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Review

# Interactions of polyphenols with carbohydrates, lipids and proteins

Lidija Jakobek *

*Josip Juraj Strossmayer University of Osijek, Faculty of Food Technology Osijek, Department of Applied Chemistry and Ecology, Franje Kuhača 20, HR 31000 Osijek, Croatia*

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ABSTRACT

Polyphenols are secondary metabolites in plants, investigated intensively because of their potential positive effects on human health. Their bioavailability and mechanism of positive effects have been studied, *in vitro* and *in vivo*. Lately, a high number of studies takes into account the interactions of polyphenols with compounds present in foods, like carbohydrates, proteins or lipids, because these food constituents can have significant effects on the activity of phenolic compounds. This paper reviews the interactions between phenolic compounds and lipids, carbohydrates and proteins and their impact on polyphenol activity.



**Contents**



## 1. Introduction

Plant foods contain components important for human development and health, like vitamins, proteins, and minerals. Phenolic compounds are plant secondary metabolites but they are also an important part of plant foods. They are being widely studied due to potential positive effects of polyphenol-rich foods. Polyphenols have shown various positive bioactivities, like anticarcinogenic properties (Bellion et al., 2010). The polyphenol influence on cardiovascular health and cancer was reviewed by Hollman et al. (2011). On the other hand, some activities of polyphenols are being reassessed, such as their direct antioxidant activities inside the organism and the biological relevance of antioxidant activities in cardiovascular disease protection (Hollman et al., 2011). It is increasingly emphasized that there are multiple bioactivities of polyphenols in the human organism that are important to understand, such as the role of their metabolites, the effects on the modulations of enzymes (Hollman et al., 2011) and interactions with other macromolecules (Le Bourvellec & Renard, 2012).

* Tel.: +385 31 224 325; fax: +385 31 207 115.
*E-mail address:* lidija.jakobek@ptfos.hr

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In order to have effects within the human organism, phenolic compounds should be released during digestion and then absorbed in the gut in a certain amount (Parada & Aguilera, 2007). That is why their bioaccessibility and bioavailability are subjects of various studies and reviews (Adam et al., 2002; Duarte & Farah, 2011; Manach, Williamson, Morand, Scalbert, & Rémésy, 2005; Serra et al., 2010). Bioaccessibility is defined as the amount of an ingested compound that is available for absorption in the gut (Palafox-Carlos, Ayala-Zavala, & Gonzalez-Aguilar, 2011). The FDA has defined *bioavailability* as the rate and extent to which the active substances or therapeutic moieties contained in a drug are absorbed and become available at the site of action (Parada & Aguilera, 2007).

Various studies deal with the determination of how much of the polyphenols can be absorbed into the circulation system after they get into the body (Adam et al., 2002; Serra et al., 2010). Evidences suggest that polyphenols are absorbed in a relatively low amount. The absorption of isoflavones and gallic acid is the best, followed by catechins, flavanones, and quercetin glucosides. Proanthocyanidins, galloylated tea catechins and anthocyanins are the least well absorbed (Manach et al., 2005). New evidence offers some new views on the bioavailability. Czank et al. (2013) studied the bioavailability of $^{13}C_5$ labeled cyanidin-3-glucoside, by collecting blood, urine, breath and fecal samples from human volunteers. The results showed that anthocyanins are more bioavailable than previously perceived (12.3 ± 1.3%) and that their metabolites are present in the circulation for ⩽48 h after ingestion. Procyanidins are abundant in many foods like apples, berries, and nuts, and are therefore consumed regularly by many people. Recent findings offers some additional understanding of the bioavailability since it was shown that not only B type dimers but also A type dimers are bioavailable (Appeldoorn, Vincken, Gruppen, & Hollman, 2009). Study has shown that the dose of polyphenol ingested has important impact in the bioavailability. Namely, higher doses can show different effects than lower doses of ingested polyphenols. Specifically, it was shown that chlorogenic acid from coffee had reduced bioavailability in humans when ingested in higher doses (Stalmach, Williamson, & Crozier, 2014). Moreover, it has become clear that nutrients like proteins, carbohydrates and lipids that surround polyphenols inside the gastrointestinal tract, have a great impact on the bioaccessibility and bioavailability of polyphenols. Indeed, many such nutrients have a very complex, porous structure which trap polyphenols and, as a consequence, change their availability for absorption. Studies conducted in recent years have shown the importance of these interactions (Chanteranne et al., 2008; Schramm et al., 2003). Moreover, these interactions with nutrients could give polyphenols a very different role. They could protect polyphenols from oxidation during their passage through the gastrointestinal tract and deliver them to the colon more intact. Here they can be metabolized under the influence of microflora. Recent studies describe the role of dietary bioactive compounds, intestinal microbiota and polyphenol metabolites (MacDonald & Wagner, 2012; Tuohy, Conterno, Gesperotti, & Viola, 2012). Furthermore, it is suggested that a positive, antioxidant environment could be created in the gastrointestinal tract, by the delivery and release of polyphenols. There polyphenols, as antioxidant compounds, can protect nutrients as proteins, lipids and vitamins, from oxidation. In addition to these mentioned activities, they also can interact with proteins producing protein precipitation and loss of nutritional value, enzymatic activity, and other biological effects (Tomás-Barberán & Andrés-Lacueva, 2012). It has become increasingly clear that polyphenols have many potential bioactivities in the human body which are affected by interactions of polyphenols with other macromolecules (Le Bourvellec & Renard, 2012).

Interactions between polyphenols and molecules from food were mostly based on different non-covalent hydrophobic interactions (Yuksel, Avci, & Erdem, 2010). Hydrogen bonds are also important as in the case of interactions between polyphenols and proteins (Frazier et al., 2010; Shpigelman, Israeli, & Livney, 2010), and polyphenols and carbohydrates (Saura-Calixto, 2011). The interaction between proteins and plant phenols can lead to covalent bonds as well (Kroll, Rawel, & Rohn, 2003). The conditions for forming covalent bonds are the capability of phenols to form quinone or semi-quinone radicals (in a two-step reaction). The reaction proceeds with polymerization (Kroll et al., 2003).

This paper reviews the recent literature about the interactions between phenolic compounds and other molecules present in food (proteins, carbohydrates, and lipids), the nature of these interactions and their significance.

## 2. Phenolic compounds

A high number of compounds belong to the group of phenolics (phenolic acids, acetophenones, phenylacetic acid, hydroxycinnamic acids, coumarins, naphthoquinones, xanthones, stilbenes, flavonoids) (Crozier, Jaganath, & Clifford, 2009). The most important ones occurring in plants are flavonoids, phenolic acids, stilbenes and lignans (Crozier et al., 2009). Their chemical structure is more or less complex and can vary from very simple molecules to very complex ones.

Flavonoids, as one of the largest group of phenolic compounds, can be further classified into several subcategories like anthocyanidins, flavonols, flavanols (catechins and proanthocyanidins), flavanones, flavones and isoflavones (Crozier et al., 2009). They have a similar basic structure consisting of two phenyl groups linked together with three-carbon bridge commonly cyclized with oxygen. They are differentiated according to the degree of unsaturation and degree of oxidation of the three-carbon segment. Moreover, various sugar molecules can be bound to the flavonoid structure over their hydroxyl groups, which make the structure of these molecules more complex. In fact they are commonly found in glycosidic forms. Glycosylation makes them more soluble in water. Acylation of the glycosides is also common. One or more of the sugar hydroxyls can be derivatized with an acid such as acetic or ferulic acid. The structure of some flavonoids can be even more complex. Gallotannins (hydrolysable tannins) and proanthoyanidins (condensed tannins) are compounds from flavanol group which have several basic units of polyphenols interconnected into a larger, more complex structure (Crozier et al., 2009; Landete, 2011). Gallotannins are esters of gallic acid and a polyol, usually glucose (Landete, 2011). Proanthocyanidins or condensed tannins are high-molecular weight polymers with flavan-3-ols as basic structural units ((epi)catechins and (epi)gallocatechins). Interflavanoid linkages are acid labile and anthocyanidin molecules are created after the acid hydrolysis in alcoholic solutions (Crozier et al., 2009).

Ellagitannins which belong to the hydrolysable tannin class are esters of hexahydroxydiphenic acid and a polyol, usually glucose or quinic acid (Landete, 2011). They can also form complex molecules.

On the other hand, phenolic acids are a group of plant phenols that have relatively simple structures but can also be linked to sugar units. They are a large group of hydrophilic phenols.

As it can be seen, phenolic compounds are a diverse group of compounds composed of simple molecules of low molecular weight up to very complex molecules of high-molecular weight. Because of the great diversity in their structure, they have different properties, such as solubility and polarity which enable them to have different interactions with other molecules. They can interact with each other and with other molecules that surround them. Bigger molecules have a much greater number of hydroxyl groups as this makes them susceptible to a very large number of interactions

with the environment. But even those with a simpler structure are often associated with sugar units which again increases the number of hydroxyl groups and raises the possibility to interact with the environment. Their structure, the arrangement of hydroxyl groups, the planarity of molecules, the arrangement of sugar units and many other factors play important roles in the activity of plant phenolics in the human body.

## 3. Plant's microstructure and localization of phenolic compounds

In order to understand interactions that can occur between polyphenols and other food ingredients, it is important to understand the basic structure of plant foods.

Plant foods produced by nature, are generally organized from molecules into assemblies and organelles that can create cells and tissues (Parada & Aguilera, 2007). Natural structures of fruits and vegetables consist of hydrated cells surrounded by the cell wall (Parada & Aguilera, 2007) with nucleus, cytoplasm and plasma membrane located within the cells; and a large central vacuole in the cytoplasm. That structure at a micro level is already recognized as a very important for the bioactivities of many compounds.

Namely, a big part of food consumption is of plant foods that have had minor processing or no processing at all. So at the moment of eating, the microstructure is in its natural original form. The digestion begins in the mouth, where changes in microstructure start happening. Mastication results in the rupture of some cells, which allows phenolic compounds and other nutrients to be released in the environment (Padayachee et al., 2012a, 2012b). In processed products, the changes in the microstructure begin already during the processing (Parada & Aguilera, 2007). In any of these cases, natural plant food, processed food or any other matrix, when the rupture of microstructural elements starts, phenolic compounds can potentially be released together with other nutrients and become available for absorption. These phenolic compounds and nutrients can also come into contact with each other which enable various interactions, possible chemical bonding, and entrapment of smaller molecules into porous structure of bigger molecules. These interactions could affect bioaccessibility, bioavailability and bioactivities of phenolic compounds.

Some food matrices enhance the accessibility of polyphenols as in the case of natural almond skin where polyphenols are more accessible than from blanched skins produced by the almond industry (Mandalari et al., 2010). A study on humans has shown that the bioavailability of chlorogenic acids from coffee can be impaired by a matrix consisting of coffee and milk (simultaneous consumption of coffee and milk) (Duarte & Farah, 2011). Milk affects the absorption of cocoa polyphenols, but according to some studies the absorption was decreased while in other it increased. This controversy was explained by the impact of polyphenol concentration (Del Rio, Borges, & Crozier, 2010). Milk could interfere with the absorption in the case of lower polyphenol concentration while it could have only minimal impact if the polyphenol concentration is high (Del Rio et al., 2010). A food matrix can influence various bioactivities of polyphenols. Cinnamon extract polyphenols can be incorporated into defatted soy flour. Polyphenols from that protein rich matrix still showed antidiabetic effects in animal studies (Cheng et al., 2012). All these described matrix effects, shown to potentially influence polyphenol bioactivities, could be partially caused by interactions between polyphenols and other molecules from food.

## 4. Interactions between polyphenols and other complex molecules

Lipids, proteins and carbohydrates are compounds often found in the environment surrounding phenolic compounds. They can come into contact with phenolic compounds and interact with them.

**Table 1**
Interactions between polyphenols and lipids, and their effects.

| Polyphenol tested | Lipid model | Effects | Reference |
|---|---|---|---|
| **Influence on emulsion properties** | | | |
| Green and black tea polyphenols | Model emulsion (olive oil, phosphatidylcholine and bile salt) | - Increased droplet size and decreased specific surface area of olive-oil emulsion | Shishikura et al. (2006) |
| **Lipase activity inhibition** | | | |
| Apple polyphenol extract and procyanidins | 4-Methylumbelliferyl oleate | - Inhibition of lipase activity (higher polymerization degree of procyanidins – higher inhibition) | Sugiyama et al. (2007) |
| Black tea polyphenol extract and polymerized polyphenol fraction | Lipid emulsion (corn oil, cholic acid, cholesteryl oleate, water) | - Inhibition of lipase activity, suppression of the increase in rat plasma triglyceride, suppression of the increase in body weight and liver lipid content | Uchiyama et al. (2011) |
| **Lipid oxidation inhibition and interaction with lipase peroxidation products** | | | |
| Quercetin, rutin, (+)-catechin, caffeic acid, chlorogenic acid, 3,4-dihydroxybezoic acid | Model emulsion Sunflower oil, stabilized by bovine serum albumin or egg yolk phospholipids | - Quercetin, rutin, (+)-catechin, caffeic and chlorogenic acid are better inhibitors of lipid oxidation than α-tocopherol or ascorbic acid | Lorrain et al. (2010) |
| Quercetin, rutin, chlorogenic acid | Model emulsion (sunflower oil stabilized by bovine serum albumin or egg yolk phospholipids | - Quercetin, rutin, chlorogenic acid highly inhibited metmyoglobin-initiated lipid oxidation<br>- Quercetin inhibited nonheme iron-initiated processes | Lorrain et al. (2012) |
| Red wine | *In vivo* study dark turkey meat cutlets | - Combination of red wine and meat prevented postprandial modification of LDL by lipid peroxidation products<br>- Possible mechanism: antioxidant properties of red wine polyphenols in the stomach, interaction with lipid peroxidation products within the gastrointestinal tract, delaying of fat absorption | Gorelik et al. (2013) |
| **Digestibility of polyphenols** | | | |
| Cocoa polyphenols | Cocoa liquor (50% fat content), cocoa powder (15% fat content) | - Fat content enhanced the digestibility of some polyphenols, especially procyanidins, during duodenal digestion. Suggestion is the interaction between fat and polyphenols | Ortega, Reguant, Romero, Macia, and Motilva (2009) |
| **Encapsulation** | | | |
| Quercetin (QC), (−)-epigallocatechin gallate ((−)-EGCG) | Lipid nanocapsules (LNC) (Labrafac, Solutol, Phospholipon) | - Lipid nanocapsules can be used as a flavonoid delivery carriers | Barras et al. (2009) |

### 4.1. Interactions with lipids

Polyphenols can interact with lipids from food sources (Table 1 and Fig. 1). Some studies have shown the potential role of these interactions in the fat absorption process (Shishikura, Khokhar, & Murray, 2006; Uchiyama, Taniguchi, Saka, Yoshida, & Yajima, 2011) which might have positive effects on health.

Dietary fats go through a digestion process that starts with mastication in which lipids are transformed into emulsions. After that they travel to the stomach and duodenum. Inside the gastrointestinal tract, emulsions are exposed to the surface-active components which help in emulsification. Furthermore, the lipase carries out a process of lipolysis, a breakdown of lipids into smaller particles which can then be absorbed (Shishikura et al., 2006). Specific emulsion properties like droplet size and surface area are important for the lipase activity (Shishikura et al., 2006). Therefore, any molecule which might act on emulsion properties or lipase activity could potentially change and affect the fat absorption process. Namely, molecules surrounding emulsions could be found inside of the oil droplet, in the water phase that surrounds the oil droplet or in the interfacial region. This partitioning is mostly determined by the polarity of molecules. Nonpolar molecules can be found in the lipid phase, polar molecules in the aqueous phase and amphiphilic molecules at the interface of these two regions. From these positions, they could change the surface or the size of the oil droplet which are important for the lipase activity. Through the influence on the emulsion properties, that kind of molecule could affect the decrease of the lipase activity and hence the decrease of fat absorption. This could eventually lead to beneficial effects on obesity.

Shishikura et al. (2006) studied the emulsification process *in vitro* and the influence of polyphenols on this process. A model emulsion from olive oil, phosphatidylcholine, and bile salt was created to stimulate small intestinal conditions (Shishikura et al., 2006). It was found that green and black tea polyphenols affected emulsions by increasing droplet size and decreasing specific surface area. Interactions between tea polyphenols and phosphatidylcholine were suggested to be the reasons for this (Shishikura et al., 2006). Phosphatidylcholine possesses hydrophilic heads at the exterior of the emulsion droplet, while polyphenols have many hydroxyl groups. They may interact creating complexes. Furthermore, polyphenols may have acted as a linker between complexes to form complex aggregates, thus increasing droplet size. Another reason for the increased droplet size can be the incorporation of tea polyphenols within the lipid layer which may lead to changes in the physicochemical properties of emulsions (increased droplet size and decreased surface area). It was suggested that the conditions of increased droplet size could cause the decrease in the lipase activity and fat absorption. Other studies also supported the inhibition of the lipase activity and fat absorption process by polyphenolic compounds. Uchiyama et al. (2011) have studied the influence of black tea polyphenols on diet-induced obesity in rats. They have shown that black tea polyphenols inhibited the lipase activity and consequently inhibited intestinal lipid absorption. Furthermore, they have shown that black tea polyphenols suppressed the increase of triglyceride levels in the rat plasma. Sugiyama et al. (2007) have studied effects of apple polyphenols and procyanidins on the lipase activity (*in vitro*) and triglyceride absorption (on mice and humans). According to their results, apple polyphenols and procyanidins also inhibited lipase activity and triglyceride absorption.

Investigations suggest that interactions between lipids and polyphenols have only a small influence on the polyphenol accessibility for absorption. For instance, Schramm et al. (2003) studied the food effects (meals rich in lipids, proteins, carbohydrates) on the absorption of cocoa flavanols in humans. They found that lipids from the meal (such as milk, butter) had only minimal effects on flavanol absorption.

On the other hand, when lipids interact with polyphenols, they can "capture" polyphenols and protect them in their passage through the gastrointestinal tract. In this way lipids might help in delivering polyphenols in the lower parts of the gastrointestinal tract. Ortega, Reguant, Romero, Macia, and Motilva (2009) studied *in vitro* digestibility of cocoa polyphenols in a matrix containing fat. They suggested that the fat content in cocoa liquor might have a protective effect on polyphenols from cocoa due to a better micellarization which enables better stability of polyphenols during digestion.

Other studies suggest that polyphenols show some potential bioactivities in the gastrointestinal tract, where they can create positive antioxidant environment or react with harmful products of the lipid peroxidation. Namely, lipids may undergo an oxidation process in the stomach leading to the increase of lipid peroxidation products. This is especially important for meat meals because meat has various polyunsaturated fatty acids, cholesterol and other compounds which are susceptible to the lipid peroxidation. Lipid peroxidation products can be absorbed and then cause different damages (Gorelik, Kanner, Schurr, & Kohen, 2013). This subject is reviewed by Kanner, Gorelik, Roman, and Kohen (2012). Polyphenols delivered to gastrointestinal tract could potentially react with these harmful products and lower their influence. Gorelik et al. (2013) studied the addition of the red wine to meat meals and the effect of the red wine on damages caused by lipid peroxidation products (malondialdehydes) created after meat meal digestion, in rats. The addition of red wine completely prevented LDL (low density lipoprotein) modifications by lipid peroxidation products. A

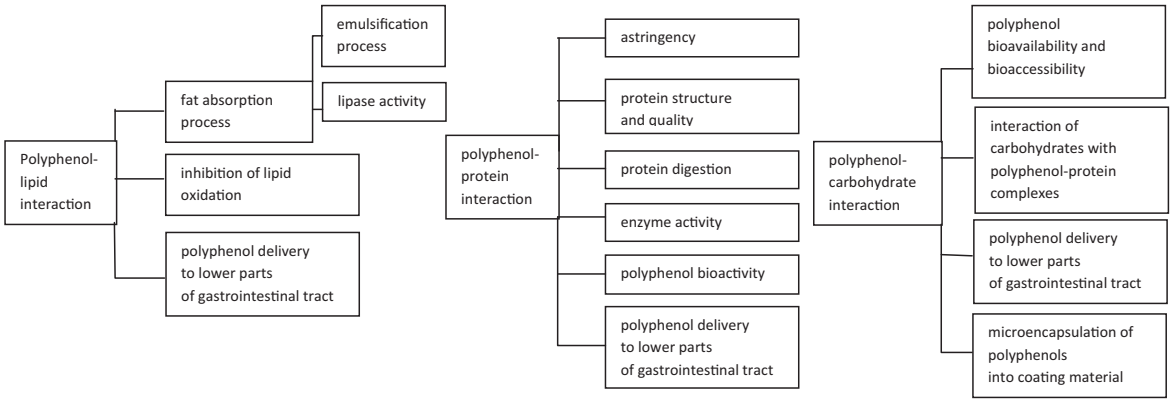


**Fig. 1.** The consequences of the interactions between polyphenols and lipids, proteins, and carbohydrates.

possible mechanism could come from wine polyphenols and their antioxidant properties. Another suggested mechanism was interaction between polyphenols and lipid peroxidation products. The delay of the fat absorption process caused by lipid–polyphenol interactions was also suggested. Other studies have also shown the inhibition of lipid oxidation by polyphenols (quercetin, rutin, (+)-catechin, caffeic acid and chlorogenic acid) (Lorrain, Dangles, Genot, & Dufour, 2010; Lorrain, Dangles, Loonis, Armand, & Dufour, 2012).

In the addition, interactions between lipids and polyphenols could be used to form nanocarriers of polyphenols through the gastrointestinal tract, which was reviewed by Santos, Ponte, Boonme, Silva, and Souto (2013). Barras et al. (2009) studied flavonoid-loaded lipid nanocapsules. Lipid nanocapsules are useful in drug delivery for water-insoluble compounds or pH sensitive compounds. They concluded that these nanocapsules could be used as flavonoid delivery carriers.

It seems that interactions between lipids and polyphenols might have a positive role in the decrease of the fat absorption process which might have a positive health effect. Besides, lipid–polyphenol interactions could result in the protection of polyphenol while they pass through the gastrointestinal tract. This potentially allows the beneficial effect of polyphenols inside the gastrointestinal tract. There the interactions between polyphenols and harmful lipid peroxidation products were suggested. Lipid peroxidation products could cause various damaging effects which could potentially be decreased by the polyphenol activity. Furthermore, the lipid–polyphenol interactions were even used in the creation of nanocapsules based on lipids which may serve as polyphenol carriers through the gastrointestinal tract.

### 4.2. Interactions with proteins

There are many papers describing protein–polyphenol interactions (Table 2, and Fig. 1). Many *in vitro* studies have shown that proteins can bind to polyphenols (Arts et al., 2002; Frazier et al., 2010; Hasni et al., 2011; Kanakis, Hasni, Bourassa, Tarantilis, & Polissiou, 2011; Nagy et al., 2012; Shpigelman et al., 2010; Stojadinovic et al., 2013; Von Staszewski et al., 2012; Yuksel et al., 2010) and that these interactions are mainly non-covalent hydrophobic interactions which may subsequently be stabilized by hydrogen bonding (Yuksel et al., 2010). Non-covalent binding includes hydrophobic-, van der Waals-, hydrogen bridge-binding and ionic interactions, it is weaker than covalent binding and it is always reversible (Nagy et al., 2012). Tea is one of the often studied systems where proteins might interact with polyphenols. Tea as one of the most popular beverages in the world is often consumed with the addition of milk. The major milk protein is casein. Recent *in vitro* study demonstrated that the binding of polyphenols from green tea with milk protein is hydrophobic (Yuksel et al., 2010). Another *in vitro* study demonstrated that the binding between polyphenols from tea with α- and β-casein is hydrophilic and hydrophobic but hydrophobic binding prevails (Hasni et al., 2011). It has also been shown that several amino acid residues participate in reactions where polyphenol–protein associations are formed (Hasni et al., 2011). Kanakis et al. (2011) studied the complexation of tea polyphenols with β-lactoglobulin, *in vitro*. The binding was hydrophilic and hydrophobic. Von Staszewski et al. (2012) studied associations between β-lactoglobulin or caseinomacropeptide and green tea polyphenols. Associations were formed which was shown by the appearance of bigger particles. The binding was hydrophobic (Von Staszewski et al., 2012). Shpigelman et al. (2010) even found that heated β-lactoglobulin binds (−)-epigallocatechin-3-gallate from tea with higher affinity than does the native protein, in an *in vitro* experiment. The binding was a combination of hydrophobic interactions and H-bonds.

Frazier et al. (2010) studied interactions of tea catechins, grape seed proanthocyanidins, mimosa 5-deoxy proanthocyanidins and sorghum procyanidins with gelatin, *in vitro*. Polyphenols interacted with gelatin which involved multiple binding sites on the protein molecule and a dominant factor in these interactions were hydrogen bonds.

Proteins and polyphenols can bind with covalent bonds as well (Kroll et al., 2003; Rohn, Rawel, & Kroll, 2002), which was reviewed by Kroll et al. (2003). Ali et al. (2012) demonstrated the appearance of covalent bonds between caffeoylquinic acid and coffee bean storage proteins. Covalent attachment was suggested between enzymes and polyphenols (α-amylase, trypsin, and lysozyme) (Rohn et al., 2002). Covalent bonds are the result of irreversible association between proteins and polyphenols, where phenols are transformed into quinones which may react with nucleophilic groups on the protein molecule (Beart, Lilley, & Haslam, 1985).

The structure and molecular weight of polyphenols play an important role in protein–polyphenol interactions. It has been shown that high molecular weight polyphenols (tannins) are able to bond more strongly or preferentially to proteins (Frazier et al., 2010). The flexibility of the polyphenol molecule appears to be important as well. Structurally flexible polyphenols have shown equal binding strength to different proteins (gelatin and bovine serum albumin) whereas less flexible polyphenols (ellagitannins) exhibited stronger binding to some proteins (gelatin) and weaker to others (bovine serum albumin) (Frazier et al., 2010). Moreover, the order of binding to proteins increased as the number of OH groups on the polyphenol molecule increased (Hasni et al., 2011; Kanakis et al., 2011). According to the mentioned studies, some structural features of polyphenol molecules are important: (i) molecular weight, (ii) structural flexibility and (iii) number of OH groups.

Protein–polyphenol interactions could have various biological effects. Interactions between salivary proteins and tannins have been studied in relation to astringency (de Freitas & Mateus, 2001; Oberque-Slier, Pena-Neira, & López-Solís, 2012; Perez-Gregorio, Mateus, & de Freitas, 2014; Sarni-Manchado, Canals-Bosch, Mazerolles, & Cheynier, 2008; Soares, Mateus, & de Freitas, 2012b; Soares et al., 2011). Astringency is an oral sensation that has been previously defined as puckering, rough and drying mouth-feel (Oberque-Slier et al., 2012). It is affected by associations between proanthocyanidins and salivary proteins. Namely, association formation will result in aggregate formation. They can reduce lubricating properties of saliva which results in unpleasant sensation in the mouth (De Freitas & Mateus, 2001). The binding is dependent on the polyphenol type and structure (De Freitas & Mateus, 2001; Perez-Gregorio et al., 2014), the pH value (Oberque-Slier et al., 2012), the salivary protein family (acidic, basic or glycosylated proline rich proteins) (Perez-Gregorio et al., 2014; Sarni-Manchado et al., 2008; Soares et al., 2011, 2012b).

Interactions can also influence protein structure, their functionality and quality. Namely, the nutritional quality of proteins depends on amino acid composition, essential amino acids, digestion etc. Compounds interfering with proteins (amino acids) could lower the protein quality. It was shown that if polyphenols bind to hydrophobic sites of proteins, the protein structure may change because only weak hydrophobic sites could remain on the surface of the protein (Yuksel et al., 2010) leading to a possible change in the protein folding and in the protein functionality. Rawel, Czajka, Rohn, and Kroll (2002) studied interactions of phenolic acids and flavonoids with soy proteins, *in vitro*. They suggested that the reaction with phenolic compounds can cause the change in the

**Table 2**
Interactions between polyphenols and proteins and their effects.

| Polyphenol tested | Protein model | Effects | References |
|---|---|---|---|
| **Attachment, the influence of polyphenol structure and other factors on the interaction** | | | |
| Grape seed procyanidins | α-Amylase, proline-rich proteins, bovine serum albumin | - Procyanidin ability to bind proteins increased with molecular weight of procyanidins | de Freitas and Mateus (2001) |
| Polyphenols | Myoglobin | - *o*-, *p*-Hydroxyphenols, *p*-quinone, gallic acid had high reactivity and caused structural changes in myoglobin | Kroll and Rawel (2001) |
| Chlorogenic acid, caffeic acid, gallic acid, flavone, apigenin, kaempferol, quercetin, myricetin | Soy proteins | - The derivatization is influenced by the number and position of OH groups on phenolic molecules | Rawel et al. (2002) |
| Green tea flavonoids | Milk proteins | - Hydrophobic bonding | Yuksel et al. (2010) |
| Grape seed proanthocyanidins, mimosa 5-deoxy proanthocyanidins, sorghum procyanidins | Gelatin | - Hydrogen bonding | Frazier et al. (2010) |
| (−)-Epigallocatechin-3-gallate | β-Lactoglobulin (BLG) | - Heated BLG binds polyphenol with higher affinity than does the native protein | Shpigelman et al. (2010) |
| (+)-Catechin, (−)-epicatechin, (−)-epicatechin gallate, (−)-epigallocatechin gallate | β-Lactoglobulin | - Hydrophobic and hydrophilic bonding<br>- Order of binding increases with increased number of OH groups | Kanakis et al. (2011) |
| (+)-Catechin, (−)-epicatechin, (−)-epigallocatechin, (−)-epigallocatechin gallate | α- and β-casein | - Interactions are more hydrophobic than hydrophilic<br>- The order of binding increases with increased number of OH groups | Hasni et al. (2011) |
| Coffee polyphenols | Coffee storage proteins | - Polyphenol oxidase activity seems to be a crucial factor for the formation of addition products | Ali et al. (2012) |
| *m*-, *o*-, *p*-Dihydroxybenzenes, ferulic acid, gallic acid | Lysozyme | - Covalent bonding | Rawel et al. (2001) |
| Chlorogenic acid, *m*-, *o*-, *p*-dihydroxybenzene, *p*-benzoquinone | α-Chymotrypsin | - Enzyme inhibition depended on the reactivity of phenols and degree of polymerization | Rohn et al. (2003) |
| **Influence on the protein structure, quality and digestibility** | | | |
| *m*-, *o*-, *p*-Dihydroxybenzenes, ferulic acid, gallic acid | Lysozyme | - Reduction of lysine and tryptophan residues<br>- Derivatives – solubility decreased over pH range, hydrophobicity increased, isoelectric point shifted to lower pH | Rawel et al. (2001) |
| Polyphenols | Myoglobin | - Enzymatic digestion of derivatized myoglobin was affected | Kroll & Rawel, 2001 |
| Chlorogenic acid, caffeic acid, gallic acid, flavone, apigenin, kaempferol, quercetin, myricetin | Soy proteins | - Interaction resulted in blocking of some amino acids (lysine, tryptophan) | Rawel et al. (2002) |
| Chlorogenic acid | β-Lactoglobulin | - The digestibility of whey protein is diminished<br>- Observed effect is not so distinct due to the high nutritional quality of whey proteins | Petzke et al. (2005) |
| Chlorogenic acid, quercetin | Soy protein | - Rats fed with soy protein derivatives showed an increase excretion of fecal and urinary nitrogen<br>- True nitrogen digestibility, biological value, net protein utilization were affected | Rohn et al. (2006) |
| Catechin, epicatechin, epigallocatechin, epicatechin gallate, epigallocatechin gallate | β-Casein | - The slowdown of protein adsorption | Aguié-Béghin et al. (2008) |
| **Influence on enzyme activity** | | | |
| *m*-, *o*-, *p*-Dihydroxybenzenes, ferulic acid, gallic acid | Lysozyme | - The peptic digestion of the derivatized lysozyme was affected | Rawel et al. (2001) |
| Caffeic, chlorogenic, ferulic, gallic acid, *m*-, *o*-, *p*-dihydroxybenzenes, quinic acid, *p*-benzoquinone | α-Amylase, trypsin, lysozyme | - The enzyme activity inhibition depended on the reactivity of phenolic and related substances, and on the substrate applied | Rohn et al. (2002) |
| Chlorogenic acid, *m*-, *o*-, *p*-dihydroxybenzene, *p*-benzoquinone | α-Chymotrypsin | - Enzyme activity affected<br>- Hydrolysis of food proteins was slowed down<br>- The affinity of enzyme to substrates decreased | Rohn et al. (2003) |
| Grape seed procyanidins | α-Amylase | - Inhibition of enzyme activity was related with the degree of polymerization of procyanidins | Gonçalves et al. (2011b) |
| **Astringency** | | | |
| Procyanidin dimer and trimer, (−)-epicatechin *O*-gallate, B2-3″-*O*-gallate | α-Amylase, proline-rich proteins (PRP) | - (+)-Catechin had higher activity for PRPs than (−)-epicatechin<br>- Procyanidin dimers linked through C(4)-C(8) interflavanoid bond had greater affinity than dimers with C(4)-C(6) linkage. Esterification of galloyl group increased activity | De Freitas and Mateus (2001) |
| Grape seed procyanidins | Proline-rich proteins | - Higher polymerized tannins predominantly precipitated with the salivary proteins<br>- Complexes found in soluble and in precipitated fractions<br>- Interactions dependent on the glycosylation state of proteins<br>- Low concentrations of tannins – glycosylated PRP–tannin complexes remained soluble, nonglycosylated PRP–tannin complexes precipitated<br>- Complexes with glycosylated PRP maintain lubrication or the oral cavity | Sarni-Manchado et al. (2008) |
| Grape seed extract | Proline-rich proteins (PRP) | - Condensed tannins interact first with acidic PRPs and statherin and then with histatins, glycosylated PRPs and basic PRPs | Soares et al. (2011) |
| Tannins | Salivary protein | - Tannins were more astringent at pH3.5 than pH7 | Oberque-Slier et al. (2012) |

(*continued on next page*)

**Table 2** (*continued*)

| Polyphenol tested | Protein model | Effects | References |
|---|---|---|---|
| Procyanidin trimer and pentagalloylglucose | Proline-rich protein (PRP) | - Acidic PRP interact with both tannins, basic PRP interact poorly with procyanidin trimer, glycosylated PRP created complexes with pentagalloylglucose<br>- Pentagalloylglucose created insoluble complexes while procyanidin trimer created soluble complexes | Soares et al. (2012b) |
| Procyanidin B3 (B3), procyanidin B2 gallate (B2G), pentagalloylglucoside (PGG) | Histatins, proline-rich proteins, statherins | - B3 – reacts with histatins, followed by basic PRP and statherins; -B2G – reacts with basic PRP, histatins and statherins; -PGG – reacts with basic PRP, followed by statherins and histatins<br>- Complexes influenced by polarity of tannins and proteins | Perez-Gregorio et al. (2014) |
| **Bioavailability of polyphenols** | | | |
| Green and black tea catechins | Milk | - Milk does not impair the bioavailability of tea catechins | Van het Hof et al. (1998) |
| Chlorogenic acids from coffee | Milk proteins | - Simultaneous consumption of milk and coffee impair the bioavailability of coffee chlorogenic acids | Duarte and Farah (2011) |
| *Artemisia dracunculus* L. polyphenols | Soy protein | - Association with soy proteins makes antidiabetic A. dracunculus polyphenols more bioavailable and bioaccessible | Ribnicky et al. (2014) |
| **Other influences on polyphenols** | | | |
| Green and black tea flavonoids | α, β, γ-casein | - Total antioxidant capacity of polyphenols was masked by the flavonoid-protein interactions | Arts et al. (2002) |
| (−)-Epigallocatechin-3-gallate (EGCG) | β-Lactoglobulin | - Complex protected EGCG against oxidative degradation | Shpigelman et al. (2010) |
| Tea polyphenols | β-Lactoglobulin (BLG) caseinomacropeptide (CMP) | - Polyphenols retain their antiproliferative activity within the complexes with BLG and CMP | Von Staszewski et al. (2012) |

net charge of the protein molecules, which can affect the solubility of these derivatives. The shift to lower pH value of the derivatives after the interaction with polyphenols was reported (Rawel et al., 2002).

Some studies suggested the blocking of some essential amino acids by polyphenols when they are bonded to proteins which could affect the availability of some amino acids. Rawel et al. (2002) suggested that phenolic acids and flavonoids, which reacted with soy proteins, might affect the blocking of lysine, tryptophan and cysteine residues in protein molecules, and hence decrease the availability of the essential amino acids, lysine and tryptophan. Several other papers reported the decrease of tryptophan and lysine residues after the interaction with polyphenols (Rawel, Kroll, & Rohn, 2001; Rohn, Petzke, Rawel, & Kroll, 2006). Petzke, Schuppe, Rohn, Rawel, and Kroll (2005) studied β-lactoglobulin treated with chlorogenic acid and tested the effects of these interactions on the protein quality and amino acid deficiency, in growing rats. Their results have shown that derivatization of β-lactoglobulin with chlorogenic acid did not lead to an additional deficiency in specific essential amino acids in growing rats.

Binding can also influence the digestion of proteins with the enzymes of the gastrointestinal tract. As a consequence of the reaction with chlorogenic acid, the digestibility of whey proteins was diminished (Petzke et al., 2005). The observed effects were not so distinct due to the high nutritional quality of whey proteins. Aguié-Béghin, Sausse, Meudec, Cheynier, and Douillard (2008) also noticed the slowdown of protein adsorption after their interaction with polyphenols. The enzymatic digestion of myoglobin (Kroll & Rawel, 2001) was affected. Petzke et al. (2005) studied N digestibility and net protein utilization in rats after they were fed with β-lactoglobulin derivatized with chlorogenic acid. They showed that only the proteins with high derivatization level could affect total N digestibility while net protein utilization remained the same. On the other hand, when rats were fed with derivatized soy proteins, increased excretion of nitrogen was shown, and nitrogen digestibility, biological value, and net protein utilization were affected (Rohn et al., 2006).

Polyphenols can bind to enzymes like α-amylase and change its activity (Gonçalves, Mateus, & de Freitas, 2011b), which can be connected to the prevention of dental caries. Namely, some functions of α-amylase can lead to the formation of dental plaque and dental caries (Rawel, Frey, Meidtner, & Kroll, 2006). By inhibiting its activity, polyphenols-α-amylase associations could have positive effects in preventing the formation of caries. Since polyphenols can bind to lysozyme, they can decrease its lytic activity (Rawel et al., 2001). Rohn et al. (2002) also demonstrated the enzyme activity inhibition by polyphenols. The activity of α-chymotrypsin was inhibited after the interaction with polyphenols (Rohn, Rawel, Wollenberger, & Kroll, 2003). As a consequence, the hydrolysis of food proteins was slower and the affinity to the substrate declined (Rohn et al., 2003).

Some studies examined the influence of polyphenol–protein interactions on polyphenol bioavailability. Earlier studies described minimal effects. Schramm et al. (2003) showed that there was only a minimal effect of proteins from meals on phenolic compound absorption (cocoa catechins) (in a study conducted on humans). Also in a study conducted *in vivo*, on human volunteers, Van het Hof, Kivits, Weststrate, and Tijburg (1998) showed that milk added to green and black tea did not influence the bioavailability of catechins. More recent studies describe positive or negative effects. Duarte and Farah (2011) suggested that the interactions between milk constituents and polyphenols from coffee may produce a negative effect on coffee polyphenol bioavailability, in humans. Ribnicky et al. (2014) studied the bioavailability of polyphenols from *Artemisia dracunculus* L. in mice, in the form of extract or in a complex with soy proteins. The results showed that polyphenols sorbed to soy protein isolate were more bioavailable and bioaccessible.

Furthermore, studies suggested additional positive effects of polyphenol–protein interactions. Namely, polyphenols could be delivered to lower parts of the gastrointestinal tract due to polyphenol–protein interactions. Certain proteins carrying polyphenols were even called nanovehicles (Shpigelman et al., 2010). Stojadinovic et al. (2013) also suggested proteins as good carriers of polyphenols in the gastrointestinal tract. These complexes could show several effects on the polyphenol activity. They might protect polyphenols against oxidative degradation as it was found for (−)epigallocatechin-3-gallate in complex with heated β-lactoglob-

ulin (Shpigelman et al., 2010). When bound to proteins, polyphenols could preserve their anti-proliferative activity which was found for green tea polyphenols (Von Staszewski et al., 2012). On the other hand, the association between polyphenols and proteins could affect the antioxidant activity of polyphenols as it was found for associations created between polyphenols and milk proteins, *in vitro* (Hasni et al., 2011). In fact, due to the protein–polyphenol interactions, the antioxidant activity of polyphenols was masked (Arts et al., 2002).

Studies discussed here have shown that polyphenol–protein interactions might influence astringency sensation in the mouth. The biological activity of proteins is also affected. By binding to proteins, polyphenols might potentially affect the availability of certain amino acids and also change the protein structure which could affect the functionality and digestibility of proteins. However, the strength of this effect could depend on the nutritional quality of proteins themselves. Polyphenols can interact with enzymes and change their enzymatic activity, which could have various consequences. Some of them are positive, as in the case of the inhibition of α-amylase activity which could be connected to the prevention of dental cavities. In the case of digestive enzyme inhibition, interactions could lead to the influence on the digestion process. Protein–polyphenol interactions might influence polyphenols as well. In the presence of proteins, some polyphenol activities could be "masked", like their antioxidant activity. Studies have also suggested the possible influence of protein–polyphenol interactions on the polyphenol bioavailability. On the other hand, due to polyphenol–protein interactions, proteins could be carriers of polyphenols through the gastrointestinal tract and protect them from oxidation reactions.

### 4.3. Interactions with carbohydrates

A large body of evidence has been shown for the interaction between polyphenols and carbohydrates (Table 3, and Fig. 1). Carbohydrates can interact with polyphenols (Le Bourvellec, Guyot, & Renard, 2009; Padayachee et al., 2012a, 2012b; Pekkinen et al., 2014; Rosa, Dufour, Lullien-Pellerin, & Micard, 2013), and it has been shown that these interactions have a significant role in the human body. In addition, several review papers have recently been published which particularly emphasize the importance of the interaction of polyphenols with dietary fiber (MacDonald & Wagner, 2012; Palafox-Carlos et al., 2011; Saura-Calixto, 2011; Tuohy et al., 2012).

Interactions of polyphenols with carbohydrates were mainly investigated experimentally *in vitro*. Polyphenol interact with various carbohydrates originated from the cell wall like pectin, cellulose or dietary fibers (Le Bourvellec et al., 2009; Padayachee et al., 2012a, 2012b). It was found that procyanidins bound to cell wall carbohydrates (Le Bourvellec, Bouchet, & Renard, 2005; Le Bourvellec et al., 2009). Studies also highlighted the increase of the interaction with the increased degree of polymerization of procyanidins and percent of galloylation (Bautista-Ortín, Cano-Lechuga, Ruiz-García, & Gómez-Plaza, 2014; Le Bourvellec et al., 2005; Watrelot, Le Bourvellec, Imberty, & Renard, 2013). Furthermore, high affinities of procyanidins for pectin were shown (Le Bourvellec et al., 2005, 2009; Watrelot et al., 2013), which was explained by the formation of hydrophobic pockets able to encapsulate procyanidins (Le Bourvellec et al., 2005). Pockets or cavities in carbohydrate molecules were highlighted as important in the interaction between cyanidin-3-*O*-glucoside and β-cyclodextrin (Fernandes et al., 2014). Padayachee et al. (2012a, 2012b) studied interactions of anthocyanins and phenolic acids with plant cell wall components (cellulose and pectin), *in vitro*. Cell wall components interacted with both anthocyanins and phenolic acids (Padayachee et al., 2012a, 2012b).

The reason for these interactions could be the formation of weak bonds (H-bonds and hydrophobic interaction) between polyphenols and cell wall components. Hydrogen bonds are formed between hydroxyl groups of polyphenols and oxygen atoms of the glycosidic linkages of polysaccharides. Covalent bonds can be formed between phenolic acids and polysaccharides. Complex porous structure and surface properties of cell walls can also be important (Fernandes et al., 2014; Le Bourvellec et al., 2005; Saura-Calixto, 2011). Wang, Liu, Chen, and Zhao (2013) studied the importance of the polyphenol structure for binding with polysaccharides. They suggested that hydroxylation (three or less OH groups) of flavonoids and galloylation of catechins improved the adsorption into oat β-glucan. Methylation or methoxylation of phenolic acids lowered the adsorption. Glycosylation exerted complicated influences (Wang et al., 2013).

Consequences of these interactions could be multiple. First of all there is an influence on the bioavailability of phenolic compounds. Some studies showed that the bioavailability decreases due to the formation of associations of carbohydrates and polyphenols, which actually capture polyphenols into their structure. Adam et al. (2002) conducted a study on a rat model, investigating ferulic acid bioavailability from supplemented diets or from a complex cereal matrix (whole and white flours). It was found that the cereal matrix limited ferulic acid bioavailability. The reason for this may be ferulic acid association with the fiber fraction through cross-linking with arabinoxylans and lignins. Indeed, some later studies showed that ferulic acid can be more available when bran structure is ruptured which results in the release of phenolic acids (Pekkinen et al., 2014; Rosa, Aura, et al., 2013). Some studies showed the possibility of carbohydrate present in the human diet to enhance the uptake of some polyphenols. For instance, in a study conducted on human volunteers, the carbohydrate consumption (bread) significantly increased the flavanol uptake (Schramm et al., 2003). This effect may have been mediated by a carbohydrate specific effect on gastrointestinal physiology (e.g. motility and/or secretion) or a carbohydrate specific enhancement of the activity of a yet unidentified carbohydrate-flavanol transporter (Schramm et al., 2003). Serra et al. (2010) also showed in a study *in vitro* that carbohydrate-rich food enhanced the uptake of the monomeric proanthocyanidins. The same study demonstrated that the absorption of dimer and trimer proanthocyanidins was repressed by the simultaneous presence of carbohydrate-rich food.

The bioavailability of polyphenols probably depends on the release of polyphenols from these associations which is influenced by various factors: polyphenol structure, complexity of polyphenol–carbohydrate structure, the possibility of enzymes to reach carbohydrates. But even non released polyphenols could have a potential positive role in the human body. Namely, more and more studies (MacDonald & Wagner, 2012; Palafox-Carlos et al., 2011; Saura-Calixto, 2011; Tuohy et al., 2012) point out various positive effects of the occurrence of polyphenol–carbohydrate association in the large intestine. Polyphenols could be transported to the large intestine where they could be released from complex structures when exposed to various enzymes and microorganisms present naturally in the colon.

There are several different effects arising from the transport of polyphenols to the colon: (i) the release of polyphenols from their associated molecules can enhance their bioaccessibility in the colon, (ii) polyphenols and carbohydrates can positively affect the growth of colon microflora, (iii) microorganisms of the digestive tract can metabolize released polyphenolic compounds, (iv) metabolites can exhibit various positive effects, (v) metabolites and polyphenols in general can create a positive antioxidant environment in the colon. These effects were described in several review papers (MacDonald & Wagner, 2012; Palafox-Carlos et al., 2011; Saura-Calixto, 2011; Tuohy et al., 2012).

**Table 3**
Interactions between polyphenols and carbohydrates and their effects.

| Polyphenol tested | Carbohydrate model | Effects | References |
|---|---|---|---|
| **Attachment, the influence of polyphenol structure and other parameters on the interaction** | | | |
| Procyanidins | Cell wall material (CWM) | - Interaction increased with the molecular weight of procyanidins<br>- Interaction decreased with drying of CWM (due to decrease of CWM porosity) | Le Bourvellec et al. (2005) |
| Apple polyphenols (procyanidins) | Cell walls from apples | - Procyanidins mainly bound to pectins | Le Bourvellec et al. (2009) |
| Proanthocyanidins | Insoluble cell wall material (CWM) | - Interaction was more related with the proanthocyanidin molecular mass than the % of galloylation | Bautista-Ortín et al. (2014) |
| Phenolic acids from purple carrot juice concentrate | Bacterial cellulose and cellulose-pectin composites | - Pure cellulose absorbed more phenolic acids in the first hour, but after several days cellulose and cellulose-pectin complexes absorbed similar levels of phenolic acids<br>- Individual phenolic acids binding; caffeic acid > chlorogenic acid > ferulic acid | Padayachee et al. (2012a) |
| Anthocyanins from purple carrot juice concentrate | Bacterial cellulose and cellulose-pectin composites | - Interaction in two stages (rapid initial stage, slow additional stage)<br>- Binding of acylated and non-acylated anthocyanins – similar pattern<br>- Ionic interactions with pectin and hydrophobic with cellulose | Padayachee et al. (2012b) |
| 23 Flavonoids (flavones, flavonols, flavanones, isoflavones, flavanols)13 phenolic acids (hydroxycinnamic and hydroxybenzoic acid) | Oat β-glucan | - Adsorption capacities among flavonoid isomers: flavonol > flavone > flavanone > isoflavone<br>- Methylation or methoxylation of phenolic acids lowered the adsorption capacities<br>- Esterification of gallic acid weakened the adsorption capacity<br>- *o*-Coumaric acid had higher adsorption capacity than *p*- and *m*-coumaric acid<br>- Galloylation improved the adsorption capacities of catechins | Wang et al. (2013) |
| Cyanidin-3-*O*-glucoside | β-Cyclodextrin (β-CD) | - Pyranic C ring was included inside the β-CD cavity, B ring lies on the plane of the wider rim of β-CD | Fernandes et al. (2014) |
| **Influence on the polyphenol bioavailability** | | | |
| Ferulic acid | Animal study - rats fed with various wheat flour | - The cereal matrix appears to limit ferulic acid bioavailability<br>- Most likely, the cause for this is ferulic acid association with the fiber fraction | Adam et al. (2002) |
| Grape seed procyanidin extract | Commercial cereal based food | - Absorption of dimer and trimer procyanidins is repressed by the presence of carbohydrate rich food<br>- The uptake of monomeric procyanidins is enhanced | Serra et al. (2010) |
| **Influence on the polyphenol–protein complexes** | | | |
| Procyanidin–trypsin complexes | Polygalacturonic acid, arabic gum, pectin, xanthan gum | - Carbohydrates prevented the association of procyanidin B3 and trypsin by a competition mechanism (ionic character of carbohydrates and the ability to encapsulate procyanidins was crucial)<br>- Aggregation inhibition; xantan gum > polygalacturonic acid > arabic gum ≫ pectin | Gonçalves et al. (2011a) |
| Salivary protein/grape seed procyanidin | Polygalacturonic acid (PG), arabic gum (AG), pectin | - Pectin inhibited interaction between polyphenols and proteins the most, followed by AG and PG<br>- PG and pectin – mechanism included the formation of a ternary complex protein/polyphenol/carbohydrate<br>- AG – mechanism is a competition with proteins for tannin binding<br>- Hydrophilic and hydrophobic interactions are important | Soares et al. (2012a) |
| **Influence on the carbohydrate fermentation** | | | |
| Ferulic acid | Arabynoxylanoligosaccharides (AXOS) | - Bound and free ferulic cid inhibited AXOS fermentation<br>- Bound ferulic acid probably sterically hinders enzyme activity | Snelders et al. (2014) |

Probably most of the polyphenols that reach the colon are polyphenols which are not absorbed in the upper parts of the gastrointestinal tract and polyphenols associated with dietary fiber (Palafox-Carlos et al., 2011; Saura-Calixto, 2011). Dietary fibers can act as an entrapping matrix and restrict the diffusion of the enzymes to their substrate which may allow polyphenols to be carried to the colon (Palafox-Carlos et al., 2011). In fact, recent findings confirm that the fibers have a role as a carrier of dietary antioxidants to the colon (Saura-Calixto, 2011). Here they can encourage the growth of beneficial bacteria and inhibit the growth of pathogenic bacteria (Saura-Calixto, 2011). The influence of whole plant foods, polyphenols and fibers on the human intestinal microbiome was described by Tuohy et al. (2012). It was also shown that polyphenols can be released from these matrixes and metabolized (Nordlund et al., 2012; Rosa, Aura, et al., 2013; Saura-Calixto, 2011). The structure of polyphenols and the food matrix can affect the process of microbial degradation (Nordlund et al., 2012; Rosa, Aura, et al., 2013). For example, it was shown that dry fermentation of rye, wheat, and oat brans, which lead to the degradation of the cell wall structure, enhances the release of phenolic acids and the accessibility of microbes to dietary fiber and bound phenolic acids. This increased the conversion of polyphenols to metabolites (Nordlund et al., 2012). The enzymatic disintegration of wheat aleurone also enhanced the formation of

polyphenolic metabolites (Rosa, Aura, et al., 2013). Metabolites can have some other positive influence (Saura-Calixto, 2011). Their common activities are antibacterial activities, anti-inflammatory activities, detoxification processes and phytoestrogenic activities (Tuohy et al., 2012). Most of the positive role relates to the protection against the risk of development of colorectal cancer (MacDonald & Wagner, 2012). MacDonald and Wagner (2012) concluded that dietary bioactive compounds and their intestinal microbiota create a complex milieu that directly affects the carcinogenic events of the colon. It was also shown that polyphenolic catabolites are able to counteract two key features of diabetic complications *in vitro* (protein glycation and neurodegeneration) (Verzelloni et al., 2011). In addition, polyphenols associated with dietary fibers can enhance the excretion of lipids, protein, water, and total fecal output; they can have positive effects on lipid metabolism, total cholesterol, LDL-cholesterol and triacylglycerides; and they can increase the antioxidant activity in the large intestine (Saura-Calixto, 2011).

Interactions between carbohydrates and polyphenols can be used for microencapsulation which includes the entrapment of the active ingredient in coating material. In that way the active ingredient is isolated (protected) from the environment until its release. Green tea polyphenols can be encapsulated on maltodextrin as a coating material (Jung, Seong, Kim, Myong, & Chang, 2013). Such microencapsulated green tea extracts can be more effective at alleviating cardiovascular risk than non-encapsulated green tea extracts (Jung et al., 2013).

Another important interaction of carbohydrates is their interaction with polyphenol–protein complexes. Namely, polyphenols can create complexes with proteins (as mentioned) which can affect nutritional quality of proteins. Furthermore, polyphenol–salivary protein complexes are important for astringency sensation of wines. Polyphenols interact also with enzymes which results in the inhibition of their enzymatic activity. Carbohydrates which are often present in food together with polyphenols, can interrupt polyphenol–protein complexes. Carbohydrates polygalacturonic acid, arabic gum, pectin and xanthan prevented the association of procyanidin B3 and trypsin (Gonçalves, Mateus, & de Freitas, 2011a). Arabic gum, pectin and polygalacturonic acid prevented association between salivary protein and grape seed procyanidins (Soares, Mateus, & de Freitas, 2012a). The interruption of polyphenol–protein association by carbohydrates can prevent some of the negative effects of these complexes, such as enzyme activity inhibition, or they can influence the perceived astringency of some food products.

Furthermore, interactions between carbohydrates and polyphenols can affect carbohydrate fermentation. Bound and free ferulic acid inhibited arabinoxylanoligosaccharides fermentation probably by sterically hindering the enzyme activity (Snelders et al., 2014).

The studies discussed here showed that polyphenolic compounds have the possibility to bind to carbohydrates. This is very important for their bioaccessibility and bioavailability in the human organism. Namely, the association with carbohydrates makes the polyphenols bioaccessible in the colon after they have been exposed to enzymes and microorganisms and released. Released polyphenols may be bioaccessible in the colon and can even be metabolized by the action of naturally present microorganisms. The role of their metabolites is still under the investigation but there is more and more evidence suggesting their various positive effects. The fact that polyphenols react with carbohydrates was used for the creation of carbohydrate carriers of polyphenols through the gastrointestinal tract. Interactions between polyphenols and carbohydrates can influence the carbohydrate fermentation.

## 5. Conclusions

An increasing number of studies have shown that interactions of polyphenols with molecules from foods (lipids, proteins, carbohydrates) can have a significant impact on the fate and role of polyphenols in the body. Since polyphenols are introduced into the body along with other food ingredients, they come into contact with them and react with lipids, proteins, and carbohydrates. The binding is mostly hydrophobic, although hydrogen bonds and covalent bonds can be created too, and various associations can be formed. Their bioactivities can be different than activities of any of these compounds individually. Lipid–polyphenol complexes may cause a decrease in the lipid absorption. In addition, access of free radicals to lipid molecules can be hindered by the presence of polyphenols in lipid molecules, which may result in reduced lipid oxidation and, consequently, in reduced occurrence of harmful lipid oxidation products. Protein–polyphenol associations might influence astringency sensation, biological activities of proteins, the availability of certain amino acids or even the digestibility of proteins. Enzyme activity inhibition is also a consequence of these interactions. One segment of interactions between polyphenols and other molecules was suggested to be very important. That is their delivery to the large intestine where they can be released and show various positive effects, like the creation of antioxidative environment, the encouragement of growth of beneficial bacteria and the inhibition of the growth of pathogenic bacteria. In addition, positive effects of their metabolites are also suggested. This was particularly recognized in the case of interactions of polyphenols with carbohydrates. It was also suggested that interactions of polyphenols with lipids, proteins and carbohydrates could affect polyphenol bioaccessibility and bioavailability.

The ability of macromolecules like lipids, proteins and carbohydrates to act as carriers of polyphenols through the digestive tract is particularly recognized. Moreover, created associations may also protect polyphenols from oxidative degradation.

It is clear that interaction between polyphenols and food ingredients are very important and that they influence on our understanding of polyphenols. Most of studies suggested positive effects of interactions which can happen between polyphenols and other food ingredients. One part of studies deals with the explanation of possible nutritional value decrease due to interactions (interactions with proteins and enzymes). Future studies should take into account interactions between polyphenols and other compounds because their contact is inevitable. It becomes more apparent that it might be possible to explain polyphenol beneficial effects by investigating these complex reactions and their consequences.

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