Chapter

Eat Tasty and Healthy: Role of Polyphenols in Functional Foods

Catarina Bessa-Pereira, Ricardo Dias, Elsa Brandão,
Nuno Mateus, Victor de Freitas, Susana Soares
and Rosa Pérez-Gregorio

Abstract

Adverse reactions to food such as allergies and celiac disease are increasingly recognized as a growing public health burden. There is currently no cure for these diseases so that there is an unmet need to evaluate different nutritional approaches aiming at improving the quality of life of affected patients and their families. In this context, healthy promising nature-derived compounds, most of which contained in fruits and vegetables, have been studied as an alternative to attenuate the epidemic. Indeed, phenolic compounds have become an emerging field of interest in nutrition in the last decades. A growing build of research suggests that phenolic compounds inhibit pro-inflammatory transcription factors by interacting with proteins involved in gene expression and cell signaling, leading to protective effects against many inflammation-mediated chronic diseases. However, the use of phenolic compounds as attenuating agents of immune reactions to food has to be aligned to the organoleptic characteristics of food, since many compounds present unpleasant taste properties, namely bitter taste and astringency. In this framework, tasty but healthy phenolic compounds arise as attractive ingredients in the design and formulation of functional foods. This book chapter is focused on revisiting the organoleptic properties of phenolic compounds while evaluating the role of these compounds in health promoting actions, namely the management of immune reactions to food such as Food Allergies and Celiac Disease.

Keywords: food allergies, celiac disease, functional foods, phenolic compounds, clean label

1. Introduction

"Healthy" and "natural" are two keywords appealing for consumers. Along with these, there is a growing demand for "functional" and "clean label" food products. The food system and consumers demand for new functional products that have potentially positive effects on health besides basic nutrition alongside to products made with few ingredients, preferably natural ones and assuring that these new ingredients are easy-to-recognize. In fact, "clean label" is a new "action" of food system to recover consumer trust, somehow lost in the past decades due to different issues, such as low transparency about ingredients. The term clean label is complex and multidimensional. While there is not a specific definition of the term, it is while accepted that clean label refers to "natural" food, with simple, well-known and short ingredients list while avoiding the use of synthetic additives [1, 2]. In this context, the use of natural extracts rich in bioactive compounds able to reduce the use of synthetic additives arise as a new reality. Consumers' of nowadays are more informed and demanding. In addition, to healthy, functional and natural, consumers are also demanding for sustainable food products. Within this framework, plant-based ingredients and bioactive compounds arise as promising tools because they comprise all these topics. This chapter will focus on a class of plant-based bioactive compounds, the phenolic compounds, and their potential to be added to functional and clean labelfoods. This chapter will start by covering the structural classification and occurrence of phenolic compounds, their health bioactivities as well as their potential application for modulation of immune reactions to food (food allergies and celiac disease). While these compounds are undoubtedly healthy, their supplementation in food can affect the sensory properties leading to unpleasant effects, namely bitter taste and astringency perception. This will be also focused inside this chapter. The technological properties of phenolic compound as new ingredients will be also discussed considering the interactions within food matrices. Despite their importance, these interactions are usually overlooked in functional and clean label foods. At the end, this chapter aims to highlight that functional foods should constitute a part of a healthy but tasteful diet.

2. Nature and occurrence of phenolic compounds: from food to waste

Phenolic compounds (PC) are secondary metabolites with a high array of unique bioactive properties, which makes them vastly appreciated for their beneficial effects on human health and well-being. PC constitute a wide family of bioactive compounds comprising more than 8000 different structures already identified [3]. Besides the great structural heterogeneity, some common features allow classifying PC into two different families: flavonoids (flavones, flavonols, flavanols, flavanones, isoflavones, and anthocyanins) and non-flavonoids (phenolic acids and derivatives, stilbenes and lignans) as summarized in **Figure 1**. In nature, these structures could also occur esterified, acylated and/or glycosylated. Indeed, the extreme diversity of these compounds joined with their extensively

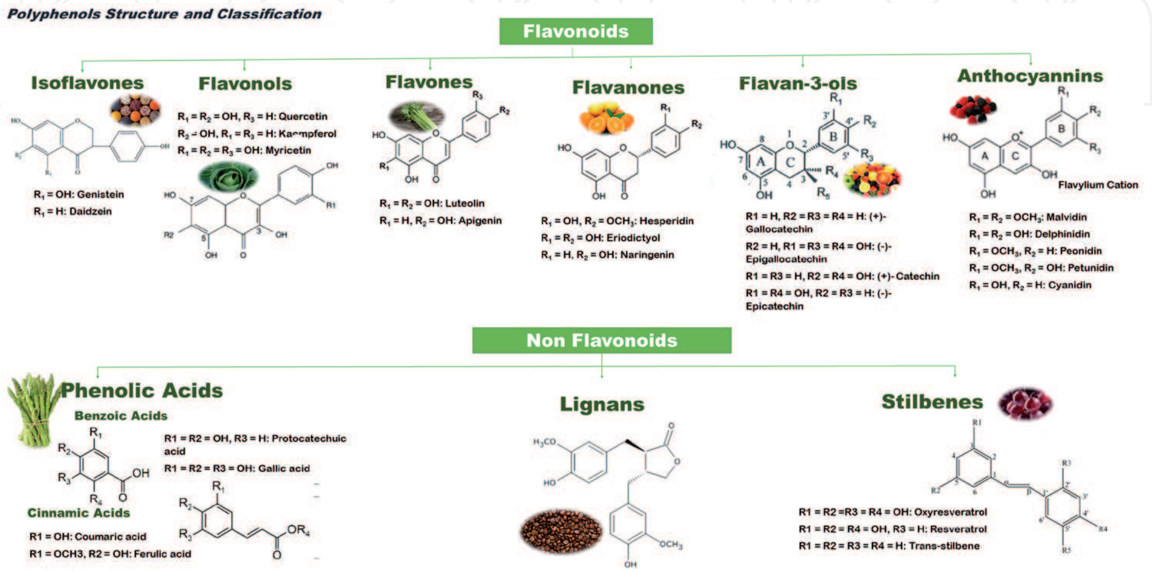

Figure 1.
Polyphenols classification and basic structures.

probed bioactivities makes them one of the most largely studied family of plant metabolites.

PC are found almost in all families of plants and are concentrated in leaf tissue, the epidermis, bark layers, flowers and fruits. The PC distribution could vary within the plant tissues. Indeed, differences in PC composition from seeds, pulp and peels have been extensively studied [4]. Overall, anthocyanin pigments are mainly accumulated in peels while flavan-3-ols appear in higher concentration in seeds [5]. Furthermore, PC occurrence in Plant Kingdom depend on biotic and abiotic factors such as genetic variations, environmental conditions and agronomic practices among others [6]. Besides these variations, the PC content could vary during processing from technological and industrial processes to homemade practices such as culinary treatments or vegetables storage [7, 8]. All these features must be considered before analyzing the real intake of PC and related health outcomes observed. Indeed, the amount of a bioactive compound required to deliver the health-related effects is the key to design a new functional food. Besides the great diversity of PC and the wide range of foods containing them, the major daily intake comes from cereal grain accounting for over 50% of their total intake. Among phytochemicals identified in cereal grain the most important are the phenolic acids and condensed tannins (flavan-3-ols polymers) [9]. In parallel, flavonoids are the main bioactive compounds found in fruits [10] and herbs and spices are rich in hidroxybenzoic acids [11].

PC are not only present in foods but also Agro-Food wastes such as fruit pomace, wood material or even waste water [12]. In this context, the valorization of Agro-Food by-products have emerged over the last years especially because of their easy obtention in large volumes with reduced costs [13]. Apart from their functionality as a source of energy, Agro-Food by-products should also be considered as value-added residues due to their chemical heterogeneity, structure and subsequent applications in the food sector as functional food ingredients or nutraceuticals contributing not only for a sustainable and circular economy but also for the implementation of zero waste politics [14].

Agro-Food wastes have been traditionally used as organic fertilizer, livestock feeds, or as a source for biofuel production [13]. The evolution in Green-chemistry with cutting-edge technology to properly obtain bioactive compounds from Agro-Food wastes opens a new perspective to produce value-added products [15]. Much evidence has been highlighted to use by-products of fruit industry or wineries, among others. Edible parts of fruits and vegetables usually contain lower amounts of bioactive compounds than skin, twings or peels non-edible portions. Indeed, wastes obtained after pressing the juice are a valuable source of PC. In parallel, winery and overall beverages industry generates large volumes of pomace (a mixture of pulp, skin, seeds, and stem) with higher amounts of PC when compared with edible fruits and vegetables [16]. Among fruit-derived by-products or wastes, apple pomace contains high amounts of flavonols, flavanols, phenolic acids, dihydrochalcones and anthocyanins [17]. Furthermore, significant amounts of a well-known antidiabetic agent named phlorizin is widely found in apple-derived by-products [18]. Peels from fruit such as banana peel, rich in phenolic acids, flavonols, flavanols, and catecholamines accounting three times the edible part of the fruit, have been reported as providing strong antioxidant and anti-microbial activities, in addition to exhibit other health benefits like reducing cholesterol and blood sugar, neuroprotective effect and anti-angiogenic activity were also described [13]. Citrus peels have been also studied to recover high-value bioactive compounds like flavones (apigenin-glucoside and diosmetin-glucoside) and flavanones (eriocitrin and hesperidin) from lemon peel and phenolic acids (hydroxybenzoic and caffeic acids) and flavanones (hesperidin and narirutin) from orange peel and pulp [19]. Potato peel has been reported as containing phenolic acids and beetroots peel and pulp contain flavonoids, phenolic acids and betalains, which exhibited good antioxidant activity and hepatoprotective effects [20]. One of the most recently studied food material was onion and garlic skin/peel, which generates huge volume of wastes especially rich in quercetin derivatives as well as other aglycone flavonoids exhibiting bioactivities like antioxidant, antimicrobial, antispasmodic, and antidiabetic activity [21]. Berries by-products such as branches obtained from elderberry processing are a valuable source of anthocyanins [22]. Furthermore, seeds/kernel which is a major waste after processing holds promise as a potential therapeutic source with numerous PC being isolated such as flavonols and gallotannins [23].

Some of the mentioned food by-products or Agro-Food wastes have been already proposed as additive in the formulation of bakery and dairy products to enhance their contents in bioactive compounds [24, 25]. In addition, the presence of natural compounds, pigments and volatile compounds can enhance the sensory properties and overall quality of the final product but some research is needed to deep in the technological effects of these new ingredients with highly probed bioactivities.

3. Phenolic compounds as modulators of immune reactions to food

Over the past several years, non-communicable diseases (NCDs) such as cancer, cardiometabolic, neurodegenerative and autoimmune disorders have become of important health concerns for consumers and a growing public health issue everywhere in the world [26]. They typically result from an imbalance between people and their environment and lifestyle patterns, including physical inactivity, tobacco usage, alcohol abuse and related metabolic risks [27]. Essential for life, diet provides a vast source of molecules that are largely harmless for the majority of the world population. Nonetheless, compelling observational and interventional evidence is now available on the implication of modern unbalanced dietary habits/diet - with its high saturated fat and sugar intake - on the incidence of low-grade, chronic, and systemic inflammation [28]. Furthermore, for some individuals, the intake of staple food like milk, eggs, nuts or bread can trigger a set of immune mechanisms that can lead to a severe allergic condition termed food allergy [29]. Besides food allergy there is a high number of immune reactions to food, some of them autoimmune disorders such as Celiac Disease. The rise of immunologic reactions to food are substantial and evolving public health issues, increasing over the last decade as epidemic [30]. Nevertheless, therapeutic options remain limited. One of the mechanisms leading to this subclinical, yet persistent adverse response to nonlife-threating situations, occurs through, for instance, food-induced structural and behavioral changes in gut microbiota [31]. The bacterial ecosystem living up in the gut play crucial roles in the induction of protective responses to pathogens, maintenance of body's homeostasis and tolerance to innocuous food antigens [32]. As a consequence, any environmental factor disturbing the richness and diversity of bacteria making up the gut microbiome could potentially affect host metabolism, impact intestinal barrier integrity and immune system functions [33]. A better understanding of the key nutritional mechanisms involved in such immune responses will likely be vital for disease prevention and development of new therapies. Indeed, consumption of antioxidants, mainly dietary phenolic compounds found in fruits and vegetables, has been related with low prevalence of immune reactions to food [34]. Used as nutraceuticals, PC are thought to dampen the onset of immune-related inflammation [35, 36]. Moreover, recent studies proved the ability of PC to bind food antigens [37, 38], which could modulate the disorders, but concerns still remain about their real function by the organism that assumes

PC through diet, because of their bioavailability, metabolism and pharmacokinetics. Scientific knowledge has to be improved to establish the basis for nutritional recommendations that help to prevent or minimize the prevalence and symptoms of immune reactions. A broad approach is herein explained to fully understand the immunomodulatory process of PC in food allergies and celiac disease from ingestion to immune systemic effects manifestation.

3.1 Food allergies

This hypersensitivity to particular proteins present in food, known as allergens, occurs when the immune system erroneously perceive foreign proteins as dangerous, initiating an allergic immune reaction [29].

The most common type of food allergy is mediated by immunoglobulin E (IgE), and is estimated to have an impact in the life of 5–8% of the children and up to 4% of the adults worldwide [39]. Food allergic reactions mediated by IgE comprise distinct phases; the allergic sensitization, where the food antigen is taken up, processed and displayed on the surface of antigen presenting cells (APCs); which, in the presence of interleukin-4 (IL-4) and/or IL-13, provide signals for the activation of the T helper 2 (TH2) subtype of T cells. Then, TH2 cells in conjugation with IL-4 and IL-13, will induce class switching in B cells, which differentiate into plasmocytes (antibody-producing cells) that secret allergen-specific IgE [40]. After the allergic sensitization, the subsequent re-exposure (elicitation phase) to the allergen, will now result in a more robust immune response. Here, the antigen-specific IgE binds to the surface receptor FcεRI expressed on mast cells and basophils. The cross-link of the FcεRI receptors with IgE will trigger mast cells and basophils degranulation, which leads to the secretion of inflammatory mediators e.g. β-hexosaminidase and histamine. In addition, allergen-induced cytokines (IL-4 and IL-13) are also released fostering the typical food allergic symptoms, which can range from mild to a life-threatening allergic reaction (anaphylaxis) [39, 40]. Given that, the incidence as well as the severity of food allergy, is gradually increasing, the search for novel therapeutics to mitigate this condition is in high demand [29].

As described earlier, there are various immune mechanisms implicated in food allergy that may, therefore, be targeted in prospective anti-allergic strategies. In this light, the extraordinary structural characteristics, wide distribution in fruits and vegetables, and the well-studied anti-inflammatory and anti-oxidant properties of PC, make these bioactive compounds fitting candidates for anti-allergic therapies [41]. In fact, various studies with PCs have suggested that some of these metabolites, especially phenolic acids and flavonoids, may exhibit certain anti-allergic benefits and although the exact mechanisms behind their action are not clear, data shows that PC can intervene at both the allergic sensitization and the elicitation phases [42, 43]. Moreover, PC can also modulate gut microbiota and potentially influence food allergy [44].

Several methodologies are currently in use to evaluate the capacity of distinct PC to interact with specific allergen proteins. Plundrich et al. performed in silico analyses to narrow down the search for PC present in cranberries/ and or lowbush blueberries (rich in anthocyanins), which could theoretically interact with Ara h 2, the most pro-allergenic protein in peanuts, specifically in the region that is thought to be the binding site for IgE [45]. This screening, in concert with further *in vitro* experiments revealed that procyanidin C1 and chlorogenic acid could potentially interact with Ara h 2 inducing conformational changes, which masked the IgE epitope [45]. Covalent interactions between chlorogenic acid and ovalbumin (OVA), the major allergen found in the egg white, also induced modifications in OVA conformation, resulting in the direct shielding of the linear IgE epitope, which attenuated allergic mechanisms [46]. Accordingly, histamine release experiments, showed that the basophil degranulation was inferior in human basophils sensitized with the OVA conjugated with chlorogenic acid when compared to OVA unconjugated, implying a decrease in the crosslinking of the FcεRI receptors via IgE-allergen interaction [46]. Also, the ability of phenolic compounds to bind to dietary allergen is pointed out as having a beneficial effect due to precipitation events [47]. Accordingly, Yichen Li et al. observed that PC from pomegranate juice could form stable complexes with cashew nuts, thus reducing allergen recognition by antibodies, and consequently the immunoreactivity to cashew nuts [47].

Despite not completely mimicking the human pathophysiology of food allergy, animal models of food allergy are important pre-clinical research tools for the food industry. These models are elected due to their capacity to simulate the most common reactions observed after the exposure to specific allergens, namely IgE production, TH2 related cytokine expression and mast cells degranulation [48, 49]. In fact, various animal models are now used to study the effect of PC as modulators of allergy. For example, the metabolites derived from epicatechin found in the circulating plasma of a mouse model of OVA allergy fed with phenolic compounds extracts isolated from apple/ or purified epicatechin, were associated with the reduction of several clinical allergic symptoms [49]. Additionally, in the ileum, the mRNA levels of the TH2 – related cytokine IL-13 and the pro-inflammatory cytokine IL-12 were decreased as well, suggesting that epicatechin could be a possible modulator of allergic reactions [49]. Also, Abril-Gil et al., used Brown Norway rats to investigate the potential protective effect of cocoa diets, which contain high amounts of flavanols (e.g. epicatechin, catechin and procyanidins) in allergic immune reactions upon OVA re-exposure [50]. Strikingly, their findings showed that while in the group of rats deprived of cocoa high levels of serum specific anti-OVA IgE were observed, in the other groups where cocoa was offered, IgE was significantly lower [50]. Moreover, the *in vitro* analysis of spleen and mesenteric lymph node cells (MLN) cytokines secretion revealed that IL-5 and IL-13 were reduced in the MLN, and that in the spleen, IL-4 was also reduced in a specific cocoa diet. Interestingly, the cocoa diet was also important for attenuating degranulation events by reducing the FcεRI and mast cell mediators (proteases) gene expression and release [50].

More recently, a mouse model (C3H/HeJ mice) representative of peanut allergy was used to evaluate the capacity of PC rich-extracts obtained from blueberry and cranberry to minimize the allergenicity of peanut proteins [51]. Here, colloidal aggregates composed of PC extracts (with different percentages) and proteins derived from peanut were introduced in the diet of peanut sensitized mice for several weeks, before challenging the mice with a higher dose of peanut flour. At the end of the experiment, it was observed that mice pre-treated with the PC aggregates, showed reduced IgE and IgG levels; and lower expression of the allergen-induced basophil activation protein marker CD63 in spleen lysates, when compared to mice kept on a diet with non-complexed peanut proteins [51].

The manifestly promising results demonstrated by these and other *in vivo* experiments, suggest that in the presence of PCs, the re-exposure to allergens result in less exuberant allergic responses. In this way, the use of these bioactive compounds hold promise to surmount the immune responses triggered by the oral administration of food antigens, contributing therefore, to the oral tolerance to dietary proteins [52].

In summary, the urgent need for effective therapeutics for food allergy and given the complex mechanisms involved in this escalating pathology, diverse anti-allergic strategies are being explored. In this perspective, the natural ability of PC to interact with food allergens, interfere with IgE interaction or production, reduce the secretion of allergic mediators and modulate the expression of allergy related cytokines make PCs attractive agents for mitigating food allergy.

3.2 Celiac disease

Celiac Disease (CD) is an immune-mediated enteropathy triggered by the ingestion of gluten proteins by genetically susceptible individuals [53]. Although there is, so far, no clear explanation for the burst of gluten-related disorders in recent years, it has been speculated that this may have occurred due to an increase in the consumption of gluten-containing foods, some based on novel wheat stains produced for technological rather than nutritional reasons, and the humans' over usage of antibiotics and pesticides, both of which rendered people more sensitive to allergenic plant proteins [54].

Mechanistically, CD is characterized by an aberrant T-cell response towards gluten peptides that, because of their high proline content, are left undigested at the gut lumen [55]. According to recent findings, some of these gluten peptides have the ability to bind to the chemokine receptor CXCR3 on the surface of intestinal epithelial cells, leading to a PKC-α dependent tight junctions disassembly and increased intestinal permeability [56]. In the lamina propria, gluten peptides are selectively deamidated by the enzyme tissue transglutaminase 2 (TG2) and later presented to gluten-specific HLA-DQ2 or HLA-DQ8-restricted CD4+ T cells by antigen-presenting cells [57]. Once activated, and in response to tissue signals provided by stressed epithelial cells, gluten-specific CD4+ T cells support the activation and differentiation of both autoreactive TG2 and gluten-specific B cells into IgA and IgG-producing plasma cells while increasing the cytolytic properties of intraepithelial cytotoxic T lymphocytes which kill distressed intestinal epithelial cells based on the recognition of stress-induced ligands e.g. MHC-class I polypeptide-related (MICA/B) and HLA-E molecules [58].

The rapid increase in the global incidence of CD, together with the growing concern of CD patients regarding their quality of life when on a gluten-excluding diet, led researchers scrambling for alternative (or complementary) ways to tackle the celiac gut's response to gluten and potentially restore tolerance [59]. Among the candidates, recent evidence brough PC into the spotlight as promising agents to be used in CD management due to their wide range of beneficial properties and positive impact on human health. Nevertheless, and despite the advances made in the past few years, there are still many unresolved questions in this area, due to the multitude of action mechanisms underlying the response to PCs intake and large interindividual variability [60].

In a CD context, PC could act at several levels: they could impair gluten digestion and peptide availability at the intestinal lumen, reduce inflammation, enhance intestinal barrier integrity and function and have a prebiotic effect through inhibition of certain pathogenic groups and stimulation of beneficial bacterial growth [61]. As shown by Dias et al. green tea PC and grape seed procyanidins can readily interact with one of the most immunoreactive gluten peptides - the 33/32-mer - primarily through an unspecific, entropy-driven, hydrophobic effect [62]. In general, these interactions were found to be similar to the interactions between polyphenols and proline-rich salivary proteins in that they are the result of cooperative binding mechanisms involving both enthalpic and entropic effects. Staggeringly, the primarily PC-binding sites within the 32-mer peptide sequence were also unveiled: they correspond to leucine, tyrosine and phenylalanine-containing domains, located in four well-defined and almost indistinguishable hydrophobic clusters, equally spaced by non-polar proline residues [63]. Subsequent transepithelial transport studies on Caco-2 cell monolayers highlighted the ability of dietary doses of

EGCG to scavenge and reduce the apical-to-basolateral translocation of the 32-mer peptide in vitro to nearly undetectable levels [62]. Still, it remains unclear whether this attenuation will have any implication in the activation and triggering of a gluten-specific T-cell mediated immune response, though the structural changes induced on the peptide upon binding provides foundational support for functional changes in its immunostimulatory action [64].

On another recent breakthrough, green tea catechins were found to prevent gluten digestion through physical interactions with gluten proteins and prevention of hydrolysis by digestive enzymes [65]. According to this study, the presence of green tea catechins resulted in a decreased formation of low molecular weight gluten peptides, decreased intestinal permeability and reduced inflammation [66]. A similar finding was also made available by Kramer and coworkers which shown a significant inhibition of IFN-γ- or gluten peptide p31–43-induced increases in CD inflammatory biomarkers including TG2, COX-2, IL-15, IL-1β, IL-6, and IL-8 by procyanidin B2-rich cocoa extracts [67].

Regarding the effect produced by PC-rich dietary patterns on gut and blood microbiomics in CD patients, data are still scarce. Nevertheless, there is now several pieces of evidence suggesting that PCs may represent a relevant factor in shaping the intestinal microbial ecosystem (i.e. the microbiota and derived metabolic products) and modifying the relative abundance of specific bacterial taxa in dysbiotic CD subjects [68]. By modulating the concentration of health-affecting microbial metabolites in the gut e.g. butyrate, polyphenols are likely to regulate a plethora of biological responses at the intestinal level that control, for instance, tight junction integrity, anti-inflammatory signaling, immune cell migration, adhesion, and cellular functions such as proliferation and apoptosis [69]. Accordingly, it has been found that treatment of CD-derived organoids with microbiota-derived bioproducts, including butyrate, improved epithelial barrier functionality and reduced gliadin-induced IFN-γ and IL-15 secretion [70]. Of note, both butyrate and lactate have been shown to exert a relevant role in regulating FoxP3 isoform expression in T cells and consequent activation of a Th17-driven immune response in CD subjects [71]. But, as well-controlled intervention studies are still lacking, future studies should be focusing on providing a proof of concept of the reliability of a PC-based dietary intervention in the context of microbiota-intestinal permeability and CD health outcomes.

4. Use of phenolic compounds as alternative to synthetic additives in functional foods

In the last 50 years, food systems have dramatically changed where the access to foods, with high levels of salt, sugars and saturated fats have become cheaper and more widely available than micronutrient rich foods—such as fresh fruits and vegetables. Consequently, the incidence of NCDs greatly increase such as obesity, type 2 diabetes as well as immune reactions to food, claiming for action. Food industry faces important challenges regarding the increase in these NCDs. In addition, besides the health challenge, other key points demand advances for the production of food and significant changes in food systems, namely population growth, rural development, globalization and climate changes.

Diverse personal, cultural or economic factors influence consumers' dietary behavior. Furthermore, political issues as well as the food labeling, marketing, information about food and policies could impact on price affecting consumer demand. Under this framework, strategies to protect vulnerable populations can be addressed to achieve a global access to healthy and sustainable diets. Based on

Figure 2.
Use of polyphenols as ingredients in functional foods.

aforementioned, PC extracts arise as ingredients able to promote health benefits while reducing the use of synthetic additives. This section summarizes the interest in using PC as new ingredients in food formulations including the effects on technological processes (**Figure 2**).

4.1 Reduction of sugar

As already mentioned, the Food Industry needs to diminish the sugar in food and beverages to minimize the impact of sugar consumption in the prevalence of metabolic disorders. Furthermore, public health policy strategies including sugar taxes for food industry accelerate the process. Zero-calorie high-potency sweeteners with improved taste perception are needed as new ingredients. To date, the scientific community has made some efforts to obtain natural sweeteners or designing synthetic compounds with high sweetening power. The most widely artificial sweeteners used in the Food Industry are aspartame, sucralose, saccharine, neotame, advantame and acesulfame potassium-k but whether the use of these sweetener affect our health is still not well understood [72]. Natural alternatives have been explored such as molasses, honey, coconut sugar, date sugar, maple syrup, agave nectar, and xylitol [73]. Most of them are carbohydrates obtained from vegetables, trees, seeds, roots, and nuts. Moreover, dihydrochalcone sweeteners are PC-derived compounds with proved beneficial health effects arising as a good alternative for sugar reduction [74]. However, difficulties associated with browning, replacement of the bulking and other properties that sucrose, glucose and fructose provide in many solid food products must be carefully analyzed.

4.2 Reduction of salt

Reducing the consumption of salt in general population has been identified as a priority intervention to reduce NCDs. Indeed, the World Health Organization has agreed to diminish 30% of salt intake by 2025. The use of vegetable extracts able to enhance flavor while improving health benefits arises as a promising alternative. Under this framework, extracts rich in PC have been already used in food industry. Indeed, green tea extracts were used to enhance the flavor of fish flesh [75], soybean isoflavones enhance the flavor quality in the muscle of grass carp while contribute to health benefits [76]. Furthermore, PC-rich extracts containing aromatic compounds such as onion, garlic, celery spices and herbs could also be a nutraceutical alternative to reduce salt.

4.3 Preservative agents

Spoilage are one of the main causes of economic loses in food industry [77]. Traditionally, the use of artificial preservative technologies such as drying, freezing, thermal treatments and more recently modified atmosphere packaging and non-thermal physical treatments (pulsed electric fields and high hydrostatic pressure) have been employed to extend shelf life of food [78]. Synthetic chemical preservatives such as, tartaric or citric acids; sulphites, sorbate, propionate and benzoate; or nitrites and nitrates, have been extensively used but in recent times the use of natural products as preservative agents acquire relevance [79]. The increase in the consumption of minimally processed foods joined with the clean label requirements boost the trend to explore the use of natural antimicrobials for food preservation. PC have been widely reported as antimicrobial agents [80]. Indeed antimicrobial extracts containing PCs have been already designed for this purposes, such as an extract of moso bamboo (Takeguard™) launched by Takex Labo (Osaka, Japan) or a mixture of different natural antimicrobial extracts (Biovia™ YM10) including green tea extract launched by Danisco DuPont [81]. **Table 1** summarizes the already tested PC from food byproducts with antimicrobial properties.

4.4 Colorant agents

Some PC are natural pigments with high potential to be incorporated into food systems as colorant agents. However, the great reactivity and lack of chemical stability make necessary to deliver these compounds in encapsulated forms. Among PC sources, flowers such as *Clitoria ternatea* petals are commonly used in health drinks and natural food colorants [95]. Moreover, Brazilian fruit peel - jabuticaba (*Plinia cauliflora* (Mart.) Kausel) and propolis from Tubuna (*Scaptotrigona bipunctata*) encapsulated in alginate beds have been tested as a new ingredient with colorant properties and health outcomes [96]. Betacyanins (red-violet) and betaxanthins (yellow-orange), from beets are also powerful antioxidants, which can be used as natural colorants in the food industry [97]. Furthermore, pecan nut shell has been already studied as a food colorant for active packaging for color stabilization [98].

4.5 Emulsifier agents

New alternatives to reduce the content of saturated fats while maintaining the emulsifying properties of sauces must be evaluated. To date, some amphiphilic plant proteins such as wheat gliadins and maize zeins have rheological properties suitable to fabricate colloidal particles for stabilizing foams and emulsions. However, in recent years the use of novel emulsifiers to obtain nutraceutical emulsions are being studied. In this context, the ability of PC to bind to proteins have been described as able to improve the chemical and physical stability of emulsions, arising as a good source of nutraceuticals while emulsifier agents. The emulsifying

Food Byproducts	Polyphenol	Target organisms	References
Coffee extract	Flavan-3-ols, hydroxycinnamic acids, flavonols, and anthocyanidins	*Pseudomonas fluorescens*, *Staphylococcus aureus*, Aspergillus flavus, *Listeria monocytogenes*, Bacillus subtilis, *Candida albicans*	[82]
Green tea waste	Flavan-3-ols (Tannins)	Staphylococcus aureus, *Escherichia coli*, Listeria monocytogenes, *Bacillus coagulans*, Shigella flexneri	[83]
Green, white and black tea extracts	Flavan-3-ols (Tannins)	Salmonella typhimurium, Listeria monocytogenes	[84]
Olive pomace	Phenolic acids (oleocanthal, deoxyloganic acid)	Escherichia coli O157:H7, Salmonella enteritidis, Listeria monocytogenes, and Staphylococcus aureus	[85]
Olive leaf extract	Phenolic acids and flavonoids	Listeria monocytogenes, Escherichia coli O157:H7, Salmonella enteritidis, Candida albicans	[86]
Pomegranate fruit peel extract	Phenolic acids and flavonoids	Salmonella spp., Listeria monocytogenes, Staphylococcus aureus, Escherichia coli, Yersinia enterocolitica, and Pseudomonas fluorescens, *Pseudomonas stutzeri*, Gram-negative bacteria, Gram-positive bacteria, and fungi	[87]
Winery products	Phenolic acids, flavonoids, stilbenes	*Bacillus cereus*, Campylobacter jejuni, Escherichia coli, Listeria monocytogenes, *Salmonella enterica*, Staphylococcus aureus, Yersinia enterocolitica	[88]
Grape pomace	Phenolic acids, flavonoids, stilbenes	Staphylococcus aureus, Salmonella, Enterococci, total aerobic mesophilic and psychrotrophic bacteria	[89]
Grape fruit seed extract	Flavonols, phenolic acids, catechins, proanthocyanidins and anthocyanins	Pseudomonas spp.	[90]
Myrtle berries seeds extract	Phenolic acids and flavonoids	Escherichia coli, Staphylococcus aureus, Salmonella typhimurium, and Bacillus cereus	[91]
Date extract	Phenolic acids and flavonoids	Escherichia coli, Bacillus subtilis, *Enterococcus faecalis*, and Salmonella spp.	[92]
Buckwheat hull extract	Flavonols (quercetin derivatives)	Gram-positive (Bacillus cereus, Staphylococcus aureus, Enterococcus faecalis) and Gram-negative bacteria (Salmonella choleraesuis, Escherichia coli, and *Proteus mirabilis*)	[93]
Pumelo peel extract	Flavonoids	Escherichia coli, *Pseudomonas aeruginosa*, Bacillus subtilis, Staphylococcus aureus, Chromobacterium violaceum, and Vibrio anguillarum	[94]

Table 1.
Polyphenols as food preservatives. Adapted from [81].

properties of proteins have also been modified by introducing polysaccharides; however, little to nothing is known about how ternary interactions could affect the physical stability of emulsions. Ternary conjugates were fabricated by covalently bonding polyphenol, protein, and polysaccharide together. The protein was used to provide surface activity, the polysaccharide to provide strong steric repulsion, and the PC to provide functional properties [99]. But, some PC have poor interfacial activity, like green tea PCs [100]. However, the interaction between green tea PC and the protein β-lactoglobulin (β-lg) (spontaneous nanocomplexes formation) was sucesfully used as an emulsifier agent in fish oil [101]. Colloidal complexes were also prepared from pea protein and grape seed proanthocyanidin and the ability of these complexes to form and stabilize oil-in-water emulsions were verified [102]. Overall, covalent and noncovalent interactions between proteins and PC have provide novel insights into the interfacial behaviors of novel emulsifiers [103].

4.6 Matrix effect

There are several factors which could influence the PC delivery to bloodstream, to their target tissues and biological activities. Disruption of the natural matrix or the microstructure created during processing may influence the release, transformation, and further absorption of some nutrients as well as functional ingredients such as PC in the digestive tract. Some *in vitro* studies verified the effect of milk proteins in PC bioaccesibility and bioactivities after consuming oat based breakfast cereals with blueberry fruit [104]. The absorption of flavanols, such as green tea catechins, is influenced by epimerization reactions, which usually occur during technological processing as well as the presence of lipids and carbohydrates. Moreover is enhanced by the presence of piperine and tartaric acid [105]. Phenolic acids and Flavanones such as hesperidin are affected by the attached sugar, which can covalently link these compounds to the cereal bran matrix [106, 107]. There are only a few examples reported on PC release from the food matrix, but existing information established a direct relationship between the absorption and dose but is sometimes linear and sometimes saturated [108]. The lack of systematic information on the effects of other components on the bioavailability of PCs needs to be performed. This information must be completed by human studies to further establish general principles affecting absorption in vivo. Information derived from such experiments could be useful for the optimal design of future bioefficacy studies for functional foods production.

5. When sensory properties can compromise the intake of potential healthy phenolic compounds

It is undeniable that PC are a key target for the Food Industry on the design of new healthy products, as widely documented in the previous sections. Nevertheless, PC account for the main organoleptic properties of food products, mainly color and taste. Anthocyanins account for the (red) color of fruits and derived products, and flavanols and tannins are linked to unpleasant taste properties, namely astringency and bitterness. So, while PC have high expectations towards the development of health-orientated and functional products, a central challenge could be aligning their applications with consumer acceptability.

5.1 PC sensory properties

Astringency is a trigeminal sensation described as a mouthfeel of dryness, roughness and puckering sensations. It is induced by different classes of compounds such as tannins, acids and alumns. In food, tannins are the main contributors to astringency perception. Several mechanisms are currently proposed to explain astringency molecular onset. The most studied one relies on the interaction and precipitation of particular families of salivary proteins, namely proline-rich proteins. The involvement of oral epithelial cells has been also reported and more recently the activation of G-protein coupled receptors was also reported. The involvement of oral mechanoreceptors is also a hypothesis despite no tangible data has been reported so far.

On the other hand, the perception of bitter taste is well characterized. Bitterness is perceived by activation of specific receptors, the bitter taste receptors (TAS2Rs). Humans express 25 TAS2Rs to perceive hundreds of bitter tasting molecules, with very wide structural features. These receptors occur at the cell-membrane of gustative cells within taste buds of human tongue. Among the wide diversity of TAS2Rs agonists reported there are several PC. In fact, some of these compounds are highly efficient agonists activating TAS2Rs at very low concentrations.

The importance of these taste properties is that they have elicited negative consumer reactions when present at high intensity in some products [109], decreasing the overall acceptability. This can compromise the intended intake of these new and functional food products.

5.2 Phenolic compounds as ingredients in functional foods

In the last years, the application of PC in functional and/or fortified foods has been widely reported. This has been mainly achieved by using either food industry by-products or wastes. Most studies use by-products from fruits (43%), followed by the application of winery (19%) and vegetable (13%) by-products [110]. Among fruit and vegetable by-products, citrus, tomato, grape, and apple by-products have been used in a wide range of food products (**Table 2**). One of these by-products is pomace (e.g. derived from apple or, grape), the main solid waste generated in juice or winemaking factories. It contains plenty of different varieties of nutritionally important compounds, such as dietary fibers, carbohydrates, PC, and minerals presenting a huge potential as a source of bioactive compounds. In addition to by-products or wastes, also some other high-PC content sources have been used to supplement food such as green tea.

Most of the reported studies use different fruit cultivars, obtained from different industry practices but without a deep characterization of the PC content. So, global relationships between PC composition-rheological-sensory properties-health inputs are not easily attained.

A cross-cut problem in most studies associated with the incorporation of these compounds in food matrices is that they can modify sensory properties leading to astringency and bitterness.

5.2.1 Addition of PC to bakery products

A significant amount of grape PC (near 70%) remains in pomace after wine making, the most important being tannins, anthocyanins, and phenolic acids, the quantities depending on the grape variety and winemaking practices. This by-product has been applied in bread, pancakes, pasta, biscuits, and other derived products. Some studies are summarized in **Table 1**.

White grape pomace has been also used to supplement biscuits [111]. In this case, the profile of PC was dominated by gallic acid, tyrosol and γ-resorcylic acid, which contributed nearly 87% of total PC. In this case, at sensory level, the replacement by grape pomace affected mainly on two attributes: fruity-acidic

PC matrix	Goal	Food product	Sensory properties				Ref.
			Physical	Color	Taste	Overall acceptability	
Wine grape pomace	Antioxidant activity	Biscuits	Reduced thickness, increased hardness	Lower lightness, higher red color, lower yellow		10% of grape pomace	[111]
	Functional food, wastes valuation, antioxidant properties	Wheat bread		Decreased brightness, increased red color	Increased bitterness, aftertaste	Zenel grape pomace was suggested to be used	[112]
Grape pomace	Healthier and high dietary fiber content	Muffins		Decreased lightness		High acceptability using at 10%	[113]
		Biscuits	No changes in thickness	Darkness	Increased bitterness	5% improved their acceptability	[114]
Grape seed extract	Healthier, extended shelf-life products	Yogurt	Increased hardness and consistency	—	Decreased taste rating	Decreased overall rating	[115]
Grape pomace	Higher antioxidant activity	Yogurt	General loss of textural quality	—	Unpleasant flavors, not enough sweet	Decreased overall rating	[116]
(Water-treated) Coffee sylverskin	Alternative fiber for oil replacement	Cake	Increased hardness, similar springiness and cohesiveness	Darker and more yellow color	Increased bitterness especially for non-treated coffee sylverskin	Water-treated coffee silverskin (up to 30%) induces no significant alterations on cake characteristics.	[117]
Tomato pomace	Alternative fiber and protein sources; increase antioxidant activity	Beef frankfurter, beef ham and meat-free sausages	Increased hardness and chewiness	Increased yellowness and lightness (meat-free sausages); highest redness	No significant changes in taste	Overall acceptance equal or higher than control	[118]
	Alternative fiber, byproduct valorization, increased health properties	Chicken sausages	Decreased chewiness and guminess, no changes in hardness	No significant changes	No significant changes	Overall acceptability (3%) equal to control	[119]

PC matrix	**Goal**	**Food product**	**Sensory properties**				**Ref.**
			Physical	**Color**	**Taste**	**Overall acceptability**	
Tomato powder	Replace synthetic colorants and reducing the nitrite level	Frankfurters	Decreased tenderness	Increased yellowness	Better flavor	Overall acceptability increased	[120]
Plant extracts (lemon balm, mint, lavender, rosemary and sage)	Functional (healthier and tastier) goat-milk new beverage	Milk-derived beverage	No significant changes	No significant changes	Some extracts (e.g. lavender) induced bitterness and astringency	Overall acceptability was found to be mint>rosemary>sage>lemon balm>lavender	[121]
Apple pomace		Cookies	Reduced thickness but no other significant changes	Decreased lightness and more brown color	Improved taste (higher fruity flavor)	Overall acceptability equal to control	[122]
	Fortification of bakery and meat products	Meat products (chicken patties and beef)	Lower hardness, springiness, cohesiveness, and chewiness	Darker and higher redness	—	—	[123]
	Increased antioxidant activity	Cider	—	Increased yellow color, higher luminosity	Higher bitterness and astringency	Overall acceptability higher than control	[124]
Rheology (dough) and texture properties							
Wine grape pomace	Antioxidant activity	Biscuits	Decreased water absorption	Reduced stability	Development time not modified		[111]
	Functional food, wastes valuation, antioxidant properties	Wheat bread	Decreased water absorption (Merlot dough); no changes to control (Zelen dough)	Increased stability	Higher development time (Merlot dough); no changes to control (Zelen dough)	Changes in all texture properties (stickier crumb, decreased crust toughness, increased sand feeling)	[112]

PC matrix	Goal	Food product	Sensory properties				Ref.
			Physical	Color	Taste	Overall acceptability	
Grape pomace	Healthier and high dietary fiber content	Muffins				hardness and chewiness increased; springiness, cohesiveness, resilience decreased	[113]
Grape peels	Supplementation of dietary fibers	Dough	Not modified	Reduced stability	Development time not modified	Higher hardness, lower adhesiveness, lower cohesiveness	[125]

Table 2.
Effect of fortification with PC in sensory properties of functional foods.

flavor notes and color. These authors studied the stability of PC during the baking process. Within the PC, the most stable ones were as follows: γ-resorcylic acid (loss of 11%) < gallic acid (loss of 18%) < tyrosol (loss of 21%) < catechin (loss of 31%) < isovanilic acid. Moreover, procyanidins B1 and B2, which were identified in the pomace were not retained after the baking process. At the end, there was an almost tenfold increase in bioactive compounds in the biscuits enriched with 30% of pomace, from 0.11 $mg.g^{-1}$ (control) to 1.07 $mg.g^{-1}$.

The stability of PC at the end of the baking process was also assessed upon supplementation of biscuits and bread with green tea extracts to increase the antioxidant ability of the final product [126]. While it was found ca. 30 and 21% of retention of epicatechin gallate and epigallocatechin gallate, respectively, for biscuits supplemented with 300 mg green tea extract per 100 g flour [127], the retention in freshly baked bread were ca. 83 and 91%, respectively [105]. At the end, it was determined that one piece of bread (53 g) containing 150 mg of GTE/100 g of flour will provide 28 mg of tea catechins, which is ~35% of those infused from one green tea bag (2 g). However, none of these studies inferred about the sensory profile of these food products.

Ross and colleagues studied the consumer acceptance of grape-seed (GS) flour-containing food products, namely pancakes and noodles [128]. The GS flour was obtained from winemaking by-products from different grapes (Merlot and Cabernet Sauvignon). Despite the PC content of the GS flour was not characterized, this organic material is well-known to have a high content in procyanidins. It was observed that the supplementation with GS flour led to a decrease on consumer acceptability of pancakes and noodles, especially for taste (bitterness), mouthfeel (astringency) and texture. This is not surprising since astringency and bitterness are the two main descriptors of procyanidins.

Coffee sylverskin, a byproduct of coffee industry highly rich in PC, has been also evaluated to supplement baking products such as cookies [129] or cakes [117]. The supplementation with this byproduct had improved the functional quality of cookies by increasing their PC contents, antioxidant capacities and *in vitro* bioaccessibilities. However, all supplementation concentrations had lowered the consumers' flavor-taste scores and overall acceptability, which was attributed to the bitter taste of this food matrix.

The use of apple pomace has functional ingredient has been recently reviewed [130] and has been applied with success in several bakery products, namely bread, scones, cakes, and muffins. The addition of 5% of the apple pomace was found to not significantly impact the sensory properties of cookies [131].

5.2.2 Addition of PC to coffee

GS pomace (derived from Chardonnay winemaking), was evaluated to be used as a functional ingredient in brewed coffee [132]. This GS pomace could be added at 6.25% replacement without significantly affecting the overall consumer acceptance of coffee compared to the control (0%). These authors chose the GS pomace from a white grape variety because it has lower levels of tannins and no anthocyanins compared to red varieties, and so it can be expected a lower contribution to bitterness and astringency. In fact, not only astringency and bitterness did not increase upon replacement as it was observed their significant reduction for all replacement percentages in comparison to the control coffee. Although the authors do not discuss this result, one hypothesis is that the white grape varieties are also well-known for a higher content in sugar. Mouthf eel and texture, pancakes made with Cabernet Sauvignon (25% replacement) showed the lowest acceptance, significantly different from 30% replacement with a higher acceptance. This result suggested that the impact of GSF concentration was more apparent for in-mouth attributes mouthf eel and texture, pancakes made with Cabernet Sauvignon (25% replacement) showed the lowest acceptance, significantly different from 30% replacement with a higher acceptance. This result suggested that the impact of GSF concentration was more apparent for in-mouth attributes.

5.2.3 Addition of PC to pasta

Gaita and colleagues supplemented pasta with grape pomace [133]. These authors quantified the PC in control pasta and in the fortified one and showed an effective enhancement of PC levels. These increases were dependent on the pomace grape variety, but in general were effective for gallic, caffeic, ferulic and coumaric acids, rutin, and resveratrol. Moreover, the pasta samples with addition of pomace to a level of 3 and 6% showed improved sensory characteristics versus the control sample while the kneading and dough processing operations have not been affected.

5.2.4 Addition of PC to dairy products

Grape pomace of Chardonnay, Moscato and Pinot noir varieties has been used to supplement yogurt [116]. A total of nine PC were characterized in fortified yogurt depending on the origin of the grape pomace: phenolic acids (gallic acid, protocatechuic acid and vanillic acid); flavan-3-ols (procyanidin B1, catechin and epicatechin) and flavonols (rutin and quercetin). For most of these PC, they were stable at least for 21 days. Independently of the origin of grape pomace, all enriched yogurts add a lower liking score, especially regarding the organoleptic properties (flavor and taste). The Moscato yogurt was less accepted, with a very low mean liking score, particularly for taste and flavor. In contrast, Chardonnay was the sample with the highest mean scores for appearance, flavor and overall liking. Several informal attributes were reported by tasters such as "not enough sweet," with "unpleasant flavors", "not homogeneous" and "grainy/sandy." However, no correlation was found with the quantified PC.

Komes and colleagues used plant extracts (lemon balm, mint, lavender, rosemary and sage) for the development of functional and nutritively valuable goat's milk-based beverages [121]. The concentration of bioactive PC (rosmarinic acid, hydroxycinnamic acid derivatives and luteolin derivatives) were significantly increased in goat's milk in dependence of the added plant extract. While the extracts alone were found to be bitter and astringent, when added to the milk, some of the final beverages had acceptable levels of these two taste properties. However, the beverage enriched with lavender extract was characterized by the highest intensity of bitterness and astringency and thus consequently low overall acceptability. On the other hand, the beverage with mint extract was one of the preferred ones. Interestingly, this beverage was the one with the highest concentration of total PC, total flavonoids and antioxidant ability while was one of the less bitter and astringent beverages. This suggests that the profile of the PC present (not the concentration) should be the key to the perceived taste properties. At the end, apart from the accomplished bioactive enrichment and stability, the new functional beverages exhibited significantly enhanced sensorial properties when compared to plain goat's milk, with the highest overall satisfactoriness determined for samples fortified with mint and rosemary extracts.

5.2.5 Addition of PC to meat products

Tomato and derived-processed products generates considerable amount of by-products in the form of pomace, peel and seeds. They are rich sources of dietary fiber and bioactive compounds. In addition to carotenes, tomato by-products are rich in vitamins as well as PC, namely phenolic acids and flavonoids. Due to their color properties, these by-products have major applications in meat and meat-derived food products, as reviewed recently [134]. The higher antioxidant activity observed for tomato waste (composed by skin and seeds) has been related with the fact that this product had the highest phenolic and flavonoid amounts, in particular rutin, quercitrin and naringenin may be more efficient as antioxidant than carotenoids with respect to preventing lipid oxidation in pressurized chicken meat. Different researches have observed some general trends in the application of tomato by-products, namely improved nutritional quality, reduced lipid oxidation and increased stability during the shelf-life period of meat products, while maintaining or increasing sensory properties and general satisfactoriness.

Green tea extracts have been also used in meat products (e.g. raw beef and chicken patties). In raw beef and chicken patties, the tea catechins treatment resulted in no significant differences in the sensory flavor, taste, and tenderness [135]. Moreover, even only a marinade with green tea instead of enrichment of meat was found to reduce the formation of heterocyclic aromatic amines while bitterness and astringency perception was neglectable [136].

At the end, surprisingly, the sensory profile reported for green tea extract-supplemented meat products (turkey burgers [126], raw beef and chicken patties [135], pan-fried beef [136] as well as other food products (biscuits, cake [137]) is usually equal or superior to the control conditions (usually containing synthetic antioxidants). Since green tea extract is well-known for its bitter and astringent taste properties this could be probably due to interactions with the food matrix compounds, as discussed ahead.

5.3 Interactions of phenolic compounds with food macronutrients

In the human diet, PC are generally consumed in foods along with macronutrients (e.g. proteins, lipids and carbohydrates). The effect of interactions between PC and food constituents is a very important topic since they can have several implications on their sensory properties and lastly on their biological effects.

5.3.1 Interaction with proteins

In food matrices, PC interaction with proteins may affect their physicochemical properties, and consequently, their sensory characteristics. The sensory implications of PC interaction with proteins are not just centered on taste. Indeed, these interactions can also influence the appearance (e.g. haze, color), aroma and texture of food products.

One of the most known effect of this interaction is haze formation in some plant-based beverages like beer, wine and fruit juice [138]. Consumers expect that these beverages are clear (free of turbidity) and to remain so during the shelf life of the product. The development of haze in beverages results in the formation of insoluble particles of colloidal or larger size that can be detected visually. This is often noted as a negative attribute affecting their acceptance and the likelihood of this product to be purchased again. Astringency and bitterness are also affected by the development of haze. Indeed, red wine astringency can be reduced by the addition of some fining agents (ovalbumin, gluten proteins or yeast protein extract) which remove reactive compounds capable of haze formation [139]. Also, in beers, the interaction between PC and malt proteins causes haze and flocculation which can be modulated by adding some fining agents that will help in the process of clarification [140]. However, fining agents should be used appropriately as they could also compromise the flavor and the overall quality of the final product. Moreover, the use of fining agents can also remove a considerable amount of PC compromising their potential health benefits. Another example of PC interaction with proteins in beverages is the case of tea. In fact, tea astringency can be rectified by the addition of milk in which PC (flavan-3-ols) interact with milk proteins (casein and whey protein) [141].

Grace and colleagues [142] studied the effect of the fortification of soy protein isolate with concentrated PC-rich fruits and vegetables (muscadine grape and kale) by sensory analysis. These authors observed that the appearance of the incorporations had resulted in different colors, a purple-red powder for the incorporation with muscadine due to the presence of anthocyanins, and a mid-intensity green with kale caused by chlorophyll incorporation into the matrix. Also, panel evaluators indicated that unfortified protein formed clumps in the mouth, while the fortified muscadine and kale matrices presented a creamy consistency in the mouth. Furthermore, the panel evaluators mentioned that muscadine-protein matrix presented a pleasant flavor with delicate notes of grape aroma, slight astringency, no bitterness, and low sourness in comparison with unfortified soy protein. On the other hand, soy protein fortified with kale showed a reminiscent flavor of cooked beans, moderate sweetness, low sourness, and no bitterness.

In all these examples above mentioned, PC interact with proteins in food matrices, contributing to a lower amount of PC available to interact with oral cavity constituents, including salivary proteins, resulting in a decrease of astringency perception [143] and also bitter taste.

5.3.2 Interaction with lipids

Contrary to PC-protein interactions that have been widely studied, interactions with other food constituents such as lipids are lacking a deeper and comprehensive research. The main references to the interaction between PC and food lipids concern on plant oils, especially olive oil. Bitterness is a key sensory attribute in olive oil determining its acceptability. However, the lipid matrix composition seems to be a determinant factor on the perception of bitter taste. García-Mesa and colleagues [144] demonstrated that two virgin oil matrices spiked with the same level of PC were able to produce different effects on bitterness, depending on the degree of unsaturation of the olive oil matrix. The most unsaturated matrices resulted in softer sensations and reduced bitterness in comparison with the less unsaturated ones.

The interest on using PC as food additives in food lipid matrices has also been growing. Indeed, lipid oxidation is the main source for food quality deterioration and generation of undesirable odors and flavors, compromising shelf-life, changing texture and color and reducing the nutritional value of food [4]. The use of green tea catechins as food additives with antioxidant properties is a good tool to increase the shelf life and to decrease the susceptibility of oxidative damage of food products. Furthermore, as previously referred, tea PC are able to interact with milk proteins suggesting a good retention in the cheese matrix [145]. Giroux and colleagues [145] evaluated the effect of green tea extract enrichment on the texture and organoleptic properties of Cheddar cheese during storage. The main effects observed were a decrease in the typical cheddar flavor, an increase in the global flavor intensity and astringency, color changes and increase in hardness. Nevertheless, the impact of green tea enrichment was dependent on the concentration used.

5.3.3 Interaction with carbohydrates

The first evidence of the interaction between PC and carbohydrates can be observed in fruits in which they interact in plant cell wall. Several classes of PC have already been described to interact with carbohydrates such as anthocyanins, phenolic acids and procyanidins [143].

In the case of red wine, PC are the main contributors to color, astringency and bitterness. Several authors have reported that yeast mannoproteins interaction with PC have numerous effects on wine sensory properties, namely on color stabilization [146], reduction of astringency [147] and increased body and mouthfeel [148]. In fact, the formation of PC-carbohydrate complexes influences their association with salivary proteins leading to a decrease on astringency perception. The same reduction trend on astringency was observed for other matrices, in which soluble pectins were added to persimmon fresh juice, resulting in the complexation with soluble tannins [149]. The interaction between PC and carbohydrates depends on their structure and physicochemical properties (e.g., ionic character and viscosity). Indeed, carbohydrates which present higher viscosity can greatly affect sensorial properties. Peleg and coworkers [150] observed that the increase of viscosity of a PC-rich cranberry juice by the addition of carboxymethyl cellulose lowered the perceived astringency at 25 °C.

In conclusion, interactions between PC and macronutrients can occur in food items and impact their sensory properties. The design of new foods with high nutrient content, tasty and affordable could be a good tool to increase the consumption of these bioactive compounds. However, the creation of these foods without comprising quality, sensory properties and functionality remains a big challenge.

At the end, most of the studies based on supplementation of food products with extracts, or with food industry by-products rich in PC are somehow empiric approaches. They find an optimal dose of an extract, by-product or waste or able to have a high expected (functional/biological) activity while the negative side-effects (e.g. low loaf volume, undesirable taste properties and textural characteristics) are minimized. While this trial-error has led to some successful examples, the use of this knowledge by the food industry depends on a more systematic approach. A deep and extensive characterization of the PC profile of the extracts, by-products and wastes should be a critical point in these studies. Furthermore, consistent data regarding the binding of the PC with food matrix components, the effect of cooking practices as well as the final bioactivities are lacking. These topics will be a valuable tool to align tastiness to healthiness in a systematic and reliable way to aid food industry towards the development of functional and clean label food.

6. Conclusions

The consumption of plant-based foods, including fruits, seeds, cereals, vegetables, and derived foodstuffs, such as beverages, has been nowadays claimed to be beneficial for human health. This awareness has been shared not only by the scientific community but also by the general public. The increase in the prevalence of non-communicable diseases and particularly the immune reactions to food, prompted the establishment of nutritional recommendations to design functional and sustainable foods. In this framework, PC have a significant potential! However, attention should be paid to PC organoleptic properties, which can compromise the final consumer acceptance.

The potential use of PC on modulation of immune reactions to food has been recently explored. In this context, PC have a double potential, before and after the food intake. From one side, the recently discovered ability of PC to bind to food immunologic proteins, and general food macromolecules such as lipids, proteins or carbohydrates could influence their bioactivities opening a new way to explore the relationship between dietary PC and health outcomes. On the other side, the modulator effects of PC on enzymatic activity, cellular redox potential, cell signaling transduction pathways or cell proliferation, as well as the ability to bind to cell receptors, that have been demonstrated sets them as potent anti-inflammatory and antioxidant compounds.

Although significant progress has been made to deepen these interactions with food macromolecules and bioactivities, considerable attention should be paid to the astringency and bitter taste elicited by PC. At the end, no matter how healthy a food is, if it does not appeal to its consumer, it is unlikely to succeed.

Going beyond, constructing food systems to all and designing foods suitable for people with specific nutritional requirements must be a priority. Under this framework, the design of clean label functional foods containing PCs as modulators of immune reactions to food while impact positively the organoleptic and technological properties of food emerge as a new reality.

Acknowledgements

The authors would like to thank FCT for their contracts: RPG (SFRH/BPD/85293/2012), EB (CEECIND/01598/2018), SS (CEEIND/01265/2018). This work was performed under the frame of FEDER (Fundo Europeu de Desenvolvimento Regional) funds through the COMPETE 2020—Operacional Programme for Competitiveness and Internationalization (POCI), and by FCT—Fundação para a Ciência e a Tecnologia—in the framework of the PTDC/OCE-ETA/32287/2017 project.

Funding

This work received financial support from the European Union (FEDER funds through COMPETE POCI-01-0145-FEDER-30448) and National Funds (FCT, Fundação para a Ciência e Tecnologia) through project PTDC/SAU-NUT/30448/2017.

Author details

Catarina Bessa-Pereira, Ricardo Dias, Elsa Brandão, Nuno Mateus,
Victor de Freitas, Susana Soares* and Rosa Pérez-Gregorio*
LAQV-REQUIMTE Departamento de Química e Bioquímica, Faculdade de Ciências da Universidade do Porto, Porto, Portugal

*Address all correspondence to: susana.soares@fc.up.pt
and maria.gregorio@fc.up.pt

References

[1] Cassiday L. Clean label: The next generation. International News on Fats, Oils and Related Materials. 2017;28(8):6-10.

[2] Asioli D, Aschemann-Witzel J, Caputo V, Vecchio R, Annunziata A, Næs T, et al. Making sense of the "clean label" trends: A review of consumer food choice behavior and discussion of industry implications. Food Research International. 2017;99:58-71.

[3] Belščak-Cvitanović A, Durgo K, Huđek A, Bačun-Družina V, Komes D. Overview of polyphenols and their properties. Polyphenols: Properties, Recovery, and Applications: Elsevier; 2018. p. 3-44.

[4] Shahidi F, Ambigaipalan P. Phenolics and polyphenolics in foods, beverages and spices: Antioxidant activity and health effects – A review. Journal of Functional Foods. 2015;18:820-97.

[5] Gomes TM, Toaldo IM, da Silva Haas IC, Burin VM, Caliari V, Luna AS, et al. Differential contribution of grape peel, pulp, and seed to bioaccessibility of micronutrients and major polyphenolic compounds of red and white grapes through simulated human digestion. Journal of Functional Foods. 2019;52:699-708.

[6] Borges LL, Alves SF, Sampaio BL, Conceição EC, Bara MTF, Paula JR. Environmental factors affecting the concentration of phenolic compounds in Myrcia tomentosa leaves. Revista Brasileira de Farmacognosia. 2013;23(2):230-8.

[7] Pérez-Gregorio MR, Regueiro J, Simal-Gándara J, Rodrigues AS, Almeida DPF. Increasing the Added-Value of Onions as a Source of Antioxidant Flavonoids: A Critical Review. Critical Reviews in Food Science and Nutrition. 2014;54(8):1050-62.

[8] Ana Sofia Rodrigues DPFA, Jesus Simal-Gándara, Maria Rosa Pérez-Gregorio Onions: A Source of Flavonoids, Flavonoids - From Biosynthesis to Human Health. In: IntechOpen, editor.2017.

[9] Abdel-Shafy H, Mansour M. Polyphenols: Properties, Occurrence, Content in Food and Potential Effects. 2017. p. 232-61.

[10] Haminiuk CWI, Maciel GM, Plata-Oviedo MSV, Peralta RM. Phenolic compounds in fruits – an overview. International Journal of Food Science & Technology. 2012;47(10):2023-44.

[11] Nakatani N. Phenolic antioxidants from herbs and spices. BioFactors (Oxford, England). 2000;13(1-4):141-6.

[12] Hellwig V, Gasser J. Polyphenols from waste streams of food industry: valorisation of blanch water from marzipan production. Phytochemistry Reviews. 2020;19(6):1539-46.

[13] Ben-Othman S, Jõudu I, Bhat R. Bioactives from Agri-Food Wastes: Present Insights and Future Challenges. 2020;25(3):510.

[14] Dias R, Oliveira H, Fernandes I, Simal-Gandara J, Perez-Gregorio R. Recent advances in extracting phenolic compounds from food and their use in disease prevention and as cosmetics. Critical Reviews in Food Science and Nutrition. 2020.

[15] Arshadi M, Attard TM, Lukasik RM, Brncic M, da Costa Lopes AM, Finell M, et al. Pre-treatment and extraction techniques for recovery of added value compounds from wastes throughout the agri-food chain. Green Chemistry. 2016;18(23):6160-204.

[16] Teixeira A, Baenas N, Dominguez-Perles R, Barros A, Rosa E,

Moreno DA, et al. Natural bioactive compounds from winery by-products as health promoters: a review. Int J Mol Sci. 2014;15(9):15638-78.

[17] Fernandes PA, Le Bourvellec C, Renard CM, Nunes FM, Bastos R, Coelho E, et al. Revisiting the chemistry of apple pomace polyphenols. Food chemistry. 2019;294:9-18.

[18] Makarova E, Górnaś P, Konrade I, Tirzite D, Cirule H, Gulbe A, et al. Acute anti-hyperglycaemic effects of an unripe apple preparation containing phlorizin in healthy volunteers: a preliminary study. Journal of the Science of Food and Agriculture. 2015;95(3):560-8.

[19] Ghasemi K, Ghasemi Y, Ebrahimzadeh MA. Antioxidant activity, phenol and flavonoid contents of 13 citrus species peels and tissues. Pak J Pharm Sci. 2009;22(3):277-81.

[20] Zin MM, Borda F, Márki E, Bánvölgyi S. Betalains, total polyphenols, and antioxidant contents in red beetroot peel (Cylindra type). Progress in Agricultural Engineering Sciences. 2020.

[21] Pal CBT, Jadeja GC. Deep eutectic solvent-based extraction of polyphenolic antioxidants from onion (*Allium cepa* L.) peel. Journal of the Science of Food and Agriculture. 2019;99(4):1969-79.

[22] Silva P, Ferreira S, Nunes FM. Elderberry (*Sambucus nigra* L.) by-products a source of anthocyanins and antioxidant polyphenols. Industrial Crops and Products. 2017;95:227-34.

[23] Mahindrakar KV, Rathod VK. Ultrasonic assisted aqueous extraction of catechin and gallic acid from *Syzygium cumini* seed kernel and evaluation of total phenolic, flavonoid contents and antioxidant activity. Chemical Engineering and Processing-Process Intensification. 2020;149:107841.

[24] Salem BR. Use of tomato pomace, mango seed kernel and pomegrabate peels powders for the productionof functional biscuits. Zagazig Journal of Agricultural Research. 2020;47(4):1011-23.

[25] Papillo VA, Locatelli M, Travaglia F, Bordiga M, Garino C, Coïsson JD, et al. Cocoa hulls polyphenols stabilized by microencapsulation as functional ingredient for bakery applications. Food Research International. 2019;115:511-8.

[26] Horton R. Offline: Time to radically rethink non-communicable diseases. Lancet. 2019;393(10184):1922.

[27] Organization WH. Preventing noncommunicable diseases (NCDs) by reducing environmental risk factors. World Health Organization; 2017.

[28] Koch W. Dietary Polyphenols—Important Non-Nutrients in the Prevention of Chronic Noncommunicable Diseases. A Systematic Review. Nutrients. 2019;11(5):1039.

[29] Yu W, Freeland DMH, Nadeau KC. Food allergy: immune mechanisms, diagnosis and immunotherapy. Nature reviews Immunology. 2016;16(12):751-65.

[30] Prescott S, Allen KJ. Food allergy: riding the second wave of the allergy epidemic. Pediatric allergy and immunology. 2011;22(2):155-60.

[31] Rinninella E, Cintoni M, Raoul P, Lopetuso LR, Scaldaferri F, Pulcini G, et al. Food Components and Dietary Habits: Keys for a Healthy Gut Microbiota Composition. Nutrients. 2019;11(10):2393.

[32] Belkaid Y, Hand TW. Role of the microbiota in immunity and inflammation. Cell. 2014;157(1):121-41.

[33] Moszak M, Szulińska M, Bogdański P. You Are What You Eat-The Relationship between Diet, Microbiota, and Metabolic Disorders-A Review. Nutrients. 2020;12(4):1096.

[34] Nurmatov U, Devereux G, Sheikh A. Nutrients and foods for the primary prevention of asthma and allergy: systematic review and meta-analysis. Journal of Allergy and Clinical Immunology. 2011;127(3):724-33. e30.

[35] Lorenz P, Heinrich M, Garcia-Käufer M, Grunewald F, Messerschmidt S, Herrick A, et al. Constituents from oak bark (*Quercus robur* L.) inhibit degranulation and allergic mediator release from basophils and mast cells in vitro. Journal of Ethnopharmacology. 2016;194:642-50.

[36] Camps-Bossacoma M, Pérez-Cano FJ, Franch À, Untersmayr E, Castell M. Effect of a cocoa diet on the small intestine and gut-associated lymphoid tissue composition in an oral sensitization model in rats. Journal of Nutritional Biochemistry. 2017;42:182-93.

[37] Vesic J, Stambolic I, Apostolovic D, Milcic M, Stanic-Vucinic D, Cirkovic Velickovic T. Complexes of green tea polyphenol, epigalocatechin-3-gallate, and 2S albumins of peanut. Food Chemistry. 2015;185:309-17.

[38] Al-Hanish A, Stanic-Vucinic D, Mihailovic J, Prodic I, Minic S, Stojadinovic M, et al. Noncovalent interactions of bovine α-lactalbumin with green tea polyphenol, epigalocatechin-3-gallate. Food Hydrocolloids. 2016;61:241-50.

[39] Broekman HCH, Eiwegger T, Upton J, Bøgh KL. IgE – the main player of food allergy. Drug Discovery Today: Disease Models. 2015;17-18:37-44.

[40] Valenta R, Hochwallner H, Linhart B, Pahr S. Food allergies: the basics. Gastroenterology. 2015;148(6):1120-31.e4.

[41] Singh A, Holvoet S, Mercenier A. Dietary polyphenols in the prevention and treatment of allergic diseases. Clinical & experimental allergy. 2011;41(10):1346-59.

[42] Singh A, Holvoet S, Mercenier A. Dietary polyphenols in the prevention and treatment of allergic diseases. Clinical and experimental allergy: Journal of the British Society for Allergy and Clinical Immunology. 2011;41(10):1346-59.

[43] Chirumbolo S. Dietary assumption of plant polyphenols and prevention of allergy. Current pharmaceutical design. 2014;20(6):811-39.

[44] Dueñas M, Muñoz-González I, Cueva C, Jiménez-Girón A, Sánchez-Patán F, Santos-Buelga C, et al. A survey of modulation of gut microbiota by dietary polyphenols. BioMed research international. 2015;2015.

[45] Plundrich NJ, Cook BT, Maleki SJ, Fourches D, Lila MA. Binding of peanut allergen Ara h 2 with Vaccinium fruit polyphenols. Food Chemistry. 2019;284:287-95.

[46] Lu Y, Li S, Xu H, Zhang T, Lin X, Wu X. Effect of Covalent Interaction with Chlorogenic Acid on the Allergenic Capacity of Ovalbumin. Journal of Agricultural and Food Chemistry. 2018;66(37):9794-800.

[47] Li Y, Mattison CP. Polyphenol-rich pomegranate juice reduces IgE binding to cashew nut allergens. J Sci Food Agric. 2018;98(4):1632-8.

[48] Schülke S, Albrecht M. Mouse Models for Food Allergies: Where Do We Stand? Cells. 2019;8(6):546.

[49] Singh A, Demont A, Actis-Goretta L, Holvoet S, Lévêques A, Lepage M,

et al. Identification of epicatechin as one of the key bioactive constituents of polyphenol-enriched extracts that demonstrate an anti-allergic effect in a murine model of food allergy. The British journal of nutrition. 2014;112(3):358-68.

[50] Abril-Gil M, Pérez-Cano FJ, Franch À, Castell M. Effect of a cocoa-enriched diet on immune response and anaphylaxis in a food allergy model in Brown Norway rats. The Journal of nutritional biochemistry. 2016;27:317-26.

[51] Bansode RR, Randolph PD, Plundrich NJ, Lila MA, Williams LL. Peanut protein-polyphenol aggregate complexation suppresses allergic sensitization to peanut by reducing peanut-specific IgE in C3H/HeJ mice. Food Chem. 2019;299:125025.

[52] Pabst O, Mowat AM. Oral tolerance to food protein. Mucosal immunology. 2012;5(3):232-9.

[53] Lindfors K, Ciacci C, Kurppa K, Lundin KEA, Makharia GK, Mearin ML, et al. Coeliac disease. Nature Reviews Disease Primers. 2019;5(1):3.

[54] de Lorgeril M, Salen P. Gluten and wheat intolerance today: are modern wheat strains involved? International journal of food sciences and nutrition. 2014;65(5):577-81.

[55] Cabanillas B. Gluten-related disorders: celiac disease, wheat allergy, and nonceliac gluten sensitivity. Critical reviews in food science and nutrition. 2020;60(15):2606-21.

[56] Sturgeon C, Fasano A. Zonulin, a regulator of epithelial and endothelial barrier functions, and its involvement in chronic inflammatory diseases. Tissue Barriers. 2016;4(4):e1251384-e.

[57] Sollid LM. The roles of MHC class II genes and post-translational modification in celiac disease. Immunogenetics. 2017;69(8-9):605-16.

[58] Jabri B, Sollid LM. T Cells in Celiac Disease. J Immunol. 2017;198(8):3005-14.

[59] Yoosuf S, Makharia GK. Evolving Therapy for Celiac Disease. Front Pediatr. 2019;7:193-.

[60] García-Conesa MT, Larrosa M. Polyphenol-Rich Foods for Human Health and Disease. Nutrients. 2020;12(2).

[61] Dias R, Pereira CB, Pérez-Gregorio R, Mateus N, Freitas V. Recent advances on dietary polyphenol's potential roles in Celiac Disease. Trends in Food Science & Technology. 2020.

[62] Dias R, Brás NF, Fernandes I, Pérez-Gregorio M, Mateus N, Freitas V. Molecular insights on the interaction and preventive potential of epigallocatechin-3-gallate in Celiac Disease. Int J Biol Macromol. 2018;112:1029-37.

[63] Dias R, Brás NF, Pérez-Gregorio M, Fernandes I, Mateus N, Freitas V. A multi-spectroscopic study on the interaction of food polyphenols with a bioactive gluten peptide: From chemistry to biological implications. Food Chem. 2019;299:125051.

[64] Van Buiten CB, Yennawar NH, Pacheco CN, Hatzakis E, Elias RJ. Physicochemical interactions with (−)-epigallocatechin-3-gallate drive structural modification of celiac-associated peptide α2-gliadin (57-89) at physiological conditions. Food & Function. 2019;10(5):2997-3007.

[65] Buiten CBV, Lambert JD, Sae-tan S, Elias RJ. Inhibition of Gliadin Digestion by Green Tea Polyphenols and the Potential Implications for Celiac Disease. The FASEB Journal. 2017;31(1_supplement):974.23–.23.

[66] Van Buiten CB, Lambert JD, Elias RJ. Green Tea Polyphenols Mitigate Gliadin-Mediated Inflammation and Permeability in Vitro. Molecular nutrition & food research. 2018;62(12):1700879.

[67] Kramer K, Yeboah-Awudzi M, Magazine N, King JM, Xu Z, Losso JN. Procyanidin B2 rich cocoa extracts inhibit inflammation in Caco-2 cell model of in vitro celiac disease by down-regulating interferon-gamma- or gliadin peptide 31-43-induced transglutaminase-2 and interleukin-15. Journal of Functional Foods. 2019;57:112-20.

[68] Kumar Singh A, Cabral C, Kumar R, Ganguly R, Kumar Rana H, Gupta A, et al. Beneficial Effects of Dietary Polyphenols on Gut Microbiota and Strategies to Improve Delivery Efficiency. Nutrients. 2019;11(9).

[69] Parada Venegas D, De la Fuente MK, Landskron G, González MJ, Quera R, Dijkstra G, et al. Short Chain Fatty Acids (SCFAs)-Mediated Gut Epithelial and Immune Regulation and Its Relevance for Inflammatory Bowel Diseases. Frontiers in Immunology. 2019;10(277).

[70] Freire R, Ingano L, Serena G, Cetinbas M, Anselmo A, Sapone A, et al. Human gut derived-organoids provide model to study gluten response and effects of microbiota-derived molecules in celiac disease. Scientific reports. 2019;9(1):7029.

[71] Serena G, Yan S, Camhi S, Patel S, Lima RS, Sapone A, et al. Proinflammatory cytokine interferon-γ and microbiome-derived metabolites dictate epigenetic switch between forkhead box protein 3 isoforms in coeliac disease. Clinical and experimental immunology. 2017;187(3):490-506.

[72] Harpaz D, Yeo LP, Cecchini F, Koon THP, Kushmaro A, Tok AIY, et al. Measuring Artificial Sweeteners Toxicity Using a Bioluminescent Bacterial Panel. Molecules. 2018;23(10):2454.

[73] Chéron J-B, Marchal A, Fiorucci S. Natural Sweeteners. In: Melton L, Shahidi F, Varelis P, editors. Encyclopedia of Food Chemistry. Oxford: Academic Press; 2019. p. 189-95.

[74] Yang W, Zhou K, Zhou Y, An Y, Hu T, Lu J, et al. Naringin dihydrochalcone ameliorates cognitive deficits and neuropathology in APP/PS1 transgenic mice. Frontiers in aging neuroscience. 2018;10:169.

[75] Ma YB, Zhang JX, Zhou XQ, Jiang WD, Wu P, Liu Y, et al. Effect of tea polyphenols on flavour, healthcare components, physicochemical properties, and mechanisms of collagen synthesis in growing grass carp (*Ctenopharyngodon idella*) muscle. Aquaculture. 2021;534.

[76] Yang B, Jiang WD, Wu P, Liu Y, Zeng YY, Jiang J, et al. Soybean isoflavones improve the health benefits, flavour quality indicators and physical properties of grass carp (Ctenopharygodon idella). PLoS ONE. 2019;14(1).

[77] Dao T, Dantigny P. Control of food spoilage fungi by ethanol. Food Control. 2011;22(3-4):360-8.

[78] Amit SK, Uddin MM, Rahman R, Islam SR, Khan MS. A review on mechanisms and commercial aspects of food preservation and processing. Agriculture & Food Security. 2017;6(1):51.

[79] Ribes S, Fuentes A, Talens P, Barat JM. Prevention of fungal spoilage in food products using natural compounds: a review. Critical reviews in food science and nutrition. 2018;58(12):2002-16.

[80] Ofosu FK, Daliri EB-M, Elahi F, Chelliah R, Lee B-H, Oh D-H. New Insights on the Use of Polyphenols as Natural Preservatives and Their Emerging Safety Concerns. Frontiers in Sustainable Food Systems. 2020;4(223).

[81] Bouarab Chibane L, Degraeve P, Ferhout H, Bouajila J, Oulahal N. Plant antimicrobial polyphenols as potential natural food preservatives. Journal of the Science of Food and Agriculture. 2019;99(4):1457-74.

[82] Monente C, Bravo J, Vitas AI, Arbillaga L, De Peña MP, Cid C. Coffee and spent coffee extracts protect against cell mutagens and inhibit growth of food-borne pathogen microorganisms. Journal of Functional Foods. 2015;12:365-74.

[83] Sung SH, Kim KH, Jeon BT, Cheong SH, Park JH, Kim DH, et al. Antibacterial and antioxidant activities of tannins extracted from agricultural by-products. Journal of Medicinal Plants Research. 2012;6(15):3072-9.

[84] Granato D, do Prado-Silva L, Alvarenga VO, Zielinski AA, Bataglion GA, de Morais DR, et al. Characterization of binary and ternary mixtures of green, white and black tea extracts by electrospray ionization mass spectrometry and modeling of their in vitro antibacterial activity. LWT-Food Science and Technology. 2016;65: 414-20

[85] Friedman M, Henika PR, Levin CE. Bactericidal activities of health-promoting, food-derived powders against the foodborne pathogens Escherichia coli, Listeria monocytogenes, Salmonella enterica, and Staphylococcus aureus. Journal of food science. 2013;78(2):M270-M5.

[86] Liu Y, McKeever LC, Malik NS. Assessment of the antimicrobial activity of olive leaf extract against foodborne bacterial pathogens. Frontiers in microbiology. 2017;8:113.

[87] Gullon B, Pintado ME, Pérez-Álvarez JA, Viuda-Martos M. Assessment of polyphenolic profile and antibacterial activity of pomegranate peel (Punica granatum) flour obtained from co-product of juice extraction. Food Control. 2016;59:94-8.

[88] Friedman M. Antibacterial, antiviral, and antifungal properties of wines and winery byproducts in relation to their flavonoid content. Journal of agricultural and food chemistry. 2014;62(26):6025-42.

[89] Sagdic O, Ozturk I, Yilmaz MT, Yetim H. Effect of grape pomace extracts obtained from different grape varieties on microbial quality of beef patty. Journal of food science. 2011;76(7):M515-M21.

[90] Bevilacqua A, Ficelo S, Corbo MR, Sinigaglia M. Bioactivity of grapefruit seed extract against Pseudomonas spp. Journal of food processing and preservation. 2010;34(3):495-507.

[91] Jabri MA, Rtibi K, Ben-Said A, Aouadhi C, Hosni K, Sakly M, et al. Antidiarrhoeal, antimicrobial and antioxidant effects of myrtle berries (Myrtus communis L.) seeds extract. Journal of pharmacy and pharmacology. 2016;68(2):264-74.

[92] Kchaou W, Abbès F, Mansour RB, Blecker C, Attia H, Besbes S. Phenolic profile, antibacterial and cytotoxic properties of second grade date extract from Tunisian cultivars (Phoenix dactylifera L.). Food chemistry. 2016;194:1048-55.

[93] Čabarkapa IS, Sedej IJ, Sakač MB, Šarić LĆ, Plavšić DV. Antimicrobial activity of buckwheat (Fagopyrum esculentum Moench) hulls extract. Food and feed research. 2008;35(4):159-64--64.

[94] Liu Z, Pan Y, Li X, Jie J, Zeng M. Chemical composition, antimicrobial

and anti-quorum sensing activities of pummelo peel flavonoid extract. Industrial crops and products. 2017;109:862-8.

[95] Chen HW, Chang YW. Encapsulation of *Clitoria ternatea* extract in liposomes by synergistic combination of probe-type ultrasonication and high-pressure processing. Journal of Food Safety. 2020;40(6).

[96] Dalponte Dallabona I, de Lima GG, Cestaro BI, Tasso IDS, Paiva TS, Laureanti EJG, et al. Development of alginate beads with encapsulated jabuticaba peel and propolis extracts to achieve a new natural colorant antioxidant additive. International Journal of Biological Macromolecules. 2020;163:1421-32.

[97] Flores-Mancha MA, Ruíz-Gutiérrez MG, Sánchez-Vega R, Santellano-EstradaE,Chávez-MartínezA. Characterization of Beet Root Extract (*Beta vulgaris*) Encapsulated with Maltodextrin and Inulin. Molecules (Basel, Switzerland). 2020;25(23).

[98] Moccia F, Agustin-Salazar S, Berg AL, Setaro B, Micillo R, Pizzo E, et al. Pecan (*Carya illinoinensis* (Wagenh.) K. Koch) Nut Shell as an Accessible Polyphenol Source for Active Packaging and Food Colorant Stabilization. ACS Sustainable Chemistry and Engineering. 2020;8(17):6700-12.

[99] Liu F, Ma C, McClements DJ, Gao Y. Development of polyphenol-protein-polysaccharide ternary complexes as emulsifiers for nutraceutical emulsions: Impact on formation, stability, and bioaccessibility of β-carotene emulsions. Food Hydrocolloids. 2016;61:578-88.

[100] Chen X, Han Y, Meng H, Li W, Li Q, Luo Y, et al. Characteristics of the emulsion stabilized by polysaccharide conjugates alkali-extracted from green tea residue and its protective effect on catechins. Industrial Crops and Products. 2019;140:111611.

[101] Von Staszewski M, Ruiz-Henestrosa VMP, Pilosof AM. Green tea polyphenols-β-lactoglobulin nanocomplexes: Interfacial behavior, emulsification and oxidation stability of fish oil. Food Hydrocolloids. 2014;35:505-11.

[102] Dai T, Li T, Li R, Zhou H, Liu C, Chen J, et al. Utilization of plant-based protein-polyphenol complexes to form and stabilize emulsions: Pea proteins and grape seed proanthocyanidins. Food Chemistry. 2020;329.

[103] Zhu X, Chen Y, Hu Y, Han Y, Xu J, Zhao Y, et al. Tuning the molecular interactions between gliadin and tannic acid to prepare Pickering stabilizers with improved emulsifying properties. Food Hydrocolloids. 2021;111.

[104] Cebeci F, Şahin-Yeşilçubuk N. The matrix effect of blueberry, oat meal and milk on polyphenols, antioxidant activity and potential bioavailability. International Journal of Food Sciences and Nutrition. 2014;65(1):69-78.

[105] Wang R, Zhou W. Stability of tea catechins in the breadmaking process. Journal of Agricultural and Food Chemistry. 2004;52(26):8224-9.

[106] Najmanová I, Vopršalová M, Saso L, Mladěnka P. The pharmacokinetics of flavanones. Critical reviews in food science and nutrition. 2020;60(18):3155-71.

[107] Wang T, He F, Chen G. Improving bioaccessibility and bioavailability of phenolic compounds in cereal grains through processing technologies: A concise review. Journal of Functional Foods. 2014;7:101-11.

[108] Sęczyk Ł, Sugier D, Świeca M, Gawlik-Dziki U. The effect of in vitro digestion, food matrix,

and hydrothermal treatment on the potential bioaccessibility of selected phenolic compounds. Food Chemistry. 2020:128581.

[109] Lesschaeve I, Noble AC. Polyphenols: factors influencing their sensory properties and their effects on food and beverage preferences. Am J Clin Nutr. 2005;81(1):330S-5.

[110] Iriondo-DeHond M, Miguel E, Del Castillo MD. Food Byproducts as Sustainable Ingredients for Innovative and Healthy Dairy Foods. 2018;10(10):1358.

[111] Mildner-Szkudlarz S, Bajerska J, Zawirska-Wojtasiak R, Górecka D. White grape pomace as a source of dietary fibre and polyphenols and its effect on physical and nutraceutical characteristics of wheat biscuits. 2013;93(2):389-95.

[112] Šporin M, Avbelj M, Kovač B, Možina SS. Quality characteristics of wheat flour dough and bread containing grape pomace flour. Food science and technology international = Ciencia y tecnologia de los alimentos internacional. 2018;24(3):251-63.

[113] Ortega-Heras M, Gómez I, de Pablos-Alcalde S, González-Sanjosé ML. Application of the Just-About-Right Scales in the Development of New Healthy Whole-Wheat Muffins by the Addition of a Product Obtained from White and Red Grape Pomace. 2019;8(9):419.

[114] Acun S, Gül H. Effects of grape pomace and grape seed flours on cookie quality. 2014;6(1):81-8.

[115] Karnopp AR, Oliveira KG, de Andrade EF, Postingher BM, Granato D. Optimization of an organic yogurt based on sensorial, nutritional, and functional perspectives. Food Chem. 2017;233:401-11.

[116] Marchiani R, Bertolino M, Belviso S, Giordano M, Ghirardello D, Torri L, et al. Yogurt Enrichment with Grape Pomace: Effect of Grape Cultivar on Physicochemical, Microbiological and Sensory Properties. Journal of Food Quality. 2016;39(2):77-89.

[117] Ateş G, Elmacı Y. Coffee silverskin as fat replacer in cake formulations and its effect on physical, chemical and sensory attributes of cakes. LWT. 2018;90:519-25.

[118] Savadkoohi S, Hoogenkamp H, Shamsi K, Farahnaky A. Color, sensory and textural attributes of beef frankfurter, beef ham and meat-free sausage containing tomato pomace. Meat Science. 2014;97(4):410-8.

[119] Yadav S, Malik A, Pathera A, Islam Rayees U, Sharma D. Development of dietary fibre enriched chicken sausages by incorporating corn bran, dried apple pomace and dried tomato pomace. Nutrition & Food Science. 2016;46(1):16-29.

[120] Eyiler E, Oztan A. Production of frankfurters with tomato powder as a natural additive. LWT - Food Sci Technol. 2011;44(1):307-11.

[121] Komes D, Bušić A, Belščak-Cvitanović A, Brnčić M, Bosiljkov T, Vojvodić A, et al. Novel Approach to the Development of Functional Goat's Milk-Based Beverages Using Medicinal Plant Extracts in Combination with High Intensity Ultrasound Treatment. Food Technology and Biotechnology. 2017;55(4):484-95.

[122] Alongi M, Melchior S, Anese M. Reducing the glycemic index of short dough biscuits by using apple pomace as a functional ingredient. LWT. 2019;100:300-5.

[123] Jung J, Cavender G, Zhao Y. Impingement drying for preparing dried

apple pomace flour and its fortification in bakery and meat products. J Food Sci Technol. 2015;52(9):5568-78.

[124] Benvenutti L, Bortolini DG, Nogueira A, Zielinski AAF, Alberti A. Effect of addition of phenolic compounds recovered from apple pomace on cider quality. LWT. 2019;100:348-54.

[125] Mironeasa S, Iuga M, Zaharia D, Mironeasa C. Rheological Analysis of Wheat Flour Dough as Influenced by Grape Peels of Different Particle Sizes and Addition Levels. Food and Bioprocess Technology. 2019;12(2):228-45.

[126] Namal Senanayake SPJ. Green tea extract: Chemistry, antioxidant properties and food applications – A review. Journal of Functional Foods. 2013;5(4):1529-41.

[127] Sharma A, Zhou W. A stability study of green tea catechins during the biscuit making process. Food Chem. 2011;126(2):568-73.

[128] Rosales Soto MU, Brown K, Ross CF. Antioxidant activity and consumer acceptance of grape seed flour-containing food products. 2012;47(3):592-602.

[129] Gocmen D, Sahan Y, Yildiz E, Coskun M, Aroufai İA. Use of coffee silverskin to improve the functional properties of cookies. J Food Sci Technol. 2019;56(6):2979-88.

[130] Lyu F, Luiz SF, Azeredo DRP, Cruz AG, Ajlouni S, Ranadheera CS. Apple Pomace as a Functional and Healthy Ingredient in Food Products: A Review. 2020;8(3):319.

[131] de Toledo NMV, Nunes LP, da Silva PPM, Spoto MHF, Canniatti-Brazaca SG. Influence of pineapple, apple and melon by-products on cookies: physicochemical and sensory aspects. 2017;52(5):1185-92.

[132] Nguyen T, Kuchera M, Smoot K, Diako C, Vixie B, Ross CF. Consumer Acceptance of a Polyphenolic Coffee Beverage. 2016;81(11):S2817-S23.

[133] Gaita C, Alexa E, Moigradean D, Poiana M-A. Designing of high value-added pasta formulas by incorporation of grape pomace skins. Romanian Biotechnological Letters. 2018.

[134] Domínguez R, Gullón P, Pateiro M, Munekata PES, Zhang W, Lorenzo JM. Tomato as Potential Source of Natural Additives for Meat Industry. A Review. 2020;9(1):73.

[135] Mitsumoto M, O'Grady MN, Kerry JP, Joe Buckley D. Addition of tea catechins and vitamin C on sensory evaluation, colour and lipid stability during chilled storage in cooked or raw beef and chicken patties. Meat Science. 2005;69(4):773-9.

[136] Quelhas I, Petisca C, Viegas O, Melo A, Pinho O, Ferreira IMPLVO. Effect of green tea marinades on the formation of heterocyclic aromatic amines and sensory quality of pan-fried beef. Food Chem. 2010;122(1):98-104.

[137] Mildner-Szkudlarz S, Zawirska-Wojtasiak R, Obuchowski W, Gośliński M. Evaluation of Antioxidant Activity of Green Tea Extract and Its Effect on the Biscuits Lipid Fraction Oxidative Stability. 2009;74(8):S362-S70.

[138] Siebert KJ. Effects of protein-polyphenol interactions on beverage haze, Stabilization and analysis. J Agric Food Chem. 1999;47(2):353-62.

[139] Marangon M, Vincenzi S, Curioni A. Wine Fining with Plant Proteins. Molecules (Basel, Switzerland). 2019;24(11):2186.

[140] Aron PM, Shellhammer TH. A Discussion of Polyphenols in Beer Physical and Flavour Stability. J Inst Brew. 2010;116(4):369-80.

[141] Rossetti D, Bongaerts JHH, Wantling E, Stokes JR, Williamson AM. Astringency of tea catechins: More than an oral lubrication tactile percept. Food Hydrocolloids. 2009;23(7):1984-92.

[142] Grace MH, Yousef GG, Esposito D, Raskin I, Lila MA. Bioactive Capacity, Sensory Properties, and Nutritional Analysis of a Shelf Stable Protein-rich Functional Ingredient with Concentrated Fruit and Vegetable Phytoactives. Plant Foods for Human Nutrition. 2014;69(4):372-8.

[143] Kardum N, Glibetic M. Polyphenols and Their Interactions With Other Dietary Compounds: Implications for Human Health. Adv Food Nutr Res. 2018;84:103-44.

[144] García-Mesa JA, Pereira-Caro G, Fernández-Hernández A, García-Ortíz Civantos C, Mateos R. Influence of lipid matrix in the bitterness perception of virgin olive oil. Food Qual Prefer. 2008;19(4):421-30.

[145] Giroux HJ, De Grandpré G, Fustier P, Champagne CP, St-Gelais D, Lacroix M, et al. Production and characterization of Cheddar-type cheese enriched with green tea extract. Dairy Science & Technology. 2013;93(3):241-54.

[146] Gonçalves FJ, Fernandes PAR, Wessel DF, Cardoso SM, Rocha SM, Coimbra MA. Interaction of wine mannoproteins and arabinogalactans with anthocyanins. Food Chem. 2018;243:1-10.

[147] Quijada-Morin N, Williams P, Rivas-Gonzalo JC, Doco T, Teresa Escribano-Bailon M. Polyphenolic, polysaccharide and oligosaccharide composition of Tempranillo red wines and their relationship with the perceived astringency. Food Chem. 2014;154:44-51.

[148] Guadalupe Z, Martínez L, Ayestarán B. Yeast Mannoproteins in Red Winemaking: Effect on Polysaccharide, Polyphenolic, and Color Composition. American Journal of Enology and Viticulture. 2010;61(2):191.

[149] Taira S, Ono M, Matsumoto N. Reduction of persimmon astringency by complex formation between pectin and tannins. Postharvest Biol Technol. 1997;12(3):265-71.

[150] Peleg H, Noble AC. Effect of viscosity, temperature and pH on astringency in cranberry juice. Food Qual Prefer. 1999;10(4-5):343-7.