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Antioxidant activity of plant secondary metabolites

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Abstract

Oxidative stress can induce the development of many different disorders. Plant secondary metabolites may act as antioxidants by neutralisation of free radicals and by stimulation of endogenous antioxidant mechanisms. One of the important secondary plant metabolites with antioxidant activity are polyphenols. They can exert activity through different mechanisms depending on their structure. Polyphenols are widely present in herbal drugs, and some of the commonly used ones are aronia berry (*Aroniae fructus*) and bilberry fruit (*Myrtilli fructus*), both rich in anthocyanins and tannins and with high antioxidant activity. The main compounds in turmeric rhizome (*Curcumae rhizome*) are curcuminoides that manifest antioxidant and anti-inflammatory activity. Furthermore, tea leaf (*Camelliae sinensis folium*) and coffee bean (*Coffeae semen*), highly present in every-day life, significantly contribute to the daily intake of antioxidants and provide necessary protection of the organism from the consequences of oxidative stress.

Key words: antioxidant activity, polyphenols, herbal drugs

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Introduction

In aerobic organisms, there is a continuous production of free radicals during oxidative metabolism. Free radicals participate in many physiological processes and as long as there is a balance between their production and antioxidant protection mechanisms, there are no cell and tissue damages. During the process of ageing of the organism, the weakening of the natural antioxidant protection mechanism and the activity of external factors (high-energy radiation, pollutants, xenobiotics) increase the generation of oxygen radicals and their toxic effects are manifested through interaction with basic cellular structures and biomolecules. Oxidative stress, and then the accumulation of oxidative damage, participate in the development of many autoimmune, inflammatory, cardiovascular and neurodegenerative disorders.

Antioxidant enzymes and non-enzymatic molecules, which prevent the formation of free radicals or remove them, are present in the human body. Due to the limited efficiency of endogenous defence systems, it is necessary to introduce exogenous antioxidants, which are present in significant quantities in medicinal plants. The phenolic compounds, vitamins C and E and carotenoids are well-known and significant secondary plant metabolites with antioxidant activity. The structure of phenolic compounds can vary from simple compounds to complex polymers. They include phenolic acids, flavonoids, anthocyanins, coumarins, anthranoids, stilbenes, lignans and tannins (1, 2).

Antioxidant activity of phenolic compounds

Antioxidant activity is achieved by suppressing the creation of free radicals (inhibition of oxidative enzymes or building complexes with metals), removing already created free radicals, and/or by stimulation of endogenous defensive antioxidant mechanisms. Plant secondary metabolites may act through one or more of the above mechanisms. Antioxidants can also act synergistically with other antioxidant systems. Phenolic compounds remove free radicals and prevent their interaction with the DNA, increase the activity of antioxidant enzymes and detoxification enzymes, and thus reduce oxidative damage, eliminate potential mediators of inflammation and carcinogens and stimulate cytoprotective mechanisms. In the modern world, due to constant exposure to various stressors (inducers of oxidative damage), it is necessary to ensure an adequate intake of antioxidant compounds, and one way to do so is the application of medicinal plants.

The structure of polyphenolic compounds affects the ability to neutralize free radicals and bind metals. The antioxidant activity of polyphenolic compounds is mostly based on the presence of OH groups and with the increase in the number of OH groups, the antioxidant activity increases. Research has shown that the presence of two hydroxyl groups in the *ortho* position increases antioxidant activity due to additional resonance stabilization and *o*-quinone formation**.** Phenolic compounds, e.g., quercetin or cyanidin with 3',4'-dihydroxy substituents in ring B and conjugation between rings A and B, show pronounced antioxidant activity. The introduction of the methyl group decreases the ability of the compound to neutralize radicals (3).

Structural characteristics of flavonoids important for antioxidant activity:

- 3,4-dihydroxy substitution in ring B, which enables good delocalization of electrons and stabilization of phenoxyl radicals;
- The presence of a 2,3-double bond in conjugation with the 4-keto group;
- 3-OH group on ring C, which increases electron delocalization along the flavonoid structure.

Quercetin meets all these parameters and has high antioxidant activity (Figure 1). The binding of the sugar component in position 3 of quercetin and the formation of rutin significantly reduces the activity (3).

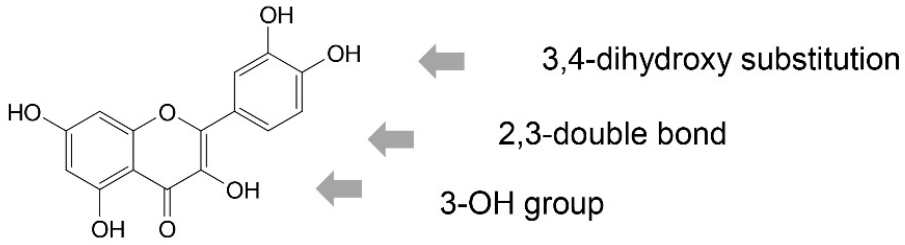

Figure 1. Structural characteristics significant for antioxidant activity
Slika 1. Strukturne karakteristike značajne za antioksidantnu aktivnost

Phenolic compounds can also act in a prooxidative manner, through autooxidation and the formation of semiquinones and superoxide ($O^{2.-}$) radicals. These radicals are very reactive and can damage important molecules such as proteins or DNA. In addition, both radicals accelerate autoxidation by forming hydrogen peroxide (H_2O_2) during the process. On the other hand, studies have documented the involvement of reactive oxygen species (ROS) in bacterial lethality, wherein the hydroxyl radical generated in Fenton's reaction was responsible for bacterial death (4, 5).

The balance between the antioxidant and prooxidant activity of phenolic compounds depends on the concentration of metal ions, the concentration of phenols and the pH of the environment (3).

Bioavailability of phenolic compounds

After oral administration, polyphenolic compounds are transported to the digestive tract, where they are broken down into compounds of lower molecular weight (caffeic acid, protocatechuic acid, protocatechuic acid aldehyde) under the influence of intestinal microbiota.

Bioavailability depends on many factors: the type of herbal drug and its processing (e.g. thermal processing), interaction with other ingredients in the intestinal tract (food and alcohol), intestinal factors (related to the person applying the herbal drug). The bioavailability of polyphenolic compounds is considered to be extremely low, only 1-

10% of the initial amount. The plasma concentration of polyphenolic compounds after resorption in the small intestine is about 1–10 μM. In addition, polyphenolic compounds are intensively metabolized in intestinal and hepatic cells (methylation, sulfation, glucuronidation). They are present in plasma as initial compounds and as metabolites (6).

About 90% of polyphenols were not absorbed in the small intestine and reached the large intestine, where they were intensively metabolized by the intestinal microbiota to components of low molecular mass. These metabolites are usually better absorbed than the initial compounds and many of them show biological effects and are mostly responsible for the biological effects of polyphenols. They can be considered 'postbiotics', i.e., metabolites created by the action of intestinal microbiota that have a positive impact on health. Additionally, the interaction between polyphenols and microbiota affects the composition and consequently the function of the microbiome. Formed metabolites can show antioxidant, anti-inflammatory and immunomodulatory effects (7, 8).

Investigations have shown that the antioxidant activity of metabolites protocatechuic acid (3,4-dihydroxy benzoic acid) and protocatechuic aldehyde (3,4-dihydroxybenzaldehyde) is achieved by radical scavenger activity and by increasing the activity of endogenous antioxidant enzymes (glutathione peroxidase (GSH-PX) and superoxide dismutase (SOD) (7, 9).

Formerly it was considered that polyphenolic compounds had weak activity in the human organism. This was based on the following considerations: (1) the reaction of polyphenols with free radicals is slow and cannot compete with antioxidants like ascorbate; (2) during metabolism, polyphenols lose their phenolic groups, change their redox properties and can no longer act as effective antioxidants, and (3) the concentration of orally applied polyphenols in body fluids is too low for effective antioxidant action. However, new research shows the following: (1) the reaction of polyphenols with radicals is very fast (new kinetic studies show that it is even 1000 times faster than it was thought); (2) the loss of the phenol group does not abolish the antioxidant activity, an aromatic molecule is required for the activity, and (3) antioxidant defence of the organism includes the action of both polyphenols and their aromatic metabolites present in μM concentrations (9, 10).

Plant antioxidant compounds are present in numerous herbal species and belong to different classes of secondary metabolites. Common herbal drugs/herbal drug preparations that are used as antioxidants are aronia (*Aroniae fructus*) and bilberry (*Myrtilli fructus*) fruits, the turmeric rhizome (*Curcumae rhizoma*), herbal drugs with purine alkaloids (green tea leaf, *Camelliae sinensis non fermentata folium*, coffee seed, *Coffeae semen;* cola seed, *Colae semen*, mate leaf, *Mate folium*), grape seed extract (*Vitis viniferae semenis extractum*), ginger rhizome (*Zingiberis rhizoma*), etc.

Aroniae fructus, aronia berry, chokeberry

Black chokeberry (*Aronia melanocarpa* L., Rosaceae) is a perennial shrub native to North America that was introduced in Europe at the beginning of the twentieth century.

Fresh fruits have an astringent taste and are rarely consumed fresh, but they are used processed in the food industry. Chokeberry or aronia fruits are one of the richest sources of polyphenols, which include anthocyanins (cyanidin-3-glucoside, cyanidine-3-galactoside, pelargonidin-3-galactoside), proanthocyanidins (polymers of (-) epicatechine and (+) catechine), flavonoids (isoquercetine, rutin, isorhamnetin-3-glucoside) and phenolic acids (chlorogenic acid, caffeic acid, *p*-coumaric aid). They also contain vitamin C, tocopherols and carotenoids (11).

The extracts of aronia fruit showed pronounced antioxidant activity. It was demonstrated through the ability to neutralize free radicals, bind metal ions and inhibit lipid peroxidation in various model systems (ORAC, TRAP, FRAP OH, NO, DPPH). Moreover, the extracts inhibited lipid peroxidation, protein carbonylation and nitration, elevated thiol concentrations, increased the activity of antioxidant enzymes (catalase, glutathione peroxidase, superoxide dismutase), protected from DNA damage, and enhanced the overall antioxidant status (12-15).

Previous studies on experimental animals showed that aronia berry extracts express anti-inflammatory, gastroprotective and neuroprotective activity (16). Aronia berry extracts showed a probiotic effect on intestinal microbiota, and a protective effect against the toxicity of heavy metals and pollutants (17). It was demonstrated that the consumption of aronia fruits lowers the level of triglycerides, total cholesterol and LDL, and reduces the development of cardiovascular diseases (18). Since they successfully inhibit oxidation, they also slow down the aging processes, and some authors consider the aronia fruit to be a geroprotector (20).

Besides the application as solid dosage forms with powdered dried aronia fruit or fruit extract, they are often consumed as food. Aronia fruits have an astringent taste and are usually consumed after freezing, drying or processing into juices or jams. Attention should be paid to the technological production process because it can affect the antioxidant and relevant biological activity (11-13).

***Myrtilli fructus*, bilberry fruit**

The bilberry or blueberry fruits (*Vaccinium myrtillus* L., Ericaceae) are used fresh (*Myrtilli fructus recens)* or dried (*Myrtilli fructus siccus*). They contain anthocyanins (cyanidin and delphinidin glycosides), proanthocyanidins (catechin and epicatechin, mostly dimers and oligomers), flavonoids, organic and phenolic acids (21, 22). According to the monograph in the European Pharmacopoeia (23), fresh bilberry fruits should contain a minimal 0.3% of anthocyanins, expressed as cyanidin 3-*O*-glucoside chloride (chrysanthemin), and dried fruits a minimal 1.0% of tannins expressed as pyrogallol (24-26).

The antioxidant activity of bilberry fruit extracts is demonstrated by the neutralization of superoxide anion, reduction of reactive oxygen and nitrogen radicals, decrease in the production of H_2O_2 and waning of oxidative damage to DNA, proteins and lipids.

Previous research on animals showed that bilberry anthocyanins with beta-carotene significantly affect retinal enzymes (inhibiting the activity of phosphoglucomutase, and increasing the activity of lactate dehydrogenase, and other enzymes). The fruit extract neutralized superoxide anion and inhibited microsomal lipid peroxidation. The phenolic fraction of bilberry significantly decreased the generation of reactive oxygen and nitrogen species (RONS) of oxidizing lipids and proteins, and reduced the extent of DNA breakage (21, 22).

Besides antioxidant, extracts of bilberry fruits also exerted anti-inflammatory, antimicrobial, cardioprotective and hypoglycemic activity. Studies on experimental animals revealed that fresh fruits showed antiedematous and vasoprotective effects, and also the improvement of microvascular circulation (22, 24, 27).

The Committee on Herbal Medicinal Products of the European Medicines Agency (EMA/HMPC) published a monograph on fresh and dried bilberry fruit based on long-standing use, where fresh fruit was used in solid dosage forms for oral use, in the form of a dry extract. This extract of fresh bilberry fruit should be indicated as a traditional herbal medicinal product to relieve symptoms of discomfort and heaviness of legs related to minor venous circulatory disturbances, or to relieve symptoms of cutaneous capillary fragility. The duration of use is 4 weeks, unless there is hypersensitivity to the active substance, in which case it is contraindicated. The use in children and adolescents under 18 years of age, and during pregnancy and lactation has not been established due to a lack of adequate data (25).

Another EMA/HMPC monograph has been published for dried bilberry fruit, where the comminuted herbal substance is used as an herbal tea, for preparation of decoction for oral use as a traditional herbal medicinal product for symptomatic treatment of mild diarrhoea (over a three-day period), or oromucosal use for symptomatic treatment of minor inflammations of the oral mucosa (for one week). It is contraindicated if there is hypersensitivity to the active substance, and it is not recommended for use in children under 12 years of age due to a lack of adequate data. On the other hand, decoctions of dried bilberry can be used during pregnancy and lactation because there is no concern regarding any malformation in humans (26).

***Curcumae rhizoma*, turmeric rhizome**

The European Pharmacopoeia gives two monographs for *Curcumae rhizoma* javanese turmeric *Curcumae zanthorrhizae rhizoma* Roxb. (syn. *C. zanthorrhiza* D. Dietrich) and turmeric rhizome, *Curcumae longae rhizoma, C. longa* L. (syn *C. domestica Valeton),* both from family Zingiberaceae. The main secondary metabolites, present in *Curcumae rhizoma*, are essential oil, polyphenols, dicinnamoyl methane derivatives, known as curcuminoids and flavonoids (28). The dried rhizome of Javanese turmeric should contain a minimum of 50 ml/kg of essential oil and a minimum of 1.0% of dicinnamoyl methane derivatives, expressed as curcumin. Whole, cured (by boiling or steaming), dried rhizome of turmeric *C. longa* with removed roots and outer surface, can

have a lower content of essential oil, a minimum of 25 mL/kg, and a higher amount of dicinnamoyl methane derivatives, expressed as curcumin, minimum 2.0% (23).

Curcumine and its analogues are liposoluble yellow pigments responsible for the characteristic colour of the turmeric rhizome (28). It is reported that curcumin is an effective antioxidant agent through multiple pathways. Curcumin acts as a scavenger of oxygen species, such as hydroxyl radical, superoxide anion, and singlet oxygen, and interferes with lipid peroxidation. It also stimulates the activities of several antioxidant enzymes and inhibits unregulated DNA damage by promoting Akt (protein kinase B) and MAPK (mitogen-activated protein kinase) pathways (28). Studies have demonstrated that the curcumin metal (Cu2+, Fe2+, Mn2+, Mg2+) complexes have better antioxidant activity compared to free curcumin (29).

Previous investigations have shown that curcumin has pronounced anti-inflammatory properties, which are attributed to the suppression of prostaglandin synthesis and inhibition of cyclooxygenase-2 (COX2), lipoxygenase (LOX), inducible nitric oxide synthase (iNOS), cytokine and transcription factors production (29).

Studies have shown that it exhibits spasmolytic, hypolipidemic, hepatoprotective, neuroprotective and cardioprotective activity. Curcumin reveals anticancer activity by promoting apoptosis and inhibiting proliferation and invasion of tumors by restricting the variety of cellular signaling pathways or intracellular transcription factors (29, 30). Another study showed that the application of the combination of turmeric rhizome fraction with cytostatics (cyclophosphamide) works synergistically *in vitro* and *in vivo*, reducing tumor volume and increasing the lifespan of experimental animals. When applying such combinations, the dose of cytostatics can be reduced and, consequently, there will be a reduction in side effects (31).

The limiting factors for effective curcumin usage are its low solubility in water, chemical instability and low bioavailability after oral administration. Recently, several approaches have been employed to reduce these issues, such as micellar solubilization, cyclodextrin complexation, crystal modification, prodrug strategies, the addition of bioavailability enhancer (piperine) and nanotechnology-based methods (29).

The Committee on Herbal Medicinal Products of European Medicines Agency (EMA/HMPC) has published two monographs for *Curcumae rhizoma*, one for *Curcumae longae rhizoma* and the another for *Curcumae xanthorrhizae rhizoma* (species name *C. xanthorrhiza* D. Dietr. has an unchecked status; the European Pharmacopoeia states *C. zanthorrhiza* Roxb., which is the accepted name). Comminuted herbal substance, liquid or dry extracts as herbal tea, and liquid or solid oral dosage forms can be used. Herbal medicinal products based on both turmeric rhizomes are indicated for symptomatic treatment of digestive disturbances, such as feelings of fullness, slow digestion and flatulence, based on long-standing use (traditional medicinal products). The duration of use is two weeks.

They are contraindicated if hypersensitivity to the active substance occurs. The use in children and adolescents under 18 years of age, or during pregnancy and lactation has

not been established due to a lack of adequate data and relevant tests on reproductive toxicity, genotoxicity, and carcinogenicity. These products are not recommended in case of obstruction of the bile duct, cholangitis, gallstones, and any other liver and biliary diseases due to the possible stimulation of bile secretion (32, 33).

Herbal drugs with purine alkaloids

Purine alkaloids are contained in well-known herbal drugs such as green tea leaf, *Camelliae sinensis non fermentata folium*, coffee seed, *Coffeae semen*, cacao seed, *Cacao semen*, cola seed, *Colae semen* and mate leaf, *Mate folium.*

The green tea leaf is a young, stabilised unfermented leaf of *Camellia sinensis* (L.) Kuntze (23). The tea leaf is rich in polyphenols, mostly phenolic acids and tannins (flavan-3-ols and their polymers) and flavonols. Common tea leaf catechins are epicatechin (EC), epicatechin-3-gallate (ECG), epigallocatechin (EGC) and mostly represented epigallocatechin-3-gallate (EGCG). Their content depends on conditions in the processes of fermentation and drying (34).

The green tea leaf should contain a minimum of 1.5% of caffeine and 8.0% of total catechins, expressed as (−)-epigallocatechin-3-O-gallate. Tea polyphenols, especially EGCG and theaflavins (formed during fermentation process), are well-known antioxidants. They neutralize free radicals, induce the endogenous antioxidant system (SOD, catalase, xanthine oxidase), and maintain intracellular redox homeostasis. Studies have shown that green tea polyphenols exert anti-inflammatory, cytotoxic, and antiproliferative activity. Polyphenols influence signaling pathways (nuclear factor kappa B, NF-κB), which consequently leads to cell cycle arrest, induction of apoptosis, modification of carcinogen metabolism, and prevention of DNA damage. They also have an antiangiogenic effect in non-liquid cancers and EGCG exerted synergistic effects with other anticancer drugs, such as curcumin, 5-fluorouracil and tamoxifen. Additionally, regular green tea consumption can be considered as chemopreventive (35, 36).

According to the EMA/HMPC monograph for *Camellia sinensis non fermentatum folium*, the comminuted herbal substance as herbal tea or solid dosage form for oral use is indicated for relief of fatigue and sensation of weakness (traditional herbal medicine). The duration of use is one week. It is contraindicated, beside hypersensitivity, in the case of gastric and duodenal ulcers, cardiovascular disorders such as hypertension and arrhythmia and hyperthyroidism.

It is not recommended for use In children and adolescents under 18 years of age, or during pregnancy and lactation. Caffeine containing products can interact with sedative substances, reducing their activity and increasing side effects caused by sympathomimetic drugs (37).

Besides green tea, coffee bean (*Coffea spp*., Rubiaceae) is another herbal drug rich in purine alkaloids that is widely consumed. The coffee bean contains caffeine (1-2%) and a smaller amount of other purine derivatives, chlorogenic, caffeic, ferulic acid and other phenolic acids. Over 85 types of coffee are known, the most famous being *C.*

arabica L. and *C. robusta* L. Linden (*C. canephora* Pierre ex. A. Froehner). Their composition is quite similar, but the ratio of polyphenolic compounds is different. The seeds of *C. arabica* contain more chlorogenic acid, while *C. robusta* contains higher contents of caffeine and total polyphenols (38). Antioxidant activity of coffee is related to its constituents: chlorogenic, caffeic, ferulic, and *n*-coumaric acids. During the roasting process, pigments melanoidins, which are strong antioxidants, are formed. Ferulic acid showed high antioxidant activity, especially the ability to inhibit lipid peroxidation in biological membranes. Ferulic acid also exerted an anti-inflammatory, anti-allergic, antibacterial and antiplatelet effect (39). The consumption of coffee or tea represents a very significant portion of the daily intake of antioxidants established for humans. Likewise, their regular intake can be considered as prevention against many inflammatory and chronic diseases (35, 36, 39).

Other herbal drugs with antioxidant activity

Many herbal drugs or herbal drug preparations that are used in everyday life manifest antioxidant activity (Table I). Some of them exert high antioxidant and anti-inflammatory activity (ginger rhizome, *Zingiberis rhizome;* cinnamon bark, *Cinnamomi cortex;* grape seed extract or French maritime pine bark extract) (40-42).

Table I Selected herbal drugs with antioxidant activity (43)

Tabela I Odabrane biljne droge sa antioksidantnom aktivnošću (43)

Biological source	Herbal drug/herbal drug preparation
Allium sativum L., *A. cepa* L., Amaryllidaceae	Garlic bulb and onion bulb
Carum carvi L., Apiaceae	Caraway fruit
Cinnamomum verum J.S. Presl, Lauraceae	Cinnamon bark
Crataegus sp. L., Rosaceae	Hawthorn leaf and flower, hawthorn fruit
Cynara cardunculus L., Asteraceae	Artichoke leaf
Fagopyrum esculentum Moench, Polygonaceae	Buckwheat aerial parts
Foeniculum vulgare Mill. ssp. *vulgare* var. *vulgare, F. vulgare* Mill. ssp. *vulgare* var. *dulce,* Apiaceae	Fennel fruit
Ginkgo biloba L., Ginkgoaceae	Ginkgo leaf
Laurus nobilis L., Lauraceae	Bay leaf, laurel

Lycium barbarum Mill., Solanaceae	Goji berry
Ocimum basilicum L., Lamiaceae	Basil aerial parts
Origanum onites L., *O. vulgare* subsp. *hirtum* (Link) letsw., Lamiaceae	Oregano aerial parts
Pinus pinaster Aiton subsp. *atlantica,* Pinaceae	Aqueous extract of bark of French maritime pine (Piknogenol ®)
Punica granatum L., Lythraceae	Pomegranate pericarp
Rosmarinus officinalis L., Lamiaceae	Rosemary leaf
Salvia officinalis L., Lamiaceae	Sage leaf
Silybum marianum (L.) Gaertn., Asteraceae	Milk thistle fruit
Thymus serpyllum L., Lamiaceae	Creeping thyme aerial parts
Thymus vulgaris L., *T. zygis* L., Lamiaceae	Thyme aerial parts
Urtica dioica L., *U. urens* L., Urticaeae	Nettle leaf
Vitis vinifera L., Vitaceae	Grape seed extract
Withania somnifera (L.) Dunal, Solanaceae	Ashwagandha, winter cherry root
Zingiber officinale Roscoe, Zingiberaceae	Ginger rhizome

Conclusion

In the modern world, due to the exposure to various inducers of oxidative damage, it is necessary to provide additional intake of antioxidant compounds. Polyphenolic compounds and drugs that contain them enable adequate protection of the organism from the consequences of oxidative stress.

Herbal drugs rich in polyphenols such as green tea leaves, bilberry fruit, chokeberry fruit or turmeric rhizomes enable not only the prevention of oxidative damage, but also of different disorders and diseases resulting from cumulative oxidative damage.

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Antioksidantna aktivnost biljnih sekundarnih metabolita

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Kratak sadržaj

Oksidativni stres može indukovati razvoj različitih poremećaja. Biljni sekundarni metaboliti mogu delovati kao antioksidansi putem neutralizacije slobodnih radikala ili stimulacijom endogenih antioksidantnih mehanizama. Polifenoli predstavljaju jedne od značajnih sekundarnih biljnih metabolita sa antioksidantnom aktivnošću. Svoje delovanje mogu ispoljiti putem različitih mehanizama u zavisnosti od svoje strukture. Polifenoli su široko rasprostranjeni u biljnim drogama i neke od uobičajeno korišćenih su plod aronije (*Aroniae fructus*) i borovnice (*Myrtilli fructus*), koje su bogate antocijanima i taninima i ispoljavaju visoku antioksidantnu aktivnost. Glavne komponente u rizomu kurkume (*Curcumae rhizome*) su kurkuminoidi, koji pokazuju antioksidantnu i antiinflamatornu aktivnost. Takođe, list čaja (*Camelliae sinensis folium*) i seme kafe (*Coffeae semen*), veoma zastupljeni u svakodnevnom životu, značajno doprinose dnevnom unosu anioksidanasa i obezbeđuju neophodnu zaštitu organizma od posledica oksidativnog stresa.

Ključne reči: antioksidantna aktivnost, polifenoli, biljne droge