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Review Article

A Review on The Potential Effects of Plant Metabolites

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ABSTRACT
Phytochemical compounds have a substantial impact on human health when they are consumed in their nutrition. These compounds have a functional role in the consistency of the color, smell, and taste of the plants. As a substitute to the synthetic chemicals used in the treatment of many chronic diseases, the interest in the use of plant materials and derivatives has been increased. Phytochemical compounds include flavonoids, phenolic acids, stilbenes, lignans, tannins, saponins, glycosides, terpenoids, carotenoids, and others. Plants consist of a mixture of both primary and secondary metabolites, many of which have been demonstrated to exhibit antioxidant, antimicrobial, antifungal, antidiabetic, antiinflammatory, anticancer, and antihypertensive properties.

Keywords: plant metabolites , phyto chemical

INTRODUCTION
Throughout history, people have processed natural plants in different ways and used them for treatment for many diseases. Although there are new drugs that come with developing technology and newly produced treatment techniques, since the dangerous side effects of these drugs cannot be ignored, interest in scientific studies on plants has increased and research on their bioactive properties has deepened (Alghadir et. al., 2022). The section that benefits from plants containing phytochemical components with various bioactive properties to treat or prevent health problems accounts for 69% of the entire world population, and this rate is higher in developing countries (Ghaedi et. al., 2015). The concept of treatment called "Complementary Medicine" has gained more importance from the past to the present, and in some countries, government incentives are given for the discovery of endemic plant species and research on their medical properties (Kulkarni and Vijiyanand, 2010; Kunwar et. al, 2022). The World Health Organization (WHO) reported that there are approximately 20,000 species of plants used in the treatment of diseases in its report based on scientific studies conducted by researchers from 91 countries on medicinal plants (Keskin, 2018; Fitzgerald et al., 2020). In this study, from the biological activities of natural phytochemicals, which are frequently used by the public today, their antioxidant, antimicrobial, antifungal, antidiabetic, anti-inflammatory, anticancer, and antihypertensive properties were reviewed.

Phytochemicals
The medicinal use of plants has increased with the discovery of the similarity between the chemical compounds used in drug production and the active substances found in plants. While the use of herbal medicines was more common in the past, as a result of the development of chemical applications, this rate has decreased gradually. However, with the research and development of new therapeutic uses of plants in recent years, the demand for natural herbal products has increased (Katiyar et al., 2012; Jose et al., 2018; Welz et al., 2018). Due to the richness of the chemical structures of plants, their use for the development of new and highly effective drug formulations has also been one of the research areas of pharmacology. In developed and developing countries, 25% of prescription drugs consist of active ingredients obtained from plants (Kulkarni and Vijiyanand, 2010; Jose et al., 2018; Mintah et al., 2019).
Bioactive compounds that develop as a result of secondary metabolic activities of plants and cannot be consumed as food but have beneficial effects on human health are called "phytochemicals" (Visioli et al., 2000; Schlaeppi, 2021). The precursors of these substances, called secondary metabolites, are intermediates, mostly consisting of products of primary metabolism; they form when the plant cell uses all available carbon for primary activities. The most known phytochemical compounds are phenolic compounds (polyphenols), tannins, saponins, carotenoids, coumarins, tocopherols, terpenes, isothiocyanates, sulfites, sulforaphanes, terpenoids, alkaloids, flavonoids, phytosterols, phytoestrogens, and indoles (Saxena et al., 2013) and are accepted as micronutrients in our diets (Howes and Simmonds, 2014). These compounds are rich in phytochemicals with antioxidant activity, which are used against many diseases

today (Vital et al., 2010). In addition to its antioxidant activities, it chelates metal ions and inhibits transcription factors that initiate and support tumor development by stimulating detoxifying enzymes (Verma et al., 2009). They also act as a degenerative, antiallergenic, anti-inflammatory, antimicrobial, antithrombotic (preventing blood clotting), anticarcinogen, antiatherogen (preventing atherosclerosis), antiulcer and vasodilator (blood vessel dilator) agent (Weisburger, 2000; Halliwell, 2007; Saqib, 2021). Apart from these properties, they also play a role in protecting plants from UV rays and providing the structural integrity of the cell wall. Studies have shown that phytochemical compounds have anticarcinogenic activity, reduce complications in cancer treatment, and have a protective role against the side effects of traditional chemotherapeutic agents (Benjamin et al., 2015; Thi and Brogger, 2015).

Phenolic Compounds

Phenolic compounds are secondary metabolites synthesized during aromatic amino acid metabolism in plants. Among the physicochemical properties of these compounds, they have the ability to condense up to eighty monomer compounds, to form residues by forming complexes with proteins, and to dissolve in water (Kisiriko et al., 2021), and about 200,000 of them have been isolated so far (Lattanzio, 2013). The ratio of currently isolated phenolic compounds is 10% when compared to all aromatic compounds, and there are hundreds of phenolic compounds waiting to be explored and discovered (Silva et al., 2005). They are present in all parts of plants at different levels and contribute to the taste, odor, and color properties of plants, as well as having antimicrobial and antioxidant effects and may cause inhibition of different enzymes. Phenolic compounds are characterized as natural sources of antioxidant requirements for metabolism and their antioxidant activities by binding free radicals or forming chelates with metals (Verma et al., 2009; Lakey-Beitia et al., 2021). These effects increase as the number of OH groups in the phenol ring they contain in their structure increases (Kisiriko et al., 2021), and they have the ability to delay, slow down, or prevent oxidation at low concentrations and to remain in a stable form when converted to free radicals (Silva et al., 2005; Scalbert and Santos, 2000). In addition to their antioxidant properties, they also have antiallergic, antimutagenic, anticarcinogenic, antiglycemic, anticholesterol, antimicrobial, anti-inflammatory, antithrombotic, vasodilator, and calming properties. They are used in the cosmetics, pharmaceutical, and food industries (Wanasundara and Shahidi, 1998; Naczk and Shahidi, 2006; Sytar et al., 2012; Abdallah et al., 2020). Studies have reported that individuals who include foods with high phenolic content in their diets have a reduced risk of coronary artery disease (Skowyra et al., 2014). Phenolic compounds increase the activity of enzymes responsible for the inhibition of cancerous cells and prevent the development of nitrosamine, which has an important role in tumor formation and cancer formation. It also regulates the ion balance in the intestinal flora and the pH in the environment. By undertaking the preservation of the integrity of the intracellular matrices, they enable the cell to resist environmental effects (Briguglio et al., 2020). Phenolic compounds are classified according to the number of phenol rings they contain and the structures that connect these rings; flavonoids (anthocyanidins, flavones, flavonols, flavanones, flavanols (catechins) and isoflavones), phenolic acids, stilbenes, and lignans (Figure 1) (Dias et al., 2021).

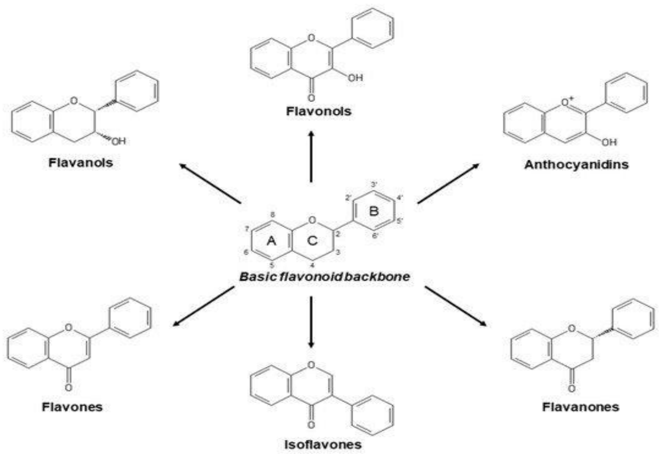


Fig.1:Basic structures of flavonoids subclasses

Flavonoids

Flavonoids, which represent an important group of phenolics, show a proportionally wide distribution in the plant flora. These compounds are formed by combining with the diphenylpropane chain and the skeleton containing 15 carbon atoms is arranged in the C6-C3-C6 configuration (Panche et al., 2016). Flavonoids are secondary metabolites with significant antioxidant activity and chelating properties (Heim et al., 2002; Sivam et al., 2010) and cannot be synthesized by humans (Sivam et al., 2010). More than 4000 flavonoids have been identified in nature, and they are named according to their ring structure, such as anthocyanidins, flavones and flavonols, flavanones, flavanols (catechins), and isoflavones. The difference between flavonoids is due to the number of hydroxyl groups in their structure, the degree of unsaturation, and the oxidation level of the triple carbon segment (Panche et al., 2016). In the literature, flavonoid compounds have been found to be antioxidants (Sharma et al., 2015; Zhong et al., 2017), anti-inflammatory (Parhiz et al., 2015), antiallergic, antiviral (Seo et al., 2016; Liang et al., 2017), antiaging (Fan et al., 2022), and anticarcinogen (cytotoxic) (Ahmed et al., et al., 2016; Butala et al., 2021). A wide variety of bioactive activities have been reported. Their regular consumption in the diet has been associated with a decrease in the incidence of certain diseases such as prostate and breast cancer (Jaganathan et al., 2014; Yiannakopoulou, 2014). At the same time, biologically effective flavonoids, also called vitamin P substances, have been reported to have inhibitory effects on bleeding and cracking in capillaries (Skowyra et al., 2014). Anthocyanins are water-soluble natural pigments found in fruits and vegetables, as well as other plants (Patra et al., 2022). They are in glycoside structure and consist of anthocyanindins in the structure of a flavilium cation called "aglycone". In the molecules of phenolic compounds forming the aglycone part, the blue color increases as the number of hydroxyl groups increases, and the red color increases as the number of methoxy groups increases (Kong et al., 2010). These pigments are esterified with sugars or combined with different molecules (such as coumaric acid, ferulic acid, caffeic acid, vanillic acid, ascorbic acid) in foods. The most common anthocyanidins are cyanidin, delphinidin, malvidin, peonidin, pelargonoidin, and petunidin. It has been reported that anthocyanins have antioxidant, antimicrobial, antiviral, anti-inflammatory, antiallergic, antimutagenic, anticarcinogenic, and antidiabetic effects (Ghosh and Konishi, 2007). Due to their antioxidant activities as well as their positive effects on color and taste, they are widely used as a natural colorant in food products such as jelly, beverages, ice cream, yoghurt, and confectionery (Ghosh and Konishi, 2007; Kong et al., 2010).

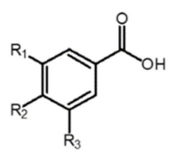
The main component of the flavonoids group is flavones, and the most important members are: routine, apigenin, chrysin, and luteolin. Commonly found in wine (red) and tomatoes, rutin is the glycoside form of quercetin. Apart from that, apigenin, in parsley and celery, luteolin, red hot pepper, and chrysin are found in the skins of the fruits (Fidan and Dundar, 2007). Flavonols, on the other hand, carry a hydroxyl group attached to the third carbon atom of the flavon. It is the most common flavonoid group found in the structure of plants, and quercetin, kaempeferol, myricetin, and fisetin are counted among the important flavonols. They are generally abundant in onions, apples, and cabbage (Ghosh and Konishi, 2007; Panche et al., 2016). Flavonone is the dihydroxy derivative of flavone, and naringenin and hesperetin are among the important flavanones. The acrid bitterness felt in grapefruit is due to naringin, a glycoside of naringenin. Hesperedin, on the other hand, is a flavanone group concentrated in citrus fruits but in the peel parts (Panche et al., 2016). Isoflavones are isomers of flavones and their structure is shown in Figure 1. Major isoflavones such as genistein, daidzein, and their glycosides genistin and daidzin are present in soybeans and soy nuts (Pascual et al., 2000; Araújo et al., 2013). Catechins are monomers of flavan-3-ols containing a hydroxyl group at the C3 atom and constitute the most common group of flavonoids in foods. Since it has two asymmetric carbon atoms in its structure, it has four different isomers. These isomers are: the hydrogen in the 2nd and 3rd carbon atoms is called (+)-catechin and (+)-gallocatechin in the trans configuration, and (-)-epicatechin and (-)-epigallocatechin in the cis configuration (Pascual et al., 2000; Zhu and Xie, 2020). It has been reported that catechins obtained from the Camilla sinensis (black tea) plant have the ability to scavenge hydroxyl radicals as high as 89% (Anggraini et al., 2021). Catechins isolated from different plants have been reported to have potent antimicrobial activity on periodontal (gum disease) pathogens such as Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis, and Prevotella intermedia (Ho et al., 2001; Nawrot-Hadzik et al., 2021). In addition, the anticancer properties of epigallocatechin gallate were examined, and it was stated that it has the ability to induce apoptosis (Ferrari et al., 2022).

Phenolic Acids

Phenolic acids constitute about one third of phenolics in free and bound forms in plants. They can bind to various plant components with ester, ether or acetal bonds (Zadernowski et al., 2009). Phenolic acids consist of two subgroups (Figure 2). These are hydroxybenzoic and hydroxycinnamic acids. Hydroxybenzoic acids are in the structure of C6-C1 phenyl methane and are found in varying amounts in plants; gallic, vanillic and syringic acids are in this group. Hydroxycinnamic acids are in the structure of C6-C3 phenylpropane. They show different properties according to the position and structure of the OH group attached to the phenylpropane ring (Skowyra et al., 2014).

The physicochemical and phytochemical properties of hydroxybenzoic and hydroxycinnamic acids, which are naturally found in the structure of plants, have been reported in various studies. Of these, gallic acid (especially green tea) is a natural antioxidant that can be extracted from plants. It is widely used in the food, pharmaceutical, and cosmetic industries (Curcio et al., 2009). It has also been reported that gallic acid has antimicrobial activity (Manso et al., 2022). Vanillic acid (4-hydroxy-3-methoxybenzoic acid) is a derivative of hydroxybenzoic acid, mostly used as a flavoring agent. It also occurs as an intermediate in the production of vanillin from ferulic acid (Walton et al., 2003). In addition to its use as a food additive, it has been reported in studies that it has anticoagulant, antioxidant, antimicrobial, and anti-inflammatory effects by reducing the pain threshold (Calixto-Campos et al., 2015). Syringic acid is another important phenolic acid. It has been reported that syringic and vanillic acids have protective properties against oxidative stress, metal chelating agents, and prevent hepatic fibrosis (stimulus return) in chronic liver damage (Itoh et al., 2010). Caffeic acid is the most abundant hydroxycinnamic acid in sunflower seeds and sunflower seeds (Laguna et al., 2019). It has been determined that caffeic acid and its derivatives have antioxidant and antimicrobial properties (Magnani et al., 2014). It has been reported that ferulic acid has antimicrobial activity against gram-positive and gram-negative (Citrobacter koseri, Escherichia coli, Enterobacter aerogenes, Helicobacter pylori, Klebsiella pneumonia, Pseudomonas aeruginosa, Shigella) bacteria found in the cell walls of plants (Usal, 2014).

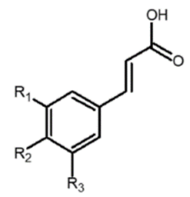
Basic structure of hydroxybenzoic acids



Acid	R_1	R_2	R_3
Benzoic	H	H	H
p-Hydroxybenzoic	H	OH	H
Protocatechuic	OH	OH	H
Vanilic	OCH_3	OH	H
Syringic	OCH_3	OH	OCH_3
Gallic	OH	OH	OH

(a)

Basic structure of hydroxycinnamic acids



Acid	R_1	R_2	R_3
Cinnamic	H	H	H
p-Coumaric	H	OH	H
Cafeic	OH	OH	H
Ferulic	OCH_3	OH	H
Sinapic	OCH_3	OCH_3	OCH_3

(b)

Fig.2:General structures of phenolic acids

Phenolic acids have been shown to inhibit the development and reproduction of some viruses such as influenza virus, respiratory syncytial virus and HIV (Ou and Kwok, 2004). It has been reported that glucosidase esters of ferulic acid have strong antioxidant activity, and the radical scavenging activity of these esters is higher than that of ferulic acid (Min et al., 2006). Coumaric acid, a derivative of cinnamic acid, has three isomers: ortho, para, and meta, depending on the hydroxyl group in its structure (Itoh et al., 2010). It has been stated that p-coumaric acid is generally used as an antioxidant in the food industry (Usal, 2014). Like ferulic acid, it has been stated that coumaric acid can inhibit microbial growth as an antimicrobial agent and is more effective than ferulic acid (Min et al., 2006). It has been shown that pyrocatechic acid, one of the important hydroxybenzoic acids found abundantly in onions and garlic from Allium species, has antimicrobial and antioxidant effects (Yunlu and Kır, 2016). Cereals are reported to contain significant levels of sinapic acid. It is stated that the most abundant hydroxycinnamic acid in rye after ferulic acid is sinapic acid and it corresponds to approximately 10% of the total amount of phenolic acid (Bondia et al., 2009). While it is emphasized that sinapic acid has antimicrobial, anticancer, and anti-inflammatory effects, it is also reported to be a strong antimutagenic agent (Niciforovic and Abramovic, 2014).

Stilbenes

Stilbenes are a group of polyphenols that are quite common in plants. The most well-known compound is resveratrol (3,5,4'-trihydroxystilbene). Resveratrol is found in large amounts in red wine and also in the outer skin of grapes (Espin et al., 2007). Stilbenes are produced by plants in response to infections due to pathogens or various stress conditions. It has been detected in more than 70 plant species, especially in grapes, strawberries, and peanuts (Skowyra et al., 2014). In a study, the ability of stilbenes isolated from red wine to act as radical scavengers was determined, and it was stated that stilbenes have an important antioxidant effect, and it was also reported that they prevent lipid peroxidation (Vincenzi et al., 2016). In a different study, the antimicrobial (Bacillus subtilis and Pseudomonas syringae) and antifungal (Aspergillus niger, Botrytis cinerea, Cladosporium herbarum, and Monilinia aucupariae) activities of stilbenes (isolated from chickpea roots) were measured by the minimum inhibition concentration method and the results were found to vary between 25-100 µg/m. (Aslam et al., 2009).

Lignans

Lignans are formed by the oxidative dimerization of two phenylpropane units. Interest in lignans and their synthetic derivatives is increasing because of their potential applicability in cancer therapy and various other pharmacological fields (Saleem et al., 2005). In a study, it was reported that the high level of lignan compounds of cow parsley plant (Anthriscus sylvestri) showed cytotoxicity against cancer cells, as well as antiviral, anti-inflammatory, and antiallergic properties (Olaru et al., 2015). In a different study, it has been reported that the lignans isolated from Myristica argentea Warb. plant have an antimicrobial effect against Streptococcus mutans, an important oral pathogen (Kayano et al., 2014). In another study, the inhibition (IC50) of lignans with different structures isolated from Litchi chinensis Sonn. plant, on human cancer cells (HepG2 and Hela) was determined as 2 µg/mL and 2.4 µg/mL, respectively, and also showed antioxidant activity close to butylated hydroxy toluene (BHT), a synthetic antioxidant (Jimenez et al., 2018).

Tannins

Tannins are another bioactive compound found in plants with a phenolic structure. Tannins are brown or light yellow-colored, amorphous substances that can be found in powder form and are divided into four basic groups: elajiitannins, gallotannins, complex tannins, and condensed tannins. Tannins have various effects on biological systems as they have metal ion chelating and protein precipitating properties (Hagerman, 2012; Skowyra et al., 2014). These compounds turn into pyrogallic acid when exposed to heat within a certain range. It has been stated that pyrogallic acid has an anticarcinogenic effect by mutating DNA. It has also been reported that tannins reduce serum lipid levels and have a regulatory effect on insulin secretion (Hagerman, 2012).

Other Phytochemical Compounds

In addition to phenolic compounds in plants, there are many bioactive compounds with different structures. Saponins, which are found in the structure of many plants, are lipophilic compounds with strong foaming properties, which can be found in steroid or triterpenoid structures, which are emphasized as anticancer agents in colon cancer and skin cancer treatments and have hypolipidemic effects (Doughari, 2012). In studies, the toxic effects of saponins at high doses have been mentioned, and they can cause poisoning, especially in cattle, by hemolyzing the blood (Garza et al., 2011). Glycosides are molecules formed by connecting the reducing group of monosaccharides to another functional group with a glycosidic bond (Doughari, 2012). It has been determined that cardiac glycosides have anticancer properties (Trenti et al., 2014). Iridoid glycoside, which is among the glycoside derivatives, is medically important, it is antidiabetic because it lowers blood glucose level (Jouad et al., 2002; Wellington and Benner, 2006), diuretic, anti-inflammatory because it relieves headaches (Boutiti et al., 2008), Since it provides pathogen inhibition, it has many activities such as antimicrobial (Sesterhenn et al., 2007). In addition, it has been reported in studies that it has antidiabetic, antibiotic, anticancer, and antiviral effects (Wellington and Benner, 2006). Terpenoids, which constitute an important group among phytochemicals, are used for their antimicrobial properties in pathogen strains resistant to drugs (Boutiti et al., 2008).

Carotenoids and tocopherols are phytochemicals that are important in nutrition and health, showing natural antioxidant properties. Carotenoids are commonly found in fruits and vegetables, along with chlorophyll in plant tissues. One of the carotenoids, β-carotene, is the precursor of vitamin A (provitamin) and turns into vitamin A when needed (Samaranayaka et al., 2011). It is stated that these compounds prevent LDL oxidation and show prooxidant properties at high concentrations, suppress tumor growth, protect DNA from peroxidation, and have immunomodulatory and anticarcinogenic effects (Tapiero et al., 2004; Yeum et al., 2009). In addition, α-tocopherol (Vitamin E) acts as a powerful antioxidant that neutralizes free radicals in the body and strengthens the immune system (Lewis et al., 2019). In addition, there are researches on its use as an antihyperglycemic, anti-inflammatory, anticancer agent, and in various food supplements (Reddy and Couvreur, 2009). Another phytochemical compound found in plants is quinone. Besides its use as a natural and artificial colorant (Sousa et al., 2015), it is among the compounds with anticancer, antiviral, antifungal, antibacterial, antitumor, and cytotoxic activities (Dongmo et al., 2015). Another compound with phytochemical properties is ascorbic acid (Vitamin C). It is important both in nutrition and because of its antioxidant properties. Studies have shown that it can be effective in the treatment of cardiovascular diseases, nervous diseases, and even some types of cancer (Sousa et al., 2015).

Antioxidant Properties of Phytochemicals

Antioxidants are chemicals that protect foodstuffs and living things that consume these foods against the oxidative damage of free radical molecules such as reactive oxygen and nitrogen species (Lobo et al., 2010; Martemucci et al., 2022). Free radicals are also formed during the transfer of electrons in the production of metabolic energy in the organism, and reactive oxygen and nitrogen types appear. Antioxidant defense systems are already present in the organism, which can keep the formation of free radicals under control and against the harmful effects of these radicals. However, in some cases, the existing antioxidant defense systems cannot completely prevent the effects of free radicals and a situation called oxidative stress may occur. Oxidative stress can cause cancer, heart, vascular, eye, brain, joint, skin, kidney, and lung disorders, as well as Type 2 diabetes, which is frequently encountered today and can increase the expression of inflammatory genes by decreasing histone deacetylase activity (Lippmann et al., 2007; Samaranayaka et al., 2011; Najafi et al., 2021).

Aerobic respiration organisms have developed antioxidant defense systems to prevent damage caused by free radicals. These systems are divided into two groups: natural and synthetic antioxidants. Natural antioxidants are also divided into two groups: enzymatic or non-enzymatic (Figure 3) (Atta et al., 2017).

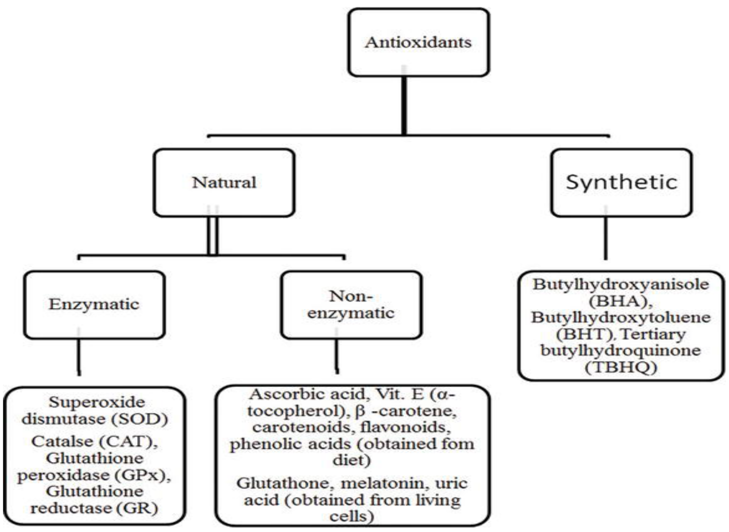


Fig.3:Classification of antioxidants

While enzymatic natural antioxidant defense systems are super oxide distumutase (SOD), catalase, glutathione peroxidase, glutathione reductase, and glutathione-S-transferase, non-enzymatic natural antioxidant systems are endogenous and exogenous factors. These compounds show their antioxidant effects by forming combinations with one or more of the reducing agent, free radical scavengers and singlet oxygen scavenger mechanisms (Lee et al., 2010).

Antioxidant balance in the human body may change due to aging and other factors such as environmental pollution, fatigue, excessive calorie intake, and high-fat diets. The body needs antioxidants of exogenous origin, such as phenolic compounds, carotenoids, vitamins C and E, in order to both prevent and delay this process, which develops in favor of oxidants (Samaranayaka et al., 2011). These substances neutralize free radicals in living things, prevent cells from being affected by these radicals, and prevent cell damage and tumor development. Thus, they provide a healthy life with minimal effects of aging (Martemucci et al., 2022).

In many studies in the literature, phenolic compounds isolated from different plants and their antioxidant capacities have been investigated, and it has been reported that they have high antioxidant activity according to their structures (Husein et al., 2014; Liu et al., 2014; Tan and Lim, 2015; Joubert and Gelderblom, 2016; Butkeviciute et al., 2022). In addition, it has been stated that various phytochemicals in plants are at equivalent levels to synthetic antioxidants (Beer et al., 2017).

Antimicrobial Properties of Phytochemicals

Antimicrobial agents are expressed as chemical or biological substances that ensure the control of disease-causing agents in the environment, limiting them to a certain level, and most importantly killing them (Canales et al., 2005). All over the world, antibiotics are used as the first line of treatment for minor and moderate infections. However, in recent years, antibiotics have started to be used unconsciously. Interruption of antibiotic use, especially during the recovery period, causes the human pathogenic bacteria existing in the metabolism to gain resistance in the following diseases, if not in the next disease (Fair and Tor, 2014). It has been observed that pathogenic microorganisms that gain resistance to drugs make it difficult to treat diseases such as AIDS, cancer, and other infectious diseases that weaken the immune system (Canales et al., 2005). In addition, these types of microorganisms transfer their properties to new species and strains, limiting the useful life of drugs, and this makes the search for new antimicrobial agents continuous (Raza, 2006). Plants with antimicrobial activity, which continue to be an important resource in the fight against infectious diseases, have been found to have a potential comparable to modern drugs in the treatment of diseases (Canales et al., 2005; Garcia, 2020).

It has been stated that phenolic compounds prevent the development of various bacteria and mold species in the environment in in vitro studies, and it has been determined that various infectious diseases that may arise from these microorganisms can be prevented and may be effective in the control of pathogens (Samy and Gopalakrishnakone, 2010; Pratyusha, 2022). There are studies in the literature investigating the antimicrobial activity of many plants. It was determined that Calendula officinalis L. plant showed the highest inhibition against P. aeruginosa among 15 different microorganisms (Larcin et al., 2015). It has been reported that the antimicrobial effect of plants containing capsaicin (Capsicum L.) on different pathogens is similar to that of commercially used antibiotics such as Amoxicillin, Imipenem, and Cefoxitin (Fuchtbauer et al., 2021).

The mechanisms of action of antimicrobial components in plants inhibit bacterial growth through a series of metabolic reactions, unlike synthetic antimicrobials (Joubert and Gelderblom, 2016; Rempe et al., 2017). Organic acids (malic acid, succinic acid, citric acid, and tartaric acid) commonly found in their structures show antimicrobial effects by lowering the pH of the intracellular or environment, by forming chelates with some metals necessary for the life of microorganisms, or by changing the permeability of the cell membrane and disrupting the substrate transport. The antimicrobial action mechanism of phenolic compounds differs in itself (Rempe et al., 2017). For example, it is stated that chlorogenic acid exerts its antimicrobial effect by breaking the cell membrane of Streptococcus pneumoniae, Staphylococcus aureus, B subtilis, E. coli, Shigella dysenteriae, and Salmonella typhimurium microorganisms (Li et al., 2014). It has been reported that quercetin has an antimicrobial effect mechanism by disrupting the cell membrane of E. coli and Helicobacter pylori and causing DNA intercalation (DNA intercalation; DNA gyrase inhibition, Type III secretion inactivation) (Wu et al., 2013). In another study, the antimicrobial effect of apigenin against H. pylori and S. aureus bacteria was explained by protein kinase inhibition (Li et al., 2014).

Antidiabetic Properties of Phytochemicals

Diabetes is a disease that can develop into a complete or a certain level of insulin deficiency and can be distinguished by high blood sugar (hyperglycemia) in its diagnosis. Today, insulin (Type 1 and, if necessary, Type 2) and orally administered antidiabetic drugs are used in the treatment of diabetes. The properties that an ideal antidiabetic drug should have should bring the plasma glucose value to the normal range, prevent the development of tissue damage, and should not have any side effects. However, there is no drug that contains all of these features, and they are generally used in single or double combinations (Ganesan et al., 2022).

The modes of action of oral antidiabetic agents, which are used to control blood sugar, are generally; increase insulin secretion, increase sensitivity to insulin, or decrease carbohydrate absorption. Antidiabetic drugs used in diabetes and their modes of action are presented in Table 1. Incretin-based agents also have glucagon (DPP-4) inhibitory effects. They are secreted from the cells of the small intestine in response to carbohydrates taken with food, and they increase the release of insulin from the pancreas and regulate the blood sugar level (Inzucchi, 2002). Sulfonylureas are not used in the treatment of Type 1 diabetes because they require a pancreas capable of secreting insulin. It has been reported that there is a risk of hypoglycemia as they provide a 1-2% decrease in fasting plasma glucose (Gardner and Shoback, 2007). Glinides increase insulin secretion by binding to different receptors than sulfonylureas. Biguanides and thiazolidinediones, which are in the class of insulin-sensitizing drugs, have been reported to reduce insulin resistance. Drugs containing alpha-glucosidase inhibitors (Table 1) delay the digestion and absorption of glucose by inhibiting enzymes that hydrolyze carbohydrates such as α-glucosidase and α-amylase in the digestive tract and also reduce postprandial hyperglycemia (Kumar et al., 2012; Aquino et al., 2003). α-Amylases (EC;3.2.1.1, endo-1,4-α-D-glucan glucohydrolase) are enzymes that hydrolyze 1,4-α-D-glycosidic bonds between glucose units in the long amylose chain. α-Glucosidases (EC; 3.2.1.20, α-D-glucoside glucohydrolase, exo-α-1,4-glucosidase) are enzymes that perform the last step of starch degradation (Aquino et al., 2003).

Table 1:Classification of oral antidiabetic drugs and their mechanism of action.

Classification	Mechanism of action
Insulin-Releasing Drugs ▪ Sulfonylureas ▪ Glinide groups	They increase insulin secretion from pancreatic β-cells.
Insulin Sensitizing Drugs; ▪ Biguanidines ▪ Thiazolidinediones	Increases the sensitivity of peripheral tissues to insulin.
Alpha-Glucosidase Inhibitors; ▪ Acarbose	In the small intestine, they inhibit carbohydrate absorption by inhibiting α-glucosidase enzymes.
Incretin Mimetic Drugs ▪ DPP-4 inhibitors	They suppress glucagon secretion from the α-cells of the pancreas and thus reduce hepatic glucose production.

The use of plants for the treatment of diabetes is very old, and it has been reported that over 800 plants are used in the treatment of diabetes (Kasali et al., 2021). Various in vitro studies have shown that most plant phenolics have the ability to inhibit enzymes involved in carbohydrate breakdown. It has been reported in studies that there are phenolic compounds that inhibit sucrase and α-glucosidase in green tea, α-glucosidase in potatoes, α-glucosidase and α-amylase in mulberry (Aquino et al., 2003). Other plant compounds, such as alkaloids, terpenoids, saponins, xanthones, and polysaccharides, have been shown to inhibit α-glucosidase and can be used to treat diabetes (Kumar et al., 2012).

Anti-Inflammatory Properties of Phytochemicals

Anti-inflammatory agents show their effects by binding the oxygen radicals that are active in the partly inflamed area or by inhibiting the formation of these radicals. Lipoxygenase and xanthine oxidase enzymes cause inflammation in the body and increase the serum level in the blood (Lavelli et al., 2000; Chen et al., 2017). Lipoxygenases (LOX, EC; 1.13.11.12) are a family of iron-containing dioxygenases that catalyze the formation of hydroperoxides by polyunsaturated fatty acids such as linoleic and arachidonic acids. They are commonly referred to as 5-, 12-, and 15-LOX due to their ability to add molecular oxygen to the 5-, 12-, or 15- carbon atoms of arachidonic acid (Wisastra and Dekker, 2014). The lipoxygenase enzymes (LOX) catalyze the reaction between unsaturated fatty acids in cis-1, 4-pentadiene structure and oxygen, and the free radicals formed as a result of this reaction are converted into compounds such as hydroperoxyeicosatetraenoic acid (HPETE) and hydroxyeicosatetraenoic acid (HETE), which have an important role in the inflammation process (Wisastra and Dekker, 2014; Ben-Nasr et al., 2015). Therefore, antioxidant defense systems that inhibit lipoxygenase enzymes responsible for inflammation also have anti-inflammatory properties (Ben-Nasr et al., 2015). The LOX enzymes are effective in the formation of many inflammation-related diseases such as arthritis (joint inflammation), asthma, coronary heart and vascular, kidney, allergic diseases, neuro-degenerative diseases such as Alzheimer's, and cancer (Mashima and Okuyama, 2015; Souleymane et al., 2016). Some of the LOX inhibitors used are banned or limited due to their high side effects. Due to such disadvantages, there is a continuous effort to develop new LOX inhibitor drugs with minimal side effects (Tomy et al., 2014).

In studies, it has been reported that different plants have LOX inhibiting capacities due to the phenolic compounds they contain (Werz, 2007; Tomy et al., 2014). Besides phenolic compounds, plant essential oils have also been shown to inhibit lipoxygenase enzymes (Loncaric et al., 2021). Another enzyme that is produced by reactive oxygen species and causes inflammation is xanthine oxidase. Xanthine oxidases (XO, EC; 1.2.3.2) catalyze the oxidation of xanthine and convert it to uric acid. Overproduction and accumulation of uric acid cause hyperuricemia, gout, and inflammation. For this reason, the use of xanthine oxidase inhibitors, which block uric acid synthesis in the body, is an important approach in the treatment of hyperuricemia-induced diseases (Wisastra and Dekker, 2014). Allopurinol (1H-pyrazolo[3,4-d]pyrimidin-4-ol) is a potent inhibitor of xanthine oxidase and has been used in the treatment of gout in recent years (Tamta et al., 2006). Studies have shown that allopurinol may cause hypersensitivity syndrome and Stevens-Johnson syndrome (a condition in which the skin and mucous membranes react severely to drugs or infection) in patients (Hammer et al., 2001). Therefore, in the treatment of inflammation, the xanthine oxidase inhibition effect of many plants has been studied, and some phenolic compounds have been reported to exert anti-inflammatory effects by inhibiting the xanthine oxidase enzyme (Zhu et al., 2004; Kim et al., 2014). In studies, it has been reported that the capacity of the extracts obtained from plants to inhibit enzymes responsible for inflammation also varies depending on the dose of the plant used, and that the increasing concentration of the plant has a positive effect on enzyme inhibition (Nunes et al., 2020).

Anticancer (Cytotoxic) Properties of Phytochemicals

Today, millions of people are diagnosed with cancer every year. In the report organized by the American Cancer Society, it is reported that approximately 2-3% of the deaths in the world during the year are caused by cancer, and approximately 3.5 million people die from cancer annually (Kathiresan et al., 2006). Cancer is a fatal disease caused by mutations that affect the uncontrolled growth, differentiation, and de-differentiation of cells. Uncontrolled growth causes a series of mutations in genes. As a result of mutations, primary tumor cells formed by a cell that undergoes uncontrolled division acquire phenotypic features in different ways (Rohrbeck and Borlak, 2009). If the tumor does not metastasize, depending on the type of cancer, the location of spread, and the severity of the disease, surgery, radiotherapy, chemotherapy, biological treatments, or hormonal treatment methods can be used (Porras et al., 2021). Chemotherapy is one of the common methods used in cancer treatment, and the drugs used activate apoptosis by stopping cell proliferation (Liang et al., 2012). However, due to the many disadvantages of anticancer drugs, the development of new generation anticancer agents has become an important research area. The cytotoxic effects of both synthetic and natural products are constantly being investigated (Cenic-Milosevic et al., 2013).

Studies have reported that approximately 50% of modern drugs used to suppress the proliferation of related cancer cells in the treatment of many types of cancer have been obtained from plants in recent years (Cenic-Milosevic et al., 2013). These compounds of plant origin are included in the composition of many drugs. For example, the drug "Paclitaxel" is a drug containing the paclitaxel compound obtained from yew tree bark and is used in the treatment of many cancers, especially breast, lung, ovarian, and pancreatic cancer. Vinca alkaloids, on the other hand, are a class of compounds found in drugs used in the treatment of blood cancer, lymph node cancers, lung cancer, and breast cancer. This drug contains “vincristine” and “vinblastine” compounds in the structure of a kind of violet plant and is used as medicine under the names of “Vinblastine” (Richter-10 mg) and “Vinblastine Sulphate”. It has been determined that the death rate and tumor formation in cancer, coronary, cardiovascular, and neurological diseases that carry serious risk are inversely proportional to the consumption of highly phenolic food sources in the diet. Studies have shown that phenolic compounds play an important role in anticancer effects and have high cytotoxic effects (Kulkarni and Vijayanand, 2010). Cytotoxicity is a common method used to determine anticancer activity based on the evaluation of the toxic effects of biological and chemical substances on cells in general (Szymanowska et al., 2018). In a study examining the cytotoxic effects of ellagic acid and curcumin, they reported that these compounds were effective (>50%) on tumor proliferation (proliferation) kinetics (Hayeshi et al., 2017). At different concentrations, four Cameroonian plant extracts: Xylopia aethiopica, Imperata cylindrica, Echinops giganteus, and Dorstenia psilurus show cytotoxic effects on human cervix (HeLa), lung (A549), breast (MDA-MB-231), ovary (SK-OV-3), blood (HL60), and liver (HepG2) cancer cells (Somaida et al., 2020). Furthermore, antiproliferative effect of kaempeferol compound isolated from Dianthus caryophyllus plant in human colon cancer (HCT-8 cell line) has been reported (Martineti et al., 2010). The anticancer activities of galangin (Zhang et al., 2013), limonene (Chidambara et al., 2012), puerarin (Xiao et al., 2011) and ursolic acid (Messner et al., 2011) from herbal phenolics have been shown in studies.

Antihypertensive Properties of Phytochemicals

Hypertension is not just a disease; it is a syndrome in which many conditions are combined. It is estimated that there are approximately 400 to 500 million hypertensive people in the world (Campbell et al., 2022) and it is the number one risk factor among preventable causes of death in the world. Medication is started in 53% of hypertension patients, and high blood pressure can be kept under control (below 140/90 mmHg) in only 27% of diagnosed hypertension patients (Carey et al., 2018). In the recent past and today, traditional methods are used in the treatment of hypertension. In addition to the many different phytochemical properties of plants, their antihypertensive properties have been demonstrated in in vitro and in vivo studies (Lobay, 2015; Uluwaduge and Thabrew, 2018). For example, it has been reported that garlic (Allium sativum L.) reduces high blood pressure, cholesterol, and triglyceride levels (Asdaq and Inamdar, 2011; Athar et al., 2019). In a study on coronary heart patients in India (432 patients), it was determined that the rate of heart attack decreased due to the lower blood pressure and cholesterol level in the group given garlic compared to the other group (Karasaki et al., 2001; Maisaroh et al., 2020). In addition, cardamom (Elettaria cardamomum), carrot (Daucus carota L.), coffee weed (Cassia occidentalis), jujube (Ziziphus jujuba), and green tea (Camellia sinensis) (Kamyab et al., 2021), ginko biloba, hawthorn, dwarf palm, red sage, licorice, American It has been reported in studies that plants such as ginseng and mullein show antihypertensive properties by reducing blood pressure (Chrysant, 2016).

CONCLUSION

Many bioactive properties of plant phytochemicals, which are important for human health, have been studied and are still being studied. The antioxidant properties of these compounds replace synthetic antioxidants, prevent the development of pathogenic microorganisms with their antimicrobial properties, balance blood glucose levels with their antidiabetic properties, reduce inflammation with their anti-inflammatory properties, reduce the risk of cancer treatment and risk with their anti-cancer properties, control blood pressure with their antihypertensive properties, and prevent the development of pathogenic microorganisms with their anti-diabetic properties. Studies have shown that they have the potential to prevent the harmful effects of free radicals and thus enable people to lead a healthier life. Nutrition with phytochemical content, especially today, is seen that it can play an important role in reducing the diseases caused by the lifestyle and respond to the consumer's desire to consume healthier products.

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