

THE ROLE OF PHENOLIC COMPOUNDS AS POTENTIAL ANTIMICROBIAL AGENTS

Abstract

Bacterial infections and intoxications are a major global health concern and diseases caused by these can worsen in some people with more complex medical circumstances, such as children, elderly, pregnant women, and immunocompromised people. Antibiotics are typically used to treat these diseases. However, antimicrobial resistance in pathogenic bacteria has retained its prominence as one of the primary global health problems in recent decades. Along with their well-known antioxidant activity of phenolic compounds, they have also inhibitory effects in pathogenic microorganisms. Due to their antimicrobial action, extracts from many fruits and vegetables with a rich phenolic compounds have been examined and promising results have been obtained. In this context, plant extracts or pure phenolic compounds can be used in the food industry as potential antibacterial agents instead of synthetic food preservatives. This chapter summarizes and discusses the phenolic compounds, classification and extraction procedure, antimicrobial activity of phenolic compounds, mechanism of action, *in vitro* studies and usage of these compounds in food system as future perspective.

Keywords: phenolic compounds; antimicrobial activity; pathogenicity;

Authors

Seda Altuntas

Department of Food Engineering
Bursa Technical University Bursa,
Turkey. seda.altuntas@btu.edu.tr

Mihriban Korukluoglu

Department of Food Engineering
Bursa Uludag University
Bursa, Turkey.
mihriban@uludag.edu.tr

I. INTRODUCTION

Phenolic compounds, which are identified by the presence of a phenol ring and one or more hydroxyl groups in their chemical structure, have become an important and popular research topic since the 90's due to the positive effects they provide on human health. Phenolic compounds represent phytochemicals present in a range of plant-derived foods, encompassing a diverse array of compounds characterized by distinct chemical structures and attributes [1]. To date, 8000 phenolic compounds have been classified into 16 different classes. The shikimic acid pathway and phenylpropanoid metabolism are responsible for the synthesis of phenolic compounds, a varied category of secondary metabolites that are widely distributed throughout plants. They play a variety of roles in plants, such as defense against pathogens and other invasive species, unsuitable temperature, unfavorable soil pH, UV radiation protection, and oxidative stress management. They are also responsible for the pigmentation of plants and their organoleptic (taste and odor) properties [2,3]. Beyond their importance in plant physiology, phenolic compounds have acquired recognition for their potential health benefits in humans. Because of their powerful antioxidant properties, phenolic compounds have been scientifically shown to protect a number of chronic diseases linked to oxidative stress, including cancer, cardiovascular, and neurological diseases. In addition, there are many clinical scientific studies demonstrating the anti-inflammatory, antimicrobial, anti-proliferative, anti-carcinogenic, anti-diabetic properties of phenolic compounds. In recent years, the study of phenolic compounds has expanded to include their interactions with the gut microbiota and their potential role in modulating gut health. These compounds may have an impact on the composition and activity of the gut microbiome, with potential implications for digestion, metabolism, and immune function. In conclusion, because of their diverse functions in both plant biology and human health, phenolic compounds represent an exciting area of research. Their importance in a variety of disciplines, from agriculture and biotechnology to nutrition and medicine, is highlighted by their antioxidant, antibacterial, and possibly gut-modulating capabilities.

II. PHENOLIC COMPOUNDS

- 1. Classification:** Phenolic compounds are defined as compounds with aromatic or aliphatic structures structurally and at least one aromatic ring to which one or more hydroxyl groups are linked [4]. Phenolics are found in plant foods such as cereal grains, vegetables, legumes, fruits, nuts, and foods processed from these plant sources (juices, wine, tea, etc.). Phenolic compounds are classified in many different ways in the literature. According to the number of phenol units in the molecule, as flavonoids and non-flavonoids, according to the number of aromatic rings, water solubility, and carbon structure [5,6].

Phenolic compounds containing carboxylic acids are called phenolic acids. The term "hydroxybenzoic acid" refers to a carboxylic acid whose functional group is directly linked to the phenol ring; the term "hydroxycinnamic acid" refers to a carboxylic acid whose functional group and the phenol ring are separated by two double-bonded carbons. Examples of hydroxybenzoic acids are salicylic acid, m-hydroxybenzoic acid, p-hydroxybenzoic acid, gallic and vanillic acid. Plant foods contain traces of these compounds or do not contain them at all. The hydroxycinnamic acids are found more in foods compared to hydroxybenzoic acids. Ferulic acid, caffeic acid, o-coumaric acid and p-coumaric acid can be given as important hydroxycinnamic acids [7]. Although phenolic acids exist in the form of esters, glycosides or amides, they can scarcely be found in free form. The variation in phenolic acids is due to the number of hydroxyl groups in the aromatic ring and the variation in placement [5].

Flavonoids are phenolic compounds that make up more than half of the more than eight thousand known phenolic compounds and are among the main polyphenols of the human diet. These compounds, together with carotenoids and chlorophyll, are responsible for the blue, purple, yellow, orange and red colors of the plant. Flavonoids consist of diphenyl propane and two benzene rings combined with a triple carbon chain. The diversity in the flavonoid structure arises from the hydroxylation, prenylation, alkalization and glycosylation reactions that change the basic molecule [5]. According to the oxidation state of the centrally located carbon ring, flavonoids are divided into 6 groups: flavonols, flavones, flavanones, flavan-3-ols, anthocyanins, and isoflavones. The main representatives of flavonols; myricetin, kaempferol and quercetin, which are abundant in leeks, broccoli and onions. Tea and red wine also contain the glycoside form of flavonols with some simple sugars such as glucose or rhamnose. The flavanols are abundant in tea, cocoa, some fruits such as apples and strawberries. Epicatechin, epicatechin gallate, and epigallocatechin gallate are examples of catechins. Flavonols are known for their antioxidant activities and have been associated with cardiovascular health benefits [8]. Flavonones such as hesperidin and naringenin are widely found in citrus fruits [9]. They have antioxidant and anti-inflammatory properties. Anthocyanins are a subclass of flavonoids that are mostly distributed in plants and are naturally occurring, water-soluble pigments. Based on the quantity and distribution of hydroxyl groups in their structure, level of glycation, and electron donors, anthocyanins exhibit strong antioxidant activity. Anthocyanins are the pigments that give many fruits and vegetables their red, purple, and blue. Well-known anthocyanin compounds include cyanidin, delphinidin, and malvidin [10]. Isoflavones such as genistein and daidzein are predominantly found in legumes, especially soybeans. Their estrogenic activity has been well-explained and are of interest for their potential health benefits, including relieving menopausal symptoms and reducing the risk of certain hormone-related cancers [11].

Lignans are formed by dimerization as a result of oxidative coupling reactions of two phenylpropanoid units. Because of their enormous structural diversity, they have different terminology and classification. The carbon chain skeleton, the way oxygen is incorporated into the skeleton, and the manner of cyclization are used to classify lignans into eight categories [12]. Lignans are commonly synthesized in flaxseed, sesame, and pumpkin. Lignans have been shown to have estrogenic and anti-estrogenic activity [7,10].

Stilbenes constitute a category of phenolic compounds naturally occurring in a diverse array of food sources, such as grapes, strawberries, peanuts, red wine, and select herbs. However, the principal dietary origins of stilbenes are peanuts and grapes. These compounds possess a fundamental chemical structure known as 1,2-diphenylethylene, with the trans configuration being prevalent in plants. Recently, stilbenes have attracted a great deal of attention for their wide range of health benefits, including anti-inflammatory, anticarcinogenic, antidiabetes, and antidyslipidemia properties. The most prominent member in this class is resveratrol, which has antioxidant properties in the cardiovascular system and may overcome multidrug resistance in malignant cells by sensitizing them to chemotherapy drugs [7,13,14].

- 2. Extraction Procedure:** The existence of strong scientific evidence revealing the relationship of dietary polyphenols between nutrition and health has led researchers to studies aiming to obtain these compounds from plant tissues with minimal damage. The family of substances known as phenolic compounds is diverse and includes both monomers like phenolic acids and highly polymerized molecules like tannins. These compounds also have conjugated forms where one or more sugar units (monosaccharides, disaccharides, or even oligosaccharides) are connected to hydroxyl groups in addition to their complex structure. Furthermore, they can bond with other compounds such as carboxylic acids, amines and lipids (terpenes). However, there are many parameters that affect the recovery of phenolic compounds from plant materials, such as solvent polarity, stability of compounds, sample preparation before extraction and extraction methods. Despite numerous qualified scientific studies, there is no widely recognized method for the extraction of all phenolics or a specific group of these compounds [8].

In the past, phenolic compounds, particularly those in their unbound state, have been extracted using several established solid-liquid extraction methods (Soxhlet, maceration, hydrodistillation, etc.) and organic solvents such as water, acetone, ethanol, and methanol. Although it is well known that the performance of the extraction is greatly influenced by the polarity of the solvent employed, it also depends on the chemical composition of the phenolic compounds to be extracted, the number and position of their hydroxyl groups, molecular size, temperature, contact time, particle size, substrate: solvent ratio, and food matrix [15].

Although traditional extraction techniques such as maceration, Soxhlet extraction, decoction and percolation have simple procedures, they have drawbacks include low extraction efficiency, labor-intensive time requirements, and high organic solvent consumption that can use harmful organic solvents that are left in trace amounts in the extracts. These disadvantages led to the recent replacement of these conventional approaches with alternative energy-based extraction processes. These techniques, which are based on green technology, reduce energy consumption, allow the use of non-toxic, biodegradable, facility-friendly solvents that can be recovered at the end of the process, provide high efficiency and purity, and low solvent consumption. In addition to traditional extraction methods, techniques such as supercritical fluid extraction, microwave assisted extraction, ultrasound assisted extraction, pulsed electric field, pulsed ohmic heating, high pressure have started to be used in the extraction of phenolic compounds and the results are promising [16,17,18].

Solvents used to extract polyphenols include water, methanol, chloroform, n-hexane, ethanol, propanol, ethyl acetate and acetone. Differences in the polarities of these solvents cause different effects on the extraction of phytochemicals. According to studies, proanthocyanidins and tannins were best extracted with acetone, flavonoids and their glycosides with ethanol, and phenolic acids and catechin with methanol. This is explained by the higher the molecular weight of the solvent, the lower the polarity, and the easier it is to extract other substances with similar molecular weights. The polarity of acetone, ethanol and methanol is 0.355, 0.654 and 0.762, respectively. Due to low polarity of acetone is ideal for the extraction of high molecular weight phenolic compounds such as condensed tannins [19].

The use of aqueous organic solvents has better extraction efficiency compared to absolute organic solvents [8]. The effect of different solvents (ethanol, methanol and acetone) and their aqueous forms on the phenolic component extraction from a traditional Chinese medicinal plant was investigated and it was determined that the total phenolic content increased as the concentration of all three organic solvents increased in the 0-70% concentration range. However, between 70-90%, it was emphasized that the phenolic component content decreased for all three organic solvents with increasing organic solvent concentration [20].

Besides the use of appropriate solvents, time and temperature are two more crucial factors that influence the yield of phenolics recovered from plant. In general, increasing time and temperature increases the solubility of the solute, extended extraction periods and heightened temperatures can lead to detrimental reactions, such as enzymatic oxidation, which result in the degradation of plant phenolics. Santos and Martins [21], in their optimization study for the extraction of phenolic compounds from edible flowers, found that the extraction of anthocyanins was most affected by the temperature parameter, while the content of phenolic compounds and

flavonoids affected the recovery efficiency the most.

The recovery of phenolics is also influenced by the solvent-to-sample ratio and the number of repeated extractions that are carried out. It has been proposed that raising the solvent-to-sample ratio encourages the extraction of phenolic compounds from plant samples; but considering the amount of solvent and determining the optimum ratio to minimize the saturation of the solvent in terms of phenolic compounds [5].

III. ANTIMICROBIAL PROPERTIES OF PHENOLIC COMPOUNDS

The use of phenol as an antiseptic is the earliest phenolic chemical use in medicine. It has been reported that a 5% (w/v) phenol solution has been compared to contemporary antiseptics that are effective against *Staphylococcus aureus* and phenol is currently used as an oral anesthetic in throat lozenges at a concentration of 1.4% [22]. The issue of microbial food safety has grown into a significant public health concern worldwide. Additionally, the emergence of multidrug-resistant bacterial strains in the food chain poses a substantial threat, reflecting the elevated risk of resistant food-borne illnesses. This concern highlighted the requirement for natural, plant-based alternatives for preserving and inhibiting bacterial growth. Phenolic compounds, have demonstrated promise not only in their antimicrobial effects but also in their potential to serve as replacements for synthetic preservatives.

- 1. The Mechanisms of Antimicrobial Activity of Phenolic Compounds:** Phenolic compounds exhibit antimicrobial activity through multiple mechanisms (Figure 1). One of the main mechanisms is that the microorganism disrupts cell membrane permeability. This leads to leakage of cellular components and ultimately to cell death. This destructive effect on the cell membrane has been associated with the hydrophobic nature of phenolic compounds, which allows them to interact with lipids and proteins present in the cell membrane [23]. Also, the antioxidant properties of phenolic compounds contribute to their antimicrobial activities. The oxidative stress caused by phenolic compounds affects the growth and survival of microorganisms by damaging their DNA, proteins and lipids. In addition to these mechanisms of action, they modulate the activity of various enzymes involved in metabolism [12,24]. Many phenolic compounds, including ferulic acid, gallic acid, carvacrol, thymol and eugenol alter the intracellular pH of the microorganism through the changes they create in the ion flow, and they block production by interfering with the energy production system [25]. Undissociated forms of phenolic acids, can pass through the phospholipid bilayer of bacterial membranes and lower the pH inside the cell. The disruption of DNA, RNA, and protein synthesis or functions, interference with intermediary metabolism [specifically the energy (ATP)-generating system], and coagulation of cytoplasmic constituents as a result of its

acidification are all reported effects of phenolics penetrating in the cytoplasm of microorganisms [26].

Studies are presented showing that Gram-positive bacteria are more sensitive to phenolic compounds than Gram-negatives [27,28,29,30]. The phenolic compounds have mechanisms of action that play a role in antimicrobial activity such as temporary or permanent damage to cell membrane permeability, changing some functions in the cell cytoplasm and changing intracellular pH [31,26]. Cueva et al. [27] investigated the effects of thirteen different phenolic acids on 3 different *Escherichia coli* strains, *Lactobacillus* spp., *S. aureus*, *Pseudomonas aeruginosa* and *Candida albicans*. They stated that Gram-positive *S. aureus* was the most sensitive bacterium to phenolic acids, and the growth of *P. aeruginosa* was not affected in the presence of any phenolic acid at the tested dose. One of the possible mechanisms explaining the antimicrobial effect of phenolic acids against pathogens has been explained as the hyperacidification of the plasma membrane interphase as a result of the dissolution of the phenolic acids. This hyperacidification changes the cell membrane potential, making the cell membrane more permeable, and also affects the sodium-potassium ATPase pump involved in ATP synthesis. Gram-positive bacteria do not possess an external membrane to hinder the diffusion of phenolic acids across their cell walls. This can result in intracellular acidification and permanent alterations in the sodium-potassium ATPase pump. On the contrary, the outer membrane of Gram-negative bacteria acts as a barrier against hyperacidification and, together with the MexE-MexF-OprN operon transport system that pumps toxins out of the cell, they are resistant to the effects of phenolic compounds. Moreover, the hydrophilic nature of the outer membrane results in repelling some phenolic molecules with hydrophobic properties [26].

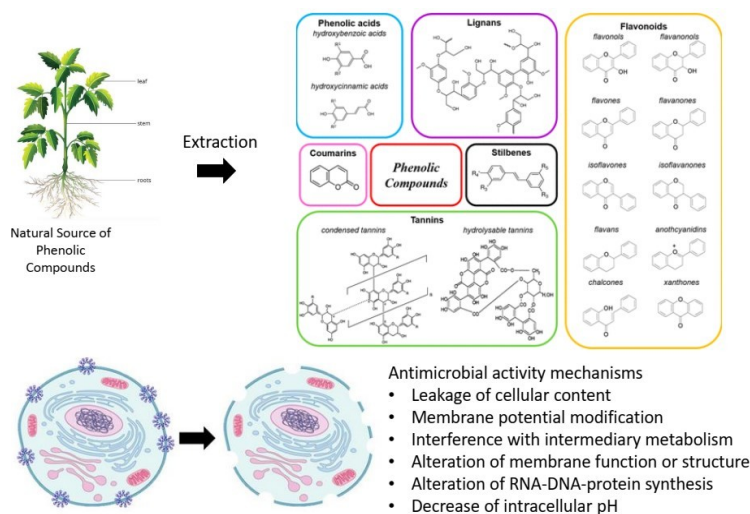


Figure 1: Main antimicrobial activity mechanisms of phenolic compounds.

2. ***In vitro* Studies of Phenolic-Rich Extracts and Pure Phenolics:** The antimicrobial properties against several microorganisms of phenolic compounds have been demonstrated in various *in vitro* studies using polyphenol-rich extracts derived from by-products and/or waste of edible plants or pure compounds. Phenolic compounds are abundant in grapes, with the majority of it being found in the skin and seeds. A methanol extract derived from grape (*Vitis vinifera* L.) pomace unveiled notable proportions of quercetin (26.3%), gallic acid (24.4%), protocatechuic acid (16.7%), and luteolin (11.4%). This extract exhibited effectiveness against antibiotic-resistant strains of *Escherichia coli* and *Staphylococcus aureus*, including methicillin-resistant *S. aureus* (MRSA), with a minimum inhibitory concentration (MIC) range of 0.3 to 3 mg/mL. In another investigation, methanol grape pomace extracts contained gallic, vanillic, syringic, p-coumaric, ellagic, and protocatechuic acids, which displayed MIC values ranging from 0.062 to 3 mg/mL against *S. aureus* and 0.2 to 2.5 mg/mL against *E. coli* [24]. Zambrano et al. [32] investigated the antimicrobial activity of residual extracts of grape, apple and pitahaya and they found that the black grape sample demonstrated a stronger inhibitory impact on most bacteria than apple and pitahaya.

Bobinaitè et al. [33] examined some properties of rowan pulp extracts prepared with different solvents and reported that the strongest antimicrobial activity against the tested strains was in the acetone extract. Researchers explained this situation by the fact that the acetone extract has the highest neochlorogenic acid content. In addition to neochlorogenic acid, it has been determined that there are studies that show the antimicrobial activity of quercetin and that it is a very strong antimicrobial and antiviral agent [34,35,36]. Quercetin is highly effective against some antibiotic-resistant bacteria, making it a promising phenolic compound by health authorities. It has been stated that among the antimicrobial and antiviral mechanisms of quercetin, there are mechanisms such as damaging the cell membrane, impairing membrane permeability, inhibiting the synthesis of nucleic acids and proteins, reducing the expression of virulence factors, dysfunctioning mitochondria, and preventing biofilm formation [36]. The suppression of ketoacyl carrier protein synthases, which are involved in bacterial fatty acid production, is assumed to be the main mechanism of quercetin's antibacterial effect. Quercetin has also been found to have antifungal effects. By lowering cell adhesion and influencing the genes involved in biofilm formation, quercetin works in conjunction with other antifungal medications like fluconazole and amphotericin B to fight fungus [34]. In a review, in which the use of natural plant-based antimicrobial compounds as an alternative to some synthetic food preservatives or biocides was discussed, the antimicrobial activity of many plant phenolic compounds was assessed and it was emphasized that the use of phenolic-rich plant extracts would be beneficial for biofilm control on food contact surfaces [26].

The antimicrobial activity of phenolic compounds varies depending on their chemical structure, concentration and the targeted microorganism. Some phenolic compounds such as resveratrol and quercetin show broad-spectrum antimicrobial activity against a wide variety of microorganisms, but phenolics such as thymol and eugenol have more specific antimicrobial effects, especially against bacteria and fungi [24,25]. Fattouch et al. [37] demonstrated in their study that chlorogenic acid is a stronger antimicrobial compound than quercetin and kaempferol. Bouarab Chibane et al. [23] investigated the antibacterial activity of 35 phenolic compounds against *L. monocytogenes* and five other bacteria at a concentration of 1 g/L. All examined polyphenols showed an inhibitory effect on *L. monocytogenes*, with 54.3% of the compounds showing a bacterial load differential (BLD) above 50%. The resveratrol and pinosylvin were the stilbenes that were most effective against this bacterium, with 100% and 97.9% of BLD, respectively. In a study, the antibacterial effects of curcumin, resveratrol, cinnephrine, p-coumaric acid and coniferyl alcohol on *E. coli* W1485 and *Bacillus cereus* strains were investigated and it is found that 240 µg/mL resveratrol inhibited *E. coli* W1485 in 48 hours and 240 µg/mL cinnamaldehyde inhibited *B. cereus* in 4 hours [38]. In a study, in which the structural, spectroscopic and biological activity of 5-O-caffeoylquinic acid (5-CQA), one of the main chlorogenic acids found in many fruits, vegetables and plants, was extensively investigated and the compound was tested against *E. coli*, *S. aureus*, *Enterococcus faecium*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Candida albicans*. It was reported that the minimum inhibitory concentration (MIC) values were 5-10 mg/mL, and the strongest antimicrobial activity was determined against *K. pneumoniae* among the microorganisms tested [39].

Studies demonstrate that phenolic compounds have antibacterial effects on not only pathogenic bacteria but also lactic acid bacteria. However, lactic acid bacteria, fortunately, were more resistant to these substances. In a study investigating the effects of six hydroxycinnamic acids and six hydroxybenzoic acids on *Lactobacillus plantarum*, *Lactobacillus hammesii*, *Lactobacillus fermentum*, *Lactobacillus reuteri*, *E. coli* and *Bacillus subtilis*. Lactic acid bacteria were significantly more tolerant to phenolic acids than *E. coli* and *B. subtilis*. It was found that *L. plantarum* metabolized all other phenolic acids except chlorogenic acid, *L. reuteri* metabolized only chlorogenic acid, *L. fermentum* metabolized p-coumaric acid and ferulic acid. The most resistant and most sensitive bacteria in the study were associated with the fact that the antimicrobial activity of phenolic acid metabolites transformed by lactic acid bacteria was 2-5 times lower than the parent compound [40]. This study strikingly reveals that the tolerance of lactic acid bacteria to phenolic compounds is due to their ability to metabolize phenolic compounds.

With a similar approach, it has been observed that lactic acid bacteria are used in sunflower flour to prevent browning caused primarily by chlorogenic acid [41]. In another study, phenolic extracts of 6 different plants, including pomegranate peel, thyme and clove, were found to contain 5 common pathogens (*B. cereus*, *E. coli*, *S. Typhimurium*, *Shigella flexneri* and *S. aureus*) and 5 common lactic acid bacteria (*L. acidophilus*, *L. delbrueckii* subsp. *bulgaricus*, *L. casei*, *L. plantarum* and *L. rhamnosus*) were investigated. The extracts inhibited food pathogens at different doses, but very high doses are required for the inhibition of lactic acid bacteria [42].

Research shows that phenolic compounds can be used as natural preservatives for food preservation owing to their preventive effects against a wide variety of foodborne pathogens, including bacteria such as *E. coli* and *Salmonella* spp., as well as molds such as *Aspergillus* species. Their potent antimicrobial activities and their widespread availability in plants make phenolic compounds promising candidates for the development of new antimicrobial agents and strategies to combat infectious diseases [30,32]. Additionally, because of the uncontrolled administration of antimicrobial medications, there has been a noticeable uptick in the development of pathogenic microorganisms that have become immune to particular antibiotics in recent times. Antimicrobial resistance within bacterial pathogens is correlated with a heightened incidence of sickness and fatalities. The complex multidrug resistance patterns found in both Gram-positive and Gram-negative bacteria create formidable obstacles for treatment and render conventional antibiotic remedies ineffectual. The synergistic antimicrobial activity of the use of phenolic compounds in combination with conventional antibiotics was evaluated in the studies of Buchmann et al. [43] and Hossain et al. [44]. Study findings show that the combination of phenolic compounds with antibiotics increases antimicrobial activity against both Gram-positive and Gram-negative bacteria. This suggests that the potentially required dose of antibiotics in patients can be reduced and the development of antibiotic resistance can be minimized.

IV. STRATEGIES TO APPLY PHENOLIC COMPOUNDS IN FOOD SYSTEM

In recent years, the large amounts of polyphenols have been reported in most of the plant food wastes and they are a cheap source of polyphenols. Seeds, pulp and peel, which are considered as fruit waste and are by-products of the fruit processing industry, constitute 30% of the total weight of some fruits [10, 45]. The residues left after wine production correspond to 20-30% by weight of the total processed grapes and approximately 70% of the grape polyphenols remain in the pulp. It is also reported that pomegranate (*Punica granatum* L.) peels, which constitute 40% of the whole fruit and are rich in phenolic compounds, are generally seen as waste and cannot be used industrially [10]. Pulp, a by-product of the cranberry juice processing industry, has also

been stated to be a good source of ellagic acid [46]. Residues from the citrus industry, notably the peel, have been identified as having elevated concentrations of total phenolic compounds in contrast to the consumable portions. For instance, the peels of apples, peaches, and pears exhibit twice the total phenolic content as observed in the fruit pulp. In the case of bananas, the edible pulp contains 232 mg/100 g of dry weight phenolics, approximately constituting a quarter of the phenolic content found in the peel [47].

There are numerous approaches that may be used to apply phenolic compounds. One key strategy involves utilizing phenolic-rich plant extracts as natural preservatives against food-borne pathogens. It's crucial to understand which are the most efficient for each food matrix and how they are more stable to achieve optimal food preservation. Phenolic compounds can be applied by dipping, spraying, washing, or rinsing and can be added directly to a solution as additives or dispersion agents. However, careful formulation and testing are crucial to ensure that the compounds' beneficial properties are retained while avoiding undesirable effects on taste and texture. Another strategy is to make phenolic chemicals in the human diet more bioavailable. This can be achieved by formulating food products in ways that improve their absorption and utilization within the body. Technologies such as encapsulation and nanoemulsions can protect phenolic compounds during digestion, ensuring they reach the target tissues intact and exert their health-promoting effects. Moreover, polyphenols can be added as an additive or incorporated into coatings or films to extend their shelf life, especially when you take into account their antioxidant properties.

Overall, integrating phenolic compounds into food systems requires a multidisciplinary approach that considers formulation, preservation, processing and regulation. By harnessing the potential of these natural compounds, the food industry can offer healthier, safer, and more sustainable products to meet the evolving demands of consumers.

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