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Dietary Fiber as a Carrier of Dietary Antioxidants: An Essential Physiological Function

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The literature addresses dietary fiber (DF) and antioxidants (AOX) separately as nonrelated compounds. This paper proposes to show that DF and AOX could be approached jointly in nutrition and health studies because around 50% of the total dietary antioxidants, mainly polyphenolics, traverse the small intestine linked to dietary fiber. These antioxidants have received little attention so far. They release the fiber matrix in the colon by the action of the bacterial microbiota, producing metabolites and an antioxidant environment. The content of polyphenols associated with DF in different foods and their potential health-related properties, including animal experiments and human trials, are reviewed. It is concluded that the transportation of dietary antioxidants through the gastrointestinal tract may be an essential function of DF.

KEYWORDS: Dietary fiber; dietary antioxidants; polyphenols; colonic fermentation; gastrointestinal health

INTRODUCTION

Dietary fiber (DF) and antioxidants (AOX) are two recognized dietary factors in the prevention of chronic disease. DF has an essential role in intestinal health and appears to be significantly associated with a lower risk of developing coronary heart disease, stroke, hypertension, diabetes, and obesity (*1*). Dietary antioxidants protect against oxidative damage to DNA, proteins, and lipids and have a significant impact on the regulation of gene expression. Intake or plasma concentration of dietary AOX has been associated with the low risk of chronic disease in healthy diets (*2*, *3*).

The abundant literature in this field (over 2600 and 3000 journal papers on DF and AOX, respectively, in the past five years, MEDLINE) addresses DF and AOX separately as nonrelated compounds, probably because of substantial differences in their chemical structures, physicochemical and biological properties, and metabolic pathways. However, our approach focuses on the fact that DF and a considerable amount of dietary AOX follow a common and synergistic physiological process within the gastrointestinal tract.

Most reported dietary AOX are a wide variety of single molecules (vitamins C and E, carotenoids, low molecular weight polyphenols, and others) solubilized and totally or partially absorbed in the upper intestine (*4*), but an appreciable amount of dietary AOX, mainly polyphenolics and some carotenoids, traverse the small intestine intact in tandem with DF. These AOX reach the colon, where they release the fiber matrix and produce metabolites and an antioxidant environment by the action of the bacterial microbiota (*5*, *6*).

The presence of polyphenols (PP) and carotenoids associated with DF may significantly affect the physiological properties and health effects of DF. This paper proposes to show that DF and AOX could be approached jointly in nutrition and health studies because of their close relationship and common fate in the gut. It also highlights the fact that transportation of AOX through the gastrointestinal tract is an essential physiological function of DF that has received little attention so far.

Dietary Fiber: A Complex of Colonic Substrates. The importance of DF for health has been defined in recent decades through active research on different gastrointestinal aspects (mobility and transit time, polyps−cancer, irritable bowel syndrome, Cröhns disease, constipation, etc.), lipid and coronary heart disease, prebiotic effect, glycemic response, satiety, and obesity(*1*). Most of this research has focused on the components included in the early definition of DF as "the remnants of plant foods remaining after hydrolysis by the enzymes of the digestive system" (*7*), which include both cell wall material and intracellular polysaccharides. These components are usually categorized by whether or not they are soluble in the human digestive fluids. Insoluble dietary fiber is made up of cellulose and other nonstarch polysaccharides along with a small amount of cell wall lignin and cutin, whereas pectins, β-glucans, arabinoxylans, galactomannans, and other indigestible polysaccharides and saccharides are typical soluble dietary fiber constituents.

However, there is now convincing evidence that the characteristics of the primary DF constituents (resistance to hydrolysis by human digestive enzymes and fermentation in the large intestine) can be extended to other indigestible food constituents (carbohydrates and noncarbohydrates) such as resistant starch, oligosaccharides, polyphenolic compounds, indigestible cell wall proteins, and animal-derived material such as aminopolysaccharides.

The need for an updated concept of DF has been raised mainly by studies on the substrates available in the human colon, along with studies on bacterial mass and energy balance (*8*).

One of the principal roles of dietary fiber is to provide substrates for fermentation by bacteria in the large intestine,

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Table 1. Substrates Available for Colonic Fermentation in Western Diets[a]

	amount (g/day)	origin
dietary fiber (as nonstarch polysaccharides and lignin)	16−21	plant foods
resistant starch	3.2−5.7	starchy foods
oligosaccharides	2−8	legumes, root vegetables, artichokes
undigested protein (resistant protein)	3−9	plant foods
undigested fat	1−3	vegetable oils and animal fat
polyphenolic compounds	0.9−2.7	plant foods and beverages
others (unabsorbed sugars, polyols, additives, organic acids)	2−10	processed foods, lactase deficiency (milk)
mucus, pancreatic enzymes, gut secretions	2−6	endogenous
total mean weight	47.7	

[a] From refs *5* and *8*−*11*.

producing various end compounds (acetate, propionate, and butyrate, ammonia, gases, H_2, CO_2, amines, phenols), energy, and biomass. This process also makes possible a function that is essential to the intestinal ecosystem: maintenance of the colonic microflora and enhancement of the immune system.

It is estimated that about 45−60 g of substrates must reach the human colon daily to reconstitute and maintain the human microflora (around 15 g of bacteria are excreted daily in human feces) (*8*, *9*). However, the daily intake of DF as traditionally defined (nonstarch polysaccharides and lignin) in European countries is estimated at around 20 g per capita (*10*), which is clearly insufficient to maintain the daily intestinal bacterial turnover.

Table 1 lists the main dietary and endogenous substances available for fermentation that have been determined from human studies on ileostomy subjects, breath hydrogen studies, and intubation of the ileum to collect effluents and from dietary intake data (*5*, *9*−*11*). The mean daily amount thought to be available for fermentation in the large intestine in persons consuming Western diets is estimated at close to 50 g, which is consistent with physiological needs. DF intake represents about 39% of this amount and provides less than half of the energy supply to the large bowel (*8*, *9*).

This substrate/energy gap speaks in favor of a broader definition of DF extending to other indigestible compounds. In this connection, numerous updated definitions consider a DF as a combination of chemically heterogeneous substances not absorbed in the small intestine, including nonstarch polysaccharides, resistant starch, oligosaccharides, sugar-alcohols, resistant protein, polyphenols, Maillard compounds, and others (*12*, *13*). On the basis of this updated concept, the intake of DF in some European areas (Spain; Murcia, Spain and Copenhagen, Denmark) has been estimated at 41.5, 62.3, and 47.5 g, respectively. These figures are more realistic, closer to the intestinal microflora and energy needs than the corresponding DF intakes determined in these regions on the basis of the traditional definition (18.3, 28.6, and 19.8 g) (*14*, *15*).

However, despite the intensive research and advances in this field, the definition of DF is still controversial. The AACC definition includes associated noncarbohydrate compounds, whereas the Codex Alimentarius defines DF as "carbohydrate polymers (dietary and synthetic) with ten or more monomeric units, which are not hydrolyzed by the endogenous enzymes in the small intestine of humans" (*16*). This definition may be useful for analysis, labeling, and commercial purposes, but it obviously presents some limitations for nutrition and health studies given that it omits major indigestible dietary constituents.

Numerous papers have addressed the chemical, physiological, and nutritional properties of the "new" DF components (resistant starch, resistant protein, oligosaccharides, synthetic polymers, and others), but little attention has been paid to associated dietary AOX (polyphenols and carotenoids).

Antioxidants associated with the DF matrix are substances that are not detected in the usual analytical procedures for either dietary AOX (targeting antioxidants extracted by aqueous−organic solvents) or DF (targeting carbohydrates and lignin). However, these antioxidant compounds make up a substantial portion of the dietary AOX; they are not minor constituents of DF, and as such they may contribute significantly to the health effects attributed to DF and dietary AOX.

DIETARY FIBER AS A CARRIER OF ANTIOXIDANTS

Dietary Antioxidants in the Small and Large Intestine. Vitamins (C, E, and A), polyphenols (flavonoids, phenolic acids, stilbenes, and tannins), and carotenoids (carotenes and xanthophylls) are the main groups of dietary AOX. Vitamins are single molecules, and their metabolism and allowances are well-known, but there are hundreds of polyphenols and carotenoids with a wide range of structures and molecular masses, and our knowledge of their intakes, bioavailability, and metabolism is currently partial and incomplete.

The biological properties of AOX depend on their bioaccessibility and bioavailability. A part of dietary AOX release the food matrix in the upper gastrointestinal tract (bioaccessibility) by direct solubilization in the intestinal fluids in physiological conditions (37 °C, pH 1−7.5) and/or by the action of digestive enzymes (enzymatic hydrolysis of protein, carbohydrates, and lipids favors the release of AOX from the food matrix). These bioaccessible AOX are at least partially absorbed through the small intestine mucose. Another part of dietary PP antioxidants (nonbioaccessible) pass undissolved and unaltered through the upper intestine in association with DF and reach the colon, where they can be fermented by the action of bacterial enzymes (*4*, *17*).

On this basis, dietary AOX can be divided into two groups: (1) antioxidants bioaccessible in the small intestine (vitamins, low molecular weight PP, and carotenoids) and (2) antioxidants not bioaccessible in the small intestine or antioxidants associated with DF. These are mainly polyphenolic compounds (polymeric PP and low molecular weight PP linked to DF and/or trapped in cores of the fiber matrix) along with minor amounts of carotenoids and others.

Most studies on dietary antioxidants refer to group 1 (*18*), whereas group 2 is usually ignored, probably because it is thought that they are minor and physiologically irrelevant food constituents. However, recent findings have shown that the group 2 AOX constitute a major proportion of the antioxidants present in foods and diets (*5*). Our approach is intended to show that the transport of these AOX is an essential physiological function of DF.

Polyphenols in Dietary Fiber: Content. PP, the most abundant AOX in our diet, are a complex group of substances with a wide range of molecular mass that can be found in plant foods and beverages either free or bound to cell wall (or DF) constituents.

PP have both hydrophobic aromatic rings and hydrophilic hydroxyl groups with the ability to bind to polysaccharides and proteins at several sites on the cell wall surface (*19*). They are linked by hydrogen bonding (between the hydroxyl group of PP and oxygen atoms of the glycosidic linkages of polysaccharides), hydrophobic interactions, and covalent bonds such as ester bonds between phenolic acids and polysaccharides. Interaction can also be dependent on specific porosity and surface properties, which can restrict the size of the molecules that penetrate. Pore size in the cell wall can range from 4 to 10 nm in diameter, which may restrict penetration of PP molecules with molecular masses larger than 10 kDa (equivalent to 34 units of catechin) (*19*−*21*).

Most literature data on food PP, assembled in several databases (*22*, *23*), comes from HPLC analysis of aqueous organic extracts of foods, and consequently biological, nutritional, and epidemiological studies generally address only extractable PP (flavonoids, phenolic acids, stilbenes and lignans, glycosides, esters, and aglycones), which are group 1 AOX (bioaccessible in the upper intestine and absorbable through the small intestine mucose). However, the usual PP analytical methods do not determine the appreciable amount of PP that remains in the residues of aqueous organic extraction, called nonextractable polyphenols (NEPP), and therefore there is an absence of data in the literature on these group 2 AOX.

NEPP are compounds, mainly polymeric tannins and hydrolyzable PP, associated with DF by the different interactions cited above. Tannins are made up of flavanol monomers (proanthocyanidins or condensed tannins) and polyesters of a sugar moiety and gallic acid or ellagic acid (hydrolyzable tannins); hydrolyzable PP are simple or oligomeric compounds linked to the cell wall structure or trapped in cores. NEPP release the fiber matrix physiologically by the action of bacterial enzymes in the colon.

To our knowledge only the intestinal microflora is able to disrupt the DF matrix and release the associated AOX in soft physiological conditions (neutral pH, 37 °C, reducing environment). The human microflora can hydrolyze, reduce, decarboxylate, demethylate, and dehydroxylate PP, producing several metabolites (dyhydroxyphenyl acids, urolithin, equol, and others). This enormous capacity to extract and transform the indigestible PP, which greatly outstrips physicochemical and biotechnological treatments, is a consequence of the genomic complexity and variety of the human microflora. The large intestine is a complex ecosystem with more than 400 different species of bacteria (>95% concentrated in the colon) containing 100 times more genes than the human genome (*24*).

The bacterial species of the human gut develop important metabolic and immune functions. Polyphenols are metabolized to a large extent by gut microbiota, producing metabolites such as hydroxyphenylacetic, phenylpropionic, and phenylbutyric acids with potential healthy effects (*25*, *26*), but there is a two-way interaction between gut microbiota and polyphenols: nondigestible components of the diet, including NEPP, modify the numbers and types of bacteria. In this context, the growth of beneficial bacteria such as *Lactobacillus* spp. and the inhibition of pathogenic bacteria (*Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans*) by the action of dietary polyphenols and their metabolites have been reported (*27*−*30*). However, current emerging evidence on these intestinal health effects of PP is largely based on in vitro and animal studies, and substantiation in humans is needed.

Determination of NEPP requires strong acidic treatments (methanol/H_2SO_4 90:10 (v/v), 85 °C, 20 h) to disrupt the cell wall structure and hydrolyze polysaccharides and proteins, allowing the release of hydrolyzable PP (*31*). An additional HCl/BuOH 97.5:2.5 (v/v) treatment (100 °C, 60 min) is required to obtain cyanidin/delphinidin solutions and insoluble phobaphenes derived from NEPA (*32*). The NEPP profile and content are determined in these two hydrolysates by HPLC-MS and spectrophotometric methods (*32*, *33*).

The strong acidic treatments may degrade some phenolic compounds, especially flavonoids, but acidic hydrolysis permits a high rate of PP recovery, and for the moment they are the only valid alternative for NEPP analysis. We previously tested different enzymatic and physicochemical procedures to release NEPP from the DF matrix with very low yields in comparison with the strong acidic hydrolysis. Among these failed attempts are enzymatic treatments (pectinases, estearases, and proteases), various solvents at high temperature and pressure, steam explosion, thiolysis, and alkali treatments. Alkaline hydrolysis, generally used in cereal products, hydrolyzes PP ester bonds but also causes partial release of the total NEPP (*31*). Anyway, novel analytical methods that minimize losses of polyphenols in hydrolysis treatments are needed.

Considerable important amounts of NEPP associated with DF following acidic treatment were first reported in some specific vegetable materials such as grape pomace, apple pomace, and carob pods. The physiological properties of these NEPP exhibited similarities with the properties of primary DF constituents (polysaccharides and lignin): nondegradation by digestive enzymes, partial colonic fermentability, and enhancement of lipid and protein excretion (*34*). In addition, they confer a specific property—antioxidant activity—on DF.

In this connection, the reported amount of PP associated with DF in 11 fruits and vegetables makes up on average around 2.5% of the DF content (*35*). Figures of the same order may be expected in other plant foods,which indicates that these compounds are not minor DF constituents. It is estimated that 80−95% of grain polyphenolic compounds are linked to cell wall polysaccharides, mainly α-arabinoxylans, as diferulates covalently bound through ester bonds (*36*).

Indeed, further studies have shown that PP appear associated with DF in all plant foods and beverages common in our diet (*5*). The highest concentrations of NEPP are found in fruits, largely consisting of proanthocyanidins (NEPA). Legumes and nuts are also sources of NEPA. Cereals and vegetables do not contain NEPA, but they are important sources of hydrolyzable PP in the diet (*5*, *33*).

With regard to the amount of PP in the diet, the literature on dietary PP intake considers only extractable polyphenols (EPP) and omits NEPP. Nevertheless, the NEPP intake in the Spanish diet, for example, is estimated at around 1 g (mainly hydrolyzable phenolics and high molecular weight proanthocyanidins) (*5*), which represent about 50% of the total intake of polyphenols, NEPP plus EPP (*37*). Intakes of the same order can be expected in Western diets. These data suggest that current research on food content and dietary intakes of PP, and on their bioavailabity, metabolism, biological properties, and potential effects on the prevention of age-related diseases, is generally focusing on the tip of the iceberg.

Ferulic acid, caffeic acid, hesperidin, naringin, catechin, epicatechin, ellagic acid, gallic acid derivatives, protocatechin, and *p*-hydroxybenzoic acid were the major individual NEPP in plant foods of the diet (*5*).

In the case of beverages, food composition tables usually report zero DF content in the most common drinks of the diet. This is mainly due to the fact that the official methods of DF analysis were developed exclusively for solid plant foods (beverages were not included in the corresponding analytical assays or interlaboratory studies). However, a certain amount of the soluble DF may be expected to pass to the beverage during the maceration

Table 2. Polyphenolic Compounds (PP) Associated with Dietary Fiber (DF)[a]

plant food	DF (% dry matter)	associated PP (% dry matter)	profile (major components)
apple with peel	16.6	0.36	proanthocyanidins, hydrolyzable PP, ferulic acid, *p*-hydroxybenzoic acid
orange	26.5	0.34	hydrolyzable PP
strawberry	24.9	0.44	proanthocyanidins, hydrolyzable tannins
onion	19.4	0.41	hydrolyzable PP
lettuce	21.0	0.67	hydrolyzable PP
beverage	mg/L	mg/L	profile (major components)
red wine	1370	533	flavonols, benzoic acids
beer (lager)	2037	103	flavonols, hydroxycinnamic acids
peach juice	2370	180	flavonols, hydroxycinnamic acids
cocoa milk drink	8206	344	flavonoids, procyanidins

[a] From refs *35*, *38*, and *48*.

and/or extraction of solid plant material. Recently, appreciable amounts of DF, as determined by a specific dialysis procedure, have been reported in brewed coffee, beer, wine, fruit juices, and other beverages (*38*). The soluble DF in drinks is made up of indigestible polysaccharides and also contains a significant amount of associated PP, mainly flavonoids and phenolic acids. Some of these data are included in **Table 2**.

NEPP are certainly the major AOX in DF, but there are other minor associated AOX such as carotenoids in fruits and vegetables and melanoidins or Maillard reaction products in processed foods (*6*, *39*). The digestion and absorption of carotenoids (β- and α-carotene, β-cryptoxanthin, lycopene, lutein, and zeaxanthin) are not complete, and as in the case of PP, a part of these dietary AOX enters the large intestine in association with DF (*6*). Also, during thermal processing of common foods (cereals, coffee, and others), polysaccharides, proteins, and phenolic compounds—mainly hydroxycinnamates—contribute to the formation of melanoidins, which are indigestible compounds that also reach the colon in association with DF (*40*). In fact, melanoidins appear in gravimetric residues from DF enzymatic-gravimetric analysis. The daily intake of carotenoids and melanoidins in DF is low in comparison with PP compounds, but their nutritional significance has yet to be elucidated.

Polyphenols in Dietary Fiber: Properties. *Antioxidant Capacity*. The appreciable amount of associated polyphenols provide to DF a significant antioxidant capacity (AC) that may have pronounced effects on its properties. The determination of DF-AC can be useful to complete the characterization of the fiber and estimate its potential health effects and applications as a functional ingredient. The AC associated with DF can be measured in extracts and hydrolysates of DF by the most common AC methods (*41*).

The antioxidant capacity of a dietary fiber is derived from the cumulative synergistic antioxidant power of polyphenols and other minor constituents (carotenoids, Maillard compounds, trace minerals, and others). This parameter provides an integrated measurement that may represent the amount of antioxidant units (Trolox equivalents) carried by a DF in the human gut.

In this context, DF with exceptional antioxidant capacity, known as antioxidant dietary fibers, have been found in mango peel, pineapple shell, guava pulp, grape pomace, acerola fruit, and some seaweeds. As food ingredients, these fibers prevent lipid oxidation in meat products and restructured fish products, maintaining nutritional quality and prolonging shelf life (*42*).

Colonic Fermentation. Fermentation of NEPP in the human colon is a physiological event that may have significant effects in intestinal health. Unabsorbed PP associated with DF are not bioavailable in the human upper intestine and reach the colon, where they become fermentable substrates for bacterial microflora along with indigestible carbohydrates. It has been hypothesized that PP/DF is able to exert a considerable reducing activity in both the small and large intestines before fermentation. Because this insoluble material remains in the gastrointestinal tract for a long time, it has the capacity to quench the soluble radicals formed in the gastrointestinal tract by a surface interaction and protein. Phenylacetic, phenylpropionic, and phenylbutyric acids and urolithins A and B are absorbable metabolites of PP colonic fermentation that may exert systemic effects (*25*, *26*). Nonabsorbable metabolites and nonfermented PP remain in the colonic lumen, where they may contribute to a healthy antioxidant environment by scavenging free radicals and counteracting the effects of dietary pro-oxidants. Also, they may have effects on modulation of the microflora, as mentioned above.

Colonic fermentation of NEPA, a major fraction of NEPP, produces metabolites that are detectable in human plasma. A higher yield of phenolic metabolites in NEPA-rich DF samples than in purified NEPA samples has been reported, which indicates that DF enhances colonic fermentation of NEPA (*25*). It also suggested that the literature results of experiments on colonic fermentation performed with simple or isolated PP are likely to differ from their actual fermentation in the human large intestine, where simultaneous and synergistic fermentation of DF occurs.

Health-Related Properties. There are very few in vivo studies addressing health-related properties of PP associated with DF in comparison with the hundreds of works focusing on EPP. **Table 3** lists some animal and human trials focusing on NEPP.

The main properties derived from the presence of appreciable amounts of DF-associated NEPP reported in animal experiments are (a) enhancement of the excretion of lipids, protein, water, and total fecal output; (b) positive effects on lipid metabolism, reducing lipid peroxidation, total cholesterol, LDL-cholesterol, and triacylglycerides in hypercholesterolemic rats; (c) better oxidative stability of chicken meat accompanied by a sparing effect on vitamin E with increasing concentration in the liver; (d) increase of antioxidant activity in the large intestine and cecum; and (e) inhibition of proliferation in the colonic epithelium by reducing the total number of crypts in rats.

These results suggest positive effects on cardiovascular disease prevention and also in gastrointestinal health, including prevention of colon cancer risk.

NEPP—hydrolyzable PP and proanthocyanidins—may produce a chemopreventive effect for colorectal cancer through different mechanisms such as generation of an antioxidant environment in the colon, inhibition of DNA oxidative damage and inflammation, induction of apoptosis, and prevention of polyp formation (*43*).

In this connection, Ferguson et al. (*13*) pointed out that because overproduction of free radicals and hence of oxidative stress has been linked to cancer, reexamination of the literature on cancer protection suggests that plant cell walls containing significant amounts of phenolic components may be the most likely to protect against cancer.

With regard to bioavailability, human trials have established that the ingestion of EPP results in increased plasma AC. As far as NEPP is concerned, a high intake of NEPA-rich DF produces an increase in plasma AC after 8 h, indicating that these PP compounds associated with DF are also bioavailable (*44*). This time is longer than in the case of EPP, 0.5−2 h (*4*), suggesting

Table 3. In Vivo Studies on Effects of Nonextractable Polyphenols (NEPP) in Intestinal Health and Cardiovascular Disease Risks

NEPP-rich material tested	experiment	effect/properties	ref
		Animal Experiments	
apple pulp, carob pod	Wistar rats fed either a DF diet free of NEPP or a DF diet rich in NEPP	increase total fecal output as well as water, nitrogen, and fat excretion in the NEPP-DF fed group; excretion of a fraction of NEPP (high molecular weight proanthocianydins)	Bravo et al. (*49*, *50*)
grape pomace, grape peels and seeds	Wistar rats fed a standard diet supplemented with cellulose, grape pomace, grape seeds, or grape peels	NEPP did not modify the production of SCFA in colonic fermentation; excretion of NEPP; increase of stool weight and protein and fat excretion	Martin-Carron et al. (*51*)
grape pomace, grape seeds	Wistar rats fed a cholesterol-added diet containing cellulose or grape pomace as source of fiber	NEPP reduce serum total cholesterol and LDL-cholesterol as well as the atherogenic index in hypercholesterolemic rats; increase of stool weight and protein and fat excretion	Martin-Carron et al.(*52*)
artichoke (hydroxycinnamic acids), grape seeds	Wistar rats fed a diet supplemented with cellulose, artichokes, or grape seeds	higher antioxidant status in large intestine and cecal contents in the artichoke and grape seeds group; enhancement of microbial enzymes to metabolize glycosides and nitrocompounds	Goñi et al. (*53*, *54*)
cocoa fiber (condensed tannins and procyanidins)	Wistar rats fed diets containing cellulose or cocoa fiber	decrease of total and LDL cholesterol and triacylglycerol levels and reduced lipid peroxidation.	Lecumberri et al. (*55*)
grape pomace	chickens fed a corn−soybean basal diet supplemented with grape pomace or vitamin E	increase of antioxidant activity in diet, ileal content, breast muscle and excreta; reduce the lipid peroxidation of meat; sparing effect with vitamin E	Brenes et al. (*56*)
grape antioxidant DF (rich in proanthocyanidins)	Wistar rats fed a cellulose diet or grape antioxidant DF diet	induction of epithelial hypoplasia in colonic mucose; reduction of apoptosis; decrease of number of crypts; antiproliferative capacity	Lopez-Oliva et al. (*57*, *58*)
grape antioxidant DF	APC_{min} mice fed standard diet and diet supplemented with 1% of grape antioxidant DF	significant reduction of the number of polyps, especially in the middle part of the colon, after 6 weeks; inhibition of intestinal tumorogenesis in small intestine	
		Human Trials	
grape DF rich in NEPP	14 healthy volunteers, acute intake of 15 g of DF rich in NEPP	increase of antioxidant capacity of plasma 8 h after ingestion	Pérez-Jimenez (*44*)
grape antioxidant DF	34 nonsmoking adults, randomized controlled parallel group trial, supplement with 7.5 g of grape antioxidant DF	significant reduction of total cholesterol, LDL cholesterol, and systolic and diastolic blood pressure; reduction of 2.5 points in the Framingham Global Risk score for cardiovascular disease	Pérez Jimenez et al. (*46*)
usual diet	12 nonsmoker healthy subjects, day before low-polyphenol diet; after overnight fast, venous blood was collected	detection in plasma of 3,4-dihydroxyphenylacetic, hydroxyphenylvaleric, and hydroxyphenylpropionic acids (metabolites of colonic fermentation of dietary nonextractable proanthocyanidins)	Saura-Calixto et al. (*25*)

Table 4. Antioxidants in the Small and Large Intestine[a]

	daily dietary intake (European diets)	absorption (%)
	Small Intestine	
vitamin A	0.6−1.4 μg	>80
vitamin C	65−161 mg	complete
vitamin E	7.8−8.3 mg	complete
selenium (selenomethionine, seleniumcysteine)	3.8−8.3 μg	>50
extractable polyphenols	1000−1100 mg	5−10
polyphenols associated with DF (nonextractable polyphenols)	900−1000 mg	0
carotenoids (β-carotene, lycopene, cryptoxanthin, lutein)	9.5−16 mg	45−50
	Large Intestine	
PP associated with DF	1270 mg (450 mg of PA plus 1250 mg of HPP)	partial absorption as single compound or fermentation metabolites; increase of intestinal antioxidant status
carotenoids	4.3−8	
extractable polyphenols (nonabsorbed in the small intestine)	900−1050 mg	
vitamins, selenium (nonabsorbed in the small intestine)	negligible	

[a] From refs *4*−*6*, *37*, and *59*.

slower absorption of NEPA than of EPP. We have found no references to human trials dealing specifically with nonextractable hydrolyzable PP, but in a rat experiment Rondini et al. (*45*) observed that the concentration of plasma ferulic acid from bran DF remained constant up to 24 h after meal but completely disappeared 4 h after free ferulic acid ingestion. This also suggests slower absorption of hydrolyzable NEPP.

With regard to systemic effects, beneficial effects on cardiovascular disease risk factors have been observed, with significant reduction of total cholesterol, LDL-cholesterol, and blood pressure, in subjects consuming DF rich in associated proanthocyanidins (*46*).

A review of in vivo studies on hydrolyzable NEPP from cereals suggests that the beneficial effects attributed to cereal DF are due to polysaccharide moieties and to the associated PP (*47*). However, these reviewed works mainly address PP linked by ester bonds to polysaccharides, which can be cleaved by the action of esterases present in both the small and large intestine (**Table 4**). Therefore, it is not possible to elucidate the proportions of PP bioaccessible in the small intestine (EPP) and the large intestine (NEPP). Be that as it may, a recent human intervention trial showed an increase of fasting blood ferulic acid concentrations after consumption of whole grain cereal, a NEPP-rich material.

Briefly then, humans trials reveal bioaccessibility and bioavailability of NEPP and their metabolites in the large intestine as well as potential health effects, but they must be seen as no more than promising preliminary results given the small number of trials that have specifically addressed these DF-associated compounds and need to be confirmed by further research.

CONCLUSIONS/REMARKS

1. DF carries an appreciable amount of AOX, mainly polyphenolic compounds, through the gastrointestinal tract.
2. Polyphenols associated with DF exhibit similar physiological properties to primary DF constituents: resistance of digestive enzymes to hydrolysis and partial fermentation in the colon.
3. PP confer specific properties on DF, mainly derived from their antioxidant capacity.
4. In vitro and animal studies have shown that PP associated with DF are bioavailable in the large intestine as colonic fermentation metabolites and as free nonfermented PP. Current emerging evidence on the intestinal health effects of PP (antioxidant status, microflora modulation), largely based on in vitro and animal studies, need to be validated in human studies.
5. Animal experiments and human trials have shown promising properties of DF rich in associated PP in the prevention of risk factors for cardiovascular and intestinal diseases.
6. PP-rich DF can be used as a functional ingredient to prevent lipid peroxidation in fish and meat products.
7. Further analytical studies are needed to minimize the partial degradation of PP produced by the strong acidic treatments required to determine NEPP.
8. The amount of PP associated with DF in the diet is estimated at about 50% of total dietary AOX.
9. PP associated with DF have been ignored until now in chemical, nutritional, and epidemiological studies, but they may contribute significantly to the health effects of DF and dietary AOX.
10. The transportation of dietary AOX through the gastrointestinal tract and the production of fermentation antioxidant metabolites in the colon appear to be essential physiological functions of dietary fiber.

ABBREVIATIONS USED

DR, dietary fiber; AOX, antioxidants; PP, polyphenols; NEPP, nonextractable polyphenols; EPP, extractable polyphenols; NEPA, nonextractable proanthocyanidins; AC, antioxidant capacity.

NOTE ADDED AFTER ASAP PUBLICATION

After the original ASAP publication of Decembar 10, 2010, changes were made to the reference listing, Table 3, and the text under Health-Related Properties. These changes are reflected in the posting of January 5, 2011.

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