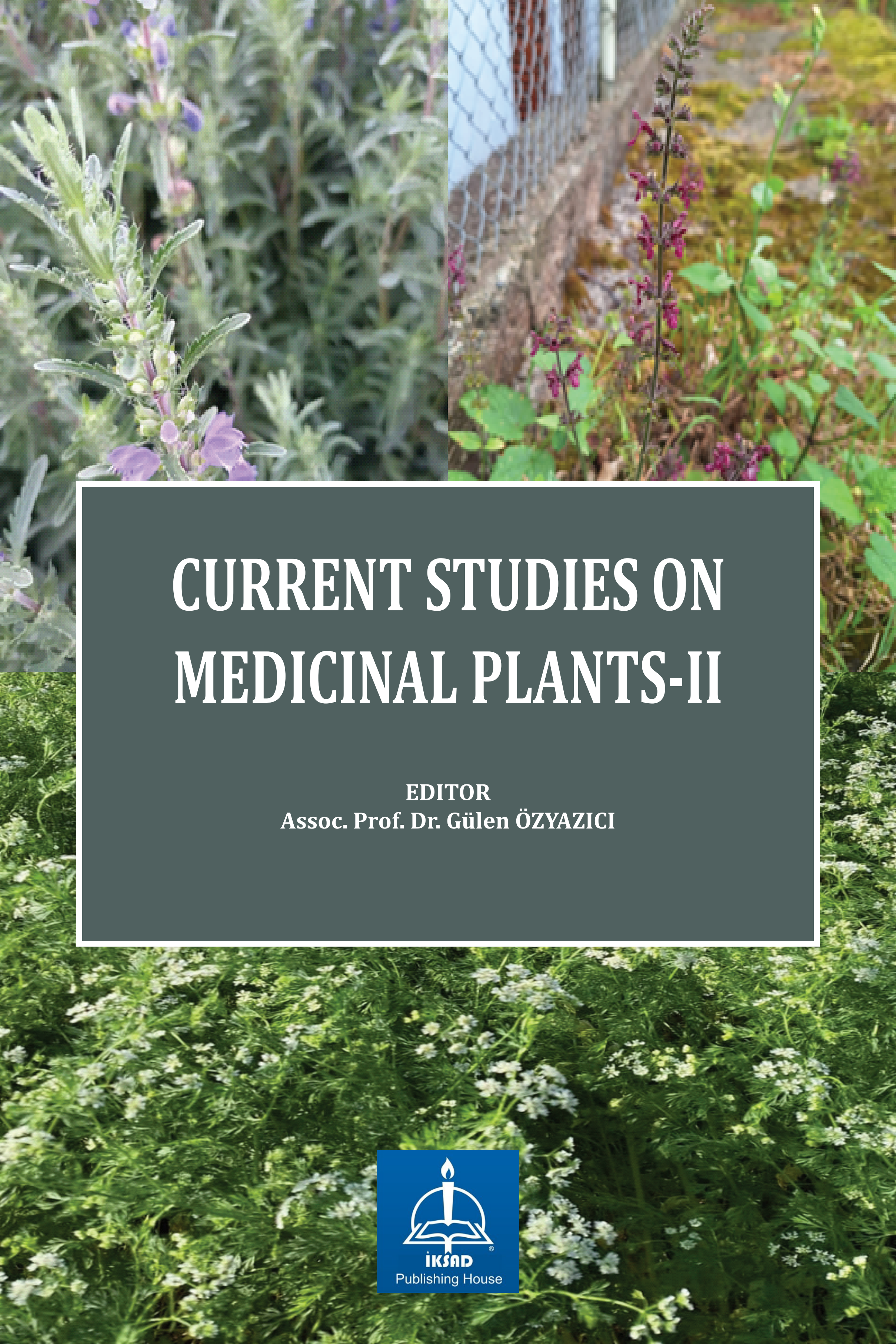


CURRENT STUDIES ON MEDICINAL PLANTS-II

EDITOR
Assoc. Prof. Dr. Gülen ÖZYAZICI

İKSAD
Publishing House

CURRENT STUDIES ON MEDICINAL PLANTS-II

EDITOR

Assoc. Prof. Dr. Gülen ÖZYAZICI

AUTHORS

Prof. Dr. Belgin COŞGE ŞENKAL

Prof. Dr. Esra UÇAR

Prof. Dr. Fatih SEYİS

Prof. Dr. Ufuk KOCA ÇALIŞKAN

Assoc. Prof. Dr. Cennet YAMAN

Assist. Prof. Dr. Gülşen GÜÇLÜ

Assist. Prof. Dr. Halil DİLMEN

Assist. Prof. Dr. Tansu USKUTOĞLU

PhD. Aysel ÖZCAN AYKUTLU

Lecturer Hatice Beyza BAŞKAL DOĞANER

Graduate Student Ahmet TOPAL

İKSAD Publishing House

Institution of Economic Development and Social
Researches Publications®
(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

ISBN: 978-625-367-841-8

Cover Design: İbrahim KAYA
September/ 2024
Ankara / Türkiye
Size = 16x24 cm

CONTENTS	

PREFACE

There are approximately 750.000 to 1.000.000 plant species in the world, of which approximately 500.000 have been identified. In addition, a large number of plants are identified each year. It has been shown that approximately 20.000 different plant species are used worldwide for medicinal purposes. More than 4000 of these species are widely used as herbal medicines, and more than 2000 herbal medicines are traded in European countries. In addition to their therapeutic purposes, medicinal and aromatic plants play a major role in many products such as essential oils, cosmetic products, health supplements, coloring agents, plant protection products and intermediate products. The market value of these plants is also increasing day by day worldwide. The growth in the natural and alternative medicine sector creates an increasing market demand for medicinal plants. In order to carry out sustainable agriculture and to evaluate the market potential in the best way, it is important for production to meet the demand in terms of quality and quantity. Although Türkiye has an important position in the world in terms of medicinal and aromatic plants, the foreign trade of these products is well below the desired level.

This book, which deals with medicinal and aromatic plants from different aspects and was prepared with the participation of valuable researchers, consists of 8 chapters. I would like to thank all our authors who contributed to the preparation of this book titled 'CURRENT STUDIES ON MEDICINAL PLANTS-II' and the employees of IKSAD publishing house who contributed to the publication phase, and I hope that this book will be useful to the scientific community.

Best regards

Assoc. Prof. Dr. Gülen ÖZYAZICI

CHAPTER I

THE EFFECTS OF MUTAGEN APPLICATIONS ON ESSENTIAL OIL QUANTITY AND COMPOSITION IN BREEDING ESSENTIAL OIL PLANTS

Assist. Prof. Tansu USKUTOĞLU[1]
Prof. Dr. Belgin COŞGE ŞENKAL[2]

DOI: https://dx.doi.org/10.5281/zenodo.13826013

[1] Pamukkale University, Field Crops Department, Faculty of Agriculture, Denizli, Türkiye. ORCID ID: 0000-0001-6631-1723, e-mail: tuskutoglu@pau.edu.tr
[2] Yozgat Bozok University, Field Crops Department, Faculty of Agriculture, Yozgat, Türkiye. ORCID ID: 0000-0001-7330-8098, e-mail: belgin.senkal@ yobu.edu.tr

INTRODUCTION

The medicinal use of plants dates back to the very beginnings of human history. On a Sumerian clay slab from Nagpur, the earliest known written record of the use of medicinal herbs to make medications dates back almost 5000 years. It included twelve drug production instructions that referenced more than two hundred different plants, some of which were alkaloid plants like mandrake, henbane, and poppies (Gurib-Fakim, 2006; Hussain et al., 2012; Petrovska, 2012). Medicinal and aromatic plants (MAPs) represent invaluable resources for the global pharmaceutical industry, with their diverse parts (roots, leaves, flowers, and seeds etc.) undergoing extensive assessment and utilization (Chen et al., 2016). Despite advancements in synthetic medicine, medicinal plants continue to play a significant role in the pharmaceutical industry. In Europe, over 1300 medicinal and aromatic plants are utilized in pharmaceuticals, with a staggering 90% of these plants sourced from wild resources. Similarly, in the United States, approximately 118 of the top 150 prescribed medications are derived from natural sources (Balunas and Kinghorn, 2005). This reliance on medicinal plants is particularly evident in developing nations, where up to 80% of the population depends solely on herbal remedies for primary healthcare. Moreover, over 25% of prescribed medicines in developed countries contain plant-based ingredients or ingredient groups (Hamilton, 2004). The growing demand for herbal medicines, natural health products, and secondary metabolites extracted from medicinal plants is contributing to a rapid expansion of their use worldwide (Chen et al., 2016; Nalawade et al., 2003).

The secondary metabolites produced by medicinal and aromatic plants (MAPs) are crucial for maintaining human health (Kolakar et al., 2018). Particularly promising for drug development are alkaloids, terpenoids, and phenylpropanoids, which are currently undergoing extensive research for their potential therapeutic applications (Li et al., 2020; Sanchita and Sharma, 2018). While wild-collected plants generally contain higher levels of secondary metabolites, cultivating medicinal plants under controlled conditions offers several advantages.

1-) Wild harvest risks adulteration, while cultivation ensures botanical accuracy.

2-) Wild harvest is unreliable, cultivation ensures steady supply.

3-) The supply can be tailored to meet the specific demands of sectors requiring these materials.
4-) Breeding wild/managed genotypes offers economic potential for medicinal plants.
5-) Cultivation permits regulated post-harvest management,
6-) Cultivated plants are easily certified organic/biodynamic, while wildcrafting standards are under development (Schippmann et al., 2007). The cultivation of medicinal and aromatic plants is of great importance due to these advantages. The selection of an appropriate variety is a critical step in the cultivation of medicinal plants, as it significantly impacts the plant's growth, yield, and quality of the desired medicinal compounds.

Mutation breeding is a faster and less laborious method compared to traditional hybridization techniques and can also be used in plants carrying rare or undesirable alleles. Therefore, it is a valuable tool for developing new varieties of MAPs and conserving biodiversity (Pandit et al., 2021).

This study compiled and analyzed relevant literature on the application of mutation breeding in MAPs, offering a comprehensive examination of this valuable technique.

1. MUTATION INDUCTION TECHNIQUES

Mutations occur spontaneously in nature. These random events cause changes in the nucleotide sequences of DNA, leading to the emergence of new gene variations. Mutations are uncommon occurrences, but the rate at which they enter genomes at each generation varies greatly among taxa: in unicellular eukaryotes, there are roughly 10^{-11} mutations per site per generation, whereas in multicellular eukaryotes, there are roughly 10^{-7} mutations per site per generation (Bergeron et al., 2023). Through the application of mutation induction techniques, the frequency of mutations in nature can be enhanced, allowing for the identification and selection of beneficial mutants. Commonly used mutagens in mutation breeding are presented in Table 1.

Table 1: Frequently utilized mutagens in plant mutation induction (IAEA, 2024)

Physical Mutagens		**Chemical Mutagens**		
Ionising radiations		**Alkylating agents**	**Base analogues**	**Acridine dye**
Ionising radiations	**Non-ionising Radiations**	Mustard gas	5-chlorouracil	Acridine orange
Particulate radiation	UV rays	EMS		Proflavine
Alpha rays		MMS		
Non-particulate radiations				
X-rays				
Gamma rays				

Physical mutagens directly damage DNA by breaking strands or causing cross-linking. In contrast, chemical mutagens modify the chemical structure of DNA, leading to misinterpretations during replication. Physical mutagens can generally induce higher mutation rates compared to chemical mutagens. However, physical mutagens also cause more lethal damage than chemical mutagens, which can directly affect selection in subsequent generations (Al-Khayri et al., 2015; Yali and Mitiku, 2022).

A total of 3.433 varieties have been developed worldwide through mutation breeding, and their distribution by region is shown in Figure 1. A total of 21 novel medicinal plant varieties have been produced to date using mutation breeding techniques (IAEA, 2024). Europe and Asia encompass approximately 88.77% of all developed varieties.

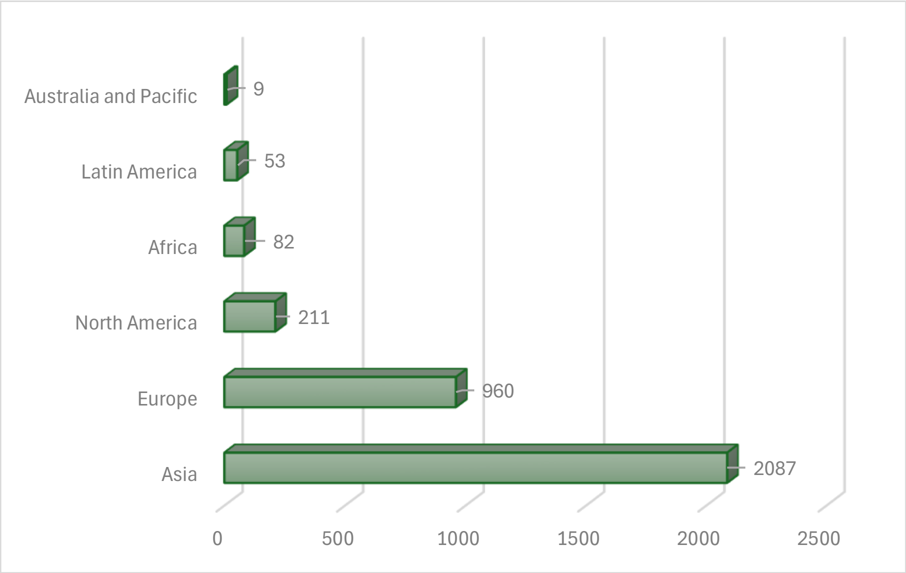


Figure 1: Distribution of reported mutant variants by region by 2024 (IAEA, 2024)

2. PROGRESS IN MUTAGENESIS IN MAPS

Rice (873), barley (307), chrysanthemum (285), wheat (265), soybean (182), and maize (89) are among the most extensively studied and mutagenized crop plants (IAEA, 2024). In addition to these crops, 21 varieties of medicinal and aromatic plants have also been developed through mutation breeding. Some of the achievements obtained through mutation breeding in MAPs are presented in Table 2.

Table 2: Achievements gained through mutation breeding in some MAPs

Common Name	Latin name	Mutagen	Achievement	Reference
Chamomile	*Matricaria recutita* L.	Gama rays SA	High oil content (1.29%-1.77%), high chamazulene content (13.98%)	(Ghareeb et al., 2022)
Sweet Basil	*Ocimum basilicum L.*	EMS	Improvement on oil content (%1.6), Control (0.6%)	(Kumari and Singh, 2024)
Pennyroyal	*Mentha pulegium* L.	Gama rays EMS	Dry weight increasing by up to 32%, oil content rising by up to 17%, and pulegone content	(Al-Amier et al., 2006)

			experiencing a remarkable 47% increase.	
Palmarosa	*Cymbopogon martinii*	Gamma rays EMS EI	revealed a notable rise in free geraniol and total oil, general enhancement in free geraniol and geranyl acetate	(Srivastava and Satpute, 1998)
Palmarosa	*Cymbopogon martinii*	Gamma rays	High oil quality, oil content (%), and herbage yield	(Srivastava et al., 2000)
Patchouli	*Pogostemon cablin* Benth	Gamma rays	Superior with plant height, herbage yield per plant, essential oil percent and monopodia length	(Lal et al., 2018)
Patchouli	*Pogostemon cablin* (Blanco) Benth.	Gamma rays	A noticeably higher proportion of patchouli alcohol, an upright plant mutant with thick, glossy, dark-green leaves	(Rekha et al., 2009)
Lavender	*Lavandula angustifolia*	EMS	Distinct in terms of essential oil composition (the proportional presence of various mono- and sesquiterpenes)	(Falk et al., 2009)
Rose	*Rosa hybrida*	Gamma rays	High terpene alcohols and oil content, higher ester contents than their original cultivar.	(Ryu et al., 2020)
Marjoram	*Origanum majorana L.*	Trimethanolamine (TMA) Diethylamine (DEA) Diethyl sulphate (DES)	One mutant had no essential oil at all, and the percentage of essential oil in marjoram was double that of the normal percentage.	(Svendsen and Scheffer, 1985)
Davana	*Artemisia pallens Bess.*	Gamma rays EMS	Flowering time plasticity (late and early flowering), high-yielding genotypes with a	(Rekha and Langer, 2007)

			bushy habit, taller plants than control plants, and high-capitulum-producing, high oil and davanone-rich genotypes	
Chrysanthemum	*Chrysanthemum morifolium*	Gamma rays	Enriched terpene profile with a lower hydrocarbon content compared to the original cultivar	(Ryu et al., 2019)
Fennel	*Foeniculum vulgare* Mill	Dimethy sulphate solution (DMS)	Increased estragole percentage	(Mostafa and Abou Alhamd, 2015)
Peppermint	*Mentha piperita* L.	Gamma rays	Increased biomass production, oil ratio, and total oil yield, with a favorable essential oil profile exhibiting high menthol levels (68-78%) and minimal menthofuran content (0.2-0.8%)	(Prasad and Kumar, 2024)

The primary goal of mutation breeding is to induce random changes in the genetic makeup of plants to generate new and beneficial traits. For this purpose, gamma rays are the most commonly used physical mutagen, while EMS is the most widely utilized chemical mutagen, to induce mutations in mutation breeding studies in MAPs. Based on the data in Table 2, significant progress has been achieved in MAPs using chemical mutagens.

MAPs have contributed a considerably role in the treatment of human diseases and the preservation of health for centuries. These plants are rich in chemical compounds called secondary metabolites, which have many biological activities. Secondary metabolites give medicinal plants their characteristic properties such as color, smell and taste, and also have various beneficial effects such as antimicrobial, anti-inflammatory, antioxidant and anticancer (Zhang et al., 2021). In addition to these properties, the production and enhancement of secondary metabolites are of great importance. Gains in yield and quality increase with mutation breeding are listed below.

1-) Development of genotypes with higher essential oil content compared to control plants

2-) Changes in the chemical structure of MAPs or an increase in the amount of desired secondary metabolites

3-) Enhanced plant dry biomass production leading to increased essential oil yield

4-) Development of new varieties with high herb yield

5-) Alterations in plant characteristics (changes in plant height or growth habit)

6-) Dramatic increases or decreases in essential oil content have been observed, and even genotypes that do not contain essential oil have been found in marjoram.

7-) Early- or late-flowering genotypes

8-) Development of varieties with more floral receptacle in plants primarily used for their flowers

In addition to these achievements, not only the quantity but also the quality of secondary metabolites has been enhanced in MAPs.

3. CONCLUSION

Mutation breeding offers a powerful tool for generating a wide range of genetic diversity by introducing novel gene combinations not found in natural variation. It can also be employed to enhance complex traits controlled by multiple genes, rather than simply focusing on simple traits governed by a single gene. This technique has proven to be a valuable tool in the development of medicinal and aromatic plants, holding the potential to significantly improve the benefits these plants offer to human health and well-being. As the concept of "returning to nature" regains prominence, researchers remain committed to further refining these methods and utilizing them to create new and superior medicinal and aromatic plant varieties.

REFERENCES

Al-Amier, H., Toaima, N., Mansour, B. M. M., El Hela, A. A., Sastry, K. S., & Craker, L. (2006). Use of mutations to improve essential oil yield and constituency in pennyroyal. Journal of Herbs, Spices and Medicinal Plants, 11(4): 91-101.

Al-Khayri, J. M., Jain, S. M., & Johnson, D. V. (2015). Advances in Plant Breeding Strategies: Breeding, Biotechnology and Molecular Tools (J. M. Al-Khayri, S. M. Jain, & D. V. Johnson, Eds.). Springer International Publishing.

Balunas, M. J., & Kinghorn, A. D. (2005). Drug discovery from medicinal plants. Life Sciences, 78(5): 431-441.

Bergeron, L. A., Besenbacher, S., Zheng, J., Li, P., Bertelsen, M. F., Quintard, B., Hoffman, J. I., Li, Z., St. Leger, J., Shao, C., Stiller, J., Gilbert, M. T. P., Schierup, M. H., & Zhang, G. (2023). Evolution of the germline mutation rate across vertebrates. Nature, 615(7951): 285-291.

Chen, S. L., Yu, H., Luo, H. M., Wu, Q., Li, C. F., & Steinmetz, A. (2016). Conservation and sustainable use of medicinal plants: Problems, progress, and prospects. Chinese Medicine (United Kingdom) (Vol. 11, Issue 1). BioMed Central Ltd.

Falk, L., Biswas, K., Boeckelmann, A., Lane, A., & Mahmoud, S. S. (2009). An effcient method for the micropropagation of lavenders: Regeneration of a unique mutant. Journal of Essential Oil Research, 21(3): 225-228.

Ghareeb, Y. E., Soliman, S. S., Ismail, T. A., Hassan, M. A., Abdelkader, M. A., Abdel Latef, A. A. H., Al-Khayri, J. M., ALshamrani, S. M., Safhi, F. A., Awad, M. F., El-Moneim, D. A., & Hassanin, A. A. (2022). Improvement of German chamomile (*Matricaria recutita* L.) for mechanical harvesting, high flower yield and essential oil content using physical and chemical mutagenesis. Plants, 11: 2940.

Gurib-Fakim, A. (2006). Medicinal plants: Traditions of yesterday and drugs of tomorrow. Molecular Aspects of Medicine, 27(1): 1-93.

Hamilton, A. C. (2004). Medicinal plants, conservation and livelihoods. Biodiversity and Conservation, 13:1477-1517.

Hussain, M. S., Fareed, S., Ansari, S., Rahman, M. A., Ahmad, I. Z., & Saeed, M. (2012). Current approaches toward production of secondary plant metabolites. Journal of Pharmacy and Bioallied Sciences, 4(1): 10-20.

IAEA. (2024). MVD Mutant Variety Database. International Atomic Energy Agency (IAEA).

Kolakar, S. S., Nadukeri, S., Jakkeral, S. A., Lakshmana, D., Hanumanthappa, M., & Gangaprasad, S. (2018). Role of mutation breeding in improvement of medicinal and aromatic crops: Review. Journal of Pharmacognosy and Phytochemistry, 3: 425-429.

Kumari, N., & Singh, M. (2024). Effect of chemical mutagen on seed germination, morphological and essential oil content in *Ocimum basilicum* L. Asian Journal of Biological and Life Sciences, 12(3): 460-465.

Lal, M., Pandey, S. K., Dutta, S., Munda, S., Baruah, J., & Paw, M. (2018). Identification of high herbage and oil yielding variety (Jor Lab P-1) of *Pogostemon cablin* (Blanco) Benth. through mutation breeding. Journal of Essential Oil-Bearing Plants, 21(1): 131-138.

Li, Y., Kong, D., Fu, Y., Sussman, M. R., & Wu, H. (2020). The effect of developmental and environmental factors on secondary metabolites in medicinal plants. Plant Physiology and Biochemistry, 148: 80-89.

Mostafa, G., & Abou Alhamd, M. F. (2015). Induction of salt tolerant mutants of *Foeniculum vulgare* by dimethyl sulphate and their identification using protein pattern and ISSR markers. J. Agric. Res, 60(2): 95-109.

Nalawade, S. M., Sagare, A. P., Lee, C. Y., Kao, C. L., & Tsay, H. S. (2003). Studies on tissue culture of Chinese medicinal plant resources in Taiwan and their sustainable utilization. Botanical Bulletin of Academia Sinica, 44: 79-98.

Pandit, R., Bhusal, B., Regmi, R., Neupane, P., Bhattarai, K., Maharjan, B., Acharya, S., & Ram Poudel, M. (2021). Mutation breeding for crop improvement: A review. Reviews Food And Agriculture, 2(1): 31-35.

Petrovska, B. B. (2012). Historical review of medicinal plants' usage. Pharmacognosy Reviews, 6(11): 1-5.

Prasad, P., & Kumar, B. (2024). Gamma irradiation induced morpho-chemical and molecular diversity in the mutagenized population of *Mentha piperita* L. Industrial Crops and Products, 210: 118036.

Rekha, K., Bhan, M. K., & Dhar, A. K. (2009). Development of erect plant mutant with improved patchouli alcohol in patchouli (*Pogostemon cablin* (*blanco*) Benth.). Journal of Essential Oil Research, 21(2): 135-137.

Rekha, K., & Langer, A. (2007). Induction and assessment of morpho-biochemical mutants in *Artemisia pallens* Bess. Genetic Resources and Crop Evolution, 54(2): 437-443.

Ryu, J., Lyu, J. Il, Kim, D. G., Kim, J. M., Jo, Y. D., Kang, S. Y., Kim, J. B., Ahn, J. W., & Kim, S. H. (2020). Comparative analysis of volatile compounds of gamma-irradiated mutants of rose (*Rosa hybrida*). Plants, 9(9): 1-15.

Ryu, J., Nam, B., Kim, B. R., Kim, S. H., Jo, Y. D., Ahn, J. W., Kim, J. B., Jin, C. H., & Han, A. R. (2019). Comparative analysis of phytochemical composition of gamma-irradiated mutant cultivars of *Chrysanthemum morifolium*. Molecules, 24(16): 3003.

Sanchita, & Sharma, A. (2018). Gene expression analysis in medicinal plants under abiotic stress conditions. Plant Metabolites and Regulation under Environmental Stress, 407-414.

Schippmann, U., Leaman, D., & Cunningham, A. B. (2007). A comparison of cultivation and wild collection of medicinal and aromatic plants under sustainability aspects. Medicinal and Aromatic Plants, 75-95).

Srivastava, H. K., & Satpute, G. K. (1998). Induction of mutations for enhanced essential oil in palmarosa (*Cymbopogon martinii*). Journal of Essential Oil Research, 10(3): 287-291.

Srivastava, H. K., Satpute, G. K., & Naqvi, A. A. (2000). Induced mutants in m2 generation and selection for enhanced essential oil yield and quality in palmarosa (*Cymbopogon martinii*, roxb.) wats., var. *martinii*. Journal of Essential Oil Research, 12(4): 501-506.

Svendsen, A. Baerheim., & Scheffer, J. J. C. (1985). Essential Oils and Aromatic Plants : Proceedings of the 15th International Symposium on

Essential Oils, held in Noordwijkerhout, the Netherlands, July 19-21, 1984. Springer Netherlands.

Yali, W., & Mitiku, T. (2022). Mutation breeding and its importance in modern plant breeding. Journal of Plant Sciences, 10(2): 64-70.

Zhang, S., Zhang, L., Zou, H., Qiu, L., Zheng, Y., Yang, D., & Wang, Y. (2021). Effects of light on secondary metabolite biosynthesis in medicinal plants. Frontiers in Plant Science, 12: 781236.

CHAPTER II

USE OF PLANT SECONDARY METABOLITIES IN AGRICULTURE

Prof. Dr. Belgin COŞGE ŞENKAL[1]
Assist. Prof. Tansu USKUTOĞLU[2]

DOI: https://dx.doi.org/10.5281/zenodo.13826018

[1] Yozgat Bozok University, Field Crops Department, Faculty of Agriculture, Yozgat, Türkiye. ORCID ID: 0000-0001-7330-8098, e-mail: belgin.senkal@yobu.edu.tr
[2] Pamukkale University, Field Crops Department, Faculty of Agriculture, Denizli, Türkiye. ORCID ID: 0000-0001-6631-1723, e-mail: tuskutoglu@pau.edu.tr

INTRODUCTION

Versatile synthesis reactions take place within the bodies of plants, and as a result, many components with different structures are formed. These natural products formed in intracellular reactions are synthesized through primary and secondary metabolism pathways (Elshafie et al., 2023). Most of these substances are secondary metabolites.

Secondary metabolites are chemical substances produced by plants and not directly related to the basic vital functions of the plant (Anulika et al., 2016). While the absence of secondary metabolites does not directly cause cell death, it is stated that it may negatively affect the organism's ability to survive in the long term (Elshafie et al., 2023). Today, there are over 100 000 secondary metabolite components, the number of which is increasing day by day (Reshi et al., 2023).

Plants, which are sources of secondary metabolites, have been used by humans as food, food supplements, traditional medicines and dyes, etc. since ancient times (Chandran et al., 2020). As knowledge about medicinal and aromatic plants increases, the use of secondary metabolites has also increased. Many plant taxa accumulate economically important organic chemicals such as alkaloids, terpenes, phenolics and glycosides. These phytochemicals, which are natural plant products, are used directly or indirectly in numerous industries (Yeshi et al., 2022).

While carrying out agricultural activities, many and large quantities of chemical products such as fertilizers, pesticides, herbicides, plant growth regulators and antibiotics are used in both plant and animal production. In recent years, excessive use of pesticides in the fight against agricultural pests has brought undesirable harm to both human life and the environment. Nowadays, environmentally friendly pesticides that are biodegradable and have high selectivity are needed all over the world. Natural products of plant origin (extracts, essential oils, etc.) are a good alternative to synthetic pesticides to reduce negative effects on human health and the environment.

1. FUNCTIONS OF PLANT SECONDARY METABOLITES

Secondary metabolites are numerous small-molecule chemical compounds produced by plant cells through primary metabolic pathways. Secondary metabolites are not found in all plants and are biologically active (antibiotic, antifungal, antiviral, etc.) components (Hussein and El-Anssary, 2019).

Secondary metabolites are formed in different ways in plants and have a wide variety of structures. They have many common features.

Secondary metabolites:

1-They are not found in all plants.

2-They are biologically active ingredients.

3- They are small molecule components.

4-They are synthesized from many primary metabolite components.

Plant secondary metabolites are classified according to their chemical structure, composition, water solubility and biosynthetic origin. The most common of these is the one that considers their biosynthetic origins (Mammadov, 2014; Chaachouay and Zidane, 2024).

The classification of plant secondary metabolites according to their biosynthetic origins is presented in Figure 1 (Mera et al., 2019; Kabera et al., 2014).

Phenolics

Phenolic substances, which are an important component of the cell wall, protect the plant from microbial attacks. They are responsible for the color formation in flowers and fruits (flavonoids and anthocyanins). At the same time, their ability to attract insects contributes to pollination and fertilization in flowers, while they play a defensive role by providing protection against predators. Tannins and phenolic resins are feeding deterrents. They contribute to the formation of disease resistance in plants. It has allelopathic effects. Some phenolics exhibit antioxidant activity. Phenolics are also used as food additives and food coloring in the food industry (Kabera et al., 2014).

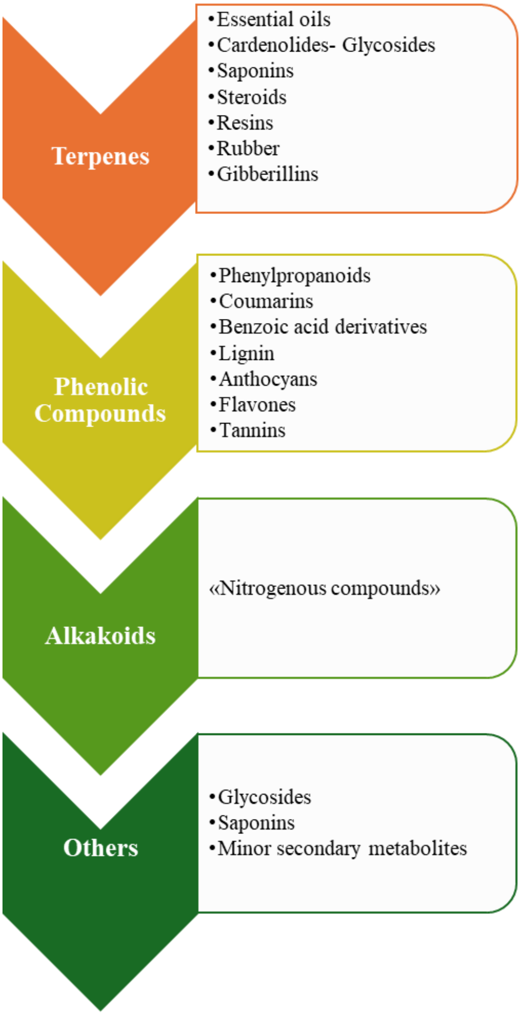


Figure 1: Classification of plant secondary metabolites

Alkaloids

They are alkali-like active substances that contain nitrogen in their structure and are toxic to many organisms. They exhibit a wide range of pharmacological activities (anticancer, analgesic, antibacterial, antihyperglycemic, etc.). They are involved in the production of therapeutic drugs in traditional and modern medicine (Awuchi, 2019).

Terpenes

Terpenes, which constitute the largest group of plant secondary metabolites, are terpene substances consisting of five-carbon isoprene units and mostly create essential oils and sometimes colors (Perveen, 2018). The most important function of terpenes in plants is ecological and physiological. In many plants, pollination occurs by insects, and plants secrete various terpenes to attract insects. Terpenes with a bitter aroma or toxic effects protect plants from being eaten by animals. Terpenes also have important functions as phytohormones (Al-Khayri et al., 2023). Terpenes, which prevent the germination of other types of plant seeds and the growth and development of foreign plants surrounding them, also repel or kill pathogenic microorganisms such as fungi, bacteria and viruses that make the plants themselves sick (Baydar, 2022).

2. ESSENTIAL OILS

Essential oil, solid or liquid, is a complex mixture of hydrophobic, volatile and aromatic properties, in which many different chemical compounds dissolve in each other and form a homogeneous solution, giving the plant its taste or characteristic smell. They are by-products of plant metabolism and are volatile secondary metabolites. It is in liquid form at room temperature (Bhavaniramya et al., 2019). Essential oils are found in the cells of organs such as leaves, flowers, stems, roots, rhizomes, fruit peels and seeds in plants (Butnariu and Sarac, 2018). Its basic compounds are terpenes, which are naturally and widely found in the plant kingdom (Figure 2). Essential oils are found in secretory ducts, secretory pockets or glandular hairs in plants. It has been determined that essential oils attract insects for fertilization in plants and have temperature-adjusting effects, thus preventing water loss. Essential oils prevent water loss by having a thermoregulating effect on the plant. These substances absorb heat from the plant due to their ability to evaporate violently and become volatile, thus helping the plant maintain its natural balance (Baydar, 2022; Akman and Güney, 2006). Essential oils are considered as “food additives, sweeteners, perfumes, cosmetics, soaps and cleaning products and plastic components”. The amount of essential oils in plants varies widely (0.01-5%) (Mammadow 2014; Bhavaniramya et al., 2019).

The main families which are rich in essential oils in the plant kingdom are "Labiatae, Rosaceae, Umbelliferae, Myrtaceae, Lauraceae, Rutaceae, Cupressaceae, Brassicaceae, Iridaceae, Zingiberaceae, Compositeae, Geraniaceae and Pinaceae" (Akman and Güney, 2006; Mammadov, 2014).

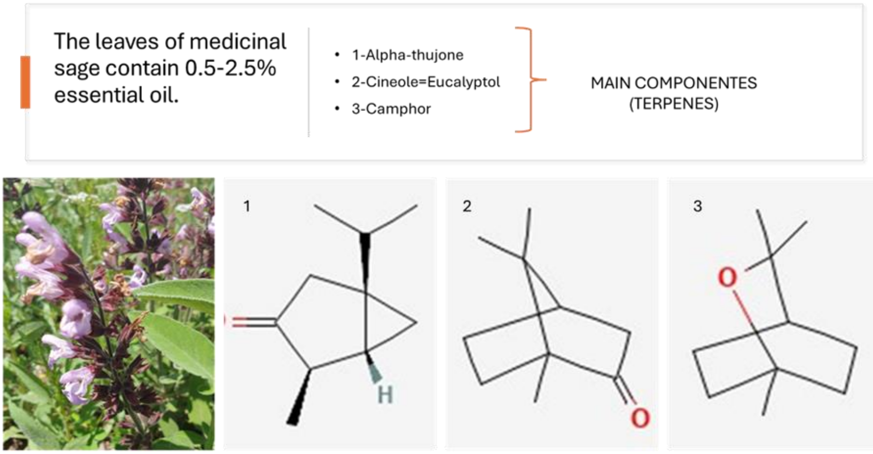


Figure 2: *Salvia officinalis* L. (Yozgat Bozok University, Research and Application Area/Divanlı-YOZGAT, 23.06.2023)
(Source: National Center for Biotechnology Information (2024). PubChem Compound Summary Retrieved May 13, 2024 from https://pubchem.ncbi.nlm.nih.gov/compound/Camphor)

2.1. The Role of Essential Oils in Plants

Although it is not known exactly why essential oils, which are not essential nutrients and building materials for plants, are produced by plants, some reasons are put forward (Figure 3).

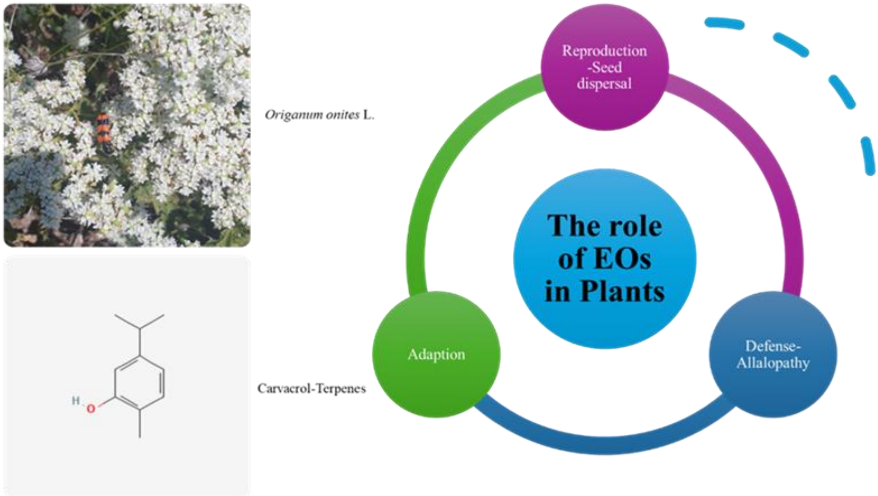


Figure 3: *Origanum onites* L. ((Yozgat Bozok University, Research and Application Area/Divanlı-YOZGAT, 20.07.2022)
Carvacrol (C10H14O-Terpene): Main component of oregano essential oil. (Source: National Center for Biotechnology Information (2024). PubChem Compound Summary for CID 10364, Carvacrol. Retrieved May 15, 2024 from https://pubchem.ncbi.nlm.nih.gov/compound/Carvacrol)

Reproduction and Seed Dispersal: The ability of plants to reproduce through pollination and the attraction of animals by essential oils in the spread of fruits and seeds to the environment and distant places reveal the main importance of these oils (Camina et al. 2023).

Adaptation: Essential oils regulate very important events such as balanced evaporation of water in plants, protection of plants from the stress caused by solar radiation, adaptation of plants to solar heat during the day and cooling at night. By balancing the movement of water, essential oils reduce stress on the plant (Sharifi-Rad et al., 2017).

Defense-Allelopathy: Essential oils undertake important functions in protecting the plant from diseases, pests and animals, in the rapid healing of wounds in the bark and wood of the plant, in protecting the plant from microorganisms and in strengthening the immune system. Essential oils give allelopathic properties to plants. Thanks to these features, the plant slows down the development of plants from other species and creates a suitable environment for its own development (Mammadov, 2014; Bhavaniramya et al., 2019; Baydar, 2022).

3. USE OF PLANT SECONDARY METABOLITIES IN AGRICULTURE

Plant secondary metabolites have very important roles in defense against various pathogens, pests and abiotic stress factors (extreme temperature stress, drought stress, flood stress, salinity stress, metal stress) (Zhang et al., 2020; Lyubenova et al., 2023).

3.1. Plant Protection

In recent years, excessive use of pesticides in agricultural areas has brought about serious environmental problems. As a result of this situation, there is a serious trend towards environmentally friendly pesticides worldwide. Natural products of plant origin are a good alternative to synthetic pesticides to reduce negative effects on both human health and the environment. Herbal pesticides:

- Due to its versatile effects, the possibility of developing a resistant population is low.
- Their degradation time is rapid, so their persistence in the environment is low.
- They do not pose a significant risk to non-target organisms.

Essential oils and plant extracts are used for pest and disease control in agriculture. It is known that essential oils and extracts obtained from various medicinal and aromatic plants have insecticidal, nematocidal, acaricidal, fungicidal and bactericidal properties. Essential oils are used to control insect populations, especially in closed areas (greenhouses, warehouses, warehouses, etc.) (Bhavaniramya et al., 2019). It has been reported that some phenolic compounds and alkaloids synthesized by plants are toxic to insects. Phenolic compounds act as toxins that inhibit the growth and development of insects (Croteau et al., 2000). Alkaloids, on the other hand, cause toxicity by affecting the nervous system, DNA replication, protein synthesis and enzyme activity of insects (Pichersky et al., 2006; Croteau et al., 2000). Monoterpenoids in the resins of coniferous trees are toxic to most insects (Mammadow, 2014).

Pyrethrins are a natural pesticide synthesized by the perennial pyrethrum plant [*Chrysanthemum cinerariaefolium* Vis., Family: Asterracea] (Figure 4) (Matsuda, 2012; Moslemi et al., 2018).

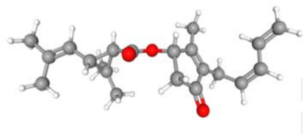
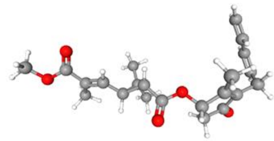
Figure 4: *Chrysanthemum cinerariaefolium* Vis.
(Source: http://www.eastafricanplants.senckenberg.de/ Access date: 28.05.2024)

They represent the most economically important natural pesticides, being neurotoxins effective against a wide range of insect species, and are widely applied in private homes, gardens, barns and organic agriculture because they are environmentally friendly (Yang et al., 2014). Due to its rapid biotransformation, its toxicity to humans and warm-blooded animals is low (Duchon et al., 2009; Sharafzadeh, 2011).

The plant extract called pyrethrum contains pyrethrin I and pyrethrin II, collectively called pyrethrins (Table 1).

It is used as powder and emulsifiable concentrates in agriculture, vegetable growing, fruit growing and floriculture. It is applied just before picking for grapes and strawberries, and after picking for other fruits and vegetables. It has a wide range of uses as powder or spray in dried fruits, hazelnuts, grain products, oilseeds and animal feed. It is applied as a repellent in products such as bagged grain, cocoa etc. (Mammadov, 2014).

Table 1: Chemical structure and uses of pyrethrin

Molecular Formula	**PYRETHRIN I** $C_{21}H_{28}O_3$	**PYRETHRIN II** $C_{22}H_{28}O_5$
Chemical Structure		
General Usage	**1-** Pre-harvest and post-harvest use in many agricultural products, **2-** Direct and indirect treatments of livestock and facilities, **3-** In commercial and industrial facilities and storage areas where raw and processed food/feed products are stored or processed.	

(Source: https://pubchem.ncbi.nlm.nih.gov/compound/5281045-5281555 Access date: 28.05.2024)

Some medicinal and aromatic plants that can be used to control pests:

Rosemary (*Rosemarinus officinalis* L.) [family LAMIACEAE]

It has been determined that rosemary essential oil is effective against storage pests and various insect and mite species (Koschier and Sedy, 2003; Isman et al. 2008).

Eucalyptus (*Eulcalyptus globulus* Labill.) [family MYRTACEAE]

Eucalyptus essential oil provides protection against harmful arthropods, provides anti-feeding activity against herbivores, and exhibits nematicidal activity (Batish et al. 2008).

Carnation (*Eugenia caryophyllus* (Sprengel) Bullock & Harrison) [family MYRTACEAE]

Eugenia caryophyllus has a potential insecticidal effect against some insects (*Callosobruchus chinensis*, *Aedes aegypti*, *Sitophilus oryzae*, etc.) (Kerdchoech et al., 2010; Matos et al., 2020).

Thyme (*Thymus vulgaris* L.) [family LAMIACEAE]

Carvacrol, thymol and linalool are the main components in thyme essential oil. The essential oil of this plant has an insecticidal effect (Khosravi and Jalali Sendi, 2013; Yazdani et al., 2014).

Lemongrass (*Cymbopogon citratus* (DC) Stapf) [family POACEAE]

Lemongrass essential oil (main components citral and 1,8-cineole) has potential activity against various insects and mites (Cavalcanti et al. 2004; Kumar et al., 2013; Sinthusiri and Soonwera, 2013). However, lemongrass extracts also have a bioinsecticide effect.

Mentha spp. [family LAMIACEAE]

Essential oils of *Mentha* species are rich in components such as menthol, menthone, mentofuran and piperitone. These components exhibit activity as biopesticides. (Mahieu et al., 2007; Papathanasopoulos et al., 2013).

Lavender (*Lavandula angustifolia* Mill.) [family LAMIACEAE]

Lavandula angustifolia has antimicrobial, antifungal, and insecticidal activities (Costa et al., 2014; Badreddine et al., 2015; Duda et al., 2015).

Apart from these, essential oils and extracts of many medicinal and aromatic plants (*Artemisia vulgaris*, *Foeniculum vulgare*, *Cuminum cymium*, *Cedrus* spp., *Piper* spp., *Vetiveria zizanoides* etc.) can be used for plant protection in agricultural activities.

3.2. Animal Health and Nutrition

Essential oils have the potential to be used in animal health and nutrition due to their biological effects (Mammadov, 2014). Essential oils given with feed have positive effects on the meat and milk quality of animals (Nehme et al., 2021). According to the results of the research conducted:

- It has been reported that spraying anise oil on the animals is effective in preventing the negative effects that occur during stress situations in dairy cows (Mammadov, 2014).

- It has been observed that the flavor and odor properties of the meat are positively affected in lambs to which essential oil mixture is added to their diet.
- Live weight gain was determined in broiler chickens.
- It has been reported that thymol and carvacrol found in thyme have a digestive stimulating effect and positively affect live weight gain and feed conversion ratio by destroying pathogenic microorganisms in the digestive system.
- It has been noted that thymol in the composition of thyme essential oil positively affects egg production.
- Rosemary essential oil added to the feed of lambs improved the sensory properties of lamb meat (Smeti et al., 2018).
- Essential oils added to feed positively affect milk quality (Morsy et al., 2012).

Intensive research is being conducted on the fact that essential oils exhibit antimicrobial activity and can be natural alternatives to traditional antibiotics in terms of animal health. Essential oils with anti-inflammatory activity have significant potential in relieving inflammatory processes. (Gheorghe-Irimia et al., 2022). It has been explained that oils such as peppermint and fennel essential oil, which have carminative properties, can be used to reduce digestive disorders in animals.

3.3. PLANT GROWTH REGULATORS

Events such as growth, development and differentiation in plants occur thanks to plant growth hormones. These substances are either produced by plants or are given externally to plants. These plant hormones, called phytohormones, are synthesized in very low amounts in one part of the plant and can be transported to other plant parts. Phytohormones cause major physiological reactions (Kumlay and Eryiğit, 2011).

These substances, mainly derived from secondary metabolites, are responsible for the adaptation of plants to environmental conditions (Aftab et al., 2010; Naeem et al. 2011; Jamwal et al., 2018). Various phytohormones play an important role in the ability of plants to adapt to different abiotic and biotic stresses such as drought, salinity and temperature (Verma et al. 2016). Some common plant secondary metabolites, such as abscisic acid, salicylic acid, gibberellins, cytokinin, jasmonic acid, and ethylene, play important roles in plant defense responses against biotic and abiotic stresses (Smolander et al., 2012).

4. CONCLUSION

In recent years, because of the widespread use of chemical pesticides in areas where plant production is carried out, resistance to diseases and pests, environmental pollution, residue and similar problems have necessitated the search for alternative methods in plant protection activities. Essential oils and other secondary metabolites obtained from plants exhibit strong activity against many pests and microorganisms in agricultural areas. Secondary metabolites, which are natural products obtained from plants, decompose in a short time, do not cause environmental pollution and do not create residues. These secondary metabolites also act as plant growth regulators. There are many studies shown that essential oils have the potential to be used in animal health and nutrition due to their wide range of biological activities. Research on the subject continues intensively around the world.

REFERENCES

Aftab, T., Khan, M.M., Idrees, M., Naeem, M., Singh, M., & Ram, M. (2010). Stimulation of crop productivity, photosynthesis and artemisinin production in *Artemisia annua* L. by triacontanol and gibberellic acid application. J. Plant Interact., 1: 273-281.

Akman, Y., & Güney, K. (2006). Bitki Biyolojisi-Botanik. Pallme Yayınları, Ankara.

Al-Khayri, J.M., Rashmi, R., Toppo, V., Chole, P.B., Banadka, A., Sudheer, W.N., Nagella, P., Shehata, W.F., Al-Mssallem, M.Q., Alessa, F.M., Almaghasla, M.I., Rezk, A.A. (2023). Plant secondary metabolites: The weapons for biotic stress management. Metabolites, 13: 716.

Anulika, N.P., Ignatius, E.O., Raymond, E.S., Osasere, O.-I., Abiola, A. H. (2016). The chemistry of natural product: plant secondary metabolites. International Journal of Technology Enhancements and Emerging Engineering Research, 4: 1-8.

Awuchi, C.G. (2019). The biochemistry, toxicology, and uses of the pharmacologically active phytochemicals: alkaloids, terpenes, polyphenols, and glycosides. J. Food Pharm. Sci., 7: 131-150.

Badreddine, B. S., Ezzine, O., Dhahri, S., Chograni, H., & Ben Jamaa, M. L. (2015). Chemical composition of *Rosmarinus* and *Lavandula* essential oils and their insecticidal effects on *Orgyia trigotephras* (Lepidoptera, Lymantriidae). Asian Pacific Journal of Tropical Medicine, 8: 98-103.

Batish, D. R., Singh, H.P., Kohli, R.K., & Kaur, S. (2008). Eucalyptus essential oil as a natural pesticide. Forest Ecology and Management, 256: 2166-2174.

Benomari, F. Z., Andreu, V., Kotarba, J., Dib, M. E. A., Bertrand, C., Muselli, A., Costa, J.& Djabou, N. (2018). Essential oils from *Algerian species* of *Mentha* as new bio-control agents against phytopathogen strains. Environmental Science and Pollution Research International, 25: 29889-29900.

Bhavaniramya, S., Vishnupriya, S., Al-Aboody, M.S., Vijayakumar, R., & Baskaran D. (2019). Role of essential oils in food safety: Antimicrobial and antioxidant applications. Grain & Oil Science and Technology, 2: 49-55.

Butnariu, M., & Sarac, I. (2018) Essential oils from plants. Journal of Biotechnology and Biomedical Science, 1: 35-43.

Camina, J.L., Usseglio, V., Marquez, V., Merlo, C., Dambolena, J.S., Zygadlo, J.A., Ashworth, L. (2023). Ecological interactions affect the bioactivity of medicinal plants. Scientific Reports, 13: 12165.

Cavalcanti, E.S.B., Morais, S.M., Lima, M.A.A, & Santana, E.W.P. (2004). Larvicidal activity of essential oils from Brazilian plants against *Aedes aegypti* L. Mem Inst Oswaldo Cruz, Rio de Janeiro, 99 (5): 541-544.

Chaachouay, N., & Zidane, L. (2024). Plant-derived natural products: A source for drug discovery and development. Drugs and Drug Candidates, 3: 184-207.

Chandran, H., Meena, M., Barupal, T., & Sharma, K. (2020). Plant tissue culture as a perpetual source for production of industrially important bioactive compounds. Biotechnology Reports, 26: e00450.

Costa, O. B., Del Menezzi, C. H. S., Benedito, L. E. C., Resck, I. S., Vieira, R. F., & Bizzo, H. R. (2014). Essential oil constituents and yields from leaves of *Blepharocalyx salicifolius* (Kunt) O. Berg and *Myracrodruon urundeuva* (Allemão) collected during daytime. International Journal of Forestry Research, 3: 1-6.

Croteau, R., Kutchan, T.M., & Lewis, N.G. (2000). Natural products (secondary metabolites), in: B. Buchanan, W. Gruissem, R. Jones (Eds.), Biochemistry and molecular biology of plants. Rockville, Maryland: American Society for Plant Physiologists, pp. 1250-1319.

Davis, E.M., & Croteau, R. (2000). Cyclization enzymes in the biosynthesis of monoterpenes, sesquiterpenes, and diterpenes. Top. Curr. Chem., 209: 53-95.

Duchon, S., Bonnet, J., Marcombe, S., Zaim, M., & Corbel, V. (2009). Pyrethrum: A mixture of natural pyrethrins has potential for malaria vector control. Journal of Medical Entomology, 46: 516-522.

Duda, S. C., Mărghitaş, L. A., Dezmirean, D., Duda, M., Mărgăoan, R., & Bobiş, O. (2015). Changes in major bioactive compounds with antioxidant activity of *Agastache foeniculum*, *Lavandula angustifolia*, *Melissa officinalis* and *Nepeta cataria*: Effect of harvest time and plant species. Industrial Crops and Products, 77: 499-507.

Elshafie, H.S., Camele, I., & Mohamed, A.A. (2023). A comprehensive review on the biological, agricultural and pharmaceutical properties of secondary metabolites based-plant origin. Int. J. Mol. Sci., 24: 3266.

Ferreira, L., Rafael, D., Lima, C., De Andrade, K., Maria, D., Navarro, F., Lafaiete, J., Alves, R., & Nelson, G. (2020). Chemical composition and insecticidal effect of essential oils from *Illicium verum* and *Eugenia caryophyllus* on *Callosobruchus maculatus* in cowpea. Ind. Crop. Prod., 145: 112088.

Gheorghe-Irimia, R.A., Tăpăloagă, D., Tăpăloagă, P. R., Ilie, L. I., Șonea, C., & Șerban, A. I. (2022). Mycotoxins and essential oils-from a meat industry hazard to a possible solution: A brief review. Food Science, 11:3666.

Hussein,R., & El-Anssary, A. (2019). Plants secondary metabolites: The key drivers of the pharmacological actions of medicinal plants. P. F. Builders (Ed.), *In: Herbal Medicine*, IntechOpen Ltd., London.

Isman, M. B., Wilson, J.A., & Bradbury, R. (2008). Insecticidal activities of commercial rosemary oils (*Rosmarinus officinalis*) against larvae of *Pseudaletia unipuncta* and *Trichoplusia ni.* in relation to their chemical compositions. Pharmaceutical Biology, 46: 82-87.

Jamwal, K., Bhattacharya, S., & Puri, S. (2018). Plant growth regulator mediated consequences of secondary metabolites in medicinal plants. J. Appl. Res. Med. Arom. Plants, 9: 26-38.

Kabera, J.N., Semana, E., Mussa, A.R., & He. X. (2014). Pplant secondary metabolites: biosynthesis, classification, function and pharmacological properties. Journal of Pharmacy and Pharmacology, 2: 377-392.

Kerdchoechuen, O., Laohakunjit, N. & Singkornard, S. (2010). Essential oils from six herbal plants for biocontrol of the maize weevil. Hortcultural Science, 45: 592-598.

Khosravi, R., & Jalali Sendi, J.J. (2013). Effect of neem pesticide (Achook) on midgut enzymatic activities and selected biochemical compounds in the hemolymph of lesser mulberry pyralid, *Glyphodes pyloalis* Walker (Lepidoptera: Pyralidae). J Plant Prot Res., 53: 238-247.

Kimbaris, A. C., Gonz´alez-Coloma, A., Andr´es, M. F., Vidali, V. P., Polissiou, M. G., & Santana-M´eridas, O. (2017). Biocidal compounds from Mentha sp. essential oils and theirstructure-activity relationships. Chemistry and Biodiversity, 14: e1600270.

Koschier, E.H., & Sedy, K.A. (2003): Labiate essential oils affecting host selection and acceptance of *Thrips tabaci* Lindeman. Crop Prot, 22: 929-934.

Kumar, P., Mishra, S., Malik, A., & Satya, S. (2013). Housefly (*Musca domestica* L.) control potential of *Cymbopogon citratus* Stapf. (Poales: Poaceae) essential oil and monoterpenes (citral and 1,8-cineole). Parasitol Res, 112: 69-76.

Kumlay, A.M., & Eryiğit, T. (2011). Growth and development regulators in plants: plant hormones. Iğdır Univ. J. Inst. Sci. & Tech., 1: 47-56.

Lyubenova, A., Georgieva, L., & Antonova, V. (2023) Utilization of plant secondary metabolites for plant protection. Biotechnology & Biotechnological Equipment, 37(1): 2297533.

Mahieu F., Owsianik, G., Verbert, L., Janssens, A., De Smedt, H., & Nilius B. (2007). TRPM8- independent menthol-induced Ca2+ release from endoplasmic reticulum and Golgi. Journal of Biological Chemistry, 282: 3325–3336.

Mammadov, R. (2014). Tohumlu Bitkilerde Sekonder Metabolitler. Nobel Yayıncılık, Ankara.

Matsuda, K. (2012). Pyrethrin biosynthesis and its regulation in *Chrysanthemum cinerariaefolium*. Top Curr Chem., 314: 73-81.

Mera, I.F.G., Falconí, D.E.G., & Córdova. V.M. (2019). Secondary metabolites in plants: main classes, phytochemical analysis and pharmacological activities. Revista Bionatura, 4:1000-1009.

Morsy, T.A., Kholif, S.M., Matloup, O.H., Abdo, M.M., & El-Shafie, M.H. (2012). Impact of anise, clove and juniper oils as feed additives on the productive performance of lactating goats. Int. J. Dairy Sci., 7:20-28.

Moslemi, A., Ades, P. K., Crous, P. W., Groom, T., Scott, J. B., Nicolas, M. E., & Taylor, P. W. J. (2018). *Paraphoma chlamydocopiosa* sp. nov. and *Paraphoma pye* sp. nov., two new species associated with leaf and crown infection of pyrethrum. Plant Pathology, 67: 124-135.

Naeem, M., Khan, M.M.A., Idrees, M., & Aftab, T. (2011). Triacontanol-mediated regulation of growth yield, physiological activities and active constituents of *Mentha arvensis* L. Plant Growth Reg., 65: 195-206.

Nehme, R., Andrés, S., Pereira, R.B., Ben Jemaa, M., Bouhallab, S., Ceciliani, F., López, S., Rahali, F.Z., Ksouri, R., Pereira, D.M., & Andennebi-Najar, L. (2021). Essential Oils in Livestock: From Health to Food Quality. Antioxidants, 10: 330.

Ntalli N. G., Ferrari F., Giannakou I., & Menkissoglu-Spiroudi, U. (2010). Phytochemistry and nematicidal activity of the essential oils from 8 Greek Lamiaceae aromatic plants and 13 terpene components. Journal of Agricultural and Food Chemistry, 58: 7856-7863.

Papathanasopoulos, A., Rotondo, A., Janssen, P., Boesmans, W., Farré, R., & Vanden Berghe, P. (2013). Effect of acute peppermint oil administration on gastric sensorimotor function and nutrient tolerance in health. Neurogastroenterology and Motility, 25: 263-271.

Perveen, S. (2018). Introductory Chapter: Terpenes and Terpenoids. IntechOpen. doi: 10.5772/intechopen.79683.

Pichersky, E., Noel, J., & Dudareva, N. (2006). Biosynthesis of plant volatiles: Nature's diversity and ingenuity. Science, 311: 808-811.

Reshi, Z.A., Ahmad, W., Lukatkin, A.S., & Javed, S.B. (2023). From nature to lab: a review of secondary metabolite biosynthetic pathways, environmental influences, and in vitro approaches. Metabolites, 13: 895.

Sharafzadeh, S. (2011). Pyrethrum, coltsfoot and dandelion: important medicinal plants from Asteraceae family. Australian Journal of Basic and Applied Sciences, 5: 1787-1791.

Sharifi-Rad, J., Sureda, A., Tenore, G.C., Daglia, M., Sharifi-Rad, M., Valussi, M., Tundis, R., Sharifi-Rad, M., Loizzo, M.R., Ademiluyi, A.O., Sharifi-Rad, R., Ayatollahi, S.A., & Iriti, M. (2017). Biological activities of essential oils: From plant chemo ecology to traditional healing systems. Molecules, 22: 70.

Sinthusiri, J., & Soonwera, M. (2013). Efficacy of herbal essential oils as insecticides against the housefly, *Musca domestica* L. Southeast Asian J Trop Med Public Health, 44: 188-196.

Smeti, S., Hajji, H., Mekki, I., Mahouachi, M., Atti, N. (2018). Effects of dose and administration form of rosemary essential oils on meat quality and fatty acid profile of lamb. Small Rumin. Res., 158: 62-68.

Smolander, A. Kanerva, S., Adamczyk, B., & Kitunen, V. (2012). Nitrogen transformations in boreal forest soils-Does composition of plant secondary compounds give any explanations? Plant Soil, 350: 1-26.

Verma, V., Ravindran, P., & Kumar, P.P. (2016). Plant hormone-mediated regulation of stress responses. BMC Plant Biol., 16: 86.

Vishnupriya, S., Al-Aboody, M.S., Vijayakumar, R., & Baskaran, D. (2019). Role of essential oils in food safety: Antimicrobial and antioxidant applications. Grain & Oil Science and Technology, 2: 49-55,

Yang, T., Gao, L., Hu, H., Stoopen, G., Wang, C., & Jongsma, M.A. (2014). Chrysanthemyl diphosphate synthase operates in plants as a bifunctional enzyme with chrysanthemol synthase activity. J. Biol. Chem., 289: 36325-36335.

Yazdani, E., Sendi, J.J., & Hajizadeh, J. (2014). Effect of *Thymus vulgaris* L. and *Origanum vulgare* L. EOs on toxicity, food consumption, and biochemical properties of lesser mulberry pyralid *Glyphodes pyloalis* Walker (Lepidoptera: Pyralidae). J Plant Prot Res., 54, 53-61.

Yeshi, K., Crayn, D., Ritmejerytė, E., Wangchuk, P. (2022). Plant secondary metabolites produced in response to abiotic stresses has potential application in pharmaceutical product development. Molecules, 27: 313.

Zhang, S.T., Zhu, C., Lyu, Y.M., Chen, Y., Zhang, Z.H., Lai, Z.X., & Lin, Y.L. (2020). Genome-wide identification, molecular evolution, and expression analysis provide new insights into the APETALA2/ethylene responsive factor (AP2/ERF) superfamily in *Dimocarpus longan* Lour. BMC Genomics, 21: 62.

CHAPTER III

PHYTOCHEMICALS AND BIOLOGICAL ACTIVITIES OF *Satureja hortensis* ESSENTIAL OIL

Assoc. Prof. Dr. Cennet YAMAN [1]
Graduate Student Ahmet TOPAL[2]

DOI: https://dx.doi.org/10.5281/zenodo.13826026

[1] Yozgat Bozok University, Department of Field Crops, Faculty of Agriculture, Yozgat,Türkiye. ORCID ID: 0000-0002-2364-8171, e-mail: cennet.yaman@ yobu.edu.tr
[2] Yozgat Bozok University, Graduate Education Institute, Department of Agricultural Sciences, Yozgat, Türkiye. ORCID ID: 0009-0003-9918-454X,
e-mail: ahmet.topal@yobu.edu.tr

INTRODUCTION

Medicinal and aromatic plants are an important source of industrial medicinal products that are widely cultivated and distributed in many regions of the world. Generally, they belong to the families Lamiaceae, Liliaceae, Gentianaceae, Boraginaceae, Papaveraceae and Rutaceae, many of which contain specie from which important bioactive compounds such as polyphenols, alkaloids and essential oils (Zhou et al., 2014). Essential oils are complex mixtures of natural substances (secondary metabolites) that plants secrete to protect themselves against predators and harsh environmental conditions.

Essential oils are widely found in the Lamiaceae family, and many species have been used as aromatic herbs and spices since ancient times. Today, there is an increasing demand for essential oils produced on large and small scales worldwide for use in cosmetics, perfume, aromatherapy and holistic medicine, as well as in the food industry (Zhou et al., 2014; Do et al., 2015; Hassanzadeh et al., 2016).

Lamiaceae (Labiatiae) is one of the largest angiosperm plant families, distributed worldwide and containing approximately 240 genera and 7,000 species (Napoli et al., 2020). The *Satureja* genus belonging to this family, consists of plants in shrub form, containing approximately 43 species that are generally aromatic and are widespread worldwide, mostly in the Mediterranean, Asia, and parts of the United States, with the remainder distributed from Western Europe and North Africa to the Altai-Western Himalayas (Duman et al., 2023). Due to its aromatic properties, the leaves and aerial parts of this genus have a unique and pleasant taste (Eminagaoglu et al., 2007). Satureja species are popular due to their pleasant smell and flavor, as well as secondary metabolites, so these species are highly preferred as medicinal plants and natural food additives (Sefidkon and Emami Bistgani, 2021). The flowers, leaves, stems and seeds of most *Satureja* species around the world have been traditionally used in the treatment of various diseases and complications such as diarrhea, nausea, myalgias, infectious diseases and gastrointestinal cramps (Güllüce et al., 2003).

Many species of *Satureja* worldwide have been pharmacologically evaluated for secondary metabolites and their therapeutic applications. One of these species, *Satureja hortensis* L. (summer savory), is one of the most popular

Satureja species. It is an annual herb that blooms with violet tubular flowers from July to September in the Northern Hemisphere. It has relatively thin leaves and grows to a height of 30-60 cm. *S. hortensis* is a well-known plant in eastern Canada (Burlando et al., 2010).

The main components of *S. hortensis* essential oil (SEO) are carvacrol, thymol, p-cymene, γ-terpinene, β-pinene, caryophyllene, α-pinene, α-terpinolene, and, α-thugene which have antimicrobial activities (Raut and Karuppayil, 2014; Nikolić et al., 2014; Farzaneh et al., 2015; Jafari et a., 2016; Sharifzadeh et al., 2016). Due to its well-known properties, SEO is used in various fields of application, from the food industry to aromatherapy, ethnomedical. Therefore, this study focused on the components of *Satureja hortensis* essential oils and its important biological activities.

1. CHEMICAL COMPONENTS OF SEO

The yield and quality of *Satureja hortensis* essential oil (SEO) are affected by factors such as genotype, plant part, harvest period and environmental conditions, as well as purification practices (Baydar et al., 2004).

For chemical profiling, water is used to extract essential essential oil from air-dried plants through 3 (British Pharmacopoeia, 1988) or 4-hour ((Farmakopea Polska VI, 2002) hydrodistillation in a clevenger-type apparatus When previous studies are examined, the SEO yield can increase up to approximately 5% (Table 1). It is affected by the location of the plant, harvest period, plant part, culture or wild form.There are studies highlighting that ultrasound and microwave assisted applications instead of traditional hydrodistillation methods are a promising approach for the extraction of SEO (Rezvanpanah et al., 2011; Memarzadeh et al., 2020; Šeregelj et al., 2022).

Table 1: Main component profile of *Satureja hortensis* essential oils presented in previous studies

Plant source	SEO yield (%)	Main components (%)	Origin	Reference
Aerial parts	1.28-4.75	carvacrol (3.1-54.60), γ-terpinene (21.3-41.4), α-terpinene (2.1-4.5), p-cymene (2.6-13.8)	Turkey, wild-growing	Başer et al., 2004
	1.30-2.67	carvacrol (41.7-63.0), γ-terpinene (23.5-41.5), p-cymene (2.6-8.1), α-terpinene (2.1-4.3)	Turkey, cultivated	
Aerial parts, beginning of flowering stage	-	Carvacrol (67.00), γ-terpinene (15.30), p-cymene (6.73), α-terpinene (1.29)	Serbia, cultivated	Mihajilov-Krstev et al., 2009
Aerial parts	-	Thymol (28.2), p-cymene (19.6), γ-terpinene (16.0), carvacrol (11.0), β-pinene (4.5), sabinene (4.4),	Iran, cultivated	Mahboubi et al., 2011
Aerial parts	2.4	Carvacrol (48.0), γ-terpinene (24.2), p-cymene (11.7), α-thujene (2.3), α-pinene (2.5), myrcene (2.5), β-pinene (1.6)	Iran, wild-growing	Farzaneh et al., 2015
Aerial parts, beginning of flowering stage	2.2-3.5	Carvacrol (41.4-50.5), γ-terpinene (32.7-38.7), p-cymene (3.4-5.5), α-terpinene (3.8-4.9)	Turkey, cultivated	Katar et al., 2017
Different storage conditions of SEO	-	carvacrol (50.69), γ-terpinene (35.4), p-cymene (2.53), α-terpinene (3.79)	Iran	Mohtashami et al., 2018
Aerial part, Flowering stage	2.47-3.65	Carvacrol (19.0–46.6), γ-terpinene (11.6–24.8), p-cymene (9.84–34.6), myrcene (1.4–2.78), β-pinene (1.2–1.98)	Iran, cultivated	Estaji et al., 2018

Aerial parts	-	carvacrol (73.24), o-cymene (7.37), γ-terpinene (6.13)	Poland	Magierowicz et al., 2019
Aerial part	1.0	carvacrol (48.51), γ-terpinene (36.63), p-cymene (3.93), α-terpinene (2.71)	Egypt	Abou Baker et al., 2020
Aerial part, Arbuscular mycorrhizal fungi and plant growth-promoting rhizobacteria	1.32-1.77	carvacrol (43.0-52.8), γ-terpinene (34.8-1.84), α-terpinene (3.0- 4.14)	Iran, cultivated	Khalediyan et al., 2021
Aerial part, Flowering stage	-	carvracol (48.7–53.25), γ-terpinene (32.7–36.8), p-cymene (3.2-3.4), α-terpinene (2.9-3.5)	South Serbia, cultivated	Ilić et al. 2023

SEO, *Satureja hortensis* essential oil

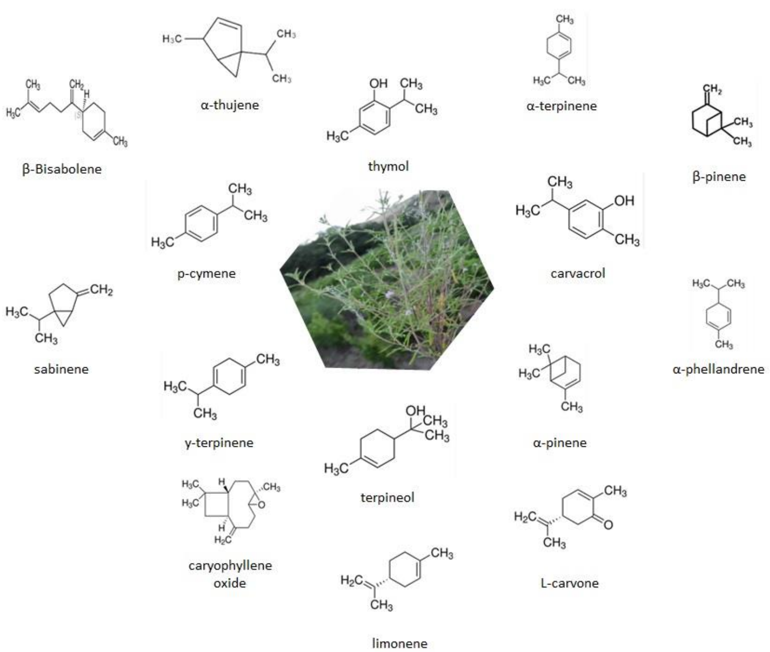


Figure 1: Essential oil components of *Satureja hortensis*

SEO consists of commercially important chemical components such as carvacrol, thymol and monoterpene hydrocarbons (p-cymene, β-pinene, camphene and limonene) (Hamidpour et al., 2014). Previous studies in Table 1 have shown that *Satureja hortensin* are chemically classified as carvacrol, thymol, p-cymene, γ-terpinene, p-cymene, α-terpinene, myrcene, β-pinene, sabinene and others (Figure 1).

As seen in Table 1, genetic and environmental factors cause diversity in the chemical profile of SEO. For example, Farmanpour-Kalalagh et al. (2020) reported that *S. hortensis* seeds and leaves have a total of 24 and 23 components, respectively, and while the seeds contain chemical components such as carvacrol, caryophyllene, estragole, the leaves contain more carvacrol, p-cymene, and γ-terpinene. Ilić et al. (2023) identified 26 compounds representing 100% of the total oil, and found carvracol (48.7–53.25%) and γ-terpinene (32.7–36.8%) as the main components of SEO in the flowering period, followed by p-cymene (3.2-3.4%), α-terpinene (2.9-3.5%).

2. BIOLOGICAL ACTIVITY OF SEO

Satureja species are one of the important medicinal and aromatic genera of the Lamiaceae family. They produce high-value phenolic compounds such as carvacrol and thymol in their essential oils. Therefore, it is widely known for its use as a food as well as for therapeutic purposes, especially as antimicrobial, anti-inflammatory, antioxidant, antidiabetic, anticancer and hepatoprotective (Hajhashemi et al., 2000; Hajhashemi et al., 2002; Christensen et al., 2009; Aşkun et al., 2012; Saeidi et al., 2013). Jafari et al. (2016) evaluated 13 species pharmacologically and found that *Satureja bachtiarica, Satureja hortensis, Satureja Montana,* and *Satureja khuzestanica* were the most active species both clinically and phytopharmacologically.

Table 2: Biological activities of *Satureja hortensis* essential oils presented in previous studies

Activity	Plant source	Main components	Origin	Reference
	Commercially available	-	Iran	Fathi et al., 2013
	Leaves/ cultivated	Carvacrol	Turkey	Feyzioglu et al., 2016
	Commercially available	Carvacrol, p-cymene, γ-terpinene	Iran	Shojaee-Aliabadi et al., 2013
	Aerial parts, wild-growing	p-Cymene, carvacrol, β-bisabolene	Iran	Samadi et al., 2015
	Commercially available	-	Iran	Sahari et al., 2012
Antioxidant	Chitosan microparticles, Commercially available	Carvacrol, p-cymene, γ-terpinene	Iran	Hosseini et al., 2013
	Aerial parts/ wild-growing	Carvacrol, thymol, α-terpinene, γ-terpinene, p-cymene	Turkey	Ceker et al., 2014
	Commercially available	Carvacrol, γ-terpinene, α-terpinene, p-cymene	Slovakia	Kačániová et al., 2017
	Aerial parts, cultivated	Carvacrol, γ-terpinene	Romania	Chambre et al., 2020
	Cultivated	Carvacrol, γ-terpinene	Egypt	Abou Baker et al., 2020
	Aerial parts/ cultivated	Thymol, carvacrol, p-cymene, other minor components	Iran	Mahboubi et al., 2011
Antimicrobial	Leaves/ chitosan nanoparticles	Carvacrol	Turkey	Feyzioglu et al., 2016
	Commercially available	Carvacrol, γ-terpinene and p-cymene	Iran	Shojaee-Aliabadi et al., 2013
	Chitosan microparticles,	Carvacrol, γ-terpinene, p-cymene	Iran	Hosseini et al., 2013

	Commercially available			
	Biopolymers, commercially available		Belgium	Iturriaga et al., 2012
	Aerial parts	γ-Terpinene, carvacrol	Iran	Sahakhiz et al., 2011
	Commercially available	Carvacrol, γ-terpinene, α-terpinene, p-cymene	Slovakia	Kačániová et al., 2017
	Leaves and flowers/ wild-growing	Carvacrol	Turkey	Gursoy et al., 2009
	Leaves/ cultivated	Thymol, γ-terpinene, carvacrol, p-cymene	Iran	Sharifzadeh et al., 2016
	Aierial parts, cultivated	Carvracol γ-terpinene	South Serbia	Ilić et al. 2023
	Aerial parts/ wild-growing	Thymol, other minor components	Iran	Shirzad et al., 2011
	Aerial parts/wild growing	Carvacrol and thymol	Turkey	Dikbas et al., 2011
	Aerial parts/ wild growing		Iran	Abdolahi et al., 2010
Antifungal	Aerial parts/ cultivated	thymol, carvacrol, synergetic effects	Iran	Abdollahi et al., 2011
	Aerial parts/ wild-growing	Carvacrol, thymol	Iran	Nabigol et al., 2011
	Leaves and flowers/ cultivated		Iran	Alizadeh et al., 2010
		Thymol, carvacrol	Iran	Alizadeh-Salteh et al., 2010
	Aerial parts/ wild-growing	carvacrol, p-cymene, γ-terpinene	Algeria,	Djenane et al., 2013
Antibacterial	Aerial parts/ wild-growing	Carvacrol thymol	Turkey,	Kotan et al., 2013
	Cultivated	Carvacrol, γ-terpinene	Egypt	Abou Baker et al., 2020

Antiparasitic	Aerial parts		Iran	Soosaraei et al., 2017
Larvicidal	Aerial parts/ wild-growing	Carvacrol, γ-terpinene, p-cymene, α-terpinene, myrcene, β-bisabolene	Czech Republic	Pavela et al., 2009
Acaricidal	Aerial parts/ wild-growing	Monoterpenes and monoterpene hydrocarbons	Iran	Ahmadi et al., 2018
Insecticidal	Aerial parts/ wild-growing	Carvacrol, thymol, p-cymene	Turkey	Tozlu et al., 2011
	Aerial parts/Ewild-growing		Turkey	Yildirim et al., 2011
	Aerial parts/cultivated	Carvacrol, γ-terpinene, p-cymene/volatile components in isolates	Czech Republic	Sajfrtova et al., 2013
Herbicidal/germination inhibition	Aerial parts	carvacrol, o-cymene, γ-terpinene	Poland	Magierowicz et al., 2019
	Aerial parts/ wild-growing	Carvacrol, γ-terpinene, minor components	Iran	Hazrati et al., 2017
Antinociceptive, Anti-inflammatory	Seeds/ wild-growing	γ-Terpinene, thymol/flavonoids, polyphenoli	Iran	Hajhashemi et al., 2012
Anticancer, Chemopreventive	Commercially available	-	Great Britain	Misharina et al., 2011
Cytotoxic effect	Cultivated	Carvacrol, γ-terpinene	Egypt	Abou Baker et al., 2020
	Aerial parts, wild-growing	Thymol, Spathulenol	Saudi Arabia	Huwaimel et al., 2023

2.1. Antimicrobial Activity

Numerous studies have been conducted focusing on the antibacterial properties of SEO and their possible importance in nutritional protection (Ghalfi et al., 2007). Essential oils damage the cell membrane by affecting enzyme activity and genetic resources in bacteria. In particular, the chemical structure of essential oils interacts with the phospholipid bilayer in the bacterial cell membrane and disrupts it (Rezvanpanah et al., 2011). SEO is rich in carvacrol and thymol, which are isomeric compounds containing a phenylic acid group in its structure. These compounds suppress the diversity of microbes, including bacteria and fungi (Razzaghi-Abyaneh et al., 2008). Oussalah et al. (2006) found that SEO was effective against the *Pseudomonas putida* strain obtained from meat, as well as *S. aureus, S. typhimurium, Listeria monocytogenes* and *E. coli*. Pintore et al. (2002) tested the antiseptic effect of SEO and noted that it had the best antibacterial effect against *Acinetobacter* spp. and *S. aureus* species. It also shows antibacterial activity against *Staphylococcus* and *E. coli* species (Wilkinson et al., 2003). In addition, it has been noted to exhibit great activity against *Enterobacter* spp. and *Enterococcus* spp., *S. pyogenes, P. mirabilis* (Wilkinson et al., 2003). Mahboubi and Kazempour (2011) revealed in their study the antimicrobial activity of SEO against various Gram-positive and Gram-negative microorganisms. Abou Baker et al. (2020) listed the tested foodborne pathogenic bacteria according to their sensitivity to SEO as follows: *Pseudomonas aeruginosa* > *Escherichia coli* = *Salmonella typhimurium* > *Staphylococcus aureus* > *Listeria monocytogenes*. Ilić et al. (2023) reported that it exhibited potent antibacterial activity against *Bacillus subtilis* (zone of inhibition 34.7-41.0 mm), *Escherichia coli* (44.3-48 mm), *Klebsiella pneumoniae* (28.3-29.0 mm) and *Proteus vulgaris* (21.0-24.3mm).

2.2. Antioxidant Activities

Many studies have indicated that Satureja essential oils are a rich source of active compounds such as carvacrol, γ-terpinene, p-cymene, thymol, linalool and β-caryophyllene.These compounds have strong antioxidant properties (Ruberto and Baratta, 2000). SEO was evaluated for antioxidant properties in oxidative stress and matrix metalloproteinase (MMP) excess expression/activity, with reference to antibacterial and antibiofilm activities against periodontal pathogens. Treatment with 1 - 5 µL/mL SEO inhibited MMP activity and H_2O_2-induced cell death (Zeidán-Chuliá et al., 2013). Behravan et al. (2007) reported that essential oil (1 - 2.5 µL/mL) of *S. hortensis* could reduce hydrogen peroxide-induced oxidative damage in rat lymphocytes. The antioxidant effects of SEO on safflower oil oxidation were examined by different relevant methods such as β-carotene bleaching, ABTS, DPPH, ferric thiocyanate and the different concentrations of the SEO showed significant activities (Fathi et al., 2013). In the DPPH assay, essential oils of *S. hortensis* plants grown in the shaded-unshaded zone showed an IC_{50} of 0.99 - 1.01 µg/mL (Ilić et al., 2023). Abou Baker et al. (2020) indicated that SEO exhibited a higher radical scavenging activity on DPPH (12.679 mg Trolox/g) and ABTS (1038.66 mg Trolox/g) radicals. It was also confirmed by Momtaz and Abdollahi (2010) and Chkhikvishvili et al. (2013) reported that SEOs exhibited high antioxidant activity.

2.3. Anti-inflammatory, Antinociceptive and Healing Activities

S. hortensis has been used in traditional treatments for bone pain and muscle relaxant. Hajhashemi et al.(2002) report that S. hortensis has been traditionally used as anti-inflammatory and an analgesic. Also, Momtaz and Abdollahi (2010) pointed out that *Satureja* species, including *S. hortensis* and *Satureja khuzestanica*, act as anti-inflammatory drugs and are equivalent to indomethacin, prednisolone and even morphine. Zeidán-Chuliá et al. (2015) revealed therapeutic effects for periodontal inflammation of SEO, reducing the live/dead bacteria ratio and increasing membrane permeability. Essential oil of *S. hortensis* seeds were evaluated by Hajhashemi et al. (2012) for possible anti-inflammatory and analgesic activities. They reported in their study that pretreatment with this oil and other extracts of *S. hortensis* reduced acetic acid-induced abdominal twitching and paw edema.

2.4. Gastrointestinal Activities

SEO was evaluated for antispasmodic activity on contractions of the isolated ileum compared to the effect of atropine and dicyclomine. The SEO (0.1 mL/100 g) was able to prevent castor oil-induced diarrhea in mice (Hajhashemiet al., 2000).

2.5. Alzheimer's Disease

Carvacrol and thymol are abundant in *Satureja* species, which can work as lower cholinesterase inhibitors and protect humans from oxidative stress and amnesia, although they do not cause negative side effects (Öztürk, 2012). Hamidpour et al. (2014) have confirmed that various *Satureja* species can protect against Alzheimer's, and even cardiovascular and diabetes.

2.6. Anti-cancer Activity

Findings from a previous study show that carvacrol has anti-carcinogenic properties and can be used as a drug in cancer treatment (Koparal and Zeytinoğlu, 2003). Hamidpour et al. (2014) reported that various *Satureja* species can protect against cancer cells.

2.7. Toxicity

An in vitro study of Behravan et al. (2006) showed that essential oil of *S. hortensis* protected rat lymphocytes from damage caused by hydrogen peroxide. Abou Baker et al. (2020) declared that the cytotoxic effect of SEO in the normal cell was determined using MTT (3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyl tetrazolium bromide). SEO showed cytotoxic effects on epithelial (phoenx-eco), kidney (THLE2) and normal lung (WI38) cells after 72 h of treatment (IC_{50} values: 31.62, 55.51 and 56.49 µg/mL, respectively).

3. CONCLUSION AND RECOMMENDATIONS

The main essential oil components of summer spice (*Satureja hortensis* L.) herb, leaves and seeds vary among genotypes and environmental factors in different locations. Most studies highlight its antimicrobial and strong antioxidant activities, which are closely related to the presence of rich monoterpenes in this species. In the future, it is necessary to conduct studies showing the application areas of SEO that can be used as a natural product.

REFERENCES

Abdolahi, A., Hassani, A., Ghosta, Y., Bernousi, I., & Meshkatalsadat, M. (2010). Study on the potential use of essential oils for decay control and quality preservation of Tabarzeh table grape. Journal of Plant Protection Research, 50(1): 45-52.

Abdollahi, A. L. I., Hassani, A., Ghosta, Y., Meshkatalsadat, M. H., & Shabani, R. (2011). Screening of antifungal properties of essential oils extracted from sweet basil, fennel, summer savory and thyme against postharvest phytopathogenic fungi. Journal of Food Safety, 31(3): 350-356.

Abou Baker, D.H., Al-Moghazy, M., & ElSayed, A.A.A. (2020). The in vitro cytotoxicity, antioxidant and antibacterial potential of *Satureja hortensis* L. essential oil cultivated in Egypt. Bioorganic chemistry, 95: 103559.

Ahmadi, Z., Saber, M., Akbari, A., & Mahdavinia, G. R. (2018). Encapsulation of *Satureja hortensis* L.(Lamiaceae) in chitosan/TPP nanoparticles with enhanced acaricide activity against Tetranychus urticae Koch (Acari: Tetranychidae). Ecotoxicology and Environmental Safety, 161: 111-119.

Alizadeh, A., Zamani, E., Sharaifi, R., Javan-Nikkhah, M., & Nazari, S. (2010). Antifungal activity of some essential oils against toxigenic *Aspergillus* species. Communications in agricultural and applied biological sciences, 75(4): 761-767.

Alizadeh-Salteh, S., Arzani, K., Omidbeigi, R., & Safaie, N. (2010). Essential oils inhibit mycelial growth of Rhizopus stolonifer. European Journal of Horticultural Science, 75(6): 278.

Aşkun, T., Tümen, G., Satil, F., & Karaarslan, D. (2012). Active constituents of some *Satureja* L. species and their biological activities. African Journal of Microbiology Research, 6(22): 4623-4633.

Başer, K.H.C., Özek, T., Kirimer, N., & Tümen, G. (2004). A comparative study of the essential oils of wild and cultivated *Satureja hortensis* L. Journal of Essential Oil Research, 16(5): 422-424.

Baydar, H., Sağdiç, O., Özkan, G., & Karadoğan, T. (2004). Antibacterial activity and composition of essential oils from *Origanum*, *Thymbra* and *Satureja* species with commercial importance in Turkey. Food Control, 15(3): 169-172.

Behravan, J., Mosaffa, F., Karimi, G. R., & Iranshahi, M. (2007). In vitro protective effects of *Satureja hortensis* L. essential oil and ethanolic extract on lymphocytes DNA. Journal of Medicinal Plants, 6(22): 64-70.

Behravan, J., Mosaffaa, F., Karimi, G., & Iranshahi, M. (2006). Antigenotoxic effects of *Satureja hortensis* L on rat lymphocytes exposed to oxidative stress. Planta Medica, 72(11): 003.

British Pharmacopoeia, (1988). HMSO, London, pp. 137-138.

Burlando, B., Verotta, L., Cornara, L., & Bottini-Massa, E. (2010). Herbal principles in cosmetics: Properties and mechanisms of action. CrC Press, Newyork.

Chambre, D. R., Moisa, C., Lupitu, A., Copolovici, L., Pop, G., & Copolovici, D. M. (2020). Chemical composition, antioxidant capacity, and thermal behavior of *Satureja hortensis* essential oil. Scientific Reports, 10(1): 21322.

Chkhikvishvili, I., Sanikidze, T., Gogia, N., Mchedlishvili, T., Enukidze, M., Machavariani, M., ... & Rodov, V. (2013). Rosmarinic acid-rich extracts of summer savory (*Satureja hortensis* L.) protect Jurkat T cells against oxidative stress. Oxidative Medicine and Cellular Longevity, Article ID 456253.

Christensen, K. B., Minet, A., Svenstrup, H., Grevsen, K., Zhang, H., Schrader, E., ... & Christensen, L. P. (2009). Identification of plant extracts with potential antidiabetic properties: effect on human peroxisome proliferator-activated receptor (PPAR), adipocyte differentiation and insulin-stimulated glucose uptake. Phytotherapy Research, 23: 1316-1325.

Ceker, S., Agar, G., Alpsoy, L., Nardemir, G., & Kizil, H. E. (2014). Antagonistic effects of *Satureja hortensis* essential oil against AFB, on human lymphocytes in vitro. Cytology and Genetics, 48: 327-332.

Dikbas, N., Dadasoglu, F., Kotan, R., & Cakir, A. (2011). Influence of summer savory essential oil (*Satureja hortensis*) on decay of strawberry and grape. Journal of Essential Oil Bearing Plants, 14(2): 151-160.

Djenane, D., Yangüela, J., Roncalés, P., & Aider, M. (2013). Use of essential oils as natural food preservatives: effect on the growth of *Salmonella* enteritidis in liquid whole eggs stored under abuse refrigerated conditions. Journal of Food Research, 2(3): 65.

Do, T.K.T., Hadji-Minaglou, F., Antoniotti, S., & Fernandez, X. (2015). Authenticity of essential oils. TrAC Trends in Analytical Chemistry, 66: 146-157.

Duman, H., Dirmenci, T., & Özcan, T. (2023). A new annual *Satureja* (Lamiaceae) species from Turkey with molecular evidence, and lectotypification of two species. Turkish Journal of Botany, 47(1): 61-72.

Eminagaoglu, O., Tepe, B., Yumrutas, O., Akpulat, H. A., Daferera, D., Polissiou, M., & Sokmen, A. (2007). The in vitro antioxidative properties of the essential oils and methanol extracts of *Satureja spicigera* (K. Koch.) Boiss. and *Satureja cuneifolia* ten. Food Chemistry, 100(1): 339-343.

Estaji, A., Roosta, H. R., Rezaei, S. A., Hosseini, S. S., & Niknam, F. (2018). Morphological, physiological and phytochemical response of different *Satureja hortensis* L. accessions to salinity in a greenhouse experiment. Journal of Applied Research on Medicinal and Aromatic Plants, 10: 25-33.

Farmakopea Polska VI. (2002). PTF(Warszawa). p. 151.

Farmanpour-Kalalagh, K., Mohebodini, M., & Sabaghnia, N. (2020). Comparison and correlation of the compositions in volatile constituents from different parts of summer savory (*Satureja hortensis* L.). International Journal of Horticultural Science and Technology, 7(3): 295-304.

Farzaneh, M., Kiani, H., Sharifi, R., Reisi, M., & Hadian, J. (2015). Chemical composition and antifungal effects of three species of satureja (*S. hortensis*, *S. spicigera*, and *S. khuzistanica*) essential oils on the main pathogens of strawberry fruit. Postharvest Biology and Technology, 109: 145-151.

Fathi, A., Sahari, M. A., Barzegar, M., & Naghdi Badi, H. (2013). Antioxidant activity of *Satureja hortensis* L. essential oil and its application in safflower oil. 67-51): 45(12, فصلنامه علمی پژوهشی گیاهان دارویی.

Feyzioglu, G. C., & Tornuk, F. (2016). Development of chitosan nanoparticles loaded with summer savory (*Satureja hortensis* L.) essential oil for antimicrobial and antioxidant delivery applications. Lwt, 70: 104-110.

Ghalfi, H., Benkerroum, N., Doguiet, D. D. K., Bensaid, M., & Thonart, P. (2007). Effectiveness of cell-adsorbed bacteriocin produced by *Lactobacillus curvatus* CWBI-B28 and selected essential oils to control *Listeria monocytogenes* in pork meat during cold storage. Letters in Applied Microbiology, 44(3): 268-273.

Güllüce, M., Sökmen, M., Daferera, D., Ağar, G., Özkan, H., Kartal, N., Polissiou, M., Sökmen, A. & Şahin, F. (2003). In vitro antibacterial, antifungal, and antioxidant activities of the essential oil and methanol extracts of herbal parts and callus cultures of *Satureja hortensis* L. Journal of Agricultural and Food Chemistry, 51(14): 3958-3965.

Gursoy, U. K., Gursoy, M., Gursoy, O. V., Cakmakci, L., Könönen, E., & Uitto, V. J. (2009). Anti-biofilm properties of *Satureja hortensis* L. essential oil against periodontal pathogens. Anaerobe, 15(4): 164-167.

Hajhashemi, V., Ghannadi, A., & Pezeshkian, S. K. (2002). Antinociceptive and anti-inflammatory effects of *Satureja hortensis* L. extracts and essential oil. Journal of Ethnopharmacology, 82(2-3): 83-87.

Hajhashemi, V., Sadraei, H., Ghannadi, A. R., & Mohseni, M. (2000). Antispasmodic and anti-diarrhoeal effect of *Satureja hortensis* L. essential oil. Journal of Ethnopharmacology, 71(1-2): 187-192.

Hajhashemi, V., Zolfaghari, B., & Yousefi, A. (2012). Antinociceptive and anti-inflammatory activities of *Satureja hortensis* seed essential oil, hydroalcoholic and polyphenolic extracts in animal models. Medical Principles and Practice, 21(2): 178-182.

Hamidpour, R., Hamidpour, S., Hamidpour, M., Shahlari, M., & Sohraby, M. (2014). Summer savory: From the selection of traditional applications to the novel effect in relief, prevention, and treatment of a number of serious illnesses such as diabetes, cardiovascular disease, Alzheimer's disease, and cancer. Journal of Traditional and Complementary Medicine, 4(3): 140-144.

Hassanzadeh, M. K., Tayarani Najaran, Z., Nasery, M. & Emami, S. A. (2016). Summer savory (*Satureja hortensis* L.). Preedy, V. R. (Ed.), Essential oils in food preservation, flavor and safety (pp. 757-764).Academic Press, UK.

Hazrati, H., Saharkhiz, M. J., Niakousari, M., & Moein, M. (2017). Natural herbicide activity of *Satureja hortensis* L. essential oil nanoemulsion on the seed germination and morphophysiological features of two important weed species. Ecotoxicology and Environmental Safety, 142: 423-430.

Hosseini, S. M., Hosseini, H., Mohammadifar, M. A., Mortazavian, A. M., Mohammadi, A., Khosravi-Darani, K., ... & Khaksar, R. (2013). Incorporation of essential oil in alginate microparticles by multiple emulsion/ionic gelation process. International Journal of Biological Macromolecules, 62: 582-588.

Huwaimel, B., Abouzied, A. S., Anwar, S., Elaasser, M. M., Almahmoud, S. A., Alshammari, B., Alrdaian, D. & Alshammari, R. Q. (2023). Novel landmarks on the journey from natural products to pharmaceutical formulations: Phytochemical, biological, toxicological and computational activities of *Satureja hortensis* L. Food and Chemical Toxicology, 179: 113969.

Ilić, Z. S., Milenković, L., Stanojević, L., Danilović, B., Šunić, L., Milenković, A., ... & Cvetković, D. (2023). Phytochemical composition and antimicrobial activities of the essential oils from summer savory (*Satureja hortensis* L.) growing in shading condition. Journal of Essential Oil Bearing Plants, 26(6): 1397-1409.

Iturriaga, L., Olabarrieta, I., & de Marañón, I. M. (2012). Antimicrobial assays of natural extracts and their inhibitory effect against Listeria innocua and fish spoilage bacteria, after incorporation into biopolymer edible films. International journal of food microbiology, 158(1): 58-64.

Jafari, F., Ghavidel, F., & Zarshenas, M. M. (2016). A critical overview on the pharmacological and clinical aspects of popular *Satureja* species. Journal of Acupuncture and Meridian Studies, 9(3): 118-127.

Kačániová, M., Terentjeva, M., Vukovic, N., Puchalski, C., Roychoudhury, S., Kunová, S., ... & Ivanišová, E. (2017). The antioxidant and antimicrobial activity of essential oils against Pseudomonas spp. isolated from fish. Saudi Pharmaceutical Journal, 25(8): 1108-1116.

Katar, D., Kacar, O., Kara, N., Aytaç, Z., Göksu, E., Kara, S., ... & Elmastaş, M. (2017). Ecological variation of yield and aroma components of summer savory (*Satureja hortensis* L.). Journal of Applied Research on Medicinal and Aromatic Plants, 7: 131-135.

Khalediyan, N., Weisany, W., & Schenk, P. M. (2021). Arbuscular mycorrhizae and rhizobacteria improve growth, nutritional status and essential oil production in *Ocimum basilicum* and *Satureja hortensis*. Industrial Crops and Products, 160: 113163.

Kizil, S., Turk, M., Özguven, M., & Khawar, K. M. (2009). Full blooming stage is suitable for herbage yield and essential oil content of summer savory (*Satureja hortensis* L.). Journal of Essential Oil Bearing Plants, 12(5): 620-629.

Koparal, A. T., & Zeytinoglu, M. (2003). Effects of carvacrol on a human non-small cell lung cancer (NSCLC) cell line, A549. Cytotechnology, 43(1): 149-154.

Kotan, R., Dadasoğlu, F., Karagoz, K., Cakir, A., Ozer, H., Kordali, S., Cakmakci, R. & Dikbas, N. (2013). Antibacterial activity of the essential oil and extracts of *Satureja hortensis* against plant pathogenic bacteria and their potential use as seed disinfectants. Scientia horticulturae, 153: 34-41.

Magierowicz, K., Górska-Drabik, E., & Sempruch, C. (2019). The insecticidal activity of *Satureja hortensis* essential oil and its active ingredient-carvacrol against *Acrobasis advenella* (Zinck.)(Lepidoptera, Pyralidae). Pesticide Biochemistry and Physiology, 153: 122-128.

Mahboubi, M., & Kazempour, N. (2011). Chemical composition and antimicrobial activity of *Satureja hortensis* and *Trachyspermum copticum* essential oil. Iranian Journal of Microbiology, 3(4): 194.

Memarzadeh, S. M., Gholami, A., Pirbalouti, A. G., & Masoum, S. (2020). Bakhtiari savory (*Satureja bachtiarica* Bunge.) essential oil and its chemical profile, antioxidant activities, and leaf micromorphology under green and conventional extraction techniques. Industrial Crops and Products, 154: 112719.

Mihajilov-Krstev, T., Radnović, D., Kitić, D., Zlatković, B., Ristić, M., & Branković, S. (2009). Chemical composition and antimicrobial activity of *Satureja hortensis* L. essential oil. Open Life Sciences, 4(3): 411-416.

Misharina, T. A., Burlakova, E. B., Fatkullina, L. D., Terenina, M. B., Krikunova, N. I., Vorob'eva, A. K., Erokhin, V. N. & Goloshchapov, A. N. (2011). Changes in fatty acid composition in the brain and liver in aging mice of high cancer risk AKR strain and effect of savory essential oil administration on leukemic process. Biomeditsinskaia Khimiia, 57(6): 604-614.

Mohtashami, S., Rowshan, V., Tabrizi, L., Babalar, M., & Ghani, A. (2018). Summer savory (*Satureja hortensis* L.) essential oil constituent oscillation at different storage conditions. Industrial Crops and Products, 111: 226-231.

Momtaz, S., & Abdollahi, M. (2010). An update on pharmacology of Satureja species; from antioxidant, antimicrobial, antidiabetes and anti-hyperlipidemic to reproductive stimulation. International Journal of Pharmcology, 6(4): 454-461.

Nabigol, A. (2011). Chemical composition and anti-fungal activities of three essential oils from Satureja spp. on four post-harvest pathogens of strawberry fruit. The Journal of Horticultural Science and Biotechnology, 86(4): 371-376.

Napoli, E., Siracusa, L., & Ruberto, G. (2020). New tricks for old guys: Recent developments in the chemistry, biochemistry, applications and exploitation of selected species from the Lamiaceae Family. Chemistry & Biodiversity, 17(3): e1900677.

Nikolić, M., Jovanović, K. K., Marković, T., Marković, D., Gligorijević, N., Radulović, S., & Soković, M. (2014). Chemical composition, antimicrobial, and cytotoxic properties of five Lamiaceae essential oils. Industrial Crops and Products, 61: 225-232.

Oussalah, M., Caillet, S., Saucier, L., & Lacroix, M. (2006). Antimicrobial effects of selected plant essential oils on the growth of a *Pseudomonas putida* strain isolated from meat. Meat Science, 73(2): 236-244.

Öztürk, M. (2012). Anticholinesterase and antioxidant activities of savoury (*Satureja thymbra* L.) with identified major terpenes of the essential oil. Food Chemistry, 134(1): 48-54.

Pavela, R. (2009). Larvicidal property of essential oils against Culex quinquefasciatus Say (Diptera: Culicidae). Industrial Crops and Products, 30(2): 311-315.

Pintore, G., Usai, M., Bradesi, P., Juliano, C., Boatto, G., Tomi, F., ... & Casanova, J. (2002). Chemical composition and antimicrobial activity of *Rosmarinus officinalis* L. oils from Sardinia and Corsica. Flavour and Fragrance Journal, 17(1): 15-19.

Raut, J. S., & Karuppayil, S. M. (2014). A status review on the medicinal properties of essential oils. Industrial Crops and Products, 62: 250-264.

Razzaghi-Abyaneh, M., Shams-Ghahfarokhi, M., Yoshinari, T., Rezaee, M. B., Jaimand, K., Nagasawa, H., & Sakuda, S. (2008). Inhibitory effects of *Satureja hortensis* L. essential oil on growth and aflatoxin production by *Aspergillus parasiticus*. International Journal of Food Microbiology, 123(3): 228-233.

Rezvanpanah, S., Rezaei, K., Golmakani, M. T., & Razavi, S. H. (2011). Antibacterial properties and chemical characterization of the essential oils from summer savory extracted by microwave-assisted hydrodistillation. Brazilian Journal of Microbiology, 42: 1453-1462.

Ruberto, G., & Baratta, M. T. (2000). Antioxidant activity of selected essential oil components in two lipid model systems. Food Chemistry, 69(2): 167-174.

Saeidi, S., Shiri, Y., Bokaeian, M., & Hassanshahian, M. (2013). Antibacterial activity of essential oil of *Satureja hortensis* against multi-drug resistant bacteria. International Journal Enteric Pathogen, 2(2): 1-4.

Saharkhiz, M. J., Zomorodian, K., Rezaei, M. R., Saadat, F., & Rahimi, M. J. (2011). Influence of growth phase on the essential oil composition and antimicrobial activities of *Satureja hortensis*. Natural Product Communications, 6(8): 1934578X1100600833.

Sajfrtova, M., Sovova, H., Karban, J., Rochova, K., Pavela, R., & Barnet, M. (2013). Effect of separation method on chemical composition and insecticidal activity of Lamiaceae isolates. Industrial Crops and Products, 47: 69-77.

Samadi, N., Masoum, S., Mehrara, B., & Hosseini, H. (2015). Application of linear multivariate calibration techniques to identify the peaks responsible for the antioxidant activity of *Satureja hortensis* L. and *Oliveria decumbens* Vent. essential oils by gas chromatography–mass spectrometry. Journal of Chromatography B, 1001: 75-81.

Sefidkon, F., & Emami Bistgani, Z. (2021). Integrative review on ethnobotany, essential oil, phytochemical, agronomy, molecular and pharmacological properties of *Satureja* species. Journal of Essential Oil Research, 33(2): 114-132.

Šeregelj, V., Šovljanski, O., Švarc-Gajić, J., Cvanić, T., Ranitović, A., Vulić, J., & Aćimović, M. (2022). Modern green approaches for obtaining

Satureja kitaibelii Wierzb. ex Heuff extracts with enhanced biological activity. Journal of the Serbian Chemical Society, 87(12): 1359-1365.

Sharifzadeh, A., Khosravi, A. R., & Ahmadian, S. (2016). Chemical composition and antifungal activity of *Satureja hortensis* L. essentiall oil against planktonic and biofilm growth of *Candida albicans* isolates from buccal lesions of HIV+ individuals. Microbial Pathogenesis, 96: 1-9.

Shojaee-Aliabadi, S., Hosseini, H., Mohammadifar, M. A., Mohammadi, A., Ghasemlou, M., Ojagh, S. M., Hosseini, S. Y. & Khaksar, R. (2013). Characterization of antioxidant-antimicrobial κ-carrageenan films containing Satureja hortensis essential oil. International journal of Biological Macromolecules, 52: 116-124.

Soosaraei, M., Fakhar, M., Teshnizi, S. H., Hezarjaribi, H. Z., & Banimostafavi, E. S. (2017). Medicinal plants with promising antileishmanial activity in Iran: a systematic review and meta-analysis. Annals of Medicine and Surgery, 21: 63-80.

Shirzad, H., Hassani, A., Abdollahi, A., Ghosta, Y., & Finidokht, S. R. (2011). Assessment of the preservative activity of some essential oils to reduce postharvest fungal rot on kiwifruits (*Actinidia deliciosa*). Journal of Essential Oil Bearing Plants, 14(2): 175-184.

Tozlu, E., Cakir, A., Kordali, S., Tozlu, G., Ozer, H., & Akcin, T. A. (2011). Chemical compositions and insecticidal effects of essential oils isolated from Achillea gypsicola, *Satureja hortensis*, *Origanum acutidens* and *Hypericum scabrum* against broadbean weevil (*Bruchus dentipes*). Scientia Horticulturae, 130(1): 9-17.

Sahari, M., Barzegar, M., Naghdi, B. H., & Vahidyan, H. (2012). Application of *Zataria multiflora* Boiss. and *Satureja hortensis* L. essential oils as two natural antioxidants in mayonnaise formulated with linseed oil. Journal: Journal of Medicinal Plants, 11(43): 69-79.

Wilkinson, J. M., Hipwell, M., Ryan, T., & Cavanagh, H. M. (2003). Bioactivity of *Backhousia citriodora*: antibacterial and antifungal activity. Journal of Agricultural and Food Chemistry, 51(1): 76-81.

Yildirim, E., Kordali, S. A. B. A. N., & Yazici, G. (2011). Insecticidal effects of essential oils of eleven plant species from Lamiaceae on *Sitophilus granarius* (L.)(Coleoptera: Curculionidae). Rom. Biotechnol. Lett, 16(6): 6702-6709.

Zeidán-Chuliá, F., Keskin, M., Könönen, E., Uitto, V. J., Söderling, E., Moreira, J. C. F., & Gürsoy, U. K. (2015). Antibacterial and antigelatinolytic effects of *Satureja hortensis* L. essential oil on epithelial cells exposed to *Fusobacterium nucleatum*. Journal of Medicinal Food, 18(4): 503-506.

Zeidán-Chuliá, F., Neves de Oliveira, B. H., Gursoy, M., Könönen, E., Fonseca Moreira, J. C., Gursoy, U. K., & Uitto, V. J. (2013). MMP-REDOX/NO interplay in periodontitis and its inhibition with *Satureja hortensis* L. essential oil. Chemistry & Biodiversity, 10(4): 507-523.

Zhou L., Xu J. & Peng Y. (2014). Medicinal Crops. Van Alfen, N. K. (Ed.), *Encyclopedia of Agriculture and Food Systems* (pp. 223-230). Elsevier, Academic Press, U.K.

CHAPTER IV

CANNABIS PHYTOCANNABINOIDS AND THEIR BIOLOGICAL ACTIVITY

Lecturer Hatice Beyza BAŞKAL DOĞANER[1]
Assoc. Prof. Dr. Cennet YAMAN [2]
Prof. Dr. Ufuk KOCA ÇALIŞKAN[3]

DOI: https://dx.doi.org/10.5281/zenodo.13826032

[1] Yozgat Bozok University, Vocational School of Health Services, Department of Pharmacy Services, Yozgat, Türkiye
ORCID ID: 0009-0002-6004-7196, e-mail: h.neyza.baskal@yobu.edu.tr
[2] Yozgat Bozok University, Faculty of Agriculture, Department of Field Crops, Yozgat,Türkiye.
ORCID ID: 0000-0002-2364-8171, e-mail: cennet.yaman@yobu.edu.tr
[3] Gazi University, Faculty of Pharmacy, Departnent of Pharmacognosy, Ankara, Türkiye
ORCİD ID: 0000-0002-5216-7588, e-mail: ukoca@gazi.edu.tr

INTRODUCTION

Hemp (*Cannabis sativa* L., Cannabaceae) is an important, a multipurpose herbaceous plant that has been cultivated since ancient times for industrial, medicinal and nutritional purposes (Vonapartis et al., 2015; Andre et al., 2016; Bonini et al., 2018). Hemp cultivation is thought to spread in China in B.C. the 2700s, and then in Asia, and then spread through Europe 2000-2200 years ago (Struik et al., 2000; Callaway, 2004).

The stalks of the hemp plant are used as fiber, which serves as raw material in the paper, textile, construction and mechanical industries (Ceyhan et al., 2002); its seeds are rich in nutrients such as nutritious oil and protein; and its leaves, flower stalks and roots contain commercially important bioactive compounds with a wide range of biological activities (Liu et al., 2022). However, in the 20th century, its cultivation was legally restricted in many countries due to the psychoactive effect of Δ-9-tetrahydrocannabinol (THC), one of the cannabis compounds (Liu et al., 2022). Subsequently, the benefits of the hemp plant were recognized and, in the commercial production of industrial hemp, according to the legal authorization of the respective governments of each country, threshold THC levels in flowering plant parts accepted as 0.1% (Colombia, several Australian states, Uruguay, Mexico and Switzerland), 0.2% (Europe) or 0.3% (USA, Brazil, China and Canada) by dry weight (Adhikary et al., 2021).

With the opening of the way for hemp cultivation, hemp is once again the center of attention in all over the world due to its multi-purpose applications and especially for its pharmaceutical properties. The cannabis plant carries about five hundred and forty-five phytochemicals of medicinal and economic importance. (Lowe et al., 2021). These include about 104 phytocannabinoids (including CBD, THC and CBG) (Table 1), 120 terpenoids, more than 26 flavonoids, phenolic amides, nitrogenous compounds, amino acids, lignans, steroids, alkaloids, fatty acids, stilbenes, vitamins, minerals and other phytochemicals (Lowe et al., 2021). They are formed in various above- and below-ground parts of the plant. The most notable compound of cannabis is cannabinoids, which are mainly found in the trichomes of the female flowers (Pollastro et al., 2018; Giupponi et al., 2020).

1. PHYTOCANNABINOIDS

Phytocannabinoids are chemically active compounds with proven therapeutic properties (Andre et al., 2016). To date, the phytocannabinoids isolated and identified from *C. sativa* are mainly divided into 10 chemical subgroups, namely THC (18 compounds), cannabigerol (CBG) (17 compounds), cannabinol (CBN) (10 compounds), cannabichromene (CBC) (8 compounds) and cannabidiol (CBD) (8 compounds) and others (Table 1) (ElSohly and Gul, 2014; Andre et al., 2016). Among phytocannabinoids, CBD and THC are generally the most abundant (Andre et al., 2016).

Table 1: Classification of phytocannabinoids in *Cannabis sativa* (ElSohly and Gul, 2014).

Chemical group	Abbreviations	Number of compounds
Δ^9-tetrahydrocannabinol	Δ^9-THC	18
Δ^8-tetrahydrocannabinol	Δ^8-THC	2
Cannabigerol	CBG	17
Cannabichromene	CBC	8
Cannabidiol	CBD	8
Cannabinodiol	CBND	2
Cannabielsoin	CBE	5
Cannabicyclol	CBL	3
Cannabinol	CBN	10
Cannabitriol	CBT	9
Others		22
Total		104

The most important psychoactive compound among the phytocannabinoids is thought to be THC and its most active isomer, the Δ9 (previously known as Δ1-THC) form in the plant. The other isomers such as the Δ8 isomer, previously called Δ6-THC, which has a relatively low psychoactive effect, is present in very low concentrations in the plant, (Mechoulam and Ben-Shabat, 1999).

Various derivatives of THC have also been synthesized, such as nabilone and dronabinol which are licensed for the alleviation of emesis, mostly due to cancer chemotherapy (Mechoulam and Ben-Shabat, 1999). Dexanabinol is the synthetic analog of THC identified by e-Therapeutics PLC as a potential anticancer agent (Juarez et al., 2021).

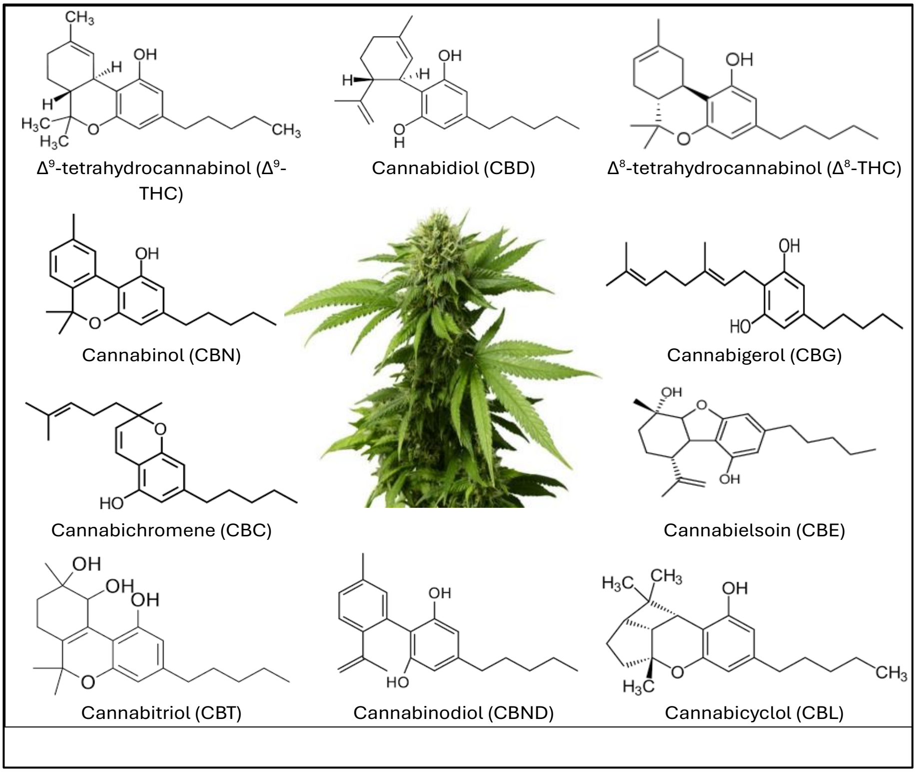


Figure 1. Structure of phytocannabinoids in *Cannabis sativa*.

Other most important compounds include cannabidiol (CBD), cannabigerol (CBG), cannabinol (CBN) that is a result of the oxidation of THC, cannabichromene (CBC) and olivetol, the precursor molecule in their biosynthesis. These phytocannabinoids are found in the plant together with carboxylic acid derivatives such as THCA, CBDA, CBGA, CBNA, CBCA. The pharmacokinetic properties of these derivatives may differ (Mechoulam and Ben-Shabat, 1999). Furthermore, these derivatives are converted into neutral cannabinoids (THC, CBD, CBG, etc.) through a decarboxylation process, whose rate depends on different factors. Essentially, the higher the temperature, the faster the conversion process (Citti at al., 2018).

2. BIOLOGICAL ACTIVITY

2.1. Traditional Use

The use of hemp to make paper, clothing and rope dates back as far as 10,000 BC in China (Abel, 2013). In the Neolithic Xianrendong region, more traces of Chinese ceramics decorated with hemp braided fibers dating back to 8000 BC have been reported. Hemp was also cultivated in Japan between 8000 and 300 BC and was used to make fiber for fabric and paper (Turner et al., 1980; Ramamoorthy et al., 2015).

However, the earliest reference to the psychotropic use of cannabis dates back to 2700 BC. Cannabis was recommended in Egypt in 1550 BC for vaginal inflammation (Veiga, 2009). In Greek medicine, Dioscorides' notes underline that the plant is psychotropic and Galen was concerned that “if we take too much it will damage the brain” (Dawson, 1934; Faulkner, 1969). It was among the 5 most important plants used in India for religious purposes. In the 1300s BC, the sacred books of the Indo-Aryans, the Atharva Veda, mentioned the stimulating and euphoric effects of cannabis (Ferrara, 2021). In Europe, hemp was used to make rope in Marseille (France) around 700 BC. The name Cannebiere (important street of the city) emphasizes the importance of hemp at that time (Bouloc, 2013).

C. sativa has been used in a wide variety of fields and has shown a high potential for usability with many applications (Clarke ve Merlin, 2016; Gedik ve Avinc, 2020; Rupasinghe et al., 2020; Gomez et al., 2021).

When we look at the use of cannabis as medicine, it is seen that various parts are utilized. There are many studies reporting the use of hemp, especially its seeds, as food (Callaway, 2004; Turner et al., 2019). The seeds are used as a hair strengthener when powdered and applied to the hair (El Khomsi et al., 2022). In addition to the above-mentioned uses, hemp seeds have been used to purify groundwater due to their high capacity to chelate polyfluoroalkyl and perfluoroalkyl substances, the so-called “eternal chemicals” (Turner et al., 2019).

The leaves are used externally as a poultice to treat eczema (El Khomsi et al., 2022) and subcutaneous tissue disorders (Klauke et al., 2014). It is also used orally in the treatment of central nervous system related disorders such as gas, cough and mucus (Rahmatullah et al., 2009; Mawla et al., 2012).

There are several studies describing the traditional uses of cannabis leaves, including the treatment of health problems such as itching, cancer, hypertension, snake and scorpion envenomation, rheumatoid arthritis (Rahmatullah et al. 2010), and gastrointestinal and circulatory disorders (Klauke et al., 2014). Cannabis leaves have sedative, narcotic and strong analgesic effects (Hussain et al., 2018).

The other part of cannabis used as medicine is the roots. They are taken orally in the form of juice and used for birth and postpartum bleeding problems, as well as for the treatment of inflammation, skin burns, joint pain, vermin and erysipelas infections (Ryz et al., 2017).

The leaves and inflorescences of *C. sativa* have been consumed as drugs in different forms due to their psychoactive effect (Clarke and Merlin, 2016; Knapp et al., 2019).

2.2. Use in Modern Medicine

Although the terminology for the health uses of the cannabis plant in historical texts differs from modern science, the traditional uses of cannabis have been comparable to those found in modern preclinical and clinical studies for phytocannabinoids and have been leading the way (Amar, 2006;; Baron, 2015; Gibbs et al., 2015; Grotenhermen et al., 2016; Weston-Green, 2018; Kuhathasan et al., 2019). Table 2 shows some biological activity studies on phytocannabinoids.

2.2.1. Antidiabetic activity

Diabetes is a chronic disease caused by the body's inability to produce or properly use insulin, a hormone produced in the pancreas that determines the level of sugar in the blood. Antidiabetic activity is usually assessed by measuring the inhibitory power of the α-amylase enzyme (Agarwal and Gupta, 2016). The enzyme α-amylase, often produced in the pancreas, converts large molecule carbohydrates into simple monosaccharides in the digestive system, increasing blood sugar levels, and then another enzyme, α-glucosidase, converts this product into glucose. Consequently, inhibiting these two enzymes can suppress the digestion of carbohydrates, delay the absorption of glucose into the blood and finally reduce the level of glucose in the blood. (Kajaria et al., 2013). Another method for assessing antidiabetic activity is aldose reductase inhibitors (ARIs). These inhibitors may prevent the reduction of glucose to sorbitol and reduce diabetes complications (Suzen and Buyukbingol, 2003). In a study, essential oils obtained from the above-ground parts of hemp with an oil ratio of 3.77 mmol ACAE/g (millimol acarbose equivalent in 1 gram extract) have been proven to perform α-glucosidase enzyme inhibition. This essential oil was also evaluated against α-amylase enzyme but did not show any significant results. (Zengin et al., 2018). A 2018 study by Smeriglio et al. showed that CBG and CBD and their acid derivatives can improve diabetic symptoms by inhibiting aldose reductase activity (Smeriglio et al., 2018). A randomized, double-blind, placebo-controlled clinical trial was conducted by Jadoon et al. (2016). In this study, 62 patients with type 2 diabetes unresponsive to insulin therapy were randomized to 5 treatment modalities; CBD (100 mg twice daily), THCV (5 mg twice daily), CBD and THCV in a 1:1 ratio (5 mg/5 mg twice daily), CBD and THCV in a 20:1 ratio (100 mg/5 mg twice daily) or matched placebo for 13 weeks. As a result, compared to placebo, THCV significantly reduced fasting plasma glucose and it was emphasized that THCV may represent a new therapeutic agent in glycemic control in individuals with type 2 diabetes (Jadoon et al., 2016).

Table 2: Biological activities of phytocannabinoids from *Cannabis sativa*

Compound	**Biological Activity**	**Source**
CBC	Antioxidant	Dawidowicz et al., 2021
	Anti-inflammatory	Delong et al., 2010
	Analgesic	Davis ve Hatoum, 1983
	Sedative	Davis ve Hatoum, 1983
	Antibacterial	Eisohly et al., 1982
	Antifungal	Eisohly et al., 1982
CBD	Tourette Syndrome	Mosley et al., 2023
	Antimelanoma, Antimelanogenic Antithyrosinase	Gaweł-Bęben et al., 2023
	Antiemetic	Grimison et al., 2020
	Parkinson's	Gugliandolo et al., 2020
	Immunomodulator	Peyravian et al., 2020
	Anti-inflammatory	Lowin et al., 2020
	Alzheimer's	Watt et al., 2017
	Antidiabetic	Jadoon et al., 2016

	Antirheumatoid	Burstein, 2015;
	Anticancer	Massi et al., 2013
	Anxiolytic	Schier et al., 2012
	Anticonvulsant	Hill et al., 2012
	Antipsychotic	Zuardi et al., 2006
	Neuroprotective antioxidant	Hampson et al., 1998
CBDA	Antioxidant	Dawidowicz et al., 2021
	Anti-inflammatory	Rock et al., 2018
	Antidiabetic	Smeriglio et al., 2018
CBG	Antidepressant	Russo et al., 2022
	Anxiolytic	Russo et al., 2022
	Reducing blood pressure	Vernail et al., 2022
	Analgesic	Russo et al., 2022
	Antidiabetic	Smeriglio et al., 2018
	Appetite stimulant	Brierley et al., 2017
THC	Tourette Syndrome	Mosley et al., 2023
	Anti-inflammatory	Li et al., 2022
	Anticancer	Li et al., 2022
	Muscle relaxant	Roychoudhury et al., 2021
	Alzheimer's	Cao et al., 2014
	Antispasmodic	Pacher et al., 2006
	Neuroprotective antioxidant	Hampson et al., 1998
	Analgesic	Sofia et al., 1973
	Antiedema	Sofia et al., 1973
THCV	Antidiabetic	Jadoon et al., 2016
	Anti-inflammatory	Bolognini et al., 2010
	Analgesic	Bolognini et al., 2010
	Antiepileptiform	Hill et al., 2010
	Anticonvulsant	Hill et al., 2010

2.2.2. Antiepileptic and anticonvulsant activities

In a study showing that CBD acts protectively by regulating neurotoxicity and hippocampal seizures in young individuals, CBD showed a higher efficacy in hippocampal-focused epilepsy than parvalbumin and extrahippocampal amygdala (Friedman ve Wongvravit 2018). In a twelve-week open-label study highlighting a 36.5% reduction in the severity of epilepsy attacks as a result of treatment, a group of patients aged 1-30 years were treated with 25 and 50 mg/kg CBD. (Devinsky et al., 2016). Preclinical research has also sought to elucidate the efficacy of CBD as an anticonvulsant in a more chronic manner. In a 28-day study in the pentylenetetrazole (PTZ) model of epilepsy, patients were treated with CBD at doses ranging from 20 to 50 mg/kg, and it was found that a reduction in seizure activity could be achieved (Farrelly et al., 2021). It is important to emphasize that other cannabinoids and combinations such as δ-9-tetrahydrocannabinolic acid, cannabidivarin, tetrahydrocannabivarin, cannabichromene and cannabigerol are effective in models of epilepsy and Huntington's disease and are also warranted in some neurodegenerative disorders such as Parkinson's (Stone et al., 2020).

2.2.3. Anti-inflammatory and analgesic activities

Many of the cannabis compounds have been shown to exhibit strong anti-inflammatory activity. The involvement of CB1 and CB2 (Cannabinoid receptors) receptors in anti-inflammatory cascades has been proven by in vivo and in vitro studies (Zurier, 2003). Some of the phytocannabinoids have been potent anti-inflammatory agents on different inflammatory models (Zurier, 2003). CB2 receptors outnumber CB1 receptors in different populations of immune cells (Croxford and Yamamura, 2005). Several studies have shown that the release of proinflammatory cytokines triggered by inflammatory agents such as lipopolysaccharide (LPS) is inhibited by stimulation of CB2 receptors (Puffenbarger et al., 2000).

Guindon and Beaulieu (2006) showed that synthetic CB1 receptor agonists and endocannabinoids are effective against neuropathic pain in animal pain models (Guindon and Beaulieu, 2006). In addition, another study reported that cannabis use reduces neuropathic pain was conducted on AIDS patients (Woolridge et al., 2005). A preparation containing THC and CBD (1:1) isolated from cannabis plant extracts was used in a clinical trial that was shown to alleviate neuropathic pain in traumatic nerve injury and multiple sclerosis and to have analgesic effects in cancer patients (Johnson et al., 2010).

2.2.4. Anticancer activity

Cancer, which is a serious cause of mortality and morbidity worldwide, had been treated with conventional methods such as chemotherapy, radiotherapy and surgery. Chemotherapy and radiotherapy, which are mostly invasive and mainly cause toxic side effects, often lead to adverse health outcomes. It is therefore clear that there is a great need for new medicines with fewer side effects and with safer use. Some of the cannabis derivative compounds have shown *in vitro* and *in vivo* activity in many cancer cell lines including prostate (Sarfaraz et al., 2006), brain (Marcu et al., 2010), cervix (Lukhele and Motadi, 2016), leukemia/lymphoma (McKallip et al., 2002) colon (Cianchi et al., 2008) and breast (Ligresti et al., 2006). Many in vivo and in vitro studies show that phytocannabinoids affect tumor progression. These include studies showing that phytocannabinoids such as THC and CBD at concentrations ranging from 5 to 65 µm inhibit proliferation and induce apoptosis in different cancer cell lines (Galve-Roperh et al., 2000; Ligresti et al., 2006; Galanti et al., 2008; McAllister et al., 2011; Solinas et al., 2013; Borrelli et al., 2014; Armstrong et al., 2015). There is also a case for improving the anticancer activity of cannabis preparations. This has been shown with the combination of certain phytocannabinoids. For example, one study revealed that Δ9-THC alone showed a lower melanoma cell death rate compared to a combination of CBD and Δ9 THC (Armstrong et al., 2015).

2.2.5. Anticoagulant activity

A study targeting the three main phytocannabinoids THC, CBD and CBN aimed to determine the possible antithrombotic effect of hemp leaf metabolites. The effect of hemp extract on thrombin activity under *in vitro* conditions was evaluated and THC and CBN showed significant IC50 (less than 50% inhibitory concentration) values (Coetzee et al., 2007). THC provided the highest activity with a value of 1.79 mg/mL. CBN also showed a high IC50 value, although not as high as THC. This study also included an *in vivo* test to determine clotting times in obese rats. In the end, compared to the control groups, the cannabis-treated rats showed an efficacy of 50%, with a twofold higher coagulation. This proved that phytocannabinoids show good anticoagulant activity.

2.2.6. Antioxidant activity

Antioxidant activity has been reported in seeds, leaves and above-ground parts of *C. sativa*. Studies on the antioxidant effects of *C. sativa* seeds are well reported in the literature. There are many studies on the antioxidant activity of *C. sativa* seeds in the literature. In a study in which the antioxidant activity of the ethanol extract of the seeds was investigated by methods such as lipid peroxidation inhibition, chelating assay and DPPH, the researchers reported that the results obtained showed that the seed organic extract showed strong antioxidant capacity with IC50 values of 1.9 mg/mL for chelating assay, 92.7 mg/mL for lipid peroxidation inhibition assay and 14.5 mg/mL for DPPH (Manosroi et al., 2019). This time the methanolic extract of the seeds was used in the study and the researchers reported an average activity against DPPH (at 500 µL/mL), showing an inhibition value of 75%. (Moccia et al., 2020). Some researchers explain this effect by the presence of phytocannabinoids and polyphenols (Mirzamohammad et al., 2021; Mechqoq et al., 2022). In a study, hemp phytocannabinoids CBG, CBD, Δ9-THC, CBN, CBGA, CBDA, Δ9-THCA were examined using ABTS, DPPH, Beta Carotene Bleaching Test, FRAP, CUPRAC, ORAC methods to determine antioxidant activity. The data presented in this study provide evidence that all cannabinoids examined show significant antioxidant activity in their ability to protect the oxidation process, scavenge free radicals and reduce metal ions. The antioxidant activity of CBG, CBD, Δ9-THC and CBN (neutral cannabinoids) is higher than Trolox as shown by the results of ABTS, CUPRAC, FRAP and DPPH assays. Cannabinoid acids that showed weaker antioxidant activity in the study showed antioxidant activity equal to or stronger than their neutral counterparts in a medium with a pH value higher than the pKa of the cannabinoid acids (CUPRAC) or in the presence of basic radicals (see ORAC) (Dawidowicz et al., 2021).

2.2.7. Dermocosmetic activity

Lipids in human skin play a crucial role in protecting it from dehydration and protecting the structure of the dermis. However, hormonal changes during menopause negatively affect the balance of the skin, making it more prone to the development of dryness (Dunn et al., 1997). Overproduction of certain enzymes such as collagenase, tyrosinase and elastase leads to atrophy of underlying tissues such as muscles and subcutaneous adipose tissue. The production of melanin in the skin is the main task of tyrosinase. Collagen, one of the structural proteins of the skin, is targeted and degraded by collagenase and elastin by elastase enzymes. One study showed that leaf extracts exhibited antithyrosinase activity and strongly inhibited the tyrosinase enzyme with an IC50 value of 0.07 ± 0.06 mg/mL (Manosroi et al., 2019). Similarly, another study showed elastase and collagenase inhibitory activities of 30% and 80%

with 1000 µg per milliliter (Zagórska-Dziok et al., 2021). This effect is mainly due to the presence of polyphenols and phytocannabinoids.

2.2.8. Neuroprotective activity

Phytocannabinoids and terpenes found in cannabis have been shown to exhibit neuroprotective properties. Several compounds found in the above-ground parts of cannabis were evaluated for their neuroprotective effects on PC-12 cells, including (e)-methyl p hydroxycinnamate, ferulic acid and p-hydroxybenzaldehyde, which showed additional protective effects against H2O2-induced damage (Liv et al., 2020). Furthermore, a study in rats reported that CBD and CBG induced neuromodulatory and neuroprotective effects (di Giacomo et al., 2020). Another study highlighted that appropriate CBD concentrations or CBD/THC ratios may be an effective therapeutic agent in the treatment after ischemic neuronal death (Landucci et al., 2021). In the study conducted by Esposito and colleagues (Esposito et al., 2007), it was emphasized that CBD can reduce neuroinflammatory responses induced by β-amyloid. On the other hand, in a study by Perez et al. using immunohistochemical analysis (Perez et al., 2013), neuronal numbers of sensory and motor neurons were determined after CBD treatment. The results showed an average neuroprotective effect of treatment with CBD with a 30% increase in synaptic protection in the spinal cord.

3. CONCLUSION AND RECOMMENDATIONS

Cannabis sativa L. contains various phytocannabinoids. Many studies have shown that these phytocannabinoids alone or in combination exhibit various biological activities. Nowadays, treatment with natural raw materials has become popular and the need for natural raw materials is increasing. Phytocannabinoids with their wide range of biological activities may meet this need. For that reason, more *in vivo* and *in vitro* biological activity and standardization studies on phytocannabinoids should be conducted in the future.

REFERENCES

Abel, E. L. (2013). Marihuana: the first twelve thousand years. Springer Science & Business Media.

Adhikary, D., Kulkarni, M., Mobini, S., Ray, A., Polowick, P., Slaski, J. J., ... & Bhowmik, P. (2021). Medical cannabis and industrial hemp tissue culture: present status and future potential. Frontiers in Plant Science, 12: 627240.

Agarwal, P., & Gupta, R. (2016). Alpha-amylase inhibition can treat diabetes mellitus. Res. Rev. J. Med. Health Sci, 5(4): 1-8.

Amar, M. B. (2006). Cannabinoids in medicine: A review of their therapeutic potential. Journal of Ethnopharmacology, 105(1-2): 1-25.

Andre, C. M., Hausman, J. F., & Guerriero, G. (2016). *Cannabis sativa*: The plant of the thousand and one molecules. Frontiers in Plant Science, 7: 174167.

Armstrong, J. L., Hill, D. S., McKee, C. S., Hernandez-Tiedra, S., Lorente, M., Lopez-Valero, I., ... & Lovat, P. E. (2015). Exploiting cannabinoid-induced cytotoxic autophagy to drive melanoma cell death. Journal of Investigative Dermatology, 135(6): 1629-1637.

Baron, E. P. (2015). Comprehensive review of medicinal marijuana, cannabinoids, and therapeutic implications in medicine and headache: what a long strange trip it's been…. Headache: The Journal of Head and Face Pain, 55(6): 885-916.

Bolognini, D., Costa, B., Maione, S., Comelli, F., Marini, P., Di Marzo, V., ... & Pertwee, R. G. (2010). The plant cannabinoid Δ9-tetrahydrocannabivarin can decrease signs of inflammation and inflammatory pain in mice. British Journal of Pharmacology, 160(3): 677-687.

Bonini, S. A., Premoli, M., Tambaro, S., Kumar, A., Maccarinelli, G., Memo, M., & Mastinu, A. (2018). *Cannabis sativa*: A comprehensive ethnopharmacological review of a medicinal plant with a long history. Journal of Ethnopharmacology, 227: 300-315.

Borrelli, F., Pagano, E., Romano, B., Panzera, S., Maiello, F., Coppola, D., ... & Izzo, A.A. (2014). Colon carcinogenesis is inhibited by the TRPM8 antagonist cannabigerol, a Cannabis-derived non-psychotropic cannabinoid. Carcinogenesis, 35(12): 2787-2797.

Bouloc, P. (2013). Hemp: Industrial Production and Uses. CABI.

Brierley, D. I., Samuels, J., Duncan, M., Whalley, B. J., & Williams, C. M. (2017). A cannabigerol-rich *Cannabis sativa* extract, devoid ofΔ 9-tetrahydrocannabinol, elicits hyperphagia in rats. Behavioural pharmacology, 28(4): 280-284.

Burstein, S. (2015). Cannabidiol (CBD) and its analogs: A review of their effects on inflammation. Bioorganic & Medicinal Chemistry, 23(7): 1377-1385.

Callaway, J. C. (2004). Hempseed as a nutritional resource: An overview. Euphytica, 140: 65-72.

Cao, C., Li, Y., Liu, H., Bai, G., Mayl, J., Lin, X., ... & Cai, J. (2014). The potential therapeutic effects of THC on Alzheimer's disease. Journal of Alzheimer's Disease, 42(3): 973-984.

Ceyhan, V., Türkten, H., Yıldırım, Ç., & Canan, S. (2022). Economic viability of industrial hemp production in Turkey. Industrial Crops and Products, 176: 114354.

Cianchi, F., Papucci, L., Schiavone, N., Lulli, M., Magnelli, L., Vinci, M. C., ... & Masini, E. (2008). Cannabinoid receptor activation induces apoptosis through tumor necrosis factor α–mediated ceramide de novo synthesis in colon cancer cells. Clinical Cancer Research, 14(23): 7691-7700.

Citti, C., Pacchetti, B., Vandelli, M. A., Forni, F., & Cannazza, G. (2018). Analysis of cannabinoids in commercial hemp seed oil and decarboxylation kinetics studies of cannabidiolic acid (CBDA). Journal of Pharmaceutical and Biomedical Analysis, 149: 532-540.

Clarke, R., & Merlin, M. (2016). Cannabis: Evolution and Ethnobotany. Univ of California Press.

Coetzee, C., Levendal, R. A., Van de Venter, M., & Frost, C. L. (2007). Anticoagulant effects of a *Cannabis* extract in an obese rat model. Phytomedicine, 14(5): 333-337.

Croxford, J. L., & Yamamura, T. (2005). Cannabinoids and the immune system: potential for the treatment of inflammatory diseases?. Journal of Neuroimmunology, 166(1-2): 3-18.

Davis, W. M., & Hatoum, N. S. (1983). Neurobehavioral actions of cannabichromene and interactions with delta 9-tetrahydrocannabinol. General Pharmacology, 14(2): 247-252.

Dawidowicz, A. L., Olszowy-Tomczyk, M., & Typek, R. (2021). CBG, CBD, Δ9-THC, CBN, CBGA, CBDA and Δ9-THCA as antioxidant agents and their intervention abilities in antioxidant action. Fitoterapia, 152: 104915.

Dawson, W. R. (1934). Studies in the Egyptian Medical Texts-III. The Journal of Egyptian Archaeology, 20(1): 41-46.

DeLong, G. T., Wolf, C. E., Poklis, A., & Lichtman, A. H. (2010). Pharmacological evaluation of the natural constituent of *Cannabis sativa*, cannabichromene and its modulation by Δ9-tetrahydrocannabinol. Drug and Alcohol Dependence, 112(1-2): 126-133.

Devinsky, O., Marsh, E., Friedman, D., Thiele, E., Laux, L., Sullivan, J.,& Cilio, M. R. (2016). Cannabidiol in patients with treatment-resistant epilepsy: an open-label interventional trial. The Lancet Neurology, 15(3): 270-278.

di Giacomo, V., Chiavaroli, A., Recinella, L., Orlando, G., Cataldi, A., Rapino, M., .& Ferrante, C. (2020). Antioxidant and neuroprotective effects induced by cannabidiol and cannabigerol in rat CTX-TNA2 astrocytes and isolated cortexes. International journal of molecular sciences, 21(10): 3575.

Dunn, L. B., Damesyn, M., Moore, A. A., Reuben, D. B., & Greendale, G. A. (1997). Does estrogen prevent skin aging?: Results from the first National Health and Nutrition Examination Survey (NHANES I). Archives of Dermatology, 133(3): 339-342.

Eisohly, H. N., Turner, C. E., Clark, A. M., & Eisohly, M. A. (1982). Synthesis and antimicrobial activities of certain cannabichromene and cannabigerol related compounds. Journal of Pharmaceutical Sciences, 71(12): 1319-1323.

El Khomsi, M., Dandani, Y., Chaachouay, N., & Hmouni, D. (2022). Ethnobotanical study of plants used for medicinal, cosmetic, and food purposes in the region of Moulay Yacoub, Northeast of Morocco. J. Pharm. Pharmacogn. Res, 10(1): 13-29.

ElSohly, M., & Gul, W. (2014). Constituents of *Cannabis sativa*. Handbook of Cannabis, 3(1093): 187-188.

Esposito, G., Scuderi, C., Savani, C., Steardo Jr, L., De Filippis, D., Cottone, P., ... & Steardo, L. (2007). Cannabidiol in vivo blunts β-amyloid induced neuroinflammation by suppressing IL-1β and iNOS expression. British Journal of Pharmacology, 151(8): 1272-1279.

Farrelly, A. M., Vlachou, S., & Grintzalis, K. (2021). Efficacy of phytocannabinoids in epilepsy treatment: novel approaches and recent advances. International Journal of Environmental Research and Public Health, 18(8): 3993.

Faulkner, R. O. (1969). The ancient Egyptian pyramid texts. Oxford Clarendon Press.

Ferrara, M. S. (2021). Peak-experience and the entheogenic use of cannabis in world religions. Journal of Psychedelic Studies, 4(3): 179-191.

Friedman, L. K., & Wongvravit, J. P. (2018). Anticonvulsant and neuroprotective effects of cannabidiol during the juvenile period. Journal of Neuropathology & Experimental Neurology, 77(10): 904-919.

Galanti, G., Fisher, T., Kventsel, I., Shoham, J., Gallily, R., Mechoulam, R., ... & Toren, A. (2008). Δ9-Tetrahydrocannabinol inhibits cell cycle progression by downregulation of E2F1 in human glioblastoma multiforme cells. Acta Oncologica, 47(6): 1062-1070.

Galve-Roperh, I., Sánchez, C., Cortés, M. L., del Pulgar, T. G., Izquierdo, M., & Guzmán, M. (2000). Anti-tumoral action of cannabinoids: involvement of sustained ceramide accumulation and extracellular signal-regulated kinase activation. Nature Medicine, 6(3): 313-319.

Gaweł-Bęben, K., Czech, K., & Luca, S. V. (2023). Cannabidiol and minor phytocannabinoids: A preliminary study to assess their anti-melanoma, anti-melanogenic, and anti-tyrosinase properties. Pharmaceuticals, 16(5): 648.

Gedik, G., & Avinc, O. (2020). Hemp fiber as a sustainable raw material source for textile industry: can we use its potential for more eco-friendly production? Sustainability in the Textile and Apparel Industries: Sourcing Natural Raw Materials, 87-109.

Gibbs, M., Winsper, C., Marwaha, S., Gilbert, E., Broome, M., & Singh, S. P. (2015). Cannabis use and mania symptoms: A systematic review and meta-analysis. Journal of Affective Disorders, 171: 39-47.

Giupponi, L., Leoni, V., Carrer, M., Ceciliani, G., Sala, S., Panseri, S.,& Giorgi, A. (2020). Overview on Italian hemp production chain, related productive and commercial activities and legislative framework. Italian Journal of Agronomy, 15(3): 194-205.

Gomez, F. P., Hu, J., & Clarke, M. A. (2021). Cannabis as a feedstock for the production of chemicals, fuels, and materials: a review of relevant studies to date. Energy & Fuels, 35(7): 5538-5557.

Gonçalves, J., Rosado, T., Soares, S., Simão, A. Y., Caramelo, D., Luís, Â., ... & Duarte, A. P. (2019). Cannabis and its secondary metabolites: their use as therapeutic drugs, toxicological aspects, and analytical determination. Medicines, 6(1): 31.

Grimison, P., Mersiades, A., Kirby, A., Lintzeris, N., Morton, R., Haber, P., ... & Stockler, M. (2020). Oral THC: CBD cannabis extract for refractory chemotherapy-induced nausea and vomiting: a randomised, placebo-controlled, phase II crossover trial. Annals of Oncology, 31(11): 1553-1560.

Grotenhermen, F., & Müller-Vahl, K. (2016). Medicinal uses of marijuana and cannabinoids. Critical Reviews in Plant Sciences, 35(5-6): 378-405.

Gugliandolo, A., Pollastro, F., Bramanti, P., & Mazzon, E. (2020). Cannabidiol exerts protective effects in an in vitro model of Parkinson's disease activating AKT/mTOR pathway. Fitoterapia, 143: 104553.

Guindon, J., & Beaulieu, P. (2006). Antihyperalgesic effects of local injections of anandamide, ibuprofen, rofecoxib and their combinations in a model of neuropathic pain. Neuropharmacology, 50(7): 814-823.

Hampson, A. J., Grimaldi, M., Axelrod, J., & Wink, D. (1998). Cannabidiol and (-) Δ9-tetrahydrocannabinol are neuroprotective antioxidants. Proceedings of the National Academy of Sciences, 95(14): 8268-8273.

Hill, A. J., Weston, S. E., Jones, N. A., Smith, I., Bevan, S. A., Williamson, E. M., ... & Whalley, B. J. (2010). Δ9-Tetrahydrocannabivarin suppresses in vitro epileptiform and in vivo seizure activity in adult rats. Epilepsia, 51(8): 1522-1532.

Hill, A. J., Williams, C. M., Whalley, B. J., & Stephens, G. J. (2012). Phytocannabinoids as novel therapeutic agents in CNS disorders. Pharmacology & Therapeutics, 133(1): 79-97.

Hussain, W., Ullah, M., Dastagir, G., & Badshah, L. A. L. (2018). Quantitative ethnobotanical appraisal of medicinal plants used by inhabitants of lower Kurram, Kurram agency, Pakistan. Avicenna Journal of Phytomedicine, 8(4): 313.

Jadoon, K. A., Ratcliffe, S. H., Barrett, D. A., Thomas, E. L., Stott, C., Bell, J. D., ... & Tan, G. D. (2016). Efficacy and safety of cannabidiol and tetrahydrocannabivarin on glycemic and lipid parameters in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled, parallel group pilot study. Diabetes Care, 39(10):1777-1786.

Johnson, J. R., Burnell-Nugent, M., Lossignol, D., Ganae-Motan, E. D., Potts, R., & Fallon, M. T. (2010). Multicenter, double-blind, randomized, placebo-controlled, parallel-group study of the efficacy, safety, and tolerability of THC: CBD extract and THC extract in patients with intractable cancer-related pain. Journal of Pain and Symptom Management, 39(2): 167-179.

Juarez, T. M., Piccioni, D., Rose, L., Nguyen, A., Brown, B., & Kesari, S. (2021). Phase I dose-escalation, safety, and CNS pharmacokinetic study of dexanabinol in patients with brain cancer. Neuro-oncology Advances, 3(1): vdab006.

Kajaria, D., Tripathi, J., Tripathi, Y. B., & Tiwari, S. (2013). In-vitro α amylase and glycosidase inhibitory effect of ethanolic extract of antiasthmatic drug-Shirishadi. Journal of Advanced Pharmaceutical Technology & Research, 4(4): 206-209.

Klauke, A. L., Racz, I., Pradier, B., Markert, A., Zimmer, A. M., Gertsch, J., & Zimmer, A. (2014). The cannabinoid CB2 receptor-selective phytocannabinoid beta-caryophyllene exerts analgesic effects in mouse models of inflammatory and neuropathic pain. European Neuropsychopharmacology, 24(4): 608-620.

Knapp, A. A., Lee, D. C., Borodovsky, J. T., Auty, S. G., Gabrielli, J., & Budney, A. J. (2019). Emerging trends in cannabis administration among adolescent cannabis users. Journal of Adolescent Health, 64(4): 487-493.

Kuhathasan, N., Dufort, A., MacKillop, J., Gottschalk, R., Minuzzi, L., & Frey, B. N. (2019). The use of cannabinoids for sleep: A critical review on clinical trials. Experimental and Clinical Psychopharmacology, 27(4): 383.

Landucci, E., Mazzantini, C., Lana, D., Davolio, P. L., Giovannini, M. G., & Pellegrini-Giampietro, D. E. (2021). Neuroprotective effects of cannabidiol but not Δ9-tetrahydrocannabinol in rat hippocampal slices exposed to oxygen-glucose deprivation: studies with cannabis extracts and selected cannabinoids. International Journal of Molecular Sciences, 22(18): 9773.

Li, D., Ilnytskyy, Y., Ghasemi Gojani, E., Kovalchuk, O., & Kovalchuk, I. (2022). Analysis of anti-cancer and anti-inflammatory properties of 25 high-THC cannabis extracts. Molecules, 27(18): 6057.

Li, J., Wang, G., Qin, Y., Zhang, X., Wang, H. F., Liu, H. W.& Yao, X. S. (2020). Neuroprotective constituents from the aerial parts of *Cannabis sativa* L. subsp. *sativa*. RSC advances, 10(53): 32043-32049.

Ligresti, A., Moriello, A. S., Starowicz, K., Matias, I., Pisanti, S., De Petrocellis, L., ... & Di Marzo, V. (2006). Antitumor activity of plant cannabinoids with emphasis on the effect of cannabidiol on human breast carcinoma. Journal of Pharmacology and Experimental Therapeutics, 318(3): 1375-1387.

Liu, F. H., Hu, H. R., Du, G. H., Deng, G., & Yang, Y. (2017). Ethnobotanical research on origin, cultivation, distribution and utilization of hemp (*Cannabis sativa* L.) in China. Indian Journal of Traditional Knowledge, 16(2): 235-242.

Liu, Y., Liu, H. Y., Li, S. H., Ma, W., Wu, D. T., Li, H. B.,& Gan, R. Y. (2022). *Cannabis sativa* bioactive compounds and their extraction, separation, purification, and identification technologies: An updated review. TrAC Trends in Analytical Chemistry, 149: 116554.

Lowe, H., Steele, B., Bryant, J., Toyang, N., & Ngwa, W. (2021). Non-cannabinoid metabolites of *Cannabis sativa* L. with therapeutic potential. Plants, 10(2): 400.

Lowin, T., Tingting, R., Zurmahr, J., Classen, T., Schneider, M., & Pongratz, G. (2020). Cannabidiol (CBD): A killer for inflammatory rheumatoid arthritis synovial fibroblasts. Cell Death & Disease, 11(8): 714.

Lukhele, S. T., & Motadi, L. R. (2016). Cannabidiol rather than *Cannabis sativa* extracts inhibit cell growth and induce apoptosis in cervical cancer cells. BMC Complementary and Alternative Medicine, 16: 1-16.

Manosroi, A., Chankhampan, C., Kietthanakorn, B. O., Ruksiriwanich, W., Chaikul, P., Boonpisuttinant, K., ... & Manosroi, J. (2019). Pharmaceutical and cosmeceutical biological activities of hemp (*Cannabis sativa* L. var. *sativa*) leaf and seed extracts. Chiang Mai J. Sci, 46: 180-195.

Marcu, J. P., Christian, R. T., Lau, D., Zielinski, A. J., Horowitz, M. P., Lee, J., ... & McAllister, S. D. (2010). Cannabidiol enhances the inhibitory effects of Δ9-tetrahydrocannabinol on human glioblastoma cell proliferation and survival. Molecular Cancer Therapeutics, 9(1): 180-189.

Massi, P., Solinas, M., Cinquina, V., & Parolaro, D. (2013). Cannabidiol as potential anticancer drug. British Journal of Clinical Pharmacology, 75(2): 303-312.

Mawla, F., Khatoon, S., Rehana, F., Jahan, S., Shelley, M. M. R., Hossain, S., ... & Rahmatullah, M. (2012). Ethnomedicinal plants of folk medicinal practitioners in four villages of Natore and Rajshahi districts, Bangladesh. Am Eur J Sustain Agric, 6: 406-416.

McAllister, S. D., Murase, R., Christian, R. T., Lau, D., Zielinski, A. J., Allison, J., ... & Desprez, P. Y. (2011). Pathways mediating the effects of cannabidiol on the reduction of breast cancer cell proliferation, invasion, and metastasis. Breast Cancer Research and Treatment, 129: 37-47.

McKallip, R. J., Lombard, C., Fisher, M., Martin, B. R., Ryu, S., Grant, S., ... & Nagarkatti, M. (2002). Targeting CB2 cannabinoid receptors as a novel therapy to treat malignant lymphoblastic disease. Blood, The Journal of the American Society of Hematology, 100(2): 627-634.

Mechqoq, H., Hourfane, S., Yaagoubi, M. E., Hamdaoui, A. E., Msanda, F., Almeida, J. R. G. D. S., ... & Aouad, N. E. (2022). Phytochemical screening, and in vitro evaluation of the antioxidant and dermocosmetic activities of four Moroccan plants: *Halimium antiatlanticum*, *Adenocarpus artemisiifolius*, *Pistacia lentiscus* and *Leonotis nepetifolia*. Cosmetics, 9(5): 94.

Mechoulam, R., & Ben-Shabat, S. (1999). From gan-zi-gun-nu to anandamide and 2-arachidonoylglycerol: the ongoing story of cannabis. Natural Product Reports, 16(2): 131-143.

Mirzamohammad, E., Alirezalu, A., Alirezalu, K., Norozi, A., & Ansari, A. (2021). Improvement of the antioxidant activity, phytochemicals, and cannabinoid compounds of *Cannabis sativa* by salicylic acid elicitor. Food Science & Nutrition, 9(12): 6873-6881.

Moccia, S., Siano, F., Russo, G. L., Volpe, M. G., La Cara, F., Pacifico, S., ... & Picariello, G. (2020). Antiproliferative and antioxidant effect of polar hemp extracts (*Cannabis sativa* L., Fedora cv.) in human colorectal cell lines. International Journal of Food Sciences and Nutrition, 71(4): 410-423.

Mosley, P. E., Webb, L., Suraev, A., Hingston, L., Turnbull, T., Foster, K., ... & McGregor, I. S. (2023). Tetrahydrocannabinol and cannabidiol in tourette syndrome. NEJM evidence, 2(9), EVIDoa2300012.

Pacher, P., Bátkai, S., & Kunos, G. (2006). The endocannabinoid system as an emerging target of pharmacotherapy. Pharmacological Reviews, 58(3): 389-462.

Perez, M., Benitez, S. U., Cartarozzi, L. P., Del Bel, E., Guimaraes, F. S., & Oliveira, A. L. (2013). Neuroprotection and reduction of glial reaction by cannabidiol treatment after sciatic nerve transection in neonatal rats. European Journal of Neuroscience, 38(10): 3424-3434.

Peyravian, N., Deo, S., Daunert, S., & Jimenez, J. J. (2020). Cannabidiol as a novel therapeutic for immune modulation. ImmunoTargets and Therapy, 131-140.

Pollastro, F., Minassi, A., & Fresu, L. G. (2018). Cannabis phenolics and their bioactivities. Current Medicinal Chemistry, 25(10): 1160-1185.

Puffenbarger, R. A., Boothe, A. C., & Cabral, G. A. (2000). Cannabinoids inhibit LPS-inducible cytokine mRNA expression in rat microglial cells. Glia, 29(1): 58-69.

Rahmatullah, M., Mollik, M. A. H., Azam, A. T. M. A., Islam, M. R., Chowdhury, M. A. M., Jahan, R., ... & Rahman, T. (2009). Ethnobotanical survey of the Santal tribe residing in Thakurgaon District, Bangladesh. American Eurasian Journal of Sustainable Agriculture, 3(4): 889-898.

Rahmatullah, M., Mollik, M. A. H., Khatun, M. A., Jahan, R., Chowdhury, A. R., Seraj, S., ... & Khatun, Z. (2010). A survey on the use of medicinal plants by folk medicinal practitioners in five villages of Boalia sub-district, Rajshahi district, Bangladesh. Adv Nat Appl Sci, 4: 39-44.

Ramamoorthy, S. K., Skrifvars, M., & Persson, A. (2015). A review of natural fibers used in biocomposites: Plant, animal and regenerated cellulose fibers. Polymer Reviews, 55(1): 107-162.

Roychoudhury, P., Wang, N. N., & Narouze, S. N. (2021). Phytocannabinoids: Tetrahydrocannabinol (THC). In Cannabinoids and Pain (pp. 71-77). Cham: Springer International Publishing.

Rupasinghe, H. V., Davis, A., Kumar, S. K., Murray, B., & Zheljazkov, V. D. (2020). Industrial hemp (Cannabis sativa subsp. sativa) as an emerging source for value-added functional food ingredients and nutraceuticals. Molecules, 25(18): 4078.

Russo, E. B., Cuttler, C., Cooper, Z. D., Stueber, A., Whiteley, V. L., & Sexton, M. (2022). Survey of patients employing cannabigerol-predominant cannabis preparations: perceived medical effects, adverse events, and withdrawal symptoms. Cannabis and Cannabinoid Research, 7(5): 706-716.

Ryz, N. R., Remillard, D. J., & Russo, E. B. (2017). Cannabis roots: a traditional therapy with future potential for treating inflammation and pain. Cannabis and Cannabinoid Research, 2(1): 210-216.

Sarfaraz, S., Afaq, F., Adhami, V. M., Malik, A., & Mukhtar, H. (2006). Cannabinoid receptor agonist-induced apoptosis of human prostate cancer cells LNCaP proceeds through sustained activation of ERK1/2 leading to G1 cell cycle arrest. Journal of Biological Chemistry, 281(51): 39480-39491.

Schier, A. R. D. M., Ribeiro, N. P. D. O., Silva, A. C. D. O., Hallak, J. E. C., Crippa, J. A. S., Nardi, A. E., & Zuardi, A. W. (2012). Cannabidiol, a *Cannabis sativa* constituent, as an anxiolytic drug. Brazilian Journal of Psychiatry, 34: 104-110.

Smeriglio, A., Giofrè, S. V., Galati, E. M., Monforte, M. T., Cicero, N., D'Angelo, V., ... & Circosta, C. (2018). Inhibition of aldose reductase activity by *Cannabis sativa* chemotypes extracts with high content of cannabidiol or cannabigerol. Fitoterapia, 127: 101-108.

Sofia, R. D., Nalepa, S. D., Harakal, J. J., & Vassar, H. B. (1973). Anti-edema and analgesic properties of Δ9-tetrahydrocannabinol (THC). Journal of Pharmacology and Experimental Therapeutics, 186(3): 646-655.

Solinas, M., Massi, P., Cinquina, V., Valenti, M., Bolognini, D., Gariboldi, M., ... & Parolaro, D. (2013). Cannabidiol, a non-psychoactive cannabinoid compound, inhibits proliferation and invasion in U87-MG and T98G glioma cells through a multitarget effect. PLoS One, 8(10): e76918.

Stone, N. L., Murphy, A. J., England, T. J., & O'Sullivan, S. E. (2020). A systematic review of minor phytocannabinoids with promising neuroprotective potential. British Journal of Pharmacology, 177(19): 4330-4352.

Struik, P. C., Amaducci, S., Bullard, M. J., Stutterheim, N. C., Venturi, G., & Cromack, H. T. H. (2000). Agronomy of fibre hemp (*Cannabis sativa* L.) in Europe. Industrial Crops and Products, 11(2-3): 107-118.

Suzen, S., & Buyukbingol, E. (2003). Recent studies of aldose reductase enzyme inhibition for diabetic complications. Current Medicinal Chemistry, 10(15): 1329-1352.

Turner, B. D., Sloan, S. W., & Currell, G. R. (2019). Novel remediation of per- and polyfluoroalkyl substances (PFASs) from contaminated groundwater using *Cannabis Sativa* L.(hemp) protein powder. Chemosphere, 229: 22-31.

Turner, C. E., Elsohly, M. A., & Boeren, E. G. (1980). Constituents of *Cannabis sativa* L. XVII. A review of the natural constituents. Journal of Natural Products, 43(2): 169-234.

Veiga, P. (2009). Oncology and Infectious Diseases in Ancient Egypt: The Ebers Papyrus’ Treatise on Tumours 857-877 and the Cases Found in Ancient Egyptian Human Material (Doctoral dissertation, University of Manchester).

Vernail, V. L., Bingaman, S. S., Silberman, Y., & Arnold, A. C. (2022). Acute cannabigerol administration lowers blood pressure in mice. Frontiers in Physiology, 13: 871962.

Vonapartis, E., Aubin, M. P., Seguin, P., Mustafa, A. F., & Charron, J. B. (2015). Seed composition of ten industrial hemp cultivars approved for production in Canada. Journal of Food Composition and Analysis, 39: 8-12.

Watt, G., & Karl, T. (2017). *In vivo* evidence for therapeutic properties of cannabidiol (CBD) for Alzheimer's disease. Frontiers in Pharmacology, 8: 234828.

Weston-Green, K. (2018). The united chemicals of cannabis: beneficial effects of cannabis phytochemicals on the brain and cognition. In Recent Advances in Cannabinoid Research. IntechOpen.

Woolridge, E., Barton, S., Samuel, J., Osorio, J., Dougherty, A., & Holdcroft, A. (2005). *Cannabis* use in HIV for pain and other medical symptoms. Journal of Pain and Symptom Management, 29(4): 358-367.

Zagórska-Dziok, M., Bujak, T., Ziemlewska, A., & Nizioł-Łukaszewska, Z. (2021). Positive effect of *Cannabis sativa* L. herb extracts on skin cells and assessment of cannabinoid-based hydrogels properties. Molecules, 26(4): 802.

Zengin, G., Menghini, L., Di Sotto, A., Mancinelli, R., Sisto, F., Carradori, S., ... & Grande, R. (2018). Chromatographic analyses, in vitro biological activities, and cytotoxicity of *Cannabis sativa* L. essential oil: A multidisciplinary study. Molecules, 23(12): 3266.

Zuardi, A. W., Crippa, J. A. D. S., Hallak, J. E. C., Moreira, F. A., & Guimarães, F. S. (2006). Cannabidiol, a *Cannabis sativa* constituent, as an antipsychotic drug. Brazilian journal of medical and biological research, 39: 421-429.

Zurier, R. B. (2003). Prospects for cannabinoids as anti-inflammatory agents. Journal of Cellular Biochemistry, 88(3): 462-466.

CHAPTER V

TEA (*Camellia sinensis* L.) AS A MEDICINAL PLANT

Asist. Prof. Emine YURTERİ[1]

PhD. Aysel Özcan AYKUTLU[2]

Prof. Dr. Fatih SEYİS[3]

DOI: https://dx.doi.org/10.5281/zenodo.13826036

[1] Recep Tayyip Erdoğan University, Faculty of Agriculture, Field Crops Department, 53300 Rize, Türkiye. ORCHID ID: 0000-0002-3770-2714, e-mail:emine.yurteri@erdogan.edu.tr

[2] Recep Tayyip Erdoğan University, Faculty of Agriculture, Field Crops Department, 53300 Rize, Türkiye. ORCHID ID: 0000-0001-5210-7617, e-mail:aysel.ozcan@erdogan.edu.tr

[3] Recep Tayyip Erdoğan University, Faculty of Agriculture, Field Crops Department, 53300 Rize, Türkiye. ORCHID ID: 000-0001-9714-370X, e-mail: fatih.seyis@erdogan.edu.tr

INTRODUCTION

A plant is deemed medicinal if it contains compounds in one or more of its organs that are useful for medicine or that can be used to make other useful drugs. This description can help you easily distinguish between plants that have been shown by research to have therapeutic features and constituents, and plants that are thought to be medicinal but have not yet undergone extensive scientific investigation (Sofowora et al., 2013).

A plant is considered "medicinal" if one or more of its organs "contain substance that can be used for therapeutic purposes, or which are precursors for chemo-pharmaceutical semi-synthesis" (Zhang, X., (2002). Tea (*Camellia sinensis* L.) is considered a medicinal herb and has been used for centuries, according to this definition.

Around the world, both traditional and modern medical systems rely heavily on plants as a natural resource. Plants and plant-derived products have been used for medicinal purposes for thousands of years.

The earliest kind of medication comes from medicinal plants, which have been used in traditional medicine across many countries for thousands of years (Khan, 2014). Human organisations have been transmitting empirical evidence of their good effects over time (Bhat, 2021).

This review will describe the detail about the medicinal value of *C. sinensis* L.

1. HISTORY AND ORIGIN OF *C. sinensis* L.

The second emperor of China, Shen Nung, is credited with discovering tea when a *Camellia sinensis* leaf blew into his cup of boiling water (2737 BCE). In 1560, Portuguese Jesuit missionary Father Jasper de Cruz became the first person in Europe to write about and taste tea. In 1650, the Dutch introduced a variety of teas and tea customs to New Amsterdam, which would later become New York. The first tea was sold as a health beverage in London, England, in 1657 at Garway's Coffee House. In 1826, John Horniman introduced the first tea for retail sales in lead-lined, sealed packages.

In order to achieve uniformity, the English business Twinings began blending tea in 1870. Iced tea was created in 1904 by the Englishman Richard Blechynden during a heat wave at the St. Louis World's Fair. When tea importer Thomas Sullivan of New York gave his customers tea in little silk bags in 1908 and they soaked the entire bag, Sullivan unintentionally created the first tea bag. The first instant tea was introduced in history in 1953. These days, Europe, North America, and North Africa are the main regions where BT is used, whereas GT is consumed across Asia.

2. IMPORTANCE OF MEDICINAL PLANTS

Medicinal plants supplement or replace modern medical remedies, which are sometimes unavailable, and also enhance the health and safety of the local community. Because of this, these plants are necessary for day-to-day living and are closely associated with a variety of social, cultural, and economic phenomena pertaining to ageing, life, health, and death (Sofowora A et al. 2013). Medicinal herbs are used in the diagnosis and treatment of diseases and disorders. For a very long time, plants have been an abundant source of safe and effective medicines (Russell-Smith et al. 2006).

It has been suggested by archaeological evidence that tea leaves soaked in boiling water were ingested by humans up to 500,000 years ago. Based on botanical evidence, China and India were among the first nations to plant tea. Nowadays, research indicates that green tea (*C. sinesis*), in particular, may offer numerous health advantages to the hundreds of millions of people who consume tea worldwide (Vitthal et al., 2008).

Because of the many health benefits of the tea plant (*C. sinensis*), which have the ability to prevent and treat a variety of illnesses, people have traditionally consumed "tea" obtained from this plant across the world. Despite its lengthy history, tea is still the most widely consumed form of tea, suggesting that little has changed in terms of the use of tea plants in recent times (Brimson et al., 2022).

The typical preparation of C. sinensis leaves is as a mixture, mostly tea, which is one of the most widely consumed drinks worldwide. Based on the fermentation method and major component quantification, there are six different types of finished *C. sinensis* tea leaves: white, green, oolong, black, dark, and yellow tea (Jiang et al., 2020). Since Southeast Asia is the home of the tea plant and has done so for around 500 years, the consumption of tea has a long history there (Wheeler et al., 2004).

Beginning in the Tang and Song Dynasties, the tea plant was valued for its pleasant scent before being acknowledged as a medicinal herb (Yang et al., 2014). Worldwide, both Eastern and Western nations consume and prefer black tea. In addition, green tea is widely utilised in the traditional Chinese medical system (Yang et al., 2014) and is preferred in Asian nations (such as China, Japan, and India) (Hayat et al., 2015). Green tea has long been used medicinally to treat heat, phlegm, thirst, and inflammation. Its anti-inflammatory and diuretic properties have even been documented in classical literature. Chinese folklore also suggests using white tea to treat diabetes, the flu, and measles (Xia te al., 2021). Additionally, drinking tea has long been advised to treat a wide range of illnesses, such as depression, indigestion, migraines, body aches, and pains, as well as detoxifying and as an energising drink to lengthen life (Ferrara et al., 2001).

3. MEDICINAL IMPORTANCE OF *C. sinensis*

Polyphenols (catechins and flavonoides), alkaloids (theophylline, caffeine, theobromine, etc.), volatile oils, polysaccharides, amino acids, lipids, vitamins (like vitamin C), inorganic elements (like aluminium, fluorine, and manganese), etc. are among the chemical components of tea leaves. However, tea's advantageous health qualities are mostly due to its polyphenol content. The flavonoides have antimicrobial, anti-allergic, anti-inflammatory, and antioxidant properties. Six major catechin components are found in green tea: epicatechin, gallocatechin, epigallocatechin, epicatechin gallate, and epigallocatechin gallate (EGCG), the last of which being the most active. According to Sharangi (2009), the percentage of polyphenols in black tea and green tea ranges from 3% to 10% and 30% to 40%, respectively.

The idea that tea improves health dates back to the 1800s. Thanks to the polyphenols included in *C. sinensis*, tea has a positive impact on health (Cooper et al., 2005 Gübür, 2015). Tea has a significant impact on the prevention and treatment of bacterial and viral infections, cancer, neurological disorders, obesity, diabetes, oxidative and inflammatory illnesses, and cardiovascular diseases (Figure 1).

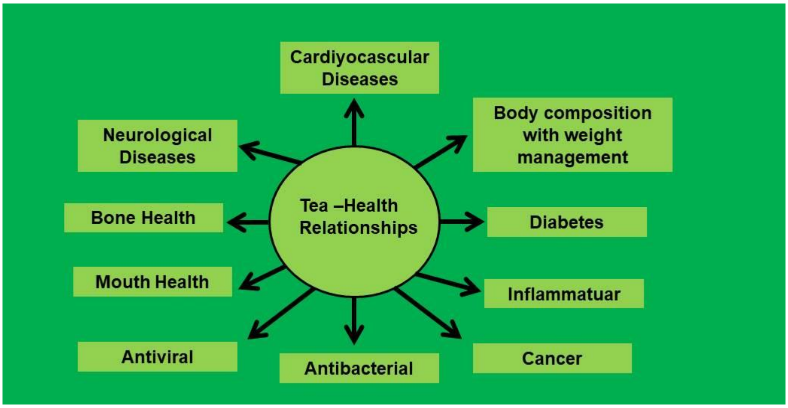


Figure 1: Tea – Health Relationship (changed from Elmas and Gezer)

This famous beverage diplays important pharmacological activities (Bhatt et al., 2004). These can be named as Anti cancer activity (Ghosh et al., 2006), lipid lowering activity (Hahimoto et al., 1987), anti carcinogenic activity (Wei et al., 1997), neuromuscular-blocking action (Higuchi et al., 1995), immunomodulatory effect (Yoshida et al., 1996), DNA effect (Murakami et al., 1999), antiviral activity (Davis et al., 1997), antibacterial activity (Yen and Chen, 1996), anti spamodic activity (Rio et al., 2002), anticataract activity (Chaudhuri et al., 1997), antioxidant activity (Sagesak et al., 1994), antidiabetic activity (Shokrzadeh et al., 2006), antigenotoxic effect (Gupta et al., 2009), hepatoprotective and antioxidant activity (Oyejide and Olushola, 2005), antibacterial effect in intestine (Raffaerella et al., 2008), anti-inflammatory activity (Chattopadhyay et al., 2004), effect on oxidative stress (Das et al., 2009) and chemoprotective activity (Ramirez-Mares et al., 2004).

4. TEA PROCESSING EFFECTS BIOACTIVE CONTENT IN TEAS

Geographical, genetic, ecological, physiological, and processing variables can all affect the chemical makeup of tea, particularly the phenolic chemicals (Pedro et al., 2019; Abdel Azeemet al., 2020). Processing has a significant impact on the phenolic composition since certain chemicals are only visible after the leaves have fermented (Abdel Azeem et al., 2020), while other compounds are broken down in the process (Chen et al., 2021). One illustration of this is the fact that unfermented green tea has higher theanine levels than fully fermented black tea (Abdel Azeem et al., 2020). Similarly, the darker the tea, the higher the content of flavin (aftained during the oxidation process of the leaves) (Braibante et al., 2014).

In addition to phenolic compounds, the composition of *C. sinensis* also contains purine nucleotide-derived secondary metabolites. In particular, there are methylxanthines-which are soluble in water and show strong central nervous system stimulation-there (Zhang et al., 2019). The two methylxanthines that mostly influence the quality of tea are theobromine and caffeine, both of which are present in higher concentrations in tea (Teng et al., 2020). Caffeine stands out among its many stimulating qualities for being a fat-soluble substance that also encourages improved focus and attention, increases fat burning (when paired with exercise), and reduces mental fatigue (Chirasani et al., 2021).

Theanine, which makes up 60–70% of the total amino acid content in tea leaves, and methylxanthines (caffeine and theobromine) stand out among the other chemicals found in teas, as do phenolic components such phenolic acids, catechins, and flavonoids (Fang et al., 2017).

The chemical composition of tea is directly influenced by the unit processes involved in its processing (Figure 2), which in turn affects its bioactive qualities, including antioxidant and sensory activity (Sun et al., 2019). Up to five unit operations-withering, panning or steaming, sweltering, rolling, and drying-are involved in the manufacture of tea herbs. According to Braibante et al. (2014), the concentration of beneficial compounds-primarily phenolic compounds-reduces more rapidly the more stages there are. Moreover, these processes change the concentrations of volatile chemicals, amino acids, theaflavins, and methylxanthines, which in turn changes their beneficial qualities and produces several kinds of tea (Figure 2).

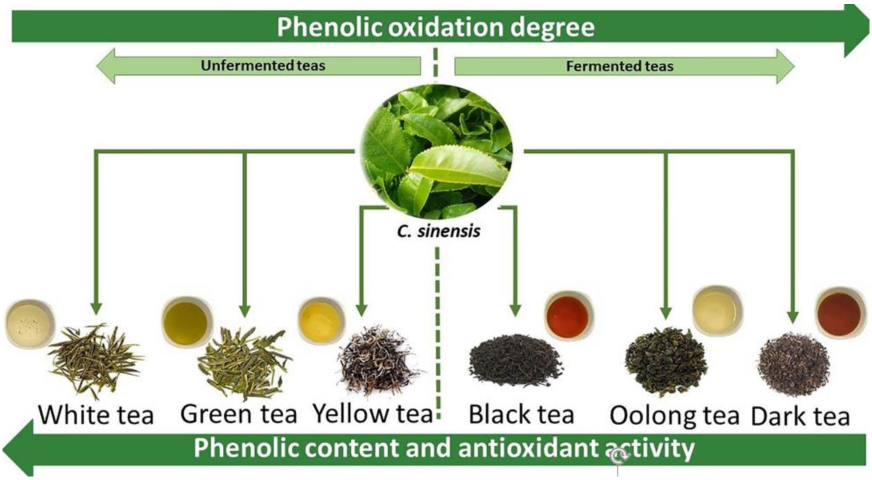


Figure 2: Effect of tea processing on phenolic content and antioxidant activity of infusions (Bortolini et al. 2019).

5. TEA - HEALTH RELATIONSHIPS

The biological functions of main secondary metabolites in tea are given in Table 1.

Table 1: The biological functions of main secondary metabolites in tea

Secondary metabolite	Function	Reference
Polyphenols	Antitumorigenesis	Khan and Mukhtar (2007)
	Antioxidant activity	Frei and Higdon (2003)
	Anticancer	Mukhtar and Ahmad (2000); Kanwar et al. (2012)
	Anticardiovascular Disease	Khan and Mukhtar (2018)
	Antioxidants, Prevent oxidative stress, modulate carcinogen metabolism	Yang et al. (2009)
Free Amino Acids	Sleep peacefully, relieve tension	Kimura et al. (2007)

	Decrease blood pressure, promote relaxation	Juneja et al. (1999)
	concentration and learning ability	Mu et al. (2015)
	Reduce hypertension	Yokogoshi et al. (1995)
	Anti-obesity	Zheng et al. (2004)
Caffeine	Anti-fatigue	Papamichael et al. (2005)
	Cardiotonic agent	Evans and Griffiths (1999)
	Vasodilation	Lopes et al. (1983)
	Improve attention	Rees et al. (1999)
	Improve physical endurance and cognitive function	Ruzton (2008)
Polysaccharides	Scavenging free radicals	Chen et al. (2009)
	Antioxidant	Wang et al. (2015)
	Immunostimulatory activity	Ferreira et al. (2015)
	Anticancer	He et al. (2013)
	Antidiabetes	Hu et al. (2005)
	Antiobesity	Wu et al. (2016)

Of course there are more investigations on secondary metabolites in tea, only a broad spectrum is given in Table 1.

6. CATECHINES

We will highlight the catechines, which are the most significant polyphenolic components in *C. sinensis*.

The bioactive polyphenolic components known as catechins are found in fresh tea leaves and green tea, and they play a significant role in the health advantages associated with tea consumption (Zhiang et al., 2016; Zheng et al., 2018). Fresh leaves of typical tea cultivars typically contain four epi-type catechins: (−)-epicatechin (EC), (−)-epigallocatechin (EGC), (−)-epicatechin gallate (ECG), and (−)-epitgallocatechin gallate (EGCG). However, heat-induced epimerization from the epi-type catechins during tea manufacturing results in the detection of their isomers in manufactured teas (Kim et al., 2007;

Liang et al., 2007). EGCG, which makes up more than 40% of the total catechin concentration in fresh tea leaves, is the most prevalent individual catechin (Zheng et al., 2018).

7. TEA FLOWERS AND THEIR MEDICINAL IMPORTANCE

Due to its pleasant flavour and biological benefits, tea has grown to become one of the most widely used functional beverages worldwide (Feng et al., 2019; Tang et al., 2019). Though in different amounts, the chemical components of tea leaves and flowers (catechins, caffeine, flavonols, polysaccharides, proteins, saponins, etc.) are comparable (Chen et al., 2018). Tea flower has been utilised as a cough suppressant, expectorant, deodorant, and skin care ingredient in traditional Chinese medicine (Yang et al., 2009).

Additionally, the flower buds have been used as a garnish for meals in Japanese cuisines such botebote-cha, Shimane, and drinks like hanaban-cha, Shimane and Kouchi, or bata bata-cha, Niigata (Yoshikawa et al., 2008; Matsuda et al., 2012). In the last few decades, there has been significant advancement in the study of the chemical makeup and biological properties of tea blossoms. Numerous biological activities of tea flower extracts have been demonstrated, including antioxidative, gastroprotective, hypoglycemic, hypolipidermic, and antiproliferative effects (Yoshikawa et al., 2005; Yang et al., 2007; Yoshikawa et al., 2008; 2009; Joshi et al., 2011; Matsuda et al., 2016; Wang et al., 2017). The presence of several functional saponins, polyphenols, polysaccharides, proteins, and vitamins in tea flowers may be responsible for these biological actions (Lin et al., 2003; Yoshikawa et al., 2005; Yang, et al., 2007; Yoshikawa, 2008; 2009; Joshi et al., 2011; Yang et al., 2012; Wang et al., 2017; Chen et al., 2018).

8. CONCLUSION

One of the most popular drinks in the world is tea, which is prepared from the leaves of the tea plant (*C. sinensis*). It is abundant in organic substances that are thought to offer several health advantages, such as mitigating the typical metabolic syndrome. The tea plant has been used for many years to cure and prevent many medical ailments. Since tea is still the most widely consumed form of the plant, there doesn't seem to have been much of a change in its intended uses. several harvesting and processing techniques have resulted in several types of tea from this plant, which vary in terms of the amount and quality of active chemicals consumed and the consequences that follow.

While tea flowers have long been thought of as the waste product of the tea plant, new research has revealed that they actually have a number of health advantages and are becoming more and more popular. In the last 20 years, a great deal of insightful and practical research has been done on the physiological genetics, isolation, identification, and assessment of functional molecules in tea flowers. Furthermore, it has been established that tea flower extract, or its bioactive components, is safe to use and at the appropriate dosage.

This book chapter highlights the importance of *C. sinensis* as a medicinal plant.

REFERENCES

Abdel Azeem, S.M., Al Mohesen, I. A., & Ibrahim, A.M.H. (2020). Analysis of total phenolic compounds in tea and fruits using diazotized aminobenzenes colorimetric spots. Food Chemistry, 332: 127392.

Bhat, S. (2021). Medicinal Plants and Its Pharmacological Values. 10.5772/intechopen.99848.

Braibante, M. E. F., da Silva, D., Braibante, Hugo, T. S., & Pazinato, M. S. (2014). A Química dos Chas. ´ Química, 36: 168-175.

Chaudhuri, T., Das, S.K., Vedasiromoni, J.R., & Ganguly, D.K. (1997). Photochemical investigation of the roots of *Camellia sinensis* L. (O. Kuntze). J. Indian Chem. Soc., 74(2): 166.

Chattopadhyay, P., Besra, S.E., Gomes, A., Das, M., Sur, P., Mitra, S., & Vedasiromoni, J.R. (2004). Anti inflammatory activity of tea (*Camellia sinensis*) root extract, Life Sci. 74(15): 1839-1849.

Chen, D., Ding, Y., Chen, G., Sun, Y., Zeng, X., & Ye, H. (2020). Components identification and nutritional value exploration of tea (*Camellia sinensis* L.) flower extract: Evidence for functional food. Food Research International, 132: 109100.

Chen, X., Ye, Y., Cheng, H., Jiang, Y., & Wu, Y. (2009). Thermal Effects on the Stability and Antioxidant Activity of an Acid Polysaccharide Conjugate Derived from Green Tea. J. Agric. Food Chem., 57: 5795-5798.

Chen, Y.Y., Zhou, Y., Zeng, L.T., Dong, F., Tu, Y.Y., & Yang, Z.Y. (2018). Occurrence of functional molecules in the flowers of tea (*Camellia sinensis*) plants: Evidence for a second resource. Molecules, 23(4): 790.

Chirasani, V.R., Pasek, D.A., & Meissner, G. (2021). Estructural and functional interactions between the Ca2+, ATP, and caffeine bindingsites of skeletal muscle ryanodine receptor (RyR1). Journal of Biological Chemistry, 101040.

Cooper, R., Morré, D.J., & Morré, D.M. (2005). Medical benefits of green tea: part I. review of noncancer health benefits. The Journal of Alternative and Complementary Medicine, 11(3): 521-528.

Das, S.A., Mukherjee, M., Das, D., & Mitra, C. (2009). Protective action of aqueous black tea (*Camellia sinensis*) extract (BTE) against ovariectomy-induced oxidative stress of mononuclear cells and its associated progression of bone loss, Phytother. Res., 23(9): 1287-1294.

Davis, A.L., Lewis, J.R., Cai, Y., Powell, C., Davis, A.P., Wilkins, J.P.G., Pudney, P., & Clifford, M.N. (1997). A polyphenolic pigment from black tea. Phytochem, 46(8): 1397-1402.

Elmas, C., & Gezer, C. (2019). Composition of tea (*Camellia sinensis*) Plant and Effects on Healh. Academical Food, 17(3): 417-428.

Evans, S.M., & Griffiths, R.R. (1999). Caffeine withdrawal: A parametric analysis of caffeine dosing conditions. J. Pharmacol. Exp. Ther., 289: 285-294.

Fang, R., Redfern, S.P., Kirkup, D., Porter, E.A., Kite, G.C., Terry, L.A., & Simmonds, M. S. J. (2017). Variation of theanine, phenolic, and methylxanthine compounds in 21 cultivars of *Camellia sinensis* harvested in different seasons. Food Chemistry, 220: 517–526.

Feng, Z., Li, Y., Li, M., Wang, Y., Zhang, L., Wan, X., & Yang, X. (2019). Tea aroma formation from six model manufacturing processes. Food Chemistry, 285: 347–354.

Ferrara, L., Montesano, D., & Senatore, A. (2001). The distribution of minerals and flavonoids in the tea plant (*Camellia sinensis*). Il Farm., 56: 397-401.

Ferreira, S.S., Passos, C.P., Madureira, P., Vilanova, M., & Coimbra, M.A. (2015). Structure–function relationships of immunostimulatory polysaccharides: A review. Carbohydr. Polym., 132: 378-396.

Frei, B., & Higdon, J.V. (2003). Antioxidant Activity of Tea Polyphenols In Vivo: Evidence from Animal Studies. J. Nutr., 133: 3275S-3284S.

Ghosh, P, Besra, S.E., Tripathi, G., Mitra, S., & Vedasiromoni, J.R. (2006). Cytotoxic and apoptogenic effect of tea root extrat and two of its steroidal Saponin of TS1 and TS2 on human leukemic cell lines K562 and U937 and on cell of CML and all patients, Leuk Res, 30(4): 459-468.

Gupta, J., Siddique, Y.H., Beg, T., Ara, G., & Afzal, M. (2009). Protective role of green tea extract against genotoxic damage induced by anabolic steroids in cultured human lymphocytes, Biology and Medicine, 1(2): 87-99.

Gübür, S. (2015). Investigation of antioxidant effect of green tea in rats feeded with diets high in crude carbohydrates, Ph.D. Thesis, Başkent University.

Hayat, K., Iqbal, H., Malik, U., Bilal, U., & Mushtaq, S. (2015). Tea and its consumption: Benefits and risks. Crit. Rev. Food Sci. Nutr., 55: 939-954.

He, N., Shi, X., Zhao, Y., Tian, L., Wang, N., & Yang, X. (2013). Inhibitory Effects and Molecular Mechanisms of Selenium-Containing Tea Polysaccharides on Human Breast Cancer MCF-7 Cells. J. Agric. Food Chem., 61: 579-588.

Higuchi, K., Suzuki, T., & Ashihara, H. (1995). Pipecolic acid from the developing fruits (pericarp and seeds) of *Coffea arabica* and *Camellia sinensis*. Colloq Sci Int Café(C. R.), 16: 389-395.

Hashimoto, F., Nonaka, G.I., & Nishioka, I. (1987). Tannins and related compounds. LVI. Isolation of four new acylated flavan-3-ols from oolong tea, Chem Pharm Bull, 35(2): 611-616.

Hu, Z.Z., Jin, G.M., Wang, L.K., & Yang, J.F. (2005). Effect of tea polysaccharides on immune functions and antioxdative activity in broilers. J. Tea Sci., 25: 61-64.

Jiang, H., Zhang, M., Wang, D., Yu, F., Zhang, N., Song, C., & Granato, D. (2020). Analytical strategy coupled to chemometrics to differentiate *Camellia sinensis* tea types based on phenolic composition, alkaloids, and amino acids. J. Food Sci., 85: 3253–3263.

Joshi, R.P., & Gulati, A. (2011). Biochemical attributes of tea flowers (*Camellia sinensis*) at different developmental stages in the Kangra region of India. Scientia Horticulturae, 130(1): 266-274.

Juneja, L., Chu, D.C., Okubo, T., Nagato, Y., & Yokogoshi. H. (1999). L-theanine - A unique amino acid of green tea and its relaxation effect in humans. Trends Food Sci. Technol., 10: 199-204.

Kanwar, J., Taskeen, M., Mohammad, I., Huo, C., Chan, T.H., & Dou, Q.P. (2012). Recent advances on tea polyphenols. Front. Biosci., 4: 111.

Khan, N., & Mukhtar, H. (2007). Tea polyphenols for health promotion. Life Sci., 81: 519-533.

Khan, N., & Mukhtar, H. (2018). Tea polyphenols in promotion of human health. Nutrients, 11: 39.

Khan, H. (2014). Medicinal plants in light of history: Recognized therapeutic modality. J. Evid. Based Integr. Med., 19: 216-219.

Kim, E., Liang, Y., Jin, J., Sun, Q., Lu, J., Du, Y., & Lin, C. (2007). Impact of heating on chemical compositions of green tea liquor. Food Chem., 103:1263-1267.

Kimura, K, Ozeki, M., Juneja, L.R., & Ohira, H. (2007). l-Theanine reduces psychological and physiological stress responses. Biol. Psychol., 74: 39-45.

Liang, H., Liang, Y., Dong, J., & Lu, J. (2007). Tea extraction methods in relation to control of epimerization of tea catechins. J. Sci. Food. Agric., 87:1748-52.

Lin, Y., S., Wu, S.S., & Lin, J.K. (2003). Determination of tea polyphenols and caffeine in tea flowers (*Camellia sinensis*) and their hydroxyl radical scavenging and nitric oxide suppressing effects. Journal of Agricultural and Food Chemistry, 51(4): 975-980.

Lopes, J.M., Aubier, M., Jardim, J., Aranda, J.V., & Macklem, P.T. (1983). Effect of caffeine on skeletal muscle function before and afterfatigue. J. Appl. Physiol. Respir. Environ. Exerc. Physiol., 54: 1303-1305.

Matsuda, H., Hamao, M., Nakamura, S., Kon'i, H., Murata, M., & Yoshikawa, M. (2012). Medicinal Flowers. XXXIII. Anti-hyperlipidemic and anti-hyperglycemic effects of chakasaponins I-III and structure of chakasaponin IV from flower buds of Chinese tea plant (*Camellia sinensis*). Chemical & Pharmaceutical Bulletin, 60(5): 674-680.

Matsuda, H., Nakamura, S., Morikawa, T., Muraoka, O., & Yoshikawa, M. (2016). New biofunctional effects of the flower buds of *Camellia sinensis* and its bioactive acylated oleanane-type triterpene oligoglycosides. Journal of Natutral Medhods, 70(4): 689-701.

Mu, W., Zhang, T., & Jiang, B. (2015). An overview of biological production of L-theanine. Biotechnol. Adv., 33: 335-342.

Mukhtar, H., & Ahmad, N. (2000). Tea polyphenols: Prevention of cancer and optimizing health. Am. J. Clin. Nutr., 71: 1698S-1702S.

Murakami, T., Nakamura, J, Matsuda, H., & Yoshikawa, M. (1999). Bioactive saponins and glycosides. XV. Saponin constituents with gastroprotective effect from the seeds of tea plant, *Camellia sinensis* L. var. assamica

Pierre, cultivated in Sri Lanka: structures of assamsaponins A, B, C, D and E. Chem Pharm Bull, 47(12): 1759-1764.

Oyejide, O.O., & Olushola, L. (2005). Hepatoprotective and antioxidant properties of extract of *Camellia sinensis* (black tea) in rats, African Journal of Biotechnology, 4(11): 1432-1438.

Papamichael, C.M., Aznaouridis, K.A., Karatzis, E.N., & Karatzi, K.N. (2005). Stamatelopoulos, K.S.; Vamvakou, G.; Lekakis, J.P.; Mavrikakis, M.E. Effect of coffee on endothelial function in healthy subjects: The role of caffeine. Clin. Sci. 109: 55-60.

Pedro, A.C., Maciel, G.M., Rampazzo, R.V., & Haminiuk, C.W I. (2019). Fundamental and applied aspects of catechins from different sources: A review. International Journal of Food Science and Technology, 55(2): 429-442.

Ramirez-Mares, M.V., Chandra, S., & Mejia, E.G. (2004). In vitro chemopreventiveactivity of *Camellia sinensis*, llexpara guariensis and A) rdisia compressa, Mutat. Res, 554: 53-65.

Raffaella, Zanchi, R., Canzi, E., Molteni, L., & Scozzoli, M. (2008). Effect of *Camellia sinensis* (L.) whole plant extract on piglet intestinal ecosystem, Annals of Microbiology, 58(1): 147-152.

Rees, K., Allen, D., & Lader, M. (1999). The influences of age and caffeine on psychomotor and cognitive function. Psychopharmacology, 145: 181-188.

Riso, P., Erba, D., Criscuoli, F., & Testolin, G. (2002). Effect of green tea extract on DNA repair and oxidative damage due to H2O2 in Jurkat T cells, Nutr. Res., 22(10): 1143-1150.

Russell-Smith, J., Karunaratne, N., & Mahindapala, R. (2006). Rapid inventory of wild medicinal plant populations in Sri Lanka. Biological Conservation, 132: 22-32.

Ruxton, C.H.S. (2008). The impact of caffeine on mood, cognitive function, performance and hydration: A review of benefits and risks. Nutr. Bull., 33: 15-25.

Sagesak, Y.M., Uemura, T., Watanabe, N., Sakata, K., & Uzawa, J. (1994). A new glucuronide saponin from tea leaves (*Camellia sinensis* var. sinensis). Biosci Biotech Biochem, 58(11): 2036-2040.

Sharangi, A.B. (2009) Medicinal and therapeutic potentialities of tea (*Camellia sinensis* L.) – A review. Food Research International, 42: 529-535.

Sofowora, A., Ogunbodede, E., & Onayade, A. (2013). The role and place of medicinal plants in the strategies for disease prevention. Afr. J. Tradit. Complement. Altern. Med., 12:10(5):210-229.

Shokrzadeh, M, Ebadi, A.G., Mirshafiee, S.S., & Choudhary, M.I. (2006). Effect of the aqueous green leaf extract of green tea on glucose level of rat, Pakistan Journal of Biological Sciences, 9(14): 2708- 2711

Sun, L., Xu, H. X., Ye, J., & Gaikwad, N. W. (2019). Comparative effect of black, green, oolong, and white tea intake on weight gain and bile acid metabolism. Nutrition, 65: 208-215.

Tang, G., Meng, X., Gan, R., Zhao, C., Liu, Q., & Feng, Y., Li, H. (2019). Health functions and related molecular mechanisms of tea components: An update review. International Journal of Molecular Sciences, 20: 6196.

Wang, Y., Li, Y., Liu, Y., Chen, X., & Wei, X. (2015). Extraction, characterization and antioxidant activities of Se-enriched tea polysaccharides. Int. J. Biol. Macromol., 77: 76-84.

Wang, Y.M., Ren, N., Rankin, G.O., Li, B., Rojanasakul, Y., Tu, Y., & Chen, Y. C. (2017). Anti-proliferative effect and cell cycle arrest induced by saponins extracted from tea (*Camellia sinensis*) flower in human ovarian cancer cells. Journal of Functional Foods, 37: 310-321.

Wei, J.X., Zuo, Q.Y., & Zhu, Y. (1997). Studies on the chemical constituents of seeds of *Camellia sinensis* var. assamica, Zhongguo Zhongyao Zazhi, 22(4): 228-230.

Wheeler, D.S., & Wheeler, W.J. (2004). The medicinal chemistry of tea. Drug Dev. Res., 61: 45-65.

Wu, T., Guo, Y., Liu, R., Wang, K., & Zhang, M. (2016). Black tea polyphenols and polysaccharides improve body composition, increase fecal fatty acid, and regulate fat metabolism in high-fat diet-induced obese rats. Food Funct., 2469-2478.

Xia, X., Wang, X., Wang, H., Lin, Z., Shao, K., Xu, J., & Zhao, Y. (2021). Ameliorative effect of white tea from 50-year-old tree of *Camellia sinensis* L. (Theaceae) on kidney damage in diabetic mice via SIRT1/AMPK pathway. J. Ethnopharmacol., 272: 113919.

Xiang, L., Wang, A., Ye, J., Zheng, X., Polito, C., Lu, J., Li, Q.S., & Liang, Y.R. (2016). Suppressive effects of tea catechins on breast cancer. Nutrients, 8: 458.

Yang, Z., Y., Jie, G.L., He, P.M., & Tu, Y. Y. (2007). Study on the antioxidant activity of tea flowers (*Camellia sinensis*). Asia Pacific Journal of Clinical Nutrition, 16(Suppl 1), 148-152.

Yang, C.S., Chen, G., & Wu, Q. (2014). Recent scientific studies of a traditional Chinese medicine, tea, on prevention of chronic diseases. J. Tradit. Complement. Med., 4: 17-23.

Yang, C.S., Lambert, J.D., & Sang, S. (2009). Antioxidative and anti-carcinogenic activities of tea polyphenols. Arch. Toxicol. 83: 11-21.

Yoshida, Y., Kiso, M., Ngashima, H., & Goto, T. (1996). Alterations in chemical constituents of tea shoot during its development. Chagyo Kenkyu Hokoku, 83: 9-16.

Yang, Z.Y., Tu, Y. Y., Baldermann, S., Dong, F., Xu, Y., & Watanabe, N. (2009). Isolation and identification of compounds from the ethanolic extract of flowers of the tea (*Camellia sinensis*) plant and their contribution to the antioxidant capacity. LWT-Food Science and Technology, 42(8): 1439-1443.

Yang, Z.Y., Dong, F., Baldermann, S., Murata, A., Tu, Y.Y., Asai, T., & Watanabe, N. (2012). Isolation and identification of spermidine derivatives in tea (*Camellia sinensis*) flowers and their distribution in floral organs. Journal of the Science of Food and Agriculture, 92(10): 2128-2132.

Yen, G.C., & Chen, H.Y. (1996). Relationship between antimutagenic activity and major components of various teas. Mutagenesis, 11(1): 37-41.

Yokogoshi, H., Kato, Y., Sagesaka, Y.M., Takihara-Matsuura, T., Kakuda, T., & Takeuchi, N. (1995). Reduction Effect of Theanine on Blood Pressure and Brain 5-Hydroxyindoles in Spontaneously Hypertensive Rats. Biosci. Biotechnol. Biochem., 59: 615-618.

Yoshikawa, M., Morikawa, T., Yamamoto, K., Kato, Y., Nagatomo, A., & Matsuda, H. (2005). Floratheasaponins A-C, acylated oleanane-type triterpene oligoglycosides with anti-hyperlipidemic activities from flowers of the tea plant (*Camellia sinensis*). Journal of Natural Products, 68(9): 1360-1365.

Yoshikawa, M., Sugimoto, S., Nakamura, S., & Matsuda, H. (2008). Medicinal flowers. XXII. Structures of chakasaponins V and VI, chakanoside I, and chakaflavonoside A from flower buds of Chinese tea plant (*Camellia sinensis*). Chemical & Pharmaceutical Bulletin, 56(9): 1297-1303.

Yoshikawa, M., Sugimoto, S., Kato, Y., Nakamura, S., Wang, T., Yamashita, C., & Matsuda, H. (2009). Acylated oleanane-type triterpene saponins with acceleration of gastrointestinal transit and inhibitory effect on pancreatic lipase from flower buds of Chinese tea plant (*Camellia sinensis*). Chemistry & Biodiversity, 6(6): 903-915.

Zhang, X., (2002) WHO Traditional Medicine Strategy *2002–2005*. World Health Organization: Geneva, Switzerland.

Zhang, L., Ho, C., Zhou, J., Santos, Jˆ anio. S., Armstrong, L., & Granato, D. (2019). Chemistry and Biological Activities of Processed *Camellia sinensis* Teas: A Comprehensive Review. Comprehensive Reviews in Food Science and Food Safety, 18(5): 1474-1495.

Zheng, G., Sayama, K., Okubo, T., Juneja, L.R., & Oguni, I. (2004). Anti-obesity effects of three major components of green tea, catechins, caffeine and theanine, in mice, Vivo, 18: 55-62.

Zheng, X., Nie, Y., Gao, Y., Huang, B., Ye, J., Lu J, & Liang, Y.R. (2018). Screening the cultivar and processing factors based on the flavonoid profiles of dry teas using principal component analysis, J. Food Compos. Anal. , 67: 29-37.

CHAPTER VI

EFFECTS OF ORGANIC FERTILIZERS ON AROMA COMPONENTS IN *Camellia sinensis* L. AT DIFFERENT LOCATIONS

PhD. Aysel ÖZCAN AYKUTLU[1]
Asist. Prof. Emine YURTERİ[2]
Prof. Dr. Fatih SEYİS[3]

DOI: https://dx.doi.org/10.5281/zenodo.13826046

[1] Recep Tayyip Erdoğan University, Faculty of Agriculture, Field Crops Department, 53300 Rize, Türkiye. ORCHID ID: 0000-0001-5210-7617, e-mail:aysel.ozcan@ erdogan.edu.tr

[2] Recep Tayyip Erdoğan University, Faculty of Agriculture, Field Crops Department, 53300 Rize, Türkiye. ORCHID ID: 0000-0002-3770-2714, e-mail:emine.yurteri@ erdogan.edu.tr

[3] Recep Tayyip Erdoğan University, Faculty of Agriculture, Field Crops Department, 53300 Rize, Türkiye. ORCHID ID: 0000-0002-3770-2714, e-mail: fatih.seyis@ erdogan.edu.tr

INTRODUCTION

Camellia sinensis (L.) O. Kuntze, known as the tea plant in our country, is an evergreen shrub belonging to the Theaceae family, growing in tropical and subtropical climates. The beverage called tea, which is obtained by collecting and processing the 2 leaves and terminal buds of the tea plant, is among the most consumed beverages in the world. Three criteria are effective in determining the quality of tea: physical appearance, infusion and flavor. Mostly, the genetic characteristics of the material, as well as agricultural and climatic conditions, are important in the formation of the quality parameters of tea shoots. (Choi OkJa et al., 2016).

Tea contains compounds such as polyphenols, caffeine, essential oils, vitamins, and flavorings that have important biological activities and are beneficial for health. Essential oils contain high amounts of terpene compounds. These terpene compounds are secondary metabolites that have many biological activities similar to other plant substances (such as phenolics, flavonoids and coumarins) (Zwenger and Basu, 2008). In folk medicine, which has been practiced from ancient times to the present day, aroma compounds with physiological effects such as sedatives are used for therapeutic purposes. More than 600 aroma compounds specific to tea have been identified to date. The unique fresh scent of the buds collected from green tea leaves is formed by linalool, cis-3-hexanol and other aroma compounds (Li et al., 2017). The characteristic structure of tea types varies according to the amount and proportion of aroma components in the tea. Depending on the volatile compounds in the tea leaves, tea aromas with green, floral or hazelnut scents emerge. Volatile compounds found in tea play an important role in determining flavor and also affect consumer preferences (Ağca et al., 2020). In addition to catechins, volatile components also contribute to the antioxidant effect and similar quality properties of tea (Li et al., 2017).

There are many factors that affect agricultural production, but one of the most important of these is fertilizer. Fertilizers serve as a driving force in increasing the yield and quality of plant products and improving food for human consumption (Colipanoand Cagasan, 2022). When the studies on the effect of nitrogen, which is an important nutrient for tea, on tea quality are examined, it has been reported that the increase in nitrogen levels has an effect on other quality parameters as well as changes in the amounts of aroma compounds and accordingly the aromatic smell of the tea changes (Owuor, 2001). However, it has been noted that K and Mg fertilizer applications contribute to the increase in aroma compounds found in tea (Ruan et al., 1999). However, due to the limited number of studies on the subject, the effect of fertilizer applications on aroma compounds has not been clearly demonstrated. More studies are needed to understand the effect of biotic and abiotic stress factors on tea quality (aroma) and the relationship between them more clearly (Yang et al., 2013).

The aim of this study was to investigate the effects of various fertilizers applied to tea plantations in different locations on the aroma compounds present in tea leaves.

1. MATERIAL AND METHOD

1.1. Plant Material

The research was carried out in tea (*Camellia sinensis* L.) plantations located in Musadağı (Çayeli/Rize) and Bölümlü (Of/Trabzon) locations. Fertilizers with different contents were applied within the scope of the experiment and samples taken from the leaves of the applied tea plants in the 1st shoot period were used as research material.

Figure 1: Images of the experiments conducted in (a) Bölümlü and (b) Musadağı locations

The coordinate information of the locations where the experiments were carried out are as follows; Bölümlü location (Figure 1a); 400 m altitude, 40°50’54’’N 41°18’32’’E, Musadağı location (Figure 1b); 180 m altitude, 41°2’52’’N 40°41’53’’E. The study was carried out according to the Randomized Blocks Factorial Experimental Design with 3 replications. In the experiment, in addition to the chemical compound fertilizer (25-5-10) used in the tea plant, 2 solid organic fertilizers (K1 and K2), 2 liquid organic fertilizers (S1 and S2) and plots belonging to the control group to which no fertilizer was applied were created. Plot sizes were determined as 30 m2 and the distance between replications was determined as 1 m.

1.2. Sample Preparation and Aroma Components Analysis

Samples of collected tea leaves were dried in the oven at 40°C for 24 hours, then ground and passed through 2 mm porous laboratory sieves to prepare for analysis. Analysis was performed using a GC-MS Device (Shimadzu, Japan) outfitted with SPME (Figure 2a). Ground plant samples weighing 0.2 g were then put into a 10 mL vial and sealed with a silicone-rubber septum lid (Figure 2b). In order to pre-condition the fiber, manufacturer guidelines were followed. The fiber was left in the headspace at equilibrium for one minute at room temperature. The fiber was placed into the needle after sampling and then moved to the injection port of the GC-MS device. The column was a CP 5MS (30 m x 0.25 mm i.d., film thickness 0.25 m). The oven temperature was set to isothermal at 220 °C for 20 minutes after being scheduled to rise from 40 °C to 240 °C at 2 °C/min. As a carrier gas, helium was employed at a constant flow rate of 1 mL/min. The FFNSC 1.2 databases were used to determine the constituents of essential oils (Seyis et al., 2022).

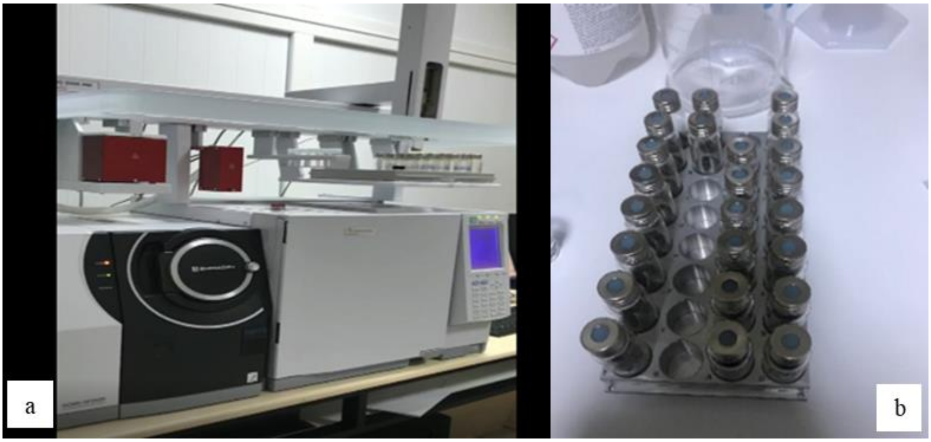


Figure 2: Images of the Gas Chromatography Mass Spectrophotometer (a) (GC-MS) device and (b) samples prepared for analysis

1.3. Data Analysis

The XLSTAT 2023 (Addinsoft, 2023) was used to perform Biplot Analysis. To visualize current variation in *Camellia sinensis* L. plant for chemical variability, this statistical program was used. Obtained data was used to produce scatter plot diagrams. Using the results of the GC-MS study, a separate biplot diagram was also produced.

1. RESULTS AND DISCUSSION

Within the scope of this study, data on the amounts of aroma components in fresh tea leaves depending on fertilizer applications carried out in different locations are given in Table 1.

According to the research results, it was determined that aroma compounds varied depending on fertilizer applications and locations. While there were a total of 84 aroma compounds in the harvested fresh tea leaf samples, caffeine compound was found to have the highest amount in all samples.

While caffeine and β-ionone compounds were detected in all tea samples, the amounts of the remaining aroma components varied depending on the sample examined. The amount of caffeine compound varied between 32.56% and 65.14%. The highest results were obtained in chemical fertilizer (65.14%, 48.21%) in terms of caffeine amount in Bölümlü and Musadağı locations, respectively, while it was followed by K1 (61.29%, 48.13%), K2 (60.28%, 47.88%), S2 (59.90%, 47.70%), S1 (54.19%, 38.56%) and control (40.99%, 37.52%) applications. However, it was determined that the caffeine content of the samples taken from Bölümlü location was higher than the samples taken from Musadağı location. In addition, β-ionone (ranging from 3.18% to 8.61%) was another important compound found in high amounts in tea leaves, although it varied according to the sample examined. Besides, only caffeine and β-ionone compounds were detected in all samples.

Table 1: Changes in aroma components in tea leaves depending on fertilizer applications (%)

Components	R.I*	R.T**	BÖLÜMLÜ						MUSADAĞI					
			Control	Chemical	K1	K2	S1	S2	Control	Chemical	K1	K2	S1	S2
Furan <2,5-	703	4.41							1.4	1.67	1.69	1.56	1.82	
Pent-2(Z)-enol	767	4.24											0.56	
Capronaldehyde	801	4.88	2.46	1.66	2.19	2.68		1.79	2.84	3.49	3.61	3.51	5.16	3.51
Formate <amyl->	823	4.15											1.28	
Hex-2(E)-enal	850	6.44				0.56							1.13	
Hex-3(Z)-enol	853	6.54							1.55	0.92	0.78		1.12	
Butyric Acid	881	6.43	1.55				1.5							
Pentanol <1-	902	4.56	3.00											
Valeric Acid	911	10.98	11.75				1.67							
Lactate <ethyl->	914	10.76	3.41							2.06		0.91		
Formate <hexyl->	929	11.86					3.77							
Butyrolactone	941	10.41	2.65											
Benzaldehyde	964	10.11						0.77						
Hexanol	967	7.00							0.82					
6- Methyl-5-Hepteno	986	11.22	1.79	2.44	2.84		2.82	2.22	3.39	2.53	2.72	2.57	4.01	1.82
Isocaproic Acid	986	10.96				1.57								
Furan <2-amyl->	991	11.37	0.97	1.16	1.09	1.18		1.08	1.16		0.88		0.88	
Valeric Acid <3-	1002	10.96			1.31			1.34		1.25		0.28	1.07	
Heptandienal	1013	12.06								1.17		0.97	1.26	0.85
Tiglate <allyl->	1025	13.36		0.82										
Eucalyptol	1032	12.88	1.67				0.92							
Benzyl Alcohol	1040	12.98	1.96		1.26		1.03	1.33	2.29	2.04	1.33	1.87	3.13	1.76
Hexenoic acid	1071	12.44	2.76							1.41		1.08		
Linalool Oxide	1080	15.11	1.11	2.73	2.75	1.15	1.06	1.36	1.92					1.21
Pyrazine <3-sec-	1089	13.56			0.74		1.24	0.86	1.14					

Linalool Oxide	1095	14.49	4.15		2.66	1.74	2.33	2.00	3.61	2.16	1.81	1.72	2.78	
Linalool	1101	15.56	1.32	1.42	1.37	1.21	1.31	1.17	2.59	1.66	1.58	2.04	2.32	
Hendecane	1101	15.84				1.16								
Pelargonaldehyde	1107	15.73	1.44	1.39	0.98	1.35		1.41	1.43	1.54	1.26	1.77	2.16	1.67
Phenethyl Alcohol	1113	16.03	1.61		0.92	0.56		0.94	3.98	2.98	2.69	3.53	3.2	2.54
Terpineol <alpha-	1138	19.02		0.83										
Limonene oxide	1142	30.72		1.42			1.74		4.00				4.31	4.48
Camphor	1149	17.23			1.09		1.25							
Menthone	1158	19.02		0.77					1.31	1.27	1.29	1.30	1.57	1.05
Non-2(E)-enal	1163	20.46									0.54			1.22
Isoisopulegol	1169	20.51							0.62					
Nona-2E,6Z-	1170	18.39				1.00								
Neomenthol	1170	15.81										1.56		
Tetrahydrofurfuryl	1179	22.78								2.76	4.39			
Heptanoate <allyl-	1182	23.61												0.62
Isopinocampheol	1195	25.75			0.57									
Capraldehyde	1208	18.21					0.73				0.48			
Nerol	1229	21.36							3.44	1.3	1.69	1.35	2.05	1.61
Pulegone	1241	30.70						2.06		3.83	4.82	4.05		
Carvone	1246	20.98		1.48		0.64								
Pentylallyl	1282	22.24			0.45									
Tridecane	1300	23.02		1.92	1.05	1.13		0.91	1.60	1.47	1.36	1.64	1.97	1.36
Terpinyl Acetate	1349	24.77					1.21							
Undecanal <2-	1369	25.86						3.53	0.92			1.67		1.88
Tetradecane	1400	26.47	0.99		1.14	1.27	6.01	2.85		0.86	0.94	1.11	1.28	1.08
Caryophyllene	1418	27.22		0.81										
Ionone <(E)-,	1421	27.41								0.92	0.78	0.95		
Aromadendrene	1438	32.42										0.60		
Geranyl Acatone	1450	28.21				2.08								

Nonane-1,3-diol	1473	34.44									0.96			
Lauryl Alcohol	1476	28.02		0.89										
Selinene <beta->	1487	29.42												2.36
Ionone <(E)-,beta	1495	29.34	3.18	3.43	4.58	4.07	3.73	4.03	8.74	7.65	8.38	8.39	8.56	8.61
Pentadecane	1500	29.74		0.92										
Citronellyl	1529	30.71				1.90								
Nerolidol	1562	34.71							1.12	0.68				
Tridec-2(E)-enal	1573	34.78												1.38
Undecalactone	1577	31.92				0.67								
Tridecyl alcohol	1580	34.46	1.18	1.13										
Caryophyllene	1587	32.44				0.56				0.57			1.03	
Phthalate	1592	40.39									0.90			
Hexadecane	1600	32.81	4.30	3.35	3.81	3.67		0.91				3.21	3.33	4.47
Tetradecanal	1614	33.18						2.35	2.40	1.07		0.92	1.16	2.44
Citronellyl Tiglate	1664	34.45				1.08								
Tridecyl methyl	1697	35.82							1.52	1.53	1.43		1.52	
Heptadecane	1700	35.75	2.77	2.38	2.25	1.87	1.57	1.24			1.34	1.22	1.10	2.32
Pentadecanol	1794	37.74				0.68								
Octadecane	1800	38.54	1.04	0.83	1.17	0.91	0.82		1.08		1.00	0.85		1.03
Caffeine	1837	38.78	**40.99**	**65.14**	**61.29**	**60.28**	**54.19**	**59.9**	**37.52**	**48.21**	**48.13**	**47.88**	**38.56**	**47.70**
Phytone	1841	38.85		1.06										1.16
Cetyl Alcohol	1884	40.15				0.64	1.47		1.05					
Nonadecane	1900	41.93		0.94	0.92		1.36	1.02						
Palmitate	1925	41.88	1.95		2.81	4.39	4.34	2.67	1.09		1.33		1.68	1.12
Isophytol	1947	42.80							2.96					
Palmitic Acid	1977	42.71			0.76		1.00	2.26						
Eicosane	2000	42.93		1.08										
Phytol	2106	46.47					2.03		1.51	3.00	1.89	1.49		0.75
Docosane	2200	47.20					0.90							

Pentacosane	2500	50.69							1.00					
TOPLAM			**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

***Retention Index, **Retention Time**

Additionally, capronaldehyde (1.66-5.16%), 6-methyl-5-hepten-2-one (1.79-4.01%), linalool oxide (1.74-4.15%), linalool (1.17-2.59%), pelargonaldehyde (0.98-2.16%), phenethyl-alcohol (0.56-3.98%), tetradecane (0.86-6.01%), methyl palmitate (1.12-4.39%), hexadecane (0.91-4.30%), heptadecane (1.10-2.77%) were other significant compounds recorded in most of the samples.

It is generally stated that linalool and hexanal compounds play an important role in determining the quality of green tea (Kato and Shibamoto, 2001). It has been stated that the accumulation of volatile components in the tea leaf is higher in April and the rates of monoterpene alcohols (linalol, linalool oxide, geraniol) from these components also increase (Hazarika et al., 1984). In the studies, it was determined that the change in volatile components in the content of tea leaves will vary depending on the region where the samples were taken (Choi et al., 2016). It is reported that choosing the appropriate raw material and location can be a logical approach to enriching the aromatic profile aimed at tea production (Ağca et al., 2020).

In the study conducted by Dai et al. (2019) examining the effects of brewing on aroma components in green tea, alcohols, aldehydes and hydrocarbons were the most abundant compounds. According to the results of the research conducted on the formation of aroma compounds during the production process in green tea (Wang et al., 2016), it was determined that the volatile components identified in the study samples belong to the alcohol, hydrocarbon, aldehyde, ketone, nitrogen compounds, lactone, phenol and ester groups.

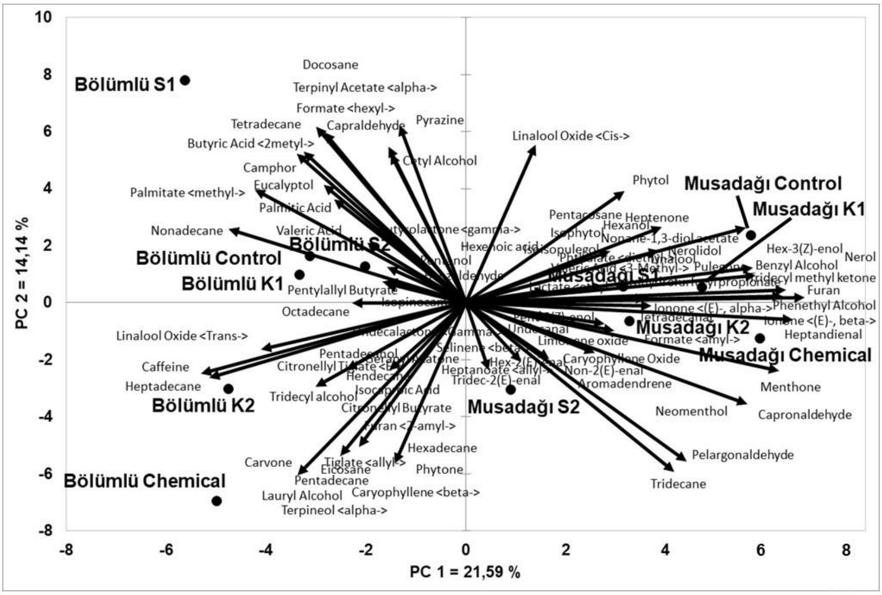


Figure 3: Biplot analysis of the essential oil composition of tea samples at the locations Bölümlü and Musadağı after organic fertilizer application

The obtained Biplot of the effect of organic fertilizers on volatile oil composition of tea samples collected from the locations Bölümlü and Musadağı can be seen in Fig. 1. Using Biplot 35.73 % of total variation based on volatile composition of tea samples could be explained. İt is clear that different organic fertilizers affected the volatile oil composition of tea samples based on locations. Although, chemical fertilizer applications different from organic fertilizer applications. Specially, caffeine could be detected at highest amounts in all samples.

2. CONCLUSION

In our study conducted to investigate the effects of liquid and solid organic fertilizers applied to tea plantations in different locations on aroma compounds in tea, it was concluded that the amount and distribution of aroma compounds varied depending on both the location and the content of organic fertilizers. When evaluated in terms of the compounds detected in all samples, caffeine content increased as altitude increased, but β-ionene, 6-methyl-5-hepten-2-one and linalool content decreased. In addition, the caffeine content of solid fertilizers was found to be higher than liquid fertilizers. In the light of this information, it can be said that altitude and fertilizer applications are effective on aroma compounds in tea leaves. However, considering that aroma compounds in tea may vary under the influence of more than one factor, more studies are needed where more locations and different cultural practices are evaluated together.

REFERENCES

Addinsoft. (2023). XLSTAT statistical and data analysis solution (New York, USA).

Ağca, A.C., Vural, N., & Şarer, E. (2020). Determination of volatile compounds in green tea and black tea from Turkey by using HS-SPME and GC-MS. İstanbul Journal of Pharmacy, 50(2): 111-115.

Choi, O. J., Jung, H. S., & Yun, K. W. (2016). Influence of different sampling site and storage duration on volatile components of Korean green tea. Research Journal of Medicinal Plants, 10(4): 309-313.

Colipano, J.M., Cagasan, U.A. (2022). A Review on the Impact of Organic, Conventional and Nano Fertilizer Application in Crop Production. Eurasian Journal of Agricultural Research, 6(2): 101-109.

Dai, Q., Jiang, Y., Liu, S., Gao, J., Jin, H., Wang, H., Xiao, M., Zhang, Z., & Li, D. (2019). The impacts of brewing in glass tumblers and thermos vacuum mugs on the aromas of green tea (*Camellia sinensis*). Journal of Food Science and Technology, 56: 4632-4647.

Hazarika, M., Mahanta, PK., & Takeo, T. (1984). Studies on some volatile flavour constituents in orthodox black teas of various clones and flushes in North-east Indi. Journal of the Science of Food and Agriculture, 35(11): 1201-1207.

Kato, M., & Shibamoto, T. (2001). Variation of major volatile constituents in various green teas from Southeast Asia. Journal of Agricultural and Food Chemistry, 49(3): 1394-1396.

Li, Y-S., Kawasaki, Y., Tomita, I., & Kawai, K. (2017). Antioxidant properties of green tea aroma in mice. Journal of Clinical Biochemistry and Nutrition, 61(1): 14-17.

Owuor, P.O. (2001). Effects of fertilisers on tea yields and quality: A review with special reference to Africa and Sri Lanka. International Journal of Tea Science, 1: 1-11.

Ruan, J., Wu, X., & Härdter, R. (1999). Effects of potassium and magnesium nutrition on the quality components of different types of teai. Journal of the Science of Food and Agriculture, 79(1): 47-52.

Sereshti, H., Samadi, S., & Jalali-Heravi, M. (2013). Determination of volatile components of green, black, oolong and white tea by optimized ultrasound-assisted extraction-dispersive liquid–liquid microextraction coupled with gas chromatography. Journal of Chromatography A, 1280: 1-8.

Seyis, F., Yurteri, E., Özcan, A., Cirak, C. & Yayla, F. (2022). Volatile secondary metabolites of *Hypericum tetrapterum* and *Hypericum bithynicum*. Biochemical Systematics and Ecology, 105: Article 104542.

Wang, C., Lv, S., Wu, Y., Lian, M., Gao, X., & Meng, Q. (2016). Study of aroma formation and transformation during the manufacturing process of Biluochun green tea in Yunnan Province by HS-SPME and GC-MS. Journal of the Science of Food and Agriculture, 96(13): 4492-4498.

Yang, Z., Baldermann, S., & Watanabe, N. (2013). Recent studies of the volatile compounds in tea. Food Research International, 53(2): 585-599.

Zwenger, S., & Basu, C. (2008). Plant terpenoids: applications and future potentials. Biotechnology and Molecular Biology Reviews, 3(1): 1-7.

CHAPTER VII

HERBAL ESSENTIAL OILS: A PROMISING ALTERNATIVE FOR CONTROLLING PHYTOPHAGOUS INSECTS

Asist. Prof. Dr. Halil DİLMEN[1]

DOI: https://dx.doi.org/10.5281/zenodo.13826052

[1] Siirt University, Faculty of Agriculture, Department of Plant Protection, Siirt, Türkiye. ORCID: 0000-0002-3802-9947, e-mail: halildilmen@siirt.edu.tr

INTRODUCTION

Pests damage agricultural products, leading to losses of yield and quality (Sharma et al., 2017). Recognizing pests is crucial for developing effective intervention strategies for agricultural production. Various strategies are employed worldwide to manage pests, primarily aimed at controlling pest populations through cultural control methods and appropriate agricultural practices. Additionally, these methods support biodiversity by aiding in the natural control of pests by predators. Furthermore, biological and ecological control methods involve the use of natural enemies to control pests. These methods encourage the use of beneficial organisms to control pest populations. However, the amount of pesticides used in agriculture worldwide was 1.795.502 tons in 1990, which increased to 3.531.959 tons in 2021 (FAO, 2024) (Figure 1).

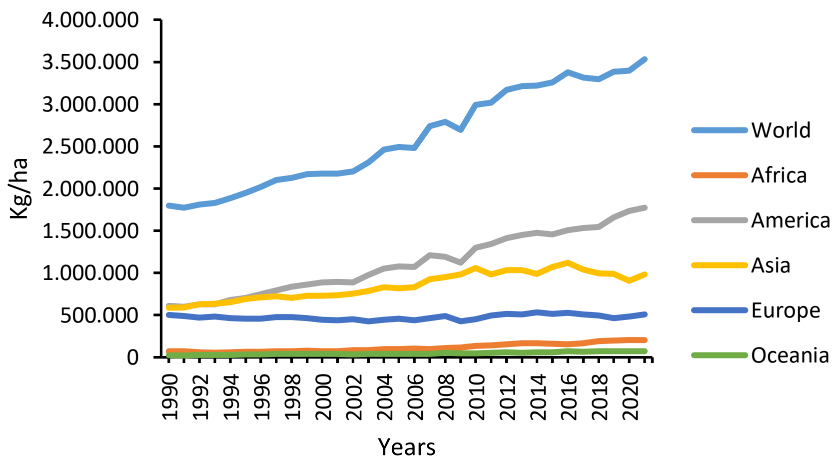


Figure 1: Worldwide pesticides use per area of cropland by region.

Although pesticides provide benefits to crops, they can negatively affect human and environmental health (Khursheed et al., 2022). Excessive pesticide use can lead to the loss of biological diversity, endangering many birds, aquatic animals, and even humans (Mahmood et al., 2016).

The rapid growth of the world's population, estimated to surpass 8 billion in November 2023 and projected to reach 10 billion by 2058 (Anonymous, 2023), presents a significant challenge in meeting the increasing demand for food and raw materials. Following World War I, the increased demands for food and raw materials resulting from population growth were met by agricultural policies known as the Green Revolution, which achieved increased productivity per unit area through the development of resilient plant species, effective irrigation, and intensive fertilization. Furthermore, a wide array of chemical inputs such as pesticides, fertilizers, vitamins, and hormones were heavily employed (Çetin, 2022). While these agricultural policies and chemical inputs aim to increase productivity per unit area, it is known that there are approximately 67.000 pest organisms that can cause up to 70% yield losses in agricultural production (Campos et al. 2019). Consequently, chemical pesticides are intensively used, especially for controlling plant diseases, pests, and weeds. However, improper agricultural practices and widespread use of chemical inputs (pesticides, fertilizers, vitamins, hormones, etc.) pose serious risks to human and environmental health.

People are directly or indirectly exposed to pesticides through intensive and indiscriminate use. Humans are often directly affected by pesticides through ingestion, dermal contact, and inhalation during their production, application, transportation, and storage (Erdoğan, 2010). As a result, more than 3 million people suffer from pesticide poisoning annually, and approximately 300,000 die from poisoning (Flores-Gutierrez et al., 2023). Furthermore, humans are indirectly affected by pesticides or residues from polluted air, water, and soil. Additionally, pesticide residues accumulated in foods such as meat, eggs, milk, vegetables, and fruits indirectly impact human health. Some pesticides, both directly and indirectly exposed, have carcinogenic, neurotoxic, and mutagenic effects (Akdoğan et al., 2012). Moreover, they trigger psychiatric and neurological diseases such as dementia, Parkinson’s disease, Alzheimer’s disease, and ALS (Özay & Arslantaş, 2016)

Plants and plant-based products are widely recognized and sought after for their use as natural pesticides and insecticides because they are effective against numerous harmful insects, readily available, inexpensive, and biodegradable (Nile et al., 2019). The adverse effects of inappropriate and excessive use of chemical pesticides have made it necessary to explore alternative pest management strategies (Mahmood et al., 2016).

Plant-based insecticides, which are derived entirely from plant sources and harmless to human health and the environment, offer a significant alternative to chemical insecticides in sustainable agriculture. These alternatives can not only help increase agricultural productivity, thus preserving farmers' incomes but also conserve ecosystems as an environmentally friendly agricultural practice. Therefore, plant-based insecticides can be an important tool for ensuring the sustainability of agriculture.

1. PLANT-BASED INSECTICIDES

Numerous plants from families such as Rutaceae, Compositae, Meliaceae, Leguminosae, Araceae, Platycodoniaceae, Solanaceae, Chenopodiaceae, Zingiberaceae, Labiatae, Loniceraceae, Umbelliferae, Polygonaceae, and Euphorbiaceae exhibit pesticide properties, containing a variety of secondary metabolites like alkaloids, terpenoids, and flavonoids (Ngegba et al., 2022).

Organic substances are synthesized by plants. While synthesized primary metabolites are used in vital activities such as growth, reproduction, and photosynthesis, secondary metabolites are aimed at creating resistance against various diseases caused by microorganisms and stress from biotic factors (Böttger et al., 2018). Plants have evolved a variety of chemical substances to defend themselves from pathogenic microorganisms and insects. These biologically active substances, known as "phytochemicals," act as repellents, toxins, deterrents to feeding, and growth regulators for insects (Şengül et al., 2022). It is known that insecticidal plant-based insecticides with repellent, antifeedant, contact, growth inhibitory, and reproductive inhibitory effects are obtained from secondary metabolites (Isman, 2017). The use of pesticides presents difficulties for environmental sustainability and global stability. As a result, increasing concern for environmental safety has led to a rising interest in pest control methods that employ eco-friendly, plant-based pesticides. Figure 2 demonstrates the process of producing an eco-friendly pesticide from the Neem tree (*Azadirachta indica*), highlighting its various insecticidal effects—repellent, toxic, growth inhibitory, and feeding deterrent—while emphasizing the benefits of low toxicity, reduced residue, and environmental sustainability."

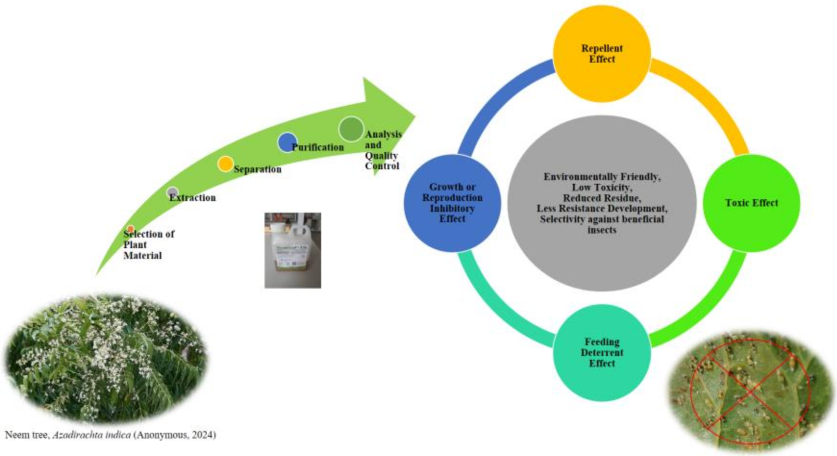


Figure 2: Extraction processes and effects of herbal essential oils

Plant-based insecticides obtained from leaves, roots, flowers, fruits, seeds, and stems of plants are used in the form of volatile oils or plant extracts (Lengai et al., 2020). Essential oils are predominantly volatile extracts of aromatic and medicinal plants (Tamokou *et al.* 2017). Essential oils are a significant source of biologically active compounds, offering a range of activities such as antibacterial, insecticidal, fungicidal, nematicidal, herbicidal, antioxidant, and anti-inflammatory effects (Kesraoui et al., 2022). Essential oils derived from plants exhibit lethal effects at different developmental stages and cause minimal harm to natural enemies (Schmutterer, 1990). Being environmentally friendly, plant-based insecticides do not pose residue problems because they dissolve easily due to environmental factors such as moisture, sunlight, and wind (Karakaş, 2018). Moreover, they exhibit low toxicity to humans and other living groups (Dalavayi et al. 2021). Plant-based insecticides have many more advantages in this regard. Owing to their environmentally friendly properties, there is growing interest in and use of plant-based products as alternatives to pesticides. In this context, many studies have been conducted to determine the effectiveness of plant-based insecticide oils and extracts against harmful insect species (Hikal et al., 2017; Kumar et al., 2019; Amala et al., 2021; Hernández-Suárez et al., 2023).

According to the results of these studies, it has been proven that components derived from plants are effective against many different harmful insect species. Among plant-based insecticides, Pyrethrum, Rotenone, and Neem are commonly used commercially, while the use of Ryania, Nicotine, Sabadilla, and volatile oils is less common. Although less common, thujone, thymol, linalool, carvacrol, eugenol, menthol, α-terpineol, 1,8-cineol, cinnamaldehyde, nicotine, and citronella are other plant-based products used in control pests (Campos et al., 2019)

Neem; It has been known in India for thousands of years and is used for medicinal, cosmetic, and agricultural purposes. It is obtained from leaves, seeds, flowers, and other parts of *Azadirachta indica*, also known as the Indian neem tree. *A. indica* contains 35 different components, but the most effective insecticide is azadirachtin. It has been shown to impact over 60 harmful insect species in various ways, including inhibiting feeding, altering morphology, reducing biological fitness, suppressing fertility, stunting growth, preventing egg-laying, and even causing sterilization (Ngegba et al., 2022).

Pyrethrum; It is obtained by drying and grinding the top parts of chrysanthemum flowers, especially *Chrysanthemum cinerariae*, *C. coccineum*, and *C. marshalli* (Soni & Anjikar, 2014). Pyrethrum, which has been known for its insecticidal properties for over 150 years, is widely used against many harmful species because of its rapid paralyzing effect on insects (Schleier III & Peterson, 2011).

Thujone; primarily derived from natural sources such as *Artemisia absinthium* (Wormwood), as well as other *Artemisia* species like sage, juniper, cedar, thyme, and mint, is a natural compound with insecticidal properties obtained from plants (Pelkonen et al., 2013). Thujone has been found to exhibit feeding deterrent, toxic, and repellent effects on insects (Lazarević et al., 2022).

Eugenol; It is a compound obtained from aromatic plants such as cloves, cinnamon, basil, turmeric, ginger, thyme, laurel, and bergamot (Khalil et al., 2017). Eugenol is widely used in medicine, especially dentistry, for local anesthesia and oral hygiene (Pavithra, 2014). Eugenol has toxic and repellent effects against aphids, psyllids, hemipterans, moths, and other insects (Czarnobai et al., 2022)

1,8-Cineol (Eucalyptol); It is a compound obtained from various aromatic plants, especially eucalyptus trees, *Mentha longifolia* (Mint), *Artemisia dracunculus* (Tarragon), *Coriandrum sativum* (Coriander), and many others (Jalilzadeh-Amin & Maham 2015). Eucalyptol, which has been used for medical purposes for many years, has been proven to have repellent and feeding inhibitory effects on various harmful insects (Batish et al., 2008).

Linalool; It is a natural compound obtained from various medicinal aromatic plants, such as Himalayan birch, orange, cinnamon, basil, thyme, and lavender (Pereira et al. 2018). Linalool is widely used for its fresh floral scent in cosmetics, household, and hygiene products (Christensson et al., 2010). Moreover, studies have shown that Linalool affects the nervous system of insects and can be used to control harmful insects (Campos et al., 2018).

As mentioned above, plant essential oils obtained from different plants can increase productivity and quality by controlling many harmful species without threatening the environment or human health. In this regard, plant-based insecticides are a potential alternative for sustainable agricultural methods, whose main purpose is to control plant pests without harming human and environmental health (Cardoso & Carmello, 2022). Alternatives to pesticides, which are intensively used against harmful insect species that cause serious yield losses in economically important plants, have been reported to have significant potential in conrol harmful insects. Some of these studies are listed in Table 1. In general, numerous studies have demonstrated that natural substances effectively reduce pest infestations in agricultural crops, orchards, and stored food products (Magierowicz et al., 2019)

Table 1: Plant essential oils used in the controlt against harmful insect species

Herbal origin medicine\ product	Harmful insect species	Host plant	Effect	References
Neem	*Sitophilus oryzae* L.	Rice	Repellent Toxic effect	Fauzi & Prastowo, 2021
	Spodoptera frugiperda (J. E. Smith)	Maize	Toxic effect	Tulashie et al., 2021
	Myzus persicae Sulzer	*Brassica* sp.	Growth and development inhibitör effect	Dohouonan & Yao, 2020
	Aphis gossypii Glover	*Gossypium hirsitum*	Toxic effect	Ali et al., 2022
Piretrum	*Sitophilus granarius L.*	*Triticum* spp.	Toxic effectli	Marchand et al., 2018
	Aphis gossypii Glover	*Cucumis sativus*	Toxic effect	Papanikolaou et al., 2018

	Phorodon humuli Schrank	*Prunus* sp.	Contact effect	Vasilev et al., 2019
Thujone	*Apis fabae* (Scop.)	*Vicia fabae*	Toxic and repellent	Harizia et al., 2021
	Ceratitis capitata (Wiedemann)	Juniperus L.	Toxic effect	Kurtca et al., 2021
Eugenol	*Trioza erytreae* (Del Guercio)	*Citrus limon*	Contact effect	Sousa et al., 2022
	Psylla pyri L.	*Pyrus communis*	Repellent	Czarnobai De Jorge et al., 2022
1,8-Cineol	*Nezara viridula* L.	*Callistemon citrinus*	Repellent	El-Gendy & El-Shafiey, 2018
	Metopolophium dirhodum (Walker)	*Triticum aestivum*	Reproductive inhibitör and repellent	Sánchez Chopa & Descamps, 2012
Linalool	*Trialeurodes vaporariorum (Westwood)*	*Solanum lycopersicum*	Toxic effect	Vicenço et al., 2021
	Myzus persicae (Sulzer)	*Capsicum annuum*	Repellent	Dardouri et al., 2019
	Ceratitis capitata (Wiedemann)	Polifag	Repellent	Papanastasiou et al., 2020
Citronella	*Bemisia tabaci (Gennadius)*	*Capsicum annuum*	Reproductive inhibitor repellent, and toxic	Saad, Roff & Idris, 2017
	Pseudococcus longispinus (Targioni Tozzetti)	*Phalaenopsis* sp.	Toxic effect	Hutapea et al., 2021
Carvacol	*Cydia pomonella L.*	Apple	Toxic effect	Konecka et al., 2020
	Acrobasis advenella (Zinck.)	*Acrobasis advenella*	Toxic effect	Magierowicz et al., 2019
	Planococcus citri (Risso)	*Citrus sinensis*	Toxic effect	Alloui-Griza et al., 2022
	Euphyllura olivina (Costa)	*Olea europaea*	Contact effect	Guessab et al., 2022

2. CONCLUSION

Herbal essential oils present a potential solution as an alternative to traditional chemical pesticides, offering potential for agricultural sustainability and environmental friendliness. The use of herbal essential oils has emerged as a significant alternative to agricultural production. Considering the environmental impacts and potential risks to human health associated with chemical pesticide use, the advantages of herbal essential oils are crucial for farmers and the agricultural industry. However, further research and development are necessary to determine the efficacy, environmental impact, and economic sustainability of this alternative. It is important to carefully consider factors such as proper dosage, application timing, and methods when using herbal essential oils. Additionally, the potential effects of these oils on other organisms, soil health, and water sources must be thoroughly evaluated. Therefore, providing farmers with education and guidance is essential for the widespread adoption of herbal essential oils in agricultural practices.

In conclusion, herbal essential oils are promising alternatives to phytophagous insects. However, additional research is needed to fully understand their effectiveness and sustainability. The broad adoption of this method in the agricultural industry could significantly contribute to agricultural sustainability and integrated pest management programs, considering its positive impacts on the environment and human health.

REFERENCES

Akdoğan, A., Divrikli, Ü., Elçi, L. (2012). Importance of pesticides and their effects on ecosystem. Academic Food Journal, 10(1): 125-132. (In Turkish).

Ali, H., Ameer, S., Qasim, M., Fiaz, S., Ali, S., Zaheer, S., ALI, B., Nawaz, M., Ali, Y., & Ahmad, N. (2022). Efficacy of botanical plant extracts on the population dynamics of cotton aphid, *Aphis gossypii* glover (Hemiptera; Aphididae). Journal of Bioresource Management, 9(2): 97-108.

Alloui-Griza, R., Cherif, A., Attia, S., Francis, F., &Lognay, G.C., & Grissa-Lebdi, K. (2022). Lethal toxicity of *Thymus capitatus* essential oil against *Planococcus citri* (Hemiptera: Pseudococcidae) and its coccinellid predator *Cryptolaemus montrouzieri* (Coleoptera: Coccinellidae). Journal of Entomological Science, 57 (3): 425-435.

Amala, K., Karthi, S., Ganesan, R., Radhakrishnan, N., Srinivasan, K., Mostafa, A.E.-Z.M., Al-Ghamdi, A.A., Alkahtani, J., Elshikh, M.S., & Senthil-Nathan, S. (2021). Bioefficacy of Epaltes divaricata (L.) n-Hexane extracts and their major metabolites against the Lepidopteran pests *Spodoptera litura* (fab.) and dengue mosquito *Aedes aegypti* (Linn.). Molecules. 26(12): 3695.

Anonymous, (2024). *Azadirachta indica*. (https://www.inaturalist.org/taxa/319135-Azadirachta-indica) (Accessed: June 7, 2024).

Anonymous, (2023). Current World Population. (https://populationmatters.org/lp-the-facts/?gad_source=1&gclid=EAIaIQobChMIrYH8Ib0hgMVMJ1aBR0tnQcREAAYASAAEgJLNPD_BwE) (Accessed: June 1, 2024).

Batish, D.R., Singh, H.P., Kohli, R.K., & Kaur, S. (2008). Eucalyptus essential oil as a natural pesticide. Forest Ecology and Management, 256(12): 2166-2174.

Böttger, A., Vothknecht, U., Bolle, C., & Wolf, A. (2018). Plant Secondary Metabolites and Their General Function in Plants. In: *Lessons on Caffeine, Cannabis & Co*. Springer International Publishing, Cham. pp. 13-17.

Campos, E.V., Proença, P.L., Oliveira, J.L., Bakshi, M., Abhilash, P.C., & Fraceto, L.F. (2019). Use of botanical insecticides for sustainable agriculture: Future perspectives. Ecological Indicators, 105: 483-495.

Campos, E.V., Proença, P.L., Oliveira, J.L., Pereira, A.E., de Morais Ribeiro, L.N., Fernandes, F.O., Gonçalves, K.C., Polanczyk, R.A., Pasquoto-Stigliani, T., & Lima, R. (2018). Carvacrol and linalool co-loaded in β-cyclodextrin-grafted chitosan nanoparticles as sustainable biopesticide aiming pest control. Scientific Reports, 8(1): 7623.

Cardoso, J.C., & Carmello, C.R. (2022). Botanical pesticides as alternatives for more sustainable crops and healthy foods.. In: *Pesticides In The Natural Environment*. Elsevier. pp. 285-315.

Christensson, J.B., Matura, M., Gruvberger, B., Bruze, M., & Karlberg, A. (2010). Linalool – a significant contact sensitizer after air exposure. Contact Dermatitis, 62(1): 32-41.

Czarnobai De Jorge, B., Hummel, H.E., & Gross, J. (2022). Repellent activity of clove essential oil volatiles and development of nanofiber-based dispensers against pear psyllids (Hemiptera: Psyllidae). Insects, 13 (8): 743.

Dalavayi Haritha, M., Bala, S., & Choudhury, D. (2021). Eco-friendly plant based on botanical pesticides. Plant Archives, 21 (1): 2197–2204.

Dardouri, T., Gautier, H., Ben Issa, R., Costagliola, G., & Gomez, L. (2019). Repellence of *Myzus persicae* (Sulzer): evidence of two modes of action of volatiles from selected living aromatic plants. Pest Management Science, 75(6): 1571-1584.

Dohouonan, D., & Yao, T. (2020). Control of green peach Aphid *Myzus persicae* (Sulzer, 1776)(Hemiptera: Aphididae) on Brassica plants. International Journal of Entomology Research, 5(3): 6-11.

El-Gendy, R.M., & El-Shafiey, S.N. (2018). Eco-friendly control strategies of green stink bug, *Nezara viridula* L.(Hemiptera: Pentatomidae): Repellency and toxicity effects of *Callistemon citrinus*, bottle brush essential oil. Journal of Plant Protection and Pathology, 9(12): 807-813.

Erdoğan, B.Y. (2010). The health and environmental effects of the pesticides commonly used in Samsun. Alınteri Journal of Agriculture Science, 19(2): 28-35.

FAO (2024). Pesticide Use, (https://www.fao.org/faostat/en/#data/RP) (Accessed :June 1, 2024)

Fauzi, S., & Prastowo, S. (2021). Repellent effect of the pandanus (*Pandanus amaryllifolius Roxb*.) and neem (*Azadirachta indica*) against rice weevil *Sitophilus oryzae L*.(Coleoptera, Curculionidae). Advances in Bioengineering & Biomedical Science Research, 5(1): 10-17.

Flores-Gutierrez, C.A., Torres-Sanchez, E.D., Reyes-Uribe, E., Torres-Jasso, J.H., Reyna-Villela, M.Z., Rojas-Bravo, D., & Salazar-Flores, J. (2023). The association between pesticide exposure and the development of fronto-temporal dementia-cum-dissociative disorders: A review. Brain Sciences, 13(8): 1194.

Guessab, A., Lazreg, F., Elouissi, M., Elouissi, A., & Daikh, Z. (2022). Larvicidal activities of essential oils against *Euphyllura olivina* Costa (Homoptera: Psyllidae). Analele Universitatii din Oradea, Fascicula Biologie, XXIX(2): 140-148.

Harizia, A., Benguerai, A., Elouissi, A., Mahi, T., & Bonal, R. (2021). Chemical composition and biological activity of *Salvia officinalis* L. essential oil against *Aphis fabae* Scopoli (Hemiptera: Aphididae). Journal of Plant Diseases and Protection, 128(6): 1547-1556.

Hernández-Suárez, E., Arjona-López, J.M., Rizza, R., Perera, S., Siverio, F., Hervalejo, A., & Arenas-Arenas, F.J. (2023). Comparative efficacy of seven biorational insecticides to manage African citrus psyllid (*Trioza erytreae*) in European organic citriculture. Biological Agriculture & Horticulture, 39(3): 194-206.

Hikal, W.M., Baeshen, R.S., & Said-Al Ahl, H.A.H. (2017). Botanical insecticide as simple extractives for pest control. Cogent Biology, 3(1): 1404274.

Hutapea, D., Rahardjoa, I.B., & Thamrin, M. (2021). Prospects of neem and citronella oil against *Pseudococcus longispinus* (hemiptera: Pseudococcidae) on Phalaenopsis. In: IOP Conference Series: Earth and Environmental Science, 11-12 August, Bogor, Indonesia.

Isman, M.B. (2017). Bridging the gap: moving botanical insecticides from the laboratory to the farm. Industrial Crops and Products, 110: 10-14.

Jalilzadeh-Amin, G., & Maham, M. (2015). The application of 1,8-cineole, a terpenoid oxide present in medicinal plants, inhibits castor oil-induced diarrhea in rats. Pharmaceutical Biology, 53(4): 594-599.

Karakaş, M. (2018). Some Important Herbal Insecticides. Turkish Journal of Scientific Reviews, 11 (2): 32-37. (In Turkish).

Kesraoui, S., Andrés, M.F., Berrocal-Lobo, M., Soudani, S., & Gonzalez-Coloma, A. (2022). Direct and indirect effects of essential oils for sustainable crop protection. Plants, 11(16): 2144.

Khalil, A.A., ur Rahman, U., Khan, M.R., Sahar, A., Mehmood, T., & Khan, M. (2017). Essential oil eugenol: Sources, extraction techniques and nutraceutical perspectives. RSC Advances, 7 (52): 32669-32681.

Khursheed, A., Rather, M.A., Jain, V., Rasool, S., Nazir, R., Malik, N.A., & Majid, S.A. (2022). Plant based natural products as potential ecofriendly and safer biopesticides: A comprehensive overview of their advantages over conventional pesticides, limitations and regulatory aspects. Microbial Pathogenesis, 173: 105854.

Konecka, E., Kaznowski, A., Grzesiek, W., Nowicki, P., Czarniewska, E., & Baranek, J. (2020). Synergistic interaction between carvacrol and Bacillus thuringiensis crystalline proteins against Cydia pomonella and Spodoptera exigua. BioControl, 65(4): 447-460.

Kumar, A., Tripathi, M.K., Chandra, U., & Veer, R. (2019). Efficacy of botanicals and bio-pesticide against *Helicoverpa armigera* in chickpea. Journal of Entomology and Zoology Studies, 7(1): 54-57.

Kurtca, M., Tumen, I., Keskin, H., Tabanca, N., Yang, X., Demirci, B., & Kendra, P.E. (2021). Chemical composition of essential oils from leaves and fruits of *Juniperus foetidissima* and their attractancy and toxicity to two economically ımportant tephritid fruit fly species, *Ceratitis capitata* and *Anastrepha suspensa*. Molecules, 26(24): 7504.

Lazarević, J., Kostić, I., Šešlija Jovanović, D., Ćalić, D., Milanović, S., & Kostić, M. (2022). Pure camphor and a thujone-camphor mixture as eco-friendly antifeedants against larvae and adults of the colorado potato beetle. Plants, 11(24): 3587.

Lengai, G.M., Muthomi, J.W., & Mbega, E.R. (2020). Phytochemical activity and role of botanical pesticides in pest management for sustainable agricultural crop production. Scientific African, 7: e00239.

Magierowicz, K., Górska-Drabik, E., & Sempruch, C. (2019). The insecticidal activity of *Satureja hortensis* essential oil and its active ingredient-carvacrol against *Acrobasis advenella* (Zinck.) (Lepidoptera, Pyralidae). Pesticide Biochemistry and Physiology, 153: 122-128.

Mahmood, I., Imadi, S.R., Shazadi, K., Gul, A., & Hakeem, K.R. (2016). Effects of pesticides on environment. K.R., Hakeem, M.S.Akhtar, S.N.A., Abdullah (Eds.) In: *Plant, Soil and Microbes*. Springer International Publishing, Cham. pp. 253-269.

Marchand, P.A., Dimier-Vallet, C., & Vidal, R. (2018). Biorational substitution of piperonyl butoxide in organic production: effectiveness of vegetable oils as synergists for pyrethrums. Environmental Science and Pollution Research, 25(30): 29936-29942.

Ngegba, P.M., Cui, G., Khalid, M.Z., & Zhong, G., 2022. Use of botanical pesticides in agriculture as an alternative to synthetic pesticides. Agriculture, 12(5): 600.

Nile, A.S., Kwon, Y.D., & Nile, S.H. (2019). Horticultural oils: Possible alternatives to chemical pesticides and insecticides. Environmental Science and Pollution Research, 26(21): 21127-21139.

Özay, Ö., & Arslantaş, D. (2016). Pesticide Exposure And Neuropsychiatric Effects. Osmangazi Journal of Medicine, 38 (Special Issue 1): 42-48.

Papanastasiou, S.A., Ioannou, C.S., & Papadopoulos, N.T. (2020). Oviposition-deterrent effect of linalool – a compound of citrus essential oils – on female Mediterranean fruit flies, *Ceratitis capitata* (Diptera: Tephritidae). Pest Management Science, 76(9): 3066-3077.

Papanikolaou, N.E., Kalaitzaki, A., Karamaouna, F., Michaelakis, A., Papadimitriou, V., Dourtoglou, V., & Papachristos, D.P. (2018). Nano-formulation enhances insecticidal activity of natural pyrethrins against *Aphis gossypii* (Hemiptera: Aphididae) and retains their harmless effect to non-target predators. Environmental Science and Pollution Research, 25(11): 10243-10249.

Pavithra, B., 2014. Eugenol-a review. Journal of Pharmaceutical Sciences and Research, 6(3): 153.

Pelkonen, O., Abass, K., & Wiesner, J. (2013). Thujone and thujone-containing herbal medicinal and botanical products: Toxicological assessment. Regulatory Toxicology and Pharmacology, 65(1): 100-107.

Pereira, I., Severino, P., Santos, A.C., Silva, A.M., & Souto, E.B. (2018). Linalool bioactive properties and potential applicability in drug delivery systems. Colloids and Surfaces B: Biointerfaces, 171: 566-578.

Saad, K.A., Roff, M.M., & Idris, A.B. (2017). Toxic, repellent, and deterrent effects of citronella essential oil on *Bemisia tabaci* (Hemiptera: Aleyrodidae) on Chili plants. Journal of Entomological Science, 52(2): 119-130.

Sánchez Chopa, C., & Descamps, L.R. (2012). Composition and biological activity of essential oils against *Metopolophium dirhodum* (Hemiptera: Aphididae) cereal crop pest. Pest Management Science, 68(11): 1492-1500.

Schleier III, J.J., & Peterson, R.K. (2011). Pyrethrins and pyrethroid insecticides. Green Trends in Insect Control, 11: 94-131.

Schmutterer, H. (1990). Properties and Potential of natural pesticides from the neem tree, *Azadirachta indica*. Annual Review of Entomology, 35 (1): 271-297.

Şengül Demirak, M.Ş., & Canpolat, E. (2022). Plant-based bioinsecticides for mosquito control: Impact on insecticide resistance and disease transmission. Insects, 13(2): 162.

Sharma, S., Kooner, R., & Arora, R. (2017). Insect pests and crop losses. R. Arora, S., Sandhu (Eds.). In: *Breeding Insect Resistant Crops for Sustainable Agriculture.* Springer Singapore, Singapore. pp. 45-66.

Soni, V., & Anjikar, A. (2014). Use of pyrethrin/pyrethrum and its effect on environment and human: a review. PharmaTutor, 2(6): 52-60.

Sousa, P.A., Neto, J., Bastos, M.M., & Aguiar, A.A. (2022). Eugenol and pulegone as potential biorational alternatives for *Trioza erytreae* (Hemiptera: Triozidae) control: Preliminary results on nymphal toxicity and applicability on *Citrus limon*. Journal of Natural Pesticide Research, 1: 100004.

Tamokou, J.D.D., Mbaveng, A.T., & Kuete, V. (2017). Antimicrobial activities of African medicinal spices and vegetables. V. Kuete (Ed.). In: *Medicinal Spices and Vegetables from Africa*. Elsevier. pp. 207-237.

Tulashie, S.K., Adjei, F., Abraham, J., & Addo, E., 2021. Potential of neem extracts as natural insecticide against fall armyworm (Spodoptera frugiperda (JE Smith)(Lepidoptera: Noctuidae). Case Studies in Chemical and Environmental Engineering, 4: 100130.

Vasilev, P., Atanasova, D., & Andreev, R., 2019. Efficacy of bioinsecticides against the hop aphid *Phorodon humuli* (Schrank)(Hemiptera: Aphididae) under laboratory conditions. Can. J. Agric. Crops, 4: 130-135.

Vicenço, C.B., Silvestre, W.P., Pauletti, G.F., de Barros, N.M., & Schwambach, J. (2021). *Cinnamomum camphora* var. *linaloolifera* essential oil on pest control: Its effect on *Trialeurodes vaporariorum* (Hemiptera: Aleyrodidae). Research, Society and Development, 10 (7): e45710716216–e45710716216.

CHAPTER VIII

CULTURAL ANTHROPOLOGY AND PLANTS

Assoc. Prof. Dr. Esra UCAR[1]

Assist. Prof. Dr. Gülşen GÜÇLÜ[2]

DOI: https://dx.doi.org/10.5281/zenodo.13826058

[1]Sivas Cumhuriyet University, Sivas Technical Sciences Vocational School, Department of Plant and Animal Production, Sivas, Türkiye
ORCID ID: 0000-0001- 6327-4779 e-mail: eucar@cumhuriyet.edu.tr
[2]Sivas Cumhuriyet University, Health Services Vocational School, Department of Health Programs, Sivas, Türkiye ORCID ID: 0000-0002-3599-213X
e-mail: gulsenguclu@cumhuriyet.edu.tr

INTRODUCTION

Since the beginning of humanity, humans have needed to fulfill three basic needs to sustain the life cycle: shelter, nutrition, and reproduction (Şeker, 2014). During periods dominated by a nomadic lifestyle, they met their nutritional needs through hunting and gathering. Agricultural production and the transition to settled life have been achieved through seed cultivation and plant cultivation. In the scope of agricultural activities, they primarily collected wild grains (Özkoçak & Koç, 2021). They initiated agricultural production by cultivating the collected seeds. As people met their needs for nutrition, clothing, and shelter, over time they also felt the need for medical treatment. They made discoveries by experiencing relief from their pains and discomforts while consuming plants for nourishment. Subsequently, they classified different organs of plants, such as fruits, roots, bark, flowers, and seeds, by chewing them and evaluating their taste and aroma, categorizing them as medicinal or poisonous (Baydar, 2019). The knowledge acquired through trial and error, evolving over centuries through various usage methods, proportions, and differences in mixtures, has culminated in the practices observed today (Koçyiğit, 2005). Ethnobotanical books spanning from ancient times to the present contain information on the characteristics and uses of medicinal and aromatic plants. Such resources encapsulate knowledge regarding the properties and applications of these plants. Even in eras predating the invention of writing, cave wall paintings depicted images of plants. Hittite inscriptions and Egyptian papyri contain information on medicinal and aromatic plants, as well as their applications (Yıldırımlı, 2004).

Plants have not only been used as food, beverages, and herbal medicine, but also considered as the harbinger of spring in Anatolia, inspiring literature and art (Kaya, 2014). Since its existence, human beings have met their needs by using the resources provided by nature. People, who lived by collecting and hunting activities in the early periods, discovered and developed agriculture by collecting seeds over time. However, their interaction with plants extended beyond mere cultivation; they also refined plants through selective breeding to enhance productivity, facilitating a transition to a more stable settled lifestyle. Humans recognized that plants not only provided sustenance but also held medicinal properties beneficial to health. Through trial and error, they identified which plants were effective against various diseases and which parts of the plants should be utilized. This ongoing process has spanned centuries, deepened the bond between humans and plants. This study examines humanity's relationship with plants, focusing on their utilization and evaluation over the centuries. This extensive evaluation process sheds light on humanity's interaction with nature and underscores the significance of plants in our lives.

1. THE BEGINNING OF AGRICULTURAL PRODUCTION

Throughout human history, anthropogenic impacts have been experienced in regions with natural vegetation, and humans have consistently interacted with plants (Türe & Böcük, 2013; Erken et al., 2022). Human beings are constantly in interaction with their environment. The hunter-gatherer lifestyle exposes individuals to risks such as hunger, famine, and at times, insufficient nutrition and perilous confrontations, leading to the possibility of death. In order to sustain their lives, they operate without laws and regulations (Zeder, 2015; Özkoçak & Koç, 2021). With the transition to settled life through the cultivation of gathered seeds, agriculture emerged as one of humanity's earliest economic activities, initiating a process that facilitated interaction between nature and humans and paved the way for modernity (Mollavelioğlu, 2009; Sarıtaş & Çoban, 2020). The data obtained from plant and animal remains indicate that farmers who fully embraced agriculture in Eastern Marmara emerged in the 6600s B.C. (Erdal, 2023). Great civilizations have flourished around major rivers. The diversity of plant species in these environments is substantial, allowing for the utilization of various plants in these regions (Yıldırımlı, 2004). According to Otaegui et al. (2017), evidence suggests that approximately 11,000 years ago, wheat breeding took place in the Sweida region of Syria. The inception of food production is presumed to have occurred in the valleys of the Yellow River and the Yangtze River. Plant domestication is thought to have occurred in regions known as the Fertile Crescent in Southwest Asia (including China), Central America, the Andes Mountains of South America, and likely the adjacent Amazon Basin and Eastern United States (Sadowski, 2017). Several thousand years after the inception of agriculture, approximately four thousand years ago, they began to implement cultural practices on the soil (Beardsworth & Keil; 2011). Agriculture has continued to evolve from its inception to the present day, with humans employing breeding methods to increase yields. Additionally, they began storing surplus produce for the following year after consuming what they had harvested. With the understanding of the importance of storage, there was a transition from subsistence farming methods to industrial agricultural practices. As a result of this transition, differences in social relationships among individuals began to be observed (Sarıtaş & Çoban, 2020). Over time, humans started to develop an attachment to the land, leading to the onset of societal life. As agricultural activities diversified, transformations also occurred in people's social relationships.

Agriculture is a holistic concept encompassing biological, environmental, social, and economic dimensions. Various agricultural activities have led to the organization of societies in religious, political, economic, and cultural aspects. As a result, this has been beneficial in making people's lives easier by contributing to their lives in different aspects (Mollavelioğlu, 2009; Standage, 2016; Sarıtaş & Çoban 2020).

2. ETHNOBOTANY

The discovery that some plants consumed for nutritional purposes happened to alleviate certain ailments led to the emergence of ethnobotany. The effective use of medicinal and aromatic plants in the treatment of diseases played a significant role in the inception of ethnobotany. Ethnobotanical research encompasses the accumulation of knowledge over extended periods regarding plants, often derived from serendipitous occurrences and refined through trial and error. This knowledge, passed down through generations, contributes to our understanding of the uses of various plants in different regions. Ethnobotanical studies serve to identify the specific purposes for which different plants can be utilized in diverse geographical areas (Kendir & Güvenç, 2010).

Ethnobotanical research is managed by various disciplines. Anthropologists, archaeologists, agronomists, foresters, botanists, and pharmacologists all approach the interaction between humans and plants from different perspectives. For instance, while biologists study plants with economic value, anthropologists have examined how plants shape perceptions of nature. In archaeobotanical research, efforts are made to gain insights into the lives of prehistoric societies based on their use of plants, while pharmacognosy focuses on the utilization of plants in medicinal formulations

(Yıldırımlı, 2004). The utilization of plants can vary from region to region. Ethnobotany examines the use of plants by specific geographical communities in terms of their nutritional, medicinal, and industrial value. The utilization patterns of plants vary according to geographical regions. Ethnobotany predominantly focuses on the utilization of plants for medicinal purposes, particularly in relation to the treatment of ailments by human populations. Preserving ancient era prescriptions, which are often undervalued in the modern age, is important. Through ethnobotany, the knowledge acquired from people's experiences and experiments should be recorded as a cultural heritage passed down from generation to generation.

It helps in preserving local culture and preventing the loss of this knowledge. Over time, as modern medications prove ineffective for certain ailments or develop resistance to some drugs, leading to the medication's ineffectiveness, people sometimes revert to natural remedies and reconnect with nature due to the significant side effects of medications. However, folk remedies continue to maintain their validity. Many of today's drugs are synthesized by taking inspiration from the major components of plants. Sometimes, drugs are produced by using plant extracts for compounds whose synthesis is impossible. As in many fields, nature is taken as a model in the pharmaceutical industry.

3. USES OF PLANTS BY HUMANS

Plants have been a constant presence in human life for centuries, exerting significant influence substantial enough to shape and diversify their livelihoods. The knowledge about plants has evolved and diversified from generation to generation, reaching the present day. Humans have utilized plants in a wide range of fields and continue to do so. In addition to being used for food, spices, and beverages, plants also prominently feature for their medicinal values. Plants with aromatic scents are sometimes utilized in various forms, such as incense or for protection against the evil eye. Additionally, plants can be used as ornamental and household items, as well as in cosmetics, landscaping, dye production, insecticides, animal feed, shelter, broom making, fuel, and other areas.

Plants were utilized as medicinal and preventative agents long before contemporary medications were developed. Since ancient times, there have been an increasing variety of plants used for health purposes. Fossils from the Middle Palaeolithic Period, 60 thousand years ago, show evidence of human use of plants for a variety of functions, including food and medicine. Plants, animals, water, and soil have all been used medicinally by humans. Through trial-and-error observation, they have experimentally discovered which plants are effective in treating particular ailments, and over time, they have shaped the local culture. With time, the plant or its parts (drugs) were no longer used directly; instead, extracts, tinctures, and distillation products were made from them.

As chemistry advanced at the start of the 19th century, several plants' pure, useful chemicals were discovered and began to be employed in medicine. The first chemicals employed as active ingredients in plant-derived medications were digitalin, which Nativelle obtained in 1868, and morphine, which Derosne and Seguin isolated in 1803-1804, and Fredrich Sertürner in 1805 (Fabricant & Farnsworth, 2001). From the perspective of public health as well as anthropology and archaeology, it is extremely valuable and significant that plants and medicinal systems with traditional uses have been documented.

In order to identify new bioactive components with the potential to serve as models for new generation drugs, it is essential that information about the plants traditionally used is recorded from the past to the present. Ethnobotanical and ethnopharmacological research must be conducted and these resources must be investigated and evaluated in terms of pharmacognosy. In the context of modern medicine, phytotherapy is accepted as a rational medical science.

A number of plants have been identified as potential models for new generation drugs. One such example is khella, which is mentioned in Eber's Papyrus and is an ancient Egyptian medicinal plant. It is known that ancient Egyptian civilisations used Khella (*Ammi visnaga*) to treat a number of diseases, particularly those affecting the urinary system. In the Middle Ages, it was used as a diuretic, and popular medicine in Egypt used its fruits to treat kidney stones. This drug is a potent spasmolytic, capable of dissolving spasm in the ureter, facilitating the passage of kidney stones. In 1946, Anrep, a pharmacologist engaged in research in Egypt, undertook an experiment that demonstrated by chance the plant's pronounced spasmolytic effect on the bronchi and coronary arteries, in contrast to its minimal effect on the ureter.

The pronounced antispasmodic effect on very small bronchi makes this plant an optimal therapeutic agent for the treatment of asthma.

Khellin, a compound derived from the fruits of *Ammi visnaga* (*Ammi visnagae fructus*), known as toothwort fruit, was employed as a bronchodilator in the United States of America (USA). In 1955, a research group synthesised analogues with fewer side effects besides khellin as potential bronchodilators because of its long-term use causing nausea and vomiting. The synthesis of cromolyn was found to prevent allergen-induced sudden bronchoconstriction in allergic asthma patients (Fabricant & Farnsworth, 2001; WHO, 2007).

Trigonella foenum-graceum, one of the oldest known medicinal plants, is known as fenugreek. It is recorded that it was used in ancient Egypt to protect mummies, in Chinese medicine as a tonic, in the treatment of oedema and weakness, and in India both as a spice and to stimulate lactation. It has been experimentally demonstrated that fenugreek seed, which is an appetite stimulant in European countries and a spice used in making pastırma in Turkish cuisine, is effective in Type 2 diabetes (Koyu, 2019).

Known in the world as Goji Berry or Wolfberry, but little known in our country, Wolfberry has made a name for itself in the 21st century as a 'super fruit'. The Goji Berry, which grows in the Himalayas, the highest mountains in the world in Tibet and Mongolia, is one of the most nutritious fruits in the world and is derived from the Solanaceae plant *Lycium barbarum*. This fruit, which is a very powerful antioxidant, has been used in Chinese medicine for 2000 years. The proteoglucans in the fruit are known as *Lycium barbarum* polysaccharides and have a wide range of pharmacological activities. In addition to atherosclerosis and diabetes, various compounds from the root bark have been reported to be effective in treating hypertension by inhibiting the renin-angiotensin system and to contain hepatoprotective compounds (Potterat, 2010; Mi et al., 2012). A 2011 study suggested that goji berry fruits contain high levels of taurine and that both fruit extracts and taurine may be used in the treatment of diabetic retinopathy by dose-dependent inhibition of PRAR-γ (peroxisome proliferator-activated receptor γ) gene transcription in human retinal pigment epithelial cells (Song et al., 2011). Another study reported that *L. barbarum* prevents neurodegeneration in the retina and may be used for the treatment of glaucoma due to its neuroprotective effects (Chan et al., 2007).

The seeds of the thistle (*Silybum marianum*) have been used for centuries in the treatment of various diseases. These seeds contain silibin, silicristin and siliadinin, which are flavolignans. They have a strong antioxidant and hepatoprotective effect. They stimulate liver regeneration in cases of toxin poisoning, hepatitis, cirrhosis and liver fibrosis. Additionally, they have anti-inflammatory and immunomodulatory properties (Bhattacharya, 2011). A study conducted in 2008 with silymarin obtained from this plant, which is known to be traditionally used in galactagogue, bitter tonic, antidepressant and liver diseases, dyspeptic complaints, diabetes and menstrual problems in Europe in the past, but nowadays more studies are being conducted. The majority of studies on liver diseases have been conducted, with the results indicating that BIO-C (micronised silymarin) reliably and effectively increases the daily milk amount in 50 healthy women at a dose of 420 mg/day following a 63-day application (Di Pierro et al., 2008).

4. CONCLUSION

In addition to their traditional applications, it is imperative to elucidate the chemical compositions of plants, establish structure-activity relationships with diverse biochemical parameters, explore numerous pharmacological activities, and validate findings through clinical applications. These *in vitro, in vivo*, and clinical studies are essential for positioning medicinal plants appropriately within the realm of healthcare. It is evident that many diseases can be treated thanks to the traditional prescriptions that have survived from the past to the present. It is recommended that pharmacognostic and ethnobotanical studies be supported in order to facilitate the applicability of phytotherapy as a rational medical science on a global scale. In addition, the sciences related to medicinal plants should establish multidisciplinary education programs and conduct research in order to reveal new current usage areas and the effectiveness of herbal resources with therapeutic value.

REFERENCES

Arranz-Otaegui, A., López-Sáez, J. A., Araus, J. L., Portillo, M., Balbo, A., Iriarte, E., ... & Ibáñez, J. J. (2017). Landscape transformations at the dawn of agriculture in Southern Syria (10.7–9.9 ka cal. BP): Plant-specific responses to the impact of human activities and climate change. Quaternary Science Reviews, 158: 145-163.

Baydar, H. (2019). Tıbbi ve aromatik bitkiler bilimi ve teknolojisi (7. Basım). Nobel Akademik Yayıncılık, Yayın, 2328, 21.

Beardsworth, A., & Keil, T. (2011). Yemek ve toplum çalışmasına bir davet: yemek sosyolojisi. Çev. A. Dede). Ankara: Phoenix Yayınları.

Bhattacharya, S. (2011). Phytotherapeutic properties of milk thistle seeds: An overview. J Adv Pharm Educ Res, 1: 69-79.

Chan, H. C., Chang, R. C. C., Ip, A. K. C., Chiu, K., Yuen, W. H., Zee, S. Y., & So, K. F. (2007). Neuroprotective effects of *Lycium barbarum* Lynn on protecting retinal ganglion cells in an ocular hypertension model of glaucoma. Experimental neurology, 203(1): 269-273.

Di Pierro, F., Callegari, A., Carotenuto, D., & Tapia, M. M. (2008). Clinical efficacy, safety and tolerability of BIO-C (micronized Silymarin) as a galactagogue. Acta Biomed, 79(3): 205-210.

Erdal Y.S. 2023. Doğu Marmara’da Tarımın Kökeni Üzerine İnsan Kalıntılarından Bir Bakış. *VIII. Biyolojik Antropoloji Sempozyumu*, 26-27 Ekim 2023.

Erken, K., Parlak, S., & Yılmaz, M. (2022). Protection of endemic taxon’s and species conservation action plans. Tree and Forest, 3(1): 33-46. (In Turkish).

Fabricant, D. S., & Farnsworth, N. R. (2001). The value of plants used in traditional medicine for drug discovery. Environmental Health Perspectives, 109(suppl 1): 69-75.

Gültekin, T., & Kaplan, M. (2021). Biyolojik ve Kültürel Antropolojik Boyutlarıyla. Editörler: Timur Gültekin, Melike Kaplan. Nobel Yayınevi.

Kaya, E. (2014). Geophytes of Turkey. Ataturk Central Horticultural Research Institute, Edition No: 96,1: 1-48, Yalova-Turkey, ISBN No:978-605-4672-88-2.

Kendir, G., & Güvenç, A. (2010). Etnobotanik ve Türkiye'de yapılmış etnobotanik çalışmalara genel bir bakış. Hacettepe University Journal of the Faculty of Pharmacy, 30(1): 49-80.

Koçyiğit, M. (2005). An Ethnobotanical Study in Yalova Pprovince (Master's thesis), İstanbul Üniversitesi, Sağlık Bilimleri Enstitüsü, İstanbul.

Koyu, E. B. (2019). Efficacy and Safety of Herbal Supplements Used in Diabetes. Journal of Nutrition and Dietetics, 47(Special Issue): 110-117. (In Turkish).

Mi, X. S., Chiu, K., Van, G., Leung, J. W. C., Lo, A. C. Y., Chung, S. K., ... & So, K. F. (2012). Effect of *Lycium barbarum* polysaccharides on the expression of endothelin-1 and its receptors in an ocular hypertension model of rat glaucoma. Neural Regeneration Research, 7(9): 645-651.

Mollavelioğlu, M. (2009). Measurement of Sustainable Agriculture and An Assessment for Turkey. (PhD Thesis*)*, Hacettepe University, Ankara. (In Turkish).

Potterat, O. (2010). Goji (*Lycium barbarum* and L. chinense): Phytochemistry, pharmacology and safety in the perspective of traditional uses and recent popularity. Planta Medica, 76(01): 7-19.

Sadowski, R.F. (2017). Neolithic Revolution. In: Thompson P., Kaplan D. (eds) Encyclopedia of Food and Agricultural Ethics. Springer, Dordrecht.

Sarıtaş, S., & Çoban, U. (2020). The Aspect of Socio-Cultural Change for South Marmara's Young Farmers. Journal of Social and Cultural Studies, 5: 80-106. (In Turkish).

Song, M. K., Salam, N. K., Roufogalis, B. D., & Huang, T. H. W. (2011). *Lycium barbarum* (Goji berry) extracts and its taurine component inhibit PPAR-γ-dependent gene transcription in human retinal pigment epithelial cells: possible implications for diabetic retinopathy treatment. Biochemical Pharmacology, 82(9): 1209-1218.

Standage, T. (2016). Altı Bardakta Dünya Tarihi. İkinci Baskı, İstanbul: Kırmızı Kedi Yayınevi.

Şeker, S. E. (2014). Digitalization, *YBS Ansiklopedi*, 1(1), 6-8. (In Turkish).

Türe, C. & Böcük, H. (2013). Biyolojik Çeşitlilik Sempozyumu 22-23 Mayıs 2013, Muğla-Marmaris. *Bildiri Kitabı*, 80-87.

WHO. (2007). WHO monographs on selected medicinal plants. WHO Library Cataloguing-in-Publication Data, 3: 23-32.

Yıldırımlı, Ş. (2004). Etnobotanik ve Türk etnobotaniği. Kebikeç İnsan Bilimleri için Kaynak Araştırmaları Dergisi, 17: 175-193.

Zeder, M. A. (2015). Core questions in domestication research. Proceedings of the National Academy of Sciences, 112(11): 3191-3198.

İKSAD
Publishing House

ISBN: 978-625-367-841-8