow, yeast β-glucan was broken down into smaller, soluble β-glucan fragments that were subsequently taken up by the CR3 of marginal granulocytes and inhibited the growth of iC3b-opsonized tumor cells.

Fungal 1,3;1,6 β-glucan's therapeutic effectiveness for cancer patients and its use as an adjuvant treatment for those taking chemotherapy to reduce hematopoiesis Weitberg et al. (2008). In this research, a β-glucan preparation was administered to patients with advanced cancers undergoing chemotherapy, and its impact on tolerability and

hematopoiesis was observed. According to the study, fungus β-glucan is well tolerated by cancer patients receiving chemotherapy and may even help them produce more hematopoiesis.

2.3. IMMUNOMODULATORY EFFECTS OF B -GLUCANS

β -Glucans have potent immunomodulatory activities proven in vitro and in animal and human-based clinical trials (Table 2).

Table 2. Immunomodulating effects of β-glucans—in vitro study (Bashir and Choi, 2017).

β-Glucan	Cell Line	Analysis	Results
Yeast p-β-glucan (Cerevan)	Wistar rat thymocytes	HPGPC, Mitogenic, and co-mitogenic activity assay	Higher stimulation indices of immunomodulatory activity.
PGG-Glucan	Human monocytic cell lines U937, HL-60, THP-1, Murine monocytes J774.1, RAW264.7, P388D(I), Murine B cell line LB27.4, Primary human fibroblasts, Keratinocytes, Bronchial epithelial cells, Murine monocyte line BMC2.3, and T cell line DO11	Whole blood chemiluminescence assay, Microbicidal assay, Measurement of cytokine secretion from whole blood, ^{3}H-PGG-Glucan binding assay, Flow cytometry, and Electrophoretic mobility shift assay	Induced activation of NF-κB-Like nuclear transcription factor in purified human neutrophils, and enhanced neutrophil anti-microbial function.
Yeast p-β-glucan (synthetic glucan)	Porcine alveolar macrophages and bone hematopoietic cell-derived dendritic cells	MTT assay, ELISA, RACE PCR, and Phagocytic activity	Enhanced cell activity and phagocytosis, and complex collaborating interaction between dectin-1 and TLRs.

β-Glucan	Cell Line	Analysis	Results
Barley β-glucan, Oat β-glucan, Fungal β-glucan	Human monocyte leukemia cell line	Size exclusion chromatography, Cytotoxicity assay, NO assay, H_2O_2 assay, Phagocytic activity, and qRT-PCR	Up-regulated inflammation related gene expression, and No production of NO, and H_2O_2.
Yeast β-glucan (WGP)	Mouse intestinal tumor cell line Colon26 produced in BALB/c mice	ELISA, and Tumor-protective effect assay	Stimulation of cytokines such as IL-2, IFN-γ, and TNF-α.
Bacterial β-glucan	Cancer cell lines, Human monocyte cell line, HPV-18-positive cervical cancer cell line, HPV-16-positive cervical cancer cell lines,	RT-PCR, IFN-γ assay, NO, and cell viability assay	Synthesis of NO in the monocyte cell lines, enhanced cytotoxic, and antitumor activity.

Cells such as macrophages, lymphocytes, natural killer (NK) cells, neutrophils, eosinophils, basophils, and mast cells in the immune system play an important role in defense against pathogenic microorganisms (Akramiene et al. 2007). Special receptors in these cells are activated by interaction with beta-glucan receptors. Macrophages are the oldest and most well-known immune response cells found in humans, animals, and simple invertebrates. Macrophages take part in changes in tissues for the release of cytokines that function in the immune system. Toxic or pathogenic stimulants such as endotoxin, bacteria, viruses, and chemical substances initiate these stimuli. ß -1,3 glucan is one of the most important immune stimulants

that are not toxic and can be administered by other means as well as completely safe orally (Czop and Austen, 1985).

β-glucans from diverse sources (oats, barley, and mushrooms) on phorbol myristate acetate differentiated THP-1 macrophages, according to Chanput et al. (2012). All β-glucans examined marginally increased inflammation-related gene expression, although the strength and patterns of expression varied. It was determined that β-glucans from various sources had diverse amounts of immunomodulatory effects.

Studies have shown that glucan is a common natural macrophage activator (Raa et al., 1992), nonspecific tumor killer, and is effective in the release of many cytokines, stimulating the general immune system through the bone marrow. Individual differences such as age, chronic infection, and malnutrition affect immune system stimulation. ß-glucan can be used to stimulate the immune system in cases where the bone marrow needs to be stimulated due to arthritis, delayed wound healing, decrease in red and white blood cells, cancer, bacterial, fungal, and viral infections (Price and Makinodan, 1972). 1,3 ß-glucan reduces the negative effect on the stimulation and activation of macrophages (Kohut et al., 1994).

In mice, a resolution has been reported several days after glucan injection into a subcutaneous malignant melanoma mass. A clearly stimulated population of macrophages was found in a biopsy from the injection site (Mansell et al., 1975). ß -glucan accelerated the healing of ulcers that normally heal slowly. Benefits were provided in the rapid regeneration of the skin and the prevention of infections (Mansell et al.,

1978). An increase in serum cytokines IL1, IL2, and interferon have been detected in systemic glucan therapy against the HIV virus in humans (Mansell, 1986).

DiLuzio et al. (1979) studied the immunostimulatory impact of yeast-derived β-glucan in A/J and C57BL/6 mice. Subcutaneous tumor implants significantly reduced the development of syngeneic anaplastic breast cancer and melanoma B16 in mice and boosted survival rates. In mice confronted with Staphylococcus aureus, yeast-glucan decreased renal necrosis. Soluble yeast-derived β-glucan showed substantial anticancer and anti-staphylococcal efficacy.

Reynolds et al. (1980) studied yeast-glucan host resistance against infectious illness response in mice, rats, and healthy cynomolgus male and female monkeys (Macaca fascicularis). The injection of yeast β-glucan before infection greatly enhanced mouse survival against Venezuelan equine encephalomyelitis (VEE) or Rift valley fever virus and Pseudomonas pseudomallei. However, post-infection dosing had little effect on mouse survival. Similarly, prior to infection, intravenous injection of β-glucan dramatically enhanced resistance to virulent Francisella tularensis. A combination dosage of yeast-glucan and VEE vaccination resulted in increased resistance to homologous viral challenge. In cynomolgus monkeys, multiple dosages had a similar effect. The adjuvant impact of yeast-glucan in the treatment of infectious disorders was investigated in this research.

In mice, oat-derived β-glucan improved immune response and tolerance to Eimeria coccidiosis. As a preventive therapy, yeast-glucan (WGP)

greatly decreased mortality due to anthrax infection and suppressed cancer cell proliferation in mice (Vetvicka et al., 2002).

Hasegawa et al. (2004) investigated the immunomodulatory effects of β-glucan formulations of Sparassis scispa extracts. SC-glucans decreased the growth of the Sarcoma-180 tumor, and the mice lived for a long period. Furthermore, human natural killer cell cytotoxicity rose while blood IgE levels and scratch index dropped. SC-glucan caused a change in Th1/Th2 balance toward Th1-dominant immunity in this research. Methotrexate is often used to treat malignant tumors and rheumatic illnesses. However, its efficacy is often hampered by major side effects and hazardous aftereffects. Sener et al. (2006) studied the preventive benefits of yeast-glucan in methotrexate-induced toxicity. The yeast-glucan treatment prevented tissue glutathione depletion, stopped a rise in tissue malondialdehyde, myeloperoxidase activity, and collagen content, and decreased tissue damage. Yeast-glucan also reduced leukocyte apoptosis and cell death. This research found that yeast -glucan may help reduce leukocyte apoptosis and oxidative tissue damage.

Shim et al. (2007) reported that they looked into the immunostimulatory properties of -glucans derived from Agrobacterium sp. in a variety of cancer cell lines and in ICR mice. On the generation of antibodies, both an adjuvant impact and an induction effect of IFN- and cytokines were seen. In eight-week-old female BALB/c mice, Vetvicka and Vetvickova (2007) studied the immunological and pharmacological effects of β -glucans from various sources, including yeast, fungus, and

grains. Yeast-derived β-glucan (glucan #300) substantially increased mouse splenocyte production of IL-2 and peripheral blood leukocyte phagocytosis. Additionally, mice's blood sugar and cholesterol levels were considerably reduced by yeast-derived β-glucan. The remainder of the tested β-glucans had quite weak immunological action. This research provided substantial evidence for the idea that the source and technique of extraction affect the immunological effects of β-glucans.

Fikarin, an algal-produced-glucan, was investigated by Vetvicka et al. (2007). In peripheral blood cells, phycarine significantly increased phagocytosis and supported Lewis lung cancer treatment. On experimentally produced leukopenia, fikarin's significant immunostimulatory effects were seen. The idea's potential for application in the treatment of gastrointestinal illnesses is supported by the discovery of the majority of it in the digestive system. Next, Vetvicka's team evaluated how various sources of -glucans affected their ability to stimulate the immune system. Yeast-derived-glucan (Betamune) substantially increased the production and release of interleukins (IL-1, 2, 4, 6, 8, and 13) and tumor necrosis factor- α, as well as activated phagocytosis (Vetvicka et al., 2008). The immunosuppressive effects of β-glucans isolated from various sources on mice were compared by Vetvicka and Vancikova (2010). The majority of the β-glucans examined were able to prevent cold stress from causing inhibition, and one of the β-glucan fractions (glucan #300) was able to keep phagocytosis at a healthy level. Additionally, glucan

#300 prevented the rise in stress-related corticosterone and maintained elevated levels of IL-6 and IL-12.

In a study, Ceyhan et al. (2012) looked at how electromagnetic radiation affected albino rats' skin's antioxidant state and the potential anti-oxidant benefits of yeast-derived β-glucans. Malondialdehyde levels and superoxide dismutase activity increases brought on by irradiation exposure were dramatically reduced by β-glucans. Yeast-derived β-glucans also reduced the loss of glutathione peroxidase activity brought on by electromagnetic radiation and marginally boosted catalase activity. Young Swiss albino mice were used in Pillai and Devi's (2013) study to examine the radioprotective effects of fungal β-glucans derived from Ganoderma lucidum. After irradiation, a considerable rise in mouse survival and a drop in the quantity of aberrant cells were seen. These investigations have shown that yeast-derived β-glucans have antioxidative and radioprotective properties and that they can reduce the oxidative skin damage brought on by electromagnetic radiation.

2.4. ANTIGENOTOXIC / ANTIMUTAGENIC / ANTIOXIDATIVE / DERMATITIS EFFECTS OF B - GLUCANS

Wistar conducted research on the effects of yeast-derived β-glucans on oxidative damage in the liver during obstructive jaundice in albino rats, according to Erkol et al. (2011). The blood levels of alanine and aspartate aminotransferases, lactate dehydrogenase, gamma-glutamyl transpeptidase, and lipid peroxide, as well as malondialdehyde, were all shown to have significantly decreased. However, the groups that

received treatments containing β-glucans generated from yeast showed considerably greater levels of glutathione and superoxide dismutase.

It has been reported that pure and active 1,3 ß-glucan is effective in the treatment of infections caused by bone marrow suppression as a result of low oral doses of radiotherapy or chemotherapy (Wyde, 1989).

Effect of a purified β-glucan preparation on canine atopy in dogs Beynen et al. (2011) reviewed in one study. Dogs received 800 ppm of β-glucan daily for an eight-week period, and clinical signs of atopic dermatitis (scaling, redness, thickness, itching, and peeling) were evaluated. Dogs fed β -glucan showed significant improvements in the overall recovery index of atopic dermatitis compared to control.

2.5. CHOLESTEROL EFFECTS OF B -GLUCANS

β -glucans have only sometimes been identified in vitro or in vivo research using animals. The benefits of β -glucans for decreasing blood pressure and cholesterol are mentioned in Table 3**.**

Table 3. Effects of β -glucans on reducing cholesterol and blood pressure in animals study (Bashir and Choi, 2017).

β-Glucan	Organism	Analysis	Results
Yeast-WGP	8-week old hypercholesterolemic BALB/c mice	Phagocytosis, and Biochemical analysis	A dose-dependent decrease in plasma cholesterol and triglyceride levels.
Yeast β-glucan	Sprague-Dawley rats	Serum total cholesterol, triglyceride, and malondialdehyde analysis	Significantly reduced and maintained cholesterol levels in blood plasma and liver. Triglyceride and

β-Glucan	Organism	Analysis	Results
			MDA levels significantly reduced.

Vetvicka and Vetvickova (2009) looked at how mice's macrophage activity and blood cholesterol levels were affected by yeast-derived β-glucans. It was shown that plasma cholesterol and triglycerides significantly decreased in a dose-dependent manner. In Sprague-Dawley rats, Kusmiati and Dhewantata (2016) looked into the anti-cholesterolemic effects of yeast-derived β -glucans. Total cholesterol in the plasma and the liver was considerably lowered to a normal level by yeast-derived β -glucans. Significant reductions in triglyceride and malondialdehyde levels were also seen.

Oral administration of beta-glucan increased the effectiveness of cholesterol-lowering drugs such as Lopid and Niacin (Donsiz, 1990). When the IL1 cytokine increases insulin secretion, the blood glucose level decreases. Macrophages are the main source of IL1 in the body, and macrophage production increases with the addition of beta-glucan to the diet. Beta-glucan meets the high antioxidant need in diabetic patients and is effective in preventing the high complication of atherosclerosis (Lang and Dobrescu, 1989).

2.6. ANTI-DIABETIC/ANTI-OBESITY EFFECTS OF B -GLUCANS

β -glucans have undergone significant research in both animal and human therapeutic trials, although no in vitro investigations have been published. Table 4 lists the effects of β-glucans on diabetes and obesity.

Table 4. Effects of β-glucans on diabetes and obesity in animals (Bashir and Choi), 2017).

β-Glucan	Organism	Analysis	Results
Lentinan	Female BALB/c mice	Spectrophotometric analysis of the total CYP contents, Western blot analysis, ECOD, EROD, and EMSA activities	Suppression of constitutive and 3-methylcholanthrene-induced CYP expression and EROD activity in liver.
Chitin-glucan	9-weeks old, male C57BL6/J mice	Oral glucose tolerance test, Microbial analysis of the cecal contents, ELISA, and Histochemical analysis	Decreased mouse gut microbiota, body weight gains, fat mass development, glucose intolerance, hepatic triglyceride accumulation and hypercholesterolemia.
Polycan	7-weeks old male hamsters	Changes in body weight, food consumption, liver weight, Serum biochemistry, Histopathological, and Histomorphometric analysis	No significant change in body weight and food consumption, serum levels of AST, ALT, triglyceride, LDL- and total-cholesterol levels. Dose-dependent reduction of atherosclerosis with relatively good protective effects on liver damage.
Yeast β-glucan + *Folium mori* extract (BG-FM)	STZ-induced diabetic rats	Changes in blood glucose levels, body weight, liver, and kidney weight, and Serum BUN, AST, ALT levels	Reduced hyperglycemic changes in the *F. mori* extract. Dose-dependent increase in anti-diabetic and hypoglycemic effect.

In high-fat diet-induced obese mice, Neyrinck et al. (2012) investigated the effectiveness of fungus-derived chitin-glucan in modifying glucose and lipid metabolism as well as the gut microbiota. We found that the gut flora underwent significant alterations along with significant cecal expansion. The growth of the adipose mass, glucose intolerance, fasting hyperglycemia, hepatic triglyceride accumulation, and hypercholesterolemia were also all considerably decreased by chitin-glucan. Consumption of chitin-glucan over an extended period of time improved the composition and/or activity of the gut microbiota, which had a beneficial impact on the emergence of obesity and associated metabolic problems.

Lim et al. (2015) investigated the anti-diabetic effects of pollyanna derived from A. pullulans on hyperlipemia and liver damage brought on by a high-fat diet (HFD) in hamsters. Serum triglyceride, alanine aminotransferase, aspartate aminotransferase, total- and LDL-cholesterol levels, as well as arteriosclerosis values showed a substantial decline. This research showed the policy's beneficial benefits in lowering HFD-induced hyperlipemia and related arteriosclerosis, as well as in avoiding liver damage.

Sohn et al. (2018) examined the effects of β -glucan extracted from *A. pullulans* and *Folium mori*. It showed a significant reduction in hyperglycemia, hepatopathy, and nephropathy.

Cavallero et al. (2002) The effects of barley-derived β -glucan on glycemic response were examined in healthy, non-diabetic men and women between the ages of 20 and 27. Both the glycemic response and

postprandial blood glucose levels decreased linearly. The potential of barley to decrease cholesterol may be aided by the fact that barley-containing foods have been demonstrated to enhance reverse cholesterol transfer.

Granfeldt et al. (2008) looked into how an oat β-glucan-containing muesli product affected postprandial insulinemia and glycemic responses. In healthy people, consumption of a muesli cereal containing 4 g of oat-derived β -glucan dramatically decreased insulin and glucose responses.

The order and Henry looked at how barley β-glucan-fortified food items (Chapati) responded to the glycemic index (Thondre and Henry, 2009). A randomized, single-blind, controlled, crossover research including healthy men and women between the ages of 26 and 50 was carried out. The research revealed a substantial decrease in the glycemic index, glucose, and postprandial blood sugar concentrations.

2.7. BONE REGENERATION/BONE DAMAGE HEALING EFFECTS OF B -GLUCANS

β-glucans have been widely researched for their antiosteoporotic, bone healing, and bone regeneration properties in both in vitro and in animal and human clinical trials. β -glucans have been shown to have antiosteoporotic properties. Table 5.

In human foetal dermal fibroblast cell lines, the wound-healing abilities of β-glucans derived from Aureobasidium pullulans have been investigated (Choi et al., 2016). He described the ability of β-glucans to

heal wounds and proposed that they may be utilized as an anti-osteoporotic treatment to promote bone growth and prevent bone resorption.

Table 5. β-glucans have been shown in animal studies to have bone regeneration and damage repair properties. (Bashir and Choi, 2017).

β-Glucan	Organism	Analysis	Results
β-glucan	2–3 months old CD-1 male mice	Chromosomal aberrations and mitotic activity	Reduced total number of cells with structural chromosomal aberrations in bone marrow and spermatogonial cells. Markedly restored mitotic activity of bone marrow cells, suppressed by anti-neoplastic drugs.
Polycalcium [Polycan and calcium lactate-gluconate (1:9)]	6-weeks old, Sprague-Dawley specific pathogen-free female ovariectomy-induced osteoporotic rats	Changes in body and bone weight, serum osteocalcium and bone-specific alkaline phosphatase levels, Urine Dpd/creatinine ratio, and Histological analysis	Markedly decreased OVX-induced osteoporotic changes. Preserved bone mass and strength.
Polycalcium (Polycan and calcium lactate-gluconate (1:9))	6-weeks old Sprague-Dawley specific pathogen-free male rats	Changes in body weight, knee thinness, cartilage glycosaminoglycan content, and Histopathological assay	Inhibited osteoarthritis related changes and induction of chondrocyte proliferation.

β-Glucan	Organism	Analysis	Results
Polycal (Polycan and calcium-gluconate (2:98))	6-weeks old male SD (Crl:CD1) rats	Changes in body weight, alveolar bone loss index, total number of buccal gingival aerobic bacterial cells, IL-1, TNF-α levels, and myeloperoxidase activity	Bacterial proliferation, periodontitis, and alveolar bone loss induced by ligature placement were significantly inhibited.
CHAP + β-glucan composite material	6-months old New Zealand male white rabbits	Radiological imaging and Histological analysis. Peripheral quantitative computed tomography, Densitometry and SEM analysis	No sign of graft rejection, stimulating effect of biomaterial on bone formation and mineralization. Enabled regeneration of bone tissue.
Polycan	An oestrogen-deficient ovariectomy model and a hypocalcemic and hypoparathyroid thyroparathyroidectomy model	Changes in bone mineral density in the femur, tibia, and lumber (L6) vertebrate using dual-energy X-ray absorptiometry, and changes in Ca bioavailability	Marked increase in the BMD of femur, tibia, and L6. Enhanced absorption and bioavailability of Ca and improved Ca balance.
Polycan	6-weeks old virgin Sprague-Dawley pathogen free female rats as an oestrogen-deficient ovariectomy model	Changes in body weight, bone mineral content, density, failure load, Histological profile, and Histomorphometric indices	Inhibited OVX-induced alterations in bone resorption. Increased serum expression levels of BLAP and all histomorphometrical indices for bone formation.

CD: Cluster of differentiation; Dpd: Deoxypyridinoline; OVX: Ovariectomy; IL: InterLeukin; TNF-α: Tumor necrosis factor-α; SEM: Scanning electron microscopy. CHAP: Carbonated hydroxyapatite; BMD: Bone mineral density; Ca: Calcium; BALP: Bone-specific alkaline phosphatase.

The anti-inflammatory properties of polycaline (polycan + calcium lactate gluconate) were examined by Park et al. in the context of ligation-induced experimental periodontitis and associated alveolar bone loss (Park et al., 2016). Continuous topical treatment of polycaline dramatically reduced periodontitis, bacterial growth, and loss of alveolar bone. These trials showed that calcium lactate gluconate and polycan formulations worked together to treat osteoarthritis effectiveness of carbonated hydroxyapatite (CHAP) granules and beta-glucans as a filler for bone deficiencies in New Zealand white rabbits was examined by Borkowski et al. (2015). In addition to the implants' considerable integration with bone tissue, the biomaterial had a stimulating impact on bone growth and mineralization and exhibited no evidence of graft rejection. The potential uses of -glucans in bone tissue regeneration and as fillers in bone defects were emphasized in this work.

In several osteoporosis model rats, Ku et al. (2015) examined the outcomes of the policy isolated from Aureobasidium pullulans. In ovariectomy thyroid-parathyroidectomy rat models, it was shown that there was a considerable rise in the bone mineral density of the femur, tibia, and L6, as well as an increase in calcium bioavailability and a reduction in calcium secretion. The hypothesis that polycan might be employed as an anti-osteoporosis agent is supported by the fact that polycan conserved bone mass and strength and accelerated bone growth (jung et al., 2016).

In dogs, β-glucans are thought to relieve symptoms of atopic dermatitis such as itching, redness, scaling, thickening, and peeling.

The most common joint disease in older cats and dogs is osteoarthritis. It has been observed to significantly reduce stiffness, lameness, and pain and improve activity in dogs with osteoarthritis. In the treatment of obesity and metabolic syndromes, they show that they reduce visceral fat, cholesterol levels, postprandial insulin, and glucose responses and boost satiety. In research examining obese dogs given beta-glucans for 90 days, similar results were shown. At the conclusion of the experiment, decreases in the levels of insulin, total cholesterol, and triglycerides were seen. Also, GLP-1 levels were elevated, suggesting that beta-glucans can affect satiety and promote better glycemic control as this hormone has a hypoglycemic effect.

In some studies, it has been observed that ß-glucan reduces mortality in fatal infections. Kournikakis et al. (2003) demonstrated the anthrax protective effects of p-1,3 glucan obtained from yeast in a study they conducted. They reported that yeast β-glucan administration in anthrax-infected animals increased the survival rate of the animals, decreased the bacterial load in the lungs, and increased the number of bacteria-free animals.

In several fish species, β-glucans have been shown to boost general immunity and resistance to infections. Kumari and Sahoo (2006), in their study to investigate the effects of ß-glucan added to the diet on innate immunity and disease resistance in Asian catfish, myeloperoxidase (MPO) and lysozyme levels, superoxide production

of 0.1% ß-glucan added to feeds, reported that it significantly increased the hemagglutination titer and the level of defense against *Aeromonas hydrophila.*

Beta-glucan has been used as a feed additive to prevent Vibrosis, Yersiniosis, and Furunculosis in shellfish (Jorgensen et al., 1993).

Erkol et al. (2011) reported that ß-glucan also has an antioxidant effect in a study conducted on rats, and the effect of ß-glucan on liver damage in obstructive jaundice was investigated. As a result of the research, they reported that β-glucan reduced liver damage and oxidative stress in rats with obstructive jaundice, as well as increased phagocytic and antioxidant effects. In serum myeloperoxidase (MPO), lipid peroxide (LPO), total and direct bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), lactate dehydrogenase (LDH), and liver tissue malondialdehyde (MDA) levels in the experimental group. They found that the values of superoxide dismutase (SOD) in serum and glutathione (GSH) in liver tissue were high. In the histopathological examination of the liver, it was stated that tissue damage was lower in the experimental group than in the control group.

Bilal et al. (2012) investigated the effects of adding ß-glucan to the diet on serum lipids and performance indices in rats fed a diet enriched with cholesterol. They reported that body weight gain (BWG), feed intake (FI), feed conversion ratio (FCR), total serum cholesterol, and LDL-cholesterol levels were significantly lower in the group fed with a diet

supplemented with fat and ß-glucan. At the end of the study, ß-glucan had no effect on serum HDL-cholesterol and triglyceride levels and negatively affected HT; They found that ß-glucan significantly reduced blood LDL and total cholesterol levels while having no impact on HDL and triglyceride levels. Therefore, ß-glucan; They claimed that it might lessen both the risk of atherosclerotic vascular disease and the liver's capacity to synthesize cholesterol.

2.8. USE OF BETA GLUCAN AS A FEED ADDITIVE

Beta-glucan provides more benefits as a feed additive compared to other immunostimulants and biological substances. The most important feed additive that can increase the standard of living in the aging process is beta-glucan. Beta-glucan is effective in defending against infections, tumors, and radiation activity, increasing antioxidant activity, maintaining lipid balance, and increasing the effectiveness of antidiabetic and other therapeutic agents.

The ß-glucan found in grain cell walls has an impact on chickens and pigs when they are fed barley. The impact of ß-glucan in chicken may be detrimental because the high viscosity it causes in the digestive track lowers food digestion and disturbs the local flora. The impact in pigs is smaller owing to decreased digestive viscosity and enhanced capacity of tiny intestinal bacteria to depolymerize β-glucan. Exogenous-glucanase usage greatly lessens or completely eliminates these negative effects while stabilizing the gut microbiome (Karunaratne and Classen, 2019).

High amounts of dietary ß-glucan (60 ppm) were greater than the negative control in the research of broiler chickens (negative control, positive control group containing 55 ppm Zn-bacitracin, 15 ppm -glucan, 30 ppm -glucan, and 60 ppm ß-glucan). Demonstrated a high survival rate and feed conversion rate. The survival and feed conversion rates of the broilers were enhanced to the same level as the 55 ppm Zn-bacitracin group when 60 ppm -glucan was added to the diet. Carcass yield, water holding capacity, pH, color, and 2-thiobarbituric acid reactive substance values—all quality indicators of chicken breast meat—were unaffected (Moon et al., 2016).

β-1,3-Glucan can be extracted from a number of sources, including cereals, fungi, and bacteria. It is a functional polymer made up of β-1,3 linked glucose. It is known that β-1,3-Glucan has anticancer, antibacterial, and antiviral properties and boosts immunity and bioactivity by encouraging the release of cytokines, activating neutrophils, natural killer cells, and macrophages (Brown and Gordon, 2005). It is well established that β -1,3-glucan activates B cells, boosts antibody synthesis, complements mAB-mediated cancer immunology, and stimulates IL-1, IL-2, and TNF-a release. Thus, β-glucan may promote immunological responses that are cell-mediated and activate macrophages, NK cells, and cytotoxic T cells (Bohn and BeMiller, 1995); (Vetvicka et al., 2007; Chen et al., 2008). Discovered that the growing performance of -glucan was unaffected (Morales-Lopez et al., 2009; Cox et al., 2010). Paenibacillus polymyxa's 1,3-1,6 β-glucan

extract did not significantly boost the organisms' ability to proliferate (Hwang et al., 2008).

Giving Atlantic salmon 1% yeast-derived beta-glucan after a lethal infection by a water-borne bacterium called Vibrio salmonicida improved their survival. While 20% of the fish in the control group survived, 60% of the fish fed yeast-derived beta-glucan survived (Raa et al., 1992).

There is a strong correlation between slowing growth after weaning and elevation of the acute phase protein haptoglobin in the blood. High haptoglobin values are accepted as an indicator of serious infection. It has been found that the haptoglobin level is reduced in weaned piglets fed with yeast glucan. This shows that piglets increase their ability to resist infection. In pigs, the risk of microbial infections generally increases during the weaning period, and the administration of yeast-derived beta-glucan as an additional nutrient during this period increases the growth rate (Dirtz et al., 1995).

Elrayeh and Yıldız (2012), growth performance, serum cholesterol, intestinal growth performance of an inulin and beta-glucan supplement (0.7% inulin; 0.014% beta-glucan; 0.7% inulin + 0.014% beta-glucan) in Ross PM3 broiler diets investigated the length and effects on the immune system. Dietary inulin supplementation substantially lengthened the intestine and cecum at the conclusion of the study. In addition to impairing performance metrics, adding 0.7 percent inulin and 0.014 percent β -glucan to meals raised blood levels of triglycerides

and total cholesterol ($P<0.001$). At the conclusion of the study, the animals in the inulin + beta-glucan group had more belly fat on their corpses than before this therapy.

Qureshi and Guo (2003) β-1,3/1,6-glucan (β-glucan) was examined as a potential immunomodulator. In vitro exposure to -glucan concentration was done on macrophages from the MQ-NCSU macrophage cell line and the abdominal infiltrate of broilers. Additionally, everyday broilers were fed diets containing 0, 20, and 40 mg/kg of β-glucan at the start, then 0, 20, and 20 mg/kg as they grew. Results It was shown that β-glucan stimulated the formation of nitrite (NO_3), interleukin-1 (IL1), and macrophages in culture. Addition of β-glucan to the feed increased macrophage phagocytic activity. In addition, primary and secondary lymphoid organs such as bursa fabricius, thymus, and spleen are larger in chicks supplemented with β-glucan. These findings showing that β-glucan enhances many basic immune responses in chicken suggest that β-glucan can be used as a possible immunomodulator.

Cheng et al. (2004), four groups were randomly formed in 160-day-old broilers, and 6-week fattening was applied. In the corn and soybean diet containing 0, 0.012, 0.025, or 0.05% glucan during the fattening period. The following factors were assessed: growth efficiency, antibody titer against the New Castle vaccine, lymphocyte blastogenesis, and peritoneal macrophage chemotaxis activity. The findings revealed no differences in antibody titer or body weight growth that were statistically significant. ß-Glucan was not added to increase lymphocyte

blastogenic. However, broilers' macrophage chemotaxis activity increased when 0.025 and 0.05 percent β-glucan were added. These findings support the idea that by altering macrophage function, ß-glucan can boost some cellular immune responses in chickens.

Lowry et al. (2005) gave oral Salmonella enteritidis (SE) to chicks that consumed the diet with and without beta-glucan. The number of SEs showed a significant difference in organs ($P<0.05$). The SE level was 76% SE positive in the liver/spleen in the group not given ß-glucan, while it was 7% SE in the group given ß-glucan. Beta-glucan has been tested for poultry as an antimicrobial immune potential in the diet as it may be an alternative to conventional antimicrobial chemotherapies.

Seljelid et al. (1985), Seljelid et al. (1987), and Rasmussen et al. (1987), β -1,3-glucan in mice in vivo. They found that it stimulated microbicidal activity and that this effect was mostly due to the activation of prostaglandin E2 and interleukin-1 (IL1) production from macrophages. The scientists also noted that β-glucan was injected into the peritoneal cavity. The total quantity of red blood cells in the peritoneal fluid of mice both before and after infection with Escherichia coli rose considerably. After 24 hours, the bacterial count in the peritoneal fluid of the mice who received ß-glucan was nil. When ß-glucan was not given to mice, bacterial counts gradually increased until the animals died after about 12 hours (Rasmussen et al., 1987; Rasmussen et al., 1990; Rasmussen and Sejelid, 1991).

The effects of administering 1,3/1.6 ß-glucan and levamisole to pregnant mares were compared. Immunoglobulin levels in colostrum and non-specific cellular and humoral responses in foals were investigated. Mares given levamisole and beta-glucan had significantly increased IgG levels in colostrum (Krakowski et al., 1999).

In a study (Altintas, 2006), ß-glucan, derived from Saccharomyces cerevisiae, is administered orally to horses whose immune systems are believed to be under stress due to clinical Babesiosis. The immune stimulant impact of ß-glucan was evaluated between the levamisole and control groups. The research included Thoroughbred and Arabian horses who had been clinically diagnosed with Babesiosis using the Giemsa painting method. The study was carried out on 18 races of horses, which weighed 380 – 480 kg while alive and 3 – 5 years old. In comparison to the beta-glucan and control groups, the levamisole group's serum ALP levels were greater on the first day ($P<0.01$). Between the first and the fourteenth day, there was a significant difference ($P<0.01$) in the beta-glucan group across all periods and in the levamisole group. The respect for the LDH and SGOT values led to the conclusion that differences in times were significant ($P<0.01$). Differences in results for hemoglobin and hematocrit were determined to be significant ($P<0.01$) in this case. The fact that ß-glucan groups' RBC, hemoglobin, and hematocrit levels returned to normal in a shorter period of time leads us to believe that ß-glucan has a significant role in hastening the patient's recovery. Levamisole group blood lymphocyte levels are significantly greater on the fourth day compared to the

fourteenth day (P<0.01). In both the levamisole group and the beta-glucan group compared to the levamisole group, quite high IgG levels were found (P<0.05).

Differences observed in results, performance, and immune response in various studies may be due to the beta-glucan source (Sadarao et al., 2020). Some sources of beta-glucan are given in Table 6.

Table 6. Some beta-glucan sources (Sadarao et al., 2020).

Food Source	Content (%)
Oats (Cereals)	4.5-5.5
Barley (Cereals)	4.5
Saccharomyces cerevisiae (Yeast)	5-7
Euglena (Algae)	90
Coriolus versicolor (Mushroom)	46.5
Sparassis crispa (Fungus)	43.6

3. REFERENCES

1. Akramiene, D., Kondrotas, ***A.,*** Didziapetriene, J., Kevelaitis, E. (2007). Effects of p-glucans on the immune system. *Medicina (Kaunas)*, 43(8), 597-606.
2. Altıntaş, I. (2006). The effect of levamisol and beta-glucans on some blood parameters and immunoglobulin G levels in horses with babesiosis. Ankara Universitesi Sağlık Bilimleri Enstitüsü PhD Thesis.
3. Bacic, A., Fincher, G.B., Stone, B.A. (2009). Chemistry, Biochemistry, and Biology of (1→3)-β-Glucans and Related Polysaccharides, 1st ed., Academic Press: Amsterdam, The Netherlands, 2009.
4. Bashir, K.M.I., Choi, J.-S. (2017). Clinical and Physiological Perspectives of β-Glucans: The Past, Present, and Future. *Int. J. Mol. Sci.*, *18*, 1906. https://doi.org/10.3390/ijms18091906
5. Beynen, A.C., Saris, D.H.J., Paap, P.M., Altena, F.V., Visser, E.A., Middelkoop, J., De Jong, L., Staats, M. (2011). Dietary β-1,3/1,6-glucans reduce clinical signs of canine atopy. *Am. J. Anim. Vet. Sci.*, 6, 146–152.
6. Bhatty, R.S. (1993). Extraction and enrichment (1,3), (1,4)-beta-D-glucan from barley and oat brans. *Cereal Chem.*,70, 73 77.
7. Bilal, T., Gürsel, F.E., Ateş, A., Keser, O. (2012). Effects of dietary p-glucan on serum lipids and performance indices in rats fed a diet enriched with cholesterol. *Pak Vet J,* 32(1), 97-100
8. Bohn, J.A., BeMiller, J.N. (1995). (1-3)-β-D-glucans as biological response modifiers: A review of structure-functional activity relationships. *Carbohydr Polym*., 28:3–14.
9. Borkowski, L., Pawłowska, M., Radzki, R.P., Bieńko, M., Polkowska, I., Belcarz, A., Karpiński, M., Słowik, T., Matuszewski, L., Ślósarczyk, A. (2015). Effect of a carbonated HAP/β-glucan composite bone substitute on healing of drilled bone voids in the proximal tibial metaphysis of rabbits. *Mater. Sci. Eng. C Mater Biol Appl*, 53: 60-67.
10. Brown, G.D., Gordon, S. (2001). Immuno recognittion. A new receptor for for beta glucan. *Nature*, 413, 36-37.

11. Brown, G.D., and Gordon, S. (2005). Immune recognition of fungal β-1, 3–1, 6-glucans. *Cell Microbiol.*,7:471–479.
12. Carpenter, K.C., Breslin, W.L., Davidson, T., Adams, A., McFarlin, B.K. (2013). Baker's yeast β-glucan supplementation increases monocytes and cytokined post-exercise: Implications for infection risk? *Br. J. Nutr*., 109, 478–486.
13. Cavallero, A., Empilli, S., Brighenti, F., Stanca, A.M. (2002). High (1→3,1→4)-β-glucan barley fractions in bread making and their effects on human glycemic response. *J. Cereal Sci*., 36, 59–66.
14. Ceyhan, A.M., Akkaya, V.B., Gulecol, S.C., Ceyhan, B.M., Ozguner, F., Chen, W. (2012). Protective effects of β-glucan against oxidative injury induced by 2.45-GHz electromagnetic radiation in the skin tissue of rats. *Arch. Dermatol. Res*., 304, 521–527.
15. Chan, W.K., Law, H.K., Lin, Z.B., Lau, Y.L., Chan, G.C. (2007). Response of human dendritic cells to different immunomodulatory polysaccharides derived from mushroom and barley. *Int. Immunol.*, 19, 891–899.
16. Chan, W.K., Law, H.K., Lin, Z.B., Lau, Y.L., Chan, G.C. (2007). Response of human dendritic cells to different immunomodulatory polysaccharides derived from mushroom and barley. *Int. Immunol.*, 19, 891–899.
17. Chanput, W., Reitsma, M., Kleinjans, L., Mes, J.J., Savelkoul, H.F., Wichers, H.J. (2012). β-glucans are involved in immune-modulation of THP-1 macrophages. *Mol. Nutr. Food Res*., 56, 822–833.
18. Chen, J. (2013). Recent advances in the studies of β-glucans for cancer therapy. *Anti-Cancer Agents Med. Chem*., 13, 679–680.
19. Chen, J., Raymond, K. (2008). β-glucans in the treatment of diabetes and associated cardiovascular risks. *Vasc. Health Risk Manag*., 4, 126–1272.
20. Chen, K.L., Weng, B.C., Chang, M.T., Liao, Y.H., Chen, T.T., Chu, C. (2008). Direct enhancement of the phagocytic and bactericidal capability of abdominal macrophage of chicks by β-1, 3-1, 6-glucan. *Poult Sci*., 87:2242–2249.
21. Chen, M., Seviour, R. (2007). Medicinal importance of fungal β-(1→3), (1→6)-glucans. *Mycol. Res*., 111, 635–652.

22. Cheng, Y-H., Lee, D-H., Wen, C-M., Weng, C-F. (2004). Effects of ß-Glucan Supplementation on Lymphocyte Proliferation, Macrophage Chemotaxis and Specific Immune Responses in Broilers. *Asian-Aust. J. Anim. Sci*. 17(8), 1145-1149.
23. Choi, J.-S., Kim, J.W., Jung, G.-W., Moon, S.-B., Cho, H.-R., Sung, S.H., Jung, J.J., Kwon, Y.S., Ku, S.K., Sohn, J.-H. (2016). Effect of a β-glucan from Aureobasidium on TGF-β1-modulated in vitro dermal wound repair. *Toxicol. Environ. Health Sci*., 8, 12–18.
24. Choromanska, A., Kulbacka, J., Rembialkowska, N., Pilat, J., Oledzki, R., Harasym, J., Saczko, J. (2015). Anticancer properties of low molecular weight oat β-glucan-An in vitro study. *Int. J. Biol. Macromol*., 80, 23–28.
25. Cox, C.M., Stuard, L.H., Kim, S., McElroy, A.P., Bedford, M.R., Dalloul, R.A. (2010). Performance and immune responses to dietary beta-glucan in broiler chicks. *Poult Sci*., 89:1924–1933.
26. Czop, J.K., Austen, K.F. (1985). A ß-glucan inhihitable receptor on human monocytes: its identity with the phagocytic receptor for particulate activators of the alternative complement pathway. *J. Immunnol*, 134:2588-2593.
27. Daou, C., Zhang, H. (2012). Oat β-Glucan: Its role in health promotion and prevention of diseases. *Compr. Rev. Food Sci. Food Saf*., 11, 355–365.
28. Daou, C., Zhang, H. (2012). Oat β-Glucan: Its role in health promotion and prevention of diseases. *Compr. Rev. Food Sci. Food Saf*., 11, 355–365.
29. Di Luzio, N.R., Williams, D.L., Mcnamee, R.B., Edwards, B.F., Kitahama, A. (1979). Comparative tumor-inhibitory and anti-bacterial activity of soluble and particulate glucan. *Int. J. Cancer*, 24, 773–779.
30. Donzis, B.A. (1990). Method and Composition for Treating Hyperlipidemia. 1990: U.S. Patent 4,891,220.
31. Dritz, S.S., Shi, J., Kielian, T.L., Goodband, R.D., Nelssen, J.L., Tokach, M.D., Chengappa, M.M., Smith, J.E., Blecha, F. (1995). Influence of dietary beta-glucan on growth performance, nonspecific immunity, and resistance to Streptococcus suis infection in weanling pigs. *J Anim Sci*,73,3341- 3350.
32. Drochner, W., Stadermann, B., Yildiz, G. (1993). Einfluss von Pektinen auf

Leistung und Stoffwechsel des Geflügels. *Übers. Tierernährung*, 21: 121-180.

33. Elrayeh, A.S., Yıldız, G. (2012). Effects of inulin and beta-glucan supplementation in broiler diets on growth performance, serum cholesterol, intestinal length, and immune system. *Turkish Journal of Veterinary & Animal Sciences,* 36 (4): 388-394. https://doi.org/10.3906/vet-1010-504
34. Ergün, A., Tuncer, Ş.D., Çolpan, İ., Yalçın, Sakine, Yıldız, G., Küçükersan, M.K., Küçükersan, S., Şehu, A., Saçaklı, P. (2019). Yemler, Yem Hijyeni Ve Teknolojisi. 7. Baskı. Detamat Matbaa. s1-448. Ankara. ISBN: 975-97808-3-8.
35. Erkol, H., Kahramansoy, N., Kordon, Ö., Büyükaşık, O., Serin, E., Ulaş, N. (2011). Effects of β-glucan on hepatic damage caused by obstructive jaundice. *Ulus Travma Acil Cerrahi Derg*, 17, 303–307.
36. Erkol, H., Kahramansoy, N., Kordon, Ö., Büyükaşık, O., Serin, E., Ulaş, N. (2011). Tıkanma sarılığında beta glukanın karaciğer hasarına etkisi. *Ulus Travma Acil Cerrahi Derg*,17(4), *303-307.*
37. Granfeldt, Y., Nyberg, L., Björck, I. (2008). Muesli with 4 g oat β-glucans lowers glucose and insulin responses after a bread meal in healthy subjects. *Eur. J. Clin. Nutr*., 62, 600–607.
38. Grau, S.J., Sirvent, P.L., Ingles, M.M., Urgell, R.M. (2015). β-glucans from Pleurotus ostreatus for prevention of recurrent respiratory tract infections. *Acta Pediatr. Esp*., 73, 186–193.
39. Hallfrisch, J., Behall, K.M. (2003). Physiological responses of men and women to barley and oat extracts (nu-trimX). I. Breath hydrogen, methane, and gastrointestinal symptoms. *Cereal Chem.*, 80, 76–79.
40. Hasegawa, A., Yamada, M., Dombo, M., Fukushima, R., Matsuura, N., Sugitachi, A. (2004). Sparassis crispa as biological response modifier. *Gan To Kagaku Ryoho*, 11, 1761–1763.
41. Hetland, G., Sandev, P. (2002). B-1,3-glucan reduces growth of Mycobacterium tuberculosis in macrophage cultures. *FEMS Immunology and Medical Microbiology*, 33, 41-45.
42. Hong, F., Yan, J., Baran, J.T., Allendorf, D.J., Hansen, R.D., Ostroff, G.R., Xing, P.X., Cheung, N.K., Ross, G.D. (2004). Mechanism by which orally

administered β-1,3-glucans enhance the tumoricidal activity of antitumor monoclonal antibodies in murine tumor models. *J. Immunol.*, 173, 797–806.

43. Hou, T.-Y., Wang, S.-H., Liang, S.-X., Jiang, W.-X., Luo, D.-D., Huang, D.-H. (2015). The screening performance of serum 1,3 β-D-glucan in patients with invasive fungal diseases: A meta-analysis of prospective cohort studies. PLoS ONE 2015, 10, e0131602.
44. Hwang, Y.H., Park, B.K., Lim, J.H., Kim, M.S., Song, I.B., Park, S.C., Jung, H.K., Hong, J.H., Yun, H.I. (2008). Effects of β-glucan from *Paenibacillus polymyxa* and L-theanine on growth performance and immunomodulation in weanling piglets. *Asian Australas J Anim Sci*., 21:1753–1759
45. Ina, K., Kataoka, T., Ando, T. (2013). The use of lentinan for treating gastric cancer. *Anti-Cancer Agents Med. Chem*., 13, 681–688.
46. Jesenak, M., Banovcin, P., Rennerova, Z., Majtan, J. (2014). β-glucans in the treatment and prevention of allergic diseases. *Allergol. Immunopathol*., 42, 149–156.
47. Jorgensen, J.B., Sharp, G.J., Secombes, J., Robertson, B. (1993). Effect of a yeast-cell-wall glucan on the bactericidal activity of rainbow macrophages. *Fish & Shellfish Immunology*, 3,267-277.
48. Jung, M.Y., Kim, J.W., Kim, K.Y., Choi, S.H., Ku, S.K. (2016). Polycan, a β-glucan from Aureobasidium pullulans SM-2001, mitigates ovariectomy-induced osteoporosis in rats. *Exp. Ther. Med*., 12, 1251–1262.
49. Juvonen, K.R., Purhonen, A.-K., Salmenkallio-Marttila, M., Lahteenmaki, L., Laaksonen, D.E., Herzig, K.-H., Uusitupa, M.I.J., Poutanen, K.S., Karhunen, L.J. (2009). Viscosity of oat bran-enriched beverages influences gastrointestinal hormonal responses in healthy humans. *J. Nutr*., 139, 461–466.
50. Karunaratne, N.D., Classen, H.L. (2019). Chapter 10. Beta-glucans and beta-glucanase in animal nutrition, do we understand their full effects? Wageningen Academic Publishers. 11 November 2019, p 171 – 191. Khoury, D.E., Cuda, C., Luhovyy, B.L., Anderson, G.H. (2012). β-glucan: Health benefits in obesity and metabolic syndrome. *J. Nutr. Metab*. Volume 2012, Article

ID 851362, https://doi.org/10.1155/2012/851362.

52. Kim, S.Y., Song, H.J., Lee, Y.Y., Cho, K.-H., Roh, Y.K. (2006). Biomedical issues of dietary fiber β-Glucan. *J. Korean Med. Sci.*, 21, 781–789.
53. Kogan, G., Pajtinka, M., Babincova, M., Miadokova, E., Rauko, P., Slamenova, D., Korolenko, T.A. (2008). Yeast cell wall polysaccharides as antioxidants and antimutagens: Can they fight cancer? *Neoplasma*, 55, 387–393.
54. Kohut, M.L, Davis, J.M., Jackson, D.A., Colbert, L.H, Strasner, A., Essig, D.A., Pate, R.R., Ghaffar, A., Mayer, E.P. (1994). Effect of exercise on macrophage antiviral function in the lung. *J, of Am. Cell. of Sports Medicine*, Vo1.26. S33.
55. Krakowski L, Krzyzannowski J, Wrona Z, Siwicki AK. (1999). The effect of nonspecific immunositimulation of pregnant mares with 1,3/1,6 glucan and levamisol on the immunoglobulins levels in collostrum, selected incidences of nonspecific cellular and humoral immunity in foals in neonatal and postnatal period. Vet. Immunol. and Immunopathol. 68:1-11.
56. Ku, S.-K., Cho, H.-R., Choi, J.-S., Kim, J.-W. (2015). Effects of polycan on calcium bioavailability in two different rat models of osteoporosis. *Toxicol. Environ. Health Sci.*, 7, 35–42.
57. Kumari, J., Sahoo, P. K. (2006). Dietary p-1,3 glucan potentiates innate immunity and disease resistance of Asian catfish, *Clarias batrachus* (L.). *JFish Dis*, 29, 95-101.
58. Kurnikakis, B., Mandeville, R., Brousseau, P., Ostroff, G. (2003). Anthrax-protective effects of yeast beta 1,3 glucans. *Med Gen Med*, 5, 1.
59. Kusmiati, and Dhewantata, F.X.R. (2016). Cholesterol-lowering effect of β-glucan extracted from Saccharomyces cerevisiae in rats. *Sci. Pharm*., 84, 153–165.
60. Lang, C.H., Dobrescu, C. (1989). Interleukin-l induced increases in glucose utilization are insulin mediated. *Life Sciences*, 45(22):21 27-34.
61. Liatis, S., Tsapogas, P., Chala, E., Dimosthenopoulos, C., Kyriakopoulos, K., Kapantais, E., Katsilambros, N. (2009). The consumption of bread enriched with β-glucan reduces LDL-cholesterol and improves insulin resistance in patients with type 2 diabetes. *Diabetes Metab*., 35, 115–120.

62. Lim, M.-K., Ku, S.-K., Choi, J.-S., Kim, J.-W. (2015). Effect of polycan, a β-glucan originating from Aureobasidium, on a high-fat diet-induced hyperlipemic hamster model. *Exp. Ther. Med*., 9, 1369–1378.
63. Lowry, V.K., Farnell, M.B., Ferro, P.J., Swaggerty, C.L., Bahl, A., Kogut, M.H. (2005). Purified beta-glucan as an abiotic feed additive up-regulates the innate immune response in immature chickens against Salmonella enterica serovar Enteritidis. *Int J Food Microbiol. Feb* 15; 98(3):309-18.
64. Manners, D.J., Masson, A.J., Patterson, J.C. (1973). The structure of a beta-(1,3) D-glucan from yeast cell walls. *Biochem. J*., 135,19- 30.
65. Mansell, PWA. (1986). Employment of soluble glucan in the treatment of patients with Acquired Immunodeficiency Syndrome. M.D Anderson Cancer Center, IND.
66. Mansell, PWA., Ichinose, I-I., Reed, R.J., Krements, E.T., McNamee, R.B., Di Luzio, N.R. (1975). Macrophage-mediated destruction of human malignant cells in vive. *J Nation Cancer Inst*, 54: 571-580.
67. Mansell, PWA., Rowden, G., Hammer, C. (1978). Clinical experiences with the use of glucan. Immune Modulation and Control of Neoplasia by Adjuvant Therapy. Raven Press, New York.
68. Mantovani, M.S., Bellini, M.F., Angeli, J.P.F., Oliveira, R.J., Silva, A.F., Ribeiro, L.R. (2008). β-glucans in promoting health: Prevention against mutation and cancer. *Mutat. Res*., 658, 154–161.
69. Moon, S.H., Lee, I., Feng, X., Lee, H.Y., Kim, J., Ahn, D.U. (2016). Effect of Dietary Beta-Glucan on the Performance of Broilers and the Quality of Broiler Breast Meat. *Asian-Australas J Anim Sci*., 29(3): 384–389. doi: 10.5713/ajas.15.0141
70. Morales-Lopez, R., Auclair, E., Garcia, F., Esteve-Garcia, E., Brufau, J. (2009). Use of yeast cell walls, β-1,3/1,6-glucans, and mannoproteins in broiler chicken diets. *Poult Sci*., 88:601–607.
71. Murphy, E.A., Davis, J.M., Carmichael, M.D. (2010). Immune modulating effects of β-glucan. *Curr. Opin. Clin. Nutr. Metab. Care*, 13, 656–661.

72. Neyrinck, A.M., Possemiers, S., Verstraete, W., De Backer, F., Cani, P.D., Delzenne, N.M. (2012). Dietary modulation of clostridial cluster XIVa gut bacteria (Roseburia spp.) by chitin-glucan fiber improves host metabolic alterations induced by high-fat diet in mice. *J. Nutr. Biochem*., 23, 51–59.
73. Nicolosi, R., Bell, S.J., Bistrian, B.R., Greenberg, I., Forse, R.A., Blacjburn, G.I. (1999). Plasma lipid cahnges after suplementation with ß glucan fiber from yeast. *Am J Clin Nutr*, 70: 208-212.
74. Ooi, V.E.C., Liu, F. (2000). Immunomodulation and anti-cancer activity of polysaccharide-protein complexes. *Curr. Med. Chem*., 7, 715–729.
75. Park, S.-I., Kang, S.-J., Han, C.-H., Kim, J.-W., Song, C.-H., Lee, S.-N., Ku, S.-K., Lee, Y.-J. (2016). The effects of topical application of polycal (a 2:98 (g/g) mixture of polycan and calcium gluconate) on experimental periodontitis and alveolar bone loss in rats. *Molecules*, 21, 527.
76. Pillai, T.G., Devi, P.U. (2013). Mushroom β-glucan: Potential candidate for post irradiation protection. *Mutat. Res*., 751, 109–115.
77. Price, G.B., Makinodan T. (1972). Immunologic deficiencies in senescence. *The Journal of Immunology*., 108 (2):403-412.
78. Qi, C., Cai, Y., Gunn, L., Ding, C., Li, B., Kloecker, G., Qian, K., Vasilakos, J., Saijo, S., Iwakura, Y. (2011). Differential pathways regulating innate and adaptive antitumor immune responses by particulate and soluble yeast-derived β-glucans. *Blood*, 117, 6825–6836.
79. Qureshi, M.A., Guo, Y. (2003). Immune enhancement by beta-1,3/1,6-glucan: A possible alternative to the use of antibiotics in poultry. WPSA, Federation of European Branches Meeting of the Working Group 10 (Turkey).
80. Raa, J., Roerstad, G., Engstad, R., Robertsen, B. (1992). In Shariff IM, Subasinghe RP, and Arthur JR. (eds). Diseases in Asian Aquaculture II.Fish Health Section, Asian Fisheries Society, Manila, Philipines, pp 39-50
81. Raa, J., Roerstad, G., Engstad, R., Robertsen, B. (1992). In Shariff IM, Subasinghe RP, and Arthur JR. (eds). Diseases in Asian Aquaculture II.Fish Health Section, Asian Fisheries Society, Manila, Philipines, pp 39-50
82. Rasmussen, L.T., Seljelıd, R. (1991). Novel immunomodulators with

pronounced in vitro effects caused by Stimulation of cytokine release. *J Cell Biochem*., 46: 60-68.

83. Rasmussen, L.T., Fandrem, J., Seljelid, R. (1990). Dynamics of blood components and peritoneal fluid during treatment of murine E. coli sepsis with β-1,3-D-polyglucose derivatives. II. Interleukin-1, tumour necrosis factor, prostaglandin E2, and Leukotriene B4. *Scan. J. Immunol.*, 32: 333-340.
84. Rasmussen, L.T., Lipsky, P.E., Seljelid, R. (1987). Production of prostaglandin E2 and Interleukin 1 by mouse peritoneal macrophages stimulated with β-1,3-D-Glucan derivatized plastic beads. *Scan. J. Immunol*., 20: 731.
85. Reynolds, J.A., Kastello, M.D., Harrigton, D.G., Crabs, C.L., Peters, C.J., Jemski, J.V., Scott, G.H., Di Luzio, N.R. (1980). Glucan-induced enhancement of host resistance to selected infectious diseases. *Infect. Immun*., 30, 51–57.
86. Sadarao, B., Das, P., Shelke, V., Chanthirasekaran, R. (2020). Beta-Glucans: A Crucial Weapon to Modulate Poultry Immune System. Kemin Industries**.**
87. Sarinho, E., Medeiros, D., Schor, D., Silva, A.R., Sales, V., Motta, M.E., Costa, A., Azoubel, A., Rizzo, J.A. (2009). Production of interleukin-10 in asthmatic children after β-1–3-glucan. *Allergol. Immunopathol. (Madr.)*, 37, 188–192.
88. Seljelid, R., Bogwald, J., Rasmussen, L. T., Larm, O., Hoffman, J., Ugelstad, J. (1985). In vivo activation of mouse macrophages with β-1,3-D-Glucan-derivatized plastic beads. *Scan. J. Immunol*, 21: 601-605.
89. Seljelid, R., Rasmussen, L. T., Larm, O., Hoffman, J. (1987). The protective effect of β-1, 3-D-Glucan-derivatized plastic beads against E. coli infection in mice. *Scan. J. Immunol*., 25: 55-60.
90. Sener, G., Eksioglu-Demiralp, E., Cetiner, M., Ercan, E., Yegen, B.C. (2006). β-glucan ameliorates methotrexate-induced oxidative organ injury via its antioxidant and immunomodulatory effects. *Eur. J. Pharmacol*., 542, 170–178.
91. Shim, J.H., Sung, K.J., Cho, M.C., Choi, W.A., Yang, Y., Lim, J.S., Yoon, D.Y. (2007). Antitumor effect of soluble β-1,3-glucan from Agrobacterium sp. R259 KCTC 1019. *J. Microbiol. Biotechnol*, 17, 1513–1520.

92. Sohn, J.-H., Kim, J.W., Jung, G.-W., Park, D.-C., Moon, S.-B., Cho, H.-R., Ku, S.K., Choi, J.-S. (2018). Effects of β-glucan and Folium mori extract combinations in STZ-induced diabetic rats: Effectiveness of various BGFM complex compositions in treating diabetes. *Curr. Nutr. Food Sci*., 14 (3), 235-246.
93. Stadermann, B., Yıldız, G., Drochner, W. (1992). Comparative investigations of various hard-to-digest carbohydrates for the causal analysis of pectin intolerance in poultry. Unpublished
94. Teas, J. (1983). The dietary intake of Laminaria, a brown seaweed, and breast cancer prevention. *Nutr. Cancer*, 4, 217–222.
95. Thondre, P.S., Henry, C.J.K. (2009). High-molecular-weight barley β-glucan in chapatis (unleavened Indian flat bread) lowers glycemic index. *Nutr. Res*, 29, 480–486.
96. Vetvicka, V. (2001). Uses of ß glucan for immunomodilation. *Journal of American Nutraceutical Assoc.(JAVA)*, 3:4
97. Vetvicka, V., Vancikova, Z. (2010). Anti-stress action of several orally-given β-glucans. Biomed. Pap. Med. Fac. Univ. *Palacky Olomouc Czech Repub*., 154, 235–238
98. Vetvicka, V., Vetvickova, J. (2007). Physiological effects of different types of β-glucan. Biomed. Pap. Med. Fac. Univ. Palacky Olomouc. *Czech Repub*., 151, 225–231.
99. Vetvicka, V., Vetvickova, J. (2009). Effects of yeast-derived β-glucans on blood cholesterol and macrophage functionality Glucans, blood cholesterol, and macrophage function. *J. Immunotoxicol*., 6, 30–35.
100. Vetvicka, V., Dvorak, B., Vetvickova, J., Richter, J., Krizan, J., Sima, P., Yvin, J.-C. (2007). Orally administered marine (1→3)-β-D-glucan phycarine stimulates both humoral and cellular immunity. *Int. J. Biol. Macromol*., 40, 291–298.
101. Vetvicka, V., Dvorak, B., Vetvickova, J., Richter, J., Krizan, J., Sima, P., Yvin, J.C. (2007). Orally administered marine (1→3)-β-d-glucan Phycarine stimulates both humoral and cellular immunity. *Int J Biol Macromol.*, 40:291–

298.

102. Vetvicka, V., Pinatto-Botelho, M.F., Santos, A.A.D., De Oliveira, C.A.F. (2014). Evaluation of a special combination of glucan with organic selenium derivative in different murine tumor model. *Anticancer Res*., 34, 6939–6944.
103. Vetvicka, V., Richter, J., Svozil, V., Dobiasova, K.R., Kral, V. (2013). Placebo-driven clinical trials of transfer point glucan#300 in children with chronic respiratory problems: Antibody production. *Am. J. Immunol*., 9, 43–47.
104. Vetvicka, V., Terayama, K., Mandeville, R., Brousseau, P., Kournikakis, B., Ostroff, G. (2002). Pilot study: Orally-Administered Yeast ß1,3-glucan prophylactically protects against Anthrax infection and Cancer in mice. *JANA*, Vol 5, No.1.
105. Vetvicka, V., Terayama, K., Mandeville, R., Brousseau, P., Kournikakis, B., Ostroff, G. (2002). Pilot study: Orally administered yeast β-1,3-glucan prophylactically protects against anthrax infection and cancer in mice. *J. Am. Nutraceut. Assoc*., 5, 1–6.
106. Vetvicka, V., Vashishta, A., Saraswat-Ohri, S., Vetvicka, J. (2008). Immunological effects of yeast- and mushroom-derived β-glucans. *J. Med. Food*, 11, 615–622.
107. Wasser, S.P., Weis, A.L. (1999). Therapeutic effects of substances occurring in higher basidiomycetes mushrooms: A modern perspective. *Crit. Rev. Immunol*. 1999, 19, 65–96.
108. Weitberg, A.B. (2008). A phase I/II trial of β-(1,3)/(1,6) D-glucan in the treatment of patients with advanced malignancies receiving chemotherapy. *J. Exp. Clin. Cancer Res*., 27, 1–4.
109. Wyde P. 1989. NSC-24™: Research report on oral and intraperitoneal applications in mice. ImmuDyne, Inc.
110. Yıldız, G. (2002). Prebiyotik Güç Sindirilebilir Karbonhidratlar ve Sağlık İçin Yararlı Besinler. *Yem Magazin*, 30: 40-43.
111. Yıldız, G., Akan, H.B. (2004). Probiyotik Olarak Kullanılan Mikroorganizmalar ve Yararları. *Yem Magazin*, 36: 37-41.
112. Yıldız, G., Dikicioğlu, T. (1999). The effect of dried Jerusalem artichoke in

addition to the laying hen rations on egg quality and blood parameters. *VIV. Poultry YUTAV*, 3-6 June 1999, İstanbul, p, 380-387. (In d.er Türkei)

113. Yoon, T.J., Kim, T.J., Lee, H., Shin, K.S., Yun, Y.P., Moon, W.K., Kim, D.W., Lee, K.H. (2008). Anti-tumor metastatic activity of β-glucan purified from mutated Saccharomyces cerevisiae. *Int. Immunopharmacol*., 8, 36–42.
114. Yun, C.H, Estrada, A., Kessel, A.V., Park, B.C., Laarveld, B. (2003). ß-Glucan, extracted from oat, enhances disease resistance against bacteriel and parasitic infections. *FEMS Immunology and Medical Microbiology*, 35, 67-75.

CHAPTER 3

CAVICOL MYIASIS

Assoc. Prof. Dr. Duygu Neval SAYIN İPEK[1]

[1] Dicle University, Faculty of Veterinary Medicine, Department of Parasitology, 21280, Diyarbakır, TURKEY; ORCID: 0000-0002-7486-232X
dneval.sayinipek@dicle.edu.tr

Cavicol Myiasis

Cavicol myiasis is myiasis caused by Diptera larvae causing pathological reactions and lesions in the body cavities. The two main cavicol myiasis seen in animals are Nasopharyngeal Myiasis and Gastrico Myiasis.

1. Nasopharagial Myiasis

Nasopharagial myiasis is the name given to myiasis in which fly larvae form the nasal fossa, frontal sinus, and pharyngeal cavity. Species in the Oestradae family and Oestrinae subfamily cause obligatory myaisis in the nasopharyngeal spaces and internal organs of ruminants and equidae. *Oestrus ovis* is the most economically important species that causes nasopharagial myiasis in sheep and goats (Wall and Shearer, 1997; Zumpt, 1965).

1.1. Oestrus ovis:

O. ovis larvae is a fly of the *Oestridae* family that causes nasal myiasis (oestrosis) of sheep and goats. Adult flies, 10-12 mm long, are yellow-brown in color and resemble honey bees. The larvae of these flies develop in the nasal cavities and sinuses of their hosts.

1.1.1. Biology

Adult females of *O. ovis* are larviparous, and they deposit the first instar larvae they store during flight directly into or inside the nasal cavities of sheep and goats. The first instar larvae, which are 1 mm in size, quickly settle in the nasal cavity, nasal septum, turbinate and ethmoid

bones. Later, they change coat and form second instar larvae which are 4-12 mm long and move towards the frontal sinuses. Here, the second instar larvae change their coat and form 20mm long third instar larvae (Wall and Shearer, 1997; Yilma and Dorchies, 1991; Zumpt, 1965). Under favorable weather conditions, the development periods of the first, second and third instar larvae take 10-25, 7-15, 13-18 days, respectively. In cold weather, the first stage larva can remain in the hypoperiodic period for months. Mature larvae that complete their development come out with sneezing and enter the pupa stage in the soil. The pupal stage lasts 19-27 days. Adult flies emerging from the pupa mate and after 12 days the female flies begin to lay larvae on their hosts. Adult flies are especially active in hot, dry weather. It has been reported that it can give three generations per year under favorable conditions. They usually give two generations in a year and adults are found in late spring and summer. When larval development stops in autumn, the first instar larvae spend the winter inside the host and do not migrate to the frontal sinuses until spring begins (Angulo-Valadez, Ascencio et al., 2011; Wall and Shearer, 1997; Yilma and Dorchies, 1991; Zumpt, 1965).

1.1.2. Pathogenesis and Clinical manifestations:

The pathological effects of *O. ovis* are partially due to the spines and mouth hooks found in the cuticles of the larvae, and the main effects are due to the biomolecular excreta and secrets secreted by the larvae to the mucosa. The ventral spine and mouth hooks, which allow the first instar larvae to quickly settle in the nasal mucosa and migrate inside the

host, cause a mechanical mucosal irritation. However, the second and third instar larvae lose their dorsal spines, so the spines are not important for the developmental process of these stages and the pathogenesis of infestation. The severity of the lesions in the ethmoid bone and sinuses is mainly related to the strong feeding activities of the third instar larvae and partially the second instar larvae. Therefore, when the second and third instar larvae are found in the ethmoid bone and sinuses, there is an increase in pathological lesions. This infestation causes hyperplasia and metaplasia in the epithelium (Hoste, Leveque et al., 2001; Tabouret, Lacroux et al., 2003).

There are three clinical stages of infestation, but sometimes these stages can be seen together. The first stage is the restlessness, nervousness caused by the flies, approaching each other and sticking their noses towards the ground or between the wool of another sheep, and as a result, a decrease in grazing activities is observed (Hoste, Leveque et al., 2001). The second stage is rhinitis and sinusitis. A few weeks after the larvae are released, runny nose and sneezing are quite pronounced and frequent. Sheep are irritable and a nasal discharge that is initially serous then becomes serous-mucous, muco-purulent and eventually a purulent discharge that may contain blood in many cases, severe. The amount of nasal discharge is not related to the number of larvae, but to the susceptibility of individuals and bacteria. In hot and dry weather, a runny nose makes breathing difficult and the hosts start to breathe through their mouths. These symptoms limit the olfactory abilities of the rams, limiting their ability to perceive estrus, which causes a

decrease in the conception rate. This results in negative feeding, such as reduced grazing and rumination time, general malnutrition, and decreased performance. Nasal and sinus infection, which is then local, shows signs of general illness causing weakness. Nervous symptoms such as ataxia, nystamus, head shaking, and teeth grinding are seen in heavily infested sheep (Dorchies, Duranton et al., 1998; Wall and Shearer, 1997). Neoplastic tumors have been reported in some breeds of sheep in the third stage. In many cases, oestrosis is clinically worsened with fever and cough, as a result of complications such as infectious bronchopneumonia, pleuropneumonia, and pasteurellosis. It has also been reported that abscesses in the lung are common. In addition, it has been reported that sheep and goats with a large number of parasites but no clinical symptoms were encountered during slaughterhouse studies (Dorchies, Wahetra et al., 2003).

1.1.3. Economic Significance

Information on economic losses caused by *Oestrus ovis* infestation is limited. Ilchmann et al. While 86 estimated a 10% decrease in milk production, 4.6 kg in meat production and 200-500 g in wool production per animal, Dorchies et al. 2003 found no difference in milk production between infested animals and healthy animals in their study. In another study, it was reported that there was a weight loss of 2 kg in rams and 1.5 kg in sheep in *O. ovis* infestations (El-Tahawy, 2010).

1.1.4. Treatment and Protection

Due to the presence of adult flies in spring and summer, recurrent infestations are seen continuously during these periods. In order to get the best results from the treatment, late summer and early winter spraying should be done when there are no adult flies. Successful spraying is based on the elimination of all larvae present in the infested animal. However, the insecticide to be used against the first stage larvae that spend the winter in the animal should have a high effect. There are two goals in the treatment of oestrosis, the first is to completely eliminate or minimize the clinical symptoms, and the second is to limit the prevalence of the parasite. To achieve these goals, treatment should be selected based on the presence of third instar larvae in the host. If there are third instar larvae, the development of the parasite is taking place, which means that they can be infested by flies again in the future, and a permanent drug should be chosen for treatment. On the contrary, if there is no third stage larvae, that is, if the first stage larva has entered the hypobiotic stage, there is no need for a permanent drug because the probability of recurrent infestation is very low. This principle is a useful tool for choosing the right drug at the right time, and this allows the rotation of drugs to be used, preventing or delaying the development of drug resistance. In France, long-acting drugs are given when sheep are taken to pasture, while drugs with a short duration of action are used when they are returned to the fold. Because at this time, the flies have died due to the cold and there is no risk of reinfestation (Tabouret, Jacquiet et al., 2001).

Many drugs such as nitroxynil, closantel, ivermectin doramectin, moxidectin, epinomectin are used in cultivation for *O. ovis* infestations. Drugs such as Closantel have a long persistence period and therefore they can be used to prevent re-infestations in seasons when flies are present It is reported that pour on 1mg / kg dose of eprinomectin has a 100% therapeutic effect, ivermectin controlled release capsules have a 100% protective effect for 100 days has been done. It has been reported that the oral use of Closantel at a dose of 10 mg/kg has a 100% protective 98% therapeutic effect (Dorchies, Alzieu et al., 1997; Habela, Moreno et al., 2006; Rugg, Gogolewski et al., 1997).

2. Gastricol Myiasis

The larvae of the genus *Gasterophilus* cause obligate gastricol myiasis in the stomach of equids such as horses, donkeys and zebras in the USA and China, especially in the Mediterranean regions (Colwell, Hall et al., 2006; Otranto, Milillo et al., 2005). Nine species have been identified in the genus *Gasterophilus* (Zumpt, 1965); 7 of them have been reported in Turkey: *G.intestinalis, G.haemorrhoidalis, G.nasalis, G.inermis, G.pecorum, G.meridionalis, G.nigricornis*. *Gasterophilus intestinalis* has a wide geographical distribution in different countries such as Morocco, Europe, Italy, Turkey and Saudi Arabia (Anazi and Alyousif, 2011; Gökçen, Sevgili et al., 2008; Otranto, Milillo et al., 2005; Pandey, Ouhelli et al., 1992).

2.1. Gasterophilus

2.1.1. Biology

The flies, whose larvae are obligatory parasitism in the digestive system of equidae, are 8-18 mm long and are free-living. Adult flies do not feed because their mouth organs are atrophied. Oviparous females lay their eggs on the forelegs, heel area, shoulder, mouth, chin, and nose hairs of Equidae. The places where the eggs are laid vary according to the species. It has been reported that *Gasterophilus intestinalis* is the most common in Turkey, and it is seen that this species lays its eggs with one egg on each hair. *G. haemorrhaidalis* lays its eggs on the cheeks, around the nose, around the upper lip, on the neck area of *G. nasalis*, on the chin of *G. inervis* and *G. nigricornis*, while *G. pecorum* sticks its eggs on the grasses in the pastures. Maggot-shaped and spiny 0.7-0.9 mm larvae emerge from the eggs in 5-10 days. As the first instar larvae take it orally, they move from the oral mucosa to the pharynx, larvae in the cheek area come to the oral cavity either by piercing the cheek skin or by their own movements. When the eggs of *G. pecorum* are taken into the mouth with grass, the larvae pierce the mucosa in the mouth and in all other *Gasterophilus* species, the larvae that come into the mouth pierce the tongue and oral mucosa, moult and become a second instar larva with a length of 5-11 mm. The larvae come to the pharynx region and attach to the mucosa, and after staying there for a month, they migrate to the phloris region of the stomach. It is reported that the larvae cling tightly to the gastric mucosa with their mouth hooks and stay there for 8-10 months. G. intestinalis larvae are red in color and adhere to the

cardiac region of the stomach. *G. nasalis* larvae are yellow in color and settle in the pyloris region of the stomach and sometimes in the duodenum. *G. pecorum* larvae are blood-red in color and are located in the fundus region of the stomach. *G. haemorrhoidalis* larvae are also red in color and remain in the rectum for a few days before being expelled from the body and cause irritation. *G. nigricornis* larvae pass through the stomach and come to the duodenum. The duration of stay of the larvae in the host is 8-11 months, although it varies according to the species. The third stage larvae, which wait in the stomach until spring, leave the gastric mucosa and pass into the intestine and are darted from there with feces. The larvae that fall into the soil enter 1-2 cm under the soil, harden and turn black in color and enter the pupal stage. The pupal period lasts 3-8 weeks. At the end of this period, the flies that emerge from the pupa fly from the end of May to the middle of August, depending on the climatic conditions. *Gastrophilus* species complete their development in about a year. Flies live for 14-20 days and fly in summer months, especially on hot days. They do not fly in cloudy, windy and rainy weather (Cogley and Cogley, 1999; Wall and Shearer, 1997; Zumpt, 1965).

2.1.2. Pathogenesis and Clinical manifestations

When the adult flies are about to lay their eggs, they disturb the animals and prevent them from eating. Because the larvae of different species of *Gasterophilus* are specifically located in one or more regions of the digestive tract, the pathological disorders they cause vary depending on the species (Agneessens, Engelen et al., 1998; Gökçen, Sevgili et al.,

2008; Höglund, Ljungström et al., 1997; Sweeney, 1990). Larvae in the mouth, tongue and buccal mucosa cause stomatitis or ulcers. Difficulty in swallowing, weakness, edema and anemia have been reported in infested equidae. (Mullen and Durden, 2009; Otranto, Milillo et al., 2005; Principato, 1988; Sandin, Skidell et al., 1999; Sequeira, Tostes et al., 2001; Wall and Shearer, 1997). The areas with hair rash due to inflammation in the migration routes of *G. inermis* larvae on the skin are called striated summer dermatitis. The larvae in the stomach are usually found in groups and they cling to the gastric mucosa through the hooks at the front ends, preventing the passage of food into the intestines and causing gastritis. When the larvae are found in large numbers, they sparsely block the pyloris area, preventing the passage of food from the stomach to the intestines. Rupturs in the stomach or duodenum and death may occur with septic peritonitis. (Otranto, Zalla et al., 2005; Soulsby, 1968; Wall and Shearer, 1997). *G.haemorrhoidalis* larvae stay in the rectum for a few days and cause irritation. There are numerous reports of human myiasis caused by *Gasterophilus spp.* (Anderson, 2006).

2.2. Treatment and Protection

Doramectin can be used intramuscularly at a dose of 200mcg/kg body weight for treatment in animals.

Since ivermectin preparations are used subcutaneously in horses, they cause local allergic reactions and pain, it is not recommended to use this way. However, it can be applied in paste form. Giving 7.5 mg/kg of rafoxanide in winter and one month after the animals graze,

Trichlorphon (neguvon) is given at a dose of 40 mg/kg after the animals are fasted for 12-18 hours, mixed with the food or by nasal-meri probe, and this application is done in 3- Its recurrence after 4 months provides a great deal of prevention of the disease (Kaufmann, 1996; Roberson and Nolan, 1988; Soulsby, 1968; Wall and Shearer, 1997).

REFERENCES

Agneessens, J., Engelen, S., Debever, P., and Vercruysse, J. (1998). Gasterophilus intestinalis infections in horses in Belgium. *Veterinary parasitology*, *77*(2-3), 199-204.

Anazi, A. D. A., and Alyousif, M. S. (2011). Prevalence of non-strongyle gastrointestinal parasites of horses in Riyadh region of Saudi Arabia. *Saudi Journal of Biological Sciences*, *18*(3), 299-303.

Anderson, J. (2006). Oestrid myiasis of humans. *The oestrid flies: biology, host-parasite relationships, impact and management. Wallingford: CABI Publishing*, 201-209.

Angulo-Valadez, C., Ascencio, F., Jacquiet, P., Dorchies, P., and Cepeda-Palacios, R. (2011). Sheep and goat immune responses to nose bot infestation: a review. *Medical and veterinary entomology*, *25*(2), 117-125.

Cogley, T., and Cogley, M. (1999). Inter-relationship between Gasterophilus larvae and the horse's gastric and duodenal wall with special reference to penetration. *Veterinary parasitology*, *86*(2), 127-142.

Colwell, D. D., Hall, M. J., and Scholl, P. J. (2006). *The oestrid flies: biology, host-parasite relationships, impact and management*. CABI.

Dorchies, P., Alzieu, J., and Cadiergues, M. (1997). Comparative curative and preventive efficacies of ivermectin and closantel on Oestrus ovis (Linné 1758) in naturally infected sheep. *Veterinary parasitology*, *72*(2), 179-184.

Dorchies, P., Duranton, C., and Jacquiet, P. (1998). Pathophysiology of Oestrus ovis infection in sheep and goats: a review. *Veterinary Record*, *142*(18), 487-489.

Dorchies, P., Wahetra, S., Lepetitcolin, E., Prévot, F., Grisez, C., Bergeaud, J.-P., Hoste, H., and Jacquiet, P. (2003). The relationship between nasal myiasis and the prevalence of enzootic nasal tumours and the effects of treatment of Oestrus ovis and milk production in dairy ewes of Roquefort cheese area. *Veterinary parasitology*, *113*(2), 169-174.

El-Tahawy, A. S. (2010). The prevalence of selected diseases and syndromes affecting Barki sheep with special emphasis on their economic impact. *Small Ruminant Research*, *90*(1-3), 83-87.

Gökçen, A., Sevgili, M., Altaş, M. G., and Camkerten, İ. (2008). Presence of Gasterophilus species in Arabian horses in Sanliurfa region. *Turkiye Parazitol Derg*, *32*, 337-339.

Habela, M., Moreno, A., Gragera-Slikker, A., Gomez, J., Montes, G., Rodriguez, P., and Alvinerie, M. (2006). Efficacy of eprinomectin pour-on in naturally Oestrus ovis infested merino sheep in Extremadura, South-West Spain. *Parasitology research*, *99*(3), 275-280.

Hoste, H., Leveque, H., and Dorchies, P. (2001). Comparison of nematode infections of the gastrointestinal tract in Angora and dairy goats in a rangeland environment: relations with the feeding behaviour. *Veterinary parasitology*, *101*(2), 127-135.

Höglund, J., Ljungström, B.-L., Nilsson, O., Lundquist, H., Osterman, E., and Uggla, A. (1997). Occurrence of Gasterophilus intestinalis and some parasitic nematodes of horses in Sweden. *Acta Veterinaria Scandinavica*, *38*(2), 157-166.

Kaufmann, J. (1996). *Parasitic infections of domestic animals: a diagnostic manual*. ILRI (aka ILCA and ILRAD).

Mullen, G. R., and Durden, L. A. (2009). *Medical and veterinary entomology*. Academic press.

Otranto, D., Milillo, P., Capelli, G., and Colwell, D. D. (2005). Species composition of Gasterophilus spp.(Diptera, Oestridae) causing equine gastric myiasis in southern Italy: parasite biodiversity and risks for extinction. *Veterinary parasitology*, *133*(1), 111-118.

Otranto, D., Zalla, P., Testini, G., and Zanaj, S. (2005). Cattle grub infestation by Hypoderma sp. in Albania and risks for European countries. *Veterinary parasitology*, *128*(1-2), 157-162.

Pandey, V., Ouhelli, H., and Verhulst, A. (1992). Epidemiological observations on Gasterophilusintestinalis and G. nasalis in donkeys from Morocco. *Veterinary parasitology*, *41*(3-4), 285-292.

Principato, M. (1988). Classification of the main macroscopic lesions produced by larvae of Gasterophilus spp.(Diptera: Gasterophilidae) in free-ranging horses in Umbria. *The Cornell Veterinarian*, *78*(1), 43-52.

Roberson, E., and Nolan, M. (1988). *Veterinary Pharmacology and Therapeutics*. Ames

Rugg, D., Gogolewski, R., Barrick, R., and Eagleson, J. (1997). Efficacy of ivermectin controlled-release capsules for the control and prevention of nasal bot infestations in sheep. *Australian veterinary journal*, *75*(1), 36-38.

Sandin, A., Skidell, J., Häggström, J., Girma, K., and Nilsson, G. (1999). Post-mortem findings of gastric ulcers in Swedish horses up to one year of age: a retrospective study 1924–1996. *Acta Veterinaria Scandinavica*, *40*(2), 109-120.

Sequeira, J., Tostes, R., and Oliveira-Sequeira, T. (2001). Prevalence and macro-and microscopic lesions produced by Gasterophilus nasalis (Diptera: Oestridae) in the Botucatu Region, SP, Brazil. *Veterinary parasitology*, *102*(3), 261-266.

Soulsby, E. J. L. (1968). Helminths, arthropods and protozoa of domesticated animals (of MSnnig's Veterinary helminthology and entomology). *Helminths, arthropods and protozoa of domesticated animals (sixth edition of MSnnig's Veterinary helminthology and entomology).*

Sweeney, H. (1990). The prevalance and pathogenicity of Gaterophilus intestinalis larvae in horses in Ireland. *Irish Veterinary Journal*, *43*(3), 67-73.

Tabouret, G., Jacquiet, P., Scholl, P., and Dorchies, P. (2001). Oestrus ovis in sheep: relative third-instar populations, risks of infection and parasitic control. *Veterinary Research*, *32*(6), 525-531.

Tabouret, G., Lacroux, C., Andreoletti, O., Bergeaud, J., Hailu-Tolosa, Y., Hoste, H., Prevot, F., Grisez, C., Dorchies, P., and Jacquiet, P. (2003). Cellular and humoral local immune responses in sheep experimentally infected with Oestrus ovis (Diptera: Oestridae). *Veterinary Research*, *34*(2), 231-241.

Wall, R., and Shearer, D. (1997). *Veterinary entomology: Arthropod ectoparasites of veterinary importance*. Springer Science & Business Media.

Yilma, J., and Dorchies, P. (1991). Epidemiology of Oestrus ovis in southwest France. *Veterinary parasitology*, *40*(3-4), 315-323.

Zumpt, F. (1965). Myiasis in man and animals in the Old World. A textbook for physicians, veterinarians and zoologists. *Myiasis in Man and Animals in the Old World. A Textbook for Physicians, Veterinarians and Zoologists.*

CHAPTER 4

CUTANEOUS MYIASIS

Assoc. Prof. Dr. Duygu Neval SAYIN İPEK[1]

[1] Dicle University, Faculty of Veterinary Medicine, Department of Parasitology, 21280, Diyarbakır, TURKEY; ORCID: 0000-0002-7486-232X
dneval.sayinipek@dicle.edu.tr

Cutaneous Myiasis

The term myiasis was used for the first time by Hope in 1940 and defined as Diptera larvae infesting vertebrate humans and animals for at least one period of their lives by feeding on their living and dead tissues, body fluids, and digested food (Boulard, Alvinerie et al., 2008; Llchmann, Betke et al., 1986; Zumpt, 1965). Myiasis, which is more common in tropical climates, is of great importance in terms of veterinary medicine due to the health problems it causes in animals and the serious damage it causes to the country's economy (Wall and Shearer, 2001a; Zumpt, 1965). Cutaneous myiasis is myiasis caused by Diptera larvae by causing swelling or deep wounds in the dermal layer or by expanding previously formed wounds. Cutaneous myiasis is divided into three groups traumatic, furuncular, and creeping myiasis, according to the main clinical signs it shows (Hall and Farkas, 2000; Zumpt, 1965).

1.Traumatic Myiasis-Wound Myiasis

Traumatic or wound myiasis is defined as a parasitic infestation that occurs as a result of feeding fly larvae in traumatic lesions in the cutaneous tissues of vertebrate hosts (Hall, 1997; Hall and Farkas, 2000). Species that cause traumatic myiasis are found in the families *Calliphoridae* and *Sarcophagidae*. In Turkey, 24 fly species that are related to these families and cause myiasis have been identified (Özdal, 2004; Sayın İpek, Şaki et al., 2011). However, it has been reported that two species, *Lucilia sericata* and *Wohlfahrtia magnifica*, which cause traumatic myiasis in cattle, sheep and many of the other animals, are

important in our country (Dik, Uslu et al., 2012; İpek and Şaki, 2010; Şaki and Özer, 1999).

1.1. Lucialia sericata

Although these speices of flies are found in many parts of the world, they are more common in holartctic regions. Adults of these flies, which are facultative traumatic myiasis agents, are 5-10 mm long and their abdomens are metallic green or coppery green. The myiasis caused by these flies, which are common in South Africa, Australia, Europe and North America, is called Blowfly strike. Studies conducted in Turkey have shown that *L. sericata* is the most common (46-82.43%) fly species that causes traumatic myiasis (Dik, Uslu et al., 2012; Özdal, 2004; Sayın İpek, Şaki et al., 2011; Sevgili, Şaki et al., 2004).

1.1.1. Biology

L. sericata is anoutogenous and needs protein for their eggs to mature. If the adult flies that emerge from the pupa get enough protein, they started to lay eggs after 5-9 days. Adult flies lay eggs on open and stinking wounds, on soiled or wet fleece, and to a lesser extent on feces. Females lay 225-250 eggs with an interval of three days.

The time from egg to adult fly varies depending on the average temperature (Wall and Shearer, 1997; Zumpt, 1965). Larvae hatch from eggs in 10-52 hours on meat in summer, and in 9.5 hours on average at 31 °C on sheep's back fleece. The larvae feed in the wound for about 5-6 days and moulting twice (Zumpt, 1965). The third instar larvae mature after 43 hours and leave the wound and fall to the ground to occurs

pupae. The larvae buried in the soil enter the prepupal stage, this period can vary between three days and a few weeks in summer conditions. The larvae that enter diapause to spend the winter are buried at a depth of 10 cm under the soil, so that they are protected from temperatures below zero degrees. They remain inactive until the soil temperature reaches about 7 °C in winter conditions. Where temperatures do not drop below freezing, reproduction continues throughout the year. Flies, which can live for a month or longer in the summer, can also go into hibernation. In the northern hemisphere, these flies can produce three or four generations a year (Pitts and Wall, 2006; Wall, French et al., 1992; Zumpt, 1965).

1.2 Wohlfahrtia magnifica

The adults of this species are 8-14 mm long, widely distributed in the tropical parts of the Palaearctic and Oriental regions from Western Europe and North Africa to the Middle East and Central Asia to China. Whole body densely pollinated whitish gray (Zumpt, 1965).

1.2.1 Biology

Wohlfahrtia magnifica larvae cause obligatory myiasis in warm-blooded vertebrates. The female fly leaves about 120-170 larvae that she removes during her life, on the open wounds of the host or near the lesioned areas opened by the bites of the ticks. These first stage larvae are very active. The fed larvae mature in 5-7 days and leave the wound to enter the pupa and fall into the soil. Larvae can also be deposited on the nasal membrane, eyes and neglected female genital organs. They

wait in the pupa stage in winter conditions and the pupae are quite durable. Flies are very active between June and September. Inactive flies in the early hours of the day and at night and on dark days fly between the hottest hours of the day (10.00-16.00) (Herms, 1946; Wall and Shearer, 1997; Zumpt, 1965).

1.3 Predisposing factors

In order for traumatic myiasis to occur in animals, it is essential that the fly population is dense and the animals become susceptible to the parasite. The fly population increases in late spring and early summer. On hot and dry summer days, the fly population decreases considerably. At the beginning of autumn, an increase in the fly population is observed again. Traumatic myiasis cases are most common in June-July (M., 1973).

Various predisposing factors can be mentioned to make animals susceptible to parasites for the formation of myiasis. Injuries such as wounds after shearing, operation wounds, wounds caused by entanglement with barbed wire create suitable environments for flies to lay eggs. Nail rot (footrot) occurring in the nail and phostitis (pizzlerot) occurring in the preputium are predisposing factors for myiasis occurring in these regions (Broughan and Wall, 2007; Loste, Ramos et al., 2005; Ruiz-Martinez, Soler-Cruz et al., 1991). It is among the factors that increase animal sensitivity in infectious diseases such as scabies caused by *Dermatophilus congolensis* (Broughan and Wall, 2007). Increased bacterial activity and fleece decomposition (fleecerot) due to prolonged wetness of the fleece on body parts contaminated with

feces and urine is one of the most important predisposing factors that increase animal susceptibility (Loste, Ramos et al., 2005; Soulsby, 1968). Microbial changes that produce special foul-smelling compounds in the mucous membrane of the odor of urine in the external genital organs are counted among the triggering factors for the formation of myiasis in these regions.

1.4. Pathogenesis and Clinical manifestations

The pathogenicity of traumatic myiasis begins with the laying of eggs or larvae of flies. Larvae cause irritation, exudation and tissue destruction with the proteolytic enzymes they secrete. They feed on dead tissue and exudations resulting from this destruction (Soulsby, 1968). *W. magnifica* larvae settle deeper into the wound, while *L. sericata* settles in the superficial tissues. This is an indication of the difference in pathogenicity between species. The skin is tense, hot and sometimes edematous. Epidermal necrosis begins at the margins of advanced wounds. A foul odor is emitted as a result of suppuration in the parts where the larvae are not present. As the larvae erode the skin, the inflamed wound area gradually enlarges. The wound can reach 0.5-20 cm in diameter and 5-8 cm in depth. A deterioration in the general condition of the animals is observed. There are clinical findings such as restlessness, anxiety, loss of appetite, fever, and increased respiratory rate (Ruiz-Martinez, Soler-Cruz et al., 1991; Soulsby, 1968). Depending on the location of the larvae, clinical signs may also differ. If it is found in the legs, it can cause lameness, if it is found in the eye, it can cause blindness, if it is found in the ear, it can cause deafness, if

it is found in the brain, it can cause nervous symptoms. In addition, if it is found in the vulva and prepitium, it can cause disorders that will affect fertility (Ruiz-Martinez, Soler-Cruz et al., 1991; Zumpt, 1965). Traumatic myiasis also causes various changes in blood values. An increase in neutrophils is observed due to the toxic products secreted by both larvae and bacteria. Anemia may occur in infested animals (Broadmeadow, O'Sullivan et al., 1984; Guerrini, 1997). If animals affected by traumatic myiasis are not treated, deaths may occur from intoxication, septicemia, shock, histolysis, or secondary infections (Guerrini, 1997).

1.5. Economic Significance

The economic importance of traumatic myiasis is quite high because it causes yield losses and treatment and prevention costs. The annual damage to the country's economies was calculated as 100-300 million dollars in Brazil and 40 million dollars in New Zealand. It has been reported that the cost for chemical protection for 4-16 weeks in England is 20-60 pounds, respectively, and 2 and 2.5 euros are spent per kg body weight of sheep (Scott, Heinrich et al., 2004; Scott, Sargison et al., 2007; Usher, Cruz et al., 1997).

1.6. Treatment and Prevention

The aim of the treatment of traumatic myiasis is to kill the larvae in the lesion and to prevent it from being reinfested with more larvae. In order to see the size of the wound, the wool in the wound area is cut and the larvae seen in the area are separated from the wound. However, it may

not be possible to separate the larvae deep in the wound. For this reason, with various drug applications, both larvae die and re-infestations are prevented (Soulsby, 1968). Today, in the treatment of traumatic myiasis, organophosphorus insecticides such as diazinon, fenthion-ethyl, coumaphos, chlorfenvinphos, carbophenothion, malation and as an alternative to these insecticides, synthetic pyrethroids, macrocyclic lactons, Insect Many drugs such as growth inhibitors have been developed (Broughan and Wall, 2006; Tellam and Bowles, 1997). To reduce contamination with urine and feces Applications such as cutting the tail, shearing the wool, separating the skin from the folded areas of the skin are the methods that can be used in the control of myiasis, provided that the wounds are well taken care of. The use of preventive drugs for intestinal nematodes reduces the risk of myiasis, especially in the pasture period (Morris, 2000; Soulsby, 1968).

2. Creeping myiasis –Subdermal myiasis

If the fly larvae that cause cutenous myiasis undergo a migration under the skin, this type of myiasis is called creeping-subdermal myiasis. Creeping myiasis is caused by seven species of flies in the *Hypoderma genus* and *Przhevalskiana* genus in the subfamily Hypodermatinae (Hall and Wall, 1995; Zumpt, 1965). The fly species that cause obligatory creeping myiasis in the northern hemisphere are *Hypoderma bovis* and *Hypoderma lineatum* in cattle, *Przhevalskiana silenus*, *P aegagrive*, *P. crossi* in goats and sheep (Boulard, 2002; Soulsby, 1968; Zumpt, 1965).

2.1. Hypoderma lineatum and Hypoderma bovis

Myiasis caused by *Hypoderma lineatum* and *Hypoderma bovis* in cattle is called hypodermosis. Hypodermosis showing a cosmopolitan distribution, is a parasitic infestation of great importance in 55 tropical and subtropical countries in the world (Scholl, 1993).

2.1.1. Biology

Among these rather large flies, *H. bovis* is 13-15 mm long, and *H. lineatum* is 12-13 mm long. The life of the adult fly, which does not take food from the outside and survives on the foods it stores in the pupal stage, is 2-25 days (Boulard, 2002; Zumpt, 1965). The flies that emerge from the pupa mate within 24 hours and female flies are ready to lay eggs 20 minutes after mating. A female can lay 300-900 eggs during her short life. There are differences between these two species, such as egg-laying behavior, egg sizes, and the migration path of the larvae in the host. They usually lay their eggs on the lower parts of the legs and body. While *H. bovis* lays one egg per hair, *H. lineatum* lays more than one egg per hair. Both species prefer sunny times to lay eggs. The larvae that emerge from the egg in 3-6 days are less than 1 mm long and come directly to the skin or hair follicles by moving down from the hairs. Within a few hours, it pierces the skin and settles in the subcutaneous connective tissue and proceeds under the back skin. Moving towards the skin of the back, *H. bovis* follows the subcutaneous nerve pathway to the spinal canal, while the larvae of *H. lineatum* move through the muscle fibers and connective tissue. After about 4 months (usually in autumn), *H. bovis* larvae reach the epidural adipose tissue of

the thoracic and lumbar vertebrae, and *H. lineatum* larvae reach the submucosa of the esophagus. The larvae found here are approximately 15 mm long. About 9 months after the eggs are laid, they are found 25 cm from the dorsal region of the larvae. During this migration, *H. bovis* larvae enter the spinal canal, while *H. lineatum* larvae wait for a while in the esophagus and come under the skin of the back without entering the spinal canal. This first stage larva, which comes under the back skin, molting and becomes the second stage larvae. The second instar larvae open holes in the skin and take their stigmas out of these holes and breathe and become the third instar larvae. The third instar larvae taken into the capsule as a result of the host reaction change their molting twice within 30-60 days and mature larvae occur. Mature *H. bovis* larvae are 27-28 mm long, and *H. lineatum* larvae are 25 mm long. In the morning (5:00-10:00), mature larvae come out of the holes in the skin in 1-3 minutes, fall into the soil and enter the pupa stage. This period lasts 17-70 days and the mature fly emerges from the pupa. The life cycle of these flies lasts about a year. In the northern hemisphere, *H. lineatum* adults are found from March to the end of June, and *H. bovis* adults from June to mid-September (Boulard, 2002; Wall and Shearer, 2001b; Zumpt, 1965).

2.1.2. Pathogenesis and Clinical manifestations

The noise and disturbing behaviors of the adults of *H. bovis* during spawning cause uneasiness in the animals. Injuries, spontaneous waste generation, slowdown in development, loss of condition and decrease in milk productivity occur during the avoidance behavior of animals

from flies. On the other hand, *H.lineatum* is very quiet and does not cause restlessness in animals. Following the laying of the eggs, edema and inflammation may occur from time to time in the place where the first larvae hatched from the egg enter. The first instar larvae of *H. lineatum* form yellow or greenish gelatinous edematous areas with dense infiltration of eosinophils during their migration in connective tissue. Rarely, in these areas, especially dead larvae, may cause anaphylactic shock due to hypersensitivity. The holes opened by the larvae coming under the back skin are prone to infections and attract other flies. One of the most important effects is that they suppress the immune system and as a result, animals are more susceptible to diseases such as bacteria, viruses and parasites. The tendency of the disease to be seen in young animals is higher in older animals (Zumpt, 1965).

2.1.3. Economic Significance of Hypodermosis

Bovine hypodermosis is one of the most economically important parasitic diseases in the world and in Turkey. In addition to causing a decrease in meat and milk yield, they also cause great economic losses in the leather industry due to the holes made by the larvae in the skin (Boulard, Alvinerie et al., 2008; Khan, Iqbal et al., 2006; Wall and Shearer, 2001a). İt is thought that it causes an overlooked loss as it causes suppression of the immune system and because animals become more susceptible to bacterial, viral and parasitic diseases (Boulard, 1989). The damage caused by hypodermosis to the national economy is 22.8 million dollars in Pakistan, and 600 in the USA $192 million was reported as, and $14 million in Canada. In a study conducted in

Afyonkarahisar in Turkey, it was reported that the annual loss in this region was 18,288 TL (Cicek, Cicek et al., 2011; Drummond, Lambert et al., 1981; Khan, 1977; Khan, Iqbal et al., 2006; Klein, 1979).

2.1.4. Treatment and Protection

Various insecticides are used in different formulations for the treatment and control of hypodermosis. In recent years, macrocyclic lactones ivermectin or similar compounds moxidectin and eprinomectin are among the most widely used drugs (Otranto, Zalla et al., 2005). However, it is very important when the drugs used in the treatment and control of hypodermosis are used. During the migration of the first instar larvae, when *H. bovis* is in the spinal canal and *H. lineatum* is in the esophagus, it can cause paraplegia (*H. bovis*) or esophagitis (*H. lineatum*) if sprayed. For this reason, the times of autumn and early winter spraying should be done consciously by knowing the migration periods of the larvae within the host, which differ according to the regional climatic conditions (Andrews, 1978; Soulsby, 1968). In the last decade, programs have been developed in many European countries for the eradication of bovine hypodermosis, and various strategies have been identified in countries where the disease is present (Andrews, 1978) However, these strategies vary according to country and environmental conditions. It has been reported that the prevalence of hypodermosis has been reduced to less than 5% with these eradication and control programs (Boulard, 2002).

2.2. Przhevalskiana Silenus

The larvae of this species, which is common in goats in the southern parts of the Palearctic belt and in northern African countries, can develop up to L2 under the back skin of sheep, so they are not considered the last host. Although the presence of *P. aegagri* and *P. crossi* has been reported in goats, except for *Przhevalskiana silenus* (Zumpt, 1965), it has been reported that these species are the same species in morphological and molecular studies (Otranto, Traversa et al., 2004; Tassi, Giangaspero et al., 1986; Tassi, Puccini et al., 1989).

2.2.1. Biology

Mature adult flies 8-14 mm long are gray olive powder in color. These flies, which do not have a mouth, live 5-10 days with the food they store in the larval stage. During the summer months, females lay 1-4 eggs, avarage 100 eggs, on the hind legs of goats, rarely on the front legs and on the short hairs on the neck and under the abdomen. Larvae that emerge from the egg in 5-19 days are white and transparent and pass into the connective tissue by piercing the skin within 2-3 hours. Larvae come under the skin of the back without entering the spinal canal or organs. Under the skin of the back, L2 is 10-12 mm long and L3 is 15-18 mm long. Adults of this species usually begin to fly in April - June, depending on the climatic conditions in their region. In December and February, second and third instar larvae develop under the skin on the back and sides of the animal from the first instar larvae. The third instar larvae fall into the soil through the hole they make in the skin to enter the pupa. The pupal stage takes place between February and April

depending on the climatic conditions (Cheema, 1977; Sayin, 1977; Zumpt, 1965).

2.2.2. Pathogenesis and Clinical manifestations

Clinical symptoms occur after the 2nd larval stage. Depending on the number of larvae in goats, restlessness, insufficient nutrition and meat, milk and hair loss occur as a result. When they pierce the skin, a yellow-red crust forms on the skin. L3 is surrounded by a hyalinized and eosinophilic capsule infiltrated by granulocytes. After granulocyte infiltration, there may be a second infiltration by lymphocytes, plasma cells, macrophages, and giant cells. Histologically, the cavity is composed of granulation tissue with a large number of granulocytes, while there is a fibrous and thick wall on the outside. If pyogenic bacteria enter with the larvae, a suppurative cavity may form in which L3 is covered with a pus-like fluid. The opened holes prepare the occasion for secondary infections (Cheema, 1977).

2.2.3. Economic Significance

There are no studies on the loss of body weight, growth retardation, decrease in milk and meat production, carcass wear and economic losses due to the holes they create in the diseased goats.

However, they stated that the tanning industry in Iraq faced serious losses due to holes in animal skins. The average weight measured in infested goats in Greece has been reported to be approximately 2.6 + 1.3 Kg lower than the average weight of non-infested goats. (Liakos, 1986).

REFERENCES

Andrews, A. (1978). Warble fly: the life cycle, distribution, economic losses and control. *The Veterinary Record*, *103*(16), 348-353.

Boulard, C. (1989). Degradation of bovine C3 by serine proteases from parasites Hypoderma lineatum (Diptera, Oestridae). *Veterinary immunology and immunopathology*, *20*(4), 387-398.

Boulard, C. (2002). Durably controlling bovine hypodermosis. *Veterinary Research*, *33*(5), 455-464.

Boulard, C., Alvinerie, M., Argenté, G., Languille, J., Paget, L., and Petit, E. (2008). A successful, sustainable and low cost control-programme for bovine hypodermosis in France. *Veterinary parasitology*, *158*(1-2), 1-10.

Broadmeadow, M., O'sullivan, B., Gibson, J., Dimmock, C., and Thomas, R. (1984). The pathogenesis of flystrike in sheep.[Symposium paper]. Sheep Blowfly and Flystrike in Sheep, Kensington, NSW (Australia), 6 Dec 1983,

Broughan, J., and Wall, R. (2006). Control of sheep blowfly strike using fly-traps. *Veterinary parasitology*, *135*(1), 57-63.

Broughan, J., and Wall, R. (2007). Fly abundance and climate as determinants of sheep blowfly strike incidence in southwest England. *Medical and veterinary entomology*, *21*(3), 231-238.

Cheema, A. (1977). Observations on the Histopathology of Warble Infestation in Goats by the Larvae of Przhevalskiana silenus. *Zentralblatt für Veterinärmedizin Reihe B*, *24*(8), 648-655.

Cicek, H., Cicek, H., Eser, M., Tandogan, M., and Sarımehmetoglu, H. O. (2011). Prevalence and economic significance of bovine hypodermosis in Afyonkarahisar province of Turkey. *Tropical animal health and production*, *43*(1), 17-20.

Dik, B., Uslu, U., and Işık, N. (2012). Myiasis in animals and human beings in Turkey. *Kafkas Univ Vet Fak Derg*, *18*(1), 37-42.

Drummond, R., Lambert, G., Smalley Jr, H., and Terrill, C. (1981). Estimated losses of livestock to pests [USA]. *CRC Handbook of Pest Management in Agriculture (USA)*.

Guerrini, V. (1997). Excretion of ammonia by Lucilia cuprina larvae suppresses immunity in sheep. *Veterinary immunology and immunopathology*, *56*(3-4), 311-317.

Hall, M. (1997). Traumatic myiasis of sheep in Europe: a review. *Parassitologia*, *39*(4), 409-413.

Hall, M., and Farkas, R. (2000). Traumatic myiasis of humans and animals. *Contributions to a manual of Palaearctic Diptera*, *1*, 751-768.

Hall, M., and Wall, R. (1995). Myiasis of humans and domestic animals. *Advances in parasitology*, *35*, 257-334.

Herms, W. (1946). Medical Entomology." Macmillan, New York.

İpek, D., and Şaki, C. (2010). External myiasis on cows, sheep and goats in Diyarbakır Province. *Journal of the Faculty of Veterinary Medicine, Dicle University*, *1*, 1-7.

Khan, M. (1977). Eradication of hypodermosis. *Veterinary parasitology*.

Khan, M., Iqbal, Z., Sajid, M., Anwar, M., Needham, G., and Hassan, M. (2006). Bovine hypodermosis: Prevalence and economic significance in southern Punjab, Pakistan. *Veterinary parasitology*, *141*(3-4), 386-390.

Klein, K. K. (1979). The economics of warble fly control. *Canadian Farm Economics*.

Liakos, B. (1986). Consequences of hypodermosis to the body weight of young goat. *Bulletin of the Hellenic Medical Veterinary Society*, *7*, 8-12.

Llchmann, G., Betke, P., and Grafe, D. (1986). Studies on oestrosis and its control in the Mongolian People'sRepublic. Mh. *Vet. Med*, *41*, 128-132.

Loste, A., Ramos, J., García, L., Ferrer, L., and Verde, M. (2005). High Prevalence of Ulcerative Posthitis in Rasa Aragonesa Rams Associated with a Legume-rich Diet. *Journal of Veterinary Medicine Series A*, *52*(4), 176-179.

M., M. (1973). *Veterinary and Medicine Arthropodology*. Ankara Üniversitesi Basımevi. Ankara.

Morris, M. C. (2000). Ethical issues associated with sheep fly strike research, prevention, and control. *Journal of Agricultural and Environmental Ethics*, *13*(3), 205-217.

Otranto, D., Traversa, D., and Giangaspero, A. (2004). Myiasis caused by Oestridae: serological and molecular diagnosis. *Parassitologia*, *46*(1-2), 169-172.

Otranto, D., Zalla, P., Testini, G., and Zanaj, S. (2005). Cattle grub infestation by Hypoderma sp. in Albania and risks for European countries. *Veterinary parasitology*, *128*(1-2), 157-162.

Özdal, N. (2004). The prevalance, development and identification of agent causing traumatic myiasis in cattle, sheep and goat in Van region. In: PhD, Yüzüncü Yıl University, Van.

Pitts, K., and Wall, R. (2006). Cold shock and cold tolerance in larvae and pupae of the blow fly, Lucilia sericata. *Physiological Entomology*, *31*(1), 57-62.

Ruiz-Martinez, I., Soler-Cruz, M., Benitez-Rodriguez, R., Perez-Jimenez, J., and Diaz-Lopez, M. (1991). Myiasis caused by Wohlfahrtia magnifica in sheep and goats in southern Spain II. Effect of age, body region and sex on larval infestation. *Isr J Vet Med*, *46*, 44-48.

Sayin, F. (1977). Incidence and seasonal activity of Przhevalskiana silenus (Brauer) in angora goats in Turkey. III Symposium on Medical and Veterinary Acaroentomology, Gdansk 25-28 September 1975. *Wiadomości Parazytologiczne*, *23*(1-3).

Sayın İpek, D., Şakİ, C., and Özer, E. (2011). Seasonal distributions of external myiasis flies determined in Diyabakır Province. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi*, *17*(3), 469-475.

Scholl, P. J. (1993). Biology and control of cattle grubs. *Annual Review of Entomology*(38), 53–70.

Scott, M. J., Heinrich, J. C., and Li, X. (2004). Progress towards the development of a transgenic strain of the Australian sheep blowfly (Lucilia cuprina) suitable for a male-only sterile release program. *Insect biochemistry and molecular biology*, *34*(2), 185-192.

Scott, P., Sargison, N., and Wilson, D. (2007). The potential for improving welfare standards and productivity in United Kingdom sheep flocks using veterinary flock health plans. *The Veterinary Journal*, *173*(3), 522-531.

Sevgili, M., Şaki, C. E., and Özkutlu, Z. (2004). External myiasis in the Şanliurfa Province: The distribution of flies. *Turkish Journal of Parasitology*, *28*, 150-153.

Soulsby, E. J. L. (1968). Helminths, arthropods and protozoa of domesticated animals (of MSnnig's Veterinary helminthology and entomology). *Helminths, arthropods and protozoa of domesticated animals (sixth edition of MSnnig's Veterinary helminthology and entomology)*.

Şakİ, C. E., and Özer, E. (1999). Myiasis Cases and Their Treatments in Cows, Sheep and Goats in Elazığ Province. *Turkish Journal of Veterinary and Animal Sciences*, *23*(3), 261-268.

Tassi, P., Giangaspero, A., Mattiucci, S., Nascetti, G., and Puccini, V. (1986). Sulla sistematica di Przhevalskiana silenus spp.: Morfologia e tassonomia biochimica. *Parassitologia*, *28*, 369-370.

Tassi, P., Puccini, V., and Giangaspero, A. (1989). Infection by the warble fly Przhevalskiana silenus Brauer, 1858, in the Italian goats. An update up to 1988. *Parassitologia*, *31*(2-3), 239-250.

Tellam, R., and Bowles, V. (1997). Control of blowfly strike in sheep: current strategies and future prospects. *International journal for parasitology*, *27*(3), 261-273.

Usher, C. B., Cruz, J., Carvalho, L., Bridi, A., Farrington, D., Barrick, R., and Eagleson, J. (1997). Prophylactic use of ivermectin against cattle myiasis caused by Cochliomyia hominivorax (Coquerel, 1858). *Veterinary parasitology*, *72*(2), 215-220.

Wall, R., French, N., and Morgan, K. (1992). Effects of temperature on the development and abundance of the sheep blowfly Lucilia sericata (Diptera: Calliphoridae). *Bulletin of Entomological Research*, *82*(1), 125-131.

Wall, R., and Shearer, D. (1997). *Veterinary entomology: Arthropod ectoparasites of veterinary importance*. Springer Science & Business Media.

Wall, R. L., and Shearer, D. (2001a). Veterinary ectoparasites: biology, pathology and control. In edition, n. (Ed.). Blackwell Science. London.

Wall, R. L., and Shearer, D. (2001b). *Veterinary ectoparasites: biology, pathology and control*. Blackwell Science. London.

Zumpt, F. (1965). Myiasis in man and animals in the Old World. A textbook for physicians, veterinarians and zoologists. *Myiasis in Man and Animals in the Old World. A Textbook for Physicians, Veterinarians and Zoologists.*

CHAPTER 5

EFFECT OF HEAT STRESS ON REPRODUCTION PERFORMANCE OF DAIRY COWS

Assoc. Prof. Dr. Tahir BAYRIL[1]

1

[1] Dicle University, Faculty of Veterinary Medicine, Department of Animal Husbandry, TR-21280, Diyarbakir – TÜRKİYE, ORCID: 0000-0001-5322-7346, E-mail:tbayril@hotmail.com

1. INTRODUCTION

Stress is defined as mental, biochemical and physiological reactions that occur in living organisms in response to the effects of internal and external factors. Many stress factors are reported in dairy cattle farming. These are referred to as factors such as transport, hierarchy among animals, climatic factors such as hot, cold and humid weather, diseases, deficiencies in care and feeding conditions, ventilation, inadequate litter use, environmental stimuli such as sound and light (Atasever et al., 2022).

Physiologically, every living thing has a comfort zone that it needs to continue its vital activities. Heat stress begins to occur when environmental temperatures exceed the limits of the comfort zone. Heat stress is the physio-pathological response of a living thing to maintain its body temperature when it is kept above the climatic range that it adapts to live. Although heat stress is associated with the ambient temperature, it is also closely related to the relative humidity and airflow in the environment. The thermo-neutral zone varies depending on the animal's species, age, sex, feed consumption, composition of the ration, housing and stall conditions, whether the skin is thick or thin, and the behavior of the animal. Administrative measures (cooling systems) and developments in feeding strategies in dairy cattle farms cause a decrease in the effect of heat stress in dairy cattle. However, the negative effects of heat stress still continue due to the extreme temperatures in summer (Abrar et al., 2015).

Since dairy cattle generally balance their body temperatures through sweating and evaporation, high relative humidity in the air affects thermoregulation negatively and air flow affects it positively. Very high relative humidity in the environment can trigger the formation of heat stress even at low temperatures. Heat stress in cows especially affects ovarian activity due to loss of appetite and feed intake and causes loss of fertility due to the decrease in oocyte-embryo quality. In bulls, it directly or indirectly affects spermatogenesis and reduces semen quality. In addition, heat stress reduces the occurrence of estrus cycle and estrus symptoms in cows, and negatively affects reproduction by causing decreases in libido in bulls (Arı, 2015).

In this review, it is a scientific study that has been revealed by making use of many scientific studies in order to determine the effect of heat stress on fertility in dairy cattle.

2. ADAPTATION MECHANISMS IN FARM ANIMALS

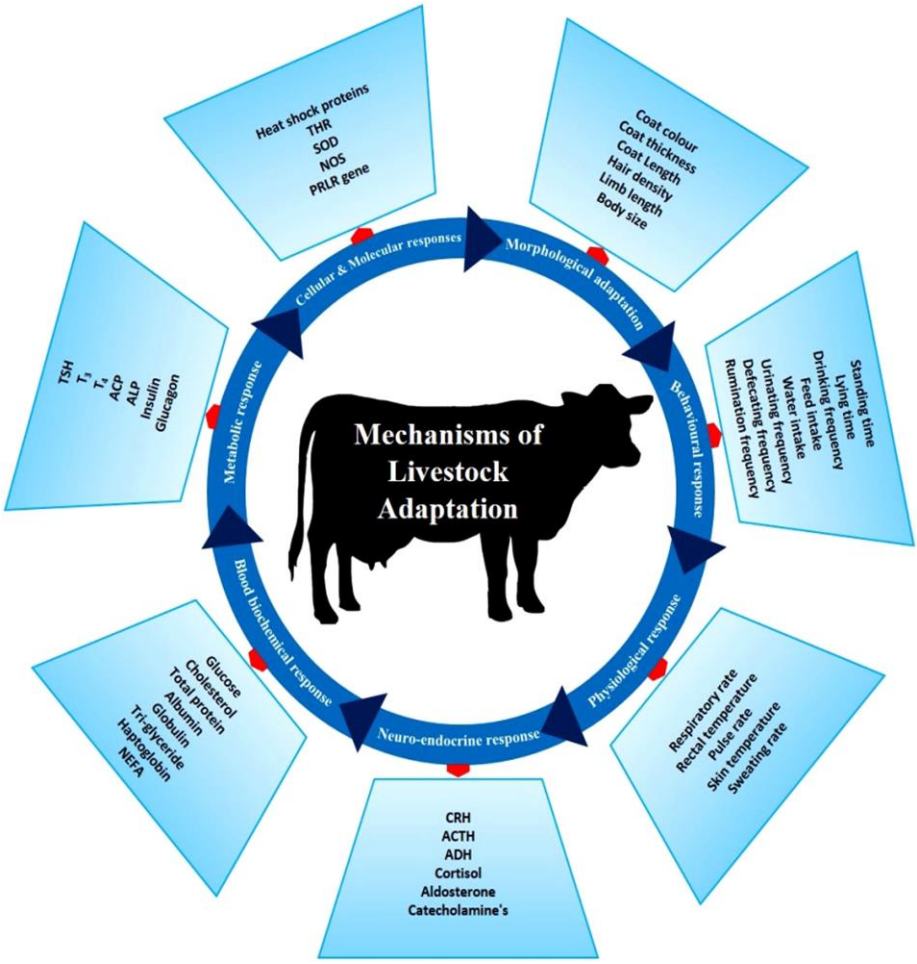


Figure 1. Different adaptive mechanisms of livestock to cope to the harsh climatic condition. These mechanisms help the animals to survive the heat stress challenges. THR= thyroid hormone receptor; SOD=super oxide dismutase; NOS =nitrous oxide synthase; PRLR =prolactin receptor; CRH=corticotropin-releasing hormone; ACTH =adrenocoticotropic hormone; ADH =antidiuretic hormone; NEFA=non-esterified fatty acids; TSH=thyroid-stimulating hormone; T3=triiodothyronine; T4 =thyroxine; ACP=acid phosphatase; ALP =alkaline phosphatase (Sejian et al., 2018).

As living things adapt to environmental differences and challenges, their adaptive abilities may tend to emerge with slow modifications in future generations. The process of adaptation in animals emerges as morphological, behavioral, physiological, neuro-endocrine, blood biochemistry, metabolic, molecular and cellular responses (Sejian et al., 2018). Morphological features are very important as balance the heat exchange between the animal and the environment. These activities include evacuating the air heated by the skin and respiratory tract or lowering the body temperature by sweating. Morphological adaptability may be more pronounced in different races within some species (McManus et al., 2009). The color of the feathers of animals is one of the most important morphological features that shape their adaptability. The shortness of the skin hair, the thinness of the skin, and the low amount of hair per unit area increase the adaptability of animals raised in hot regions (Sejian et al., 2018). Animals with light hair color reflect 50-60% of sunlight compared to those with dark hair color. This creates an advantage in animals with light coat and skin color (McManus et al., 2009).

Heat distribution in cattle is best done through the skin. The large diameter, volume, circumference and density of the sweat gland positively affect the adaptation to the warm environment (Jian et al., 2016). Small-sized cattle breeds bred in tropical regions are more adaptable than large-bodied cattle. The reasons for this are that they have less feed and water consumption. The fact that the ratio of testicular volume and artery length to testicular tissue volume is

higher in cattle bred in regions where heat stress is intense is due to the testicular thermoregulation feature (Brito et al., 2004).

One of the most important adaptation characteristics of animals to heat stress is behavioral adaptation. When animals begin to experience heat stress, the first thing they do is to seek shade. Animals under stress prefer shady areas to reduce the negative effects of heat. Studies show that dairy cattle tend to use shaded areas more in sunny and warm environments (Curtis et al., 2017). One of the common behavioral responses to temperature increase in cattle is to reduce feed intake. Studies have shown that farm animals consume less feed in summer. This behavioral response is done to balance the metabolic heat that increases with feed intake (Spiers et al., 2004; Shilja et al., 2016). In addition, there is an increase in the frequency of drinking water in cattle due to the increase in environmental temperature (Valente et al., 2015; Shilja et al., 2016). Cattle raised in and adapted to desert regions compensate for the high water loss by making their urine more concentrated (Chedid et al., 2014).

Physiologically, ruminants try to balance the body against increasing environmental temperature through respiration and sweating. Depending on the increase in ambient temperature, there is an increase in the respiratory rate and sweating rate in animals. It tries to prevent the metabolism from heating up even more by evaporating the moisture in the body with the cooling mechanisms in the respiratory and skin (Kadzere et al., 2002; Berman, 2006). n the studies, it was reported that the respiratory rate of Angus, Nellore and Sahiwal cattle

breeds increased when exposed to heat stress. Even in cattle adapted to tropical regions, respiratory rates increase (Valente et al., 2015).

It is known that the hormones released from the adrenal and thyroid glands have important roles in balancing the increased ambient temperature and regulating metabolism in animals. In studies conducted on animals exposed to different types of heat stress, it is reported that plasma cortisol levels are quite high (Wojtas et al., 2014; Marina and von Keyserlingk, 2017).

3. EFFECT ON OOSIT-EMBRYO DEVELOPMENT AND EMBRYO MORTALITY

The negative effects of heat stress on fertility parameters in cattle species are quite high. Dairy cattle are exposed to heat stress with the effect of increasing environmental temperature in summer. As the ambient temperature rises, oocyte maturation and embryonic development are compromised and thus, a decrease in pregnancy rates occurs (Wolfenson et al., 2000). There are mechanisms that inhibit the growth of oocytes due to heat stress. The most important of these is reductions in the synthesis of the preovulatory surge in estradiol and luteinizing hormones. Weakness and delay occur in maturation of follicles and cause inactivity in cattle ovaries (Hansen, 2007). In cattle exposed to heat stress, the dominance of dominant follicles decreases and follicle selection is delayed (Khodaei-Motlagh et al., 2011).

In dairy cattle, the blood progesterone level decreases with the increase in environmental temperature. Decreased progesterone level

results in abnormalities in oocyte maturation, inability to placental implantation, and embryonic losses (Khodaei-Motlagh et al., 2011). During heat stress, uterine blood flow decreases and uterine temperature increases accordingly. These changes that occur in the uterus suppress embryonic development and lead to embryonic losses (Singh et al., 2013).

In ruminants, decreases are observed in the estradiol-17 beta concentration due to the increase in temperature in the summer months. These reductions cause silent estrus by suppressing oestrus symptoms in cattle (De Rensis and Scaramuzzi, 2003). In addition, heat stress increases ACTH and cortisol secretion and blocks estradiol-induced sexual behaviors. When the body temperature exceeds 40°C in farm animals, the developing follicles are damaged and become lifeless (Roth et al., 2000; Sing et al., 2013).

Embryo viability decreases in cows exposed to heat during early pregnancy. In addition, early embryos on the 1st day after fertilization are more sensitive to heat stress than later embryos. The increase in body temperature in the early embryonic period has a negative effect on the development of embryos. Likewise, in early embryos (1-8 cells), heat stress significantly reduces the rate of reaching the blastocyst and the number of cells in the blastocyst (Zhandi et al., 2009; Namekawa et al., 2010).

4. EFFECT ON PUBERTAL DEVELOPMENT

In cows exposed to heat stress, the androgen produced by the effect of LH in theca cells on the ovaries is insufficient to be converted to estrogen in granulosa cells with the effect of FSH secreted from the pituitary (Ball and Peter, 2004). A low level of estrogen causes the LH peak necessary for ovulation to not be seen, while the deficiency of inhibin hormone level causes a continuous release of FSH from the pituitary. Although the FSH level is high, the theca and granulosa cells, which are exposed to heat stress, cannot produce enough estrogen. Therefore, estrus is delayed or cannot be seen. It has been reported that as a result of the negative effects of the follicles due to heat stress, the decrease in estrogen production leads to the formation of a small number of oxytocin receptors in the uterine endometrium, and the low PGF2α release caused by the binding of oxytocin produced in the ovaries to the receptors in the uterus, paves the way for the delay of luteolysis (Samall, 2013).

As a result of the hormonal balance deteriorating due to heat stress, it causes a decrease in the synthesis of PGF2α, which is released from the uterine endometrium and is responsible for the lysis of the corpus luteum. This may cause permanent corpus luteum. In addition, the inability of the corpus luteum to produce enough P4 as a result of chronic heat stress also disrupts the development of the uterine glands and does not allow the formation of a suitable environment for the development of the embryo. Depending on the heat stress, the uterine environment being physiologically unsuitable for the development of

the embryo before implantation and implantation will cause early embryonic deaths (Wolfenson et al., 2000).

5. EFFECT ON FERTILITY

Changes in sexual behavior and pregnancy rate in dairy cattle are among the most important characteristics affected by environmental factors. In dairy cattle with high milk yield, the period from calving to first insemination, the rate of conception at first insemination, the number of inseminations per pregnancy, service period and calving interval are more affected during periods of high thermal stress. Heat stress, which increases and reaches a peak level in summer, decreases the duration and intensity of estrus symptoms, prolongs the duration of anoestrus and increases the silent heat rate. Depending on these changes, while the number of inseminations per pregnancy increases in dairy cattle, is a decrease in fertilization rates (Hansen, 1999; Barash et al., 2001).

There is a very important relationship between the pregnancy rate, which is one of the important indicators of reproductive performance in dairy cattle, and the level of heat stress. It is an important source of information about the level of body temperature being affected by thermal stress (Dikmen et al., 2009). It is a known fact that the body temperatures of cows affected by heat stress increase (Tucker et al., 2008). When cows raised under suitable conditions (body temperature = 38.5^{o}C and ambient temperature = 21^{o}C) are inseminated, a pregnancy rate of 48% is obtained; It has been determined that the

pregnancy rate decreases by 0% when the cows are inseminated when their body temperature rises to 40^{o}C and the ambient temperature to 32.2^{o}C (Altınçekiç, 2012). In addition to a clear decrease in the pregnancy rate in cows under the influence of heat stress, it is known that there are many secondary changes such as changes in ovarian activity, negative effects on embryonic development, changes in uterine functions and environment (Roth, 2008; Hansen, 2009).

6. EFFECT OF HEAT STRESS ON PREPARTUM PERIOD

Cows in the dry period are less likely to be affected by environmental heat since they are not in the lactation period. However, sudden physiological, nutritional and environmental changes that may occur during this period can cause stress (Bajagai, 2011). These changes make dairy cows more sensitive to heat stress and adversely affect postpartum cow health, milk and reproductive efficiency. The dry period in dairy cattle is important as it is a preparation period for udder development, rapid fetal growth and lactation period. The heat stress that may occur in this process may affect the endocrine responses, which may increase fetal losses in dairy cows, decrease calf birth weight, and decrease follicle and oocyte maturation associated with the postpartum estrous cycle cycle (Nardone et al., 2010). In dairy cattle, there is an increase in non-esterified fatty acid concentrations in the blood due to heat stress that may occur before birth, while decreases in thyroid hormones and placental estrogen levels occur. These events can lead to changes in the growth of the breast and placenta, nutrition of the calf in the womb, and milk

production. Studies have reported that calf birth weight and milk yield are lower in cows exposed to heat stress during late pregnancy. The reason for this was expressed by the decrease in thyroxine, prolactin, growth hormone and glucocorticoid concentrations in the bloodstream (Collier et al., 1980; Avendano-Reyes et al., 2006).

7. CONCLUSION

Heat stress, which increases with global warming, is more effective on breeding and production parameters of dairy cattle, and large economic losses occur due to decreases in milk production and decreases in fertility. These high economic losses have become a major concern for dairy producers. In all countries of the world, many measures are taken to prevent these losses. The most important of these is that the cooling systems and water spray equipment are located in the shelters. In addition, the techniques of minimizing the energy losses of animals before thermal stress by developing feeding strategies come to the fore. However, despite these measures, economic problems in dairy cattle breeding still continue. For this reason, the most important criterion to prevent these losses in tropical regions or regions where heat stress is intense is the development of breeds adapted to the region.

REFERENCES

Abrar, A., Tiwari, R.P., Mishra, G.K., Biswadeep, J., Munner A.D., Asif A.B. (2015). Effect of Environmental Heat Stress on Reproduction Performance of Dairy Cows. International Journal of Livestock Research, ISSN 2277-1964 ONLINE.

Altınçekiç, Ş.Ö., Koyuncu, M. (2012). Derleme: Çiftlik Hayvanları ve Stress. Hayvansal Üretim, 53:1, 27-37.

Arı, U.Ç. (2015). Physiologic and Hormonal Effects of Heat Stress on Reproduction in Cattle. Turkiye Klinikleri J Reprod Artif Insemin-Special Topics. 1(1);1-10.

Bajagai, Y.S. (2011). Global climate change and its impacts on dairy cattle. Nepalese Veterinary Journal, 30, 2-16.

Atasever, S., Erdem, H., Kul, E. (2022). Süt sığırlarında verim üzerine etkili bazıiklimsel stres faktörleri Erişim:https://docplayer.biz.tr/16341974-Sut-sigirlarinda-verim-uzerine-etkili-bazi-iklimsel-stres faktorleri.html.

Avendano-Reyes, L.F.D., Alvarez-Valenzuela, A., Correa-Calderon, J.S., Saucedo-Quintero, P.H., Robinson and Fadel, J.G. (2006). Effect of cooling Holstein cows during the dry period on postpartum performance under heat stress conditions. Livestock Science, 105:198-206.

Ball, P.J.H., Peters, A.R. (2004). Anatomy. pp: 26-27. In: Reproduction in cattle. 3rd edition Blackwell Publishing, Oxford, Great Britain.

Barash, H., Silanikove, N., Shamay, A., Ezrat, E. (2001). Interrelationships among ambient temperature, day lenght, and milk yield in dairy cows under a Mediterranean climate. J. Dairy Sci. 84, 2314- 2320.

Berman, A. (2006). Extending the potential of evaporative cooling for heatstress relief. Journal of Dairy Science 89, 3817–3825.

Brito, L.F., Silva, A.E., Barbosa, R.T., Kastelic, J.P. (2004). Testicular thermoregulation in Bos indicus, crossbred and Bos taurus bulls: relationship with scrotal, testicular vascular cone and testicular morphology, and effects on semen quality and sperm production. Theriogenology 61, 511–528.

Chedid, M., Jaber, L.S., Giger-Reverdin, S., Duvaux-Ponter C., Hamadeh, S.K. (2014). Water stress in sheep raised under arid conditions. Canadian Journal of Animal Science 94, 243–257.

Collier, R.J., Simerl, N.A., Wilax, C.J. (1980). Effect of month of calving on birth weight, milk yield and birth weight - milk yield interrelationships. Journal Dairy Science, 63 (1): 90.

Curtis, A.K, Scharf, B., Eichen, P.A., Spiers, D.E. (2017). Relationships between ambient conditions, thermal status, and feed intake of cattle during summer heat stress with access to shade. Journal of Thermal Biology 63, 104–111.

De Rensis, F., Scaramuzzi, R.J. (2003). Heat stress and seasonal effects on reproduction in the dairy cow: A review. Theriogenology, 60: 1139-1151.

Dikmen, S., Hansen, P.J. (2009). Is the temperatu-re-humidity index the best indicator of heat stress in lactating dairy cows in a subtropical environ-ment?. J. Dairy Sci., 92, 109-116.

Hansen, P.J., Arechiga, C.F. (1999). Strategies for managing reproduction in the heat-stressed dairy cow. J Dairy Sci; 82: 36–50.

Hansen, P.J. (2007). Exploitation of genetic and physiological determinants of embryonic resistance to elevated temperature to improve embryonic survival in dairy cattle during heat stress. Theriogenology, 68(1): S242-249.

Hansen, P.J., Drost, M., Rivera, R.M., Paula Lopes, F.F., AlKatanani, Y.M., Krininger, C.E., III, Chase, Jr. C.C. (2001). Adverse impact of heat stress on embryo production: Causes and strate-gies for mitigation. Theriogenology,55, 91–103.

Jian, W., Ke, Y., Cheng, L. (2016). Physiological responses and lactation to cutaneous evaporative heat loss in Bos indicus, Bos taurus, and their crossbreds. Asian-Australasian Journal of Animal Sciences 28, 1558–1564.

Kadzere, C.T., Murphy, M.R., Silanikove, N., Maltz, E. (2002). Heat stress in lactating dairy cows: a review. Livestock Production Science 77, 59–91.

Khodaei-Motlagh, M., Shahneh, A.Z., Masoumi, R., Derensis, F. (2011). Alterations in reproductive hormones during heat stress in dairy cattle. Afr. J. Biotechnol., 10(29): 5552-5558.

Marina, L.P. von Keyserlingk, A.G. (2017). Invited review: Effects of heat stress on dairy cattle welfare. Journal of Dairy Science 100, 8645–8657.

McManus, C.M, Paludo, G.R., Louvandini, H., Gugel, R., Sasaki, L.C.B. Paiva, S.R. (2009). Heat tolerance in Brazilian sheep: physiological and blood parameters. Tropical Animal Health Production 41, 95–101.

Namekawa, T., Ikeda, S., Sugımoto, M., Kume, S. (2010). Effects of astaxanthincontaining oil on development and stress related gene expression of bovine embryos exposed to heat stress , Reprod Domest Anim., **45**: 387-391.

Nardone, A., Ronchi, B., Lacetera, N., Bernabucci, U. (2006). Climate effects on productive traits in Livestock. Veterinary research communications, 30(1): 75-81.

Roth, Z., Meidan, R., Braw-Tal, R., Wolfenson, D. (2000). Immediate and delayed effects of heat stress on follicular development and its association with plasma FSH and inhibin concentration in cows. J. Reprod. Infertil., 120(1): 83-90.

Roth, Z. (2008). Heat Stress, the Follicle, and Its Enclosed Oocyte: Mechanisms and Potential Strategies to Improve Fertility in Dairy Cows. Reprod Dom Anim, 43:2, 238–244.

Samal, L. 2013. Heat stres in dairy cows-reproductive problems and control measures. International Journal of Livestock Research, 3: 14-23.

Sejiaan, V., Bhatta, R., Gaughan, J., Dunshea, F., Lacetera, N. (2018). Review. Adaptation of animals to heat stress. Animal, 12(S2), 431-444. Doi:10.1017/S1751731118001945

Singh, M., Chaudhari, B.K., Singh, J.K., Singh, A.K., Maurya, P.K. (2013). Effects of thermal load on buffalo reproductive performance during summer season. J. Biol. Sci., 1(1): 1-8.

Shilja, S., Sejian, V., Bagath, M., Mech, A., David., C.G., Kurien., E.K., Varma, G., Bhatta, R. (2016). Adaptive capability as indicated by behavioural and physiological responses, plasma HSP70 level, and PBMC HSP70 mRNA

expression in Osmanabadi goats subjected to combined (heat and nutritional) stressors. International Journal of Biometeorology 60, 1311–1323.

Spiers, D.E., Spain, J.N., Sampson, J.D., Rhoads, R.P. (2004). Use of physiological parameters to predict milk yield and feed intake in heat-stressed dairy cows. Journal of Thermal Biology 29, 759–764.

Tucker, C.B., Rogers, A.R.., Schütz, K.E. (2008). Effect of solar radiation on dairy cattle behavi-our, use of shade and body temperature in a pas-ture-based system. Animal Behaviour Science, 109, 141–154.

Wojtas, K., Cwynar, P., Kolacz, R. (2014). Effect of thermal stress on physiological and blood parameters in merino sheep. Bulletin of the Veterinary Institute in Pulawy 58, 283–288.

Wolfenson, D., Roth, Z., Meidan, R. (2000). Impaired reproduction in heat-stressed cattle: Basic and applied aspects. Anim. Reprod. Sci., 60-61: 535-547.

Valente, É.E.L,, Chizzotti, M.L., Oliveira, C.V.R., Galvão, M.C., Domingues, S.S., Rodrigues, AC., Ladeira, M.M. (2015). Intake, physiological parameters and behavior of Angus and Nellore bulls subjected to heat stress. Semina: Ciências Agrárias 36, 4565–4574.

Zhandı, M., Towhıdı, A., Nasr-Esfahanı, M., Zare-Shahneh, A. (2009). Unexpected detrimental effect of ıgf-1 on bovine oocyte developmental competence under heat stress. J Assist Reprod Genet; 26: 605-611.

CHAPTER 6

FROM FARM TO TABLE HEALTHY NUTRITION

Prof. Dr. Murat Sedat BARAN[1]

[1] Dicle University, Veterinary Faculty, Department of Animal Nutrition, and Nutritional Diseases, 21280, Diyarbakır,TURKEY; ORCID: 0000-0002-7297- 8556; E-mail: msedatbaran@dicle.edu.tr

1. INTRODUCTION

As it is known, food and nutrition are the basic needs of humanity. The prerequisite for producing healthy animal foods is to provide healthy raw materials. The main condition for producing healthy raw materials; is to obtain the main animal products such as meat, milk and eggs from healthy animals that are raised in healthy conditions in enterprises with modern technology and are under the control of a veterinarian on a regular basis.

It is known that some heavy metals naturally found in the soil, industrial toxins (dioxins) contaminating grasses, mycotoxins and heavy metals from feed used in animal feeding, and some other contaminants are transmitted to food during the feeding of cattle in pastures. (Baran, 2018). Veterinary drugs (antibiotics, antiparasitic, digestive system drugs) used for therapeutic purposes in livestock and drugs that affect feed efficiency and live weight gain are still important quality and public health problems today.

Safe food and feed from farm to table; It is food and feed that does not carry physical, chemical and biological risks, starting from the primary production stage until reaching the consumer (table) or animal.

2. ISSUES TO BE CONSIDERED IN THE PRIMARY PRODUCTION STAGE

- In herbal production, the licensed drug recommended for the product should be used in sufficient doses, with the appropriate tool, and at the appropriate time.

- The time between spraying and harvesting is very important for food safety. The time required between the last spraying and the harvest must be adhered to.
- Medicines used to ensure traceability and vaccinations for animal health should be done regularly and on time. Veterinary drugs should not be used without a veterinary prescription.
- Care should be taken to ensure that animals' stables and pens and transportation are in suitable conditions and that they are cleaned.
- Records of feed, veterinary drugs and vaccines should be kept to ensure traceability.

3. GENETICALLY MODIFIED ORGANISMS (GMO) FEEDS USED IN ANIMAL NUTRITION, GMO TECHNOLOGY AND RELIABILITY OF GMO FEEDS

All interested parties who import, process and use GMO feeds are obliged to notify the Ministry of entry and circulation of the products and to keep the necessary records up-to-date. If the soy and corn varieties approved for use as feed by the Biosafety Board contain more than 0.9 % GMO, it must be stated on the label. In our country, as in the EU, products obtained from farm animals fed with GMO feed should be labeled in terms of GMO.

Modern biotechnology techniques that enable a living species to gain distinct genetic characteristics by transferring genes from another living species or interfering with the existing genetic structure are called gene technology, and organisms that have gained new features by using this

technology are called Genetically Modified Organisms (GMO). The aim of GMOs produced today is to reduce agricultural production costs by making plants resistant to diseases and pests, and to increase product quality by improving the appearance, nutritional value, processing or storage properties of the plant or product to be obtained (Konanç and Öztürk, 2011).

A number of dangers (allergenicity, toxicity, carcinogenicity, resistance to antibiotics, etc.) that GMO products may pose in terms of human health also raise concerns about animal health.It is thought that animals fed with GMO feeds may pass on to their meat and eggs and accumulate there, and this may adversely affect the health of people who consume these products. In addition to the proteins, fats, carbohydrates, minerals and vitamins found in many GMO foods we consume, we also consume the DNA of these foods. The World Health Organization (WHO) concluded that the consumption of DNA, including genes derived from genetically modified crops, does not pose any risk. The Food and Drug Administration (FDA) has allowed the GMO content of GMO foods and feeds to be 0.9 % (Konanç and Öztürk, 2011).

In studies conducted on animals, it has been determined that GMO products do not affect animal performance in general. In a similar study conducted with GMO and non-GMO corn dairy cattle, it was reported that there was no difference in animal feed consumption, udder health, milk yield and milk quality (fat, protein, lactose). Although it has been confirmed by many scientific studies that there is no genetic material (transgenic DNA) belonging to the transgenic feed type in animal

products such as meat, milk and eggs obtained from animals fed with feeds containing GMOs, it should not be ignored that these products cause different negative effects after years. Products containing GMOs; It is stated as a serious danger that it will reduce genetic diversity, disrupt natural fauna and flora, destroy gene resources, increase foreign dependency in agriculture, and that genes of resistance to antibiotics can be passed on to human or animal genes (Konanç and Öztürk, 2011).

4. IMPORTANCE OF FEED SUPPLY AND NUTRITION IN ORGANIC LİVESTOCK

According to the organic livestock criteria, the nutrition of animals is very important both in terms of allowing people to be fed with more reliable healthy foods (without chemical residues) and in terms of the welfare of the animals (Baran, 2022_b).

Feeding has an important place in the realization of organic animal husbandry in organic agriculture. Organic livestock is generally recommended for businesses engaged in organic plant production. Organic livestock is mostly based on pasture (Baran, 2018; Baran, 2022_b).

In organic animal production, we can list the issues to be considered regarding feed supply and animal nutrition as follows;

In enterprises engaged in organic animal breeding, pastures and pastures must comply with organic agriculture rules, that is, chemical fertilization and struggle should not be made in the said areas. Animals

should be fed with organically grown feedstuffs (Baran, 2022$_a$; Öztürk et al., 2013; Peker, 2021).

Genetically modified organisms cannot be used as feed and feed additives. Antibiotics, drug substances, efficiency enhancers, etc. feed additives cannot be used in animal feding (Tekeli, 2004; Eleroğlu et al., 2014, Anonim, 2018). The rations of animals should contain at least 60 % daily roughage, hay or silage (Baran, 2022$_b$).

5. EFFECTS OF MYCOTOXINS IN FEEDS ON ANIMAL HEALTH

Microorganisms are generally the leading causes of spoilage and poisoning in foods and animal feeds. Molds, which are naturally found in air and soil among microorganisms, are an important source of contamination for agricultural products and feed; It is seen as an important spoilage factor in feeds due to their resistance to environmental conditions and their rapid reproduction (Baran, 2019).

6. MITOTOXIN CONTAMINATION IN FEED-FOODSTUFFS

In developing countries, climate and product storage conditions are generally conducive to the production of fungi and mycotoxins. Mycotoxicosis is a disease that occurs with the consumption of feed and foods contaminated with mycotoxins and causes a wide variety of biological factors. Liver and kidney toxicity, adverse effects on the central nervous system, and estrogenic effects are some of the undesirable biological effects of mycotoxins. Many mycotoxins are also carcinogenic. The fact that mixed feeds consist of very different

raw materials increases the risk of contamination of the feed with various mycotoxins (Aksu and Baytok, 2011; Baran, 2019).

Fungal Contaminations: Contamination of feed products with mycotoxins consists of several sources. These; contaminated raw materials (in the field or at the storage stage), contamination during the storage of the feed, contamination during the distribution stage. (Baran, 2019).

7. FROM FEED TO FOOD SAFETY

Animal feeding is the starting point of the food safety chain within the "farm to fork" approach, and many factors that lead to contamination of animal feeds constitute the key point in the transition from animal to human. The transition of toxic components from feed and feed additives to foods of animal origin needs to be controlled in terms of human health.

In feed production, the physical, chemical and microbiological processes of the products of animal origin, which are obtained after the life cycle of the animal consuming this feed, go through physical, chemical and microbiological processes, starting from the stages of raw material supply from the field, arrival at the factory, addition of feed additives and leaving the factory as a final product. Elimination of the dangers that may occur in terms of safety is of great importance in terms of a safe food approach.

There is a close relationship between the animal products that people consume and the quality of animal feed. Therefore, when evaluated in

terms of human health, it is of great importance to evaluate feed and feed additives in terms of the following risk factors in the transition from feed to live animal, to food of animal origin, to human.

8. SOURCES OF CONTAMINATION IN FEED

Heavy metals are toxic and undesirable components such as pesticides, veterinary drugs and dioxin.

Heavy Metals: Animals that are fed especially near industrial areas can be contaminated with substances such as lead and mercury through the natural feed they consume due to the presence of environmental pollutants, accumulation occurs in the foods obtained from these animals, and human health may be adversely affected as a result.

Contamination Caused by Feed Pests: Insects can be found in many feedstuffs, they can contaminate the feed with their feces, odors, and when they become discernible in the feed, the feed can already lose its quality of being a feed.

Veterinary Medicines and Feed Additives: Feed additives used to control diseases or increase performance can form residues in feeds. The amount of use of veterinary drugs and feed additives should be constantly controlled from the perspective of HACCP. Feed additives must have at least one of the following features; It should positively affect the properties of animal products, meet the nutrient needs of animals, especially affect the flora in the digestive system or the digestion of feed, and affect animal production, performance positively (Baran, 2019).

Bacterial Contamination: Contamination of Salmonella and other microorganisms to animal feeds, which is a step in the transmission of pathogenic microorganisms to foods of animal origin, may originate from the feed raw materials itself, as well as from contamination during the transportation, storage and various stages of compound feed production (Baran, 2019).

9. THE TOXIN THAT ENTERS OUR TABLE WITH OUR FOOD: DIOXIN

Dioxin and similar compounds are environmental pollutants that can be found almost everywhere and threaten human and animal health, called "very toxic man-made compounds". Society is exposed to dioxin especially through animal fats in the foods they consume. The accumulation of dioxins in the animal body is mostly through the consumption of contaminated plants by animals.

Among the dioxins, the most well-known polychlorludibenzo-para-dioxins (PCDD), polychlorodibenzofurans (PCDF), polychlorinated biphenyls (PCB) are toxic environmental pollutants that can be found everywhere and threaten human and animal health. Due to their low water solubility, they have the potential to accumulate in foods. Dioxin, mostly from animal foods, meat and meat products, milk and dairy products and sea products and less; exposure through plant foods. The release of dioxins to the environment is caused by the burning of chemical and medical wastes in incinerators, the use of chlorine-containing methods in the paper industry, the production of chlorinated

herbicides, and dioxins are among the first class carcinogens (Baytok and Bingöl, 2011).

9.1. Dioxin Sources

Dioxins are formed by the combustion of organic materials at temperatures above 250 ^{o}C. It is known that dioxins are transmitted to animals and their meat grazing around furnaces where solid wastes are incinerated in this way. In addition, dioxins can occur in iron mines, chemical processes such as car wheel production, and the use of chlorine-containing substances in the wood industry (Baytok and Bingöl, 2011).

9.2. Dioxin in Foods

Humans are exposed to dioxins by consuming foods containing more than 90% animal fats. Dioxin is mostly taken into the human body by the consumption of meat, dairy and fish products. Dioxin levels in milk obtained from animals fed by grazing outside especially in industrialized regions and in summer months and in products obtained from these milks can reach dangerous levels from time to time.

9.3. Dioxin Toxicity

Dioxins are stored in the fat tissues of humans and animals; As a result of lactation, stress and hunger, it can pass into the blood and maintain its toxic effects for a long time. In animal studies, it has been determined that even very low amounts of dioxins have a highly toxic effect**.** Cancer (especially digestive, liver and breast cancers), developmental disorders, birth defects such as cleft palate, defective kidney formation,

heart diseases, nausea, respiratory distress, reproductive disorder, high blood pressure and asthma can occur as a result of exposure to dioxin and similar compounds has been reported. Many disease such as cancer (especially digestive, liver and breast cancers), developmental disorders, birth defects such as cleft palate, kidney formation disorders and heart diseases, nausea, respiratory difficulties, reproductive disorders, high blood pressure and asthma are caused by exposure to dioxins and similar compounds (Baytok and Bingöl, 2011).

9.10. Protection From Dioxin

Exposure to various treatments (electrostatic precipitators reduce dioxin ratio by over 90%) and dioxin-containing fly ash resulting from the incineration of hospital wastes, city garbage, harmful wastes and solid wastes is one of the methods that can be used to reduce the harmful effect (Baytok and Bingöl, 2011).

10. HYGIENIC FEED PRODUCTION

Within the farm-to-table safe food processes applied in many countries, there are feed factories in the first step of animal food production. For this reason, it is important to produce hygienically safe feed and to keep these feeds under control until they are consumed by the animal. In recent years, HACCP system applications have been used to produce safe and hygienic feed in feed factories. As it is known, HACCP is expressed as "Hazard Analysis Critical Control Points".

In order to get good yield from farm animals, to have better quality of animal products and to protect the health of animals, they should be fed

with safe and hygienic feeds. Since the personnel in charge of feed production constitute the most important part of the system; personnel should be trained and they should perform production techniques in a hygienic and correct manner (Baran, 2019).

11. SAFE FEED CONCEPT

Safe animal feeds come as the first step in animal production within the food safety approach from farm to table. Safe animal feeds are expressed as "feeds that do not pose any adverse effects on human and animal health and do not carry physical, chemical and biological risks". In addition, the use of safe feed is important for meat, dairy and egg enterprises in terms of maintaining and maintaining quality.

Safe feed production includes the use of quality raw materials, the absence of harmful additives to animal health in the raw materials, and the fulfillment of the requirements of hygiene and technical issues at the factory level (Baran, 2019).

12. CONCLUSION

It should be ensured that the quality elements are at the highest level in the period between the feeding of farm animals with hygienic feeds, the acquisition of feed raw materials, the processing of the feeds at the production stages, giving them to the consumption of animals, and the production of animal-derived products for human consumption. In order to solve the problem of harmful contamination in feed, the application of the HACCP system in feed factories is also important for the reliability of the produced feed.

As it is known, there is a terrible information pollution in the written and visual media. The fact that people who are not experts in the subject lead the society with information of dubious scientific nature, negatively affects the balanced and adequate nutrition of our people. We have to enlighten our people with correct and scientific approaches.

According to the results of the research examined, there is no significant difference between the feeds obtained from traditional or transgenic plants in terms of nutrient content, digestibility and performance of the animals; It can also be said that there are no residues such as DNA or DNA particles in the organs and tissues of animals. However, it cannot be said that this applies to all transgenic products. In particular, scientists should intensify their research on the nutrient content of transgenic feed ingredients, feed value and whether they can form residues in animal products.

Risk-based controls should be increased in terms of both quality criteria and undesirable substances such as antibiotics, mycotoxins, pesticides and dioxins in feeds.

As a result; It should be aimed to expand a food safety chain to include feed raw materials and additives, starting from feed producers and farms, and to highlight the organic products that have developed in recent years.

REFERENCES

1. Aksu, T., Baytok, E. (2011). İnsan ve Hayvan Sağlığı Açısından Bitmeyen Tehlikeye Güncel Bir Yaklaşım (Yem-Gıda Maddelerinde Mikotoksin Bulaşıklığı), *VI. Ulusal Hayvan Besleme Kongresi (Uluslararası Katılımlı),* 485-491, Samsun.
2. Anonim. (2018). Organik Tarımın Esasları ve Uygulamasına İlişkin Yönetmelik. 18.10.2010 tarih ve 27676 sayılı *Resmi Gazete*.
3. Baran, M.S. (2018). Hayvan Besleme ve Beslenme Hastalıkları Ders Kitabı. 1. Baskı, Diyarbakır.
4. Baran, M.S. (2019). Yemler Yem Hijyeni ve Teknolojisi. Dicle Üniv. Vet. Fak. Ders Kitabı, Diyarbakır.
5. Baran, M.S. (2022_a). Towards A Precısıon Anımal Nutrıtıon. Chapter 8, Poultry Nutrıtıon In Organıc Anımal Productıon, 173-186, Ankara.
6. Baran, M.S. (2022_b). Towards A Precısıon Anımal Nutrıtıon. Chapter 9, Feedıng In Organıc Lıvestock, 187-204, Ankara.
7. Baytok, E., Bingöl, N.T. (2011). Gıdalarımızla Soframıza ve Hayatımıza Giren Toksin: Dioksin, *VI. Ulusal Hayvan Besleme Kongresi (Uluslararası Katılımlı),* 528-535, Samsun.
8. Eleroğlu, H., Yıldırım, A., Şekeroğlu, A. (2014). Organik Tavukçulukta Mera Kompozisyonu, Besleme ve Barındırma Teknikleri. *Tavukçuluk Araştırma Dergisi* 11(1): 16-27.
9. Konanç, K., Öztürk, E. (2011). GDO Teknolojisi, Hayvan Beslemede Kullanılan GDO'lu Yemler ve Bu Yemlerin Güvenilirliği, *VI. Ulusal Hayvan Besleme Kongresi (Uluslararası Katılımlı),* 499-503, Samsun.
10. Öztürk, A.K., Türkoğlu, M., Eleroğlu, H. (2013). Türkiye'de Organik Hayvansal Üretimde Kanatlı Yetiştiriciliği, *Doğu Karadeniz 1. Organik Tarım Kongresi,* 100–108, Kelkit/Gümüşhane.
11. Peker, M.U. (2021). Organik Kanatlı Yetiştiriciliği, *Apelasyon Dergisi*: 2021 07 / Sayı: 92.

12. Tekeli, A. (2004). Organik Hayvansal Üretim. Çukurova Üniversitesi Zootekni Günleri, Adana.

CHAPTER 7

IMPORTANCE OF ANIMAL WELFARE IN DAIRY CATTLE BREEDING

Assoc. Prof. Dr. Tahir BAYRIL[1]

[1] Dicle University, Faculty of Veterinary Medicine, Department of Animal Husbandry, TR-21280, Diyarbakir – TÜRKİYE, ORCID: 0000-0001-5322-7346, E-mail:tbayril@hotmail.com

1. INTRODUCTION

The increase in the socio-economic and cultural level of people has also increased their sensitivity to living things and nature. This sensitivity has increased the interest in the welfare of animals and has led to the emergence of some concepts related to animal rights(Akbaş, 2013). Developments in animal welfare in the globalizing world have reached a significant level in the last decades. Changing the population balance from rural to urban areas; Factors such as the effect of the written-visual media and non-governmental organizations, the significant increase in the number of pet owners in cities, and the increase in the education and economic level of the society have led to an increased interest in animal welfare (Ünal, 2007).

The importance given to different aspects of animal welfare varies relatively, with ethologists and ecologists placing more emphasis on behavioral aspects, zootechnists focusing on high productivity, physiologists on the absence of stress, and veterinarians on the absence of disease (Fraser, 2008). An animal is in a good state of well-being if it is healthy, comfortable, well-fed, safe and able to display innate behaviors and is not suffering from unpleasant conditions such as pain and fear. Good animal welfare requires disease prevention and veterinary treatment, appropriate housing, management and nutrition, and humane treatment and humane killing of animals (Mellor and Webster, 2014; Suárez et al., 2017).

In the welfare evaluation; There is a growing worldwide effort to develop objective indicators that provide information about the animal's quality of life, are scientifically reliable and can be used practically by professionals. Shortening of life span of animals, diseases, abnormal behaviors, increase in adrenal activity, body damage, regression in growth and reproductive efficiency, suppression of immunity are indicators of decline in animal welfare (Knierim and Winckler, 2009; Wemelsfelder and Mullen, 2014).

Animals are sensitive beings with positive and negative emotions, and therefore parameters or protocols used in the assessment of animal welfare should encompass not only the animals' sensory experiences with regard to their physical health but also the conditions in which they live. High milk yield is one of the main reasons for lowering welfare of cows. However, high milk yield is not by itself an absolute factor reducing animal welfare, many other environmental and management problems cause animal welfare losses and decrease milk yield (Trevisi et al., 2006).

2. HOUSING AND ANIMAL WELFARE

Although the first thing that comes to mind when it comes to shelter planning is the structure where the animals will be sheltered, but the enterprise should be considered as a whole. Factors such as barns for milking cows, calves, calves, heifers and dry cows to be sheltered, milking parlor, solid-liquid manure warehouses, machinery equipment building, feed warehouses, silage pit, various protection structures,

and the house where the owner or worker will take shelter should be considered together (Velioğlu and Şentürk, 2020).

The comfort of resting and promenade areas, thermal comfort and ease of movement criteria constitute the principle of good accommodation and welfare (Welfare Quality 2009). They developed a total of 50 criteria in a study of extensively reared cattle in New Zealand. They used the definition of good environment instead of good hosting in the extensive system. In a good environment, they have determined 4 criteria as access to pasture, shelter, restriction in a certain area and internal hazards (Kaurivi et al., 2019).

Whether or not farm animals have good shelter conditions is also an important indicator of animal welfare. In addition to good shelter conditions, adequate bedding and walking area for livestock, the bedding material used is also considered an important indicator of welfare. Dairy cattle spend most of their lives in shelters. Lactation cows spend about 8 to 13 hours of the time spent in the barns lying down. In a study of 3122 cows raised in tied and free-stall barns in Canada and the United States, it was reported that the cows rested for an average of 11 hours. It has been determined that the cows rest at the stops for at least 6 hours and at most 16 hours (Charlton et al., 2014; Solano et al., 2016; Westin et al., 2016). The tendency to rest at the stall is usually more during the night phase of the day. Cows in the dry period and in the pasture, on the other hand, perform an average of 9 hours of resting per day. The success or failure of the farm management will have an impact on the length of stay and rest of the

animals in the shelters. Since feeding, milking and access to the milking parlor are long-term processes, they affect the resting time negatively (Beauchemin, 2018). Since drinking water, sheltering and social behaviors take less time during the day, it will not have a negative effect on the rest period (Val- Laillet et al., 2009).

Before starting the planning of the barns, the climatic environmental demands of the cattle should be known and the effects of the negative effects on the animals should be predicted in advance. Suitable temperature values for dairy cattle vary according to age, breed, feeding and care conditions and animal species. For cattle, the temperature of 10-15°C is known as the most suitable temperature values. However, the temperature being between 5-25°C does not cause significant negative effects on yield and animals. Although low or high humidity does not affect meat and milk yield much, changing humidity with very high or very low temperature can be a problem. Humidity in the barn is required to be between 60-80%. Adequate lighting is important for animal health and the comfort of barn workers. For this purpose, maximum use of sunlight should be made, and artificial lighting should be used together with it. Natural lighting is provided by windows in closed shelters. Windows are structures used in barns for the purpose of providing daylight and ventilation. The window area should not be less than 1/20 of the floor area according to the climatic conditions. Artificial lighting is also very important for the comfort of employees while caring and

feeding activities in cattle. A 100-watt light bulb is sufficient for every 37-46 m2 of the barn floor area (Velioğlu and Şentürk, 2020).

Dehorning can help reduce negative interactions between animals. Decreased area and manger length requirement for hornless animals and easier handling of hornless animals are among the other beneficial aspects of the application (Grondahl-Nielsen et al., 1999). It is known that after this application, which is based on removing the horn button in calves and burning the horn roots for a short time at high temperature, the animals show a general stagnation (Daş, 2005). Although painkillers are used during the application, the procedure is painful and stressful. However, it is reported that short-term stress and pain at an early age will not have a serious effect on the animal, and short-term pain and stress will not adversely affect welfare (Puppe, 2003).

The emergence of new technologies and their use in the field of livestock show a rapid increase. This leads to changes in the housing standards of dairy cattle breeding. Milking systems and herd management programs, especially developed towards the end of the 20th century, are used in many commercial dairy farms (USDA, 2016). The development of sensing technologies and intelligent computing models has had positive effects on the improvement of animal welfare (Jukan et al., 2017). With these technologies, the health of animals is monitored and controlled remotely. Thus, routine health checks are made before animals are brought to shelters and animals can easily show their natural behaviors in pasture and shelters

(Warren et al., 2003). In the future, new sensing technologies and smart computing devices will be further integrated with dairy barns. These technologies will determine the health and shelter needs of animals and will enable them to increase their natural behavioral abilities and express them more easily (de Mol et al., 2013).

3. NUTRITION AND ANIMAL WELFARE

Obtaining high quality products in dairy cattle breeding is a very difficult process. In this process, animal welfare is important in terms of keeping both moral, ethical and production efficiency at the highest level. The most important of the basic costs of milk and meat production is the feed used in animal feeding. Feeding management is as important as the quality and amount of feed in order for dairy cows to be fed adequately. When housing density increases in intensive production systems, dairy cows frequently move within the feeding area, social stress increases, and competition between feeding activity and animals, which may have harmful consequences, also increases. For this reason, both the design and ease of use of the feeding systems, which will provide the animals with feed and water, as well as the amount and placement in the shelter are important. Because, all animals kept together should be provided with access to the manger and feed at the same time (Huzzey et al., 2006; Greiveldinger et al., 2009).

Until the last 10 years, there were no systems for breeders to measure the amount of feed consumed by individual animals and to determine

its relationship with yield. Today, commercial companies have developed collar and ear tag-based systems that are associated with the individual animal's feeding or feeding behavior time. In addition, feed mixed wagons have been developed for the preparation of ration contents according to the yields of the animals throughout the year. These mixed wagons are linked to programs with internet access, and how much feed the animals consume is calculated and associated with welfare (Keenan, 2019). In fact, companies have recently taken the process even further, integrating spectroscopic analysis equipment into the feeding wagon (Barbi et al., 2010).

In dairy cattle farms with intensive breeding, cows fed with appropriate ration programs may not have much problems with feeding. The negative energy balance that occurs in the early lactation period is also minimal. Availability of adequate feeding area causes a decrease in agonistic behavior among animals. Intensive milk production in cows fed only on pasture areas may increase the risk of weight loss due to malnutrition (Phillips, 2002; Roche et al., 2006). Competition is increasing among cows fed limited daily feed and grazed on pasture. This makes it difficult for cows with low social rank to access food and causes heifers to reach less feed. Grazing of dairy cattle in the pasture causes feed deficit in summer and winter, and feed excess in autumn and spring. This nutrient deficit can be eliminated by silage (Holmes et al., 2002).

The energy requirement of high-yielding dairy cows is also high, and this need is greatest especially in the first part of lactation. Low

energy intake of high-yielding dairy cows compared to daily life and productivity needs causes negative energy balance, and during this period dairy cows lose their body condition excessively by having to use their body reserves (Pryce et al., 2000; Matthews et al., 2012). Selection studies for high milk yield increase milk production, and if the energy needed by animals cannot be met with daily feed in order to provide this production, more body reserves are used to close the increasing deficit. In addition, when other daily activities are taken into account, time constraints appear as another important factor for cows to exhibit eating behavior to meet their increased feed needs (Serbester et al., 2012).

There is an inverse relationship between milk yield and heat stress in dairy cattle in terms of yield characteristics (West, 2003). Cows with multiple calvings and high milk yield are more affected by heat stress than those with low yields and single calving. In order for lactating cows to maintain high milk yields, their feed consumption must also be high. However, due to heat stress, feed consumption decreases and energy deficiency occurs (Bernabucci et al., 2014). Negative energy balance due to heat stress is higher in cows in early lactation. The negative energy balance formed after birth is followed by metabolic diseases and decreases in reproductive performance (Drackley, 1999).

Water is one of the most important nutrients for health and performance due to the high milk yield of dairy cattle (NRC, 2001). Water is necessary for the digestion and metabolism of nutrients, the

absorption and transport of nutrients, the removal of waste products from the body, and the maintenance of fluid and temperature balance (Murphy, 1992). Increasing water intake to heat stress is a physiological reaction. In hot periods, water intake will increase to meet the water lost through sweat, respiratory tract, feces, urine and milk (Holter and Kentsel, 1992). When water intake is low, changes in animal performance, health status and behavior will occur (Cardot et al., 2008). Due to low water intake, an increase in hematocrit value and blood urea amount, slowdowns in respiratory rate and rumen movements occur in animals (Steiger Burgos et al., 2001). In addition, animals cluster around drinkers due to increased water intake, and increases in aggressive behavior are observed (Little et al., 1980).

4. BEHAVIORS AND ANIMAL WELFARE

In the evaluation of cattle welfare, behavioral, production and physiological indicators are taken into consideration and the resulting symptoms are interpreted to determine whether the animal is under stress or the degree of stress (Keyserlingk et al., 2009). An animal's emotions, namely the level of arousal, are expressed as emotional behaviors. Seven emotional action-oriented systems have been demonstrated in cattle. These include exploration, anxiety/fear, assertiveness/dominance, emotional bonds in animal-animal and human-animal relationships, play behavior and sensations related to pleasures/lust (Mellor, 2012). In all periods, if the animal's needs are not met, it can be said that the welfare is deteriorated. In addition,

the fact that animals are excluded from anxiety and fear shows that they experience more or less pleasurable emotions, and this causes a positive reflection on the welfare indicators of the animal (Weary et al., 2017).

Cattle are herd animals and they establish relationships with social behaviors. They have a very strong herd instinct and a herd hierarchy is established at an early age. The earlier the cattle come together, the sooner they adapt to the social order. Communications that begin in the early period lead to the formation of tighter bonds. During these periods, they often interact with each other, such as play behaviors and mutual grooming. Individuals, who become dominant with their aggressive behavior from an early age, form a hierarchy by displaying aggressive and defensive behavior in the following periods. Especially during the feeding period, this dominant behavior allows them to consume more feed. This causes animals with dominant characters to develop faster and to be larger in size (Şahin, 2013).

In herds that do not have a social hierarchy, individuals will compete for power in order to be accepted. This will lead to increased fights and unrest in the herd. The introduction of a young animal or an outside animal into a herd with a social hierarchy causes short-term turmoil. This state of confusion ends when the newly arrived animals find a place in the herd (Tölü, 2005). Animals want to dominate the herd, protect their offspring, isolate their sexual partners, and claim resources such as feed, water, shade, and resting area. In their fights,

they may exhibit different fighting techniques specific to the species and/or individuals, such as attacking, escaping, intimidating, replacing each other, and exhibiting a deceptive attitude (Barroso et al., 2000). From an early age, game behaviors, which are copies of agonistic behaviors, are played among animals. However, they report that the likelihood and level of agonistic behaviors increase with increasing age (Cornetto et al., 2002).

Inadequate planning of herd management and management causes stress among animals. It is not possible for the animal under stress to socialize and give the desired level of efficiency. When dairy cows feel comfortable physically, physiologically and psychologically, they will show their production abilities. For this reason, it is necessary to take measures to prevent the herd or the animals in the herd from being exposed to social stress. If it is desired to create a socially strong herd, cattle should be raised together from a young age and they should be allowed to have physical contact between them. Animals raised in separate compartments show aggressive behavior and take longer to socialize when brought together later. In addition, cattle whose paddocks and stops are changed are exposed to social stress and their productivity begins to decrease. For this reason, relocations should not be made as much as possible. If this change is mandatory, animals should be relocated as a group, not individually (Göncü, 2018).

5. CONCLUSION

The future of dairy cattle will be revealed by the behaviors of three stakeholder groups. This group consists of industry, the people, and the animals themselves. Certain behaviors of animals are more critical and prioritized than other factors. Therefore, it is necessary to establish the conditions in which dairy cattle can exhibit their natural behaviors and to evaluate these conditions through ethological researches. According to the results of these studies, it is important to establish suitable shelters, feeding strategies and natural behavior areas for animals.

REFERENCES

Akbaş, A.A. (2013) Çiftlik hayvanlarında davranış ve refah ilişkisi. MAKÜ Sağ. Bil. Enst. Derg. 1 (1): 42-49.

Barroso, F.G., Alados, C.L., Boza, J. (2000). Social hierarchy in the domestic goat: effect on food habits and production. Appl. Anim. Behav. Sci. 69, 35-53.

Beauchemin, K.A. (2018). Invited review: Current perspectives on eating and rumination activity in dairy cows. J. Dairy Sci. 101:4762–4784. https: / / doi .org/ 10 .3168/ jds .2017 -13706.

Bernabucci, U., S. Biffani, L. Buggiotti, A. Vitali, N. Lacetera, and A. Nardone. (2014). The effects of heat stress in Italian Holstein dairy cattle. J. Dairy Sci. 97:471–486. https: / / doi .org/ 10 .3168/ jds.2013 -6611.

Cardot, V., Y. Le Roux, S. Jurjanz. (2008). Drinking behavior of lactating dairy cows and prediction of their water intake. J. Dairy Sci. 91:2257–2264. https: / / doi .org/ 10 .3168/ jds .2007 -0204.

Charlton, G.L., D.B. Haley, J. Rushen, de Passille A.M. (2014). Stocking density, milking duration, and lying times of lactating cows on Canadian freestall dairy farms. J. Dairy Sci. 97:2694 2700. https: / / doi .org/ 10 .3168/ jds .2013 -6923.

Cornetto, T., Estevez, I., Douglass, L.W. (2002). Using artificial cover to reduce aggression and disturbances in domestic fowl. Appl. Anim. Behav. Sci. 75, 325–336.

Daş, G. (2005). Oğlaklarda boynuz köreltme. Hasad Hayvancılık 20 (239): 24-26.

de Mol, RM., G. Andre, E.J.B. Bleumer, J.T.N. van der Werf, Y. de Haas, van Reenen C.G. (2013). Applicability of day-to-day variation in behavior for the automated detection of lameness in dairy cows. J. Dairy Sci. 96:3703–3712. https: / / doi .org/ 10 .3168/ jds .2012 -6305.

Drackley, J.K. (1999). Biology of dairy cows during the transition period: The final frontier? J. Dairy Sci. 82:2259–2273.

Fraser, D. (2008). Understanding Animal Welfare: The Science in its Cultural Context. Wiley-Blackwell, Oxford.

Göncü, S. (2018). Sığır davranışları ve sürü yönetimi. Akademisyen kitabevi. Yenişehir-Ankara.

Grondahl-Nielsen, C., Simonsen, H.B., DAmkjer Lund, J., Hesselhort, M. (1999). Behavioural, endocrine and cardiac responses in young calves undergoing dehorning without and with use of sedation and analgesia. Veterinary Journal 158: 14-20.

Holmes, C.W, Brookes, I.M, Garrick, D.J, MacKenzie, D.D.S, Parkinson, T.J Wilso n, G.F. (2002). "Feeding the herd: Management of feed demand in the pastoral dairy farm system". In Milk Production from Pasture, 69-89. Palmerston North, , NZ: Massey University.

Holter, J.B., W.E. Urban, Jr. (1992). Water partitioning and intake prediction in dry and lactating Holstein cows. J. Dairy Sci. 75:1472 1479. https: / / doi .org/ 10 .3168/ jds .S0022 -0302(92)77904-1.

Jukan, A., Masip-Bruin, X., Amla, N. (2017). Smart computing and sensing technologies for animal welfare: A systematic review. ACM Comput. Surv. 50:1. https: / / doi .org/ 10 .1145/ 3041960.

Kaurivi, Y.B., Laven, R., Hickson, R., Stafford, K., Parkinson, T. (2019). Identification of suitable animal welfare assessment measures for extensive beef systems in New Zealand. Agriculture. 9(3): 66; Doi:10.3390/Agriculture9030066.

Keyserlingk, M.A.G., von Rushen, J., de Passillé, A.M., Weary, D.M. (2009). Invited review:The welfare of dairy cattle – key concepts and the role of science. J. Dairy Sci., 92: 4101–4111

Knierim, U., Winckler, C. (2009). On-farm welfare assessment in cattle: validity, reliability and feasibility issues and future perspectives with special regard to the Welfare Quality (R) approach. Animal Welfare, 18 (4): 451- 458. Special Issue: SI

Little, W., Collis, K.A., Gleed, P.T., Sansom, B.F., Allen, W.M., Quick, A. J. (1980). Effect of reduced water intake by lactating dairy cows on behavior, milk yield and blood composition. Vet. Rec.106:547–551. https: / / doi .org/ 10 .1136/ vr .106 .26 .547.

Matthews, L.R., Cameron, C., Sheahan, A.J., Kolver, E.S., Roche, J.R. (2012). Associations among dairy cow body condition and welfare-associated behavioral traits. Journal of Dairy Science, 95(5):2595-2601.

Mellor, D.J., Webster, J.R. (2014). Development of animal welfare understanding drives change in minimum welfare standards. Revue scientifique et technique-office international des epizooties, 33:121-130.

Mellor, D.J. 2012. Animal emotions, behaviour and the promotion of positive welfare states. N. Z. Vet. J., 60: 1–8.

Murphy, M.R. (1992). Symposium: Nutritional factors affecting animal water and waste quality: Water metabolism of dairy cattle. J. Dairy Sci. 75:326–333. https: / / doi .org/ 10 .3168/ jds .S0022 -0302(92)77768 -6.

National Research Council (NRC). (2001). Nutrient Requirements of Dairy Cattle. 7th rev. ed. National Academy Press, Washington, DC.

Phillips, C.J. Social behaviour. 2002. Cattle Behaviour and Welfare, 84–122. Oxford, , UK: Blackwell Publishing.

Pryce, J.E., Coffey, M.P., Brotherstone, S. (2000). The genetic relationship between calving interval, body condition score and linear type and management traits in registered Holsteins. J. Dairy Sci., 83:2664–2671.

Puppe, B. (2003). Stressbewältigung und Wohlbefinden– verhaltensphysiologische Ansatzpunkte einer Gesundheitssicherung bei Tieren. Arch. Tierz. 46:52-56.

Roche, .JR, Berry, D.P., Kolver, E.S. (2006). Holstein-Friesian strain and feed effects on milk production, body weight, and body condition score profiles in grazing dairy cows. Journal of Dairy Science, 89: 3532–3543.

Serbester, U., Çinar, M., Hayırlı, A. (2012). Sütçü ineklerde negatif enerji dengesi ve metabolik indikatörleri. Kafkas Univ Vet Fak Derg, 18(4):705-711.

Solano, L., Barkema, H.W., Pajor, E.A., Mason, S., LeBlanc, S.J., Nash, C.G. Haley, R., Pellerin, D.B.D., , Rushen, J., de Passille, A.M., Vasseur, E., Orsel, K. (2016). Associations between lying behavior and lameness in Canadian Holstein-Friesian cows housed in freestall barns. J. Dairy Sci. 99:2086–2101. https: / / doi .org/ 10.3168/ jds .2015 -10336.

Steiger Burgos, M., Senn, M., Sutter, F., Kreuzer, M., Langhans, W. (2001). Effect of water restriction on feeding and metabolism in dairy cows. Am. J. Physiol. Regul. Integr. Comp. Physiol. 280:R418–R427. https: / / doi .org/ 10 .1152/ ajpregu .2001 .280 .2 .R418.

Suárez, V.H., Martínez, G.M., Bertoni, E.A. (2017). Mastitis, a health-related indicator of dairy cow welfare and productivity. Dairy and Vet Sci J., 4(5): JDVS.MS.ID.555650.

Şahin, R. (2013). Hayvanlarda sosyal davranışlar. Hatipoğlu yayınları, 2.Baskı, Beşevler-Ankara.

Trevisi, E., Bionaz, M., Piccioli-Cappelli, F., Bertoni, G. (2006). The management of intensive dairy farms can be improved for better welfare and milk yield. Livestock Science, 103(3):231-236.

Tölü, C. (2005). Keçilerde sosyal hiyerarşi ve agonistik davranışlar üzerine araştırmalar. Yüksek lisans tezi, Çanakkale Onsekiz Mart Üniversitesi, Fen Bil. Enst., Zootekni Anabilim Dalı, Çanakkale.

USDA. (2016). Dairy 2014: Milk quality, milking procedures, and mastitis on U.S. Dairies, 2014. Accessed Jul. 12, 2019. https: / / www .aphis .usda .gov/ animal health/ nahms/ dairy/ downloads/ dairy14/ Dairy14 dr Mastitis .pdf.

Ünal, N. (2007). Hayvan refahı. Vilsan Dergi, 2(5), 25–26.

Warren, S., Nagl, L., Schmitz, R., Yao, J., Hildreth, T., Erickson, H., Poole, D., Andresen, D. (2003). A distributed infrastructure for veterinary telemedicine. In Proceedings of the 25th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (IEEE Cat. No. 03CH37439). 2:1394–1397.

Weary, D.M., Droege P., Braithwaite V.A. (2017). Behavioural evidence of felt emotions: approaches, inferences and refinements. Adv. Stud. Behav., 49: 27–48.

Welfare Quality. (2009). Welfare Quality Assessment Protocol for Cattle (Dairy and Beef Cattle). Erişim: https://edepot.wur.nl/233467. Erişim Tarihi: 13.05.2022. Welfare Quality Consortium: Lelystad, the Netherlands.

Wemelsfelder, F., Mullen, S. (2014). Applying ethological and health indicators to practical animal welfare assessment. Revue Scientifique et Technique-Office International des Epizooties, 33 (1): 111-120.

West, J.W. (2003). Effects of heat-stress on production in dairy cattle. J. Dairy Sci. 86:2131–2144. https: / / doi .org/ 10 .3168/ jds .S0022-0302(03)73803 -X.

Westin, R., Vaughan, A., de Passille, A.M., DeVries, T.J., Pajor, E.A., Pellerin, D., Siegford, J.M., Vasseur, E., Rushen, J. (2016). Lying times of lactating cows on dairy farms with automatic milking systems and the relation to lameness, leg lesions, and body condition score. J. Dairy Sci. 99:551–561. https: / / doi .org/ 10 .3168/ jds.2015 -9737.

Val-Laillet, D., Guesdon, V., von Keyserlingk, M.A.G., de Passille, A.M., Rushen, J. (2009). Allogrooming in cattle: Relationships between social preferences, feeding displacements and social dominance. Appl. Anim. Behav. Sci. 116:141–149. https: / / doi .org/ 10.1016/ j .applanim .2008 .08 .005.

Velioğlu, E.K., Şentürk, E. (2020). Hayvancılığa giriş, Mesleki ve Teknik Anadolu Lisesi 9. Sınıf ders kitabı, T.C. Milli Eğitim Bakanlığı,Ankara.

CHAPTER 8

IRISIN: SMALL MYOKIN WITH WIDE EFFECT

Assist. Prof. Dr. Polat İPEK[1]

[1] Dicle University, Faculty of Veterinary Medicine, Basic Veterinary Science, Department of Physiology, 21280, Diyarbakır, TURKEY; ORCID: 0000-0003-1756-9757; E-mail:ipekpolat911@hotmail.com

Introduction

The skeletal muscle is the largest organ in the body and in addition to its function in the movement system, it also secretes some signaling cytokine peptides that have autocrine, paracrine and endocrine effects. These cytokines, which are produced by muscle fibers and secreted into the blood, are called "myokin" (myokin peptides). During or after physical activities, many myokines are secreted from the skeletal muscle into the circulation. Therefore, skeletal muscle is considered a true endocrine organ (Akın and Arıkan, 2020; Arıkan and Akın, 2019; Avcı, 2015; Sarıoğlu, 2021; Şahin and Altay, 2018).

Myokins released in response to exercise have an effect on energy metabolism and are also involved in the development of different physiological phenomena such as osteogenesis, myogenesis, fat oxidation, endothelial function and fat tissue browning (Akın and Arıkan, 2020). Many studies have shown that the release of myokines increases with exercise and therefore has important roles in the treatment of obesity (Sarıoğlu, 2021; Şahin and Altay, 2018).

Interleukin-6 (IL-6) was the first myokine to be discovered, and since its discovery, skeletal muscle has been found to have the capacity to express many more myokines. One of these myokine is iris, which is also called a hormone due to its paracrine, autocrine and endocrine effects (Akcan, 2018; Berberoğlu and Hacışevki, 2021; İnci and Ünübol Aypak, 2016; Şahin and Altay, 2018).

Irisin has attracted the attention of many researchers with its discovery. Because this hormone is effective on weight loss as well as increasing energy expenditure in living beings and is envisaged as a promising molecule in the future in the fight against metabolic diseases (Akın and Arıkan, 2020; Arıkan and Akın, 2019; Sarıoğlu, 2021; Şahin and Altay, 2018). Some studies have been conducted on the effect of changes in blood plasma level of irisin hormone on treatment in obesity, metabolic syndrome, insulin-independent diabetes and cardiovascular diseases (Bayraktar and Tekce, 2021; Erden, 2014; Sarıoğlu, 2021; Sınar, Acar et al., 2020; Şahin and Altay, 2018). However, there are currently limited studies on this hormone in the literature (Bayraktar and Tekce, 2021; Erden, 2014; Şahin and Altay, 2018). It is estimated that the investigation and clear explanation of the iris and its functional mechanism will play a key role in the understanding of many diseases and their development (Demirel, Şahintürk et al., 2021).

Irisin Hormones

Irisin is a newly discovered peptide hormone, which is stimulated by exercise or muscle activity, released from the muscles and affects fat oxidation in adipose cells and regulates thermoregulation. Studies have shown that this peptide structure also plays an active role in insulin resistance and energy metabolism (Akcan, 2018; Aslan and Yardımcı, 2017; Balgetir and Kocaman, 2016; Moon and Mantzoros, 2014).

Irisin, which is described as a myokine because it is mostly secreted from muscle tissue, is also an adipokine because it is also secreted from adipose tissue (İnci and Ünübol Aypak, 2016; Sarıoğlu, 2021). In addition, as a result of immunohistochemical studies; It is reported that small amounts of irisin are secreted by the testis, pancreas, liver, brain, heart and stomach (Bayraktar and Tekce, 2021).

Irisin is the proteolytic product of the membrane protein known as fibronectin type III domain 5 (FNDC5) in muscles (Aslan and Yardımcı, 2017). This protein, which is released from myocytes during physical activity, protects the person from metabolic diseases and acts as a link between muscle tissue and other tissues, was first reported by Bostrom et al. (Akın and Arıkan, 2020; Bayraktar and Tekce, 2021; İnci and Ünübol Aypak, 2016; Sarıoğlu, 2021; Şahin and Altay, 2018). This first protein discovered is a membrane protein called fibronectin type III domain 5 (FNDC5), the expression of which is regulated by PGC-1α (Avcı, 2015; Deniz, 2017; İnci and Ünübol Aypak, 2016; Sarıoğlu, 2021; Sınar, Acar et al., 2020; Şahin and Altay, 2018). Irisin is released from skeletal muscle into the blood as a proteolytic product of FNDC5 molecules during physical activity (Arıkan and Akın, 2019; Erden, 2014; Perakakis, Triantafyllou et al., 2017; Sarıoğlu, 2021; Sınar, Acar et al., 2020; Şahin and Altay, 2018). The most important physiological task of the irisin, which is currently known, is to provide the development of brown adipose tissue from white adipose tissue. Irisin is normally present in the blood at a basal level. However, during acute or intense physical activity, it release from skeletal muscle to the blood

increases and it binds to its receptor in the subcutaneous adipose tissue, causing both the browning of white adipose tissue and stimulating the expression of UCP1 via a PPARγ-mediated mechanism. As a result; decrease in white adipose tissue, which is the energy store of the body, increase in energy expenditure and weakening are shaped. Therefore, irisin has been reported as a new thermogenic hormone that converts chemical energy into heat energy and regulates energy metabolism (Sarıoğlu, 2021; Sınar, Acar et al., 2020; Şahin and Altay, 2018).

Structure of the Irisin

The precursor form of irisin is the membrane-based fibronectin type III domain 5 (FNDC5) protein. Studies have reported that transmembrane FNDC5 is larger than cellular FNDC5. Fibronectin type III domain 5 is synthesized as a type I membrane protein, then cut proteolytically and the amino (N) terminal part of the protein is released into the extracellular fluid. This final proteolytic product which is released into the extracellular fluid is irisin (Aslan and Yardımcı, 2017; Demirel, 2021; Erden, 2014; Sarıoğlu, 2021; Tekin, 2015).

Irisin was first reported by Boström et al. This peptide with a glycoprotein structure is the largest hormone in the myokine class with a molecular weight of 12 kDa. The name of the irisin hormone comes from the name iris. Iris; the Greek messenger goddess. Since this hormone sends signals from muscle to other tissues, Boström et al. They named it irisin, inspired by the Greek Messenger Goddess Iris (Aslan and Yardımcı, 2017; Bayraktar and Tekce, 2021; Boström, Wu et al.,

2012; Erden, 2014; İnci and Ünübol Aypak, 2016; Perakakis, Triantafyllou et al., 2017; Sarıoğlu, 2021).

FNDC5 is a membrane-based protein with 206 aa found in skeletal muscle tissue. The iris occurs when 94 aa of FNDC5 is lost during physical exercise. The proteolytic enzyme that cleaves FNDC5 to form the iris is currently unknown (Demirel, 2021; Demirel, Şahintürk et al., 2021; Tekin, 2015).

Amino acid sequence of irisin "Asp - Ser - Pro - Ser - Ala - Pro - Val - Asn - Val - Thr - Val - Arg - His - Leu - Lys - Ala - Asn - Ser - Ala - Val - Val - Ser - Trp - Asp - Val - Leu - Glu - Asp - Glu - Val - Val - Ile - Gly - Phe - Ala - Ile - Ser - Gln - Gln - Lys - Lys - Asp - Val - Arg - Met - Leu - Arg - Phe - Ile - Gln - Glu - Val - Asn - Thr - Thr - Thr - Arg - Ser - Cys - Ala - Leu - Trp - Asp - Leu - Glu - Glu - Asp - Thr - Glu - Tyr - Ile - Val - His - Val - Gln - Ala - Ile - Ser - Ile - Gln - Gly - Gln - Ser - Pro - Ala - Ser - Glu - Pro - Val - Leu - Phe - Lys - Thr - Pro - Arg - Glu - Ala - Glu - Lys - Met - Ala - Ser - Lys - Asn - Lys - Asp - Glu - Val - Thr - Met - Lys - Glu". There are also forms of irisin with different amino acid numbers (39, 49, 53, 70 and 112 amino acids). However, it is not yet known which of these forms is more active and whether they have different physiological roles (Demirel, 2021; Demirel, Şahintürk et al., 2021).

Irisin, the proteolytic product of FNDC5, has been well protected evolutionarily in mammals. For example, while irisin is 100% similar in mice and humans, the similarity rate for insulin is 83%. This ratio is

90% for the hormone glucagon and 83 for the hormone leptin (Arıkan and Akın, 2019; Aslan and Yardımcı, 2017; Demirel, Şahintürk et al., 2021; Erden, 2014; İnci and Ünübol Aypak, 2016; Perakakis, Triantafyllou et al., 2017; Sarıoğlu, 2021; Tekin, 2015).

Irisin Receptors

Although many studies have been conducted on the functions of the iris in the target tissues and organs; The irisin receptors that mediate these functions are still unknown. In the first study on irisin, it was suggested that irisin exerts its effects through a type of cell surface receptor.

It is clear that the discovery of the receptors that mediate the effect of irisin in which tissues and the identification of their expression sites with future research will contribute to the understanding of the physiological importance of irisin (Boström, Wu et al., 2012; Demirel, Şahintürk et al., 2021; Erden, 2014; Gülmez and Atakişi, 2019; Tekin, 2015).

Main Tissues Synthesizing Irisine

Irisin was first detected in skeletal muscle. However, in later studies, it has been reported that it is synthesized and secreted in many tissues and organs in different parts of the body, and its main source is skeletal muscles and adipose tissue (Akın and Arıkan, 2020; Sarıoğlu, 2021; Sınar, Acar et al., 2020).

Studies have revealed the presence of irisin hormone in 47 different tissues and organs, mainly in adipose tissue, brain, heart, stomach, cerebrospinal fluid, testis, lung, spleen, breast milk, saliva and purkinje cells in the cerebellum (Aslan and Yardımcı, 2017; Demirel, Şahintürk et al., 2021; Erden, 2014; Gülmez and Atakişi, 2019; Öztürk, 2021; Perakakis, Triantafyllou et al., 2017; Sarıoğlu, 2021).

It is stated that irisin, which plays a key role in glucose homeostasis, is secreted in very small amounts from the pancreas and liver (Akcan, 2018). It is an analogue of irisin "lymphokine" secreted from skeletal muscle and liver and named as "myokine" (Demirel, Şahintürk et al., 2021; Gülmez and Atakişi, 2019; Perakakis, Triantafyllou et al., 2017).

Although irisin secretion increases after physical exercise, the plasma concentration of irisin varies in pathological conditions such as body fat profile, presence of obesity, any drug use, and kidney failure. (Akın and Arıkan, 2020).

In mice, 72% of the circulating iris originates from muscle tissue, and the remainder from adipose tissue. In humans, the expression of FNDC5 in adipose tissue is 100-200 times lower than in skeletal muscle (Akcan, 2018).

Excretion of Irisin

In CT scan (or computed tomography examination) for irisin excretion, it was reported that the highest radioactive irisin uptake was in the gallbladder, followed by kidney and liver involvement. It was observed

that the radioactivity in the liver and kidneys decreased rapidly after the 60th minute, and continued to decrease more slowly after the 120th minute (Arıkan and Akın, 2019).]. As a result of a study conducted with blood samples taken from kidney failure patients; It has been reported that irisin concentration is significantly (23%) decreased after hemodialysis relative to pre-dialysis concentrations. The result of this study also shows that the irisin is partially dialyzable (Arıkan and Akın, 2019; Ebert, Focke et al., 2014).

Effect Mechanism of the Irisin

Discussions on irisin expression and possible mechanisms of action are still ongoing. In recent years, some studies have suggested that irisin is a molecule released by skeletal and cardiac muscle in response to exercise and acts as a messenger. In addition, some studies have shown that irisin hormone converts white adipose tissue to brown adipose tissue, promotes glucose uptake in skeletal muscle and heart, regulates glucose and lipid metabolism and improves pancreatic cell function, and has therapeutic effects in insulin resistance and insulin-independent diabetes. Many such physiological effects of irisin are mediated by activation of p38 mitogen-activated protein kinase (p38 MAPK) and extracellular signal-regulated kinase (ERK) (Demirel, Şahintürk et al., 2021).

Adipose tissue cells are divided into three as white, beige and brown (İnci and Ünübol Aypak, 2016).

One of the primary functions of brown adipose tissue is thermogenesis. When the body is exposed to cold, body temperature drops. In response to this decrease, the number of mitochondria in brown adipose tissue cells increases, resulting in thermoregulation Irisin follows two pathways inside the cell for energy expenditure and heat increase.

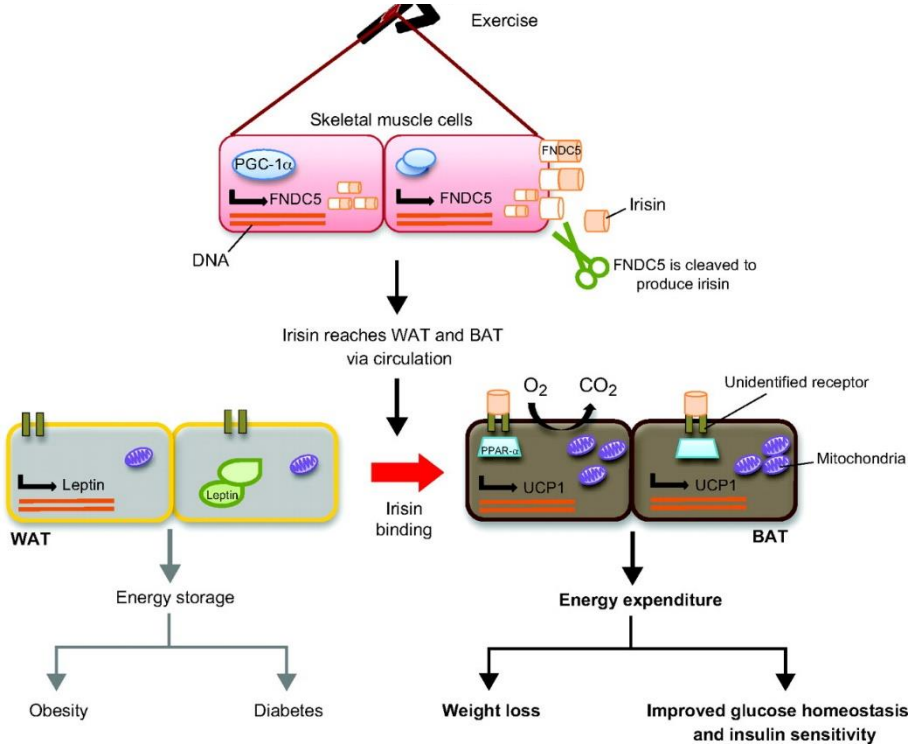
Irisin follows two pathways for energy expenditure and heat increase, inside of the cell;

First Way; By binding to the receptor on the white adipose tissue cell surface, irisin activates the adenylate cyclase enzyme in the cell membrane. Thus, it causes an increase in cyclic adenosine monophosphate (cAMP) within the cell. Increasing cAMP level activates protein kinase. Protein kinase enables the activation of hormone sensitive lipase (HSL). With the effect of activated HSL, both lipolysis occurs and energy expenditure increases.

Second Way; When irisin binds to the white adipose tissue cell surface, it stimulates the white adipose tissue cell nucleus through an as yet unknown mechanism. By stimulating the white adipose tissue cell nucleus, uncoupling protein 1 (UCP1) increases mRNA expression approximately 7-1500-fold, and with the increase of UCP1, white adipose tissue turns into brown adipose tissue. UCP1 in the inner membrane of the mitochondria of the cell that turns into brown adipose tissue causes proton escape to the mitochondrial matrix by disrupting the proton gradient formed in the inner membrane of the mitochondria as a result of oxidative phosphorylation. This stops the synthesis of

ATP. During this proton escape, heat generation takes place (Arıkan and Akın, 2019; Aslan and Yardımcı, 2017).

Fig. 1. Exercise-induced adipose tissue browning through PGC-1 α and irisin (Castillo-Quan, 2012).



Measurement of the Irisin

Circulating irisin levels are analyzed using the "Enzyme-Linked Immuno Sorbent Assay (ELISA)" method and the expression of the FNDC5 mRNA gene by using real-time polymerase chain reaction (Real time-PCR) method because it gives fast results, is practical, applicable and economical. However, it has been reported that protein expression does not fully reflect the circulating irisin level. The measurement can also be performed in the pericardium of the muscle, in the rectum area of the large intestine, in the heart, kidney, liver, lung and adipose tissue. In addition, studies for the measurement of normal irisin levels in the circulation; different results have been reported in mice and humans (İnci and Ünübol Aypak, 2016; Sarıoğlu, 2021).

REFERENCES

Akcan, F. (2018). *Farklı şiddetlerde uygulanan aerobik ve anaerobik egzersizlerin sporcu ve sedanterlerde serum irisin seviyesine akut etkisinin incelenmesi*. (Doktora Tezi) Gaziantep Üniversitesi Sağlık Bilimleri Enstitüsü. Gaziantep.

Akın, G., and Arıkan, Ş. (2020). Sağlıklı genç yetişkinlerde dayanıklılık antrenmanlarının irisin hormon düzeyine etkisi. *SPORMETRE Beden Eğitimi ve Spor Bilimleri Dergisi*, *18*(1), 242-252.

Arıkan, Ş., and Akın, G. (2019). İrisin ve Egzersiz. *Türk Spor Bilimleri Dergisi*, *2*(2), 106-114.

Aslan, N. N., and Yardımcı, H. (2017). Obezite üzerine etkili yeni bir hormon: İrisin. *Gümüşhane Üniversitesi Sağlık Bilimleri Dergisi*, *6*(3), 176-183.

Avcı, B. (2015). *Sağlıklı genç erişkin bireylerde sistemik dolaşım irisin düzeyleri*. (Yüksek Lisans Tezi) Trakya Üniversitesi Sağlık Bilimleri Enstitüsü. Edirne.

Balgetir, F., and Kocaman, N. (2016). Deneysel Diyabetik Ratların Beyin Dokusunda İrisin İmmünreaktivitesi Üzerine Losartanın Etkileri. *Firat Med J*, *21*(2), 63-66.

Bayraktar, B., and Tekce, E. (2021). Anadolu Merinoslarında İrisin hormon yanıtı üzerine bazı fizyolojik parametrelerin etkisi. *Etlik Veteriner Mikrobiyoloji Dergisi*, *32*(2), 1-6.

Berberoğlu, H. T., and Hacışevki, A. (2021). An overvıew of the effects of ırısın on metabolic disorders. *Gazi Sağlık Bilimleri Dergisi*, *6*(2), 33-41.

Boström, P., Wu, J., Jedrychowski, M. P., Korde, A., Ye, L., Lo, J. C., Rasbach, K. A., Boström, E. A., Choi, J. H., and Long, J. Z. (2012). A PGC1-α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. *Nature*, *481*(7382), 463-468. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3522098/pdf/nihms383119.pdf

Castillo-Quan, J. I. (2012). From white to brown fat through the PGC-1α-dependent myokine irisin: implications for diabetes and obesity. *Disease models & mechanisms*, *5*(3), 293-295.

Demirel, S. (2021). *İrisinin iletim tipi arterlerdeki fonksiyonel etkileri ve olası etki mekanizmalarının izole organ banyosu modelinde araştırılması*. (Doktora Tezi) Bursa Uludag University. Sağlık Bilimleri Enstitüsü. Bursa.

Demirel, S., Şahintürk, S., and Özyener, F. (2021). İrisin ve vasküler kontraktilite üzerine etkileri. *SDÜ Tıp Fakültesi Dergisi*, *28*(1), 163-170.

Deniz, M. (2017). *Anaerobik eşikteki iş gücünde yapılan egzersizin irisin, nesfatin-1 ve oksidatif stres üzerine olan etkilerinin belirlenmesi*. (Doktora Tezi) Fırat Üniversitesi Sağlık Bilimleri Enstitüsü. Elazığ.

Ebert, T., Focke, D., Petroff, D., Wurst, U., Richter, J., Bachmann, A., Lossner, U., Kralisch, S., Kratzsch, J., Beige, J., Bast, I., Anders, M., Bluher, M., Stumvoll, M., and Fasshauer, M. (2014). Serum levels of the myokine irisin in relation to metabolic and renal function. *Eur J Endocrinol*, *170*(4), 501-506. https://doi.org/10.1530/EJE-13-1053

Erden, Y. (2014). *Sıçanlarda intraserebroventriküler irisin uygulamasının beyindeki eşleşme bozucu (Uncoupling) protein ailesi üzerine etkileri*. (Doktora Tezi) Fırat Üniversitesi Fen Bilimleri Enstitüsü. Elazığ.

Gülmez, C., and Atakişi, O. (2019). Yeni hormonlar: R-Spondin-1, Nesfatin-1 ve İrisin. *Caucasian Journal of Science*, *6*(1), 37-50.

İnci, A., and Ünübol Aypak, S. (2016). İrisin ve metabolik etkileri. *Turkiye Klinikleri J Endocrin*, *11*(1), 15-21. https://doi.org/10.5336/endocrin.2016-49995

Moon, H. S., and Mantzoros, C. S. (2014). Regulation of cell proliferation and malignant potential by irisin in endometrial, colon, thyroid and esophageal cancer cell lines. *Metabolism*, *63*(2), 188-193. https://doi.org/10.1016/j.metabol.2013.10.005

Öztürk, D. (2021). Egzersiz ve enerji homeostazı ile ilgili hormonlar. https://www.researchgate.net/publication/352991930

Perakakis, N., Triantafyllou, G. A., Fernandez-Real, J. M., Huh, J. Y., Park, K. H., Seufert, J., and Mantzoros, C. S. (2017). Physiology and role of irisin in glucose homeostasis. *Nat Rev Endocrinol*, *13*(6), 324-337. https://doi.org/10.1038/nrendo.2016.221

Sarıoğlu, B. (2021). İrisin Hormonu. *Sağlık ve Toplum*, *31*(3), 59-66.

Sınar, D. S., Acar, N. E., and Yıldırım, I. (2020). Enerji Metabolizması, Obezite ve Hormonlar. In *Türkiye Spor Bilimleri Dergisi* (Vol. 4, pp. 30-60).

Şahin, E., and Altay, D. U. (2018). Yeni tanı almış metformin kullanan tip 2 diyabetes mellituslu hastalarda serum irisin seviyelerinin incelenmesi. *Dicle Tıp Dergisi*, *45*(1), 43-49.

Tekin, S. (2015). *Beslenmenin hipotalamik kontrolünde irisin hormonunun etkilerinin araştırılması*. (Doktora Tezi) İnönü Üniversitesi Sağlık Bilimleri Enstitüsü. Malatya.

CHAPTER 9

STUDIES OF THE NEW HORMONE IRISIN

Assist. Prof. Dr. Polat İPEK[1]

[1] Dicle University, Faculty of Veterinary Medicine, Basic Veterinary Science, Department of Physiology, 21280, Diyarbakır, TURKEY;
ORCID: 0000-0003-1756-9757; E-mail:ipekpolat911@hotmail.com

Introduction

Irisin, a recently discovered hormone, which plays a role in energy metabolism, is a myokine and adipokine with a molecular weight of 12 kDa, composed of 112 amino acids, and is released from myocytes during physical activity (Bayraktar and Tekce, 2021). It has been shown that irisin plays a key role in energy metabolism and glucose homeostasis (Demirel, Şahintürk et al., 2021).

Because of irisin is a myokine derived from fat and muscle tissue and which is more affected by exercise, studies have focused more on exercise, obesity and glucose metabolism. Studies examining the relationship of nutritional type and content with irisin remained limited (Sarıoğlu, 2021).

Irisin and Exercise

Although the health-protecting effect of regular physical exercise has been proven, there are many unanswered information regarding the molecular, cellular and systemic mechanisms that reveal these effects (Aslan and Yardımcı, 2017; Deniz, 2017; Sarıoğlu, 2021).

Exercise is an effective factor in the browning of white adipose tissue. The connection between the browning of the white adipose tissue and the exercise is made by the irisin secreted from the muscle tissue. Irisin, which is separated from FNDC5 and released into the blood by a proteolytic mechanism that is not yet known, reaches the white adipose tissue, interacts with an unknown receptor and causes the conversion of

white adipose tissue to brown adipose tissue (Aslan and Yardımcı, 2017). That's why, irisin is also thought to be an exercise protein (Aslan and Yardımcı, 2017; Avcı, 2015).

Due to the fact that it increases energy consumption and has regulatory effects on glucose metabolism, irisinin is thought to be a guiding agent in the fight against important diseases such as obesity and diabetes (Özçelik, Algül et al., 2017; Sarıoğlu, 2021).

Mildly elevated irisin levels with exercise lead to increased energy expenditure without any change in movement or food consumption. This has an important role in controlling body weight and balancing blood sugar (Berberoğlu and Hacışevki, 2021).

In many laboratories in the world that study metabolism, studies are still being carried out to determine how the irisin molecule will have an effect through or without physical exercise (Aslan and Yardımcı, 2017). Böstrom et al., who were the first to discover the irisin hormone, stated that irisin in mice increased due to exercise (Akcan, 2018; Aslan and Yardımcı, 2017).

In another study conducted with irisin, it was reported that; it caused a temporary increase (around 20%) in the first 1 hour in circulating irisin levels after moderate exercise. (Kraemer, Shockett et al., 2014). In a similar study, it was reported that circulating irisin levels increased in healthy subjects in response to acute exercise, while muscle FNDC5 mRNA and circulating irisin levels decreased in parallel with the

decrease in body mass after bariatric surgery in obese subjects (Avcı, 2015; Huh, Panagiotou et al., 2012).

Exercise-related increases of irisin levels may also reduce food intake and increased energy consumption. It is important to clarify the effects of exercise on hormones such as leptin, nesfatin-1 and irisin in the regulation of energy homeostasis, how it stimulates the release of these hormones and maintains energy balance, as it can be used as a non-pharmacological treatment in the future (Öztürk, 2021).

Irisin and Obesity

Obesity, which is the accumulation of fat in adipose tissues in amounts that disrupt human health, has recently become an important public health problem in the world (Aslan and Yardımcı, 2017; Sınar, Acar et al., 2020). According to the World Health Organization (WHO) reports, the obesity rate in the world has doubled in the last 30-40 years. As in the whole world, obesity is seen as an increasing problem especially among young individuals in our country. It is thought that this situation will increase diseases such as cardiovascular disease, dyslipidemia, diabetes, insulin resistance, hypertension (Aslan and Yardımcı, 2017).

Although there are studies showing that as the amount of adipose tissue increases, irisin levels in the circulation decrease; there are also studies reporting that circulating irisin levels increase as waist circumference, waist/hip ratio and leptin levels increase. While the majority of irisin hormone in the circulatory system of individuals with normal body mass index (BMI) and no metabolic disease is secreted from muscle

cells, the amount of irisin secreted due to the increase in body fat mass in obese individuals is higher in adipose tissue (Sarıoğlu, 2021).

Genetic, personal and environmental factors that play a role in the development of obesity cause disturbances in energy metabolism. The effects of hormones, one of these factors, on energy metabolism is one of the current research topics. Therefore, it is important to know these hormones, which are also associated with weight gain (Sınar, Acar et al., 2020). Indeed, studies on obesity show that there is a positive correlation between irisin and BMI (Aslan and Yardımcı, 2017).

Irisin causes heat production by blocking ATP during the fat burning process. In a study investigating irisin levels in different body indices, it was determined that circulating irisin levels in obese individuals were higher than in anorexic and normal weight individuals (Aslan and Yardımcı, 2017; Stengel, Hofmann et al., 2013).

In studies conducted on children, it is stated that circulating irisin levels are higher in those with insulin resistance and metabolic syndrome; In a study by Reinehr et al., determined that the irisin level in obese children with impaired glucose tolerance was higher than those in obese children with normal glucose tolerance and normal weight, and reported that irisin level was associated with adolescence and insulin resistance, but not with weight in childhood (Aslan and Yardımcı, 2017; Reinehr, Elfers et al., 2015). In another study conducted in children, was reported that the increase in insulin resistance with the onset of puberty increased plasma irisin levels (Aslan and Yardımcı, 2017).

Irisin and Diabetes

Diabetes is a chronic metabolic disease of genetic origin that can lead to serious complications accompanied by disorders in carbohydrate, lipid and protein metabolism due to insufficient insulin secretion or insulin resistance in target tissues (İpek, Taşdemir et al., 2019; Şahin and Altay, 2018).

It has been reported that irisin level is lower in individuals with Type-2 diabetes than in healthy individuals. It has been found that increases in the level of irisin in the blood increase energy expenditure and improve diet-induced insulin resistance. Therefore, irisin has started to be considered as a hormone that may be effective in the treatment of metabolic diseases such as obesity and Type-2 diabetes, and it has been an important area of interest to investigate and understand the mechanism of action of this hormone (Şahin and Altay, 2018).

Effects of Irisin on Metabolic Syndrome and Vascular Tonus

The discovery of the iris has raised the hope that it may be a potential new agent that can be used in the treatment of many metabolic diseases, especially obesity and diabetes mellitus.

Metabolic syndrome, which is one of the most important health problems of today and its frequency is increasing; is characterized by insulin resistance, hyperglycemia, hypertension, hyperlipidemia, and abdominal obesity (Demirel, 2021; Demirel, Şahintürk et al., 2021). Studies show that irisin level decreases with advancing age in patients with metabolic syndrome, and there is a negative correlation between

HbA1c, one of the metabolic syndrome markers, and irisin (Demirel, Şahintürk et al., 2021). In addition, it has been reported that irisin may play a role in the regulation of blood pressure due to the close relationship between irisin and metabolic diseases (Fu, Han et al., 2016).

A study; in which human irisin was administered to rats centrally (3rd cerebral ventricle) and peripherally; was found that peripheral irisin administration reduced blood pressure in both control and hypertensive rats; administration of the central iris has been found to increase blood pressure and cardiac contractility, reversing atenolol-induced cardiac inhibition (Sarıoğlu, 2021; Zhang, Chang et al., 2015).

It is thought that with the increase in the knowledge about the role of FNDC5 in future studies, it can direct new drug development studies and clinical applications for the treatment of metabolic disorders (Cao, Zheng et al., 2019).

In a study conducted in mice; was concluded that irisinin improves endothelial function in the aorta of obese mice induced by high-fat diet, provides the protective effect of irisinin by activation of the AMPK-eNOS signaling pathway, and in the light of these results, irisinin plays an important role in modulating endothelial function in obesity, and may have important clinical effects in the prevention and treatment of cardiovascular diseases in obesity (Demirel, Şahintürk et al., 2021; Han, Zhang et al., 2015).

In a study investigating the effects of iris on vascular activity; that irisinin induces both endothelia-dependent and independent relaxation in mouse mesenteric arteries, that endothelial-dependent relaxation of irisine is mediated by the NO-cGMP-dependent pathway, and that endothelium-independent relaxation is due to the inhibition of Ca2+ flow through VDCCs and intracellular Ca2+ release through both IP3R and RyR channels, and according to the experimental findings obtained, irisinin is a useful agent in the treatment of abnormal vasoconstriction-related diseases such as hypertension. but more detailed studies are needed to determine the effectiveness of irisinin in the treatment of hypertension (Demirel, Şahintürk et al., 2021; Jiang, Wan et al., 2015).

Other Studies of Irisin

The irisin molecule is thought to be a potential agent for use in the treatment of many diseases (Berberoğlu and Hacışevki, 2021). Although irisin hormone is mainly synthesized from muscle tissue, few studies show the presence of irisin in neuronal areas (Erden, 2014).

Irisin has positive effects on bones as it induces bone formation, reduces the risk of fractures and increases osteoblast differentiation. In addition, irisin has positive effects on the nervous system by preserving neurogenesis, reducing some proinflammatory cytokines and preventing neuron damage by reducing oxidative stress. It has important roles in modulating glucose homeostasis in the liver. It serves the regeneration and function of beta cells in the pancreas, ensures the survival of beta cells, and increases the secretion of certain hormones,

including insulin and glucagon. It is also thought to be of great importance in terms of the treatment of obesity and various obesity-related diseases (Berberoğlu and Hacışevki, 2021).

It has been reported that irisin secreted from breast tissue is important for growth, energy regulation and development of the gastrointestinal tract in neonatals. It has a role in reproductive function and in meeting the necessary energy needs depending on the growth of the fetus and in metabolic changes related to pregnancy. There are also studies reporting that men have higher serum irisin levels than women in terms of gender (Bayraktar and Tekce, 2021).

Conclusion

Health is one of the most important concepts for all living creatures. Scientific studies in the field of health contribute positively to life expectancy and quality of life. For this; scientific studies in the field of health are important (Akcan, 2018).

In recent years; Alternative treatment methods for obesity and related metabolic diseases with increasing incidence are being studied intensively (Sarıoğlu, 2021).

Irisin, now defined as a myokine, is the proteolytic product of the fibronectin type III domain 5 protein (Aslan and Yardımcı, 2017). The irisin molecule; has also been called a hormone because it has paracrine, autocrine and endocrine effects (İnci and Ünübol Aypak, 2016). This hormone; is stated that it is triggered by exercise from muscle tissue

(Akcan, 2018). Although the mechanisms that provide the effect of this hormone on diseases are not yet clear, it has been reported that it has a high prognostic and therapeutic potential in many studies carried out so far (Gülmez and Atakişi, 2019).

Moreover; Knowing the yet undiscovered receptors of the irisin molecule and the tissues in which these receptors are located is important for understanding the mechanisms underlying the relationship between circulating irisin concentration and metabolic diseases associated with obesity (Berberoğlu and Hacışevki, 2021).

In this context;

To develop new therapeutic approaches in medicine and veterinary; It is important to carry out more long-term and complex studies on irisin (Berberoğlu and Hacışevki, 2021).

REFERENCES

Akcan, F. (2018). *Farklı şiddetlerde uygulanan aerobik ve anaerobik egzersizlerin sporcu ve sedanterlerde serum irisin seviyesine akut etkisinin incelenmesi*. (Doktora Tezi) Gaziantep Üniversitesi Sağlık Bilimleri Enstitüsü. Gaziantep.

Aslan, N. N., and Yardımcı, H. (2017). Obezite üzerine etkili yeni bir hormon: İrisin. *Gümüşhane Üniversitesi Sağlık Bilimleri Dergisi*, *6*(3), 176-183.

Avcı, B. (2015). *Sağlıklı genç erişkin bireylerde sistemik dolaşım irisin düzeyleri*. (Yüksek Lisans Tezi) Trakya Üniversitesi Sağlık Bilimleri Enstitüsü. Edirne.

Bayraktar, B., and Tekce, E. (2021). Anadolu Merinoslarında İrisin hormon yanıtı üzerine bazı fizyolojik parametrelerin etkisi. *Etlik Veteriner Mikrobiyoloji Dergisi*, *32*(2), 1-6.

Berberoğlu, H. T., and Hacışevki, A. (2021). An overvıew of the effects of ırısın on metabolic disorders. *Gazi Sağlık Bilimleri Dergisi*, *6*(2), 33-41.

Cao, R. Y., Zheng, H., Redfearn, D., and Yang, J. (2019). FNDC5: A novel player in metabolism and metabolic syndrome. *Biochimie*, *158*, 111-116. https://doi.org/10.1016/j.biochi.2019.01.001

Demirel, S. (2021). *İrisinin iletim tipi arterlerdeki fonksiyonel etkileri ve olası etki mekanizmalarının izole organ banyosu modelinde araştırılması*. (Doktora Tezi) Bursa Uludag University. Sağlık Bilimleri Enstitüsü. Bursa.

Demirel, S., Şahintürk, S., and Özyener, F. (2021). İrisin ve vasküler kontraktilite üzerine etkileri. *SDÜ Tıp Fakültesi Dergisi*, *28*(1), 163-170.

Deniz, M. (2017). *Anaerobik eşikteki iş gücünde yapılan egzersizin irisin, nesfatin-1 ve oksidatif stres üzerine olan etkilerinin belirlenmesi*. (Doktora Tezi) Fırat Üniversitesi Sağlık Bilimleri Enstitüsü. Elazığ.

Erden, Y. (2014). *Sıçanlarda intraserebroventriküler irisin uygulamasının beyindeki eşleşme bozucu (Uncoupling) protein ailesi üzerine etkileri*. (Doktora Tezi) Fırat Üniversitesi Fen Bilimleri Enstitüsü. Elazığ.

Fu, J., Han, Y., Wang, J., Liu, Y., Zheng, S., Zhou, L., Jose, P. A., and Zeng, C. (2016). Irisin lowers blood pressure by improvement of endothelial dysfunction via AMPK-Akt-eNOS-NO pathway in the spontaneously

hypertensive rat. *Journal of the American heart association*, *5*(11), e003433. https://doi.org/10.1161/JAHA.116.003433

Gülmez, C., and Atakişi, O. (2019). Yeni hormonlar: R-Spondin-1, Nesfatin-1 ve İrisin. *Caucasian Journal of Science*, *6*(1), 37-50.

Han, F., Zhang, S., Hou, N., Wang, D., and Sun, X. (2015). Irisin improves endothelial function in obese mice through the AMPK-eNOS pathway. *American Journal of Physiology-Heart and Circulatory Physiology*, *309*(9), H1501-H1508.

Huh, J. Y., Panagiotou, G., Mougios, V., Brinkoetter, M., Vamvini, M. T., Schneider, B. E., and Mantzoros, C. S. (2012). FNDC5 and irisin in humans: I. Predictors of circulating concentrations in serum and plasma and II. mRNA expression and circulating concentrations in response to weight loss and exercise. *Metabolism*, *61*(12), 1725-1738. https://doi.org/10.1016/j.metabol. 2012.09.002

İnci, A., and Ünübol Aypak, S. (2016). İrisin ve metabolik etkileri. *Turkiye Klinikleri J Endocrin*, *11*(1), 15-21. https://doi.org/10.5336/endocrin.2016-49995

İpek, P., Taşdemir, E., and Koçyiğit, Y. (2019). Investigation of possible antidiabetic effects of potentilla fulgens in diabetic rats and comparison with other antidiabetics. *The Medical Journal Of Haydarpaşa Numune Training and Research Hospital*, *59*(1), 1-7.

Jiang, M., Wan, F., Wang, F., and Wu, Q. (2015). Irisin relaxes mouse mesenteric arteries through endothelium-dependent and endothelium-independent mechanisms. *Biochemical and biophysical research communications*, *468*(4), 832-836. https://doi.org/10.1016/j.bbrc.2015.11.040

Kraemer, R. R., Shockett, P., Webb, N. D., Shah, U., and Castracane, V. D. (2014). A transient elevated irisin blood concentration in response to prolonged, moderate aerobic exercise in young men and women. *Horm Metab Res*, *46*(2), 150-154. https://doi.org/10.1055/s-0033-1355381

Özçelik, O., Algül, S., Deniz, M., Baydaş, F., and Tan, F. (2017). Sabah ve gece yapılan aerobik egzersizin antrenmanlı deneklerde serum irisin düzeyine etkilerinin belirlenmesi. *Genel Tip Dergisi*, *27*(1), 1-5.

Öztürk, D. (2021). Egzersiz ve enerji homeostazı ile ilgili hormonlar. https://www.researchgate.net/publication/352991930

Reinehr, T., Elfers, C., Lass, N., and Roth, C. L. (2015). Irisin and its relation to insulin resistance and puberty in obese children: a longitudinal analysis. *J Clin Endocrinol Metab*, *100*(5), 2123-2130. https://doi.org/10.1210/jc.2015-1208

Sarıoğlu, B. (2021). İrisin Hormonu. *Sağlık ve Toplum*, *31*(3), 59-66.

Sınar, D. S., Acar, N. E., and Yıldırım, I. (2020). Enerji Metabolizması, Obezite ve Hormonlar. In *Türkiye Spor Bilimleri Dergisi* (Vol. 4, pp. 30-60).

Stengel, A., Hofmann, T., Goebel-Stengel, M., Elbelt, U., Kobelt, P., and Klapp, B. F. (2013). Circulating levels of irisin in patients with anorexia nervosa and different stages of obesity–correlation with body mass index. *Peptides*, *39*, 125-130. https://doi.org/10.1016/j.peptides.2012.11.014

Şahin, E., and Altay, D. U. (2018). Yeni tanı almış metformin kullanan tip 2 diyabetes mellituslu hastalarda serum irisin seviyelerinin incelenmesi. *Dicle Tıp Dergisi*, *45*(1), 43-49.

Zhang, W., Chang, L., Zhang, C., Zhang, R., Li, Z., Chai, B., Li, J., Chen, E., and Mulholland, M. (2015). Central and peripheral irisin differentially regulate blood pressure. *Cardiovasc Drugs Ther*, *29*(2), 121-127. https://doi.org/10.1007/s10557-015-6580-y

CHAPTER 10

FUNCTIONAL FOOD; EGG ENRICHED WITH CONJUGATED LINOLEIC ACID

Assoc. Prof. Dr. Özlem DURNA AYDIN[1]

[11] Kafkas University, Veterinary Faculty, Department of Animal Nutrition, and Nutritional Diseases, 36040, Kars, TURKEY; ORCID: 0000-0003-4532-6795; E-mail:odurna36@gmail.com

1. INTRODUCTION

Today, consumers who are conscious about health, change their food preferences and turn to foods that provide special physiological effects in the body, reduce the risk of formation of certain diseases, preventive, therapeutic and meet the basic nutritional requirements of the body. The increasing market of these products, which are called functional foods, provides new opportunities to the food industry (Karagözlü and Bayerer, 2004). Foods contain nutrients that individuals need for their normal development and growth. Recent developments in food and nutrition science show that foods are effective in regulating various body functions and preventing some diseases, as well as meeting the individual's nutritional needs (Korhonen, 2002).

Food has three main functions: nutritive, sensory and physiological. While nutritive and sensory functions are found in every food, some foods have physiological functions. However, with the help of various technological processes applied in recent years, physiological functions can be added to foods (Ekşi, 2005). In other words, functional foods are obtained by changing the nutrient composition during their production or by removing the harmful components in their structure after they are produced and limiting their levels, or by increasing the level if the health-friendly components are naturally present in their structure and adding them if they are not found (Jiménez-Colmenero et al., 2001).Functional food production first started in Japan in 1980, and in the USA and EU countries in 1990 (Kırış and Velioğlu, 2001). The

physiological benefits of functional foods derive from two major sources.

2. FATS

Fats are organic substances that are insoluble in water, soluble in organic solvents such as ether, benzene, chloroform and acetone, and can be esterified. It is mainly composed of carbon, hydrogen and oxygen, but some of them are found in nitrogen, phosphorus and sülfür. Fatty acids are organic compounds with carboxyl functional groups.Their closed formula is R-COOH. The fatty acid consists of alkyl and carboxyl group as shown below. The chain length is usually 12-24 carbons. Two and multiples of two contain carbon atoms. The most common fatty acids are 16-18 C. Unsaturated fatty acids contain one or more double bonds in their structure. They significantly affect the physical and chemical properties of the oil. They are generally of vegetable origin. Some of the important unsaturated fatty acids are linoleic acid (18 °C), linolenic acid (18 °C), arachidonic acid (20 °C) and oleic acid (18 °C). The double bonded C atoms in unsaturated fatty acids are called cis or trans, depending on whether the H atoms to which they are attached are on the same side of the chain or in opposite directions. If the H atoms are on the same side, they are called cis, and if they are in the opposite direction, they are called trans (Kara, 2009).

2.1. Essential Fatty Acids

They are fatty acids that contain double bonds in their structure and must be taken with food in animals. The reason why these fatty acids are so important is that they are an essential part of the cell membrane phospholipid layer at the cellular level and are the precursors of signaling molecules such as steroids and prostaglandins (Pariza et al., 2001). These molecules have important roles in metabolism, such as controlling blood pressure, blood coagulation, blood lipid levels, immune and inflammatory responses (Kara, 2009).

2.2. Conjugated fatty acids

Fatty acids are divided into conjugated and unconjugated fatty acids, as shown in Figure 1, according to the location of the double bonds. The double bonds in the structure of conjugated fatty acids are in a saturated and unsaturated form, that is, the separation of two double bonded carbons with a single bonded C (Metin 1996). CLA has two unsaturated double bonds at different carbon positions in the fatty acid chain. In conjugated linoleic acid molecules, unlike linoleic acid, a single bond comes after one double bond. This single bond is followed by a double bond (Chin et al. 1992). CLA is formed when one or both double bonds of linoleic acid, one of the three essential fatty acids, are changed by reactions (Kaptan et al., 2017).

a-─CH2─CH=CH─CH=CH─ (conjugated fatty acid chain)

b-─CH=CH─CH2─CH=CH─ (unconjugated fatty acid chain)

Figure 1. Representation of conjugated fatty acids (Metin 1996)

Among the conjugated fatty acids, the most known and studied is CLA isomers, which is the conjugated fatty acid form of linoleic acid (Kara, 2009).

2.3. Conjuge Linoleic Acid (CLA)

Conjugated linoleic acid (CLA) is a fatty acid with two conjugated unsaturated double bonds at different carbon positions in the fatty acid chain (Çelik, 2006). Conjugated linoleic acid occurs in two ways. One of them is the formation of linoleic acid in the rumen as an intermediate during the biohydrogenation of stearic acid, and the other is that CLA is formed in the mammary glands through the enzyme Δ9desaturase. Conjugated linoleic acid contains 28 different isomers. The most active of these are cis-9, trans-11 and trans-10, cis-12 isomers. (Kara, 2009). Interest in CLA started in 1979 with the discovery of its anticarcinogenic and antimutagenic effects in cooked beef. Studies have shown that CLA has effects such as reducing body fat accumulation, antidiabetic, reducing the risk of arteriosclerosis, increasing bone mineralization and strengthening the immune system. (Bell and Kenelly, 2001; Khanal and Olson, 2004). According to Kara

(2009), the relations of conjugated linoleic acid with animal husbandry, human health and nutrition are the subjects that are emphasized.

Conjugated linoleic acid is a fatty acid that is a mixture of conjugated positional and geometric isomers of linoleic acid (octadecadionic acid) containing 2 double bonds with 18 carbon atoms in its natural state (Yavuz, 2011). CLA was discovered by chance in 1979 in a study by Michael W. Pariza on the cooking temperature and time of beef burgers. In the study conducted to show that the fatty acids in grilled beef are procarcinogenic, it was noticed that they have anticarcinogenic properties, contrary to what was thought (Pariza and Hargraves 1985). After a study found that CLA has an anticarcinogenic effect, its importance has gradually increased (Ha et al., 1987; Ercoşkun et al., 2005). It has recently attracted attention with its anticarcinogenic, antimutagenic, anti-inflammatory, antidiabetic, arteriosclerosis (atherosclerosis) and body fat deposition, enhancing bone mineralization, antioxidant effects, and metabolic rate-increasing effects, and recently playing an important role in functional food production (Kaptan et al., 2017).

3. EGG ENRICHED WITH CONJUGATED LINOLEIC ACID

Conjugated linoleic acid (CLA) is a mixture of positional and geometric isomers of linoleic acid (linoleic acid; cis-9, cis-12 octadecadienoic). The cis-9, trans-11 isomer of CLA is formed as an intermediate during the biohydrogenation of linoleic acid to vacsenic acid by rumen bacteria in ruminant animals. Therefore, CLA is naturally found in milk and meat obtained from ruminant animals (Harmon, 1999).

Although CLA was defined many years ago, its positive effects on health have been determined in recent years. He states that CLA reduces the risk of cancer (skin, stomach, breast and intestine), prevents the formation of atherosclerosis and diabetes, affects the immune system and bone composition, and reduces body fat content. For this reason, studies have been started to increase the CLA content of eggs (Açıkgöz and Önenç, 2006).

Raes et al. (2002) determined that when they added 1g/100g of CLA to egg feed, the level of monounsaturated fatty acids decreased, the level of saturated fatty acids increased, but the level of polyunsaturated fatty acids did not change. Researchers stated that this may be due to the increase in desaturase activity of CLA.

Jones et al. (2000), on the other hand, determined that the CLA content in the eggs of white Leghorn breed chickens fed with 1 g/kg feed CLA supplemented feeds approached the CLA level found in the products of ruminant animals (~3mg CLA / g fat). However, enrichment of eggs in terms of CLA negatively affects their consumability (color, hardness, taste) (Aydin et al., 2001; Watkins et al., 2003) and output power (Aydin et al., 2001).

In one study, four different levels of CLA (0.0, 0.5, 0.75, 1.0) were given to 25-week-old laying hens to produce eggs enriched with conjugated linoleic acid (CLA). The same four levels of CLA significantly increased the CLA, saturated fatty acids (SFA) content in the egg yolk, while significantly decreased the monounsaturated fatty

acids (MUFA) content. But polyunsaturated fatty acids (PUFA) levels were not affected (Franczyk-Żarów et al., 2019).

Rumenic acid (RmA), an omega-7 conjugated linoleic acid (CLA) and its conjugated linolenic acid (CLnA) precursors, α-eleostearic acid (α-ESA) and punicic acid (PunA) are suspected. They have a wide array of biological activities such as antidiabetic, anti-inflammatory and anticancer properties. Humans cannot synthesize or insufficiently synthesize these fatty acids, which must be obtained through diet. In this context, the development of a widely consumed food enriched with RmA and related CLnA may be a solution to supply these health-promoting fatty acids to the human diet. Chicken eggs have a special place as a cheap and balanced source of high-quality amino acids and essential fatty acids, as well as various minerals and vitamins. Additionally, its multifunctional properties make it an ingredient in many food formulations. The fatty acid profile of the eggs was improved when the laying hens were fed a flaxseed-rich feed with CLnA-rich seed oil. Consuming eggs enriched with omega-3 fatty acids, CLA and CLnA twice daily for three months reduced abdominal obesity in people at risk of developing metabolic syndrome. Therefore, these eggs are recommended as functional foods to be included in a healthy and balanced diet for disease prevention (Njembe and Tatiana, 2021).

4. CONCLUSION

Many functional foods of plant or animal origin have been used in human nutrition in order to eliminate nutrient deficiencies and reduce

the risks of chronic diseases due to aging. Egg is an animal food with functional properties in terms of its natural nutrient composition. In addition, today, as a result of developments in science and technology, it is possible to produce functional eggs enriched with one or more nutrients. Functional eggs are more expensive than commercial eggs. However, considering the positive effects of eggs on quality of life and health, this price difference can be ignored.

REFERENCES

Açıkgöz, Z., Önenç, S.S. (2006). Fonksiyonel yumurta üretimi. *Hayvansal Üretim* 47(1): 36-46.

Aydin, R., Pariza, M. W., Cook M.E. (2001). Olive oil prevents the adverse effects of dietary conjugated linoleic acid on chick hatchability and egg quality. *The Journal of Nutrition*, 131(3): 800-806.

Bell, J. A. and Kenelly, J. J. (2001). Conjugated linoleic acid enriched milk: a designer milk with potential. *Advances in Dairy Technology*, 13: 213-228

Çelik L. (2006). Konjuge linoleik asidin ruminatlarda biyosentezi, fizyoloji ve lipid metabolizması üzerine etkileri. *Hayvansal Üretim* 47(1): 1-7.

Ekşi, A. (2005). Bilimsel ve yasal açıdan gıdaların fonksiyonelliği. Gıda Kongresi, 19-21 Nisan, Bornova, İzmir, 6-12s.

Ercoşkun H., Uğuz Ş., Kıralan M. (2005). Konjuge linoleik asit. *Gıda Mühendisleri Odası Gıda Mühendisliği Dergisi* 9(19): 42-46

Franczyk-Żarów, M., Szymczyk, B.,Kostogrys, R.B. (2019). Effects of dietary conjugated linoleic acid and selected vegetable oils or Vitamin E on fatty acid composition of hen egg yolks. *Annals of Animal Science*, 19 (1): 173-188.

Ha, Y.L., Grimm, N.K., Pariza, M.W. (1987). Anticarcinogens from ground beef: heat altered derivates of linoleic acid. *Carcinogenesis*, 8: 1881-1887.

Harmon, B. G. (1999). The roles of conjugated linoleic acid in food producing animals. *ASA Tecnical Bulletin* Vol.AN25,

Jiménez-Colmenero, F., Carballo, J., Cofrades, S. (2001). Healthier meat and meat products: their role as functional foods. *Meat Science*, 59: 5-13.

Jones, S., Ma D.W.L., Robinson F.E., Field C.J., Clandinin M.T. (2000). Isomers of conjugated linoleik asit (CLA) are incorporated into egg yolk lipids by CLA-fed laying hens. *Journal of Nutrition*, 130(8):2002-2005.

Kara O. (2009). *Konjuge linoleik asit metabolizması ve sağlık üzerine etkileri* (Yüksek Lisans Tezi). Namık Kemal Üniversitesi Fen Bilimleri Enstitüsü, Tekirdağ

Kaptan, B., Öksüz, Ö., Bilgi,n B. (2017). *Manda sütü yağı konjuge linoleik yağ asitleri kompozisyonlarının belirlenmesi*. Namık Kemal Üniversitesi Bilimsel

Araştırma Projeleri Koordinasyon Birimi (NKUBAP) Bilimsel Araştırma Projesi Sonuç Raporu.

Karagözlü, C., Bayerer, M. (2004). Peyniraltı Suyu Proteinlerinin Fonksiyonel Özellikleri ve Sağlık Üzerine Etkileri. *Ege Üniversitesi Ziraat Fakültesi Dergisi*, 41 (2):197-207.

Khanal R. C, Olson K.C. (2004). Factors affecting conjugated linoleic acid (CLA) content in milk, meat, and egg: A review. *Pakistan Journal of Nutrition*, 3: 82-98

Kırış, S., Velioğlu, S. (2001). Hiper besleyici gıdalar. *TÜBİTAK Bilim ve Teknik Dergisi*, 56-57.

Korhonen, H. (2002). Technology options for new nutritional concept. *International Journal of Dairy Tecnology*. 55(2): 79-87

Metin, M. (1996). Süt Teknolojisi sütün bileşimi ve işlenmesi. *Ege Üniversitesi Mühendislik Fakültesi Yayınları* No:33

Njembe, N., Tatiana, M. (2021). *Conjugated linolenic acids of plant origin: bioconversion in laying hens, enrichment of egg yolk and impact of their consumption on human health* (Doctoral dissertation, UCL-Université Catholique de Louvain).

Pariza, M.W., Hargraves W.A. (1985). A beef-derived mutagenesis modulator inhibits initiation of mouse epidermal tumors by 7,12-dimethylben-z[a]anthracene. *Carcinogenesis*; 6: 591-3

Pariza,, M.W., Park, Y., Cook, M.E. (2001). The biologically active isomers of conjugated linoleic acid. *Progress in Lipid Research* 40, 283-298

Raes, K., Huyghebaert, G., De Smet, S., Nollet, L., Arnouts, S., Demeyer, D. (2002). The deposition of conjugated linoleic acids in eggs of laying hens fed dietsvarying in fat level and fatty acid profile. *Journal of Nutrition* 132: 182-189

Yavuz H. (20119. Konjuge linoleik asit üretimi, hayvansal ürünlerdeki önemi ve sağlık üzerine etkileri. VII. Ulusal Zootekni Öğrenci Kongresi. 115-119

Watkins, B.A., Feng, S., Storm, A.K., Devitt, A.A., Yu, L., Li, Y. 2003. Conjugated linoleic acids alter the fatty acid composition and phys,ical properties of egg

yolk and albumin. *Journal of Agricultural and Food Chemistry,*. 51: 6870-6876

CHAPTER 11

RENDERING; ANIMAL SPECIES DETECTION IN RENDERING PRODUCTS WITH DNA TECHNOLOGY

Assoc. Prof. Dr. Özlem DURNA AYDIN[1]

[1] Kafkas University, Veterinary Faculty, Department of Animal Nutrition, and Nutritional Diseases, 36040, Kars, TURKEY; ORCID: 0000-0003-4532-6795; E-mail:odurna36@gmail.com

1. INTRODUCTION

Proteins are made up of 20 different amino acids. These amino acids are essential for the formation, maintenance, and repair of muscles, tissues, and organs. Forages (grass grass, corn, sorghum, etc., green or dried plants) contain limited protein, while meat-bone meal, feather meal, blood meal, poultry by-product meal and fish meal contain high protein. Each protein consists of certain amino acids arranged in a certain way. Combining amino acids in different combinations and in different ways of ordering determines the properties and biological function of the protein they form. Proteins can change types through fragmentation and recombination called catabolism. For example, the protein that the animal eats is first broken down into amino acids in its structure and then reassembled in a certain shape and sequence to form muscle protein. Poultry can use up to 22 amino acids to form different proteins. 12 of these amino acids are essential. In other words, the bird can create these within its own body. The remaining amino acids must be taken with the diet (Kutlu and Görgülü, 2003). In addition, animal protein sources are richer in essential amino acids than vegetable protein sources. For this reason, it is often necessary to include animal protein sources in the rations in order to meet the essential amino acid needs of especially poultry and monogastric animals.

2. RENDERING PROCESS AND FEATURES

The rendering process, which is carried out in special facilities for this work, in order to use the fresh residues released during the slaughter of

both mammals and poultry as a feed source in animal nutrition, consists of the following stages;

- ✓ raw materials are collected
- ✓ milled
- ✓ heated to sterilization level,
- ✓ the oil is separated
- ✓ dried until the dry matter percentage is 92-93% and ground to become a homogeneous raw material (NRA, 2000).

The heat and systems applied in the rendering system;

1) 135-145 ^{O}C for 30 minutes (Stord Duke System)
2) 22-23 min. 125 ^{0} C with Duration (Stord Bartz System)
3) 20-25 min. for 125 ^{o}C (Anderson Carver Greenfield System)
4) Two-stage heat is applied. In the beginning, 3-7 minutes. for a period of 95 ^{o}C, then 20 min. It is 120-130 ^{o}C for a period of time (Protect De Watering System).

3. RENDERING PRODUCTS

We can describe the rendering products, which are an important raw material source in animal feeds, as follows:

Degreasing of fresh residues formed during the slaughter of both mammals and poultry in the rendering system and fine grinding and residues rich in amino acids, mineral substances (Ca and P), essential

fatty acids and many vital nutrients are called 'rendering products'(Demirulus and Aydın, 1996).

3.1. Meat Flour

The fact that meat flour is especially rich in lysine amino acids plays an outstanding role in better evaluation of the proteins of feed raw materials, such as wheat grains, which are poor in these amino acids. However, as the bone ratio of meat flour increases, the essential amino acid content decreases. For this reason, it is essential that meat flour does not contain too many bones. Because amino acids are very few in the gelatin glue part of the bone. For this reason, in order to limit the amount of bone to be found in meat flour, it is stipulated that the phosphorus content should not be more than 2.5%. In terms of durability, the fat content of meat flour should not exceed 10%. Meat flour does not contain vitamins A and D, but is rich in vitamin B12, niacin and choline. As it can be easily understood when their structure is examined, meat meal comes in second place after fish meal among animal feeds in terms of biological value of protein. Meat flour can be safely added to chick and chicken feeds between 3-7% (Akyıldız, 1983).

3.2. Meat-Bone Meal

The nutrient content of meat-bone flour varies depending on the technology applied. Overcooking negatively affects flavor and quality. At the same time, the bone ratio in the raw material is also effective on the quality of meat-bone flour. Depending on the bone ratio, the amount

of phosphorus and crude protein varies. In meat-bone flour, phosphorus can be between 2.4-6.4% and crude protein can be between 35-55%. On the other hand, it is undesirable to have a high level of crude fat in meat-bone flour, because it restricts the feed consumption of animals and affects the quality of the feed by becoming bitter easily (Akyıldız, 1983). Meat-bone flour can be used as a protein source, as it is rich in calcium and phosphorus, it can also be used to meet these needs (Büyükşahin, 1985).

3.3. Bone Meal

According to the technology in which bone flours are obtained, crude protein, crude oil, calcium and phosphorus contents vary. In general, bone meal is obtained in different ways, including in open boilers and pressure steam boilers. The bone meal obtained in open boilers is called "raw bone meal" or "unheated bone meal". In this method, the bones are sterilized since they are cooked in open cauldrons for a long time without applying steam (Göğüş, 1976). They contain a minimum of 25% crude protein and a maximum of 4% crude fat. The amount of ash is over 40% and includes 28-30% calcium and 13-19% phosphorus. Since the ratio of calcium and phosphorus (2/1) is optimal, they are added to the rations in order to maintain the calcium-phosphorus balance (Özgen, 1986). Their protein or fat content is low, as steam provides a large separation of proteins and fats. Bone flours obtained by this method contain 6-8% crude protein, 1.5-3% crude fat, 30% calcium and 14% phosphorus. Bone meal proteins are of low value and of little importance in terms of essential amino acids. It is mainly used

in the nutrition of ruminants as a source of calcium and phosphorus (Büyükşahin, 1985).

3.4. Chicken flour

This product is a by-product of poultry slaughterhouses and includes unused entrails and other inedible parts of poultry carcasses, excluding feathers. The calcium level in it should not be higher than 2.2 times the actual phosphorus level. The main difference between the products obtained at different enterprises is due to the applied processing method. For example, chicken flour from a further processing plant contains bones separated from the carcass. On the other hand, since the mentioned bones will not be found in enterprises that sell the slaughtered chickens as whole carcasses, the first product usually contains a higher percentage of ash than the other (Kutlu, 2003).

3.5. Blood Meal

After slaughtering the animals in slaughterhouses and meat combinations, the blood is collected, heated until it coagulates, the water is filtered, dried and ground to obtain blood meal. In the production of blood meal, contamination of the blood with foreign substances and unwanted substances such as stomach contents, urine and fertilizer should not be allowed. The most important factor affecting the quality of blood flours is the processes applied during drying, especially if the applied temperature is high, lysine is inactivated. Lysine in this state is of no nutritional value, especially for

monogastrics. In addition, the high temperature applied reduces the digestion level of blood meal (Büyükşahin, 1985).

3.6. Hydrolyzed Feather Flour

Hydrolyzed feather meal produced under high heat and pressure has high crude protein (80%). Due to the keratin and disulfide bonds in its structure, its digestibility is considered low and it is not preferred in poultry nutrition (Coşkun et al. 1997). However, it is used as a nitrogen source in organic agriculture. Hydrolyzed feather meal can be used together with other protein sources in broiler rations with up to 8% success. However, it should be used around 3-4% (Akyıldız, 1983).

3.7. Animal Fats

Adding fat to cattle and poultry diets reduces production costs and increases the profitability of raising these animals. Adding oil to animal feeds has the following benefits (Kutlu and Görgülü, 2003);

- ✓ Intake of essential fatty acids
- ✓ Increased absorption of fat-soluble vitamins
- ✓ Being an effective energy source
- ✓ Prevention of dust formation
- ✓ Animals eat more willingly
- ✓ Prevention of constipation
- ✓ Reducing the negative effect of heat stress

- ✓ Increased egg weight
- ✓ Increase in milk yield

The use of animal fat in feeds of farm animals is not as common as the use of vegetable oil. Animal fats such as tallow, virgin oil and bone oil are used as an energy source in animal feeds, provided that they are not spoiled.

In order for it to be well utilized by the animal, the melting point should be above 40°C and these oils should not be heated at temperatures above 60°C (Akyıldız, 1983).

Determining the origin of animal products is important for economic value, belief, ethical and health reasons. In particular, due to the widespread occurrence of Mad Cow Disease (BSE) in the late 20th century, decisions were taken by the European Union (EU) Commission for the preparation of rendering products, their use in animal rations and their control (96/449/EC, 2000/766/EC, 2001/999/EC, 2002/1774/EC, 2003/1234EC).

4. SPECIES DETECTION IN RENDERING PRODUCTS WITH DNA TECHNOLOGY

Different electrophoretic and immuno-chemical methods (ELISA, SDS-PAGE) are used for species determination of meat products. However, these methods are not sensitive enough because peptide and epitope structures are negatively affected, especially in products exposed to high heat treatment such as rendering products (Lahiff et al., 2001; Tajima et al., 2002). For this reason, DNA-based methods, which

are more stable, have started to be preferred for species determination of meat products (Tajima et al., 2002; Dalmasso et al 2004). By using Polymerase Chain Reaction (PCR) technology, different marker systems (RFLP, RAPD, mtDNA, rRNA, minisatellite, microsatellite) can be used to identify species at the DNA level more sensitively, quickly and economically. For this purpose, ruminate, poultry, fish, pig, horse Marker systems have been developed for, carnivore, mouse and rat species (İlhak and Arslan 2007, Martin et al. 2007).

Wing and feather particles were observed in the examination of the rendering product (bait) using the Nikon H-III (Tokyo, Japan) imaging system adapted to the Nikon SZM-2T (Tokyo, Japan) stereomicroscope (Figure 1) (Kurar et al., 2012).

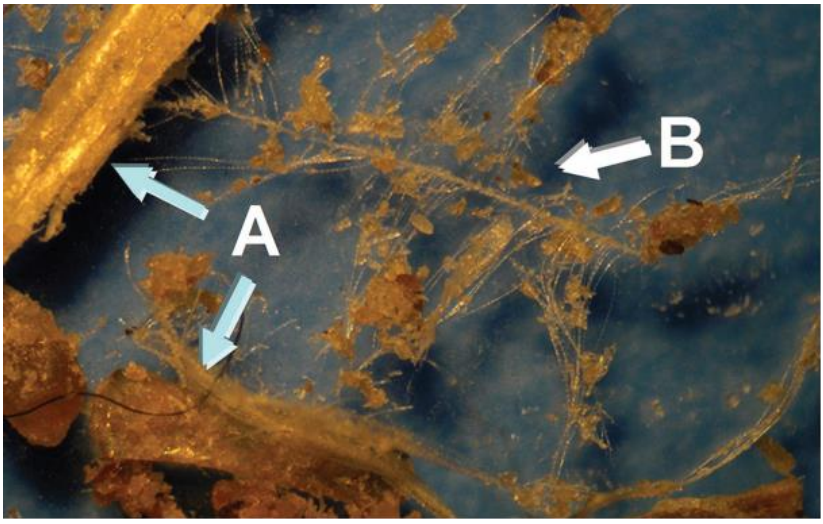


Figure 1. Microscopic examination of the feed sample. A; wing and B; feather particles.

Observation of bone and tissue particles constitutes the basis of microscopic examinations used in the identification of products of animal origin. However, this method is quite time consuming and requires special experience. In addition, microscopic methods only provide information about zoological classification (mammal, poultry, fish, etc.) (Dalmasso et al. 2004). Although the samples were treated with high temperatures (133 ^{0}C, 3 bar, 20 minutes), the observation of wing and feather particles indicates that the sample may be of avian origin (Kurar et al., 2012).

In heat-treated products, as in proteins, DNA breaks down as a result of thermal denaturation. Ebbehol and Thomsen (1991) reported that DNA isolated from heat-treated meat products was highly fragmented (<300 bp). In addition, the amount of DNA isolated from heat-treated products is 10 times less than from fresh tissues (Lahiff et al. 2001), reducing the target DNA copy number for PCR reactions. Some negative factors that occur during the preparation of these products and suppress PCR can be carried into the reaction (Fumiere et al., 2006). For this reason, different isolation methods have been developed since the efficiency of the DNA isolation method used is important (Lahiff et al., 2001). In this study, DNA isolation was performed using two different methods based on organic (phenol/chloroform) and detergent (DTAB). Although PCR amplification was observed in DNA samples isolated by both methods, DTAB method was observed to be more effective in DNA isolation from hydrolyzed wing-feather samples as a result of spectrophotometric

analyzes. The detergent-based method is easier than the organic method and is more reliable for the user and the environment.

DNA markers to be used in species identification studies of heat-treated animal products are created according to two criteria. These are that the PCR target region is small and has repeat regions in the genome. Since DNA isolated in rendering products is highly fragmented (Ebbehol and Thomsen 1991), it is critical to use primers that yield small PCR products (<300 bp) (Dalmasso et al 2004).

The use of DNA marker systems with high copy ratio in the genome is preferred in species determination studies (Tajima et al 2002). For this purpose, mitochondrial DNA (mtDNA) marker systems are widely used. ~2500 copies of mtDNA can be found in the cell (Lahiff et al 2001, Tajima et al 2002). mtDNA sequence differences allow generation of species-specific PCR markers (Bellagamba et al., 2006).

5. CONCLUSION

By processing meat, poultry and fishing industry residues with appropriate technology and using them as feed; It will provide the following advantages in terms of animal nutrition and the country.-The processing of these industrial residues contributes to the prevention of environmental pollution that threatens health norms. -As such valuable raw materials are not wasted and used as fodder, it contributes significantly to animal husbandry and therefore to the country's economy.

Since feeds of animal origin are rich in protein, they are used as a protein source with high biological value in the feeds of birds that need high protein. Because these feeds are rich in essential amino acids and especially lysine, they are important sources for meeting the amino acid needs of poultry. The fact that feeds of animal origin are rich in mineral substances, especially calcium and phosphorus, as well as some vitamins, complement the feed of plant origin in these aspects.

In short, animal-based feed raw materials, which are so valuable for balanced nutrition and healthy breeding of poultry, have a great importance for the country's livestock and therefore the feed industry. This resource, which is not widely used in our country, needs to be produced using appropriate technologies in a way that has nutrient content and hygiene in accordance with standards. In this way, it will contribute to both the prevention of environmental pollution and the creation of economic added value by encouraging the evaluation of slaughterhouse wastes.

It has been concluded that the DNA test panel can be successfully used in the determination of species and composition of rendering products and meat products used as human food and prepared at high temperatures.

REFERENCES

Kutlu, H.R. ve Görgülü, M. (2003). Genel Hayvan Besleme. Ders Notu. Ç.Ü. Ziraat Fak. Zootekni Bölümü, Adana.

Akyıldız, P. (1983). Yemler Bilgisi Ve Teknolojisi. A.Ü. Ziraat Fakültesi Yayınları No.368,Ders Kitabı No.234, Ankara.

Demirulus, H., Aydın A. (1996). Y.Y.Ü. Ziraat Fak. Zootekni Böl. VAN Ekoloji Çevre Dergisi Nisan-Mayıs-Haziran, Sayı:19

Kurar, E., Özşensoy, Y., Bülbül, M. D., Nizamlıoğlu, M. (2012). DNA teknolojisi ile rendering ürünlerinde tür tespiti: Bir vaka raporu. Eurasian Journal of Veterinary Sciences, 28(2), 122-125.

NRA (2000). Rendering Ürünlerinin Bio-Güvenliği ve Besin Değeri..S.42, İzmir.

Büyükşahin H, 1985. Hayvansal Kökenli Yemlerin Hayvan Beslemedeki Yeri. Yem Sanayi Dergisi. Sayı. 44:10-18

Özgen, H. (1986). Hayvan Besleme S.Ü. Yayınları. No. 16. Veteriner Fakültesi Yayınları. 5: 63

Göğüş, K. (1976). Hayvansal Kökenli Yemler ve Bazı Önemli Özellikler. Yem Bülteni. Cilt 1(2):18-21

Kutlu, H.R. (2003). Yemler Bilgisi ve Yem Teknolojisi. Ders Notu. Çukurova Üniversitesi Ziraat Fakakültesi Zootekni Bölümü, Adana.

Lahiff, S., Glennon, M., O'Brien, L., Lyng, J., Smith, T., Maher, M., Shilton, N. (2001). Species-specific PCR for the identification of ovine, porcine and chicken species in meat and bone meal (MBM). Molecular and Cellular Probes, 15: 27-35

Tajima, K., Enishi, O., Amari, M., Mitsumori, M., Kajikawa, H., Kurihara, M., Yanai, S., Matsui, H., Yasue, H., Mitsuhashi, T., Kawashima, T., Matsumoto, M. (2002). PCR detection of DNAs of animal origin in feed by primers based on sequences of short and long interspersed repetitive elements. Bioscience, Biotechnology, and Biochemistry, 66: 2247-2250.

Dalmasso, A., Fontanella, E., Piatti, P., Civera, T., Rosati, S., Bottero, M.T. (2004). A multiplex PCR assay for the identification of animal species in feedstuffs. Molecular and Cellular Probes,, 18: 81-87.

Ilhak, O.I., Arslan, A, (2007). Identification of meat species by polymerase chain reaction (PCR) technique. Turkish Journal of Veterinary and Animal Sciences, 31: 159-163.

Martín, I., García, T., Fajardo, V., Rojas, M., Hernández, P.E., González, I., Martín, R. (2007). Technical note: detection of cat, dog, and rat or mouse tissues in food and animal feed using species-specific polymerase chain reaction. Journal of Animal Science, 85: 2734-2739.

Fumiere, O., Dubois, M., Baeten, V., Von Holst, C., Berben, G. (2006). Effective PCR detection of animal species in highly processed animal byproducts and compound feeds. Analytical and Bioanalytical Chemistry, 385: 1045-1054.

Bellagamba, F., Comincini, S., Ferretti, L., Valfre, F., Moretti, V.M. (2006). Application of quantitative real-time PCR in the detection of prion-protein gene species-specific DNA sequences in animal meals and feedstuffs. Journal of Food Protection, 69: 891-896

CHAPTER 12

SHOULD WE FEED CATTLE AD LIBITUM OR RESTRICTED?

Prof. Dr. Hüseyin NURSOY[1]

[1] Bingöl University Faculty of Veterinary Medicine, Department of Animal Nutrition and Nutritional Diseases, 12000, Bingöl, TURKEY; ORCID: 0000-0002-5524-2459;E-mail:hnursoy@bingol.edu.tr.

INTRODUCTION

Free or Ad Libitum Feeding: Ad libitum in Latin means "unlimited" and in English it means "optional, full and spontaneous" in music. Abbreviation for "ad lib." it is in the form (1). "Ad libitum" in the veterinary field; this means that animals can freely consume the feed at all times, eat as much as they want whenever they want, and that there is always feed in front of them. Long-term ad libitum feeding or access to food 24 hours/day for monogastric animals such as horses, donkeys, rabbits, cats, dogs, mice, rats; it causes an increase in overweight, heart and respiratory diseases, foot and reproductive problems and cancer formation (2). Regardless of the age and physiological periods of the cattle, the excess of energy and protein can cause reproductive and calving problems. In general, it is recommended to give these animals roughage such as pasture and dry grass (except corn silage) ad libitum in terms of reproductive health and cheapness. As feed intake increases, Live Weight (LW), Live Weight Gain (LWG) and Feed Conversion Ratio (FCR) gains may not increase linearly (3).

Programmed / Restricted / Limited Feeding: Animals are fed according to certain predetermined measures such as breed, LW, LWG, milk yield, egg yield, FCR, etc. feed intake in fixed quantities. For this purpose, NRC (National Research Council, USA), INRA (Institut national de la recherche Agronomique, France), ARC (Agricultural Research Council, UK), FEDNA (Fundación Española para el Desarrollo de la Nutrición Animal, Spain), CVB (Centraal Veevoederbureau; Central Bureau for Livestock Feeding, Germany),

TNS (Trouw Nutrition Spain, Spain), Rhône-Poulenc, Adisseo, Degussa, Evonik, etc. tables of some public and private institutions in the world, such as cattle and other animals, reporting the daily nutrient requirements can be used. If these tables are followed, animals neither become obese by feeding ad libitum nor show signs of hunger. Among those programmed or restricted in these tables; feeding time, for example, allowing access to 16 hours/day feed instead of 24 hours, feed type, restriction of forages or concentrates separately, and some feed ingredients (Dry Matter (DM), metabolic energy (ME), net energy (NE), crude protein (CP), minerals and vitamins (4). Since the digestive tract is not constantly filled with restricted feeding, the digestibility of the feeds increases, liver abscess is related to both restriction and lowering of the energy content. While roughage, which has low energy content, does not make fat and is cheaper, can be given to cattle ad libitum periodically; Concentrated feeds can be given on a limited basis. Thus, while the problems caused by hunger are reduced, other problems do not occur. In cattle, tongue movements increase, cortisol increases, glucose and insulin decrease, NEFA and β-hydroxy butyrate increase in fasting states. For example, by giving concentrated feeds with high energy content to male young cattle during their growth period, their survival rate, energy and protein needs are reduced, and more nutrients can be spent on yield or muscle development. Well; restricted feeding of feeds with high energy content during the growth period is better than giving roughage ad libitum during the same period (2, 3).

CALVES NUTRITION

In recent years, ad libitum administration of Milk Replacers (MR) to calves has been discussed. Brends et al. (5) Fat content or energy value rather than lactose consumption controls daily feed intake, fat intake is higher than MR in calves given full-fat milk. and 150 g/1 liter they emphasized that attention should be paid to dilute. In their study by Schaff et al. (6) in which they examined the first 8-week period, at the first 5 weeks of Holstein and Holstein x Charolais cross-breed calves, with ad libitum administration of MR, approximately 15 liters/day can be drunk by a calf and there is no diarrhea in this period. After the 5th week, it was observed that the amount of MR drinking in the calves suddenly decreased to 6 liters, despite this decrease, the consumption of starter feed did not decrease, and 6 liters of milk replacer was consumed on a daily basis. It has been reported that the LW in the restricted feeding group, in which 6 liters of milk replacer is given on a constant basis, approaches 70 kg and is lower than the group (80 kg) given ad libitum MR. Rosenberger et al. (7) programmed the feeding of 6, 8, 10 liters and 12 liters of pasteurized milk per day to female-male calves with an average birth weight of 40 kg with automatic milk drinking machines that can heat up to 0.5 liter of 40^{o}C every hour until the first 42 days. During the trial (first 68 days), starter feed and a mixture of meadow grass+English grass grass were given ad libitum. In the study, the calves drank the most 9.6 kg of pasteurized milk per day, there was a statistically significant difference between the groups given 6 and 12 liters in LWG, the consumption of starter feed

was not different in the groups programmed to 6 and 12 liters, the consumption of starter feed and LWG of excessive milking after weaning. Researchers stated that since milk of 10% of LW causes physiological and mechanical hunger in calves, milk of this rate should be given for the first 42 up to 15% of LW. Gerbert et al. (8) stated that the calves of meat breeds constantly suckle their mothers, that is, they drink milk ad libitum, and reported that there is no problem in these calves, but the opposite is the case in dairy breeds. They reported that less than 6 liters of milk or MR given to dairy calves in 2 meals caused abnormal behavior and digestive problems. Researchers suggest that the abomasum are overfilled as calves receive more milk and MR, especially with the automatic MR machines that have been used in recent years, and to prevent this situation, the daily amount of milk or MR should be divided into at least 2-3 meals. It can be recommended to start calf starter feeds within the first week and to start high quality and soft textured roughage after the first month (4).

BEEF CATTLE NUTRITION

Starting from weaning up to approximately 300 kg LW or up to 1 year of age, bacgrounding rations containing 40-70% quality roughage are offered to young cattle to be fattened. The DM content of the rations should not below 75% should be 13-14% CP (urea can be used very little) and at least 2600 ME/kg energy. These cattle can be given silage from the age of 6 months. In this period, DM consumption is about 3% of LW. According to the desired LWG, the roughage ratio

in the ration can be reduced up to 40%. During this period, silage or high quality hay is given ad libitum, additionally 3-6 kg of concentrated feed is fed per animal. In general, quality roughage is given as DM at a rate of 2.5% of LW. Finishing rations containing 75-85% concentrate feed up to approximately 450-550 kg (approximately 250-300 kg carcass is obtained) are given to young bulls from about 300 kg LW or from 1 year old until slaughter. The DM of the ration should contain 11% CP and at least 2900 ME/kg energy. In this period, DM consumption is 2.5% of LW. According to the desired LWG, the roughage ratio in the ration can be reduced up to 10% (3,4,9).

Pittaluga et al. (10), a 106-day trial was applied to Angus beef cattle with an average fattening starting weight of 281 kg, with ad libitum corn silage and corn-weighted feeding and restricted feeding up to 85% of ad libitum, and then all experimental animals were given the above-mentioned ration ad libitum. . Up to an average of 544 kg body weight, the LWG was 1.45 kg/day and the 106-182 days of the next period of feed restriction in the first 106-day period of the trial. was found to be compensated within days. In a study conducted with Scilacci (3), for Angus young cattle, 3 feeding levels were tested as ad libitum, 20% ad libitum restricted and 30% ad libitum restricted. High moisture corn and corn silage feeds were used in the study. Daily feed consumption was 5.9 kg/day, 4.7 kg/day and 4.1 kg/day, respectively and showed significant differences ($P<0.01$). There was no statistical difference in LWG ($P>0.05$). This was probably due to the high amounts of NEm, NEg and crude protein provided by the restricted feed

rations. Although the feed conversion ratio (FCR) was not statistically different between ad libitum and 20% restricted cattle (6.69 and 6.09, $P>0.05$, respectively), it was more efficient ($P<0.01$) with a feed consumption of 4.65 kg per kg LW in the 30% restricted ration group. a situation has been observed. Researchers have revealed that cattle fed with limited diets provide 21% less FCR yield than those fed ad libitum or have more meat with less feed.

Mathison and Engstrom (11), controlled or non-ad libitum feeding in beef cattle, due to regular daily feed intake (DFI); They reported that it should be preferred because of the decrease in daily movement activity in animals, increase in nutrient digestibility, less excretion of feces, decrease in live weight variations and less internal fat formation. In another trial with 2 groups, the researchers reported that in male beef cattle between 363-516 kg LW, 96% less feed was given compared to the ad libitum group and ad libitum; reported that none of the parameters (LW, DFI (mean 9.68 kg/day), LWG (mean 1.6 kg/day), FCR (6/1), Carcass Weight (mean 300 kg)) were affected. They also stated that ad libitum administration of ground corn reduced nutrient digestibility, whereas barley administration did not.

In an article published by Faulkner and Berger (12), the following determinations were made: Farmers engaged in open feedlots want their animals to be meated and slaughtered as soon as possible. For this purpose, they consume concenrate feed by ad libitum. However, in recent years, instead of this tendency, it can be ensured that the slaughter live weight does not decrease by using -20-7% or an

average of 5.5% less feed in order to be cheaper. The only parameter that can be used here is to restrict the feed at rates varying between 5-20% according to ad libitum feeding. In particular, FCR decreases by -1-9% on average by 3.5%. This is an important economic gain, profit.

It has been reported that although restricted feeding, which is given 5-15% less per day compared to ad libitum feeding, has a negative effect on LWG in the finishing periods of beef cattle, it has positive effects on FCR (13). Galyean et al. (13), in another supportive study (14), when 1 year old male beef cattle with an average live weight of 374 kg were fed wheat-weighted concentrate and roughage ad libitum feeding or 85% of ad libitum feeding with restricted feeding respectively 6.82 and 6.16. In other experiments, when the Hereford beef cattle with an average body weight of 293 kg were fed wheat-density concentrate and roughage ad libitum feeding or 80% of the ad libitum feeding with restricted feeding, the LWG was 1.29 kg/day and 1.20 kg/day, respectively. Although it decreased very little like days, FCR values were realized as 7.14 and 6.91, respectively. In another trial of the same article, the researchers found that although slaughter LW (587 kg and 572 kg), LWG (1.36 kg/day and 1.27 kg/day) increased, respectively, in beef cattle consuming ad libitum and 80% restricted feeds (9.46 kg/day). and 8.66) were lower in the restricted feed group. In addition, the advantages of restricted feeding in other factors such as feed cost, feeder and bedding cleanliness, and the low amount of feces were revealed by the researchers are listed.

The metabolic rates and body temperatures of the 2 groups that were restricted by ad libitum and 75% of the ad libitum in open fattening (feedlot) cattle were examined and it was observed that the body temperature was 0.5 ^{o}C higher due to the increase in respiration rate in the ad libitum fed group. Researchers have recommended limited feeding of beef cattle in summer temperatures (15).

Scilacci (3) reported that the ration with low NEg (=0.99 Mcal/kg DM) value was ad libitum and the ration with high NEg (=1.32 Mcal/kg DM) value was ad libitum for beef cattle with an average body weight of 280 kg for 84 days. 85% less administration; reported that the high-energy but limited diet had higher LW, LWG NEg intake and rumination time (444.3 min/day), but lower feed consumption and feed consumption/LWkg. Mader et al. (16) reported that the mean DFI was 7 kg/day and the daily metabolic energy intake was 5.71 Mcal/day in fattening cattle with an average of 239 kg of feed given ad libitum and at the beginning of the experiment, and there was no difference between the groups.

Silva et al. (17), the final LW, LWG and FCR parameters of the ration containing 40% corn silage and 60% concentrated feed in the DM, given ad libitum and 85% of this amount in the finishing periods of Holstein x Zebu crossbreed cattle with an average live weight of 318 kg. reported to be unaffected. Researchers recommend 85% restricted feeding because it causes DM consumption and P deficiency. Vizcarra et al. (18), male beef cattle with an average trial starting body weight of 251 kg, which were restricted for 2 hours a day, 1 hour after each new

meal, after the ad libitum and 2 times increased feeds at 06:00 and 14:00 in the morning were collected, or no feed was given. observed that the parameters of LW, LWG, FCR and DFI were statistically lower among the group. Researchers also reported that there was no difference between the normal ground and flake corn state in terms of the parameters examined.

HEIFERS AND DAIRY COWS NUTRITION

Hicks et al. (14), when corn-density concentrates and roughages were fed ad libitum feeding or 89% of ad libitum feeding with restricted feeding in female heifers aged 1 year with an average weight of 329 kg, the FCR values were 8.78 and 8.06, respectively. This reduces the feed cost. Roberts et al. (19), in heifers fed ad libitum and a ration restricted to 80% of it and fed for 140 days after weaning; It is reported that there is 26% lower feed consumption and LWG it reaches puberty 20 days later but weaker, there is no difference in the rate of conception, and as a result, restricted feeding is recommended.

The benefits of limited or limited administration of Total Mixture Ration (TMR) in ruminants are listed as follows: Normal rumen functions and movements are more frequent, nutrient digestibility increases due to less feed passing through the reticulo-rumen, and for this reason, such feed restrictions should be avoided especially in middle and last lactations. possible is recommended. In ruminants, ad libitum (24 hours) and limited (19 hours) administration of TMR did not affect daily DM consumption, live weight, milk yield, milk components, and daily average pH. It was found that they ruminate

(424 min./day) (20). It has been reported that even if the feed consumption decreases with the ad libitum feed given to dairy cows by 4-12%, the milk yield and FCR parameters are the same. Researchers have also determined that the 10% restriction also causes a decrease in methane gas production (21).

Loor et al. (22) stated that in the 60-day dry period of dairy cows, 14.4 kg of DM feed was consumed per day by ad libitum feeding of rations with a net energy value of 1.6 Mcal in kg/DM, consisting of corn silage and alfalfa silage, and that those who were fed restricted (given 80% of their net energy needs) They determined that they consumed 7.3 kg of DM feed. Researchers suggested that 140% of net energy need does not cause obesity in cows, but it has negative effects on genomic markers in liver hepatocytes (Figure 1), increases the risk of ketosis, and should be fed moderately instead of ad libitum feeding.

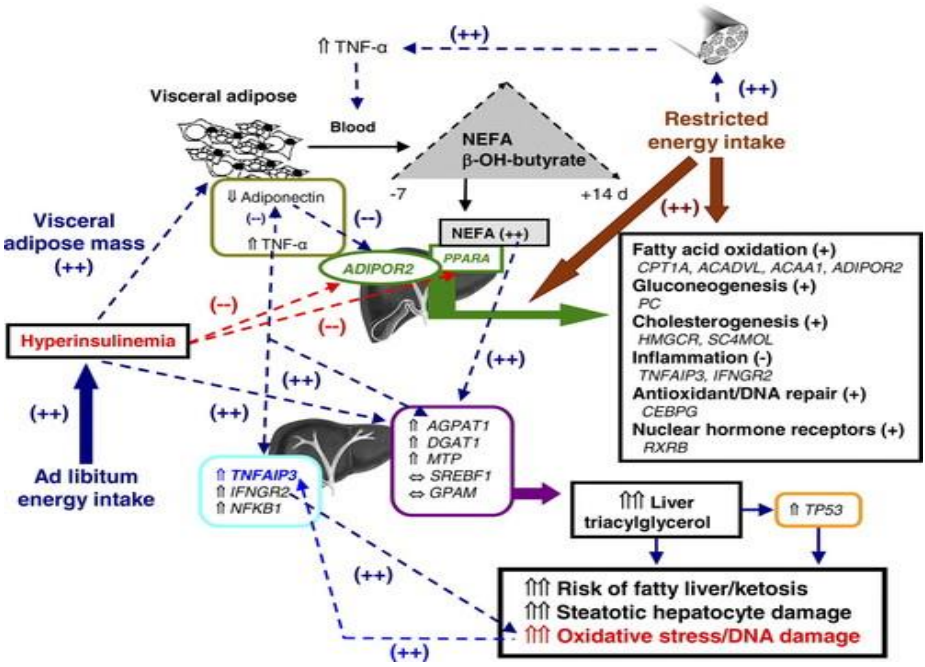


Figure 1. Negative effects of ad libitum feeding on organs in cattle.

CONCLUSIONS

As a result; Based on the literatures of data in this review, the following can be said:

1- Calves should not be given ad libitum milk or MR a milk drinking program up to 15% of LW can be applied in the first 6 weeks. Calf starter feeds should be started within the first week and roughage should be started after the first month.

2- The cattle to be fattened may not be fed ad libitum after weaning. Feeding should be done according to the nutritional needs given in the tables of organizations such as NRC.

3- It can be said that limited feeding is beneficial for heifers and the energy value of the feed given ad libitum to dairy cows should be reduced.

REFERENCES

1-Ad libitum meaning, https://legal-dictionary.thefreedictionary.com/ad+libitum, Accessed: 06.06.2022.

2-Tolkamp, BJ., D'Eath, RB., ve Phillips, CJC. (Ed.). Hunger associated with restricted feeding systems. In CJC. Phillips (Ed.), *Nutrition and the Welfare of Farm Animals*. Springer International Publishing, 16, 11-27, 2016.

3-Morgan A. Scilacci. Effect of traditional roughage-based or limit-fed, high-energy diets on growth performance and digestion in newly received growing cattle and subsequent implications on feedlot growth performance and carcass characteristics and effect of Enogen corn hybrids or conventional hybrids in diets containing corn coproducts on performance and digestion in newly received growing cattle. Kansas State University, A THESIS, 2019.

4-H. Nursoy. Feeds and Animal Nutrition Lecture Notes, Bingöl University Faculty of Veterinary Medicine, 2022.

5-H. Berends, H.van Laar, L.N. Leal, W.J.J.Gerrits, J.Martín-Tereso. Effects of exchanging lactose for fat in milk replacer on ad libitum feed intake and growth performance in dairy calves. Journal of Dairy Science, 103, 5, 4275-4287, 2020.

6-Christine T. Schäff, Jeannine Gruse, Josefine Maciej, Manfred Mielenz, Elisa Wirthgen, Andreas Hoeflich, Marion Schmicke, Ralf Pfuhl, Paulina Jawor, Tadeusz Stefaniak, Harald M. Hammon. Effects of Feeding Milk Replacer Ad Libitum or in Restricted Amounts for the First Five Weeks of Life on the Growth, Metabolic Adaptation, and Immune Status of Newborn Calves. PLoS One., 11(12) 30; 1-24, 2016.

7-K. Rosenberger , J.H.C. Costa, H.W. Neave , M. A. G. von Keyserlingk, DM Weary. The effect of milk allowance on behavior and weight gains in dairy calves. J Dairy Sci,. 100(1):504-512, 2017.

8-C. Gerbert, D. Frieten , C. Koch, G. Dusel , K. Eder, T. Stefaniak, J. Bajzert, P. Jawor , A. Tuchscherer, H.M. Hammon. Effects of ad libitum milk replacer feeding and butyrate supplementation on behavior, immune status, and health

of Holstein calves in the postnatal period. J Dairy Sci., 101(8):7348-7360, . 2018.

9-David G. Hinton., Supplementary Feeding of Sheep and Beef Cattle 2007, Landlinks Press Csiro Publishing, Collingwood, VIC, Australia.

10- Alejandro Pittaluga, Mairim Ortiz, Alejandro E. Relling. Effect of feed ıntake and calcium salts of palm oil ınclusion on growth performance and carcass characteristics of feedlot finishing steers. Journal of Animal Science 100 (Supplement_2): 99-100, 2022.

11-Mathison, G.W., Engstrom, D.F. Ad libitum versus restricted feeding of barley- and corn-based feedlot diets. Can. J. Anim. Sci. 75: 637-640, 1995.

12-Dan B. Faulkner ve Larry L. Berger. Limit Feeding Beef Cattle. Product of Extension Beef Cattle Resource Committee, BCH-5175, 2021.

13-Galyean M.L., Hatfield E.E. Stanton T.L. Review: Restricted and Programmed Feeding of Beef Cattle-Definitions, Application, and Research Results. The Professional Animal Scientist, 15, 1, 1-6, 1999.

14-R. B. Hicks, F. N. Owens, D. R. Gill, J. J. Martin, C. A. Strasia Effects of Controlled Feed Intake on Performance and Carcass Characteristics of Feedlot Steers and Heifers. *Journal of Animal Science*, 68, 1, 233–244, 1990.

15-T. L. Mader, S. M. Holt, G. L. Hahn, M. S. Davis, D. E. Spiers. Feeding strategies for managing heat load in feedlot cattle. *Journal of Animal Science*, 80, 9, 2373–2382, 2002.

16- T. L. Mader J. B. Gaughan and B A. Young. Feedlot Diet Roughage Level for Hereford Cattle Exposed to Excessive Heat Load. Haskell Agricultural Laboratory (Northeast Research and Extension Center) 13, 1999.

17-F. A. S. Silva, S. C. Valadares Filho, L. A. Godoi, B. C. Silva, M. V. C. Pacheco, D. Zanetti, P. D. B. Benedeti, F. F. Silva and T. L. Felix. Effect of duration of restricted-feeding on nutrient excretion, animal performance, and carcass characteristics of Holstein × Zebu finishing steers. *Animal Production Science*, *60*(4), 535-544.https://doi.org/10.1590/1809-6891v21e-63329, 2020.

18-Víctor Manuel González-Vizcarra, Alejandro Plascencia, Daniel Ramos-Aviña, Richard Avery Zinn. Influence of substituting steam-flaked corn for dry rolled corn on feedlot cattle growth performance when cattle are allowed either ad libitum or restricted access to the finishing diet. Asian-Australasian Journal of Animal Sciences (AJAS), 30, 11: 1563-1567, 2017.

19-A. J. Roberts, E. E. Grings, M. D. MacNeil, R. C. Waterman, L. Alexander and T. W. Geary. Reproductive performance of heifers offered ad libitum or restricted access to feed for a 140-d period after weaning. Proceedings, Western Section, American Society of Animal Science, 58, 255-258, 2007.

20-D. Cavallini, L. M. E. Mammi, M. Fustini, A. Palmonari, A. J. Heinrichs and A. Formigoni. Effects of ad libitum or restricted access to total mixed ration with supplemental long hay on production, intake, and rumination. J. Dairy Sci., 101:10922–10928, 2018.

21-A. Fischer, N. Edouard P. Faverdin. Precision feed restriction improves feed and milk efficiencies and reduces methane emissions of less efficient lactating Holstein cows without impairing their performance. Journal of Dairy Science, 103, 5, 4408-4422, 2020.

22-Juan J. Loor, Heather M. Dann, Nicole A. Janovick Guretzky, Robin E. Everts, Rosane Oliveira, Chery A. Green, Noah B. Litherland, Sandra L. Rodriguez-Zas, Harris A. Lewin, and James K. Drackley. Plane of nutrition prepartum alters hepatic gene expression and function indairy cows as assessed by longitudinal transcript and metabolic profiling. Physiol Genomics 27: 29–41, 2006.

BÖLÜM 13

TENDINITIS IN HORSES AND TREATMENT OPTIONS

Assist. Prof. Dr. Emine ÇATALKAYA[1]

[1] Dicle University, Faculty of Veterinary Medicine, Department of Surgery, Diyarbakir/Türkiye, ORCID: 0000 0001 7884 5407
eminecatalkaya21@gmail.com

1. INTRODUCTION

Tendons and ligaments, which are quite flexible, start from bones or muscles and end in joints. They passively transfer power for joint movement and are tensile-resistant structures. (Dyson 2003, O'Sullivan 2007). Musculus flexor digitorum superficialis and musculus interosseus medius tendon support against excessive tension in the metacarpophalangeal and metatarsophalangeal joints (Seyrek-Intas et al. 2002, Jorgensen et al. 2003, Whitton et al. 2007). Tendonitis is the rupture of tendon fibers at the fibrillar or fascicular level and the resulting inflammatory reactions as a result of excessive stretching and trauma of the tendons. (Alkan et al. 1995, Seyrek-Intas et al. 2002).

Tendon injuries are frequently encountered in humans and sports horses. It has been reported that it accounts for approximately 46% of musculoskeletal injuries in sports horses (Tsang et al. 2019). Tendinitis is a condition that significantly affects the sporting life of the horse and may even cause the horse's racing life to end if it is not treated on time and in accordance with the rules (Jorgensen et al. 2003, Dakin 2017). As a matter of fact, it has been reported that 7-43% of the race life in purebred English horses is terminated due to tendinitis of Musculus flexor digitalis superficialis (MFDS) (Jorgensen et al. 2003). Tendinitis is mostly seen in the tendons of the Musculus flexor digitalis superficialis (MFDS), Musculus flexor digitalis profundus (MFDS) and Musculus interosseus medius, which are located on the palmar surface of the front limb (Samsar and Akın

1998, Rick 2003, Dyson and Genovese 2003, Arıcan et al. 2008, Sarrafian et al. 2012). Rarely, tendonitis is seen in the tendons of Musculus extensor carpi radialis, Musculus extensor digitalis lateralis, Musculus extensor digitalis communis, Musculus extensor digitalis pedis longus.

Tendinitis usually occurs in the flexor tendons and bilaterally, but often one foot is more affected than the other (Rick 2003, Jorgensen et al. 2003, Yücel 2005). It has been reported that Thoroughbred English and Thoroughbred Arabian racehorses frequently participate in long-distance races, training is done at race pace, and genetic predisposition affects tendinitis formation in MFDS (Jorgensen et al. 2003, Rick 2003, Tsang et al. 2019). Inflammation of the musculus flexor digitorum profundus (MFDP) is more common in the hind limb and has been reported to be usually unilateral (Dyson 2003).

2. ETIOLOGY

Tendinitis in horses occurs for various preparatory and constructive reasons. Among the predisposing reasons are high body weight but thin and weak tendons (Jorgensen et al. 2003), orthopedic problems such as "X" or "O" legs, shakiness, dog-handedness, long snot of the nail and flat heel. In addition, faulty nail cutting and shoeing errors are also effective in the formation of tendinitis (Yücel 2005, O'Sullivan 2007). Obstacles and high jumps in horses are also among the predisposing causes of tendinitis (Dyson 2003, Smith 2003, Smith and Allen 2004). Constructive reasons are factors such as frequent and

high effort training and running (Jorgensen et al. 2003), participation in races with insufficient training, wet and slippery running tracks, and working on poorly grounded (rough) terrains (Smith 2003, Rick 2003, Smith and Allen 2004, Yücel 2005).

The forelimbs bear more than half of the horse's body weight. In addition, due to the weight of the rider or the wrong posture of the rider, the weight affecting the front extremity of the horse is among the etiological factors. During the gallop of the horse, when one of the forelegs hits the ground alone and the entire load of the body is transferred to this foot, the biomechanical tension in the tendons is at the maximum level, causing tendinitis cases to occur mostly in the front extremities and mostly in the flexor tendons (Alkan et al. 1995, Jorgensen et al. 2003, Smith and Allen 2004, Yücel 2005). In a study, it was reported that tendinitis is seen 67% of the time after a race or training (Alkan et al. 1995).

3. CLINICAL APPEARANCE

Subclinical, acute and chronic forms of aseptic tendinitis are seen. Subclinical tendinitis is difficult to diagnose, difficult to diagnose by palpation and ultrasonographic examination. Flexor tendon inflammations are mostly localized in three parts of the metacarpal or metatarsal region (Smith 2003, Smith and Allen 2004, Smith 2007, Whitton et al. 2007).

These are respectively;

- MFDP is often inflamed in the area immediately below the carpal joint or in the proximal 1/3 of the metacarpus (O'Sullivan 2007),

- MFDS is frequently inflamed due to thinning of the tendon in the middle 1/3 of the metacarpus or metatarsus (Yücel 2005, O'Sullivan 2007),

- In the distal 1/3 of the metacarpus and metatarsus, it can be listed as inflammation of the Musculus Interosseus medius, mostly with the squeezing or inflammation of the volar annular ligament (Dyson and Genovese 2003, Yücel 2005, O'Sullivan 2007).

A local deformity is observed in acute tendinitis. The affected tendon section usually curves outward on inspection. The degree of lameness seen is directly proportional to the severity of the injury. Generally, lameness has the character of severe pressure lameness. There are typical signs of inflammation such as pain, swelling and temperature increase on palpation (Gills 1997, Smith 2003, Smith and Allen 2004, Smith 2007, Whitton et al. 2007, Roger and Smith 2008).

One of the most important findings of tendinitis is pain. The painful response detected in the systematic palpation of the flexor tendons with the thumb and index finger from proximal to distal in the semi-flexion position of the foot may be a sign of tendinitis. However, not

every horse with tendinitis will respond painfully (Bertoni et al. 2013). Another sign of tendinitis is edema. Soft or semi-hard, diffuse or focal fluid accumulation is felt on palpation. Slight crepitation is felt on palpation when the foot is in the flexed position. Subcutaneous edema may not only be due to tendon damage, but may also be due to incorrectly applied bandages, externally applied drugs, and subsolear abscesses. Therefore, differential diagnosis is important. Clinical symptoms are more severe when musculus interosseus medius and MFDS inflammation are together. If tendinitis occurs in the lower 1/3 of the MFDS and the inflammation spreads to the volar anular ligament, swelling occurs in the tendon and tendon sheaths that coincide with the upper part of the sesamoid bones, due to the compression of the inflamed MFDS by the volar annular ligament and at the same time the pressure of the inflamed ligament. This swelling shows itself with a curvature when viewed from the side and from the back (Rick 2003, Dyson 2003, Dyson and Trotter 2003, Yücel 2005, O'Sullivan 2007). Local temperature increase is the earliest and most common sign of MFDS tendon injury (Jorgensen et al. 2003). Regional thickening and temperature increase can also be seen in tendinitis due to the cicatrix tissue formed at the end of the healing period. local temperature rise is detected by palpation or thermography. Therapeutic vegetable oils and barn bandage applied to the area should not be confused with tendinitis as they cause temperature increase. In addition, increased pulsation in digital arteries in tendinitis draws attention (Smith 2003, Smith and Allen 2004, Yücel 2005).

Chronic tendinitis occurs when acute tendinitis is not treated or when the factor that causes tendinitis is constantly affected. In chronic tendinitis, a thickening is seen in the region, and an outward curvature is seen in the tendon line descending from top to bottom in a side view. The curvature of chronic tendinitis cannot be removed with any treatment.

Septic tendinitis, on the other hand, is shaped due to traumas in which skin integrity is impaired (such as sharp object wounds, cut wounds), infections in surrounding tissues (tendovaginitis, bursitis, arthritis, etc.) and generalized infections (Jorgensen et al. 2003, Yücel 2005).

4. DIAGNOSIS

Diagnosis of tendon injuries is usually easily made by observation and/or palpation of the swelling. Inspection of the tendons should be done carefully with the animal foot on the ground, with the tendons taut, and with the tendons loose after the foot is raised, and should always be compared with the other leg. Severe pain in the metacarpophalangeal joint hyperextension when the contralateral limb is raised indicates superficial digital flexor tendinitis and/or concomitant damage to the suspension ligament.

While diagnosis can often be made without diagnostic imaging, ultrasonography is an invaluable diagnostic technique for confirming the injured structure and assessing severity (Gills 1997). Ultrasonographic examination performed earlier than four days after injury may lead to erroneous results due to the initial enlargement of

the lesion associated with proteolytic enzyme activity, but aggressive early anti-inflammatory therapy may minimize these changes. A probe of 10 MHz and above should be used in ultrasonographic examination (Padaliya et al. 2015). There is no standard examination method for ultrasonographic examination. However, it is recommended to evaluate the metacarpus region by dividing it into seven regions transversely and 3 regions longitudinally (Roger KW and Smith MA 2008, Padaliya et al. 2015). It is recommended to perform both transversal and longitudinal examination when performing a tendon examination (Arıcan et al. 2008, Roger KW and Smith MA 2008). Both extremities should be evaluated to identify common concomitant pathology (Temizoglu 2005, Roger KW and Smith MA 2008). In order to make full good ultrasonographic examinations of the extremities, the horse can be sedated with low doses of α_2 agonist agents (Detomidin HCl, Xylazine HCl), and shaving the area and degreasing with alcohol is essential for better examination. Sufficient amount of ultrasound gel should be used so that no air remains between the ultrasound probe and the tendon, and the probe should be placed vertically on the tendon. Otherwise, artifacts may cause misdiagnosis (Roger KW and Smith MA 2008, Yavuz et al. 2010).

The most common ultrasonographic signs of injury are:

* An increase in tendon cross-sectional area

* Generalized or focal hypoechoic (dark) areas within the tendon

* Disruption of longitudinal striated structure

* Changes in the shape and margin of the tendon are observed, especially in injuries to the tendon sheaths (Roger and Schramme 2003, Roger and Smith 2008, Padaliya et al. 2015).

5. PROGNOSIS

The results of tendinitis treatment in flat race and performance horses have been unsatisfactory, mostly because of the high probability of recurrence (Gills 1997, Roger and Schramme 2003, Roger and Smith 2008). This risk is seen more in racehorses. Ultrasonographic grading of the injury is important at the beginning of the treatment in tendon injuries in purebred and standard breed horses. Evaluation of the condition of tendon fibers in the pre-exercise ultrasonographic examination is important in terms of preventing recurrence of tendinitis. Although beta-aminoproprionitrile fumarate (BAPN) can improve the prognosis of the most severely affected horses, the efficacy of this treatment alone is relatively minor.

6. TREATMENT

Over the years, many treatment methods have been tried. However, there is always the possibility of recurrence. It is very important to know the stages of tendon healing in determining the treatment in cases of tendon inflammation. Treatment should be determined whether the tendinitis to be examined is in acute, subacute or chronic

stages and treatment should be started accordingly. (Roger and Schramme 2003).

6.1. Acute (inflammatory) phase

In early treatment, physical therapy (rest, cold application and pressure bandage) is important to reduce inflammation and limit the effect of proteolytic enzymes that disrupt tendon tissue (Dowling et al. 2000, Roger and Schramme 2003). Treatment with 20 minutes of cold hydrotherapy should be initiated immediately after the injury. Cold hydrotherapy has been shown to be safer for cooling than ice application. Even at this early stage, recommendations for relieving inflammation, maximizing healing, and controlled movement should be made. These movements are achieved by early passive and active movement of injured tissues. To be successful, the degree or frequency of movements must remain below the horse's pain threshold. Controlled movements can be initiated with a 15-minute light physical therapy session that includes a series of 10 to 30 carpal and metacarpophalangeal extensions and flexions performed at short intervals during the first 72 hours. Cold application and bandage application should be continued between physical therapy sessions. After 72 hours, sessions should be done once or twice a day. When the inflammation is reduced and the horse's extremity is more comfortable, light active loading exercise can be applied. Local application of dimethyl sulfoxide (DMSO) may be useful to accelerate edema resolution (Roger and Schramme 2003).

There is a theoretical basis for the use of anti-inflammatory agents that have a protective effect on connective tissue (steroids, polysulfated glycosaminoglycans [PSGAG] and hyaluronan). Systemic administration of short-acting steroids should be done within the first 24 to 48 hours to avoid any interaction with subsequent fibroplasia. PSGAGs have been shown to inhibit proteolytic enzymes in vitro and can be administered intralesional. Although not licensed for intralesional use, this route may be more effective than the systemic route and intratendular administration can be easily combined with needle-based tendon splitting (Dowling et al. 2000, Roger and Schramme 2003). Surgical treatment at this stage includes percutaneous tendon division, which has been shown to accelerate resolution of the ultrasonographically seen 'core lesion'. Tendon division can be accomplished with a scalpel or, less invasively, by needle puncture, when combined with intratendular drug therapy. It has been shown that desmotomy of the accessory ligament increases the tension in the suspensor ligament and may cause an increased incidence of desmitis (Roger and Schramme 2003).

6.2. Subacute (fibroblastic) phase

Regular ultrasonographic monitoring in early and walking exercises aims to improve the quality of the scar tissue formed at this stage. If the ultrasonographic cross-sectional area of the healed tendon increases by more than 10% after initiation of early active movements, the exercise level should be reduced.

To improve the quality of scar tissue, beta-aminoproprionitrile fumarate (BAPN) can be injected intratendinally 30 to 90 days after injury (Roger and Schramme 2003). This drug inhibits lysyl oxidase, the enzyme that promotes cross-linking of collagen molecules. Thus, it is thought that collagen fibers will be aligned longitudinally with controlled exercise, preventing cross-linking of collagen fibers (Dowling et al. 2000). Although early clinical trials in the US and UK have shown a benefit in more severe cases, subsequent outcomes have been variable and therefore this treatment should only be considered for the most severely affected cases. It should be noted, however, that BAPN is not available as a licensed drug.

Sodium hyaluronate was used both intratendinous and peritendinous in tendinitis cases and gave good results. Sodium hyaluronate has been experimentally obtained to reduce adhesion formation and accelerate healing in tendon injuries (Roger and Schramme 2003). In addition, growth factors and/or cell-based treatments are also used intratendinally in the treatment of tendinitis. Both insulin-like growth factor 1 (IGF-1) and transforming growth factor beta (TGF-β) reach their peak concentrations in the injured tendon within 10 days of tendon injury (Roger and Schramme 2003, Roger and Smith 2008). Bone marrow, a source of stem cells, has been hypothesized as a growth factor and direct injection of bone marrow into damaged suspensory ligaments has been reported to be beneficial (Herthel 2001). Other cell-based treatments involving the use of expanded stem cells in vitro are under investigation (Smith et al. 2003), but more

work is required to determine whether these new treatments are effective.

Platelet-rich plasma (PRP) is the plasma component obtained by centrifugation of whole blood and containing a higher concentration of platelets than whole blood. The fact that it contains many growth factors has brought the use of PRP injections in the treatment of various musculoskeletal diseases (Yilmaz and Kesikburun 2013). Platelets contain many proteins, cytokines and other factors that initiate and regulate wound healing. The growth factors they contain are responsible for stimulating neovascularization and fibroblast chemotaxis and are stimulators for fibroblast proliferation and collagen synthesis (Dilicikik et al. 2018). In a study by Boswell et al. (2014) in horses, they reported that PRP with low leukocytes and high platelet concentration resulted in the administration of more anabolic growth factor and less proinflammatory cytokines, which reduced inflammation and increased matrix gene synthesis. Likewise, in a study by McCarrel et al. (2012), they emphasized that inflammatory cytokines in the tendon increased after the injection of PRP with a high concentration in terms of WBC into the MFDS tendon. In another study by Schnabel et al. (2007), it was reported that PRP increased the regulation of anabolic gene expression in the tendons of the Musculus flexor digitorum superficialis.

6.3. Chronic phase

A controlled exercise program with regular ultrasonographic examinations to detect early signs of recurrence is a good treatment approach in cases of chronic tendinitis. It has been argued that bilateral desmotomy of the accessory ligament of MFDS gives positive results in the treatment of horses with MFDS tendinitis to prevent recurrence after recovery.

Undoubtedly, the main advance in helping to recover from tendon injuries has been the use of diagnostic ultrasonography as a rehabilitation tool. An initial ultrasonographic evaluation at least four to seven days after injury provides prognostic information and a baseline against which subsequent measurements of cross-sectional area can be compared, thus enabling a semiobjective assessment of tendon healing. It is obvious that predetermined ultrasonographic criteria must be met before a horse with a tendon injury can move on to the next level of a controlled exercise program (especially levels 2, 3 and 4). If the horse's exercise intensity is to be increased, it should be constant or reduced in cross-sectional area (i.e. <10% increase in cross-sectional area at any level) compared to previous examination, with an improvement in echogenicity and fiber pattern of the tendon (Roger and Schramme 2003). Clinical studies suggest that early pre-galop exercise often results in clinical deterioration in BAPN-treated horses, and it is therefore recommended that pre-galop exercise should not be resumed until eight months after BAPN therapy (Dowling et al. 2000, Roger and Schramme 2003).

6.4. Special therapies

Individual conditions may benefit from other specific treatment modalities. For example, intrathecal tears in the deep digital flexor tendon within the digital sheath and tear of the suspensory ligament at the level of the metacarpophalangeal joint seem to benefit from arthroscopic debridement. Extracorporeal shock wave therapy (SWT) has been advocated for many tendon and ligament injuries, but its effectiveness has not been fully proven. It has also been suggested that lateral plantar metatarsal neurectomy combined with fasciotomy is an alternative method (Dowling et al. 2000, Roger and Schramme 2003).

7. CONCLUSION

Tendo damage heals with repair rather than regeneration, and therefore preventive measures should be preferred (Dakin 2017). From this study, four strategies can be suggested for the prevention of tendinitis in horses.

Protective strategies;

* The quality of the tendon can be maximized by starting light exercises early before skeletal musculature maturity and increasing tendon strength/resistance to injury.

* Exercises performed after skeletal-muscular maturity can be performed with controlled ultrasonographic examination.

* The risk factors associated with tendinitis can be reduced. For example; Conditions such as the frequency of the horse's exercise, the floor surface on which it is working, the weight of the rider, regular hoof care, and shoeing errors should be reviewed.

* Early detection methods can be developed using more sensitive ultrasonography or serological markers.

REFERENCES

Alkan, Z., Salih, M., Bumin, A., Sarıerler, M. (1995) Atlarda fleksor tendoların ultrasonografik muayenesi. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi* 1 (1-2): 31-35.

Arıcan, M., Çalım, K.N., Kocabıyık, A., Yavuz, Ü. (2008) Atlarda ön ekstremite fleksor tendinitis'in ultrasonografik muayene ile değerlendirilmesi. *Veteriner Bilimleri Dergisi* 24 (2): 19-26.

Bertoni, L., Forresu, D., Coundry, V., Audigie, F., Denoix, J.M., Mira, M.C. (2013) Fractures of the third trochanter in horses: 8 cases (2000–2012) *Journal of the American Veterinary Medical Association* 243 (2): 261-266.

Boswell, S.G., Schnabel, L.V., Mohammed, H.O., Sundman, E.A., Minas, T., Fortier, L.A. (2014) Increasing platelet concentrations in leukocyte-reduced platelet-rich plasma decrease collagen gene synthesis in tendons. *American of Journal Sports Medicine* 42 (1): 42-49.

Dakin, S.G. (2017) A review of the healing processes in equine superficial digital flexor tendinopathy. *Equine Veterinary Education* 29 (9): 516-520.

Dilicikik, U., Demirel, H.A., Dönmez, G., Sargon, M.F., Birant, E., Doral, M.N. (2018) The effect of PRGF on healing of clamp-induced tendinopathy in animals. *Spor Hekimliği Dergisi* 53 (2): 51-58.

Dowling, B.A., Dart, A.J., Hodgson, D.R., Smith, R.K.W. (2000) Superficial digital flexor tendonitis in the horse. *Equine Veterinary Journal* 32 (5): 369-378.

Dyson, S.J. (2003) The Deep Digital Flexor Tendon, Desmitis of the Accessory Ligament of the Deep Digital Flexor Tendon. Diagnosis and Management of Lameness in the Horse ISBN 0-7216-8342-8 Copyright © 2003, Elsevier Science (USA). All rights reserved. Chapter: 71-72 pages: 644-654.

Dyson, S.J., Genovese, R.L. (2003) The Suspensory Apparatus. Diagnosis and Management of Lameness in the Horse ISBN 0-7216-8342-8 Copyright © 2003, Elsevier Science (USA). All rights reserved. Chapter: 73 pages: 654-673.

Dyson, S.J., Trotter, G. (2003) The Distal Phalanx and Distal Interphalangeal Joint.Diagnosis and Management of Lameness in the Horse ISBN 0-7216-8342-8 Copyright © 2003, Elsevier Science (USA). All rights reserved. Chapter: 34 pages: 310-325.

Gills, C.L. (1997) Rehabilitation of Tendon and Ligament Injuries. *Proceedings of the 43rd AAEP Annual Convention*, December 7-10, p. 306-309. Arizona/USA.

Herthel, D.J. (2001) Enhanced suspensory ligament healing in 100 horses by stem cells and other bone marrow components. *Proceedings of the 47th AAEP Annual Convention*, November 24-28, p. 319-321.

Jorgensen, J.S., Genovese, R.L., Ross, M.W., Dyson, S.J. (2003) Superficial Digital Flexor Tendonitis. Diagnosis and Management of Lameness in the Horse ISBN 0-7216-8342-8 Copyright © 2003, Elsevier Science (USA). All rights reserved. Chapter: 70 pages: 628-644.

McCarrel, T.M, Minas, T., Fortier, L.A. (2012) Optimization of leukocyte concentration in platelet-rich plasma for the treatment of tendinopathy. *Journal of the Bone Joint Surgery American* Oct 3; 94(19): e143(1-8).

O'Sullivan, B.C. (2007) Injuries of the Fleksor Tendons: Focus on the Superficial Digital Flexor Tendon. (C)Elsevier Inc. All rights reserved. *Clinic Technique Equine Practice* 6: 189-197.

Padaliya, N.R., Ranpariya, J.J., Kumar, D., Javia, C.B., Barvalia, D.R. (2015) Ultrasonographic assessment of the equine palmar tendons. *Veterinary World* EISSN: 2231-0916: 208-212.

Rick, M.C. (2003) Lameness of the Arabian Racehorse. Diagnosis and Management of Lameness in the Horse ISBN 0-7216-8342-8 Copyright © 2003, Elsevier Science (USA). All rights reserved. Chapter:112 p: 930-933.

Roger, K.W.S., Schramme, M. (2003) Tendon injury in the horse: Current theories and therapies. *In Practise* pp: 529-539.

Roger, K.W., Smith, M.A. (2008) Ultrasonography in the Dıagnosis of Lameness. *Proceedings of the 10th International Congress of World Equine Veterinary Association*, January 28 – February 1, Moscow, Russia.

Roger, K.W., Smith, M.A. (2008) Tendon and Ligament Injury. Proceedings of the 54th Annual Convention of the American Association of the Equine Practioners, December 6-10 p. 475-501, San Diego, California.

Samsar, E., Akın, F. (1998) Özel Cerrahi. Tamer Matbaacılık, Ankara.

Sarrafian, T.L., Case, J.T., Kinde, H., Draft, B.M., Read, D.H., Moore, J.D., Uzal, F.A., Stover, S.M. (2012) Fatal musculoskeletal injuries of Quarter Horse racehorses: 314 cases (1990–2007), *Journal American Veterinary Medicine Association* 241:935–942.

Schnabel, L.V., Mohammed, H.O., Miller, B.J. (2007) Platelet rich plasma (PRP) enhances anabolic gene expression patterns in flexor digitorum superficialis tendons. *Journal Orthopaedic Research* 25 (2): 230-240.

Seyrek-Intas, D., Celimli, N., Kaya, M. (2002) Atlarda tendo hastalıklarında ultrasonografik muayenenin sağaltım yönteminin seçimi üzerine etkisi. *Veteriner Cerrahi Dergisi* 8: 35–40.

Smith, R.K.W. (2003) Pathophysiology of Tendon Injury.Diagnosis and Management of Lameness in the Horse ISBN 0-7216-8342-8 Copyright © 2003, Elsevier Science (USA). All rights reserved. Chapter:70 pp: 616-628.

Smith RKW (2007) Mesenchymal stem cell therapy for equine tendinopathy. ISSN 0963-8288 print/ISSN 1464-5165 online ª 2007 Informa UK Ltd. (Informa Healthcare).

Smith, R.K.W., Allen, E.G. (2004) Tendon and ligament physiology 2004, Elsevier Limited. All rights reserved. Chapter:8 pp:130-151.

Temizoglu, M.D. (2005) Atlarda biceps brachii kası ve tendosunun ultrasonografik değerlendirmesi. *Ankara Universitesi Veteriner Fakultesi Dergisi* 52:77-83.

Tsang, A.S., Dart, A.J., Biasutti, S.A., Jeffcott, L.B., Smith, M.M., Little, C.B. (2019) Effects of tendon injury on uninjured regional tendons in the distal limb: An in-vivo study using an ovine tendinopathy model. *PLOS ONE* April 23: 1-24.

Whitton, R.C., Hodgson, D.R., Rose, R.J. (2007) İskelet -Kas Sistemi, Klinik Pratikte At Hekimliği (2007), Medipres yayıncılık, Chapter:4 p: 97-179.

Yavuz, Ü., Demirkan, I., Korkmaz, M. (2010) Atların Ön Bacak Fleksor Tendolarında Akut Peritendinitislerin Termografik, Ultrasonografik ve Radyografik Tanısı. *Kocatepe Veteriner Dergisi* 3 (1): 31-40.

Yılmaz, B., Kesikburun, S. (2013) Plateletten Zengin Plazma Uygulamalar. *Turk Fizyoloji Tıp Rehabilitasyon Dergisi* 59: 338-344.

Yucel, R. (2005) Atların Ortopedik Hastalıkları, Aktif yayıncılık, İstanbul.

BÖLÜM 14

THE EFFECTS OF PROBIOTICS AND PREBIOTICS ON ANIMALS AND THEIR FUTURE

Assoc. Prof. Dr. Oktay KAPLAN[1]

[1] Dicle University, Veterinary Faculty, Department of Animal Nutrition, and Nutritional Diseases, 21280, Diyarbakır,TURKEY; ORCID: 0000-0001-6143-8987; E-mail:okaplan61@gmail.com

1.INTRODUCTION

Probiotic; It is expressed as live microorganisms that have a beneficial effect on the host and improve the intestinal microbial balance. Today, the definition made by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) in 2002 was changed by the International Association of Probiotics and Prebiotics (ISAPP) in 2013 as "living organisms that, when taken in adequate amounts, have positive effects on the health of the host." updated to " (Pyne et al., 2012; Hill et al., 2014; Markowiak and Slizewska, 2017). Because of their beneficial effects on health and growth stimulation, probiotics are widely used especially in ruminant nutrition and poultry feed. Such formulations may contain one or more selected strains of microorganisms and, depending on the species and age of the host animals, they may be administered as a powder, suspension, capsule, pellet, gel or paste. They are used periodically or continuously as additives for feed and premixes directly (Anadon et al., 2014; Güler et al. 2019).

Prebiotics are indigestible food ingredients and carbohydrates that promote the growth of colon bacteria that positively affect human and animal health (Naidu et al., 1999). In other words, they are selectively fermented compounds that can make beneficial changes in the composition and activity of the gastrointestinal microflora (Gibson and Roberfroid, 1995). It is reported that 8-40 g/day should be taken for prebiotics to show the physiological effects stated (Rao, 2001). The most widely known prebiotic substances are oligosaccharides (Shin et

al., 2000). Oligosaccharides are indigestible polysaccharides consisting of 3-10 sugar units linked by glycosidic bonds. Oligosaccharides used as prebiotics; Since they have the ability to bind to fimbriae that allow pathogenic microorganisms to adhere to the intestinal surface, they prevent the colonization of pathogenic microorganisms and cause their excretion through feces (Spring, 1998).

2. USE OF PROBIOTICS AND PREBIOTICS IN ANIMAL NUTRITION

2.1. Use of probiotıcs and prebıotics in ruminants

2.1.1. Effect of probiotics and prebiotics on feed utility

Probiotics have found application areas, especially in cattle, in order to affect the composition of the microflora in the foregut and intestine in ruminants (Aytuğ et al., 1990). Various studies have been conducted on the use of probiotics in calves and lambs. Based on the results of 17 separate studies, Hooper reported that the average daily body weight gain increased by 5.7%, feed efficiency was improved by 5.6%, diarrhea events decreased by 37.3% and mortality rate decreased by 27.3% in calves given probiotics (Hooper, 1990). Gill gave probiotics to 307 calves for 28 days. Disease events in calves were also reduced by 10.9% (Gill et al., 1987). Gorgulu et al. (2001) in their study on the increase in live weight, immune system and feed conversion in calves fed with probiotics; reported that probiotics given with milk, colostrum, milk replacer feed or liquid beverages had a reducing effect on diarrhea cases, increased feed efficiency and increased daily live weight. Seo et al. (2011) in their study on feed efficiency, competition with pathogens

and milk yield, they found an increase in feed efficiency and live weight gain of probiotic additives, and a decrease in diarrhea cases. They reported that animals receiving probiotic additives were weaned more easily and the digestion of the consumed feeds increased, so that the feed additive also affected the early rumen development. Lubbadehl et al. reported in their study that the addition of probiotics to lactating goat and lamb feeds did not provide a significant increase in feed consumption and feed efficiency, but caused a decrease in cholesterol levels in lambs (Lubbadehl et al., 1999). Antunovic et al. (2005), in their study on weaned lambs; They stated that with the addition of probiotics, an increase in live weight and feed consumption was achieved, blood iron levels increased, and calcium, urea and glucose levels were reduced.

In another study conducted in sheep; It has been reported that probiotics cause an increase in the digestibility of nutrients, feed consumption, milk yield and quality (Hillal et al., 2011). Roodposhti and Dabiri (2012), in their study on calves, stated that the addition of prebiotics could significantly improve the increase in live weight in the sixth, seventh and eighth weeks and reduced the number of E. coli in feces. Hooper reported that average daily body weight gain increased by 6.4%, daily feed consumption increased by 6.1%, and lamb mortality decreased by 81.3% in lambs fed with probiotic added feed (Hooper, 1989). In addition to studies reporting positive effects of probiotics in calves, there are also studies reporting no statistically significant effects (Vanbelle et al., 1990).

2.1.2 Use of probiotics and prebiotics ın dairy cows

Many studies have stated that probiotics have a significant effect on the nutrition of dairy cows (Uygur, 1999). Many studies have shown that the use of probiotics in dairy cows has a positive effect on rumen parameters. As a matter of fact, in these studies, it was reported that a significant increase in the number of cellulolytic bacteria was achieved with the use of probiotics. It has been shown that the degree of digestion of cellulose in roughage increases, the utilization from lactic acid increases, the utilization from ammonia improves, and the rumen pH remains stable in the neutral range. It is reported that probiotics used in feeding dairy cows increase dry matter consumption by 1-2 kg/day and accordingly milk production by 1-1,5 kg/day (Karaayvaz and Alçiçek, 1999). The physiological reason for the positive effect of yeasts is mostly based on improving rumen conditions and increasing cellulotic activity (Alçiçek et al. 1998). Yeast cultures are added to the rations of lactating and dry dairy cows to potentially increase milk yield and dry matter intake and support the development of ruminal fermentation (Metin and Yanar, 2003). The most commonly used probiotic yeasts in the nutrition of ruminants are Saccharomyces cerevisiae and Torulopsis candida. Although it has only recently been recognized in our country, the use of probiotic Saccharomyces cerevisiae as a feed additive dates back to the 1980s in the USA (Karaayvaz, 2004). For this purpose, the effects of adding Saccharomyces cerevisiae to the rations were investigated in a trial initiated 21 days before calving in Jersey cows and continued for 140 days after calving. With the progress of the

experiment, it was observed that the cows that were added to their rations with Saccharomyces cerevisiae increased their dry matter consumption much more than those that were not added. The weight loss in the cows of the group that was added Saccharomyces cerevisiae to their ration after birth was much less than that of the cows that were not added. When the treatment groups were compared in terms of reaching the maximum milk yield of cows after calving, it was determined that this period was shorter in those fed Saccharomyces cerevisiae. However, the difference in total milk yield in this 140-day period after birth was not significant, and milk composition was not affected significantly (Metin and Yanar, 2003). In the case of the use of probiotics originating from Saccharomyces cerevisiae, dry matter consumption in dairy cows increased by 1.4 kg per day (Erasmus et al. 1992; Bakal, 1999; Karaayvaz and Alçiçek, 1999). Ayad et al. (2013), in their study on milk production and some biochemical parameters, found that milk production, milk fat and some biochemical parameters improved in animals fed with feed containing probiotics. In another study, the content of milk was examined. In this study, animals were given a ration consisting of grain, meadow grass, mixed feed, mineral substances and vitamins. In addition, 10 g/day Saccharomyces cerevisiae per animal was added to the rations every day. As seen in Table 1, the following results were obtained (Bakal, 1999).

Table 1: Effect of probiotic use on milk content.

Parameter	Trial Groups		Effect
	Control	Saccharomyces cerevisiae	
Milk production (kg/day)	24,6	25,9	+1,3 kg
Milk Fat production (g/day)	910	948	+4%
Protein production (g/day)	787	839	+7%

It has been observed in Table 2 that Aspergillus oryzae culture extracts improve rumen fermentation and consequently milk yield by reducing methane production (Frumholtz et al. 1989; Karaayvaz and Alçiçek, 1999).

Table 2: Effect of Aspergillus oryzae culture on milk yield.

Lactation Days	Milk yield kg/day	
	Control	Aspergillus oryzae
40-90	35,6	38,9
91-120	36,1	38,3
121-150	33,3	34,7

2.2. Use of probiotics and prebiotics in poultry feed

In poultry, lactic acid bacteria are usually dominant on the cell epithelium of the crop. Here, they adhere to starch particles to produce organic acids and reduce the pH to 4.5 or below, facilitating the digestion of feed. The microflora formed in the crop also constitutes the source of the intestinal microflora (Jernigan et al., 1985). In many studies conducted since the 1970s with the aim of using probiotics as growth factors in poultry, positive and negative results have been obtained regarding animal performance (Krueger et al., 1972; Jernigan

et al., 1985). In the first of two separate studies that he conducted with chicks by adding L. acidophilus to their feed, the live weight gain and feed efficiency were worse by 0.4% and 3.3%, respectively, in the 21-day trial period, and in the second, at the end of the 49-day trial period, the live weight gain increased by 2.31%. reported that utilization was not affected (Watkins and Kratzer., 1983; Watkins and Miller., 1983). In a study on Japanese quails, it was determined that prebiotic-probiotic combination and organic acid combinations added to their rations positively affected the development of intestinal villi of quails (Çakır et al., 2008). In another study, the effect of prebiotic-probiotic combination and organic acid combination applied to the diets of Japanese quails on the intestines was examined histochemically and differences in intestinal morphology, especially increases in mucin and serotonin secreting cell densities were detected. According to the results obtained from these studies, it is understood that prebiotic-probiotic and organic acid combinations have positive effects on the histological structures of the intestines in quail nutrition against the negative effects of antibiotics (Şimşek et al., 2012; Kaplan et al. 2018). At the end of the study carried out by Özcan et al. (2022) on quails, the highest live weight and live weight gain were determined in the liquid probiotic group, while the lowest live weight was determined in the count group. When the live weights recorded during the experiment were examined, the highest value was determined in the group that added liquid probiotics. When the feed conversion rate and feed consumption data were examined in the study, statistically significant differences were found between the experimental and control groups. In the

examinations performed on ileum tissue, the difference between the groups in terms of villus length and crypt depth was found to be insignificant. While there was a difference between the groups in terms of liver, gizzard and other internal organ weights from the addition of probiotics to the ration, no statistical difference was found in terms of heart weights. Differences were found between males and females in the carcass and, accordingly, in almost all parameters. Considering that this difference is due to gender, comparisons were made between the same sex and different groups. As a result; Considering its positive effects on fattening performance and other measured parameters, it was concluded that the use of probiotics in both powder and liquid form in quails will contribute positively to performance (Özcan et al. 2022). Kim et al. (2017), probiotic feeds used; reported that it has positive effects on the nutrition of chickens, digestive system, immune system and resistance to diseases.

Ivanovic et al. (2012) investigated the effect of probiotic nutrition on pH, chemical composition and fatty acids of meat. As a result; They stated that the addition of probiotics significantly reduced the fat, increased the water content in drumstick and breast meat, and caused differences in acid value. As a result, they stated that probiotics can be effective on fatty acid oxidation and change the taste of meat, and increase meat quality depending on its chemical composition. Guo et al. (2017), in their study; showed that long-term probiotic supplementation increased feed efficiency, eggshell durability, and decreased the number of Escherichia coli in feces. They stated that the

increase in the beneficial bacteria population increased the production performance. In laying hens given Lactobacillus cultures by Krueger et al. (1972), egg production increased by 3.03%, feed efficiency increased by 7.41%, fertility and hatching rate were not affected. Nursoy et al. added varying levels of yeast culture (Saccharomyces cerevisiae) to the laying hen rations and found that egg production, feed consumption, feed injury and egg weights were similar in all groups. Egg shape index was significantly higher in group II (0.2% yeast) and group III (0.3% yeast) compared to other groups. There was no difference between the groups in terms of egg shell breaking strength, egg shell thickness, egg yolk index, egg albumin index, Haugh unit, egg yolk color scores and egg quality values (Nursoy et al. 2004).

In a study by Alp et al., the addition of Lactiferm-L5 (Streptococcus faecium M-74, 5*10.9/g) alone and together with some antibiotics (avoparcin, virginiamycine, zinc bacitracin) to broiler feeds resulted in viability at the sixth and seventh weeks of slaughter age. reported that it did not have a significant effect on weight gain, feed efficiency, carcass yield, abdominal fat accumulation, small intestine weight and serum cholesterol amount (Alp et al., 1993). Chen and Chen (2003) found that the growth power, gut structure and length of broiler chickens fed with prebiotics increased in their study. In this study, it was reported that the live weight, feed conversion ratio, carcass weight and gut length of broilers increased. Zhou et al. (2010) stated in their study that probiotics are beneficial in daily weight gain and final weight of broilers. In studies, it has been determined that the live weight gain

and feed efficiency increase with the addition of a prebiotic preparation to the broiler rations (Kumprech et al., 1997).

2.3. Usıng probiotics and prebiotics in silage making

Organic acids, enzymes, antioxidants, nutrients and microorganisms are used as additives in silage production. Probiotics are added to the silage material by spraying in the form of a suspension of microorganisms along with dry yeast and $CaCO_3$ in the amount of 10.7 CFU/g (Shockey et al., 1988). Lactic acid bacteria added to the silage increase the amount of organic acids and decrease the pH of the silage, thus stopping the growth of enterobacteria, molds and yeasts in the silage (Kent et al., 1988). The increase of lactic acid bacteria in the silage suppresses the growth of proteolytic bacteria due to the anaerobic environment created by them, thus minimizing protein degradation in the silage of roughage containing high protein such as leguminous. It has been reported that silage made by adding lactic acid bacteria positively affects milk yield and milk protein of cows (Kung et al., 1987). Luther, on the other hand, determined that probiotic added silage increased feed efficiency in fattening calves (Luther, 1986).

3. SAFETY OF PREBIOTICS AND PROBIOTICS AND LEGAL REGULATIONS

There are no legal restrictions on the use of Lactibacillus-derived probiotics in America, Europe and Asia (Reid, 1999). However, there are hesitations about genetically modified microorganisms. Concerns about genetically modified microorganisms are increasing in the public

(Kuipers et al., 2000). In a study, Lactobacillus species were detected in 8 (0.24%) of 3317 blood samples obtained from sick people between 1989 and 1992, and as a result of their research, these factors were found to be effective. revealed that there is no interest among probiotic Lactibacillus (Kırjavainen et al., 1999).

The recommended daily dose of inulin and oligofructose is 1-4 g in the USA and 3-11 g in Europe. Inulin-type herbal fructans are considered natural food additives in many European countries and harmless in the United States. It has been stated that Nisin has been used in brine products, cheeses and other dairy products in many countries since the 1950s. The United States Food and Drug Administration (FDA) allowed the use of nisin in pasteurized dairy products in 1998 to prevent the reproduction of C. botulinum spores and toxin formation (Holton, 2000).

4. PROBIOTICS AND THE FUTURE OF PREBIOTICS

Research on probiotics has been inconclusive for the following reasons:

a-The presence of a large number of probiotic species and strains.

b-The characteristics of these factors are not fully clarified.

c-The effect of different storage conditions on these factors is not fully understood.

d-Even a single strain produces different effects according to individuals.

e-The high cost of detailed clinical applications (Klaenhammer, 2000).

The benefits of using probiotics and prebiotics or synbiotics are emphasized. However, although the beneficial effects resulting from the combined effects of inulin-type fructans and Bifidobacterium have been revealed in human and animal trials, there are still questions to be answered today.

For example;

a-How long is the persistence of the bifidogenic effect when the diet is stopped?

b-What exactly is the functional benefit from the synbiotic effect?

c-How clear is its reliability, although the benefit from dominating Bifidobacteria in the gut is not yet clear and has not been demonstrated in detail? like (Roberfroid, 2000),

In future studies on probiotics, it has been reported that the benefits of probiotic-effective bacteria and their interactions with the body will be clearly demonstrated, and its use against the formation of antibacterial resistance, which is becoming increasingly risky, will become widespread (Reid, 1999). It has not been clearly demonstrated how probiotics act as immunomodulators in the intestinal flora in health and disease (Erickson et al., 2000). Although the inhibitory effect of probiotics and prebiotics on cancer stem cells has been reported in experimental animals, there is a lack of information on the dose and duration of use (Brady et al., 2000). The production of antigens that improve cellular immunity by bacteria and their noncovalent attachment to the cell wall of a probiotic bacteria, and thus vaccination

using food, are among the research topics (Kuipers et al., 2000). The relationship of probiotics used as food supplements with many diseases has been investigated, and the data on the effects of today's dietary habits on human health are increasing. In recent years, when human genome projects have been put into practice and genetic differences between humans have been investigated, the effects of nutrition on individuals have varied. Most of the chemicals we take into our bodies through nutrition affect our genes. With further studies, it is possible that human life can be extended by arranging the right diet according to genetic structure in the near future. For this reason, the interest in nutritional genetics, which is the combination of two fields such as nutrigenetics and nutrigenomics, is increasing day by day in order to examine the positive and negative aspects of the diet-gene relationship on health (Ayhan and Soylu 2015). It is reported that bacteriocins such as nisin and niskicholine will be used in packaging materials and food preservation in the future (Holton, 2000). In food technology, it is aimed to suppress saprophytes and pathogens in order to increase the durability of the product and reduce the risk of infection. Today, studies are carried out in several branches (Kuipers et al., 2000).

These;

a-Suppression of stress-inducing genes: For this purpose, to make Lactobacillus more resistant to heat shock, sudden pH drop and external autolytic factors, and to develop hybrid strains that synthesize the desired proteins.

b-Metabolic engineering: It is aimed to obtain information about the metabolic activities of the agent with the help of mathematical models created in the computer environment, starting from the decoding of the genetic code of the bacterium and the understanding of the enzymes it produces. In this way, the bacteria can be prevented from producing the unwanted metabolite. For example, L. lactis produced lactate and acetoin. By transferring the acetolactate decarboxylase gene from Streptococcus mutans to L. lactis, 50% of the sugars are converted to diacetyl (butter flavor), and by transferring the dehydrogenase gene from B. spaericus, more than 99% of the sugars are converted to alanine (flavouring and sweetening).

c-By improving the proteolysis ability of L. lactis, progress has been made in increasing the aroma formation in cheeses and the production of lytic products such as bacteriocin.

d-Attachment system: To create target points where the beneficial substances secreted by the probiotic agent can hold.

REFERENCES

Alçiçek, A., Şayan, Y., Özkul., H. (1998). Ruminantların Beslenmesinde Probiyotik Kullanımında Yeni Gelişmeler, Hayvansal Üretim Dergisi. 38: 32-38.

Alp, M., Kahraman, R., Kacobağlı, N., Eren, M., Şenel, H.S. (1993). Lactiferm-L5 Ve Bazı Antibiyotiklerin Broyler Performansı, Abdominal Yağ Ve İnce Bağırsak Ağırlığı İle Kan Kolesterolüne Etkileri. İst. Üniv. Vet. Fak. dergisi. 19(2):145-157.

Anadon, A., Castellano, V., Martínez-Larrañaga, M.R. (2014). Regulation and guidelines of probiotics and prebiotics. In: Ötles S, editor. Probiotics and prebiotics in food, nutrition and health. Boca Raton, FL: CRC Press, LLC Taylor & Francis Group; 91–113.

Antunovic, Z., Speranda, M., Liker, B., Seric, V., Steiner, Z., Domacinovic, M. (2005). Influence of feding the probiotic pioneer to growing lambs on performances and blood composition. Acta Veterinaria, 55(4), 287-300.

Ayad, M.A., Benallou, B., Saim, M.S., Smadi, M.A., Meziane T. (2013). Impact of feeding yeast culture on milk yield, milk components, and blood components in Algerian dairy herds. Journal of Veterinary Science and Technology. 4(2), 1-5.

Ayhan N.Y ve Soylu M. (2015). Nütrisyonel Genomik-İnsan Yaklaşımı. Turkiye Klinikleri J Nutr Diet-Special Topics.1(3):25-30

Aytuğ, C.N., Alaçam, E., Özkoç, Ü., Yalçın, B.B., Türker, H., Gökçen, H. (1990). Koyun- Keçi Hastalıkları ve Yetiştiriciliği. Tüm Vet. Hayavancılık Hizmetleri Yay. No:2, İstanbul.

Bakal, A. 1999. Ruminantların beslenmesinde probiyotik kullanımı. Bitirme Tezi, Ege Ü. Z. F. Zootekni Bölümü.

Brady, L.J., Gallaher, D.D., Busta, F.F. (2000). The role of probiotic cultures in the prevention of colon cancer. Journaj of Nutr, 130:410-414.

Chen, Y.C., Chen, T.C. (2003). Effect of adding chicory fructans in feed on broiler growth performance, serum cholesterol and intestinal lenght. International Journal of Poultry Science. 2(3), 214-219.

Çakır S., Midilli M., Erol H., Şimşek N., Çınar M., Altıntas A., Alp H., Altıntas L., Cengiz Ö., Antalyalı A. (2008). Use of combined probiotic-prebiotic, organic acid and avilamycin in diets of Japanese quails. Revue Méd. Vét., 159, 565-569.

Erasmus, L.J., Botha, P.M., Kisner, A. (1992). Effect of yeast culture supplement on production, rumen fermentation, and duodenal nitrogen flow in dairy cows. J. of Dairy Science. 75, 3056-3065.

Erickson, K.L. and Hubbard, N.E. (2000). Probiotic immunomodulation in health and disease. J Nutr, 130:403-409.

Frumholtz, P.P., Newbold, C.J., and Wallace, R.J. (1989). Influence of Aspergillus oryzae fermentation extract on the fermentation of a basal ration in the rumen simulation technique (Rusitec). J. Agric. Sci. 113:169-172. doi:10.1017/S002185960008672X.

Gibson, G.R. and Roberfroid, M.B. (1995). Dietary modulation of the human colonic microbiota introducing the concept of prebiotics. J. Nutr. 125, 1401-1412.

Gill, D.R., Smith, R.A., Ball, R.L. (1987). The effect of probiotic feeding on health and performance of newly-arrived stocker calves. Anim. Sci. Research Report. 202-204.

Gülmez M. ve Güven, A. (2002). Probiyotik, prebiyotik ve sinbiyotikler. Kafkas Üniv. Vet. Fak. Derg. 8, 83-89.

Görgülü, M., Öngel, E., Yurtseven, S., Kutlu, H. R., Siuta A., 2001. Effects of probiotic on growing performance and health of calves. Çukurova Üniversitesi Ziraat Fakültesi Dergisi, 16, 73-78.

Guo, J. R., Dong, X.F., Liu, S., & Tong, J.M., 2017. Effects of long-term Bacillus subtilis CGMCC 1.921 supplementation on performance, egg quality, and fecal and cecal microbiota of laying hens. Poultry Science. 96(5), 1280-1289.

Güler, A., Kaplan., O., Bozkaya, F., 2019. Bazı kaba yemlere ilave edilen probiyotiklerin in vitro organik madde sindirimi ve metan üretimi üzerine etkileri. Harran Üniv Vet Fak Derg. 8 (1): 93-98.

Hill, C., Guarner, F., Reid, G., Gibson, G.R., Merenstein, D.J., Pot, B., Sanders, M.E. 2014. The International Scientific Association for Probiotics and Prebiotics

consensus statement on the scope and appropriate use of the term probiotic. Nature Reviews Gastroenterology & Hepatology, 11(8), 506-514.

Hillal, H., El-Sayaad, G., Abdella, M., 2011. Effect of growth promoters (probiotics) supplementation on performance, rumen activity and some blood constituents in growing lambs. Archiv Tierzucht. 54(6), 607-617.

Holton W.C. 2000. Fresh ideas for food safety. Environ Health Perspec, 108(11):516-519.

Hooper, P. 1989. The role of probiotics (intestinal inoculants) in productinon animals, World Associations of Veterinary Food Hygienists(jubilee) İnternational Sympoisum in Stockholm, 2-7 July, 27-30.

Hooper, R. 1990. Probiotics-İntestinal İnoculants For Production Animals. In: Probiotics in Animal Nutrition Of Animals. Sbornik Prednasek.19-21 November 1990: Brno. Pp. 69-88.

Ivanovic, S., Pisinov, B., Maslic-Strizak, D., Savic, B., Stojanovic, Z. (2012. Influence of probiotics on quality of chicken meat. African Journal of Agricultural Research, 7, 2191-2196.

Jernigan, M.A., Miles, R.D., Arafa, A.S. (1985). Probiotics in Poultry Nutrition. A - World's Science. 41(2):99-107.

Kaplan, O., Avci, M., Denek, N., Baran, M.S., Nursoy, H., Bozkaya, F. (2018). Influence of humic acid addition to drinking water on laying performance and egg quality in Japanese quails. Indian J. Anim. Res., 52(9) 1309-1312.Doi: 10.18805/ijar.B-874.

Karaayvaz, B. K. ve A. Alçiçek. (1999). Süt İneklerinin Beslenmesinde Probiyotik Kullanımı Uluslararası Hayvancılık Kongresi, İzmir, 233-236.

Karaayvaz, B.K. (2004). Probiyotiklerin Kuzu Besisinde İn-Vivo ve İn-Vitro Etkilerinin Araştırılması. Ege Ü. Fen Bilimleri Enstitüsü Doktora Tezi.

Krueger, W.F., Bradley, J.W., Patterson, R.H. (1972). The interaction of gentian violet and Lactobacillus organisms in the diet of Leghorn hens. Poultry Sci. 56, 1729.

Kent, B.A., Aramber, M.J., Walters, J.L. (1988). Effects of bacterial inoculant on alfalfa haylage: ensiling characteristics and milk production response when fed to dairy cows in early lactation. J. Dairy Sci., 71, 2457-2461.

Kırjavainen, P.V., Tuomola, E.M., Crittenden, R.G., Ouwehand, A.C., Harty, D.W.S., Morris, L.F., Rautelin, H., Playne, M.J., Donohue, D.J., Salminen S.J. (1999). İn vitro adhesion and platelet aggregation properties of bacteremia-associated lactobacilli. İnfect immun, 67(5):2653-2655.

Kim, H.W., Miller, D.K., Yan, F., Wang, W., Cheng, H.W., Yuan, H., Kim, B. (2017). Probiotic supplementation and fast freezing to improve quality attributes and oxidation stability of frozen chicken breast muscle. LWT- Food Science and Technology, 75, 34-41.

Klaenhammer, T.R. (2000). Probiotic bacteria: today and tomorrow. Journal Nutr, 130:415-416.

Klaenhammer, T.R. (2000). Probiotic bacteria: today and tomorrow, Journal of Nutrition 130:415-416.

Kuipers O.P., Buist G. and Kok J. (2000). Current strategies for inprovent food bacteria. Res Microbiol, 151:815-822.

Kumprech, I., Zobac P., Sikse V., Sefton AE., Spring P. (1997). Effect of dietary, mannanoligosaccharide level on live weight and feed efficiency of broilers. Proceedings Int. Symp. Nondigestible Oligosaccharides. Graduate School Vlag, Wageningennl, 144.

Kung, L., Satter, L.D., Jones, B.A., Genin, K.W., Sudoma, A.L., Enders, G.L., Kim, H.S. (1987). Microbial inoculation of low moisture alfalfa silage. J. Dairy Sci. 70, 2069-2077.

Lubbadehl, W., Haddadin, M.S.Y., Al-Tamimi, M.A., Robinson, R.K. (1999). Effect on the cholesterol content of fresh lamb of supplementing the feed of Awasi ewes and lambs with Lactobacillus acidophilus. Meat Science, 52, 381- 385.

Luther, R.M. 1986. Effect of mikrobial inoculation of whole-plant corn silage chemical characteristics, preservation and utilization by steers. J. Anim. Sci., 63, 1329-1336.

Markowiak, P., & Śliżewska, K. (2017). Effects of probiotics, prebiotics, and synbiotics on human health. Nutrients, 9(9), 1021.

Metin, J. ve Yanar. M. (2003). Probiyotikler ve sığır yetiştiriciliğinde kullanımı. Yem Magazin dergisi. 34: 47-50.

Mussatto, S.I., Mancilha, I.M. (2007). Non-digestible oligosaccarides. Carbohidrate Polymers, 68, 587- 597.

Naidu A.S., Bidlack WR., Clemens RA. (1999). Probiotic spectra of lactic acid bacteria. Crit. Rev. Food Sci. Nutr. 38, 13-126.

Nursoy, H., Kaplan, O., Oğuz, M. N., Yılmaz, O. (2004). Effects Of Varying Levels Of Yeast Culture On Yield And Some Parameters İn Laying Hen Diets. Indian Veterinary Journal.81: 59-62.

Özcan, C, Tufan, T., Karakoç, Z., İrak, K., Arslan, C., Kaplan, O. (2022). The Effect of Using Different Forms of Probiotic (Bacillus sp.) on Fattening Performance, Blood and Carcass Parameters in Japanese quail (Couturnix Couturnix Japonica). ISPEC Journal of Agr. Sciences 6(1): 178-188.

Pyne, D.B., West, N.P., Cripps, A.W. (2012). Probiotics and immune response to exercise. European Journal of Sport Science. 7(1), 51-59.

Roodposhti, P. M. and Dabiri, N. (2012). Effects of probiotic and prebiotic on average daily gain, fecal shedding of *Escherichia coli*, and immune system status in newborn female calves. Asian-Australasian Journal of Animal Sciences, 25(9), 1255 – 1261.

Rao V.A. (2001). The prebiotic properties of oligofructose at low intake levels. Nutr. Res., 21, 843-848.

Reid G. (1999). The scientific basis for probiotic strains of lactobacillus. Appl Environ Microbiol. 65(9): 3763-3766.

Roberfroid M.B. (2000). Prebiotics and probiotics: are they functional food. Am J. Clin Nutr, 71:1682-1687.

Sarıca, Ş. 1999. Kanatlı hayvan beslemede probiyotik kullanımı. Hayvansal Üretim Dergisi. 39-40: 105-112.

Seo, Y.S., Lim, J.Y., Choi, B.S., Kim, H., Goo, E., Lee, B., Hwang, I. (2011). Complete genome sequence of Burkholderia gladioli BSR3. Journal of bacteriology.

Shin HS., Lee H., Pestka JJ., Ustunol Z. (2000). Growth and viability of commercial Bifidobacterium spp. in skim milk containing oligosaccharides and inulin. J. Food Sci., 65, 884-887.

Shockey, W.L., Dehority, B.A., Conrad, H.R. (1988). Effects of microbial inoculant on fermentation of poor quality alfalfa. J. Dairy Sci., 71, 722-726.

Spring P. (1998). The effect of age and environment on the avian gastrointestinal microflora and its role in the development of competitive exclusion products. Feed Compounder.18, 16-20.

Şimşek N., Can I., Karadeniz A., Kara A., Gumus R. (2012). Effects of dietary various supplementations on the mucin and serotonin releasing cell numbers in small intestine of quails. Revue Med. Vet. 163, 328-334.

Uygur, A.M. (1999). Hayvan besleme ve yem endüstrisinde biyoteknolojiden yararlanma olanakları, E. Ü. Fen Bilmleri Enstitüsü Yüksek Lisans Tezi.

Watkins, B.A. and Kratzer, F.H. (1983). Effect of oral dosing of Lactobacillus strains on gut colonization and liver biotin in broiler chick. Poultry Sci. 62, 2088-2094.

Watkins, B.A. and Miller, B.F. (1983). Competitive gut exclusion of avian pathogens by Lactobacillus acidophilus in gnotobiotic attacks. Poultry Sci. 62, 1772-1779.

Vanbelle, N., Teller, E., Focant, M. (1990). Probiotics in Animal Nutrition. A Review. Arciv Animal Nutrition 40:543-567.

Zhou, X., Wang, Y., Gu, Q., Li, W. (2010). Effect of dietary probiotic, *Bacillus coagulans*, on growth performance, chemical composition, and meat quality of Guangxi Yellow chicken. Poultry science, 89(3), 588-593.

CHAPTER 15

THE EGG PRODUCTION, GROWTH, SLAUGHTER AND CARCASS CHARACTERISTICS OF NATIVE GEES (*Anser anser*) RAISED UNDER BREEDERS CONDITIONS IN KARS; II. GROWING, SLAUGHTER AND CARCASS CHARACTERISTICS

Assoc. Prof. Dr. Kadir ONK[1], Prof. Dr. Turgut KIRMIZIBAYRAK[2]

[1] Department of Animal Breeding and Husbandry, Faculty of Veterinary Medicine, Kafkas University, 3610, Kars, Türkiye. https://orcid.org/0000-0002-5618-2988, kadironk@hotmail.com
[2] Department of Animal Breeding and Husbandry, Faculty of Veterinary Medicine, Kafkas University, 3610, Kars, Türkiye. https://orcid.org/0000-0003-3626-6137, turgut98@hotmail.com

1. INTRODUCTION

Many countries in the world are trying to utilize different nutritional sources as well as increasing production in order to meet the food deficit. Geese among the species of poultry are also utilized as nutrient in various geographies across the world. Even though geese do not grow as fast as other poultry animals that are commercially raised, they possess lower costs for raising due to their low protein requirements. Among domesticated poultry, they are the most durable animals with longest service life in production. Life span of geese generally vary between 10 and 60 years, this time may be 3-5 years in average in geese raised for their meat and may increase up to 10 years for extensive raising (Puchajda et al. 1989; Tilki and Inal 2004a).

Even though goose breeding is performed under various production values in all of the countries in the world, it is more intense in countries with cold climate. Goose and duck meat have an important place in some of Eastern European countries, as well as East and Southeast Asian Countries (Ibtisham et al. 2017; Uhlirova et al. 2018).

It is possible to see goose breeding in all regions of Türkiye. Traditional family type extensive breeding is performed mostly in Northeastern Anatolian, South Anatolian, West Black Sea, Central Anatolia regions based on regions, almost in all of the provinces, particularly in Ardahan, Kars, and Muş. In family type extensive breeding, geese are raised for 8-10 months after they hatch and then slaughtered. Family business sell those geese which are not raised for intra-family requirements either

alive or slaughtered at the market. (Tilki and İnal 2004b; Tuik 2007). Growth performance is affected by some factors such as genotype, selection rate, age, gender, nutrition, stocking density, environment and production system (Fanatico et al. 2007; Wang et al. 2009). Although incidents happening during incubation or after hatching may influence growth too, drawing conclusions in this regard seems difficult because of the insufficient studies about this issue. (Tona et al. 2004; Sabry et al. 2013).

Slaughter and carcass characteristics of geese change in respect of breed, variety, selection level, gender, age, nutrition, production system and fattening period (Fortin et al. 1983; Tilki and Inal 2004b; Shi et al. 2010; Liu et al. 2011). Stocking density, production season, environmental condition at slaughter and the interactions of these factors may also effect on these characteristics (Castellini et al. 2002; Karacay et al. 2008).

Most of the studies conducted on poultry focused on chicken, quail, and turkey. Even though the number of studies on goose breeding in Türkiye is not sufficient, limited number of studies on goose concentrated on slaughter and carcass characteristics under intensive breeding conditions. This study was conducted to determine growth, slaughter and carcass traits of geese under breeder conditions in province of Kars, where goose breeding is common in Türkiye.

2. MATERIAL AND METHODS

2.1. Animal

The study was conducted on geese belonging to a total of 60 goose breeders in central district and various settlements in the province of Kars, Türkiye. Breeders were not interferred during growing period of geese. The breeders fed the geese in the first week with milk, milk bread mixture and fresh herbs. Then they fed chick feeds n addition to fresh herbs until one month old. After one month geese grazed on the pasture. One month before the slaughter, in addition to the pasture, geese were fed with barley break in the evenings.

The numbers of geese used in this study were 1367 geese in hatching and 1079, 1067, 1061, 1057, 1044, 963, and 408 geese aged 30, 60, 90, 120, 150, 180, and 210 days, respectively.

2.2. Growth monitor

Geese used in the study were attached a wing number and weighed after they had hatched. They were weighed at hatch date and in 30-day intervals starting from the date of hatching to determine live weight and changes in live weight during the study.

2.3. Determination of slaughter and carcass traits

Slaughtering of geese was done in central Kars and its vicinity. The geese were did not receive additional feeding for 12 h before slaughtering, but water continued to be supplied until slaughter. The

weights of the geese were measured before slaughter. Geese were killed by exsanguination with a neck cut that severed the carotid artery and jugular vein. The blood weights were determined by waiting 15-20 minutes after slaughtering and weighing the geese second time. Then, after feather removal with dry and wet method which included immersing the geese in hot water (60-65°C) for 1-3 minutes, the geese were weighed the third time to determine feather weights.

The abdomen of the geese was opened, firstly the abdomen fat was removed and weighed and then after removing and cleaning the internal organs, gizzard, heart, liver, lung, intestine and intestinal fat were weighed separately. After removal of the internal organs, the carcass was cleaned and hot carcass weights were determined as percentage of live weight at slaughter. Then, after waiting at +4 0C for 24 hours, carcass was weighed again to determine the cold carcass weights.

Carcass yield, and blood, feather, head, feet, liver, heart, gizzard, intestines and abdominal fat relative weights are calculated as a percentage of live weight at slaughter. In order to determine slaughter and carcass traits, 511 (174 at 180 days of age, 337 at 210 days of age) of 1055 geese whose growth were followed in this study were slaughtered. Carcass traits were determined by cutting carcasses of 153 (52 at 6 months of age, 101 at 7 months of age) of the geese slaughtered. These 511 geese were randomly selected among the 1055 geese whose growth were observed from hatching to slaughter. In this study, while live weight, carcass and its parts were measured with a scale with 0.1g

sensitivity and internal organs were measured with a scale with 0.01g sensitivity.

2.4. Statistical analysis

General Linear Model in SPSS 18.0 statistical computer program was used to examine the factors affecting growth, slaughter and carcass traits of geese. According to this model;

For hatching weight of geese, the following equation was formed:

$Y_{ijk} = \mu + a_i + b_j + e_{ijk}$.

Y_{ijkl}: Examined efficiency trait of any goose, μ: Expected mean, a_i: Maternal feather color (i: 1-5; white, black, brown, pied, and grey), b_j: group of egg weight (j: 1-5; ≤140.00, 140.01-150.00, 150.01-160.00, 160.01-170.00 ve 170.01≥) and e_{ijkl}: Term of error.

For growth traits of geese aged between 30-120 days, the following equation was formed:

$Y_{ijklm} = \mu + a_i + b_j + c_k + d_l + e_{ijklm}$.

Y_{ijkl}: Examined efficiency trait of any goose, μ: Expected mean, a_i: Maternal feather color (i: 1-5; white, black, brown, pied, and grey), bj: group of egg weight (j:1-5; ≤140.00, 140.01-150.00, 150.01-160.00, 160.01-170.00 ve 170.01≥), c_k: Sex (k: 1-2; male and female), d_l: Hatching weight group (d_l: 1-5; ≤ 89.99, 90.00-94.99, 95.00-99.99, 100.00-104.99 and 105.00≥) and e_{ijklm}: Term of error.

For slaughter and carcass traits of geese, the following equation was formed:

$Y_{ijkl} = \mu + a_i + b_j + c_k + e_{ijkl}$.

Y_{ijkl}: Examined efficiency trait of any goose, μ: Expected mean, a_i: Maternal feather color (i: 1-5; white, black, brown, pied, and grey), b_j: Sex (j: 1-2; male and female), c_k: age of slaughter (k: 1-2; 6 and 7 months) and e_{ijkl}: Term of error.

Duncan test was used in SPSS 18.0 statistical program to compare significance between groups in terms of examined traits.

3. RESULTS AND DISCUSSION

Table 1 shows live weights of geese in different periods of the growth in terms of examined factors. Maternal feather coluor, egg weight, and sex were determined to have a significant effect on hatching weight ($P<0.001$). Hatching weight was determined to be the highest in chicks with grey feather and the lowest in chicks with white feather in terms of maternal feather color and the highest in eggs heavier than 170 g and the lowest in eggs lighter than 140 g among egg weight groups.

There were statistically significant differences in maternal feather color in terms of followed time periods of the growth ($P<0.05$-0.001). Generally, growth was greater in chicks obtained from mothers with white and grey color and lower in those obtained from pied mothers among the maternal feather color group. In terms of egg weight, the

highest mean live weight in periods of growth was determined in geese hatching from eggs heavier than 160.01 g. Mean live weight at the examined age was found to statistically increase as weight of the egg increased. As hatching weight increased in early periods of the growth (30-90 days) live weight increased statistically in terms of the effect of hatching weight on growth. The growth difference between hatchlings heavier than 90.00 g disappeared since 120 days of age, however, growth in hatchlings lighter than 90.00 g had the lowest live weight in every period of the growth. Mean live weight of male geese was higher in all months compared to female geese.

Table 2 shows mean and standard error values of slaughter traits in geese in terms of sex and slaughter age. Statistically significant differences were determined between weights of slaughter, hot carcass, blood, feather, head, foot, heart, liver, lung, gizzard, and intestine in terms of sex ($P<0.05$-0.001). While weights of blood, head, foot, heart, liver, and lung were insignificant in terms of slaughter age ($P>0.05$), there were statistically significant differences between other examined traits ($P<0.05$-0.001). While slaughter, feather and gizzard weights and foot, heart, liver and gizzard rates were high at 210 days of age, blood, feather, head, lung rates were high at 180 days of age.

Table 1 - Live Weights of Geese in Different Periods of Growth (Hatching - 210 Days of Age) in Terms of The Examined Factors.

Group	Hatching weight (g)		30 day		60 day		90 day		120 day		150 day		180 day		210 day	
	n	$\overline{X} \pm S_{\overline{X}}$	n	$\overline{X} \pm S_{\overline{X}}$	n	$\overline{X} \pm S_{\overline{X}}$	n	$\overline{X} \pm S_{\overline{X}}$	n	$\overline{X} \pm S_{\overline{X}}$	n	$\overline{X} \pm S_{\overline{X}}$	n	$\overline{X} \pm S_{\overline{X}}$	n	$\overline{X} \pm S_{\overline{X}}$
Maternal Feather Colour		***		***		**		**		*		**		***		***
White	376	93.39 ± 0.41c	286	971.93 ± 10.65a	285	1861.46 ± 20.10a	285	2820.54 ± 24.11a	285	3480.55 ± 28.60a	285	4055.33 ± 31.78a	252	4489.23 ± 35.08b	108	4826.81 ± 54.16ab
Black	321	93.92 ± 0.44c	259	925.12 ± 10.85b	255	1820.17 ± 20.57b	253	2724.18 ± 24.72c	251	3372.54 ± 29.38b	239	3927.29 ± 33.45bc	215	4383.26 ± 36.85c	97	4646.01 ± 58.70b
Brown	162	95.25 ± 0.59b	130	895.40 ± 14.28c	129	1744.94 ± 26.98c	126	2708.14 ± 32.77cd	126	3376.54 ± 38.84b	126	3958.27 ± 43.10b	126	4459.88 ± 45.28b	67	4648.01 ± 64.10b
Piebald	457	93.43 ± 0.36c	367	917.75 ± 9.05b	361	1829.17 ± 17.17b	360	2708.46 ± 20.60cd	358	3374.69 ± 24.53b	357	3908.45 ± 27.34c	339	4313.40 ± 29.34d	121	4478.84 ± 48.30c
Grey	51	100.18 ± 1.06a	37	977.87 ± 27.50a	37	1865.14 ± 51.80a	37	2768.93 ± 62.00b	37	3458.44 ± 73.48a	37	4033.59 ± 81.56a	31	4553.72 ± 92.71a	15	5007.48 ± 137.80a
Egg Weight (g)		***		***		**		**		***		***		***		***
≤140.00	91	79.28 ± 0.81e	71	875.98 ± 22.52c	70	1727.61 ± 42.64c	67	2584.15 ± 52.02d	66	3182.30 ± 61.97d	63	3667.32 ± 69.98c	63	4075.38 ± 74.28d	45	4403.80 ± 99.49d
140.01 – 150.00	175	90.43 ± 0.61d	136	895.36 ± 15.99c	135	1816.61 ± 30.19b	135	2743.59 ± 36.16c	135	3409.49 ± 42.87c	130	3966.38 ± 47.99bc	123	4438.55 ± 52.22c	59	4705.41 ± 77.33c
150.01 – 160.00	428	95.98 ± 0.43c	338	951.81 ± 10.75b	334	1872.30 ± 20.34a	332	2790.84 ± 24.39b	331	3468.62 ± 28.92b	326	4032.74 ± 32.28b	299	4503.22 ± 35.67b	97	4671.17 ± 60.37c
160.01 – 170.00	407	103.08 ± 0.40b	322	976.71 ± 10.87a	316	1826.92 ± 20.63b	315	2794.15 ± 24.75b	313	3477.22 ± 29.38ab	313	4072.59 ± 32.62ab	295	4526.67 ± 35.30b	110	4800.89 ± 56.06b
170.01≥	266	107.42 ± 0.47a	212	988.15 ± 13.52a	212	1877.45 ± 25.51a	212	2817.51 ± 30.54a	212	3525.13 ± 36.19a	212	4143.92 ± 40.16a	183	4655.68 ± 44.65a	97	5025.88 ± 61.86a
Hatching Weight (g)				***		***		***		**		**		**		**
<90.00			239	832.75 ± 12.62e	236	1600.42 ± 23.85d	233	2577.94 ± 28.70c	231	3298.66 ± 34.10c	223	3857.81 ± 38.22c	215	4300.57 ± 41.41c	114	4686.36 ± 60.67b
90.00 – 94.99			157	903.52 ± 14.84d	153	1799.91 ± 28.21c	151	2807.25 ± 34.06ab	151	3462.49 ± 40.38a	151	4032.26 ± 44.85ab	142	4502.81 ± 48.69a	57	4912.41 ± 76.02a
95.00 – 99.99			210	932.44 ± 13.28c	209	1832.84 ± 25.09c	208	2741.49 ± 30.16b	208	3399.75 ± 35.76b	205	3966.59 ± 39.93b	194	4426.14 ± 43.33b	81	4760.11 ± 65.88ab
100.00 – 104.99			167	973.96 ± 15.01b	166	1910.62 ± 28.38b	166	2791.67 ± 34.07ab	164	3440.60 ± 40.51ab	162	3990.09 ± 45.27ab	149	4457.53 ± 49.78ab	53	4694.47 ± 81.06b
105.00≥			306	1045.35 ± 12.68a	303	1977.09 ± 23.95a	303	2811.89 ± 28.80a	303	3461.26 ± 34.15a	303	4036.17 ± 37.97a	263	4512.45 ± 41.99a	103	4553.81 ± 64.70c
Sex		***		***		***		***		***		***		***		***
Male	719	96.32 ± 0.37	555	973.30 ± 9.36	551	1900.18 ± 17.68	548	2860.44 ± 21.29	547	3568.96 ± 25.25	539	4169.73 ± 28.20	500	4654.20 ± 30.78	215	4895.93 ± 44.95
Female	648	94.15 ± 0.36	524	901.91 ± 9.36	516	1748.18 ± 17.69	513	2631.66 ± 21.34	510	3256.14 ± 25.34	505	3783.46 ± 28.31	463	4225.60 ± 31.36	193	4546.93 ± 48.07
General	1367	95.24 ± 0.30	1079	937.60 ± 7.98	1067	1824.18 ± 15.07	1061	2746.05 ± 18.20	1057	3412.55 ± 21.60	1044	3976.59 ± 24.13	963	4439.89 ± 26.59	408	4721.43 ± 38.75

[a,b,c,d,e]: The differences among the values bearing different superscript on the same row line are significant (P<0.05), **: P<0.01,***: P<0.001

Table 2 - Mean and Standard Error Values of Slaughter Traits in Geese in Terms of Sex and Slaughter Age

Slaughter traits	Sex			Slaughter age			General (n=511)
	Male (n=267)	Female (n=244)		180 day (n=174)	210 day (n=377)		
	$\overline{X} \pm S_{\overline{x}}$	$\overline{X} \pm S_{\overline{x}}$	P	$\overline{X} \pm S_{\overline{x}}$	$\overline{X} \pm S_{\overline{x}}$	P	$\overline{X} \pm S_{\overline{x}}$
Slaughter weight (g)	4696.61 ± 41.02	4361.40 ± 42.88	***	4384.62 ± 48.01	4673.39 ± 36.89	***	4529.01 ± 33.13
Blood weight (g)	221.83 ± 2.11	212.06 ± 2.20	***	218.68 ± 2.47	215.20 ± 1.90	-	216.94 ± 1.70
Blood percentage (%)	4.77 ± 0.05	4.92 ± 0.05	*	5.02 ± 0.06	4.67 ± 0.04	***	4.84 ± 0.04
Feather weight (g)	336.70 ± 2.11	326.41 ± 2.21	***	328.40 ± 2.47	334.71 ± 1.90	*	331.56 ± 1.70
Feather percentage (%)	7.25 ± 0.06	7.58 ± 0.06	***	7.58 ± 0.70	7.25 ± 0.05	***	7.42 ± 0.05
Head weight (g)	166.23 ± 1.38	157.65 ± 1.45	***	160.55 ± 1.62	163.34 ± 1.25	-	161.94 ± 1.12
Head percentage (%)	3.57 ± 0.03	3.65 ± 0.03	*	3.70 ± 0.03	3.52 ± 0.03	***	3.61 ± 0.02
Foot weight (g)	126.72 ± 1.42	120.77 ± 1.49	*	123.21 ± 1.28	124.28 ± 1.67	-	123.75 ± 1.15
Foot percentage (%)	2.72 ± 0.03	2.80 ± 0.03	*	2.66 ± 0.03	2.86 ± 0.03	***	2.76 ± 0.02
Heart weight (g)	38.09 ± 0.40	36.14 ± 0.41	***	36.77 ± 0.36	37.46 ± 0.46	-	37.11 ± 0.32
Heart percentage (%)	0.82 ± 0.01	0.84 ± 0.01	-	0.80 ± 0.01	0.86 ± 0.01	***	0.83 ± 0.01
Liver weight (g)	75.68 ± 0.95	72.08 ± 0.99	**	72.94 ± 0.85	74.81 ± 1.11	-	73.88 ± 0.76
Liver percentage (%)	1.63 ± 0.02	1.68 ± 0.02	-	1.58 ± 0.02	1.73 ± 0.03	***	1.65 ± 0.02
Lung weight (g)	36.60 ± 0.39	35.09 ± 0.41	**	35.59 ± 0.45	36.10 ± 0.35	-	35.84 ± 0.31
Lung percentage (%)	0.79 ± 0.01	0.81 ± 0.01	*	0.82 ± 0.01	0.78 ± 0.01	***	0.80 ± 0.01
Gizzard weight (g)	184.05 ± 1.80	174.62 ± 1.89	***	168.27 ± 1.62	190.40 ± 2.11	***	179.33 ± 1.46
Gizzard percentage (%)	3.97 ± 0.04	4.06 ± 0.05	-	3.64 ± 0.04	4.39 ± 0.05	***	4.02 ± 0.04
Intestine weight (g)	145.75 ± 1.52	139.77 ± 1.59	**	139.69 ± 1.37	145.83 ± 1.78	**	142.76 ± 1.23
Intestine percentage (%)	3.13 ± 0.03	3.24 ± 0.03	**	3.36 ± 0.04	3.02 ± 0.03	***	3.19 ± 0.03

-: insignificant (P > 0.05), *: P<0.05, **: P<0.01, ***: P<0.001

Table 3 - Mean and Standard Error Values of Slaughter Traits in Geese in Terms of Different Feather Color

Slaughter traits	Feather colour						
	Black (n=110)	White (n=122)	Brown (n=45)	Piebald (n=203)	Grey (n=31)		General (n=511)
	$\overline{X} \pm S_{\overline{x}}$	$\overline{X} \pm S_{\overline{x}}$	$\overline{X} \pm S_{\overline{x}}$	$\overline{X} \pm S_{\overline{x}}$	$\overline{X} \pm S_{\overline{x}}$	P	$\overline{X} \pm S_{\overline{x}}$
Slaughter weight (g)	4614.66 ± 56.53a	4452.86 ± 52.84ab	4613.57 ± 86.85a	4414.74 ± 41.15b	4549.19 ± 103.74ab	*	4529.01 ± 33.13
Blood weight (g)	220.22 ± 2.90	216.94 ± 2.72	215.69 ± 4.46	214.13 ± 2.11	217.73 ± 5.33	-	216.94 ± 1.70
Blood percentage (%)	4.80 ± 0.07	4.92 ± 0.06	4.70 ± 0.10	4.90 ± 0.05	4.89 ± 0.12	-	4.84 ± 0.04
Feather weight (g)	328.99 ± 2.91	32.36 ± 2.72	331.87 ± 4.47	326.55 ± 2.12	338.01 ± 5.34	-	331.56 ± 1.70
Feather percentage (%)	7.21 ± 0.08b	7.54 ± 0.08a	7.27 ± 0.13ab	7.49 ± 0.06a	7.57 ± 0.15a	*	7.42 ± 0.05
Head weight (g)	161.34 ± 1.91	161.11 ± 1.78	164.75 ± 2.93	160.96 ± 1.39	161.55 ± 3.50	-	161.94 ± 1.12
Head percentage (%)	3.52 ± 0.04b	3.65 ± 0.04ab	3.60 ± 0.06ab	3.68 ± 0.03a	3.60 ± 0.07ab	*	3.61 ± 0.02
Foot weight (g)	123.56 ± 1.96	122.68 ± 1.83	124.45 ± 3.01	121.05 ± 1.43	126.99 ± 3.60	-	123.75 ± 1.15
Foot percentage (%)	2.70 ± 0.04	2.78 ± 0.04	2.72 ± 0.06	2.76 ± 0.03	2.84 ± 0.07	-	2.76 ± 0.02
Heart weight (g)	37.18 ± 0.55	36.66 ± 0.51	37.12 ± 0.84	36.07 ± 0.40	38.55 ± 1.00	-	37.11 ± 0.32
Heart percentage (%)	0.81 ± 0.01	0.83 ± 0.01	0.81 ± 0.02	0.83 ± 0.01	0.86 ± 0.02	-	0.83 ± 0.01
Liver weight (g)	74.35 ± 1.30	75.05 ± 1.22	75.22 ± 2.00	72.44 ± 0.95	72.33 ± 2.39	-	73.88 ± 0.76
Liver percentage (%)	1.62 ± 0.02	1.70 ± 1.65	1.65 ± 0.05	1.66 ± 0.02	1.63 ± 0.05	-	1.65 ± 0.02
Lung weight (g)	35.89 ± 0.54	36.49 ± 0.50	36.04 ± 0.82	35.20 ± 0.39	35.59 ± 0.98	-	35.84 ± 0.31
Lung percentage (%)	0.78 ± 0.01	0.83 ± 0.01	0.79 ± 0.02	0.81 ± 0.01	0.79 ± 0.02	-	0.80 ± 0.01
Gizzard weight (g)	177.71 ± 2.49	177.81 ± 2.33	182.70 ± 3.82	173.52 ± 1.81	184.91 ± 4.56	-	179.33 ± 1.46
Gizzard percentage (%)	3.89 ± 0.60	4.03 ± 0.06	4.04 ± 0.09	3.98 ± 0.04	4.14 ± 0.11	-	4.02 ± 0.04
Intestine weight (g)	144.35 ± 2.10	139.40 ± 1.96	143.41 ± 3.22	142.30 ± 1.53	144.34 ± 3.85	-	142.76 ± 1.23
Intestine percentage (%)	3.15 ± 0.04	3.16 ± 0.04	3.14 ± 0.07	3.25 ± 0.03	3.22 ± 0.08	-	3.19 ± 0.03

a,b: The differences among the values bearing different superscript on the same row line are significant (P<0.05), -: insignificant (P>0.05), *: P<0.05

Table 3 show mean and standard error values of slaughter traits in geese with different feather colour. In terms of colours, slaughter weight and feather and head rates were significant ($P<0.05$) and other examined traits were insignificant ($P>0.05$). While black and brown geese had the highest slaughter weight, pied geese had the lowest slaughter weight. Feather ratio had the highest value in geese with grey feather and the lowest value in geese with black feather.

Table 4 shows mean and standard error values of carcass traits in geese in terms of sex. There were statistically significant differences between neck, thigh, breast, back, abdominal fat, internal fat, hot and cold carcass weights in terms of sex ($P<0.05$-0.01). Carcass weights were determined as high in male geese and low in female geese.

Table 5 shows mean and standard error values of carcass traits in geese by slaughter age. While wing weight and rates of thigh, wing, internal fat, and abdominal fat from the statistically investigated traits were insignificant ($P>0.05$), statistically significant differences were determined between other examined traits ($P<0.05$-0.01).

While mean hot and cold carcass weights were 3153.84 and 3103.80 g for geese slaughtered at 180 and 210 days of age; means of neck, breast, thigh, wing, back, internal fat and abdominal fat were 202.18, 879.95, 707.24, 453.42, 608.79, 107.89 and 158.53 g, respectively. In addition, approximately 50% of the difference between carcass weights of geese slaughtered at age of 180 and 210 days was observed to be arising from abdominal and internal fat increase.

Table 6 shows mean and standard error values of carcass traits in geese with different feather coluor. It was determined that while differences between hot and cold carcass weight regarding different feather colour were statistically significant ($P<0.05$), differences between other traits were insignificant ($P>0.05$). Geese with black and brown feather color had the highest hot and cold carcass weight, geese with pied feather colour had the lowest carcass weight.

In the study, hatching weights were determined as 94.15 and 96.32 g for female and male geese and the mean hatching weight was 95.24 g. Hatching weights ranged between 93.39-100.18 g for maternal feather color groups and between 78.28-107.42 g for egg weight groups. It was found that hatching weights were lower than 101.2-120.1 g reported by Ünal et al. (2005); similar to values between 92-97 g reported by Knizetova et al. (1994), 94.63 g reported by Aslan and Saatci (2003) for native geese in Kars and 95.5 and 94.2 g reported by Tilki and Inal (2004a) for geese originated from Başkuyu and Tatlıcak; and higher than 82.7-90.6 g reported by some researchers (Shanaway 1987; Boz et al. 2017a).

Table 4 - Mean and Standard Error Values of Carcass Traits in Geese in Terms Of Sex

Carcass traits	Sex						
	Male		Female			General	
	n	$\overline{X} \pm S_{\overline{x}}$	n	$\overline{X} \pm S_{\overline{x}}$	P	n	$\overline{X} \pm S_{\overline{x}}$
Hot carcass weight (g)	267	3288.02 ± 34.90	244	3019.66 ± 36.48	***	511	3153.84 ± 28.19
Hot carcass dressing percentage (%)	267	69.77 ± 0.18	244	68.94 ± 0.19	***	511	69.36 ± 0.14
Cold carcass weight (g)	267	3235.87 ± 35.99	244	2971.72 ± 34.42	***	511	3103.80 ± 27.81
Cold carcass dressing percentage (%)	267	68.66 ± 0.18	244	67.85 ± 0.18	***	511	68.25 ± 0.14
Neck weight (g)	267	205.74 ± 2.39	244	198.63 ± 2.50	*	511	202.18 ± 1.93
Neck percentage (%)	267	6.45 ± 0.08	244	6.78 ± 0.08	***	511	6.62 ± 0.06
Chest weight (g)	75	918.87 ± 20.65	78	841.04 ± 19.78	**	153	879.95 ± 14.77
Chest percentage (%)	75	28.81 ± 0.12	78	28.10 ± 0.12	***	153	28.46 ± 0.09
Leg weight (g)	75	731.51 ± 16.88	78	682.98 ± 16.17	*	153	707.11 ± 12.08
Leg percentage (%)	75	22.89 ± 0.10	78	22.80 ± 0.10	-	153	22.84 ± 0.07
Wing weight (g)	75	469.29 ± 12.10	78	437.56 ± 11.59	-	153	453.42 ± 8.65
Wing percentage (%)	75	14.13 ± 0.09	78	14.11 ± 0.09	-	153	14.24 ± 0.07
Back weigh (g)	75	644.51 ± 14.49	78	573.07 ± 13.88	***	153	608.79 ± 10.37
Back percentage (%)	75	20.19 ± 0.10	78	19.17 ± 0.10	***	153	19.68 ± 0.07
Intestinal fat weight (g)	267	112.37 ± 2.11	244	103.41 ± 2.20	**	511	107.89 ± 1.70
Intestinal fat (%)	267	3.09 ± 0.06	244	3.10 ± 0.06	-	511	3.10 ± 0.05
Abdominal fat weight (g)	267	165.47 ± 3.74	244	151.59 ± 3.91	*	511	158.53 ± 3.02
Abdominal fat percentage (%)	267	5.06 ± 0.10	244	5.05 ± 0.10	-	511	5.06 ± 0.08
Fire (%)	267	1.59 ± 0.02	244	1.59 ± 0.02	-	511	1.59 ± 0.01

-: insignificant (P > 0.05), *: P<0.05, **: P<0.01,***: P<0.001

Table 5 - Mean and Standard Error Values of Carcass Traits in Geese in Terms of Slaughter Age

Carcass traits	Slaughter age					General	
	180 day		210 day				
	n	$\overline{X} \pm S_{\overline{x}}$	n	$\overline{X} \pm S_{\overline{x}}$	P	n	$\overline{X} \pm S_{\overline{x}}$
Hot carcass weight (g)	174	3010.11 ± 40.84	337	3297.58 ± 31.38	***	511	3153.84 ± 28.19
Hot carcass dressing percentage (%)	174	68.44 ± 0.21	337	70.28 ± 0.16	***	511	69.36 ± 0.14
Cold carcass weight (g)	174	2960.86 ± 40.29	337	3246.73 ± 30.96	***	511	3103.80 ± 27.81
Cold carcass dressing percentage (%)	174	67.31 ± 0.21	337	69.19 ± 0.16	***	511	68.25 ± 0.14
Neck weight (g)	174	201.39 ± 2.80	337	202.98 ± 2.15	-	511	202.18 ± 1.93
Neck percentage (%)	174	6.91 ± 0.09	337	6.33 ± 0.07	***	511	6.62 ± 0.06
Chest weight (g)	52	830.60 ± 24.15	101	929.30 ± 17.17	**	153	879.95 ± 14.77
Chest percentage (%)	52	28.46 ± 0.14	101	28.45 ± 0.10	-	153	28.46 ± 0.09
Leg weight (g)	52	664.42 ± 19.74	101	750.06 ± 14.04	**	153	707.24 ± 12.08
Leg percentage (%)	52	22.73 ± 0.12	101	22.96 ± 0.08	-	153	22.84 ± 0.07
Wing weight (g)	52	424.17 ± 14.15	101	482.69 ± 10.06	**	153	453.42 ± 8.65
Wing percentage (%)	52	14.10 ± 0.11	101	14.14 ± 0.08	-	153	14.24 ± 0.07
Back weigh (g)	52	577.56 ± 16.95	101	640.03 ± 12.05	**	153	608.79 ± 10.37
Back percentage (%)	52	14.51 ± 0.11	101	14.71 ± 0.08	-	153	19.68 ± 0.07
Intestinal fat weight (g)	174	104.52 ± 2.46	337	111.27 ± 1.89	*	511	107.89 ± 1.70
Intestinal fat (%)	174	3.21 ± 0.07	337	3.18 ± 0.06	-	511	3.10 ± 0.05
Abdominal fat weight (g)	174	140.52 ± 3.74	337	176.53 ± 3.36	***	511	158.53 ± 3.02
Abdominal fat percentage (%)	174	4.73 ± 0.11	337	5.39 ± 0.09	***	511	5.06 ± 0.08
Fire (%)	174	1.64 ± 0.02	337	1.55 ± 0.01	***	511	1.59 ± 0.01

-: insignificant (P > 0.05), *: P<0.05, **: P<0.01,***: P<0.001

Table 6 - Mean and Standard Error Values of Carcass Traits in Geese with Different Feather Color

Carcass traits	Feather colour													
	Black		White		Brown		Piebald		Grey			General		
	n	$\overline{X} \pm S_{\overline{X}}$	n	$\overline{X} \pm S_{\overline{X}}$	n	$\overline{X} \pm S_{\overline{X}}$	n	$\overline{X} \pm S_{\overline{X}}$	n	$\overline{X} \pm S_{\overline{X}}$	P	n	$\overline{X} \pm S_{\overline{X}}$
Hot carcass weight (g)	110	3232.88 ± 48.10a	122	3083.72 ± 44.96ab	45	3226.42 ± 73.89a	203	3062.58 ± 35.01b	31	3163.62 ± 88.26ab	*	511	3153.84 ± 28.19
Hot carcass dressing percentage (%)	110	69.83 ± 0.24	122	69.03 ± 0.23	45	69.71 ± 0.37	203	69.08 ± 0.18	31	69.13 ± 0.45	-	511	69.36 ± 0.14
Cold carcass weight (g)	110	3182.49 ± 47.44a	122	3034.84 ± 44.35ab	45	3175.55 ± 72.86a	203	3014.63 ± 34.53b	31	3111.48 ± 87.06ab	*	511	3103.80 ± 27.81
Cold carcass dressing percentage (%)	110	68.74 ± 0.24	122	67.93 ± 0.23	45	68.60 ± 0.37	203	68.00 ± 0.18	31	67.98 ± 0.45	-	511	68.25 ± 0.14
Neck weight (g)	110	204.35 ± 3.30	122	201.99 ± 3.08	45	207.42 ± 5.07	203	195.83 ± 2.40	31	195.83 ± 2.33	-	511	202.18 ± 1.93
Neck percentage (%)	110	6.50 ± 0.11	122	6.74 ± 0.10	45	6.63 ± 0.16	203	6.60 ± 0.08	31	6.63 ± 0.20	-	511	6.62 ± 0.06
Chest weight (g)	30	902.52 ± 31.29	33	842.49 ± 30.64	27	898.94 ± 33.45	42	841.07 ± 26.03	21	914.74 ± 36.70	-	153	879.95 ± 14.77
Chest percentage (%)	30	28.56 ± 0.18	33	28.40 ± 0.18	27	28.36 ± 0.20	42	28.50 ± 0.15	21	28.47 ± 0.22	-	153	28.46 ± 0.09
Leg weight (g)	30	723.16 ± 25.58	33	684.18 ± 25.05	27	724.28 ± 27.35	42	671.67 ± 21.28	21	732.93 ± 30.01	-	153	707.24 ± 12.08
Leg percentage (%)	30	22.91 ± 0.15	33	23.01 ± 0.15	27	22.78 ± 0.16	42	22.78 ± 0.13	21	22.75 ± 0.18	-	153	22.84 ± 0.07
Wing weight (g)	30	459.52 ± 18.33	33	432.62 ± 17.95	27	460.70 ± 19.60	42	434.21 ± 15.25	21	480.08 ± 21.50	-	153	453.42 ± 8.65
Wing percentage (%)	30	14.47 ± 0.14	33	14.48 ± 0.14	27	14.43 ± 0.15	42	14.57 ± 0.12	21	14.73 ± 0.16	-	153	14.24 ± 0.07
Back weigh (g)	30	615.22 ± 21.96	33	579.40 ± 21.50	27	635.51 ± 23.48	42	579.09 ± 18.27	21	634.74 ± 25.75	-	153	608.79 ± 10.37
Back percentage (%)	30	14.55 ± 0.14	33	14.56 ± 0.14	27	14.50 ± 0.15	42	14.64 ± 0.12	21	14.80 ± 0.16	-	153	19.68 ± 0.07
Intestinal fat weight (g)	110	111.09 ± 2.90	122	104.51 ± 2.71	45	112.28 ± 4.46	203	107.33 ± 2.11	31	104.25 ± 5.32	-	511	107.89 ± 1.70
Intestinal fat (%)	110	3.41 ± 0.84	122	3.32 ± 0.08	45	3.47 ± 0.13	203	3.49 ± 0.06	31	3.32 ± 0.15	-	511	3.10 ± 0.05
Abdominal fat weight (g)	110	156.59 ± 5.15	122	149.48 ± 4.81	45	160.17 ± 7.91	203	155.86 ± 3.75	31	170.53 ± 9.45	-	511	158.53 ± 3.02
Abdominal fat percentage (%)	110	4.89 ± 0.13	122	4.91 ± 0.12	45	4.98 ± 0.20	203	5.11 ± 0.10	31	5.41 ± 0.24	-	511	5.06 ± 0.08
Fire (%)	110	1.57 ± 0.02	122	1.59 ± 0.02	45	1.58 ± 0.03	203	1.57 ± 0.02	31	1.66 ± 0.04	-	511	1.59 ± 0.01

-: insignificant (P > 0.05), *: P<0.05

The effect of maternal feather color and egg weight on hatching weight was determined to be significant (P<0.001). This difference was associated with the fact that egg weights of geese with grey maternal feather color were higher. Hatching weight was similar to 93.0-97.4 g reported by Saatcı et al. (2005) for all geese with other feather color except for geese with grey feather color. In terms of live weights, a continuous growth was determined in geese in all stages of the growth starting from hatching. Growth of geese was very fast until 90 days of age and was slower particularly between 120 and 210 days after 90 days.These results were similar to the results of numerous studies (Saatci et al. 2011; Kokoszynski et al. 2014; Boz et al. 2017a).

In the study, mean live weights at 30, 60, 90, 120, and 150 days of age were found to be 937.6, 1824.0, 2746.1, 3412.6, and 3976.5 g, respectively. These values were lower than values reported by many researchers (Tilki et al. 2005; Bochno et al. 2006; Saatci and Tilki 2007; Wolc et al. 2008; Boz et al. 2017a) for geese from different breeds and raised under intensive conditions.

Live weights of male geese were significantly higher than those of female geese at all weeks. This result confirms previous studies. (Kapkowska et al. 2011; Liu et al. 2011; Murawska 2013; Boz et al. 2017a).

It was found that mean live weight at age of 180 days was 4439.89 g and this value was 4654.04 and 4225.48 g for male and female geese in the study. These results were lower than the values between 5060-6220

g reported by some researchers (Fortin et al. 1983; Mourot et al. 2006; Lisowski et al. 2008); similar to 4797.2 and 4771.9 g reported by Tilki and İnal (2004a) for geese originating from Armutlu and Tatlıcak; and higher than 4197.9 g reported for geese originating from Başkuyu.

Mean live weight at 210 days of age obtained in the study was 4721.43 g and this value was 4895.93 and 4546.93 g for male and female geese. These values were determined to be lower than 5556-6269 g the values reported by Knizetova et al. (1994).

Differences between live weights determined in different months in the study and live weights determined in other studies may be associated with factors such as genetics, breed, care, feeding, and shelter. Because the geese used in study were raised extensively and generally breeders do not mostly give concentrated feed, the measured live weights were found to be lower than those reported in other studies.

As a result of study, it was found that slaughter weights in terms of sex were 4496.61 and 4361.40 g for male and female geese, and the mean slaughter weight was 4529.01 g. Slaughter weight of male geese was higher than slaughter weight of female geese in the study. This is compatible with the results of studies conducted on local geese and other breeds of goose (Stevenson 1985; Guy et al. 1996; Şahin et al. 2003, Tilki and Inal 2004b; Tilki et al. 2005; Kırmızıbayrak et al. 2011, Sarıca et al. 2015; Boz et al. 2017b).

Slaughter weights determined in the study were lower than 6712 and 5584 g reported by Guy et al. (1996) for male and female geese, 5208 and 4877 g reported by Tilki et al. (2005) for male and female geese. They were detected to be similar to 4226 g by Mazanowski et al. (2005) for White Koluda and Slovak geese and averagely 4716.2 g reported by Kırmızıbayrak (2002) native geese of Kars region; and were higher than 4014.9 g reported by Tilki and İnal (2004b) for geese originating from Başkuy.

Slaughter weights in terms of feather color were the highest in black and brown feather geese (4614.66-4613.57g) and the lowest in pied feather geese (4414.74g).

Feather weight which is one of the important products obtained from geese was 331.56 g in average, and 336.70 and 326.41 g in male and female geese in the study. Feather weight determined in male and female geese were lower than 637.9 and 518.2 g reported by Çelik and Bozkurt (2009) and 434.8 and 370.8 g reported by Tilki and Inal (2004b); and higher than 229.5 and 195.5 g reported by Saatcı (2008), and 290.0 and 255 g reported by Boz et al. (2017b) The fact that male geese had more feather than female geese in the study showed also similarity with previous researchs (Tilki et al. 2004; Tilki et al. 2005; Saatcı 2008; Boz et al. 2017b).

Liver is another important product of goose. Mean liver ratios were determined to be 1.63% and 1.68% for male and female geese. Liver ratio in male and female geese was lower than 2.6 and 3.76% reported

by Çelik and Bozkurt (2009) and 2.82 and 2.84% reported by Cave et al. (1994); similar to the ratios between 1.59-1.67% reported by Kirchgeβner et al. (1997); and higher than values between 1.15 and 1.55% reported by Fortin et al. (1983).

Hot and cold carcass yield were determined as 69.36% and 68.25%. Male geese had higher value than female geese in terms of hot and cold carcass yield. Hot and cold carcass yield for male and female geese in this study were lower than 72.37-73.68% reported by Kırmızıbayrak et al. (2011) and 71.76 and 70.49% reported by Tilki and Inal (2004b) for male and female geese; similar to 68.00% reported by Stevenson (1985) for female geese and 68.70% by Tilki et al. (2004) for avarege percentage of male and female geese, and higher than values between 60.00-67.50% reported in other several studies by Lisowski et al. (2008); Çelik and Bozkurt (2009); Boz et al. (2017b).

The fact that carcass yields determined in the study were higher than the results reported in some studies makes us think that native geese may be more appropriate for fattening compared to many other goose breeds. In addition, differences between studies may be associated with different slaughter age, feeding types, and fattening times.

In the study, neck, breast, thigh, wing, back, internal fat and abdominal fat rates constituting parts of the carcass were 6.62, 28.46, 22.84, 14.24, 19.68, 3.10, and 5.06%, respectively.

Breast and thigh are among the most valuable parts of the carcass. The total percantage of these was 51.30% of the carcass. Wing, back, and neck are among the least valuable parts of the carcass. The total percantage of these was 40.54%, and the total of internal and abdominal fat rate was 8.16%. These results were similar to the results of numerous studies (Fortin et al. 1983; Tilki and İnal 2004b; Şahin et al. 2008; Çelik and Bozkurt 2009; Boz et al. 2017b; Uhlirova et al. 2018; Mancinelli et al. 2019).

4. CONCLUSIONS

This study revealed significant information about growth, slaughter, and carcass traits of native geese raised under breeder conditions in the province of Kars where geese breeding is performed most commonly in Türkiye.

Consequently, current conditions appropriate for geese raising in Kars region should be evaluated and the requirement for quality brood to improve broiler ability of geese raised should be met.

If artificial incubation becomes prevalent in the region, egg yield and production of goose meat can be increased relatively

5. REFERENCES

Bochno, R., Murawska, D., Brzostowska, U. (2006). Age-Related changes in the distribution of lean fat with skin and bones in goose carcasses. *Poult Sciences* 85: 1987-1991.

Boz, M.A., Sarica, M., Yamak, U.S. (2017a.) Production traits of artificially and naturally hatched geese in intensive and free-range systems: I. Growth traits. *British Poultry Science* 58: 132-138.

Boz. M.A., Sarica M., Yamak U.S. (2017b). Production traits of artificially and naturally hatched geese in intensive and free-range systems: II: slaughter, carcass and meat quality traits. *British Poultry Science* 58: 166-176.

Cartoni Mancinelli, A., Mattioli, S., Dal Bosco, A., Piottoli, L,, Ranucci, D., Branciari, R., Cotozzolo, E., Castellini, C. (2019). Rearing Romagnola geese in vineyard: pasture and antioxidant intake, performance, carcass and meat quality. *Italian Journal of Animal Science* 18: 1-9.

Castellini, C., Mugnai, C., Dal Bosco, A. (2002). Effect of organic production system on broiler carcass and meat quality. *Meat Science* 60: 219-225.

Cave, N.A., Grunder, A.A., Butler, G., Fortin, A., Pawluczuk, B. (1994). Influence of age, sex and pre-slaughter holding conditions on live weight and carcass traits of broiler geese. *Archiv fur Geflugelkunde* 58: 106-110.

Celik B, Bozkurt, Z. (2009). Slaughter and carcass traits of native geese reared in Muş Province. *Journal of Lalahan Livestock Research Institute* 49: 37-46.

Fanatico, A.C., Pillai, P.B., Emmert, J.L., Owens, C.M. (2007). Meat quality of slow and fast-growing chicken genotypes fed low-nutrient or standard diets and raised indoors or with outdoor access. *Poult Sciences* 84: 1321-1327.

Fortin, A., Grunder, A.A., Chambers, J.R., Hamilton, R.M.G. (1983). Live and carcass characteristics of four strains of male and female geese slaughtered at 173, 180, and 194 days of age. *Poult Sciences* 62: 1217-1223.

Guy, G., Rousselot-Pailley, D., Rouvier, R. (1996). Comparison of meat geese performance fed with or without grass. *Archiv fur Geflugelkunde* 60: 217-221.

Ibtisham, F., An, L., Li, T., Niu, Y., Xiao, M., Zhang, L., Jia, R. (2017). Growth patterns of two Chinese native goose breeds. *Brazilian Journal of Poultry Science* 19: 203-210.

Kapkowska, E., Gumulka, M., Rabsztyn, A., Poltowicz, K., Andres, K. (2011). Comparative study on fattening results of Zatorska and White Kołuda geese. *Annals of Animal Science* 11: 207-217.

Karacay, N., Ocak, N., Sarica, M., Erener, G. (2008). Effect of carbohydrate supplementation provided through drinking water during feed withdrawal on meat and liver colours in broilers *Journal of the Science of Food and Agriculture* 88: 479-484.

Kirchgeβner, M., Jamroz, D., Eder, K., Pakulska, E. (1997). Carcass quality and fatty acid composition in growing geese fed various rations. Archiv fur Geflugelkunde 61: 191-197.

Kırmızıbayrak, T., Onk, K., Yazıcı, K. (2011). Effects of age and sex on slaughtering and carcass characteristics of Turkish native geese reared in free range production conditions in Kars province *Journal of the Faculty of Veterinary Medicine, Kafkas University* 17:41-45.

Kırmızıbayrak, T. (2002). Slaughter and carcass traits of native geese reared in local breeder conditions in Kars. *Turkish Journal of Veterinary and Animal Sciences*, 26: 667-670.

Knizetova, H., Hyanek, J., Veselsky, A. (1994). Analysis of growth curves of fowl. III. Geese. *British Poultry Science* 35: 335-344.

Kokoszynski, D., Bernacki, Z., Grabowicz, M., Stanczak, K. (2014). Effect of corn silage and quantitative restriction on growth performance, body measurements, and carcass tissue composition in White Koluda W31 geese. *Poultry Science* 93: 1993-1999.

Lisowski, M., Slawınska, A., Dluzniewska, P., Mazanowski, A., Bennarczyk, M. (2008). Analysis of DNA polymorphism (RAPD-PCR) and reciprocal effects of geese crossbreeds. *Folia Biol (Krakow)* 56: 159-164.

Liu, B.Y., Wang, Z.Y., Yang, H.M., Wang, J.M., Xu, D., Zhang, R., Wang, Q. (2011). Influence of rearing system on growth performance, carcass traits, and meat quality of Yangzhou geese. *Poult Science* 90: 653-659.

Mazanowski, A., Bernacki, Z., Kisiel, T. (2005). Meat traits and meat chemical composition in hybrids of Graylag (*Anser anser L.*) with White Koluda and Slovakian geese. *Animal Science Papers and Reports* 23: 15-32.

Mourot, J., Guy, G., Peinıau, P., Hermier, D. (2006). Effects of overfeeding on lipid synthesis, transport and storage in two breeds of geese differing in their capacity for fatty liver production. *Animal Research* 55: 427-442.

Murawska, D. (2013). The effect of age on the growth rate of tissues and organs and the percentage content of edible and inedible components in Koluda White geese. *Poult Science* 92: 1400-1407.

Puchajda, H., Faruga, A., Siekiera, J. (1989). Using Bilgoraj geese for two the cycles. *Acta Acad Agric Tech Olst Zootech* 32: 187-193.

Saatcı M, Kırmızıbayrak T, Aksoy AR, Tilki M. (2005). Egg weight, shape index and hatching weight and interrelationships among these traits in Native Turkish Geese with different coloured feathers. *Turkish Journal of Veterinary and Animal Sciences* 29: 353-357.

Saatcı M. 2008. Effects of age, sex, feather colour, body measurements, and body weight on down and feather yield in native Turkish geese. *Turkish Journal of Veterinary and Animal Sciences* 32: 293-297.

Sabry, M.I.E., Yalcin, S., Turgay-Izzetoglu, G. (2013). Interaction between breeder age and hatching time affects intestine development and broiler performance *Livestock Science* 157: 612-617.

Sahin, T., Tilki, M., Kaya, I., Ünal, Y., Aksu Elmalı, D. (2008). Effect of different protein levels for finishing period on fattening performance and carcass traits in native Turkish geese. Journal of Animal and Veterinary Advance 7: 1364-1369.

Sarica, M., Boz, M.A., Yamak, U.S. (2015). Slaughter and carcass traits of white and multicolor geese reared in backyard in Yozgat. *Turkish Journal of Agriculture - Food Science and Technology* 3: 142-147.

Shi, S.R., Wang, Z.Y., Zou, J.M., Jiang, N. (2010). Effects of dietary threonine on growth performance and carcass traits of Yangzhou geese. Czech Journal of Animal Science 55: 382-387.

Stevenson, M.H. (1985). Effects of diets of varying energy concentrations on the growth and carcass composition of geese. . *British Poultry Science* 26: 493-504.

Tilki, M., Inal, Ş. (2004a). Yield traits of geese of different origins reared in Turkey-II. Growth traits. *Turkish Journal of Veterinary and Animal Sciences* 28: 157-163.

Tilki, M., İnal, Ş. (2004b). Yield traits of geese of different origins reared in Turkey-III. Slaughter and carcass traits. *Turkish Journal of Veterinary and Animal Sciences* 28: 165-171.

Tilki, M., Saatcı, M., Kırmızıbayrak, T., Aksoy, A.R. (2004). Slaughter and carcass traits of geese raised in Boğazköy-Kars. *The Journal of the Faculty of Veterinary Medicine, University of Kafkas* 10: 143-146.

Tilki, M., Saatcı, M., Kırmızıbayrak, T., Aksoy, A.R. (2005). Effect of age on growth and carcass composition of native Turkish geese. *Archiv fur Geflugelkunde* 69: 77-83.

Tona, K., Onagbesan, O., De-Ketelaere, B., Decuypere, E., Bruggeman, V. (2004). Effects of age of broiler breeders and egg storage on egg quality, hatchability, chick quality, chick weight, and chick posthatch growth to forty-two days. *Journal of Applied Poultry Research* 13: 10-18.

TUIK. (2018). Turkish Statistical Institute. http://www.tuik.gov.tr (Accessed 12.10. 2018).

Uhlirova, L., Tumova, E., Chodova, D., Vlckova, J., Ketta, M., Volek, Z., Skrivanova, V. (2018). The effect of age, genotype and sex on carcass traits, meat quality and sensory attributes of geese. *Asian-Australasian Journal of Animal Sciences* 31: 421-428.

Unal, Y., Kaya, I., Saatcı, M., Yıldız, S., Oncuer, A. (2005). Effect of feeding with different protein level on fattening performance of Geese. *Journal of Lalahan Livestock Research Institute*. 45: 33-39.

Wang, K.H., Shı, S.R., Dou, T.C., Sun, H.J. (2009). Effect of a free-range raising system on growth performance, carcass yield, and meat quality of slow-growing chicken. *Poult Sciences* 88: 2219-2223.

Wolc, A., Barczak, E., Wezyk, S., Bodowski, J., Bielinska, H., Szwaczkowski, T. (2008). Genetic evaluation of production and reproduction traits in two selected lines of geese under multitrait animal model. *Animal Science Papers and Reports*. 26: 71-78.

Acknowledgments

This study is a summarized part of the author's doctoral thesis.

This study was presented as a summary oral presentation at the 8th Balkan Animal Science Conference Balnimalcon 2017, 6-8 September 2017, Prizren, Kosovo.

Funding & Thanks

This study was supported by the Kafkas University Scientific Research Projects Commission, with the project number of 2007VF06 and we would like to thank Kafkas University Scientific Research Commission for this support.

CHAPTER 16

WATER QUALITY FOR POULTRY

Prof. Dr. Hüseyin NURSOY[1]

[1] Bingöl University Faculty of Veterinary Medicine, Department of Animal Nutrition and Nutritional Diseases, 12000, Bingöl, TURKEY; ORCID: 0000-0002-5524-2459; E-mail:hnursoy@bingol.edu.tr.

Introduction

Drinking of water, which constitutes 70% of the bird's body; species, age, sex, physiological condition, disease states such as diarrhea, dehydration, evaporation with breath, yield level, ambient temperature, ambient humidity, other in-house conditions, feed consumption, feed composition and form, water temperature, drinker type and regular water may vary depending on many factors such as presentation (1). The water used in poultry production must have certain properties. Although it differs according to age, sex and species in poultry, 55-77% of their body consists of water. Eggs contain about 65% water. Water is actually a nutrient. Because it contains dozens of minerals and trace elements in molten state. Water is an important medium for the composition of tissues and cells and for the realization of most metabolic events in the body. Water is used a lot in the digestion of foods and feeds and elimination of wastes in the body (2). Since birds do not have sweat glands, they expel the excess heat from their bodies by evaporating water through the air sacs associated with the lungs. Birds drink twice as much water as the feed they consume at normal house temperatures. However, water intake can increase 2-4 times under heat stress. Water and feed consumption decreases in diseases caused by the digestive system or infection, such as diarrhea. In applications such as vaccines, drugs, and antibiotics, the task of being a carrier of water emerges (2, 3, 4). Since the digestive systems of poultry are different from other animals, feeding and irrigation should be as ad libitum. Digestive canal and duration are short in poultry, their

feed and water intake capacities are quite limited. The water they need to take daily should always be ready. Birds that cannot get the appropriate amount and quality of water can lead to low productivity and problems such as shedding and shedding at an advanced stage. The excess of dissolved minerals in the water may cause poisoning, resulting in low yield and performance reductions (2, 4).

Water Drinking in Poultry

Water drinking in poultry is higher than metabolic body weight when compared to mammals due to high body temperature, high feed efficiency, high metabolic rate, and difference in digestion and waste products (5). Lott et al. (6) reported that there is a high correlation of 98% between water drinking and feed intake. Açıkgöz et al. (1) stated that there is a 1/2 ratio between feed and water intake in layers. In poultry, first the feed and then the water are consumed. Substances of the ration such as dry matter, salt, protein, fat and cellulose affect water drinking. The presence of more than 20% soybean meal and tapioca in the diet increased water drinking and started the wet litter syndrome. As a result of substitution of cereals such as barley, wheat and rye with high beta-glucan content in poultry feeds instead of corn, the amount of water in the feces increased. In cases where limited feeding is applied every other day to prevent the breeders from getting fat, water drinking is also significantly reduced. Kırkpınar et al. (7) reported that high environmental temperatures reduced feed consumption (the water taken with feed also decreases) in poultry, whereas water consumption increases. Açıkgöz et al.(1) said that, feed intake decreases and water

drinking increases at high enviroment temperatures, Because more water is drunk because the heat is dissipated by breathing. As the ambient temperature rises, the water/feed consumption ratio increases. The moisture content in the manure of chickens that receive water 4 times a day for 15 minutes decreases from 78.20% to 75.59%. The water temperature should be 10-15 ^{o}C for poultry.

According to a study by Xin (8) with a high regression coefficient (R^2=0.99) in chickens, the water drinking of 1-56 days old broilers was formulated as follows:

Daily Drinking Water, liters/day = (-2.78+4.70x A+0.128xA^2 - 0.00217xA^3)/1000

(A: Age of chicken in days)

Deeb and Cahaner (9) stated that water drinking of broiler chickens is higher than in layer hens and this is directly related to body weight, and they consume approximately 9.3% of live weight. Darden and Marks (10) reported that brown chickens drink more water than white chickens, and in the same way, water drinking of quails for meat purposes is higher depending on live weight compared to egg laying types. Cemek et al. (2) reported, daily water intake of male turkeys increased from 0.3 liters/day to 1.3 liters/day when the water temperature was increased from 10°C to 37.8°C. Likewise, the water requirements of turkeys depend on factors such as age, breed, type, gender, characteristics of rations, production conditions and ambient and water temperatures. May et al. (11) said that, the water drinking by

the drip drinker system (nipple) at low temperature in broilers is the same as in hanger type drinkers. However, due to frequent breathing at high temperatures, the water drinking in the nipples is less. Feddes et al. (12). Deeb and Cahaner (9) and Darden and Marks (10) found that male chickens drink 4-9% more water than females. Marks (13) reported in his study that the protein ratio was 20% and 28% in quails, and that water drinking was low in the low protein group and high water drinking in the high protein group.

Table 1. Drinking of Ad-libitum Water at Different Environmental Temperatures in Poultry, Liter per 1000 Animals (10, 13, 14).

PoultryTypes	**Periods**	**20ºC**	**32ºC**
Leghorn hen	4. week	50	75
	12. week	115	180
	18. week	140	200
	%50 egg	150	250
	%90 egg	180	300
Broiler	1. week	24	40
	3. week	100	190
	6. week	240	500
Turkey	1. week	24	50
	4. week	110	200
	12. week	320	600
	18. week	450	850
Duck	1. week	28	50
	4. week	120	230
	8. week	300	600
Goose	1. week	28	50
	4. week	250	450
	6. week	350	600
Quail	1. week	10.7	-
	4. week	80	-
	8. week	110	-

Effects of Water Quality in Poultry

For the water to be healthy must meet many criteria; flavor, acidity, alkalinity, odor, color, turbidity, salinity, electrical conductivity, pH, biochemical oxygen value, hardness, anion, cation, herbicide, pesticide, bacterial presence etc.

Effects of Acidity and Alkalinity of Water on Birds: The pH of drinking water normally used is in the range of 5-9. However, a pH other than 6-9 can cause corrosion in surface of metallic equipment (3). The optimum water pH for poultry is between 6.5-7.8 (14). Drinking water pH range of 2-10 in poultry affects of water drinking. With the increase of acidity in water, the color changes to red, and with the increase of alkalinity, it turns blue and digestion is adversely affected. The effects of vaccines and drugs added to these quality of waters also decrease. The water is slightly acidic rather than alkaline; It can prevent the development of bacteria such as Salmonella, E. Coli and Clostridium (15). Although it is often stated that pure water is the best water, the freshest water for poultry is water containing very little dissolved carbon dioxide and oxygen, which is also used for humans and other animals. The animal consumes more of these waters. Poultry perceives two tastes, salty and spicy. The bitter taste in the water is due to alkaloids and these bitter waters are less drinkable. It is also possible to reduce this bitterness with organic acids such as citric or acetic acid (2, 4).

Table 2. The effects of Some Physical and Chemical Parameters of Water Quality (16).

Physical Parameters	**Effects**
Color	The color of the water may change if any substance is added with acid and alkaline waters.
Taste and odor	Pathological microorganism contamination and algae (algae), plankton, etc. Physical contamination such as water spoils the taste and color of the water.
Temperature	Hot waters allow the reproduction of pathogenic bacteria in particular.
Inorganics	
Aluminum	Provides turbidity (flocs of aluminum).
Chloride	Causes bad taste
Copper	Increases the corrosion of mechanical equipment through which water passes, creates a yellow color.
Hardness	Forms deposits in metal pipes and boilers. It causes excessive use of soap. It is the cause of bad taste.
Hydrogen sulfide	Causes odor and bad taste.
Iron	Iron causes water to be red-brown in color.
pH	PH is an important parameter for disinfection, for example, the effectiveness of chlorine and ozone is directly dependent on pH.
Sulfate	Sulfate makes the water taste bad.
Total dissolved solids (TDS)	Total dissolved solids provide the formation of taste.
Organics	
Dichlorobenzenes	Increase odor.
Ethylbenzene	Increases odor.
Monochlorobenzene	Increases the odor and spoils the taste.
Styrene	Enhances Odor.

Toluene	Enhances odor.
Trichlorobenzene	Increases odor.
Xylene	Increases the odor, spoils the taste.
Detergents	Increases lather, odor and bad taste.
Disinfectants and its by-products	
Chlorine	Increases odor, spoils taste
Chlorophenols	Increase odor.

Effects of Salinity of Water on Birds: It is the concentration of ions such as Na, Mg, S, Cl, Ca or total dissolved matter in the water. Excess of these elements is toxic. However, for example, Ca gives sweetness to the water, it is desirable that phosphates be in an amount of water against bacterial growth, Na and Mg sulfates are laxative. Sodium and chloride ions in salt are important ions that determine the salinity of water (17). Atoms or molecules that gain or lose electrons are called ions. For example; Sodium atom contains 11 electrons and 11 protons. If 1 electron loses, a Na+ ion or cation is formed, which has 10 electrons and 11 protons (can give 1 electron to the medium) with 1 missing electron, thus 1 excess or free proton. Likewise, while the Cl atom has 17 protons and 17 electrons in its normal or neutral state, if it gains 1 electron, a Cl - chloride ion or anion with 18 electrons and 17 protons is formed. Carboxyl molecule is a molecule that can react R-COOH→R-COO- + H+ anionic, amino group R-NH_2 + H+→ R- NH_3+ cationic (18). Eleroğlu and Sarıca, (3), if the common salt (NaCl) ratio of the ration is normal and there is 4000 ppm of salt in the water; Water loss, decrease in growth rate, decrease in feed intake and death occur in

chickens, turkeys and ducklings, that the birds have difficulty in tolerating salt in the water and that common salt (NaCl) added to the drinking water of layer hens for 7 weeks at the rate of 0.05-0.5% has diarrhea effect. And they report that it reduces growth and egg shell quality, however, 2 g/kg salt in the feed is less effective. Salinity and electrical conductivity are similarly considered in Total Dissolved Solids (TDS) amount. According to NRC (19), the amount of TDS in water for livestock should be 0-1000 ppm. However, this value can be accepted up to 2000-3000 ppm. However, the reliable upper limit of the same value was reported as 4000 ppm in previous studies (2, 14, 15), and the animal consumes these waters less (15).

Table 3. TDS Classification for Waters of Poultry, (20).

TDS Quantity	**Remarks**
Less than 1000 ppm	No problem in these waters
1000-2999 ppm	In some cases, temporary diarrhea may be seen.
3000-4999 ppm	It increases diarrhea and death rate, and a decrease in growth is observed especially in turkeys.
5000-6999 ppm	It can be used with little control in farm animals. It is not given to those who are pregnant or lactating. Not used for poultry.
7000-10000 ppm	Not used for poultry.
Higher than 10000 ppm.	It can never be used when the salt content is higher than 10000 ppm.

Determination of Salinity: All organic substances and other ionizable substances in water are measured by 3 methods (21): *1-Electrical Conductivity Method*: It is the ability of water to conduct electricity. The ability of pure water to conduct electricity is 0.5-2 μmho/cm, and it increases with temperature (17). Water that has the ability to conduct electricity and contains ions is called electrolyte. Electrolytes are defined by their ionic valence rather than their weight. Atoms such as C, O and N are non-electron exchange atoms such as minerals and trace elements (18,22). *2-Specific Gravity Method*: The dissolved solids or salinity densimeter in the water is measured and corrected with temperature. *3- Chloride (Argentometric) Method*: All -CO_3 in water dissociate into ions such as chloride and bromide. This is a salinity method based on the detection of ions. When chlorides approach 250 ml/g in water, they form a salty taste (17). Damron and Kelly (23) reported that 6% common salt (NaCl) added to the feed of layer hens did not change the specific gravity of the egg, while Pourreza et al. (24) reported that 2000 ppm or 2 g/liter and above salt in the water reduced the egg shell quality, but water containing 1000 ppm or 1 g/liter salt did not have a negative effect.

Table 4. Electrical Conductivty (EC) values of Water Indicator of Salinity to be Used for Poultry, (20).

EC	Classification	Remarks
<1000 mg/l < 1.5 dS/m	Perfect	It can be used for all.
1000-3000 mg/l 1.5 – 5.0 dS/m	Very good	Very little transient diarrhea.
3000-5000 mg/l 5.0 – 8.0 dS/m	Good for livestock, not suitable for poultry.	It increases the rate of diarrhea and death, and a decrease in growth is observed especially in turkeys.
5000-7000 mg/l 8.0 – 11.0 dS/m	Limited use for livestock. Not suitable for poultry. It can be used with little control in farm animals.	It can be used with little control in farm animals. It is not given to those who are pregnant or lactating. Not used for poultry.
7000-10000 mg/l 11.0 – 16.0 dS/m	Very little use.	Not for use with poultry. Not for all other animals.
>10000 mg/l >16.0 dS/m	Absolutely not given.	It cannot be used when the salt content is high.

Effects of Water Hardness on Birds: The hardness of a water; It is mainly due to the dissolved calcium or magnesium salts in it, or it is the soap precipitating capacity of the water. There are 0-60 mg/l dissolved Ca and Mg in soft waters, 61-120 mg/l in medium hard waters, 121-180 mg/l in hard waters and 180 mg/l and above in very hard waters. If Ca and Mg are found as carbonate, this hardness can be removed by boiling. However, if there is a sulfate root, this hardness is continuous and is not removed by boiling (17, 21). A French Hardness Grade (FHG) is equivalent to 10 mg/L of calcium carbonate. Hardness in water causes congestion in water distribution systems, Sodium (Na) and Potassium (K) are not causes of hardness (22). Eleroğlu et al. (4) stated that extremely hard water reduces water loss, joint diseases and the rate of poor quality egg shells in poultry, and that hard water that will affect the

metabolism in the body should not be given to the animals continuously, as well as soft water. The same investigators reported that there was a positive correlation between feed conversion and magnesium, a negative correlation with calcium ($p<0.05$), a positive correlation between live weight, dissolved oxygen, bicarbonate, hardness and magnesium, and a negative correlation between nitrate and nitrogen. Atteh and Leeson (25) reported that the amount of magnesium carbonate in the water above 100 ppm in 3 week old broiler chickens improved feed efficiency, but caused leg abnormalities, and the amount of calcium carbonate above 100 ppm did not show a similar effect. Gardiner et al. (26) observed that extremely hard water increased leg disorders, water loss and poor eggshell quality in farm animals. Koelkebeck et al. (27) found that giving Na_2CO_3 water during heat stress in laying hens had a positive effect on egg shell quality. Likewise, it has been determined that carbonated drinking water increases the feed efficiency and vitality of broiler chickens (28). Damron and Flunker (29) reported that increasing the total amount of usable calcium in the drinking water of laying hens to 0.2% by using calcium lactate improves the shell quality. Raported by Jensen et al. (30), the opinions regarding the fact that not removing the hardness in water causes fatty liver syndrome have not been proven experimentally yet. The hardness of drinking water for humans and animals should be soft or medium hard according to the FHG. It is beneficial to avoid the use of very hard water, which will disrupt the chemical balance for poultry. (3). It is possible to soften or completely reset hard water. The use of softener reduces the hardness of the water, but the TDS does not change. For this purpose, soda-lime,

aluminum sulphate, trisodium phosphate, zeolites and ion exchange resins are used (31). Resin is a solid or semi-fluid, easily soluble, natural secretion substance formed in some plants and trees, especially pines. Hardness in water can be softened by substances that cause ion exchanges, such as pine resin. However, over time these resins can become saturated with calcium and magnesium salts. To prevent this, they need to be changed at certain intervals (14). The resin particles used as an ion exchanger in water softening, purification and filtration processes are in an insoluble matrix structure with a diameter of 0.3-2 mm. They have a highly developed porous structure. Mg^{+2}, Ca^{+2} etc. causing hardness. As the electrons of the ions pass through the resin particles, they are replaced by the H+ ions in the structure of the resin and these ions become attached to the resin. The particles of the resin matrix, Mg^{+2}, Ca^{+2} etc. Its ability to retain ions is more than sodium. Basic resins hold anions and acidic resins hold cations (31, 32)

Table 5. Hardness Degrees of Water to be Used for Poultry (20,33).

French Hardness Grade, 1 FHG=10mg $CaCO_3$/liter	**American Hardness Grade, AHG, 1 mg $CaCO_3$/liter**	**Hardness Degrees**
0-6	-	Dessert
7-13	0-75	Soft
14-28	76-150	Medium hard
29-42	151-300	Hard
42- and above	300 and above	Very Hard

Effects of Nitrates, Nitrites and Sulfates in Water on Poultry: The quality of water mostly depends on nitrate, nitrite, sulfates and total

dissolved solids. Major sources of nitrate and nitrite on earth; plant and animal wastes, nitrogen fertilizers and nitrogen-rich soils. Nitrates are converted to nitrite in ruminants and cause ammonia poisoning. They convert hemoglobin in oxygen-carrying red blood cells to methemoglobin. Even 1 mg/l of nitrite is more dangerous than nitrate. In such cases, the water should be changed (2). All animals need sulfur to form amino acids. Sulphates in water are not actually toxic. However, especially in ruminants, sulfates turn into sulfites and become toxic substances. The negative effect of nitrate level in the range of 3-20 mg/l on performance in poultry has not been determined yet (3). Littlefield (34) found in his study in broilers that nitrate levels higher than 20 mg/l had a negative effect on body weight gain, feed efficiency and performance. Adams et al. (35) reported that 4000 ppm $MgSO_4$ added to layer rations reduced water intake by 15% and egg production by 76%. Ağaoğlu et al. (36) reported that nitrate and nitrite amounts in 366 natural springs/fountains, wells and other drinking waters in Van were determined in standards, but they found high levels of 0.7-0.12 ppm nitrite in 2 tap waters and 0.323 ppm in 1 well water.

Table 6. Criteria for Poultry Acceptable Nitrate, Nitrite and Sulfate (20, 33).

Substance	**Acceptable limits, mg/liter**	**Maximum Limits, g/liter**
Nitrate, NO_3	1-5	25
Nitrite, NO_2	0.4	4
Sulphate, SO_4	15-40	200

High Fluorine in Poultry Drinking Water: According to the World Health Organization (WHO) (37), the fluorine levels in waters to be used for humans and animals are less than <1.5 mg/l, which is beneficial

for the organism. However, excess fluorine (>1.5 mg/l) is harmful to humans and animals, and can cause black spots on teeth and bone problems. Fluorine is high in surface waters obtained from areas with high groundwater and waters in volcanic areas. Varol and Varol (38) stated that the Ağrı Tendürek Volcanic area, Uşak, Isparta and Eskişehir are the places where fluorosis (disease caused by excessive fluoride in waters) is most common in Türkiye. Researchers have reported that fluoride taken with water is the biggest source for humans and animals, it passes from the small intestines to the blood, spreads throughout the body without binding to proteins, and 99% of it accumulates in the bones and teeth. In addition, studies in sheep, rats and rabbits report that excessive fluoride ingested with drinking water causes renal congestion, live fetus rate, congestion in the lungs, destruction of the respiratory system epithelium, necrosis, fibrillation in the heart muscle, and impaired glucose metabolism.

Table 7. Fluorine Levels in Drinking Waters According to the Legislation of the Ministry of Health of Türkiye (39).

Classification	**Fluorine Level, ppm**
High Quality Water	<1
Lightly Contaminated Water	1.5
Dirty Water	2
Very Contaminated Water	>2000

Effects of Microbiological Contaminations in Water on Poultry: As drinking water sources for poultry; well water, spring water, stream, river, lake etc., agricultural irrigation water or network water is used. Agricultural waters may have high salinity or TDS, toxic substances

and microbiological contaminations. Therefore, maximum importance should be given to healthy water. In the world and in our country, toxications of water-dependent animals are not common (2). Ağaoğlu et al. (40) said that coliform bacteria are normally found as saprophytes in the intestines of humans and animals. Detection of these microorganisms in the water means that the feces are mixed, that is, there is a sewage leak. In Table 6, acceptable amounts of bacterial populations in waters are given. Most bacteria and blue-green algae (Cyanobacteria) multiply above 20^{o}C. These bacteria can change the color of water to green, blue or even red. For this reason, it is of great benefit for poultry and other livestock to have a water temperature below 20^{o}C (14).

Table 8. Microbiological Limits in Drinking and Spring Waters, (41).

Microbiological Parameters	**Standard Values, CFU/ml**
Total Bacteria	0-1000
Total Coliform	0-50
Fecal Coliform (E. coli)	0
Enterococci	0
Salmonella	0
Pseudomonas auruginosa	0
Clostridum perfringens	0
Pathogenic staphylococci, It can grow in 72 hours at 22^{o}C and 24 hours at 37^{o}C	5-20
Parasites	0
Other microbiological organisms	0

The nitrate and nitrite in the waters increase the growth of algae and the increase of the algae causes botulism (food-feed poisoning). Although

there is no evidence-based relationship between the presence of algae or blue-green algae in water and toxications, it is assumed that it causes the formation of other toxic substances. Therefore, algae growth should be reduced in drinkers or other water sources with algae. Some of the algae or blue-green algae produce toxins. In order to reduce algae growth or organic contamination in water tanks, sunlight should not shine. In addition, 1 mg/l copper sulfate can also be used. However, copper poisoning is also a risk (2). Grizzle et al. (42) reported that nitrate with low concentration did not affect coliform bacteria and performance in broilers, but the combination of these two factors was harmful. Alemdar et al. (43) found enterococci in 30%, coliforms in 12%, sulphite-reducing anaerobes in 24% and E. coli bacteria that should not be present in 8% of 164 tap and tank waters they examined in Bitlis. In a different study conducted by Yalçın et al. (44), total bacteria above the standards were found in 10-57% of the water we drink and in 36% of the spring waters. In the drinking water samples taken from broiler farms, 41-97% bacteria and 1% E. coli bacteria were found (3). The physical, chemical and microbiological quality criteria of the water to be used for poultry are given in Table 6 collectively.

Table 9. Normal Physical, Chemical and Microbiological Quality Criteria of Water to be Used for Poultry, (2,20,45).

A) Physical and Chemical Parameters		***C) Inorganic Contamination Parameters***	
Temperature, °C	20-25	Mercury, mg/l	0.01-0.003
pH	6.5-9.5	Cadmium, mg/l	0.05-0.08
Dissolved oxygen, mg/l	8	Lead, mg/l	0-0.05
Oxygen saturation, %	90	Arsenic, mg/l	0.025-0.2
Mg (mg/l)	0.01-0.05	Copper, mg/l	0.002-0.6
Sulfate ion, mg/l	200	Chromium, mg/l	0.05-1
Ammonium nitrogen, mg/l	0.2	Uranium, mg/l	0.2
Nitrite nitrogen, mg/l	0.002	Cobalt, mg/l	10
Nitrate nitrogen, mg/l	5	Nickel, mg/l	1
Total phosphorus, mg/l	0.02	Zinc, mg/l	1.5
Total dissolved matter, mg/l	500	Cyanide (total), mg/	10
Color, Pt-Co unit	5	Fluoride, mg/l	1000
Sodium, mg/l	50-150	Free chlorine, mg/l	10
Cl, mg/l	50-150	Sulfur, mg/l	2
B) Organic Parameters		Iron, mg/l	0.2-0.3
Chemical oxygen demand, mg/l	25	Manganese, mg/l	0.01-0.05
Biological oxygen demand, mg/l	4	Boron, mg/l	5
Total organic carbon, mg/l	5	Selenium, mg/l	0.05
Total kjdeldahl-nitrogen, mg/l	0.5	Barium, mg/l	1000
Oil and grease, mg/l	0.02	Aluminum, mg/l	0.3
Surfactants that react with methylene blue, mg/l	0.05	***D) Radioactivity***	
Phenolic substances, mg/l	0.002	Alpha-activity, bq/l	0.1
Mineral oils and derivatives, mg/l	0.02	Beta-activity, bq/l	1
Total pesticide, mg/l	0.001		

REFERENCES

1-Açıkgöz, Z., Bayraktar, H., Altan, A. "Yüksek sıcaklıkta yumurta tavuklarının su tüketimi–verim performansı arasındaki ilişki", Hayvansal Üretim, 43(1): 25-31, 2002.

2-Cemek, B., Çetin, S., Yıldırım, D., "Çiftlik ve kümes hayvanlarının su tüketimi ve su kalite özellikleri, Tarım Bilimleri Araştırma Dergisi 4(1): 57-67, 2011.

3-Eleroğlu, H., Sarıca M., "Kanatlı üretiminde içme suyu kalitesi", 4. Ulusal Zootekni Bilim Kongresi, Cilt 1: 318-324**.** 1-3 Eylül**.** SDÜ. Ziraat Fakültesi Zootekni Bölümü**,** Isparta**,** 2004.

4-Eleroğlu, H., Yıldırım A., Şekeroğlu, A., "Organik tavukçulukta içme suyu özellikleri beslemedeki önemi ve su kalitesini artırmaya yönelik uygulamalar", Türkiye II. Organik Hayvancılık Kongresi, 24-26 Ekim 2013.

5-Saleh. K. Nofal R.. Younis H.. Ragab M. "Preliminary results of rectional selection for water consumption ın Japanese quail" 2nd Mediterraean Summit of WPSA. 107-109. 2009.

6-Lott, BD., Dozier, WA., Simmons, JD., Roush, WB., "Water flow rates in commercial broiler houses", Poult. Sci., 82: 102 [S56]. 2003.

7-Kırkpınar, F., Özdoğan, M., Taluğ, AM., "Kanatlılarda su metabolizması ve suyun performans üzerine etkileri", Hayvancılık'96 Ulusal Kongresi, İzmir, 390-397, 18-20 Eylül 1996.

8-Xin, H., "Feed and water consumption, growth. and mortality of male broilers", Poult. Sci., 73(5): 610-616, 1994.

9-Deeb, N., Cahaner, A., "Genotype- by- environment interaction with broiler genotypes differing in growth rate 3. growth rate and water consumption of broiler progeny from weight selected versus non selected parents under normal and high ambient temperatures", Poult. Sci., 81: 293-301, 2002.

10-Darden, JR., Marks, HL., "Divergent selection for growth in japanese quail under split and complete nutritional environments. 2. Water and feed ıntake patterns and abdominal fat and carcass lipid characteristics", Poult. Sci., 67: 1111-1122. 1988.

11-May JD., Lott, BD., Simmons, JD.,"Water consumption by broilers in high cyclic temperatures: bell versus nipple waterers", Poultry Sci., 76: 944-947, 1997.

12-Feddes, JJ, Emmanuel, EJ, Zuidhoft, MJ., "Broiler performance, body weight variance, feed and water intake, and carcass quality at different stocking densities, Poultry Science, 81(6): 774-779, 2002.

13-Marks, HL., "Selection environment ınfluences on feed and water ıntake of japanese quail following long-term selection for 4-week body weight", Poultry Science 60: 2571-2580. 1981.

14-Leeson, S., Summers JD., "Commercial poultry nutrition", 3rd edition, University Books, Ontario, Canada, 2008.

15-Göncü, KS., Özkütük, K., Görgülü, M., "Sığır yetiştiriciliğinde su gereksinmesi ve içme suyu kalite özellikleri", Hasad Dergisi, Ağustos 24, Sayı 279: 44-51, 2008.

16-Uzun, S., "Su kalitesinin iyileştirilmesinde ozon kullanımı ve kimyasal etkileri", Turk Hij Den Biyol Derg., 68(2): 105-113 | DOI: 10.5505/TurkHijyen. 2011.46330, 2011

17-Özyuvacı, N., "Su kalitesi tayininde kullanılan parametreler ve orman ekosistemleri ile ormancılık uygulamalarının bunlar üzerindeki etkileri", Journal of the Faculty of Forestry Seri B, Cilt 43(1-2): 69-84,1993.

18-Vander, AJ., Sherman JH., Luciano DS., "Human Physiology", 5.Ed. New York (1990).

19-NRC, National Research Council, "Nutrient requirements of ring-necked pheasants, japanese quail, and bobwhite quail, nutrient requirements of poultry (9th rev. ed)", National Academy Press, Washington DC., USA. p. 45, 1994

20-FAO, Water quality guideline for livestock and poultry production for parameters of concern in agrıcultural drainage water (Table A2.1. Guide for the use of saline water for livestock and poultry), http://www.fao.org/docrep/005 /y4263e/y4263e0f.htm, Accessed: 01.03.2016

21-Anonim, Tuzluluk Tayini, http://www.yesilaski.com/tuzluluk-ve-elektriksel-iletkenlik-tayini.html, Erişim Tarihi: 01.03.2016

22-Ersoy, E., Bayşu N., "Biyokimya", AÜ. Veteriner Fakültesi Yayınları No 408, Ankara, 1986.

23-Damron, BL., Kelly, LS., "Short-term exposure of laying hens to high dietary sodium chloride levels", Poultry Sci., 66(5): 825-828, 1987.

24-Pourreza, J., Nili, N., Edriss, MA., "Relationship of plasma calcium and phosphorus to the shell quality of laying hens receiving saline drinking water", British Poultry Science, 35(5): 755-762, 1994.

25-Atteh, JO., Leeson, S., "Influence of increasing the calcium and magnesium content of the drinking water on performance and bone and plasma minerals of broiler chickens", Poultry Sci., 62: 869-874, 1983.

26-Gardiner, E., Chernos, R., "Water quality on poultry farms", Can. Poultryman. 68(8): 36-37, 1981.

27-Koelkebeck, KW., Harrison, PC., Madindou, T., "Research note: Effect of carbonated drinking water on production performance and bone characteristics of laying hens exposed to high environmental temperatures", Poultry Sci., 72: 1800-1803, 1993.

28- Okelo, PO., Carr, LC., Harrison, PC., Douglas, LW., Byrd, VE., Wabeck, CW., Schreuders, PD., Wheaton, FW., Zimmermann, NG., "Effectiveness of using cool roost. cool and carbonated drinking water to relieve heat stress in hens", Annual International Meeting of the American Society of Agricultural Engineers, ASAE, 98, 4038. 1998.

29-Damron, BL., Flunker, LK., "Calcium supplementation of hen drinking water", Poultry Sci., 74: 784-787, 1995.

30- Jensen, LS., Maurice, DV., Chang, CH., "Relationship of mineral content of drinking water to liver lipid accumulation in laying hens", Poultry Sci., 56: 260-266, 1977.

31-Bilici İ, "Sert su arıtma yöntemleri", Ders Notları, web.hitit.edu.tr/dersnotlari /İbrahim bilici- 15.10.2014-5P2A.pdf, 2014.

32-Yalçın, E., Akdemir, Ö., "İskenderun demir çelik fabrikası enerji tesisi saf su hazırlama ünitesinin incelenmesi", Ege Üniversitesi MMO Bilimsel Çalışmalar Teskon, 2015.

33- Watkins, S., "Water: Identifying and correcting challenges", Avian Advice University of Arkansas Cooperative Extension Service, Fayetteville, 10(3): 10-15, 2008.

34-Littlefield, LH., "Drinking water nitrates and chick performance", Poultry Sci., 56: 1352-1360, 1977.

35-Adams, AW., Cunningham, FE., Munger, LL., "Some effects on layers of sodium sulfate and magnesium sulfate in their drinking water", Poultry Sci., 54: 704-714, 1975.

36-Ağaoğlu, S., Alişarlı, M., Alemdar, S., Dede, S., "Van bölgesi içme ve kullanma sularında nitrat ve nitrit düzeylerinin araştırılması", YYÜ Vet Fak Derg, 18(2): 17-24, 2007.

37-WHO, "Fluorine and fluorides. (Environmental health criteria No: 36)", World Health Organization, pp. 25-26, Geneva, 1984.

38-Varol, E., Varol, S., "Çevresel bir hastalık olarak florozis ve insan sağlığı üzerine etkisi" TAF Prev Med Bull, 9(3): 233-238, 2010.

39-Sağlık Bakanlığı, "Doğal kaynak, maden ve içme suları ile tıbbi suların istihsali, ambalajlanması ve satışı hakkında yönetmelik, T.C. Sağlık Bakanlığı, 26 Temmuz 2000/24121 sayılı Resmi Gazete", Başbakanlık Basımevi, Ankara, 2000.

40-Ağaoğlu, S., Ekici, K., Alemdar, S., Dede, S., "Van ve yöresi kaynak sularının mikrobiyolojik, fiziksel ve kimyasal kaliteleri üzerine araştırmalar", Van Tıp Dergisi, 6 (2): 30-33, 1999.

41-Sağlık Bakanlığı, "17 Şubat 2005 sayılı Resmi Gazete'de İnsani tüketim amaçlı sular hakkındaki yönetmelik, T.C. Sağlık Bakanlıgı, (Değişiklik 07 Mart 2013/25730 sayılı Resmi Gazete)", Başbakanlık Basımevi, Ankara, 2013.

42-Grizzle, JM., Armbrust, TA., Bryan, MA., Saxon, AM., "Water quality II: The effect of water nitrate and bacteria on broiler growth performance", J. Appl. Poult. Res. 6: 48-55, 1997a.

43-Alemdar, S., Kahraman, T., Ağaoğlu, S., Alişarlı M., "Bitlis ili içme sularının bazı mikrobiyolojik ve fizikokimyasal özellikleri", Ekoloji, 19(73): 29-38, 2009.

44-Yalçın, E., Akdemir, Ö., "İskenderun demir çelik fabrikası enerji tesisi saf su hazırlama ünitesinin incelenmesi", Ege Üniversitesi MMO Bilimsel Çalışmalar Teskon, 2015.

45-Sağlık Bakanlığı, İnsani tüketim amaçlı sular, TS266/Nisan 2005, Türk Standartları Enstitüsü, Ankara, 2005.

CHAPTER 17

WHAT ARE PROBIOTICS AND PREBIOTICS, HOW ARE THEIR EFFECTS?

Assoc. Prof. Dr. Oktay KAPLAN[1]

[1] Dicle University, Veterinary Faculty, Department of Animal Nutrition, and Nutritional Diseases, 21280, Diyarbakır,TURKEY; ORCID: 0000-0001-6143-8987; E-mail:okaplan61@gmail.com

1. INTRODUCTION

Nutrition; It includes the adequate, balanced and healthy intake of the nutrients it needs depending on the productivity level, gender, species and age of the living thing. Adequate and balanced consumption of nutrients; It is effective in growth and development, sustaining life, protecting, improving and developing health, and increasing the quality of life (Mansoor, 2015). Not enought feeding; although it seriously affects growth, development and health, some cases can lead to irreversible problems, discomfort and even death. However, nutrition can be the direct cause of many diseases and plays an important role in the easy establishment and severe course of many other diseases (Baysal, 2010).

Nutrition is of great importance for livestock as well as for humans. In addition to the use of productive breeds for the development of animal husbandry, adequate and balanced nutrition is required. It is stated that the growth, development and efficiency of animals are proportional to the level of feed efficiency. Accordingly, in order to obtain high efficiency, it is necessary to maximize the use of feed and to protect animal health (Kutlu and Özen, 2009).

When added to feeds in animal nutrition; Substances that are easy to digest by animals, are absorbed in the intestines of animals and transported to the body, improve feed efficiency, positively affect quality and provide economic benefits are expressed as "feed additives" (Kutlu and Şahin, 2017). It is known that antibiotics, which have been used as growth factors in compound feeds for a long time, prevent the

growth of beneficial microorganisms as well as pathogenic microorganisms in the digestive tract of animals. In case of long-term use, pathogenic microorganisms gain resistance to antibiotics and cause a decrease in the effects of antibiotics in treatment. In addition, there are hesitations about the use of antibiotics on the grounds that they threaten human health because they leave residues in animal products. For this reason, the use of probiotics as an alternative to yield-enhancing antibiotics has been emphasized in recent years. (Kahraman et al. 1996; Kaplan et al. 2018; Güler et al. 2019; Özcan et al. 2022). Especially after the prohibition of antibiotics, probiotics and prebiotics have gained importance as alternative feed additives (Ziggers, 2006).

In line with the advances in recent years, it is stated that the annual growth of the probiotic industry in the next 8 years, with a prebiotic growth forecast of 12.7%, will continue to expand the public awareness and acceptance of both probiotics and prebiotics (Mano et al., 2018; Jackson et al., 2019).

2. DEFINITIONS OF PROBIOTIC AND PREBIOTIC

The English equivalent of the word probiotic is “for life”. The origin of this word came about when Nobel Prize-winning Russian researcher Elie Metchnikoff researched why villagers in Bulgaria live long. He attributed the reason for this long life to excessive consumption of yogurt and fresh fermented milk products, and introduced us to probiotic bacteria (Cruywagen et al., 1996; Diler, 2007).

The definition of probiotics has been made in various ways. The term probiotic, which was first defined by Fuller in 1989 as "feed containing live microorganisms that restore the intestinal balance of the host animal", was expanded in 1992 by Havenaar and Huisin't Veld as "a single or mixed culture of living microorganisms that increase the benefit of beneficial microflora in humans and animals". Lastly, it was defined by Guarner and Schaafsman in 1998 as “a certain number of living microorganisms that provide a significant health gain beyond ensuring a healthy life” (Klaenhammer, 2000). It is a live microbial feed additive given orally or by adding to the feed (Kahraman et al. 1996; Yalçın et al. 1996). Commercial probiotic preparations contain live bacteria, fungi, yeast cultures and various enzymes. These preparations may consist of only one microorganism strain, or they may contain up to eight microorganism strains (Fuller, 1989; Yalçın et al. 1996; Nursoy et al. 2004; Özcan et al. 2022).

Prebiotic; It is expressed as non-digestible and short-chain carbohydrates that ferment in the intestine without being digested by enzymes that have beneficial effects on animal health, provide the development of colon bacteria and increase their activities (Demirci et al., 2017). Prebiotics are also expressed as non-digestible components that can benefit the host organism by stimulating the growth or activity of one or more, but limited numbers of probiotics in the colon (Manning and Gibson, 2004). As a final definition, ISAPP 2010 defined a dietary prebiotic as “a selectively fermented ingredient that causes specific changes in the composition and activity of the gastrointestinal

microbiota, thereby conferring benefits on the health of the host" (Gibson et al., 2011).

Prebiotics; It can be produced in three different ways such as microbiological or enzymatic synthesis, extraction from plants and enzymatic hydrolysis of polysaccharides (Gulewicz et al., 2003). Examples of foods that naturally contain prebiotics are yams, asparagus, sweet potatoes, wheat, onions, bananas, apples, mushrooms, forest fruits, honey, chicory root, citrus fruits, garlic, and leeks. Among the prebiotics found in foods, fructooligosaccharides, soybean oligosaccharides, galactooligosaccharides, isomaltooligosaccharides, glucooligosaccharides, xylooligosaccharides, palatinose, inulin and lactulose can be counted (Mussatto and Mancilha, 2007).

Microorganisms commonly used in probiotic production are Lactobacillus and Streptococcus (Fuller, 1989; Yalçın et al. 1996). The European Food Safety Authority (EFSA) has evaluated more than 100 microorganisms as safe and allowed them to be used as food additives. Some of the microorganisms used as probiotics are given in Table 1 (Kum and Sekkin, 2012). Probiotic bacteria, unlike pathogenic bacteria, are gram positive and anaerobic and not pathogenic. Lactobacillus, Leuconostoc, Pediococcus, Streptococcus type bacteria produce lactic acid. In addition, Lactobacillus bacteria are the bacteria that are the most resistant to gastric pH and can maintain their vitality during the passage through the digestive tract (Yalçın et al. 1996).

Table 1. Some of the microorganisms used as probiotics.

Bakteriler		
Bacillus spp.	**Enterococcus spp.**	**Leuconoctoc spp.**
Bacillus cereus	*Enterococcus faecium*	*Leuconoctoc mesenteriodes*
Bacillus coagulans	*Enterococcus facelis*	**Pediococcus spp.**
Bacillus lentus	**Lactobacillus spp.**	*Pediococcus acidilactici*
Bacillus licheniformis	*Lactobacillus acidophilus*	*Pediococcus cerevisiae*
Bacillus pumilis	*Lactobacillus brevis*	*Pediococcus freudenreichii*
Bacillus subtilis	*Lactobacillus buchneri*	*Pediococcus shermanii*
Bacillus toyoi	*Lactobacillus bulgaricus*	**Streptococcus spp.**
Bacterioides spp.	*Lactobacillus bifidus*	*Streptococcus diacetylactis*
Bacteroides amyplophilus	*Lactobacillus casei*	*Streptococcus faecium*
Bacteriodes ruminicola	*Lactobacillus cellobiosus*	*Streptococcus infantarius*
Bacteroides suis	*Lactobacillus curvatus*	*Streptococcus intermedius*
Bifidobacterium spp.	*Lactobacillus delbrueckii*	*Streptococcus lactis*
Bifidobacterium adolescentis	*Lactobacillus farciminis*	*Streptococcus thermophilus*
Bifidobacterium animalis	*Lactobacillus fermentum*	**Vibrio spp.**
Bifidobacterium bifidum	*Lactobacillus gasseri*	*Vibrio fluvialis*
Bifidobacterium breve	*Lactobacillus helveticus*	*Vibrio proteolyticus*
Bifidobacterium infantis	*Lactobacillus johnsonii*	*Vibrio pelagius*
Bifidobacterium lactis	*Lactobacillus kefirio*	
Bifidobacterium longum **Clostridium spp.**	*Lactobacillus lactis*	
Clostridium butyricum	*Lactobacillus paracasei*	
	Lactobacillus plantarum	
	Lactobacillus pontis	
	Lactobacillus reuterii	
	Lactobacillus rhamnosus	
	Lactobacillus sakei	
	Lactobacillus salivarius	
	Lactobacillus zeae	

Mayalar ve Küfler		
Aspergillus spp.	**Saccharomyces spp.**	**Rhodotorula spp.**
Aspergillus niger	*Saccharomyces boulardii*	*Rhodotorula rubra*
Aspergillus oryzae	*Saccharomyces bayanus*	*Torulopsis spp.*
Aspergillus species	*Saccharomyces cerevisiae*	*Torulopsis candida*

symbiotics; Synbiotic substances, named after the synergistic effect of prebiotics and probiotics, are defined as nutrients or additives that contain probiotics and prebiotics together (Douglas and Sanders, 2008). The best known synbiotics are Bifidobacterium + fructooligosaccharides (FOS), Lactobacillus+lactilol, Bifidobacterium + galactooligosaccharides (GOS) combinations (Gülmez and Güven, 2002). Synbiotics are thought to increase probiotic stability in the gastrointestinal tract. The main prebiotics used in foods are given in Table 2.

In a study in which 30 healthy volunteers were fed for two weeks in a synbiotic mixture prepared with B. lactis Bb-12 and FOS, it was revealed that more important results could be obtained than pure probiotics (Rastall and Maitin, 2002). In another study, 50 of 100 female patients with abdominal pain, bloating and gas problems were given FOS, L. paracasei, L. rhamnosus, L. acidophilus and Bb. lactis combination, 50 of them were treated with placebo, and better results were obtained in patients treated with synbiotics (Waitzberg et al., 2013).

Table 2: Main prebiotics used in foods (Mussatto and Mancilha, 2007; Parracho and et al., 2007).

-Inulin -Lactulose -Fructooligosaccharides -Galacto-oligosaccharides -lactosucrose -Gluco-oligosaccharides -Raftilin -Oligomate	-Xylo-oligosaccharides -Palatinosis -Pyrodextrins -Sorbitol -Isomalto-oligosaccharides -soybean oligosaccharides -Gentio-oligosaccharides

3. PROBIOTIC AND PREBIOTIC PROPERTIES

We can summarize the properties of probiotics used in animal nutrition as follows.

-It must be adapted to the normal intestinal flora of the animal to which it is given and isolated from it.

-It must be alive and in the desired concentration.

-It should not be pathogenic and non-toxic.

-It must have the ability to exert beneficial effects in pets, such as increasing growth and increasing resistance to disease.

-It should be resistant to stomach acid, bile and lysozyme enzymes in the intestines while passing through the stomach, and should be activated quickly and show a high ability to multiply.

-They should be able to maintain their vitality during technological processes in feed production.

-It should be able to maintain its stability feature at room temperature before or after adding to the feed.

-It should have the ability and durability to be used for a long time in storage, feed and field conditions (Yalçın et al., 1996; Alçiçek et al., 1998; Sarıca, 1999).

Since probiotics are sensitive to environmental conditions, attention should be paid to feed processing techniques, storage conditions, interaction with feed additives added to mixed feed, pH of the environment, and the characteristics of the carrier used (Sarıca, 1999). Commercial probiotic preparations are prepared in different forms such as powder, granule, pellet, liquid suspension, capsule. When the microorganisms produced are dried in accordance with the freezing technique, they can maintain their vitality for a long time (Sarıca, 1999; Karaayvaz, 2004). Probiotics lose their vitality to a great extent during feed processing techniques (steam pelleting and extrusion processes). For this reason, moisture, temperature and pressure should be considered while adding probiotics to feeds during pelleting in feed factories. Especially Fe and Cu ions, especially mineral premixes, high-density vitamin premixes (especially vitamin K), feed additives such as antifungal and antioxidant can also have a detrimental effect on probiotics (Vanbelle, 1990).

Probiotic preparations should be stored at a temperature of 22-25 degrees and in a dry place. When the storage temperature rises above 30 degrees, bacteria lose their viability (Jones and Thomas, 1987). Although the number of probiotics decreases over time in mixed feeds with low moisture content, since they remain viable for a longer period of time in this type of mixed feed, feeds with probiotic additions should

be stored appropriately in a dry and cool place (Yalçın et al. 1996). In order for probiotics added to diets to be effective as feed additives, to improve the bacterial balance in the gut; stability and ability to survive in feed, and the ability to reproduce after passing through the stomach should have one or more of the features (Jacela et al., 2010).

Five basic important criteria for the classification of prebiotics; It is expressed as resistance to digestion in the upper parts of the digestive tract, fermentation with intestinal microbiota, positive effect on host health, selective stimulation of growth of probiotics, stability in various food or feed processing conditions (Wang, 2009; Slizewska et al., 2013). For a food to have prebiotic properties; It should be resistant to stomach acid, not hydrolyzed by digestive enzymes, not absorbed in the upper parts of the gastrointestinal tract, hydrolyzed by microorganisms in the intestine, and stimulate the proliferation of more microorganisms that have a positive effect on health (Gibson and Roberfroid, 2008). Future prebiotic compounds; It has been disclosed that it can be chemically or structurally modified by the application of high pressure, acid, enzyme and oxidation treatments to change the functionality. It is also stated that unique prebiotic combinations in optimized blends can provide the ability to create new benefit profiles (Lam and Cheung, 2019).

Oligosaccharides cannot be hydrolyzed or absorbed in the small intestine, whereas Lactobacillus spp. and Bifidobacterium spp. They can be fermented by and show prebiotic properties (Marx et al., 2000). Oligosaccharides are found naturally in plants such as chicory, leeks,

artichokes, wheat, soy, legumes, bananas, onions, garlic, asparagus, artichokes and tomatoes, as well as commercially produced by the enzymatic hydrolysis of polysaccharides or by synthesizing from monosaccharides and disaccharides (Manning and Gibson, 2004). In the food industry, fructooligosaccharides, galactooligosaccharides, transgalactooligosaccharides (TOS), xylooligosaccharides (XOS), gentio, lactulose (LAC), lactosucrose, inulin (INU), isomaltooligosaccharides, soybean oligosaccharides (SOS) are the most commonly used prebiotics (Shin et al., 2000). Inulin is one of the substances that has become widespread in food in recent years. Inulin, Lactobacillus spp., and Bifidobacterium spp. It can be fermented by and shows prebiotic properties (Marx et al., 2000; Yildiz et al., 2006). It is reported that free oligosaccharides, one of the natural components of mammalian milk, are found at the highest level in colostrum and protect the newborn against cholera and urinary system infections (Hanson et al., 1999; Yağcı, 2002; Macfarlane et al., 2008). In a study, FOS, INU, GOS, SOS, XOS, LAC were determined by Bifidobacterium animalis subsp. The effect of Lactis BB-12 on growth performance and acidity development was tried to be determined in vitro, and it was determined that all of the tested prebiotics encouraged bacterial growth at certain levels between pH 4.02-5.06, and XOS showed the most positive effect (Şener et al., 2008).

4. PROBIOTIC AND PREBIOTIC EFFECTS ON ANIMALS

In recent years; There has been a significant increase in the number of studies investigating the potential health benefits associated with

probiotics and prebiotics. Many tests have been conducted to validate clinical studies for prebiotics and probiotics. With these clinical studies, it is suggested that probiotics will be used as adjuncts for many treatments such as viral-bacterial infection, lowering serum cholesterol, reducing the risk of colon cancer, lactose intolerance and intestinal microbiota. Due to the situation of probiotics related to animal health and diseases and especially their importance on the immune system, they can be used to stimulate the immune system from birth (Willing et al., 2012). In many studies; There are data showing that probiotics can stimulate the immune system, reduce serum cholesterol, reduce lactose intolerance, reduce diarrhea, control infections, act as antibiotics, suppress tumors and protect against colon/bladder cancer (Corliss et al., 2013).

4.1. EFFECTS OF PROBIOTICS ON ANIMALS

Probiotics taken with foodstuffs should reach the intestine alive and the food should contain at least 106 cfu/g or more live probiotic microorganisms (Akman, 2009). At the same time, it is stated that the microorganisms to be used remain alive during the shelf life and production of the food (Vuyst et al., 2008). Molecular and genetic studies; showed that probiotics have beneficial effects involving four mechanisms (Markowiak and Slizewska, 2017).

1. Antagonism through the production of antimicrobial agents,
2. Adhesion to the epithelium and competition with pathogens for nutrients,
3. Immunomodulation of the host,

4. Inhibition of bacterial toxin production.

In addition, L. acidophilus reduces the serum cholesterol level by affecting the absorption of cholesterol in the intestines. Probiotics play an important role in the prevention of intestinal infections and in the treatment of cancer. The continuous use of antibiotics leads to the formation of bacterial strains resistant to many antibiotics, but healing is delayed due to the destruction of the intestinal flora. Despite these disadvantages of antibiotics, probiotics prevent diseases, accelerate the return of intestinal flora to normal, and ensure healthy development by increasing the animal's self-recovery and feed utilization. In addition, since probiotics are not absorbed from the digestive tract, they do not leave residues in tissues like antibiotics (Sarıca, 1999; Kaplan et al 2018). The modes of action of probiotics, which are quite complex; It varies depending on the probiotic microorganism and its strain, the amount given to the animal, the type and physical condition of the animal, and whether there is a stressful situation in the animal such as adverse environmental conditions (Yalçın et al. 1996).

Probiotics are used to increase feed digestibility, reduce the negative effects of environmental conditions, and increase vitamin and mineral absorption in animals. Stress can cause deterioration of the intestinal flora balance of animals and increase of pathogens. In this way, the amount of feed efficiency in animals decreases and the yield decreases. In order to prevent such negativities, higher efficiency feeds are obtained with probiotics added to the feeds (Niewold, 2007).

The effects of probiotics are listed below;

4.1.1. REDUCING THE NUMBER OF PATHOGENIC BACTERIA

Probiotics produce inhibitory antimicrobial peptides (microsin, bacteriocin) that inhibit the growth of pathogenic bacteria by acting as a direct antagonist on pathogenic microorganisms. It has been shown that S. boulardii suppresses the growth of Candida albicans, Salmonella typhi, Shigella, Escherichia coli (Hennequin and Kaufmann-Lacroix, 2002). It has been determined that the activities of bifido bacteria in the intestine are beneficial for human health, produce antimicrobial substances, and inhibit the activities of some microorganisms such as Staphylococcus aureus, Bacillus cereus, Escherichia coli, Pseudomonas fluorescens, Salmonella typhosa, Shigella dysenteriae, Bacteriodes vulgatus (Heczko et al., 2006).

Probiotic microorganisms inhibit the growth of pathogenic bacteria by synthesizing organic acids such as acetic acid and lactic acid, lowering the pH of the environment and synthesizing H_2O_2. They also increase bowel movements depending on the decrease in the pH of the environment (Mathieu et al., 1993). Lactobacillus acidophilus produces lactic acid, hydrogen peroxide and various bacteriocins (acidolin, acidophilin, lactosidin) that have antibacterial effects against intestinal pathogens. Lactic acid lowers the pH of the environment, creating an unsuitable situation for other bacteria. Hydrogen peroxide, on the other hand, plays a role in the antagonistic effect against intestinal pathogens (Heczko et al., 2006). Probiotics are microorganisms that specifically activate the development of intestinal microflora. It forms the basis of

the barrier that provides protection against pathogens. The composition of the intestinal flora together with the intestinal immune system allows resistant bacteria for protective function. In addition, intestinal microflora has an important place for vitamin synthesis and metabolism of foreign compounds (Marteau et al., 2002). The flora in the digestive system has an important place for both human and animal health.

4.1.2. ADHESION TO THE BOTTOM SURFACE

Probiotics inhibit the growth and invasion of pathogens in many ways. These substances compete with pathogenic bacteria for a limited number of sites in the mucus layer and epithelial cells, prevent the adhesion of pathogens, make it difficult for pathogens to enter with their number and volume advantages, and prevent the translocation of pathogens by strengthening the epithelial barrier. Probiotic is of great importance due to its effect on undesirable microorganisms that reproduce in the intestinal tract, such as Coli bacteria. With the use of probiotics, a protective layer is formed on the intestinal wall and the growth and reproduction of unwanted bacteria is prevented (Alçiçek et al. 1998; Özcan et al. 2022).

In a study, it was determined that S. boulardii competed for Entamoeba histolytica receptors in erythrocytes and reduced the number of trophozoites (Grand and Watkins, 1976). Compositions on the bacterial cell surface may mediate the adhesion of bacteria to intestinal epithelial cells. In an adhesion study with L. gasseri, it was seen that proteins and carbohydrates are necessary for adhesion, and divalent cations (Ca^{+2}) are also effective in adhesion. It has been thought that the adhesion of

Lactobacilli to human intestinal cells is due to the mechanism consisting of different combinations of proteins and carbohydrates on the bacterial surface (Tuomolo et al., 1999). In Table 3, the effect area and mechanism of some probiotics are given.

Table 3: Site of action and mechanism of some probiotics.

Probiotic	Effect zone	Mechanism of action
Lactic acid bacteria	Small intestine	Formation of antimicrobial active substances, formation of essential or some intermediate products to adhere to feed and intestinal wall.
Saccharomyces cerevisiae	Rumen and small intestine	Disintegration of cell wall, effect on rumen volatile fatty acids and pH value, formation of intermediates for various microorganisms.

4.1.3. COMPETITION FOR NUTRITIONAL ELEMENTS

Probiotics inhibit the reproduction of pathogens by consuming the nutrients they need for reproduction: S. boulardii prevents the reproduction of C. difficile by consuming the monosaccharides needed by Clostridium difficile (Castagliuolo et al., 1999).

4.1.4. EFFECT OF ENZYME ACTIVITY

They have an effect on metabolism. They increase the activity of lactase, maltose and sucrase by affecting the intestinal enzyme activity. It is reported that S. boulardii provides maturation of polyamines and aminopeptidases (Mathieu et al., 1993).

4.1.5. EFFECTS ON TOXIN AND TOXIN RECEPTORS

Probiotics reduce the intestinal absorption of toxic substances such as indole, amine, and ammonia (Guerin-Danan et al., 1998). S. boulardii 54 kDA protein has protease activity and acts directly on C. difficile toxin A by preventing the toxin from binding to the receptor. In animal models, it has been shown that cAMP, adenylate cyclase activity decreases with the effect of 120 kDA protein, and water sodium hypersecretion decreases (Reid et al., 2003).

4.1.6. EFFECTS ON THE IMMUNE SYSTEM

It is stated that probiotics have antibacterial effects and have many positive effects on allergic disease and immune system (Holzapfel and Schillinger, 2002). The immune effect of the gut microbiota, including probiotic bacteria, is based on three cases (Borchers et al., 2009). The first of these is the induction and maintenance of immunological tolerance against environmental antigens (nutrition and respiratory), the second is the induction and control of immunological reactions against pathogens of bacterial and viral origin, and the third is; prevention of auto-aggressive and allergic reactions. In an animal experiment with Bifidobacterium breve, it was determined that antibody production increased in peyer's patches. When L. casei shirota strain was given, an increase in the number of T helper and a decrease in the level of IgE were shown (Kognoff, 1993).

Studies on the clinical use of probiotic microorganisms are increasing day by day. Positive effects related to especially intestinal system

diseases, liver, H. pylori, oral and dental health, urogenital system diseases, lactose intolerance, relief of constipation symptoms, stimulation of immune system, allergy, cancer, prevention of various types of diarrhea, regulation of cholesterol level are mentioned. There are many studies on its use in diarrhea due to antibiotic use, which is one of the intestinal system diseases, and inflammatory bowel diseases such as ulcerative colitis, chron's disease, spastic colon (irritable bowel syndrome), necrotizing enterocolitis (Kınık and Gürsoy, 2006).

4.1.7. EFFECTS ON ANTIBIOTIC-RELATED DİARRHOEA

Oral antibiotics in infections destroy the pathogenic microorganisms as well as the beneficial bacteria naturally found in the intestinal flora. As a result, antibiotic-associated diarrhea may occur (Gönç and Akalın, 1995). Meta-analyses show that the most effective probiotic species in this type of diarrhea is Saccharomyces boulardii (Cremonini et al., 2002; Vrese and Marteau, 2007). D'Souza et al. administered S.boulardii (2*500 mg) to 97 hospitalized patients receiving antibiotic treatment; They were followed for 7 weeks. While antibiotic diarrhea developed in 14 patients (14.6%) in the control group (n=9614), diarrhea was found in only 7 (7.2%) of those given S. boulardii (P=0.02) D'Souza et al., 2002. In a study on calves, they stated that probiotics shorten the duration of diarrhea of different origins, reduce lactose sensitivity, decrease bacterial enzyme activity and positively affect the immune system (Verstegena and Williams., 2002).

4.1.8. USAGE IN INFLAMMATORY BOTTOM DISEASES

Ulcerative Colitis (UC): UC is an inflammatory bowel disease characterized by continuous mucosal inflammation extending from the rectum to the colon (Seksik et al., 2008). In a study, 120 individuals with UC were randomly divided into 3 groups consisting of 40 individuals. The first group was given probiotics (2*10/9 cfu/day), the second group was given prebiotics (8.0 g/day psyllium), the third group was given synbiotic (2*10/9 cfu/day+8.0 g/day psyllium). At the end of the 2'nd and 4'th weeks, the results of the blood samples taken from 32 randomly selected individuals were evaluated. Emotional functions in the group using probiotics, intestinal functions in the group using prebiotics, and improvement in both systemic and social functions in the group using synbiotics, as well as a decrease in C-reactive protein (CRP) levels were reported in the individuals in the group using synbiotics (Fujimori et al., 2009).

Chron's Disease: It is a chronic inflammatory bowel disease that can be seen along the digestive tract and can lead to lesions. The effects of Escherichia coli Nissle 1917 and placebo were investigated in cases controlled with steroids. Symptoms disappeared in 70% of those who used E.coli Nissle 1917 for one year and in 30% of those who took placebo for one year (Malchow et al., 1997).

Spastic Colon-Irritable Bowel Syndrome (IBS): IBS is one of the most common gastrointestinal system diseases characterized by abdominal pain, distention, constipation and diarrhea symptoms (Kajander et al., 2005). B. longum LA101, Lb. in 160 patients with IBS.

acidophilus LA102, L. lactis LA103 and S. thermophilus LA104 in a study evaluating the effect of LAB's containing 1*10/10 cfu in total on symptoms, at the end of the 4th week, indigestion, abdominal pain were evaluated 42.6% in IBS symptoms, 41% in abdominal pain, 9 reductions were detected (Holowacz et al., 2008).

Helicobacter Pylori: It has been reported that Helicobacter pylori, which is the main cause of gastritis and peptic ulcer, isolated from endoscopic biopsy specimens of human gastric mucosa, may also be indirectly associated with gastric cancer (Felley and Michetti, 2003). In particular, Lactobacillus has been reported to be the most effective species in preventing the adhesion of H. pyloris to the mucosa (Lesbros-Pantaflickova et al., 2007).They isolated the microorganisms named Lactobacillus cristapus, L. kefiri, L. ferentoshensis, Kluyveromyces lactis, Issatchen orientalis from traditional yogurt produced and consumed in America. They reported that these microorganisms inhibit the growth of H. pylori by mechanisms such as the production of lactic acid and other organic acids, ethanol production, and bacteriocin production (Oh et al., 2002). In another study, it was stated that L. salivarus, which has the ability to produce high amounts of lactic acid, can be used to inhibit the growth of H. pylori and to prevent the binding and colonization of L. reuteri to the receptors in the gastric mucosa by competing with H. pylori (Aiba et al., 1998).

Effect on Liver Functions: Hepatic encephalopathy is an important complication of end-stage liver cirrhosis and liver failure (Solga, 2003). In this disease, it is reported that probiotics reduce the ammonia level

and bacterial urease level of the blood carried in the portal vein that brings blood from the intestines to the liver, and decrease ammonia absorption and intestinal permeability by lowering the pH (Solga, 2003). Control of encephalopathy requires some measures to help reduce the production and absorption of intestinal ammonia or other potentially toxic nitrogenous compounds. Probiotics can inhibit microorganisms with enzyme activity, especially gram-negative microorganisms, by producing inhibitory compounds, reducing the pH, producing short-chain fatty acids, and competing to adhere to the intestinal lumen (Tuohy et al., 2003). The administration of two types of probiotics (in capsules) containing Bifidobacterium, L. acidophilus and Enterococcus species or B. subtilis and E. faecium to 50 patients with cirrhosis for 14 days by Zhao et al. effects on the levels were investigated. As a result of the study, it was determined that the number of Bifidobacteria in the colon increased, blood and fecal ammonia levels and the amount of plasma endotoxin decreased (Zhao et al. 2004).

4.2. EFFECTS OF PREBIOTICS

In the use of prebiotics in the nutrition of animals, the properties of oligosaccharides to increase lactic acid level, increase the pH of the digestive system, and increase the number of beneficial bacteria are beneficial. On the other hand, it has been reported that mannanoligosaccharides improve intestinal mucosa, increase intestinal villi, and increase maltase, aminopeptidase and alkaline phosphatase activity, especially in the jejunum (Iji et al., 2001; Tunç, 2007).

4.2.1. EFFECTS ON HEALTH

Prebiotics are also defined as compounds that can provide beneficial physiological effects on the host, can be metabolized by intestinal microorganisms, and regulate the composition and activity of the intestinal microbiota (Bindels et al., 2015). Prebiotics can act as agents that alter the response of the immune system by increasing or decreasing the strength of the immune system without microorganisms in the intestinal flora (Kunova et al., 2011). The most widely known group of prebiotics is expressed as oligosaccharides (Shin et al., 2000). Oligosaccharides; It is metabolized by species belonging to Lactobacillus and Bifidobacterium genera, causing the formation of short-chain fatty acids. Short chain fatty acids; It has positive effects on health such as preventing colonocytes, increasing sodium absorption, increasing mucosal blood flow, reducing blood cholesterol levels, regulating the immune system, regulating cell proliferation and providing energy (Kavas, 2011).

Prebiotics cause many physiological effects. Some of those; To increase the number of Bifidobacterium in the colon, increase calcium absorption, increase stool weight, shorten gastrointestinal transit time and lower blood lipid levels. Moreover; increased Bifidobacterium in the colon; It benefits host health by producing compounds that will inhibit possible pathogens, lowering blood ammonia levels, and producing vitamins and digestive enzymes (Sharma et al., 2012).

Prebiotics can be used as an additional supplement to probiotics. It is stated that in addition to providing long-term stability in foods or feeds

during the shelf life, they also exhibit positive effects on resistance to processing, consistency and aroma of products. In addition, resistance to acids, proteases and bile salts in the gastrointestinal tract can be considered as other positive properties of prebiotics. Prebiotics eliminate the need for competition with bacteria by selectively stimulating the microorganisms in the intestinal tract of the host, and thus, by stimulating the intestinal microbiota, it determines the fermentation activity and benefits the host by affecting the level of short-chain fatty acids (VandenAbbeele et al., 2013; Sivieri et al., 2014). In fact, prebiotics cause a decrease in intestinal pH and provide osmotic water retention in the intestine (Crittenden and Playne, 2009).

5. RESULT

Broad technological advances in data collection and analytical tools are aimed at enabling the discovery of new candidate probiotics and prebiotics, as well as providing deeper insights into their interactions with the microbiome and host. It is stated that human clinical trials have been developed as well as in vitro and in vivo research to determine the more comprehensive extent of prebiotic effects. Existing targets for prebiotics are now expanding beyond lactic acid bacteria to a broader spectrum of microbial responders (Gibson et al., 2017).

As a result; The use of additional supplements such as probiotics and prebiotics as feed additives, which do not have the risk of leaving residue in animals, has gained importance instead of using the preferred antibiotic for improving performance, health, and efficiency as well as for treatment. In addition, these feed additives regardless of age, species

and gender; It has been determined that it has positive effects on the immune and gastrointestinal system, as well as the effects of benefiting from feed, increase in live weight, increase in growth and development performance. Prebiotics and probiotics have many positive effects on health such as reducing the number of pathogenic microorganisms by showing an inhibitory effect, producing digestive enzymes and improving intestinal functions, as well as increasing the level of antibodies and increasing macrophage activity by improving the immune system. Based on research, the use of probiotics and prebiotics for disease is increasing day by day. It has positive effects on the protection of animal health, especially on the gastrointestinal and immune system. It can be said that testing new combinations in future studies will have a high potential to create an alternative to feed additives.

6. REFERENCES

Aiba, Y., Suzuki, N., Kabir, AMA., Takagi, A., Koga, Y. (1998). Lactic acid-mediated suppression of Helicobacter pylori by the oral administration of Lactobacillus salivarious as a probiotic in a gnotobiotic murine model. Am. J. Gastrol., 93, 2097-2101.

Akman, E. (2009). Bazı laktik asit bakterilerinin probiyotik özelliklerinin incelenmesi, Yüksek lisans tezi, İ.T.Ü. Fen Bilimleri Enstitüsü, İstanbul.

Alçiçek, A., Şayan, Y., ve Özkul. H. (1998). Ruminantların Beslenmesinde Probiyotik Kullanımında Yeni Gelişmeler, Hayvansal Üretim, 38: 32-38.

Baysal, A. (2010). Genel Beslenme 13. Baskı, Hatiboğlu Yayınevi, Ankara.

Bindels, L.B., Delzenne, N.M., Cani, P.D., Walter, J. (2015). Towards a more comprehensive concept for prebiotics. Nature Reviews Gastroenterology & Hepatology, 12(5), 303-310

Borchers, A.T., Selmi, C., Meyers, F.J., Keen, C.L., Gershwin, M.E. (2009). Probiotics and immunity. J. Gastroenterol. 44, 26-46.

Castagliuolo, LM., Riegler, MF., Valenick, I., La Mont, JT., Pathoulakis, C. (1999). Saccharomyces boulardii; protease inhibits the effects of Clostridium difficile toxins A and B in human colonic mucosa. İnfect. Immun., 67, 302-307.

Corliss, A., O'Bryan, Dolar, Pak., Philip, G., Crandall, Sun., Ok, Lee and Steven, C., Ricke, (2013). The role of prebiotics and probiotics in human health O'Bryan et al., J Prob Health, 1:2.

Cremonini, F., Di Caro, S., Nista, E.C. (2002). Meta-analysis: the effect of probiotic administration on antibiotic-associated diarrhoea. Aliment. Pharmacol. Ther., 16, 1461-1467.

Crittenden, R., Playne, M.J. (2009). Prebiotics. In Handbook of Probiotics and Prebiotics; Lee, Y.K., Salminen, S., Eds.; John Wiley & Sons Inc.: Hoboken, N.J., USA, 535–561.

Cruywagen, C.W, Jordaan, I, Venter, L. (1996). Effect of Lactobacillus acidophilus supplementation of milk replacer on preweaning performance of calves. J Dairy Sci, 79(3): 483-486.

Demirci, M., Sağdıç O., Çavuş, M., Pehlivanoğlu, H., Çağlar, M.Y., Yılmaz, M.T. (2017). Prebiyotik Oligosakkaritlerin Kaynakları, Üretimleri ve Gıda Uygulamaları. Avrupa Bilim ve Teknoloji Dergisi. Cilt. 6, No. 10, S. 20-31.

Diler, A. (2007). Probiyotik+Enzim Kombinasyonunun Esmer Irkı Buzağılarda Yemden Yararlanma ve Büyüme Performansı Üzerine Etkileri. Yüksek Lisans Tezi. Atatürk Üniv Fen Bilimleri Enstitüsü, Zootekni Programı. Erzurum.

D'Souza, AI., Rajkumar, J., Cooke, J., Bulpitt, C.J. (2002). Probiotics in prevention of antibiotic associated diarrhoea. Meta-analysis. British Med. J., 324, 1361.

Douglas L.C. and Sanders M.E. (2008). Probiotics and prebiotics in dietetics practice. J. Am. Dietetic Assoc., 108, 510-521.

Felley, C., Michetti, P. (2003). Probiotics and Helicobacter pylori. Best Practice & Research Clinic. Gastroenterol., 17, 785-791.

Fujimori, S., Gudis, K., Mitsui, K., Seo, T., Yonezawa, M., Tanaka, S., Tatsuguchi, A., Sakamoto, C.A. (2009). Randomized controlled trial on the efficacy of synbiotic versus probiotic and prebiotic treatment to improve the quality of life in patients with ulcerative colitis. Nutrition. 25:520–525. doi: 016/j.nut.2008.11.017.

Fuller, R. (1989). A Review. Probiotics İn Man And Animals. J.Appl. Bact., 66:365-378.

Gibson, G.R., Roberfroid, M.B. (2008). Handbook of Prebiotics. Boca Raton, Florida: CRC Press.

Gibson, G. R., Scott, K. P., Rastall, R. A., Tuohy, K. M., Hotchkiss, A., Dubert-Ferrandon, A., Buddington, R. (2011). Dietary prebiotics: current status and new definition. Food Science & Technology Bulletin Functional Foods. 7(1), 1-19.

Gibson, G. R., Hutkins, R., Sanders, M.E., Prescott, S.L., Reimer, R.A., Salminen, S.J., Scott, K., Stanton, C., Swanson, K.S., Cani, P.D., Verbeke, K., Gregor Reid, G. (2017). Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. Nat. Rev. Gastroenterol. Hepatol. 14, pp. 491-502

Gönç, S., Akalın, A.S. (1995). Yoğurtta canlı olarak bulunan Lactobacillus acidophilus ve Lactobacillus bifidus'un organizma ve sağlık üzerine etkisi. Gıda.20 (2): 75-80.

Grand, RJ., Watkins, J.B. (1976). Development of the human gastrointestinal tract. A review. Gastroenterol., 70, 790-810.

Guerin-Danan, C., Chabene,t C., Pedone, C., Po-pot, F. (1998). Milk fermented with yogurt cultures and lactobacillus casei compared with yogurt and gelled milk influence on intestinal microflora in healthy infants. J. Clin. Nutr., 67, 111-117.

Gulewicz, P., Ciesiolka, D., Frias, J, Vidal-Valverde, C., Frejnagel, S., Trojanowska, K., Gulewicz, K. (2003). Simple method of isolation and purification of α-galactosides from legumes. Journal of Agricultural and Food Chemistry. 48, 3120–3123.

Gülmez, M., Güven, A. (2002). Probiyotik, prebiyotik ve sinbiyotikler, Kafkas Üniversitesi Veteriner Fakültesi Dergisi, 8(1),83-89.

Güler, A., Kaplan., O., Bozkaya, F. (2019). Bazı kaba yemlere ilave edilen probiyotiklerin in vitro organik madde sindirimi ve metan üretimi üzerine etkileri. Harran Üniv Vet Fak Derg. 8 (1): 93-98.

Hanson L., Dahlman-Höglund A., Karlsson M. (1999). Normal microbial flora of gut. In "Probiotics", Other Nutrition, Workshop Series, 42, 217-228. Hanson L., Yolken R. Eds., Lippincott Raven Publishers, USA.

Heczko,PB., Strus, M., Kochan, P. (2006). Critical evaluation of probiotic activitiy and lactic acid bacteria and their effects. J. Phsiol. Pharm., 57(Suppl 9), 5-12.

Hennequin, C., Kaufman-Lacroix. (2002). Possible role of catheters in Saccharomyces boulardi fungemia. Eur. J. Clin. Mikrobiol. İnfect. Dis., 19,16-20.

Holowacz, SD., Bieuvelet, S., Burckel, A., Cazauble, M., Dray, X., Marteau, P.A. (2008). Double blind randomized controlled trial of probiotic combination in 100 patients with irritable bowel syndrome. Gastroentèrologie Cliniq. Et biolog., 32, 147-152.

Holzapfel, W.H., Schillinger, U. (2002). İntroduction top re-and probiotics. Food Research International. 35, 109-116.

Iji, P.A., Saki, A.A., Tivey, D.R. (2001). Intestinal structure and function of broiler chickens on diets supplemented with a mannan oligosaccharide. J. Sci. Food Agric., 81: 1186-92.

Jacela, J.Y., DeRouchey, J.M., Tokach, M.D., Goodband, R.D., Nelssen, J.L., Renter, D.G., Dritz, S.S. (2010). Feed additives for swine: Fact sheets–prebiotics and probiotics, and phytogenics. Journal of Swine Health and Production, 18(3), 132-136.

Jackson, S.A., Schoeni, J.L., Vegge, C., Pane, M., Stahl, B., Bradley, M., Goldman, V.S., Burguiere, P., John B. Atwater, J.B., Mary Ellen Sanders, M.S. (2019). Improving End-User Trust in the Quality of Commercial Probiotic Products. Front. Microbiol., 10, p. 739.

Jones, C.D. and Thomas, C.N. (1987). The Maintenance Of Strain Specifity And Bile Tolerance When Producing Stable Bacteria. Alındı: Biotechnology İn The Feed Industry (Ed. T.P.Lyons). Alltech Technical Publication. Kentucky, 157-166.

Kahraman, R., Alp, M., Kocabağlı, N., Irmak, G. Ve Şenel, H.S. (1996). The Effects Of Fastrack And Sodium Bicarbonate On Performance Of Broilers. Tr. J.Of Veterinary And Animal Sciences 20:383-386.

Kajander, K., Hatakka, K., Poussa, T., Farkkila, M., Korpela, R. (2005). A probiotic mixture alleviates symptoms in irritable bowel syndrome patients: a controlled 6-month intervention. Alimentary Pharm. Therap., 22, 387-394.

Kaplan, O., Avci, M., Denek, N., Baran, M.S., Nursoy, H., Bozkaya, F. (2018). Influence of humic acid addition to drinking water on laying performance and egg quality in Japanese quails. Indian J. Anim. Res., 52(9) 1309-1312.Doi: 10.18805/ijar.B-874.

Karaayvaz, B.K. (2004). Probiyotiklerin Kuzu Besisinde İn-Vivo ve İn-Vitro Etkilerinin Araştırılması. E. Ü. Fen Bilimleri Enstitüsü Doktora Tezi, İzmir, 149 s.

Kavas, N. (2011). Fonksiyonel Keçi Peyniri Üretiminde Sinbiyotik Mikrokapsüllerin Kullanımı ve Canlılıklarının İncelenmesi. Doktora Tezi. Ege Üniversitesi Fen Bilimleri Enstitüsü.

Kınık, Ö., Gürsoy, O. (2006). Probiyotik bakterilerin klinik uygulamalarında yeni gelişmeler-I, Ege Üniv. Ziraat Fak. Derg., 43, 181-188.

Kognoff, M.F. (1993). Immunology of the intestinal tract. Gastroenterology, 105, 1275-1280.

Lesbros-Pantoflickova D., Corthesy-Theulaz I., Blum A.L. (2007). Helicobacter pylori and Probiotics. J. Nutrition, 137, 812-818.

Kum, C., Sekkin, S. (2012). Alternative approaches to antibiotics. Turkiye Klinikleri Journal of Veterinary Sciences Journal, 3(3), 84-116.

Kunova, G., Rada, V., Lisova, I., Rockova, S., Vlkova E. (2011). In vitro fermentability of prebiotic oligosaccharides by lactobacilli. Czech J Food Sci, 29(1), S49-S54.

Kutlu H., ve Şahin, A. (2017). Kanatlı Beslemede Güncel Çalışmalar ve Gelecek için Öneriler Hayvansal Üretim 58(2): 66-79.

Kutlu, H.R., Özen, N. (2009). Hayvan Beslemede Son Gelişmeler. VI. Ulusal Zootekni Bilim Kongresi, Atatürk Üniversitesi, Erzurum.

Lam, K.L., Cheung P.C. (2019). Carbohydrate-based prebiotics in targeted modulation of gut microbiome. J. Agric. Food Chem., 67, pp. 12335-12340

Macfarlane GT., Steed H., Macfarlane S. (2008). Bacterial metabolism and health-related effects of galacto- oligosaccharides and other prebiotics. J. Appl. Microbiol. 104, 305-344.

Malchow, H.A. (1997). Crohn's disease and Escherichia coli. A new approach in therapy to maintain remission of colonic Crohn's disease. J. Clinic. Gastroenterol., 25, 653-658.

Manning, T.S., Gibson, G.R. (2004). Prebiotics. Best practice & research clinical gastroenterology, 18(2), 287- 298.

Mansoor, S. (2015). Nutrition education curriculum for training physicians in medical colleges of Pakistan. Pakistan Armed Forces Medical Journal, 65(3), 382-385.

Mano, M.C.R., Numa, I.A.N., Silva, J.B., Paulino, B.N., Pessoa, M.G., Pastore, G.M. (2018). Oligosaccharide biotechnology: an approach of prebiotic revolution on the industry Appl. Microbiol. Biotechnol., 102, pp. 17-37

Markowiak, P., & Śliżewska, K. (2017). Effects of probiotics, prebiotics, and synbiotics on human health. Nutrients, 9(9), 1021.

Marteau, P., Seksik, P., Jian, R. (2002). Probiotics and intestinal health effects: a clinical perspective. British Journal of Nutrition. 88 (1), 51.

Marx, S.P., Winkler, S., Hartmeier, W. (2000). Metabolization of beta-(2,6)-linked fructose-oligosaccharides by different bifidobacteria. FEMS Microbiology Letters. 182, 163-169.

Mathieu, F., Sudirman, I., Rekhif, N. (1993). Mesenterocin 52, a bacteriocin produced by Leuconostoc Mesenteroides Ssp. Mesenteroides Fr 52. J. Appl. Bacteriol., 74,372-379.

Mussatto, S.I., Mancilha, I.M. (2007). Non-digestible oligosaccarides. Carbohidrate Polymers, 68, 587-597.

Niewold, T.A. (2007). The Nonantibiotic anti-inflammatory effect of antimicrobial growth prometers, the real mode of action? A hypotesis. Poult. Sci. 86, 605-609.

Nursoy, H., Kaplan, O., Oğuz, M. N., Yılmaz, O. (2004). Effects Of Varying Levels Of Yeast Culture On Yield And Some Parameters İn Laying Hen Diets. Indian Veterinary Journal.81: 59-62.

Oh, Y., Osato, MS., Han, X., Bennett G., Hong WK. (2002). Folk yoghurt kils Helicobacter pylori. J. Appl. Microbiol., 93, 1083-1088.

Özcan, C, Tufan, T., Karakoç, Z., İrak, K., Arslan, C., Kaplan, O. (2022). The Effect of Using Different Forms of Probiotic (Bacillus sp.) on Fattening Performance, Blood and Carcass Parameters in Japanese quail (Couturnix Couturnix Japonica). ISPEC Journal of Agr. Sciences 6(1): 178-188.

Parracho H., McCartney A.L., Gibson, G.R. (2007). Probiotics and prebiotics in infant nutrition. Proc. Nutr. Soc. 66, 405-411.

Rastall AR., Maitin, Y. (2002). Prebiotics and synbiotics: towards the next generation. Current Opinion Biotechnol. 13, 490-496.

Reid, G., Jass, J., Sebulsky, MT., Mc Cormick, J.K. (2003). Potential uses of probiotics Reid in clinical practice. Clinic Microbiol. Rev., 16, 658-672.

Sarıca, Ş. (1999). Kanatlı hayvan beslemede probiyotik kullanımı. Hayvansal Üretim 39-40: 105-112.

Seksik, P., Dray X., Sokol H, Marteau P. (2008). Is there any place for alimentary probiotics, prebiotics or synbiotics, for patients with inflammatory bowel disease Molec. Nutr. Food Res., 52, 906-912.

Sharma, S., Agarwal, N., Verma, P. (2012). Miraculous health benefits of prebiotics. International Journal of Pharmaceutical Sciences and Research, 3(6), 1544.

Shin, H.S., Lee, H., Pestka, J.J., Ustunol, Z. (2000). Growth and viability of commercial Bifidobacterium spp. in skim milk containing oligosaccharides and inulin. Journal of Food Science, 65, 884-887.

Sivieri, K., Morales, M.L.V., Saad, S.M.I., Adorno, M.A.T., Sakamoto, I.K., Rossi, E.A. (2014). Prebiotic effect of fructooligosaccharide in the simulator of the human intestinal microbial ecosystem (SHIME (R) Model). Journal of Medicinal Food,17, 894–901.

Slizewska, K., Nowak, A., Barczynska, R., Libudzisz, Z. (2013). Prebiotyki-definicja, właściwości i zastosowanie w przemyśle. Żywność Nauka Technologia Jakość, 20(1).

Solga, S.F. (2003). Probiotics can treat hepatic encephalopathy. Medical Hypotheses, 61, 307-313.

Şener A., Temiz A., Toğay S.Ö., Bağcı U. (2008). Çeşitli prebiyotiklerin Bifidobacterium animalis Subsp. Lactis Bb-12'nin gelişimi ve asitlik geliştirme özelliği üzerine in vitro etkileri. Türkiye 10. Gıda Kongresi, Erzurum.

Tunç, M.A. (2007). Humatların koyunlarda rumen parametreleri ve bazı kan değerleri üzerine etkisi. Yüksek Lisans Tezi, Atatürk Üniv. Hayvan Besleme ve Beslenme Hastalıkları A.D., Erzurum, 9.

Tuohy, K.M., Probert, H.M., Smejkal C.W., Gibson G.R. (2003). Using probiotics and prebiotics to improve gut health. Drug Discov. Today, 8, 692-700.

Tuomolo E.M., Ouwehand A.C., Salminen S.J. (1999). The effect of probiotic bacteria on the adhesion of pathogensto human intestinal mucus. FEMS Immunol. Medical Microbiol.,26, 137-142.

Waitzberg D.L., Loqullo, L.C., Bittencourt, A.F., Torrinhas, R.S., Shiroma, G.M., Paulino, N.P., Teixeira-da-Silva, M.L. (2013). Effect of synbiotic in constipated adult women– A randomized, double-blind, placebo-controlled study of clinical response. Clin. Nutr. 1, 27-33.

Wang, Y. (2009). Prebiotics: Present and future in food science and technology. Food Research International, 42, 8-12.

Willing, B.P., Malik, G., Van, Kessel, A.G. (2012). Nutrition and gut health in swine. In: Chiba L.I., editor. Sustainable swine nutrition. Chichester: Wiley. 197–213.

Vanbelle, N., Teller, E., Focant, M. (1990). Probiotics in Animal Nutrition. A Review. Arciv Animal Nutrition 40:543-567.

Verstegena, M.W.A., Williams, B.A., (2002). Animal Biotechnology, ISSN: 1532-2378, Alternatives to the use of antibiotics as growth promoters for monogastric animals, Department of Animal Sciences, Animal Nutrition Group, Wageningen University 13(1), 113-127.

VandenAbbeele, P., Venema, K., Van de Wiele, T., Verstraete, W., Possemiers, S. (2013). Different human gut models reveal the distinct fermentation patterns of arabinoxylan versus inulin. Journal of agricultural and food chemistry, 61(41), 9819-9827.

Vrese, M., Marteau, P.R. (2007). Effects of probiotics and prebiotics. J. Nutrition, 137, 803-811.

Vuyst, L., Falony, G., Leroy, F. (2008). Probiotics in fermented sausages. Meat Science, 80, 75-78.

Yalçın, S., Çiftçi, İ., Önal, A. G. Ve Yılmaz, A. (1996). Tuyem " 3. Uluslararası Yem Kongresi ve Yem Sergisi'' 30-33.

Yağcı R. (2002). Prebiyotikler ve probiyotikler. Çocuk sağlığı ve hastalıkları dergisi. 45, 337-344.

Yildiz G, Sacakli P, Gungor T. (2006). The effect of dietary Jerusalem artichoke (Helianthus tuberosus L.) on performance, egg quality characteristics and egg cholesterol content in laying hens**.** Czech J. Anim. Sci., 51, 349–354.

Zhao, H.Y., Wang, H.J., Lu Z., Xu S.Z. (2004). Intestinal microflora in patients with liver cirrhosis. Chinese. J. Dig. Dis., 5, 64-67.

Ziggers, D. (2006). Feed additives, what they were and what they have become. Feed Technology, 10(1), 16-19.

ISBN: 978-625-8323-21-4