

## Review Article

# Evaluating the Potential of Phytochemicals as Natural Substitute for Synthetic Antioxidant

### ABSTRACT

**Aims:** The aim of this review has been to investigate the antioxidant potential of flavonoids as a subgroup of polyphenols and ultimately entirely and partially substitute the synthetic antioxidant with natural them.

**Methodology:** All relevant databases were searched for the terms including 'phytochemical', 'polyphenol', 'flavonoid', 'natural additive', as well as 'antioxidant activity' combined with *in vivo* and *in vitro* phrases.

**Results:** Free radicals are among the damaging factors to macromolecules. The oxidative reaction caused by these radicals is one of the reasons for food spoilage, which causes unpleasant odor, loss of taste, damaged tissue and appearance, and loss of nutritional value of exposed material. The common antioxidants employed in foods include Butylated hydroxytoluene (BHT), Butylated hydroxyanisole (BHA), Tert-butyl hydroquinone (TBHQ), and Propyl gallate (P.G.). Synthetic antioxidants have adverse effects such as causing mutation and carcinogenicity in the human body despite their high performance; hence, many studies have been carried out on replacing them with natural antioxidants. Phytochemicals and a widespread group of them known as polyphenols possess a high antioxidant activity. A major subset of polyphenols, Flavonoids, are secondary metabolites in plants with many applications. These compounds are potential antioxidants because of their capabilities, such as scavenging the free radicals donating hydrogen atoms, electrons, and chelate metal cations. The antioxidant mechanism of action of flavonoids is transferring hydrogen toward free radicals. Accordingly, the more the flavonoid structure makes the hydrogen transfer faster and easier, the more the flavonoid's antioxidant power will be. Therefore, the antioxidant activity of the flavonoids with hydroxy groups in their structure is higher among the different flavonoids.

**Conclusion:** Besides health promotion and some disease prevention effects, various *in vitro* studies have shown that flavonoids possess a high antioxidant activity that is competitive with synthetic antioxidants. However, for being commercially available, these compounds should have become extracted from a low price source with a high-performance method.

**Keywords:** antioxidant, flavonoids, food preservation, phytochemical, polyphenol,

### 1. INTRODUCTION

Most food products are made up of various chemical components that are easily oxidized. Lipids (fats, oils, and waxes) have the most significant potential to lose electrons in general. Lipid auto-oxidation in food products initiated by metal ions exposure, metallo-protein catalysts, light, heat, or ionizing radiation can deteriorate the color, flavor, texture, quality, and safety of food. Food fats are chemically made of triglycerides, and oxidation occurs at the unsaturated sites of the triglycerides, resulting in rancidity [1,2]. Free radicals are the most frequent oxidants in biological systems. Free radicals are atoms, molecules, or ions with one or more unpaired electrons, turning them to highly reactive and unstable. In order

to stabilize themselves, unpaired electrons in these free radicals seek out and acquire electrons from other substances. However, the first assault pairs the odd electron, another free radical is produced in the process, resulting in a chain reaction. The free radicals cause considerable damages to the macromolecules in organisms of bodies, including DNA, proteins, lipids, and carbohydrates. The damages caused by free radicals are also referred to as oxidative damages [3-6].

Free radicals are frequently derived from oxygen, nitrogen, and sulfur molecules in biological systems. These free radicals are constituents of the reactive oxygen species (ROS), reactive nitrogen species (RNS), and reactive sulfur species (RSS) molecular families. Free radicals such superoxide anion ( $O_2^{\bullet-}$ ), per hydroxyl radical ( $HO_2^{\bullet}$ ), hydroxyl radical ( $O.H^{\bullet}$ ), nitric oxide, and other species like hydrogen peroxide ( $H_2O_2$ ), singlet oxygen ( $O_2$ ), hypochlorous acid ( $HOCl$ ), and peroxyxynitrite ( $ONOO^-$ ) are forms of ROS. Nitric oxide is converted to RNS by reacting with  $O_2^{\bullet-}$  to generate  $ONOO^-$ . By reacting thiols with ROS, RSS is quickly produced. The production of ROS occurs as a result of cellular metabolism and functional activities [1,7].

Antioxidants are one of the factors which prevent oxidative damages. The structure of antioxidants is such that although they release hydrogen atoms, the reactivity of these atoms is extremely low [8]. In general, antioxidants are divided into synthetic and natural groups. Because synthetic antioxidants are cheaper and more accessible and show high efficiency and stability, they were gradually considered as alternatives to their natural type after World War II [9]. Phytochemical and among them the phenolic compounds are known to be the most important natural antioxidants, and they are recognized as excellent antioxidants due to their capacity of scavenging free radicals, donating hydrogen atoms, electrons, and chelate metal cations [10,11]. Nowadays, synthetic antioxidants are more commonly used in industries, the most common of which include Butylated hydroxytoluene (BHT), Butylated hydroxyanisole (BHA), Tert-butyl hydroquinone (TBHQ), and Propyl gallate (P.G.). Many other suggested compounds have antioxidant activity, but only a few can be used in foods. Ethoxyquin (EMQ) is a synthetic antioxidant with a non-phenolic structure, the use of which is not permitted for humans compared to other antioxidants mentioned earlier; however, it is used for food preservation in animal feeding [12]. The use of antioxidants in foods has been limited by the regulatory laws of one country or international standards [13], so the consumption of synthetic antioxidants is limited due to their toxic effects and carcinogenicity. Since the carcinogenicity of synthetic antioxidants has been observed, the necessity of using alternatives without adverse effects is becoming increasingly important [14]. Therefore, in recent years, the demand for natural antioxidants, especially plant origins, has increased because of growing concern among consumers about these synthetic antioxidants due to their toxicological effects [15-17]. Hence, this review has been conducted to investigate the antioxidant activity of phytochemicals, emphasizing *in vitro* studies to shed light on the potential of flavonoids to be utilized as natural antioxidants in food and examine their capability to substitute the synthetic antioxidants.

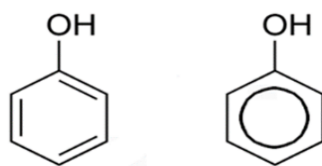
## 2. METHODOLOGY

This review has been conducted to investigate the antioxidant activity of phytochemicals, especially flavonoids, and their potential to entirely or partially substitute synthetic antioxidants in food products. All relevant databases were searched for the terms including 'phytochemical', 'polyphenol', 'flavonoid', 'natural additive', as well as 'antioxidant activity' combined with *in vivo* and *in vitro* phrases. It should also be mentioned that in the process of selecting relevant papers, priority was given to the research providing *in vitro* information regarding the antioxidant activity of phytochemicals. Data was collected through search using Scopus, Pubmed, Web of Science, Science Direct, Google Scholar databases, and related books and reliable websites, as well as prominent conferences and congresses with various publication dates ranging from 1981 to 2021.

### 3. DISCUSSION

Phytochemicals are chemical compounds and bioactive substances of plants that are naturally found in plants associated with biological activities beneficial for human health. These compounds are categorized by their chemical structures and include polyphenols (flavonoids and non-flavonoid polyphenols), carotenoids, phytosterols, betalains, and organosulfur. Phytochemical compounds cause the color, odor, and taste of plants to be changeless and play an important role in the plant defense system. More than 5000 pigments in plants are considered phytochemicals. These compounds can reveal their biological activity through various mechanisms such as antiviral, antibacterial properties, antioxidant, anti-inflammatory, anticancer, modulation of enzyme activities, stimulation of the immune system, gene expression, regulation of cholesterol synthesis, and blood pressure. They can also improve health and prevent diseases [18, 19]. Studies have shown that due to the presence of these compounds in the fruits and vegetables-rich diets, they can delay aging, reduce inflammation and the oxidative stress risk and also decrease the risk of chronic diseases such as cardiovascular diseases, arteriosclerosis, cancer, diabetes, cataract, neurological diseases, and disorders of the cognitive function [20-22]. Fruits, vegetables, legumes, and whole grains are the primary sources of phytochemicals in the diet [23]. There are different methods for extracting phytochemical compounds. These compounds can be extracted from plants through physical and chemical methods such as ultrasonication, super-critical fluid extraction, solvent extraction, and cold pressing [18, 24]. It should be pointed out that many phytochemicals are insoluble in aqueous solutions and do not have acceptable oil solubility. These compounds are chemically unstable and will decompose rapidly if being exposed to the external environment and adjacent to oxygen, temperature, light, pH, and some other reactive substances.

Phenolic compounds or polyphenols are important groups of phytochemical compounds in plants [25, 26]. Phenolic compounds have excellent antioxidant characteristics and are often found in fruits and vegetables [27]. These compounds include flavonoids, flavanols, anthocyanins, anthraquinones, benzoyl acetyl, and their derivatives. Polyphenols have two general classes, one is flavonoids, and the other is phenolic acids. Different parts of the plant produce compounds that are mainly phenolic and are known as natural antioxidants. Compounds such as flavonoids, coumarins, tocopherols, carotenoids, organic acids, and derivatives of cinnamic acid are phenolic antioxidants from the plant source. In this category of compounds, the hydroxyl group is directly bonded to an aromatic hydrocarbon [28]. There are at least 8000 known structures of phenolic compounds, the simplest of which is Phenol shown in Figure 1 [25]. Phenolic compounds are known for their antioxidant activity that depends on the structure, especially the number and location of hydroxyl groups and the nature of substituents in aromatic rings [29].



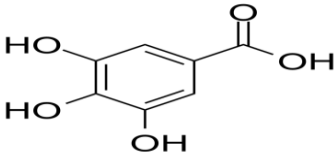
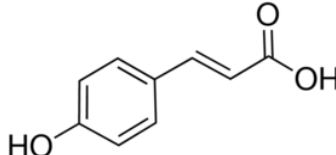
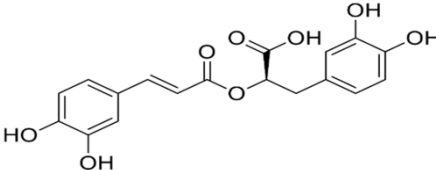
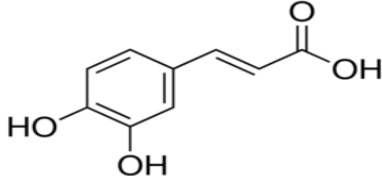
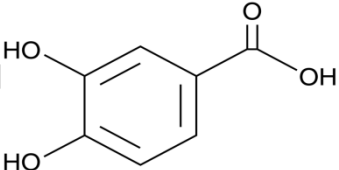
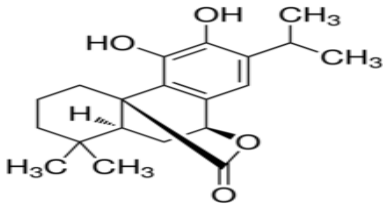
**Fig. 1. Phenol, the most straightforward component of phenolic compounds**

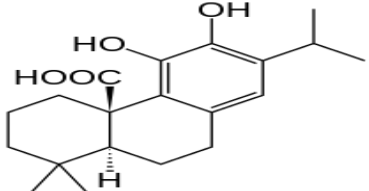
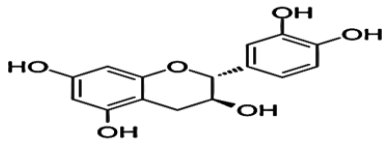
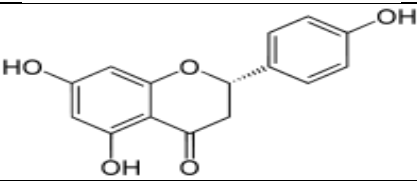
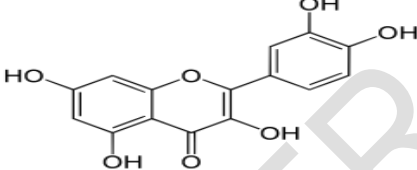
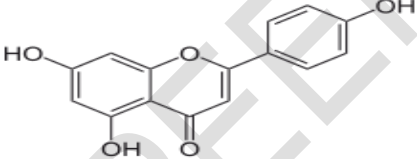
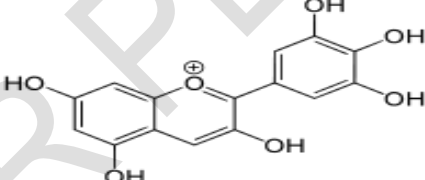
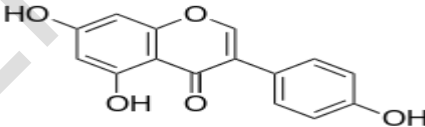
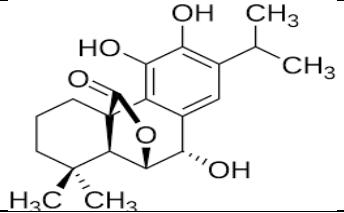
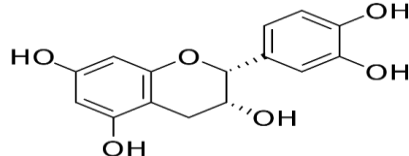
Phenolic compounds are referred to as health promotion compounds and have the capability of preventing chronic heart disease [30, 31]. The antioxidant characteristics of phenolic compounds depend on their capability of giving electrons to trap free radicals by the formation of stable phenoxyl compounds [32].

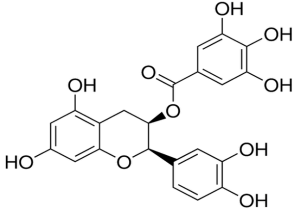
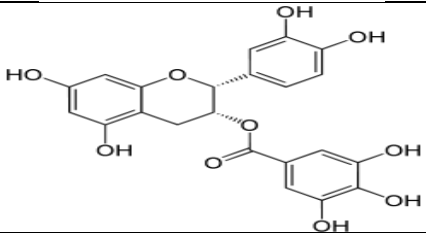
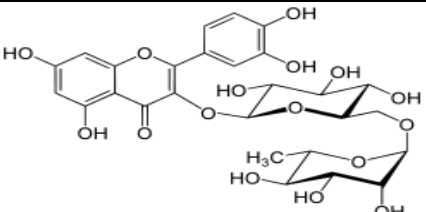
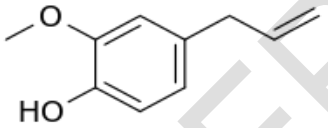
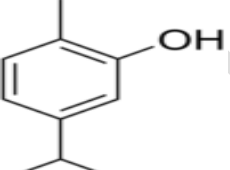
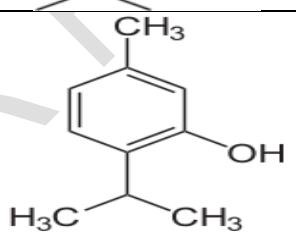
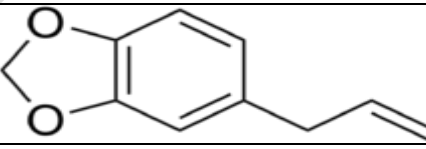
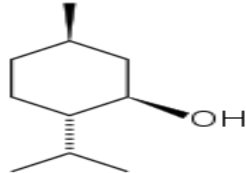
Plants have always been excellent food sources for the consumption of valuable bioactive compounds [33]. These natural antioxidants have been extracted from plants in the form of essential oils and

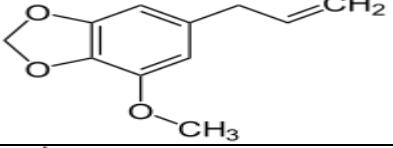

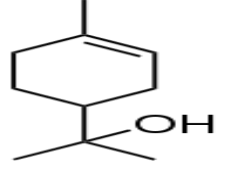
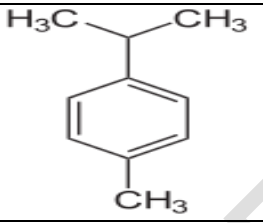
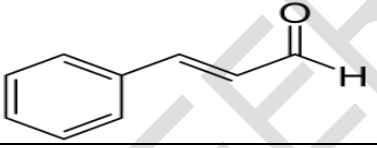
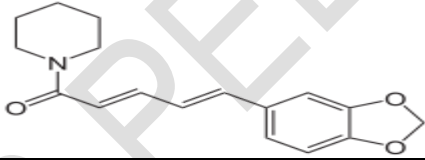
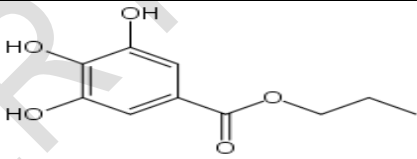
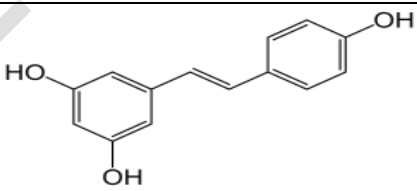
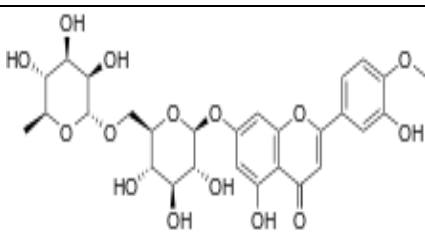
extract from various sources such as fruits (grapes, pomegranates, dates, kinnow), vegetables (broccoli, potatoes, drumstick, pumpkin, Indian turmeric, nettle), medicinal plants, and spices (tea, rosemary, oregano, cinnamon, common sage, thyme, peppermint, ginger, clove) and have been investigated for reducing fat oxidation [34-39]. Phenolic compounds are discovered in combination with saccharides (monosaccharides and polysaccharides) bonded to one or more phenolic groups. Although some phenolic compounds are ubiquitous, others are specific to particular plant families and are found in particular plant organs or at specific stages of plant growth [40]. Important phenolic compounds in plants that have been reported to possess antioxidant activity in *in vitro* and *in vivo* studies are listed in Table 1.

**Table 1. The phenolic compounds with high antioxidant activity**

Name	Chemical formula	Structure	Reference(s)
Gallic acid	$C_7H_6O_5$		Gallic acid prevents the melanogenesis, rancidity, and spoilage of fats and oils due to its antioxidant nature, facilitating its application as food additives in various eatable materials like baked goods, candy, chewing gums, and cosmetics [41,42].
p-Coumaric acid	$C_9H_8O_3$		p-coumaric acid occurs widely in the cell walls of graminaceous plants. It decreases low-density lipoprotein peroxidation, shows antioxidant and antimicrobial activities, and plays a vital role in human health. It is a good antioxidant and a good antimicrobial; therefore, it is a natural alternative instead of synthetic additives [43].
Rosmarinic acid	$C_{18}H_{16}O_8$		A significant number of herbal preparations and food supplements containing rosmarinic acid are marketed with claims for beneficial health effects. Due to lipid peroxidation and bacterial growth inhibition, Rosmarinic acid is approved for use as a natural antioxidant and/or preservative in the food industry [44].
Caffeic acid	$C_9H_8O_4$		Natural phenolic antioxidants, including caffeic and ferulic acids, gained attention as photoprotective agents. Caffeic acid is a $\alpha$ -tocopherol protective in low-density lipoprotein. Furthermore, their combination with other products, such as chlorogenic and caftaric acids, showed more potent antioxidant activity in various systems [45].
Protocatechuic acid	$C_7H_6O_4$		Protocatechuic acid is a type of widely distributed naturally occurring phenolic acid. Protocatechuic acid has structural similarities with gallic acid, caffeic acid, vanillic acid, and syringic acid, which are well-known antioxidant compounds. Hence, it could therefore be used in the pharmacological or food industry as a natural antioxidant [46].
Carnosol	$C_{20}H_{26}O_4$		Several <i>in vitro</i> studies were reviewed regarding the antioxidant activity of the carnosol and carnosic acid. Using the 2,2-diphenyl-1-picrylhydrazyl method, these bioactive compounds were validated for their antioxidant activity. Also, using the thiobarbituric acid, superoxide anion, and lipid-free radicals scavenging activity assays and Rancimat methods (determination of oxidative stability of fat), carnosol has been reported to inhibit lipid peroxidation

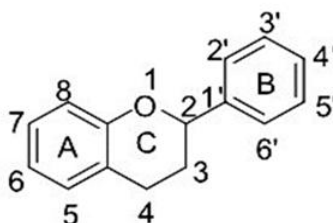
Carnosic acid	$C_{20}H_{28}O_4$		through the lipid-free radical scavenging mechanism. These studies have shown the antioxidant potential of carnosol and carnosic acid, whose properties are closely related to other biological activities, such as cytoprotective and anticancer, primarily due to their ability to neutralize reactive oxygen species [47].
Flavanol (catechin)	$C_{15}H_{14}O_6$		It has been revealed that catechin is antioxidant at all concentrations and attributed the antioxidant behavior to iron chelation. Consequently, catechin has been a widely used antioxidant in combination with other biopolymers for the development of active food packaging [48,49].
Flavanone (naringenin)	$C_{15}H_{12}O_5$		Naringenin has exhibited higher antioxidant capacity and hydroxyl and superoxide radical scavenger efficiency than naringin. Additionally, naringenin has shown greater effectiveness in the protection against oxidative damage to lipids in a dose-dependent manner [50].
Flavonol (quercetin)	$C_{15}H_{10}O_7$		Due to the capacity of quercetin to scavenge free radicals and bind transition metal ions, quercetin is considered a powerful antioxidant. Because of these qualities, quercetin can prevent lipid peroxidation [51].
Flavone (Apigenin)	$C_{15}H_{10}O_5$		Apigenin is a widely distributed flavonoid responsible for antioxidant potential and chelating redox-active metals. The antioxidant mechanism of apigenin includes oxidant enzymes inhibition, modulation of redox signaling pathways, reinforcing enzymatic and nonenzymatic antioxidants, metal chelation, and free radical scavenging [52].
Anthocyanin (delphinidin)	$C_{15}H_{11}O_7^+$		Anthocyanins are polyphenols with the known antioxidant activity which can be responsible for various biological activities. The antioxidant capacity of plant-derived anthocyanins has been demonstrated with various assay methods, including ORAC, FRAP, TEAC, and DPPH. [53].
Isoflavone (genistein)	$C_{15}H_{10}O_5$		Genistein has been widely studied as an antioxidant, with some research claiming that it may have the ability to scavenge reactive oxygen and nitrogen species (ROS and RNS) effectively [54].
Rosmanol	$C_{20}H_{26}O_5$		Comparison between rosmanol and synthetic antioxidants has shown that rosmanol possesses an antioxidant capacity four times higher than synthetic antioxidants of BRT and BRA [55].
Epicatechin	$C_{15}H_{14}O_6$		Catechin and epicatechin are two flavan-3-ol stereoisomers that, according to their structure, have comparable radical scavenging and antioxidant activity. Both have the ability to bind the iron ion and scavenge hydroxyl, peroxy, and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals [56].

Epicatechin gallate(ECG)	$C_{22}H_{18}O_{10}$		Evaluation of radical scavenging activity of some catechins <i>in vitro</i> revealed that in each of the assays, including DPPH, ABTS, and FRAP after epigallocatechin gallate, epicatechin gallate had the highest potential [57].
Epigallocatechin gallate (EGCG)	$C_{22}H_{18}O_{11}$		Epigallocatechin gallate effectively protected against supercoiled DNA nicking caused by peroxy and hydroxyl radicals. In scavenging the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical, epigallocatechin gallate had a synergistic impact with $\alpha$ -tocopherol, demonstrating a direct free radical scavenging potential [58].
Rutin	$C_{27}H_{30}O_{16}$		Rutin has exhibited strong DPPH radical scavenging activity. In addition, rutin possesses effective inhibition property of lipid peroxidation. The antioxidant activity of rutin is competitive with various antioxidants such as BHT and Vc (ascorbic acid) [59].
Eugenol	$C_{10}H_{12}O_2$		Antioxidant activity of eugenol has been evaluated with different assays such as DPPH, ABTS, and DMPD are competitive with inhibiting potential for lipid peroxidation of standard antioxidants including BHA, BHT, $\alpha$ -tocopherol, and Trolox [60].
Carvacrol	$C_{10}H_{14}O$		The antioxidant activity of carvacrol has been shown through a series of <i>in vitro</i> assays, including hydroxyl radical, superoxide, nitric oxide, DPPH, and ABTS radical scavenging assays [61].
Thymol	$C_{10}H_{14}O$		Different reports regarding antioxidant properties of thymol are due to its ability to donate H-atoms from phenol hydroxyl groups, which could react with peroxy radicals to produce stabilized phenoxyl radicals and, consequently, terminate lipid peroxidation chain reactions [62].
Safrole	$C_{10}H_{10}O_2$		The antioxidant activity of safrole oil has been reported to be comparatively lower than the Trolox reference standard, which is known to have high antioxidant activity. However, free radicals scavenging activity of safrole is still considered eminent [63]
Menthol	$C_{10}H_{20}O$		Different studies have reported that the antioxidant activity of some of the plant-derived essential oils is related to menthol; for instance, the radical scavenging activity of peppermint essential oil is associated with the presence of menthol and menthone, which contains the hydroxyl radical ( $\cdot$ O.H.) [64, 65].

Myristicin	$C_{11}H_{12}O_3$		While evaluating the myristicin with DPPH and ABS methods revealed its antioxidant activity inadequacy compared to BHA, the synergetic effect of myristin with other antioxidants can be considered [66].
Eucalyptol	$C_{10}H_{18}O$		Previous researches have shown that there might be a direct relationship between the high scavenging activity of essential oil over BHT and the high content of Eucalyptol in the essential oil [67, 68].
Terpineol	$C_{10}H_{18}O$		Due to various biological activities, terpineol is a proper compound to be improved the shelf life of food products, as it has been shown to be effective for enhancing the antioxidant activity of chitosan biopolymer to inhibit free radicals mediated deterioration [69].
<i>p</i> -Cymene	$C_{10}H_{14}$		Previous investigations on DPPH free radical scavenging by some plant-derived essential oils have revealed that <i>p</i> -Cymene, as one of the main constituents, plays a prominent role in the antioxidant activity of the essential oils [70].
Cinnamaldehyde	$C_9H_8O$		Cinnamaldehyde enhances the antioxidant defense against reactive oxygen species and reduces the levels of lipid peroxidation products, and increases the activities of antioxidant enzymes [71].
Piperine	$C_{17}H_{19}NO_3$		Piperine interacts readily with highly oxidizing radicals and binds redox-active metal ions, indicating that it could potentially function as an effective antioxidant [72].
Propyl gallate	$C_{10}H_{12}O_5$		As it has become determined by free radical scavenging assays, the propyl gallate compound has the potential to inhibit lipid oxidation which is competitive with TBHQ [73].
Resveratrol	$C_{14}H_{12}O_3$		In different studies, resveratrol has exhibited a robust reducing power, chelating activity on $Fe^{2+}$ , free radical-scavenging, hydrogen peroxide scavenging, and hydroxyl radical scavenging activities [74].
Diosmin	$C_{28}H_{32}O_{15}$		The <i>in vitro</i> studies on diosmin showed its free radical scavenging activity. The hydroxyl free radical scavenging and superoxide free radical scavenging activities of diosmin have been evidenced by the <i>in vitro</i> studies [75].

### 3.1 The Structure of Flavonoids and Their Antioxidant Activity

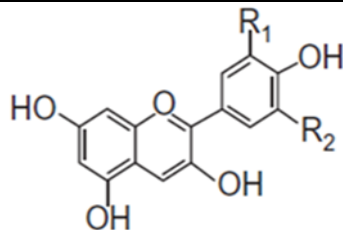
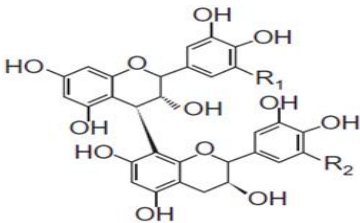
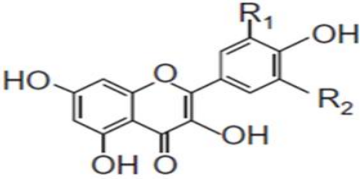
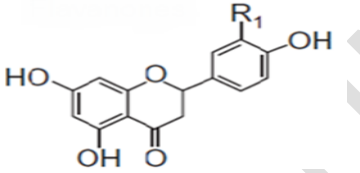
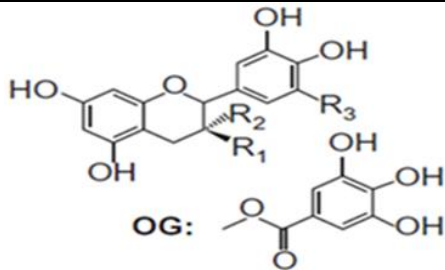
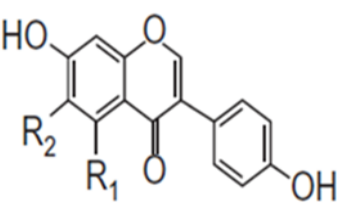
Flavonoids are the largest group of phytochemicals and are also considered as the most widespread group of polyphenols found in fruits and vegetables. Flavonoids have excellent antioxidant properties and can exhibit their antioxidant activity by scavenging free radicals and reactive oxygen species, chelating the metals, and preventing the oxidation of low-density lipoproteins (LDLs) [27, 76]. Flavones are the most basic structures of flavonoids. From the structural point of view, all flavonoids possess a C6-C3-C6 carbon skeleton in which the carbon atoms are arranged in three phenolic rings A, B, and C, and the C ring normally contains oxygen [77, 78]. Figure 2 indicates a Phenylbenzopyrane as the basic structure of flavonoids.



**Fig. 2 basic structure of flavonoids (Phenylbenzopyrane)**

Flavonoids have different families, each of which has different members. The flavonoid families include Flavones, Isoflavones, Flavonols, Flavanones, Dihydroflavonols, Flavan-3-ols (monomers), Proanthocyanidins (oligomeric flavan-3-ols), and Anthocyanidins. These families, along with their members, are shown in Table 2 [79].

Table 2. Flavonoids family

Primary structure		R groups alterations		
Anthocyanidins				
	R1	R2		
	Pelargonidin	H	H	
	Cyanidin	OH	H	
	Delphinidin	OH	OH	
	Peonidin	OCH3	H	
	Petunidin	OCH3	OH	
Malvidin	OCH3	OCH3		
Proanthocyanidins (oligomeric flavan-3-ols)				
	R1	R2		
	Procyanidin B1 EC (4b-8)-C	H	H	
	Prodelfinidin B1 EGC-(4b-8)-GC	OH	OH	
Flavonols				
	R1	R2		
	Kaempferol	H	H	
	Quercetin	OH	H	
	Myricetin	OH	OH	
Flavanones				
	R1			
	Naringin	H		
	Eriodictyol	OH		
	Hesperetin	OCH3		
Flavan-3-ols (monomers)		R1	R2	R3
	(+)Catchin	OH	H	H
	(-)Epicatechin	H	OH	H
	(+)Gallocatechol	OH	H	OH
	(-)Epigallocatechin	H	OH	OH
	(+)Catechin gallate	OG	H	H
	(-)Epigallocatechin gallate	H	OG	H
	(+)Gallocatechin gallate	OG	H	OH
	(-)Epigallocatechin gallate	H	OG	OH
Isoflavones		R1	R2	
	Daidzein	H	H	
	Genistein	OH	H	
	Glycitein	H	OCH3	

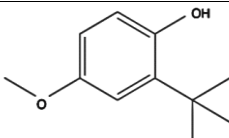
## 3.2 Regulations Regarding Synthetic and Natural Antioxidants

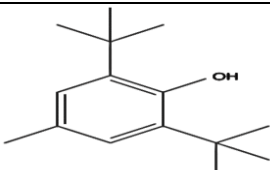

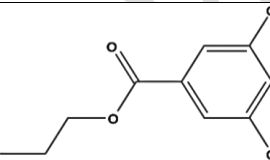
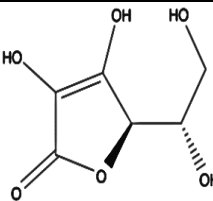
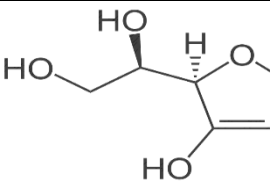
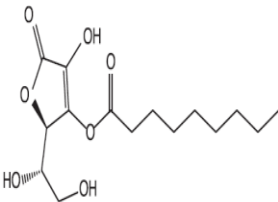
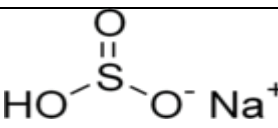
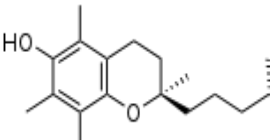
Many scientists claim that there should be a shift away from synthetic antioxidants due to the growing interest in natural food antioxidants; however, it has not yet occurred, and thus the natural or synthetic origin of the various antioxidants currently used in the food industry is not specified in the official tables showing the amounts and permissions for the use of each additive in each type of food [80]. The Codex Alimentarius Commission is the worldwide standard-setting authority in charge of regulating and establishing the framework of food regulations that guide the use of antioxidants in foods. Since food regulatory systems and legal frameworks in respect to the use of antioxidants as food additives differ by country, these criteria are neither required nor immediately applicable [81]. The European Food Safety Authority (EFSA) of the European Union and the Food and Drug Administration (FDA) of the United States of America are the two primary guiding authorities in charge of regulating the licensing of food additives across the world [82]. Under the E.U., regulation E.C. No 1129/2011 specifies a list of antioxidants, categorized according to their E-numbers, that are regulated in the section of "other food additives." The natural antioxidants recognized as food additives by the E.U. include rosemary extracts (E392), ascorbic acid (E300), and tocopherols (E306–E309), according to this regulation [83]. Food products and ingredients are monitored by various authorities in the United States of America, the most relevant of which is the U.S. Food and Drug Administration (FDA). The FDA's regulations for food items are listed in Title 21 of the Code of Federal Regulations of the United States. There is no distinct category for natural antioxidants in the Code of Federal Regulations (21 CFR 182; 21 CFR 172), as there is in European regulations [84–86]. Although natural antioxidants such as ascorbic acid and tocopherols are specifically designated for use in food, the U.S. regulation is far more comprehensive than the European one and includes additional substances that fall into other categories yet have demonstrated antioxidant activity. Several of the compounds allowed for use as coloring adjuncts, spices, or natural flavorings, such as flavonoids like phloretin glycoside, carotenoids like carotene and astaxanthin, or extracts of rosemary or sage, have recognized the antioxidant potential. In the case of phloretin, astaxanthin, and sage extract are not listed as food additives in any category in E.U. regulations, although they are classified for technical applications in U.S. standards [87, 88]. Considering the mentioned regulations, it is evident that regardless of utilization of natural or synthetic antioxidants, the optimal choice of antioxidant for each food matrix should be determined on a case-by-case basis, as *in vitro* antioxidant activities are not always reproduced in the food, and there are frequent changes due to food processing or interactions with other food matrix components that have antioxidant or prooxidant activities [89].

## 3.3 Antioxidants in Food Preservation

Once lipid oxidation in a food matrix is analyzed over time, there is frequently a lag phase during which the deposition of lipid oxidation by-products is moderate. This lag phase is associated with the presence of antioxidants in the food matrix, which limit the synthesis of free radicals that target fatty acids, as well as the low free radical generation that precedes the concentration of hydroperoxides and  $\beta$ -scission reactions [80]. The objective of the food industry is to extend the lag period during which the concentrations of the components that cause rancidity taste are below human detection limits. When the food matrix lacks natural antioxidants and/or includes significant endogenous prooxidants, the most typical technique employed by food manufacturers to limit oxidation is to add antioxidants directly to the food matrix [89]. In the context of food science, the phrase "antioxidant" refers to substances that prevent lipid peroxidation and other oxidative reactions, hence preserving the freshness and shelf-life extension of foods. The method of action is the same whether the antioxidant is natural or synthetic, and it comprises free radical scavenging, metal chelating, and singlet oxygen quenching [90, 91]. Due to their stability, low cost, and wide availability, synthetic antioxidants are frequently employed. Phenolic antioxidants are the most extensively used synthetic antioxidants in the food industry, with Butylated hydroxyanisole (BHA) (E320), Butylated hydroxytoluene (BHT) (E321), Propyl gallate (P.G.) (E310), and Tert-butyl hydroquinone (TBHQ) (E319) being the most common. In table 3, some critical information regarding the chemical structure as well as health-related concerns about the consumption of these antioxidants has been revealed [80, 92–101]. Despite the fact that these synthetic antioxidants are widely used and tightly regulated, there are concerns about their safety owing to overdose usage and/or misuse; for instance, combining various antioxidants may exacerbate their toxic effects. High concentrations of chemical synthetic antioxidants may induce DNA damage or *in vitro* toxicity in some tissues [102–105]. The food industry is attempting to reduce the use of synthetic compounds by substituting natural alternatives in response to consumer concerns that they are being exposed to potentially toxic chemical synthetic compounds through their regular diet. Though, just because plant antioxidants are natural, it does not mean they are safe by default; toxicity tests are always required for each case [102].

**Table 3. Chemical structures of food industry antioxidants**

Antioxidants	Molecular formula	Carcinogenic potential	Allergenic potential	Chemical structures
Butylated hydroxyanisole (BHA)	$C_{11}H_{16}O_2$	Category 1 (use within limit on body = 5.2 % w/w; face >100% w/w; hands >100 % w/w)	Moderate sensitizer (max dose = 0.0729 $\mu\text{g}/\text{cm}^2/\text{hr}$ )	
		Acceptable daily intake (ADI)*: below 1.0 mg/kg body weight		

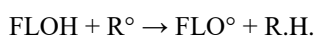
Butylated Hydroxytoluene (BHT)	C <sub>15</sub> H <sub>24</sub> O	–	Weak sensitizer (max dose = 14.6 µg/cm <sup>2</sup> /hr)	
		Acceptable daily intake (ADI): 0.25 mg/kg body weight		
tert-Butylhydroquinone (TBHQ)	C <sub>10</sub> H <sub>14</sub> O <sub>2</sub>	–	–	
		Acceptable daily intake (ADI): 0.7 mg/kg body weight		
Propyl Gallate (P.G.)	C <sub>10</sub> H <sub>12</sub> O <sub>5</sub>	–	Moderate sensitizer (max dose = 0.0255 µg/cm <sup>2</sup> /hr)	
		Acceptable daily intake (ADI): 0.5 mg/kg body weight		
Ascorbic Acid (Vitamin C)	C <sub>6</sub> H <sub>8</sub> O <sub>6</sub>	Category 3 (use with precaution)	–	
		Acceptable daily intake (ADI): there is no safety concern for the use of ascorbic acid (E300), sodium ascorbate (E301), and calcium ascorbate (E302) as food additives at the reported uses and use levels, and there is no need for a numerical ADI for ascorbic acid and its salts.		
Erythorbic acid	C <sub>6</sub> H <sub>8</sub> O <sub>6</sub>	–	–	
		Acceptable daily intake (ADI): 6 mg/kg body weight		
Ascorbyl Palmitate	C <sub>22</sub> H <sub>38</sub> O <sub>7</sub>	–	Weak sensitizer (max dose = 7.29 µg/cm <sup>2</sup> /hr)	
		Acceptable daily intake (ADI): considering the available data, the Panel concluded that there is no safety concern for the use of ascorbyl palmitate (E304(i)) and ascorbyl stearate (E304(ii)) as food additives at the reported uses and use levels		
Sodium bisulfite	NaHSO <sub>3</sub>	–	–	
		Acceptable daily intake (ADI): 0.7 mg SO <sub>2</sub> equivalent/kg body weight		
alpha-tocopherol	C <sub>29</sub> H <sub>50</sub> O <sub>2</sub>	–	–	
		Acceptable daily intake (ADI): 11-13 mg/kg body weight		

\*Mentioned quantities are specified for adults. For more details or quantity for a specific age group, please refer to the released document at [European Food Safety Authority](#).

### 3. 4 The Structure of Flavonoids and Their Antioxidant Properties

Flavonoids are active polyphenol compounds that are found in almost all fruits and vegetables. Aglycones, glycosides, and methylated derivatives are different forms of flavonoids. Aglycones are produced when the glycosyl group in a glycoside is replaced by a hydrogen atom. Glycosides are composed of two parts — sugars (glycons) and non-sugars (aglycones) — and play different roles in plants [6]. Various species of flavonoids differ in terms of oxidation rate and C-ring substituent; in other words, the presence of one double bond, one carbonyl group, and one hydroxy group in the pyranil C ring is used to classify them into species and subspecies.

The substituents of A and B rings with hydroxy groups are used to identify the available members in a species. Flavonoids in plants are often derived from glycosylate and play a role in the production of shining blue, reddish-yellow, and reddish-orange shades in leaves, flowers, and fruits. Regardless of the variety of fruits and vegetables, flavonoids are found in seeds, nuts, buds, spices, herbal medications, and some drinks such as wine, especially red and tea wines, and in smaller quantities in beer. The antioxidant properties are among the most important properties of flavonoids. Flavonoids are highly effective antioxidants in general, and it has been observed that they protect the body against cardiovascular diseases by reducing the oxidation of low-density lipoproteins (LDLs). In many studies, flavonoid-rich plant extracts have been used to prevent food oxidation [7]. Despite the many benefits of synthetic antioxidants compared to natural ones, such as their low prices, the use of antioxidants in food has been limited by regulatory laws of one country or international standards [13]. Hence, the use of synthetic antioxidants is limited due to their toxic effects and carcinogenicity. Synthetic antioxidants have a limit of using 0.02% fat of food [6]. Since the carcinogenic properties of synthetic antioxidants have been observed, the necessity of the use of alternatives without adverse effects has become increasingly important [14]. Therefore, in recent years, the demand for natural antioxidants, especially of plant origin, has increased due to the increasing concern among consumers about these synthetic antioxidants considering potential toxicological effects [17]. As a whole, flavonoids are highly effective antioxidants, and there are pieces of evidence that they protect the body against cardiovascular diseases by reducing the oxidation of low-density lipoproteins (LDLs). Flavonoids both prevent lipid peroxidation and act as scavengers of radicals such as superoxides, lipid peroxy, and hydroxyls, and also lead to inactivation of single oxygen molecules and prevention of the activity of lipooxygenases. The high potency of flavonoids in inhibiting free radicals relates to their ability to transfer a hydrogen atom from a hydroxy group to the free radical and ultimately stabilize it:



Flavones and catechins are the most powerful flavonoids with antioxidant properties that can protect the body against reactive oxygen species (ROS). According to many studies, the free radical scavenging activity for flavonoids has been reported as the following [6, 106]:

Myricetin > quercetin > rhamnetin > morin > diosmetin > naringenin > apigenin > catechin > 5,7-Dihydroxy-3,3',4'-trimethoxyflavone > robinin > kaempferol > flavone

Different factors affect the antioxidant properties of flavonoids. One of the most important factors is the structure of flavonoids. The presence of hydroxyl and glycosylated groups has a significant effect on the antioxidant properties of flavonoids. The presence of glycosylated groups reduces the antioxidant properties of flavonoids. On the other hand, the presence of hydroxy groups increases the antioxidant properties of flavonoids. For maximum free radical scavenging activity, flavonoids must have a hydroxy group at the 4' and 3' positions of the B ring, a conjugated double bond between carbon 2 and 3, an Oxo group at the 4 position of the C ring, a hydroxy group on carbon 3 in the C ring, and a hydroxy group on carbon 5 in the A ring (refer to Figure 2). Flavonoids, along with their hydroxy groups, act as free radical scavengers, and the presence of many hydroxy groups, especially in the B ring, increases their antioxidant activity. The hydroxyls of the B ring are the first active stations in traversing the oxidation chain. The three structural groups are responsible for determining the scavenging activity of free radicals and antioxidant activity of flavonoids: a catechol section in the B ring, a conjugated double bond at the positions 2 and 3, an oxo group with the carbonyl group function in the ring C, and the presence of hydroxy groups at the positions 3 and 5 [106, 107]. Thus, it is noteworthy that flavonoids can exhibit different antioxidant activities according to their structure.

Flavonoids are classified as non-nutrients in the scientific food realm. They have typically been eliminated from food crops because of their inhibitory effects on digestive enzymes, astringency and bitterness, and poor absorption after intake. However, as a result of their inclusion in regular meals, several therapeutic benefits such as antioxidant properties in animal studies, the decrease of cardiovascular disease and high blood pressure, and antiallergic, anti-inflammatory, and anti-diabetic activities were recognized. As a result, flavonoids are now considered third-order functional components (food factors) that have biological regulatory roles [108]. Flavonoids are also important in food preservation and industry. The phrase "sustainable intensification" was created by the Royal Society of London, which denotes current agricultural practices aiming at raising food production while also safeguarding biodiversity and environmental processes. Food waste minimization is one of the most critical elements of "sustainable intensification." As a result, there is a growing demand for postharvest storage technology and food preservatives research [109, 110]. Since today's consumers are concerned about the usage of chemically synthesized preservatives, natural products are being prioritized. At the same time, industries are putting a greater focus on the usage of plant-derived antioxidant and antibacterial components to improve shelf life. In this setting, the antioxidant activity of flavonoids may not only preserve food stability over time but also provide protection against necrotrophic fungi and food-borne diseases. The antioxidant mechanism of flavonoids in food systems is mainly connected to their capacity to prevent lipid autooxidation, which is a primary cause of food quality degradation and shelf-life reduction [111]. Flavonoids can donate hydrogen atoms to lipid radicals, resulting in more stable antioxidant radicals that are less susceptible to autooxidation. Antioxidant action mechanisms of flavonoids include direct scavenging of ROS, inhibition of ROS formation via chelation of trace elements (e.g., quercetin has iron-chelating and iron-stabilizing properties), or inhibition of free radical-generating enzymes (e.g., glutathione S-transferase, microsomal monooxygenase, mitochondrial succinoxidase, NADH oxidase), and activation of antioxidant defenses (e.g., upregulation of antioxidant enzymes with radical scavenging ability). A synergy of some of these mechanisms, such as radical

scavenging activity along with some enzyme function inhibition, may also occur [112-114]. The capacity of flavonoids to lower the susceptibility of fresh fruits and vegetables to particular postharvest infections may also contribute to their antioxidant effect in extending shelf life [109, 115]. Flavonoids, exceptionally high hydroxylated anthocyanins, can prevent the growth of grey mold (produced by *Botrytis cinerea*), causing the dynamics of the ROS burst to be disrupted during infection. Flavonoids may bind and inactivate proteins and may form complexes with bacterial cell walls, giving them antibacterial action against a variety of pathogens [116-118]. Flavonoids have been employed in a variety of dietary applications due to their beneficial characteristics. They have been used as active antioxidant materials in the packaging of oxygen-sensitive foods to extend shelf life and improve bioactive component content [119]. They have also been used to minimize lipid oxidation in cooked pork patties and raw mackerel fillets [120]. Considering all mentioned information regarding the antioxidant potential of flavonoids, it is evident that, besides their health-promoting effects, they can be utilized as food additives to extend their shelf life.

## 4. CONCLUSION

As one of the significant subgroups of polyphenols, flavonoids are crucial secondary chemicals known as phytochemicals generated by plants that serve a variety of activities, including growth and development and stress resistance. The high demand and interest in the utilization of flavonoids in food processing, as well as their health-promoting effects, has resulted in the increased acknowledgment of positive aspects of flavonoids for human health. It is evident that as an important subset of the phytochemicals family, flavonoids possess a considerable antioxidant activity that is competitive with synthetic antioxidants. Flavonoids are abundant in vegetables, flowers, and seeds, and approaches to extract these compounds from these natural sources have been developed for use as food additives and preservatives. However, on a commercial scale, the extraction of flavonoids directly from the mentioned sources does not seem to be profitable. Hence, it seems that attempting to find a proper source for extraction, such as plant wastes as well as designing a high-performance extraction method, would be a critical step for these compounds to be applied on food products as preservatives.

## REFERENCES

1. Atta EM, Mohamed NH, Silaev AA. Antioxidants: An overview on the natural and synthetic types. *European Chemical Bulletin*. 2017;6(8):365-75. <https://doi.org/10.17628/ecb.2017.6.365-375>
2. Latifi Z, Khesht SG, Daneshniya M. Detection of olive oil adulteration in terms of monitoring the U.V. and I.R. spectral patterns during thermal oxidation. 4th International Conference on Applied Researches in Science & Engineering At: Vrije Universiteit-Brussel. 2019. <https://en.civilica.com/doc/1000635/>
3. Halliwell B. Free radicals and antioxidants: updating a personal view. *Nutrition reviews*. 2012 May 1;70(5):257-65. <https://doi.org/10.1111/j.1753-4887.2012.00476.x>
4. Traystman RJ, Kirsch JR, Koehler RC. Oxygen radical mechanisms of brain injury following ischemia and reperfusion. *Journal of Applied Physiology*. 1991 Oct 1;71(4):1185-95. <https://doi.org/10.1152/jappl.1991.71.4.1185>
5. Nogala-Kalucka M, Korczak J, Dratwia M, Lampart-Szczapa E, Siger A, Buchowski M. Changes in antioxidant activity and free radical scavenging potential of rosemary extract and tocopherols in isolated rapeseed oil triacylglycerols during accelerated tests. *Food Chemistry*. 2005 Nov 1;93(2):227-35. <https://doi.org/10.1016/j.foodchem.2004.09.021>
6. Daneshniya M, Maleki MH, Liavali H, Hassanjani M, Keshavarz Bahadori N, Mohammadi M, Jalilvand Nezhad H. Antioxidant activity of flavonoids as an important phytochemical compound in plants. In *Proceedings of the 2nd International Congress on Engineering, Technology and Innovation*, Darmstadt, Germany 2020.
7. Daneshniya M, Maleki MH, Liavali HM, Hassanjani MR. Phenolic compounds extracted from plants as potential antioxidants. In *Proceedings of the 2<sup>nd</sup> International Congress on Engineering, Technology and Innovation*, Darmstadt, Germany 2020.
8. Pokorný J. Are natural antioxidants better—and safer—than synthetic antioxidants?. *European journal of lipid science and technology*. 2007 Jun;109(6):629-42. <https://doi.org/10.1002/ejlt.200700064>
9. Halliwell B, Murcia MA, Chirico S, Aruoma OI. Free radicals and antioxidants in food and in vivo: what they do and how they work. *Critical Reviews in Food Science & Nutrition*. 1995 Jan 1;35(1-2):7-20. <https://doi.org/10.1080/10408399509527682>
10. Afanas' ev IB, Dcrozsko AI, Brodskii AV, Kostyuk VA, Potapovitch AI. Chelating and free radical scavenging mechanisms of inhibitory action of rutin and quercetin in lipid peroxidation. *Biochemical pharmacology*. 1989 Jun 1;38(11):1763-9. [https://doi.org/10.1016/0006-2952\(89\)90410-3](https://doi.org/10.1016/0006-2952(89)90410-3)
11. latifi Y, Chaharlang M, Daneshniya M, khaki Arani S, Barzаноoni M, Boghori P. Antioxidant and antimicrobial properties of methanolic extract of green walnut skin. *FSCT*. 2021; 17 (108) :127-136 <https://doi.org/10.52547/fsct.17.108.127>

12. Latifi Z, Daneshniya M, Khademi F. Effect of preservative of Anarijeh (*Froriepia subpinnata*) extract on shelf life of silver carp fish (*Hypophthalmichthys molitrix*) at superchilling temperature (-3 °C). In Proceedings of the 4th International Conference on Applied Researches in Science and Engineering 2019. <https://en.civilica.com/doc/1000639/>
13. Dorman HD, Bachmayer O, Kosar M, Hiltunen R. Antioxidant properties of aqueous extracts from selected Lamiaceae species grown in Turkey. *Journal of Agricultural and Food Chemistry*. 2004 Feb 25;52(4):762-70. <https://doi.org/10.1021/jf034908v>
14. Ardabili AG, Farhoosh R, Khodaparast MH. Frying stability of canola oil in presence of pumpkin seed and olive oils. *European journal of lipid science and technology*. 2010 Aug;112(8):871-7. <https://doi.org/10.1002/ejlt.200900257>
15. Formanek Z, Kerry JP, Higgins FM, Buckley DJ, Morrissey PA, Farkas J. Addition of synthetic and natural antioxidants to  $\alpha$ -tocopheryl acetate supplemented beef patties: effects of antioxidants and packaging on lipid oxidation. *Meat science*. 2001 Aug 1;58(4):337-41. [https://doi.org/10.1016/S0309-1740\(00\)00149-2](https://doi.org/10.1016/S0309-1740(00)00149-2)
16. Biswas AK, Keshri RC, Bisht G.S. Effect of enrobing and antioxidants on quality characteristics of precooked pork patties under chilled and frozen storage conditions. *Meat science*. 2004 Mar 1;66(3):733-41. <https://doi.org/10.1016/j.meatsci.2003.07.006>
17. Jayathilakan K, Sharma GK, Radhakrishna K, Bawa AS. Antioxidant potential of synthetic and natural antioxidants and its effect on warmed-over-flavour in different species of meat. *Food Chemistry*. 2007 Jan 1;105(3):908-16 <https://doi.org/10.1016/j.foodchem.2007.04.068>
18. Puri M, Sharma D, Barrow CJ. Enzyme-assisted extraction of bioactives from plants. *Trends in biotechnology*. 2012 Jan 1;30(1):37-44. <https://doi.org/10.1016/j.tibtech.2011.06.014>
19. Yadav RN, Agarwala M. Phytochemical analysis of some medicinal plants. *Journal of phytochemistry*. 2011 Dec 14;3(12). <https://updatepublishing.com/journal/index.php/jp/article/view/2737>
20. Eliassen AH, Hendrickson SJ, Brinton LA, Buring JE, Campos H, Dai Q, Dorgan JF, Franke AA, Gao YT, Goodman MT, Hallmans G. Circulating carotenoids and risk of breast cancer: pooled analysis of eight prospective studies. *Journal of the National Cancer Institute*. 2012 Dec 19;104(24):1905-16. <https://doi.org/10.1093/jnci/djs461>
21. Pojer E, Mattivi F, Johnson D, Stockley CS. The case for anthocyanin consumption to promote human health: a review. *Comprehensive Reviews in Food Science and Food Safety*. 2013 Sep;12(5):483-508. <https://doi.org/10.1111/1541-4337.12024>
22. Tanaka T, Shnimizu M, Moriwaki H. Cancer chemoprevention by carotenoids. *Molecules*. 2012 Mar;17(3):3202-42. <https://doi.org/10.3390/molecules17033202>
23. Tokusoglu Ö, Hall III CA, editors. *Fruit and cereal bioactives: sources, chemistry, and applications*. 1st ed. CRC press; 2011 Mar 14. <https://doi.org/10.1201/b10786>
24. Latifi, Z., Sadeghi, F., Azizi, J., Daneshniya M., Measuring of phytochemical and antioxidant compounds and identification of main phenolic compound in Anarijeh plant (*Froriepiasubpinnata*) extract by RPHPLC method. 13<sup>th</sup> International Conference on Engineering & Technology, Norway. 2019.
25. Bravo L. Polyphenols: chemistry, dietary sources, metabolism, and nutritional significance. *Nutrition reviews*. 1998 Nov 1;56(11):317-33. <https://doi.org/10.1111/j.1753-4887.1998.tb01670.x>
26. Daneshniya M, Maleki MH, Mohammadi MA, Ahangarian K, Kondeskalaei VJ, Alavi H. Antioxidant and Antimicrobial Activity of *Ferula* Species' Essential Oils and Plant Extracts and their Application as the Natural Food Preservatives. *South Asian Research Journal of Natural Products*. 26Apr.2021; 4(3):1-23. Available from: <https://www.journalsarjnp.com/index.php/SARJNP/article/view/30133>
27. Heim KE, Tagliaferro AR, Bobilya DJ. Flavonoid antioxidants: chemistry, metabolism and structure-activity relationships. *The Journal of nutritional biochemistry*. 2002 Oct 1;13(10):572-84. [https://doi.org/10.1016/S0955-2863\(02\)00208-5](https://doi.org/10.1016/S0955-2863(02)00208-5)
28. Amorati R, Valgimigli L. Modulation of the antioxidant activity of phenols by non-covalent interactions. *Organic & biomolecular chemistry*. 2012;10(21):4147-58. <https://doi.org/10.1039/C2OB25174D>
29. Balasundram N, Sundram K, Samman S. Phenolic compounds in plants and agri-industrial by-products: Antioxidant activity, occurrence, and potential uses. *Food chemistry*. 2006 Jan 1;99(1):191-203. <https://doi.org/10.1016/j.foodchem.2005.07.042>
30. Harborne JB, Williams CA. Advances in flavonoid research since 1992. *Phytochemistry*. 2000 Nov 1;55(6):481-504. [https://doi.org/10.1016/S0031-9422\(00\)00235-1](https://doi.org/10.1016/S0031-9422(00)00235-1)
31. Holtekjølen AK, Bævre AB, Rødbotten M, Berg H, Knutsen SH. Antioxidant properties and sensory profiles of breads containing barley flour. *Food chemistry*. 2008 Sep 15;110(2):414-21. <https://doi.org/10.1016/j.foodchem.2008.02.054>
32. Lam RY, Woo AY, Leung PS, Cheng CH. Antioxidant actions of phenolic compounds found in dietary plants on low-density lipoprotein and erythrocytes in vitro. *Journal of the American College of Nutrition*. 2007 Jun 1;26(3):233-42. <https://doi.org/10.1080/07315724.2007.10719606>

33. Tayel AA, EL-TRAS WF. Plant extracts as potent biopreservatives for *Salmonella typhimurium* control and quality enhancement in ground beef. *Journal of Food Safety*. 2012 Feb;32(1):115-21. <https://doi.org/10.1111/j.1745-4565.2011.00357.x>
34. Devatkal SK, Narsaiah K, Borah A. Anti-oxidant effect of extracts of kinnow rind, pomegranate rind and seed powders in cooked goat meat patties. *Meat Science*. 2010 May 1;85(1):155-9. <https://doi.org/10.1016/j.meatsci.2009.12.019>
35. Huang B, He J, Ban X, Zeng H, Yao X, Wang Y. Antioxidant activity of bovine and porcine meat treated with extracts from edible lotus (*Nelumbo nucifera*) rhizome knot and leaf. *Meat science*. 2011 Jan 1;87(1):46-53. <https://doi.org/10.1016/j.meatsci.2010.09.001>
36. Wójciak KM, Dolatowski ZJ, Okoń A. The effect of water plant extracts addition on the oxidative stability of meat products. *Acta Scientiarum Polonorum Technologia Alimentaria*. 2011 Jun 30;10(2):175-88. [https://www.food.actapol.net/pub/4\\_2\\_2011.pdf](https://www.food.actapol.net/pub/4_2_2011.pdf)
37. Das AK, Rajkumar V, Verma AK, Swarup D. Moringa oleifera leaves extract: a natural antioxidant for retarding lipid peroxidation in cooked goat meat patties. *International journal of food science & technology*. 2012 Mar;47(3):585-91. <https://doi.org/10.1111/j.1365-2621.2011.02881.x>
38. Latifi Z, Daneshniya M, Khademi F. Effect of preservative of Anarijeh (*Fraxinus subpinnata*) extract on shelf life of silver carp fish (*Hypophthalmichthys molitrix*) at superchilling temperature (-3 °C). In *Proceedings of the 4th International Conference on Applied Researches in Science and Engineering 2019*. <https://en.civilica.com/doc/1000639/>
39. Ebadi M, Latifi Z, Daneshniya M. Optimization of the Antioxidant Effect of Ethanolic Extract of Thistle (*Carduus pycnocephalus* L.) by Response Surface Method and Comparison of the Antioxidant Effect of Extract and Essential Oil on Oxidative Soybean Oil Resistance. *Journal of food science and technology (Iran)*. 2021 Jan 10;17(108):151-64. <https://doi.org/10.52547/fsct.17.108.151>
40. Cheynier V. Phenolic compounds: from plants to foods. *Phytochemistry reviews*. 2012 Jun;11(2):153-77. <https://doi.org/10.1007/s11101-012-9242-8>
41. Singleton VL. Naturally occurring food toxicants: phenolic substances of plant origin common in foods. *Advances in food research*. 1981 Jan 1;27:149-242. [https://doi.org/10.1016/S0065-2628\(08\)60299-2](https://doi.org/10.1016/S0065-2628(08)60299-2)
42. Su TR, Lin JJ, Tsai CC, Huang TK, Yang ZY, Wu MO, Zheng YQ, Su CC, Wu YJ. Inhibition of melanogenesis by gallic acid: Possible involvement of the PI3K/Akt, MEK/ERK and Wnt/β-catenin signaling pathways in B16F10 cells. *International journal of molecular sciences*. 2013 Oct;14(10):20443-58. <https://doi.org/10.3390/ijms141020443>
43. Boz H. p-Coumaric acid in cereals: presence, antioxidant and antimicrobial effects. *International Journal of Food Science & Technology*. 2015 Nov;50(11):2323-8. <https://doi.org/10.1111/ijfs.12898>
44. Marchev AS, Vasileva LV, Amirova KM, Savova MS, Koycheva IK, Balcheva-Sivenova ZP, Vasileva SM, Georgiev MI. Rosmarinic acid-From bench to valuable applications in food industry. *Trends in Food Science & Technology*. 2021 Nov 1;117:182-93. <https://doi.org/10.1016/j.tifs.2021.03.015>
45. Magnani C, Isaac VL, Correa MA, Salgado HR. Caffeic acid: a review of its potential use in medications and cosmetics. *Analytical Methods*. 2014;6(10):3203-10. <https://doi.org/10.1039/C3AY41807C>
46. Kakkar S, Bais S. A review on protocatechuic acid and its pharmacological potential. *International Scholarly Research Notices*. 2014;2014. <https://doi.org/10.1155/2014/952943>
47. Andrade JM, Faustino C, Garcia C, Ladeiras D, Reis CP, Rijo P. *Rosmarinus officinalis* L.: an update review of its phytochemistry and biological activity. *Future science OA*. 2018 Feb 1;4(4):FSO283. <https://doi.org/10.4155/fsoa-2017-0124>
48. Sugihara N, Ohnishi M, Imamura M, Furuno K. Differences in antioxidative efficiency of catechins in various metal-induced lipid peroxidations in cultured hepatocytes. *Journal of health science*. 2001;47(2):99-106. <https://doi.org/10.1248/jhs.47.99>
49. Sivakanthan S, Rajendran S, Gamage A, Madhujith T, Mani S. Antioxidant and antimicrobial applications of biopolymers: A review. *Food Research International*. 2020 Oct 1;136:109327. <https://doi.org/10.1016/j.foodres.2020.109327>
50. Cavia-Saiz M, Busto MD, Pilar-Izquierdo MC, Ortega N, Perez-Mateos M, Muñiz P. Antioxidant properties, radical scavenging activity and biomolecule protection capacity of flavonoid naringenin and its glycoside naringin: a comparative study. *Journal of the Science of Food and Agriculture*. 2010 May;90(7):1238-44. <https://doi.org/10.1002/jsfa.3959>
51. Baghel SS, Shrivastava N, Baghel RS, Agrawal P, Rajput S. A review of quercetin: antioxidant and anticancer properties. *World J Pharm Pharmaceutical Sci*. 2012 May 1;1(1):146-60. [https://www.researchgate.net/publication/267333748\\_A\\_review\\_of\\_quercetin\\_Antioxidant\\_and\\_anticancer\\_properties](https://www.researchgate.net/publication/267333748_A_review_of_quercetin_Antioxidant_and_anticancer_properties)

52. Kashyap P, Shikha D, Thakur M, Aneja A. Functionality of apigenin as a potent antioxidant with emphasis on bioavailability, metabolism, action mechanism and in vitro and in vivo studies: A review. *Journal of food biochemistry*. 2021 Sep 26:e13950. <https://doi.org/10.1111/jfbc.13950>
53. Miguel MG. Anthocyanins: Antioxidant and/or anti-inflammatory activities. *Journal of Applied Pharmaceutical Science*. 2011;1(6):7-15. <http://hdl.handle.net/10400.1/6317>
54. Weng L, Zhang F, Wang R, Ma W, Song Y. A review on protective role of genistein against oxidative stress in diabetes and related complications. *Chemico-biological interactions*. 2019 Sep 1;310:108665. <https://doi.org/10.1016/j.cbi.2019.05.031>
55. Nieto G, Ros G, Castillo J. Antioxidant and antimicrobial properties of rosemary (*Rosmarinus officinalis*, L.): A review. *Medicines*. 2018 Sep;5(3):98. <https://doi.org/10.3390/medicines5030098>
56. Yilmaz Y. Novel uses of catechins in foods. *Trends in Food Science & Technology*. 2008 Feb 1;17(2):64-71. <https://doi.org/10.1016/j.tifs.2005.10.005>
57. He J, Xu L, Le Yang XW. Epigallocatechin gallate is the most effective catechin against antioxidant stress via hydrogen peroxide and radical scavenging activity. *Medical Science Monitor: International Medical Journal of Experimental and Clinical Research*. 2018;24:8198. <https://doi.org/10.12659/MSM.911175>
58. Hu C, Kitts DD. Evaluation of antioxidant activity of epigallocatechin gallate in biphasic model systems in vitro. *Molecular and Cellular Biochemistry*. 2001 Feb;218(1):147-55. <https://doi.org/10.1023/A:1007220928446>
59. Yang J, Guo J, Yuan J. In vitro antioxidant properties of rutin. *LWT-Food Science and Technology*. 2008 Jul 1;41(6):1060-6. <https://doi.org/10.1016/j.lwt.2007.06.010>
60. Gülçin İ. Antioxidant activity of eugenol: A structure–activity relationship study. *Journal of medicinal food*. 2011 Sep 1;14(9):975-85. <https://doi.org/10.1089/jmf.2010.0197>
61. Aristatile B, Al-Numair KS, Al-Assaf AH, Veeramani C, Pugalendi KV. Protective effect of carvacrol on oxidative stress and cellular DNA damage induced by UVB irradiation in human peripheral lymphocytes. *Journal of biochemical and molecular toxicology*. 2015 Nov;29(11):497-507. <https://doi.org/10.1002/jbt.20355>
62. Viuda-Martos M, Ruiz Navajas Y, Sánchez Zapata E, Fernández-López J, Pérez-Álvarez JA. Antioxidant activity of essential oils of five spice plants widely used in a Mediterranean diet. *Flavour and Fragrance Journal*. 2010 Jan;25(1):13-9. <https://doi.org/10.1002/ffj.1951>
63. Eid AM, Hawash M. Biological evaluation of Safrole oil and Safrole oil Nanoemulgel as antioxidant, antidiabetic, antibacterial, antifungal and anticancer. *BMC Complementary Medicine and Therapies*. 2021 Dec;21(1):1-2. <https://doi.org/10.1186/s12906-021-03324-z>
64. Wu Z, Tan B, Liu Y, Dunn J, Martorell Guerola P, Tortajada M, Cao Z, Ji P. Chemical composition and antioxidant properties of essential oils from peppermint, native spearmint and scotch spearmint. *Molecules*. 2019 Jan;24(15):2825. <https://doi.org/10.3390/molecules24152825>
65. Sun Z, Wang H, Wang J, Zhou L, Yang P. Chemical composition and anti-inflammatory, cytotoxic and antioxidant activities of essential oil from leaves of *Mentha piperita* grown in China. *PloS one*. 2014 Dec 10;9(12):e114767. <https://doi.org/10.1371/journal.pone.0114767>
66. Lim H, Shin S. Antibacterial and Antioxidant Activities of the Essential Oil from the Roots of *Anthriscus sylvestris*. *Yakhak Hoeji*. 2012;56(5):320-5. <https://www.koreascience.or.kr/article/JAKO201217642691877.page>
67. Mimica-Dukić N, Božin B, Soković M, Mihajlović B, Matavulj M. Antimicrobial and antioxidant activities of three *Mentha* species essential oils. *Planta medica*. 2003 May;69(05):413-9. <https://doi.org/10.1055/s-2003-39704>
68. Larayetan RA, Okoh OO, Sadimenko A, Okoh AI. Terpene constituents of the aerial parts, phenolic content, antibacterial potential, free radical scavenging and antioxidant activity of *Callistemon citrinus* (Curtis) Skeels (Myrtaceae) from Eastern Cape Province of South Africa. *BMC complementary and alternative medicine*. 2017 Dec;17(1):1-9. <https://doi.org/10.1186/s12906-017-1804-2>
69. Chaudhari AK, Singh A, Singh VK, Dwivedy AK, Das S, Ramsdam MG, Dkhar MS, Kayang H, Dubey NK. Assessment of chitosan biopolymer encapsulated  $\alpha$ -Terpineol against fungal, aflatoxin B1 (AFB1) and free radicals mediated deterioration of stored maize and possible mode of action. *Food chemistry*. 2020 May 1;311:126010. <https://doi.org/10.1016/j.foodchem.2019.126010>
70. Reza M, Nejad S. Antibacterial and Antioxidant Activity and Essential Oil Composition of *Grammosciadium scabridum* Boiss. from Iran. *Zeitschrift für Naturforschung C*. 2014.
71. Subash-Babu P, Alshatwi AA, Ignacimuthu S. Beneficial antioxidative and antiperoxidative effect of cinnamaldehyde protect streptozotocin-induced pancreatic  $\beta$ -cells damage in wistar rats. *Biomolecules & therapeutics*. 2014 Jan;22(1):47. <https://doi.org/10.4062/biomolther.2013.100>
72. Carp OE, Moraru A, Pinteala M, Arvinte A. Electrochemical behaviour of piperine. Comparison with control antioxidants. *Food Chemistry*. 2021 Mar 1;339:128110. <https://doi.org/10.1016/j.foodchem.2020.128110>

73. Alamed J, Chaayasit W, McClements DJ, Decker EA. Relationships between free radical scavenging and antioxidant activity in foods. *Journal of agricultural and food chemistry*. 2009 Apr 8;57(7):2969-76. <https://doi.org/10.1021/jf803436c>
74. Hussein MA. A convenient mechanism for the free radical scavenging activity of resveratrol. *International Journal of Phytomedicine*. 2011 Oct 1;3(4):459. <https://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.868.4033&rep=rep1&type=pdf>
75. Queenthly SS, John B. Diosmin exhibits anti-hyperlipidemic effects in isoproterenol induced myocardial infarcted rats. *European journal of pharmacology*. 2013 Oct 15;718(1-3):213-8. <https://doi.org/10.1016/j.ejphar.2013.08.031>
76. Chu YH, Chang CL, Hsu HF. Flavonoid content of several vegetables and their antioxidant activity. *Journal of the Science of Food and Agriculture*. 2000 Apr;80(5):561-6. [https://doi.org/10.1002/\(SICI\)1097-0010\(200004\)80:5<561::AID-JSFA574>3.0.CO;2-%23](https://doi.org/10.1002/(SICI)1097-0010(200004)80:5<561::AID-JSFA574>3.0.CO;2-%23)
77. Pietta PG. Flavonoids as antioxidants. *Journal of natural products*. 2000 Jul 28;63(7):1035-42. <https://doi.org/10.1021/np9904509>
78. Ververidis F, Trantas E, Douglas C, Vollmer G, Kretzschmar G, Panopoulos N. Biotechnology of flavonoids and other phenylpropanoid-derived natural products. Part I: Chemical diversity, impacts on plant biology and human health. *Biotechnology Journal: Healthcare Nutrition Technology*. 2007 Oct;2(10):1214-34. <https://doi.org/10.1002/biot.200700084>
79. Laura A, Moreno-Escamilla JO, Rodrigo-García J, Alvarez-Parrilla E. Phenolic compounds. In *Postharvest physiology and biochemistry of fruits and vegetables* 2019 Jan 1 (pp. 253-271). Woodhead Publishing. <https://doi.org/10.1016/B978-0-12-813278-4.00012-9>
80. Gutiérrez-del-Río I, López-Ibáñez S, Magadán-Corpas P, Fernández-Calleja L, Pérez-Valero Á, Tuñón-Granda M, Miguélez EM, Villar CJ, Lombó F. Terpenoids and polyphenols as natural antioxidant agents in food preservation. *Antioxidants*. 2021 Aug;10(8):1264. <https://doi.org/10.3390/antiox10081264>
81. Manassis G, Kalogianni AI, Lazou T, Moschovas M, Bossis I, Gelasakis AI. Plant-derived natural antioxidants in meat and meat products. *Antioxidants*. 2020 Dec;9(12):1215. <https://doi.org/10.3390/antiox9121215>
82. Carochio M, Morales P, Ferreira IC. Antioxidants: Reviewing the chemistry, food applications, legislation and role as preservatives. *Trends in Food Science & Technology*. 2018 Jan 1;71:107-20. <https://doi.org/10.1016/j.tifs.2017.11.008>
83. European Parliament and Council Commission Regulation (E.U.) No 1129/2011 of 11 November 2011 Amending Annex II to Regulation (E.C.) No 1333/2008 of the European Parliament and of the Council by Establishing a Union List of Food Additives (Text with EEA Relevance). Available online: <https://op.europa.eu/en/publication-detail/-/publication/28cb4a37-b40e-11e3-86f9-01aa75ed71a1>
84. Oswell NJ, Thippareddi H, Pegg RB. Practical use of natural antioxidants in meat products in the U.S.: A review. *Meat science*. 2018 Nov 1;145:469-79. <https://doi.org/10.1016/j.meatsci.2018.07.020>
85. FDA U.S. (Food and Drug Administration). CFR—Code of Federal Regulations Title 21 Part 172. Food Additives Permitted for Direct Addition to Food for Human Consumption. Available online: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=172>
86. FDA U.S. (Food and Drug Administration). CFR—Code of Federal Regulations Title 21 Part 182. Substances Generally Recognized as Safe. Available online: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?CFRPart=182> (accessed on 15 July 2021).
87. FDA U.S. (Food and Drug Administration). Substances Added to Food (Formerly EAFUS). Available online: <https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=FoodSubstances> (accessed on 10 January 2022).
88. European Commission Food Additives Database. Available online: [https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=FoodSubstances&sort=Sortterm\\_ID&order=ASC&startrow=1&type=basic&search=ASCORBIC](https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=FoodSubstances&sort=Sortterm_ID&order=ASC&startrow=1&type=basic&search=ASCORBIC) (accessed on 17 January 2022).
89. Barden L, Decker EA. Lipid oxidation in low-moisture food: A review. *Critical reviews in food science and nutrition*. 2016 Nov 17;56(15):2467-82. <https://doi.org/10.1080/10408398.2013.848833>
90. Yang X, Sun Z, Wang W, Zhou Q, Shi G, Wei F, Jiang G. Developmental toxicity of synthetic phenolic antioxidants to the early life stage of zebrafish. *Science of the Total Environment*. 2018 Dec 1;643:559-68.
91. Lin D, Xiao M, Zhao J, Li Z, Xing B, Li X, Kong M, Li L, Zhang Q, Liu Y, Chen H. An overview of plant phenolic compounds and their importance in human nutrition and management of type 2 diabetes. *Molecules*. 2016 Oct;21(10):1374. <https://doi.org/10.3390/molecules21101374>
92. Kwan YH, Tung YK, Kochhar JS, Li H, Poh AL, Kang L. 2-Regulation of cosmetics. *Handbook of Cosmeceutical Excipients and their Safeties*, Yu Heng Kwan, Yee Kei Tung, Jaspreet Singh Kochhar, Hairui Li, Ai-Ling Poh, and Lifeng Kang (Eds.). Woodhead Publishing. 2014:7-22. <https://www.elsevier.com/books/handbook-of-cosmeceutical-excipients-and-their-safeties/kwan/978-1-907568-53-4>

93. EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS). Scientific Opinion on the re-evaluation of butylated hydroxyanisole–BHA (E 320) as a food additive. *EFSA Journal*. 2011 Oct;9(10):2392. <https://doi.org/10.2903/j.efsa.2011.2392>
94. EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS). Scientific Opinion on the re-evaluation of butylated hydroxytoluene BHT (E 321) as a food additive. *EFSA Journal*. 2012 Mar;10(3):2588. <https://doi.org/10.2903/j.efsa.2012.2588>
95. EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS). Statement on the refined exposure assessment of tertiary-butyl hydroquinone (E 319). *EFSA Journal*. 2016 Jan;14(1):4363. <https://doi.org/10.2903/j.efsa.2016.4363>
96. EFSA Panel on Food Additives and Nutrient Sources Added to Food (ANS). Scientific Opinion on the re-evaluation of propyl gallate (E 310) as a food additive. *EFSA Journal*. 2014 Apr;12(4):3642. <https://doi.org/10.2903/j.efsa.2014.3642>
97. EFSA Panel on Food additives and Nutrient Sources added to Food (ANS). Scientific Opinion on the re-evaluation of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) as food additives. *Efsa Journal*. 2015 May;13(5):4087. <https://doi.org/10.2903/j.efsa.2015.4087>
98. EFSA Panel on Food Additives and Nutrient Sources added to food (ANS). Scientific Opinion on the re-evaluation of erythorbic acid (E 315) and sodium erythorbate (E 316) as food additives. *EFSA Journal*. 2016 Jan;14(1):4360. <https://doi.org/10.2903/j.efsa.2016.4360>
99. EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS). Scientific Opinion on the re-evaluation of ascorbyl palmitate (E 304 (i)) and ascorbyl stearate (E 304 (ii)) as food additives. *EFSA Journal*. 2015 Nov;13(11):4289. <https://doi.org/10.2903/j.efsa.2015.4289>
100. EFSA Panel on Food additives and Nutrient Sources added to Food (ANS). Scientific Opinion on the re-evaluation of sulfur dioxide (E 220), sodium sulfite (E 221), sodium bisulfite (E 222), sodium metabisulfite (E 223), potassium metabisulfite (E 224), calcium sulfite (E 226), calcium bisulfite (E 227) and potassium bisulfite (E 228) as food additives. *Efsa Journal*. 2016 Apr;14(4):4438. <https://doi.org/10.2903/j.efsa.2016.4438>
101. EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA). Scientific Opinion on Dietary Reference Values for vitamin E as  $\alpha$ -tocopherol. *EFSA Journal*. 2015 Jul;13(7):4149. <https://doi.org/10.2903/j.efsa.2015.4149>
102. Lourenço SC, Moldão-Martins M, Alves VD. Antioxidants of natural plant origins: From sources to food industry applications. *Molecules*. 2019 Jan;24(22):4132. <https://doi.org/10.3390/molecules24224132>
103. Xu X, Liu A, Hu S, Ares I, Martínez-Larrañaga MR, Wang X, Martínez M, Anadón A, Martínez MA. Synthetic phenolic antioxidants: Metabolism, hazards and mechanism of action. *Food Chemistry*. 2021 Aug 15;353:129488. <https://doi.org/10.1016/j.foodchem.2021.129488>
104. Liu R, Mabury SA. Synthetic phenolic antioxidants: A review of environmental occurrence, fate, human exposure, and toxicity. *Environmental science & technology*. 2020 Sep 11;54(19):11706-19. <https://doi.org/10.1021/acs.est.0c05077>
105. Baran A, Yildirim S, Ghosigharehaghaji A, Bolat İ, Sulukan E, Ceyhun SB. An approach to evaluating the potential teratogenic and neurotoxic mechanism of BHA based on apoptosis induced by oxidative stress in zebrafish embryo (Danio rerio). *Human & experimental toxicology*. 2021 Mar;40(3):425-38. <https://doi.org/10.1177/0960327120952140>
106. Gülçin İ. Antioxidant activity of food constituents: an overview. *Archives of toxicology*. 2012 Mar;86(3):345-91. <https://doi.org/10.1007/s00204-011-0774-2>
107. Heijnen CG, Haenen GR, Van Acker FA, Van der Vijgh WJ, Bast A. Flavonoids as peroxynitrite scavengers: the role of the hydroxyl groups. *Toxicology in vitro*. 2001 Feb 1;15(1):3-6. [https://doi.org/10.1016/S0887-2333\(00\)00053-9](https://doi.org/10.1016/S0887-2333(00)00053-9)
108. Terahara N. Flavonoids in foods: a review. *Natural product communications*. 2015 Mar;10(3):1934578X1501000334. <https://doi.org/10.1177/1934578X1501000334>
109. D'Amelia V, Aversano R, Chiaiese P, Carputo D. The antioxidant properties of plant flavonoids: their exploitation by molecular plant breeding. *Phytochemistry Reviews*. 2018 Jun;17(3):611-25. <https://doi.org/10.1007/s11101-018-9568-y>
110. Petersen B, Snapp S. What is sustainable intensification? Views from experts. *Land use policy*. 2015 Jul 1;46:1-0. <https://doi.org/10.1016/j.landusepol.2015.02.002>
111. Shahidi F, Ambigaipalan P. Phenolics and polyphenolics in foods, beverages and spices: Antioxidant activity and health effects—A review. *Journal of functional foods*. 2015 Oct 1;18:820-97. <https://doi.org/10.1016/j.jff.2015.06.018>
112. Kumar S, Pandey AK. Chemistry and biological activities of flavonoids: an overview. *The scientific world journal*. 2013 Oct;2013. <https://doi.org/10.1155/2013/162750>

113. Agrawal AD. Pharmacological Activities of Flavonoids: A Review. *International Journal of Pharmaceutical Sciences and Nanotechnology*. 2011 Aug 31;4(2):1394-8. <https://doi.org/10.37285/ijpsn.2011.4.2.3>
114. Kaleem M, Ahmad A. Flavonoids as nutraceuticals. In *Therapeutic, probiotic, and unconventional foods* 2018 Jan 1 (pp. 137-155). Academic Press. <https://doi.org/10.1016/B978-0-12-814625-5.00008-X>
115. Neha P, Pandey-Rai S. Biochemical activity and therapeutic role of antioxidants in plants and humans. *Plants as a Source of Natural Antioxidants*; CABI Publishing: Wallingford, UK. 2014 Feb:191-224. [https://www.researchgate.net/publication/267395391\\_Biochemical\\_Activity\\_and\\_Therapeutic\\_Role\\_of\\_Antioxidants\\_in\\_Plants\\_and\\_Humans](https://www.researchgate.net/publication/267395391_Biochemical_Activity_and_Therapeutic_Role_of_Antioxidants_in_Plants_and_Humans)
116. Zhang Y, Butelli E, De Stefano R, Schoonbeek HJ, Magusin A, Pagliarini C, et al. Anthocyanins double the shelf life of tomatoes by delaying overripening and reducing susceptibility to gray mold. *Current Biology*. 2013 Jun 17;23(12):1094-100. <https://doi.org/10.1016/j.cub.2013.04.072>
117. Zhang Y, De Stefano R, Robine M, Butelli E, Bulling K, Hill L, Rejzek M, Martin C, Schoonbeek HJ. Different reactive oxygen species scavenging properties of flavonoids determine their abilities to extend the shelf life of tomato. *Plant Physiology*. 2015 Nov;169(3):1568-83. <https://doi.org/10.1104/pp.15.00346>
118. Hintz T, Matthews KK, Di R. The use of plant antimicrobial compounds for food preservation. *BioMed research international*. 2015 Oct 11;2015. <https://doi.org/10.1155/2015/246264>
119. López de Dicastillo C, Nerín C, Alfaro P, Catalá R, Gavara R, Hernández-Muñoz P. Development of new antioxidant active packaging films based on ethylene vinyl alcohol copolymer (EVOH) and green tea extract. *Journal of agricultural and food chemistry*. 2011 Jul 27;59(14):7832-40. <https://doi.org/10.1021/jf201246g>
120. Viji P, Binsi PK, Visnuvinayagam S, Bindu J, Ravishankar CN, Srinivasa Gopal TK. Efficacy of mint (*Mentha arvensis*) leaf and citrus (*Citrus aurantium*) peel extracts as natural preservatives for shelf life extension of chill stored Indian mackerel. *Journal of food science and technology*. 2015 Oct;52(10):6278-89. <https://doi.org/10.1007/s13197-015-1788-1>