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Metabolic Stimulation of Plant Phenolics for Food Preservation and Health

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antioxidants, pentose phosphate pathway, phenolic phytochemicals, food preservation, postharvest preservation, noncommunicable chronic diseases

Abstract

Plant phenolics as secondary metabolites are key to a plant's defense response against biotic and abiotic stresses. These phytochemicals are also increasingly relevant to food preservation and human health in terms of chronic disease management. Phenolic compounds from different food crops with different chemical structures and biological functions have the potential to act as natural antioxidants. Plant-based human foods are rich with these phenolic phytochemicals and can be used effectively for food preservation and bioactive enrichments through metabolic stimulation of key pathways. Phenolic metabolites protect against microbial degradation of plant-based foods during postharvest storage. Phenolics not only provide biotic protection but also help to counter biochemical and physical food deteriorations and to enhance shelf life and nutritional quality. This review summarizes the role of metabolically stimulated plant phenolics in food preservation and their impact on the prevention of oxidative stress–induced human diseases.

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1. INTRODUCTION

Antioxidants: chemical substances that in low concentrations delay or prevent the oxidation of a substrate

Oxidative stress: breakdown of cellular homeostasis due to the imbalance between concentrations of prooxidants and antioxidants, which leads to the damage of cells and cellular organelles

Food preservation: processes designed to improve quality and longevity of food by preventing microbial, chemical, and physical deterioration

Noncommunicable chronic diseases (NCDs): noninfectious chronic diseases with long durations and slow progression, such as cancer, diabetes, cardiovascular disease

Shelf life: length of time a perishable item can be stored without any significant loss or deterioration

Phenolic metabolites make up the most abundant and heterogeneous group of biochemicals in plant-based foods. Phenolics are plant secondary metabolites with a large array of diverse compounds that differ significantly in chemical structure and function depending on the plant species (Bors & Michel 2002). Structurally, phenolic compounds have an aromatic ring with one or more hydroxyl substitutes, including their functional derivatives (Rice-Evans et al. 1995). Phenolics found in plant-based foods, such as fruits and vegetables, include phenolic acids, flavonoids, lignans, stilbenes, tannins, coumarins, and proanthocyanidins. In plants, phenolics can function as antimicrobials, natural pesticides, signal substances, attractants for pollinators, protective agents against abiotic UV radiation, insulating material, and constituents of the cell wall (Shahidi & Naczk 2004). Among phenolics, anthocyanins determine the colors of the fruits, flowers, and leaves of most plant species. Animals, including humans, cannot synthesize phenolics in their tissues and therefore derive them only from consumption of a plant-based diet. Plant phenolics are the main source of dietary antioxidants and potentially provide protection against oxidative stress–induced diseases to humans (Sarkela et al. 2001).

There is an increasing interest in phenolic research as it has diverse applications and is relevant to understanding plant responses to biotic and abiotic stresses, improving food quality and food preservation, applications in materials science, and use of bioactive molecules for human and animal disease management (Shetty & Wahlqvist 2004). Chemical stability, easy identification, widespread distribution, and chemical variability make phenolics useful for multiple functions and applications (Naczk & Shahidi 2004). This review emphasizes the special role of metabolically active phenolics in food preservation and their implication in the prevention of noncommunicable chronic diseases (NCDs) in humans. It also provides insight on the current understanding of improvements to phenolic profiles through the metabolic stimulation of food to increase shelf life and to protect against biotic and abiotic stresses in fruits and vegetables during pre- and postharvest conditions. Advancements in the metabolic basis for plant phenolic research, and in particular the focus on the chemical and biochemical rationale for function, help us understand the underlying principles of food phenolics in food preservation and their potential roles in human health. In addition to their preservation mechanism, phenolics also potentially enhance the bioactive nutraceutical properties of food, which has relevance in several chronic disease management strategies, especially NCDs.

2. PHENOLICS: A PLANT DEFENSE RESPONSE

Plant defense response and countering mechanisms against herbivores and pathogens involve different strategies ranging from physical barriers such as waxy layers, thorns, or resin ducts, to chemical resistance provided by secondary metabolites (Treutter 2006). Secondary metabolites of plants that provide protection against macro- and microorganisms are alkaloids, terpenes, steroids, glycosides, and phenolics. Phenolics provide a plant defense mechanism against viruses, bacteria, fungi, and herbivorous animals (Hay & Fenical 1988). The diversity and heterogeneity of phenolic compounds in plants provide a broad spectrum of protective defenses against wide arrays of pathogens and pests (Nicholson & Hammerschmidt 1992). The mechanism through which phenolics provide protection against pathogens is either constitutive resistance or induced resistance (Levin 1971) (**Figure 1**). Although some phenolics or phenolic acids can counter pathogenesis directly, metabolically induced changes in phenolic profiles are essential for disease or insect resistance. Simple phenolics such as chlorogenic acid and caffeic acid or complex phenolics such as tannins can be directly toxic to many microorganisms. Water-soluble phenolic compounds such

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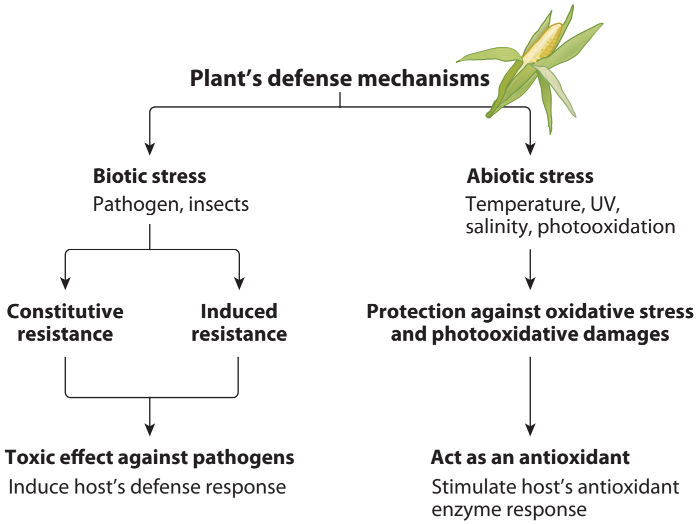

Figure 1

Plant's defense mechanisms involving phenolics for biotic and abiotic stress tolerance.

as catechol or protocatechuic acid induce resistance in onion varieties against *Colletotrichum circinans* infection (Levin 1976). Phenolics can also help in signal transduction and can play a crucial role in plant-microbe interactions, including symbiosis and nitrogen fixation in legumes. Beyond providing a shield against biotic stresses, phenolics can also protect plant cells and tissues against oxidative damages induced by abiotic stresses.

Therefore, secondary metabolites, including phenolics, are no longer considered by-products of primary metabolism and metabolic wastes or toxic substances stored in vacuoles; rather, they are now recognized widely as valuable molecules with diverse relevant biological functions. Flavonol is the most abundant of flavonoids found in ancient bryophytes, which provide protection against photooxidative damage to cells. One important biological function of flavonoids is to assist plant reproduction by attracting and recruiting plant pollinators and seed dispersers (Winkel-Shirley 2002). However, the main evolutionary purpose of phenolics, including flavonoids, is to provide protection against abiotic UV radiation. Studies of *Arabidopsis* mutants further strengthen the hypothesis that flavonoids are primary UV absorbents in plant tissues (Bieza & Lois 2001). Phenolics present in plant cells can also stimulate plant synthesis and the activity of other antioxidant enzymes, which in turn provide protection against biotic stresses. Phenolics play other physiological roles in plant cells, but the most significant is as antioxidants against oxidative stresses (Close & McArthur 2002). The principal mechanism of flavonoids for UV protection also involves better redox regulation and quenching of oxidants. Increased flavonols improve the stress tolerance capacity in plant tissues by enhancing antioxidative potential and simultaneously improving the nutritional quality of food crops (Shetty & McCue 2003).

3. PHENOLIC CHEMISTRY

Phenolic metabolites make up a large group of natural compounds distributed widely in fruits, vegetables, cereals, legumes, oilseeds, and other plants (Tsao 2010). There are approximately 8,000 currently known phenolic and polyphenolic metabolites with typical phenolic structural features (Bravo 1998). However, the term polyphenols is somewhat confusing and vague as it covers different subgroups of phenolic acids and flavonoids that vary significantly in the structure, stability, bioavailability, and physiological functions related to plant defense response and potentially to human health (Tsao 2010, Young et al. 2011). The wide distribution and diversity of phenolic metabolites in different groups of plants have led scientists to categorize these secondary compounds according to their relevance in plant defense and reproductive functions. The classification of phenolic metabolites and polyphenols is largely based on their origin, biological function, and chemical structure. Chemically, natural phenolic metabolites can range from simple molecules such as phenolic acids with a single ring structure to highly polymerized phenolic compounds such as tannins. These phenolic compounds, resulting from plant metabolic responses, may occur in conjugated form with one or more sugar residues such as monosaccharaides, disaccharides, or even oligosaccharides linked to hydroxyl groups (Bravo 1998). Glucose is the most common of the sugar residues, which also include galactose, rhamnose, xylose, arabinose, and glucuronic and galacturonic acids (Bravo 1998). Other compounds such as carboxylic and organic acids, amines, lipids, and other phenolic metabolites also occur.

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The most common and widely distributed groups of phenolic metabolites are phenolic acids and flavonoids, which are used in food preservation and potentially human disease management. Phenolic acids can be divided into two main types, benzoic acid and cinnamic acid derivatives based on C1-C6 and C3-C6 backbones, respectively (Tsao 2010). Simple phenolics present in food may be derived from decarboxylation of phenolic carboxylic acids, thermal degradation of lignin, or microbial activity (Shahidi & Naczk 1995). There are many free and bound phenolic acids in fruits and vegetables and bound phenolics in grains and seeds, which can be released by acidic or alkaline hydrolysis or by enzymes (Tsao 2010). Cleaved phenolic acids present in seeds can be released during germination and sprouting. More than 2,000 flavonoids have been identified and further characterized in different subgroups such as anthocyanins, flavan-3-ols, flavones, flavanones, flavonols, and more (Harborne 1994, Young et al. 2011). The general structure of flavonoids includes a C6-C3-C6 backbone with two phenolic C6 rings. The structural differences and glycosylation patterns of common flavonoids define their biological activities, including potential antioxidant activity (Tsao 2010). Flavanols or flavan-3-ols are commonly known as catechins, which are isomers with *trans* configuration, and epicatechins are of *cis* configuration. Flavanol stereoisomers occur in many fruits, mostly in the skins of grapes, apples, pears, and berries (Tsao et al. 2003). Condensed tannins are considered proanthocyanidins, whereas anthocyanidins occur in the glycosidic form (Yoshida et al. 2000). Some phenolic metabolites such as capsaicinoids in chili peppers and avenanthramides in oats are polyphenolic amides and have N-containing functional substituents (Tsao 2010). Other than phenolic acids, flavonoids, and phenolic amides, there are several other phenolic metabolites found in plant-based foods that have health relevance. Such phenolics are resveratrol from grapes and red wine, ellagic acid and its derivatives from berries, lignans from flax, curcumin from turmeric, and rosmarinic and ellagic acids from herbs and spices.

The most important biological function of phenolic metabolites with structural significance is antioxidant activity. Antioxidants are chemical substances present in low concentrations, compared to primary metabolites such as proteins, lipids, and carbohydrates, and delay or prevent oxidation of substrates (Aruoma 1999). Phenolic metabolites or synonym polyphenols can act as antioxidants by scavenging singlet oxygen or free radicals in cells (Rice-Evans et al. 1995). The antioxidative properties of phenolic metabolites are mainly due to their ability to donate hydrogen from hydroxyl groups positioned along the aromatic ring in order to terminate free-radical oxidation of lipids and other biomolecules and their forming aryloxyl radicals (Foti et al. 1994). Among phenolics, monophenols are less potent as hydrogen-donating radical scavengers than polymeric phenols (Figueroa-Espinoza & Villeneuve 2005). Phenolic metabolites also combat free radicals through the stimulation of host antioxidant enzyme responses (Shetty & Wahlqvist 2004). The antioxidant potential varies widely among phenolic metabolites due to their chemical structure, and studies have revealed the underlying mechanisms of such variations (Bors & Michel 2002). For example, polymeric phenolics such as tannins are superior antioxidants because their eventual oxidation leads to oligomerization via phenolic coupling and enlargement of numerous reactive sites (Bors & Michel 2002). Different mechanisms are involved in the antioxidative potential of phenolic metabolites, including polymeric forms, which ultimately determine their role as dietary antioxidants for food preservation and human disease management.

4. PHENOLIC METABOLITES IN FOOD

Phenolic metabolites are virtually present in all plant foods, but their levels vary significantly among diets depending on the type and quantity of plant-based food sources. Plant foods overall are excellent sources of dietary antioxidants as they have rich phenolic profiles. Plant phenolics are receiving increased interest in designing functional foods to combat environmental and lifestyle-induced oxidation-associated diseases (Shetty 2004, Shetty & Wahlqvist 2004). Higher consumption of phenolic-rich, plant-based foods could potentially provide cost-effective prevention and a complementary strategy to pharmaceutical drugs for the management of the early stages of major chronic diseases such as cardiovascular disease, diabetes, and potentially cancer (Labriola & Livingston 1999). Phenolic characterization of plant-based foods also can increase our understanding of the role that phenolic metabolites have in food preservation, which can address global food security issues resulting from large-scale spoilage and waste of fresh foods.

Most dietary plant-based phenolics are metabolized by colonic microbes before absorption, but a smaller amount can be absorbed directly in the upper gastrointestinal tract (Selma et al. 2009). Gut bacteria modulate the biological activity of dietary phenolics by various mechanisms, and this metabolic process is a prerequisite for absorption. The mode of action and systemic effects of dietary phenolic metabolites largely depend on synergistic action and are affected by other constituents present in the diet (Liu 2003).

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5. ROLES OF PHENOLICS FROM FOOD PRESERVATION TO CHRONIC DISEASE MANAGEMENT

Phenolics from plant-based foods have a major role both in food preservation and in human disease management. One major global challenge is to provide food security for the growing world population in part from crop diversity that will not only meet macro- and micronutrient needs but also provide bioactive moieties in food to counter chronic diseases such as NCDs associated with obesity. Although advancements in agricultural sciences during the past five decades have led to increased food production and better nutrition, this strategy, in addition to posing ecological sustainability challenges, has led to an increased public health burden: lifestyle-associated obesity derived from excess macronutrient intake, contributing to, in some cases, micronutrient imbalances among the extremely poor. Present global grain stocks are sufficient to feed 12 billion people, but still 1 billion people are hungry, and 1.3 billion tons of food are lost or wasted annually due to a lack of sufficient storage or to spoilage after field harvest (Hubert et al. 2010). At the same time, there are nearly 1.5 billion people consuming more macronutrients than required, resulting in rapid emergence of NCD obesity. Even in poor communities globally, excess empty calories and deficiencies in micronutrients are major health challenges that can be prevented with the consumption of a diverse array of foods, especially fresh fruits and vegetables that spoil easily. Efficient and improved food preservation is essential to reducing such food security imbalances that are linked to health disparities. Therefore, food preservation not only can help mitigate food security concerns but also may reduce NCD-associated human health issues and benefit global ecology through increased food diversity, especially by increasing the intakes of legumes, fruits, and vegetables. Since phenolic metabolites naturally protect the plant cellular system against many biotic and abiotic stresses, they may contribute to the improvement of postharvest qualities of grains, legumes, fruits, and vegetables (Cisneros-Zevallos 2003). Flavor, color, and the nutritional quality of foods largely depend on their phenolic compositions and the transformation of different phenolic compounds during postharvest stages. The antioxidant activity of phenolics present in specific foods not only helps to combat diseases when consumed but also provides postharvest protection against microbial and chemical degradation of food (Pinedo et al. 2007).

Phytochemicals: naturally occurring chemical compounds of plants with protective and disease prevention properties

Enzymatic browning: enzyme-catalyzed oxidation of phenols in fruits and vegetables, which leads to brown pigmentation

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5.1. Role of Phenolic Metabolites in Food Preservation

Due to physical, chemical, and microbial reactions, all plant-based foods deteriorate and lose quality and potential shelf life at some rate after harvest (Gould 1996). Many different methods, such as freezing, smoking, heating, sun drying, irradiation, and chemical treatments, have been used alone or in combination to preserve foods. According to global estimates, 10% of cereal and 40% of vegetables and fruits, including 75% of peas and beans, are lost annually during storage (Lacroix & Ouattara 2000). If meat, poultry, and fish are included, the overall estimate would be much larger. Without proper countermeasures and protection, postharvest storage loss not only increases the price of food and reduces its availability and accessibility, but it may also increase the amount of food contaminated by foodborne pathogens and insects. Contaminated food increases the risk of human illnesses and also reduces the nutritional quality of the food.

Agricultural and horticultural produce that is rich in phenolic bioactive ingredients provides a mixture of phytochemicals with potential health benefits (Shetty & McCue 2003). These same bioactive phenolic compounds also can improve storage quality and increase the shelf life of fruits, vegetables, legumes, and grains. Maturity; agronomic practices; and postharvest handling, processing, and storage conditions influence the biochemical characteristics and phenolic composition of fruits and vegetables. Many early investigations were focused on the physical characteristics of plant-based foods to determine their quality parameters. However, as bioactive phytochemical compounds of plant-based foods have been identified as providing relevant health benefits, it is useful to understand the changes and relevance of this quality parameter during postharvest storage (Ayala-Zavala et al. 2007). During postharvest storage and handling, several factors such as species, variety, microbial load, presence of pests, temperature, light condition, humidity, radiation exposure, packaging, and chemical treatments significantly influence the biochemical properties and rate of the deterioration of plant-based food (Bengtsson & Hagen 2008) (**Figure 2**).

During the postharvest stages, grains, pods, fruits, and vegetables are detached from their host mother plants, but they continue to respire and have metabolic activities. The longevity, eating quality (taste), and changes in the chemical compositions of agricultural and horticultural produce are determined by a series of biotic and abiotic factors during the pre- and postharvest stages. The principal contributing factor is respiration, as the higher the rate of respiration, the more rapidly the produce deteriorates. Another important factor is enzyme-catalyzed browning reactions, which involve oxidation of phenolic compounds by polyphenol oxidase (PPO) to quinones, followed by transformation of the quinones to dark pigments (Friedman 1997, Lee & Whitaker 1995). Browning due to PPO activity can significantly contribute to the loss of food during postharvest storage. Browning by PPO can be aggravated by cellular disruption through vibration, rough handling, mechanical damages, and aging. For food such as mushrooms, the loss due to browning can be as high as 40% (Beaulieu et al. 1999). Hence, prevention of enzymatic browning is a major concern for farmers and food industries during postharvest storage.

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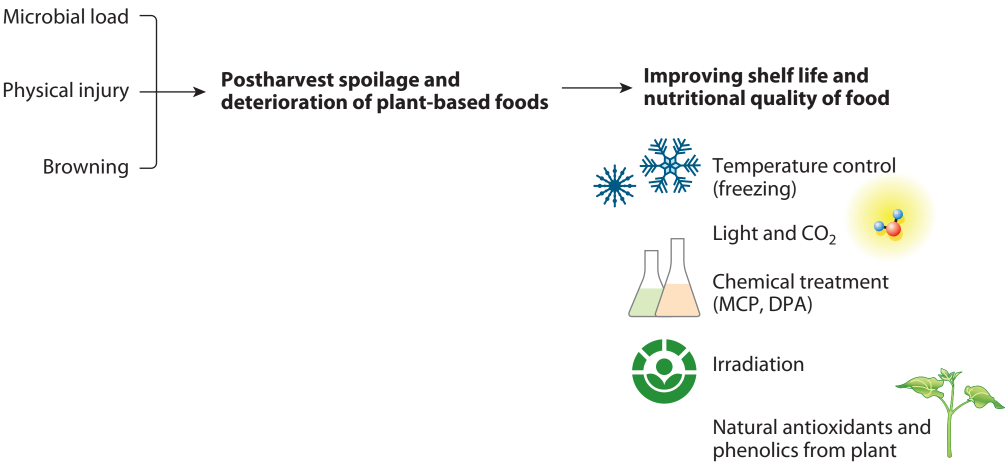

Figure 2

Major factors contributing to food spoilage and several physical and biochemical conditions for improving the postharvest storage quality of plant-based foods. Abbreviations: DPA, diphenylamine; MCP, methylcyclopropene.

5.2. Factors Influencing Storage Quality and Phenolic Composition of Plant-Based Food

Low temperatures generally slow respiration rates, ripening, senescence processes, and the growth of pathogenic and spoilage microorganisms, and thus keep plant-based foods healthy during postharvest storage. Some studies revealed that cold storage (0 and 1°C) did not affect non-phenolic phytochemicals such as β-carotene, α-carotene, and total carotenoids of carrots during storage (Koca & Karadeniz 2008, Kidmose et al. 2006). In contrast, minor degradation of carrot carotenoids during cold storage was observed (Howard et al. 1999, Kopas-Lane & Warthesen 1995). Another study revealed that total anthocyanin content in strawberries increased gradually at 10°C but decreased at 0 and 5°C after 5 days of storage (Ayala-Zavala et al. (2004), whereas total phenolic compounds remained at constant value during the storage period (13 days). Total phenolic content increased in Jonagold apples after 120 days of storage at 0°C, and it was positively correlated with an increase in ethylene during the same period (Leja et al. 2003). MacLean et al. (2006) observed a small reduction in anthocyanins and an increase in chlorogenic acid but no change in the overall content of phenolic compounds in Red Delicious apples during 120 days of cold storage. Goncalves et al. (2004) studied the bioactive compounds of four different cultivars of cherries during postharvest storage and found that phenolic contents generally decreased with storage at 1–2°C and increased with storage at 15 ± 5°C. The phenolic content of Hayward kiwifruit increased after 6 months of storage at 0°C followed by a week at ambient temperature (25°C) (Tavarini et al. 2008). The soluble phenolic and ascorbic acid contents of tomatoes increased during storage at increased temperatures (Toor & Savage 2006).

Radiation treatment is effective in preventing infection of plant-based foods by insects and pathogens (Lacroix & Ouattara 2000). Microorganisms, including bacteria, can be eliminated from vegetables with 1–3 kGy or 100 krad of irradiation (Lacroix & Ouattara 2000). Higher vitamin C content was observed in clementines for the entire preservation period after an irradiation treatment (Abdellaoui et al. 1995). Greater synthesis of flavonoids in oranges was observed with the combination of irradiation and storage at 20°C (Oufedjikh et al. 2000). Elimination of pathogenic bacteria such as *Pseudomonas talasii* and *Mycogone perniciosa*, along with reduction of PPO activity and the browning reaction, was observed in mushrooms after irradiation with 1 kGy (Skou et al. 1974).

Lighting conditions and oxygen concentration also contribute significantly to the quality parameters of plant-based foods during the storage period. The phenolic content of fruits and vegetables generally increases with elevated light or UV irradiation. A tenfold greater concentration of quercetin glycoside content was observed in sun-exposed clusters of Pinot noir grapes (Price et al. 1995). More anthocyanin and quercetin compounds were observed in sun-exposed apples, whereas other major phenolic compounds such as catechins, phloridzin, and chlorogenic acid were not significantly different for apples grown in the sun or the shade (Awad et al. 2001). A high correlation between phenolic compounds and oxygen concentration (>21 kPa) was observed in many fruits during postharvest storage. Greater anthocyanin and quercetin contents were in sun-exposed than shaded portions of Jonagold and Elstar apples (Lancaster et al. 2000). Zheng et al. (2008) determined that a high oxygen concentration increased the phenolic content of blueberries during storage. The oxidative stress induced by higher oxygen concentrations may contribute to the higher phenolic content, as this stress-induced condition stimulates the pentose phosphate, shikimate, and phenylpropanoid pathways.

Other than physical conditions, use of chemical treatments, including natural products or antioxidant stimulators from plant-based foods, is increasingly gaining popularity for improving postharvest storage quality. Chemical treatment with hexanal vapor and 1-methylcyclopropene (MCP) treatments increase firmness, superoxide dismutase activity (SOD), and ascorbate peroxidase activity in sweet cherries (Sharma et al. 2010). The same study revealed that the levels of anthocyanins or phenolic content either increased or remained the same during 30 days of storage. Chen et al. (2010) determined that 1-MCP vacuum infiltration treatments significantly improved the physiological quality of Suli pears during cold storage. The anthocyanin content of strawberries continuously decreased after treatments with natural antimicrobials (methyl jasmonate, ethanol, or combinations of both) (Ayala-Zavala et al. 2005); however, total phenolic compounds and antioxidant activity capacity increased sharply during the first 5 days at 7.5°C. Peel browning of Bartlett pears was reduced by diphenylamine and ethoxyquin treatments (Feng et al. 2004).

Natural nonphenolic antioxidants are generally used to mitigate biochemical deterioration such as enzymatic browning in fruits. This provides protection against both microbial and chemical degradation (Wu et al. 2004). Ascorbic acid is the most widely used antioxidant; cysteine, N-acetylcysteine, calcium salts, citric acid, and other organic acids are also used to increase the shelf life of fruit. An antioxidant dipping treatment (1% ascorbic acid + 1% citric acid) increased the ascorbic acid content and total phenolic metabolites of fresh-cut apples (Cocci et al. 2006). Robles-Sanchez et al. (2009) determined that fresh-cut mango cubes had a higher total phenolic content after antioxidant dipping treatments. Sun et al. (2010) determined that ascorbic acid with 1% chitosan solution increased SOD and catalase activities, resulting in higher ascorbic acid and glutathione contents in the pulp of treated litchi. The ascorbic acid content of fruits and vegetables varies widely and largely depends on genotypes, preharvest climatic conditions, cultural practices, maturity, harvesting methods, and postharvest handling (Lee & Kader 2000). It generally decreases with longer storage time; low temperatures; and bruising, trimming, and other mechanical injuries (Lee & Kader 2000). Phenolic phytochemicals such as cinnamic acid, cinnamaldehydes, coumarins, capsaicin, and tannins have an anti-*Helicobacter pylori* effect (Bae et al. 1999). Chun et al. (2005) detected a high antimicrobial activity for oregano extracts against *H. pylori*. Moreno et al. (2006) suggested that the antimicrobial efficacy of rosemary extracts was dependent on their phenolic composition, and the primary bioactive compounds present in the extracts were carnosic acid and rosmarinic acid. The antimicrobial effect of these phenolic phytochemicals during storage

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also occurs for foodborne pathogens and some human pathogens such as *H. pylori* (Shetty & Lin 2005).

Chitosan derivatives can improve the postharvest quality of food (Muzzarelli et al. 2012), which could be also achieved by soluble chitosan oligosaccharide due to stimulation of phenolic metabolites (Sarkar et al. 2010). Many strains of filamentous and edible fungi contain chitin in their tissues. Applying chitosan to plants induces a series of plant defense reactions, including an increase in the production of glucan hydrolases and phenolic compounds and synthesis of specific phytoalexins that possess antifungal activity (Muzzarelli et al. 2012). Chitosan-treated fruit and vegetables have an increased shelf life due to a reduction of respiration rate and water loss through semipermeable chitosan coating (Bautista-Baños et al. 2006). In addition, chitosan-treated tomatoes were resistant to *Rhizoctonia* (Mazaro et al. 2009). Similarly, coating rice seeds with chitosan improved seedling growth and root activity and was inhibitory to fungi (Zeng & Shi 2009). Water-soluble chitosan derivatives are also very effective in inhibiting some bacterial strains (Muzzarelli et al. 1990, Jung et al. 2010).

α-amylase: an enzyme present in human saliva and the pancreas that helps to break down starch into simple sugars such as maltose and glucose

α-glucosidase: an enzyme that helps to break down starch and disaccharide to glucose

The phenolic content and antioxidant activity of fruits and vegetables also change with maturity, ripening, and storage time. Advanced stages of ripeness of high bush blueberries showed higher anthocyanin content (Kalt et al. 2003). Postharvest preservation of fruits largely depends on the antioxidant activity of phenols during storage. A study with four different cultivars of apples revealed an initial increase of SOD activity in well-preserved cultivars during storage (5°C for 120 days) (Adyanthaya et al. 2009). The high SOD activity in this study correlated with a high phenolic content and high total antioxidant activity.

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5.3. Phenolics to Combat Noncommunicable Chronic Diseases

Phenolic phytochemicals possess antimutagenic, anticarcinogenic, and antiglycemic properties and potentially can be targeted for the prevention of chronic diseases through the design and development of health-promoting foods and food ingredients. Phenolic phytochemicals can help maintain cellular homeostasis and protect cells against oxidative stress–induced malfunction and related pathogenesis. Most of the diseases including chronic NCDs involve the breakdown of the cellular redox (oxidation-reduction) balance and production of reactive oxygen species, which eventually leads to apoptosis and necrosis (Voehringer 1999).

Dietary phenolic phytochemicals and their metabolites may influence digestion, absorption, and metabolism of dietary carbohydrates such as starch and sucrose. Cells respond to phenolic phytochemicals mainly through direct interactions with receptors or enzymes involved in metabolic processes of digestion and signal transduction, or through modifying gene expressions. This may result in a modification of the redox status of the cell that can trigger a series of redox-dependent reactions (Ordovas 2006). Dietary phenolic metabolites from different plant-based sources influence glucose metabolism by several mechanisms, such as inhibition of carbohydrate digestion and glucose absorption in the intestine, stimulation of insulin secretion from the pancreatic β-cells, modulation of glucose release from the liver, activation of insulin receptors and glucose uptake in the insulin-sensitive tissues, and modulation of hepatic glucose output (Hanhineva et al. 2010). Carbohydrate digestion and glucose absorption are obvious targets for better glycemic control after high carbohydrate meals, and α-amylase and α-glucosidase are the key enzymes responsible for the digestion of dietary carbohydrates to glucose. Inhibition of these digestive enzymes could reduce the rate of glucose release and absorption in the small intestine and consequently suppress postprandial hyperglycemia (Hanhineva et al. 2010). Many in vitro studies have revealed that phenolic metabolites, including flavonoids (anthocyanins, catechins, flavanones, flavonols, flavones, and isoflavones), phenolic acids, and tannins (proanthocyanindins and ellagitanins), inhibit α-amylase

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and α-glucosidase activities (Hanhineva et al. 2010). Polyphenolic extracts of foods, including berries (strawberries, raspberries, blueberries, and black currants), vegetables (pumpkin, beans, and eggplants), green and black tea, and red wine, also inhibited α-amylase and α-glucosidase in in vitro studies (Cheplick et al. 2007, 2010; Pinto et al. 2008; McCue et al. 2005; Kwon et al. 2008).

The high phenolic content of apple cultivars was associated with enhanced postharvest preservation and α-glucosidase inhibition during 120 days of storage (Adyanthaya et al. 2010). A probable role of the phenolics in apples in the reduction of the risk of developing type 2 diabetes is in the modulation of postprandial glucose. Barbosa et al. (2010) also correlated phenolic content with α-glucosidase inhibition in aqueous and ethanol extracts of 10 different apple cultivars after harvest. Red Delicious and Honeycrisp apples had higher phenolic content and high total antioxidant activity. Higher phenolic content, antioxidant activity, and α-glucosidase inhibition was observed in the peel extracts compared to pulp extracts. The aqueous pulp extracts had greater α-amylase inhibition compared to the peel. The major phenolic compounds in the peel extracts were quercetin derivatives, protocatechuic acid, and chlorogenic acid, whereas pulp extracts had quercetin derivatives, chlorogenic acid, and *p*-coumaric acid. In another postharvest study, a similar correlation was observed between phenolic content and α-glucosidase inhibition in both peel and pulp extracts of six different apple cultivars during six months of storage. Apples treated with 1-MCP remained firm and retained total phenolic content, total antioxidant activity, α-glucosidase, and α-amylase inhibitory activities in both peel and pulp extracts during the storage period (D. Sarkar, C. Ankolekar, D. Greene, and K. Shetty, unpublished results). The effect of the chemical treatment (1-MCP) was more prominent in the peel compared to the pulp extracts (D. Sarkar, C. Ankolekar, D. Greene, and K. Shetty, unpublished results). All of these in vitro studies revealed a strong association between phenolic content and α-glucosidase inhibitory activity and supported the promising use of apples as a possible dietary countermeasure and part of complementary strategies to reduce and manage the risk of type 2 diabetes developments in the early stages and to manage diabetic complications.

Similar enzyme inhibitory activity was also observed in in vitro studies with different pear cultivars. Pear cultivars from Oregon and Massachusetts, including Red Anjou, Green Anjou, Bartlett, and Starkrimson, had high phenolic content, antioxidant activity, and α-glucosidase inhibitory activities in both peel and pulp extracts (D. Sarkar, C. Ankolekar, D. Greene, and K. Shetty, unpublished results). High α-amylase inhibitory activity was also observed in the aqueous pulp extracts of these pear cultivars. Similarly, different sweet cherry and tart cherry cultivars have the potential for type 2 diabetes management based on enzyme inhibition model studies. Out of 22 different cherry cultivars, many (Montmorencey, Jubileum, Northstar, Baleton) had high phenolic content, antioxidant activity, and α-glucosidase inhibitory activities. We observed high α-glucosidase inhibition and low α-amylase inhibition in almost all cherry cultivars (D. Sarkar, A.C.L. Barbosa, C. Ankolekar, D. Greene, and K. Shetty, unpublished results). Therefore, cherries offer the potential for good postprandial blood glucose management without the common side effects associated with high α-amylase inhibition.

Phenolic metabolites also influence glucose transporters and thus mediate intestinal absorption of glucose. Several flavonoids, including chlorogenic, ferulic, caffeic, and tannic acids, quercetin monoglucosides, tea catechins, and naringenin inhibit Na^+-dependent sodium-dependent glucose transporter-1 (SGLT1)-mediated glucose transport (Welsch et al. 1989, Li et al. 2006). Several studies conducted in animal models also revealed that phenolic metabolites can alter postprandial blood glucose response. Song et al. (2005) observed that hyperglycemia was significantly decreased in diabetic rats after administration of glucose with quercetin. In another study, Hanamura et al. (2006) reported a reduction of plasma glucose levels in mice after administration of maltose with a crude acerola phenolics' fraction, suggesting inhibition of α-glucosidase activity and intestinal

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glucose transport. Berries, a rich source of anthocyanins, significantly decreased the peak glucose increment by reducing the rate of sucrose digestion or absorption from the gastrointestinal tract (Törrönen et al. 2010). Soybean isoflavonoids have a positive impact on β-cell function. Choi et al. (2008) determined that isoflavonoids, such as genistein and daidzein, preserved in mice insulin production by β-cells. Flavonoids, such as quercetin, luteolin, and apigenin, also provide protective function against β-cells. Dietary phenolics may also influence glucose metabolism through stimulation of peripheral glucose uptake in both insulin-sensitive and insulin-nonsensitive tissues (Park et al. 2007).

Flavonoid intake can also lower the risk of coronary disease and cancer. A high intake of flavonoids (approximately 30 mg/day) was associated with a 50% reduction in the coronary heart disease mortality rate (Montonen et al. 2005). The mechanism of action of flavonoids against cardiovascular diseases includes inhibition of low density lipoprotein oxidation and inhibition of platelet aggregation and adhesion (Ceriello et al. 1992). Phenolic metabolites are also capable of inhibiting cholesterol esterification and intestinal lipoprotein secretion (Kaplan & Aviram 2005). Due to the high antioxidant activity of phenolics, they can regulate cellular function through inhibition of prooxidant enzymes, induction of antioxidant enzymes, and inhibition of the redox-sensitive transcription factors (Ceriello 2003). These studies, along with other epidemiologic studies, suggest that phenolics can have therapeutic roles with health-protective benefits by acting as modifiers of many physiological functions in the human body. Fruits such as apples, pears, and cherries and cultivars with high phenolic content not only have the potential to control postprandial hyperglycemia using in vitro enzyme models but also have the additional potential to manage cellular redox imbalances to prevent diabetic complications through free-radical, scavenging-linked antioxidant activity. Further clinical studies in animal models, human clinical studies, and epidemiologic studies are needed to validate the biochemical rationale developed from these in vitro studies for type 2 diabetes and chronic heart disease management.

6. DIFFERENT MECHANISMS TO STIMULATE PHENOLIC CONTENT AND PROFILES IN FOOD

Phenolic phytochemicals have an important role in the development of functional foods for current and future health and wellness through dietary strategies, particularly to manage chronic diseases (Shetty & McCue 2003). Enhancing phenolic phytochemicals in plant-based food sources can help prevent disease and aid in the management of NCDs, as this can provide reduced-cost alternatives to drug treatments at later stages of disease that are not affordable in many less-developed countries and among the poor in well-developed countries. Novel tissue culture and bioprocessing technologies have been developed for consistent production of bioactive and optimized dietary phytochemical profiles in food crops and also in medicinal plants (Shetty 1997, Shetty & Wahlqvist 2004). Direct application of natural antioxidants as a seed treatment or during pre- and postharvest treatments can improve the phenolic content of plant-based products (Sarkar et al. 2010). Metabolic innovations are available to improve the biosynthesis of phenolic metabolites in different plant systems by controlling the regulation of the pentose phosphate pathway (PPP) (Shetty & Wahlqvist 2004). Previous research in our laboratory has revealed that biosynthesis can be enhanced through biochemical and microbial stimulations (Randhir & Shetty 2006, Sarkar et al. 2010). Phenolic compounds in plants are derived through the pentose phosphate, shikimate, and phenylpropanoid pathways (Shetty 1997, 2004). The first rate-limiting step of the PPP is glucose-6-phosphate dehydrogenase (G6PDH) activity (Phang 1985), which converts glucose-6-phosphate into ribulose-5-phosphate and also produces reducing equivalents [nicotinamide adenosine di-phosphate hydrogen (NADPH)] for cellular

Pentose phosphate pathway (PPP): biochemical pathway that generates nicotinamide adenosine di-phosphate hydrogen (NADPH) and pentose phosphate derivatives to support anabolic need

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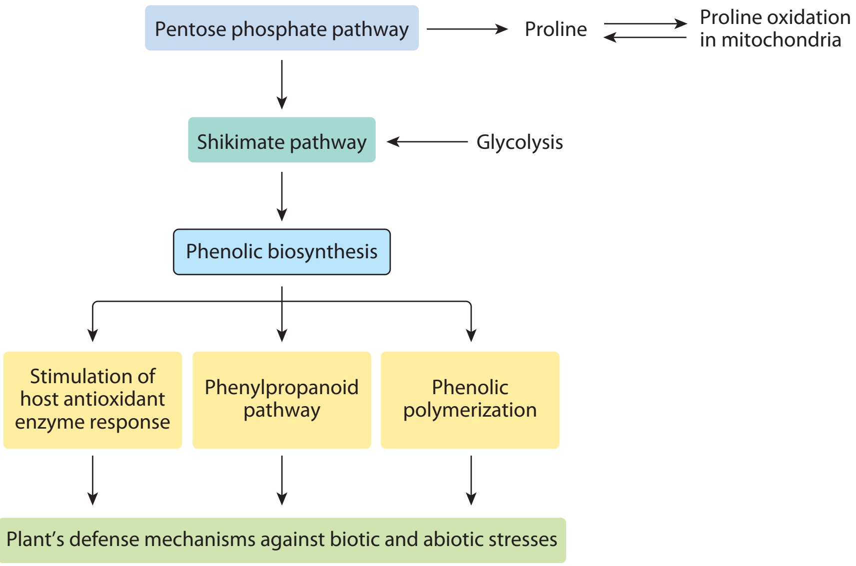

Figure 3

Stimulation of phenolic biosynthesis, which improves plant's defenses against biotic and abiotic stress through the upregulation of the proline-associated pentose phosphate pathway (adapted from Shetty 1997).

anabolic reactions. The PPP also generates from glycolysis erythrose-4-phosphate, which along with phosphoenol pyruvate, is channeled to the shikimate pathway to produce phenylalanine, which is directed through the phenylpropanoid pathway to produce phenolic metabolites (Shetty & Wahlqvist 2004).

A model has been proposed to meet the cellular requirement of reducing equivalents, whereby phenolic metabolites can enhance the antioxidant defense response in plant systems through upregulation of the PPP (Shetty 1997) (**Figure 3**). The proline-associated PPP can stimulate both the shikimate and phenylpropanoid pathways; therefore, modulation of this pathway can lead to the stimulation of phenolic biosynthesis and other antioxidant enzymes in plants (Shetty 1997, Shetty & McCue 2003). Proline, in association with the PPP, can play a key role in the metabolic regulation in this defense mechanism (Hare et al. 1999, Shetty 2004). The demand for NADPH for proline synthesis in the cytosol may increase the cellular NADP+/NADPH ratio to activate G6PDH, the first rate-limiting enzyme of the PPP (Shetty 2004). These insights for the proposed model were gained when the proline analog, azetidine-2-carboxylate, an inhibitor of proline dehydrogenase, was used and an enhanced tolerance to this analog could stimulate proline synthesis, which drives the demand for NADPH and thereby phenolic synthesis (Elthon & Stewart 1984, Shetty 2004, Shetty & Wahlqvist 2004). Another analog, hydroxyproline, which is a competitive inhibitor of proline incorporation into proteins, can drive overexpression toward phenolic synthesis (Sarkar et al. 2010) or at low levels can deregulate proline synthesis via feedback inhibition (Shetty & Wahlqvist 2004). Therefore, deregulation of the PPP can drive metabolic flux toward erythrose-4-phosphate for biosynthesis of shikimate and phenylpropanoid metabolites. At the same time, proline serves as a reducing equivalent by donating protons, instead of NADH, for adenosine triphosphate synthesis through oxidative phosphorylation in the mitochondria (Hare & Cress 1997).

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On the basis of the above insights, the overall defense mechanism of plants is based partly on both phenolic biosynthesis and its correlation with the stimulation of an antioxidant enzyme response to counter mitochondrial oxygen malfunction (Shetty & Wahlqvist 2004). Within a plant system model, acid plus exogenous phenolic proline analogs and precursor combinations and microbial elicitors can be used to stimulate phenolic biosynthesis and other antioxidant enzymes to counter oxidative stress in plants. Proline and G6PDH correlations during phenolic response were also associated with phenolic content, potential polymerization of phenolics by guaiacol peroxidase, and antioxidant activity based on the free-radical scavenging activity of phenolics and other antioxidant enzymes such as SOD (Shetty & Wahlqvist 2004). This redox pathway–linked model provides a scientific foundation for developing different dynamic metabolic stimulation strategies to harness the benefits of phenolic phytochemicals from food and medicinal plants for food preservation with enriched phenolic phytochemicals and for human health through optimization of phenolic metabolite-enriched functional foods and nutraceuticals to counter chronic diseases such as NCDs. Such pathways are accessible through a variety of plants across a diverse ecology with different abiotic and biotic stresses and reproductive functions. Such food crop diversity can provide ingredient sources for food preservation and human health while allowing management of diverse ecological systems.

Therefore, studying plant defense responses that involve antioxidant protection can be useful in developing more health-optimized antioxidant-enriched agricultural food crops in diverse ecological niches and cropping systems. Phenolic biosynthesis in plant systems can be stimulated through different avenues such as seed treatment, manipulation of the soil rhizosphere, and external application of natural antioxidants during early growth stages and also during preharvest or postharvest treatments with natural bioprocessed elicitors (**Figure 4**). Mobilization of antioxidant enzymes directly correlating with phenolic metabolic responses in seeds and in other plant parts

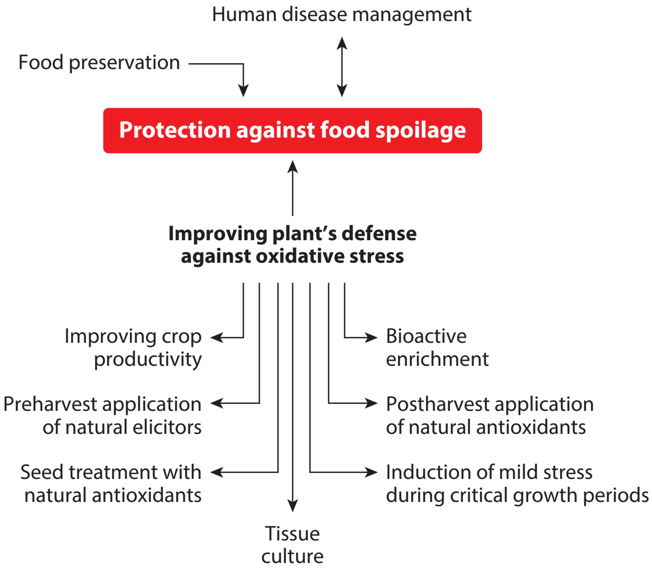

Figure 4

Pre- and postharvest applications of new technologies and tools for improving food preservation and enhancing bioactive compounds in plant-based foods, done in an effort to combat the global epidemic of noncommunicable chronic diseases.

is an efficient and effective strategy to harness the health-beneficial compounds from diverse food crops grown under diverse ecological conditions. Legumes and other plants have been studied by using such scientific rationale to stimulate health-relevant and antimicrobial plant bioactives (Randhir et al. 2007). Fermentation of food with beneficial bacteria can also enhance phenolic -linked antioxidant activity (Ankolekar et al. 2011) and, when such fermented bioactive ingredients are used, they could improve preservation and the shelf life of fruits and vegetables during postharvest storage.

7. CONCLUSIONS

Diverse biological functions of phenolic metabolic responses and metabolites accumulated in dietary crop plants provide multiple opportunities to utilize bioactive compounds for food preservation and for human health applications. The major biological function of accumulated phenolic metabolites is their ability to counter oxidative stress correlated with higher antioxidant potential. Metabolic manipulation of food phenolics can prevent both biotic and abiotic degradation and spoilage of food during postharvest storage. Advances in the understanding of phenolic chemistry and biochemistry will expand the scope of the application of phenolics from crop production improvement to postharvest preservation applications. The improvement in the end-use quality of plant foods by enrichment with plant phytochemicals has significance in agricultural production for more efficient management of diverse agricultural ecologies and has potential applications in human health for managing NCDs. Selective modification and stimulation of phenolic profiles using metabolic innovations during postharvest stages may enhance both quality and longevity during storage. Such an approach can be important in meeting the global challenges of food security from crop diversity and for advancing increased consumer demand for healthy foods to manage NCDs, while also addressing the challenges of sustainability in maintaining ecological diversity.

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SUMMARY POINTS

1. The evolutionary role of phenolics in plants mainly is to provide defense against abiotic and biotic stresses, and it has relevance in plants' reproductive functions.
2. Understanding plant defense response mechanisms involving phenolics also helps to utilize this large group of potentially targeted bioactive compounds for different applications ranging from crop protection to food preservation in postharvest stages to human health benefits for NCD prevention.
3. The diversity of the chemical structures of phenolic metabolic responses in diverse crops and the diverse ecological niches that are under redox control enable the recruitment of an antioxidant defense response that determines a phenolic compound's main biological function coupled with related functional benefits.
4. Phenolic metabolites from a variety of plant-based foods are the main sources of dietary antioxidants and potentially provide significant benefits to human health when consumed through diet.
5. Modification of phenolic biosynthesis with new metabolic innovation strategies and tools can help to achieve enhanced postharvest preservation of plant-based foods with concurrent benefits for human health.

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FUTURE ISSUES

1. Research related to sourcing natural phenolic metabolites from dietary crops through metabolic innovations during the pre- and postharvest stages of food crop production is beneficial for more efficient ingredient design strategies for food preservation and human health applications. It is important to understand the specific mechanisms of food phenolics in sourced crop systems for improving bioactive quality and for monitoring the changes of phenolic profiles during postharvest storage conditions.
2. Research focusing on industrial and agricultural applications of phenolic metabolites for food crop bioactive profiles is needed in the future.
3. Animal and clinical studies with phenolic-enriched foods and food ingredient profiles of consistent quality will strengthen the present understanding of phenolics for human health applications, especially for diet-linked NCD conditions.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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