Food processing strategies to enhance phenolic compounds bioaccessibility and bioavailability in plant-based foods

Albert Ribas-Agustí, Olga Martín-Belloso, Robert Soliva-Fortuny, and Pedro Elez-Martínez

Department of Food Technology, Agrotecnio Center, University of Lleida, Av. Alcalde Rovira Roura 191, Lleida, E-25198, Spain

ABSTRACT

Phenolic compounds are important constituents of plant-based foods, as their presence is related to protective effects on health. To exert their biological activity, phenolic compounds must be released from the matrix during digestion in an absorbable form (bioaccessible) and finally absorbed and transferred to the bloodstream (bioavailable). Chemical structure and matrix interactions are some food-related factors that hamper phenolic compounds bioaccessibility and bioavailability, and that can be counteracted by food processing. It has been shown that food processing can induce chemical or physical modifications in food that enhance phenolic compounds bioaccessibility and bioavailability. These changes include: (i) chemical modifications into more bioaccessible and bioavailable forms; (ii) cleavage of covalent or hydrogen bonds or hydrophobic forces that attach phenolic compounds to matrix macromolecules; (iii) damaging microstructural barriers such as cell walls that impede the release from the matrix; and (iv) create microstructures that protect phenolic compounds until they are absorbed. Indeed, food processing can produce degradation of phenolic compounds, however, it is possible to counteract it by modulating the operating conditions in favor of increased bioaccessibility and bioavailability. This review compiles the current knowledge on the effects of processing on phenolic compounds bioaccessibility or bioavailability, while suggesting new guidelines in the search of optimal processing conditions as a step forward towards the design of healthier foods.

KEYWORDS

Food processing; phenolic compounds; bioaccessibility; bioavailability; plant-based food

Introduction

Fruits and vegetables are beneficial in a healthy diet (WHO and FAO, 2003). Their consumption is related to a number of health effects, which can be attributed to the biological activity of phenolic compounds and others (Tomás-Barberán and Andrés-Lacueva, 2012). Phenolic compounds are a large group of secondary metabolites that are ubiquitous in plants and can be in significant amounts in some plant-derived foods (Haminiuk et al., 2012). Actually, phenolic compounds are the largest group of dietary antioxidants in humans (Scalbert and Williamson, 2000). Many of their beneficial properties have been reported with regard to their antioxidant activity and their ability to scavenge reactive oxygen species. Furthermore, they can participate in signal transduction with positive effects on cell metabolism. In this sense, some authors have related these biological activities with reduced risk of cancer and cardiovascular diseases (Scalbert et al., 2005).

Phenolic compounds constitute a huge and heterogeneous group with more than 8,000 identified compounds, which can be classified by their molecular structure (Figure 1). The common molecular trait of all phenolic compounds is the presence of one or more aromatic rings, with at least one hydroxyl group (phenol group). They can be simple molecules with one phenol, such as phenolic acids, or complex structures with two or multiple phenol groups, such as stilbenes and flavonoids. Flavonoids is one of the main groups of phenolic compounds, which consists in two aromatic rings connected by a heterocycle. Flavonols, flavones, isoflavonones, flavanones, flavan-3-ols, and anthocyanidins are the most common sub-classes of flavonoids and they differ from each other by the structure of their heterocycle. In addition, their native form is often polymerized or conjugated with sugars or organic acids. Proanthocyanidins (condensed tannins) are an example of oligomeric or polymeric forms composed of flavan-3-ols units. Glycosylation is very common in flavonoids, except for flavan-3-ols. In consequence, a huge range of structures exists with different chemical and biological properties (Crozier et al., 2009).

Plant origin and food processing are the two main factors that affect the presence and amount of the different classes of phenolic compounds in food. Some edible plants are very rich in phenolic compounds, including most fruits and vegetables (Rothwell et al., 2013). Once ingested, the health effects derived from the phenolic compounds depend on to what extent they are released from the matrix, absorbed in the gastrointestinal tract and available for metabolism. Bioaccessibility is the fraction of compounds that is released from the food matrix during digestion and becomes available for small intestinal absorption; on the other hand, bioavailability refers to the fraction of compounds that is absorbed, distributed by the circulatory system and subjected to metabolism and elimination. Many factors are involved in the bioaccessibility and bioavailability of phenolic compounds, from their chemical structure and interactions.
with the food matrix to the nutritional condition and genetic factors of the host. Therefore, in order to fully assess the nutritional properties of food, attention should be paid to those factors affecting bioaccessibility or bioavailability of phenolic compounds.

Food processing affects phenolic compounds bioaccessibility and bioavailability in different ways. Firstly, higher content in food normally implies more released and absorbed compounds in the intestine. Plants synthesize phenolic compounds as a defense mechanism against biotic or abiotic stress conditions. Thus, postharvest treatments that emulate such stress conditions can be used to stimulate the accumulation of phenolic compounds in raw fruits and vegetables (Amarowicz et al., 2009). On the other hand, food processing often induces the degradation of phenolic compounds, thus reducing their amount in processed foods. However, processing can also lead to chemical or physical modifications in food in such a way that fosters the release and absorption of phenolic compounds during digestion.

Comprehensive work has been done regarding the phenolic compounds content in food and the effects of food processing on their content and stability (Rothwell et al., 2013). More recently, the interest has been also focused on bioaccessibility and bioavailability, as these approaches are more tightly associated to the effects on health. The number of studies on phenolic compounds bioaccessibility or bioavailability is currently expanding (Crozier et al., 2010). Bioavailability is estimated by \textit{in vivo} analysis of the metabolites in blood and/or urine after consumption, while bioaccessibility is assessed by \textit{in vitro} methodologies that estimate the amount of compounds available for intestinal absorption (Carbonell-Capella et al., 2014). The \textit{in vivo} methodologies are more realistic approaches to the determination of health effects. However, their implementation is difficult and expensive and normally limits the number of samples to be assessed. This can be simplified by the use of \textit{in vitro} methodologies that emulate digestion, release and absorption of food nutrients in the gastrointestinal tract, facilitating the assessment of multiple processing conditions. In food technology research, the assessment of phenolic compounds bioaccessibility using \textit{in vitro} simulated digestion is a common tool as a tentative estimation to bioavailability (Motilva et al., 2015).

The main and primary objective of food processing is to provide safe and nutritious food. Recent advances in food technology have made new processing methodologies available in addition to the traditional processes, which are able to render added value to food products by enhancing their nutritional properties, without losing sight of their microbiological safety. In this sense, variables and intensities of these technologies can be modulated in order to improve the phenolic compounds bioaccessibility and bioavailability. Even if there is good knowledge on the phenolic compounds content in food, there is a serious lack of information on the effect of food processing on their bioaccessibility or bioavailability. This review compiles the existing data, with a focus on works assessing bioaccessibility or bioavailability, and proposes some strategies in order to explore those processing conditions that unlock phenolic

\textbf{Figure 1.} Classes and chemical structures of dietary phenolic compounds.
compounds bioaccessibility and bioavailability from the food matrix. Finally, this work is intended to encourage new research in an area with promising findings in the near future.

**Chemical structure of phenolic compounds in plant-based foods affecting their bioaccessibility and bioavailability**

The molecular structure of phenolic compounds has an influence on their bioaccessibility and bioavailability, and more precisely, the class of compound, molecular size and pattern of glycosylation are relevant features to be considered. Actually, there is a vast array of chemical properties among phenolic compounds in plant-based foods due to their huge diversity of structural forms (Figure 1). The acidic conditions of the gastric digestion do not significantly affect the structure of most phenolic compounds (Rios et al., 2002; Manach et al., 2004). Therefore, as a general rule, polymeric or glycosylated phenolic compounds need to be transformed in the small or large intestine before being absorbed. This is the case of most flavonoids that are glycosylated in their native form, except flavan-3-ols, which are mainly present in their oligomeric or polymeric forms (proanthocyanidins). Flavonoid glycosides are too hydrophilic to be absorbed by passive diffusion in the small intestine. In fact, they are deglycosylated in the lumen of the small intestine by the lactase phlorizin hydrolase and incorporated into the enterocytes by passive diffusion (Day et al., 2000). Another way of absorption is the incorporation into the epithelial cells of the small intestine by active transport through sodium-glucose transporter proteins, being subsequently deglycosylated by a cytosolic β-glucosidase (Gee et al., 2000). Glucose- and probably arabinose- and xylose-conjugated flavonoids can be hydrolyzed and absorbed in the small intestine, even faster than the corresponding aglycones (Gee et al., 2000). On the contrary, rhamnose- and rutinoside- (glucose and rhamnose disaccharide) conjugated flavonoids cannot be hydrolyzed until they reach the colon, where they are degraded by the rhamnosidases of the colonic microbiota and absorbed in the colon (Hollman et al., 1999). The highly unstable anthocyanidins are an exception to this general rule, since they are absorbed only in the glycosylated form (anthocyanins) (Prior and Wu, 2006). Nevertheless, anthocyanins are also very sensitive to degradation during processing and digestion, so very low bioavailability values are expected for anthocyanins, in the order of <0.1% of the intake (Hollands et al., 2008). On the contrary, isoflavones are considered the most bioavailable phenolic compounds, in the order of 40% for daidzin (Manach et al., 2005). As a general trend, the bioavailability of phenolic compounds that need to be hydrolyzed by the colon microbiota is lower if compared to those compounds that are readily absorbed in the small intestine (Manach et al., 2004).

In proanthocyanidins, the degree of polymerization (DP) influences their bioavailability. Most of the dietary proanthocyanidins pass through the small intestine and reach the colon, especially those with high DP (Kahle et al., 2007). When they arrive at the large intestine they are extensively modified by the colonic microbiota, producing a vast array of phenolic acids and also probably some monomeric and dimeric flavan-3-ols, which are readily absorbed in the colon (Serra et al., 2011; Ozdal et al., 2016). In the colon, the catabolism and absorption of metabolites is more intense with low-polymerized proanthocyanidins. High-molecular-weight proanthocyanidins easily form complexes with macromolecules during digestion, hindering their transformation and absorption (Serrano et al., 2009).

Part of the dietary phenolic acids is absorbed in the small intestine and the rest is further modified and absorbed in the colon (Crozier et al., 2010). For instance, after consumption of coffee, 30% of caffeoylquinic acid and derivatives were absorbed in the small intestine and the rest passed to the large intestine (Stalmach et al., 2010). These compounds are degraded afterwards by esterases of the colon microbiota, yielding caffeic acid and other absorbable metabolites (Del Rio et al., 2010). Polymeric compounds containing gallic acid (gallotannins) are also hydrolyzed by the colon microbiota (Serrano et al., 2009).

It is worth mentioning that the microbiota modifications and the final bioactive forms in which phenolic compounds reach the organism are highly dependent on the subject. After absorption, phenolic compounds or their colonic metabolites are transported by the portal vein to the liver, where they undergo further modifications by conjugation, such as glucuronidation, sulfation and methylation, known as phase II metabolism. Some phenolic metabolites can reach the liver already conjugated in the enterocytes (Spencer et al., 1999). Almost all the phenolic compounds present in plasma are phase II metabolites; thus the health effects of the dietary compounds are mostly due to the biological activity of their glucuronide, sulfate or methyl metabolites.

**Matrix interactions in plant-based foods affecting phenolic compounds bioaccessibility and bioavailability**

In order to be bioavailable, dietary phenolic compounds must be released from the food matrix during small intestinal digestion (bioaccessible) or as a result of the colon microbiota metabolism. In this regard, food matrix composition has a great influence on phenolic compounds bioaccessibility and bioavailability. On the one hand, matrix interactions may hinder the release and solubilization of phenolic compounds in the chyme. On the other hand, phenolic compounds can form unavailable forms through chemical modifications. On the contrary, matrix interactions can also prevent phenolic compounds from degradation through the gastrointestinal tract until their absorption site (Bohn, 2014). The hydrophobic aromatic rings and the hydrophilic hydroxyl groups enable phenolic compounds to create weak and strong interactions with different types of molecules, mainly macromolecules such as polysaccharides, proteins and lipids (Jakobek, 2015).

**Polysaccharide interactions**

Raw fruits and vegetables are rich in dietary fiber, which consists of an ensemble of different polysaccharides, such as cellulose, hemicelluloses and pectic polysaccharides. They form the cell wall, an outer layer that confers structural support to the plant cells and the whole tissues. These macromolecules form an intricate network that interacts with the surrounding media. There is evidence that the presence of polysaccharides in food
interfere with the assimilation of phenolic compounds. Phenolic compounds are more easily released from food matrices in poor dietary fiber, such as juices and beverages (Palafoux-Charles et al., 2011). This interference can be explained by the interactions that can be native in the raw material itself, originated by food processing or created during the transit through the gastrointestinal tract. Actually, when assessing bioavailability, phenolic compounds can be divided between those easily released from the matrix during digestion and those linked to the dietary fiber. In a western diet, it is estimated that about 50% of the phenolic compounds intake is associated with dietary fiber, which can be only absorbed if the interactions have been successfully hydrolyzed by the colonic microbiota (Saura-Calixto, 2011).

Some phenolic compounds in their native form are strongly bound to cell wall hemicelluloses. In this regard, aleurone and pericarp of cereals are rich in ferulic acid esterified to hemicellulose (Manach et al., 2004). However, other phenolic compounds are stored at the vacuole of plant cells, so the interactions with the cell wall polysaccharides occur when the cells are disrupted during processing or mastication.

Le Bourvellec et al. (2004) found that procyanidins were rapidly adsorbed to cell wall polysaccharides. The nature of this effect was hydrogen bonding and hydrophobic interactions. The adsorption of procyanidins to polysaccharides was not affected by pH in the range of 2.2 – 7.0 and it increased with increasing ionic strength or decreasing temperature. The amount of procyanidins bound to polysaccharides increased with the molecular weight, DP, the percentage of galloylation, and the percentage of catechin units in the structure, although the affinity changed between different polysaccharides (Le Bourvellec et al., 2005).

Phan et al. (2015) found that some water-soluble phenolic compounds (phenolic acids, phenolic acid esters, flavan-3-ols and anthocyanidins) created fast and spontaneous interactions with isolated cellulose, up to 0.6 g/g cellulose. This study suggested that phenolic compounds are adsorbed to cellulose regardless their native charge, via hydrogen bonding and hydrophobic forces. Another work (Phan et al., 2016), showed that pH and temperature affected the binding capacity of cyanidin-3-glucoside and ferulic acid to cellulose, but it was not affected by NaCl concentration. The highest affinity was observed at pH 5.0 and 4°C (cyanidin-3-glucoside) and pH 5.5 and 20°C (ferulic acid). On the contrary, pH, temperature and NaCl concentration had no significant influence to the binding capacity of catechin to cellulose.

Many pectin interactions have been reported. Anthocyanins such as cyanidin glycosides create ionic interactions with pectin, and the extent of the binding gradually increases with the time of contact and the pectin content (Padayachee et al., 2012a). Similarly, phenolic acids such as caffeic acid, ferulic acid and some derivatives interact with pectin, but slower than how they do with cellulose, probably due to repulsive forces created by the negative charges in both compounds. The molecular size seems to be not an influencing factor for the phenolic acids affinity to pectin (Padayachee et al., 2012b). On the other hand, procyanidins bind to pectin with higher affinity to what has been observed for xyloglucan (hemicellulose), starch or cellulose, probably because of the capacity of pectin to create hydrophobic pockets that are able to encapsulate procyanidins.

Phenolic compounds make interactions with starch as well, both amylose and amylopectin molecules (Zhu, 2015). As a consequence of these interactions, starch and phenolic compounds change their physicochemical and nutritional properties. Starch can create weak binding with phenolic compounds through hydrogen bonds, or create stronger inclusion complexes through hydrophobic forces between amylose single helices and phenolic compounds, which remain entrapped in the complex.

Interactions with polysaccharides have a large impact on the phenolic compounds bioaccessibility and bioavailability. Less than 2% of bound anthocyanins and phenolic acids were released during in vitro gastric and small intestinal digestion (Padayachee et al., 2013). This means that almost all the bound compounds are delivered to the large intestine, where they are subject to possible modifications by the gut microbiota. The higher the dietary fiber content in cereals, the lower the bioaccessibility of phenolic compounds (Chitindingu et al., 2015). In this sense, the ferulic acid bioavailability in rats was reduced in a cereal matrix due to the interactions with hemicelluloses (Adam et al., 2002). The elimination of these interactions by enzymatic hydrolysis resulted in an increase in the bioavailability of ferulic acid and other phenolic acids (Anson et al., 2011).

On the contrary, the interaction with other polysaccharides which act as protective carriers through the gastrointestinal tract can result in an increase of the bioavailability. This is the case of the starch inclusion complexes: genistein bioavailability in rats was increased when it was in complexation with amylose (Cohen et al., 2011). In this line, it is suggested that uptake of monomeric procyanidins can be increased if consumed together with a polysaccharide-rich meal (Serra et al., 2010) or carbohydrate-rich foods, including polysaccharides and/or low molecular weight sugars (Schramm et al., 2003). It is not clear if the positive effect of low weight polysaccharides is due to modifications in the matrix interactions or to the stimulation of digestive processes that enhance intestinal uptake, such as increased motility and secretion or the activation of membrane transporters (Schramm et al., 2003; Helal et al., 2014).

**Protein interactions**

The interaction between phenolic compounds and proteins has been an issue of concern since they can affect the nutritional quality of food (Świeca et al., 2013). After binding with phenolic compounds, proteins including digestive enzymes can undergo configurational changes that alter their physiological activity (Bandyopadhyay et al., 2012; Xiao and Kai, 2012). Temperature, pH and chemical structure of protein and phenolic compound affect their possible interaction (Ozdal et al., 2013). Phenolic compounds with higher molecular weight, more structural flexibility and more hydroxyl groups in the structure have more capacity to interact with proteins (Jakobek, 2015). On the other hand, proteins with higher content in proline are advantaged in the interactions with phenolic compounds, especially with galloylated procyanidins (Bandyopadhyay et al., 2012). The nature of these interactions is mainly noncovalent, such as hydrogen bonding and hydrophobic interactions (Yuksel et al., 2010; Nagy et al., 2012).

Frazier et al. (2010) found spontaneous interactions between proteins and proanthocyanidins through multiple binding sites.
of the protein. They form complexes that precipitate at pH values near the protein isoelectric point, which are facilitated when the ratio proanthocyanidin/protein is high (Adamczyk et al., 2012). Milk addition to a proanthocyanidin-rich cinnamon beverage produced an immediate formation of insoluble casein complexes, quenching 28% of the free proanthocyanidins. However, the precipitated complexes were again released during gastric digestion (Helal et al., 2014). It is possible that low molecular weight carbohydrates, such as sucrose, inhibit the formation of insoluble protein-proanthocyanidin aggregates by competition for hydrogen-bonding sites of proanthocyanidins. For example, Helal et al. (2014) found that the addition of sucrose or honey increased the bioaccessibility of polymeric proanthocyanidins from a cinnamon beverage by decreasing their interaction with proteins.

Hydroxycinnamic acids form relatively strong interactions with human serum albumin (HSA), dominated by hydrophobic forces and hydrogen bonding (Muralidharra and Prakash, 1995). The interaction between caffeoylquinic acid and milk proteins decreased during digestion but did not disappear (Dupas et al., 2006). In the case of stilbenoids, their affinity to HSA was enhanced by the presence of methoxy- or hydroxyl groups in the structure, while glycosylation weakened the interaction. The higher the stilbene lipophilicity, the stronger the protein binding, which is also dominated by hydrophobic forces (Cao et al., 2016).

Contradictory effects have been identified between protein interactions and their effect on phenolic compounds bioaccessibility or bioavailability, from negative to neutral and positive effects (Ozdal et al., 2013; Jakobek, 2015). Milk addition to coffee brought on casein-caffeoylquinic acid interaction, but it did not reduce the cell uptake of caffeoylquinic acid (Dupas et al., 2006). In this sense, other works have shown no significant effects of milk protein interactions on the bioaccessibility of tea procyanidins (van der Burg-Koorevaar et al., 2011) or cocoa procyanidins (Neilson et al., 2009), as well as on the bioavailability of tea flavonols (Hollman et al., 2001), tea procyanidins (Van Het Hof et al., 1998; Kyle et al., 2007) or cocoa procyanidins (Roura et al., 2007; Neilson et al., 2009). Other authors have found negative effects of milk protein interactions, e.g., on fruit juice phenolic compounds bioaccessibility (Rodriguez-Roque et al., 2014; Rodriguez-Roque et al., 2015), coffee hydroxycinnamic acids bioaccessibility (Tagliazucchi et al., 2012a) and bioavailability (Duarte and Farah, 2011), as well as on black tea proanthocyanidins effects on vascular function (Lorenz et al., 2007). In contrast, milk interactions also appeared to boost phenolic compounds bioaccessibility and bioavailability. Green et al. (2007) found that milk addition increased tea proanthocyanidin recovery in a simulated in vitro digestion. Protein interactions in a green tea-enriched cheese resulted in a more than twofold increase in the total phenolic compounds bioaccessibility (Lamothe et al., 2016). It has been also observed that chalcones were more bioavailable in complexation with soy proteins (Ribnicky et al., 2014).

**Lipid interactions**

While phenolic compounds can inhibit lipase activity and the formation of lipid droplets in the small intestine, thus affecting the overall fat absorption process, lipid interactions have limited effect on the bioaccessibility and bioavailability of phenolic compounds (Jakobek, 2015). Ortega et al. (2009) suggested a protective effect of the fat matrix on cocoa procyanidins and flavonoids during duodenal digestion, although it did not protect phenolic acids from their degradation. However, the fat content in cocoa did not affect the bioaccessibility of phenolic compounds. In another study, there was a positive correlation between the milk fat content and the bioaccessibility of hydroxycinnamic acids in coffee with milk, although bioaccessibility was initially compromised by protein interactions (Tagliazucchi et al., 2012a). Rodriguez-Roque et al. (2014) found that the addition of milk in juice beverages improved the bioaccessibility of lipophilic constituents such as carotenoids but not that of hydrophilic compounds such as phenolic acids and flavonoids, although possible effects could have been masked by milk protein interactions. In another work, the bioaccessibility of phenolic compounds in orange juice with added skimmed milk was higher than in orange juice with added whole milk, denoting a possible detrimental effect of milk fat in the matrix (He et al., 2016). However, the effect of the milk fat was not observed in grape and apple juices. In any case, the clearest effect of lipid matrices can be expected on lipophilic compounds, such as curcuminoids. Fu et al. (2016) found enhanced curcuminoid bioaccessibility in buttermilk yogurt in comparison to aqueous dispersions, due to better micellarization during digestion.

**Food processing affecting phenolic compounds bioaccessibility and bioavailability**

**Mechanical processing**

**Milling and grinding**

The release of phenolic compounds from solid plant-based foods is favored by the mechanical disruption and the acidic conditions of digestion (Tagliazucchi et al., 2012b). Logically, grinding and other unit operations that result in the diminution of the particle size foster phenolic compounds extractability during digestion and enhance their bioaccessibility. Baking whole wheat bread with reduced bran particle size, obtained by fractionation, resulted in increased phenolic acids bioaccessibility (Hemery et al., 2010) (Table 1). In another work, the proanthocyanidin bioaccessibility in fermented cocoa beans decreased 10% after roasting, but it increased up to 117% after blending the roasted beans to obtain cocoa liquor (Gültekín-Ozgüven et al., 2016).

**Juicing**

Juicing yields a liquid fraction with the soluble compounds separated from the solid fraction with most of the insoluble cell wall polysaccharides. Some phenolic compounds will remain in the insoluble fraction due to interactions with polysaccharides. For example, in orange juicing, the flavonoid content decreased 8-fold when the albedo and the fibrous matrix were discarded (Aschoff et al., 2015) (Table 1). However, the remaining compounds probably are more bioaccessible in juice than in the whole fruit, where polysaccharide interactions can be important. In this sense, Aschoff et al. (2015) found that flavanone bioaccessibility in orange juice increased by 450% compared to...
the orange segments with the fibrous matrix. Differences between juice and whole fruit matrices can be diminished in the colon, after the action of the colonic microbiota. According to this, Brett et al. (2009) found no significant differences between the flavanone bioavailabilities in orange fruit and juice.

**Encapsulation**

Several processing technologies allow the formation of small vesicles, from nano- to milli- scale, consisting of encapsulated phenolic or other bioactive compounds surrounded by a “wall” material. Encapsulation of phenolic compounds can improve their stability during food processing and digestion as well as improve their absorption and extend their life in the bloodstream, resulting in improved bioavailability (Yao et al., 2015). For example, uptake of the lipophilic curcuminoids can be improved by their encapsulation into liposomes (Takahashi et al., 2009) (Table 1). In this line, oil-in-water nanoemulsions are proposed as delivery systems of lipophilic compounds, since their bioavailability can be improved due to their increased solubility and absorption in the gastrointestinal tract (Odriozola-Serrano et al., 2014; Salvia-Trujillo et al., 2017). Other methodologies have successfully encapsulated phenolic compounds in nanoparticles, by using amphiphilic copolymers for the encapsulation of resveratrol (Shao et al., 2009) and chitosan or gelatin for flavan-3-ols (Hu et al., 2008; Shuta et al., 2009). Fang and Bhandari (2010) reviewed and discussed the more widely used processes for the encapsulation of phenolic compounds and their possible effects on bioavailability.

**Enzymatic and chemical treatments**

Enzyme treatments can be used to reduce the matrix interactions that hinder phenolic compounds bioavailability. Namely, polysaccharide-degrading enzymes destabilize the integrity of cell walls and increase the extractability of vacuolar phenolic compounds. On the other hand, the use of hemicellulases can lead to an increased extractability of cell wall bound-phenolic acids. The latter can be particularly effective in bread and other cereal-based foods rich in cell wall bound-phenolic acids (Wang et al., 2014). In this sense, fermentation with hemicellulase (xylanase), β-glucanase, α-amylase and ferulic acid esterase in wheat bran increased phenolic acids bioavailability and the production of 3-phenylpropionic acid, end product of the ferulic acid colonic metabolism (Anson et al., 2009; Anson et al., 2011) (Table 2).

Very little information is available on the effect of chemical treatments on phenolic compounds bioaccessibility or bioavailability. It is assumed that antioxidants help the preservation of phenolic compounds at least during the food shelf life. Oven-dried and freeze-dried pumpkin ours exhibited higher bioaccessibility of total polyphenols when they were pre-treated with sodium metabisulphite (Aydin and Gocmen, 2015). Acidification or basification may affect both matrix interactions and phenolic compounds stability. However, there is low margin of

### Table 1. Changes in phenolic compounds bioaccessibility or bioavailability in mechanically processed food.

| Processed food                  | Processing conditions                                                                 | Compounds                        | Effect of processing*                                                                 | Reference                        |
|--------------------------------|----------------------------------------------------------------------------------------|----------------------------------|---------------------------------------------------------------------------------------|----------------------------------|
| Ultramine ground whole wheat bread | Bran: three grinding steps with 0.3 mm selection grid.                                  | p-Coumaric acid, sinapic acid, ferulic acid | p-Coumaric acid: 79% bioaccessibility increase. Sinapic acid: 15% bioaccessibility decrease. Ferulic acid: 35% bioaccessibility increase. With respect to whole wheat bread. | Hemery et al. (2010)               |
| Cryogenic ground whole wheat bread  | Bran: cryogenic grinding (−100°C).                                                      | p-Coumaric acid, sinapic acid, ferulic acid | p-Coumaric acid: 140% bioaccessibility increase. Sinapic acid: 35% bioaccessibility decrease. Ferulic acid: 18% bioaccessibility increase. With respect to whole wheat bread. | Hemery et al. (2010)               |
| Electrostatically separated whole wheat bread  | Bran: cryogenic grinded bran + two steps of electrostatic separation (negatively charged particles). | p-Coumaric acid, sinapic acid, ferulic acid | p-Coumaric acid: 184% bioaccessibility increase. Sinapic acid: 25% bioaccessibility increase. Ferulic acid: 41% bioaccessibility increase. With respect to whole wheat bread. | Hemery et al. (2010)               |
| Natural cocoa liquor             | Blending + 150°C 60 min + crushing (cocoa nib) + grinding                               | Procyanidins                     | 17% bioaccessibility increase (with respect to dried and fermented cocoa beans).       | Gültekin-Özgüven et al. (2016)     |
| Cocoa powder                    | Blending + 150°C 60 min + crushing (cocoa nib) + grinding + CaCO3, 80–100°C 10–12 h final pH 8.2 + pressing (cocoa butter discarded) + pulverizing | Procyanidins                     | 75% bioaccessibility decrease (with respect to dried and fermented cocoa beans).       | Gültekin-Özgüven et al. (2016)     |
| Orange juice                                   | —                                                                                   | Narirutin, hesperidin            | 5-fold increase in bioaccessibility (plasma concentration, AUC 0–2h).                 | Aschoff et al. (2015)             |
| Orange juice                                   | —                                                                                   | Naringenin, hesperetin           | No effect on bioavailability (plasma metabolites concentration)                      | Brett et al. (2009)              |
| Liposome-encapsulated curcumin                       | Dispersion in a lecithin aqueous solution + microfluidization                      | Curcumin                         | 396% bioavailability increase in rats (plasma concentration, AUC 0–2h).               | Takahashi et al. (2009)           |

AUC: area under the curve.

*Effect with respect to the unprocessed food.
maneuver, since pH changes dramatically modify the sensory properties and microbiological safety of food products. Alkali- zation of a cocoa liquor to obtain cocoa powder resulted in a 52% decrease of procyanidins bioaccessibility with respect to the natural cocoa liquor (Gültekin-Özgüven et al., 2016).

**Thermal processing**

Phenolic compounds are degraded at high temperature; thus thermal treatments reduce the phenolic compounds content in food and jeopardize the amount that is finally absorbed. On the other hand, high temperature also induces other modifications that can be positive for the phenolic compounds bioavailability, such as degradation or modification of cell wall polysaccharides, proteins and other matrix factors that may lead to an increased extractability of phenolic compounds during digestion. Actually, the bioavailability in a thermally treated food product compared to its raw material is a balance between the compounds that have been destroyed during processing and those remaining that have been released and could be absorbed thanks to the thermally-induced matrix changes (Parada and Aguileran, 2007). The extent to which temperature affects phenolic compounds depends on the protective effect that the matrix may exert but also to the chemical properties and thermal stability of the compound.

**Domestic cooking**

Cooking cherry tomato tilted the balance towards an increased bioavailability of naringenin and caffeoylequinic acid (Bugianesi et al., 2004) (Table 3). Accordingly, increased naringenin bioavailability was reported for cooked tomato sauce (Martínez-Huélamo et al., 2015). In tomato, heating before discarding the skin usually enhances the extraction of skin flavonoids and their bioaccessibility (Kamiloglu et al., 2014). In raw cardoon stalks, only 2% of phenolic compounds (mainly caffeoylequinic acid derivatives) remained unmodified after in vitro gastrointestinal digestion, but the percentage was much higher in griddled (60%) or fried cardoon stalks (67%) (Juárez et al., 2017). In a Compositae wild vegetable (Symurus deltoides), blanching and microwave heating induced a severe decrease of the phenolic acids bioaccessibility (85–93%) (Son and Shim, 2015). In mushrooms, whose antioxidant activity is accounted for their content in phenolic compounds, the polar water-soluble antioxidants were more resistant to cooking (boiling, frying, grilling and microwaving) than the less polar methanol-soluble antioxidants (Soler-Rivas et al., 2009). In this work, the effect of the different cooking methodologies was dependent on the mushroom species, and boiling was found to be the thermal treatment with higher impact on the antioxidant activity. In fact, boiling, frying and other cooking methods with direct contact with the cooking media have higher effect on the phenolic compounds content than methods with indirect contact, such as steaming, where leaching losses are more limited (Palermo et al., 2014; Kaulmann et al., 2016). Accordingly, de Lima et al. (2017) found that the total phenolic compounds content in cooked cassava was higher when cooking by steaming rather than microwaving or boiling (25.8, 18.0, and 16.6 mg GAE 100 g–1 respectively). In addition, this work showed that bioaccessibility of the remaining compounds after cooking was higher after steaming (74.5%) than after boiling (72.9%) or microwaving (72.7), showing that in this case, the cooking method influenced both the stability of phenolic compounds and those matrix factors affecting their bioaccessibility.

In cereals, where phenolic acids bioaccessibility is strongly influenced by polysaccharide interactions, domestic cooking can be used to promote phenolic compounds extractability (Wang et al., 2014). Roasting was observed to be the best domestic cooking method (amongst pressure cooking, boiling and microwave heating) to keep, and in some cases increase, the phenolic compounds bioaccessibility in pearl millet, finger millet, sorghum and wheat (Hithamani and Srinivasan, 2014a; 2014b). Roasting was also the best cooking method to promote the phenolic compounds bioaccessibility in green gram and chickpea (Hithamani and Srinivasan, 2014a). Also in legumes, pressure cooking released matrix-bound phenolic acids and flavan-3-ols from cranberry beans (Chen et al., 2015). On the other hand, roasting cocoa beans reduced by 10% the bioaccessibility of procyanidins (Gültekin-Özgüven et al., 2016).

Rodriguez-Mateos et al. (2014) studied the effect of the baking process on the bioavailability of blueberry phenolic compounds, mainly anthocyanins, procyanidins and phenolic acids. To this end, they assessed the fate of a detailed list of 22 metabolites in plasma after ingestion of a blueberry drink and a

### Table 2. Changes in phenolic compounds bioaccessibility or bioavailability in enzymatically or chemically processed food.

| Processed food | Processing conditions | Compounds | Effect of processing | Reference |
|----------------|-----------------------|-----------|----------------------|-----------|
| Whole wheat bread with fermented and enzymatic treated bran | Bran: fermentation with xylanase, β-glucanase, α-amylase, cellulase, ferulic acid esterase, 20°C 20h | Ferulic acid, vanillic acid, 3,4-dimethoxybenzoic acid | Ferulic acid: 400% bioaccessibility increase, 167% bioavailability increase (plasma concentration, AUC 0–24h). Vanillic acid: 79% bioavailability increase (plasma concentration, AUC 0–24h). 3,4-Dimethoxybenzoic acid: 83% bioavailability increase (plasma concentration, AUC 0–24h). As compared with whole wheat bread with native bran. 44% bioaccessibility decrease (with respect to dried and fermented cocoa beans). | Gültekin-Ozgun et al. (2016) |
| Alkalized cocoa liquor | Blending + 150°C 60 min + crushing (cocoa nib) + grinding + CaCO3 80–100°C 10–12 h final pH 8.2 | Sum of identified procyanidins | | |

AUC: area under the curve.

*Effect with respect to the unprocessed food.
Table 3. Changes in phenolic compounds bioaccessibility or bioavailability in thermally processed food.

| Processed food               | Processing conditions | Compounds                        | Effect of processing                                  | Reference                  |
|-----------------------------|-----------------------|----------------------------------|-------------------------------------------------------|----------------------------|
| Tomato sauce                | 99°C 60 min           | Naringenin, phenolic acids       | Naringenin: bioavailability increase (naringenin and naringenin glucuronide plasma and urine concentration). Phenolic acids: no effect on bioavailability | Martinez-Huélamo et al. (2015) |
| Cooked tomato               | 100°C 15 min          | Naringenin, chlorogenic acid     | Bioavailability increase (plasma concentration). No effect on bioaccessibility. | Bugianesi et al. (2004)    |
| Cooked tomato puree         | Peeling (skin removal) + chopping + 77°C 15 min + sieving + 80°C 13 min | Total polyphenols, total flavonoids | Total flavonoids: 22% bioaccessibility increase. | Kamiloglu et al. (2014)    |
| Cooked tomato pieces        | Chop + 75°C 15 min    | Total polyphenols, total flavonoids | No effect on bioaccessibility.                       | Kamiloglu et al. (2014)    |
| Cooked tomato paste         | Chop + 70°C 20 min + sieving (skin removal) + 80°C 70 min | Total polyphenols, total flavonoids | Total flavonoids: 900% bioaccessibility increase. | Kamiloglu et al. (2014)    |
| Cooked tomato juice         | Peeling (skin removal) + grating + 72°C 20 min + sieving + 70°C 5 min | Total polyphenols, total flavonoids | Total flavonoids: 900% bioaccessibility increase. | Kamiloglu et al. (2014)    |
| Frieded cardoon             | 115°C 10 min + 108°C 5 min in olive or sunflower oil | Sum of identified phenolic compounds | 1747% (olive oil), 1876% (sunflower oil) bioaccessibility increase. | Juaniz et al. (2017)       |
| Griddled cardoon            | 150°C 10 min + 110°C 5 min | Sum of identified phenolic compounds | 3330% bioaccessibility increase.                      | Juaniz et al. (2017)       |
| Roasted cocoa beans         | Blending + 150°C 60 min | Sum of identified procyanidins   | 10% bioaccessibility decrease (with respect to dried and fermented cocoa beans). | Gültkin-Ozgüven et al. (2016) |
| Black carrot jam and marmalade | Peeling + slicing + sugar/sweetener + 100°C (boiling) 30 min + pectin + cooking (concentration) + citric acid (pH 3) | Total polyphenols, identified phenolic acids | Processing decreased 10% total phenolic content. For the remaining compounds, processing increased their bioaccessibility 7–13% (total phenolic content) and 5–31% (phenolic acids). | Kamiloglu et al. (2015)    |
| Blanched wild vegetable     | 100°C 1, 3, 5 min     | Sum of identified phenolic acids | 85% (1 min), 86% (3 min), 88% (5 min) bioaccessibility decrease. | Son and Shim (2015)        |
| Microwaved wild vegetable   | 700W 30 s, 1 min, 2 min | Sum of identified phenolic acids | 93% (30 s), 93% (1 min), 91% (2 min) bioaccessibility decrease. | Son and Shim (2015)        |
| Roasted finger millet       | 150°C 5 min           | Total polyphenols, total flavonoids, sum identified phenolic acids | Total flavonoids: 900% bioaccessibility increase. | Hithamani and Srinivasan (2014b) |
| Pressure cooked finger millet | Grinding + pressure cooking (15 psi) 15–20 min | Total polyphenols, total flavonoids, sum identified phenolic acids | Total flavonoids: 18% bioaccessibility decrease. | Hithamani and Srinivasan (2014b) |
| Boiled finger millet        | Grinding + 100°C 5, 10, 15 min | Total polyphenols, total flavonoids, sum identified phenolic acids | Total flavonoids: 2% bioaccessibility increase. | Hithamani and Srinivasan (2014b) |
| Microwaved finger millet    | Grinding + 300, 450, 600 W 3 min (in water) | Total polyphenols, total flavonoids, sum identified phenolic acids | Sum identified phenolic acids: 27% bioaccessibility decrease. | Hithamani and Srinivasan (2014b) |
| Roasted pearl millet        | 150°C 5 min           | Total polyphenols, total flavonoids, sum identified phenolic acids | Total flavonoids: 20% bioaccessibility increase. | Hithamani and Srinivasan (2014b) |
| Pressure cooked pearl millet | Grinding + pressure cooking (15 psi) 15–20 min | Total polyphenols, total flavonoids, sum identified phenolic acids | Total flavonoids: 64% bioaccessibility increase. | Hithamani and Srinivasan (2014b) |
| Treatment                  | Method/Condition | Total polyphenols, total flavonoids, sum identified phenolic acids | Sum identified phenolic acids: bioaccessibility change |
|----------------------------|------------------|------------------------------------------------------------------|--------------------------------------------------------|
| Boiled pearl millet        | Grinding + 100°C 5, 10, 15 min | Total polyphenols, total flavonoids, sum identified phenolic acids | 37% bioaccessibility increase. Total polyphenols, total flavonoids: No effect on bioaccessibility. |
| Microwaved pearl millet    | Grinding + 300, 450, 600 W 3 min (in water) | Total polyphenols, total flavonoids, sum identified phenolic acids | Sum identified phenolic acids: 33% decrease (5 min) and 10% (10 min), 23% (15 min) bioaccessibility increase. Total polyphenols: no effect (300 W) and 16% (450W), 25% (600 W) bioaccessibility decrease. Total flavonoids: no effect on bioaccessibility. Sum identified phenolic acids: 60% (300 W), 19% (450 W), 4% (600 W) bioaccessibility increase. |
| Roasted wheat              | 150°C 5 min      | Total polyphenols, total flavonoids, sum identified phenolic acids | Total polyphenols: 26% bioaccessibility decrease. |
| Pressure cooked wheat      | Grinding + pressure cooking (15 psi) 15 min | Total polyphenols, total flavonoids, sum identified phenolic acids | Total flavonoids: no effect on bioaccessibility. Sum identified phenolic acids: no bioaccessibility in native wheat, 221 µg/g bioaccessible in roasted wheat. |
| Boiled wheat               | Grinding + 100°C 10 min | Total polyphenols, total flavonoids, sum identified phenolic acids | Total polyphenols, total flavonoids: No effect on bioaccessibility. Sum identified phenolic acids: no bioaccessibility in native wheat, 30 µg/g bioaccessible in pressure cooked wheat. |
| Microwaved wheat           | Grinding + 450 W 4 min (in water) | Total polyphenols, total flavonoids, sum identified phenolic acids | Total polyphenols: 20% bioaccessibility decrease. Total flavonoids: no effect on bioaccessibility. Sum identified phenolic acids: no bioaccessibility in native wheat and in boiled wheat. |
| Roasted sorghum            | 150°C 5 min      | Total polyphenols, total flavonoids, sum identified phenolic acids | Total polyphenols: 15% bioaccessibility decrease. |
| Pressure cooked sorghum    | Grinding + pressure cooking (15 psi) 15 min | Total polyphenols, total flavonoids, sum identified phenolic acids | Total flavonoids: no effect on bioaccessibility. Sum identified phenolic acids: 264% bioaccessibility increase. Total polyphenols, total flavonoids: No effect on bioaccessibility. |
| Boiled sorghum             | Grinding + 100°C 10 min | Total polyphenols, total flavonoids, sum identified phenolic acids | Total polyphenols, total flavonoids: No effect on bioaccessibility. Sum identified phenolic acids: 38% bioaccessibility increase. Total polyphenols: 12% bioaccessibility decrease. Total flavonoids: no effect on bioaccessibility. Sum identified phenolic acids: 2% bioaccessibility increase. Total polyphenols: 23% bioaccessibility decrease. |
| Microwaved sorghum         | Grinding + 450 W 4 min (in water) | Total polyphenols, total flavonoids, sum identified phenolic acids | Total flavonoids: 56% bioaccessibility decrease. Sum identified phenolic acids: 22% bioaccessibility decrease. Total polyphenols: 11% bioaccessibility increase. |
| Roasted green gram         | 150°C 5 min      | Total polyphenols, total flavonoids, sum identified phenolic acids | Total flavonoids: no effect on bioaccessibility. Sum identified phenolic acids: 38% bioaccessibility increase. Total polyphenols, total flavonoids: No effect on bioaccessibility. Sum identified phenolic acids: 17% bioaccessibility decrease. Total polyphenols, total flavonoids: No effect on bioaccessibility. |
| Pressure cooked green gram | Grinding + pressure cooking (15 psi) 15 min | Total polyphenols, total flavonoids, sum identified phenolic acids | Total polyphenols, total flavonoids: No effect on bioaccessibility. Sum identified phenolic acids: 38% bioaccessibility increase. Total polyphenols, total flavonoids: No effect on bioaccessibility. Sum identified phenolic acids: 17% bioaccessibility decrease. Total polyphenols, total flavonoids: No effect on bioaccessibility. |
| Boiled green gram          | Grinding + 100°C 10 min | Total polyphenols, total flavonoids, sum identified phenolic acids | Total flavonoids: no effect on bioaccessibility. Sum identified phenolic acids: 38% bioaccessibility increase. Total polyphenols, total flavonoids: No effect on bioaccessibility. Sum identified phenolic acids: 17% bioaccessibility decrease. Total polyphenols, total flavonoids: No effect on bioaccessibility. |

(Continued on next page)
| Processed food                  | Processing conditions                              | Compounds                                                                                                                                                                                                 | Effect of processing*                                                                                      | Reference                          |
|--------------------------------|---------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|-----------------------------------|
| Microwaved green gram          | Grinding + 450 W 4 min (in water)                 | Total polyphenols, total flavonoids, sum identified phenolic acids                                                                                                                                       | Sum identified phenolic acids: 29% bioaccessibility increase. Total polyphenols: 17% bioaccessibility decrease. | Hithamani and Srinivasan (2014a) |
| Roasted chickpea               | 150°C 5 min                                       | Total polyphenols, total flavonoids, sum identified phenolic acids                                                                                                                                       | Total flavonoids: no effect on bioaccessibility. Sum identified phenolic acids: 11% bioaccessibility decrease. Total polyphenols: 17% bioaccessibility increase. | Hithamani and Srinivasan (2014a) |
| Pressure cooked chickpea       | Grinding + pressure cooking (15 psi) 15 min       | Total polyphenols, total flavonoids, sum identified phenolic acids                                                                                                                                       | Total flavonoids: no effect on bioaccessibility. Sum identified phenolic acids: 46% bioaccessibility increase. Total polyphenols: 11% bioaccessibility decrease. | Hithamani and Srinivasan (2014a) |
| Boiled chickpea                | Grinding + 100°C 10 min                           | Total polyphenols, total flavonoids, sum identified phenolic acids                                                                                                                                       | Total flavonoids: no effect on bioaccessibility. Sum identified phenolic acids: 25% bioaccessibility increase. Total polyphenols: 9% bioaccessibility decrease. | Hithamani and Srinivasan (2014a) |
| Microwaved chickpea            | Grinding + 450 W 4 min (in water)                 | Total polyphenols, total flavonoids, sum identified phenolic acids                                                                                                                                       | Total flavonoids: no effect on bioaccessibility. Sum identified phenolic acids: 11% bioaccessibility increase. Total polyphenols: 17% bioaccessibility increase. | Hithamani and Srinivasan (2014a) |
| Blueberry baked bun            | - Dough with freeze-dried blueberry powder: proving 30°C - Filling with freeze-dried blueberry powder: cooking 90°C - Dough + filling: proving 30°C + cooking 180°C | Sum of phenolic compounds (mainly anthocyanins, procyanidins and phenolic acids)                                                                                                                     | Sum identified phenolic acids: 31% bioaccessibility increase. No effect on bioavailability (AUC 0–6h) with respect to blueberry powder drink. | Rodriguez-Mateos et al. (2014)    |
| Pasteurized fruit juice with water | 90°C 60 s                                      | Sum identified phenolic acids, sum identified flavonoids, total polyphenols                                                                                                                             | Sum identified phenolic acids: 37% bioaccessibility decrease. Sum identified flavonoids: 19% bioaccessibility decrease. Total polyphenols: 14% bioaccessibility decrease. Sum identified phenolic acids: 11% bioaccessibility increase. | Rodriguez-Roque et al. (2015) |
| Pasteurized fruit juice with milk | 90°C 60 s                                       | Sum identified phenolic acids, sum identified flavonoids, total polyphenols                                                                                                                             | Sum identified flavonoids: 22% bioaccessibility increase. Total polyphenols: 3% bioaccessibility increase. Sum identified phenolic acids: 3% bioaccessibility increase. | Rodriguez-Roque et al. (2015)    |
| Pasteurized fruit juice with soy milk | 90°C 60 s                                     | Sum identified phenolic acids, sum identified flavonoids, total polyphenols                                                                                                                             | Sum identified flavonoids: 21% bioaccessibility increase. Total polyphenols: 3% bioaccessibility increase. | Rodriguez-Roque et al. (2015)    |
| Pasteurized apple juice        | 80, 90°C 30 s                                    | Sum of identified phenolic compounds                                                                                                                                                                   | No effect on bioaccessibility. 34% (80°C), 27% (90°C) bioaccessibility increase. 19% (80°C), 29% (90°C) bioaccessibility increase. | He et al. (2016)                  |
| Pasteurized grape juice        | 80, 90°C 30 s                                    | Sum of identified phenolic compounds                                                                                                                                                                   | No effect on bioaccessibility. (compared to nonpasteurized orange juice) Bound phenolic acids: 29% total tract bioaccessibility increase in pigs. Free phenolic acids: no effect on total tract bioaccessibility in pigs. | Aschoff et al. (2015)             |
| Pasteurized orange juice       | 80, 90°C 30 s                                    | Sum of identified phenolic compounds Naringin, hesperidin                                                                                                                                               | No effect on bioaccessibility. 34% (80°C), 27% (90°C) bioaccessibility increase. 19% (80°C), 29% (90°C) bioaccessibility increase. | He et al. (2016)                  |
| Pasteurized orange juice       | Continuous, 70°C 80 L h⁻¹ and 90°C 60 L h⁻¹     | Total polyphenols, free phenolic acids (remaining compounds after treatment)                                                                                                                                                 | Bound phenolic acids: 29% total tract bioaccessibility increase in pigs. Free phenolic acids: no effect on total tract bioaccessibility in pigs. | Hole et al. (2013)                |
| Food                  | Treatment | Bioactive Compounds                                                                 | Bioavailability Change | Reference                      |
|----------------------|-----------|-------------------------------------------------------------------------------------|------------------------|--------------------------------|
| Extruded dehulled oats | 110°C     | Bound phenolic acids, free phenolic acids (remaining compounds after treatment)     | Bound phenolic acids: 14% total tract bioaccessibility increase in pigs. | Hole et al. (2013)            |
| Extruded sorghum     | 50% whole grain - 50% bran + α-amylase | Procyanidins                                                                      | Free phenolic acids: no effect on total tract bioaccessibility in pigs. | Gu et al. (2008)              |
| Dried figs           | Sundrying (31–34°C daily average) 8 days | Caffeoylquinic acid, quercetin rutinoside, cyanidin glucoside, cyanidin rutinoside | Caffeoylquinic acid: 50% (yellow fig) and 60% (purple fig) bioaccessibility increase. Quercetin rutinoside: 21% (yellow fig) and 33% (purple fig) bioaccessibility decrease. Cyanidin glucoside, cyanidin rutinoside: 100% (purple fig) bioaccessibility decrease. | Kamiloglu and Capanoglu (2013) |
| Dried tomato         | 70°C 36 h | Total polyphenols, total flavonoids                                                 | Total polyphenols: 200% bioaccessibility increase. Total flavonoids: no effect on bioaccessibility. | Kamiloglu et al. (2014)       |

AUC: area under the curve.
*Effect with respect to the unprocessed food.
baked product with blueberry powder. Bioavailability was determined as the area under de curve (AUC). Despite the AUC was higher for 4 metabolites and it was lower for other 4 metabolites after intake of blueberry baked product, if compared to the blueberry drink, no difference in the bioavailability of overall phenolic compounds was found.

**Pasteurization and sterilization**

The effects described for cooking are softened when using the mild time and temperature conditions of pasteurization. Again, the positive or negative effect will depend on compounds stability, matrix protective effects and existing interactions. In orange juice, there was found that continuous pasteurization or flash-pasteurization of orange juice had no effect on the flavanone bioaccessibility if compared to unprocessed juice (Aschoff et al., 2015) (Table 3). However, results largely depend on treatment conditions. In another work on batch pasteurization, the phenolic compounds bioaccessibility in orange and grape juices was enhanced, although there was no effect in apple juice, probably due to a matrix effect or different thermal stabilities of the apple phenolic compounds (He et al., 2016). Rodriguez-Roque et al. (2015) found interesting matrix effects: pasteurization had a negative effect on the bioaccessibility of total polyphenols, phenolic acids and flavonoids in a mixed-fruit beverage, with 14%, 37% and 19% decreases, respectively. On the contrary, pasteurization had a positive effect in juice with a protein-rich matrix (soy or cow milk), with 3%, 3–11% and 21–22% increase in the bioaccessibilities of total polyphenols, phenolic acids and flavonoids, respectively (Table 3).

The amount of phenolic compounds in jams and marmalades is much smaller if compared to fresh fruit (Hollands et al., 2008). Marmalade and jam processing of black carrots decreased drastically the total phenolic (89–90%) and phenolic acids (49–97%) contents. However, the bioaccessibility of the remaining compounds was higher if compared to the unprocessed carrots (7–13% increase for total phenolic content and 5–31% increase for phenolic acids), probably due to matrix changes during thermal treatment (Kamiloglu et al., 2015).

Canning of fruit and vegetables is associated to washing, peeling and blanching steps followed by a thermal processing in a sealed liquid medium. Thus, the canning process involves extensive loss of water-soluble and heat-sensitive compounds, which finally ends to a decreased amount of phenolic compounds if compared to the fresh fruit and vegetables (Rickman et al., 2007). However, the effects of canning on phenolic compounds bioaccessibility or bioavailability still need to be investigated.

**Extrusion**

The combination of high temperature, high pressure and high shearing conditions of extrusion affects phenolic compounds bioaccessibility and bioavailability. Extrusion is a common processing for cereals that are intended for breakfast meal or feed. In this sense, Hole et al. (2013) found that extrusion of barley or dehulled oat increased by 29% and 14% the total tract bioaccessibility of bound phenolic acids in pigs, due the release of cell wall polysaccharide interactions, while extrusion had no effect on the bioaccessibility of free phenolic acids (Table 3). Extrusion is also reported to depolymerize sorghum proanthocyanidins with DP ≥ 6 (Awika et al., 2003), which would facilitate the intestinal absorption of these compounds. Accordingly, extrusion of sorghum with the addition of α-amylase enhanced procyanidin bioavailability in pigs (Gu et al., 2008).

**Drying**

Drying and freeze-drying promote drastic changes in the food matrix, affecting cellular structures, matrix interactions and stability of phenolic compounds (Betoret et al., 2015). Aydin and Gocmen (2015) compared the effects of freeze-drying and conventional hot-air oven drying on the bioaccessibility of phenolic acids in pumpkin flour. Highest bioaccessibilities were obtained with oven drying, probably due to its higher effect on the matrix. In tomato, oven-drying enhanced the total polyphenols bioaccessibility by twofold but not that of total flavonoids, showing that the positive effect on total polyphenols was most probably limited on phenolic acids (Kamiloglu et al., 2014) (Table 3). In agreement, another work showed that sun-drying positively affected the caffeoylquinic acid bioaccessibility (50–60% increase) in figs, but it negatively affected flavonoids bioaccessibility (21–33% decrease for quercetin rutinoside) and more intensely anthocyanins, which disappeared from dried purple figs (Kamiloglu and Capanoglu, 2013). The drying process also affects proanthocyanidins, which are reported to disappear or polymerize during prunes and raisins processing (Prior and Gu, 2005).

**Cold processing**

**Freezing**

Changes in phenolic content after freezing or during frozen storage seem to be strongly dependent on the commodity (Rickman et al., 2007). González et al. (2003) found that two early cultivars of raspberry contained greater amount of anthocyanins after freezing in liquid nitrogen, while their content decreased in other two late cultivars. Although anthocyanins are highly unstable phenolic compounds, their content in red fruits during frozen storage is slightly affected (González et al., 2003; Hollands et al., 2008). Other works have shown a detrimental effect of freezing on the phenolic compounds content in fruit juices (Gil-Izquierdo et al., 2002; Johnson et al., 2015). Likewise, freezing reduced the total phenolic content in apple after in vitro gastric digestion (Dalmau et al., 2017). On the other hand, freezing damages the food matrix due to the formation of ice crystals, and the damage is enhanced if the freezing process is slow (Van Buggenhout et al., 2006). These matrix changes probably entail increased extractability during digestion but also higher susceptibility to oxidation and degradation, especially if freezing is followed by thermal treatment (Oliveira et al., 2016). Based on these considerations, significant effects of freezing on phenolic compounds bioaccessibility or bioavailability could be expected. Nevertheless, to the best of our knowledge, no works have yet been performed on this matter.

**Nonthermal processing**

As has been previously mentioned for the thermal processing, high temperature induces changes in the food matrix that may be beneficial for the release and bioavailability of phenolic...
From the nutritional point of view, the use of high pressure is the same time that better preserves the sensory properties. High pressure is used as an alternative to the thermal pasteurization for the inactivation of food pathogens and enzymes, at high pressures than high temperatures. Furthermore, high pressure can lead to the rupture of cellular structures and enhance the bioaccessibility and bioavailability of bioactive compounds. Two main processing technologies use high pressure conditions: high pressure homogenization (HPH) and high pressure processing (HPP). HPH is a hydrodynamic processing that very promising since most bioactive compounds better resist high pressures than high temperatures. Two main processing technologies use high pressure conditions: high pressure homogenization (HPH) and high pressure processing (HPP). HPH is a hydrodynamic processing that increases the homogeneity of purees or liquid foods with the application of 3 to 500 MPa. HPP is a hydrostatic processing technology used in solid or liquid batch systems, which are usually packaged, that uses 150 to 900 MPa (Betoret et al., 2015).

Rodriguez-Roque et al. (2015) found that bioaccessibility of phenolic acids and flavonoids in mixtures of fruit beverages with water, cow milk and soy milk matrices treated with HPP was higher than in thermally treated beverages, although it was lower for total polyphenols (Tables 3 and 4). In this study, the phenolic compounds bioaccessibility was improved in most cases by HPP when compared to the untreated beverages, compounds. However, the positive matrix changes are counteracted by the thermally-induced degradation of the bioactive compounds as well as texture modifications that end to reduced palatability. Some novel technologies, such as high pressure treatment, pulsed electric fields and ultrasounds, have emerged in the recent years as alternatives to the thermal processing. In some cases, the interest in such technologies relies on their capacity to achieve an equivalent microbiological safety than the obtained by thermal pasteurization, but with improved sensory and/or nutritional properties. In other cases, the positive effect on phenolic compounds bioavailability would justify their use only for nutritional purposes.

### High pressure treatment

High pressure is used as an alternative to the thermal pasteurization for the inactivation of food pathogens and enzymes, at the same time that better preserves the sensory properties. From the nutritional point of view, the use of high pressure is

### Table 4. Changes in phenolic compounds bioaccessibility or bioavailability in nonthermally processed food.

| Processed food               | Processing conditions | Compounds                                      | Effect of processing* | Reference         |
|------------------------------|-----------------------|------------------------------------------------|-----------------------|-------------------|
| HPH apple juice              | 250 MPa 10 min        | Sum of identified phenolic compounds           | 29% bioaccessibility decrease. | He et al. (2016)  |
| HPH grape juice              | 250 MPa 10 min        | Sum of identified phenolic compounds           | No effect on bioaccessibility. | He et al. (2016)  |
| HPH orange juice             | 250 MPa 10 min        | Sum of identified phenolic compounds           | No effect on bioaccessibility. | He et al. (2016)  |
| HPP-treated fruit juice with water | 400 MPa 5 min     | Sum identified phenolic acids, sum identified flavonoids, total polyphenols | Sum identified phenolic acids: 12% bioaccessibility decrease. | Rodriguez-Roque et al. (2015) |
| HPP-treated fruit juice with milk | 400 MPa 5 min       | Sum identified phenolic acids, sum identified flavonoids, total polyphenols | Total polyphenols: 18% bioaccessibility decrease. | Rodriguez-Roque et al. (2015) |
| HPP-treated fruit juice with soy milk | 400 MPa 5 min     | Sum identified phenolic acids, sum identified flavonoids, total polyphenols | Total polyphenols: 15% bioaccessibility increase. | Rodriguez-Roque et al. (2015) |
| PEF-treated fruit juice with water | 35 kV cm⁻¹ in 4 μs pulses, 200 Hz, 1800 μs (high intensity, bipolar mode) | Sum identified phenolic acids, sum identified flavonoids, total polyphenols | Total polyphenols: 21% bioaccessibility decrease. | Rodriguez-Roque et al. (2015) |
| PEF-treated fruit juice with milk | 35 kV cm⁻¹ in 4 μs pulses, 200 Hz, 1800 μs (high intensity, bipolar mode) | Sum identified phenolic acids, sum identified flavonoids, total polyphenols | Total polyphenols: 3% bioaccessibility decrease. | Rodriguez-Roque et al. (2015) |
| PEF-treated fruit juice with soy milk | 35 kV cm⁻¹ in 4 μs pulses, 200 Hz, 1800 μs (high intensity, bipolar mode) | Sum identified phenolic acids, sum identified flavonoids, total polyphenols | Total polyphenols: 16% bioaccessibility increase. | Rodriguez-Roque et al. (2015) |
| Sonicated and dried cashew apple bagasse | 20 kHz, 75 W cm⁻², 2–10 min | Total polyphenols                            | Sum identified flavonoids: 23% bioaccessibility decrease. 400% (2 min) and 300% (10 min) bioaccessibility increase with respect to nonsonicated dried cashew apple bagasse. | Fonteles et al. (2016) |

HPH: high pressure homogenization; HPP: high pressure processing; PEF: pulsed electric fields.

*Effect with respect to the unprocessed food.
especially in milk and soy milk matrices (Table 4). However, it has also been reported that in some cases the matrix network and interactions are strengthened under high pressure, thus hindering the release of bioactive compounds during digestion (Colle et al., 2010). In line with this statement, He et al. (2016) observed that HPH-treated apple, grape and orange juices had lower bioaccessibility than thermally-pasteurized juices.

**Pulsed electric fields (PEF) treatment**

PEF processing consists of the application of very fast and highly intense electrical discharges on a food product that has been placed between two electrodes (Siemer et al., 2014). One of the main effects of the application of PEF to food systems is that cell membranes undergo electroporation, *i.e.*, irreversible membrane permeabilization that has a lethal effect for most food pathogens. Therefore, high-intensity PEF is an alternative to thermal pasteurization (Soliva-Fortuny et al., 2009). Given the effects on the food matrix, and more precisely on the integrity of cell walls and membranes, interesting consequences regarding the bioaccessibility and bioavailability of phenolic compounds could be predicted from PEF application. In this sense, its use has been proposed to release cell wall-bound phenolic acids from sorghum flour and apple pomace (Lohani and Muthukumarappan, 2016). PEF treatment, under certain conditions, has been successfully used to increase the phenolic compounds content in apple fruit juices (Schilling et al., 2008; Grimì et al., 2011; Turk et al., 2012), while other works have shown no significant differences between PEF-treated and thermally-treated tomato juice or PEF-treated (Odriozola-Serrano et al., 2009) and untreated apple juice (Schilling et al., 2007).

Very few works have addressed the effect of PEF processing on phenolic compounds bioaccessibility or bioavailability. Rodríguez-Roque et al. (2015) found that in most cases high-intensity PEF processing of fruit-based beverages increased the phenolic compounds bioaccessibility when compared to the thermally-pasteurized fruit beverages, in water or milk matrices, except for the total polyphenols bioaccessibility of fruit beverage in soy milk (Tables 3 and 4). Even if moderate-intensity PEF is nonlethal for pathogens, their use can provoke plant stress and activate the secondary metabolism. In this sense, moderate-intensity PEF has been proposed to enhance phenolic compounds content in tomato (Vallverdú-Queralt et al., 2013).

**Ultrasound treatment**

Low frequency ultrasounds (16–100 kHz) induce changes in the physical and chemical properties of food, mainly by effect of cavitation, which occurs during the propagation of ultrasound waves through a liquid medium. This phenomenon consists in the generation of gas bubbles which grow and collapse after several compressing and decompressing cycles, ending in explosions at the nanoscale level with structural effects on proteins and membranes (Soria and Villamiel, 2010). Therefore, microstructure changes can be induced by ultrasounds, with potential implications for the matrix-phenolic interactions. In food industry, ultrasounds treatment has been proposed as a unit operation before drying, as ultrasounds effects can enhance the mass transfer and the drying efficiency. Sonication improved the quality of dried cashew apple bagasse, with an important enhancement (400%) of the total phenolic bioaccessibility (Fonteles et al., 2016).

**Food processing as a strategy to increase phenolic compounds bioaccessibility and bioavailability**

Food processing can be used as a tool for the enhancement of phenolic compounds bioavailability in plant-based foods. There are two principal prerequisites thereof: (i) limited processing-induced degradation of phenolic compounds and (ii) a minimum of matrix changes, e.g. destruction of molecular interactions, that entail an enhanced release of phenolic compounds and/or higher absorption in the gastrointestinal tract.

The particle size reduction or the changes in the solubility properties obtained by mechanical processing, the inhibition of matrix interactions by enzymatic or chemical treatment, and the matrix destruction under thermal or nonthermal processing make the different technologies described in this review able to accomplish the second requirement at different degrees. Concerning the stability of phenolic compounds under food processing, the literature data show that in most cases phenolic compounds are sensitive to high temperature. Therefore, food processing not using high temperature acquires an advantageous position. Nonthermal processing deserves separate mention, since they can be used as a substitute of the conventionally used thermal processing. When designing a strategy to increase phenolic compounds bioaccessibility and bioavailability, the choice of single or combined food processing technologies may be considered depending on the expected

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**Figure 2.** Use of nonthermal food processing to increase phenolic compounds bioaccessibility (%) from fruit juice-based beverages. a. Water-fruit juice beverage; b. Milk-fruit juice beverage; c. soymilk-fruit juice beverage. PEF, Pulsed electric fields (35 kV/cm 1.8 ms); HPP, high pressure processing (400 MPa 5 min); TT, thermal treatment (90°C 60 s); TPC, total phenolic compounds; TF, total flavonoids; TPA, total phenolic acids. Different letters between treatments show significant difference. Adapted from Rodríguez-Roque et al. (2015).
impact of each technology but indeed also on the requirements of the food product.

The contradictory results shown sometimes when using the same technology (Tables 1–4) indicate that the effects easily turn into positive or negative, in terms of phenolic compounds bioaccessibility or bioavailability, depending on the operating conditions and also on the nature of the phenolic compounds and the matrix of the plant-based food. Figure 2 shows that the use of PEF or HPP, under certain operating conditions, resulted in enhanced bioaccessibility of phenolic compounds in plant-based fruit beverages with respect to thermal treatment. The effects depended on the nature of the matrix (water-fruit juice, milk-fruit juice or soy-milk juice) and on the group of the phenolic compounds (total phenolics, total flavonoids or total phenolic acids). Therefore, there is an interesting potential of food processing as strategy to increase phenolic compounds bioaccessibility and bioavailability, but a thorough exploration of the effects under different operation conditions is needed in order to find the most appropriate strategy for each food product.

Conclusions

Bioavailability of phenolic compounds largely depends on their chemical structure and the matrix effects and interactions. Food processing, beyond its traditional use to stabilize and produce long-lasting food products, can be also used as a tool to increase phenolic compounds bioavailability, given that many of the physical and chemical constraints for their bioavailability can be modulated by food processing. From the literature it can be stated that it is possible to find processing conditions to intentionally facilitate the release of phenolic compounds from the matrix during digestion. Bioavailability of phenolic compounds in processed food is a balance between those compounds lost during processing and those finally absorbed into the organism. Therefore, food technologists need to find the operating conditions that tip the balance in favor of bioaccessibility and bioavailability. The finding of these compromise operating conditions will be achieved thanks to the information provided by the current and future research that is conducted in this area. The choice between bioaccessibility or bioavailability assessment in future research will require a previous consideration of the advantages and drawbacks of each methodology. Indeed, bioavailability of phenolic compounds is a better approximation to their biological effects on the organism; however, the costs of sampling from interventional studies and fully assessing the whole absorbed metabolites limit their implementation. In addition, the large interindividual variability makes difficult to obtain reliable results from bioavailability studies. On the other hand, results from in vitro bioaccessibility studies including gastric and duodenal digestion are limited to those compounds that are available for absorption in the small intestine (bioaccessible), lacking in the determination of the colonic metabolites after interaction with the microbiota. However, the determination of the nonbioaccessible compounds is also relevant from a nutritional point of view, given their positive effects on the good functioning of the intestinal microbiota and inhibitory effects on gut pathogens. The simplicity, low cost, good reproducibility and high throughput of the bioaccessibility methods have made them a popular choice in the field of food sciences. Regarding technologies, special attention must be paid to emerging nonthermal processing treatments, which have shown little or no detrimental effects on the phenolic content, while inducing matrix changes that potentially entail higher uptake during digestion. However, to date very few works have addressed the impact of food processing on phenolic compounds bioaccessibility or bioavailability and the scarce information is even more limited for nonthermal technologies. Therefore, the research in this area appears to be challenging but promising as future results will have direct consequences on the functional properties of vegetable-based food products.

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