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BIOLOGICALLY ACTIVE PLANT COMPOUNDS AND THEIR MECHANISMS OF ACTION: REVIEW

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ABSTRACT

Introduction and Purpose: Numerous studies conducted over the past few decades have confirmed that active compounds isolated from plants have multiple biological effects, including antioxidant, antimicrobial, anticancer, antiallergic, and anti-inflammatory properties. The primary focus of phytochemical research has been on phenolic compounds and their potential applications in medicine, cosmetics, pharmacy and agriculture.

The aim of this work is to highlight the significance of biologically active components isolated from plants and to clarify their mechanisms of action at the cellular level, with the goal of contributing to the development of plant-based antimicrobial and antioxidant agents.

Materials and Methods: In this scientific paper, we present the research results on biologically active compounds from plants and their mechanisms of action at the cellular level to summarize this field of study and, in part, contribute to the development of biologically active plant-derived compounds. During the database search, we used the following keywords: "biologically active plant compounds," "antimicrobial activity," and "antioxidant properties of plants."

Results: Plants are characterized by a mixture of various active mechanisms with different pharmacological profiles, allowing them to affect multiple diseases, unlike synthetic drugs, which are designed to inhibit or stimulate a single pharmacological pathway. The antimicrobial potential of essential oils and plant extracts is due to the presence of many pharmacologically active compounds, and their mode of action on bacterial cells depends on the concentration of the active substance, the type of microorganism, and the structure of their cell wall. Biologically active compounds isolated from plants are associated with antioxidant

activity in biological systems, as they play an important role in the absorption and neutralization of free radicals.
Discussion and Conclusion: In recent years, significant efforts have been made to isolate and examine biologically active compounds from plants and their antioxidant and antimicrobial properties. Special attention has been given to the mechanisms of action of these compounds on microbial cells. Biologically active compounds affect the transmembrane pH gradient and membrane integrity of microbial cells, causing leakage of intracellular contents, disruption of transport and energy production processes, as well as the respiratory chain, and play an important role in the absorption and neutralization of free radicals. A review of the literature concludes that the plant world represents an inexhaustible source of biologically active compounds with antimicrobial and antioxidant properties, which should continue to be studied to contribute to the development of plant-based antimicrobial and antioxidant agents.
Keywords: Biologically Active Compounds, Antimicrobial Properties, Antioxidant Activity.

INTRODUCTION

The use of medicinal plants in the prevention and treatment of various health issues dates back to ancient civilizations. Knowledge about the beneficial effects of numerous medicinal plant species and their proper usage has been passed down from generation to generation. Today, in many developing regions, between 70 and 95% of the population still relies on plants as a primary form of medicine, and many countries have integrated traditional plant-based remedies into their main healthcare systems through regulatory frameworks (RBG Willis, 2017). However, the use of plants in treatment is not limited to underdeveloped countries; plants are increasingly used in developed countries where modern medicine is readily available (Bošković, 2017).

According to the World Health Organization (WHO, 1997), plants represent an inexhaustible natural resource for the production of various medicines. The WHO has developed a strategy for the application of traditional herbal medicines, including a set of technical guidelines and documents related to the safety, efficacy, and quality assurance of medicinal plants and herbal materials (WHO, 2007). With advancements in scientific instrumental methods, it has become possible to achieve detailed characterization of biologically active compounds from medicinal plant species.

Numerous studies conducted over the past few decades have confirmed that active compounds isolated from plants exhibit multiple biological effects, including antioxidant, antimicrobial, anticancer, antiallergic, and anti-inflammatory properties. Scientists are in search of new natural sources of antioxidants that could replace synthetic ones in cosmetics, pharmaceuticals, and the food industry.

Phenolic compounds are highly prevalent in the plant kingdom. Major dietary sources of polyphenols include legumes (pulses and beans), cereals (corn, barley, oats, sorghum, rice, and wheat), nuts, oilseeds (rapeseed, flaxseed, olive seeds, and canola), beverages (fruit juices, tea, coffee, beer, wine, and cocoa), as well as fruits and vegetables (Khatoon et al., 2018). Phenolic compounds and flavonoids are associated with antioxidant activity in biological systems, mainly due to their redox properties, which play an important role in the absorption and neutralization of free radicals, mitigate the effects of singlet and triplet oxygen, or decompose peroxides (Saha et al., 2008). Besides their pronounced antioxidant activity, phenolic compounds contribute to the prevention of carcinogenesis and mutagenesis.

The antimicrobial potential of plant extracts is attributed to the presence of various pharmacologically active substances, and the mode of their action on bacterial cells depends

on the concentration of the active substance, the type of microorganism, and the structure of their cell wall.
The aim of this work is to highlight the significance of biologically active components isolated from plants and to clarify their mechanisms of action on cells, with the objective of contributing to the development of plant-based antimicrobial and antioxidant agents.

METHODOLOGY

In this scientific paper, we presented the results of research on biologically active compounds from plants and their mechanisms of action on cells in order to summarize this area of research and partially contribute to the development of biologically active compounds from plants. During the database search, we used the following keywords: "biologically active plant compounds," "antimicrobial activity," and "antioxidant properties of plants."

RESULTS AND DISCUSSION

In the process of photosynthesis, plants synthesize a large number of organic compounds, secondary metabolites, which were not given much importance until a few decades ago. However, recent research has shown that these compounds play an essential role in plant development, particularly in surviving adverse conditions (Kliebenstein, Osbourn, 2012). Secondary metabolites influence intercellular communication and reproduction in plants, and they are produced as a response to biotic and abiotic stress (Hartmann, 2007). They serve as a defense mechanism for plants against various herbivores and microorganisms (Bošković, 2017). On the other hand, some secondary metabolites play a role in attracting pollinating insects and other animals (Kaufman, 1999; Briskin, 2000; Wink, 2003). There are 14 basic classes of secondary metabolites, which are presented in Table 1 (Wink, 2003).

Table 1. Classes of Plant Secondary Metabolites according to Wink (2003)

Classes of Plant Secondary Metabolites	***Approximate Number***
Alkaloids	21000
Amines	100
Cyanogenic glycosides	60
Glucosinolates	100
Non-protein amino acids	700
Monoterpenes	2500
Sesquiterpenes	5000
Diterpenes	2500
Triterpenes, saponins, sterols	5000
Tetraterpenes	500
Flavonoids, Tannins	5000
Polyacetylenes, fatty acids	1500
Polyketides	750
Phenylpropanoids	2000

Numerous studies have confirmed that secondary metabolites have beneficial effects on human health, and are therefore referred to as biologically active components. The greatest interest in phytochemical research has been focused on phenolic compounds and their potential applications in medicine, pharmacy, and agriculture. They play a very important

physiological and morphological role in plant growth and reproduction, protection against pathogens and predators, and also contribute to the formation of color and sensory properties of flowers, fruits, and vegetables (Bošković, 2017). In plant organisms, polyphenols perform a range of functions that have a significant impact on the ecophysiology of plants: they act as antioxidants, antimicrobial agents, and visual attractants for some pollinating insects (Heim et al., 2002). As natural sources of polyphenolic compounds, the literature most often mentions aromatic and medicinal herbs, fruits, vegetables, and cereals (Naczk, Shahidi, 2006).
Flavonoids have shown numerous therapeutic effects: antimicrobial, antiviral, anticancer, anti-inflammatory, and others. The cardioprotective role of flavonoids is attributed to their ability to inhibit lipid peroxidation, capture ("trap") free radical electrons, chelate transition metal ions (Fe2+, Cu2+, Zn2+, and Mg2+), activate antioxidant enzymes, and inhibit oxidases (Heim et al, 2002). Many flavonoids can act as cofactors for numerous enzymes, and they are also used in the fight against skin aging, as anti-cellulite products, and skin whitening products (Bošković, 2017). Flavonoids significantly contribute to strengthening capillaries, anti-inflammatory effects, protection from radiation, softening of the skin, and others (Svobodova, 2003; Malinowska, 2013).

Antioxidant Activity of Plant Extracts

In the past decade, significant attention has been given to the antioxidant activity of biologically active compounds isolated from plants. The bioactive compounds of plants stimulate the immune system, block the formation of carcinogens, reduce oxidation, slow the growth rate of cancer cells, reduce inflammation, trigger apoptosis, prevent DNA damage, and regulate hormones such as estrogen and insulin, whose excess levels are linked with an increased risk of breast and colon cancer (Karamac et al., 2019). Plants contain a wide range of antioxidants, and it is difficult to measure the antioxidant capacity of each compound individually. In order to assess the biological activity of plant extracts, the first step is to determine their antioxidant capacity (Bošković, 2017). A large number of methods have been developed for determining antioxidant activity in plants: total antioxidant capacity, inhibition of lipid peroxidation, DPPH method for antioxidant activity, and the ability to “scavenge” hydroxyl radicals. Repair antioxidants are particularly important as they act through specific mechanisms, restoring or removing damaged vital biomolecules that occur under oxidative stress conditions. The mechanism of action of antioxidants is shown in Figure 1.

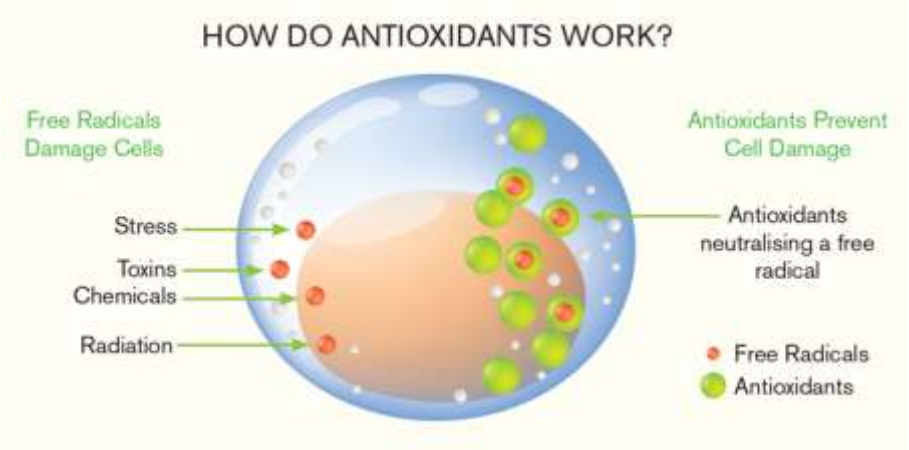

Figure 1. Mechanisms of Action of Antioxidants

It is assumed that polyphenolic antioxidants, such as flavonoids in red wine, along with antioxidants from olive oil and fresh fruits and vegetables, which are abundant in Mediterranean cuisine, may provide protection against coronary heart disease. Many flavonoids, such as quercetin and catechin, have shown to be better antioxidants than vitamins C and E (Svobodova, 2003). Amarowicz et al. (2008) report that, compared to simple phenolic compounds, tannins are 15-30 times more effective in destroying peroxyl radicals, which is why they are considered important biological antioxidants. Research results on the antioxidant activity of ethanolic extracts from plants *Anchusa officinalis*, *Echium vulgare* and *E. italicum* using multiple methods have confirmed that they possess exceptionally good antioxidant activity (Bošković, 2017a; Bošković, 2018; Bošković, 2022), due to the presence of high amounts of phenols, flavonoids, and tannins in these plants.

Antimicrobial Activity of Plant Extracts

Due to the increasing occurrence of bacterial resistance to a large number of antibiotics, as well as the ability of plants to synthesize biologically active compounds, the use of natural antimicrobial agents of plant origin in the biological control of pathogenic bacteria is gaining greater importance (Đukić, Vesković, 2015). Rapid technological advancement and the application of new, increasingly efficient methodologies have allowed the identification and characterization of numerous antibacterial agents in recent years (Katz and Baltz, 2016).

Plants are characterized by a combination of various active mechanisms with different pharmacological profiles, allowing them to impact multiple ailments, unlike synthetic drugs, which are designed to inhibit or stimulate only one pharmacological pathway (Della Loggia, 2000). The advantage of plant-derived compounds over synthetic drugs lies in the broader pharmacological complexity that plants possess (Bošković, 2017). HPLC analysis of selected plant species from the Boraginaceae family confirmed the presence of numerous pharmacologically active substances, with rosmarinic acid and rutin being the most dominant, both of which have proven antioxidant, anti-inflammatory, and anticancer activities (Bošković, 2017a; Bošković, 2018; Bošković, 2022).

According to research by Skandamis et al. (2006), extracts from certain plant species contain a wide range of reactive groups, so their antimicrobial effect cannot be attributed to a single, specific mechanism but rather involves multiple target sites within the microorganism cell. Phenolic compounds affect the transmembrane pH gradient and membrane integrity, causing leakage of intracellular contents, disruption of transport processes, energy production, and the respiratory chain (Bošković, 2017). The hydrophobicity of plant extracts enables their integration into cell membrane lipids, making the membrane more permeable and leading to apoptosis of the microbial cell. Figure 2 illustrates the mechanisms of action of plant extracts on microbial cells.

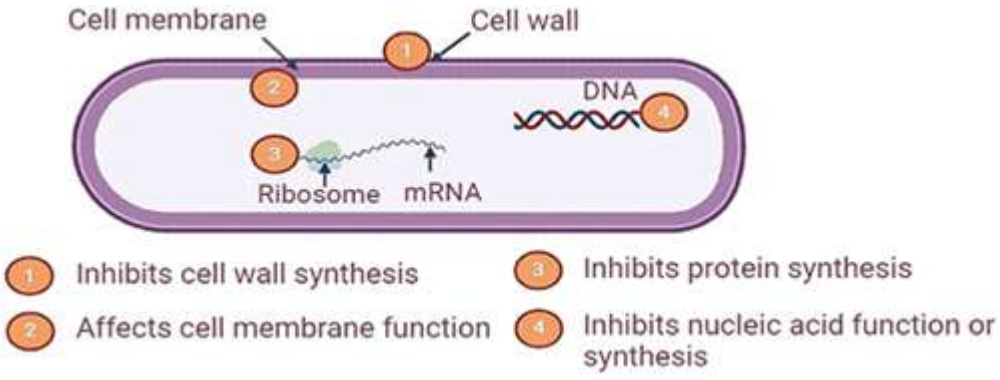

Figure. 2. Mechanisms of Action of Plant Extracts on Microbial Cells

The methods commonly used in practice for determining the antimicrobial potential of medicinal plants and essential oils are the microdilution method and the disk diffusion method. The microdilution method has become the preferred technique for evaluating the antibacterial potency of plant extracts or compounds due to its efficiency, reproducibility, and ability to assess a wide range of concentrations in a small sample volume (Balouiri et al., 2016).

Numerous studies on selected plant species have shown that only certain plant species exhibit exceptionally good antimicrobial activity, expressed by the minimum inhibitory concentration.

MIC value is defined as the lowest concentration of the assayed antimicrobial agent that inhibits the visible growth of the microorganism tested, and it is usually expressed in µg/mL or mg/L (Balouiri et al., 2016). There is a large body of evidence suggesting that plant extracts and polyphenols have the ability to disrupt the structure of the bacterial plasma membrane, causing the formation of pores, leakage, altering electrical charge, altering polarity, increasing permeability, modifying fluidity, delocalizing membrane proteins, and other phenomena responsible for antibacterial activity (Alvarez-Martínez et al., 2021).

According to the results of studies (Bošković, 2022) the applied solvents significantly affected the content of phenolic compounds in and their antimicrobial and antioxidant properties. A large number of studies have confirmed that polar solvents are significantly more effective than non-polar ones in isolating bioactive components, which has led to enhanced antioxidant and antimicrobial properties of plant extracts. The antimicrobial properties of selected plant species were examined using the microdilution method on gram-positive and gram-negative bacteria by Bošković (2018), who found that the ethanolic extract of *Anchusa officinalis* exhibited excellent antimicrobial activity (MIC=3.94 µg/mL) against *Proteus vulgaris*, *Salmonella enteritidis*, *Enterococcus faecalis*, *Enterococcus faecium*, *Salmonella typhimurium*, and *Candida albicans*, and that the chloroform and acetone extracts were effective against *E. faecalis* and *C. albicans* (MIC=7.875 µg/mL). Meanwhile, the chloroform extract of *Echium vulgare L.* showed the strongest activity against *P. mirabilis*, *S. typhimurium*, *L. ivanovii*, and *S. aureus* (MIC=3.91 µg/mL), and the ethanolic extract exhibited the greatest antimicrobial activity against *K. pneumoniae*, *S. enteritidis*, and *C. freundii* (3.91 µg/mL) (Bošković, 2022). The observed antimicrobial effects are closely linked to the total phenol concentration and the broad range of biological activities, including antithrombotic, cardioprotective, vasodilatory effects, as well as the high antioxidant potential of the tested extracts (Bošković, 2017).

According to the research by Lakušić et al. (2013), there are significant differences in antimicrobial effects not only between different plant species but also within the same species

collected in different geographical regions and at different times, which can be attributed to the impact of climatic and edaphic factors.

Pseudomonas aeruginosa (PA) is a gram-negative bacterium that can cause nosocomial infections, including respiratory tract infections, burn and wound infections, urinary tract infections and bloodstream infections (Wei et al., 2024). Chakotiya et al. (2016) assessed the antibacterial potential of *Glycyrrhiza glabra* stem extract and *Mentha piperita* leaf extract against multidrug-resistant *P. aeruginosa* and their findings revealed that these extracts displayed significant activity, with minimum inhibitory concentrations of 10 µg/mL and 25 µg/mL. While extracts of *E. vulgare* exhibited very poor antimicrobial potential against *Pseudomonas aeruginosa* (500 µg/ml) (Bošković, 2022).

CONCLUSION

In recent years, significant efforts have been made to isolate and study biologically active compounds from plants, focusing on their antioxidant and antimicrobial properties. Special attention has been given to the mechanisms of action of these compounds on microbial cells. Biologically active compounds affect the transmembrane pH gradient and the integrity of the microbial cell membrane, causing leakage of intracellular content, disruption of transport and energy production processes, and the respiratory chain. They are also associated with antioxidant activity in biological systems, as they play an important role in absorbing and neutralizing free radicals. Based on a review of the literature, it has been concluded that the plant kingdom represents an inexhaustible source of biologically active compounds with antimicrobial and antioxidant properties, which should continue to be explored to contribute to the development of plant-based antimicrobial and antioxidant agents.

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THE IMPORTANCE OF BEING READY FOR POSSIBLE EARTHQUAKE INCIDENTS FOR ANIMAL AGRICULTURE

HAYVAN TARIMINDA OLASI DEPREM OLAYLARINA HAZIR OLMANIN ÖNEMİ

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ÖZET
Deprem, insanlar ve diğer canlıların yanı sıra hayvanlar için de çok önemli bir tehdittir. Bir zooteknist ziraat mühendisi veya hayvan yetiştiricisi olarak, deprem olayı öncesinde, sırasında ve sonrasında çiftlik hayvanlarımıza bakım ve koruma çalışmaları yapmalıyız. Çiftlik hayvanlarını güvenli barınaklarda güvence altına alınmaları, onlara yem ve su tedarik etmeyi ve enkaz altında kalması gibi potansiyel tehlikelerden korunmaları sağlanmalıdır. Bunları yapabilmek için onları ölümden, yaralanmadan, susuzluktan, açlıktan, dolayısıyla üretim kayıplarından korumak konusunda öncesinde, sırasında ve sonrasında yapılması gerekenleri yapmak için bir eylem planımızın olması gerekiyor. Teknik personeller, sağ ve sağlıklı hayvan yetiştiricileri, deprem yaşandığında hayvanlarının güvenliğini sağlamalı ve onları güvende tutmak için harekete geçmelidir, ancak öncelikle kendilerini bu olaydan korumalıdır. Hayvanları binalardan ya da yapılardan uzak, açık bir alana taşımalılar, suya ve yeme erişimlerini sağlamalılar ve refah durumlarını izlenmelidir. Depremler bittikten sonra hayvanlar canlılık, yaralanma ve mevcut durumlarından kurtarmak için hala yardıma ihtiyaç duyma açısından kontrol edilmeleri gerekebilir. İhtiyaç duyulması halinde veteriner hizmetlerinin özellikle AFAD'dan ulaşılacak veteriner hekim veya zooteknist ziraat mühendisi veya yardımcı personel tarafından yapılması gerekmektedir. Hayvan barınaklarının onarılması ve yem kaynaklarının sağlanması, en azından hayvanların hayatta kalmaları için hayvan refahının sürdürülmesi amacıyla gerekmektedir. Sonuç olarak; deprem öncesinde alınacak önlemler hayvanların hayatta, güvende, sağlıklı ve üretken kalması açısından önemlidir.
Anahtar kelimeler: deprem, çiftlik hayvanları, yem temini, yaralanmalar, binalar, refah

ABSTRACT
The Importance of Being Ready for Possible Earthquake Incidents for Animal Agriculture
Earthquake is very important threat for animals as well as humans and other living things. As a zoo technician or animal keeper, we have to practice caring and protecting our farm animals before, during, and after an earthquake event. This may include preparing farm animals by securing them in safe structures, providing them with food and water supplies, and ensuring they are protected from potential dangers such as falling debris. In order to do these, we must have an action plan what should be done, before, during and after with respect to protecting them from death, injury, thirst and hunger, consequently production losses. When an earthquake occurs, farmers must ensure the safety of their animals and take action to keep them secure, but firstly they must protect themselves from this event. Perhaps, they will transfer animals to an open area away from buildings or constructions, ensuring they have free access to water and feed, and monitoring their welfare condition. After the earthquake incidences were finished, farmers may need to control their animals with respect to liveness, injuries and still needing help for rescuing them their current situations. If they need, the veterinary medications