TUE-SSS-BFT(R)-01

ANTIMICROBIAL ACTIVITY OF PROPOLIS – A REVIEW

Tsvetomira Boneva, Student
Department of Chemistry, Food and Biotechnologies,
University of Ruse "Angel Kanchev", Razgrad Branch
E-mail: s222611@stud.uni-ruse.bg

Prof. Stanka Damyanova, DSc
Department of Chemistry, Food and Biotechnologies,
University of Ruse "Angel Kanchev", Razgrad Branch
E-mail: sdamianova@uni-ruse.bg

Abstract: *Propolis (bee glue) is sticky resinous material produced by honeybees from various plant sources. This product of bee secretion is composed of resins, waxes, polyphenols, polysaccharides, volatile materials and other secondary metabolites that are responsible for its bioactive characteristics such as antibacterial, anti-angiogenic, antiulcer, anti-inflammatory, antioxidant and anti-viral activities. Worldwide, researchers are studying the complex composition of propolis to unveil its biological potential. Propolis and its derivatives show broad spectrum of antimicrobial activity against different types of bacteria and enhance the efficacy of conventional antibiotics especially against multidrug-resistant microorganisms. Currently, antimicrobial drug resistance is having a serious impact on healthcare around the globe and bee glue should be evaluated adequately to better elucidate its potential application in various fields of medicine.*

Keywords*: propolis, antimicrobial, antibacterial.*

INTRODUCTION

Propolis is a natural resinous substance produced by honeybees from plant materials such as tree buds, sap flows, and other botanical sources. Bees collect these resins and mix them with wax and enzymes, creating propolis. They use it to seal gaps in their hives, reinforce hive structure, and protect against external threats like pathogens (Velikova et al., 2014). It is a complex mixture of bioactive compounds, including polyphenols, flavonoids, terpenes, and phenolic acids (Yapici, İzol and Tarhan, 2023). Propolis has a long history of use in traditional medicine due to its antimicrobial, anti-inflammatory, antioxidant, and immunomodulatory properties (Almuhayawi, 2020). Understanding these properties can lead to the development of new therapeutic agents for various health conditions. Propolis exhibits broad-spectrum antimicrobial activity against bacteria, fungi, viruses, and protozoa (Sa-eed et al., 2023). Investigating the mechanisms underlying this activity can help identify novel antimicrobial compounds and strategies to combat infectious diseases, especially in the context of rising antibiotic resistance (Bouchelaghem, 2022).

EXPOSURE

Chemical composition of propolis

A great deal of research has been conducted on the chemical composition of propolis, which is strongly dependent on factors such as geographic location, plant sources, and bee species (Velikova et al., 2014). Hundreds of compounds have been recognized in samples collected from various geographical areas. However, typical components of propolis include resins, waxes, essential oils, polyphenols, terpenes, amino acids, small amounts of vitamins and minerals, enzymes, sugars, and other trace elements (Tumbarski et al., 2023). These categories include various active compounds, such as flavones, caffeic acid, isovanillin, vanillin, butanoic acid, malic acid, alanine, benzoic acid, coumaric acid, gentisic acid, ferulic acid, vanillic acid, pinocembrin, pinobanksin, galangin, thymol, luteolin, terpenes, lignans, myricetin, decanoic

acids, chrysin, quercetin, kaempferol and more (Yapici, İzol and Tarhan, 2023). The therapeutic properties of propolis are mainly attributed to volatiles, flavonoids, and phenolic compounds, which are well known as antioxidant and antimicrobial active ingredients (Almuhayawi, 2020).

Table 2.Some types of propolis (Bouchelaghem, 2022).

Type	**Region**	**Main compounds**	
Poplar propolis	Mostly from Eurasian regions	Acetyloxycaffeate Caffeic acid Chrysin Dihydroflavonols Galangin Henolics	Phenylpropanoids Pinobanksin Pinocembrin Prenyl caffeate Salicylic acid
Mediterranean propolis	Greek, Cyprus, Malta, Sicily, Bulgaria,Turkey, Greece, Algeria, Croatia,Morocco	Communic acid Diterpenic acids Hydroxyditerpenic acid Imbricataloic	Isoagatholal Isocupressic acid Pimaric acid Pinocembrin
Yellow propolis	Cuba Brazil	Acetyl triterpenes Flavanones Lanostane Lupane Oleanane	Polymethoxylated Sterols Triterpenic alcohols Ursane
Brown propolis	Brazil Cuba	Artepillin C Baccharin Caffeic acids Chlorogenic acids Drupanin Kaempferide	Kaempferol *p*-coumaric Phenylpropanoid Polyisoprenylated benzophenones Prenylated phenylpropanoids
Red propolis	Brazil Cuba	Artepellin C Biochanin A Flavone Homopterocarpin Liquiritigenin Lupeol Medicarpin	Methyl abietate Methyl *o*-orsellinate Naringenin Neovestitol Pterocarpans Vestitol β-amyrin
Green propolis	Brazil Taiwan	Apigenin Artepillin C Caffeic acid Chrysin Cinnamic acid	Ferulic acid Kaempferide Narigenin Pinobanksin Rutin

Several types of propolis have been classified based on chemical composition and plant origin (Velikova et al., 2014). The process of standardization of propolis is extremely challenging due to its exceptionally inconsistent composition (Tumbarski et al., 2023).

Antimicrobial efficacy of propolis

The antimicrobial efficacy of propolis and some of its individual components have been documented against bacteria, viruses, fungi, and protozoa (Bouchelaghem, 2022). Various research indicated that propolis was more effective against Gram-positive bacteria in comparison to Gram-negative ones (Almuhayawi, 2020). Propolis is thought to exert its antibacterial activity by either enhancing the immunity of the organism or by acting directly on the microorganism (Sa-eed et al., 2023). The geographic location from which propolis is collected affects its antibacterial potential due to previously mentioned differences in chemical composition (Velikova et al., 2014).

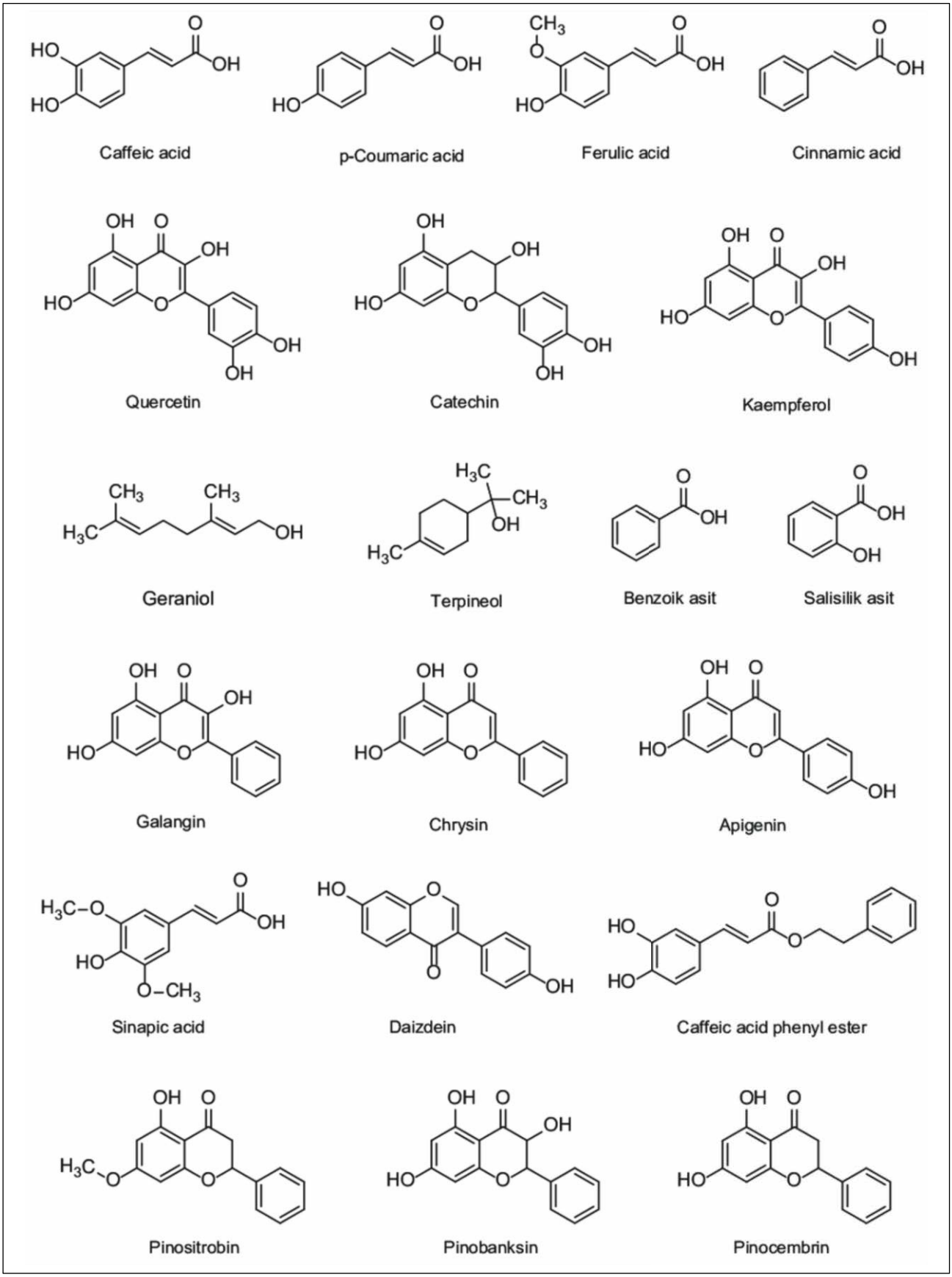

Fig. 1. Chemical structures of some bioactive compounds found in propolis (Yapici, 2023).

Best propolis activity was noted using Middle Eastern propolis, which was extremely effective against both Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Escherichia coli*) bacteria (Bouchelaghem, 2022). Artepillin C is one of the various phenolic mixes found in

propolis and exhibited efficient antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) (Velikova et al., 2014). Also, kaempferide was highly effective against *Enterococcus faecalis, Listeria monocytogenes, and Staphylococcus saprophyticus* (Tumbarski et al., 2023). Quercetin, yet another flavonoid found in propolis, binds to the subunit of *Escherichia coli* DNA gyrase to hinder bacterial activity (Sa-eed et al., 2023). Furthermore, it is assumed that propolis can cause fractional bacterial lysis and can affect bacterial proteins. Numerous investigations have confirmed a synergistic action among anti-infection agents and propolis. For example, chloramphenicol in the presence of Bulgarian propolis showed synergism against *Salmonella typhi*, and the combination of four Brazilian red propolis and fluconazole were effective against *Candida sp.* (Bouchelaghem, 2022). Other flavonoids like pinocembrin and apigenin were investigated and revealed antibacterial activity against *Streptococcus mutans* (Tumbarski et al., 2023). Likewise, pinocembrin has shown antibacterial properties against *Klebsiella pneumoniae, Listeria monocytogenes, Staphylococcus aureus, Pseudomonas aeruginosa, Streptococcus sobrinus, Enterococcus faecalis,* and *Streptococcus mutans* (Yapici, İzol and Tarhan, 2023). On the other hand, apigenin has shown efficacy against the following Gram-negative bacteria: *Pseudomonas aeruginosa, Klebsiella pneumoniae, Salmonella enterica serotype Typhimurium, Proteus mirabilis, and Enterobacter aerogenes* (Almuhayawi, 2020). Cinnamic acid caught attention by showing potent efficacy against *Bacillus spp., Micrococcus flavus, Pseudomonas aeruginosa, Yersinia ruckeri, Vibrio spp., Escherichia coli, Mycobacterium tuberculosis, Listeria monocytogenes, Enterobacter cloacae*, and *Salmonella enterica serotype Typhimurium* (Sa-eed et al., 2023). These examples are a small piece of all the research that has been done, and a lot more are to be investigated.

There are numerous studies with different components of propolis and their effect over a variety of pathogenic microorganisms, all of them proving the value of this natural substance. Besides the antimicrobial efficacy of the compounds themselves, it is worth noting the synergetic impact on bacterial resistance to conventional antibiotics (Sa-eed et al., 2023).

Antimicrobial mechanism of action of propolis

Several possible antimicrobial mechanisms of action of propolis have been proposed.

Nucleic acid synthesis inhibition refers to the disruption or interference with the process of synthesizing nucleic acids, namely DNA and RNA, within a cell. This interference can occur through various mechanisms (inhibition of DNA replication and RNA transcription) and is often targeted in antimicrobial therapy to inhibit the growth and replication of pathogens, thus resulting in reducing the affinity to development of biofilms (Bouchelaghem, 2022). Nucleic acid synthesis inhibition is a fundamental mechanism underlying the action of many antimicrobial agents.

Alteration of cytoplasmic membrane function refers to the disruption or modification of the structure and integrity of the cell membrane in microorganisms. The cytoplasmic membrane, also known as the plasma membrane, is a vital component of all cells, serving multiple essential functions such as maintaining cell integrity, regulating the passage of molecules in and out of the cell, and generating energy via electron transport chains in prokaryotes (Sa-eed et al., 2023).

Altering the function of the cytoplasmic membrane can have profound effects on microbial viability, causing energy metabolism inhibition (disrupting the generation of ATP), interference with transport proteins embedded in the membrane leading to disruption of essential cellular processes. Furthermore, certain agents can cause damage to the membrane structure, compromising its permeability and integrity, leading to cell lysis.

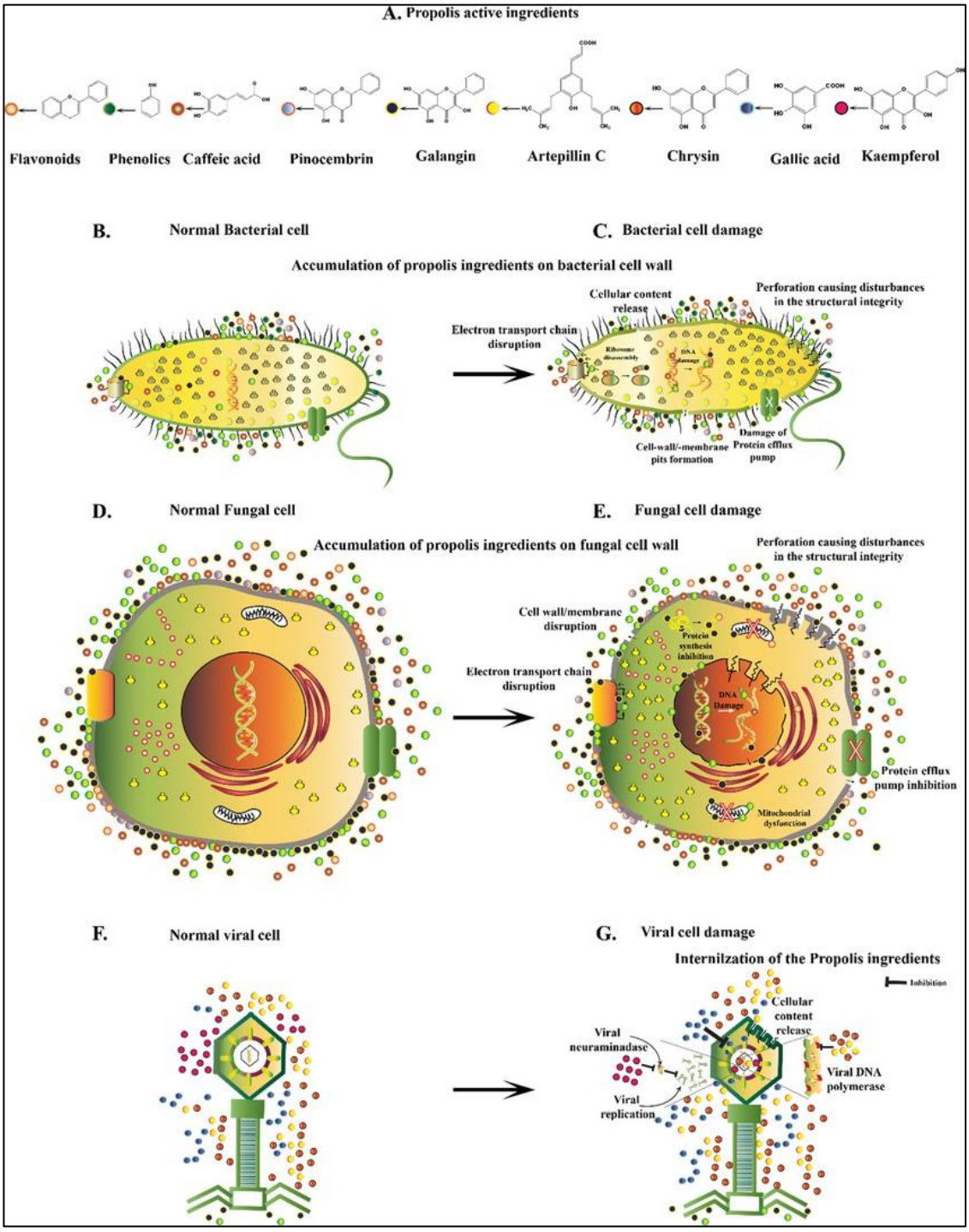

Fig. 2. Mechanism of antimicrobial action of propolis compounds (Ghosh, 2022)

Due to the different quality, quantity, and ratios of each component of propolis, it is difficult to predict the predominant biological activity of this natural substance, as it is also considered that these components act synergistically. Currently, very little is known about the molecular mechanism associated with the biological effects of propolis, and the mechanisms of interaction with microorganisms are still not clear (Yapici, İzol and Tarhan, 2023).

CONCLUSION

Propolis is an effective natural product that shows significant biological activity directly interacting with the microbial cells or by stimulating the immune system of the host cells. Its chemical composition is extremely heterogenic strongly dependent on geographical origin and plant sources. Yet, studies define some of its major compounds as highly effective antimicrobial

agents demonstrating both single and synergetic action even against multidrug-resistant microorganisms. Further research should be conducted to clarify the methods of interaction of propolis with microorganisms at molecular level.

Acknowledgments: The authors acknowledge the support of the Science Fund of the University of Ruse, Bulgaria (project 2024/BRz-02).

REFERENCES

Almuhayawi, M., (2020). Propolis as a novel antibacterial agent. *Saudi Journal of Biological Sciences*, 27(11), 3079-3086, URL: https://doi.org/10.1016/j.sjbs.2020.09.016.

Bouchelaghem, S. (2022). Propolis characterization and antimicrobial activities against Staphylococcus aureus and Candida albicans: A review. *Saudi Journal of Biological Sciences*, 29(4), 1936-1946. URL: https://doi.org/10.1016/j.sjbs.2021.11.063.

Ghosh, S., Al-Sharify, Z. T., Maleka, M. F., Onyeaka, H., Maleke, M., Maolloum, A., Godoy, L., Meskini, M., Rami, M., Ahmadi, S., Al-Najjar, S., Al-Sharify, N., Ahmed, S., & Dehghani, M. H., (2022). Propolis efficacy on SARS-COV viruses: a review on antimicrobial activities and molecular simulations. *Environmental Science and Pollution Research,* 29, 58628–58647

Sa-eed, A., Donkor, E., Arhin, R., Tetteh-Quarcoo, P., Attah, S., Kabotso, D., Kotey, F., & Dayie, N., (2023). In vitro antimicrobial activity of crude propolis extracts and fractions. *FEMS Microbes*, 4, xtad010. URL: https://doi.org/10.1093/femsmc/xtad010.

Tumbarski, Y., Todorova, M., Topuzova, M., Gineva, G., Yanakieva, V., Ivanov, I., & Petkova, N. (2023). Comparative Study on Physicochemical, Antioxidant and Antimicrobial Properties of Propolis Collected from Different Regions of Bulgaria. *Journal of Apicultural Science,* 67(1), URL: https://sciendo.com/article/10.2478/jas-2023-0004.

Velikova, M., Bankova, V., Sorkun, K., Houcine, S., Tsvetkova, I., & Kujumgiev, A. (2014). Propolis from the Mediterranean Region: Chemical Composition and Antimicrobial Activity. *Zeitschrift für Naturforschung C*, 55(9-10), 790 - 793. URL: https://doi.org/10.1515/znc-2000-9-1019.

Yapici, İ., İzol, E., & Tarhan, A. (2023). Significant bioactive components in bee products, *Bee and Bee Products,* 1 - 16, Orient Publications.

