

Antibacterial properties of Maillard reaction products: Molecular mechanisms and influencing factors (Review)

ZHONGSHUANG HU¹, JIAO LI¹, XIANGHUAN WU¹, YONGZHONG WEI¹, XUDONG LI² and JING JI^{1,2}

¹School of Food and Pharmacy, Shanghai Zhongqiao Vocational and Technical University, Shanghai 201514, P.R. China;

²School of Agriculture and Biology, Shanghai Jiaotong University, Shanghai 200240, P.R. China

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Abstract. The Maillard reaction, a non-enzymatic process involving the interaction between carbonyl and amino groups, has attracted substantial interest in biomedical research due to the antibacterial properties of its products. Maillard reaction products (MRPs) exhibit broad-spectrum activity against both foodborne bacteria and pathogenic strains, including antibiotic-resistant strains. These compounds inhibit microbial growth, regulate virulence and disrupt biofilm formation through mechanisms such as metal chelation, membrane disruption and interference with bacterial metabolism. As a result, MRPs emerge as promising alternatives to conventional antibiotics. In the biomedical field, MRPs hold potential for applications in medical device coatings and gut microbiota modulation, where they can prevent microbial colonization and influence host-microbe interactions. However, concerns regarding their safety, cytotoxicity and structural complexity pose significant challenges for broader implementation. Future research should focus on elucidating the structure-activity relationships of MRPs, optimizing their production and evaluating their long-term effects in biological systems. The present review provides an in-depth examination of the antibacterial mechanisms of MRPs, with a particular focus on identifying the bioactive molecules responsible for their activity. Additionally, it explores the potential biomedical applications of MRPs as sustainable antimicrobial agents.

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1. Introduction

The Maillard reaction, a non-enzymatic process involving the covalent bonding of carbonyl and amino groups, is well established in food chemistry (1); it produces a diverse range of compounds, including those responsible for flavor, aroma and color (2). In recent decades, its biomedical relevance has gained significant attention due to the biological activities of Maillard reaction products (MRPs), which show potential in various medical applications (1,2). MRPs exhibit a broad spectrum of biological properties, including antioxidant, anti-inflammatory and antihypertensive activities (1,2). A subclass of MRPs, advanced glycation end-products (AGEs), has been strongly linked to chronic diseases, such as cardiovascular disorders, type 2 diabetes, atherosclerosis and coronary artery disease (3-5). Emerging evidence suggests that AGEs may also contribute to antibacterial defense by enhancing immune responses and altering gut microbiota. These effects influence host-microbe interactions and support their potential in antimicrobial applications (6,7). Beyond these physiological effects, MRPs also interact with microorganisms, including bacteria, fungi and viruses, significantly reducing microbial growth and activity (8-11). Furthermore, *in vivo*, MRPs influence microbial ecology and host-microbe interactions, shaping gut microbiota composition (6,7,12).

In addition to their antibacterial properties, MRPs regulate microbial processes through multiple mechanisms, including inhibition of microbial adhesion, disruption of DNA integrity, modification of enzyme activity, regulation of gene expression, and alteration of microbial traits such as biofilm formation, virulence, acid resistance, invasiveness and mutagenicity (13-18). These properties make MRPs valuable not only for food preservation but also for gut microbiota modulation and pathogen control strategies in medical and industrial applications.

Correspondence to: Dr Zhongshuang Hu or Professor Jing Ji, School of Food and Pharmacy, Shanghai Zhongqiao Vocational and Technical University, 3888 Caolang Road, Shanghai 201514, P.R. China

E-mail: hzs@shzq.edu.cn

E-mail: xiaoxiaohill@alumni.sjtu.edu.cn

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The antibacterial properties of MRPs vary throughout the Maillard reaction due to changes in their chemical structures and mechanisms of action (19-21). The Maillard reaction progresses through three distinct stages, each yielding compounds with specific chemical and biological properties (2,21). In the initial stage, a reducing sugar reacts with a free amino group, forming unstable Schiff bases that rearrange into more stable keto-amines, known as Amadori products. During the intermediate and advanced stages, the degradation of Amadori products is influenced by pH. Under acidic conditions, degradation primarily follows a 1,2-enolization pathway, yielding furfural (from pentoses) or hydroxy-methyl-furfural (from hexoses). Under alkaline conditions, degradation proceeds via 2,3-enolization, producing reductones and various fission products, such as acetol, pyruvaldehyde and diacetyl. These compounds undergo further transformations, including oxidative cleavage and retro-aldol fragmentation, generating highly reactive α -dicarbonyl compounds (22). In the final stage, the reaction produces complex, high-molecular-weight (HMW) polymers called melanoidins. These brown-colored compounds exhibit diverse chemical compositions, including carbohydrate backbones with nitrogen-containing components and protein-based structures incorporating chromophores and phenolic residues (23-25).

Antibacterial activity is crucial in the medical field due to its broad applications. However, the rise of antibiotic-resistant bacteria poses a significant challenge despite the success of numerous antibiotics in clinical use. This issue underscores the urgent need for innovative approaches to antibiotic discovery and creative antimicrobial strategies (26). The Maillard reaction occurs naturally without requiring additional chemical compounds and has been recognized for its potential to modify bioactive properties (1). Therefore, it offers an environmentally friendly and efficient platform for developing antibacterial agents. The effectiveness of MRPs as antibacterial agents depends on reaction conditions such as heating time, temperature, water activity, pH and reactant composition. These factors influence the structural and functional properties of MRPs, ultimately affecting their antibacterial activity (9,19,27).

The present review provides an in-depth analysis of the antibacterial properties of MRPs; their antibacterial effects against various bacteria are examined, the bioactive molecules responsible for this activity are identified and the underlying mechanisms are elucidated. Additionally, the review explores key reaction conditions influencing the formation of antibacterial MRPs. Furthermore, potential medical applications are emphasized and future research directions are proposed to enhance understanding of their structure-activity relationships and optimize their practical use.

2. Antibacterial potential of MRPs

The antibacterial properties of MRPs were first documented in the 1960s, with early studies noting reduced germination times in *Bacillus subtilis* spores and shortened lag phases in *Propionibacterium* cultures in autoclaved media (9). Subsequent research has since expanded our understanding of the direct impact of MRPs on a wide range of microorganisms. For instance, MRPs derived from simple sugar-amino acid model systems, such as xylose-phenylalanine and

glucose-alanine, have demonstrated significant inhibitory effects against various bacterial species, including *Bacillus cereus*, *Bacillus subtilis*, *Brevibacillus brevis*, *Clostridium perfringens*, *Listeria monocytogenes*, *Staphylococcus aureus* (*S. aureus*), *Aeromonas hydrophila*, *Escherichia coli* (*E. coli*) and *Salmonella enterica* serovar *Typhimurium* (19,27-33). Similarly, MRPs synthesized from polysaccharides and hydrolyzed proteins, as well as those formed through the self-reaction of amino saccharide model systems (such as glucose-squid skin, glucose-chitosan and glucose-whey protein) have shown potent antibacterial activity against *Bacillus subtilis*, *Clostridium perfringens*, *S. aureus*, *E. coli*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, *Proteus vulgaris*, *Vibrio harveyi* and *Vibrio parahaemolyticus* (10,34-42).

The antibacterial potential of MRPs extends beyond laboratory-generated model systems (29,32,37,38,43-45). MRPs derived from natural sources, such as biscuits and roasted coffee, have also exhibited significant antibacterial activity, indicating a broad and diverse antimicrobial spectrum. Notably, Gram-positive bacteria tend to be more susceptible to MRPs than Gram-negative bacteria, likely due to structural differences in their cell walls (29,32,46). However, certain MRPs have demonstrated stronger antibacterial activity against Gram-negative bacteria, suggesting that the efficacy of MRPs is highly dependent on their specific bioactive components and mechanisms of action (32,38). Notably, MRPs have also been found to inhibit clinically relevant bacterial strains, including *E. coli*, *Helicobacter pylori* (*H. pylori*), *Pseudomonas aeruginosa*, *Vibrio harveyi*, multidrug-resistant *Pseudomonas aeruginosa*, methicillin-susceptible *S. aureus* and methicillin-resistant *S. aureus* (41,47-49). These findings highlight the potential applications of MRPs in medical settings. Additionally, MRPs derived from model systems have demonstrated inhibitory effects on yeast and mold growth, as well as antiviral activity, further emphasizing their broad-spectrum antimicrobial properties (8,10,34).

3. Bioactive antibacterial compounds in MRPs

Due to the inherent complexity of the Maillard reaction, detailed molecular studies on the antibacterial properties of MRPs remain limited, particularly for HMW compounds (21). Unlike conventional antibiotics, which have well-defined structures and concentrations that facilitate direct comparisons across different studies, MRPs exhibit significant variability in composition. Although methods such as disc diffusion and minimum inhibitory concentration assays are commonly employed to evaluate the antibacterial activity of MRPs, a standardized protocol for comparing their efficacy across studies is currently lacking (43,50-52). This complexity poses challenges in cross-study comparisons and necessitates alternative investigative approaches. Typically, the extent of the Maillard reaction is inferred from the browning intensity of MRPs, measured by absorbance at 420 nm, which serves as an indirect indicator of their concentration-dependent effects (32). Despite these challenges, limited studies have demonstrated that MRPs exhibit inhibitory effects against pathogens such as *S. aureus* and *H. pylori*, comparable to certain antibiotics such as levofloxacin and amikacin, as assessed by disc diffusion assays (49).

Aminoreductone (AR) and glycated peptides. AR and glycated peptides are early-stage MRPs with notable antibacterial activity (53,54). AR has been identified in thermally processed milk and has been shown to inhibit the proliferation of foodborne bacteria, including *S. aureus*, *Bacillus subtilis*, *Enterococcus faecalis*, *Listeria innocua*, *Listeria monocytogenes*, *E. coli* and *Salmonella typhimurium* (55,56). AR, formed in a lactose-butylamine model system, has also been reported to inhibit the proliferation of *Pseudomonas aeruginosa* and antibiotic-resistant bacteria, including multidrug-resistant *Pseudomonas aeruginosa*, methicillin-susceptible *S. aureus* and methicillin-resistant *S. aureus* (48,49). Moreover, AR has demonstrated significant antibacterial activity against *H. pylori* under acidic conditions, both *in vitro* and in a mouse infection model, highlighting its potential for the treatment of infectious gastric diseases (47). The antibacterial mechanism of AR is considered to involve interference with bacterial cell wall integrity and membrane permeability, with its efficacy influenced by factors, such as cell wall thickness, lipid composition and surface charge (48,49). Additionally, AR has been shown to enhance the effectiveness of conventional antibiotics, such as amikacin and levofloxacin, although the underlying mechanism of this synergy remains unclear (49).

Glycopeptides, a significant class of antibacterial agents, serve as a critical platform for antibiotic discovery (57). Several glycopeptides, such as vancomycin and teicoplanin, are widely used in clinical settings. Additionally, numerous glycopeptides synthesized from sugar-free amino acids have been evaluated for their antibacterial activity against various microorganisms (54). Notably, glycopeptides formed during the early stages of the Maillard reaction, such as histidine-asparagine-lactose glycopeptide and gluten-hydrolysate-glucosamine glycopeptide, have demonstrated enhanced antibacterial activity compared with their native counterparts (35,36,54,58).

α -dicarbonyl compounds. α -dicarbonyl compounds are intermediate-stage products of the Maillard reaction and are widely present in both processed and unprocessed foods (59-61). These highly electrophilic compounds readily interact with proteins, potentially altering their bioactivity (50). Among the most extensively studied α -dicarbonyls are diacetyl, glyoxal and methylglyoxal (MGO), which have demonstrated significant antibacterial properties against various bacterial strains, including *E. coli*, *Pseudomonas fluorescens*, *S. aureus*, *Salmonella typhimurium* and *Salmonella enteritidis* (45,51,62,63). Furthermore, glyoxal, MGO and diacetyl have shown a strong negative correlation with bacterial viability, suggesting that α -dicarbonyl compounds contribute significantly to the antibacterial activity of MRPs (50). Notably, MGO has been reported to impair biofilm formation by disrupting fimbriae and flagella at lower concentrations, while at higher concentrations, it compromises microbial membrane integrity (64,65). However, the antibacterial effects of MRPs cannot be solely attributed to α -dicarbonyl compounds. Other MRP components, such as melanoidins, also play a role in the overall antibacterial activity. It is likely that these components act synergistically, enhancing antibacterial efficacy through complementary mechanisms such as membrane disruption and metal chelation (Fig. 1A) (66).

Additionally, some α -dicarbonyl compounds undergo cyclization and condensation to form pyrazoles, pyrazines, furans and pyrroles, which have been demonstrated to exhibit antibacterial activity in their purified form rather than as components of MRPs (67-71). Although direct evidence linking these compounds to the antibacterial effects of MRPs is limited, their structural similarity to known antibacterial agents suggests that they may contribute to MRP-mediated antimicrobial activity (31). Further research is needed to elucidate their precise mechanisms of action.

Melanoidins. The formation of HMW compounds, particularly melanoidins, marks the late stage of the Maillard reaction (23). Melanoidins are primarily responsible for the characteristic brown coloration of heat-treated foods and have gained attention for their multiple bioactivities, including antioxidant, antihypertensive, prebiotic and antibacterial properties (32). Numerous studies have demonstrated their broad-spectrum antibacterial activity against both foodborne and pathogenic bacteria. Moreover, HMW melanoidins exhibit stronger antibacterial activity than their low-molecular-weight (LMW) counterparts (11,20,32).

Structurally, melanoidins derived from model systems primarily consist of furans, carbonyl compounds, pyrroles, pyrazines and pyridines (23). Additionally, melanoidins are negatively charged, with HMW fractions exhibiting a greater negative charge than LMW fractions. These structural characteristics contribute to their bioactivity, particularly in antibacterial mechanisms (23,72).

Melanoidins, as anionic hydrophilic polymers, exhibit strong metal-binding properties, effectively chelating essential metals such as iron, copper and magnesium (Fig. 1A) (39,66,73). Since iron is crucial for bacterial proliferation and magnesium serves as a key activator of numerous enzymes, the sequestration of these metals by melanoidins may contribute to inhibition of bacterial proliferation (29,39,66,73-75). By depriving bacteria of these essential nutrients, melanoidins interfere with their metabolic functions and survival. Additionally, MRPs have been reported to exert bactericidal effects on Gram-negative bacteria by causing irreversible damage to both the inner and outer membranes (23). Notably, magnesium chelation has been reported as a potential inducer of membrane disruption, suggesting that melanoidins may contribute to bacterial membrane damage by sequestering magnesium and disrupting membrane integrity (66). This dual action, nutrient depletion and membrane disruption, enhances their antibacterial properties.

In addition to nutrient deprivation, melanoidins may exert bactericidal effects on Gram-negative bacteria by disrupting both the inner and outer membranes (20). Studies have shown that magnesium chelation can destabilize bacterial membranes, suggesting that melanoidins may enhance this effect by sequestering magnesium and interfering with membrane integrity (66). Moreover, melanoidin treatment has been observed to increase dye uptake, promote pore formation and induce intracellular component leakage, ultimately leading to bacterial cell death (20,23,39,76,77). This suggests that melanoidins not only act as metabolic inhibitors but also function as membrane disruptors, further contributing to their antibacterial efficacy.

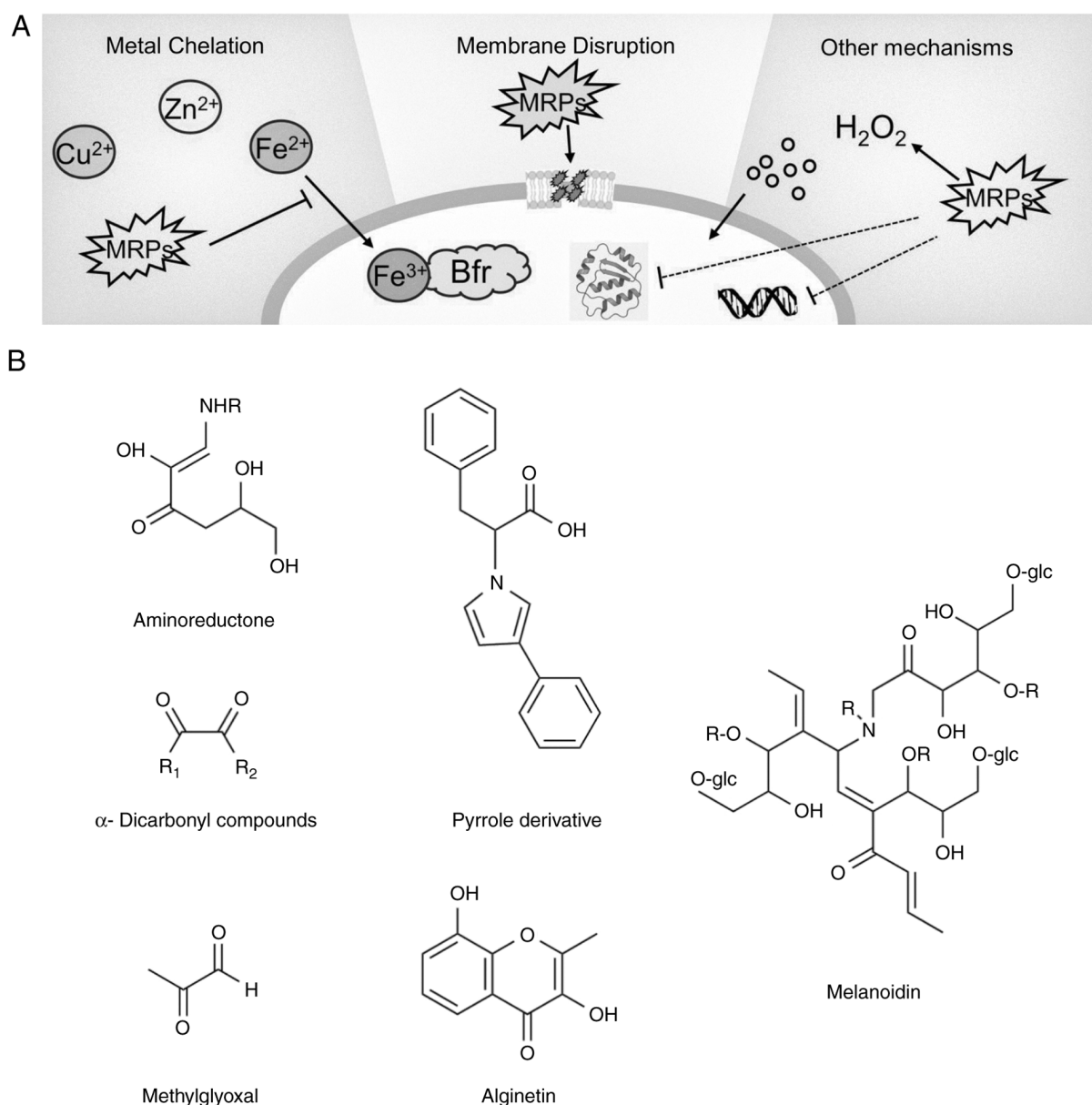


Figure 1. Antibacterial mechanisms and representative compounds of MRPs. (A) Schematic representation of the primary antibacterial mechanisms of MRPs. These mechanisms include metal ion chelation, membrane disruption, interference with bacterial metabolism and modulation of oxidative stress. Collectively, these processes contribute to the broad-spectrum antimicrobial activity of MRPs against a wide range of microorganisms. (B) Chemical structures of selected bioactive compounds derived from MRPs, which are responsible for their antimicrobial properties. These compounds encompass aminoreductone, α -dicarbonyl compounds (with R1 and R2 representing variable substituents), pyrrole derivatives, methylglyoxal, alginetin and melanoidin. Melanoidin is depicted with its carbohydrate backbone as an integral component of its structural framework. MRPs, Maillard reaction products.

Other bioactive molecules. In addition to the well-characterized antibacterial compounds found in MRPs, several other bioactive molecules contribute to their antimicrobial properties (Fig. 1A). Phenols, quinones, nitrogen-containing heterocycles (such as 1,4-dihydropyridines) and hydrogen peroxide (H_2O_2) have all been reported to exhibit antibacterial activity. These compounds likely exert their effects by interfering with microbial metabolic pathways, disrupting bacterial cell walls, proteins and nucleic acids, and ultimately impairing bacterial survival (31,42,78-80). For instance, alginetin (3,8-dihydroxy-2-methylchromone), a flavonoid-derived polyphenol, has been isolated from a xylose-phenylalanine model system and identified as a contributor to the inhibitory effects on *Bacillus cereus* and *Salmonella typhimurium* (31).

Although these compounds have been identified as potential contributors to the antibacterial properties of MRPs, their specific roles within complex Maillard reaction systems remain to be fully elucidated. Future research should focus on determining their precise mechanisms of action and evaluating their synergistic effects with other bioactive MRPs.

4. Factors affecting the antibacterial activity of MRPs

The antibacterial properties of MRPs are influenced by a variety of factors, including reaction conditions, reactant composition and external environmental parameters (19). Key variables such as pH, temperature, reaction duration and reactant selection significantly impact the yield, chemical

composition and biological activity of MRPs. Understanding these factors is crucial for optimizing the production of MRPs with enhanced antibacterial efficacy (19,22,81).

Effect of pH. The pH of the reaction system plays a critical role in determining the kinetics, composition and bioactivity of MRPs (22,82). Studies have revealed that under alkaline conditions, amino acids and sugars react more efficiently, leading to increased browning intensity and enhanced antibacterial activity (19,37,38,82). Alkaline conditions enhance the nucleophilicity of amino groups, accelerating their interaction with carbonyl compounds and facilitating the formation of Schiff bases and Amadori products (83-85). However, extreme alkalinity (pH>12) has been reported to reduce the formation of melanoidins, likely due to degradation reactions that disrupt polymerization (86). The impact of pH also varies across different reaction stages. In the intermediate and advanced stages, pH influences the breakdown of Amadori products, thereby modulating the production of α -dicarbonyl compounds and metal-chelating melanoidins (22,73,87). Notably, MRPs derived from glucosamine self-reaction exhibit antibacterial activity at pH 5 but not at pH 7, suggesting that pH not only affects the reaction pathway but also alters the functional properties of the final MRPs (88). Further research is needed to determine whether dynamically adjusting pH during the Maillard reaction can be used as a strategy to fine-tune the antibacterial activity of MRPs.

Effect of heating method. The method and intensity of heating significantly influence the antibacterial properties of MRPs. Prolonged reaction times and elevated temperatures generally enhance the formation of HMW compounds, which have been associated with stronger antibacterial activity (19,23,36,50). This effect is primarily attributed to the greater extent of Maillard reaction progression, leading to increased production of bioactive melanoidins and α -dicarbonyl intermediates (73,89). However, excessive heating can have detrimental effects. Overly complex molecular structures may form, reducing the metal-chelating abilities and bioactivity of MRPs. Moreover, prolonged thermal processing may generate unwanted byproducts, some of which could be cytotoxic or detrimental. To address these challenges, alternative processing techniques have been explored. Mild-temperature Maillard reactions (for example, $\sim 40^{\circ}\text{C}$) have been investigated for their ability to generate bioactive MRPs while minimizing undesirable byproducts (35). Additionally, emerging technologies such as ultrasound-assisted Maillard reactions and γ -irradiation have been explored as innovative, non-toxic strategies to enhance the antibacterial properties of MRPs (46,90).

Influence of sugar selection. The choice of sugar reactants critically impacts the composition and bioactivity of MRPs. Most studies have focused on reducing sugars, such as glucose and fructose, due to their high reactivity and prevalence in food systems (9,19,32,37). However, pentose sugars, including xylose and ribose, have been reported to produce MRPs with superior antibacterial activity compared with hexoses such as glucose (41). This difference is likely due to the stronger reducing properties of pentoses, which accelerate Maillard reaction kinetics and promote the formation of highly reactive

intermediates (32,91). In addition to monosaccharides, the use of oligosaccharides and polysaccharides can further modulate the antibacterial properties of MRPs (34,36,76,92). Polysaccharides not only serve as reactants but also provide carbohydrate backbones that contribute to the structural diversity of HMW melanoidins (25).

Influence of amino acid selection. Amino acid composition is another crucial determinant of the antibacterial activity of MRPs. Different amino acids lead to the formation of distinct reaction products, resulting in variations in bioactivity (23,70). For instance, MRPs derived from glucose-tryptophan systems have shown stronger antibacterial effects against *E. coli* than those produced from other amino acids (29). Similarly, xylose-phenylalanine MRPs exhibit potent antibacterial activity against *Bacillus cereus* and *Brevibacillus brevis* (32). These findings suggest that the antibacterial potential of MRPs is highly dependent on the specific amino acid involved, though variations in experimental conditions and microbial targets may contribute to differences in observed efficacy. One possible explanation for these differences is the variation in metal-chelating properties and π -electron interactions among different amino acid-derived MRPs, which may influence their ability to disrupt bacterial membranes (23). Additionally, amino acids with nucleophilic side chains, such as lysine, react more readily with reducing sugars, accelerating the formation of Schiff bases and altering the overall reaction kinetics (85).

In more complex Maillard reaction systems, antimicrobial peptides (AMPs) may also form as a result of amino acid modifications. AMPs, such as human LL-37, exert antibacterial effects through membrane disruption, facilitated by their cationic secondary structures, hydrophobic domains and specific amino acid residues (for example, proline, histidine and tryptophan) (93). The Maillard reaction can simultaneously induce peptide degradation and cross-linking, leading to the formation of novel bioactive peptides with enhanced antibacterial properties (37,94). Notably, research has identified several novel AMPs, including those with specific amino acid sequences such as RVAPEEHPTL and WLPVVR, from MRPs of half-fin anchovy hydrolysates and glucose. These peptides demonstrate stronger inhibitory effects against *E. coli* (42). This finding suggests a potential link between the Maillard reaction and antimicrobial peptide generation. These include overlapping amino acid compositions (for example, proline and cysteine), a net cationic charge and antibacterial activity mediated by bacterial membrane disruption (42,95-98).

Notably, MRPs formed in glycolaldehyde and bovine serum albumin model systems have been reported to inhibit lipopolysaccharide (LPS) uptake by macrophages, a property shared by certain AMPs that neutralize LPS toxicity by direct binding (97,99). However, whether these MRPs interact with LPS through the same mechanism as AMPs remains unclear, warranting further investigation.

These findings suggest that the antibacterial potential of MRPs is highly dependent on the specific amino acid involved. While certain amino acids enhance antimicrobial activity through metal chelation and membrane disruption, variations in experimental conditions and microbial targets may also contribute to differences in observed efficacy. Further studies

are needed to systematically compare the effects of different amino acids on MRPs bioactivity under controlled conditions.

Influence of sugar-to-amino acid ratio. The ratio of sugar to amino acids significantly affects the composition, MW distribution and antibacterial efficacy of MRPs (100). Higher sugar concentrations tend to promote the formation of HMW melanoidins, which exhibit strong metal-chelating and antioxidant properties that contribute to bacterial inhibition (91). However, excessive sugar levels can lead to over-polymerization, resulting in insoluble compounds with diminished bioactivity (101). Conversely, increasing the amino acid concentration shifts the reaction toward the production of nitrogen-containing LMW compounds, such as Strecker aldehydes and pyrazines, which are known for their direct antibacterial effects (32). Therefore, optimizing the sugar-to-amino acid ratio is crucial for enhancing the antibacterial activity of MRPs. Additionally, the sugar-to-amino acid ratio influences the pH of the reaction system, further modulating the composition and bioactivity of MRPs (101). A high sugar proportion typically lowers the pH, enhancing inhibition against acid-sensitive bacterial strains, whereas a higher amino acid content can promote the formation of nitrogenous heterocyclic compounds with distinct antibacterial mechanisms (32).

Other contributing factors. Several additional factors, including metal ions, water activity and external additives, further influence the formation and antibacterial properties of MRPs (9). Increased phosphate buffer concentrations have been shown to accelerate glucose consumption, indicating enhanced Maillard reaction progression (83). Similarly, the presence of iron and copper ions has been reported to catalyze Maillard reactions and promote the formation of reactive oxygen species and dicarbonyl compounds, which could enhance MRP antibacterial efficacy (102). Moreover, certain additives, such as sulfites, act as reducing agents that scavenge reactive carbonyl groups and inhibit formation of MRPs (103). Other inhibitors, including polyphenols, may also interfere with the antibacterial activity of MRPs, although their precise roles remain underexplored (104). These intricate mechanisms highlight the importance of optimizing reaction parameters to maximize the antibacterial potential of MRPs. Further research is needed to determine how carbonyl scavengers and reaction modifiers affect different stages of the Maillard reaction and their impact on the bioactivity of MRPs.

5. Structure-activity relationship trends of antibacterial MRPs

Establishing definitive structure-activity relationships for MRPs is challenging due to their structural variability. However, emerging evidence reveals several trends that can guide the development of MRPs with enhanced antibacterial properties (Fig. 1B).

Bioactive groups and molecular moieties. The presence of electrophilic α -dicarbonyl compounds has been associated with direct antibacterial effects, likely due to their reactivity with nucleophilic residues in bacterial biomolecules (62,105). Additionally, the anionic and hydrophilic nature of melanoidin

contributes to metal ion chelation and facilitates interactions with bacterial membranes (23). Other reactive groups, such as phenolic hydroxyls and quinones, may also participate in redox-based mechanisms that disrupt microbial cellular function (106,107). The MW of MRPs also influences their antibacterial potency. HMW compounds, such as melanoidins, generally exhibit stronger antibacterial activity, potentially due to their enhanced metal-chelating capacity and membrane-disruptive properties (75,81).

Integral structural properties of MRPs. Beyond specific functional groups, several integral structural features of MRPs have been linked to enhanced antibacterial activity. These include negative surface charge, electrophilic carbonyl groups, aromatic rings and nitrogen-containing heterocycles, all of which may interfere with bacterial metabolism, enzyme function or membrane integrity (108–110). The choice of reaction precursors also plays a critical role. MRPs derived from pentose sugars and aromatic amino acids (for example, xylose-phenylalanine systems) tend to exhibit stronger antibacterial activity than those formed from hexoses and aliphatic amino acids, possibly due to the formation of more reactive or structurally diverse intermediates (32).

6. Application and perspectives

The stage-specific properties and diverse antibacterial mechanisms of MRPs offer significant potential in food science and biomedical applications. In the food industry, MRPs have been explored as natural preservatives due to their ability to inhibit spoilage microorganisms and foodborne pathogens. Their incorporation into food packaging materials has been investigated to extend shelf life and enhance food safety (78). Additionally, MRPs can be used as functional ingredients in processed foods, not only for their antimicrobial properties but also for their flavor-enhancing and antioxidant effects.

In biomedicine, MRPs present promising applications as alternative antimicrobial agents. Given the rise of antibiotic-resistant bacteria (methicillin-resistant *S. aureus* and vancomycin-resistant *Enterococci*), MRPs could serve as non-antibiotic alternatives that reduce selective pressure on bacterial resistance. Their potential extends to medical device coatings, where they could prevent microbial colonization and biofilm formation on implantable materials, thereby reducing hospital-acquired infections. Moreover, MRPs have been proposed as therapeutic agents for gut microbiota modulation, influencing the composition of intestinal bacteria and potentially benefiting human health (7).

Beyond direct applications, MRPs offer a platform for antibiotic discovery. Their complex chemical structures and interactions with microbial targets provide a unique opportunity to identify bioactive compounds with novel antibacterial mechanisms. Screening MRPs for AMPs or small molecules could contribute to the development of next-generation antibiotics.

However, despite their potential, several challenges remain. Concerns about the safety and cytotoxicity of MRPs, particularly regarding their HMW fractions, must be addressed through rigorous toxicological assessments. Additionally, the structural heterogeneity of MRPs poses difficulties

in standardization and reproducibility, which are crucial for regulatory approval in food and medical applications. Furthermore, technological challenges must be addressed to enhance the practical utility of MRPs. The complex chemical structure of MRPs can lead to instability during processing and storage, which may affect their bioavailability and antibacterial efficacy. Techniques such as microencapsulation can help protect MRPs and enhance their stability (111).

In medical applications, MRPs face technological challenges but show promise. In medical device coatings, the complex structure of MRPs can cause adhesion issues and inconsistent distribution, reducing antibacterial activity. They also risk oxidative degradation and hydrolysis, affecting long-term stability. To tackle these issues, strategies such as incorporating MRPs into polymer matrices (for example, chitosan films) enhance their mechanical and antimicrobial properties (77,112). In wound dressings, MRPs from heated glucose/fructose-arginine solutions, when combined with poly-caprolactone to form nanofibrous membranes, effectively suppress bacterial proliferation without cytotoxicity to human fibroblasts, suggesting potential as novel wound dressings (113).

Future research should focus on optimizing the Maillard reaction parameters to selectively produce MRPs with desirable bioactivity while minimizing undesirable byproducts. Advanced analytical techniques, such as mass spectrometry-based metabolomics, could facilitate the characterization of bioactive MRP components, enabling the refinement of their functional applications. By integrating multidisciplinary approaches from microbiology, food science and materials engineering, MRPs hold great promise as sustainable antimicrobial agents for diverse industrial and clinical applications.

7. Conclusion

MRPs represent a promising class of antibacterial agents with broad-spectrum activity, including efficacy against antibiotic-resistant pathogens. Their antibacterial properties are influenced by reaction conditions and reactant composition, highlighting the importance of controlling the Maillard reaction to optimize MRP bioactivity. The underlying antimicrobial mechanisms of MRPs, including metal chelation, membrane disruption, enzyme inhibition and interference with bacterial metabolism, provide a strong foundation for their potential applications.

The diversity of MRPs, from early-stage compounds such as ARs to late-stage melanoidins, enables a wide range of applications in food preservation, alternative antimicrobial therapies and biomedical innovations. However, further research is necessary to elucidate their precise structure-activity relationships, improve production techniques and assess their safety for long-term use.

Collaboration across disciplines, including microbiology, food science, pharmaceutical chemistry and materials engineering, will be essential to fully harness the potential of MRPs. By overcoming current challenges and optimizing their functional properties, MRPs could emerge as sustainable and effective antimicrobial solutions for food safety, medical applications and public health.

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Authors' contributions

ZH was responsible for the literature search, manuscript writing and discussion. JL, XW and YW critically revised the content of the manuscript. XL and JJ conceived the topic of review for the study and revised the manuscript. All authors read and approved the final version of the manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Use of artificial intelligence tools

During the preparation of this work, artificial intelligence tools were used to improve the readability and language of the manuscript or to generate images, and subsequently, the authors revised and edited the content produced by the artificial intelligence tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

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