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REVIEW

The role of polyphenols in food safety: mitigating the formation of acrylamide and hydroxymethylfurfural and their health risks

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Abstract

The formation of toxic compounds such as acrylamide (AA) and hydroxymethylfurfural (HMF) during thermal food processing (>120 °C) represents a significant risk to human health, as they have been associated with neurotoxic, genotoxic, and carcinogenic effects. However, several studies have shown that polyphenols can reduce the levels of these toxic compounds. In this context, this review examines the potential of polyphenols to mitigate the formation of AA and HMF via distinct mechanisms during the Maillard reaction (MR). In general, these compounds interact with precursors and intermediates of the MR. Thus, polyphenols represent a natural and effective strategy for improving food safety, thereby promoting the development of healthier products. However, Future challenges remain, including the elucidation of the chemical mechanisms involved in the action of polyphenols, an in-depth study of factors such as pH, temperature, and food matrix, toxicological and metabolic evaluations, regulatory aspects, the use of clean and sustainable technologies for obtaining polyphenols, optimization of extraction methods, and application in food matrices while considering sensory effects. A multidisciplinary approach will be vital to achieving the effective and safe application of polyphenols in the food industry.

Keywords: Polyphenols; Maillard reaction; Inhibition; Hydroxymethylfurfural; Acrylamide.

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1. Introduction

Fried, baked, and grilled foods have flavors, aromas, and colors that are attractive and sensorially acceptable to consumers (Yu et al., 2024; Zhang et al., 2023). Many of these characteristics are due to chemical reactions known as the Maillard reaction, which occur within the food matrix during the cooking process (Pedreschi et al., 2021). This reaction is initiated by proteins and carbohydrates, with high temperatures and water content serving as the primary catalysts of this chemical phenomenon (de Sousa Fontes et al., 2024).

The Maillard Reaction (MR) is a chemical process that promotes the formation of compounds such as melanoidins, pyrazines, thiophenes, furans, pyrans, pyrroles, and pyrimidines, which improve the development of flavors, colors, and aromas through different chemical pathways (Tang et al., 2024). However, this chemical process also favors the development of toxic compounds such as acrylamide (AA) and 5-hydroxymethylfurfural-dehyde (HMF), which are recognized as potentially carcinogenic compounds (Borba et al., 2024), linked to neurological damage (Dong et al., 2025),

reproductive (Thangamany et al., 2025), endocrine (Baraka et al., 2024), genetic (Kontaş Yedier et al., 2022), cellular (Farodoye et al., 2024), hepatic (Alejolowo et al., 2024), digestive (Chen et al., 2024), respiratory (Ji et al., 2018), cardiovascular (Huang et al., 2018a), and inflammatory (Liu et al., 2025).

HMF is synthesized via the MR pathway due to the thermal decomposition of carbohydrates in foods subjected to high temperatures (T° > 120 °C) (Tang et al., 2024). This compound has a furan ring attached to a formyl group and a hydroxyl group, with a molecular weight of 126.11 g/mol (Varelis, 2024). Meanwhile, AA is a compound generated in starchy products subjected to high temperatures (T° > 120 °C) due to a reaction between reducing sugars and asparagine (Bachir et al., 2023; Xue et al., 2023). This compound is formed by an amino group linked to a vinyl group and a carboxyl group, with a molecular weight of 71.08 g/mol (Bachir et al., 2023). Both compounds (HMF and AA) are polar molecules with low molecular weights and high solubility in water, which favors their easy adsorption in the gastrointestinal tract and subsequent distribution in organs through the bloodstream (Wu et al., 2024). Thus, these compounds pose a critical challenge in food safety, highlighting the need for effective strategies that reduce their formation without compromising the sensory characteristics of foods (Yu et al., 2024).

Polyphenols are secondary metabolites whose chemical structure is composed of phenolic rings, which must always be hydroxylated, with a molecular weight that varies between 150 and 3000 g/mol (El-Saadony et al., 2024). These compounds can be classified as flavonoids (flavonols, flavanones, isoflavones, neoflavanoids, chalcones, anthocyanins, flavones, flavanonols, and flavanols) and non-flavonoids (stilbenes, phenolic acids, and lignans) (El-Saadony et al., 2024). Polyphenols stand out for their antioxidant capacity, which has been linked to the treatment and prevention of diseases related to oxidative stress (Piazza et al., 2024), as well as other bioactive properties such as neuroprotective (Dong et al., 2025), antiglycan (Wang et al., 2025), anti-inflammatory (Alejolowo et al., 2024), antidiabetic (Zouaoui et al., 2025), cytoprotective (Gupta et al., 2024), genoprotective (Wang et al., 2022), and anticancerogenic (Chang et al., 2025).

Interestingly, polyphenols are not only associated with health benefits, but also with their ability to inhibit the formation of toxic compounds during thermal processing of food (T° > 120 °C), such as advanced glycation end products (Valle-Sánchez et al., 2025), furfural (Zheng et al., 2024), heterocyclic amines (Xie et al., 2025), as well as polycyclic aromatic hydrocarbons (Timón et al., 2025). Therefore, several studies have focused on evaluating the ability of these compounds to reduce the formation of HMF and AA during the MR. In beef patties, Yu et al. (2024) observed that rosemary, turmeric, and bay leaf inhibited AA formation by ~44%, 46%, and 40%, respectively, and HMF formation by ~73%, 15%, and 77%, in hamburgers. The polyphenols present in these herbs probably inhibit the formation of compounds during the MR, reducing HMF formation. On the other hand, Zhang et al. (2023) mentioned that polyphenols can interact with reducing sugars, reducing their availability for the formation of HMF and AA. Similarly, Assefa et al. (2025) incorporated phenolic extracts of kesse, koseret, and tosign into potato chips, achieving 63.4%, 58.5%, and 44.8% inhibition of AA formation, respectively.

Furthermore, these products maintained good sensory acceptability (flavor, odor, and color). However, the mechanisms of interaction between polyphenols and MR intermediates are still a matter of debate. Thus, this review compiles information on the potential of polyphenols to inhibit the formation of toxic compounds (HMF and AA) during high-temperature food processing, while also providing alternatives for developing safe and sensorially acceptable foods.

2. Compounds derived from the Maillard reaction (MR)

MR is a chemical process between reducing sugars (glucose and fructose) and amino acids in thermally processed foods (>120 °C), such as baked goods, coffee, and meat products (He et al., 2019). However, if MR is not controlled, it can generate substances harmful to health, such as AA, HMF, and advanced glycation end products (Figure 1).

MR is divided into three stages. During the first stage, reducing sugars and amino compounds (amino acids and proteins) react by condensation processes, producing glucosamines that are rearranged into Amadori and Heyns products (Yang et al., 2025). In the second stage, Amadori products are decomposed through enolizations, forming deoxysones and volatile compounds such as aldehydes, ketones, and pyrazines, which contribute to the aroma (Zhang et al., 2025). In the third stage, reactive intermediates undergo dehydration, fragmentation, cyclization, and polymerization, allowing the formation of melanoidins, nitrogenous polymers responsible for the brown color and toasted aroma in foods (Chen et al., 2025).

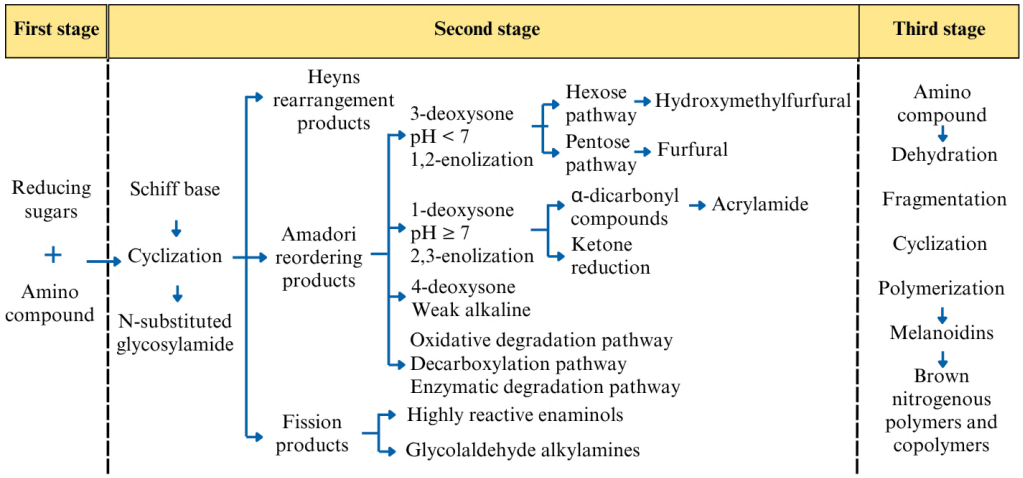

Figure 1. Stages and products of the Maillard reaction.

2.1. Factors affecting MR

During food processing, MR depends on factors such as pH, temperature, and water content, which can accelerate or retard its progress (Table 1). For example, a pH > 7 accelerates the reaction due to the formation of reactive intermediates such as Schiff bases, while acidic media (pH < 7) slow the formation of these compounds (de Sousa Fontes et al., 2024). On the other hand, high temperatures (> 120 °C) exponentially accelerate the reaction due to the increase in the kinetic energy of the molecules, facilitating the interaction between reducing sugars and amino acids (García-Ríos et al., 2024).

Regarding water content, a lower water activity accelerates the reaction, as it concentrates the sugars and amino acids and favors the formation of key intermediates, such as α-dicarbonyl compounds, Schiff bases, and Amadori products (Tang et al., 2024). These factors promote the formation of compounds such as melanoidins (brown pigment) and volatile substances responsible for flavor (sulfur compounds) and aromas (pyrazines, pyrans, thiophenes, furans, pyrroles, and pyrimidines), as well as toxic compounds such as AA and HMF (Table 1) (Pucci et al., 2024).

3. Toxic compounds: Acrylamide (AA) and hydroxymethylfurfural (HMF)

AA is an unsaturated amide composed of a carbon-carbon double bond linked to a carbonyl group and an amide group (Figure 2a) (Capuano & Fogliano, 2011). This molecule can be formed by the interaction between reducing sugars and the α-amino group of L-asparagine or other free amino acids (Auñon-Lopez et al., 2025). It can also be formed by the decomposition of furan intermediate compounds with carbonyl groups of the MR (Dong et al., 2025).

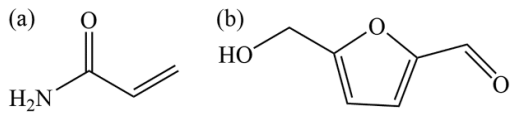

Figure 2. Structural composition of acrylamide (a) and hydroxymethylfurfural (b).

HMF is a heterocyclic compound ($C_6H_6O_3$), which contains a ring attached to a hydroxyl group and a carbonyl group (Figure 2b) (Capuano & Fogliano, 2011). During MR, reducing sugars such as glucose, fructose, and sucrose are decomposed at high temperatures (> 120 °C), forming HMF (Huang et al., 2024). The increase in temperature accelerates the sugar degradation reactions and the low moisture content concentrates these substrates, resulting in the formation and accumulation of HMF (Guan et al., 2023).

3.1. Health implications of acrylamide (AA) and hydroxymethylfurfural (HMF)

Ingestion of food contaminated with AA is the main route of absorption (Jackson & Al-Taher, 2022). After adsorption, AA enters the bloodstream and is transported to the liver, where it is metabolized by the cytochrome P450 monooxygenase (CYP2E1) enzyme, resulting in the generation of glycidamide (Settels et al., 2008). This compound can form adducts with DNA, interfering with normal DNA replication and gene transcription (Settels et al., 2008). This induces the production of reactive oxygen species (ROS), such as superoxide anion and hydrogen peroxide, generating an intracellular redox imbalance by exceeding the endogenous antioxidant capacity (Yang et al., 2021). ROS interact with DNA, causing modifications such as oxidation of nitrogenous bases and breakage of single strands (Farodoye et al., 2024).

Table 1
Compounds formed during the Maillard reaction

Factors	Process parameters	Precursor compounds	Compounds generated	References
Temperature Time	145 °C 10, 20, 40, 60, 80, 120, and 180 min	Fatty acids (oleic acid, linoleic acid, and linolenic acid), carbohydrates, reducing sugars (glucose), and glutathione	Volatile compounds (thiophenes, furans, sulfides, aldehydes, alcohols, ketones, and carboxylic acids), and glutathione-Amadori compounds	Du et al. (2025)
Temperature Time pH	37 and 95 °C 10, 90, 120, and 1440 min ~6 to ~8	Peptides, amino acids (cysteine, alanine, asparagine, arginine, etc.), proteases (flavorzyme and trypsin), reducing sugars (ribose), and proteins	Volatile compounds (pyrazines, furans, aldehydes, and sulfides)	Nishimura & Abe (2025)
Time	6 weeks, 1 to 18 years	Reducing sugars, deoxyglucosone, carbohydrates, amino acids, and α-dicarbonyl compounds	Toxic compounds (HMF, furfural, 5-methylfurfural, glyoxal, methylglyoxal, 2,3-butanedione, and 2,3-pentanedione), and volatile compounds (furanoids, aldehydes, sulfides, alcohols, pyrazines, ketones, and oxazoles)	Huang et al. (2024)
Time Temperature	1.5 and 3.5 min 130 and 190 °C	Proteins, lipids, amino acids (lysine), lipid hydroperoxide, malondialdehyde, thiobarbituric acid, and polyunsaturated fatty acids	Toxic compounds (AGEs and AA), and volatile compounds (alcohols and furans)	Auñon-Lopez et al. (2025)
-	-	Proteins, amino acids (lysine and arginine), reducing sugars, peptides, and α-dicarbonyl compounds	Toxic compounds (AGEs)	Bieck et al. (2025)
Time Temperature	1, 3, 6, 12, 15, 18, 21, 24, 27, and 30 min 200, 220, and 240 °C	Protein, reducing sugars, and α-dicarbonyl compounds	Pigments (melanoidins)	Lee et al. (2024)
Time Temperature pH Salinity Humidity	10, 20, 30, 40, 50, 60, 120, and 180 min 40, 60, 80, 100, 120, 140, 160, and 200 °C 2.41, 3, 5.25, 6.40, and 7.83 NaCl (0, 2, 4, 6, 8, 10, 12, 14, and 16%) Soak in water for 15 to 60 min (~10 to ~25%)	Reducing sugars, amino acids, and oils	Toxic compounds (HMF and furfural)	Guan et al. (2023)
Time Temperature pH	60 min 121 °C 4 and 6	Amino acids (thiamine, cysteine, asparagine, etc.), fatty acids, reducing sugars (glucose, mannose, fructose, maltose, ribose), lipids, carbohydrates, and proteins	Volatile compounds (ketones, aldehydes, hydrocarbons, alcohols, esters, furans, acids, phenols, thiols, thiazoles, thiophenes, pyrazines, and pyrroles)	de Sousa Fontes et al. (2024)
Temperature	UHT treatment	Amino acids (lysine, glycine, alanine, etc.), α-dicarbonyl compounds, furosine, furans, proteins, carbohydrates, lipids, and reducing sugars (glucose, dextrin, maltose, maltotriose)	Toxic compounds (HMF, AA, and furfural)	Pucci et al. (2024)
Time Temperature Humidity	190, 210, and 230 °C 7, 10, and 14 min ~15 to ~50%	Carbohydrates, lipids, proteins, reducing sugars, amino acids (lysine, arginine, histidine, serine, etc.), and α-dicarbonyl compounds	Toxic compounds (AGEs, HMF, methylglyoxal, and glyoxal), pigments (melanoidins), and volatile compounds (aldehydes, ketones, alcohols, sulfides, terpenes, acids, hydrocarbons, phenols, esters, and ethers)	Tang et al. (2024)
Time Temperature	2.5 min 180 °C	Reducing sugars (fructose, glucose), carbohydrates (sucrose), and amino acids (asparagine)	Toxic compounds (AA, HMF, and furan)	García-Ríos et al. (2024)
Time Temperature Humidity	40, 150, 160, 170, and 180 °C ~45% to ~54%	Lipids, malondialdehyde, proteins, and reducing sugars	Toxic compounds (AGEs)	Y. Liu et al. (2024)

HMF: Hydroxymethylfurfural; AA: Acrylamide; AGEs: Advanced Glycation End Products; UHT: Ultra High Temperature.

Additionally, within the cell membrane, ROS initiate reactions with lipids, triggering a process of lipid peroxidation that forms compounds such as malondialdehyde and 4-hydroxynonenal, which disrupt the cell membrane's integrity and act as cytotoxic agents (Quasmi et al., 2025). ROS also affects the structure and function of proteins by oxidation, altering metabolic pathways and activating inflammatory responses and apoptosis, which favors genetic instability and promotes mutations (Gupta et al., 2024).

The International Agency for Research on Cancer (IARC) classified AA in group 2A of carcinogens, and the European Food Safety Authority limited its intake to between 0.4 and 1.9 µg/kg to reduce its presence in starchy foods exposed to high temperatures, such as potato products, cereals, coffee, baby food, and bakery items (Borba et al., 2024).

On the other hand, the ingestion of food contaminated with HMF can have carcinogenic effects (Table 2). HMF is metabolized in the liver to 5-sulfoxymethylfurfural (SMF) by enzymes such as sulfotransferases (Monien et al., 2009). This compound is highly reactive, with the ability to form adducts with DNA, which can generate genotoxic mutations that favor the initiation of the carcinogenic process (Pastoriza de la Cueva et al., 2017). Moreover, it can induce oxidative stress and activate proinflammatory pathways, promoting genetic instability and abnormal cell proliferation (Capuano & Fogliano, 2011). Therefore, the IARC has classified HMF as a possible human carcinogen (Group 2B), establishing the median lethal dose at 40 mg/kg of HMF in honey (Borba et al., 2024). In this regard, Table 2 summarizes how the intake of relatively low doses of both compounds (HMF and AA) can trigger toxicological effects, as well as the possible mechanisms that lead to this damage to biological systems.

4. Polyphenols: an alternative to mitigate toxic compounds

Polyphenols are molecules composed of at least one benzene ring, which must always be hydroxylated (Huamán-Castilla et al., 2024). These compounds are secondary metabolites, which, unlike primary metabolites (lipids, amino acids, or carbohydrates), are not essential for growth or reproduction. However, they perform defensive functions against pathogens, herbivores, UV radiation, and abiotic stress. These compounds are generally present within cellular vacuoles, which are protected by a structural matrix composed of polymers (Pedreschi et al., 2018). To date, more than 8000 phenolic compounds have been identified, ranging from low molecular weight molecules (~120 Da) to high molecular weight polymeric complexes (~20 kDa) (El-Saadony et al., 2024).

Due to their chemical structural diversity, polyphenols can be classified as extractable and non-extractable (Huamán-Castilla et al., 2024). For example, extractable polyphenols, such as monomers and oligomers (catechins, anthocyanins, and phenolic acids), are soluble and are released at mild thermal temperatures (between 30 and 70 ºC) under atmospheric conditions (Harun et al., 2025). However, the polymers (condensed tannins and lignans) remain attached to the cell wall by covalent bonds or hydrophobic interactions (Figure 3) (Huang et al., 2025).Thus, advanced techniques at high temperatures and high pressures are required to extract these compounds.

Polyphenols can also be classified as flavonoids and non-flavonoids (Figure 4). This depends on the number of aromatic rings, the type of bonds between them, the length of side chains, and the presence of functional groups (methoxy, carbonyl, glycosyls, and esters) (El-Saadony et al., 2024). Flavonoids are subdivided according to the position of the phenyl group, the degree of hydroxylation, methylation and glycosylation (Yuan et al., 2025). These compounds are formed by two aromatic rings, connected by a three-carbon chain that forms a heterocyclic ring (Huamán-Castilla et al., 2024). Meanwhile, non-flavonoids lack this heterocyclic structure and are characterized by having one or more aromatic rings with hydroxyl groups (Pathiraja et al., 2023).

Polyphenol content can be determined by colorimetric methods such as the Folin-Ciocalteu method, which measures total phenol content based on its ability to reduce a reagent (Huamán-Castilla et al., 2024). However, this method provides a general or global value of the total polyphenols present in the sample. Therefore, chromatographic techniques coupled with mass spectrometry report quantitative values of the concentration of specific polyphenols or polyphenolic profiles (Tyagi et al., 2025). However, the phenolic profile is affected by the type of plant species (Purves et al., 2025), the part of the plant (Shi et al., 2025), as well as agronomic factors (Gao et al., 2025). In general, the leaves have high concentrations of flavonols and flavones, while the fruits are rich in anthocyanins, flavanols, and phenolic acids (Debnath-Canning et al., 2020).

Table 2
Health effects of acrylamide and hydroxymethylfurfural intake

Compounds	Administration dose	Study organism	Induced toxicity	References
Acrylamide	20 mg/kg – 21 d	Male Sprague-Dawley rats	Muscle weakness, ataxia, and disorders in nerve fibers	Dong et al. (2025)
	60 µg/kg – 56 d	Male and female Sprague-Dawley rats	Damage to testicular and ovarian tissues, cellular apoptosis, effects on the neurological and immune systems	Thangamany et al. (2025)
	5 mg/kg – 28 d	Mice	Neuronal damage and inflammation of brain tissue	Liu et al. (2025)
	0.5, 1, 2 mM – 24 h y 15, 30 y 50 mg/kg – 28 d	HepG2 cells and male BALB/c	Mitochondrial dysfunction, apoptosis, and liver injury	Li et al. (2025)
	0.125 y 0.25 mM – 180 d	Zebrafish	Transgenerational toxicity, neurological damage, reproductive and motor dysfunctions	Wang et al. (2024)
	0,1, 0,5, 2,5, 12,5 mg/kg – 28 a 30 h	Chicks	Delayed neural tube development	Becit-Kizilkaya et al. (2024)
	20 mg/kg – 28 d	Male Wistar rats	Oxidative stress, reproductive and neuroendocrine dysfunctions	Baraka et al. (2024)
	25, 50 y 100 mg/kg – 7 d	Flies (*Drosophila melanogaster*)	Apoptosis, oxidative stress and mitochondrial dysfunction	Farodoye et al. (2024)
	20 mg/kg – 21 d	Male Wistar rats	Liver damage and oxidative stress	Alejolowo et al. (2024)
	19.13 mg/kg – 28 d	Female Wistar rats	DNA damage, muscle weakness, oxidative stress, cellular atrophy, liver damage, and neuronal degeneration	Gupta et al. (2024)
	20 mg/kg – 60 d	Male Sprague-Dawley rats	Gastric damage, histological alterations, DNA damage, and apoptosis	Abd-Elhakim et al. (2024)
	50 mg/kg – 7 d y 1, 2, 4, 8, 12, 16 mmol/L – 24 h	Male Kunming mice and HepG2 cells	Liver damage, oxidative stress, apoptosis, and autophagy	Li et al. (2024)
	0.005, 0.01, 0.05, 0.1, 0.5, 1, 5 y 10 mM – 24, 48 y 72 h	Human lung cells (BEAS-2B)	Carcinogenesis, DNA strand breaks, morphological and cytoplasmic changes	Kontaş Yedier et al. (2022)
	10, 25, 50, 85, 100, 175, 350, 700 y 1400 µg/mL - 24 h	HepG2 cells	Cell cycle arrest, DNA damage, cytotoxicity, and apoptosis	Wang et al. (2022)
	0.5, 1, 1.25, 1.5 y 2 mM – 24, 36 y 48 h	BV2 cells	Decreased cell viability, cytotoxicity, effects on cell morphology, neurotoxicity, and inflammation	Wang et al. (2022)
	25 mg/kg – 7 d	Male Swiss mice	RNA damage, impaired testicular development, proteomic alterations, and developmental disorders	Trigg et al. (2021)
	2.5, 10 y 50 mg/kg – 14 d	Female Wistar-Albino rats	Weight loss, hormonal disruption, apoptosis, autophagy, potential development of polycystic ovary syndrome, and premature ovarian aging	Aldawood et al. (2020)
	0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4 y 5 mM – 144 h	Zebrafish	Cardiovascular damage, heart asymmetry, deterioration of cardiac valves, apoptosis, abnormal development of myocardium and endocardium	Huang et al. (2018b)
	0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, and 5 mM – 96 h	Zebrafish embryos	Reduced blood flow, mortality, oxidative stress, cardiovascular damage, and developmental disorders	Huang et al. (2018a)
Hydroxymethylfurfural	5, 12.5, 25, and 50 Mm – 12 h	Flies *(Drosophila melanogaster)*	Oxidative stress, intestinal damage, impaired growth and development	Chen, et al. (2024)
	30 and 300 mg/kg – 21 d 0.1, 0.5, 1, 5, 10, and 50 mM – 24 h	Male albino mice and TM3 Leydig cells	Reduction in testosterone levels and cytotoxicity	Orta Yilmaz & Aydin (2024)
	1 mg/kg – 12 months	Mice	Sarcopenia, chronic and systemic inflammation	Xu et al. (2023)
	2, 4, 8, and 16 mM – 24 h	Human gastric epithelial	Apoptosis and oxidative stress	Qiu et al. (2022)
	0.5, 1, and 2 mg/mL	Male mice and human umbilical vein endothelial cells	Cell deformation, allergy, and inflammation	He et al. (2020)
	250 mg/kg – 3 times a week for 4 weeks	Albino mice	DNA damage, oxidative stress, altered liver structure and function	El Bohi et al. (2020)
	10 mg/kg – 3 d	Mice	Respiratory condition and oxidative stress	Ji et al. (2018)

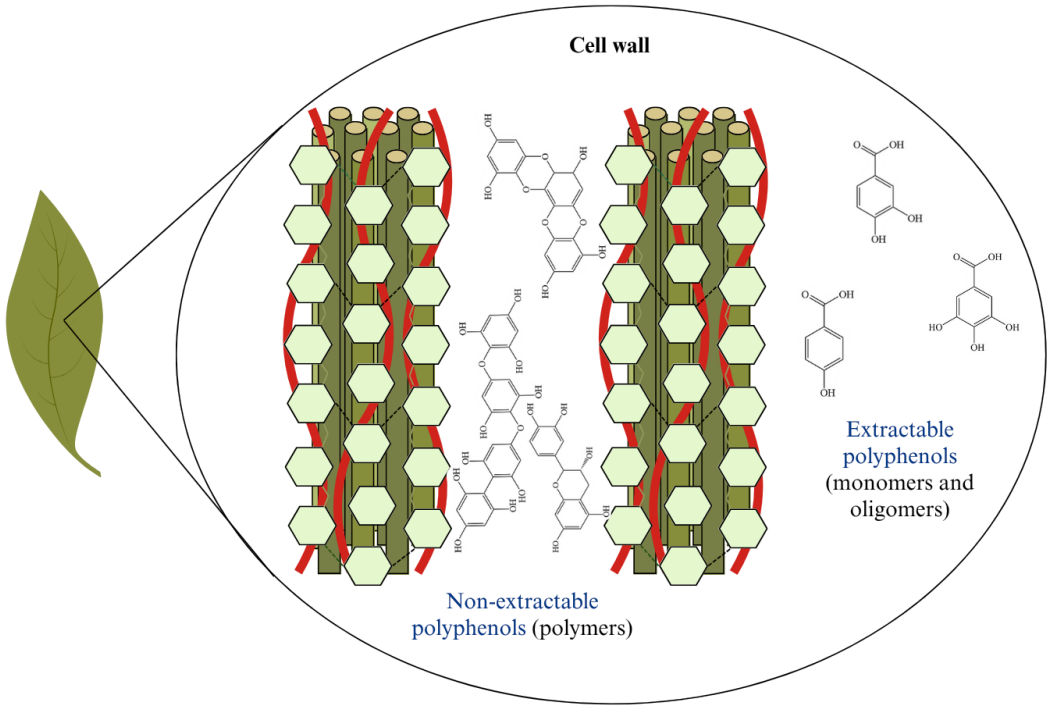

Figure 3. Interaction of polyphenols with the plant matrix.

4.1. Inhibitory effect of polyphenols on acrylamide (AA) and hydroxymethylfurfural (HMF)

While polyphenols have antioxidant properties, these compounds can also inhibit different stages of MR (early, advanced, and final stages) (Figure 5). This effect could reduce the formation of toxic products such as AA and HMF (Wang et al., 2025).

In the first stage of MR, polyphenols can interact with precursor compounds, such as reducing sugars (glucose and fructose), and specific amino acids, primarily lysine and asparagine (Troise et al., 2020). This interaction enables polyphenols to form adducts with the precursors, thereby reducing the formation of Schiff and Amadori base compounds by approximately three times (Zhang et al., 2023).

These interactions occur through Van der Waals forces, hydrophobic interactions, and hydrogen bonds (Pedreschi et al., 2018). In this regard, Zou et al. (2025) found that the use of vanillin, chlorogenic acid, and gallic acid forms adducts through hydrogen bond interactions with the ketone group of fructose. Wen et al. (2021) found that theaflavins establish interactions between their hydroxyl groups and the carbonyl group of glucose. Jiang et al. (2021) reported that the interaction between catechin and glucose is mediated by a nucleophilic addition mechanism.

Consequently, these interactions between polyphenols and reducing sugars prevent the isomerization of glucose into fructose, as well as the formation of Amadori products (Bayati & Poojary, 2025).

Regarding amino acids, when polyphenols are oxidized, they become highly electrophilic quinones, which can interact with amino acids that have nucleophilic groups in their side chain, such as lysine, cysteine, histidine, tyrosine, and tryptophan (Mertens et al., 2020). These interactions occur through addition reactions, where the thiol group (–SH) of cysteine and the amino group ε ($–NH_2$) of lysine interact with the electrophilic carbons of the quinone, forming covalent adducts (C–S or C–N) (Pham et al., 2019). In the case of aromatic amino acids such as tyrosine and histidine, π-stacking interactions and oxidative couplings occur, particularly under alkaline pH conditions and the presence of oxygen (Shamagsumova et al., 2023). These interactions block the functional sites of the amino acids, which are key to the initiation of the first step of the MR (Liang et al., 2024).

In the second step, polyphenols act as nucleophiles towards the carbonyl group of HMF, reacting with it by nucleophilic addition to form stable adducts, such as catechin-HMF-anthocyanin, catechin-HMF-catechin, anthocyanin-HMF acetals, and catechin-HMF (Zamora & Hidalgo, 2018). In this regard, Lee et al. (2020) described that the carbon atoms at the C6 and C8 positions of the polyphenol epigallocatechin gallate act as nucleophilic centers,

forming adducts with HMF. This reaction is particularly efficient with polyphenols that have multiple hydroxyl groups, such as quercetin, epicatechin, epicatechin gallate, epigallocatechin gallate, and gallic acid (Zamora & Hidalgo, 2018).

During the third stage, polyphenols can interact with Strecker aldehydes by nucleophilic addition mechanisms or covalent bond formation (Nonier Bourden et al., 2008). Phenolic hydroxyl groups, especially in activated positions of the aromatic ring, act as nucleophiles that attack the electrophilic carbon of the carbonyl group of aldehydes (Bi et al., 2024). In this regard, Xie et al. (2025) found that myricetin can interact with formaldehyde, acetaldehyde, and phenylacetaldehyde, reducing the capacity of AA formation. Li et al. (2014) demonstrated that naringenin reacts by nucleophilic addition at the C6 and C8 positions of its aromatic ring with phenylacetaldehyde, a precursor for the formation of AA and HMF. Likewise, catechin can react with aldehydes, forming alkyl-aryl bonds by nucleophilic addition of its hydroxyl groups, generating adducts that block the progression of reactions during MR (Constantinou & Koutsidis, 2016).

On the other hand, since AA and HMF are contaminants generated by thermal processing, multiple investigations have been conducted to analyze different processing strategies that inhibit these compounds by using polyphenols, aiming to obtain safe products. These findings are summarized in Table 3.

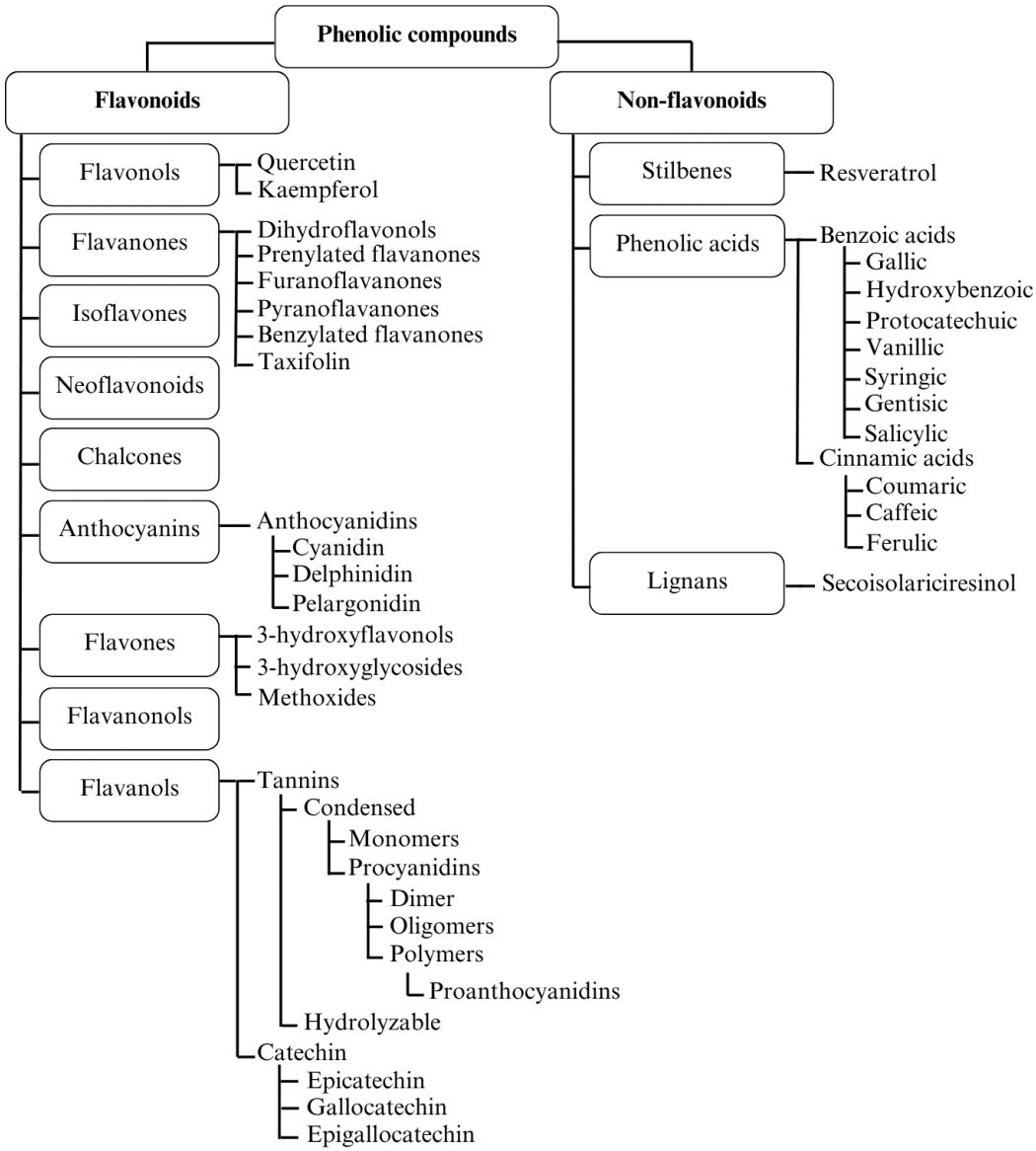

Figure 4. Structural classification of polyphenols.

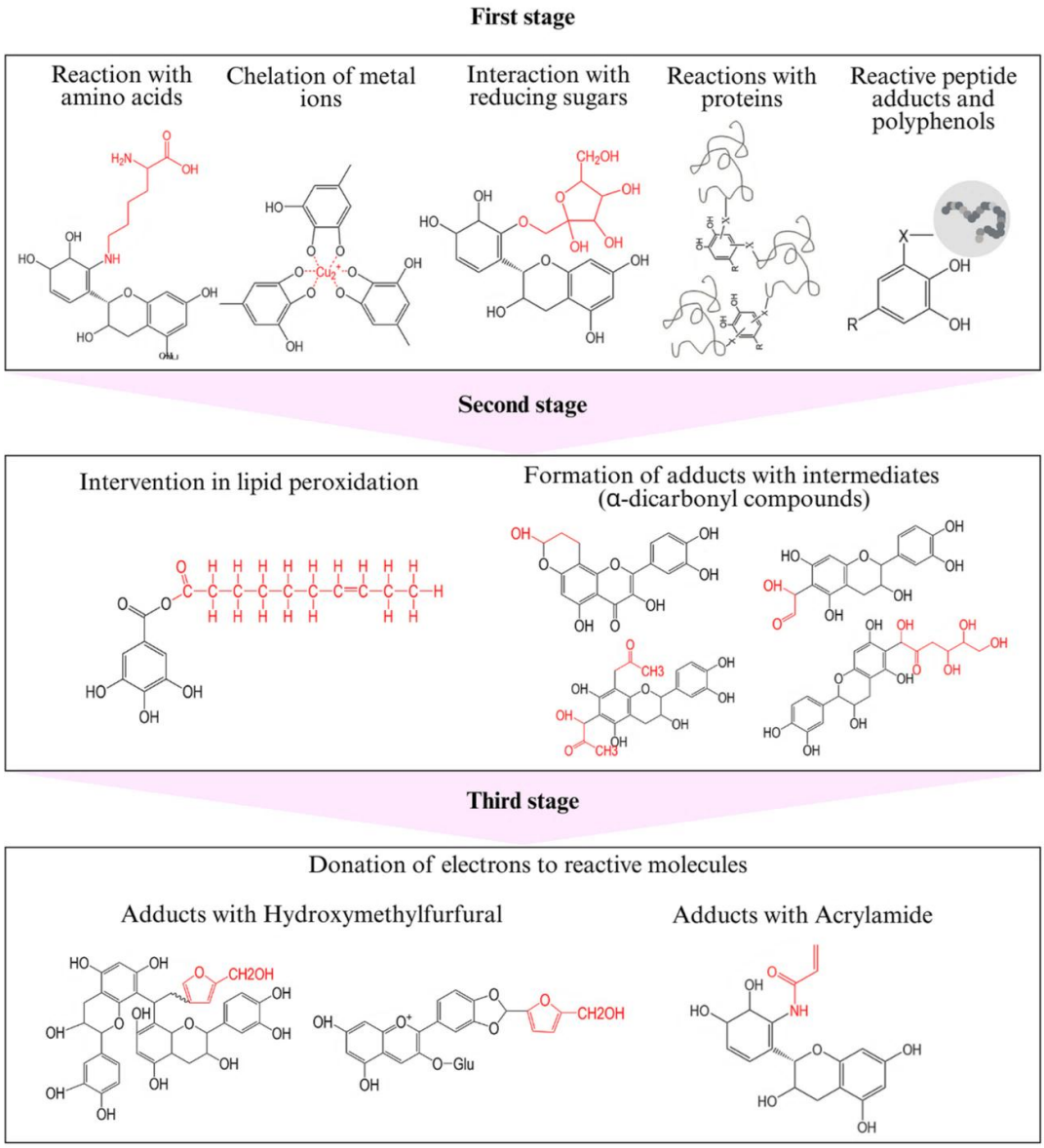

Figure 5. Stages and mechanisms of intervention of polyphenols in the inhibition of acrylamide and hydroxymethylfurfural.

5. Future challenges

Progress in the study of polyphenols as potential simultaneous inhibitors of AA and HMF has been significant in recent years. However, their effective implementation in real food systems requires a comprehensive approach that considers both the chemical mechanisms involved and the technological and regulatory aspects. The incorporation of polyphenol extracts as functional ingredients represents a promising alternative for developing safe foods, while also providing health benefits due to their bioactive properties.

From a chemical perspective, it is necessary to delve deeper into the influence of parameters such as pH, temperature, and food matrix composition on the reactive capacity of polyphenols since the molecular structure of the phenolic compound and environmental conditions determine these interactions. Another aspect is the toxicological and metabolic evaluation of the adducts generated at each stage of the MR process to confirm their safety.

At the technological level, the predominant use of conventional extraction methods with organic solvents persists; therefore, it is recommended to move toward clean and sustainable technologies that recover higher molecular weight polyphenols, thereby maximizing cost efficiency. Furthermore, it has been demonstrated that polyphenols in extract form act synergistically to inhibit both toxic compounds, exhibiting greater efficacy than the use of isolated polyphenols or powdered plant matrices.

Table 3
Polyphenols applied in food and Maillard reaction model systems to reduce hydroxymethylfurfural and acrylamide

Source of polyphenols	Extraction method	Extraction conditions	Food and formulation	Inhibitory potential	Reference
Kesse, koseret, and tosign	SLE	96% ethanol for 8 h	Potato (120 mg/L)	Reduction of AA (~63%, ~59%, and ~45%)	Assefa et al. (2025)
Echium amoenum	-	-	Cookies (0.5, 1, 1.5, 2, 2.5, 3%)	Reduction of AA (~66%)	Mofidipour et al. (2025)
Ginger, black pepper, star anise, fennel, bay leaf, *Kaempferia* rhizome	-	-	Roasted chicken (1.5%)	Reduction of HMF (~25%) and AA (~86%)	Wang et al. (2025)
Epigallocatechin, dihydromyricetin, and procyanidin	-	-	Low-lactose milk (0.1, 0.2, 0.3, 0.4, and 0.5 mg/mL)	Reduction of HMF (~48%)	Na et al. (2024)
Rosemary, turmeric, and bay leaf	UAE	Methanol at room temperature for 10 min, followed by a water bath at 80°C for 20 min. Ultrasonic bath for 5 min and water bath at 80°C for 20 min	Roast beef burgers (0.5%)	Reduction of AA (~44%, ~46%, and ~40%) and HMF (~73%, ~15%, and ~77%), respectively	Yu et al. (2024)
Blackcurrant pomace and red cabbage residues	SLE	50% methanol acidified with HCl (pH 2) and 70% acetone	French fries (20%)	Reduction of AA up to ~66% and HMF up to ~55%	Zhang et al. (2023)
Ginger and kaempferol	-	-	Cookies (5, 10, and 15 g/kg of ginger and 0.05, 0.10, and 0.15 g/kg of kaempferol)	Reduction of AA up to ~52%	Xue et al. (2023)
Wild roses, elderberries, sea buckthorns, rowans, blueberries, and hawthorns	-	-	Cookies (0.5% of lyophilized samples)	Decrease in AA by ~59% (hawthorn), ~71% (rowan), ~87% (wild rose), ~89% (sea buckthorn), ~91% (elderberry), and ~94% (blueberry)	Borczak et al. (2022)
Sorghum bran, grape seed, and green tea	SLE	Sorghum bran was extracted with 75% acetone under continuous stirring for 2 h	Bread (0.5%, 1%, and 1.5%)	Reduction of AA from ~22% up to ~70%	Chen et al. (2022)
Gallic acid	-	-	Glucose/arginine and sucrose/arginine model systems (0.01 mol/L)	Mitigation of HMF formation by ~49% in the MR glucose/arginine system and ~54% in the MR sucrose/arginine system	Abrantes et al. (2022)
Tea residues	Untreated, fermented, and cooked at high temperature	Fragmentation of six polyphenols: hydroxybenzoic acids (protocatechuic acid, gallic acid, and vanillic acid) and hydroxycinnamic acids (p-coumaric acid, caffeic acid, and ferulic acid)	Cookies (1%, 2%, and 3%)	Inhibition of AA up to ~36% with protocatechuic acid. Inhibition of HMF up to ~52% with protocatechuic acid	Ma et al. (2022)
Green tea	-	-	Bread (0.1% and 0.5%)	Reduction of AA up to ~25%	Onacik-Gür et al. (2022)
Virgin olive oil wastewater	-	-	Cookies (0.05%, 0.1%, and 0.2%)	Reduction of AA up to ~55%	Troise et al. (2020)
Ginger	-	-	Cookies (1%, 3%, 5%, and 7%)	Reduction of AA by ~6%	Yang et al. (2019)
Seeds and sprouts of bitter and common buckwheat	UAE	70% ethanol, 1:10 ratio by sonication for 30 min	Bread (0.00011%)	Reduction of AA by ~24%, ~27%, 17%, and ~17%, respectively	Jing et al. (2019)
Pomegranate flower	SLE	96% ethanol at 45°C for 24 h	Donuts (100 mL extract, 0.75 g/mL)	Reduction of AA up to ~12%	Heydari Ashkezari & Salehifar (2019)
Catechin, quercetin, gallic acid, ferulic acid, and caffeic acid	-	-	Bread (0.1%, 0.5%, 1%, and 2%)	Reduction of AA from ~16% up to ~95%	Mildner-Szkudlarz et al. (2019)

Tara	SLE	Water at 60°C for 30 min 0.1 M NaOH in water (pH 11) for 30 min	Bread (0.05%, 0.06%, 0.075%, 0.1%, and 0.15%)	Reduction of AA by ~85% and HMF by ~90%	Pedreschi et al. (2018)
Rapeseed press cake	SLE	NaOH at 0,1 M in water (pH 11), 30 min	Cookies (6.5% and 12.9%)	Reduction of AA up to ~67%	Troise et al. (2018)
Epicatechin	-	-	French fries (1 mg/mL) and asparagine-glucose model (0.025%)	Reduction of HMF up to ~70%	Qi et al. (2018c)
Sorghum bran	SLE	70% acetone, 29.5% water, and 0.5% acetic acid for 1 h. Flavanol fractionation	French fries (0.01, 0.03, 0.1, 0.3, and 1 mg/mL) and asparagine-glucose model (50, 100, and 200 µg/mL)	Reduction of HMF up to ~50%	Qi et al. (2018b)
	UAE	70% acetone, 29.5% water, and 0.5% acetic acid. Sonication for 10 min for 1 h. Proanthocyanidin fractionation	French fries (0.01, 0.03, 0.1, 0.3, and 1 mg/mL) and asparagine-glucose model (50, 100, and 200 µg/mL)	Reduction of AA up to ~44%	Qi et al. (2018a)
Quercetin	-	-	Bread (1.90 mg/g)	Inhibition of HMF by ~86%	Zhang & An (2017)
Epicatechin, epicatechin gallate, caffeic acid, ferulic acid, 3-caffeoylquinic acid, 4-caffeoylquinic acid, 5-caffeoylquinic acid, 3,4-dicaffeoylquinic acid, 3,5-dicaffeoylquinic acid, and 4,5-dicaffeoylquinic acid	-	-	Waxy corn starch system, wet-to-dry and dry (0.1, 0.5, and 1 µmol/g)	Reduction of AA from ~15% up to ~75%	Constantinou & Koutsidis (2016)
Grape pomace	UAE	70% methanol, sonication for 10 min, room temperature for 60 min, followed by 5 min sonication	French fries (0.025%, 0.05% and 0.1%) and asparagine-glucose model system (50, 100, and 200 µg/mL)	Reduction of AA up to ~90%	Xu et al. (2015)
Pomegranate peel, olive mill wastewater, cranberry bush juice, and polyphenols (Epicatechin, oleuropein, punicalagin, caffeic acid, chlorogenic acid, and ellagic acid)	SLE	Prior depectinization at 9000 rpm for 10 min. Pomegranate peel was subjected to agitation for 1 h with methanol	Cookies (0.2 g/100 g flour) and glycine-glucose and asparagine-fructose model system (30 µmol/100 g flour)	Reduction of AA from ~31% up to ~85% in the MR system and reduction from ~10% up to ~19% in cookies	Oral et al. (2014)
Wild oregano, thyme, cinnamon, bougainvillea, and green tea	SLE	Water at 60°C for 24 h	French fries (1 g/L)	Inhibition of AA by ~17%, ~39%, and ~62% with oregano, cinnamon, and green tea extract, respectively	Morales et al. (2014)
Rosemary and tocopherols	-	-	Sunflower oil for frying French fries (1000 mg/kg)	Inhibition of AA up to ~38%	Urbančič et al. (2014)
Bamboo leaves and tea	-	-	Cookies (0.2 g/kg and 0.1 g/kg)	Inhibition of AA up to ~64% and ~43%	Li et al. (2012)
Cinnamon bark, clove, coriander fruit, cumin seeds, turmeric rhizome, purple onion, grape seed proanthocyanidins, curcumin, eugenol, and cinnamaldehyde	SLE	Water at 80°C for 30 min	Cookies (0.25%, 0.5%, 1%, 2%, and 4%) and asparagine-glucose model system (0.05%, 0.1%, 0.25%, 0.5%, 1%, and 2%)	Inhibition of AA up to ~51% in cookies using clove extract and ~62% in the model system using proanthocyanidins	Zhu et al. (2011)
35 dietary plants (spices, fruits, tea, beans, and herbs) and 11 phenolic compounds	SLE	Water at 80°C for 30 min in a water bath shaker	Asparagine-glucose reaction system (0.1 mg/mL)	Inhibition of AA up to ~75% with mint and up to ~53% with p-coumaric acid	Zhu et al. (2009)
Rosemary, *Dictamnus*, epicatechin, and epigallocatechin gallate from green tea	SLE	Water for 1 min at 13500 rpm	Bread (1%, 10%) and glucose-asparagine model system (0.1 and 1 mM)	Reduction of AA up to ~67%	Hedegaard et al. (2008)
Bamboo leaves	SLE	30% ethanol for 1 h	Chicken wings (0.001%, 0.01%, 0.05%, 0.1%, 0.5%, and 1%)	Reduction of AA up to ~59%	Zhang et al. (2007)

HMF: Hydroxymethylfurfural; AA: Acrylamide; UAE: Ultrasound-Assisted Extraction; SLE: Solid-Liquid Extraction; MR: Maillard Reaction.

On the other hand, although the inclusion of these compounds could modify sensory properties of the food, such as color or flavor, the available evidence indicates that these effects are minimal and depend on the applied concentration. Finally, the need to validate the efficacy of these compounds under real production, storage, and distribution conditions is highlighted. To achieve the effective and safe application of polyphenols in the food industry, a multidisciplinary approach combining food science, biotechnology, process engineering, and food regulation will be essential.

6. Conclusions

Polyphenols are metabolites present in various plant matrices, which are effective in inhibiting the generation of acrylamide (AA) and hydroxymethylfurfural (HMF) during heat treatment of food. This capacity is defined by several interaction mechanisms during the different stages of the Maillard reaction, acting primarily as antioxidants that neutralize free radicals and eliminate carbonyl compounds that are precursors of AA and HMF. Therefore, the ability of these compounds to reduce the presence of these harmful substances offers a promising avenue for improving food safety. However, the effectiveness of polyphenols varies depending on the type of plant matrix and food processing parameters, suggesting the need to optimize extraction and application methods in specific food matrices.

Despite the progress made, key future challenges must be addressed to ensure the effective incorporation of polyphenols into real food systems. First, there is a need to further explore the chemical mechanisms behind the actions of polyphenols, especially how factors such as pH, temperature, and food matrix composition affect their reactivity. Additionally, a thorough toxicological and metabolic assessment of the adducts formed at each stage of the Maillard reaction is necessary to verify their safety for human consumption. It is also advisable to shift toward using clean and sustainable technologies for polyphenol extraction to enhance efficiency and reduce environmental impact.

Regarding the sensory aspect, although adding these compounds might alter some sensory properties of the food, such as color or flavor, available evidence indicates that these effects are minor and depend on the concentration used. Finally, the importance of validating the effectiveness of these compounds in actual production, storage, and distribution conditions is emphasized. To ensure the safe and effective use of polyphenols in the food industry, a multidisciplinary approach that combines food science, biotechnology, process engineering, and food regulation will be necessary.

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