VETERINARY SCIENCE AND CURRENT STUDIES I

EDITORS
Doç. Dr. Oktay KAPLAN
Prof. Dr. Mehmet ÇİFTÇİ

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Assoc. Prof. Dr. Oktay KAPLAN
Prof. Dr. Mehmet ÇİFTÇİ

AUTHORS
Prof. Dr. Gültekin YILDIZ
Prof. Dr. Halil Selçuk BIRICIK
Prof. Dr. Hüseyin NURSOY
Prof. Dr. Mehmet ÇİFTÇİ
Assoc. Prof. Dr. Berna DUMAN AYDIN
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Dr. Selcen ARSLAN
İlker ALTINTAŞ
Muhammet Alperen HAMEŞ

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

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Iksad Publications – 2024©

ISBN: 978-625-378-032-6
Cover Design: İbrahim KAYA
December / 2024
Ankara / Türkiye
Size: 16x24cm

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PREFACE

Veterinary medicine is becoming more and more critical in terms of both protecting animal health and indirectly contributing to human health. The health of animals plays a vital role both in improving their welfare individually and in preventing problems that may threaten human health such as zoonotic diseases. For this reason, veterinary doctors should be professionals who not only have medical knowledge but also can adapt to constantly changing technology and scientific developments. Veterinary medicine is not only a field limited to clinical interventions; it also has a wide range of responsibilities such as animal rights, ethical issues, health policies and public health. Progress in the field of veterinary medicine is possible not only by having existing knowledge, but also by continuously updating this knowledge.

This book aims to bring together the most up-to-date approaches of veterinary medicine and to shed light on veterinarians, students and anyone interested in the field who want to discover scientific advances and new treatment methods in this field. Believing that veterinary medicine will gain even greater importance in the coming years, we hope that the book "Veterinary Science and Current Studies I" will be both a practical information and an inspiring source.

EDITORS
Doç. Dr. Oktay KAPLAN[1]
Prof. Dr. Mehmet ÇİFTÇİ[2]

[1] Dicle University, Veterinary Faculty, Department of Animal Nutrition, and Nutritional Diseases, 21280, Diyarbakır, Turkiye; ORCID: https://orcid.org/0000-0001-6143-8987; E-mail: okaplan61@gmail.com

[2] Department of Animal Nutrition and Nutritional Diseases, Faculty of Veterinary Medicine, University of Firat, 23119, Elazig, Turkiye; ORCID: https://orcid.org/0000-0002-3009-8710; Email: mciftci@firat.edu.tr

CHAPTER I

THE EFFECT OF LEVAMISOL AND BETA-GLUCANS ON SOME BLOOD PARAMETERS AND IMMUNOGLOBULIN G LEVELS IN HORSES WITH BABESIOSIS

Prof. Dr. Gültekin YILDIZ[1]
İlker ALTINTAŞ[2]

DOI: https://dx.doi.org/10.5281/zenodo.14550957

[1] Ankara University, Faculty of Veterinary Medicine, Department of Animal Nutrition & Nutritional Diseases, Ankara, Türkiye; gyildiz@ankara.edu.tr
ORCID ID: 0000-0002-1003-9254
[2] Ankara University Health Sciences Institute Graduate Student.
ilkeraltintas2005@hotmail.com ORCID Kimliği: 0009-0005-2351-4156

Introduction

Babesiosis is a common disease caused by tick-borne protozoan parasites of the *Babesia* genus. It is characterized by symptoms such as fever, depression, anorexia, jaundice, and hemoglobinuria (Stephen et al., 1998).

The immune-stimulating effects of polysaccharides have been widely studied in recent years (Vetvicka, 2003). Animals treated with beta-glucan recover more quickly from infections caused by microorganisms like viruses, bacteria, fungi, and parasites (Engstad and Robertsen, 1994).

Beta-glucan plays a crucial role in stimulating macrophages (Vetvicka, 2003). The anti-infective properties of β-glucan can be attributed to its immune-enhancing capabilities (Wyde, 1989). It is known to have immunomodulating effects, enhancing immunity against a wide range of microbial infections (Quintin et al., 2012; Vetvicka, 2021).

β-1→3-D -glucans are key components of microbial cell walls and can be secreted by both pathogenic and non-pathogenic fungi, such as *Saccharomyces cerevisiae* (Bartnicki-Garcia, 1968). These β-1→3-D-linked glucose polymers are recognized as pathogen-associated molecular patterns (PAMPs), which can influence biological responses (Gordon, 2002).

Known for decades for its immunomodulatory effects, β -glucan, derived from fungi and yeasts, boosts immunity against various infections by modifying biological responses. It has been successfully used in rat models and in vitro studies focusing on sepsis and SIRS (Lacerenza et al., 2024).

A study by Lacerenza et al. (2024) explored the effects of preventive β -glucan supplementation in horses with endotoxemia, focusing on the modulation of inflammatory responses. Horses from experimental groups showed clinical signs and hematological changes associated with endotoxemia, such as elevated heart rate, body temperature, and increased levels of bilirubin, glucose, lactate, and cytokines like TNF-a, IL-6, and IL-10. Importantly, β-glucan did not compromise liver or kidney function. The β-glucan group had higher serum total protein, globulins, and IL-8 levels compared to Controls. Additionally, peritoneal fluid analysis revealed lower neutrophil concentrations and higher macrophage concentrations in the β -glucan group. While β -glucan did not reduce clinical endotoxemia signs, its preventive use seemed to modulate immune responses, suggesting its potential for prophylactic use in endotoxemia treatment in horses.

Endotoxemia in horses, caused by diseases like colic, pleuropneumonia, and metritis, is a serious condition that can lead to death. This study highlights the importance of finding treatments or preventative measures for this condition. Yeast-derived β-glucans, particularly those from *Saccharomyces cerevisiae,* are known to have immune-modulating properties. The study suggests that supplementing horses with β -glucans can enhance their immune response to endotoxemia induced by intravenous injection of E. coli lipopolysaccharide (Lacerenza et al., 2024).

Preventive oral supplementation with β-glucan at 10 mg/kg/day for 30 days led to changes in immune response, including higher serum total proteins, globulins, IL-8 levels, and changes in peritoneal inflammatory cells, though clinical endotoxemia signs were not significantly reduced (Lacerenza et al., 2024).

Currently, β -glucan from yeast is widely used as a protective substance against infections due to its ability to stimulate both innate and adaptive immunity (Chen et al., 2012; Masuda et al., 2013). These polymers activate the immune response through the complement system, either directly or with the help of antibodies, and produce chemotactic factors that guide leukocytes to infection sites. Additionally, β-glucan has been shown to activate leukocytes, stimulating their phagocytic and antimicrobial activities, as well as the production of pro-inflammatory mediators (Cloetens et al., 2012). Studies have demonstrated its protective effects against various pathogens such as *Leishmania major, Candida albicans, Streptococcus suis,* and *Escherichia coli* (Vetvicka, 2011; Santos et al., 2019).

Moreover, β-glucan has been shown to modify responses to pro-inflammatory stimuli, such as sepsis. In murine models of polymicrobial sepsis, β-glucan reduced morbidity and mortality, underscoring its anti-inflammatory potential by promoting the interleukin-1 antagonist receptor (IL-1 RA) pathway, which counteracts inflammation (Williams et al., 1991; Luhm et al., 2006).

The preventive use of β-glucan resulted in higher levels of serum total proteins and globulins compared to the control group, suggesting a better immune response. Globulins, especially immunoglobulins, are directly involved in antigen binding and the immune response (Walther et al., 2015). Additionally, β-glucan supplementation led to a change in the cell composition

of peritoneal fluid, with lower neutrophil concentrations and higher macrophage concentrations compared to the control group, though the total nucleated cell count remained unchanged. These findings align with previous studies showing that endotoxemia induced by intravenous LPS does not alter total white blood cell counts in peritoneal fluid (Valadao et al., 1995).

Levamisole, known for its nonspecific immune-enhancing effects, including increased lymphocyte proliferation, macrophage phagocytosis, and enhanced neutrophil chemotaxis sensitivity, has been used to support immune systems under stress (Aydın, 1998). A study by Krakowski et al. (1999) found that administering both beta-glucan and levamisole to pregnant mares increased immune globulin levels in their colostrum and influenced foals' immune responses, though results were somewhat controversial.

While β-glucan has shown promise in rat models and in vitro studies for treating sepsis and SIRS, it has not been extensively evaluated for clinical babesiosis in horses. Thus, this study aims to assess whether yeast-derived B-glucan, with its ability to modulate systemic immunity, could benefit the treatment of clinical babesiosis in horses by modulating the systemic inflammatory response.

This study seeks to investigate the immune-stimulating effects of *Saccharomyces cerevisiae-der*ived β-glucan, administered orally to horses with presumed immune suppression due to clinical babesiosis, and compare the outcomes between levamisole and control groups.

- **Materials and methods**

The study carried out on 18 races horses aged between 3-5 years old and have 380-480 live weights in Ankara Hippodrome of Jockey Club of Turkey. In the study the horses, which showed babesiosis symptom clinically and were detected by the Giemsa painting technique were used.

The horses divided into three groups as control, beta glucan and levamisol. The patients with babesiosis were separated to each group one by one. Standard treatment (Imidocarb, oxitetracycline, liquid support) for the disease was practiced to the horses in the Control Group. During the study in addition to the standard treatment 0,2 mg/kg BW dosage of beta glucan (Imuneks®), which is obtained from *Saccharomyces cerevisiae* is orally given to beta glucan Group every day. And to the third group named Levamisol Group

2.5 mg/kg BW dosage of levamisol (Nilverm®) is orally given every other day be sides the standard treatment. Levamisol and beta glucan are given to the test animals either in carrot or apple or by injection in to the mouth. Practices have begun just after the determination of the disease and continued 14 days.

In the period of the disease the horses are fed with unlimited dry hay in the first week and beginning from the second week they are fed with about 1 kg of oats besides unlimited dry hay.

The horses whose immune systems are thought to be under pressure related to clinical babesiosis are taken into the investigation after measuring their RBC, IgG levels and serum ALP, LDH, SGOT, CK, total protein and total bilirubin levels. For hemogram analysis Hemavet 850 automatic equipment; and for fıxing ALP, LDH, SGOT, CK, total protein and total bilirubin levels Humolyzer 2000 CD automatic equipment (whose calibration have been regulated for horses) have been used.

Blood samples are taken from *Vena jugularis* of the horses in the morning on the determination day of the disease (first day), and on the following 4^{th}, 7^{th} and 14^{th} days.

For the determination of IgG level blood serums taken on the 14^{th} day were used. Determination of IgG level was done with Elisa kit (Bethyl, USA).

Analyses of research results are done with Repeated Measurement Varian's Analyses Technique. Group factor has three levels as control, beta glucan and levamisol; time factor has four levels 1^{st}, 4^{th}, 7^{th} and 14^{th} days. Observation numbers are different in subgroups.

To determine the differences between groups and times Bonferroni and Duncan tests, which are among multi-comparison techniques, are used (Sümbüloglu and Sümbüloglu, 1995; David, 2000). For statistical calculations SPSS 18.0 program is used. In Duncan test;

A, B, C = Capital letters are used for the result of statistical comparison between groups in each time. ($p<0.01$).

a, b, c = Minor letters show statistical comparison of the differences between time averages in each group. ($p<0.01$).

- **Results**

In calculations done according to ALP levels Group x Time interaction is found to be important from the point of view of statistic. ($p<0.01$) (Table 1).

In calculations done according to LDH, SGOT, CK (Table 1) and RBC, hemoglobin and hematocrit values (Table 2), total bilirubin, total protein, IgG (Table 3) levels Group x Time interaction is found to be not important from the point of view of statistic. Differences between groups are not statistically important. Differences between times are statistically important ($p<0.01$).

In calculations done according to lymphocyte and monocyte values Group x Time interaction is found to be important from the point of view of statistic ($p<0.01$) (Table 2).

- **Discussion**

The serum alkaline phosphatase (ALP) values (Table 1) in this study showed a decrease in the beta-glucan group on day 4 and in the levamisole group on day 14. Specifically, the decrease was 14.1% in the levamisole group and 15.9% in the beta-glucan group. In both the control and treatment groups, the ALP values remained within the normal reference range (Canadian Council on Animal Care, 1993), suggesting that neither levamisole nor beta-glucan had a significant impact on ALP levels. However, when evaluating the ALP values over time, significant differences were observed between the first-day values and those at later time points in the beta-glucan group ($p<0.01$). A similar observation was made between the first and 14th-day values in the levamisole group ($p<0.01$), indicating a time-dependent effect of both treatments.

It is believed that beta-glucan may partially prevent an increase in lactate dehydrogenase (LDH) levels (Table 1). The observed time-dependent decrease in LDH values across all groups suggests a positive treatment response. Babesiosis, a parasitic disease known to cause hemolysis (Stephen et al., 1998), results in the breakdown of erythrocytes, which subsequently leads to an increase in LDH enzyme levels (Blackmore and Brobst, 1981). As the disease progresses, LDH levels rise but later decrease due to the effects of the treatments. By day 14, LDH values were still elevated compared to normal values (Merck Veterinary Manual, 2005), likely because of the prolonged half-life of the LDH enzyme (Robinson and Edward, 1998). These findings indicate that while treatment may reduce LDH levels, the normalization of these levels may take longer.

Regarding serum glutamic oxaloacetic transaminase (SGOT) levels, all groups showed values above the normal reference range (Canadian Council on

Animal Care, 1993; Merck Veterinary Manual, 2005). This is not unexpected since SGOT is produced by the liver, erythrocytes, and muscles (Blackmore and Brobst, 1981), and hemolysis during the clinical progression of babesiosis contributes to an increase in SGOT levels. SGOT levels typically return to normal within 7-10 days after hemolysis (Andrews and Reed, 1986). Statistical analysis revealed significant changes over time ($p<0.01$), with initial increases in SGOT levels followed by a decrease as the treatment progressed.

An increase in both SGOT and creatine kinase (CK) levels, especially in the absence of recent strenuous exercise, suggests that the muscles may have been affected by the disease (Kobluk et al., 1995). In this study, blood serum CK levels decreased from day 1 to day 14 (Table 1), indicating a possible improvement in muscle health as a result of the treatment.

When examining red blood cell (RBC) counts, a decrease was observed in the levamisole group on day 4. This could be due to a slower progression of the disease in the horses in this group. In contrast, beta-glucan appeared to prevent the decline in RBC counts, helping to maintain RBC levels within normal limits (Canadian Council on Animal Care, 1993).

The blood hemoglobin values reached normal levels (Canadian Council on Animal Care, 1993) on day 4 in the beta-glucan group and on day 7 in the control group (11.1-19.0 g/dl). However, the fact that hemoglobin levels did not normalize by day 14 in the control group suggests that disease progression had a more significant impact on recovery in this group. The same observation was made for hematocrit values (Table 2), indicating that beta-glucan treatment may shorten the recovery time by at least one week compared to the other groups.

Blood lymphocyte values (Table 2) remained within normal limits (Canadian Council on Animal Care, 1993; Garlinghouse and Fleming, 2005). In the levamisole group, lymphocyte levels were significantly higher on day 4 compared to day 14 ($p<0.01$), suggesting an initial immune response followed by a return to baseline levels. This increase in lymphocyte levels may reflect an immune system response to the babesiosis infection, with a gradual normalization occurring after the treatment.

Monocyte levels (Table 2) showed interesting trends in both the beta-glucan and levamisole groups. In the beta-glucan group, monocyte levels were high on day 1 but decreased rapidly over time, whereas in the levamisole group,

there was a significant increase in monocytes on day 4 ($p<0.01$). This suggests that beta-glucan exerted its effects early, when macrophage activation was crucial to control tissue destruction and injury. By day 14, monocyte levels in all groups returned to normal ranges (Garlinghouse and Fleming, 2005), suggesting that tissue repair was underway.

When evaluating total protein values, no significant differences were found between the groups or over time (Table 3). This lack of variation could be attributed to the rehydration caused by intravenous fluid support provided to all groups during treatment.

Total bilirubin levels were elevated on day 1 in all groups (Table 3), which is a typical finding in cases of babesiosis, as the disease leads to immune system suppression and hemolysis. The increase in bilirubin is likely a result of hemolysis induced by the parasitic infection. The observed decrease in bilirubin levels across all groups suggests that the Standard treatment effectively addressed the underlying hemolysis.

IgG levels were measured on the 14th day using the ELISA technique. While no significant statistical differences were found between groups, numerical differences were noted (Table 3). These differences were not considered statistically significant due to the small sample size, which limited the statistical power of the analysis. It is expected that future studies with a larger sample size will provide more definitive results.

Normal IgG levels in mature horses range from 900-2400 mg/dl, with an average of 1650 mg/dl (Jorgensen, 1991). In this study, the average IgG levels in the beta-glucan group were within the normal range, while both the levamisole and control groups had levels below the normal limit. Despite this, all groups' IgG values fell within the normal range by day 14. The effect of beta-glucan on IgG levels was not found to be statistically significant, suggesting that while beta-glucan may have influenced immune function, its effect on IgG levels was not substantial compared to the other treatments.

In conclusion, the results of this study indicate that beta-glucan and levamisole treatments had varying effects on several key clinical parameters. Both treatments showed potential benefits, such as reducing LDH and SGOT levels, maintaining RBC counts, and supporting immune function, but the effects were not always significant. Further studies with larger sample sizes are needed to better understand the role of these treatments in the management of

babesiosis and their impact on immune function and recovery in infected horses.

- **Conclusion**

As a result, beta glucan has a positive effect as a feed additive and this effect is more powerful than classical treatment practiced against babesiosis and levamisol additive, and this effect has been supported statistically in many blood parameters, and increase in IgG has not found to be statistically important.

- **Acknowledgements**

We thank The Department of Virology, Veterinary Faculty of Ankara University for helping about IgG levels detection.

Table 1. Serum ALP, LDH, SGOT and CK values for all groups**.**

		n	1. day	4. day	7. day	14. day	General
			x ± Sx	x ± Sx	x ± Sx	x ± Sx	x ± Sx
ALP, IU/L	C	6	247,78±17,17 Ba	282,08±49,13 Aa	288,35±44,77 Aa	300,25±30,28 Aa	279,62±31,87
	B	3	224,27±24,28 Bb	377,10±69,48 Aa	333,63±63,32 Aa	317,57±42,82 Aa	313,14±45,07
	L	4	379,40±21,03 Aa	346,20±60,18 Aab	365,52±54,84 Aab	297,07±37,09 Ab	347,05±39,03
	G	13	283,82±12,14	335,13±34,74	329,17±31,66	304,96±21,41	
LDH, IU/L.	C	6	740,70±89,49	878,00±157,89	610,26±86,80	530,90±52,63	689,96±73,98
	B	3	388,97±126,6	668,57±223,29	717,33±122,76	428,53±74,43	550,85±104,62
	L	4	628,80±109,6	1102,20±109,4	609,53±106,31	480,50±64,46	705,40±90,60
	G	13	586,16±63,28ab	883,04±111,64a	645,78±61,38ab	479,98±37,21 b	
SGOT, IU/L.	C	6	480,10±46,40	556,38±73,78	541,93±77,86	446,45±83,69	508,22±59,99
	B	3	494,53±65,63	666,60±104,34	740,77±110,11	655,03±118,35	639,23±84,84
	L	4	396,65±56,83	499,72±90,36	463,82±95,36	436,55±102,50	449,19±73,47
	G	13	459,76±32,81 b	574,24±52,17ab	582,17±55,06a	512,68±59,18ab	
CK, IU/L	C	6	649,72±454,0	243,95±800,47	173,75±332,89	182,92±87,44	312,58±409,80
	B	3	370,00±642,9	279,93±1132,0	138,70±470,77	175,57±123,66	241,05±579,54
	L	4	1028,55±556	1994,20±980,4	829,53±407,70	237,93±107,09	1022,30±501,9
	G	13	682,75±321,1	839,36±556,01	380,32±235,39	198,80±61,83	

C: Control; B: β-glucan; L: Levamisole; General: G: General Average

Table 2. Blood haemogram values for all groups**.**

		n	1. day	4. day	7. day	14. day	General
			x ± Sx	X ± Sx	x ± Sx	x ± Sx	x ± Sx
RBC,	C	6	6,40±0,54	6,66±0,62	7,86±0,63	7,98±0,54	7,22±0,47
$1x10^{12}$ / L	B	3	7,29±0,62	9,11±0,87	9,33±0,89	9,25±0,77	8,74±0,66
	L	3	7,82±0,76	6,45±0,87	7,50±0,88	7,52±0,77	7,32±0,66
	G	12	7,17±0,40	7,41±0,46	8,23±0,47	8,25±0,40	
Hemoglobin,	C	6	9,18±0,81	9,25±0,89	11,10±0,79	11,41±0,59	10,24±0,58
g/dl.	B	3	9,40±1,15	12,80±1,26	13,33±1,12	12,73±0,84	12,07±0,82
	L	3	10,37±1,15	8,60±1,26	10,73±1,12	10,90±0,84	10,15±0,82
	G	12	9,65±0,61 b	10,22±0,66 b	11,72±0,59ab	11,68 ±0,44 a	
Hematokrit,	C	6	26,73±1,88	27,77±2,31	33,55±2,17	34,38±1,57	30,61±1,37
%	B	3	29,43±2,66	37,26±3,27	38,77±3,07	37,50±2,22	35,74±1,93
	L	3	30,73±2,66	26,23±3,27	30,93±3,07	32,46±2,22	30,09±1,93
	G	12	28,97±1,40b	30,42±1,72 b	34,42±1,62ab	34,78±1,17 a	
Lymphocyte,	C	6	3,37±0,52 b	4,90±0,55 a	4,74±0,65 a	3,83±0,45 ab	4,21±0,48
$1x10^{9}$ / L.	B	3	4,47±0,74 a	3,94±0,78 a	3,68±0,91 a	4,40±0,63 a	4,12±0,68
	L	3	3,30±0,74 b	5,19±0,78 a	4,17±0,91 ab	3,31±0,63 b	3,99±0,68
	G	12	3,71±0,39	4,67±0,41	4,20±0,48	3,84±0,33	
Monocytes,	C	6	0,71±0,21 a	0,60±0,23 a	0,93±0,23 a	0,52±0,15 a	0,69±0,16
$1x10^{9}$ / L	B	3	1,22±0,29 a	0,43±0,33 b	0,31±0,33b	0,76±0,22 ab	0,68±0,23
	L	3	0,75±0,29ab	1,20±0,33 a	1,02±0,33 ab	0,60±0,22 b	0,89±0,23
	G	12	0,90± 0,15	0,74±0,17	0,75±0,17	0,63±0,11	

C: Control; B: β -glucan; L: Levamisole; General: G: General Average

Table 3. Serum total protein, bilirubin and IgG values for all groups**.**

		n	1. day	4. day	7. GÜN	14. GÜN	General
			x ± Sx	x ± Sx	x ± Sx	x ± Sx	x ± Sx
Total	C	6	62,37±5,88	62,80±4,16	58,95±3,33	60,28±2,64	61,10±3,52
Protein,	B	3	60,40±8,31	63,47±5,88	63,97±4,71	58,73±3,73	61,64±4,98
g/L.	L	4	66,67±7,20	59,27±5,09	60,72±4,08	63,75±3,23	61,10±4,31
	G	13	61,14±4,15	61,84±2,93	61,21±2,35	60,92±1,86	
Total	C	6	14,28±3,24	6,27±1,39	2,23±0,81	4,22±1,62	6,75±1,46
Bilirubin,	B	3	13,77±4,59	4,97±1,97	2,57±1,14	1,97±2,29	5,82±2,06
^mol/L.	L	4	11,07±3,97	7,07±1,70	4,27±0,99	3,05±1,99	6,37±1,78
	G	13	13,04±2,29 a	6,10±0,98 b	3,02 ±0,57 c	3,08±1,15 c	
IgG, mg/dl	C	6				710,16±189,65	
	B	6				1511,00±1179,3	
	L	6				844,50±444,74	
	G	18				1021,89±191,55	

C: Control; B: β -glucan; L: Levamisole; General: G: General Average

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CHAPTER II

DIABETES MELLITUS

Muhammet Alperen HAMEŞ[1]
Dr. Selcen ARSLAN[2]
Prof. Dr. Mehmet ÇİFTÇİ[3]
Assoc. Prof. Dr. Oktay KAPLAN[4]

DOI: https://dx.doi.org/10.5281/zenodo.14550977

[1]University of Harran, Birecik Vocational School, Laboratory and Veterinary Health, Birecik, Turkiye; **Orcid:** https://orcid.org/0000-0002-0508-3488; **E-mail:** alperenhames@harran.edu.tr

[2]Republic of Turkey Ministry of Agriculture and Forestry, Elazığ Directorate of Provincial Agriculture and Forestry, 23040, Elazig, Turkiye; **Orcid:** https://orcid.org/0000-0001-9910-6187; **E-mail:** cencincon@gmail.com

[3]Department of Animal Nutrition and Nutritional Diseases, Faculty of Veterinary Medicine, University of Firat, 23119, Elazig, Turkiye; **Orcid:** https://orcid.org/0000-0002-3009-8710; **E-mail:** mciftci@firat.edu.tr

[4]Dicle University, Veterinary Faculty, Department of Animal Nutrition, and Nutritional Diseases, 21280, Diyarbakır, Turkiye; **Orcid:** https://orcid.org/0000-0001-6143-8987; **E-mail:** okaplan61@gmail.com

1. Introduction

With the advancement of technology in the modern world, there has been an increase in the incidence of some diseases because of less active lifestyle (İnce, 2010). The most common of these diseases is diabetes mellitus (DM), an endocrine disease resulting from impaired carbohydrate tolerance. The primary etiology of DM is the destruction or impaired function of pancreatic beta cells, which are involved in the production of insulin (type I) or the reduction or absence of the insulin hormone due to diminished insulin receptor sensitivity in cells (type II) (Rooman et al., 2000). The main reasons for the emergence of the disease include genetic causes, immunological causes, malnutrition, sedentary life and other environmental factors (Rossini et al., 1993). In the comparison between the years 2000 and 2013, DM became the leading cause of disease burden, with a 60% increase (from 10th place in 2000 to 4th place in 2013). According to World Health Organisation (WHO) data, the number of diabetic patients increased from 108 million in 1980 to 422 million in 2014. While the prevelance of diabetes among the global population was 4.7 % in the 1980s, this figure increased to 8.5 % in 2014. In 2016, more than 1.6 million people died directly due to diabetes. 2.2 million deaths were attributed to high blood glucose. In total, about 3.7 million people die each year from DM and high blood sugar. In 2016, the WHO estimated that diabetes was the 7th leading cause of death globally. DM should be taken into consideration not only in terms of the increase in mortality rate but also in terms of causing chronic diseases. As a matter of fact, DM is the main cause of blindness, kidney failure, heart attack, stroke and lower limb amputation (Anonim, 2020).

Today, antidiabetic agents and insulin are commonly used in the treatment of diabetes (Sepici et al., 2004). Insulin utilisation is inevitable especially in the treatment of Type I DM. However, oral antidiabetic drugs cause disorders in kidney, liver and gastrointestinal systems, and diarrhoea. On the other hand, long-term use of insulin causes psychological problems in people (Hou et al., 2005). Furthermore, studies on herbal products with antioxidant and hypoglycaemic properties have intensified as a consequence of the search for alternative methods, given the inadequacy of these drugs in preventing chronic diseases caused by DM (Hou et al., 2005; Eddouks et al., 2005).

1.1. History of Diabetes Mellitus

Diabetes mellitus is a lifelong metabolic disease characterised by symptoms including high blood glucose level (hyperglycaemia), presence of glucose in urine (glucosuria) and lipid disorders (dyslipidaemia) (Bağrıaçık, 1997). The history of diabetes dates back to ancient times. In the Egyptian Ebers Papyrus (BC-1500), it was named as a disease in which a lot of urine was urinated and sugar was excreted with urine. Arateus of Cappadocia (AD-200) was the first scientist to use the name diabetes. In the medieval period, the disease was called 'mellitus', which means honeyed urine, because of the sugar in the urine of the patients. In the same period, Ibn-i Sina (Avicenna) obtained a brown waste when he boiled and evaporated the urine taken from diabetic patients (Bağrıaçık, 1997). Thomas Willis (17th century) re-detected that the urine of diabetic patients was sweet and named the disease as DM for the first time (Zoltan and Willis, 2004). In 1869, Paul Langerhans identified small cell communities in the pancreatic gland. These cell communities are called 'Islets of Langerhans' today. Insulin is secreted from beta cells in this islet and glucagon is secreted from alpha cells and mixed into the blood. These two hormones act jointly to stabilise the blood sugar level (Tura et al., 2006). Banting et al., (1991), in their study on dogs, administered a solution derived from the dog's pancreas to a canine model with a surgically removed pancreas exhibiting symptoms of diabetes. The administration of this solution resulted in a notable reduction in the animal's blood sugar levels. Following this study, the same researchers isolated insulin in 1991.

1.2. Classification of Diabetes Mellitus

The initial classification of diabetes was initially divided into two categories: 'Juvenile Diabetes Mellitus' and 'Adult Onset Diabetes Mellitus'. This was based on the time of onset of the disease. However, this classification was subsequently revised due to the its inability to adequately explain the clinical manifestations of the disease. The American Diabetes Association classifies DM into four clinical categories (American Diabetes Association, 2010).

I) Type I DM

a) Immune mediated DM

b) Idiopathic DM

II) Type II DM
a) DM caused by insulin resistance
b) DM caused by insufficient insulin secretion
III) Other Specific Types of DM
a) Genetic defects in β cell function
b) Genetic defects in insulin function
c) Exocrine pancreas diseases
d) Endocrinopathies
e) Drug or chemical origin
f) Infections
g) Rare forms of immune-mediated diabetes
h) Other genetic syndromes sometimes associated with diabetes
IV) Gestational Diabetes Mellitus (GDM)

I) Type I Diabetes Mellitus

a) Immune Mediated DM**:** This form of diabetes, also referred to as insulin-dependent DM, Type I DM or childhood DM, is a condition characterised by an insufficient insulin production due to the damage of beta cells in the pancreas, necessitating a life reliant on insulin. In addition to genetic predisposition, a number of environmental factors have been identified as contributing to the immune destruction of beta cells. Immune-mediated DM accounts for 5-10% of all DM cases. In this form of DM, the rate of beta cell destruction is highly variable. It is rapid in some individuals, predominantly infants and children, while in others, predominantly adults, it is slower. Some patients, especially children and adolescents, may present with ketoacidosis as the first sign of the disease (American Diabetes Association, 2010).

b) Idiopathic DM**:** Some forms of Type I DM have no known aetiology. Some of these patients have persistent insulinopenia and are prone to ketoacidosis. Very few patients with Type I DM have idiopathic DM, and these are of African or Asian descent. Individuals with this form of diabetes suffer from episodic ketoacidosis. Idiopathic Type I DM is hereditary, not related to autoimmunity (American Diabetes Association, 2010).

II) Type II Diabetes Mellitus

This form of DM is also called as adult-onset, secondary, and non-insulin-dependent DM. It typically manifests in individuals of advanced age. In this form, the beta cells remain intact, and there is no issue with the formation, secretion, and storage of insulin. The issue arises from a deficiencey in the number of insulin receptors present in the cells where insulin is active, or from insulin resistance. In consequence of these factors, the cells are unable to absorb sufficient quantities of insulin, which results in the onset of Type II DM. Individuals diagnosed with Type II DM frequently report an increase in body weight. This is due to the fact that the level of insulin present is insufficient to maintain normal blood glucose levels, but rather at a level that allows for the storage of fat (Yılmaz, 1999). Type II DM represents 90-95% of all diagnosed cases of DM. The incidence rate is higher in individuals with advanced age, obesity, a family history of diabetes, a sedentary lifestyle and certain racial groups (Numanoğlu, 2017).

III) Other Specific Types of Diabetes Mellitus

a) Genetic Defects in β Cell Function

Defects in beta cells results in development of a form of DM known as Maturity-Onset Diabetes of the Young (MODY). MODY is a form of a diabetes that manifests in adulthood but is observed in individuals at relatively young ages (Satır et al., 2009). The term MODY was first employed in 1974 to describe a form of DM that presents in individuals with a strong family history of the disease (Tattersall, 1974). This form is characterised by the following distinctive features: the patients are under the age of 25, there is a history of DM in two generations before the age of 25 in the family, and insulin is not required. It is estimated that this form of DM constitutes between 1 and 2% of all cases of DM. (McDonald and Ellard, 2013). It is hypothesised that 80% of all MODY cases are caused by defects in the glucokinase (GCK), hepatocyte nuclear factor 1-α (HNF1A) and hepatocyte nuclear factor 4-α (HNF4A) genes (Ellard et al., 2008). Glucokinase is an enzyme that catalyses the conversion of glucose to glucose-6-phosphate in the metabolic pathway of glucose. A consequence of in this enzyme defect is the impairment of glucose perception and sensitivity in pancreatic beta cells (Tuhan et al., 2014). Consequently, a moderate elevation in fasting blood glucose levels will be identified in

individuals under the age of 25. Pharmacological intervention is seldom employed in the treatment of these patients, and the disease can be managed effectively through dietary and lifestyle modifications (McDonald and Ellard, 2013; Shields et al., 2010).

b) Genetic Defects in Insulin Function

Insulin is rendered ineffective in the target tissue as a consequence of structural and functional defects in the insulin receptor (INSR) resulting from homozygous and heterozygous mutations. The clinical manifestations of of the condition range from mild to severe depending on the severity of the defect (Doğan et al., 2016). Type A insulin resistance is the result of autosomal dominant mutations in the INSR gene. It presents with the mildest clinical findings among INSR defects. The condition is characterised by the presence of polycystic ovaries and diabetes without obesity in female patients (Musso et al., 2004). In males, the condition typically manifests after the age of 20, exhibiting characteristics akin to those observed in Type II DM (Doğan et al., 2016). Rabson Mendelhall Syndrome is the result of autosomal recessive mutations in the INSR gene. Patients present with prenatal-onset growth retardation with severe insulin resistance, decreased subcutaneous adipose tissue and muscle atrophy (Bathi et al., 2010). Lipoatrophic diabetes is caused by defects in the peroxisome proliferator-activated receptor gene (PPARG), which plays a role in insulin sensitivity, and the laminin A gene (LMNA), which acts as a transcription factor related to adipogenesis (Diker-Cohen et al., 2015). In lipoatrophic DM, patients present to the physician because of severe hypertriglyceridemia, hyperglycemia and acanthosis nigricans, despite the absence of obesity (Demir et al., 2016).

IV) Gestational Diabetes Mellitus (GDM)

It is defined as glucose tolerance disorder at different levels, initially identifies during the prenatal period. Such conditions carry inherent risks for both mother and child (Oğuz, 2016). In fact, one study has shown that GDM has a negative effect on the reproductive performance of male offspring and on the oxidant/antioxidant balance in testicular and pancreatic tissue in the post-pubertal period (Türk et al., 2018). A single or two-stage glucose tolerance test may be employed in the diagnosis. In terms of treatment, continuous

monitoring of the patient's blood glucose level, medical nutrition therapy, exercise and, if necessary, medical therapy can be employed. The administration of insulin represents the most significant method within the domain of pharmacological intervention (Oğuz, 2016).

1.3. Causes of Diabetes Mellitus

Causes of DM include age, gender, genetics, obesity, diet and physical activity. Type I diabetes occurs in the first 9 months following birth or between the ages of 12 and 14. Type II DM usually occurs after the age of 40 (Goday, 2002). It has been found that diabetes is more common in women than in men, but it is more common in men in Japan (Bağrıaçık, 1997). Studies have revealed that 40% of patients with Type II DM have a family history (Kartal, 2006). Obesity is one of the major problems of the world. Obesity creates an environment for many diseases. In fact, the likelihood of DM increases by 25% in people with a body mass index over 25. In addition, 67% of patients diagnosed with Type II DM are overweight and 46% are obese (Numanoğlu, 2017). Causes such as overnutrition, unbalanced diet based on carbohydrates or fat due to poor economic situation trigger the development of DM (Numanoğlu, 2017). Excess energy as a result of a sedentary lifestyle leads to weight problems as the energy to be expended decreases due to reduced activity. As a result, irregular blood pressure, heart and lung problems will negatively affect the effective use of glucose (Kartal, 2006).

1.4. Diagnosis of Diabetes Mellitus

A diagnosis of diabetes can be readily made when the specific symptoms of the disease are observed. However, in cases where disease conditions without any discernible symptoms cannot be identified through random laboratory findings, the condition may persist undiagnosed for years. In the diagnosis of DM, a fasting plasma glucose level is above 126 mg/dL or above on two consecutive mornings following an overnight fast is indicative of the disease (Numanoğlu, 2017). Furthermore, if the plasma glucose level obtained at any point during the day is above the level of 200 mg/dL in the ‘Oral Glucose Tolerance Test (OGTT)’, the individual is diagnosed with diabetes (Kartal, 2006).

1.4.1. Clinical Findings

The initial symptoms observed in patients include an increased desire to consume water, frequent urination, and an elevated frequency of nocturnal urination, accompanied by a sensation of hunger, excessive food intake, xerostomia, prolonged wound healing, blurred vision, weakness, and vaginal itching in women (Bozkurt and Yıldız, 2008).

1.4.2. Laboratory Findings

1.4.2.1. Fasting Blood Glucose Measurement

It can be posited that the blood glucose value of an individual is within the normal range if the results of two consecutive tests conducted on different days on an empty stomach are below 100 mg/dL. This is contingent upon the individual having fasted for at least eight hours prior to the test. A reading of less than 100 mg/dL on the test day indicates a normal blood glucose level. A reading between 100 and 125 mg/dL suggests the presence of potential DM, while a reading above 126 mg/dL is indicative of DM (Dinççağ, 2011).

1.4.2.2. Postprandial Blood Glucose Measurement

A plasma glucose level exceeding 140 mg/dL two hours after the ingestion of a meal by the individual under suspicion can be used as a diagnostic criterion for DM (Numanoğlu, 2017).

1.4.2.3. Oral Glucose Tolerance Test

In this test, the individual under suspicion, is provided with a diet and permitted normal physical activity for a period of three days. Subsequently, the individual is required to abstain from food for a period of 10 to 16 hours, after which a blood sample is taken and analysed while subject is still fasting. Subsequently, the individual under suspicion is administered 75 g of glucose dissolved in 250-300 ml of water, and a second blood sample is taken and measured two hours later. Should the blood glucose level exceed 200 mg/dL as a result of the measurement, a diagnosis of DM is rendered (Numanoğlu, 2017).

1.4.2.4. Measurement of Glucosylated Haemoglobin (HbA1c)

A HbA1c value of less than 6.5% indicates a normal blood glucose level. A value of less than 7.5% suggests the presence of potential DM, while a value of 7.5% or above is indicative of DM (Kartal, 2006).

1.5. Treatment of Diabetes Mellitus

The principal treatment modalities for DM are insulin administration, oral antidiabetic drugs, dietary modification, and exercise. It is not uncommon for patients to experience difficulties when attempting to alter their lifestyle and adapt to their treatment regimen (Visser and Snoek, 2004).

1.6. Insulin

The pancreas contains both endocrine and exocrine secretory areas. These areas, which synthesise and secrete hormones, are collectively referred to as the 'Islets of Langerhans'. The human pancreas contains one million islets. The pancreatic islets are composed of three main types of cells: insulin-secreting beta cells (comprising approximately 50% of the cells in human islets), glucagon-secreting alpha cells (35-40%) and somatostatin-secreting delta cells (10-15%) (Cabrera et. al., 2006). The formation of active form of insulin necessitates intense posttranslational modification in the form of proteolytic cleavage during its production (Nawaz et al., 2017). The production of insulin commences with the translation of a messenger RNA transcript into an inactive protein, preproinsulin. This inactive form is synthesised from the endoplasmic reticulum. Subsequently, the posttranslational process assembles the N-terminal signal sequence and forms disulfide bridges. Ultimately, the polypeptide is truncated at two positions, thereby releasing the intervening carbon chain. Consequently, the active form of insulin is packaged in secretory cells for storage (Amihăesei and Chelaru, 2014). As a consequence of an increase in blood glucose levels following the ingestion of food, the secretion of insulin is initiated. Indeed, it is hypothesised that blood glucose level is measured directly by the pancreas, resulting in the secretion of insulin from beta cells accordingly. Furthermore, polypeptides occurring in the digestive system such as gastrin, secretin, cholecystokinin and glucagon, which are present in the digestive system, have also been demonstrated to play a role in insulin secretion (Zobalı, 2000). The levels of insulin and glucagon present in

the blood plasma are directly correlated with the quantity of glucose that is absorbed into the body as a result of the ingestion of nutrients. Insulin and glucagon work in concert to regulate blood glucose levels (Fidan, 2007).

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CHAPTER III

HERBAL PRODUCTS USED IN DIABETES TREATMENT

Dr. Selcen ARSLAN[1]
Muhammet Alperen HAMEŞ[2]
Prof. Dr. Mehmet ÇİFTÇİ[3]
Assoc. Prof. Dr. Oktay KAPLAN[4]

DOI: https://dx.doi.org/10.5281/zenodo.14550993

[1]Republic of Turkey Ministry of Agriculture and Forestry, Elazığ Directorate of Provincial Agriculture and Forestry, 23040, Elazig, Turkiye;
Orcid: https://orcid.org/0000-0001-9910-6187, E-mail: cencincon@gmail.com
[2] University of Harran, Birecik Vocational School, Laboratory and Veterinary Health, Birecik, Turkiye; Orcid: https://orcid.org/0000-0002-0508-3488; E-mail: alperenhames@harran.edu.tr
[3]Department of Animal Nutrition and Nutritional Diseases, Faculty of Veterinary Medicine, University of Firat, 23119, Elazig, Turkiye; Orcid: https://orcid.org/0000-0002-3009-8710; E-mail: mciftci@firat.edu.tr
[4]Dicle University, Veterinary Faculty, Department of Animal Nutrition, and Nutritional Diseases, 21280, Diyarbakır, Turkiye; Orcid: https://orcid.org/0000-0001-6143-8987; E-mail: okaplan61@gmail.com

1. Introduction

Plants have been used for therapeutic purposes in every period of human existence. In Egyptians (1550 BC), information about 450 diseases was given in a papyrus and it was determined that herbal and animal origin drugs were used in the treatment of these diseases (Karaman and Cebe, 2016). In turn, Hippocrates (460-377 BC) mentioned about 400 plants for the treatment of diseases. In the first century, Dioskorides' book "Materia Medica" gave information about 500 medicinal plants and their therapeutic properties. Ibn-i Sina (Avicenna, 980-1037 AC) left over a hundred scientific works. In these works, he mentioned about 900 medicinal plants used for therapeutic purposes (Baytop, 1999). The word 'Phytotherapy', which means 'Treatment with Medicinal Plants', was first used by the French physician Henri Leclerc (1880-1955) (Çubukçu et al., 2002).

As indicated by data from the World Health Organization (WHO), approximately 21.000 of the 70.000 plants utilized for medicinal purposes globally are employed in the pharmaceutical industry. Türkiye is the 18th most prominent exporter of medicinal plants among 110 countries (Yılmaz et al., 2010). The utilization of medicinal plants in the management of diabetes commenced during the first quarter of the twentieth century. In studies on *Galega officinalis L.,* it was determined that guanidine derivative compounds in the structure of the plant have hypoglycaemic effect (Karaman and Cebe, 2016). In Türkiye, the rate of use of herbal products by patients with diabetes has been found to vary between 27 and 36% (Ceylan et al., 2009; Ilhan et al., 2016).

Sarıkaya et al., (2010) has been reviewed information about the species, genera and families of plants used frequently for antidiabetic purposes in Turkish traditional medicine. In their analysis on the distribution of families used in the treatment of diabetes, the researchers reported that the most frequently used family was Rosaceae, with a prevalence of 21% (Uğurlu ve Seçmen, 2008). After *Rosaceae, Lamiaceae* was the most frequently used family with 14% (Yeşilada et al., 1995) and *Berberidaceae, Cistaceae, Liliaceae, Loranthaceae* and *Polygonaceae* were the least used families with 2.1% (Puavilai et al., 1999). In the same review, the information provided regarding the genera utilized in the treatment of diabetes revealed that the most frequently used genus is *Urtica sp.,* with a frequency of 4.23% (Jia et al., 2009).

This was followed by *Rosa sp, Teucrium sp* and *Thymus sp,* with a frequency of 3.5% (Heydari et al., 2010) by *Morus sp* and *Rubus sp,* with a frequency of 2.82% (Nassar et al., 2012) and *Allium sp, Artemisia sp, Berberis sp, Cerasus sp, Cistus sp, Crataegus sp, Mentha sp, Pyrus sp, Vicia sp* and *Viscum sp,* with a frequency of 2.11% (Puavilai et al., 1999). In the same review, the most commonly used plant species in the treatment of diabetes were *Urtica dioica* with 3.6% (Heydari et al., 2010), *Rosa canina* and *Teucrium polium* with 2.9% (Nassar et al., 2012), *Cerasus mahaleb* and *Viscum album* with 2.16% (Puavilai et al., 1999).

In their review on herbal products and food supplements used in the treatment of diabetes, Aslan and Orhan (2010) posited that hypoglycaemic drugs and herbal products exert their effects by stimulating insulin production in the beta cells of the pancreas, and they are only useful in patients with Type II diabetes through this mechanism of action, as they do not affect patients with Type I and Type II diabetes patients, in whom the ability to produce insulin is lost. While some of the herbal products used in this group increase insulin release, some of them decrease blood glucose level thanks to insulin-like compounds. In the review, it was also stated that herbal products that increase insulin sensitivity show their effects by increasing the sensitivity of peripheral insulin receptors in cases of resistance to insulin. Furthermore, it was posited that the deceleration of carbohydrate absorption within the digestive system precipitates a decline in blood glucose levels. It was additionally proposed that herbal products (the majority of which contain fibre) that inhibit carbohydrate absorption demonstrate efficacy in this manner, albeit through disparate mechanisms of action. The ingestion of these fibrous products at mealtimes has been demonstrated to reduce glucose absorption and to lower the satiety blood glucose level.

Numanoğlu (2017) has reported in his master's thesis in which the use of herbal support products of individuals with type II diabetes was evaluated that 70.6 % of female patients and 48.5 % of male patients used herbal products and that the patients mostly used black cumin (21.5 %), cinnamon (20.0 %), garlic (19.2 %) and blueberry (11.8 %) and benefited effectively from these products. In the same study, it was determined that the sources of information about these products were environment (57.5 %), media (27.5 %) and internet (15 %).

In this study, the most commonly used antidiabetic herbal products will be emphasised.

1.1. Cinnamon (*Cinnamomum sp*.)

One of the most widely used spices in the world is cinnamon with its unique flavour. Cinnamon is a species of the genus Cinnamomum from the Lauraceae family (Koyu, 2019). Although there are about 250 species of Cinnamomum genus, 4 of them are used as spices. The most commonly used ones are Ceylon (*Cinnamomum zeylanicum*) and Chinese (*Cinnamomum aromaticum*) cinnamon (Kawatra ve Rajagopalan, 2015). Chinese cinnamon has a thicker skin and is less fragrant. Chinese cinnamon is dried in the sun; Ceylon cinnamon is dried in the shade. Although both types of cinnamon contain tannin and essential oil at the level of 1-2%, their chemical contents are different from each other. For example, Chinese cinnamon contains cinnamyl aldehyde at the level of 85-90% while Ceylon cinnamon contains it at the level of 65-70% (Aslan and Orhan, 2010; Gürson and Özçelikay, 2005). It has been documented that *Cinnamomum zeylanicum* possesses potent antioxidant properties, which have been linked to enhanced semen quality (Yüce et al., 2013). Additionally, it has been proposed that *Cinnamomum zeylanicum* possesses the capacity to mitigate testicular and sperm damage induced by carbon tetrachloride (Yüce et al., 2014), some chemotherapeutics (Sarıözkan et al., 2016), and heat stress (Türk et al., 2015). The anti-diabetic property of cinnamon is attributed to the presence of procyanidin type A polymers in its structure, which have been demonstrated to enhance insulin receptor autophosphorylation and augment insulin sensitivity (Chase and Mc Queen, 2007). In addition, substances such as cinnamylaldehyde and methyl eugenol in the essential oil content of cinnamon have anti-diabetic properties. In clinical studies, it has been reported that Chinese cinnamon is more effective than Ceylon cinnamon (Aslan and Orhan, 2010). Khan et al., (1990) found that cinnamon increased the effect of insulin and reduced insulin resistance. In other studies, it was determined that cinnamon polyphenols showed an insulin-like effect on human and animal cells (Sangal, 2011; Imparl-Radosevich et al., 1998) and increased the effectiveness of insulin by 20-fold (Cao et al., 2007). In a study conducted by Khan et al., (2003) 60 volunteer patients with type II diabetes aged 40 and above were administered powdered cinnamon at doses of

1, 3, and 6 grams. The results demonstrated a significant reduction in blood glucose levels, with a mean decrease of 18-29%. Similarly, Safdar et al., (2004) divided 30 volunteer type II patients into 3 groups and gave capsules containing cinnamon at the level of 1, 3 and 6 grams for 40 days. The results showed that cinnamon significantly reduced blood glucose levels. Kim et al., (2005) administered cinnamon extract at the levels of 50, 100, 150 and 200 mg/kg orally to rats for six weeks and found that blood glucose level was significantly lower in the group using cinnamon extract at the level of 200 mg/kg compared to the control group. In addition, Verspohl et al., (2005) conducted a study on rats to determine the anti-diabetic effect of cinnamon and found that blood glucose level decreased with the effect of cinnamon. As a result of all these studies, cinnamon should be used at a daily dose of at least 1 gram in order to see its hypoglycaemic effect. In addition, depending on the blood glucose level, the daily dose can be increased to 6 grams, but it is recommended that the daily dose should not exceed 6 grams (Aslan and Orhan, 2010).

1.2. Black Cumin Seed (*Nigella sativa*)

Nigella sativa (*Nigella sativa*) is a flowering plant from the Ranunculacea (buttercup family). It is used under names such as black seed, black cumin or seed of blessing (Mollazadeh and Hosseinzadeh, 2014). Black cumin is a plant that grows naturally in South America, North Africa, Western Asia and Anatolia. The seeds and oil of black cumin have been used for years against many ailments. The most important chemical components in black cumin seeds are imoquinone, thymohydroquinone, dithymoquinone and thymol (Koyu, 2019). The effects of black cumin on diabetes have been demonstrated through a number of mechanisms. These include the enhancement of insulin sensitivity in the liver, the inhibition of gluconeogenesis, the promotion of glucose utilisation in muscles, the reduction of glucose absorption in the digestive system, the stimulation of insulin secretion and the augmentation of beta cell number in the pancreas (Razavi and Hosseinzadeh, 2014). In a study performed by Bamosa et al., (2010) 94 type II diabetic patients were given black cumin seeds at different doses (1, 2 and 3 g/day) as supportive treatment as well as anti-diabetic drugs for 12 weeks, it was determined that there was an average 56 mg / dL decrease in fasting blood glucose levels and an average 1.52% decrease in HbA1c levels in the group using 2 g / day dose. In a study conducted

by Najmi et al. (2008), patients with insulin resistance were administered black cumin oil (2.5 mL x 2) in conjunction with atorvastatin and metformin over a six-week period. The results demonstrated that the decrease in fasting blood glucose level in the group given black cumin oil in addition to atorvastatin and metformin was highly significant compared to the groups given other anti-diabetics alone. In a study conducted on rats, three groups were formed, one of the groups received insulin treatment, the other group did not receive any treatment, and the third group was given the ethanol extract of black cumin seed (300 mg / kg / day) for 30 days. At the end of the study, the blood glucose levels of the animals in the group receiving black cumin extract were significantly lower than those in the group receiving no treatment, but slightly higher than those in the group receiving insulin treatment (Kaleem et al., 2006). In a separate study, diabetic rabbits were divided into four groups. The first three groups were administered glibenclamide, ethanol, and methanol extracts of black cumin at a dose of 100 mg/kg/day for a period of two weeks, respectively. The fourth and final group served as a control and did not receive any treatment. At the end of the study, it was determined that the blood glucose levels of the animals in the three intervention groups were significantly lower than the untreated group. However, the researchers stated that glibenclamide was more effective than black cumin extracts in reducing blood glucose levels (Ikram and Hussain, 2014). In addition to these studies on black cumin with positive results, various studies have been conducted on its toxic effects. Indeed, Zaoui et al., (2002) conducted a study on mice to determine the toxic level of black cumin oil and found that the lethal dose 50 (LD50) value was 28.8 mL/kg in oral administration and 2.06 mL/kg in intraperitoneal administration. Additionally, in a case study conducted in Türkiye, a 62-year-old woman with diabetes was administered black cumin seed tablets (2-2.5 g/day) for a period of six days. Following this, the patient exhibited symptoms of acute renal failure, which was subsequently identified as a potential adverse reaction associated with black cumin seed (Arslan et al., 2013).

1.3. Ginger (*Zingiber officinale Roscoe*)

Ginger (*Zingiber officinale Roscoe*), which belongs to the Zingiberaceae family, is an herbaceous perennial plant with yellow and red flowers that can reach one metre in height. It is cultivated in countries such as China, India,

Indonesia, Vietnam and Japan. Roots and rhizomes of ginger are used as spices and for medicinal purposes (Güceyü et al., 2019). Gingerols in its composition give a sharp flavour to ginger. Apart from this, there are zingiberen and shogaols in its composition (Semwal et al., 2015). Ginger is used in the treatment of abdominal pain, arthritis, non-alcoholic fatty liver disease, primary dysmenorrhoea and nausea caused by pregnancy and chemotherapy (Lai et al., 2016; Daily et al., 2015; Bryer, 2005; Panahi et al., 2012; Grzanna et al., 2005). The anti-diabetic effect of ginger is manifested through the inhibition of α-amylase and α-glucosidase enzymes, the translocation of glucose transporter protein-4 (GLUT-4), and an increase in insulin sensitivity (Li et al., 2012).

In a double-blind placebo-controlled study (Arablou et al., 2014) conducted to determine the effects of ginger consumption on glycaemic status, lipid profile and some inflammation markers in patients with type 2 diabetes (70 people), patients were randomly divided into ginger and control groups. Patients were given 1600 mg wheat flour and 1600 mg ginger daily for placebo instead of ginger for 12 weeks. The results showed that ginger significantly reduced fasting plasma glucose and HbA1c levels compared to the placebo group. In another study conducted in diabetic patients (88 people), it was found that fasting blood glucose levels decreased by 10.5% in patients taking 3 g/day ginger for 8 weeks, but increased by 21% in patients in placebo group. In the same study, it was determined that HbA1c levels in patients consuming ginger decreased significantly compared to patients in the placebo group (Mozaffari-Khosravi et al., 2014). In contrast to these, as a result of a randomised, double-blind placebo-controlled study on 64 patients with type II diabetes, it was found that it had no effect on fasting blood glucose and HbA1c levels (Mahluji et al., 2013).

It is important to consider certain aspects of ginger usage. Given that ginger has the capacity to exert a pronounced inhibitory effect on thromboxane synthase, it may result in an extended bleeding time. Accordingly, it is recommended that this substance should be used only under the supervision of a qualified medical practitioner by individuals who are currently taking anticoagulant medications or who have underlying blood clotting disorders (Merrily and Kuhn, 2002; Dulger, 2012).

1.4. Nettle (*Urtica spp.*)

Stinging nettle belongs to '*Urticaceae*' family and its fresh and dried flowering green parts (herba), leaves, seeds and root parts are used for medicinal purposes (Baser, 2011). It grows spontaneously in forested areas, rivers and roadsides in Türkiye (Davis, 1988). One of the important features of nettle is the redness that results from the burning effect of the green part of the plant when it comes into contact with the skin. This phenomenon can be attributed to the presence of histamine and acetylcholine compounds in their feathers (Baser, 2011). In addition, formic acid, serotonin, choline and betaine are also found in nettle leaves (Emmelin and Feldberg, 1948; Collier and Chester, 1956; Atasu and Cihangir, 1984). Betaine purified from nettle extracts was found to accelerate blood coagulation in experimental animals (Atasu and Cihangir, 1984). The most important species of stinging nettle are the perennial large nettle (*Urtica dioica L.*), also called bitter nettle, the annual small nettle (*Urtica urens L.*), also called sweet nettle, and the annual black nettle (*Urtica pilulifera*).

The impact of nettle on diabetes is shown by an increase in insulin secretion from the pancreas and a reduction in glucose absorption (Çıkladilmez, 2013). In a study, the hypoglycaemic effect of *Urtica dioica* (250 mg/kg) was investigated in hyperglycaemia induced by oral glucose test, and also in experimental diabetes induced by alloxan in rats. The results demonstrated that *Urtica dioica* given 30 minutes before the oral glucose test decreased the plasma glucose level and this decrease reached up to 33% one hour after glucose loading. In contrast, it was found that *Urtica dioica* had no hypoglycaemic effect in alloxan-induced diabetic rats. The researchers found that glucose absorption in the jejunum part of the digestive system decreased from 11 mg to 8.05 mg for 2 hours, suggesting that the antihyperglycaemic effect of nettle may be related to the decrease in glucose absorption from the intestine (Bnouham et al., 2003). In another study, the effects of *Urtica dioica* leaves given at a dose of 100 mg/kg/day on high blood glucose levels and pancreatic beta cells in rats with streptozotocin-induced diabetes were investigated both as protective and therapeutic. For protective effect, *Urtica dioica* was given for five days before diabetes mellitus, and as a result, an increase in beta cell count and a decrease in blood glucose level were determined in the group given nettle compared to the group not given nettle.

For therapeutic purposes, nettle was given to animals for 4 weeks and hypoglycaemic effect and improvement in beta cells were observed (Golalipour et al., 2011). Although nettle is generally regarded as safe, it has been associated with a number of side effects, including nausea, sweating, diarrhoea, and allergic reactions when it comes into contact with the skin surface. In addition, given its ability to alter the menstrual cycle, it is advisable that those contemplating pregnancy should refrain from using it. Furthermore, given that, hormonal fluctuations during pregnancy can have adverse effects on the foetus, it is not recommended pregnant women use nettle.

1.5. Power Pomegranate (*Momordica charantia L.*)

Power pomegranate, which belongs to the Cucurbitaceae family, is eaten and consumed as a vegetable in various regions of the world (Chaturvedi, 2012). In Türkiye, it is also grown in gardens as an ornamental plant (Demirezer et al., 2017). Power pomegranate is one of the leading natural products used against diabetes in Southeast Asia. It has an insulin-like effect due to a polypeptide compound known as 'p-insulin', 'plant insulin' or 'polypeptide-P'. This component found in pomegranate is similar to bovine insulin in terms of pharmacokinetics and its effect starts within 30-60 minutes and lasts for 4 hours (Baldwa et al., 1977; Leatherdale et al., 1981). The mechanism of the hypoglycaemic effect of pomegranate is thought to increase glucose utilisation in skeletal muscles, decrease glucose absorption from the intestines, suppress gluconeogenesis (by inhibiting two enzymes glucose-6-phosphatase and fructose 1,6 bisphosphatase) and protect beta cells and their functions (Joseph and Jini, 2013).

Sundaram et al., (2009) reported that potato pomegranate given to rats with streptozotocin-induced diabetes mellitus decreased serum glutamic-ocaloacetic transaminase (SGOT), alanine aminotransferase (ALT) activities and urea concentration and increased serum total protein and albumin levels. Tripathi and Chandra (2009) also administered potassium pomegranate fruit extract to rats with diabetes mellitus and examined blood glucose level and heart tissue oxidative stress indicators. They found that the rising blood glucose level decreased in the diabetes group receiving pomegranate, the increasing lipid peroxidation level decreased in the heart tissue, on the contrary, decreasing glutathione (GSH), superoxide dismutase (SOD), catalase (CAT) and

glutathione peroxidase (GSH-Px) activities increased. Sathishsekar and Subramanian (2005) determined that plasma glucose levels decreased with increased CAT, SOD, GSH-Px activities in pancreatic tissue due to the effect of potato pomegranate seed extract given to rats in which diabetes was induced by applying streptozotocin. Although no adverse effects have been observed following oral administration or subcutaneous injection of potassium pomegranate and it is reported to be safe, intravenous administration is not recommended because it is thought to be toxic (Akpınar, 2013). Furthermore, it is hypothesised that certain compounds present within the plant's structure may induce infertility in both men and women. In addition, it has been asserted that the plant is contraindicated for use by breastfeeding mothers, given the potential for transfer of the active compounds to the infant via breast milk. Similarly, the plant should be avoided by pregnant women, as it has been claimed to induce uterine contractions. (Aslan and Orhan, 2010). However, pomegranate has been demonstrated to possess potent antioxidant property (Türk et al., 2008). This property has been linked to improvements in sperm quality (Türk et al., 2008) and a reduction in testicular damage caused by carbon tetrachloride (Türk et al., 2016).

1.6. Garlic (Allium sativum L.)

The herbaceous plant known as garlic is native to the steppes of Central and Western Asia. It comprises roots, stems, leaves and cloves, and produces greenish-white or pink flowers. The plant typically reaches a height of 25-100 cm. The most important characteristics of the plant are its pungent odour, appetising and also burning flavour. The chemical composition of garlic includes 63.8% water, 28.2% carbohydrate, 5.3% protein, 0.2% fat and 1.1% cellulose (Ayaz and Alpsoy, 2007). Garlic also contains essential oils containing sulphur (allicin, alliin, ajoen); vitamins A, C, E, B1, B2; magnesium, selenium minerals; polyphenols (Rahman, 2001). The compound named allicin (diallylthiosulfinate) is responsible for the sharp odour and burning flavour of garlic. This compound is formed as a result of the breakdown of alliin in the structure of garlic by alliinase enzyme (Thomson and Ali, 2003). Alliin is converted into allicin as a result of bruising, crushing and chopping of garlic (Agarwal, 1996). The most commonly produced garlic types in Türkiye are Kastamonu, Balıkesir, Black, Spanish and Italian garlic (Kütevin and Türkeş,

1987). The most commonly produced varieties are Kastamonu garlic, which is also called as white garlic, and dark (black) garlic. White garlic has also been employed in the context of medical treatment (Baytop, 1999). White garlic, which has good bioavailability but low consumption due to its pungent odour and taste, is transformed into black garlic using heat treatment (Ergin, 2019). Some of the sulfur-containing compounds (aliisin) in the structure of garlic have the ability to regulate glucose metabolism. The important privilege is that if the blood glucose level is low, it does not lower it further (Ergin, 2019). Black garlic consumption has been reported to be effective against diabetes and obesity (Jung et al., 2011). Three-week-old mice were given 5% black garlic for seven weeks in a study on mice with type II diabetes by Lee et al., (2009). As a result of the study, it was determined that black garlic showed strong antioxidant properties, prevented fatty liver and diabetic complications. In addition to its beneficial effects, excessive consumption of garlic can also result in allergic reactions due to the presence of sulfur compounds in its structure. In addition, excessive consumption of raw garlic can cause intestinal gases and irritation of the normal flora in the mucosa of the digestive tract.

1.7. Kişniş (Coriandrum sativum L.)

Coriander is an annual herbaceous plant belonging to the Umbelliferae family. It typically grows to a height of 20–60 cm. (Akgül, 1993). The spice obtained from the plant contains essential oil, tannin, resin and sugar. The most significant constituents of the essential oil are linalool (60-70%), gamma-terpinene (6%), alpha-pinene, camphor, jeraniol, p-cymene, jeranyl acetate, limonene, aldehydes, esters and alcohols (Özbek et al., 2006). Although information regarding the effect of coriander on diabetes is not sufficient, it is thought to be due to the synergistic effect of bioactive compounds such as linalool, geranyl acetate and gamma-terpinene (Laribi et al., 2015). It was established that the administration of coriander extract at a dosage of 20 mg/kg to animals with obesity, hyperglycaemia and hyperlipidaemia resulted in a reduction in insulin resistance and triglyceride levels, as well as a restoration of normal blood glucose levels (Asgarpanah and Kazemivash, 2012; Aissaoui et al., 2011). There are studies reporting that coriander extract reduces hyperglycaemia and increases insulin secretion by reducing glucose uptake and metabolism (Gray and Flatt, 1999; Swanston-Flatt et al., 1990). Sreelatha et al.,

(2009) have also confirmed that coriander leaves and stems have a high level of andiabetic effect and can be used for medicinal purposes. In contrast to aforementioned studies, Öntürk and Özbek (2009) administered trans-caryophyllene and eugenol (the active ingredients of coriander) to diabetic mice and observed that these substances had no effect on fasting blood glucose (FBG) in healthy animals, but increased FBG level in diabetic animals.

1.8. Blueberry (*Vaccinium myrtillus*)

Blueberry is a perennial plant from the heather family (Ericaceae), which is grown in forested areas, reaching a height of 30-45 cm. The leaves are up to 2.5 cm long, ovate, slightly notched and bright green in colour. The flowers are reddish or greenish pink in colour and bell-shaped. The berries are blue, black and purple in colour (Murray, 1995). In addition, the chemical composition of blueberries was determined to be 83 g water, 0.7 g protein, 0.5 g fat, 15 g carbohydrate, 0.8 g fibre (cellulose) and 62 calories of energy per 100 g (Batu and Kırmacı, 2006). The composition of essential oils obtained from blueberries in Türkiye is limonene, alpha pinene, linalool and linalyl acetate (Akgül and Bayrak, 1989). The essential oil of *Myrtus communis* has been found to contain the following components: 1,8-cineole (18.2%), linalool (16.3%), myrtle acetate (14.5%), linalyl acetate (6.7%), terpineol (6.5%), -pinene (6.4%), geranyl acetate (5.5%), limonene (3.4%), geraniol, neryl acetate and methyl eugenol (between 1% and 2%) (Ozek, 2000).

In Türkiye, it is grown as a grape fruit especially in the eastern Black Sea region. Blueberry has been reported to posses a protective effect against chronic diseases such as cancer, cardiovascular, cerebrovascular, atherosclerosis and diabetes. This effect is mainly associated with the antioxidant properties of phenolic compounds present in its structure (Wu et al., 2002). In this context, it was determined that FBG and HbA1c levels decreased as a result of the study in which 200 ml/day blueberry juice was given for 3 months to individuals with Type II disease for 6-17 years (Chambers and Camire, 2003). Demir (2014) also examined the effects of water extracts of *Myrtus communis L.* plant fruit on diabetes and diabetes complications in streptozotocin-induced rats and found a significant decrease in the glucose levels of the groups given different doses of fruit extract (250, 500 and 1000 mg/kg), while an increase in the glucose level of the diabetic control group was determined. Sepici et al., (2004)

administered the essential oil obtained from the leaves of *Myrtus communis L.* at different doses (10, 20, 40, 50 and 100 mg/kg) orally to normal and diabetic rabbits and investigated its hypoglycaemic effect. At the end of the study, they determined that while the plant used in rabbits without diabetes (normal) had no effect, blood glucose levels decreased in rabbits with alloxan-induced diabetes. They determined that the effective dose in the study was 50 mg/kg. In addition to the aforementioned beneficial effects, ingestion of the substance over an extended period may result in poisoning. Furthermore, the presence of tannins in its structure may induce feelings of nausea and digestive discomfort (Çıkladilmez, 2013).

2. Conclusion

Given the prevalence of herbal products in the treatment of a wide range of diseases, it is unsurprising that they also play an important role in the management of diabetes. In studies examining the impact of herbal products on diabetes, it has been observed that traditional medicines derived from herbal sources paved the way for the development of novel antidiabetic pharmaceuticals. Indeed, the drug metformin, which is currently employed in the treatment of diabetes, is derived from a plant product (Galega officinalis). However, due to the toxicity of the active substance (guanidine) present in the plant, this plant was not employed directly in the treatment regimen. Instead, new biguanidines that exert an effect on diabetes but are non-toxic were developed based on this plant. In light of these considerations, it becomes evident that plants can exert beneficial or detrimental effects.

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CHAPTER IV

PASTURES AND RANGELANDS FOR RUMINANTS

Prof. Hüseyin NURSOY[1]

DOI: https://dx.doi.org/10.5281/zenodo.14556034

[1] Bingöl University Faculty of Veterinary Medicine Department of Animal Nutrition and Nutritional Diseases, 12000, Türkiye nursoymalatya@hotmail.com
Orcid ID: ORCID: 0000-0002-5524-2459

1. INTRODUCTION

Pastures and rangelands; are our natural resources where the cost of feed, which constitutes 70% of the production cost for farm animals and especially ruminants, is the cheapest and easiest to obtain. Pastures are the main feed source of traditional animal husbandry in many parts of the world. Approximately 70% of farm animal feed in the world is provided from these areas, 16% of the world's food production is also provided from pastures (Çomaklı and Tufan, 2021). In the world are 26% of agricultural areas, i.e. 3.4 billion hectares, are pastures and rangelands. While countries such as China, Australia, the USA and Brazil are ranked first, Turkey is ranked 46th (Nursoy and Aldemir, 2019). Our country's approximately 78 million hectares of land area, approximately 10,811 million hectares, is pastures (approximately 1 million ha) and rangelands (9.7 million ha). Meadow and pasture areas in our country have decreased by 63% in the last 60 years (Nursoy and Yılmaz, 2002). The rate of meeting the daily feed needs of animals from meadows and pastures is 97% in Ireland, 83% in England, 71% in France, 54% in the Netherlands and 40% in the USA (Nursoy and Aldemir 2019). Pastures and rangelands areas in Turkey can only meet 33.7% of the roughage needs required for animal husbandry. A total of 31 million tons of production was achieved in 2018 in meadow and pasture areas and areas where forage crops are cultivated. It has been found that the roughage required for adequate feeding of 19 million cattle is 86 million tons. The deficit in this area is 55 million tons (Çıray, 2022).

We observe that the forage crop planting rates in total field lands in the world are 49.8% in Australia, 36.5% in Germany, 31.4% in the Netherlands; 25.8% in France, 25.4% in the UK and 23.0% in the USA. However, in less developed countries, this rate is 11.7% in Greece, 17.0% in Romania and 6.3% in Bulgaria. For this reason, we can say that there is a significant linear relationship between the level of development of a country in agriculture and the importance it gives to forage crop agriculture. For example, in Muş province in Turkey, it ranks 1st with 1 million 397 thousand tons of alfalfa production in 60 thousand hectares of land. and makes significant contributions to animal husbandry. (Anonymous, 2021)

In Turkey, the area of forage crops planted and the production of forage crops have been on the rise since the 1990s. In 1990, 3 million acres of forage crops were planted, and in 2021, they reached 25 million acres. While the

production of forage crops was around 4.5 million tons in 1990, approximately 61 million tons of forage crops were produced in 2021. The highest amount of forage crops were planted in 2021, on an area of 25 million acres. In 2020 and 2021, the years of highest production, approximately 61 million tons of forage crops were produced (Çıray, 2022).

2. DEFINATION OF PASTURE AND RANGELAND

Pasture are generally flat, densely growing in areas close to the surface of the groundwater, dense and tall, and generally composed of tuberous plants that do not have roots, stems or leeches. When the meadow grasses are short or suitable for grazing after mowing, these meadows are also called bottom pastures. Pastures are forage areas formed by sparse, short-statured root-stemmed and leech plants in barren lands with sloping, rugged and deep groundwater (Nursoy and Aldemir 2019). Pastures can also be found in flat areas, provided that the groundwater is deep. If the vegetation is lush due to rainfall or irrigation, pastures can also be mowed. “Under the Forest” and “Inside the Forest” pastures are also used as a feed source in animal husbandry. Artificial pastures and meadows are forage areas whose vegetation is created by human hands and fertilized and irrigated when necessary. “Temporary pastures” are artificial pastures established with one-year lifespan forage crops such as vetch, red clover, barley, rye, and sorghum, and “Continuous Pastures” are artificial pastures established by planting long-lived forage crops (Nursoy and Yılmaz, 2002; Nursoy and Aldemir 2019). Plateaus are flat areas used as pastures and meadows during certain periods of the year on mountain ranges that are at least 500 meters above sea level. The vegetation consists of mountain meadows and plateau steppe plants. Dry grass can be obtained by mowing plateaus that have high vegetation and cannot be reached by animals. In our country, plateaus are visited between May and July and grazing is done for 60-140 days (Nursoy and Yılmaz, 2002).

3. IMPORTANCE OF PASTURE AND RANGELAND

Nearly 18% of the total area in our country is covered with meadow pastures; It constitutes a significant part of the plant resources that are the basic factor for other living things (Anonymous, 2021). They are the most economical feed source for animals. In fact, a significant part of the quality roughage in our country is provided from meadow pastures. In addition, pasture

animal husbandry is the most economical animal husbandry model without any expense. In animal husbandry, 70% of operating expenses are feed expenses (Minson 1990). Meadow pastures are important in terms of animal health and reproductive biology. Since animals need to be mobile in organic animal husbandry, pastures are needed. Meadow pastures are important in preventing erosion. In fact, pastures constitute a significant part of the areas subject to erosion in our country. They extend the life of facilities such as dams and ponds. Since 87% of meadow pastures consist of class V-VII lands, there is no possibility of evaluating these areas differently (Nursoy and Aldemir 2019). It reduces the greenhouse effect by balancing the amount of CO_2 in the atmosphere. Shrub pastures meet some of the fuel need in rural areas. Meadow pastures are gene centers. They have economic value in terms of animal feeding. They are a source of nectar and nectar in beekeeping (Çomaklı and Tufan, 2021). Ruminant animals should be given roughage containing at least 18% crude cellulose for the reproduction and development of rumen microorganisms, the physical movements of the rumen and the prevention of hardening (keratinization) of rumen wall epithelium (Nursoy and Yılmaz, 2002). Ruminant animals that feed as herbivores can meet a significant portion of their nutrient needs from meadows and pastures or dried and ensiled roughage. For example, all of the daily nutrient needs of cows that give 18 kg/day of milk and sheep up to the first 15th week of their pregnancy can be met with quality roughage. In addition, 40-70% of the rations of cows with high milk yield and 90-100% of the rations of dry cows and breeding heifers are used (McDonald et al., 1990; Nursoy and Yılmaz, 2002). In recent years, instead of roughage with a cellulose ratio of more than 18% in rations/concentrate feed with a cellulose ratio of less than 18%, the amounts of cell wall materials such as NDF (Neutral Detergent Fiber) and ADF (Acid Detergent Fiber) in total rations are taken into account. For example, the minimum ADF ratio that should be present in rations of dairy cows is 19% and the NDF ratio is 25%. 75% of the NDF ratio should be provided from roughage. Cattle and sheep should consume 2% of their live weight as roughage or 1.2% of NDF on a daily basis (Nursoy and Yılmaz, 2002). There are some advantages to feeding ruminants on pasture: The harvesting, transportation, storage and conservation processes of the product in the field increase the cost of the feed. In a pasture-based feeding program, there are no such expenses. Areas where agricultural

machinery cannot enter and where cultivated agriculture cannot be carried out (steppe areas, areas with a lot of rocks, etc.) are being evaluated. The opportunity for other animals, especially breeding animals, to exercise in clean, oxygen-rich air and the lack of contact with other animals also reduce the risk of epidemic diseases in animals on pasture (Nursoy and Yılmaz, 2002). As a result of consuming nutrients in plants and some unknown beneficial substances fresh, disorders related to nutritional deficiencies are less common. Since the energy needs of grazing animals are 3-10% higher than those that stay in place, their feed consumption also increases. For example, the feed consumption of meadow grasses consumed in their natural state by cattle and sheep is 20-59% higher than their silage. In addition to these advantages of feeding ruminants on pasture, there are also some disadvantages such as the low yield obtained from the unit area due to walking and chewing during grazing, not being suitable for modern feeding techniques, and the inability to control the nutrient consumption of animals (Nursoy and Yılmaz, 2002; Nursoy and Aldemir 2019).

4. PASTURE AND RANGELAND MANAGEMENT

Training of shepherds using pastures should be included. Pastures should be grazed within their capacity. In a study conducted in Erzurum, it was determined that a 250 kg live weight native breed cattle needs 18-20 da pasture area. Although the time to start grazing varies by region, the average for Erzurum can be accepted as May 15. Grazing should be continued for an average of 5 months until October 15. Uniform grazing of the pasture should be ensured. It should be grazed with an animal species suitable for the pasture conditions. Grazing should be started from low altitude areas. In order to reduce grazing pressure in pastures, stable animal husbandry should be encouraged especially near large settlements and rotation pastures should be established within the field land. This situation is of great importance especially in culture breed animal husbandry. Spring grazing in pastures reduces productivity by half. Grazing of pastures in spring has become a tradition in our country. This practice should be prevented with farmer trainings. In our country, the harvest is late in the meadows. According to the researches, it has been determined that the harvest is done on average 15 days late in our country and this situation reduces the quality of the meadow grass by 55. The harvest should be done on

the 15-20th of July, when the plants start to bloom. The mowing height should be 5-6 cm. The mowing height should be 5-6 cm. In the harvest and preservation of the grass, the mowing time should be adjusted well and quality grass production should be ensured. Drum mowing machines are recommended in the harvest of the meadow. In addition, some negative practices on the pasture lands should be stopped. Some of these are inappropriate quality changes and the recycling practices of the areas destroyed for various reasons (quarries, mineral exploration, etc.) in the pasture areas should be carried out in accordance with the technique (Çomaklı and Tufan, 2021).

5. GRAZING METHODS

In order to benefit from the vegetation cover for many years without reducing the productivity of the pasture, it is necessary to perform appropriate grazing in pastures. Attention should be paid to issues such as not grazing the pasture soil while it is wet, especially in the spring, grazing it when the plant is at least 15 cm tall, and stopping grazing 3-4 weeks before the first frosts (plant height should be at least 5-10 cm) in the fall so that it is resistant to winter and stores reserve nutrients. For the continuity of the pasture, plants should be allowed to form seeds every few years (Nursoy and Yılmaz, 2002). As a result of heavy grazing above the capacity of the pasture, decreases are observed in the photosynthesis, carbohydrate storage, root development, seed production, water retention and aeration capacities of the soil. Since the plants cannot withstand cold and drought, wild plants increase and erosion accelerates. However, these negativities are not observed in light or normal grazing below the grazing capacity. In the pasture separated into paddocks, the sections with high yields are grazed in the first year and the other sections are grazed in the following years. As explained below, there are generally three types of grazing methods: continuous, rotational and resting rotational (Tosun and Altın, 1986; Gençkan 1985, Minson, 1990):

5.1. Continuous Grazing: It is the continuous grazing of animals in a certain pasture area throughout the season or year. It is a method used in low-yield pastures. Since the amount of grass per animal is not certain, spot grazing is performed. Since plant seeds do not form in this grazing method, the continuity of the pasture is also eliminated

5.2. Rotation Grazing: This method is mostly applied in pastures where there are many plants that can reproduce with roots and stem shoots without needing seeds. The basis of the method is based on giving the plants a certain resting period. For this, the pasture is divided into 3 or more paddocks in terms of grazing capacity and grazing period, each paddock is grazed for certain periods and then rested. The resting period is generally between 15-42 days after grazing in forage grasses and legumes. Fertilizer and irrigation can be applied to plants in the resting period. This method, which is applied in pastures with high productivity, reduces selectivity or spot grazing and allows for regular and uniform grazing. In pastures that are very lush, irrigated, fertilized and have high productivity, rotational grazing can be done by surrounding the pasture section with mobile electric or normal fences. In this way, the yield loss that may occur due to trampling is also reduced (Table 1).

Table 1. Rotation grazing method (3 days grazing, 20 days resting)

Year	**Grazing Periods**	**Pasture Paddocks**		
		A	**B**	**C**
First year	First	Graze	------	------
	Medium	------	Graze	------
	Last	------	------	Graze
Second year	First	------	Graze	------
	Medium	------	------	Graze
	Last	Graze	------	------
Third year	First	------	------	Graze
	Medium	Graze	------	------
	Last	------	Graze	------

5.3. Resting Rotation Grazing: This method is recommended for pastures with weakened vegetation and whose plants can reproduce by seed. This method is based on the principles of delaying grazing until the plant seeds mature by grazing the pasture paddocks in a row and late for two consecutive years. One purpose of resting rotation grazing is to ensure that annual weeds that grow early in the spring in the pasture are heavily grazed by animals while they are young and green, thus combating weeds in that area. Weeds in different areas can be cleaned in this way every year.

Resting rotation grazing is done for different purposes.

A -) Grazing to strengthen the existing vegetation: It is a grazing method applied for the purpose of improving pastures where plants that reproduce with plant roots and stems are the majority and where plants grow weak due to reasons such as heavy grazing and drought. Grazing is started from the part with the best vegetation, and the part with weak vegetation is rested (Table 2).

Table 2. Grazing to strengthen existing vegetation

Year	**Grazing Periods**	**Pasture Paddocks**		
		A	**B**	**C**
First year	First	------	Graze	Graze
	Medium	Graze	------	------
	Last	------	Graze	Graze
Second year	First	Graze	------	Graze
	Medium	------	Graze	------
	Last	Graze	------	Graze
Third year	First	Graze	Graze	------
	Medium	------	------	Graze
	Last	Graze	Graze	------
Fourth year	First	------	Graze	Graze
	Medium	Graze	------	------
	Last	------	------	Graze

B) Grazing for the purpose of achieving seeding: This method can be successful in cases where the desired plants are present in sufficient quantities in any pasture vegetation, these plants can reproduce by seed, and annual weeds are present in low quantities in the pasture. This method is the process of obtaining the seeds of the desired plants and distributing the seeds to the pasture area by both rubbing and eating by animals (Tablo 3).

Table 3. Grazing to achieve seeding

Year	**Grazing Periods**	**Pasture Paddocks**		
		A	**B**	**C**
First year	First	------	------	Graze
	Medium	-----	Graze	------
	Last	Graze	------	------
Second year	First	------	Graze	------
	Medium	------	------	Graze
	Last	Graze	------	------
Third year	First	------	------	Graze
	Medium	Graze	------	------
	Last	------	Graze	------
Fourth year	First	Graze	------	------
	Medium	------	------	Graze
	Last	------	Graze	------
Fifth year	First	Graze	------	------
	Medium	------	Graze	------
	Last	------	------	Graze
Sixth year	First	------	Graze	------
	Medium	Graze	------	------
	Last	------	-------	Graze

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BÖLÜM V

INSECT PROTEIN FOR BROILERS

Prof. Hüseyin NURSOY[1]

DOI: https://dx.doi.org/10.5281/zenodo.14551164

[1] Bingöl University Faculty of Veterinary Medicine Department of Animal Nutrition and Nutritional Diseases, 12000, Türkiye nursoymalatya@hotmail.com
Orcid ID: ORCID: 0000-0002-5524-2459

1.INTRODUCTION

In our country and in the world, broiler chicken production is carried out in the form of conventional and organic production. Our country ranks 1st in Europe and 8th in the world with 2,418,000 tons of chicken carcass meat production annually (AVEC, 2022; TEPGE, 2023). 60-82.76% of the production costs in broiler enterprises arise from feed costs (Yeni and Dağdemir, 2023). Since broiler chickens grow very quickly, they need 20-23% Crude Protein (CP) and essential amino acids such as 0.11% lysine and 0.4% methionine in the ration, especially in the first 3 weeks (Marco et al., 2015) and 5% Crude Fat (EE) in the finishing periods on the 25th-35th days (Abdullatif and Azzam, 2023). These needs; Our country's needs are met from plant sources such as imported soybean meal (SBM) and sunflower seed meal, animal sources such as meat meal, meat-bone meal, chicken meal or fish meal, and vegetable oils used in human nutrition. Our country imported $6 billion worth of feed and $1.9 billion worth of full-fat soybeans in 2022 (TGDF, 2023). Animal proteins are risky in terms of Salmonella and other microorganisms, expensive, and since they fall into the rendering product category according to European Union criteria (EC Regulation, No: 999/2001), they carry the phenomenon of species-based "cannibalism". Rendering products have also been banned in our country since 2017 (Regulation on Animal By-Products Not for Human Consumption, 2017/44). Within the framework of this regulation, a species cannot consume by-products of its own species, in other words; chicken slaughterhouse by-products, which are an important source of protein, cannot be used in chicken rations. This situation causes us to import more SBM. Synthetic amino acids, which are completely imported, are both quite expensive and not accepted in organic animal husbandry.

INSECT PROTEINS

Insects and especially their larvae (worms) and pupae (Photo 1-2) are the natural food of all birds in nature; and nearly 1900 insects and their larvae are an important source of protein and fat in the nutrition of more than 2 billion people in China, Vietnam, South Korea, Japan, Mexico, most African and South American countries (Özek, 2016; Aksoy and El, 2021). With the "Innovative Food Regulation" (Regulation No. 2015/2283) that came into force in January 2018 by the European Food and Safety Authority (EFSA), the

consumption of insect-based foods has been permitted and legally marketable. It is reported that the global market for edible insects (larvae) or their flour in European countries will increase by 47% by 2026 (Aksoy and El, 2021). Jackson (2023) states that the Black Soldier Fly (BSF), (Black Soldier Fly, Hermetia illucens Linnaeus 1758)) larva (Photo 1) will reach $ 1.3 billion in sales in global markets by
2027.

Photo 1. Black Soldier Fly (BSF), (Black Soldier Fly, Hermetia illucens Linnaeus 1758) and larvae (Tomas et al., 2020; Jackson, 2023)

Depending on their species, life stages (egg, larva, pupa and adult) and the substrates they are raised on, insects; DM content in the larval period is 30-43.6%, normal CP content is 10.9-78.8%, HY ratios are 10.2-47%, ω-3 and ω-6 fatty acids are 16.5-24% in total fat (With this feature, it is used in newborn and child nutrition) and it is reported that the bioavailability of riboflavin, pantothenic acid, B_{12} and A vitamins is high (Işık and Karapınar, 2017; Aksoy and El, 2021; Khalifah et al. 2023). Insects make good use of wastes such as feces, which cause environmental pollution in animal shelters, as substrate. The Black Soldier Fly (BSF) is an environmentally friendly insect that feeds and grows on human feces and can reduce feces by 50% (Sevilmiş et al., 2019). Under suitable conditions, 180 kg live weight is obtained from BSF in 42 days or 58 tons of pupa in 5 months in 1 m^2 area (Kar et al., 2018). It is reported that the feed conversion efficiency of the Cricket (Acheta domesticus) is 2 times higher than chickens, 4 times higher than pigs and 12 times higher than cattle, and that they can contribute to the ecological system with advantages such as consuming much less water than other animals and producing less greenhouse gas (Aksoy and El, 2021). It is stated that the Meadow Cricket (Gryllus testaceus Walker) can be raised with up to 50 insects in a 4-liter container and that it also reduces the use of pesticides in some insects used in biological control (Işık and Karapınar, 2017). Insects reproduce by leaving capsules containing their eggs. The total life span of the Black Soldier Fly (BSF) is 40-44 days. Adult BSF, which have a very short life span of five to eight days, mate immediately, and after mating, the female BSF lays 500-900 fertile eggs. The larval period of BSF is 13-18 days depending on the substrate, and the pupal period is a minimum of 8 days. A BSF in the adult stage lives for a maximum of 5-8 days (De Smet et al., 2018). The total life span of the Flourworm or Yellow Flourworm (WW) (Tenebrio molitor Linnaeus 1758) is considerably longer than flies like BSF, between 142-442 days. Adults that are one to three months old can reach up to 28 mm in length after laying their fertile eggs and enter the larval stage of 10-12 days, becoming pupae in 3-4 months and adults in 12-20 days (Aracagök et al., 2023), (Photo 2).

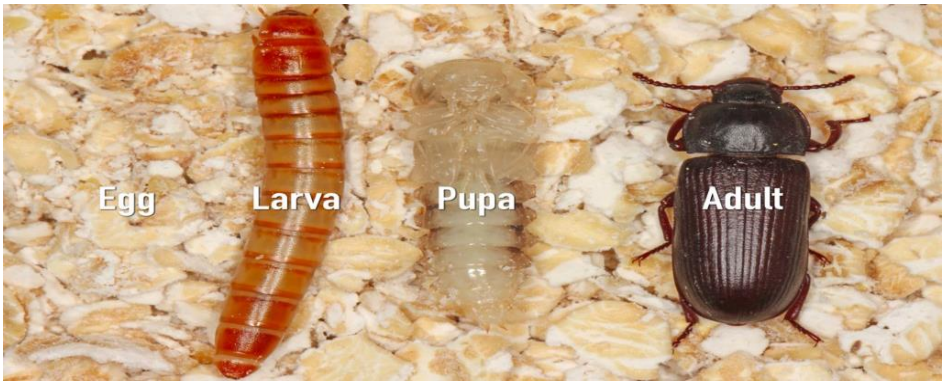

Photo 2. Mealworm or Yellow Mealworm (MW), (Tenebrio molitor Linnaeus 1758), (Biotas.org, 2023)

As a source of protein, amino acids and fat (ω-3 and ω-6 fatty acids); Cricket, Field Locust, Turkistan Cockroach, Black Soldier Fly (BSF) (Photo 1), Mealworm (MW) (Photo 2), Buffalo Worm, Morio Worm, houseflies, ants, Wax Moth and many other insect species can be used. It is recorded that insects have amino acid contents close to fish meal except for some amino acids and some amino acid digestibility such as lysine is better than fish meal (92.1%) (Işık and Kırkpınar, 2017, De Marco et al., 2015). Oibiokpa et al. (2018) stated that the cricket (Gryllus assimilis) protein has a protein efficiency ratio (PER) of 1.78, a net protein utilization ratio (NPR) of 3.04 and a biological value of 93.02%, and that casein has higher values than casein with values of 0.86, 2.74 and 73.45%, respectively. It has been determined that insect utilization has antibiotic, antiviral (attacin alloferon, defensin A, etc.) and prebiotic properties in poultry. It is thought that insect chitins may also have similar functions (Özek, 2016; Aksoy and El, 2021). It is reported that a new peptide (HF-1) from housefly (Musca domestica) larvae inhibits strains of pathogens such as Escherichia coli, Pseudomonas aeruginosa, Salmonella typhimurium, Shigella dysenteriae, Staphylococcus aureus and Bacillus subtilis (Aksoy and El, 2021).

ADDITION OF INSECT LARVAE TO BROILER DIETS

Use of Dry BSF Larval Meal Alone: BSF alone should not be used 100% instead of SBM in starter and finisher diets of broiler chickens (Hossain and Bhuiyan, 2023), BSF larvae meal replaced by SBM at 25% and 50% levels

improves growth performance (Mat et al., 2021), and adding 15% BSF meal to the diet; It is reported that it does not affect feed consumption, performance, cooking loss and sensory properties and positively changes calcification in the tibia bone (Uushona, 2015). Loponte et al. (2017) reported that the appearance of BSF alone as black in yellow feed slightly reduces feed intake, whereas Ognik et al. (2020) reported that BSF larvae meal used in turkeys at a rate of 15% has positive effects on feed conversion ratio (FCR). Dry BSF larvae added to the ration alone at a rate of 15%; It has been found that it has no negative effect on blood Ca, erythrocytes and leukocytes and increases serum P, Glutathione peroxidase and SOD activity (Dabbou et al., 2018; Hossain and Bhuiyan, 2023), that chitin in BSF reduces cholesterol and triglycerides in serum (Borrelli et al., 2017) and does not affect blood glucose and total protein concentrations (Hossain and Bhuiyan, 2023). Use of Dry MW Larvae Meal Alone: The above statement for BSF is also valid for MW. In other words; MW alone should not be used 100% instead of SBM in the starter and finisher diets of broiler chickens (Hossain and Bhuiyan, 2023). Biasato et al. (2018) reported that the use of MW at 5, 10 and 15% levels in Ross 308 male chickens for 53 days increased the live weight, daily live weight gain, feed consumption, decreased the FCR value, but did not change the carcass weight. Bovera et al. (2016) stated that the use of MW at 29.62% of the ration in male chickens on days 30-62 did not change the live weight, daily live weight gain and carcass yield, but reduced the ileal digestibility of DM and CP, and that the MW rate of 29.62% was too much in the ration. It is reported that the MW added to the ration at 10% alone was 2346 g and the control group was 2262 g at the end of the 35-day trial, total feed consumption and FCR values were similar with 3823 and 3808 g/bird, 1.66 and 1.72 values, respectively, carcass yield was higher in the MW group with 1937 g and 1778 g, respectively, fecal score, diarrhea, feathering, pododermatitis were not different in the MW group, and some saturated fatty acids were high in the MW group (Vasilopoulos et al. 2023). Bisato et al. (2019) reported that MW used at 5, 10 and 15% levels had effects on intestinal microbiota and mucin secretion and caused decreases in the number of some bacteria.

Table 1. Comparison of nutrient compositions of SBM, Fish Meal and MW and BSF larvae (in Normal Feed).

	SBM (INRA, 2023)	Fish Meal (INRA, 2023)	Meal Worm (MW) (INRA, 2023)	Black Soldier Fly (BSF) (Marco et al., 2015; INRA, 2023; Auza et al., 2023)
DM, %	87.7-93.2	92.1-92.3	94.6	91.7-93.52
CP, %	43.5-48.5	62.6-69	47.7	33.7-58.05
EE, %	1.5-8.9	9.1-9.5	33.7	11-49
CF, %	3.9-6.3	0	4.8	8.7-14.8
Ash, %	6.1-7.1	14-17.8	3.4	10.7-11.90
Ca, %	0.34	3.11-4.48	0.22	1.28-3.96
Total P, %	0.62	2.29-2.76	0.73	0.66-0.93
Lysine, %	2.12-3.06	4.68-5.20	3.07	2.18-2.86
Metionine,%	0.62-0.69	1.66-1.92	0.93	0.68-0.95
AMEn*, kkal/kg	2220-2720	3120-3370	4890	2866-4400

*: AMEn (Apparent Metabolic Energy Adjusted for Nitrogen), MJ/kg DM = 4164.187 + 51.006 x EE (DM'de %) - 197.663 x Ash (DM'de %) - 35.689 x CF (DM'de %) - 20.593 x NDF (DM'de %), (Alvarenga et al., 2015).

Tablo 2. Usage rates of insect proteins instead of SBM and fish meal in broiler diets (in normal feed, %)

FEEDS	SBM	Fish Meal	Meal Worm (MW)	Black Soldier Fly (BSF)	MW/BSF:50/50
Starter Rations, First 21 days					
Corn, %7.6	52	70	59	58	58
SBM, %48	39	-	22	13	13
Fish meal, %65	-	26	-	-	-
MW, %47	-	-	15	-	-

BSF, %45	-	-	-	25	-
MW/BSF, %46	-	-	-	-	25
Sun flower oil	5.7	-	-	-	-
Limestone	1.65	2.68	2.38	2.38	2.38
DCP	0.50	0.50	0.50	0.50	0.50
Salt	0.30	0.30	0.30	0.30	0.30
DL-Metionine	0.60	0.35	0.55	0.55	0.55
L-Lysine HCL	0.08	-	0.01	0.10	0.10
Vitamin-Mineral premix [1]	0.15	0.15	0.15	0.15	0.15
Ethoxyquin	0.01	0.01	0.01	0.01	0.01
Anticoccidial	0.01	0.01	0.01	0.01	0.01
Toplam	100	100	100	100	100
Calculated					
CP, %	22.67	22.43	22.20	22.12	22.34
AMEn, kkal/kg[2]	3080	3007	3100	3022	3179
Digestible Lysine, %	1.21	1.45	1.27	1.20	1.27
Digestible Metionine+Cystein, %	0.94	0.93	0.93	0.93	0.94
Finishing Rations, Last 21 days					
Corn, %7.6	60	72	66	62	65
SBM, %48	31	-	13	7	8
Fish meal, %65	-	21	-	-	-
MW, %47	-	-	17	-	-
BSF, %45	-	-	-	25	-
MW/BSF, %46	-	-	-	-	23
Sun flower oil	5.7	3	-	2	-
Limestone	1.65	2.68	2.38	2.38	2.38
DCP	0.50	0.50	0.50	0.50	0.50
Salt	0.30	0.30	0.30	0.30	0.30
DL-Metionine	0.60	0.35	0.60	0.55	0.55
L-Lysine HCL	0.08	-	0.10	0.10	0.10
Vitamin-Mineral	0.15	0.15	0.15	0.15	0.15

premix [1]					
Ethoxyquin	0.01	0.01	0.01	0.01	0.01
Anticoccidial	0.01	0.01	0.01	0.01	0.01
Toplam	100	100	100	100	100
Calculated					
CP, %	19.44	19.29	19.37	19.54	19.53
AMEn, kkal/kg[2]	3129	3174	3192	3176	3186
Digestible Lysine, %	1.02	1.20	1.11	1.05	1.10
Digestible Metionine+Cystein, %	0.90	0.84	0.90	0.90	0.91

[1]: Vitamins per 5 kg (A, 2.400.000 IU; D_3, 1.000.000 IU; E, 16.000 IU; K, 800 mg; B_1, 600 mg; B2,1600 mg; B6, 1000 mg; B12, 6 mg; niacin, 8000 mg; folic acid, 400 mg; pantotenic acid, 3000 mg; biotin 40 mg) ve minerals (cobalt, 80 mg; copper, 2000 mg; iodine, 400; Fe, 1200 mg; manganese, 18.000 mg; selenium, 60 mg, zinc, 14.000 mg).
[2]: AMEn (Apparent Metabolic Energy Adjusted for Nitrogen), MJ/kg DM = 4164.187 + 51.006 x EE (DM'de %) - 197.663 x Ash (DM'de %) - 35.689 x CF (DM'de %) - 20.593 x NDF (DM'de %), (Alvarenga et al., 2015).

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BÖLÜM VI

FEATHER COLORATIONS IN CHICKENS AND SOME DEFINITIONS

Associate Professor Osman KARABULUT[1]

DOI: https://dx.doi.org/10.5281/zenodo.14551185

[1] Department of Biometrics, Faculty of Veterinary Medicine, Aksaray University, Aksaray – Turkey.ORCID ID: 0000-0002-8142-2365
Email: okarabulut02@gmail.com

1. INTRODUCTION

Feather colors in chickens not only beautify the flock but also provide information about breeds and genetics. Whether aiming for a decorative farmstead or striving for optimal egg production, understanding these colors and patterns can assist in selecting the desired chickens for the coop (Perfectpoultry, 2024).

The formation of chicken feather colors is primarily influenced by two main color pigments: black and red. In other words, every recognized color variation in chickens is derived from these two pigments, and they can be intensified, diluted, or hidden to create the color spectrum seen in different breeds. Through selective breeding, humans have mastered the art of manipulating these genetic traits, producing an incredible spectrum of feather colors. Many colors have been created through the strategic interaction of black and red pigments via breeding practices (Nie et al., 2021; Aksoy, 1998).

Feather colorations on a chicken's body are not just for aesthetic purposes; they also reflect the breed's genetic heritage and can affect their adaptability to different environments. The differences in feather colors between roosters and hens are usually distinct and play an important role in the visual dynamics of the flock. Roosters typically have more vibrant and varied colors, showcasing shiny feathers, bold patterns, and longer, more extravagant tail feathers. These bright feathers serve not only to attract females but also to assert dominance and ward off rivals. In contrast, hens usually have plainer, more uniform feather colors, which help with camouflage while protecting their eggs (Erensayın, 1991).

Although it does not receive much attention in the scientific world, one of the most fascinating aspects of poultry farming, both for enthusiasts and backyard chicken owners, is the wide range of feather colors in chickens. For this reason, the definitions of feather colorations have been established by breeders, though in some cases, different regions may use alternate definitions. This section aims to cover the common definitions.

To better understand how to identify chickens by their feather colors and determine their breeds, one must examine how feather colors are defined. Since it is necessary to know the morphological regions of a chicken when describing the locations of colors on feathers, these regions are introduced with a Picture (Figure 1).

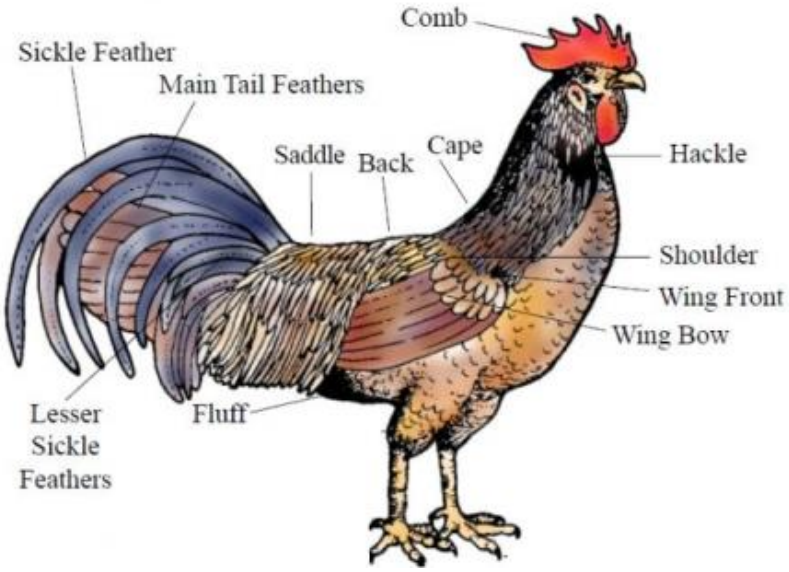

Figure 1. Morphological regions of a rooster.
Reference: Jacob, 2024.

2. Black-Breasted Red

Roosters are very colorful and quite different from hens. Roosters have black body feathers and black tails, along with red feathers, and parts of the hackles, back, shoulders, and wings. Hens, on the other hand, have brown body feathers, yellow-orange hackles feathers or black-mixed gold hackles feathers, a salmon-colored chest, and a black tail. Within the Black-Breasted Red color scheme, there can be small variations between breeds. The key feature is that the bird should have black breast feathers, and in order to be considered Black-Breasted Red, it should have only black and red feathers (Star Milling, 2024).

Figure 2. Black-Breasted Red colored rooster and hen**.**
Reference: Rosecomb Bantam Federation, 2024.

3. Bay

The Bay feather color in chickens is a rich, reddish-brown tone, typically with warm chestnut undertones. This distinct coloration can create a striking contrast with lighter feather patterns or add depth to darker patterns (Star Milling, 2024).

Figure 3. Bay colored hen and rooster.
Reference: Lesley, 2022.

4. Birchen

Birchen is a color where the main body and tail of the chicken are completely black, regardless of gender. In both males and females, the head and hackle feathers, as well as the hackle feathers in males, are covered with silvery-white feathers, each with a narrow black line running through the center of each feather. The chest feathers are black, adorned with a fine silver edging (Animal World, 2024).

Figure 4. Birchen colored rooster and hen.
Reference: Dunlap Hatchery, 2024.

5. Black

Chickens with pure black feathers contain eumelanin pigmentation throughout all parts of the feathers. The head, neck feathers, back, saddle, sickles, and wing bows can display a sheen ranging from beetle-green to purple tones, which can be especially rich in male birds, but are also noticeably present in females (Star Milling, 2024).

Figure 5. Black colored rooster and hen.
Reference: Armstrong, 2024.

6. Blue Body Color

This feather color, which is a diluted form of black, is typically described as a slate-grey appearance that characterizes any bird with this color. Some breeds have black-laced blue varieties, while others may be slate blue, lemon blue, or blue-grey. The color known as "self blue" in the United States and "lavender" in the United Kingdom is characterized by a uniform, pale bluish-grey color across all feathers (Animal World, 2024).

Figure 6. Blue Body Color.
Reference: The Every Day Mom Life, 2023

7. Buff

This color defines a uniform tone of orange-yellow. Some varieties are entirely buff in color, while others have black accents on the tail, neck, or wings. This soft color tone is uniform and consistent, giving the chicken's feathers a smooth and pleasing aesthetic (Animal World, 2024).

Figure 7. Buff Colored Chicken and Rooster.
Reference: The Home Steading Hippy, 2023.

8. Chestnut

Feathers of chestnut color have a rich, reddish-brown hue. They are typically in a warm, dark brown tone with a distinct red or mahogany shade, resembling the color of a chestnut tree. This color can be quite vibrant and is usually evenly distributed across the feathers, though some variations and patterns may also ocur (Perfect Poultry. 2024).

Figure 8. Chestnut Colored Hen.
Reference: Poultry Keper, 2015

9. Cinnamon

It is a dark, reddish-buff feather color, and this color varies in adult hens with brownish and white feathers. These rich, earthy tones, resembling cinnamon, give the bird a distinctive and generally attractive appearance (Perfect Poultry. 2024).

Figure 9. Cinnamon Colored Rooster And Hen.
Reference: Backyard Chicken Chatter, 2022.

10.Columbian

This color pattern consists of white and black markings. The rooster's head, back, and thighs are white. The hackle feathers are green-black with white laceing, while the main tail and sickle feathers are completely black. In hens, the bodies are white, with black necks featuring white laceing and some black tail feathers (Animal World, 2024; Perfect Poultry. 2024).

Figure 10. Columbian Colored Rooster And Hen.
Reference: Marcum, 2023.

11.Crele (Cuckoo Black-Breasted Red)

Crele is a color pattern resulting from the combination of the cuckoo striping pattern with Black-Breasted Red. Birds with this type of coloration have cuckoo feathers adorned with yellow, orange, and red highlights. Roosters display these highlights in the hackle feathers, shoulders, and saddle feathers, while hens only show these highlights in the hackle feathers (Perfect Poultry. 2024; Star Milling, 2024).

Figure 11. Crele Colored Chicken And Rooster.
Reference: The Chicken Coop Company, 2024.

12.Fawn

Fawn chicken feathers are typically light, tawny brown or beige in color, often with a slight reddish or yellowish undertone. This color can vary, but it generally resembles the color of a fawn. In some breeds, fawn feathers may also have fine patterns or shading variations, which contribute to the overall appearance (Perfect Poultry. 2024).

Figure 12. Fawn Body Color.
Reference: Backyard Chickens, 2013.

13.Duckwing

This feather color is characterized by a distinct striped pattern in contrasting colors along the male's wing. Duckwing feathers can come in gold, blue gold, silver, blue silver, and fawn silver tones (Perfect Poultry. 2024).

Figure 13. Duckwing Colored Rooster.
Reference: My Pet Chicken, 2024a.

14.Golden Laced

This feather color pattern is characterized by red/gold and black. Roosters have red head, hackle feathers, back, and saddle feathers, while the belly feathers are black, and the tail is a shiny greenish-black. The wing bow and chest are red/gold in color, and each feather has even black laceing. Hens have red/gold heads and black hackle feathers, which are embroidered with red laced. The body feathers are red/gold with black laceing (Animal World, 2024).

Figure 14. Golden Laced colored rooster.
Reference: Sunset Valley Chicks, 2021.

15.Mille Fleur

The Mille Fleur feather color pattern is a striking combination of rich reddish-brown feathers adorned with black and white tips, creating a speckled or mille-fleurs effect. The feathers are mahogany in color, and each tip ends with a crescent-shaped black bar followed by a V-shaped white shine (Perfect Poultry. 2024).

Figure 15. Mille Fleur Body Color.
Reference: My Pet Chicken, 2024b.

16.Partridge

The Partridge body color is quite similar to Black-Breasted Red, especially in roosters, where the resemblance is so strong that describing one would easily describe the other as well. The noticeable differences, however, are seen in the hen's feather pattern. The hackle feathers are black in the center, surrounded by a thin reddish-bay edge, and the overall body color is the same reddish-bay, decorated with beautiful black lines. Each feather has three black lines, and the main tail is black, though only the top two feathers differ, matching the same pattern as the body. This intricate pattern is visually striking (Star Milling, 2024).

Figure 16. Partridge body color.
Reference: The Country Small Holder, 2023**.**

17.Red

The color is a rich dark red or mahogany red. Roosters have bright red neck, back, and saddle feathers, along with greenish-black tail feathers and chest. Hens have colors that range between gold, salmon, brown, and black tones. The rich dark red or mahogany red feather color is an intensified version of the Buff color (Perfect Poultry. 2024).

Figure 17. Red colored rooster.
Reference: Chicken Scratch Poultry, 2020.

18.Red Pile

This color pattern is seen in both Modern and Old English Game chicken breeds. Roosters generally have white bodies, with red/orange hackle feathers, saddle feathers, and wing bows. Hens are either white or salmon in color, with golden-colored heads (Star Milling, 2024).

Figure 18. Red Pile Body Color.
Reference: Weymouth, 2023.

19.Salmon

The color is a reddish or pinkish buff that resembles cooked salmon and is used to describe the chest of Black-Breasted Red chickens. In the salmon feather color variety, the hens' chest and lower body are white, while the rest of the body is salmon-colored. In roosters, the color variation is more diverse (Star Milling, 2024).

Figure 19. Salmon Body Color.
Reference: (Happy Chicken Coop, 2021.

20.Silver

It is a color pattern characterized by silvery white. Roosters have various shades of white, black, and greenish-black feathers, while hens have a salmon-colored chest, a gray body, and white hackle feathers with a black stripe running through the center (Star Milling, 2024).

Figure 20. Silver colored hen.
Reference: SASSO, 2024.

21.Silver Laced

The Silver Laced chicken pattern is characterized by bright silvery-white ground feathers, each framed with a sharp black edge, creating a striking laced effect. The under feathers are black, and the tail is a shiny greenish-black. The wing bow and chest are silver in color, with neat black laced patterns on each feather. The hen's head is silver, while the hackle feathers are black, adorned with silver lacing. The body feathers are silver, covered with black laced (Animal World, 2024).

Figure 21. Silver Laced Colored Hen and Rooster.
Reference: The Happy Chicken Coop, 2017.

22.Silver Penciled

This color pattern is characterized by silver and black. Roosters have silver heads, with hackle, back, and saddle feathers in silver, each featuring a black stripe down the center. The chest and under feathers are black, while the tail is a shiny greenish-black. Hens have a pattern similar to the Partridge, but in silver instead of reddish bay. The head is silver, and the hackle feathers are black, adorned with silver lace detailing. The body feathers are silver, with three black penciling on each feather, giving the overall appearance a steel-grey look (Animal World, 2024; Star Milling, 2024).

Figure 22. Silver Penciled Body Color.
Reference: Kasmala & Dicarlo, Feb 9, 2023.

23.Silver Spangled

The Silver Spangled feather color features bright, greenish-black spangles on silvery-white feathers. This gives the chickens a polka dot or "spangled"appearance (Perfect Poultry. 2024).

Figure 23. Silver Spangled Colored Hen and Rooster.
Reference: Livestock Conservancy, 2024.

24.Wheaten

Wheaten chicken feathers resemble the color of yellow wheat. Hens are mostly wheat-colored, but their hackle and tail feathers are darker. Roosters, on the other hand, are more varied in color, but they are generally a more orange version of Black-Breasted Red (Animal World, 2024).

Figure 24. Wheaten Body Color.
Reference: Sky Blue Egg, 2012.

25.White

In White chickens, the entire surface of the feathers is pure white due to the absence of melanin pigmentation in all parts of the feathers. Both hens and roosters are entirely white throughout their bodies (Star Milling, 2024).

Figüre: 25. White colored rooster.
Reference: Homesteader, October 18, 2022.

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BÖLÜM VII

FEATHER TYPES IN CHICKENS

Associate Professor Osman KARABULUT[1]

DOI: https://dx.doi.org/10.5281/zenodo.14551225

[1] Department of Biometrics, Faculty of Veterinary Medicine, Aksaray University, Aksaray – Turkey.
ORCID ID: 0000-0002-8142-2365
Email: okarabulut02@gmail.com

1. INTRODUCTION

Feathers are distinctive and significant structures that set birds apart from other animals. Feathers cover almost the entire body of a chicken, although the legs of most chicken breeds are bare; however, in some breeds, feathers can be seen extending down the legs and even on the toes.

Chickens have different types of feathers, each serving a unique purpose. These feathers not only protect the chicken from external factors but also facilitate efficient flight. However, the situation is different for poultry breeders. If a breeder is concerned with the productivity of the chicken, the structure and colour of the feathers provide valuable information about the bird's egg or meat production or its gender. Sometimes, breeders examine the feather structure and colour to determine the purity of a breed, while those wishing for an aesthetically pleasing appearance in their yard may also prioritize the feathers' structure and colour. Therefore, this section will provide information about the parts and types.

2. MORPHOLOGICAL PARTS OF THE FEATHER

Feathers can be found in different morphological structures in various regions of the chicken's body. However, in general, a standard feather consists of the following parts: vane, rachis, calamus, shaft, bar, afterfeather, downy barb, and barbule (Bitchin' Chickens, 2020; Natural Chicken Keeping, 2012).

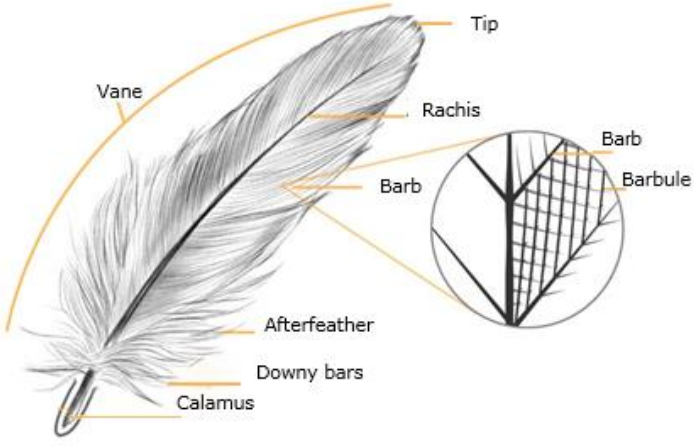


Figure 1. Standart bir tüyün kısımları.
Reference: Natural Chicken Keeping, 2012.

2.1. Shaft

The central part of the feather, running longitudinally, is a hollow rod-like structure that is attached to the bird's skin or bone, narrowing as it extends toward the tip of the feather. The portion of the shaft that lies beneath the skin is known as the calamus, also referred to as the hollow shaft or quil, while the part above the skin is called the rachis (Osváth et al., 2020).

The shaft is rigid, whereas the rachis is elastic and bends when force is applied, returning to its original shape once the force is removed. The rachis can be straight, arched, or sickle-shaped, depending on the location of the bird (Phillipsen, 2020; Wang & Meyers, 2017).

2.2. Vane:

The central shaft of the feather gives rise to the vane, which forms a wide, flat, two-dimensional plane. Vanes may appear solid, but they are actually composed of many small, hair-like structures that extend parallel to one another, called barbs. The barbs that collectively form the vane create a highly organized lattice structure, tightly interwoven through the barbules between the barbs, resulting in a tightly woven configuration (Sullivan et al., 2016).

The rigid vane functions as a rudder during flight, helping to utilize the force of the air effectively during takeoff and landing (Deng, 2016).

2.3. Afterfeather

The barbs located beneath the vane, closer to the rachis and parallel to the vane, are looser in structure compared to the vane. These barbs are more commonly used for temperature regulation rather than for flight, as they are found in the downy part of the feather (Chicken Fans 8 September, 2022).

3. FEATHER TYPES ACCORDING to THEIR MORPHOLOGICAL STRUCTURES

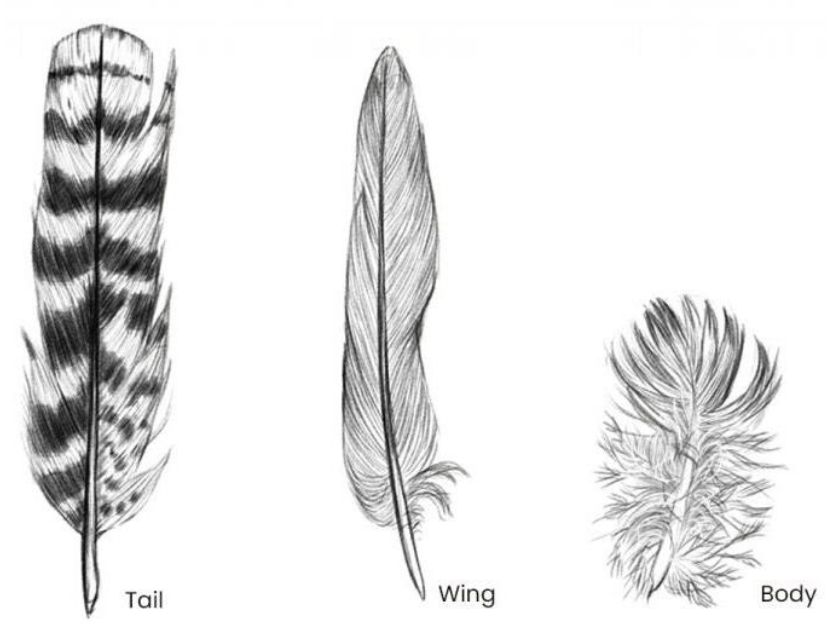
Feathers vary based on their location and the functions they serve. These include Contour feathers, Semiplumes, Down feathers, Powder down, Bristles, and Filoplumes.

3.1. The Contour feather

The contour feathers, which most of us are familiar with, are crucial for flight and general body coverage. They are composed of vanes formed by the barbs on either side of a central shaft. The vanes of contour feathers must be rigid and flexible for flight (Greij, September 14. 2024; Tatomir, 2023).

Tiny muscles around the follicle, the point where the feather emerges from the skin, ensure that the contour feather maintains its correct orientation. These muscles also allow for partial control over the feather's position. As a result, contour feathers can be raised or lowered at will, often as entire sections rather than individually. Birds can fluff up or compress their feathers to regulate body temperature. However, there are other reasons why birds move their feathers. For instance, birds may raise their contour feathers to appear larger and more threatening in order to intimidate a rival or predator (Phillipsen, 2020).

There are three types of contour feathers, based on their location and function: tail, wing, and body feathers.

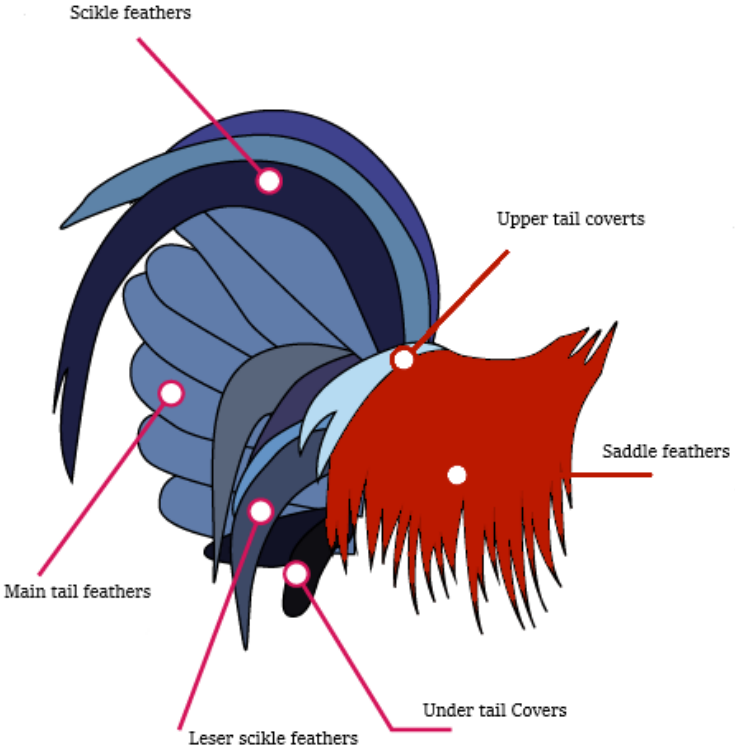


Figüre 3.1. The Contour feathers.
Reference: Drawing with Pri, March 12.2021.

3.1.1. Tail feathers

Chicken tail feathers, although seemingly simple adornments, reveal a wealth of information about the bird's sex, age, and even health. While both male and female chickens have tail feathers, there are significant differences in their size, shape, colour, and function. Understanding these variations provides a deep insight into the fascinating world of poultry (Chicken Fans 8 September, 2022).

Roosters typically have much longer and more elaborate tail feathers than hens. These feathers, known as sickles, curve gracefully upwards, creating a distinctive and eye-catching appearance. The length and curvature of these feathers can vary depending on the chicken breed; some breeds may have exceptionally long and flowing tails (Valto, November 19,2024).



Figüre 3.1.1. Tail Feathers.
Reference: Chicken Fans, 8 September, 2022.

3.1.1.1. Sickle Feathers

These are the distinctive and characteristic long, curved feathers of the rooster's tail. Sickle feathers are the long, sickle-shaped feathers found only in the rooster's tail. They are typically very flamboyant and eye-catching. Hens, on the other hand, do not have these feathers in their tails (The Science of Birds November, 12, 2020).

Figür 3.1.1.1. Sickle feathers (Clorofil, 2019)

3.1.1.2. Saddle Feathers

These feathers, located just above the tail, contribute to the overall fullness and beauty of the rooster's plumage. Saddle feathers are the feathers found on chickens' backs, between the neck and the tail. Most roosters have bright, long, and pointed saddle feathers, while hens have shorter and rounder feathers. These feathers cover both the upper and lower parts of the back (Avian Report 2024).

Although these feathers serve as a rudder in flight, helping the bird steer in the desired direction, chickens have very limited flight abilities, so the feathers remain primarily ornamental. Additionally, these feathers are popular in fly fishing, where they are used as artificial flies (Valto, November 19,2024).

Figür 3.1.1.2. Saddel Feathers.
Reference: Amazon, 2024.

3.1.1.3. Main Tail Feathers

The main tail feathers in chickens are long, stiff feathers extending from the tail and are primarily used for steering and balance during flight. These feathers are critical for flight control, helping the bird adjust its direction and also assisting in braking during landing. Main tail feathers are usually the longest and most prominent feathers on the tail, giving the chicken its characteristic tail shape. Although chickens are not strong fliers, these feathers still provide some control during short flights or gliding. The main tail feathers are attached to the last section of the chicken's backbone, known as the pigostyle (Chicken Fans 8 September, 2022).

3.1.1.4. Greater Sickle Feathers

Greater sickle feathers are long, curved feathers found in the tails of roosters. These feathers are characteristic of roosters and are generally longer and more prominent than those in hens. Due to their sickle-like shape, they curve upwards and outwards, often appearing quite striking and elegant. They

play a role in courtship displays and help the rooster appear more impressive and dominant (Chicken Fans 8 September, 2022).

3.1.1.5. Lesser Sickle Feathers

Lesser sickle feathers in chickens are shorter and less prominent feathers found in the rooster's tail, situated just below the greater sickle feathers. These feathers are also curved, but they generally have a less dramatic appearance compared to the greater sickle feathers. While they are longer and more decorative than the tail feathers of hens, they do not have the same striking, upward-curving shape. Like the greater sickle feathers, lesser sickle feathers contribute to the rooster's overall tail structure, enhancing its appearance during courtship displays and helping it appear more impressive to other hens.

3.1.1.6. Upper Tail Coverts

Upper tail covert feathers are smaller, round feathers located just above the main tail feathers, covering the upper part of the tail. These feathers help soften and shape the overall appearance of the tail by concealing the base of the longer tail feathers. While not as long or striking as the main tail feathers, upper tail covert feathers provide a neat and polished look, contributing to the overall appearance of the bird's plumage. In roosters, these feathers may be more prominent and contribute to the fullness and beauty of the tail (Valto, November 19,2024).

3.1.1.7. Under Tail Covert feathers

Under tail covert feathers are small feathers located beneath the main tail feathers. They cover the underside of the tail and help refine and shape the appearance of the tail's base. These feathers are generally shorter and softer compared to the main tail feathers. Under tail covert feathers also help protect the more delicate areas beneath the tail and give the bird's overall plumage a neat, rounded appearance. In roosters, these feathers contribute to the fullness and attractiveness of the tail, while in hens, they serve a similar function by providing a tidy appearance (Chicken Fans 8 September, 2022).

3.1.2. Wing contour feathers

These are the feathers that provide thrust during takeoff, allowing the bird to fly upwards and gain altitude. The wings consist of three main sections of feathers: coverts, primaries, and secondaries (Greij, September 14. 2024).

3.1.2.1. Covert feathers

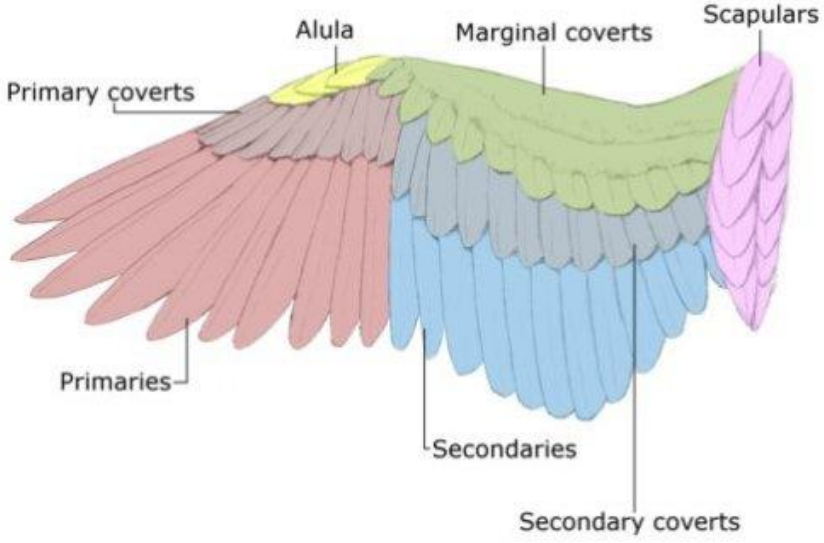
Covert feathers on chickens are small, round feathers located on the upper parts of the wings, closest to the body. They help cover and protect the larger flight feathers, such as the primaries and secondaries, and are essential for smooth and efficient wing movement. While covert feathers are not as long or stiff as the primary and secondary feathers, they contribute to the bird's overall aerodynamics and feather structure, ensuring that the wings are well-organized and functional.

3.1.2.2. Primary feathers

Primary feathers on a chicken are long, strong feathers located on the outer edge of the wings. These feathers are the largest and most important for flight, providing the thrust necessary for takeoff and forward movement. In chickens, primary feathers are crucial for maintaining control and balance during short flights or gliding. They are stiff and long, extending from the tip of the wing and attaching to the outermost part of the wing. Typically, there are ten primary feathers on each wing, though the number may vary slightly depending on the breed (Avian Report 2024).

3.1.2.3. Secondary feathers

Secondary feathers on a chicken are located in the middle section of the wing, attached closer to the body. These feathers are typically shorter than the primary feathers but still play an important role in flight. Secondary feathers provide lift and assist with balance and control during flight, especially when the bird flaps its wings. They are generally longer and more flexible than primary feathers, working in coordination with the primary feathers to help the chicken maintain balance and maneuver while flying or gliding. In chickens, secondary feathers are also important for covering the body and contributing to the overall shape and appearance of the wings (Chicken Fans 8 September, 2022).



Figür 3.1.2. Wing contour feathers.
Reference: Bitchin' Chickens, 2020.

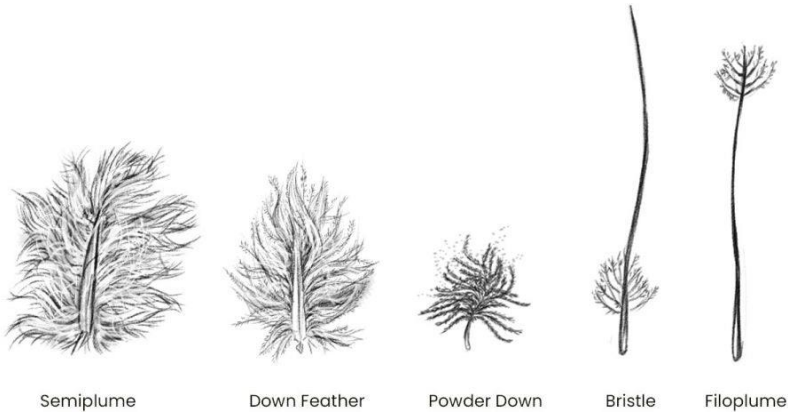
3.1.3. Body contour feathers

Body contour feathers are the smallest feathers and cover the edges of the body and wings. These feathers are especially prominent along the neck, back, and wings, helping the chicken maintain its form and aerodynamics, particularly in flight or escape situations. Body contour feathers act as a barrier to protect the skin from external factors such as dirt, moisture, and debris. They also help regulate the chicken's body temperature, with the downy part of the feathers trapping air close to the body to provide warmth. Although chickens are not long-distance fliers, body contour feathers help provide some lift and control during short flights or when escaping from predators (The Scıence of Bırds, November 12, 2020).

3.2. Other feather

These feathers are located beneath the stiff contour feathers and primarily serve an insulating function. They provide support to the contour feathers against external impacts. Depending on their location, they may also serve

different roles. Here, information is provided about five types of feathers: Semiplume, Down feathers, Powder down feathers, Bristle feathers, and Filoplume feathers (Greij, September 14. 2024; Drawing with Pri, March 12.2021).



Figüre 3.2. Other feathers
Reference: Drawing with Pri, March 12.2021

3.2.1. Semiplume feathers

Semiplume feathers are the second type of feathers found alongside a shaft, but unlike the stiff contour feathers, they are soft and light. Most semiplumes are hidden beneath the contour feathers for insulation purposes, but some grow larger and are used in courtship displays, as seen in the tail feathers of swans (Avian Report 2024).

3.2.2. Down feather

Down feathers are attached to the skin on one end but do not contain a shaft. The barbules, which branch off from the barbs, spread from the tip of the calamus. These feathers are short, fluffy, and loose. Both semiplumes and down feathers serve an insulating function, helping to protect the bird from heat and cold (Greij, September 14. 2024).

3.2.3. Powder down feather

Powder down feathers are a special type of feather that produces a powder-like substance. Similar to semiplumes, the barbs of powder down

feathers continuously grow, with the tips of the barbs disintegrating into a fine powder. Birds spread this powder onto their other feathers while grooming, which helps waterproof their plumage and keep parasites away. Powder down feathers are typically found in the chest and pelvic regions of the bird (Valto, November 19,2024).

3.2.4. Bristle feather

Bristle feathers are short and stiff, and unlike other feathers, they lack barbs except at the base of the shaft. These feathers are typically found around the eyes and near the base of the beak. It is believed that they provide sensory information The Scıence of Bırds (November 12, 2020).

3.2.5. Filoplume feather

Filoplume feather hollow shaft ve şaftt'tan oluşur ancak uçlarına yakın birkaç küçük barb bulunur. Bu tüyler contour tüylerinin etrafında, özellikle de kanatlara yakın yerlerde bulunur. Etkili bir uçuş için rüzgâr ve hava basıncı hakkında duyusal bilgi sağladıkları tahmin edilmektedir (Avian Report 2024).

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BÖLÜM VIII

MORPHOLOGICAL, PHYSIOLOGICAL, BEHAVIORAL CHARACTERISTICS AND BASIC NUTRITIONAL REQUIREMENTS OF HONEY BEES (*APIS MELLIFERA L.)*

Assist. Prof. Dr. Aydın DAŞ[1]

Assist. Prof. Dr. Besime DOĞAN DAŞ[2]

DOI: https://dx.doi.org/10.5281/zenodo.14551264

[1] Department of Animal Science, Faculty of Veterinary Medicine, Harran University, Şanlıurfa, Türkiye. adas@harran.edu.tr, Orcid ID: 0000-0003-0371-5434

[2] [1]Department of Animal Science, Faculty of Veterinary Medicine, Harran University, Şanlıurfa, Türkiye. bdas@harran.edu.tr, Orcid ID: 0000-0003-2163-2632

INTRODUCTION

Honey bees produce products with economic value such as honey, beeswax, pollen, propolis, royal jelly, and bee venom. They also provide pollination, which is important in plant production (Yılmaz, 2016). In order for plants to produce seeds and fruits, flowers must be pollinated. Honey bees are the best pollinators, especially in open areas. The fact that 1/3 of human food consists of plants that require bee pollination will cause a decrease of approximately 30% in plant production in the absence of pollination (Karadeniz, 2012).

Pollination by bees ensures continuity and diversity of flora. Increases the quality and quantity of products obtained in plant production within agricultural activities (Karadeniz, 2012). In plants, there is an increase in the rate of fruit formation, fruit size, the number of seeds in the fruit and other characteristics related to the quality of the fruit (Lampeitl, 2007). It has also been stated that the flowers of plants pollinated by bees are less damaged by frost events (Kesdek, 2012). In the absence or inadequacy of other pollinator vectors, honey bees ensure the protection of endangered plant species through pollination (Çakmak, 1999), and contribute to the development of wildlife and the increase in diversity in plants and animals by multiplying and spreading these plants (Aksoy, 2024).

Morphological Characteristics of Honey Bees

Honey bees are social insects that live in communities called colonies. There are three types of individuals in a bee colony: queen bee, worker bee and male bee. Queen bee and worker bee are female individuals and develop from fertilized eggs. Honey bees undergo complete metamorphosis, each individual turns into an adult honey bee after the egg laid in the honeycomb cell, then the larva, prepupa and pupa stages. The queen bee is the most important individual in the colony, and plays both the mother and indirect father role in transferring the genetic structure to the offspring. Male bees have no other function other than mating. Unlike queen bees and worker bees, males do not have stingers and therefore do not have any defense mechanisms (Winston, 1987; Silici and Özkök, 2009). Bees are included in the insect class, which is the richest class of the arthropod phylum of the animal kingdom.

The body of the bee is soft and covered with a dense hair cover. The bee body consists of three parts: head, thorax and abdomen. The head contains eyes, feelers and feeding organs. The second part of the body, the thorax, is connected to the head by a thin, mobile neck. The thorax and abdomen consist of rings called segments (Özbakır, 2011; Mucsi, 2020)

The head of bees resembles a triangle. The head contains eyes, feelers and mouth parts. The eyes consist of a pair of compound (comb) eyes and three simple eyes. Each of the simple eyes consists of thousands of small units. The compound eye is formed by the union of approximately 3,000 simple eyes in the queen bee, 4,000 in the worker bee and more than 8,000 in the male bee. Bees provide the senses of smell, taste and touch-feeling thanks to a pair of feelers located on their head. They have the ability to move in all directions with the help of very strong muscles. Bees have a licking-sucking mouth type. They show a tearing feature with the help of their lower jaws. The lower jaw and lower lip extend together to form a proboscis in the form of a proboscis. The length of the tongue is between 6-7 mm. The bee; The tongue part, which is covered with hairs, consists of intertwined hard and various rings, and there are narrow, hairless parts between these rings. Worker bees use their upper jaws for tasks such as collecting pollen, processing wax in honeycomb construction, and holding and grasping anything. In bees, the proboscis is used to collect liquid nutrients such as nectar, honey, syrup or water (Winston, 1987).

In bees, the thorax movement consists of four segments. The first segment of the abdomen is connected to the last segment of the thorax. There are three pairs of legs and two pairs of wings, one pair from each of the three segments in the thorax. Therefore, the thorax is the movement center of the bee. Honey bees have two pairs of wings. The wings are made of two very thin membranes and are supported by chitinized veins (Winston, 1987).

The abdomen of bees contains internal organs such as the stomach, intestines and reproductive organs, as well as wax glands and a sting. There are 10 abdominal segments in the honey bee larva. However, the first abdominal segment merges with the thorax and the adult bee has 9 segments. The last abdominal segments are also intertwined, so the worker and queen bee appear to have 6 segments. The 8th, 9th and 10th segments are reduced and hidden inside the 7th segment. Worker bees have wax glands on their 4th, 5th, 6th and 7th front plates. Each of these segments has a pair of wax glands (wax mirrors)

on the right and left. On the inner surface of the 7th abdominal segment of worker bees and near the front edge of the dorsal plate, there is a scent gland (nasanof gland) consisting of large cells. Worker bees and queen bees have a sting at the end of the abdomen. The sting is a thin, pointed defensive organ that protrudes from the sting chamber (Özbakır, 2011; Winston, 1987).

The Queen Bee

The queen bee is the mother of all individuals in the colony. They lay 1000-1500 eggs during the breeding season, forming the source of genetic variation. The diploid (2n:32) queen bee also assumes the role of a father in a way by storing the sperm of the male bees. Queen bees, who complete the incubation period in 16 days, store the sperm they receive from 7-17 male bees in a mating flight in their sperm sac. This flight may be repeated several times due to insufficient mating. Queen bees, who use the sperm in their sperm sac to fertilize the eggs, do not go on mating flights again throughout their lives (Woyke, 1962). The queen bee, who is the only individual in the colony that lays eggs and ensures the continuity of the colony, can lay up to 2000 eggs per day, depending on many factors such as nectar abundance and the size of the colony worker bee population (Genç and Dodoloğolu, 2003). Queen bees, which can live for 3-4 years under normal conditions, are used for a maximum of two years in technical beekeeping, depending on the use of spermatozoids stored in their sperm sacs. In the event that queen bees that do not leave the hive except for fertilization flights and swarming during their lifetime die for any reason or lose their ability to lay eggs, a few of the offspring that are suitable for queen bee production are raised as queen bees by taking them to a different feeding program. The absence of offspring of suitable age for queen rearing in the hive results in the destruction of the colony (Amiri et al., 2017; Korkmaz and Öztürk, 2004).

The Worker Bee

Worker bee; is the female offspring of the queen bee and carries diploid chromosome (2n:32) since it develops from fertilized eggs. It shows structural and functional differences from the queen bee. Worker bees, whose incubation period is 21 days, are individuals responsible for all tasks such as raising offspring, weaving combs, collecting honey and defending the colony. Worker

bees, which reflect all physiological and behavioral characteristics of the colony, constitute the most crowded group of the colony. Their crowdedness is accepted as an indicator of colony strength and productivity (Suwannapong et al, 2011). Although worker bees, whose numbers are expressed in thousands, develop from fertilized eggs, they do not have the ability to reproduce due to the underdevelopment of their ovaries and sperm sacs. However, if they escape the pheromone pressure secreted by the queen bee and offspring present in the colony, it is possible for one or more worker bees to lay eggs in the case of pseudo-queen bee formation. However, since they do not go on mating flights, they lay infertile eggs (Andrew et al., 2001). The number of male bees that develop from infertile eggs and have an incubation period of 24 days varies depending on the season. They are structurally larger than worker bees and smaller than the queen bee. Male bees, who have no other duty than mating with virgin queens, do not participate in any activity within the hive (Czekonska et al., 2013).

The Male Bees

Male bees are formed from unfertilized eggs. They are carriers that make approximately 10 million copies of the genetic message they receive from the queen bee and pass it on to the next generation. Although male bees are seen as a tool for genetic copying, they are as important as the queen bee because they will form the paternal lines of the colony individuals that will be formed (Erkan and Kızıltaş, 2017).

While male bees have different genotypes due to the differences in the unfertilized eggs of the queen bee, the spermatozoa produced by a male bee have the same genetic structure. Male bees, which cannot fulfill any of the honey, pollen collection or in-hive responsibilities of worker bees in the colony, can be easily distinguished from other individuals on the comb thanks to the two compound eyes that almost completely cover their heads. Although they are not as tall as the queen bee, they are larger and wider than worker bees. Since they have a very short tongue structure, they cannot collect nectar from flowers.

Similarly, since they do not have glands, they cannot secrete beeswax and royal jelly. Since they do not have stingers, they cannot defend themselves. Their numbers in the colony vary depending on the season. Generally, in early

spring and late autumn, while no male bees are observed in the colony, their numbers begin to increase in the spring as the weather warms up, depending on environmental conditions and colony strength (Koeniger, 2005). Worker bees regulate the production of male bees by building large honeycomb cells and caring for and feeding the individuals in the cells. When their numbers are desired to be limited, the eggs, larvae and pupae left in the large honeycomb cells are destroyed and their development is prevented. Male bees, whose numbers reach their highest level with the swarming season, are thrown out of the hive and left to die as the nectar decreases. Male bees that emerge from the cells make their first flights when they reach approximately one week of age. Flights, which are generally made in the afternoon, begin with the purpose of getting to know the environment and later head towards areas called gathering (mating) areas. Male bees, which cannot fly unless the air temperature reaches 20 °C, make about 2-4 flights per day. Although they reach sexual maturity when they reach approximately 8 days of age, the most suitable ones for mating and artificial insemination are those aged 12-15 days. Drones, whose reason for existence is to mate, mate by following the unmated, virgin queen bee that leaves the hive in the air. Drones, who normally have a life span of 40-50 days, die when they mate with a virgin queen bee because they lose their mating organs (Güler, 2008).

Physiological And Behavioral Characteristics of Honey Bees

Characteristics such as wintering ability, brood area, survival rate, honey yield and flight efficiency used to determine the performance characteristics of honey bee colonies in the regions where they are located are defined as physiological characteristics, while characteristics such as plundering, aggressiveness, swarming and propolis collection are defined as behavioral characteristics (Rutner, 1988).

Wintering Ability (%): In the autumn maintenance of colonies, the number of frames with bees is determined and they are allowed to enter winter, and in the following spring maintenance, the number of frames with bees is determined again. The difference between the number of frames with bees determined at the entrance and exit of wintering colonies is determined with the help of the relation as follows;

Wintering Ability=Number of frames with bees emerging from spring/Number of frames with bees entering winter x 100 (Genç, 1990).

Broode Area (cm^2/colony): The broode quantities of colonies are based on the principle of determining the open and closed brood area in cm^2 at 21-day intervals or only the closed broode areas every 12 days.

The broode area develops in an ellipse shape on the comb. In a healthy colony, there are an average of 4 brood cells in a 1 cm^2 broode area. The measurements are applied separately to both sides of the broode frames and are added together to determine the total area in each frame (Doğaroğlu and Ortaç, 1992).

Survival (%): The ability to adapt a population is determined by its survival.

Using the number of queens lost by colonies at various periods, the survival rate of groups is determined by dividing the number of queens by the number of groups. Accordingly, the survival rate of colonies is determined as a percentage by utilizing the number of colonies that died out during the trial period (Gözenler, 2000).

Cleaning (Hygienic) Behavior (pupa count/colony): The most reliable way to eliminate negativities such as residue left by drug use especially in bee products, negative effects on bees and disease agents gaining immunity over time is to determine disease-resistant bee breeds and develop new genetic material from them. Because worker bees of different age groups that make up the colony have the ability to clean all kinds of crumbs, debris, mites on each other or dead eggs, larvae or pupae in their honeycomb cells and throw them out of the nest or groom each other. This skill is an acquisition provided by the genetic structure. It is a character that is primarily evaluated in both adaptation and selection breeding. The colony's removal of the brood in open or closed cells that have died for any reason and throwing them out of the hive is considered as cleaning (hygienic) behavior. Worker bees also display this behavior when removing the diseased source from the nest in case of any disease occurring in the colony environment (Guzman-Novoa, 2011; De Roode and Lefèvre 2012).

Pollen Production Efficiency (g/colony): In order to determine the pollen production efficiency of the colony, when most of the plant species and varieties in the region are in flower, traps are opened in the colony in the evening after the forager bees return to the hive. The traps are closed at noon the next day. The pollen collected in each trap is weighed separately and the amount of pollen collected by the colony (g/time) is determined (Dreller and Tarpy 2000).

Honey Yield: The amount of honey obtained at the end of a production year in beekeeping is an important indicator of the success of colony management. Honey yield is a result of the environment, colony management and the genetic characteristics of the bee, and can vary depending on the size of the colony population. The size of the colony population can vary depending on the age of the queen bee, the egg-laying rate and the survival rate of the worker bees. There is a positive relationship between the amount of brood in the colony and the honey yield it produces (Ebbersten, 1978; Woyke, 1984; Kumova, 2000).

Flight Activity (number/colony): There is a high level of correlation between the flight activity of colonies and their ability to reach and benefit from food sources. This feature provides information about food gathering power. Determination of flight activity is based on determining the number of worker bees that leave the hive at short intervals at certain times of the day. This feature determines the ability of colonies to benefit from food sources, and also provides an idea about the pollination efficiency of colonies. Stand somewhere to the side of the hive and count the worker bees that leave the hive flight hole and flight board for 30 or 60 seconds. Measurements are made in the same time interval in the trial colonies, taking into account the hours during which the bees fly during the day. The average number of worker bees that leave or enter each colony (number/colony) is determined (Erickson et al., 1975).

Plundering; Honey bees try to collect nectar and pollen whenever they can fly normally, regardless of the source. Especially in periods when nectar is scarce in nature, worker bees from strong colonies occasionally attack weak colonies to carry their honey to the hives, which is defined as plundering.

Plundering is a bee behavior that is completely undesirable and should be taken into consideration in technical beekeeping, as it leads to the loss of colonies and the spread of diseases between hives and even between apiaries. Plundering behavior can be prevented by following the rules regarding colony maintenance and management, such as not keeping weak and strong colonies side by side, leaving a reasonable distance between colonies, narrowing the hive's flight holes, closing the hive's cracks and crevices, feeding the colony inside the hive, not leaving the hives open for long periods, and not spreading sugary substances around the hive (Graham, 2003; Öder, 2006; Korkmaz, 2013).

Aggressiveness (number of stings/colony): Aggressiveness or bee stings is an undesirable feature because it makes it difficult for the breeder to work and increases stress in the colony. It negatively affects productivity. Bee races show different aggressive behaviors from each other. These behaviors of colonies change depending on the period and conditions. When making a definition or being able to say that this race is more docile than that race, a sufficient number of measurements and observation values made in different periods are required. Therefore, the aggressiveness of colonies is compared at the same time and under equal conditions. The method is to create stress in the colonies and the reactions of the bees are drawn onto materials such as leather, suede, cloth, etc. Oval balls made of black cloth with dimensions of 5*4 cm are used. The ball is hung in front of the hive flight hole with a rope and is shaken for 30 or 60 seconds. The number of stings hitting the ball during this time (number/colony) is determined.

Swarming Tendency (%): Swarming is a natural but preventable form of reproduction in which a honey bee colony spontaneously divides into two smaller colonies. Swarming usually occurs after a few weeks when nectar and pollen resources are abundant, and depending on the climate and flora, over a 4-6 week period between the end of spring and the beginning of summer. During the swarming phase, some of the queen bees and worker bees in the colony, thousands, sometimes tens of thousands of worker bees, fill their honey stomachs with honey and form a bee cloud in front of the hive and leave the hive en masse with a loud buzz. These bees that leave the hive form a cluster in the form of a grape cluster on a tree, bush or a suitable place near the hive with

the queen bee within a few minutes (Graham, 2003; Korkmaz, 2013). This type of swarming behavior is due to genetic structure. Especially in urban areas, swarming of colonies must be prevented (Melathopoulos et al., 2018; UC anr, 2018; Boma, 2019; Matsuzawa and Kohsaka, 2021).

Propolis Collection: Propolis collection is one of the most difficult processes that honey bees struggle with. Since bees usually tend to collect propolis from the upper parts of trees, it is quite difficult to observe this behavior. Bees use their hind legs and upper jaws to collect the resinous, mucilaginous exudate found in the buds and shoots of plants, and moisten and soften it in their mouths. Meanwhile, bees increase the biological value of the propolis they turn into pellets by adding some enzymes they secrete from their mouths. The propolis turned into pellets is packed into the pollen basket on the hind legs with the help of their front and middle legs. It takes about 15-16 minutes for a propolis load that a bee can carry with its two legs to be stored, and the propolis is carried to the hive with the pollen basket.

Worker bees that perform their duties inside the hive bite and pull the propolis from the bees that return to the hive with the propolis load, tearing it into small pieces and carefully pressing and sticking it to the place where they will use it. Bees mix some beeswax into the propolis used to cover any part of the hive. The bee, which breaks off a piece of the propolis load, hits the propolis lump and makes the remaining piece smooth again. The complete discharge of the propolis load varies between one and a few hours, depending on its use in the hive and the number of worker bees that bring the propolis load.

A worker bee discharges the propolis it collects into the hive in 30 minutes. Since propolis is collected only on hot days and during the hot hours of the day, the bee that discharges the propolis load will tend to collect another propolis if it has enough time. Propolis is collected by 12-21 day old field worker bees that weave the comb, feed the larvae, disinfect the comb cells, secrete wax and are generally responsible for colony management, and is used immediately in the necessary places (Kumova et al., 2002).

Basic Nutritional Requirements of Honey Bees

The basic nutritional needs of honey bees are evaluated on an individual and colony basis. These nutritional requirements show some differences

according to gender, development period, especially adult worker bee age groups, reproductive functions in queen and drone bees and season. The carbohydrate source of honey bees is provided by nectar or secretions, while the protein source is pollen and bee bread. Honey converted from nectar, bee bread from pollen and royal jelly produced by consuming them contain the carbohydrates and proteins that honey bees need, as well as vitamins, minerals, amino acids and fats. Although the water needs of the colony are mainly provided by nectar, water is also carried to the hive by field bees when needed. Like all living things, honey bees need water to survive.

Water is necessary not only to maintain osmotic balance in adult bees, but also to prepare liquid food for the brood and to cool the hive on hot days. The need for foragers to collect water in a honeybee colony increases when high temperatures make it necessary to cool the hive interior by evaporation, and decreases when the danger of overheating has passed. Although there are individual differences, it has been reported that honeybees prefer saltwater sources, especially those containing sodium (Lau and Nieh, 2016).

Carbohydrates; The energy required for wax secretion and comb weaving, cleaning the hive interior, feeding other brood and adult bees, adjusting the temperature of the hive interior and brood area, flight of foragers collecting pollen and nectar, and other activities inside and outside the hive are provided by carbohydrates. Carbohydrates that meet the energy requirement are derived from sucrose, a disaccharide found in the composition of nectar, and its monosaccharide components glucose and fructose. The proportion of these sugars varies between 10-70% depending on the plant species from which the nectar is collected (Nicolson and Thornburg, 2007). The energy content of a flower nectar depends on its volume and sugar concentration. Bees can distinguish small differences in nectar concentration and prefer those with high concentrations (Nicolson, 2011). Adult bees can benefit from carbohydrates such as glucose, fructose, sucrose, trehalose, maltose and metiltose, but they cannot use rhamnose, xylose, arabinose, galactose, mannose, lactose, raffinose, melibiose, stachyose, dextrin, insulin and some of them are toxic carbohydrates (Barker, 1977). Nectar contains sugars as well as water and some other substances that give honey its unique taste. The water content of nectar varies according to its source and environmental conditions. Although amino acids are in lower concentrations, especially in insect-pollinated plant nectars, they are

among the most abundant substances in the nectar composition after sugars. It has been stated that the amount of proline in nectar has an attractive feature for honey bees, and similarly, glycine is attractive and improves the learning ability of honey bees. Proline is also evaluated as a quality criterion in honey. Other substances found in the composition of nectar have been reported by various researchers as organic acids, terpenes, alkaloids, flavonoids, glycosides, vitamins, phenolics and oils (Nicolson, 2011). When worker bees fill their honey stomachs with nectar and return to the hive, the nectar is taken orally by these bees or by other bees in the hive and stored in the honeycomb cells. The process of nectar conversion to honey is initiated in the honey stomach of field worker bees, and the moisture content is reduced to between 16-20% during the ripening process by adding invertase, diastase and glucose oxidase enzymes. Due to their social organization, nurse worker bees are responsible for the nutrition of all other individuals in the colony. Nurse worker bees must also consume pollen and honey to produce royal jelly, which is the food for their offspring (Kunert and Crailsheim, 1988). A worker bee larva reaches an average weight of 150 mg after a 5-day feeding period, while drone larvae reach 340 mg after a 6.5-day feeding period (Özbakır and Alişiroğlu, 2019). The total amount of carbohydrates to raise a worker bee is estimated to be roughly 59.4 mg and 98.2 mg for a drone (Rortais et al., 2005). An adult honey bee requires approximately 4 mg of usable sugar per day to survive. It has been reported that forager worker bees that collect pollen and nectar for each hour of flight require approximately 8-12 mg of sugar (Balderrama et al., 1992). It has been reported that the annual honey requirement of a honey bee colony is approximately 60-80 kg (Winston, 1987). In colonies that do not receive additional feeding after honey harvest, if carbohydrate deficiency occurs in the spring when winter reserves are depleted and nectar sources are poor, the number of larvae raised is also limited (Brodschneider and Crailsheim, 2010).

Proteins; Pollen, the male gametophyte of flowering plants, is the main protein source of bees and also a source of micronutrients. Pollen consists of proteins, lipids, sugars, fibers, mineral salts, amino acids, phenolic compounds and vitamins in terms of chemical composition. The presence of high concentrations of reduced sugars, essential amino acids and unsaturated/saturated fatty acids, Zn, Cu, Fe and a high K/Na ratio makes honeybee pollen important for human diets as well. The main components of

pollen are; The proportion varies between 13-55% and is carbohydrates (fructose, glucose, sucrose), 10-40% proteins (amino acids, enzymes), 0.3-20% crude fibers and 1-10% lipids (fatty acids, sterols, hydrocarbons) (lö, 2017). Honey bees require ten amino acids for development: arginine, histidine, lysine, tryptophan, phenylalanine, methionine, threonine, leucine, isoleucine and valine. Although the protein and amino acid content of pollen depends on the botanical origin, the essential amino acid concentration is stable regardless of the botanical origin; especially glutamic acid, aspartic acid, proline, leucine, lysine, arginine and serine amino acids have been reported to be abundant in pollen content by various researchers (Szczęsna, 2006). The chemical composition of pollen collected by hand from flowers, obtained from pollen traps and honeycomb cells (bee bread) varies (Roulston et al., 2000). Pollens with different surface shapes collected from flowers by forager worker bees are moistened with a certain amount of nectar and carried to the colony in pollen baskets located on their hind legs. Pollen, which has more nectar, salivary secretion and microbial content added to it in the hive, is usually stored in the cells close to the brood area and consumed in the form of bee bread, which has a higher nutritional value. The pollen consumption and requirements of worker bees vary depending on their age and their role in the colony. Pollen consumption and metabolism in the colony are not equally common among all bees. Especially 8-day-old worker bees are the primary pollen processors and distributors of the colony due to the highest proteolytic activity in their stomachs among other individuals. During the first 8-10 days of their lives, worker bees must consume pollen to develop their hypopharyngeal and mandibular glands and to produce larval nutrients. Protein-rich royal jelly is produced not only to feed the brood, but also to feed the queen bee, especially in adults. Unlike honey, pollen is stored in smaller amounts, and when there is no field activity, the stores are consumed more quickly. Larvae are particularly dependent on protein, and brood production is strongly affected by protein deficiency, and cannibalism (brood eating) behavior can be observed. There is a significant relationship between the average capping time of larval cells and pollen arrival; the less pollen stored in the hive during the development of the larvae, the earlier the larval cells are capped (Schmickl and Crailsheim, 2001; Schmickl and Crailsheim, 2002). The response of honey bees to deficiencies in the quantity or quality of their pollen reserves has been to increase the gross

amount of pollen brought to the hive, rather than specializing in collecting pollen with a higher protein content (Pernal and Currie, 2001). The addition of nectar to pollen of different sizes and shapes facilitates its transportation to the hive in worker bee pollen baskets. Bee bread is of great importance for colony survival and population development, especially in early spring (Brodschneider and Crailsheim, 2010). Colony population growth and worker bee quality are significantly affected by diet composition. According to the results of a field study conducted to determine the optimal dietary protein concentration in honey bee nutrition, a crude protein content of 29.5–34.0% was recommended in the honey bee diet in early spring. High protein content in the diet had the opposite effect, shortening lifespan and reducing population growth (Zheng et al., 2014).

The composition of royal jelly, which is the other protein source of the colony, consists of 60-70% water, 9-18% proteins, 7-18% carbohydrates, 3-8% lipids, essential amino acids, vitamins and minerals. However, royal jelly contains niacin (vitamin B3), pyrioxidine (B6), thiamine (B1), riboflavin (B2), pantothenic acid, folic acid, biotin, as well as magnesium, potassium, calcium, zinc, iron and copper minerals, and small amounts of polyphenol compounds (Bogdanov, 2017). Honey bees are unique even among social insects because only female larvae fed with high-quality and abundant royal jelly can be raised as queen bees. Larvae to be raised as queen bees are fed intensively with mandibular gland secretions for the first three days, and then with a mixture of both mandibular and hypopharyngeal gland secretions. Worker bee larvae are fed with hypopharyngeal gland secretions for the first few days of the larval period, and then are fed with a mixture of royal jelly, honey and pollen for the remaining days.

The larva's first food (first 3.5 days) is rich in protein, while its last food is rich in carbohydrates.

After adult emergence, worker bees feed from honey and pollen cells around the brood area, and also from other worker bees through their mouthparts (trophallaxis). Drone larvae are provided with lower quality protein, a higher amount of food due to their long development period and body size (Winston 1987). The effects of honey bee pheromones on feeding and food collection should not be forgotten.

Both queen bees and brood produce primary pheromones that strongly affect cooperative brood care.

Honey bee larvae, which cannot feed themselves, emit pheromones, affecting the behavior and physiology of nurse worker bees, encouraging them to provide appropriate feeding resources and stimulating more pollen collection. (Sagili and Pankiw, 2009).

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CHAPTER IX

AN OVERVIEW OF ANIMAL RESCUE ACTIVITIES OF FIRE SERVICES

Prof. Dr. Halil Selçuk BIRICIK[1]

DOI: https://dx.doi.org/10.5281/zenodo.14551274

[1] Afyon Kocatepe Üniversitesi, Veteriner Fakültesi, Afyonkarahisar, Türkiye. hsbiricik1@email.com, Orcid ID: orcid.org/0000-0003-4974-1611

INTRODUCTION

Disasters affect both animals, people and also need response. Animal rescue is the transfer of the animal from risky area to the safe place by using modern rescue attempts. Animal rescue is a collaboration between search and rescue team, firefighter and veterinarian to obtain a successful result. Rescue teams must work together with the vets that sedate and inject sedatives to the animals in order to contribute the animal welfare.

In this study, animal rescue activities, institutional capacities, opinions and suggestions of Fire Department Personnel working in Balıkesir, Artvin, Konya, Şanlıurfa and Van Municipalities in our country in fire and other emergencies were compiled.

Balıkesir fire service

Fig. 1: Balıkesir Disaster coordination center

Fig. 2: Snake, cat and dog catching devices in Balıkesir Fire Service

Firefighters are mostly involved in rescue activities related to cats (trapped in high places) in the city centre.

During a cat rescue incident, a staff member was given a rabies shot as a result of a scratch. There are unnecessary reports of cases that do not require rescue. The public needs to be made aware of uncomplicated, non-rescue incidents.

Fig. 3: Cat stuck in tree

The prominent views of the fire department personnel can be listed as follows:

The images of hundreds of animals dying and being injured in the fires that started in agricultural lands in Diyarbakır and Mardin in June 2024 and caused the death of 15 people affected us greatly. As is known; In the large fire that started on June 20 in the border villages of Diyarbakır and Mardin, hundreds of sheep and goats raised in the region died so far, and many animals were taken for treatment.

Fig. 4: Burnt sheep in Mardin field fire (June 2024)

Fig. 5: Burn treatment in a fire-affected animal

Burning stubble in agricultural lands harms animals and nature. A public service announcement should be prepared on this issue, and the public should be made aware of the effects of fire on animals on TV channels (Note: This issue should be taken into consideration as animals were severely affected in the Diyarbakır and Mardin fires in June).

Fig. 6: Firefighters' response to the fire

Recently, 100 goats died in a barn fire. Large animals such as cattle should not be kept tied in a barn. During the winter months, animals knock over electric heaters in barns, causing fires.

The institutions responsible for animal rescue in disasters such as fire, earthquake, flood or individual cases are not clear. Is it the General Directorate of Nature Conservation and National Parks under the Ministry of Agriculture and Forestry, AFAD or the Fire Departments? In some cities, AFAD comes to the fore in this regard, and in others, the Fire Department. While the Fire Department generally intervenes in cases within the city, AFAD teams intervene in cases in rural areas. The institutions responsible for animal intervention in disasters and their boundaries should be determined.

The number of fire department personnel is insufficient. Certified trainings for animal rescue cases (approach to large and small animals, holding and tying, first aid, rescue equipment) should be initiated and teams consisting of animal-loving personnel should be formed.

Artvin Fire service

Firefighting, a 310-year-old organization, is not yet registered as a profession.

Animals were intervened in forest fires. Animals such as turtles and hedgehogs are affected more because they cannot escape.

Fig 7: A turtle affected by a forest fire

Rescue operations are carried out in rural areas in cases of large animals falling into wells and also in barn fires. Inter-institutional cooperation (AFAD, Agriculture Directorates, Nature Conservation Organization) is insufficient. There are veterinarians within the municipality, but in many animal rescue cases, sufficient contribution is not received for on-site intervention.

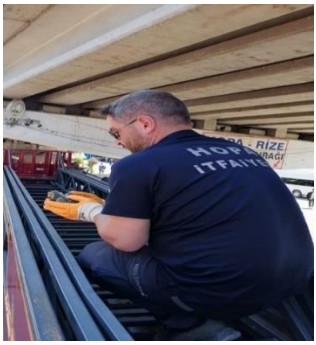

Fig. 8: After Artvin Hopa Firefighter rescued the seagull from the area where it was stuck

Fig. 9: After rescuing a dog that fell into a stream

Van Fire service

Fig. 9: Reed (wetland) area next to Van Castle

Fig. 10: Van Fire Department personnel's intervention to the Mardin field fire in June 2024

Fig.11: Van Fire Department personnel rescue turtles in fire

Fig. 12: Van Fire service cow rescue

The majority of the reed (wetland) areas in Turkey are located near Lake Van. The reed areas within the borders of Erciş, Gevaş and Muradiye districts are home to many bird species. Fires occur frequently in these reeds. Sometimes villagers start fires to scare away the pigs sheltering in the reeds, especially the piglets die because they cannot escape, and then a fire is reported. When firefighters arrive at the scene, groaning sounds are heard but they cannot approach because of the flames. In one case, the explosion sound of a bloated burning pig was heard from all sides. Many reptiles and insects, especially turtles, die because they cannot escape the flames. In addition, these reed areas, which are home to many bird species, completely destroy their nests as a result of fires, and countless birds lose their lives.

In woodshed and shed fires, poultry animals are seen dying from smoke. Cows have been witnessed dying in barn fires.

As fire department personnel, the main problem in animal rescue is the lack of rescue equipment. If this deficiency is completed, we will be successful.

Fig. 13: Van Fire service cow rescue

Fig. 14: Cow rescue in Muradiye district of Van city

When dogs and cats are stuck somewhere, they become aggressive when you go to rescue them and approach the animal. A sedative needs to be administered. Veterinary support is required for this, but sometimes it is not possible to reach veterinarians immediately. It is even more difficult to find a veterinarian, especially at night. For this reason, every fire department should have a veterinary staff.

Ventilation gaps in buildings are a big problem for firefighters. There are two problems; first, there are no filters placed on the ventilation gaps on the top of the buildings, so birds and cats fall through these gaps. Second, builders make the gaps very narrow to save space. Firefighters who go down into the ventilation gap to save the animal have a hard time intervening, they get stuck inside. They also make the ventilation windows inside the houses narrow to save costs, if they were wide, it would be easier to reach the animals that fall into the gap.

Fig. 15: Van Fire Department rescues bird that fell into ventilation shaft

Konya Fire service

Fig. 16: Rescue equipment

Fig 17: Konya Firefighters

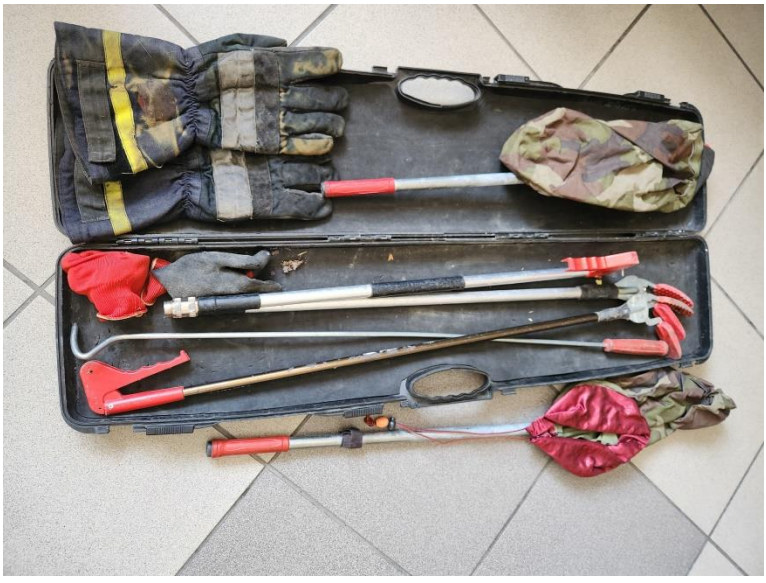

Fig. 18: Konya Fire service animal rescue equipments

In the city center, the fire department personnel are wasting their time due to false reports, mostly about cats. Cats naturally go to the tops of trees, but citizens still report them to be rescued.

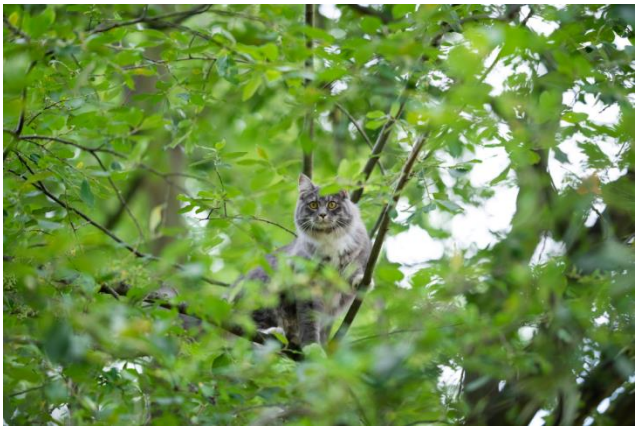

Fig. 19: Cat climbing tree top

Straw bales are obtained by separating grains such as wheat, barley, and oats from their ears and then compressing the remaining parts of the plant using a baling machine, and are used in animal husbandry. Although it has very low nutritional value, it is commonly given to animals as feed in Turkey. Farmers, especially those involved in cattle breeding, feed the bales they have prepared in the summer to their animals in the winter. Large enterprises stack thousands of bales next to barns, and since they do not divide the bales, when a fire starts, all the bales burn, and also spread to the barn and the animals die. In such a fire, the cows burn inside the barn and are immediately slaughtered before they die.

Since there is no water left in Konya, the wells are idle. When the covers are left open, animals fall into the wells many times. We save them using tripods. Konya has large agricultural lands (barley, wheat). In the summer months, when the grass dries, there are stubble fires, people throw cigarettes, the fires start and quickly reach other areas. Many animals, especially snakes, are harmed in these fires.

Fig. 20: After rescuing dog

Fig. 21: Fire breaks out in a wheat field in Konya

Fig. 22: Konya Municipality stubble fire poster

Fig. 23: Konya Municipality stubble fire poster

Şanlıurfa Fire service

Fig.24: Animal husbandry in caves in Urfa

Şanlıurfa Fire Department has a leading place in our country in terms of animal rescue equipment. There is a model horse brought from England to be used in drills at the fire station, as well as belts that enable the safe rescue of large and small animals that fall or get stuck in places such as wells, canals, streams, lifting equipment such as cranes, and special equipment that can pull out large animals stuck in mud.

Fig. 25: Manakin horse

Fig. 26: Cow rescue sling

Firefighters are participating in rescue operations related to cats, which climb to high places in the city center.

Şanlıurfa Fire Department personnel went to the region in June to provide support in responding to fires that started in agricultural fields in Diyarbakır and Mardin, resulting in the deaths and injuries of hundreds of animals.

Şanlıurfa has large agricultural fields (barley, wheat, lentils, chickpeas, corn), especially in the summer months, when the grass dries out from May, there are many stubble fires, people passing by throw cigarettes, fires start in the fields because of a cigarette and quickly spread to other areas. Many animals, especially snakes, are harmed in these fires.

Fire department personnel are insufficient in number. In order to intervene in animal rescue cases in case of fire and other emergencies, a team consisting primarily of animal-loving personnel should be established within each fire department, these teams should be trained and they should intervene in cases involving animals at the first stage.

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CHAPTER X

SMALL ANIMAL SEDATION AND INJECTABLE ANESTHESIA

Prof. Dr. Halil Selçuk BIRICIK[1]

[1] Afyon Kocatepe Üniversitesi, Veteriner Fakültesi, Afyonkarahisar, Türkiye. hsbiricik1@email.com, Orcid ID: orcid.org/0000-0003-4974-1611

INTRODUCTION

The "*anesthesia"* means "lack of sensation". Anesthesia is performed by giving agents depressing nerve function. With general anesthesia, the animal is unconscious for a short time period. During this condition, there is muscle relaxation and a complete loss of pain sensation. Other types of anesthesia include local anesthesia for localized area of skin or a tooth, and spinal anesthesia, resulting in anesthesia of a special part of the body.

Within the last 15 years there has been a significant changes in anaesthesia is conducted in dogs. Introduction of new drugs has broadened choices for anaesthesia protocols and enabled use of appropriate combinations to meet demands of increasingly sophisticated medical and surgical procedures. Monitoring equipment has become available specifically for veterinary medicine and its cost is such as to make its purchase feasible in general veterinary practice.

Stages of anesthesia: There are several stages to delivere anesthesia to small animals. Firstly, there is the pre-anesthetic animal assessment and preparation. On the procedure, there is preanesthesia with sedatives and opioids permitting endotracheal intubation for induction of the anesthetic. Maintenance of anesthesia following induction is usually with a inhalant anesthetics like isoflurane or sevoflurane, via endotracheal intubation.

While the animal is under anesthesia; heart and respiratory rate, central nervous system functions are controlled continuously so the depth of anesthesia can be adjusted urgently. During and after the anesthesia, emergency agents and equipments for their use should be available to maintain good circulation of blood. During the recovery period, veterinarian experienced in the determination of anesthesia recovery problems should monitor the animal.

Definitions

Premedication: preanesthetic medication refers to a drug treatment given to an animal before a surgical or invasive medical procedure. These agents are sedative or analgesic, and are frequently given intramuscularly or subcutaneously to sedate the animal for several procedures.

Induction: The administration of an anesthetic drug or combinations at the beginning of anesthesia that results in a state of general anesthesia. These drugs are generally given intravenously.

General Anesthesia: A state of unconsciousness with the absence of pain sensation over the whole body, through the administration of anesthetic agents.

Maintenance: On going situation of general anesthesia. Inhalation anesthetics are used for maintenance of anesthesia because they allow control of the anesthetic state and also at low cost. However, intravenous agents can also be used to maintain a surgical level of general anesthesia.

Analgesic: An agent used to achieve relief from pain. Analgesic drugs act in various ways on the peripheral and central nervous systems, and include non-steroidal anti-inflammatory drugs, and opioids (such as morphine and pethidine).

A hypnotic is a depressant of the central nervous system which enables the animal for sleeping more easily, or a drug used to increase the depth of sleep. A sedative is an agent which relieves anxiety and concluding tends to make it easier for the animal to rest or sleep. Many drugs are in both the sedative and the hypnotic categories, the differentiation usually being increase or decrease in the dose.

A tranquillizer is a drug with a effective action in relieving anxiety without producing sedation. They affect behaviour and the classification of these drugs are done as 'major' and 'minor'. Equines that have been given tranquilizers are aware of their environment but appear more relaxed.

A sedative is an agent that reduces excitement, therefore allowing the animal to become sleepy. These include xylazine (Rompun), detomidine (Dormosedan) and romifidine (SediVet). These drugs are short-acting and provide reliable sedation with little analgesia (pain relief). Sedated horses are unaware of their surroundings, but these drugs cannot prevent all reactions such as kicking, and may even increase the risk. Sedatives are commonly used to facilitate short veterinary procedures.

Pre-Anesthetic Status

The aim of the preanesthetic control is to determine risk factors that influence the animal's ability to tolerate anesthesia. The evaluation consists of anemnesis, physical status, age, breed, temperament, operation, use of deep sedation and the experience of veterinary anesthesist.

There are five general classifications of animal physical status, including:

- Normal healthy animal
- Animal with mild systemic disease
- Animal with severe systemic disease
- Animal with severe systemic disease that is a constant threat to life
- Animal who is not thought to survive without the operation

Parameters to be evaluated includes:

Anemnesis: Identify risk factors, including previous anesthetics used, known disease conditions, adverse agent responses.

Physical examination: A wide physical examination may show risk factors, such as arrhythmia or anormal lung capacity.

Age: Older animals have increased anesthetic risk because of changes in cardiovascular and respiratory parameters. Diseases develops more commonly in aged animals. Very young animals can be at increased risk from hypoglycemia, hypothermia.

Breed: Brachycephalic dogs and cats are more susceptible to upper airway obstruction. Greyhounds have longer sleeping time after administering several anesthetics such as propofol or thiopental. Some breeds of and cats may be predisposed to cardiac disease in parallel older age.

Experience of anesthetist: Previous education in different anesthesia techniques will facilitate their use. Also, an experienced surgeon may be

faster and cause less tissue trauma to the animal.

Preanesthetic preparation

Starvation for about 12 hours usually ensures a dog will have an empty stomach. Water need not be given until preanesthesia is given or until about 2 hours prior to anesthesia. Laboratory evaluation can help useful via data about the general health position of the animal prior to anesthesia. A complex physical examination to determine any disturbances must be carried out.

Intravenous catheterization: The common used venous access is cephalic vein. Other veins for venous catheter usage include the tarsal, saphenous, auricular and jugular veins.

Preanesthetic drugs: A planned preanesthesia helps smooth induction and has anesthetic reducing effect during anesthesia. There are many choices available. Sedative and opioid combination (neuroleptanalgesia) is very popular especially acepromazine-morphine combination), and produces better restraint and analgesia as preanesthesia. Premedication in dogs usually includes administration of anticholinergic, sedative, and opioid drugs, the combination preferred depending on the conditions.

Acepromazine

Produces mild sedation at clinically used dose (0.01 – 0.05 mg/kg) The doses of acepromazine reduce with increasing weight of the animal; for i.m. usage in small dogs, 0.05–0.10 mg/kg; for dogs 10 to 20 kg, 0.05 mg/kg; for dogs 20 to 40 kg, 0.03–0.05 mg/kg: with a maximum dose of 3 mg for most big sized dogs.

- Anti-arrhythmic
- It is necessary at least 20 min for good activity following IV injection.
- Longer duration
- Preanesthesia dose of 0.04 mg/kg intramuscularly has little cardiovascular effect in normal dogs.

- Will cause hypotension in old, risky, or hypovolemic animals via direct myocardial depression and peripheral vasodilation, and should not be used in these risky animals.
- Boxer breeds are very sensitive to phenothiazine and acepromazine as 0.02 mg/kg intramuscularly can cause collapse with the animal as bradycardic and hypotensive. For this, it is suggested low dose of acepromazine be given, and atropine be used with acepromazine in this breed.
- Inexpensive, and usually given for sedation and premedication.

Diazepam/Midazolam

Diazepam or midazolam are not used alone to normal dogs as they may cause excitability. They are often administered in combination with an opioid for sedation or preanaesthesia and within this combination contribute to higher degree sedation than would be obtained by the opioid alone. Diazepam and midazolam are frequently given i.v. just before intravenous agents such as thiopental.

- Minor tranquillizan agents
- Satisfactory muscle relaxation
- Minimal cardiopulmonar effect
- 0.05 – 0.4 mg/kg IV, IM, SQ
- Diazepam may be irritant to the tissue so better to avoid giving it intramuscularly.

Xylazine

Xylazine is the first α_2 adrenoceptor agonist to be widely used in animal anesthesia. Given i.m. to dogs in doses of 1–3 mg/kg it provides good sedation and also hypnosis. The drug is titled as a sedative and, as might be expected, increasing the dose causes to greater sedation as well as increased duration of sedation. High doses is related with riskious cardiovascular effects and longer recovery, so that high doses cannot be suggested. An unwanted effect in dogs is vomiting as sedation develops. In dogs, xylazine often causes a rise in arterial blood pressure and dose-dependent respiratory depression. Atropine may be given to prevent bradycardia. Other side effects

similar in other species; Hyperglycemia, gastrointestinal motility depression.

Medetomidine

- Occur less vomiting than xylazine
- 5-40 mcg/kg IM, SQ have been given to provide sedation. Following intravenous administration dysrhythmias can occur, so it is not recommended
- Duration of sedation is approximately for one hour
- The potential effects of medetomidine in dogs are very similar to those of xylazine, it causes bradycardia, hyperglycemia, and increased urine production. It causes arterial hypertension related with dose rate increase.

Romifidine

- It is from alpha 2 agonists
- Reduces the amount required for the anesthetic induction in dose related manner
- Provides dose dependent cardiovascular depression
- 10-80 mcg/kg IM, SQ

Opioids

- Morphine, pethidine (meperidine), hydromorphone, and oxymorphone are good analgesics for orthopaedic interventions.
- Mostly used to produce analgesia in dogs
- Produce better sedation and analgesia when used with other sedatives
- Morphine is cheap and is used in the dose of 0.25-1 mg/kg IM, SQ.
- IV morphine causes histamine release especially if given as a rapid bolus, but slow administration is less likely to cause problems
- Oxymorphone causes less vomiting than morphine and hydromorphone, so is better choice for patients with head trauma, eye injury and gastrointestinal disturbances
- Combination of benzodiazepines with butorphanol (or buprenorphine) is a helpful alternative to the combination with pure

opioids for brachycephalics decreasing the risk of respiratory depression

- Opioids induce minimal changes in cardiovascular parameters

Anticholinergics

- Anticholinergics are not mostly given as division of preanesthetic phase
- Atropine or glycopyrrolate may be used for animals with high resting vagal tone and procedures likely to increase vagal stimulation

Recommended dosages are; atropine 0.02-0.04 mg/kg IV, IM, SQ; and glycopyrrolate 2-10 mcg/kg IV, IM, SQ

Neuroletanalgesia

Some combinations of neuroleptanalgesia are enough to start anaesthesia that is necessary for endotracheal intubation in older or sick dogs.

The supplement of an opioid effect positively the degree of sedation and analgesia than achieved by use of the sedative or opioid alone. In addition, the combination allows a decrease in dose rate of one or both the drugs while performing effective sedation. Reduced dose rates cause in less respiratory or cardiovascular depression, less airway obstruction in brachycephalic breeds, and less agent to be metabolized for recovery. Furthermore, following the procedure the opioid drug can be antagonized by injection of naloxone. Sedative-opioid combinations are options for procedures such as radiography, examinations, bandage applications and minor orthopaedic interventions, and for preanaesthesia.

Acepromazine, 0.05 mg/ kg, with morphine, 0.5–1.0 mg/kg, or oxymor- phone, 0.05–0.1 mg/kg, or the addition of medetomidine, 0.03–0.04 mg/kg, with butorphanol, 0.2 mg/kg, given i.m. will induce profound sedation. The combinations of acepromazine, 0.05 mg/kg, with pethidine, 3–4 mg/kg, or butorphanol, 0.2–0.4 mg/kg, or buprenorphine, 0.01 mg/kg, cause mild to moderate sedation.

Intravenous Administration

Intravenous technique in dogs are commonly used into the cephalic vein, but other convenient sites include the lateral saphenous vein, the femoral vein, the jugular vein and, in unconscious dogs, the sublingual veins. Whichever vein is preferred, alert dogs should be handled correctly. Muzzles can be used in dogs showing an inclination to bite. The muzzles should be of the type with a quick release, delay in removal of a muzzle in a dog that has vomited during start of anaesthesia may lead to inhalation of the vomited material.

Hematoma occurrence after venipuncture should be prevented by application of pressure to the site for an adequate period, about a minute. A hematoma is not only painful for the dog; it may prevent subsequent use of the preferred vein for venepuncture for following days.

Ketamine

Ketamine dose rates providing anaesthesia in dogs produces excessive muscle tone and causes convulsions. Thus, ketamine should not be used as alone for dog anaesthesia. It should be administered in combination with various sedative agents to start anaesthesia for short term procedures or for maintenance with isoflurane, desflurane or sevoflurane.

- The dose of ketamine which provides anesthesia in dogs is very near to that which causes seizures
- Ketamine is related with increased muscle rigidity and excessive salivation
- Ketamine causes increases in heart rate, cardiac output, and blood pressure
- Many sedatives are used with ketamine to induce deep sedation or light anesthesia

Medetomidine at 5 – 40 mcg/kg with ketamine at 2-5 mg/kg given either IM or IV provides deep sedation often recumbency. Butorphanol 0.1-0.4 mg/kg IV, IM can be added in this combination for better sedation, analgesia and muscle relaxation.

Medetomidine can be changed by xylazine 0.1-0.5 mg/kg, resulting in shorter duration of effect

Ketamine-Diazepam

This combination provides less cardiovascular depression than xylazine-ketamine. A common combination used for starting of anaesthesia is 0.25 mg/kg of diazepam and 5 mg/kg of ketamine administered intravenously together.

Tiletamine and Zolazepam

Telazol up to 4 mg/kg IV to effect or intramuscularly causes deep sedation or little anesthesia

- Side effects related with ketamine-diazepam use can also be seen
- Typically used to provide enough sedation in dogs
- Other sedatives and opioids can be combined to cause more potent so as to increase sedation, analgesia and duration of effect, and reduce side effects.

Etomidate

Etomidate is a short acting non-barbiturate intravenous anaesthetic. Induction of anaesthesia with etomidate is related with little or no change in cardiovascular parameter and with less depressive effect than thiopental, and etomidate does not cause the heart to disrhythmias. In experimental researches with dogs, little negative cardiovascular effect was determined during anaesthesia with etomidate. It causes reduction of intracranial pressure.

Thiopental

The solution of thiopental have a very high pH and the agent can only be administered intravenously. It should always be administered in dogs as a 2.5% or weaker solution for more concentrated solutions are ot suitable and dan- gerous. A 5% solution causes thrombosis of the vein and, if any is injected perivascularly, produces complications overlying tissues and skin.

- Induction in unpremedicated dogs can be used at the dose of 15 mg/kg IV given the half dose as a rapid bolus and the remaining given titrated to effect
- In little premedicated dogs 7 mg/kg is enough to start anesthetic

induction

- Multiple administration will require the drug to be metabolized, and the dog will have a longer recovery lasting for 24 hours or more
- Maximum total dose for a healthy dog is 30 mg/kg.

Propofol

Propofol is frequently used in dogs. The dose for induction of anaesthesia in unpremedicated dogs is 6 mg/kg and premedication with 0.02–0.05 mg/kg of acepromazine decreases the dose to about 4 mg/kg. Females are more sensitive than males. Propofol has been used for start of anaesthesia in dogs. Medetomidine, 20–40 μg/kg, decreases the preferred dose of propofol to 2–4 mg/kg.

- It produces rapid induction and is very rapidly eliminated from the plasma.
- 6 mg/kg IV is enough dose for the anesthetic induction. Respiratory arrest is not commonly seen particularly with rapid IV bolus. It is best given as titrated to effect to produce anesthetic depth just enough to allow endotracheal intubation by slow administration
- It is non-accumulative and maintenance of anesthesia for longer duration can be achieved using a constant rate of infusion.

Monitoring

- Monitoriation is important to maintain a good plane of anesthesia and to prevent excessive insult to the cardiovascular, respiratory, and central nervous systems.
- Anesthetic depth can be controlled by observation of these signs: physical movement or jaw chewing in response to stimulation, eye position and degree of muscle tone, and presence or absence of palpebral reflexes etc.
- Parameters used to monitor the cardiovascular system include heart rate, pulse pressure, mucous membrane color, and capillary refill time.
- Direct blood pressure measurement can provide continuous hemodynamic status of the animal and can be easily accomplished

through catheterizing the auricular artery.

- The ECG is useful to monitor cardiac dysrhythmias.
- The respiratory system is controlled by monitoring respiratory rate and volume.
- It can be determined by observing the emptying of the rebreathing bag of the anesthetic machine during respiratory cycles.
- Pulse oximetry and/or arterial blood gas analysis gives information of the ventilatory efficiency
- Ocular reflexes are observed to monitor the central nervous system. The palpebral reflex is lost at light planes of anesthesia in ruminants, so it is of little value during anesthesia of these species.
- Ophthalmic ointment should be applied to the eyes during anesthesia to prevent corneal injury.
- Body temperature is also an important parameter to monitor during anesthesia.

Recovery

Recovery from anesthesia can be prolonged in hypothermic conditions, causing in increased morbidity. Provide adequate thermal support until the dog's temperature is consistently rising and approaching normal. A detailed anesthesia will reduce perioperative morbidity and arrange perioperative conditions. Monitoring are important to help that potentially reversible situations do not become irreversible. **Supporting to dog must be maintained during the recovery period.**

- Normal body temperature should be maintained during operation
- Warm blanket, circulating warm water blanket are very helpful to keep the body temperature
- Endotracheal tube must remain in place until starting swallowing reflex to protect the airway, and with return of strong muscle tones
- If animals pretreated with reversible agents, recovery can be achieved by reversing the drugs with specific antagonists. Atipamezole and naloxone are two primary examples and they are best used titrated to effect.

Cat Anesthesia

- Cats are not similar to dogs and their behavioral and physio-anatomical differences make anesthesia more difficult than in dogs.
- Cats have resistance to physical restraint and IV sedative/anesthetic administration in unpreanesthetised cats can be extremely difficult. It would, therefore, be necessary to administer good premedicants to facilitate anesthetic induction in cats.
- Provided that the potential risk is thought, proper premedication, a smooth anesthetic induction, careful monitoring, appropriate attention to the oxygenation, ventilation and circulation will ensure a very low morbidity rate in cats.

Preanesthetic preparation

- Starvation for about 12 hours usually helps a cat will have an empty stomach and water need not be deprived of until or about 2 hours prior to anesthesia
- Laboratory evaluation can provide useful prescreening information about the general health status of the patient prior to anesthesia
- A thorough physical examination to determine any abnormalities must be done. Auscultation for cardiac dysrhythmias and murmurs, or abnormal lung sounds will give useful information regarding possible cardiopulmonary disease.
- Control animal's physiology in risky animals (e.g. fluid deficit, acid-base abnormality)
- Intravenous catheter placement is not as easy as in dogs so heavier premedication may be required for easy procedure
- The common site of venous catheterization is cephalic vein
- Other veins for venous catheter placement include the saphenous and jugular veins

Preanesthetic agents

- A reliable preanesthetic sedation facilitates smooth induction and has anesthetic sparing effect during maintenance
- There are many alternatives available. Sedative/opioid (e.g.

midazolam and hydromorphone), or dissociative/sedative (e.g. ketamine and midazolam) combinations are popular, and they produce better restraint and analgesia than that achieved by single drug administration with less side effects (e.g. ketamine induced muscle rigidity when used alone).

Acepromazine

- Provides mild sedation at clinically accepted doses. Acepromazine may be administered at dose rates of 0.03 to 0.10 mg/kg. In cats the sedation provided is very variable and is seldom adequate to assist in control of an animal.
- Anti-arrhythmic
- Requires at least 20 min for good effect even after IV injection, and 30 to 45 min when given IM, and longer for SQ
- Longer duration
- A young, healthy cat can tolerate the premedication dose of 0.05 mg/kg with minimal cardiovascular effect
- However, in animals under risk in severe cardiac failure and with decreased circulatory volume its use is not preferred.

Diazepam/Midazolam

- When given alone, they produce no enough sedation in cats. Diazepam and other benzodiazepines provide no obvious sedation when given to domestic cats. They are used in preanesthesia for their muscle relaxant effects and their use is associated with an increased duration of action of other drugs administered in anaesthesia.
- They are primarily used as premedicants to counteract ketamine induced muscle rigidity and convulsions
- Because of their minimal cardiopulmonary depression, they can be a suitable premedicant for cats with cardiopulmonary diseases
- Diazepam is given in doses of up to 0.5 mg/kg i.m.; 0.1 – 0.5 mg/kg IV, IM, SQ for diazepam and 0.1 to 0.3 mg/kg IV, IM, SQ for midazolam

- Diazepam is more irritant to the tissue so is recommended not to be administered intramuscularly.

Xylazine

Xylazine has been mostly used, but it can cause variable results. When its dose increase, depth and duration of sedation provided increase.

- Doses of 1 to 3 mg/kg by the i.m. route may be administered to give mild to fairly profound sedation; s.c. injection may be used but gives less reliable results.
- Vomiting occur as the drug starts to exert its effect
- Cardiovascular depression can be profound
- Typically used as a premedicant prior to ketamine anesthesia
- As seen in other species Other side effects such as hyperglycemia, diuresis, gastrointerstinal motility depression can also occur.
- Largely displaced by medetomidine in small animals.

Medetomidine

- Medetomidine has currently completely used instead of xylazine and a dose of 80 μg/kg appears to give sedation similar in type and depth to that achieved by 3 mg/kg of i.m. xylazine. Duration of effect is dose related, but after an i.m. dose of 80 μg/kg clinically useful effects last for approximately 1 hour and recovery appears to be complete in about two hours.
- Unwanted effects are as expected for an α_2 adrenoceptor agonist, significant bradycardia and transient arterial hypertension followed by hypotension, depression of respiratory rate, pallor of mucous membranes. It causes less vomiting than xylazine
- A sublingual spray at 15-30 mcg/kg can be helpful to sedate an unrestrained cat. IV administration is associated with more severe form of dysrhythmias, so generally is not suggested
- Sedation lasts approximately for one hour, but can be antagonized by its revesal agent atipamezole if indicated
- The pharmacologic effects of medetomidine in cats are very similar to those of xylazine

- It is important to note that increasing the dose of alpha 2 agonists does not increase the depth of sedation, but rather prolongs the duration of sedation.

Romifidine

- The most recent alpha 2 agonists
- Reduces the amount required for the anesthetic induction in dose related manner
- Provides dose dependent cardiovascular depression
- 10-100 mcg/kg IM, SQ

Opioids

- When given alone, it may induce excitement so is best given with sedatives. When combined with other sedatives it provides better analgesia and sedation
- Morphine is cheap and is used in the dose of 0.1-0.2 mg/kg IM, SQ. This dose is much less than in dogs, but morphine is less well metabolized in cats than in dogs
- Combination of benzodiazepines with buprenorphine (or butorphanol) is a helpful choice to the combination with pure opioids for cats reducing the risk of respiratory depression
- Opioids induce minimal changes in cardiovascular parameters

Anticholinergics

- Anticholinergics are used to reduce excessive salivation (particularly with use of ketamine)
- 0.02 to 0.04 mg/kg IV, IM, SQ is the recommended dose for atropine
- Atropine causes visual disturbance so cats need to be handled carefully

Anesthesia Induction

Anesthetic induction is best performed using rapid-acting IV drugs. Intravenous induction helps for rapid airway control and allows for titration of the induction drug to effect within the given dosage range. Sick,

debilitated, or depressed cats will require less agent than healthy, alert animals.

Ketamine

- Ketamine given at 10 to 20 mg/kg IM produces recumbency in the cat within 3-5 minutes. Muscle rigidity and excessive salivation is not commonly seen
- A wide range of sedatives are combined with ketamine to reduce these undesired effects and also to decrease the amount of ketamine through a synergism
- Ketamine may cause increased heart rate, cardiac output, and blood pressure

Ketamine-acepromazine

Acepromazine 0.02-0.1 mg/kg IM added to ketamine 10 to 20 mg/kg IM, reduces the muscle rigidity and provides condition similar to general anesthesia

Ketamine-medetomidine

Medetomidine at 10 - 50 mcg/kg added to ketamine at 5 mg/kg, produces deep sedation often recumbency. Butorphanol 0.1-0.4 mg/kg IM can be included in this combination for better analgesia, sedation and muscle relaxation.

Medetomidine can be substituted by xylazine 0.5 – 1.0 mg/kg, with shorter duration of sedation as xylazine has a shorter half life

Ketamine-Diazepam/Midazolam

This combination causes less cardiovascular depression than medetomidine- ketamine

Diazepam 0.25 mg/kg and ketamine 5 mg/kg given as IV bolus induces anesthesia in 1-2 minutes

Butorphanol 0.1-0.4 mg/kg IV can be included in this combination for better analgesia and muscle relaxation.

Tiletamine and Zolazepam

Telazol up to 4 mg/kg IV to effect or IM produces deep sedation or light anesthesia

- Undesired effects seen with ketamine-diazepam can be seen

- Typically used to provide deep sedation in intractable cats
- Other sedatives and opioids can be mixed to make the constituent more potent so as to increase sedation, analgesia and duration of effect, and reduce side effects.

Thiopental

- Thiopental, barbiturate anesthetic, is given i.v. and in cats it should be used as a 1.25 % for use in cats. Very small doses as 2 mg/kg will be needed following heavy premedication with α_2 adrenoceptor agonists. If thiopental is to be used as the sole agent, maximum dose can reach to 20 mg/kg, but at these high doses, anesthetic recovery will take several hours and the effects will still be observable the next day. If recovery is longer, the cat must be kept warm, against hypothermia risk.
- Induction in unpremedicated cats can be achieved at the dose of 15 mg/kg IV given the half dose as a rapid bolus and the remaining given titrated to effect
- In lightly premedicated cats 7 mg/kg is enough to start anesthetic induction

Recovery is through redistribution of the agent from the brain into the other tissues.

Propofol

- Propofol has been used mostly in cats as an i.v. anaesthetic. The dose needed to induce anaesthesia is 6 to 7 mg/kg in both unpremedicated animals and in animals premedicated with 0.03 mg/kg acepromazine
- Advantages and disadvantages of propofol for dogs as described above similarly apply to cats
- 6 mg/kg IV is administered slowly titrated to effect to induce anesthesia, and in most premedicated cats one third to half of the calculated dose is sufficient to allow endotracheal intubation.

Alphaxalone-Alphadolone

- General anesthesia can be started by administering this steroid anesthetic
- Induction is usually smooth and rapid, but occasionally vomiting and laryngeal spasm can be observed
- 9 mg/kg IV produces about 15 minute anesthesia with minimal respiratory depression and cardiovascular stability is good
- Saffan given at 18 mg/kg IM induces anesthesia in 10 minutes which effect lasts 10 to 20 minutes
- Although contraindicated for use in dogs, Saffan is a safe induction and maintenance agent in cats

Monitoring

- Anesthetic monitoring in a veterinary clinic is similar to that found in any human hospital.
- The Veterinary anesthetist is trained to monitor the animal throughout the entire intervention, from induction until recovery. The anesthetist adjusts the anesthetic levels according to the patient's vital signs and ensures that the animal remains stable throughout the procedure.
- Anesthetic monitoring is important to maintain a satisfactory plane of anesthesia and to prevent excessive insult to the cardiovascular, respiratory, and central nervous systems.
- Anesthetic depth can be measured by observation of the following signs: physical movement or jaw chewing in response to stimulation, eye position and degree of muscle tone, and presence or absence of palpebral reflexes etc.
- Variables used to monitor the cardiovascular system include heart rate, pulse pressure, mucous membrane color, and capillary refill time.
- Direct blood pressure measurement can provide continuous hemodynamic status of the animal and can be easily accomplished through catheterizing a peripheral artery.

- The ECG is useful to monitor cardiac dysrhythmias. It shows the rate and pattern of the heartbeat. It will detect and show unusual heartbeats titled *arrhythmias.* If unusual heartbeats are determined, the anesthetist will do appropriate changes in anesthesia and/or emergency medications.
- The respiratory system is evaluated by monitoring respiratory rate and volume.
- stimulation, eye position and degree of muscle tone, and presence or absence of palpebral reflexes etc.
- Variables used to monitor the cardiovascular system include heart rate, pulse pressure, mucous membrane color, and capillary refill time.
- Direct blood pressure measurement can provide continuous hemodynamic status of the animal and can be easily accomplished through catheterizing a peripheral artery.
- The ECG is useful to monitor cardiac dysrhythmias. It shows the rate and pattern of the heartbeat. It will detect and show unusual heartbeats titled *arrhythmias.* If unusual heartbeats are determined, the anesthetist will do appropriate changes in anesthesia and/or emergency medications.
- The respiratory system is evaluated by monitoring respiratory rate and volume.
- Pulse oximetry and/or arterial blood gas analysis provide information of the ventilatory efficiency. It may be used to monitor the amount of oxygen in the animal's blood and the pulse rate. This instrument should always be used in conjunction with other monitoring equipments.
- Ocular reflexes are used to monitor the central nervous system.
- Ophthalmic ointment should be applied to the eyes during anesthesia to prevent corneal injury.
- Body temperature is also an important parameter to monitor during anesthesia. Because of the tendency for anesthetized animals to lose body heat, supplemental heat sources are often required to maintain adequate body temperature. It is performed by inserting a

temperature probe into the esophagus or the rectum. Either too low or too high a body temperature can cause dangerous complications. Maintenance of normal body temperature is especially important in animals under risk.

Perioperative pain management

- Use of opioids in cats within the perioperative period has not been as widespread as in dogs. However, with more research and better pharmacologic understanding, veterinarians have increased to use opioids in cats
- The central nervous system excitement can be decreased with concurrent administration of sedatives, but other side effects such as respiratory depression, vomiting and dysphoria are still possible
- In addition to opioids, α2-adrenergic agonists, local anesthetics, and nonsteroidal anti- inflammatory drugs (NSAIDs) can be used to provide analgesia. Since cat is more sensitive to develop NSAID-related toxicity, careful selection of dosing and choice of agents is necessary to avoid complications.

Recovery

- Recovery is a critical period of anesthesia that includes an animal support, monitoring, and record keeping. It starts when the anesthetic gas is turned off. It does not end at the time of extubation.
- Animals recovering from anesthesia require monitoring by veterinary anesthetist in the recognition of complications. Although many complications occur throughout anesthesia, most anesthetic related deaths occur during recovery.
- Cats are sensitive to develop hypothermia during recovery due to their small size and this can significantly prolong the recovery and increase oxygen demand of the muscle tissues.
- Warm blanket, circulating warm water blanket are very effective to keep the body temperature, infrared lamps are also useful external heat sources

- If animal is pre-treated with reversible agents, recovery can be accelerated by reversing the drugs with specific antagonists. Atipamezole and naloxone are two primary examples and they are best used titrated to effect.

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BÖLÜM XI

MIRACLES OF THE BEE - THE EFFECTS OF BEE BREAD ON HEALTH

Assoc. Prof. Dr. Berna DUMAN AYDIN[1]

DOI: https://dx.doi.org/10.5281/zenodo.14551690

[1] Dicle Üniversitesi, Vetriner Fakültesi, Besin/Gıda Hijyeni ve Teknolojisi Bölümü Diyarbakır, Türkiye. berna.dumanaydin@dicle.edu.tr,
Orcid ID: 0000. 0001. 6116. 3274

INTRODUCTION

Chronic diseases that are difficult to diagnose and treat have started to emerge as a result of the rapid increase in consumption with the increasing world population and the use of less physical activity to access food with the developing technology. People want to improve their quality of life for reasons such as increased treatment costs, loss of labor force, prolonged life expectancy, and a large percentage of the population being elderly (Margaoan et al., 2019).

Today, the understanding of food production and consumption is undergoing a significant change and the development of functional foods is becoming an important sector in the food market. Value- added and health-oriented products that positively affect our well-being and quality of life beyond basic nutritional properties are defined as "functional foods". This term emphasizes the positive association of bioactive compounds in these foods with health (Barta et al., 2022).

In recent years, there has been a growing interest in so-called "functional foods", foods that can provide not only basic nutritional and energy requirements, but also additional physiological benefits to the consumer. The term "functional food" was first used in Japan in the 1980s and applied to processed foods containing ingredients that provide benefits of some physiological function. Today, a functional food is defined as a food that produces a beneficial effect on one or more functional functions, improves well-being and reduces the risk of suffering from a specific medical condition (Gómez-Caravaca et al., 2006).

Apitherapy and Functional Foods

Apitherapy is the use of bee products to prevent or treat disease and promote healing. It can also be defined as the science of using honey bee products to maintain health in case of illness or accident and to help the individual regain health (Trumbeckaite et al., 2015).

The origins of apitherapy date back 6000 years to ancient Egyptian medicine. The Greeks and Romans also used bee products for medicinal purposes and this was expressed 2500 years ago by Hippocrates as "let food be medicine and medicine be food". Today, medical science and technology encompass medical standards of care, self-care practices, health insurance and community health systems. Therefore, it is important to promote and popularize

apitherapy, which has been an effective method for centuries, as a simple, practical and feasible self-care method (Barta et al., 2022, Zhu and Wongsiri, 2008).

Traditional and alternative medicine practices related to health are used in all cultures. With the 2014 Regulation on Traditional and Complementary Medicine Practices, traditional and complementary medicine practices that can be officially applied in our country have been determined. One of these practices is apitherapy (Resmi Gazete, 2014).

In recent years, interest in ecological, functional, balanced and healthy foods has been growing rapidly. Many companies in the food industry are focusing on exploring natural food sources with high nutritional value and potential benefits such as disease prevention and health promotion. For this reason, some food manufacturers are paying more attention to beekeeping products such as pollen, honey, bee bread, propolis and royal jelly. Today, these products are recognized as functional foods that contribute positively to both physiological and psychological health by enriching nutritional value (Bobis et al., 2010). While bee products have historically been used therapeutically and for food consumption, recent studies have shown that they contain important details that can be validated as food supplements due to their biological properties that may be pharmaceuticals (Margaoan et al., 2019).

Table 1. Biological and functional effects of bee products

Product	Functional and biological properties of bee products
Bal	antibacterial, antifungal, antiviral, antioxidative, prebiotic, anti-inflammatory, anticarcinogenic, probiotic
Pollen	antibacterial, antifungal, antioxidative, immunomodulating, radioprotective, hepatoprotective
Bee bread	Antibacterial, antifungal, antiviral, antioxidant, prebiotic, anti-inflammatory, anticarcinogenic, anti-inflammatory, analgesic, immunomodulatory, anticancer
Royal Jelly	antibacterial, antifungal, antiviral, antioxidative, biostimulant, immunomodulatory,radioprotective, anticarcinogenic
Propolis	antibacterial, antifungal, antiviral, antioxidative, antiparasitic, immunomodulatory, anti-inflammatory, analgesic, hepatoprotective, anticarcinogenic
Bee Venom	antibacterial, anti-inflammatory, immunoactivating, immunosuppressive, analgesic,radioprotective, anticarcinogenic

(Bogdanov et al., 2008, Bogdanov, 2011)

Recently, free radicals and reactive oxygen species (ROS) have been implicated in the development of aging and lifestyle-related diseases such as diabetes, obesity and hypertension. Nowadays, consumer demand for natural foods with pharmaceutical effects is on the rise. In this context, bee bread stands out as a food containing natural ingredients and bee bread extracts have been found to exhibit high antioxidant properties and scavenging power against free radicals such as superoxide anion radical and hydroxyl radical (Nagai et al., 2004).

According to research data, bee products are rich in phytochemicals such as carotenoids, phenolic acids and especially flavonoids, as well as proteins, minerals, nucleic and amino acids, polyphenols, carbohydrates, phytosterols, vitamins and sugars. The medicinal importance of these products has been known since antiquity. Bee bread has been found to have antioxidant, antibacterial, antiviral, anti-inflammatory and anticancer properties due to its complex chemical composition. In recent years, interest in the chemicals

responsible for these effects has increased. Considering their beneficial effects in food production and human health, bee products have broad research potential and production perspectives as natural and valuable ingredients (Nakajima et al., 2019, Veiga et al., 2017, Yıldırım et al., 2016, Liu et al., 2016, Rimbach et al., 2017, Bogdanov 2011, Yücel et al., 2017).

Bee Bread

The nutritional needs of the honey bee Apis mellifera are met by pollen, nectar and water collection. Nectar is the primary source of carbohydrates; pollen provides proteins, lipids, vitamins and minerals. Forager worker bees collect pollen, which is then filled into the cells of the brood comb by other bees, usually younger, and a small layer of honey is deposited on top of the pollen to prevent spoilage. This chemically altered pollen store is called bee bread. Bee bread, a natural bee product obtained by bees through lactic acid fermentation of bee pollen in the comb cells, is also called perga or ambrosia. Bee bread is consumed by adult bees and used in larval feeding (Karaman et al., 2017, Gıllıam, 1979, Ivanisova et al., 2015).

According to scientific studies, the nutritional value of bee bread varies according to the variety of plants, season and geography from which it is harvested. It contains more than 300 compounds such as amino acids, sugars, fatty acids, minerals, organic acids, polyphenols and vitamins, making bee bread a valuable dietary supplement. The chemical composition of bee bread is biochemically similar to the pollen from which it is made. However, bee bread differs in that it contains more carbohydrates and enzymes, is richer in vitamins K and B, contains less protein and fat, and shows lower pH values due to lactic acid. Thanks to its biochemical diversity, this natural product can be used for strengthening the immune system, regulating digestive system function, antimicrobial, anti-aging and anti-anemic activities. It also has positive effects in supporting endocrine and nervous system functions, promoting tissue regeneration and eliminating various forms of toxins (Andelkovic et al., 2012, Barene et al., 2015, Ivanisova et al., 2015, Kieliszek et al., 2018, Khalifa et al., 2020).

Bee bread is rich in some important enzymes produced by the bee and delivered to the honey, such as amylase, invertase, phosphatases, transferases

and glucose oxidase, which increase digestibility by converting large molecular weight molecules into low molecular weight molecules such as polysaccharides and proteins, and some important enzymes originating from nectar, honeydew or pollen, such as catalase and phosphatase, and enzyme cofactors such as biotin, glutathione and NAD (Bakour et al, 2022).

Although lactic acid bacteria, Bifidobacterium sp., Saccharomyces sp., Pseudomonas sp., Streptococus sp., Candida sp., Torulopsis sp. are found in the natural digestive flora of honey bees, LAB and Bifidobacterium are known to play an important role in fermentation (Gilliam et al., 1974, Olofsson et al., 2008).

Bee bread is a product produced by adding microorganisms originating from the saliva of bees to pollen. These microorganisms form a microbiome that plays an important role in the nutrition of the bees' larvae and the health of adult bees. Bee bread is rich in microorganisms that may have probiotic properties. It has been frequently repeated in studies that beneficial fungi such as Aspergillus, Penicillium, Rhizopus and Cladosporium are found in bee bread (Dimov et al., 2021, Yoder et al., 2013). It has also been reported to be rich in lactic acid bacteria such as "Apilactobacillus kunkeei, Lactiplantibacillus plantarum, Fructobacillus fructosus, Levilactobacillus brevis and Lactobacillus delbrueckii subsp. Lactis (Iorizzo et al., 2020), Leuconostoc mesenteroides, Enterococcus faecalis and Bacillus species" (Muhammed et al., 2020).

Pollen has a protective layer called exine, which is difficult to digest. This layer consists of components such as carbohydrates, proteins, lipids and phenolic substances. Bee bread is fermented by worker bees with a mixture of pollen and nectar and stored in combs. Through fermentation, the exine layer of the pollen is partially broken down and the bee bread becomes fully digestible, replacing the pollen, which is not fully digestible. Furthermore, this process increases the bioavailability of bee bread resulting in higher absorption by human intestinal epithelial cells. Since the proteins in bee bread are more biologically active and therefore easily absorbed, bee bread contains significantly higher amounts of peptides and free amino acids. Thanks to the composition of all essential amino acids, bee bread has several times better composition than many valuable products containing animal protein. Due to the proportions of its components, bee bread can be considered as a good food supplement and a good food additive in vitamin deficiency caused by

malnutrition or monotypic diet (Habryka et al., 2016, Khalifa et al., 2020, Zuluaga et al., 2015).

Some studies have shown the antimicrobial potential of bee bread for the prevention and treatment of bacterial and fungal infections in animals and humans due to its high polyphenol and LAB content (Pelka et al., 2021, Margaoan et al., 2019).

Samples of bee bread and bee pollen have shown potential activity against the growth of both gram positive and gram negative bacteria that are resistant to antibiotics. This would be a very interesting approach to control more dangerous strains of microorganisms in medical sciences. As microorganisms have developed resistance to common antibiotics, it has become necessary to look for an alternative approach to this situation. Considering the non-toxic natural origin and antimicrobial effects of bee bread, it is concluded that their possible use as natural additives is of great interest in academic situations, food cosmetics and pharmaceutical industries due to a growing trend towards the replacement of synthetic preservatives with natural ones (Abouda et al., 2011). In a study in which bee pollen was found to have higher values in terms of chemical and antioxidant capacity than bee bread, it was reported that bee bread is more suitable for human consumption as a food supplement in terms of bioavailability and longer storage (Mayda et al., 2020).

In a study on the chemical and palynological properties of bee bread, it was found that bee bread contains more pollen from plants that are easily accessible or preferred by bees and that there are changes in the pollen content, fatty acid composition and chemical composition of bee bread samples of different geographical origins (Kaplan et al., 2019).

Bee Bread has been shown to have antimicrobial, antioxidant, anti-radical, anti-cancer and anti- inflammatory properties. The main chemical components of bee bread include carbohydrates, proteins and vitamins, as well as minerals, fatty acids and enzymes, natural antibiotics, antioxidants and hormones, phenolic compounds (kaempferol, myricetin, luteolin, etc.). Bee Bread is recognized as a useful food supplement. In recent years, there has been great interest in the use of bee bread in the treatment of many diseases (Dranca et al., 2020, Khalifa et al., 2020).

Bee bread has been shown to protect against the reactivity of tumor cells and has other biological properties such as antimicrobial and hepatoprotective

effects (Sobral et al., 2017, Eswaran and Bhargava, 2014, Ceksteryte and Balzekas, 2014), making it a promising therapeutic option for some disease conditions (Suleiman, 2021) as it has compounds that can reduce oxidative stress, inflammation and apoptosis and inhibit microbial growth

Probiotic Effects of Bee Bread

Bee bread is a probiotic-rich natural product containing a diverse and complex spectrum of microorganisms such as bacteria and fungi involved in the bee bread production process through lactic fermentation of bee pollen (Margaoan et al., 2019). In studies on bacteria isolated from bee bread, bacillus strains and lactobacilli strains with probiotic properties were found (Mohammad et al., 2020, Toutinee et al., 2022).

It was found that selected strains of A. kunkeei, which maintain a symbiotic life with the honeybee and are mostly isolated from bee bread, can be used for probioticizing fruit preparations frequently used in the diet of hospitalized and immunocompromised patients, and that strains of A. kunkeei species showed a similar performance to Lacticaseibacillus rhamnosus used as a probiotic control in terms of survival during simulated gastrointestinal transit (Vergalito et al., 2020).

Freshness and quality are of utmost importance for maximum benefit from bee bread. It is stated that the biological activity of bee bread that is not stored under suitable conditions or kept for a long time (more than one year) is greatly reduced and even completely lost after a certain period of time. Therefore, it is recommended that bee bread should be stored under suitable conditions (cool, out of direct sunlight, moisture-free and dry environment) and consumed immediately if possible (Karaman et al., 2017). Bee bread contains components necessary for the normal development and continuity of a living organism. It contains approximately 20% protein, 3% fat, 24-35% carbohydrate, 3% vitamins and minerals. It is also rich in vitamins A, B1, B2, B6, B12, C, D, E and P and trace elements such as potassium, magnesium, calcium, copper, iron, sulfur, chlorine and manganese. Thanks to the protein, vitamins, minerals and especially microorganisms beneficial for microbiota, bee bread is used as a supportive treatment for many diseases by experts (Karaman et al., 2016, Regrut et al., 2016, Didaras et al., 2020).

Anti Anemic Effects of Bee Bread

In a study investigating the effect of bee bread against anemia induced in the laboratory environment, bee bread improved the biochemical parameters caused by lead acetate, this result was supported by hematological, biochemical and histological analyzes and it was reported that bee bread can be used as a support for anemia treatment (Hazır and Silici, 2019).

In a study investigating the antioxidant activity and protective effect of bee bread (honey and pollen) in aluminum-induced anemia, elevation of inflammatory constituents and hepato-renal toxicity in mice, bee bread exhibited antioxidant activity and had a significant protective effect on aluminum- induced toxicity in mice, decreased hemoglobin and C-reactive protein, It was found to improve the elevation of monocyte and leukocyte counts, normalize the elevation of liver enzymes and blood urea nitrogen, and it was stated that this mechanism of action may be related to the antioxidant and anti-inflammatory activity of bee bread extract (Bakour et al., 2017)

Anti-Inflammatory Effects of Bee Bread

BP and BB contain polyphenols with anti-inflammatory properties, anti-cancer phytosterols, fatty acids and polysaccharides that support the immune system. Bee bread also contains compounds that have the potential to reduce inflammation and strengthen immunity. Therefore, bee bread can be used as a food supplement with anti-inflammatory effects (Margaoan et al., 2019)

Antimicrobial Effect of Bee Bread

Studies reveal that bee bread extracts show antimicrobial activity against various bacteria. In particular, a more pronounced activity was observed on Gram-positive bacteria. Bee bread was effective against Gram-positive bacteria such as Staphylococcus aureus, Bacillus cereus, Staphylococcus epidermidis, Bacillus thuringiensis, Clostridium perfringens, Bacillus subtilis, methicillin-susceptible Staphylococcus aureus (MSSA) and Listeria monocytogenes. It also

shows antimicrobial activity against Gram-negative bacteria such as Pseudomonas aeruginosa, Escherichia coli, Salmonella enterica, Enterobacter cloacae, Salmonella typhimurium, Haemophilus influenza, Klebsiella

pneumonia, Shigella, and Salmonella typhi. These results suggest that bee bread offers a broad spectrum of antimicrobial activity against different bacterial species (baltrusaityte et al., 2007, Abouda et al., 2011, Ivanisov et al., 2015, Didaras et al., 2021).

Antitumoral Effect of Bee Bread

Bee bread reduces oxidative stress by increasing the activities of antioxidant enzymes (glutathione-S-transferase, superoxide dismutase, glutathione peroxidase, catalase, glutathione reductase) and increasing total antioxidant capacity levels (Zakaria et al., 2021, Bakour et al., 2022).

In a study investigating the palynological analysis, chemical composition, antioxidant activity and cytotoxic effect of bee bread against lung, prostate cancer and human neuroblastoma cell lines in humans, it was reported that bee bread can be used in medical fields due to its antioxidant and anticancer properties (Dervişoğlu et al., 2022).

In a study conducted by Sobral et al. in 2017, the antitumor effect of bee bread on different human tumor cell lines such as breast adenocarcinoma, non-small cell lung cancer, cervical carcinoma, hepatocellular carcinoma and tumor-free liver cells was examined. According to the results of the research, it was reported that bee bread samples showed moderate antitumor activity, but these samples did not produce any toxic effects on normal cells (Sobral et al., 2017).

The Effects of Bee Bread Against Obesity

It has also been shown to have a hypocholesterolemic property, significantly reducing 15.7% of total cholesterol and 20.5% of LDL levels in overweight and obese patients (Kas'ianenko et al., 2011).

In a study of phenolic compounds and anti-atherogenic effect of bee bread in high-fat diet-induced obese rats, it was suggested that 0.5 g/kg/day of bee bread had anti-atherogenic properties in high- fat diet-induced obese rats, probably partly due to the presence of phenolic compounds with high antioxidant and hypocholesterolemic properties (Othman et al., 2019).

Bee bread ameliorated obesity-induced lipid peroxidation. It has been shown that obesity causes an increase in the number of apoptotic cells and bee bread reduces it. Bee bread administration (200 mg/kg/day) had positive effects

on weight control and other parameters (Doğanyiğit et al., 2020). (2019) reported that bee bread contains large amounts of unsaturated fatty acids and sometimes has very favorable n-6/n-3 fatty acid ratios and that this composition indicates the high nutritional value of bee bread (Ciric et al., 2019).

İvanisova et al. found that bee bread is a good source of antioxidants as well as a good antimicrobial agent (Ivanisova et al., 2015).

The daily dose for an adult should be about 20-40 g. It is enough to eat one tablespoon of bee bread every day to replenish and strengthen an organism. As a product characterized by a stronger activity than pollen, bee bread is usually administered in smaller quantities or over a short period of time (Komosinska et al., 2015).

Bee Bread as an Indicator

As a result of a study on the usability of bee bread and hatching bee brood for assessing monocyclic aromatic hydrocarbon levels in the environment, it was reported that the use of bee bread is a valuable source of information for measuring and monitoring monocyclic aromatic hydrocarbon pollution in the environment (Zieba et al., 2020).

In studies investigating the presence of heavy metals in bee products, it has been reported that there are more heavy metals in pollen than in bee bread and that this may be due to metal loss during the transformation of pollen into bee bread, and that bee products including bee bread in terms of heavy metal presence are valuable indicators of environmental pollution (Zhelyazkova, 2018, Roman et al., 2016).

As a result, Hippocrates said, "Let food be medicine and medicine be food". In 1850, the German philosopher Ludwig Feuerbach coined the phrase "Man is what he eats". Feuerbach's view is in line with Hippocrates and the Asian wisdom in Traditional Chinese medicine and Ayurveda. "Diet is the foundation of health" and "Tell me what you eat and I will tell you who you are" emphasize, as Jean Anthelme Brillat-Savarin notes, that what we eat shapes us. Phytochemical and biological research reveals the potential for bee bread to be used in the food and pharmaceutical industry as functional food ingredients and/or natural medicinal products with antioxidant properties. However, further studies on bee pollen and other bee products are needed. These studies need to be supported by more in-depth investigations

examining the interrelationships between botanical origin, total phenolic content, flavonoids, vitamins, lipids and other biologically active compounds content and pharmacological properties.

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BÖLÜM XII

HEALTH EFFECTS OF BLACK GARLIC

Assoc. Prof. Dr.Berna DUMAN AYDIN [1]

[1] [1] Dicle Üniversitesi, Vetriner Fakültesi, Besin/Gıda Hijyeni ve Teknolojisi Bölümü Diyarbakır, Türkiye. berna.dumanaydin@dicle.edu.tr,
Orcid ID: 0000. 0001. 6116. 3274

INTRODUCTION

With the changes brought by the age, people are conscious of having a healthier quality of life and prefer to take preventive measures instead of treating health problems to increase their life span and quality. At the beginning of these preferred measures, food and nutrition are in the first place, and in nutrition, they prefer functional foods that protect and improve well-being and reduce the risk of disease occurrence.

Garlic is among the oldest cultivated plants. Its origin probably predates written history in Central Asia. It has been part of folk medicine for thousands of years and the Codex Ebers, an Egyptian medical papyrus dating back to about 1550 BC, contains more than 800 therapeutic formulas, 22 of which mention garlic as an effective remedy for various ailments, including heart problems, headaches, bites, worms and tumors. Along with the Egyptians, Aristotle, Hippocrates and Aristophanes recommended garlic for its medicinal effects (Block, 1985).

It has been widely used throughout history both as a seasoning for food and as a medicinal plant. Garlic can increase appetite and aid digestion. The main effective components in garlic are organosulfur compounds and bioactive enzymes. Among them, allicin is well known for its pharmacological properties, including anti-bacterial, anti-hyperlipidemia, anti-tumor and immunomodulatory activity. However, despite its numerous medicinal properties, garlic is recommended to be consumed in moderation due to its reported toxicity at high doses. Excessive consumption of garlic can cause damage to the intestinal lining and stomach, anemia, contact dermatitis, and a decrease in serum protein and calcium In addition, raw garlic produces a strong pungent odor that penetrates the skin and causes an unpleasant body and breath odor in humans (Yoo et al., 2014, Zhang et al., 2015, Kim et al., 2012).

Black garlic is a fermented product of the fermentation process of fresh garlic, characterized by its black color, which does not have the unpleasant taste and smell of fresh garlic. It is usually obtained by processing fresh garlic at high temperature for 60 to 90 days without any additional processing. Although the details of the process are a trade secret, some researchers have reported that black garlic can be prepared at a temperature ranging from 65 to 90 C and a relative humidity of 60-80% Black garlic is an increasingly well-known garlic preparation that is fermented at high humidity and temperature regulated not

only to remove the strong unpleasant flavor of fresh garlic, but also to improve its nutritional composition, bioactivities and taste values. During heat treatment, many reactions occur in the black garlic product, including the Maillard reaction. The Maillard reaction can cause changes in the nutrient content, color, texture, taste and aroma of garlic. Many studies have reported that black garlic has a wide range of health benefits such as anticancer, antioxidant, antiallergic, hypocholesterolemic and hepatoprotective activities, especially since its antioxidant properties are stronger than fresh garlic (Tran et al., 2020a, Yuan et al., 2016, Yoo et al., 2014, Chen, 2014, Kim et al., 2012).

Black garlic does not have the strong odor of fresh garlic because allicin, the compound responsible for the unique pungent odor, is converted to water-soluble antioxidant compounds including S-allylcysteine and S-allylmercaptocysteine during the ripening process (Kim et al., 2012).

In recent years, black garlic has become a prominent functional food due to its wide-ranging biological functions, including cardioprotective, antioxidant, anti-inflammatory, anticancer, hyperlipidemia-lowering, antiobesity, hepatoprotective and neuroprotective effects (Tran et al., 2020b).

Black garlic is reported to be superior to fresh garlic in terms of sensory and utilization properties and biological effects (especially antioxidant activities). Black garlic has high nutritional value, shows memory and nervous system protective effects, anti-cancer, anti-obesity, anti-inflammatory, immune-boosting, anti-allergic, liver-protective, heart-protective, oxidative stress-reducing and post-alcohol syndrome-relieving effects. Therefore, black garlic could potentially be marketed as an innovative healthy snack or functional food (Qiu et al., 2019).

Hepatoprotective Effect

In a study investigating the effect of black garlic on experimentally induced liver injury, the results suggest that black garlic has hepatoprotective properties and can be used as an adjunctive therapy to prevent or manage liver injury. In particular, the effect of black garlic on protecting liver cells is remarkable, suggesting that this product could be a potential dietary supplement to support liver health (Shin et al., 2014).

In fermented garlic, much of the foul odor from fresh garlic is removed and many sulfur-containing compounds beneficial to health are formed.

Through the heating process, the unstable and unpleasant compounds in raw garlic are converted into stable and tasteless compounds. As a result, black garlic usually has a sweet-sour taste instead of an unpleasant odor and taste, and does not cause abdominal pain or other gastrointestinal problems. Black garlic is reported to have stronger antioxidant activity than fresh garlic and shows better efficacy in preventing metabolic diseases and alcoholic hepatotoxicity (Zhang et al., 2015, Kimura et al., 2017, Yuan et al., 2016, Lee et al., 2009).

It was concluded that the diet supplemented with black garlic powder reversed the hepatotoxic changes caused by CCl4 administration and that black garlic powder is a hepatoprotective agent worth treating liver damage and this protective activity of black garlic may be due to its antioxidant properties (Hussein et al., 2019).

In rats fed high-fat diets containing black garlic, body weight gain, fatty liver and serum triglyceride increase were suppressed, thus it was reported that black garlic intake may be beneficial for the suppression of high-fat diet-induced obesity in rats (Chang et al., 2017).

Anti-Cancer effect;

The pharmacological activities of black garlic, such as cholesterol-lowering, anti-allergic, high antioxidant activity, can improve the immune system, inhibit HT29 cell growth in colon cancer, anti-tumor, reduce hyperglycemia and dyslipidemia, hepatoprotective, and induce apoptosis in cell human leukemia U937 (Tran et al., 2018).

In the study investigating the effect of black garlic extract on gastric cancer cells in vivo and in vitro, it was reported that black garlic extract treatment inhibited the growth of SGC-7901 cells by inducing apoptosis in vitro, More importantly, it has been reported that black garlic extract is an effective anticancer product in a mouse model and that these beneficial effects may be due in part to the antioxidant and immunomodulatory activities of black garlic extract (Wang et al., 2012).

Antioxidant Effect

Black garlic contains abundant antioxidant compounds including polyphenols, alkaloids, flavonoids, S-allyl-cysteine and antioxidant intermediates derived from the Maillard reaction (Choi et al., 2014).

The high polyphenol content of black garlic has obvious DPPH- radical and -OH radical scavenging activities and can increase serum antioxidant enzyme activities while significantly reducing serum Malone Dialdehyde content in mice (Wang et al., 2017).

In a study in which the antioxidant capacity of garlic was measured, it was reported that the polyphenol content of black garlic was significantly higher than that of raw garlic, thus black garlic had a higher capacity to absorb oxygen radicals (Liu et al., 2018).

Cardioprotective Effect

In a study on the potential bioprotective effects of black garlic against cardiovascular diseases, fermented black garlic samples and their Amadori products (AC) were found to promote angiogenesis, prevent thrombus formation by rescuing chemically induced vascular lesions in zebrafish, and reduce the risk of cardiovascular disease by preventing H2O2-induced damage of endothelial cells (Zhang et al., 2019).

Black garlic extract shows anti-atherogenic effects in rabbits by reducing fatty streak development, cholesterol deposition in the vessel wall and the development of fibro-fatty plaques in the neointima of cholesterol-fed rabbits, as well as reducing the progression of coronary artery calcification (CAC) (Efendy et al., 1997).

Antimicrobial Effect

The results of the study investigating the inhibition effect of black garlic extract prepared with methanol on pyocyanin and elastase production and biofilm formation, which are synthesized by Pseudomonas aeruginosa PA01 and play an important role in its pathogenesis, show that black garlic has antimicrobial properties and may be a potential therapeutic agent especially against pathogens such as Pseudomonas aeruginosa (Özaydın et al., 2020).

The ethanolic (30%) extract of fermented black garlic exhibited antibacterial activity against 11 bacterial strains causing oral diseases. Short

and long incubation with this extract inhibited the growth of more than 90% of salivary bacteria (Vlachojannis et al., 2018).

In the study using black garlic paste, the antimicrobial activity of black garlic pulp extract (BGPE) was examined. BGPE showed antimicrobial effect against Gram-positive (Listeria monocytogenes, Staphylococcus aureus) and Gram-negative (Escherichia coli O157:H7, Salmonella Typhimurium) foodborne pathogens and its effect against Gram-positive bacteria was found to be stronger (Kang et al., 2017).

In a study investigating the antibacterial effect of black garlic extract against Escherichia coli, black garlic extract showed antimicrobial effect Black garlic fermentation, fermentation of garlic (Allium sativum L) increased its antioxidant activity and total phenolic compounds, and organosulfur compounds such as S-allylcysteine (SAC) and flavonoid compounds were reported to be the active substances that played the most role in the prevention of Escherichia coli in black garlic (Harun et al. , 2021)

Sasaki (2017) investigated the antimicrobial effect of black garlic extract and showed that the extract was effective against MRSA (methicillin-resistant Staphylococcus aureus), Pseudomonas aeruginosa and enterohemorrhagic Escherichia coli O157:H7.

In a study investigating the antibacterial effect of garlic, it was found that 1 mg/ml concentration of black garlic in isopropanol or ethyl acetate solvent effectively inhibited the growth of E. coli and S. aureus. Especially the potential of black garlic fermented for 3-4 weeks as a therapeutic agent was emphasized (Setiyoningrum et al., 2021).

In a study, black garlic was shown to have the highest antioxidant and antimicrobial activities compared to fresh garlic, especially an effective potential against methicillin-resistant Staphylococcus aureus (Botas et al., 2019).

In a study on black garlic, it was found that black garlic extracts showed stronger bacteriostatic effect against Gram-positive bacteria, especially Bacillus subtilis and Staphylococcus aureus, compared to Gram-negative bacteria, such as Escherichia coli and Pseudomonas aeruginosa. As a result, it was concluded that black garlic aged under optimal conditions exhibited enhanced antioxidant activity and effective bacteriostatic properties, making it a valuable functional food ingredient (Chang et al.)

In another study in which black garlic was studied, the results showed that the antimicrobial activity of black garlic against Streptococcus mutans and Enterococcus faecalis was significantly increased ($P < 0.05$). However, no significant difference ($P > 0.05$) was observed in antimicrobial activity against Streptococcus pyogenes (Halimah and Hasan, 2021).

Neuroprotective Effect

Studies have shown that the ethanolic extract of black garlic can prevent the impairment of working memory from the oxidative stress induced by mono sodium glutamate, which causes the impairment of working memory of rats, without causing deficiencies in the number of pyramidal cells in the medial prefrontal cortex, inhibit its detrimental effects on spatial memory and total number of pyramidal neurons, improve motor coordination function and the number of Purkinje cells in the cerebellar cortex of the rat brain (Nurmasitoh et al, 2018, Aminuddin et al., 2015, Hermawati et al., 2015).

It is suggested that black garlic alleviates neuroinflammation and cognitive impairment in the elderly and Alzheimer's patients, which is a pathological evidence of Alzheimer's disease, and black garlic may be a good supplementary food for improving cognitive functions (Nillert et al., 2017).

Anti-inflammatory Effect

Black garlic has anti-inflammatory activity through its bioactive components S-allylcysteine, polyphenols and flavonoids and can be used as an alternative anti-inflammatory agent in phytotherapy (Salsabila et al., 2021).

Kim et al. (2014) reported in their study that black garlic extract is less toxic than fresh garlic extract and that black garlic has anti-inflammatory activity that reduces the production of LPS-induced inflammatory mediators and cytokines by regulating MAPK and NFjB activation in RAW 264.7 macrophages and that the study findings suggest that black garlic extract may be useful as an anti-inflammatory agent against fatal sepsis (Kim et al., 2014).

Effect on Skin Health

In a study investigating the effects of black garlic on dermatitis in mice, it was shown that black garlic extract, which exerts anti-allergic activity, has both antioxidant activity and anti-inflammatory effects in vitro and in vivo, and

in the same study, black garlic extract has anti-dermatitic activity by inhibiting the activation of macrophages, It has been reported that these effects are due to the rich phenolic compounds and flavonoids of black garlic extract and therefore the use of black garlic as a functional food for phyto-medicine and treatments of inflammatory diseases, including contact dermatitis (You et al. , 2019).

In a study in which black garlic extract obtained by maceration method was made into nanoparticles using silver reducing agent, the nanoparticles obtained were used in the production of peel-off masks and their properties were tested. The results showed that the mask with black garlic nanoparticles had a strong antioxidant activity (21,168 ppm), the particle size was 59.47 nm and exhibited good properties according to viscosity, spreadability and drying tests. The nano-sized black garlic particles are able to penetrate the skin pores more effectively and thus help repair damaged skin cells (Andiarna et al., 2024).

Effect on Kidney Health

In a study on the renal health of black garlic, black garlic offers protective effects against glomerular histopathological damage in hyperuricemic rats, and 240 mg/day dose was found to be the most effective. These results suggest the potential use of black garlic in the prevention of renal complications related to hyperuricemia (Wahyudin et al., 2024).

Antiviral Effect

In the study examining the antiviral effect of black garlic extract (BGE) against herpes simplex virus-2 (HSV-2) infections and its ability to reduce oxidative stress, it was revealed that BGE can inhibit viral infection and show a protective effect by reducing oxidative stress in cells (Horowitz et al., 2024).

Use in Food Production

The effect of natural antioxidants from black garlic (BG) on the quality parameters of pork jerky using nitrite replacement for 60 days was studied. The addition of BG did not alter parameters such as nutrient composition, pH, water activity and shear strength, but improved weight loss and color stability. Moreover, protein oxidation was lower in BG-containing formulations and TBARS and carbonyl compound values were lower than in the control group.

The results indicate that BG can be an effective alternative to nitrite and can improve the oxidative stability of dried meats (Lopes et al., 2024).

In the study using different concentrations of black garlic powder (BGP), it was found to improve the properties of ready-to-eat pork meatballs. BGP reduced lipid oxidation and increased redness and thiol content. It also decreased the pH level after heating and significantly improved the texture and sensory properties of meatballs with 2% BGP. As a result, BGP was shown to be effective in improving sensory quality and oxidative stability (Kim et al 2019).

In the study investigating the effect of black garlic on polycyclic aromatic hydrocarbons (PAHs) content and toxic potential of beef meatballs supplemented with black garlic, black garlic greatly reduced the formation of harmful PAH compounds in meatballs and reduced the cancer-related risk on human health to almost negligible levels. In particular, black garlic aged at 70 °C for 45 days and added at 1% gave the most effective results. Therefore, black garlic can be used as an effective natural additive to reduce PAH formation and exposure in meatballs (Aoudeh et al., 2023).

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ISBN: 978-625-378-032-6