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Plant-Derived Food Antioxidants and Their Effects on Health

Duygu DOĞAN[1], Emine OKUMUŞ[2]*, İsmet MEYDAN[1]

[1] Van Yuzuncu Yil University, Health Services Vocational School, Zeve Campus, 65080, Tuşba, Van, Turkey
[2] Van Yuzuncu Yil University, Faculty of Engineering, Department of Food Engineering, Zeve Campus, 65080, Tuşba, Van, Turkey

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* *Corresponding author: emineokumus@yyu.edu.tr*

Abstract

Antioxidant foods and ingredients have an important place in the food industry. Many ingredients such as fruits, vegetables, grains and seeds are rich in antioxidants. Antioxidants have become the focus of attention thanks to their protective effect against pathological processes caused by oxidative stress. Apart from this, they exhibit range of biological effects such as anti-inflammatory, anti-aging and anti-diabetic. Traditionally, herbal medicines and dietary foods are sources of antioxidants that protect people from external factors. Obtaining and evaluating antioxidants from foods and medicinal plants is very important for their application in drugs and food additives. Phenolic compounds are bioactive compounds commonly found in many plant tissues, including fruits and vegetables. These compounds, which are used as antioxidant sources, have potential protective roles on health, even though they are not nutrients. In recent studies, polyphenols show antioxidant effects by modulating cell signaling pathways. Thanks to the benefits of polyphenols as protective and therapeutic agents; it shows that it can be consumed in a rich diet, used as a food supplement and used as pharmaceutical drugs. Apart from this, the amount of polyphenols consumed has a great impact on health. This review examines the contents and effects of antioxidants found in foods with sample studies. It is crucial for the food industry to clearly present rich ingredients found in food science for progress in this field. It is necessary to raise awareness by renewing the antioxidant contents in foods and furthering their benefits in the health sector.

Key Words: Food, antioxidants, polyphenols, flavonoids, health.

Bitkisel Kaynaklı Gıda Antioksidanları ve Sağlık üzerindeki Etkileri

Öz

Gıda endüstrisinde antioksidan gıdalar ve bileşenler önemli bir yere sahiptir. Meyveler, sebzeler, tahıllar ve tohumlar gibi birçok içerik antioksidan açısından zengindir. Antioksidanlar, oksidatif stresin neden olduğu patolojik süreçlere karşı koruyucu etkileri sayesinde ilgi odağı haline gelmiştir. Bunun dışında anti-inflamatuar, anti-aging ve anti-diyabetik gibi çeşitli biyolojik etkiler de gösterirler. Geleneksel olarak bitkisel ilaçlar ve diyet gıdaları insanları dış etkenlerden koruyan antioksidan kaynaklarıdır. Gıdalardan ve şifalı bitkilerden antioksidanların elde edilmesi ve değerlendirilmesi, bunların ilaç ve gıda katkı maddelerinde uygulanması açısından oldukça önemlidir. Fenolik bileşikler, meyve ve sebzeler de dahil olmak üzere birçok bitki dokusunda yaygın olarak bulunan biyoaktif bileşiklerdir. Antioksidan kaynağı olarak kullanılan bu bileşikler, besin maddesi olmasa da sağlık üzerinde potansiyel koruyucu rollere sahiptir. Yapılan son çalışmalarda polifenoller, hücre sinyal yolaklarını modüle ederek antioksidan etki göstermektedirler. Polifenollerin koruyucu ve tedavi edici ajan olarak faydaları sayesinde; zengin bir diyetle tüketilebileceğini, gıda takviyesi ve farmasötik ilaç olarak kullanılabileceğini göstermektedir. Bunun dışında tüketilen polifenol miktarının sağlık üzerinde büyük etkisi vardır. Bu derlemede gıdalarda bulunan antioksidanların içerikleri ve etkileri örnek çalışmalarla incelenmektedir. Gıda endüstrisinin, gıda biliminde bulunan bu zengin içerikleri net bir şekilde sunması, bu alanda ilerleme sağlanması açısından büyük önem taşımaktadır. Gıdalardaki antioksidan içeriklerinin yenilenmesi ve sağlık sektöründeki faydalarının daha da ileri götürülerek farkındalığın arttırılması gerekmektedir.

Anahtar Kelimeler: Gıda, antioksidanlar, polifenoller, flavonoidler, sağlık.

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1. INTRODUCTION

The interest in antioxidants found in foods stems from the fact that they can improve human health and lead to a better quality of life (Amarowicz and Pegg 2019). Thanks to the content of polyphenolic compounds, one of the most researched bioactive classes, many functional products have been created in the food industry and health sector (Valls et al. 2009; Caleja et al. 2017). Polyphenols in food types such as fruits, vegetables, grains and legumes play an important role in reducing the risk of disease, thanks to their physiological benefits as well as their high nutritional values (Fig.1) (Kaushal et al. 2022).

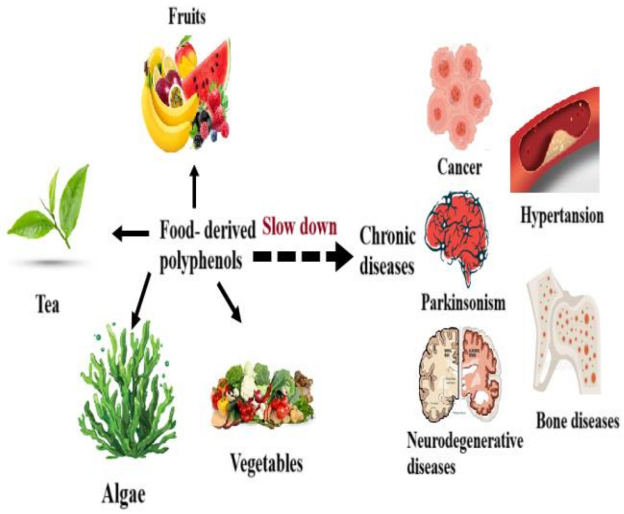

Fig.1 Effects of food-derived polyphenols on chronic diseases (Xu et al. 2024).

Polyphenols are one of the phytochemicals with polyhydroxy compounds that provide the most effective protection against pathogenic attacks and radiation. (Mutha et al. 2021).

The structure of polyphenols varies from simple molecules such as phenolic acids to higher order molecules such as tannins (Tresserra-Rimbau et al. 2018). Polyphenol subgroups vary according to the number of phenol rings they contain and the structural components connecting the rings (Ouideau et al. 2011). Polyphenols have remarkable biological effects such as preventing reactive oxygen and nitrogen species, providing electron transfer to free radicals, activating antioxidant enzymes and eliminating oxidative stress. (De Araújo et al. 2021).

Absorption of polyphenols is metabolized by hepatic enzymes and intestinal microflora in the intestine (Panche et al. 2016). Polyphenols are divided into subclasses as flavonoids, phenolic acids, stilbenes, tannins and lignans (Di Lorenzo et al. 2021). The largest subclass of polyphenols are flavonoids (Tresserra-Rimbau et al. 2018). Flavonoids, are secondary plant metabolites that serve as signaling molecules, detoxifying agents, antioxidants and are responsible for the protection of plants against biotic and abiotic stresses (Mutha et al. 2021; Kaushal et al. 2022). They are divided into flavanols, flavanones, flavonols, flavonones, isoflavones and anthocyanins (Neri-Numa et al. 2020). Bioflavonoids are found in remarkable concentrations in fruits, vegetables and tea (Frutos et al. 2019). Flavonoids show many nutraceutical properties such as anticancer, anti-inflammatory, antidiabetic, antioxidant, antiproliferative and immunomodulatory, as shown in Table 1 (Kaushal et al. 2022).

Table 1 Natural antioxidants in foods and the diseases they are effective in treating (Li et al. 2014).

Natural antioxidants	Target diseases	Foods rich in natural antioxidants
Flavonoids	Cardiovascular disease, arthritis, Alzheimer's disease, stroke (Jiang et al. 2013; Khan and Dangles 2014; Jiang et al. 2014; Zhang et al. 2014).	Plants, berries, honey
Flavanols (catechin)	Arteriosclerosis, coronary heart disease, and alcoholic liver (Kurosawa et al. 2005; Suzuki et al. 2013).	Cocoa bean
Flavanols (epigallocatechin-3-gallate)	Aging, Alzheimer's disease, diabetes, cardiovascular diseases, tumors and inflammation (Rezai-Zadeh et al. 2005; Baba et al. 2012; Bornhoeft et al. 2012; Riegsecker et al. 2013; Zuo et al. 2014).	Green tea
Flavanols (catechin, epicatechin, gallocatechin)	Diabetes, cardiovascular diseases (Du et al. 2007; Hokayem et al. 2013).	Red wine, grape seeds
Isoflavonoids	Prostate, ovarian, cervical and breast cancers (Wu et al. 1998; Suter et al. 2011; Aufderklamm et al. 2014; Lee et al. 2014)	Soybean
Anthocyanins	Cardiovascular disease, neurodegenerative diseases, Breast cancer, liver cancer (Zafra- Stone et al. 2007; Bishayee et al. 2010; Tremblay et al. 2013; Noratto et al. 2014).	Black rice, purple sweet potato, blueberry, mulberry and other dark foods, peaches.

The functionality of flavonoids depends on the presence of conjugated double bonds, which determine the number and orientation of active hydroxyl groups (-OH) in the aromatic ring (B ring), and are responsible for their ability to eliminate free radicals and chelate metals. Thanks to this, they gain antioxidant properties (Mondal et al. 2020). Increasing concentrations of free radicals disrupt the redox balance and cause oxidative damage (Gupta et al. 2014). This imbalance lies at the basis of diseases such as cancer, Parkinson's, diabetes and Alzheimer's (Labat-Robert et al. 2014). Consuming antioxidants is of great importance to clear these radicals and maintain balance. Obtaining antioxidants from foods is the most powerful alternative both for the treatment of diseases and for preventing negative reactions (Li et al. 2014).

2. Polyphenols

Polyphenols are natural compounds containing one or more phenol groups, found in many food sources. They are secondary defense metabolites used especially against pathogenic effects and ultraviolet radiation (Tresserra-Rimbau et al. 2018; Silva et al. 2020). More than 8000 classification definitions have been made in phenolic compounds (Cory et al. 2018). In foods; It is used to provide flavour, color, odor and oxidative stability (Lattanzio 2013). It is also responsible for the preservation and diversity of fruits, vegetables and flowers. Shikimite acid and phenylpropanoid pathways are among the pioneers of biosynthesis in providing phenolic compounds (Ferreira et al. 2017). As a result of the research, it has been stated that long-term consumption of plant polyphenols provides protection against cancer, diabetes, cardiovascular diseases and neurodegenerative diseases (Kardum and Glibetic 2018). Phenoxyl radicals are formed thanks to the electron acquisition of phenolic groups in polyphenols. These structures cause a positive deterioration in the oxidative chain reactions within the cell (Mutha et al. 2021). Consuming a diet rich in polyphenols not only protects against oxidative damage but can also act as an antioxidant (Mustafa et al. 2020). Polyphenols are effective on carcinogenesis during the induction of cell defense systems such as detoxifying and antioxidant enzyme systems. It provides inhibition on anti-inflammatory and anti-cellular growth signaling pathways, limiting the cell cycle and resulting in cell death. In this way, they have an anticancer effect by changing the epigenome of cancer cells (Briguglio et al. 2020). Current research emphasizes that polyphenols play an important role during aging. It has been stated that polyphenolic compounds can regulate the redox state of cells and prevent deterioration in biological molecules such as nucleic acids, lipids and proteins. It is possible by directly scavenging reactive oxygen species or by interacting with transcription factors that regulate the antioxidant response. It has been observed that it provides high expression of antioxidant enzymes such as superoxide dismutase and catalase (Gomes et al. 2012). In addition, polyphenol compounds found in foods are of interest due to their effects on the intestinal microbiota. They do this in two ways; they can directly control their conformation and can be broken down into smaller fragments by intestinal microbes, thus forming metabolites that can be easily absorbed from natural compounds. (Pascale et al. 2018). It has been stated that 5-10% of the total polyphenol intake is absorbed in the small intestine, and the remaining part accumulates in the large intestine and undergoes enzymatic change by the intestinal microbiota (Meccariello and D' Angelo 2021). The majority of natural polyphenols are generally yellow, red and purple pigments and can absorb harmful rays. Natural polyphenols also have a sunscreen effect by reducing radiation-related tissue disorders, oxidative stress and negative traces on DNA caused by harmful rays (Nichols and Katiyar 2010; Dunaway et al. 2018). As an alternative source of phenolic compounds derived from many fruits and vegetables, food-agricultural waste has also recently become a stimulating area of research by scientists. Being environmentally friendly, sustainable and at a lower cost, it becomes a valuable opportunity for recycling (Ayala- Zavala et al. 2018). For example; approximately 70% of the polyphenols in grapes used in winemaking remain in the pulp (Albuquerque et al. 2020). Different forms of polyphenolic compounds have been found to have sugar residues attached to hydroxyl groups or directly to the aromatic carbon (Kondratyuk and Pezzuto 2004) . Citrus peels, seeds and pulp are an important source of hydroxycinnamic acid, flavone glycosides, flavones and flavone aglycones. Pineapple peels are a source of gallic acid, catechin, epicatechin and ferulic acid. Onion peels contain quercetin and kaempferol. Apart from this, it has been stated that wheat straw, wheat bran, sawdust and coffee grounds are rich in polyphenols (Panzella et al. 2020). Recently, monofloral honeys have attracted great attention due to their phytochemical content, which is associated with antioxidant and cancer prevention effects. They contain phenolic compounds such as vanillic acid, caffeic acid, p-coumaric acid, ferulic acid, quercetin and kaempferol. Monofloral honeys are becoming potential therapeutic agents by preventing apoptosis and cell number increase in various cell channels (Mărgăoan et al. 2021). Unlike plants, microorganisms are seen as sources of new bioactive compounds for medicinal and agricultural purposes. Microbes can be grown more rapidly under controlled conditions, thus enabling their use as potential bioactive substances for nutraceutical applications. Actinomycetes, one of these microorganisms, are isolated from various habitats and show antioxidant effects. It has been stated that they have a brain-protective effect as well as a suppressive effect on hydroxyl radicals (Chandra et al. 2020). Mushrooms; It contains phytochemicals such as anthocyanidins, carotenoids, isoflavonoids and flavonoids. They stated that mushroom antioxidants show protective effects through different mechanisms at various stages of the oxidation process. The inhibitory properties of mushroom species against premature death are directly proportional to the amounts of powerful antioxidants such as glutathione. It was found that the polysaccharide extract of Dictyophora indusiata, an edible mushroom, showed 72.26% antioxidant properties against lipid peroxidation. It has been stated that extracts obtained from the Russula virescens plant have a hydroxyl radical scavenging effect in relation to their amounts (Hasnat et al. 2014; Liu et al. 2017; Mwangi et al. 2022). Seaweeds, which are used as another antioxidant source, may contain up to eight interconnected phenol rings. In this way, they have an antioxidant effect thanks to the presence of bioactive structures such as carotenoids, gallic acid, quercetin, myricetin, flavones, flavonols, flavanones, isoflavones, phenolic acids and tannins. They contribute directly or indirectly to the inhibition of the oxidation process (Kumar et al. 2021). Although lactobacillus and bifidobacteria strains, which have proven their functionality as probiotics, are used in many food supplements, they have recently attracted attention with their antioxidant effects. Human-derived Lactobacillus and Bifidobacterium DPPH have proven to have a high antioxidant effect as a result of free radical scavenging and ABTS radical scavenging analyses. This suggests that probiotic subspecies may be effective as a complementary part in foods on symptoms associated with oxidative stress (Kim et al. 2020).

Although we examined plant sources in terms of polyphenolic components in our research, there are also animal sources as another alternative. It has been reported that insects, which are a source of nutrition in various cultures, are rich in phenolic compounds. Gallic acid, hydroxybenzoic acid, *p*-coumaric acid, ferulic acid, tricin, luteolin, quercetin, isovitexin are some of the common polyphenols in edible insects. Blaps rynchopetera Fairmaire, an insect from the family Tenebrionidae, has been used in Chinese traditional medicine to treat coughs, gastritis, and some types of cancer (Torres-Castillo and Olazarán-Santibáñez 2023). Polyphenols; It can be classified as flavonoids, phenolic acids, stilbenes and lignans (Fig. 2) (Rana et al. 2022).

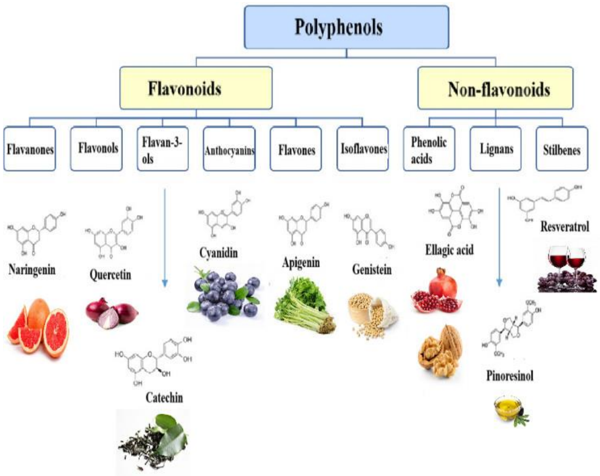

Fig. 2 Structure and diversity of polyphenols (Anhê et al. 2019).

2.1. Phenolic acids

Phenolic acids are the simplest subclass of polyphenols. They contain phenolic rings and carboxylic acids in their structure. It has derivatives as hydroxybenzoic acid and hydroxycinnamic acid (Fig. 3) (Heleno et al. 2015; Durazzo et al. 2019).

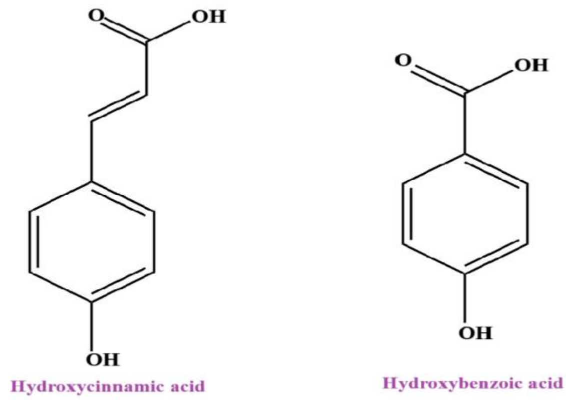

Fig. 3 Chemical structures of hydroxybenzoic acid and hydroxycinnamic acid (De Oliveira et al. 2023).

Phenolic acids are the dominant phenolic compounds obtained from plant sources, cereals, legumes and oilseeds (Fig. 4). Phenolic acids are glycosylated and found bound to other molecules in the cell wall (De la Rosa et al. 2019). Examples of hydroxybenzoic acids include salicylic acid, gallic acid and vanillic acid; Examples of hydroxycinnamic acid are coumaric acid, caffeic acid and chlorogenic acid (Ferreira et al. 2017).

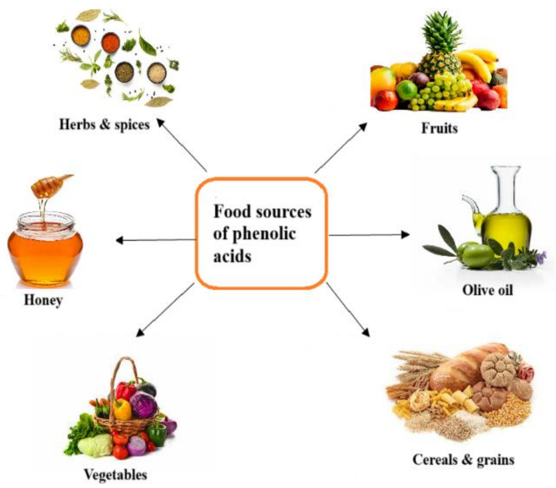

Fig. 4 Phenolic acids and food sources (Ali et al. 2020).

Table 2. Flavonoid subgroups and the nutrients they contain (Nieman and Mitmesser 2017).

Flavonoids	Sample Polyphenols	Food Sources
Simple Flavonoids		
Flavan-3-ols	(+) –catechins, (-)-epicatechin, (-)-epigallocatechin-3-gallete	Green tea, chocolate, tree fruits, grapes, red wine
Flavanones	Hesperetin, Naringenin, Eriodictyol	Citrus fruits and juices
Flavones	Luteolin, Apigenin	Parsley, celery seed, oregano
Isoflavones	Daidzein, Genistein, Glycitein	Soybeans, soy-based foods, legumes
Flavonols	Quercetin, Kaempferol, Myricetin, Isohamnetin	Onions, apples, tea, berries
Anthocyanins	Cyanidin, Delphinidin, Malvidin, Pelargonidin, Peonidin, Petunidin	Most berries, Stone fruits

2.2. Flavonoids

Flavonoids are water-soluble compounds found in glycoside conjugated form in fruits and vegetables (Acosta-Estrada et al. 2014). They are secondary metabolites responsible for both the scent and color of the flower (Panche et al. 2016). Flavonoids are known to be found in more than 8000 compounds (Durazzo et al. 2019).

Flavonoids chemically consist of 15 carbon atoms contained within two benzene rings and connected by a heterocyclic pyran ring (Fig. 5) (Mark et al. 2019).

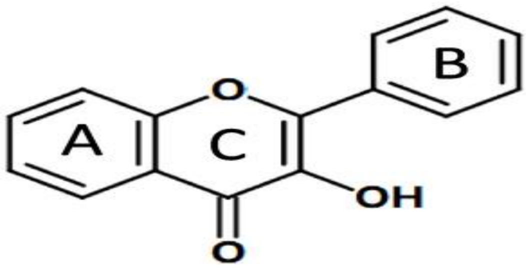

Fig. 5 Chemical structure of flavonoids (Rodriguez et al. 2021).

The various subclasses of flavonoids, differ according to the bond between the B and C rings and the substitution of the C ring (Fig.6) (Kaushal et al. 2022).

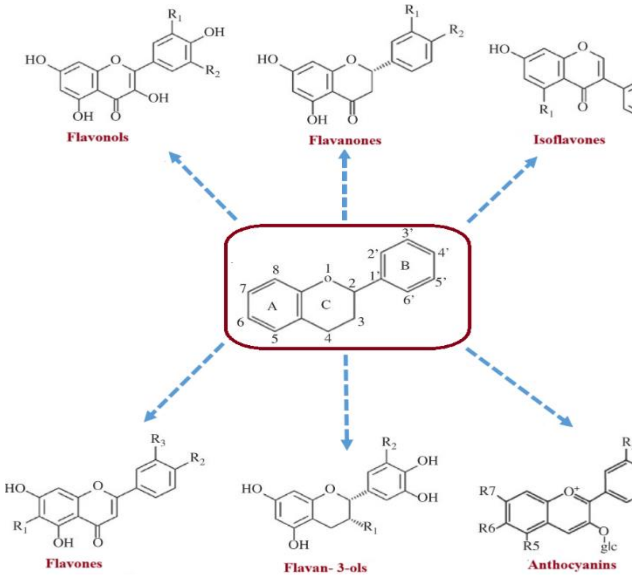

Fig. 6 Generic structures of major classes of flavonoids (Gentile et al. 2018).

Flavonoids occur in nature as a result of esterification, glycosylation and polymerization reactions. Condensed tannins may occur as the polymerization product of flavonoids (Ferreira et al. 2017). Flavonoids are found in many classes of food sources, including blueberries, oranges, lemons, grapefruits, and pomelo. Subclasses of flavonoids and the foods in which they are found are shown in Table 2. The amount of flavonoids found in foods may vary depending on how the foods are processed (Guven et al. 2019). For example, fruits and vegetables are primarily separated into peel and stem parts. However, research shows that removing the peel and stem parts significantly reduces the amount of antioxidants found in fruits and vegetables (Atınç and Kalkan 2018).

Flavonoids also have positive effects on human health. They are known to be important antioxidants for suppressing free radical formation, clearing free radicals by reducing lipid peroxidation, and protecting antioxidant systems (Fig. 7) (Jiang et al. 2020; Duan et al. 2021). In addition, these molecules have biological activities such as antimicrobial, antiviral, hepatoprotective, nephroprotective, anti-inflammatory, cardiovascular protective effects and potentially cancer prevention (Rodriguez et al. 2021; Mouffouk et al. 2021).

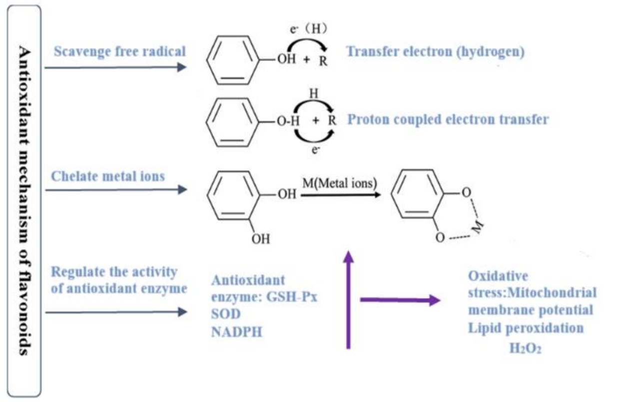

Fig 7. Antioxidant mechanisms of flavonoids. GSH-Px: glutathione peroxidase; SOD: Superoxide dismutase (Lv et al. 2021).

2.2.1 Flavanols (Flavan-3-ols)

Flavanols are 3-hydroxy derivatives of flavanones. Flavanols are also known as flavan-3-ols due to the hydroxyl group attached to the 3rd position of the C rings (Sapian et al. 2021). The most common flavanol monomers are catechin, epicatechin, catechin gallate, epicatechin gallate, gallocatechin, epigallocatechin, gallocatechin gallate, and epigallocatechin gallate (Dias et al. 2021). These ingredients are found in various products such as apples, peaches, cocoa powder, hazelnuts, dark chocolate, strawberries and grapes (Seleem et al. 2017). Flavanols cause nitric oxide (NO) to be released into the blood. It has been stated that flavanol consumption can prevent damage to blood vessels in people who smoke (Pascual- Teresa et al. 2010). Consumption of flavanol-rich foods has a healing effect on endothelial functions and is preventive for cardiovascular diseases (Guven et al. 2019). In addition, it has important effects on health such as clearing free radicals, mediation and inhibition of enzymes, anticarcinogenic, antiviral, positive modulation of hemostasis, and improvement in insulin sensitivity (Ottaviani et al. 2011; Engin et al. 2018).

2.2.2 Flavanones

Flavanones are diversified as naringenin, hesperetin and eriodicthiol (Maleki et al. 2019). They are characteristic components of the citrus fruits, such as lemon, sweet orange, tangerine, grapefruit and tomato (Khan et al. 2020). It is present in the trunk, branch, leaf, root, flower and fruit parts of plant groups (Khan and Dangles 2014). The antioxidant activity of flavanones depends on their number and the spatial position of the hydroxyl group attached to the phenol ring. These compounds show high antioxidant activity in hydrophilic environments (Khan and Dnaglrs 2014; Guven et al. 2019). Naringenin flavanones can inhibit nitrate and nitrite production and proinflammatory cytokines and reduce intestinal edema (Bodet et al. 2008). Flavanones, which have anticancer effects, have the potential to block tumor proliferation. They have an antimutagenic effect thanks to their UV light absorbing properties (Brodowska 2017; Guven et al. 2019). It has been stated that it is beneficial in reducing inflammatory responses caused by SARS-CoV-2 infection (Tutunchi et al. 2020).

2.2.3 Flavonols

Rutin, quercetin, kaempferol and myricetin are the most well-known types. Lettuce, cranberries, apples, peaches and red peppers are valuable sources of quercetin and kaempferol. Also, there is rutin in spinach leaves; myricetin in hazelnuts, strawberries and tea (Dias et al. 2021). Flavonols act as antioxidants by protecting biomolecules from oxidative damage (Guven et al. 2019). Rutin has antibacterial, antiviral, antifungal, antiallergic, antidiabetic, antioxidant, anticancer, neuroprotective effects as well as healing properties for the thyroid glands (Al-Dhabi et al. 2015). Quercetin protects low-density lipoprotein from oxidation, preventing oxidative damage to cellular structure and blood vessels caused by free radicals (David et al. 2016). Kaempferol modulates important elements in inflammation, metastasis, apoptosis and inflammation-related signaling pathways (Hussain et al. 2024). Myricetin is a compound that has cytotoxic effects on various types of cancer. It can inhibit enzymes that are effective in the initiation and progression of cancer (Semwal et al. 2016).

2.2.4 Flavones

Luteolin, apigenin and chrysin are the most common types of flavones (Maleki et al. 2019). Mostly vegetables, fruits, nuts, grains, seeds and plant-based drinks are rich in flavones (Maleki et al. 2019; Wen et al. 2020). These molecules have regulatory properties for enzyme systems that are effective in many diseases (Hariri et al. 2017). They also have immunomodulatory effects and play an important role in reducing total cholesterol (Hostetler et al. 2017; Zaragozá et al. 2020). Apigenin can be used as a hepatoprotective agent in liver damage caused by oxidative stress by regulating multiple genes at high doses in vivo (Ali et al. 2017). Luteolin has antioxidant activity that chelates metal ions and scavenges free radicals. It also inhibits prooxidant enzymes and prevents the formation of free radicals (Xu et al. 2019). Luteolin crosses the blood-brain barrier, important for central nervous system diseases (Ashaari et al. 2018).

2.2.5 Isoflavones

Isoflavones are divided into genistein, daidzein, glycitein (Maleki et al. 2019). Mainly found in legumes; soybeans, green peas, chickpeas, black beans, lima beans and lupins. It has also been found in low amounts in broccoli, cauliflower, barley and hazelnuts (Ko 2014; Křížová et al. 2019). Isoflavones have effects such as relieving menopausal symptoms, hepatoprotective effect, and cardiovascular protection (Gómez-Zorita et al. 2020; Alipour and Karimi- Sales 2020; Ma et al. 2020). A study conducted on obese rats has shown that it has an improving effect on kidney functions (Pessoa et al. 2020). Daidzein inhibits isoenzymes of human alcohol dehydrogenase (ADH) and mitochondrial aldehyde dehydrogenase, which are degraded in human alcohol metabolism (Hämäläinen et al. 2007). Genistein is an important therapeutic agent in cancer treatments. In addition, it can prevent bone density loss by directly acting on osteoblasts on the bone (Nazari-Khanamiri and Ghasemnejad-Berenji 2021).

2.3 Anthocyanins

Anthocyanins are produced from flavonols, which contain a hydroxyl group and also have two double bonds (Ayala-Zavala et al. 2018; Mark et al. 2019). The most common anthocyanins are; cyanidin, delphinidin, pelargonidin, peonidin, malvidin and petunidin (Khoo et al. 2017). Anthocyanins are found mostly in red fruits and vegetables such as red onion, radish, red cabbage, red lettuce, eggplant, purple sweet potato, strawberry, plum, blackberry, raspberry, cherry, grape (Fig. 8) (Paun et al. 2011; Chaves- Silva et al. 2018). In addition to its antioxidant, anticancer, antibacterial, antidiabetic, antiangiogenic properties, it is effective in preventing cardiovascular diseases, vision health, obesity, and neurological disorders (Khoo et al. 2017). Anthocyanins are used as natural colorants, especially by the food industry (Carocho et al. 2015).

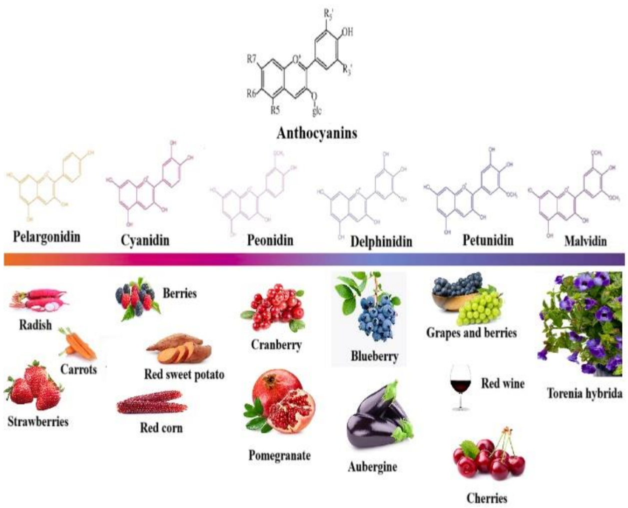

Fig. 8 Food sources rich in anthocyanins (Posadino et al. 2023).

2.4 Stilbenes

Stilbenes are polyhydroxyphenolic compounds with a chemical structure containing two benzene rings linked together by a double bond (Durazzo et al. 2019; Mark et al. 2019). More than 400 stilbenes are known. However, stilbene synthase, the key enzyme involved in stilbene biosynthesis, is restricted to a limited and heterogeneous group of plants (Riviere et al. 2012; Caleja et al. 2017). It is found in various foods such as grapes, peanuts, mulberries, strawberries, wine, celery (El Khawand et al. 2018). They have various biological activities including antitumor, anti-inflammatory, antioxidant, antibacterial, antiviral and antidiabetic (Su et al. 2022). The most well-known and important stilbene is resveratrol (Albuquerque et al. 2020). It is present in more than 70 plant species, including grapes and peanuts (Su et al. 2022). Resveratrol exhibits anti-cancer activity due to its chemopreventive and chemotherapeutic properties (Elshaer et al. 2018). It has been reported to be effective in many types of cancer such as lung, colon, breast, skin, prostate, ovary, liver, leukemia, and thyroid (Sirerol et al. 2016).

2.5 Tannins

Tannins are water-soluble polyphenolic compounds found in plant tissues. They have been reported to give an astringent and bitter taste to some fruits in particular (Durazzo et al. 2019; Albuquerque et al. 2020). The main classification and structures of tannins are shown in fig.9. Hydrolyzable tannins are formed by the hydrolysis of simple phenols in an acidic or basic environment to produce phenolic acid or carbohydrate molecules (Formation of gallotannin from gallic acid) (Durazzo et al. 2019). Condensed tannins are formed by the condensation of two or more flavan-3-ol unit monomers (Mora et al. 2022).

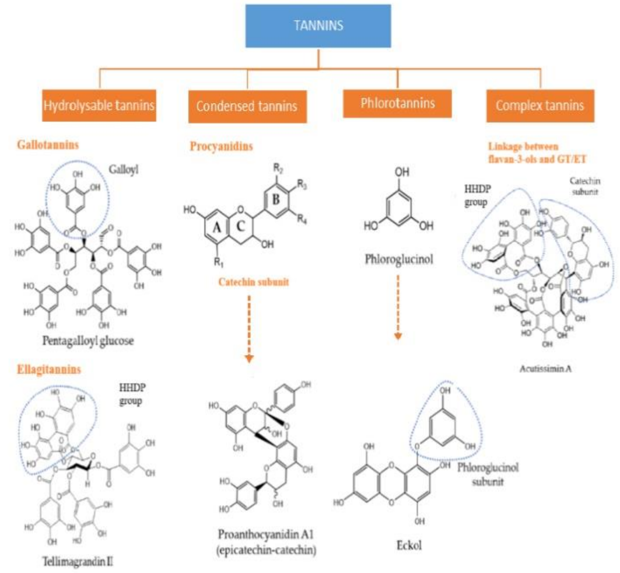

Fig. 9 Classification and general structures of tannins. R: Radical; GT: Gallotannins; ET: Ellagitannins; HHDP: Hexahydroxydiphenol (Fraga- Corral et al. 2021).

Tannins have a significant effect in preventing diseases such as cancer, heart, allergies, Alzheimer's and Parkinson's (Panzella and Napolitano 2017). In addition, tannins have antimicrobial effects and prevent the growth of fungi, yeast, bacteria and viruses (Fraga- Corral et al. 2021). Its antimicrobial properties are attributed to the hydrolysis of the ester bond between gallic acid and polyols, which are hydrolyzed after ripening in many fruits (Kumar et al. 2021).

2.6 Lignans

Lignans consist of two phenylpropanoid units (Rocchetti et al. 2022). It is found in grains, fruits and vegetables, especially flaxseed is the most important source (Luna-Guevara et al. 2018). Animal test evidence has shown that flaxseed and pure lignans have anticancer effects on various types of cancer (De Silva and Alcorn 2019). Lignans have been observed to have significant antioxidant activity and also inhibit lipid peroxidation (Fig. 10) (Shadidi et al. 2019). In addition to other bioactivities, it also has estrogenic and antiestrogenic effects (Caleja et al. 2017).

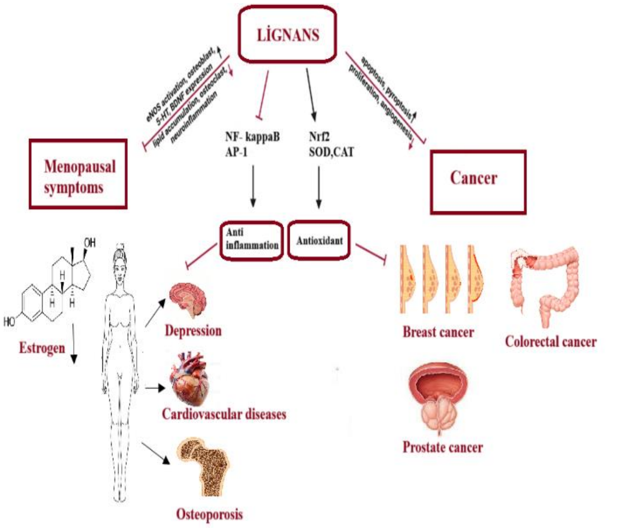

Fig. 10 Scheme of therapeutic properties of lignans. Nrf2: Nuclear factor erythroid 2; SOD: Superoxide dismutase; CAT: Katalaz; AP-1: activator protein; NF-kappaB: Nuclear factor kappa B (Jang et al. 2022).

3. Antioxidant mechanism of action and bioavailability

Phenolic compounds have antioxidant effects such as scavenging free radicals and inhibiting lipid oxidation (San Miguel-Chávez 2017). Many oxidations are caused by the hydroxyl radical (HO) formed by the electron transfer reaction between iron and hydrogen peroxide (Fenton reaction) (Bié et al. 2023). The formation of excessive amounts of reactive hydroxyl radicals and the reduction of hydrogen peroxidase increase free metal ions. Polyphenols can reduce the amount of high amounts of free radicals because they can chelate both metal ions and free radicals (Mishra et al. 2013). Polyphenols can react with non-polar compounds in the hydrophobic inner membrane of the plasma membrane. As a result of the reaction, the oxidation rate of lipids and proteins changes. Flavonoids in the membrane core can protect membrane structure and function (Hussain et al. 2016). Polyphenols can regulate NO production as a result of their interaction with nitric oxide synthase (NOS). Flavonoids such as quercetin and luteolin have been reported to inhibit xanthine oxidase (XO), a source of free radicals (Belščak-Cvitanović et al. 2018). At least four mechanisms have been listed by which polyphenols combat ROS. It can directly eliminate ROS thanks to the presence of phenolic hydroxyl groups in its primary structure. The ROS scavenging capacity of polyphenols varies depending on the hydroxyl groups in their structure, the positions they contain and the glycosylation of phytochemical molecules (Luo et al. 2021). The second mechanism is the effect on the production of endogenous antioxidants and oxidase enzymes. The first mechanism that neutralizes oxidants is sodium oxide dismutase 1 (SOD1) in the cytosol and SOD2 in the mitochondrial matrix, which converts superoxide to hydrogen peroxide with the intracellular enzyme. Hydrogen peroxide is neutralized by catalase (CAT) and glutathione peroxidases (GSH-Px) by converting it into more water and oxygen (Singh et al. 2015). Third, polyphenols regulate the Nrf2-mediated pathway. Nrf2; SOD is a transcriptional factor responsible for regulating the expression of detoxifying enzymes such as GPx1, GSH, GST. It shows activity by binding to antioxidant response elements located in the promoter regions of enzyme genes (Kobayashi and Yamamoto 2005). The last one is that polyphenols can counter ROS by regulating microRNAs. MicroRNAs; They are endogenous, non-coding and single-stranded RNAs. It binds to mRNA to repress and induce translation to regulate various biological pathways in many diseases, including cell proliferation and death, aging, and cancer (Fig.11)(Kim et al. 2014). Ji et al. stated that kaempferol showed antioxidant activity by affecting the expression of NADPH oxidase and NF-kB signaling pathway in mice of different age groups (Kim et al. 2010). Kim et al. reported that proanthocyanidins prevent ROS production and oxidative stress by reducing the activity of the MAPK (Mitogen- activated Protein kinase) pathway, which is activated by stress (Kim et al. 2011). In the study, it was observed that chlorogenic acid easily chelates with iron ions and prevents OH production thanks to the Fenton reaction, thus protecting the cells from oxidative damage (Yang et al. 2021). Cao et al. it has been observed that furofuran sesamin reduces ROS and MDA levels. It has been stated that it shows antioxidant activity on oxidative stress caused by fluoride in the liver by increasing antioxidant enzyme levels (Cao et al. 2020).

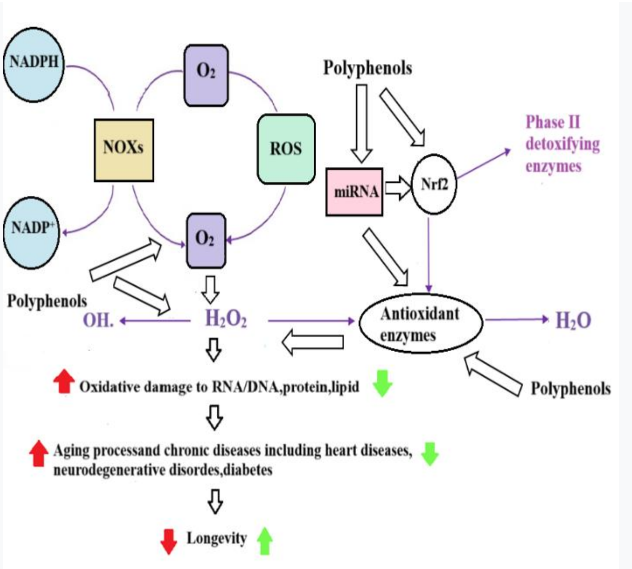

Fig. 11 Schematic diagram of polyphenols antioxidant mechanisms. Nrf2: Nuclear factor erythroid 2; ROS: reactive oxygen species (Luo et al. 2021).

The health effects of polyphenols are related to their concentration and their bioaccessibility and bioavailability after ingestion (Bié et al. 2023). Bioavailability is defined as the proportion of an ingested nutrient that is absorbed after digestion into the body. The measurement of bioavailability is dependent on estimates of antioxidants absorbed (Palafox- Carlos et al. 2011). Polyphenols bind to fiber-like macromolecules, forming chemical and colloidal complexes that reduce or increase their bioavailability and thus may interact with other food products in the intestine (Crozier et al. 2010; Ashley et al. 2019). Many polyphenols are found in foods as unabsorbable esters, glycosides or polymers. Before absorption, they must be hydrolyzed by enzymes in the intestine or by colon microflora. Some of the polyphenols are broken down by intestinal microbiota to form aromatic acids (Crozier et al. 2010; Bié et al. 2023). Polyphenols that are not absorbed in the small intestine reach the colon and undergo biotransformation by the microbiota (Pérez-Chabela and Hernández-Alcántara 2018). Flavonoids are generally glycosides with a hydrophilic structure and therefore have low bioavailability because they cannot be well absorbed in the intestine. Low bioavailability, coupled with oxidative degradation and metabolic alterations, precludes nutraceutical and pharmaceutical benefits (Manach et al. 2004; Maaliki et al. 2019). Bioaccessibility is expressed as the amount of food component that can pass through the intestinal barrier after the component is released from the solid food matrix. Only antioxidants released from fruits and vegetables by the action of digestive enzymes and intestinal microflora are bioaccessible in the intestine (Palafox- Carlos et al. 2011). Bioavailability studies on polyphenols do not take bioaccessibility into account. Although the bioavailability of all foods is different, molecules isolated from foods or chemically synthesized are mainly used (Saura- Calixto et al. 2007).

4. Examples on therapeutic effects of polyphenols

4.1 Gastroprotective effects

The protective effect of natural flavonoids against peptic ulcer was investigated in the study conducted by Zhang et al. (2020) He listed 60 types of flavonoids that have gastroprotective effects in peptic ulcer models. It has been stated that flavonoids have a good therapeutic effect on peptic ulcers both in combination with existing drugs and as a result of nanocapsulation (Zhang et al. 2020). Thanks to many molecular mechanisms of flavonoids, they can affect the glucose mechanism in the small intestine, muscle, fat, liver and pancreas. It has been reported that it inhibits enzymes involved in the digestion and absorption of carbohydrates, such as α- amylase and α-glucosidase, thus contributing to the reduction of post-meal glycemia (Hanhineva et al. 2010).

4.2 Antioxidant effect and oxidative stress

Ultrasound causes an increase in the extraction of substances that have antioxidant effects. The highest activity in the antioxidant effect of apple waste extracts obtained with the help of ultrasound was determined as leaves, peel and pulp, respectively (Arslan 2023). Cocoa polyphenols were administered as a treatment to mice with alcoholic fatty liver. The level of PLOOH, an oxidative stress indicator of phospholipid hydroperoxide, was significantly reduced in the liver of animals. This is an indication that cocoa polyphenols provide a protective effect on the liver (Suzuki et al. 2013). The antioxidant effect of the scarlet spur apple species, which has a high phenolic content, was investigated separately as peel, pulp and leaf. DPPH (2,2-diphenyl-1-picrylhydrazyl) and ABTS+ (2,2'-azino-bis 3-ethylbenzothiazoline-6-sulfuric acid) radical scavenging assays were used and it was determined that the highest antioxidant effect was especially seen in the apple leaf (Arslan et al. 2024). In a study, mice fed a high-fat and sugary diet were given green tea polyphenol solution (0, 0.8, 1.6, 3.2 g/L, respectively) instead of water for 4 weeks. Green tea polyphenols have been found to reduce large arterial permeability and ROS levels, as well as NAD(P)H oxidase protein expression levels in mice on a high fat and sugar diet. Since NAD(P)H oxidase is an important source of ROS in vivo, green tea polyphenols have been reported to have antioxidant effects (Zuo et al. 2014). At the beginning of the experiment, 3 groups were formed from 66 healthy adults who consumed less than 2 portions of vegetables and fruits in 1 day.. They were given placebo (water), black currant juice in low concentrations and black currant juice in high concentrations, respectively. As a result of the study, it was determined that people who took black currant juice had lower F2-isoprostane content, an indicator of oxidative stress, than those who took placebo. The cardiovascular system health index for blood flow regulation was reported to be significantly higher than the placebo group (Khan et al. 2016).

4.3 Neuroprotective effect

As an example of research, hesperetin was studied in an Alzheimer's rat model. In the 3-week study, 10 and 20 mg/kg hesperetin and hesperetin nanoparticles were injected. It was stated that it treated learning and cognitive disorders by reducing increased oxidative stress. It was also reported that hesperetin nanoparticles were more effective than the other hesperetin-applied group (Kwon et al. 2018). Grapes with high polyphenol content; 1.5 ml/kg concentrate was administered as a dietary supplement to transgenic mice with Parkinson's disease. As a result of the study, it was observed that it significantly increased memory reconsolidation (Tikhonova et al. 2020). It has been noted that supplementation at 10 mg/kg EC per day significantly improved 6-hydroxydopamine (OHDA) lesioned Parkinson's disease in male rats compared to the treated control group. It provided a neuroprotective effect by increasing locomotor activity and decreasing rotational behavior (Bitu Pinto et al. 2015).

4.4 Antidiabetic effect

Gallic acid and p-coumaric acid were observed to decrease serum glucose levels in diabetic rats. They provided an antidiabetic effect with an increase in insulin values (Abdel- Moneim et al. 2017). Fenugreek (Trigonella foenum-graecum) has long been used in traditional medicine for the treatment of many health problems, including diabetes. It has a strong α-glucosidase activity under in vitro conditions (95.24%). The treatment results on intraperitoneal glucose tolerance test in diabetic rats have shown good responses. It has been stated that fenugreek has a strong healing effect on diabetes (Laila et al. 2023). Polyphenols found in grapes have been used in the treatment of type 2 diabetes patients and it has been stated that they can prevent insulin resistance, oxidative stress and similar harmful conditions caused by fructose (Hokayem et al. 2013). Apigenin and naringenin were administered intragastricly at a dose of 50 or 100 mg/kg once a day for 6 weeks. Significantly reduced blood glucose, serum lipids, malondialdehyde levels. It improved NO production in diabetic rats by increasing SOD level (Ren et al. 2016). Guo et al. showed a significant reduction in fasting glucose levels following dietary cyanidin-3-glucoside supplementation (0.2%) for 5 weeks. In this way, it has been observed that it increases insulin sensitivity. It alleviated hepatic TAG (triacylglycerol) content and steatosis in genetically diabetic mice (Guo et al. 2012). The antidiabetic effects of nine medicinal and aromatic plant extracts (peppermint, spearmint, yarrow, sage, yellow cantoron, thyme, lavender, lemon balm, echinacea) were investigated due to their enzyme inhibition related to type-2 diabetes. It was predicted that these plants could be used as α-glucosidase inhibitors. In particular, the highest antidiabetic effect was determined in peppermint, St. John's wort and sage, respectively (Arslan and Çam 2022).

4.5 Anticancer effect

The polyphenols found in peach fruit were treated with 0.8-1.6 polyphenols every day in mice transplanted with breast cancer cells. It showed an inhibitory effect on the growth and metastasis of cancer cells, and the tumor volume of mice in the treatment group was significantly reduced (Noratto et al. 2014). Resveratrol, a stilbene polyphenol, has been demonstrated with anticancer activity such as induction of apoptosis in human hepatocellular carcinoma (HCC), induction of epidermal growth factor receptor (EGFR) cell death via signaling pathway, regulation of AMP-activated protein kinase enzyme (AMPK) (Gao et al. 2017; Jin et al. 2017). It has been reported that a diet containing abundant amounts of blueberries significantly reduced light-induced retinal damage in rats after 7 and 2 weeks of administration. This has been shown to have a protective effect on nerve cells due to the anthocyanins found in blueberries (Tremblay et al. 2017). In the analysis carried out with the participation of more than 57,000 individuals between the ages of 50-64, it was stated that plasma lignan concentration and colon cancer incidence, especially in women, are related and that high lignan concentration can prevent colon cancer formation (Johnsen et al.2010; Ortiz et al. 2022).

4.6 Antimicrobial effect

Teaflavins found in black tea are known to have antiviral activity and have anti-human immunodeficiency virus-1 (anti-HIV-1) effects. Teaflavin 3' gallate and teaflavin 3'digallate have shown an antiviral effect on coronavirus by restricting chymotrypsin protease (Sharma and Rao 2009). It was determined that the extracts obtained from air and microwave dried peach leaves had inhibitory effects on E. coli and L. monocytogenes. These results show that peach leaf extracts can be used as antimicrobial agents for pathogenic microorganisms (Şen Arslan et al. 2021). In a study conducted on 32 elderly (60-70 years old) people treated with G. biloba extract, there was an increase in small vessel blood flow and red blood cell volume after treatment with 270 mg *G. biloba* extract and placebo compared to the control group. It has been reported that the use of G. biloba extract significantly increases GSH levels. Apart from this, it has been found to improve skin and liver microcirculation (Li et al. 2014). In a study, the antibacterial effects of dragon fruit, prickly pear and red beet peel extracts were investigated. It was determined that prickly pear extract had the most effective minimum inhibitory concentration. It was stated that each extract caused a decrease in the growth rates of both gram-positive and gram-negative bacteria (Şen Arslan 2024). Today, it is known that many polyphenolic compounds have many benefits in medicines and health.

5. RESULT AND DISCUSSION

Polyphenols constitute a natural variety containing various chemicals and enzymes. Studies have shown that these compounds have a healing effect on health thanks to consumable foods. It has been stated that they are effective against chronic conditions such as cancer, diabetes, cardiovascular diseases. They are strong antioxidant sources, especially thanks to their ability to cleanse reactive species. Due to their strong activity, these compounds could be used as potential materials fo r a possible treatment of diseases. The use of natural antioxidants as natural food additives after the processing process in foods should become a future goal. Discovering new bioactive components by transferring the properties of these foods with high bioavailability should be the main goal of scientific analysis.

CONFLICT OF INTEREST

The authors declared no conflict of interest. The authors declared that this study hasn’t received financial support.

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