Polyphenols in food industry, nano-based technology development and biological properties: An overview

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REVIEW ARTICLE

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Polyphenols in food industry, nano-based technology development and biological properties: An overview

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Abstract

There is a growing interest in bioactive compounds particularly polyphenols as dietary sources, food ingredients with several putative beneficial activities such as antioxidant and antimicrobial properties. Understanding the underlying mechanisms of plant-derived phenolic compounds can substantially help develop solutions and technologies to better control and alleviate oxidative stress, inflammation, and consequently cancer. Studies have indicated that the loading of natural phytoconstituents into appropriate nanoparticles can develop and broaden biological applications. There is a wide range of applications derived from nanotechnology and nanomedicine through developing the packaging, preservation, and bioavailability of natural phytochemical. The present paper provides an overview and highlight on the importance and potential of natural polyphenols particularly in food and pharmaceutical industries. Furthermore, nanotechnology approaches, bioavailability, and potential adverse effects are also discussed.

KEYWORDS

bioavailability, food industry, nanotechnology, polyphenolic compounds

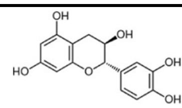
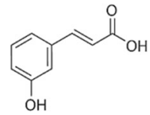
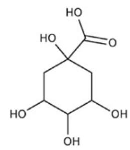
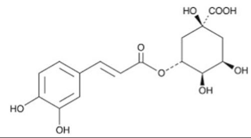
1 | INTRODUCTION

Herbal medicines are attracting further attentions—thanks to high efficacy against a wide range of diseases (Cohen, 2000). Over the past decades, many studies were mainly focused on plant active ingredients, given the capacity to improve human health (Valdés et al., 2015). Polyphenols, secondary metabolite biosynthesized by higher plants, are known for potential health attributions to mitigate a variety of human disorders. Accompanied by enzymes and other subcellular molecules, polyphenols play important roles in preventing degenerative, cardiovascular, and neurodegenerative diseases with the capacity to act as antioxidant, anallergic, anti-inflammatory, antitumor, anti-infective, and antihypertensive agents (Daglia, 2012). The Chemical structure and characteristics of selected phenolic compounds as discussed in the present review paper have been listed in the Table 1.

2 | NATURAL POLYPHENOLS

Plants have historically played a key role in man's life, for instance, medical communities used beneficial plants for a variety of medicinal purposes (Shahidi & Ambigaipalan, 2015). Phytochemicals including phenolic compounds are basically plant-derived compounds which can be found in fruits, vegetables, beans, cereals, and plant-based beverages, for example, tea and wine, and it is believed to have a protective role against diseases (Asif, 2015). Herbal foods, with wide range of structures, naturally contain compounds like polyphenols (Dragovic-Uzelac et al., 2007). Despite different classifications made on polyphenols based upon origin, biological function, and chemical structure (Tsao, 2010), there are two main categories being the focus of the present review; phenolic acids/alcohols and phenolic flavonoid/nonflavonoid groups. Polyphenols are the biggest group of phytochemicals that are biologically

TABLE 1 Chemical structure and characteristics of selected phenolic compounds.

Compound	Chemical name	Classification	Formula	Molar mass (g/mol)	Structure
Catechin	Flavan-3-ol	Flavonoid	$C_{15}H_{14}O_6$	290.26	
m-Coumaric acid	3-Hydroxycinnamic acid	Phenolic acid	$C_9H_8O_3$	164.16	
Quinic acid	Cyclohexanecarboxylic acid	Phenolic acid	$C_7H_{12}O_6$	192.17	
Chlorogenic acid	3-(3,4-dihydroxycinnamoyl) quinic acid	Polyphenol	$C_{16}H_{18}O_9$	354.31	

active compounds, and widely recognized in herbal diet with substantial roles in the protection mechanism upon infectious agents, and abiotic stresses, that is, ultraviolet (UV) radiation and precipitation (Dragovic-Uzelac et al., 2007). There is a diverse function of phenolic compounds in plants, for example, contributing to the colors of fruits and leaves, protecting plants from herbivores, attracting or repeling bugs, encouraging pollination and seed dispersal and protecting agents against UV light (Nichenametla et al., 2006). In human diet, phenolic compounds are related to characteristics of taste, palatability, nutritional value, and acceptability of fresh and processed food (Stintzing & Carle, 2004). Flavonoid groups have similar carbon skeleton of diphenyl propanes and two benzene rings (Ring A and B) linked with a linear three-carbon chain. Approximately 4000 flavonoids have so far been identified in plants. The major nonflavonoid groups include the phenolic acids which are derived from benzoic acid, and include protocatechuic, gallic, caffeic, coumaric, and ferulic acids, all of which are major derivatives of cinnamic acid, second stilbenes and third lignans that are chemically available in *cis*- and *trans*-isomeric forms made by phenylpropane units oxidative dimerization (D'Archivio et al., 2007; Fiorentino et al., 2007). One of the major polyphenolic compounds, widely used today, is hydroxycinnamic acid that belong to the phenolic acid groups and can be found in almost all plants. Caffeic acid is the major indicative of hydroxycinnamic acids which is mostly present in foods in the form of ester with quinic acid and chlorogenic acid (Clifford, 2004; Rice-Evans et al., 1996). Composition of chlorogenic acid in daily coffee drinkers is 0.5–1 g, though coffee abstainers normally ingest <100 mg/day and excess typically enter the blood in the colon (Olthof et al., 2001). Other polyphenolic compounds exhibit major functions in human health. For instance, the extraction of active ingredients from green tea can significantly reduce most of the oxidation indices (Jongberg et al., 2013). Examples are lipid oxidation and carbonyls formation in Bologna-type sausages that were significantly reduced, without any effects on thiol and protein crosslinks (indicators of proteins oxidation) (Ahmad et al., 2015). Olive leaf is another polyphenol-rich source mostly made up of eleuropein, tyrosol, caffeic acid, and hydroxytyrosol with antimicrobial properties (Jafari et al., 2017).

3 | PHENOLIC ACIDS

Phenolic acids that are nonflavonoid polyphenolic compounds can be categorized in two major groups; cinnamic acid and benzoic acid which are subordinates of C1–C6 and C3–C6 backbones. Free phenolic acids and grains are abundantly exist in fruit and vegetables and bran or hull bound-shaped phenolic acids are plentiful in seeds (Adom & Liu, 2002; Chandrasekara & Shahidi, 2010; DellaGreca et al., 2007; Kim et al., 2006). Although the amount of hydroxybenzoic acid in edible plants is not very high, several tens of milligrams per kilogram fresh weight can be found in onions, black radish, and specified red fruits (Shahidi & Naczk, 1995). In addition, intricated structures such as hydrolyzable tannins are exist in hydroxybenzoic (ellagitannins in red fruit like strawberries, blackberries and raspberries, and gallotannins in mangoes) (Clifford & Scalbert, 2000). Caffeic, ferulic, *p*-coumaric, and sinapic acids are constituent of hydroxycinnamic acids and are more abundant than hydroxybenzoic acids. Quinic acid esters, glycosylated derivatives, tartaric acid, and shikimic acid are the linked forms. Chlorogenic acid is found in majority of fruits and is abundant in coffee, for instance, a single cup may contain between 70 and 350 mg chlorogenic acid, caffeic, and quinic acid (Clifford, 1999).

4 | FLAVONOIDS

Common structures of flavonoids are C6–C3–C6, in which both C6 units in Ring A and Ring B possess a phenolic nature. Flavonoids are typically classified into anthocyanins, flavones, flavanones, flavan-3-ols and flavonols based upon chromane ring, Ring C alterations and the hydroxylation pattern. The Ring B in most flavonoids are attached to the Ring C and C2 position, however, few flavonoids such as neoflavonoids and isoflavones have the Ring B linked with Ring C, C3 and C4 positions (Tsao, 2010). An important subclass of flavonols are kaempferol and quercetin typically known as the most frequent flavonoids present in diet. They exist at relatively small magnitude of 15– 30 mg/kg fresh weight. Onions (up to 1.2 g/kg fresh wt), boroccoli, curly kale, blueberries and leeks are the most abundant sources (Macheix & Fleuriet, 1990). The Ring B in Isoflavones is connected to C3 position of Ring C which are mostly present in the leguminous family of plants. Beans, particularly soybean are rich in two major isoflavones, that is, daidzein and genistein, along with biochanin A, formononetin, and glycetein (Mazur et al., 1998; Wang & Murphy, 1994).

5 | DIFFERENCE IN POLYPHENOL CONTENT OF FOOD

Substantial resources for polyphenols are beverages and fruits like red wine and tea. Polyphenols such as quercetin can be found in all plant-based products, that is, vegetables, cereals, fruits, legumes, tea, fruit juices, wine, infusions, and so forth but, others are peculiar to particular foods, that is, phloridzin in apples, isoflavons in soya, and flavanones in citrus fruit. Often times, the combination of polyphenols in food is complex and little is known. Most literature report flavanol monomers (epicatechin) or oligomers (procyanidin B2), chlorogenic acid and small quantities of other hydroxycinnamic acids, two glycosides of phloretin, quercetin glycosides, and anthocyanins such as cyanidin 3-galactoside in the skin of certain species of red apples. Diversity of polyphenol composition in different apples has been widely investigated. The polyphenol profiles in different species of apples are essentially the same, but their level may vary between 0.1 and 5 g total polyphenols/kg fresh weight and may be as much as 10 g/kg in cider apples (Guyot et al., 1998; Sanoner et al., 1999). The composition of the polyphenol is less recognized in many plants and the data are mostly bounded to one or few species and sometimes do not have eatable groups. Exotic fruits and cereals have not been analyzed yet. The polyphenol content of plants is dependant upon other parameters, that is, environmental factors, the level of ripeness at the harvest time, storage and processing, among which, environmental factors play essential role. These agents may be pedoclimatic (sun exposure, soil type, rainfall) or agronomic (culture in hydroponic culture, greenhouses or fields fruit yield per tree, biological culture etc.). Disposal to light has also a serious impact on flavonoids and the ripeness rate remarkably affect the concentration and proportion of the various polyphenols (Macheix & Fleuriet, 1990). It is a difficult task to specify a certain amount of polyphenol per each family of plants, in that, an immense magnitude of analysis is needed to collect such data. For instance, the *p*-coumaric acid content analyses in 500 red wines demonstrated genetical factors were more important than exposure to light (Clifford, 2000). Industrial food processing is another factor that defines the content of polyphenols whilst legume seeds dehulling fruit peeling and bolting and decoration of cereals can damage and affect polyphenols content. Given the contact among cytoplasmic polyphenol oxidase (PPO) and phenolic substrate of vacuoles, the grinding of plant tissues may incite oxidative damage of polyphenols. In such cases, polyphenols are changed into pigments that are brown and have various degrees of polymerization like during the procedure of making jam or fruit canning. Because of the fact juicing requires clarification or stabilization steps, particular flavonoids take account of haze formation and discoloration are then removed. For this reason, manufactured juices contain low flavonoid content. The esters of hydroxycinnamic acid are typically hydrolyzed by pectinolytic enzymes during processes (Rice-Evans & Miller, 1996).

6 | INTESTINE ABSORPTION AND METABOLISM

The mechanism of intestinal absorption and metabolism is not very well known. It is demonstrated that abundant hydrophilic properties of polyphenols can pass through cell walls of intestinal tracks via passive diffusion. In case of ferulic and cinnamic acid, the mechanism of uptake in the jejunum of rat is based upon Na^+-dependent active transport (Ader et al., 1996). All flavonoids in human diet, but for flavanols, appear as glycosylate thus influencing absorption. Some surgically treated rats have been used to demonstrate the possible absorption of some flavonoids such as quercetin and daidzein in the gastric level, but not their glycosides level (Crespy et al., 2002; Piskula et al., 1999). Aglycones and some glucosides are the only compounds that small intestine can absorb, whilst polyphenols linked to a rhamnose moiety ought to reach the colon, therefore, rhamnosidases of the microflora hydrolyze them before absorption (Hollman & Katan, 1997; Manach et al., 1995). Given the smaller exchange area and lower density of transport systems, the nutrients absorption occurs less promptly in the colon than small intestine, however, the absorption of glycosides with rhamnose are lower. The highest absorption in human occurs 0.5–0.7 h after ingestion of quercetin 4′-glucoside and 6–9 h after the ingestion of the same quantity of rutin (quercetin-3-rutinoside). The bioavailability of rutin is only 15%–20% compared to quercetin 4′-glucoside (Graefe et al., 2001; Hollman et al., 1999). Polyphenol absorption relies on preferences and dietary habits. About one-third of total phenols is depend on phenolic acids, and two thirds on flavonoids. It is most likely that individuals who heavily drink coffee take further phenolic acids than flavonoids. The absorption of flavones, isoflavones, and flavonols is moderately lower than that of phenolic acids and other flavonoids, and oxidized polyphenols. Polyphenols are abundant in chocolate, and even a little intake of chocolate may considerably impact on absorption of total polyphenol and more specifically on the catechin (Arts et al., 1999).

7 | BASIC CHALLENGES IN POLYPHENOLS INVESTIGATION

Phenolic compounds, particularly flavonoids, are an important constituent in human cuisine. Quercetin, genistein, daidzein, kaempferol, apigenin, lutelin, biochanin, and myricetin are few to name amongst others. The concentration of plant-derived phenolic compounds in the human cuisine may substantially vary. For example, edible parts of vegetables and fruits typically contain 10 mg/kg of quercetin (Hertog et al., 1992). There are multiple factors that can potentially influence and transform the bioavailability of phenolic compounds in the human body, such as sulfation, glucuronidation, metabolization, and methylation (Bravo, 1998). Despite the complications of using polyphenol compounds, in vitro and in vivo studies have shown as the best therapeutic target for use in the market (Balentine et al., 2015). It is, therefore, of prime importance to choose the best dose of polyphenolic compounds so that desirable health effects can be achieved (Smoliga et al., 2012). It is obviously required to conduct further studies to detect the optimal doses needed. For instance, quercetin may be an effective compound against various illnesses, despite the fact that the addition of quercetin to long-term diet can lead to further decrease in the lifetime of mice (Jones & Hughes, 1982). Given the complex reactions that may occur over the course of food processing, one should be aware of polyphenol interactions with other food ingredients, such as dietary fibers or proteins (Gleichenhagen & Schieber, 2016), as such compounds have paradoxically illustrated pro-oxidant (generating oxygen radical) properties rather than antioxidant features which is therefore of a particular concern when incorporating into industrial applications (Andarwulan et al., 2010; Boots et al., 2008; Gülçin, 2010; Lamson & Brignall, 2000; Obied, 2013; Olas et al., 2001; Scalbert et al., 2005). Concentrations of polyphenolic compounds in the gastrointestinal tract is adequate to produce in vivo reactive oxygen species (ROS) as a result of their pro-oxidants activity (Halliwell, 2008). Polyphenolic compounds are also recognized as prooxidants which indicates the over use of such compounds as a down regulator of endogenous antioxidants (Halliwell, 2011).

7.1 | Nanotechnology approach in food preservation

Nanotechnology is a novel field that has attracted great attention and the prospective applications of this concept in food crafts has been extensively scrutinized its potential applications in food industry. Size and physicochemical features of nanoparticles with dimensions ranging between 1 and 100 nm are the advantages of polyphenols as active compounds. There are however disadvantages when incorporated as functional food ingredients, such that low solubility, bioavailability, and stability (Milinčić et al., 2019). The history of using the fundamentals of so-called nanotechnology techniques in food industry dates back to few decades ago. Examples are low-fat products like mayonnaise from emulsified fat droplets dilution by containing water droplets that are in nano size (Chaudhry & Castle, 2011). Nanotechnology is an important tool and an efficient option of nanoparticle uses in industry such as cosmetics, food additives, food processing, food safety, functional foods, and detection techniques of foodborne pathogens (Ranjan et al., 2014). To observe and manipulate matters at the nanoscale, the produced nanomaterials have an inner structure or further external dimensions on 1–100 nm scale. Unlike their macroscale counterparts, such materials have unique properties such as thermodynamic, solvability, color, rigidity, toxicity, diffusivity, ocular, magnetic features owing to their exquisite physiochemical features and great ratio of surface to volume (Franci et al., 2015). To increase the absorption of bioactive compounds in the gastrointestinal tract through active endocytosis or enhance bioactivity in circulation of body via particular spot, the nanoparticle delivery system encapsulates and is delivered by nanocarriers. The incorporation of ingredients, colors, polyphenols, fugacious additives, bacteria, and enzymes in little capsules can therefore stabilize, and secure them from processing, health and nutritional damages as a unique way in food industries (Ghorbanzade et al., 2017). In a survey, the sensory and physicochemical quality of yogurt samples with nano-encapsulated fish oil with nano-liposomes indicated that properties were closer to control sample in terms of sensory attributes in yogurt with fish oil than free fish oil yogurt. In a similar experiment curcumin isolated from turmeric (*Curcuma longa*) showed a decreased amount of antioxidant activity and remained resistant after pasteurization (Sari et al., 2015). The preparation of nanocapsules with curcumin have been described to be the one-pot procedure for the milliard reaction prevention in milk model (Olas et al., 2001). In another study, Coradini et al. (2014) introduced the curcumin and resveratrol coencapsulation in nanocapsules of pcl/grape seed oil (polymer/oil). To measure cassava starch films as recyclable coverage, another study evaluated the incorporation of lycopene-PCL nanocapsules (Assis et al., 2017) or peppermint oil as a plant extract was applied—thanks to antimicrobial properties in which PCL nanocapsules were filled with lutein via the interfacial deposition technique (Brum et al., 2017). Nanotechnology can also enhance other properties and contribute to the generation of stronger colorings, flavorings, nutritional additives, lower cost of processing and/or ingredients (Ingale & Chaudhari, 2018). For instance, the unfavorable activities of PPO and pectin methyl esterase in crisp apples can be controlled through an additive with great potential for utilizing in the production of nano coatings. The encapsulation of α-tocopherol indicated enhanced effects on nopal mucilage—thanks to activity of α-tocopherol in the nanoemulsion system. Nanoemulsion of nopal mucilage and α-tocopherol in submicrometer size are the reason for firmness and color preservation during refrigeration (Saxena et al., 2017). Carotenoids, as a food additive, are sensitive to oxygen, light and auto-oxidation impacts. In addition, they are almost unstable in food (Guadarrama-Lezama et al., 2014). It is therefore essential to first encapsulate the desired compounds in a delivery before incorporation into the food system. Alongside with carotenoids, polyunsaturated fatty acids such as omega-3 fatty acids and conjugated linoleic acid (CLA) have multiple beneficial effects on health. Examples of physiological effects associated with of omega-3 fatty activity include lowering the risk of cardiovascular disorder, helping the growth of infants and reducing immune and mental response problems (Ishak et al., 2017). There are also multiple functions associated with CLA, that is, growth progression, reduce atherosclerosis severity, and antagonizing the influences of immune system incitement (Dhabhar et al., 1994). There are various legally permissive supplements in cuisines such as citric acid, nitrites, acetic acid, sulfites, lactic acid, sorbic acid, benzoic acid, sodium diacetate, sodium benzoate, methyl and ethyl paraben, sodium propionate, and propyl paraben, which are chemical additives frequently used in food crops as food preservatives (Smith & Hong-Shum, 2011). There are nanomaterials with antimicrobial characteristics that could damage the integrity of bacteria membrane through electrostatic interaction. Furthermore, free radical made by nanoparticles can enforce oxidative stress, damage DNA, membrane, and mitochondria of the bacterial cells (Hajipour et al., 2012). The susceptivity of various microorganisms to nanomaterials is varied because of several phenomena as follows: (i) the structure of the cell wall in bacteria, the hydrophobicity, hydrophilicity and presence of external layer charge; (ii) the likelihood and potential to form biofilm, as pathogenic species tend to form biofilm; (iii) growth rate: fast-growing bacterial species are less resistant to NPs compared to slow-growing species. Such phenomena is due to the lack of stress-response genes.

Nano antimicrobials with high bactericidal properties are typically categorized into two groups: organic-based materials that mostly contain nanostructured chitosan and inorganic nano antimicrobials like silver, zinc oxide, titanium dioxide, nanoclys, copper nanomaterial, and carbon nanotubes. The low bioavailability and solubility and interaction ability with food ingredients are characteristics of antimicrobial agents (Carmona-Ribeiro & de Melo Carrasco, 2014). With nanocarriers, it is feasible to preserve antimicrobials from activity loss as undesirable interactions with other components in cuisine are inevitable. Furthermore, nanocarriers can enhance bioavailability, solubility, and consistency during food processing and help sustain volatile antimicrobial compounds (Hosseini et al., 2017). Nanoencapsulation could be employed as a technique to improve the viability of probiotics—an essential feature for such category and maintain therapeutic effects that is, suppression of food-borne pathogens, during food processing, storage, and gastrointestinal transition (Shukla, 2012). Functional features of food such as antimicrobial and antioxidant activity or physicochemical properties can be improved upon using nanoparticle, which contains phenolic compounds, during food process. A beneficial method for protecting the active compounds features during food consumption and processing is nanoencapsulation (Sarkar et al., 2017). Furthermore, for the purposes of quality and safety control, nanotechnology-based sensor systems have been progressed as realistic solutions rather than conventional analytical methods (Zhang & Chen, 2019).

8 | POLYPHENOLS AS ANTIMICROBIAL AGENTS

Over the past two decades, secondary metabolites, particularly polyphenols, have been extensively investigated and held promises to provide an alternative solution to curing chronic illnesses (i.e., as cardiovascular disease, cancer, osteoporosis, diabetes mellitus, and neurodegenerative diseases). Such capacity is firstly attributed to properties such as free radical scavenging, antioxidative, and metal chelating activities in such class of compounds and secondly the ability to prohibit and/or reduce a variety of enzymes, such as telomerase (Naasani et al., 2003), cyclooxygenase (Hussain et al., 2005; O'Leary et al., 2004), or lipoxygenase (Sadik et al., 2003; Schewe et al., 2001). Furthermore, the interaction of polyphenols with cell receptors and signal transduction pathways have recently gained momentum and a large body of information continue to shed lights on mechanistic pathways—thanks to advanced analytical techniques and recent progress made in molecular biology (Kong et al., 2000; Spencer et al., 2003; Wiseman et al., 2001). The antimicrobial effects of flavonols, tannins, and flavan-3-ols have also been extensively investigated in many microorganisms. Recent evidence also suggests a synergism with antibiotics which, in principle, can inhibit a number of microbial virulence factors. Examples are the neutralization of bacterial toxins, the suppression of biofilm formation, and host ligands adhesion's decrement. To ignore the synthetic preservatives or progress creative remedy for different microbial infectious treatment (Jayaraman et al., 2010; Saavedra et al., 2010), the antimicrobial properties of such class of polyphenols have been suggested to be used for developing new food preservatives (Rodríguez Vaquero et al., 2010) and is expected to ultimately contribute to the expansion and introduction of new food preservatives. The polyphenol compounds and their bactericidal properties are summarized in Table 2.

9 | USING POLYPHENOLS AS A NOVEL STRATEGY IN CORRELATION WITH ANTI-INFECTIVE DRUGS

Infectious diseases are one of the leading accounts for morality in human. Overusing drugs like antibiotics creates health-related problems such as antibiotic resistance in bacteria, viruses or parasites and induce biofilm formations. This could ultimately leads to a series of disease like AIDS, gonorrhea, malaria, pneumonia, influenza, diarrhea, tuberculosis, and chronic infections (Daglia, 2012). Antibiotics can kill bacteria or/and other microorganisms or suppress cell growth and reproduction (Martinez, 2009). Few studies have reported a novel strategy in which secondary metabolites such as polyphenols act as inhibitory compounds against fungi, phytophagous insects, and/or bacteria with enhanced efficacy, thereby can decrease antibiotic dosage and subsequently alleviate side-effects thereafter (Coutinho et al. 2008, 2009; Garo et al., 2007). The synergistic effects of flavonols in association with rifampicin antibiotic was illustrated against clinical rifampicin-resistant methicillin-resistant *Staphylococcus aureus* (MRSA) isolates (Lin et al., 2008). By only utilizing flavonols (kaempferol and quercetin), a slight β-lactamase inhibition was observed, however, when combined with rifampicin antibiotic, the inhibitory properties increased upto 57.8% and 75.8%, respectively (Bernard et al., 1997). Other research have investigated the synergistic effects of epigallocatechin gallate (EGCG)[1] in combination with various β-lactam antibiotics against MRSA (Hu, Zhao, Asano, et al., 2002; Hu, Zhao, Yoda, et al. 2002; Stapleton, Shah, Anderson, et al., 2004; Stapleton, Shah, Hamilton-Miller, et al., 2004). Another study reported the presence of five main compounds of gallocatechin gallate, EGCG, EGC, epicatechin, and ECG, in different percentages, in the extraction of polyphenol from green tea with antibacterial properties against 17 strains of methicillin-susceptible *S. aureus* and 13 of clinical MRSA isolates (Cho et al., 2008).

10 | BIOAVAILABILITY OF DIETARY POLYPHENOLS

Polyphenol is believed to be the most abundant antioxidant in human diet and their structural variability affect the bioavailability (Manach et al., 2004). The biological attributions of polyphenols are affected by consumption amount and bioavailability. Among the various polyphenols, bioavailability seems to greatly vary and the most common polyphenols in human's diet are not necessarily those leading to the most concentrations of active metabolites in target tissues (Manach et al., 2005). Both phenolic acids isoflavones and, like gallic acid and caffeic acid, followed by catechins, flavanones, and quercetin glucosides are the most well absorbed polyphenols but with diverse kinetics. The large molecular weight polyphenols are least absorbed polyphenols such as the galloylated tea catechins, proanthocyanidins, and the anthocyanins (Gonthier et al., 2003). A rise in flavanols absorption such as catechins is reported when tea polyphenols were managed as a capsule rather than consumption as black or green tea (Chow et al., 2005; Henning et al., 2004). When polyphenols reach the colon, they are metabolized via the microflora into a vast low molecular weight phenolic acids arrangement. Total metabolites of plasma concentrations with the comparative urinary exclusion ranged between 0.3% and 43% of the ingested dose and ranged between 0 and 4 μmol/L with an absorbance of 50 mg aglycone equivalents which is basically dependant on the polyphenol (Manach et al., 2005).

11 | ANTIOXIDANT ACTIVITY OF POLYPHENOLS

There is a large body of literature that indicates a wide range of diseases are related to oxidative stress due to reactive oxygen and nitrogen species. Polyphenols were claimed to be more effective to the antioxidant

[1] Epigallocatechin gallate.

TABLE 2 Antimicrobial effect of polyphenols (Daglia, 2012).

Polyphenol	Effect	
Flavan-3-ol flavonol	Antibacterial	*Vibrio cholerae–Streptococcus mutans–Campylobacter jejuni* *Clostridium perfringens–Escherichia coli–Bacillus cereus* *Helicobacter pylori–Staphylococcus aureus–Lactobacillus acidophilus* *Actinomyces naeslundii–Prevotella oralis–Porphyromonas gingivalis–Prevotella melaninogenica–Fusobacterium nucleatum–Chlamydia pneumoniae*
	Antiviral	Adenovirus–Enterovirus–Flu virus
	Antifungal	*Candida albicans* *Microsporum gypseum* *Trichophyton* *Mentagrophytes* *Trichophyton rubrum*
Condensed tannins	Antibacterial	*S. mutans* *E. coli* *S. aureus*
	Antiviral	influenza A virus type-1 herpes simplex virus (HSV)
Hydrolysable tannins	Antibacterial	*Salmonella–Staphylococcus–Helicobacter–E. coli–Bacillus clostridium–Campylobacter lysteria*
	Antiviral	Epstein–Barr virus Herpes virus HSV-1 and HSV-2
	Antifungal	*Candida parapsilosis*
Phenolic acid	Antibacterial	*S. aureus–Listeria monocytogenes* *E. coli–Pseudomonas aeruginosa*
Neolignan	Antibacterial	*Mycobacterium tuberculosis*

activities in fruits than vitamin C (Wang et al., 1996). Polyphenol compounds can be appeared as a vigorous antioxidant and can also neutralize free radicals by giving a hydrogen atom or electron. Certain hydroxylation patterns and the highly conjugated system as in 3-hydroxy group in flavanols, are identified to be pivotal in the antioxidant activities. The generation of free radicals are typically induced by the repression of polyphenol, thereby decrease the oxidation's rate through prohibiting the formation of free radicals precursors and deactivation of the radical species. A such, polyphenols play as an attributive radical scavenger of the lipid peroxidation chain reactions (chain breakers). To cease the chain reactions, the electron donation of chain-breakers to the free radicals ultimately results in the neutralization of free radicals and transformed into more stable and less reactive species (Guo et al., 2009; Pietta, 2000; Rice-Evans et al., 1996). A number of in vitro antioxidant model systems have been developed to assess the total antioxidant activities and can demonstrate, to some extend, how polyphenols act as antioxidants, hence shed light on the mechanism of actions in human health (Prior et al., 2005).

12 | PRO-OXIDANT ACTIVITY AND CELLULAR EFFECTS OF POLYPHENOLS

Polyphenol compounds can exhibit anticancer and antioxidant properties but under certain conditions they have shown some pro-oxidant activities (Rucinska et al., 2007). For instance, antioxidants can exert a pro-oxidant activity in the presence of metal ions (Yordi et al., 2012). Their pro-oxidant activity is based upon a phenoxyl radical production or redox complex with a metal ion transition. Phenoxyl radicals reaction with oxygen converts oxygen to H_2O_2 but also contribute to the formation of a complex mixture of semiquinones and quinones (Hodnick et al., 1988). Polyphenols with phenolic ring were metabolized via peroxidase to produce prooxidant phenoxyl radicals that, in some cases were sufficiently reactive to cooxidize GSH or NADH accompanied by extensive oxygen uptake and ROS production. Polyphenols with catechol rings also demonstrated to co-oxidize ascorbate which is likely to interfere by semiquinone radicals (Han et al., 2007).

13 | FUTURE PERSPECTIVES

Phenolic phytochemicals are widely spread across the plant kingdom. They are a class of chemical compounds comprising one or more hydroxyl groups (–OH) bonded directly to an aromatic hydrocarbon group. The hydroxyl groups are usually the functional moieties that determine the biological activity of each phenolic compound. Phenolics are typically found as esters or glycosides rather than as free compounds. Polyphenolic compounds and other plant natural phytochemical (flavonoids, anthocyanin, saponins) play essential roles in food industry and preservation techniques. Furthermore, various biological activities including free radicals inhibiting, antimicrobial, antiobesity, and anticancer of different plant extracts and isolated compounds have been reported. The limitation of dietary supplementation (i.e., low stability, poor solubility and bioavailability) can be removed by applying nanotechnology-based encapsulation systems such as nano-emulsion, liposomes, and phytosomes. Meanwhile, the microbial spoilage, lipid oxidation, and short shelf life are currently the challenges and nanoencapsulation of polyphenolic compounds in food science can substantially help tackle such drawbacks.

AUTHOR CONTRIBUTIONS

Fatemeh Omidfar: Data curation; funding acquisition; methodology; writing—original draft. **Fatemeh Gheybi**: Data curation; investigation; validation; writing—review and editing. **Mohsen Zareian**: Funding acquisition; methodology; writing—review and editing. **Ehsan Karimi**: Investigation; project administration; validation; visualization; writing—review and editing.

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The authors declare no conflicts of interest.

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Data sharing applies to this article.

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