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CULTIVATION, IMPORTANCE AND POSSIBILITES OF APPLICATION OF MEDICINAL PLANTS IN MEDICINE

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Abstract: Medicinal and aromatic plants are intensively studied and applied in traditional and official phytotherapy. Medicinal plants can be cultivated or collected from nature. The pharmacological activity of plants is mainly due to the products of secondary metabolism. Recently, more and more attention has been paid to the study of the chemical structure and pharmacological activity of herbal drugs, which contain polyphenols due to their antioxidant and anti-inflammatory effect, and thus a beneficial effect on health.

Keywords: medicinal plants, importance, cultivation, biological activity, application in medicine.

Introduction

In the production of food on the planet level, the primary role belongs mainly to angiosperms, but this group of plants also includes species that are intensively used in pharmacy and medicine (Jančić, 2004; Šarčević-Todosijević et al., 2018). The cultivation of medicinal plants is no different from the cultivation of other crops, and in order to achieve optimal yields, optimal habitat conditions are necessary, as well as the timely application of agrotechnical measures. Medicinal plants can be cultivated or collected from nature (Kovačević, 2004). The area of the Balkans is very rich in medicinal plant species, but due to favorable climatic conditions, they can also be successfully grown on plantations (Šarčević-Todosijević et al., 2018; Šarčević-Todosijević et al., 2022a).

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Medicinal and aromatic plants are intensively studied and applied in traditional and official phytotherapy, but also in food production as spices and preservatives. The biological effect exerted by medicinal or aromatic plant species mainly depends on the main constituents of each species, but also on the amount of these constituents in the plant. The products of secondary metabolism are mainly responsible for the pharmacological activity of plants. Recently, more and more attention has been paid to the study of the chemical structure and pharmacological activity of herbal drugs containing polyphenols because their antioxidant and anti-inflammatory effects, and thus their beneficial effects on health. Epidemiological studies indicate that the long-term use of plant polyphenols in the diet has a preventive effect on the occurrence of cancer, diabetes, inflammatory, cardiovascular, neurodegenerative diseases, as well as aging-associated diseases. In addition to antibacterial and antifungal properties, natural components of plants are an important source for developing new antiviral drugs due to their availability and low side effects (Beckman, 2000; Kovačević, 2004; Arts and Hollman, 2005; Đorđević et al., 2020; Šarčević-Todosijević et al., 2022b; Popović et al., 2018a; 2018b; 2019; 2020; 2021).

Material and Methods

In this study an analysis of the production of medicinal plants was also done. On the desk research is based. A number of scientific papers results of domestics and foreign authors in the thematic fields is also analyzed and quoted. The analytical-synthetic method was used during the discussion and formulation of conclusions.

Results and discussion

In global food production, the primary role belongs to plant production, with the most important being angiosperms. Angiosperms also include species that are intensively used in pharmacy and medicine. Whether it is crop production for food or medical purposes, optimal crop yields can only be obtained through agricultural production based on scientific principles (Jančić, 2004; Đukić et al., 2007; Šarčević-Todosijević et al., 2018; Šarčević-Todosijević and Vojvodić, 2020). Cultivation of medicinal plants is not significantly different from cultivation of any other crop. In order to achieve optimal yields of medicinal plants, as well as the synthesis of pharmacologically active ingredients, optimal conditions of the habitat, especially the soil, are necessary.

According to the data of the Statistical Office of the Republic of Serbia, the areas under medicinal and aromatic plants in the period from 2002 to 2006 tend to decrease, from 1.832 ha in 2002 to 1.211 ha in 2006. From 2007 to 2009, the areas under medicinal and aromatic plants increased, and in 2012 there was a decrease and these areas amounted to only 1.337 ha (table 1).

Table 1. Production of medicinal and aromatic herbs in Serbia

Year	2002	2006	2012	2022	Interval variation
Area, ha	1832	1211	1337	1300	621

In cultivation of medicinal plants, care should be taken in the selection of the most suitable taxon (species or variety) for cultivation in a certain region, selection of soil, cultivation and preparation of the soil, selection of the optimal way to establish plantations (type of planting material and planting time), application of agrotechnical measures for cultivation and protection of the plants. Plants should be harvested at the stage of ontogenetic development, in which the quality of the drug is the most optimal. Some medicinal plants cannot be cultivated as plantations, because they produce pharmacologically active substances in the required quantities only in natural habitats. Such plants must be collected from nature (Kovačević, 2004). The Balkans is very rich in medicinal plant species. In the Košutnjak locality, Šarčević-Todosijević et al. (2018) collected and determined 32 plant species within 24 angiosperm families. All collected species show wide range of pharmacological activities and are used in phytotherapy (Šarčević-Todosijević et al., 2018; Šarčević-Todosijević et al., 2022a).

However, in the climatic conditions of the Balkans, medicinal herbs can be cultivated successfully. Miloradović (2018) investigated the impact of agro-ecological conditions in southern Banat and Pomoravlje on morphological characteristics, herb yield and quality of essential oil obtained by distillation of fresh immortelle biomass (*Helichrysum italicum*). These studies have shown that by choosing the most favorable system of production technology, commercial yields can be expected already from the second year of cultivation, as well as that Italian immortelle (*Helichrysum italicum*) can be successfully grown in continental areas, in this case in the hilly areas of Central Serbia, as well as in the plains of Vojvodina (Miloradović et al., 2018).

Filipović et al. (2021) conducted the first published research in the Republic of Serbia about the vegetative propagation of Pannonian thyme (*Thymus pannonicus*). In addition to morphological polymorphism, species of the genus

Thymus are characterized by a large chemical polymorphism in the composition of the essential oil, which exhibits strong inhibitory activity against *Helicobacter pylori* and other bacteria, as well as against *Candida albicans*. It is used in the auxiliary therapy and prevention of gastritis and in alleviating diseases of the respiratory tract and the gastrointestinal system. In the paper, they examined the impact of the application of three different phytohormones (INCIT2, INCIT 5 and INCIT 8, all based on α -Naphthalene Acetic Acid (NAA), with the cuttings of two forms of Pannonian thyme (the L-16 form, with hairy leaves, and the L-9 form, with hairless leaves), established during two periods (March and May), on the percentage of the rooted cuttings and the morphological properties of the seedlings. The variant without the application of the phytohormones was taken as the control. Based on the achieved results, Filipović et al. (2021) point out that INCIT 2 proved to be the most suitable phytohormone for the rooting of Pannonic thyme cuttings, with the average percentage of rooted cuttings of 61.3%. The lowest rooting percentage was recorded in the control variant, only 29.4%. Satisfactory rooting was found in the cuttings treated with INCIT 8 (57.6%). The L-16 form cuttings showed a higher rooting rate, an average of 53.8%, whereas the L-9 form cuttings had a lower average percentage of rooted cuttings (45.0%) for both plant establishment periods. Greater success and quality in the rooting of cuttings was recorded in the second (May) period of plant establishment, averaging 58.1%, which was higher by 17.4% than the percentage of rooted cuttings in the first establishment period (40.7%) (Filipović et al., 2021).

Popović et al. (2018) conducted an experiment with *Phacelia tanacetifolia* cultivar NS Priora in two variants: control, without nutrition and variant with nutrition, in organic cropping system. *Phacelia tanacetifolia* is commercial species, which has long been used for bee nutrition, and after acacia, it produces the most nectar. Foliar nutrition had a positive effect on all the tested characteristics. Analysis of variance was found highly significant effect of nutrition on leaf length, yield of biomass and plant height. This research indicated the justification of growing honey plants, especially the species *Phacelia tanacetifolia*, in a health-safe organic cultivation system (Popović et al., 2018a; 2020).

The pharmacological effect of medicinal or aromatic plant species mainly depends on the main constituents of each species, but also on the amount of these constituents in the plant. The therapeutic effects of medicinal plant species are very broad, they include antibacterial, antiviral, anti-inflammatory, antioxidant, anticancer, cytotoxic, spasmolytic, diuretic, sedative and many

other effects (Kovačević, 2004; Šarčević-Todosijević et al., 2019a,b; 2022b; Dročić et al., 2020; Đorđević et al., 2020; Popović et al., 2022; Petrović et al., 2022).

Polyphenols are a very important group of compounds, secondary metabolites of plants, due to their beneficial effect on health. Epidemiological studies indicate that the long-term use of plant polyphenols in the diet has a preventive effect on the occurrence of various diseases. As natural antioxidants, they are important in the prevention and treatment of cancer, inflammatory, cardiovascular and neurodegenerative diseases, and intake of fruits and vegetables, especially seeds and nuts, is associated with a lower risk of developing chronic and degenerative aging-associated diseases. Polyphenols include phenolic acids, flavonoids, coumarins, stilbenes and lignans, as well as polymerized forms such as tannins and lignin (Beckman, 2000; Kovačević, 2004; Arts and Hollman, 2005; Đorđević et al., 2020; Popović et al., 2020; 2021; Šarčević-Todosijević et al., 2022b).

The most common ingredients of *Ginkgo biloba* extract, one of the plant species most often used in phytotherapy, are also polyphenols (flavonoids). This plant has become increasingly important in the last thirty years, after the discovery and definition of a standardized extract EGb 761 (EGb 761 - standardized *Ginkgo biloba* leaf extract). This extract contains 24% heterosides and 6% ginkgolide and bilobalide. *Ginkgo* extract contains a number of active substances, which show effectiveness in the treatment of arterial and cerebrovascular insufficiency, dementia, vertigo, asthma, allergies, memory improvement, and acts as a strong antioxidant (Dubey et al., 2004; Kovačević, 2004).

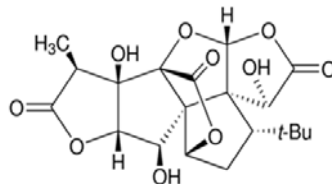


Figure 1. Ginkgolide A (Kovačević, 2004)

Defeudis (2002) from the *Institute for BioScience* in the USA, conducted studies on the effectiveness of the application of bilobalide. *In vivo* studies have indicated that systemically administered bilobalide can reduce cerebral edema, decrease cortical infarct volume in certain stroke models, and reduce cerebral ischemia. *In vitro* studies indicate that bilobalide has multiple mechanisms of action that may be associated with neuroprotection. These mechanisms include preservation of mitochondrial ATP synthesis, inhibition of apoptotic damage

induced by staurosporine or by serum-free medium, suppression of hypoxia-induced membrane deterioration in the brain and actions of increasing the expression of the mitochondrial DNA-encoded COX III subunit of cytochrome c oxidase and the ND1 subunit of NADH dehydrogenase. Considering that it has multiple mechanisms of action, Defeudis (2002) points out that bilobalide could be useful in developing therapy for disorders involving cerebral ischemia and neurodegeneration.

Hop (*Humulus lupulus* L.) is also a source of numerous biologically active polyphenolic compounds. A significant compound, 8-prenylnaringenin (8-PN), belonging to the group of prenylated flavonoids, was shown to be a potent phytoestrogen. Due to its estrogenic effects, administration of 8-PN represents a novel therapeutic approach to the treatment of menopausal and post-menopausal symptoms. Application of 8-PN in the treatment of menopause has been clinically examined with good results. Other biological activities include the potential to prevent bone-resorption or tumor suppression. However, the use of phytoestrogens is often considered due to possible adverse effects associated with long-term use (Štulíková et al., 2018).

Pharmacologically active ingredients of plants that are widely used are also essential oils. Stevanović (2021) examined the antimicrobial and antiviral activity of essential oils of aromatic plant species *Origanum vulgare*, *Calluna vulgaris*, *Helichrysum italicum*, *Satureja montana* and *Thymus vulgaris* on strains of bacteria *Staphylococcus aureus* and fungi *Candida albicans* and *Candida krusei*. The antimicrobial activity of essential oils was tested by determining the minimum inhibitory concentration (MIC), as well as the potential of essential oils to reduce the biofilm of the tested strains of microorganisms. The essential oils showed significant antimicrobial activity, in the range of 0.078-5 mg/ml for *S. aureus* and 0.156-5 mg/ml for *C. albicans* and *C. krusei*. *Calluna vulgaris* essential oil (MIC=0.078 mg/ml) showed the highest antimicrobial activity against *S. aureus*, and *Helichrysum italicum* essential oil (MIC=0.156 mg/ml) against *Candida* sp. The significant potential of all oils in the reduction of biofilms produced by the tested types of microorganisms was also determined (Stevanović, 2021).

Due to the presence of various bioactive compounds, primarily essential oils, the plant species *Matricaria chamomilla* (chamomile) has anti-inflammatory properties (Kovačević, 2004). The phytochemistry composition of essential oils and extracts of *M. chamomilla* has been intensively studied and it has been determined that the plant contains over 120 constituents. Due to the mentioned chemical composition, *M. chamomilla* exhibits a wide range of biological activities, such as antioxidant, antibacterial, antifungal, antiparasitic,

insecticidal, antidiabetic, anticancer and anti-inflammatory (Mihyaoui et al., 2022). In addition to chamomile, numerous metabolites that exhibit strong antimicrobial, antiviral, anti-inflammatory, antioxidant, antimutagenic and anticancer biological activity have been isolated from the immortelle drug (*Helichrysum* sp.) (Miloradović, 2018).

Natural plant components are also an important source for developing new antiviral drugs due to their availability and low side effects. Most of the research is conducted on finding an antiviral drug that will inhibit various enzymes associated with the life cycle of the virus, so the connection between the structure of flavonoids and these enzymes was observed. Baicalin, isolated from the plant species *Scutellaria baicalensis*, inhibits HIV infection and viral replication. Different combinations of flavones and flavonols show synergism, so kaempferol and luteolin show a synergistic effect against Herpes Simplex Virus (HSV). Synergism can also occur between flavonoids and other antiviral agents (Hegi, 1981; Kovačević, 2004).

Conclusion

The area of the Balkans is very rich in medicinal plant species, but due to favorable climatic conditions, medicinal plants can also be successfully grown on plantations. The cultivation of medicinal plants is no different from the cultivation of other crops, and in order to achieve optimal yields, optimal habitat conditions are necessary, as well as the timely application of agrotechnical measures. The pharmacological effect that medicinal or aromatic plant species exhibit mainly depends on the main ingredients of each species, but also on the amount of these ingredients in the plant. Recently, more and more attention has been paid to the study of the chemical structure and pharmacological activity of herbal medicines, which contain polyphenols because of their beneficial effect on health. Natural components of plants are an important source for the development of new antiviral drugs.

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