Phenolic-Protein Interaction: Effects on Functional Properties of Phenolics and Advantages on Phenolic Delivery Platform Development

Gokce Altin[1], Eda Nur Ayar[2] and Beraat Ozcelik[3]

[1] Istanbul Technical University

Received: 9 December 2018 Accepted: 2 January 2019 Published: 15 January 2019

Abstract

The interaction between phenolics and proteins is one of the most research areas in food, pharmaceutical, and cosmetic fields since these interactions affect the functional properties of proteins and phenolics. By using this phenomena, organoleptic properties of phenolic compounds can be engineered, foaming and gelling properties of proteins can be increased, and also novel delivery platforms for phenolics can be designed. During the construction of phenolic-protein interaction, both covalent and non-covalent bonds occur. Formation of these bonds depends on the type of phenolic compounds and protein and also environmental conditions such as pH, temperature and ionic strengths. Understanding the exact mechanism behind these interactions are leading to generate tunable food, drug, and cosmetic products.

Index terms— interaction, antioxidant capacity, bio accessibility, sensory quality, delivery of phenolics.

1 Introduction

henolic compounds, abundantly present in plants, account for one-third of the dietary phenols and are a large family of phytochemicals (Herrmann & Nagel, 1989). The phenolic compounds have numerous physiological functions, such as anti-inflammatory, antimutagenic, and antioxidant properties through phenolic compounds' potential to protect from oxidative stress (Lee et al., 2005; Altin, Gültekin-Özgüven & Ozcelik, 2018). The studies on animals and also human submits that phenolic compounds in daily diet have significant roles in protection from several diseases including certain types of cancers, cardiovascular diseases, and prevention of osteoporosis (Ali, H., 2012). Even insignificant structural differences in the location, number, or form of substituted groups can directly affect the bio-distribution, free concentration, and metabolism of phenolic compounds, and resulting affect to their bioactivity (Jaldappagari et al., 2013).

Interactions between the different food compounds have been commonly identified and it is known to have influence on the biological, functional and, nutritional properties of food products. The interaction of phenolic compounds-proteins seems to be the most important one using different aspects. Phenolic acids could be interacted by non-covalently and covalently with proteins, and the interactions of protein-phenolic may affect the biological and functional properties of phenolics as well as proteins (Charlton et al., 2002). The bioactivity of a compound after the consumption is related to its bioaccessibility and bioavailability. Based on the type of interaction between phenolics-proteins can be increased or decreased their bioaccessibility and bioavailability. In the sensory aspect, organoleptic quality of food product such as color, bitterness, and astringency, is directly affected form phenolic-protein interaction. (De Freitas & Mateus, 2012; Chung, C., Rojanasasithara, T., Mutilangi, W., & McClements, D. J., 2017).

In last decade, numerous studies are focusing on delivery of phenolics, since to contribute the functionality of phenolics is crucialsince they have several positive effects on health such as antioxidant, antimicrobial, anti-inflammatory, anti-carcinogenic, and hepatoprotective effect. Protein-phenolic conjugates and protein-based nanoparticles are the most common studied techniques about a delivery of phenolics, which can be used in food, pharmaceutical, and cosmetic sector.

Therefore, understand the exact mechanism between phenolic-protein interaction not only leads to the observation of nutritional and sensory changes on foods but also enhance to develop novel strategies for functional foods and dietary supplement area. While the interactions can be analyzed considering several aspects, it still is a challenge for food analysis and researchers (Czubinski, J., & Dwiecki, K., 2017). To comprehend the roles of proteins and phenols in interaction, it is essential to designate the nature of the physicochemical and chemical interactions of the proteins-phenolic acids (Ali, H., 2012). The bonding types can be characterized by spectroscopic methods, microscopic methods, thermodynamic methods, bioinformatics methods, electrophoretic and chromategraphic methods.

The goal of this review is to give researchers an overview of the currently used methods for identification of bonding type, negative and positive effects of interaction on food quality, bioaccessibility, bioavailability as well as to introduce the novel delivery strategies that base on phenolic-protein interaction.

II. Type of Bindings that Contributes to the Interaction

The phenolic-protein interaction is mainly contributed via non-covalent bonds, which are weaker than covalent bonds and they are always reversible. Among the covalent bonds, hydrogen bonds provide more stable complex than Van-der -Waals interactions, dipole-dipole interactions and hydrophobic interactions (Yuksel et al., 2010; **??**agy et al., 2012; **??**akobek 2015). While non-covalent bonds commonly occur in proteinphenolic interaction, in some case covalent interaction can also be formed (Gallo et al., 2013;El-Maksoud et al., 2018;Sui et al., 2018). To determine the phenolicprotein interaction is necessary for the biological activity of phenolics as well as proteins. There are several approaches to investigate this interaction such as, spectroscopic methods, microscopic methods, thermodynamic methods, bioinformatics methods, electrophoretic and chromatographic methods. Several studies focus on to investigate phenolic-protein interaction. Previous studies and their findings are summarized in Table 1. To obtain the excat result during determination of the binding type, different techniques are used together (Table 1).

The proteomic approach is one of the novel bioinformatic technique to identify the binding type. Gallo et al. (2013), investigated the type of interactions between cocoa polyphenols and milk proteins by proteomic technique. They characterized the interaction of ?-lactoglobulin (?-Lg) with catechin and epicatechin, moreover identified the amino acid residue at the binding site. For this aim, they used the matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF-MS) and the electrospray ionization tandem quadrupole/orthogonal-acceleration time-of-flight mass spectrometer (ESI-Q-TOF MS/MS). In these analyses, tryptic peptides of ?-Lg have allowed the identification of the binding site as the free thiol group of cysteine and found that while polyphenols covalently bound with ?-Lg, they interact with casein via non-covalent bonds. In another study, fluorescence, circular dichroism spectroscopy, and docking studies were used for characterization of the interaction between ?-Lg and cyanidin-3-O-glucoside According to this study, the interaction was mainly contributed by both hydrogen bonding and the hydrophobic interaction (Cheng et al., 2017). Furthermore, after the binding of cyanidin-3-O-glucoside to ?-Lg, the secondary structure of the ?-Lg was changed in which the major structure of ?-sheetincreased and the minor structure of ?-helix decreased. The changes in secondary structure of proteins after the phenolic interaction also identified in different studies (Zhang et al., 2014;Al-Hanish et al., 2016;Jia et al., 2017). The significant reduction of ?helix and an increase of ?-sheet and turn structures were determined in ?-lactalbumin and ?-Lg in the phenolic-protein complex (Zhang et al., 2014). Also, Jia et al. (2017) observed the conformational changes on the secondary structure of ?-Lg, after phenolic compound attachment, via circular dichroism and Fourier transform infrared. According to their findings, after the binding of the phenolic compound, the surface hydrophobicity of ?-Lg was changed. Thus ?-helix to ?-structures transition occurred. The noncovalent interactions between ?-lactalbumin and epigallocatechin-3-gallate were determined by circular dichroism and Fourier transform infrared spectroscopy (Al-Hanish et al., 2016). Based on their findings, epigallocatechin-3-gallate caused the conformational changes in ?-lactalbumin, which were inducing ?-helix to ?-structures transition.

Not only the non-covalent bonds but also the covalent bonds also occur in a phenolic-protein complex. Sui et al. (2018) demonstrated the conformational changes on soy proteins in the presence of anthocyanins. They used three-dimensional fluorescence and Fourier transform infrared spectroscopy to determine the interaction character. They reported that the covalent bonds occurred more abundant than non-covalent bonds in soy protein isolate-anthocyanin complex. The conformational changes on the secondary structure of soy protein isolate also detected as a decrease in ?-sheets and an increase in ?-turns and random coils.

2 III. Interaction Effect on Nutritional and Antioxidant Quality of Foods

The interaction of phenolics-proteins and starch may be one of the mostfundamental factors affecting the nutraceutical quality of the food products. There are several studies that is confirmed by earlier studies including phenolic-protein **??**Arts et The chemical structure of phenolic compounds is the enhancive reason for interaction with major food components. In other words, a hydroxyl group and carboxylic acids give rise to increasing of phenolic interaction with proteins, carbohydrates, lipids, and (Bravo, 1998; Alu'datt, Rababah, Ereifej, Brewer, & Alli, 2013; Escarpa & Gonzalez, 2001). As mentioned before, phenolic acids and proteins bring about two main types of interactions (covalent or noncovalent) that result in two kinds of precipitation of proteins. First one is multisite interactions, that is, several phenolics bind to one protein molecule and the second one is multidentate interactions, that is, one phenolic binds to several protein sites or protein molecules. A study by Rawel, Meidtner, and Kroll (2005) stated that the non-covalent binding of phenolic compounds does not affecton the secondary structure of the proteins while may induce to distinct alteration in the tertiary structure of proteins. However, it has been indicated that the covalent binding of phenolics compounds may affect both tertiary and secondary structures of proteins (Kroll et al., 2003). Moreover, these interactions may also end in changes in the thermal stability, solubility, and digestibility of food proteins (Kroll et al., 2003;Ozdal et al., 2013). S. Wu et al. (2018) have studied on 71 phenolic acids, and the derivatives of these phenolics were chosen to estimate the binding affinity with ?-lactoglobulin. According to their study, the potential mechanisms for increased binding affinity is the inclusion of the hydrogen bond in the interaction between the ?-lactoglobulin and phenolic acids. The interaction between ?-lactoglobulin-phenolic acid has enhanced antioxidant activity when compared tothat of the phenolic acids alone (S. Wu et al., 2018). This study gives perspective for understanding the relationship between the chemical structure of phenolic acids and the affinity for ?-lactoglobulin.Volume XIX Issue I Version I Year 2019 (D D D D) L minerals

Most of the nutritional concern of phenolics focus on their side effects caused by the capability of phenolics to conjugate and precipitate protein, lipids, minerals and carbohydrates resulting in reducing food digestibility (Bravo, 1998). On the other hand, several studies indicated that regarding the bio-functional impact of the naturally occurring interactions between phenolics with food constituents such as antioxidant effects become inadequate (Bravo, Saura-Calixto, and Goni, 1992; Alu'datt, Rababah, Ereifej, Brewer, et al., 2013).

3 IV. Interaction Effect on Organoleptic Quality of Foods

Polyphenol compounds are currently present in multiform beverages and food products. Several properties of phenolic compounds are using in the food industry. Antioxidant properties of phenolic compounds have been utilized in the food industry to stabilize cysteine proteases and to prolong shelf-life of processed products (Howell, 2005). Also, phenolic compounds including anthocyanins, ?-carotene, riboflavin, and curcumin are using as natural food colorants in beverage products (Mortensen, 2006).

These compounds have poor solubility and limited chemical stability which is challenging as a natural colorant in food products and beverages (Chung, C., Rojanasasithara, T., Mutilangi, W., & McClements, D. J., 2017). On the other hand, phenolic-protein interaction is using to maintain the stability of phenolic-colorants. The interaction between protein and phenolic compounds is initially starting with a hydrophobic effect and is stabilized by hydrogen bonding (Oh, Hoff, Armstrong, & Haff, 1980;Siebert, 1999). Thus, different research groups are studying on improvement of the stability of phenolic-colorants by using phenolic-protein interaction phenomena. Chung et al. (2015) proved that when heated whey protein isolates are added to model beverage systems containing ascorbic acid, it is improved the color stability of anthocyanins in the beverage. Ascorbic acid has a strong effect to tint ofthe anthocyanins in these systems. (Mercadante & Bobbio, 2007;Poei-Langston & Wrolstad, 1981). Recently, Chung and co-workers studied beverage products containing ascorbic acid. They examined the effect of polypeptides and amino acids on the color stability of anthocyanins. Also, the product containing ascorbic acid and an amino acid is two times more convenient regarding to the average half-life of the anthocyanin than alone ascorbic acid added the product (Chung C. et al., 2017).

Astringency sensation and bitterness are another important sensory attribute for wine. Interaction and precipitation of proline-rich proteins, especially, salivary proteins by tannins is estimated to be the general explanation of astringency onset **??**Charlton et **??**018) found evidence that the interaction of proline-rich proteins by tannins is disparate when the proteins are present simultaneously or alone. However, protein-phenolic interaction and co-protein interaction via tannins may be responsible and need to be more investigated.

In respect of food processing, there are only limited studies to confirm the effects of phenolic-protein interactions. Indeed, for the food industry, the interaction is exploited as refining and clarification treatments to improve haze stability (Cosme, Ricardo-da-Silva, & Laureano, 2008). There are few studies on improving textural properties via the phenolic-protein interaction. Wu, Clifford, and Howell (2007) reported that the forming and the gelling potential of egg albumin protein could be significantly increased by addition of the instant green tea. In another study, green tea powder added to weat dough to enhance viscous/elastic modulus and the stability of wheat dough. **??**Wang et al., 2015). Having obtaining protein-phenolic interaction between fruit extract and soy protein isolate in a glutenfree rice noodle, improved noodle quality, and the dough is achieved **??** enhanced via interaction of pea protein isolate with green tea extract to the supported both antioxidant activity and network.

Beyond that, presence of phenolic compounds at a nutritional daily intake had no adverse impact on protein digestibility. However, the high dose consumption of a phenolic extract may appear destructive to humans who consume low protein amount. Hence, consuming polyphenol supplements needs to be given to the benefit/risk balance with dedicated care (Dufour, C. et al., 2018).

4 V. Interaction Effect on Bioaccessibility/Bioavailability of Phenolics

To demonstrate the bioactivity of a compound on human health, it should have a sufficient bioaccessibility and bioavailability. While bioaccessibility refers to the (%) undecomposed (bioactive) fraction of a compound after gastro-intestinal digestion, bioavailability represents the (%) metabolized fraction of a bioactive compound. Both bioaccessibility and bioavailability of phenolic compounds can be improved, impeded or unaltered when co-delivered with other foods like rich in protein, carbohydrate, fat or fiber **??** There is currently a natural affinity between polyphenols and proteins (Bandyopadhyay, Ghosh, & Ghosh, 2012). Thereby, protein-rich food matrices can be stabilized and concentrate anthocyanins and also other phenolics Roopchand, Grace et al., 2012;Roopchand et al., 2013). Grape and blueberry polyphenol-enriched protein matrix have been studied for oral administration, and the hypoglycemic effect obtained in mice indicates that the phenolic-protein complex is bioactive. (Roopchand et al., 2013). In another study, it is reported that anthocyanins are conserved by the sorption to defatted soy flour while transiting through the upper gastrointestinal tract by permitting huge amounts to be gained to the colon (Ribnicky D. M. et al., 2014). Pineda-Vadilloet al. (2016) studied on protein-rich products enriched with grape extracts. As a result, they showed that the food matrix has no affect on the antioxidant activity; while the antioxidant capacity was steady during the oral and gastric phases, it considerably increased during the intestinal phase of digestion. There is also another study, that supports the approach of the noncovalently polyphenols-proteins interaction which are hydrolyzing during digestion, and there was no effect on the absorption of polyphenols and proteins (Budryn, G., & Nebesny, E., 2013). These studies indicated that becoming complex with the protein matrix does not affect the bioaccessibility of anthocyanins/polyphenols negatively (Budryn, G. & Nebesny, E. 2013; Ribnicky D. M. et al., 2014; Pineda-Vadillo et al., 2016). In the previousin vivo models, it was demonstrated that the bioavailability of milk and coffee can reduce when they are consumed together (Duarte & Farah, 2011). The different inferences among various studies may be the potential of some phenolics to be complex with digestive enzymes and food matrix. The previous study of **??**ohn et al. (2002) confirmed that the activity of selected digestive enzymes such as trypsin and ?-amylase was a decline in the case of protein-phenolic interaction. Thereby, the interaction has caused to the antioxidant activity of phenolic compounds reduce as it cannot leave the protein-phenolic complex. However, the interaction of phenolic-protein occur only some functional groups and the un-interacted part still can be show activity (Rohn, **??**awel, & Kroll, 2002;Alminger, M. et al., 2014). Indeed, being complex with polyphenols is known to reduce protein digestibility via protecting proteins from enzyme degradation or through interaction with digestive enzymes.

5 VI. Delivery Techniques based on Phenolic-Protein Interaction

Phenolic compounds are highly unstable bioactive compounds due to exposure to degradation by light, soluble oxygen or enzymes. The basic goal of delivery techniques is to protect the phenolic compounds from adverse environmental conditions. Protein-based delivery techniques are one of the novel strategies from this area, and there are numerous studies about this subject. The delivered phenolic compounds, as well as the delivery system, is summarized in Table **??**. These strategies can mainly divide into two groups; (i) protein-phenolic conjugates and (ii) protein-based nanoparticles.

6 a) Protein-phenolic conjugates

Protein-phenolic conjugates can be used to enhance antioxidant activity of a protein as well as its stability (Frazier et al., 2010;Wu et al., 2011;El-Maksoud et al., 2018) or to reduce the degradation level of delivered phenolic compounds. Since the non-covalent interactions are reversible, the stable structure cannot be obtained by non-covalent bonds. Besides, these types of interactions lead to alterations on protein and phenolic compound structure, hence their functionality and nutritional value are changed (Mehanna et al., 2014;Ozdal et al., 2013). Conversely, conjugates are constructed with covalent bonds. Hence stable structure can be obtained. El-Maksoud et al. phenolic compound that they used in conjugate was caffeic acid, and ?-lactoglobulin was selected for protein part of conjugates. They reported that the conjugates showed better water solubility than native ?-lactoglobulin and non-covalently bond ?-lactoglobulin-caffeic acid complex. Moreover, the thermal stability of ?lactoglobulin significantly was increased with this conjugate.

In the view of nutraceutical delivery aspect, protein-phenolic conjugates offer several advantages. investigated the physicochemical properties of ?-carotene emulsions stabilized via chlorogenic acid-lactoferrin-glucose/polydextrose conjugates. They indicated that the produced conjugate offered better emulsifying properties such as the physicochemical stability of ?-carotene emulsions can be conserved during the freeze-thaw treatment. Besides, chemical stability of ?-carotene in the emulsions against ultraviolet light exposure can enhanced by the conjugate. Therefore, they suggested that the conjugates containing protein, polyphenol and carbohydrates could be a smart building block for delivery systems . In another study, the chemical stability of curcumin to degradation at physiological pH and of resveratrol to degradation under ultraviolet irradiation conditions was obtained by zeinepigallocatechin gallate conjugates (Liu et al., 2018).

7 b) Protein-based nanoparticles

Zein and gliadin are the prolamine-type proteins which generally occur in in cereals such as corn and wheat, respectively. The four major components of zein are ?, ?, ? and ?-zein (Hu & McClements, 2015). Since both zein and gliadin contain the high amount of nonpolar amino acids in their primary structure, they are soluble in aqueous ethanol solution (60-90%), but insoluble in water ??Rombouts et al., 2009; ??hukla & Cheryan, 2001). Because of their highly hydrophobic nature, these proteins can be easily converted into spherical colloidal nanoparticles, which are effective delivery agents for phenolic compounds (Chen, Zheng, McClements, & Xiao, 2014). Previous studies reported that protein-based nanoparticles are suitable and effective delivery agents for different phenolic compounds (Table ??). During the formation of proteinbased nanoparticles with phenolics, non-covalent interactions such as electrostatic interaction, hydrogen bonding, and hydrophobic interactions were involved in the structure (Dai et al., 2018). On the other hand, these interactions mainly depend on the type of protein and phenolic compounds. Joye et al. (2015) studied on binding ability of resveratrol to the zein and gliadin. They assumed that hydrogen bonds are the main force that contributed to the interaction between resveratrol and zein. However, the hydrophobic interactions constructed the resveratrol-gliadin interaction. In another study about curcumin delivery by zein-nanoparticles, are indicated that hydrogen bonds between the phenolic hydroxyl groups in curcumin and the carbonyl group in amide bonds in zein were attributed to the formation of proteinbased nanoparticle with polyphenol (Dai et al., 2017;Sun et al., 2017). These nanoparticles are not only protecting the related phenolic compounds form adverse environmental conditions, beyond that they support the controlled released of the phenolics. Liang et al. (2017) reported that the controlled release property of epigallocatechin gallate was improved by zein/ chitosan nanoparticles and according to Sun et al. (2017), controlled release of curcumin during in vitro digestion, can be obtained by zein-shellac composite colloidal particles. In another study, in vitro release of curcumin as well as its stability are improved by zein nanoparticles (Dai et al., 2018). The authors suggested that curcumin might bind to zein in tyrosine residue. Since, the aromatic side groups and double bonds in zein molecules could absorb UV light (Luo et al., 2013), zein nanoparticles enhance the stability of curcumin against UV light. The zein-lecithin composite nanoparticles also improved the stability of curcumin against UV irradiation, high ionic strength and thermal treatment (Dai et al., 2017).

8 VII. Conclusion

The interaction between phenolic compounds and proteins is an important phenomena since it affects the functionality, biological activity and nutritional quality of protein and phenolics. The interaction is contributed with both non-covalent and covalent bonds that depend on the type of protein and phenolics as well as the environmental conditions. Depending on the bonding type, there occur conformational changes in protein structure. There are several techniques for determining the bounding type such as spectroscopic methods, microscopic methods, thermodynamic methods, bioinformatics methods, electrophoretic and chromatographic methods. The delivery of phenolics in the desired system can be done by novel agents which are constructed with proteins. Indeed, the bonding type is important to select the novel delivery strategies. If the protein functionality is important in delivery system, then the covalent bonds are crucial to eliminating the structural changes. But if the controlled released of phenolic is desired, the non-covalent bonds are wanted.

9 Volume Issue I Version I

[1] [2] [3] [4]

[4]Phenolic-Protein Interaction: Effects on Functional Properties of Phenolics and Advantages on Phenolic Delivery Platform Development

1

Polyphenol	Protein	Determination Method	Type of Interaction	
Green tea	Milk proteins	Fluorescent probe	Hydrophobic interactions	Protein surface h
flavanoids		binding method	between catechin and ?-	was
		Isothermal titration calorimetry	casein.	hydrophobic bind milk proteins and
Pelargonidin	Dairy proteins:	Fluorescence	Hydrophobic interactions	the structural cor
		spectroscopy	between pelargonidin-?-	the milk proteins
	?-lactoglobulin		lactoglobulin	binding process
	Caseinate		Hydrogen bonding between pelargonidin-caseinate	
Chlorogenic acid	?-lactoglobulin	Fluorescence	Hydrogen bonding and	The secondary st
Ferulic acid		spectroscopy	Van der Waals interactions between ?-	lactoglobulin

Figure 1: Table 1 :

[Pineda-Vadillo et al.] , C Pineda-Vadillo , F Nau , C G Dubiard , V Cheynier , E Meudec , M Sanz-Buenhombre .

[Wang et al.] , Q Wang , Y Li , F Sun , X Li , P Wang , J Sun .

[Wu et al.] , S Wu , Y Zhang , F Ren , Y Qin , J Liu , J Liu .

[Charlton et al. ()] , A J Charlton , N J Baxter , M L Khan , A J Moir , E Haslam , A P Davies , M P Williamson . 2002.

[Dupas et al. ()] , C J Dupas , A C Marsset-Baglieri , C S Ordonaud , F M G Ducept , M. -N Maillard . 2006.

[Roopchand et al. ()] , D E Roopchand , M H Grace , P Kuhn , D M Cheng , N Plundrich , A Pouleva . 2012.

[Czubinski and Dwiecki ()] 'A review of methods used for investigation of protein-phenolic compound interactions'. J Czubinski , K Dwiecki . *International Journal of Food Science & Technology* 2017. 52 (3) p. .

[Ozdal et al. ()] 'A review on protein-phenolic interactions and associated changes'. T Ozdal , E Capanoglu , F Altay . *Food Research International* 2013. 51 p. .

[El-Maksoud et al. ()] 'Adding functionality to milkbased protein: Preparation, and physico-chemical characterization of ?-lactoglobulin-phenolic conjugates'. A A A El-Maksoud , I H A El-Ghany , H S El-Beltagi , S Anankanbil , C Banerjee , S V Petersen , Guo . 10.1016/j.foodchem.2017.08.101. `https://doi.org/10.1016/j.foodchem.2017.08.101` *Z* 2018. August 2017. p. .

[Wu et al. ()] 'Analysis of binding interaction between (?)-epigallocatechin (EGC) and ?-lactoglobulin by multispectroscopic method'. X Wu , H Wu , M Liu , Z Liu , H Xu , F Lai . *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* 2011. 82 (1) p. .

[Mercadante and Bobbio ()] 'Anthocyanins in foods: Occurrence and physicochemical properties'. A Mercadante , F O Bobbio . *Food colorants chemical and functional properties*, C Socaciu (ed.) (Boca Raton, FL, USA) 2007. CRC Press. p. .

[Lee and Lee ()] 'Antiproliferative effects of dietary phenolic substances and hydrogen peroxide'. H J Lee , C Y Lee . *Journal of agricultural and food chemistry* 2005. 53 (6) p. .

[Xiao et al. ()] 'Assembly of kafirin/carboxymethyl chitosan nanoparticles to enhance the cellular uptake of curcumin'. J Xiao , S Nian , Q Huang . *Food Hydrocolloids* 2015. p. .

[Mcdougall et al. ()] 'Assessing potential bioavailability of raspberry anthocyanins using an in vitro digestion system'. G J Mcdougall , P Dobson , P Smith , A Blake , D Stewart . *Journal of Agricultural and Food Chemistry* 2005. 53 (15) p. .

[Rawel et al. ()] 'Binding of selected phenolic compounds to proteins'. H M Rawel , K Meidtner , J Kroll . *Journal of Agricultural and Food Chemistry* 2005. 53 p. .

[Roopchand et al. ()] 'Biochemical analysis and in vivo hypoglycemic activity of a grape polyphenol-soybean flour complex'. D E Roopchand , P Kuhn , A Poulev , A Oren , M A Lila , B Fridlender . *Journal of Agricultural and Food Chemistry* 2012. 60 (36) p. .

[Roopchand et al. ()] 'Blueberry polyphenol-enriched soybean flour reduces hyperglycemia, body weight gain and serum cholesterol in mice'. D E Roopchand , P Kuhn , L E Rojo , M A Lila , I Raskin . *Pharmacological Research* 2013. 68 (1) p. .

[?wieca et al. ()] 'Bread enriched with quinoa leaves-The influence of protein-phenolics interactions on the nutritional and antioxidant quality'. M ?wieca , ? S?czyk , U Gawlik-Dziki , D Dziki . *Food chemistry* 2014. 162 p. .

[Mortensen ()] 'Carotenoids and other pigments as natural colorants'. A Mortensen . *Pure and Applied Chemistry* 2006. 78 (8) p. .

[Yuksel et al. ()] 'Characterization of binding interactions between green tea flavanoids and milk proteins'. Z Yuksel , E Avci , Y Kemal . 10.1016/j.foodchem.2009.12.064. `https://doi.org/10.1016/j.foodchem.2009.12.064` *Food Chemistry* 2010. 121 (2) p. .

[Arroyo-Maya et al. ()] 'Characterization of flavonoid-protein interactions using fluorescence spectroscopy: Binding of pelargonidin to dairy proteins'. I J Arroyo-Maya , J Campos-Terán , A Hernándezarana , D Julian . 10.1016/j.foodchem.2016.06.105. `https://doi.org/10.1016/j.foodchem.2016.06.105` *Food Chemistry* 2016. 213 p. .

[Altin et al. ()] 'Chitosan coated liposome dispersions loaded with cacao hull waste extract: Effect of spray drying on physico-chemical stability and in vitro bioaccessibility'. G Altin , M Gültekin-Özgüven , B Ozcelik . *Journal of Food Engineering* 2018. 223 p. .

[Coffee antioxidant properties: effects of milk addition and processing conditions Journal of Food Science] 'Coffee antioxidant properties: effects of milk addition and processing conditions'. *Journal of Food Science* 71 (3) p. .

[Poei-Langston and Wrolstad ()] 'Color degradation in an ascorbic acid-anthocyaninflavanol model system'. M Poei-Langston , R Wrolstad . *Journal of Food Science* 1981. 46 (4) p. .

[Jia et al. ()] *Comparison of binding interaction between blactoglobulin and three common polyphenols using multi-spectroscopy and modeling methods*, J Jia , X Gao , M Hao , L Tang . 10.1016/j.foodchem.2017.01.131. https://doi.org/10.1016/j.foodchem.2017.01.131 2017. 228 p. .

[Lee et al. ()] 'Development of a gluten-free rice noodle by utilizing protein-polyphenol interaction between soy protein isolate and extract of Acanthopanax sessiliflorus'. D S Lee , Y Kim , Y Song , J H Lee , S Lee , S H Yoo , K W Lee , H J Hur . *Journal of the Science of Food and Agriculture* 2016. 96 (3) p. .

[Alu'datt et al. ()] 'Distribution, antioxidant and characterisation of phenolic compounds in soybeans, flaxseed and olives'. M H Alu'datt , T Rababah , K Ereifej , I Alli . *Food Chemistry* 2013. p. .

[Budryn and Nebesny ()] 'Effect of green and roasted coffee antioxidants on quality and shelf life of cookies and chocolates'. G Budryn , E Nebesny . *Journal of Food Processing and Preservation* 2013. 37 (5) p. .

[Mehanna et al. ()] 'Effect of interaction phenolic compounds with milk proteins on cell line'. N S Mehanna , Z M R Hassan , H M F El-Din , A A E Ali , R Amarowicz , T M El-Messery . *Food and Nutrition Sciences* 2014. 5 p. .

[Duarte and Farah ()] 'Effect of simultaneous consumption of milk and coffee on chlorogenic acids' bioavailability in humans'. G S Duarte , A Farah . *Journal of Agricultural and Food Chemistry* 2011. 59 (14) p. .

[Li et al. ()] 'Effect of superfine green tea powder on the thermodynamic, rheological and fresh noodle making properties of wheat flour'. M Li , J H Zhang , K X Zhu , W Peng , S K Zhang , B Wang , . . Zhou , HM . *LWT-Food Science and Technology* 2012. 46 (1) p. .

[Ribnicky ()] 'Effects of a high fat meal matrix and protein complexation on the bioaccessibility of blueberry anthocyanins using the TNO gastrointestinal model (TIM-1)'. D M Ribnicky . *Food Chemistry* 2014. 142 p. .

[Bravo et al. ()] 'Effects of dietary fiber and tannins from apple pulp on the composition of feces in rats'. L Bravo , F Saura-Calixto , I Goni . *British Journal of Nutrition* 1992. 67 p. .

[Siebert ()] 'Effects of protein-polyphenol interactions on beverage haze, stabilization, and analysis'. K J Siebert . *Journal of Agricultural and Food Chemistry* 1999. 47 (2) p. .

[Efficient sorption of polyphenols to soybean flour enables natural fortification of foods Food Chemistry] 'Efficient sorption of polyphenols to soybean flour enables natural fortification of foods'. *Food Chemistry* 131 p. .

[Liang et al. ()] 'Encapsulation of epigallocatechin gallate in zein/chitosan nanoparticles for controlled applications in food systems'. J Liang , H Yan , X Wang , Y Zhou , X Gao , P Puligundla , X Wan . 10.1016/j.foodchem.2017.02.106. https://doi.org/10.1016/j.foodchem.2017.02.106 *Food Chemistry* 2017. 231 p. .

[Chung et al. ()] 'Enhanced stability of anthocyanin-based color in model beverage systems through whey protein isolate complexation'. C Chung , T Rojanasasithara , W Mutilangi , D J Mcclements . *Food Research International* 2015. 76 p. .

[Wang et al. ()] 'Fabrication and characterization of carboxymethyl chitosan and tea polyphenols coating on zein nanoparticles to encapsulate bcarotene by anti-solvent precipitation method'. M Wang , Y Fu , G Chen , Y Shi , X Li , H Zhang . 10.1016/%20j.foodhyd.2017.10.036. https://doi.org/10.1016/j.foodhyd.2017.10.036 *Food Hydrocolloids* 2018. 77 p. .

[Hu and Mcclements ()] 'Fabrication of biopolymer nanoparticles by anti solvent precipitation and electrostatic deposition: Zeinalginate core/shell nanoparticles'. K Hu , D J Mcclements . *Food Hydrocolloids* 2015. 44 p. .

[Joye et al. ()] *Fluorescence quenching study of resveratrol binding to zein and gliadin: Towards a more rational approach to resveratrol encapsulation using water-insoluble proteins*, I J Joye , G Davidov-Pardo , R D Ludescher , D J Mcclements . 10.1016/j.foodchem.2015.03.128. https://doi.org/10.1016/j.foodchem.2015.03.128 2015. 185 p. .

[Liu et al. ()] *Food Hydrocolloids Fabrication and characterization of protein-phenolic conjugate nanoparticles for co-delivery of curcumin and resveratrol*, F Liu , D Ma , X Luo , Z Zhang , L He , Y Gao , D Julian . 10.1016/j.foodhyd.2018.01.017. https://doi.org/10.1016/j.foodhyd.2018.01.017 2018. 79 p. .

[Dai et al. ()] 'Food Hydrocolloids Fabrication of zein and rhamnolipid complex nanoparticles to enhance the stability and in vitro release of curcumin'. L Dai , R Li , Y Wei , C Sun , L Mao , Y Gao . 10.1016/j.foodhyd.2017.11.003. https://doi.org/10.1016/j.foodhyd.2017.11.003 *Food Hydrocolloids* 2018. 77 p. .

[Cao et al. ()] 'Food Hydrocolloids Interfacial properties of whey protein foams as in fl uenced by preheating and phenolic binding at neutral pH'. Y Cao , Y L Xiong , Y Cao , A D True . 10.1016/j.foodhyd.2018.04.020. https://doi.org/10.1016/j.foodhyd.2018.04.020 *Food Hydrocolloids* 2018. 82 p. .

[Karefyllakis et al. ()] 'Food Hydrocolloids Physical bonding between sun fl ower proteins and phenols: Impact on interfacial properties'. D Karefyllakis , S Altunkaya , C C Berton-Carabin , A Jan , V Goot , Der , C V Nikiforidis . 10.1016/j.foodhyd.2017.07.018. https://doi.org/10.1016/j.foodhyd.2017.07.018 *Food Hydrocolloids* 2017. 73 p. .

[Yang et al. ()] 'Food matrix affecting anthocyanin bioavailability: Review'. M Yang , S I Koo , W O Song , O K Chun . *Current Medicinal Chemistry* 2011. 18 (2) p. .

[Sui et al. ()] *Functional and conformational changes to soy proteins accompanying anthocyanins: Focus on covalent and non-covalent interactions*, X Sui , H Sun , B Qi , M Zhang , Y Li , L Jiang . 10.1016/j.foodchem.2017.11.090. https://doi.org/10.1016/j.foodchem.2017.11.090 2018. November 2017. p. .

[Howell ()] N K Howell . *Ingredient Interactions: Effects on Food Quality*, 2005. CRC Press. (nd Ed)

[Oh et al. ()] 'Hydrophobic interaction in tannin-protein complexes'. H I Oh , J E Hoff , G S Armstrong , L A Haff . *Journal of Agricultural and Food Chemistry* 1980. 28 (2) p. .

[Tagliazucchi et al. ()] 'In vitro bio-accessibility and antioxidant activity of grape polyphenols'. D Tagliazucchi , E Verzelloni , D Bertolini , A Conte . *Food Chemistry* 2010. 120 (2) p. .

[S ?ieca et al. ()] 'In vitro digestibility and starch content predicted glycemic index and potential in vitro antidiabetic effect of lentil sprouts obtained by different germination techniques'. M S ?ieca , U Gawlik-Dziki , B Baraniak . *Food Chemistry* 2013. 138 (2-3) p. .

[Karakaya ()] 'In vitro digestion of dairy and egg products enriched with grape extracts: Effect of the food matrix on polyphenol bioaccessibility and antioxidant activity'. S Karakaya . *Food Research International* 2016. 88 p. .

[Alminger et al. ()] 'In vitro models for studying secondary plant metabolite digestion and bioaccessibility'. M Alminger , A M Aura , T Bohn , C Dufour , S N El , A Gomes , S Karakaya , M C Martínez-Cuesta , G J Mcdougall , T Requena , C N Santos . *Comprehensive Reviews in Food Science and Food Safety* 2014. 13 p. .

[Keppler et al. ()] 'Influence of mathematical models and correction factors on binding results of polyphenols and retinol with b-lactoglobulin measured with fluorescence quenching'. J K Keppler , M C Stuhldreier , F Temps , K Schwarz . *Food Biophysics* 2014. 9 (2) p. .

[Chai et al. ()] 'Interaction between amylose and tea polyphenols modulates the postprandial glycemic response to highamylose maize starch'. Y Chai , M Wang , G Zhang . *Journal of Agricultural and Food Chemistry* 2013. 61 p. .

[Girard et al. ()] 'Interaction mechanisms of condensed tannins (proanthocyanidins) with wheat gluten proteins ?'. A L Girard , S R Bean , M Tilley , S L Adrianos , J M Awika . 10.1016/j.foodchem.2017.11.054. https://doi.org/10.1016/j.foodchem.2017.11.054 *Food Chemistry* 2018. August 2017. p. .

[Zhang et al. ()] 'Interaction of milk whey protein with common phenolic acids'. H Zhang , D Yu , J Sun , H Guo , Q Ding , R Liu , F Ren . 10.1016/j.molstruc.2013.11.009. https://doi.org/10.1016/j.molstruc.2013.11.009 *Journal of Molecular Structure* 2014. 1058 p. .

[Zhang et al. ()] *Interaction of phenolic acids and their derivatives with human serum albumin: Structureaffinity relationships and effects on antioxidant activity*, Y Zhang , S Wu , Y Qin , J Liu , J Liu , Q Wang . 10.1016/j.foodchem.2017.07.100. https://doi.org/10.1016/j.foodchem.2017.07.100 2018. January 2017. p. .

[Liu et al. ()] 'Interaction of phenolic acids with trypsin: Experimental and molecular modeling studies'. B Liu , H Xiao , J Li , S Geng , H Ma , G Liang . 10.1016/j.foodchem.2017.01.126. https://doi.org/10.1016/j.foodchem.2017.01.126 *Food Chemistry* 2017. 228 p. .

[Arts et al. ()] 'Interactions between flavonoids and proteins: Effect on the total antioxidant capacity'. M J T J Arts , G R M M Haenen , L C Wilms , S A J N Beetstra , C G M Heijnen , H Voss . *Journal of Agricultural and Food Chemistry* 2002. 50 (5) p. .

[Jaldappagari et al. ()] 'Interactions of polyphenols with plasma proteins: insights from analytical techniques'. S Jaldappagari , S Balakrishnan , A H Hegde , N L Teradal , P S Narayan . *Current drug metabolism* 2013. 14 (4) p. .

[Frazier et al. ()] 'Interactions of tea tannins and condensed tannins with proteins'. R A Frazier , E R Deaville , R J Green , E Stringano , I Willoughby , J Plant , I Mueller-Harvey . *Journal of Pharmaceutical and Biomedical Analysis* 2010. 51 p. .

[Cheng et al. ()] 'International Journal of Biological Macromolecules Spectrofluorimetric and molecular docking studies on the interaction of cyanidin-3-O-glucoside with whey protein, ? -lactoglobulin'. J Cheng , J Liu , G Prasanna , P Jing . 10.1016/j.ijbiomac.2017.07.119. https://doi.org/10.1016/j.ijbiomac.2017.07.119 *International Journal of Biological Macromolecules* 2017. 105 p. .

[Gawlik-Dziki et al. ()] 'Leaves of quinoa (Chenopodium quinoa Willd.) as a source of natural source inhibitors of xanthine oxidase'. U Gawlik-Dziki , M Dziki , D Tomi?o , J Baraniak , B . *Bromatologia i Chemia Toksykologiczna* 2012. 45 (3) p. .

[Al-Hanish et al. ()] 'Noncovalent interactions of bovine alactalbumin with green tea'. A Al-Hanish , D Stanic-Vucinic , J Mihailovic , I Prodic , S Minic , M Stojadinovic , T C Velickovic . 10.1016/j.foodhyd.2016.05.012. https://doi.org/10.1016/j.foodhyd.2016.05.012 *Food Hydrocolloids* 2016. 61 p. .

[Herrmann and Nagel ()] 'Occurrence and Content of Hydroxycinnamic and Hydroxybenzoic Acid Compounds in Foods'. K Herrmann , C W Nagel . *Critical Reviews in Food Science and Nutrition* 1989. 28 p. .

[Liu et al. ()] 'On enhancing the solubility of curcumin by microencapsulation in whey protein isolate via spray drying'. W Liu , X D Chen , Z Cheng , C Selomulya . *Journal of Food Engineering* 2016. 169 p. .

[Hemar et al. ()] *Original article Investigation into the interaction between resveratrol and whey proteins using fluorescence spectroscopy*, Y Hemar , M Gerbeaud , C M Oliver , M A Augustin . 10.1111/j.1365-2621.2011.02728.x. https://doi.org/10.1111/j.1365-2621.2011.02728.x 2011. p. .

[Liu et al. ()] 'Physicochemical properties of b -carotene emulsions stabilized by chlorogenic acidlactoferrin -glucose/polydextrose conjugates'. F Liu , D Wang , H Xu , C Sun , Y Gao . 10.1016/j.foodchem.2015.09.047. https://doi.org/10.1016/j.foodchem.2015.09.047 *FOOD CHEMISTRY* 2016. 196 p. .

[Ho et al. ()] 'Physicochemical stability of lycopene-loaded emulsions stabilized by plant or dairy proteins'. K K H Y Ho , K Schroën , M F S Martín-González , C C Berton-Carabin . 10.1016/j.foostr.2016.12.001. https://doi.org/10.1016/j.foostr.2016.12.001 *Food Structure* 2017. 12 p. .

[Polyphenol/peptide binding and precipitation Journal of agricultural and food chemistry] 'Polyphenol/peptide binding and precipitation'. *Journal of agricultural and food chemistry* 50 (6) p. .

[Bravo ()] 'Polyphenols: chemistry, dietary sources, metabolism, and nutritional significance'. L Bravo . *Nutrition Review* 1998. 56 p. .

[Sun et al. ()] 'Preparation, characterization and stability of curcumin-loaded zein-shellac composite colloidal particles'. C Sun , C Xu , L Mao , D Wang , J Yang , Y Gao . 10.1016/j.foodchem.2017.02.001. https://doi.org/10.1016/j.foodchem.2017.02.001 *Food Chemistry* 2017. 228 p. .

[Zhang et al. ()] 'Preparation, physicochemical characterization and in vitro digestibility on solid complex of maize starches with quercetin'. L Zhang , X Yang , S Li , W Gao . *LWT -Food Science and Technology* 2011. 44 p. .

[Ali ()] 'Protein-phenolic interactions in food'. H Ali . *Eurasian J Anal Chem* 2012. 7 (3) p. .

[Song and Yoo ()] 'Quality improvement of a rice-substituted fried noodle by utilizing the protein-polyphenol interaction between a pea protein isolate and green tea (Camellia sinensis) extract'. Y Song , S H Yoo . *Food chemistry* 2017. 235 p. .

[Kroll et al. ()] 'Reactions of plant phenolics with food proteins and enzymes under special consideration of covalent bonds'. J Kroll , H M Rawel , S Rohn . *Food Science and Technology Research* 2003. 9 p. .

[Bandyopadhyay et al. ()] 'Recent developments on polyphenolprotein interactions: Effects on tea and coffee taste, antioxidant properties and the digestive system'. P Bandyopadhyay , A K Ghosh , C Ghosh . *Food & Function* 2012. 3 (6) p. .

[Sharifi-Rad et al. ()] 'Salvia spp. Plants-from farm to food applications and phytopharmacotherapy'. M Sharifi-Rad , B Ozcelik , G Alt?n , C Da?kaya-Dikmen , M Martorell , K Ramírez-Alarcón , . . Coutinho , HD M . *Trends in Food Science & Technology* 2018.

[Chung et al. ()] 'Stability improvement of natural food colors: Impact of amino acid and peptide addition on anthocyanin stability in model beverages'. C Chung , T Rojanasasithara , W Mutilangi , D J Mcclements . *Food chemistry* 2017. 218 p. .

[Dai et al. ()] 'Structural characterization, formation mechanism and stability of curcumin in zein-lecithin composite nanoparticles fabricated by antisolvent co-precipitation'. L Dai , C Sun , R Li , L Mao , F Liu , Y Gao . 10.1016/j.foodchem.2017.05.134. https://doi.org/10.1016/j.foodchem.2017.05.134 *Food Chemistry* 2017. 237 p. .

[Zhang ()] 'Structure-affinity relationship of the interaction between phenolic acids and their derivatives and ?-lactoglobulin and effect on antioxidant activity'. H Zhang . *Food chemistry* 2018. 245 p. .

[Soares et al. ()] 'Study of human salivary proline-rich proteins interaction with food tannins'. S Soares , I García-Estévez , R Ferrer-Galego , N F Brás , E Brandão , M Silva , . . Mateus , N . *Food Chemistry* 2018. 243 p. .

[Chen et al. ()] 'Tangeretin-loaded protein nanoparticles fabricated from zein/b-lactoglobulin: Preparation, characterization, and functional performance'. J Chen , J Zheng , D J Mcclements , H Xiao . *Food Chemistry* 2014. 158 p. .

[He ()] 'Tannins improve dough mixing properties through affecting physicochemical and structural properties of wheat gluten proteins'. G He . *Food Research International* 2015. 69 p. .

[Wu et al. ()] 'The effect of instant green tea on the foaming and rheological properties of egg albumen proteins'. W Wu , M Clifford , N K Howell . *Journal of the Science of Food and Agriculture* 2007. 87 (10) p. .

[Tagliazucchi et al. ()] 'The first tract of alimentary canal as an extractor. Release of phytochemicals from solid food matrices during simulated digestion'. D Tagliazucchi , E Verzelloni , A Conte . *Journal of Food Biochemistry* 2012. 36 (5) p. .

[Gallo et al. ()] *The interaction of cocoa polyphenols with milk proteins studied by proteomic techniques*, M Gallo , G Vinci , G Graziani , C Simone , De , P Ferranti . 10.1016/j.foodres.2013.07.011. https://doi.org/10.1016/j.foodres.2013.07.011 2013. FRIN. 54 p. .

[Escarpa and Gonzalez ()] 'Total extractable phenolic chromatographic index: an overview of the phenolic class contents from different sources of foods'. A Escarpa , M Gonzalez . *European Food Research and Technology* 2001. 212 p. .

[De Freitas and Mateus ()] 'Updating Wine Pigments'. V De Freitas , N Mateus . *Recent Advances in Polyphenol Research*, C Santos-Buelga, M T Escribano-Bailon, & V Lattanzio (ed.) 2010. p. .