

Review

Polyphenolics in Grape Seeds—Biochemistry and Functionality

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ABSTRACT Grape seeds are waste products of the winery and grape juice industry. These seeds contain lipid, protein, carbohydrates, and 5–8% polyphenols depending on the variety. Polyphenols in grape seeds are mainly flavonoids, including gallic acid, the monomeric flavan-3-ols catechin, epicatechin, galocatechin, epigallocatechin, and epicatechin 3-*O*-gallate, and procyanidin dimers, trimers, and more highly polymerized procyanidins. Grape seed extract is known as a powerful antioxidant that protects the body from premature aging, disease, and decay. Grape seeds contain mainly phenols such as proanthocyanidins (oligomeric proanthocyanidins). Scientific studies have shown that the antioxidant power of proanthocyanidins is 20 times greater than vitamin E and 50 times greater than vitamin C. Extensive research suggests that grape seed extract is beneficial in many areas of health because of its antioxidant effect to bond with collagen, promoting youthful skin, cell health, elasticity, and flexibility. Other studies have shown that proanthocyanidins help to protect the body from sun damage, to improve vision, to improve flexibility in joints, arteries, and body tissues such as the heart, and to improve blood circulation by strengthening capillaries, arteries, and veins. The most abundant phenolic compounds isolated from grape seed are catechins, epicatechin, procyanidin, and some dimers and trimers.

KEY WORDS: • catechins • epicatechin • grape seed • polyphenolics

INTRODUCTION

PHENOLICS ARE BROADLY DISTRIBUTED in the plant kingdom and are the most abundant secondary metabolites found in plants.¹ These phenolic substances or polyphenols include many classes of compounds ranging from phenolic acids, colored anthocyanins, simple flavonoids, and complex flavonoids.² All phenolic compounds possess an aromatic ring bearing one or more hydroxyl groups. The phenolic compounds in grapes and grape products (juice and wine) can be divided into two groups: (a) phenolic acids and related compounds and (b) flavonoids. The most common phenolic acids in grape include cinnamic acids (coumaric acid, caffeic acid, ferulic acid, chlorogenic acid, and neochlorogenic acid) and benzoic acids (*p*-hydroxybenzoic acid, protocatechuic acid, vanillic acid, and gallic acid). Flavonoids include colorless flavan-3-ols (such as catechin, epicatechin, and their polymers and their ester forms with galactic acid or glucose), colored flavanones (the most common flavanone in food is quercetin), and red and blue anthocyanins.

Many foods and food material contain phenolics, such as cereals and legumes (barley, corn, nuts, oats, rice, sorghum, wheat, beans, and pulses), oilseeds (rapeseed, canola, flaxseed, and olive seeds), fruits and vegetables, and beverages (fruit juices, tea, coffee, cocoa, beer, and wine). Caffeic and coumaric acids are common in apples, pears, and grapes. In addition, apples and pears are rich in chlorogenic acid, and grapes are usually rich in gallic acid. Hertog *et al.*³ assayed for phenolic compounds in the edible portion of 28 vegetables and nine fruits consumed in the Netherlands and found onions, kale, broccoli, French beans, and string beans contained relatively high quercetin levels. Apples contain the highest quercetin level compared with other fruits. In another report the level of total phenolics of sunflower seeds, wheat germ, buckwheat, and several fruits, vegetables, and medicinal plants measured by the Folin–Ciocalteu method was shown to vary from 169 to 10,548 mg/100 g of dry product.⁴ The contents of total phenolic compounds in some common plants are listed in Table 1.

Tea is a major source of polyphenols. The major constituents of tea polyphenols are flavanols [(+)-catechin, (–)-epicatechin, and (–)-epicatechin gallate], flavonols (quercetin, kaempferol, and their glycosides), flavones (vitexin and isovitexin), and phenolic acids (gallic acid and chlorogenic acid). They constitute up to 30% of the dry weight of green tea leaves⁵ and 9–10% of the dry weight of black tea leaves.^{6,7} Pine tree bark is another plant rich in

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TABLE 1. TOTAL PHENOLIC COMPOUNDS OF SOME FRUITS AND VEGETABLES

Product name	Total phenolics (mg/100 g)
Solin seed	473
Flax seed	509
Sunflower seed	1,601
Buckwheat seed	726
Wheat germ	349
Sweet berry	2,098
Blueberry	4,180
Red onion scale	10,548
Sunflower hull, purple	9,747
Echinacea flower head	5,467
Echinacea root	3,841
Buckwheat hulls	3,900
Potato, purple	781
Horseradish root	481

Data are from Velioglu *et al.*⁴ The total phenolics were measured by the Folin-Ciocalteu method and expressed as ferulic acid equivalents.

polyphenols. The first polyphenol preparation for pharmaceutical purposes was made from pine bark.⁸

Phenolic compounds play an important role in overall organoleptic properties of foods. Phenolics contribute to the bitterness and astringency of fruits and fruit juices, because of the interaction between phenolics, mainly procyanidins, and the glycoproteins in saliva.⁹ Anthocyanin is responsible for the orange, red, blue, and purple color of many fruits and vegetables such as apples, berries (*e.g.*, blueberry and grapes), beets, and onions. Colorants produced from grape skin are considered nontoxic and are categorized as being in the GRAS (generally recognized as safe) class, and as such are used by the food industry as a color additive.¹⁰ Juice clarified by ultrafiltration is lighter than that made by traditional filtration because of the removal of polyphenols with a high degree of polymerization (DP). Sensory evaluation studies showed that tetrameric procyanidins are more bitter, while the other high polymeric components are more astringent, on an equivalent weight basis.¹¹ The yellow and brown colors of fruit juice are produced largely by the oxidation reaction between polyphenols and oxygen in the presence of polyphenol oxidase. Phenolics are considered to be the most important compounds affecting flavor as well as color differences among white, pink, and red wines; they are the natural ingredients of wine that react with oxygen and are crucial to the preservation, maturation, and aging of wine.¹² However, the presence of polyphenols can also cause some undesirable effects during the storage of fruits and juice. For example, the polyphenol-protein¹³ and polyphenol-polysaccharide¹⁴ interactions are the most frequent causes of haze in beer, wine, and clarified juice. The existence of polyphenols in clarified beverages also affects the color stability because of slow oxidation during storage. Ultra-

filtration has been utilized commercially to produce stable beverages (*e.g.*, juice, wine, and beer).

DISTRIBUTION OF PHENOLIC COMPOUNDS IN GRAPE AND GRAPE SEEDS

Phenols represent the third most abundant constituent in grapes and wines after carbohydrates and fruit acids.¹² The phenolic compounds are broadly distributed inside grapes. When extracting a single grape variety, the composition of phenolics depends upon whether the extraction is performed on whole grape pulp, skin, or seeds. The total extractable phenolics in grape are present at only about 10% or less in pulp, 60–70% in the seeds, and 28–35% in the skin. The phenol content of seeds may range from 5% to 8% by weight.¹⁵ The most abundant phenolics isolated from grape seeds are catechins (catechin, epicatechin, and procyanidins) and their polymers.^{16,17} Thorngate and Singleton¹⁸ studied the distribution of catechin, epicatechin, and procyanidins of grape seeds in Pinot Noir and Cabernet species. They found that the outer soft coat contained the majority of those compounds with exception of epicatechin in the Cabernet Sauvignon cultivar.

FACTORS INFLUENCING PHENOLIC CONTENT AND COMPOSITION OF GRAPE SEEDS

Revilla *et al.*¹⁹ showed that the content of phenolics (catechin and procyanidins) in grapes is clearly affected by four agroecological factors: the cultivar, the year of production (*i.e.*, the climatic condition from year to year), the site of production (the effect of geographic origin of grapes, soil chemistry, and fertilization), and the degree of maturation.

The composition of red grape phenolics is different from that of white grape. It was shown by Lee and Jaworski²⁰ that the phenolic compounds commonly found in white grapes (seeds removed) are esters of hydroxycinnamic acid, catechins, and procyanidins. Lee and Jaworski²¹ also identified three other phenolics in white grapes grown in New York. They were catechin-gallate, catechin-catechin-gallate, and β -1,3,6-tri-*O*-galloyl-D-glucose. Phenolics in red grapes contain mainly hydroxycinnamic acid-tartaric acid esters, procyanidins, flavonol glycosides, and anthocyanins.²² Anthocyanins are the major coloring components of red grapes.

Variety of grapes

Kovac *et al.*²³ compared 19 cultivars of winemaking grapes harvested at about the same stage of maturity in 1987 and found the total content of catechins and procyanidins varied from 414 to 2,593 mg/kg of grape. Among the 19 cultivars, Pinot Gris and Pinot Noir (belonging to *Vitis vinifera*) had the highest content of catechin and procyanidins in seeds and entire clusters. Similar results were obtained for table grapes by Revilla *et al.*²⁴ However, the total phenolic content of table grapes is significantly lower

than that of winemaking grapes. The data published by Fuleki and Silva²⁵ illustrate the compositional variation of catechins (catechin and epicatechin) and procyanidins (B1, B2, B3, B4, B1-3-*O*-g, B2-3-*O*-g, C1 T2) in grape seeds of different cultivars. These authors studied the phenolic composition of grape seeds from the *vinifera*, *hybrid*, and *labrusca* type of red and white grape cultivars grown in the Niagara region of Ontario, Canada (Table 2).

Climatic condition

Revilla *et al.*²⁴ examined the content of catechin, epicatechin, and procyanidins (B1, B2, B3, B4, and C1) in seeds of *cv. Muscat* of Hambourg sampled at El Encin (Spain). The content of these individual phenolics was very variable during the period from 1992 to 1993, despite their similar degree of maturity.

Site of production

Tempranillo grapes were sampled from four different sites around Madrid in Spain in September 1994, and the total content of catechins and procyanidins in seeds determined varied from 108 to 225 mg/kg of grape, depending on the geographic origin.²⁴

Degree of maturity

Several studies have reported that a number of grape cultivars (Tempranillo, Garnacha, and Cabernet Sauvignon)

grown in central Spain had the highest concentration of catechins and procyanidins during the early stages of development. The total content of catechins and procyanidins in seeds decreased dramatically during September. The amount of these compounds in seeds was nearly fivefold more at the end of August compared with the levels at the beginning of October.¹⁹

STRUCTURE, NOMENCLATURE, AND PROPERTIES OF PHENOLICS

Structure and DP of grape seed polyphenols

The phenolic compounds in grape seeds are essentially all flavonoids. The presence of flavan-3-ol monomers, dimers, and trimers has been extensively reported. Catechin, epicatechin, and epicatechin-3-*O*-gallate are monomers.²⁶ Flavan-3-ols easily condenses into oligomeric procyanidins and polymeric compounds (condensed tannins). The dimeric procyanidins are often referred as B-series, and the trimeric procyanidins as C-series. Five different dimers (procyanidin B1, B2, B3, B4, and B5) and two trimers (C1 and C2) were identified from grape skin and seeds. These dimers and trimers are composed of catechins and epicatechins. Fuleki and Silva²⁵ isolated and identified a total of 11 monomers, dimers, and trimers by reversed-phase high-performance liquid chromatography (HPLC) from the seeds of red grapes. Some authors have reported that the DP could reach much higher numbers. Prieur *et al.*¹⁷ showed a DP of 16 units by employing gel permeation chromatography and normal-

TABLE 2. PHENOLIC COMPOSITION OF SEEDS OF DIFFERENT GRAPE VARIETIES

Cultivar	Color	Level (mg/100 g)			
		Monomers	Dimers	Dimer gallates	Trimers
Vinifera					
Cabernet	Red	232	169	43	26
France					
Cabernet	Red	125	95	11	32
Sauvignon	Red	228	375	108	67
Gamay					
Merlot	Red	143	97	37	23
Pinot Noir	Red	437	235	41	84
Chardonnay	White	141	126	17	9
Riesling	White	49	54	4	7
Hybrid					
Baco Noir	Red	204	292	54	53
DeChaunac	Red	213	40	4	17
Marechal Foch	Red	88	141	24	10
Vincent	Red	439	238	54	28
Brights 12	Red	75	40	14	9
V65115	Red	119	30	7	18
Seyval	White	44	16	Tr	Tr
Labrusca					
Concord	Red	125	98	13	10
Elvira	White	95	45	7	5
Niagara	White	155	49	10	17

Data are from Fuleki and Silva.²⁵ Monomers included (+)-catechin and (-)-epicatechin, expressed as (+)-catechin equivalents; dimers and trimers as B2 equivalents; and dimer gallates as B2-3'-*O*-gallate equivalent. Tr, trace.

phase HPLC. It may be possible that the higher polymers observed by those authors are due to oxidative polymerization after extraction from seeds. The structures of catechins (monomers) and some procyanidins are shown in Fig. 1.

Physical properties of polyphenols

The physical properties (*e.g.*, melting point, absorption of light, and optical rotation) of polyphenols are as follows.²⁷

Molecular weight. The molecular weights of three monomers, catechin, epicatechin, and epicatechin-(3-*O*)-gallate, based on their molecular structure, are 293, 294, and 445, respectively. According to the DP, the MW of procyanidin dimer, trimer, and tetramer are 580, 870, and 1,160, respectively. These molecular weight differences are the basis for separation by gel permeation chromatography and membrane fractionation.

Solubility. Some phenolics are water-soluble, and some are lipid-soluble. In general, catechins are lipid-soluble, and procyanidins are water-soluble. Therefore, it is relatively easy to separate procyanidins from catechins. Since procyanidins are water-soluble, they can be extracted by water without introducing any organic solvents. This ensures the safety of grape seed extract as a dietary supplement. Their water and lipid solubilities are also of prime importance in understanding their antioxidant activities.²⁸

Melting point. The melting points of catechin, epicatechin, and epicatechin-3-gallate are 174°C, 236°C, and 236°C, respectively.

Absorption of light. The maximum absorption of light occurs at $\lambda_{\max} = 264\text{--}280$ nm.

Optical rotation (in ethanol). $[\alpha]_D$ of catechin, epicatechin, and epicatechin-3-gallate is 0°, 58.3°, and 188°, respectively.

Chemical and biochemical properties of polyphenols

Hydrogen donation. Phenolics contain multiple hydroxyl groups (-OH). They are hydrogen-donating antioxidants and singlet oxygen quenchers.²⁹ This makes polyphenols a class of reducing agents. They are also very potent metal chelating agents. They can trap and quench free radicals and break the chain reaction. Their antioxidant potentials are four to five times that of vitamin C or E.

Stability. Grape seed polyphenols are very sensitive to oxygen, light, acid, and alkaline, but relatively less sensitive to heat. Colorless phenolics such as catechin and epicatechin are easily oxidized in fruits and vegetables because of the presence of polyphenol oxidase, which is responsible for the bruising of fruits (*e.g.*, apples, pears, and peaches) and vegetables and the browning of juice.

Polyphenol-protein interaction. Phenolics from grape seeds have a special affinity for some proteins and certain protein building blocks (*e.g.*, proline-rich proteins).^{30,31} These reactions between polyphenol and protein can be used in the extraction of polyphenols and proteins from plant material. Also, by inhibiting or activating certain enzymes, fruits can become resistant to microbial attack, and in the production of beer, wine, and fruit juice, the formation of haze can be reduced.^{13,32} There are four kinds of interactive bonds between phenolic compounds and protein: hydrogen, hydrophobic, ionic, and covalent bonds.³³ Phenols may combine with protein reversibly by hydrogen bonding, or irreversibly by oxidation followed by covalent condensations. A study on the nature of protein-phenol interaction in beverages showed that the interaction involved hydrogen bonds, hydrophobic interactions, and some covalent bonding.¹³ The interaction of polyphenols with bovine serum albumin was used to study the anti-ulcer activity of grape seed extract *in vitro*.³⁴ Many proteins can be precipitated by polyphenols. This property can be used to quantify proteins, for example, the hemoglobin assay,³⁵ gelatin assay,³⁶ and bovine serum albumin assay.³⁷ The polyphenol-protein interaction in food matrix such as seeds, meals, or flours may also reduce the nutritional value of proteins from these sources. In addition, it has been reported that both condensed tannins and hydrolyzable tannins have antinutritional effects on livestock. Chicks fed a tannin-rich diet showed diminished weight gain and lower nutrient utilization, particularly protein as indicated by an increase in fecal nitrogen level.³⁸ However, it is important to keep in mind that the observed antinutritional effects in these studies may not be totally due to tannin, but may be due to non-tannin materials that occur exclusively with tannin.³⁹

Coloring reactions in inorganic acid and alkaline conditions. Proanthocyanidins, the major polyphenols of grape seed extracts, are colorless. When heating in an acid medium, they yield a red color. This procedure was used to measure all substances that collectively are proanthocyanidins.⁴⁰ In alkaline solution, they react with reagents and produce a blue color.

IMPORTANCE OF GRAPE PHENOLICS TO HUMAN HEALTH

Grape phenolics, including flavonoids and related polyphenols from grape, wine, and grape seeds, have generated remarkable interest based on positive reports of their antioxidant properties and ability to serve as free radical scavengers. The beneficial effects of grape seed polyphenols are due to their free radical scavenging capability, but the antioxidant activity of grape seed polyphenols is superior to other well-known antioxidants, such as vitamin C, vitamin E, and β -carotene. Some clinical data have shown that procyanidin oligomers from grape seeds are 20 times more potent than vitamin C and 50 times more potent than vitamin E as antioxidant.⁴¹ Besides their antioxidant activity,

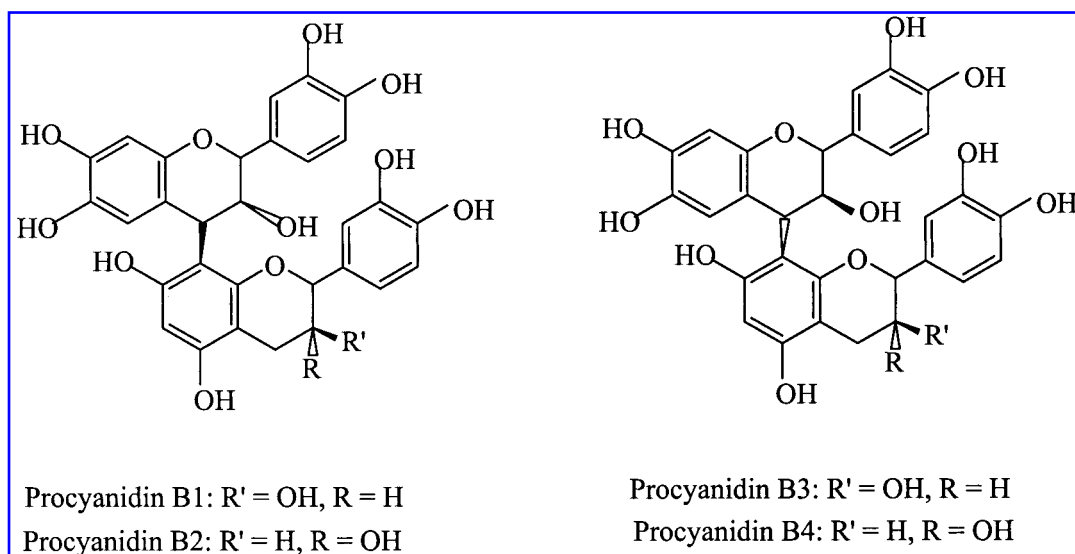
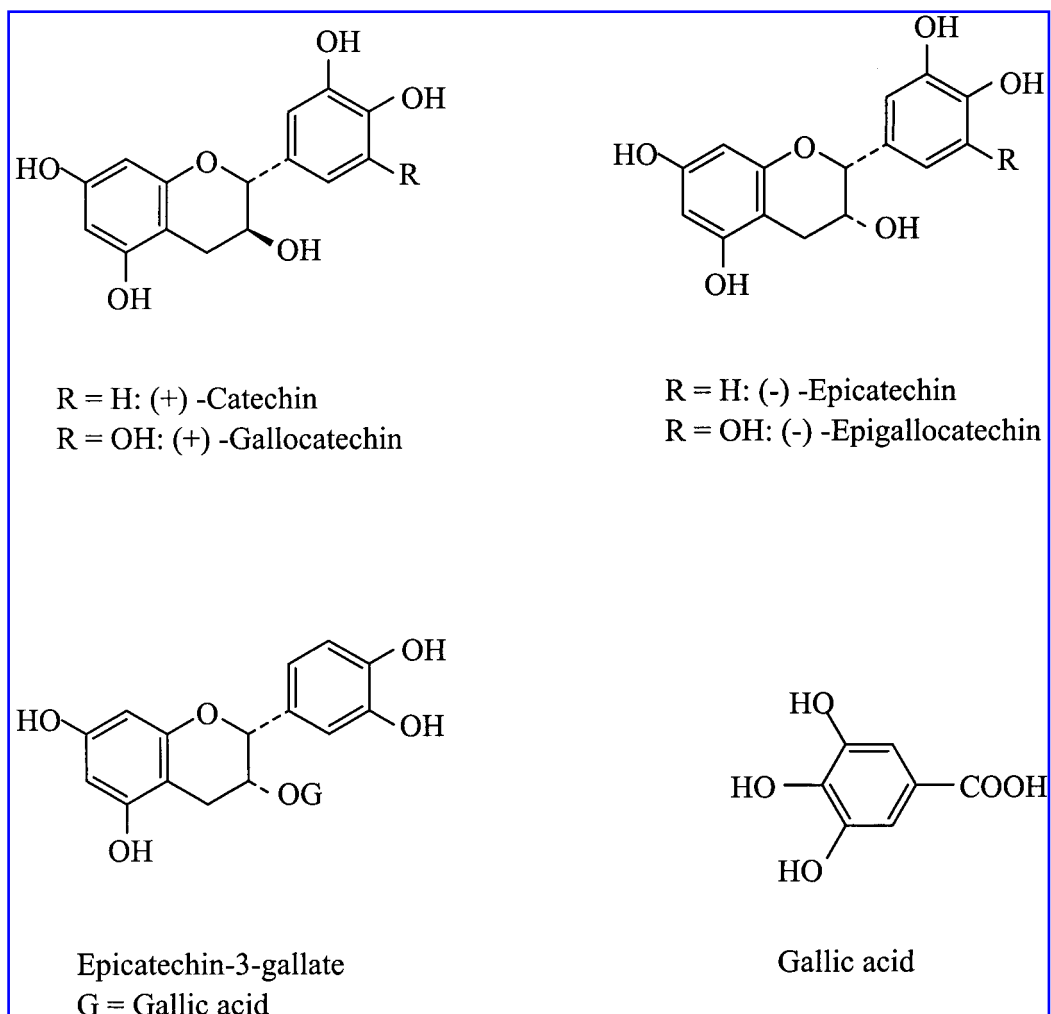


FIG. 1. Structures of major polyphenols identified in grape seed extract.

grape seed polyphenols also inhibit some enzymes that catalyze the release of histamine, which is responsible for inflammation and allergies.

Masquelier⁴² found that the bioflavonoids extracted from grape seeds were superior to those from pine bark in both concentration and antioxidant effect. Phenolics scavenge free radicals, and this property interferes with the initiation and propagation of free radical chain reactions in test systems. Another important property of these phenolic compounds is their apparent water and lipid solubility properties. Silva *et al.*⁴³ reported that epicatechin 3-*O*-gallate and various procyanidins obtained from grape seeds, including catechin monomers, are potent scavengers of superoxide radical ($O_2^{\bullet-}$) and hydroxyl radicals ($\bullet OH$) in aqueous models. Gallic acid esterification increased the free radical scavenging capacity of the dimer procyanidins.

Several studies have indicated that grape, wine, and grape seed extracts inhibit the oxidation of low-density lipoprotein (LDL).⁴⁴⁻⁴⁶ When wine extracts containing oligomeric procyanidins were diluted 1,000 times, their activity in inhibiting the oxidation of isolated human LDL far exceeded that of the vitamin C and E.⁴⁷ It has been constantly demonstrated *in vitro* and in clinical studies that red wine phenolics and grape phenolics inhibit LDL oxidation and inhibit platelet aggregation, thus preventing coronary heart disease.^{47,48} About 63% of the total phenolics in the seeds are in the red wine. Polyphenols (mainly catechins and procyanidins) of grape seed play a major role in the inhibition of LDL oxidation and platelet aggregation. Kanner *et al.*⁴⁹ found that lipid peroxidation catalyzed by biological catalysts such as myoglobin, cytochrome c, and iron ascorbate, was inhibited by red wine phenolics (some were from the fermentation of grape seeds and skin) at a concentration of 0.2, 0.35, and 0.9 μg of phenolics/mL. They also determined the antioxidative capacity of wine phenolics and α -toco-

pherol in a system containing LDL. The results showed that the antioxidation potential of wine phenolics was more than twice of that of α -tocopherol.

Cardiovascular disease is associated with modifications in fatty acid metabolism and excessive lipid peroxidation of LDL. These oxidation products are also implicated in the formation of thromboxane, which leads first to enhanced platelet aggregation, then to artery blockage, and finally to thrombosis.⁵⁰ The accumulation of lipid oxidation products from LDL can be attributed to the low levels of plasma antioxidants. Grape seed polyphenols reduce the risk of heart disease by inhibiting the oxidation of LDL. Procyanidins from grape seeds constitute the active ingredient of proprietary products widely used in some Western European countries for the treatment of circulatory disorders. Phenolics protect vitamins from early oxidation and make vitamins available for their primary functions. There is synergy between antioxidants, such as vitamin C and E, selenium, and carotenoids.

Phenolics of grape seeds may help to inhibit enzyme systems that are responsible for the production of free radicals and that are associated with inflammatory reactions. Procyanidins intervene in the synthesis and release of many substances that promote inflammation, for example, histamine, serine protease, prostaglandins, and leukotrienes.⁵¹⁻⁵³ Procyanidins also inhibit the activation of hyaluronidase, a proteoglycan splitting enzyme that attacks various tissues during inflammation. This action is related to the antihistamine effect and the ability to strengthen cell membranes of basophils and mast cells, which contain the allergens, thus preventing the hypersensitivity to pollens and food allergens.⁵⁴

Vennat *et al.*⁵⁵ reported the anti-ulcer activity of procyanidin prepared by fermentation of an extract of rhizomes of *Fragaria vesca* (the preparation contains mainly dimers) on a reserpine-induced ulcer model. Saito *et al.*³⁴ also in-

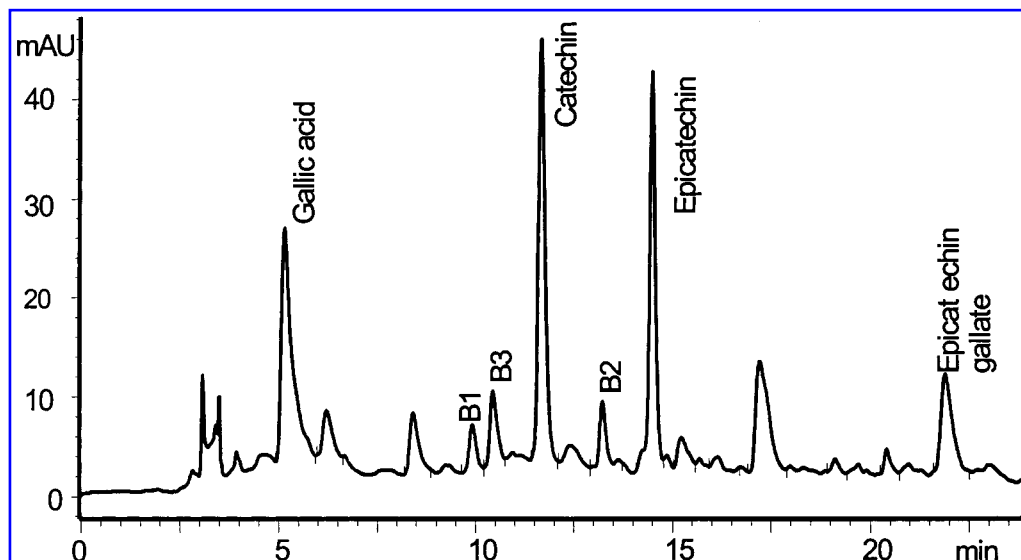


FIG. 2. HPLC profile of grape seed extraction by 50:50 ethanol/water solution at room temperature.

vestigated the anti-ulcer activity of grape seed extracts composed of longer oligmers of procyanidins in rats. The mucosal injury was induced by oral feeding of 60% ethanol containing 150 mM hydrochloride. The anti-ulcer activity was estimated by gastric mucosal lesion. Procyanidins inhibit mucosal injury by trapping and quenching oxygen-derived free radical peroxide *via* a radical scavenging effect on gastric mucosa.

A variety of procyanidins have been shown to prevent the growth of cancer cells. Liviero and Puglisi⁵⁶ investigated the anti-mutagenic activity of procyanidins from grape *V. vinifera* (VVL) on yeast *Saccharomyces cerevisiae* (strain S288C). The mitochondrial antimutagenesis was measured by the production of respiratory deficient mutants and the nuclear antimutagenic activity was evaluated by using the forward mutation system from L-canavanine sensitivity to L-canavanine resistance. They found that VVL at 0.5 mg/mL induced a 65% decrease of the mitochondrial spontaneous mutability in *Saccharomyces* strain S288C. At the same concentration, VVL reduced the mutation rate for the nuclear genetic determinant canavanine sensitivity by 92%.

Several important tissues in the body are predominantly composed of fats. Conspicuous in this regard is the brain. A recent *in vivo* study⁵⁷ indicated that grape seed proanthocyanidin extract had better protective effects than vitamin E, vitamin C, vitamin E plus C, and β -carotene against 12-*O*-tetradecanoylphorbol-13-acetate-induced lipid peroxidation and DNA fragmentation in liver and brain tissues of mice, as well as against the production of free radicals in the peritoneal macrophages (*i.e.*, immune cells) of these same mice. This study was performed by oral administration of the above antioxidants to female mice, and the protective effects were evaluated by measuring chemiluminescence, as an index of reactive oxygen species production, cytochrome c reduction, lipid peroxidation, and DNA fragmentation (Table 3).

Another anticarcinogenic study conducted by Jang *et al.*⁵⁸ illustrated that resveratrol, a natural product derived from grapes, inhibited tumor initiation, promotion, and progression. The results showed that: (1) resveratrol acted as an antioxidant and antimutagen, and induced phase II drug-metabolizing enzymes (anti-initiation activity); (2) it medi-

ated anti-inflammatory effects and inhibited cyclooxygenase and hydroperoxidase function (antipromotion activity); (3) it induced human promyelocytic leukemia cell differentiation (antipromotion activity); and (4) it inhibited the development of preneoplastic lesions in carcinogen-treated mouse mammary glands in culture and inhibited tumorigenesis in a mouse skin cancer model. Changes in pH change the charge characteristics of phenolics. At the pH of grape juice and wine, phenolics are almost neutral. Vernhet *et al.*¹⁴ reported that polyphenolic fractions, including native tannins isolated from grape seeds and recovered from wine, carried no charge or negligible charges at pH 3.5. Phenolics are negatively charged under alkaline condition. Silva *et al.*⁴³ found that certain polyphenols, for example, epicatechin-3-*O*-gallate and procyanidins B2 and B2 3'-*O*-gallate, had higher superoxide radical trapping activity at pH 9 than at pH 7.5.

SUMMARY

Many foods and food material contain phenolics, such as cereals and legumes, oilseeds, fruits, and vegetables, as well as beverages (fruit juices, tea, coffee, cocoa, beer, and wine). The phenolic compounds in grapes (seed, skin, and pulp) and grape products (juice and wine) can be divided into two groups, phenolic acids and flavonoids. Some common phenolic acids found in grapes include coumaric, caffeic, ferulic, chlorogenic, neochlorogenic, *p*-hydroxybenzoic, vanillic, and gallic acids. Some flavonoids include catechin, epicatechin, procyanidins and their polymers and ester forms, quercetin, and red and blue anthocyanins. The total extractable phenolics in grape are present in about 10% or less in pulp, 60–70% in the seeds, and 28–35% in the skin.

The pharmacological and nutraceutical benefits derived from phenolic compounds are closely related to their antioxidant and singlet oxygen quenching ability. These phenolic compounds are able to trap and quench free radicals, and their antioxidant potentials have been shown to be four to five times that of vitamin C or E. They are also very potent metal chelating agents.

Grape seed polyphenols are very sensitive to oxygen, light, acid, and alkaline, but relatively less sensitive to heat.

TABLE 3. COMPARISON OF THE PROTECTIVE EFFECTS OF GSPE, VITAMIN C, VITAMIN E SUCCINATE, AND β -CAROTENE AGAINST TPA-INDUCED HEPATIC AND BRAIN LIPID PEROXIDATION, DNA FRAGMENTATION, AND PERITONEAL MACROPHAGE ACTIVATION IN MICE

	GSPE	Vitamin C	Vitamin E	β -Carotene
Chemiluminescence reduction in peritoneal macrophages	70%	18%	47%	16%
Cytochrome c reduction	65%	15%	37%	19%
DNA fragmentation reduction in				
Hepatic tissue	47%	1%	30%	11%
Brain tissue	50%	14%	31%	11%
Lipid peroxidation inhibition		Dose-dependent		

GPSE, grape seed proanthocyanidin extract; 12-*O*-tetradecanoylphorbol-13-acetate.

They may combine with proteins reversibly by hydrogen or hydrophobic ionic bonding, or irreversibly by oxidation followed by covalent condensations. These reactions between polyphenol and protein can be used in the extraction of polyphenols and proteins from plant material and in the reduction of haze during the processing of beer, wine, and fruit juice. The polyphenol–protein interaction in food matrix such as seeds, meals, or flours may also reduce the nutritional value of proteins from these sources, but it is important to note that the observed antinutritional effects in these studies may be due to non-tannin materials in the food matrix.

Many techniques that were developed to study the oxidative stability of fats and oils have been adapted to measure polyphenol antioxidant activity. Some of these methods include the rancimat method, ferric-inducing antioxidant potential assay, chemiluminescence, trolox spectrophotometric analysis, β -carotene bleaching, and free radical scavenging capacity assays.

There are no satisfactory solvent extraction systems that would be suitable for isolation of all classes of phenolics. However, for the purpose of analysis, phenolics in grape and other foods are extracted by various organic solvents, usually alcohols (methanol, ethanol, and alcohol–water mixtures), acetone, and ethyl acetate. By selecting the optimum solvent combination and solvent-to-sample ratio, high recoveries of phenolics can be obtained.

A number of spectrophotometric methods have been developed to quantitate the levels of phenolic compounds in plant materials. Some of these methods are used to determine total phenolic compounds; some are used for a specific group or class of phenolic compounds. The Folin–Denis and the Folin–Ciocalteu assays are two widely used methods that can measure total phenolics in food products. The Prussian blue test and the vanillin method are two additional spectrophotometric methods that can be used to determine total phenolics. Other methods include titration with potassium permanganate and the protein precipitation method.

The method of choice for the separation, isolation, purification, and identification of phenolic compounds is chromatography. Chromatographic techniques will not only separate individual phenolic compounds but also give both quantitative and qualitative results. Paper chromatography and thin-layer chromatography were the earliest techniques developed, and they are still used today. The development of gas chromatography and HPLC, along with more sophisticated detectors (mass spectrometer, diode array), has greatly improved the separation performance and quantitation of polyphenols.

Much of the interest in phenolic compounds from grape seeds stems from their antioxidant properties and their ability to serve as free radical scavengers. Research suggests that grape seed oil helps protect the body from sun damage, improve vision, improve flexibility in joints, improve blood circulation, and reduce LDL oxidation and the occurrence of coronary heart disease.

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