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REVIEW

Recent approaches in the application of antimicrobial peptides in food preservation

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Abstract

Antimicrobial peptides (AMPs) are small peptides existing in nature as an important part of the innate immune system in various organisms. Notably, the AMPs exhibit inhibitory effects against a wide spectrum of pathogens, showcasing potential applications in different fields such as food, agriculture, medicine. This review explores the application of AMPs in the food industry, emphasizing their crucial role in enhancing the safety and shelf life of food and how they offer a viable substitute for chemical preservatives with their biocompatible and natural attributes. It provides an overview of the recent advancements, ranging from conventional approaches of using natural AMPs derived from bacteria or other sources to the biocomputational design and usage of synthetic AMPs for food preservation. Recent innovations such as structural modifications of AMPs to improve safety and suitability as food preservatives have been discussed. Furthermore, the active packaging and creative fabrication strategies such as nano-formulation, biopolymeric peptides and casting films, for optimizing the efficacy and stability of these peptides in food systems are summarized. The overall focus is on the spectrum of applications, with special attention to potential challenges in the usage of AMPs in the food industry and strategies for their mitigation.

Keywords Applications · Challenges · Packaging · In silico · Fabrication · Bioinformatics · Nanoparticles

Introduction

Outbreaks of foodborne diseases listed on FDA website reveal a dangerous trend. A total of 24 outbreaks are mentioned in 2023 resulting in illness or hospitalization (https://www.fda.gov/food/outbreaks-foodborne-illness/investigations-foodborne-illness-outbreaks). Some food microbes such as strains of *Listeria monocytogenes, Salmonella, Escherichia coli* are pathogenic and responsible for severe diseases; nevertheless, there are other microbes including but not limited to *Brochothrix thermosphacta*, *Carnobacterium spp.*, *Lactobacillus spp.*, *Lactococcus spp.*, that may not cause illnesses, yet food spoilage caused by these microbes can be economically devastating. The actual amount of economic loss caused by food spoilage is unknown, although it is believed that 25% of food produced worldwide is lost owing to spoilage microbes (Bondi et al. 2014). Reducing food spoilage and FBDs is the main goal of using food preservation techniques, such as thermal or non-thermal treatments, food additives, and improved packaging. Artificial preservatives like sorbates, nitrites, and benzoates inhibit microbial activity, antioxidants like formaldehyde, butylated hydroxytoluene, and butylated hydroxyanisole are used to stop food from oxidizing. However, a growing number of individuals are looking for minimally processed foods free of artificial substances because they are worried about the safety of chemical preservatives.

Antimicrobial peptides (AMPs) are a diverse class of molecules that all living things produce and are considered a part of innate immunity. These are sometimes also referred to as peptide antibiotics (Zasloff 2002). They are peptides that range in size from 7 to 100 amino acids. A lot of research interest has been generated by AMPs' capacity to fight bacteria that are resistant to drugs. Additionally, some AMPs have immune-modulatory qualities that support

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pathogen clearance in an indirect manner. They have found a role in diverse fields such as healthcare, agriculture, and the food industry. These peptides are classified based on their diverse sources, amino acid composition, activity, and structural attributes (Huan et al. 2020). Sources of AMPs encompass animals, plants, microorganisms, and recently synthetic AMPs. AMPs grouped on the basis of their amino acid composition include peptides rich in either proline, glycine, histidine, or tryptophan, while their activity can be characterized as either broad-spectrum or specific to certain pathogens. Structural classifications include α-helical, β-sheet, loop, and extended peptides. Mechanisms of action of AMPs include killing microbes by disrupting the cell membrane, inhibiting the production of proteins and nucleic acids, or binding to specific targets inside the cell, ultimately leading to cell death (Yonezawa et al. 1992; Graf et al. 2017; Boix-Lemonche et al. 2020).

Researchers are currently investigating the potential of AMPs to inhibit the growth of microbes, for extending the shelf life of various food products, and prevention of FBDs (Zhang et al. 2021; Baindara and Mandal 2022; Jha and Singh 2023). Nevertheless, there are still a number of technical obstacles that need to be addressed before AMPs may be used in food preservation. These include issues with large-scale synthesis, toxicity, haemolytic activity, stability, immunogenicity, and other possible drawbacks. Recent research investigations have focused on a number of solutions intended to alleviate the aforementioned limitations. These comprise rational design and modification of AMPs, biocomputational and bioinformatics analysis based in silico designing and active packaging systems (Agyei et al. 2018; Aguilera-Puga et al. 2023; Jordan et al. 2024).

AMPs derived from variety of sources as preservatives in different food types

In response to customer demands for safer and more natural food preservation techniques, AMPs present a possible substitute for conventional chemical preservatives. In addition to antimicrobial activity, AMPs have demonstrated antioxidant activity, which is of interest to the food industry (Lima et al. 2019). Some of the AMPs have the potential of being used as food additives and are classified as 'Generally Regarded as Safe' (GRAS) such as natural variants of Nisin (Nisin-A, Z, F, Q, U, U2, H, P) which are among the most important FDA approved AMPs as food preservative (Field et al. 2023). There are many similar approved/GRAS AMPs which include but not limited to Natamycin (Meena et al. 2021), Enterocin AS-48 (Dijksteel et al. 2021), Lactoferricin (Singh et al. 2023), ε-Polylysine and Pediocin PA-1 (Luz et al. 2018; Santos et al. 2018). Several AMPs have been evaluated for their potential to inhibit microbes in a number of food matrices, some of which are summarized as follows or in Table 1.

Table 1 Details of various AMPs evaluated against microbes in different foods

S.N	Name of the AMP	Source	Mechanism of action	Target microbes	Food	References
	11SGP and RBAH	Pea and Red kidney bean	Antibacterial and antioxidant	Bacterial and fungal species	Buffalo meat	El-Saadony et al. (2021)
	Glycinin basic peptide	Soybean	Suppression of spore germination	*Aspergillus niger* and *Penicillium* spp.	Wet noodles	Hou et al. (2017)
	Iturin V	*Lactobacillus* sp. M31	Disintegration of cell wall	*Vibrio* species	Fish	Singh et al. (2021)
	EAFP1	*Eucommia ulmoides*	Interfere with elongation of fungal cell wall	Pathogenic fungal species	Tomato, Wheat	Huang et al. (2002)
	ABP	*Momordica charantia L*	Destroying the cell membrane of bacteria	*Staphylococcus aureus, Escherichia coli*	Minced meat products	Jabeen and Khanum (2017)
	Enterocin AS-48	*Enterococcus faecalis A-48–32*	Endospore structure disarray	*Alicyclobacillus acidoterrestris*	Fruit juices	Grande et al. (2005)
	Mytimacin-4	*Mytilus galloprovincialis*	Attack intracellular structures	Pork spoilage bacteria	Pork	Dong et al. (2024)
	Melittin	*Apis mellifera*	Membrane disruption	*S. aureus, E. coli, Listeria monocytogenes*	Beef	Rouhi et al. (2024)
	Tilapia Piscidin 4	Nile tilapia	Increase membrane permeability	*Candida albicans, Rhizopus oryzae*	Tomato, Fruit juices	Hazam et al. (2024)

Milk and dairy products

Milk and its products are a vital source of nutrition, but they are susceptible to spoilage by microorganisms, leading to economic losses. Natural bio-preservatives, such as AMPs, offer a promising solution to preserve milk and its products without compromising their nutritional quality or safety (Mohanty et al. 2016). A novel AMP named LCWAP designed by screening amino acid sequences from the whey acidic protein (WAP) of large yellow croaker (*Larimichthys crocea*) exhibited a minimal inhibitory concentration (MIC) of 15.6 µg/mL against *Staphylococcus aureus* in milk and inhibited biofilm formation up to 94.3%, without showing cytotoxic effects on normal human hepatocytes (Yang et al. 2020). Similarly, a peptide Cerein 8A was found to reduce *Listeria monocytogenes* in milk by 3 log cycles over 14 days at 4 °C and decreased viable counts by 2 log cycles on contaminated cheese surfaces over 30 days (Bizani et al. 2008). Another study reported liposome-encapsulated Nisin and BLS P34 for preserving Minas frescal cheese by controlling *L. monocytogenes* in which these AMPs showed 88.9 and 100% entrapment efficiency in liposomes, respectively. These treatments significantly reduced the bacterial counts compared to the control during 21 days of storage of cheese at 7 °C (Malheiros et al. 2012).

Fruits and vegetables

AMPs have shown promise in inhibiting the growth of spoilage microorganisms and extending the shelf life of fruits and vegetables without the use of synthetic additives. Overall, the focus of research is shifting towards preserving fruits and vegetables in ways that are both effective and environmentally friendly. Arulrajah et al. (2021) studied antifungal peptides from kenaf seeds to extend the shelf life of tomato puree. Mixture of these peptides when applied to tomato puree significantly reduced fungal counts and delayed growth of *Aspergillus niger* and *Fusarium* sp. up to 14 and 23 days at 25 °C and 4 °C respectively. Shwaiki et al. (2020) examined Snakin-1, a peptide extracted from potato tubers, against *Zygosaccharomyces bailii*, a yeast responsible for spoilage in different beverages such as Fanta Orange (Coca-Cola, Ireland) (pH 3.1), SuperValu (Chilled 169 Cranberry Juice) (pH 2.7) and apple juice (CYPRINA) (pH 3.5), and observed a complete inhibition of *Z. bailii* in all juices at 200 µg/mL. A cationic antimicrobial peptide PAF56 inhibited spore formation, disrupted cell membranes, and was non-toxic to human red blood cells when it was evaluated in preservation of citrus fruits by targeting *Penicillium digitatum*, *Penicillium italicum*, and *Geotrichum candidum,* demonstrating its potential as an effective agent for postharvest citrus disease control (Wang et al. 2021). The antimicrobial peptide CB-M was studied by Yang et al. (2023) against *Botrytis cinerea*, a fungus causing Gray mold disease in cherry tomatoes, tomatoes, and grapes fruits. Results showed a strong dose dependent inhibitory effect on spore survival and mycelial growth of *B. cinerea* thus reducing the disease.

Meat, fish or sea food

Meat and fish are prized for their nutritional value and taste, but they are highly perishable due to microbial contamination and altered sensory properties because of lipid oxidation. Dang et al. (2020) found *Musca domestica* derived AMPs to increase membrane permeability and inhibition of bacterial growth in chilled pork at concentrations 0.4 to 0.8 mg/ml with negligible hemolytic activity against human erythrocytes. Nie et al. (2021) designed chimeric lysins by fusing *Salmonella* phage lysin with the peptide LeuA-P, which could effectively reduce the microbial counts in contaminated chilled chicken and extend its shelf life by seven days. Similar studies have reported the use of AMPs to minimize lipid oxidation and reduce the bacterial count in meat or meat products (Przybylski et al. 2016; Jabeen and Khanum 2017). AMPs have also been found to play a crucial role in preserving fish or sea food by inhibiting microbial growth (Shabir et al. 2018; Ning et al. 2019). Sm-A1, a peptide derived from turbot viscera, was successfully loaded into poly vinyl alcohol-chitosan hydrogel which could effectively protect the salmon muscle from the microbiological contamination and texture deterioration (Bi et al. 2020). Peng et al. (2018) investigated the effect of Nisin along with 1% chitosan as preservatives on the quality of Jumbo squid and reported a reduction in both microbial growth and nutritional loss.

Cereal crops and their products

AMPs have been found to be effective in protection of various cereal crops or their products. Unclean conditions in storage godowns make food grain unfit for human consumption due to microbial deterioration. AMPs LR14 were studied for the prevention of wheat grain spoilage under storage which prevented fungal growth even after a prolonged storage for more than 2 years (Gupta and Srivastava 2014). Furthermore, transgenic technology has been used for heterogenous expression of AMPs in crops like rice and maize which provides them with resistance against phytopathogens (Noonan et al. 2017; Tang et al. 2023). Additionally, studies have reported the efficacy of AMPs in improving shelf life of cereal derived food products such as cakes and noodles (Xiao and Niu 2015; Luz et al. 2018; Lu et al. 2022).

Challenges of the AMPs applications

The application of AMPs in general, and particularly for food preservation, has many challenges. These include high production costs, possible toxicity for eukaryotic cells, a lack of stability, antigenicity and development of resistance, that need to be addressed. The final fate of the AMPs, including their absorption, distribution, metabolism, excretion, and toxicity (ADMET), are other aspects to be looked into for efficient therapeutic efficiency (Okella et al. 2022).

The major challenge that synthetic AMPs face in their application in food preservation is the expensive cost of synthesis, which impedes the large-scale production and usage of these peptides. The poor stability of AMPs is another major challenge due to their susceptibility to the action of proteases or other environmental factors such as temperature and pH. AMPs stability has also been associated with geometrical features such as ovality, lipophilicity, radius of gyration, and polar surface area. The thermostability of AMPs is very important in food production since thermal treatments are generally used during food processing (Al-sahlany et al. 2020).

Another major problem with applications of AMPs is their possible toxicity to the host cells. Due to hydrophobic structure with positive charges, AMPs have both advantage of broad-spectrum bioactivity and problem of potential biotoxicity (Wei and Zhang 2022). Although the nonspecific mechanism of action of AMPs is a major advantage in terms of broad-spectrum activity encompassing a wide range of microorganisms, there may be chances of uptake of these AMPs by off-target cells instead or in addition to the target cells. It may result in undesired effects on eukaryotic cells, leading to toxicity or hemolytic activity. Natural AMPs with cationic charges can interact with negative ions on the surface of the cell membrane, and then form oligomers to destroy cells (Spaller et al. 2013). These potential toxicities may be reduced by change in amino acid composition of peptides or by attachment with biomaterials (Wei and Zhang 2022). In addition, certain microbiota that are part of the digestive system may uptake these AMPs and develop resistance against the peptides, resulting in a risk of dissemination of the resistance through horizontal gene transfer to pathogens (Crits-Christoph et al. 2022; Tajer et al. 2024).

Further, there are many elements in foods such as proteases and peptidases that can react with or interact with AMPs, thereby reducing their bioactivity (Udenigwe and Fogliano 2017). Also, reactions can occur between amino groups on peptides with carbonyl groups on reducing sugars present in foods, resulting in inactive form of peptides (Lund and Ray 2017). The need for studies on the behavior of AMPs within complex food systems is imperative since the effect of some food processing parameters on AMP activity, such as temperature and pH, is often studied separately.

Improved design or modification of AMPs

There are many strategies for rationally designing AMPs for improved efficiency against microbes, reduced toxicity, and increased stability (Rai et al. 2016; Giacometti and Buretić-Tomljanović 2017; Agyei et al. 2018). Important concerns in applications of AMPs and designing strategies to mitigate these concerns are shown as Fig. 1.

The effective functioning of AMPs requires adherence to appropriate design principles. It involves creating the AMP units, or AMP moiety, to be available for the best possible performance. Even the size and aggregation of the newly created peptides affect the functional characteristics of the AMPs. In order to achieve the interaction of the proper domain, the hydrophilic and hydrophobic regions of a composite AMP assembly should be oriented appropriately, e.g., the systematic evolution of ligands by exponential enrichment (SELEX) forms. Certain peptides may operate better even when combined with single-stranded oligonucleotide versions of nucleic acids (Lee et al. 2022). The biological activity of AMPs has been demonstrated to be enhanced via hybridization, which involves covalently joining two or more peptide segments to reap the benefits of each fragment (Tian et al. 2019).

The multiple hurdle concept is another approach wherein combinations of natural antimicrobials with nonthermal processing technologies such as ultrasound, pulsed-electric field, high pressure, and ozone treatment have shown potential synergistic effects. Applying these nonthermal techniques may cause bacterial cell membranes to deteriorate or make them more vulnerable to AMPs, which would increase the lethality of these peptides (Molinos et al. 2008).

Various strategies like cyclization, capping, lipidation, glycosylation, dimerization/multimerization, dendrimerization, phosphorylation, acetylation have been explored for increasing the stability of the AMPs (Rounds and Straus 2020; Bitencourt et al. 2023; Kumari et al. 2023; Mironov et al. 2024). Cyclization (Liu et al. 2017) and peptide stapling (Selvarajan et al. 2023) have been employed to enhance the stability of the AMPs against proteolytic degradation. Another way to improve AMP stability against proteases is to cap the AMPs. Attaching an acyl group or hydrophobic end modification are some of the N- or C-terminal capping methods to improve the stability of AMPs (Zhong et al. 2019). Dimerization or multimerization is obtained by incorporating the peptide side chains or peptide branches in the α- or ε-amino groups of certain amino acids (Santos-Filho

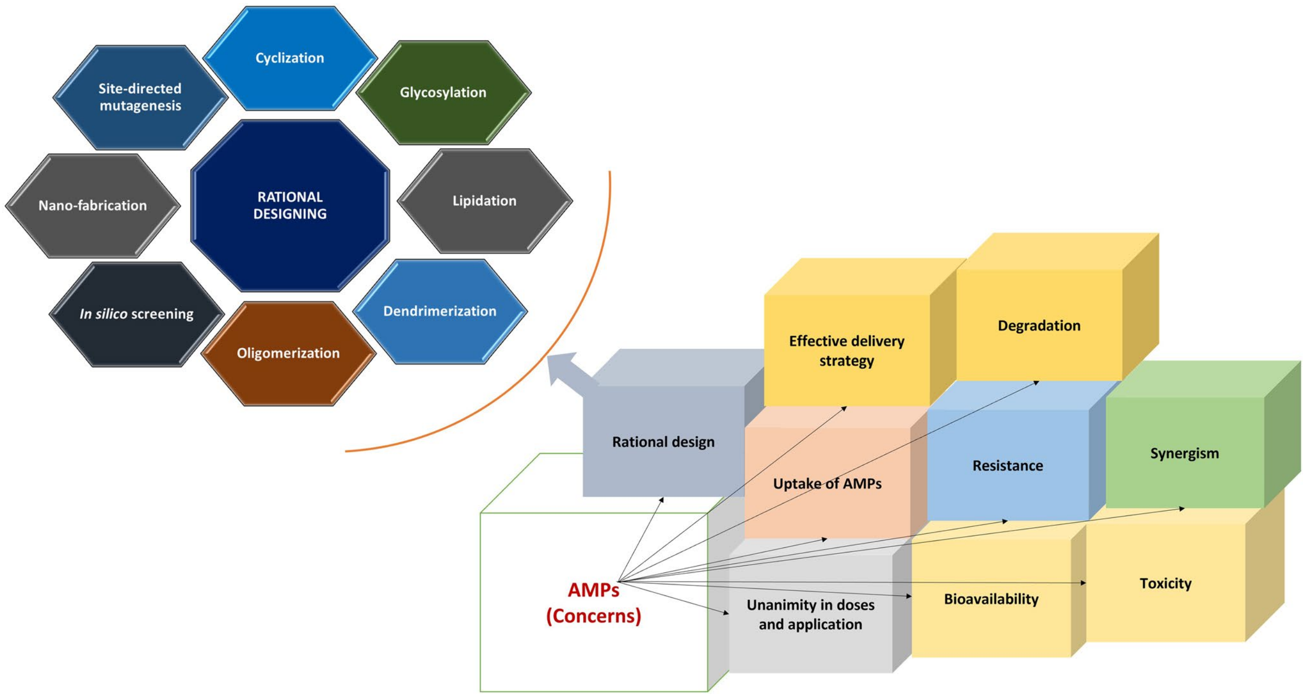

Fig. 1 Important concerns in applications of AMPs and designing strategies to mitigate these concerns

et al. 2021). Using this strategy, more peptide monomers are grouped, which eventually boosts the stability of the whole unit by providing protection against proteolytic degradation due to steric hindrance (Bitencourt et al. 2023).

To create AMPs that are both highly active and less toxic, different approaches have been used, which include truncating the original peptides while preserving the active component and site-directed alteration of the amino acid residues (Huan et al. 2020).

In silico analysis for AMP prediction and discovery

AMPs in their initial days of discovery were isolated from different natural sources, but now a days, synthetic AMPs are also in application. These molecules are well known for their diverse modes of action against pathogens, which reflects their potential in terms of therapeutic and food preservative usage. However, a few limitations have also been identified with the applications of AMPs (Lombardi et al. 2015; Zhao et al. 2016; Oshiro et al. 2019), as mentioned earlier. These limitations can be overcome through in silico analysis using a combination of bioinformatics or computational models with the aim of improving the performance, biocompatibility, and safety of AMPs. The classical methods, such as isolation and identification of AMPs, are very time-consuming and laborious. For the practical use of AMPs as food preservatives, it is important to reduce the experimental time spent identifying AMPs. A number of computational models have been developed for the effective design and discovery of AMPs through in silico analysis. These models have helped in the rapid and accurate prediction of peptides that can be chemically synthesized and investigated for their suitability for use as food preservatives. In general, these predictive computational models are broadly based on empirical methods and machine learning (ML) approaches (Porto et al. 2012).

The empirical methods used for AMP design are qualitative in nature. These models are governed by rules or patterns of antimicrobial activity. Practical issues may arise for empirical approaches because of their low accuracy and complex analysis. In contrast, the ML models have demonstrated their usefulness in well-structured screening and prediction of AMP sequences. The models used on such platforms make final inferences using comprehensive training data (Jia et al. 2015). One popular machine learning approach for creating and optimizing AMPs is the quantitative structure activity relationship, or QSAR model (Mitchell 2014). This model uses physicochemical parameters and amino acid sequences to envisage the biological action of AMPs (Hilpert et al. 2008).

Interestingly, the combination of the predictive and generative machine learning (ML) models is opined to be best suited for the designing of AMPs (Aguilera-Puga et al. 2023). The ML platforms use various algorithms like support vector machine (SVM), K-nearest neighbor (KNN), random forest (RF), and neural network (NN). The SVM algorithms consider factors like amino acid composition, physiochemical properties, and structural features of AMPs. These can also be used to forecast peptide membrane activity with high predictive value. The KNN algorithms rely on pattern recognition methods. Xiao et al. (2013) demonstrated the use of the fuzzy K-nearest neighbor (F-KNN) method and multi-label classifier which finally classify AMPs into different types based on activity. The RF algorithm-based methods predict AMPs using the distribution pattern of properties of peptides acquired from available AMPs and non-AMPs sequences (Lawrence et al. 2021), while the NN method can be used to identify the pattern in a sequence database and model the structure–activity relationship of AMPs (Wang et al. 2024).

In addition to the popular ML methods, de novo computational prediction platforms have helped generate a variety of peptide sequences with different amino acid compositions, interaction structures, and modes of action (Hiss et al. 2010). These platforms use information on amino acid frequency and position preferences which offers insights into the structure and amphipathicity of peptides (Porto et al. 2012).

An evolutionary/genetic algorithm-based approach has been utilized recently using fitness functions like activity descriptors and data gathered from databases to identify a variety of AMPs (Torres and de La Fuente-Nunez 2019). Using these algorithms in conjunction with other models like NNs and computational tools such as molecular docking, the output potential of AMP prediction can be further enhanced. Table 2 provides details on several models and tools for in silico investigation of AMPs.

Workflow for in silico analysis

Adoption of a prudent AMPs analytical workflow or pipeline is necessary for a thorough assessment of the antibacterial potential, physicochemical characteristics, and biocompatibility of peptides in order to design and identify appropriate AMPs with a broad range of activity. A typical workflow for AMP development or in silico prediction may have four stages of analysis (Melo et al. 2021; Aguilera-Puga et al.

Table 2 Description of various tools and ML models available for in silico AMP design

S. N	Name of the tool/Model	Algorithm/Platform	Link	References
1	iAMPpred	SVM algorithm	http://cabgrid.res.in:8080/amppred/	Meher et al. (2017)
2	iAMP-L2	fuzzy K-nearest neighbor (F-KNN)	http://www.jci-bioinfo.cn/iAMP-2L	Xiao et al. (2013)
3	Mutator	Amino acid substitution	http://split4.pmfst.hr/mutator/	Kamech et al. (2012)
4	AntiBP2	SVM algorithm	http://crdd.osdd.net/raghava/antibp2/	Lata et al. (2009)
5	ClassAMP	RF and SVM algorithms	http://www.bicnirrh.res.in/classamp/	Joseph et al. (2012)
6	DBAASP	RF algorithm	https://dbaasp.org/home	Vishnepolsky et al. (2022)
7	Joker	Linguistic model for de novo prediction	https://github.com/williamfp7/Joker	Porto et al. (2018)
8	CAMP	SVM, RF and artificial neuronal network (ANN)	http://www.camp.bicnirrh.res.in/index.php	Waghu and Indicula-Thomas (2020)
9	AMPscanner	Hosts RF and multivariate adaptive regression splines (MARS) based classifier and ANN based AMP classifier	https://www.dveltri.com/ascan/	Veltri et al. (2018)
10	AntiMPmod	SVM	webs.iiitd.edu.in/raghava/antimpmod/	Agrawal and Raghava (2018)
11	dbAMP	RF	http://csb.cse.yzu.edu.tw/dbAMP/predict.php	Jhong et al. (2019)
12	ampir	SVM	https://github.com/legana/ampir	Fingerhut et al. (2020)
13	amPEPpy	RF	https://github.com/tlawrence3/amPEPpy	Lawrence et al. (2021)
14	ADAM	SVM, Hideen Markov Model (HMM)	http://bioinformatics.cs.ntou.edu.tw/ADAM	Lee et al. (2015)
15	IAMPE	(KNN), SVM, RF	http://cbb1.ut.ac.ir/	Kavousi et al. (2020)
16	CalcAMP	Multi-layered Perceptron (MLP)	https://github.com/CDDLeiden/CalcAMP	Bournez et al. (2023)
17	DiffAMP	ANN	https://github.com/wrab12/diff-amp	Wang et al. (2024)

2023). Gathering experimental data on amino acid composition, structure, biological activity, and physiochemical characteristics is the initial stage. In the second stage, the information is converted to a digital format that supports ML so that it may be analyzed. The third step comprises the actual use of ML models with selection of algorithms having high accuracy and reliability. In the fourth phase, the best AMP candidate is identified, which can be validated for activity. Various in vitro biocompatibility analysis parameters like hemolysis prediction, water solubility prediction, toxicity prediction, peptide half-life prediction, and protease susceptibility analysis can also be included (Melo et al. 2021). One of the important aspects of in silico analysis is antigenicity prediction, as designed AMPs should be free from antigenicity. Various safety analysis databases and tools to design AMP are given in Table 3.

Active food packaging and creative fabrication of AMPs

Food packaging is an important aspect of today's food industry, as it plays a major role in safeguarding the quality of products and the safety of consumers. In smart packaging, functionality beyond the standard function of serving as a physical barrier between the product and its surroundings is included. Various types of packaging on the basis of the engineered functionality of the package include ergonomic packaging, informative packaging, responsive packaging, and active packaging (Singh and Heldman 2001; Brockgreitens and Abbas 2016).

Active packaging is achieved by incorporating antimicrobial agents into the packaging material and ensuring a controlled release over an extended period to preserve the food quality. The mechanism of packaging of AMPs can be summed up by three interconnected sections, which include the incorporation system, which comprises the addition of AMPs into the packaging material; the release system, which ensures the diffusion of peptides from the surface of the package to the food; and the interaction and inhibition system, involving the interaction and subsequently destruction of microbes present in the food (Sultana et al. 2021).

For the purpose of enhancing efficacy and stability in a range of applications, including food packaging, AMPs are manufactured or encapsulated in a variety of ways, as described as follows.

Nanoencapsulation

One of the most common methods used for the fabrication of AMPs for active packaging of food is nanoencapsulation. The two primary stages in nanoencapsulation are incorporating antibacterial agents into their appropriate carriers and reducing their size to the nanoscale. The stability of AMPs is generally improved by nanoencapsulation, which also offers controlled release, high adsorption, defense against environmental variables, and less unfavorable interactions with food ingredients. Additionally, it gives the loaded particles a larger surface area than the bigger particles for higher efficacy. The efficiency of AMPs has been improved by their integration into nanoparticles such as lactoferrin, chitosan, polycaprolactone, polyethylene oxide, liposomes, poly (lactic-co-glycolic acid) commonly known as PLGA and even extending to binary or ternary complexes of such nanoparticles in order to preserve the physiochemical properties of food items (Duarte and Picone 2022). There are a variety of nanoencapsulation systems, including nanofibers, liposomes, nanoemulsions.

Nanofibers can be synthesized using artificial or natural polymers. These possess a large surface area of contact, which makes it possible to load more than one molecule at once. They are produced by various methods, such as

Table 3 List of AMP activity analysis tools

S. N	Name	Activity	Link	Reference
	HemoPred	Predicts hemolytic activity	http://codes.bio/hemopred/	Win et al. (2017)
	HemoPI/Hemolytik	Predicts hemolytic and non-hemolytic peptides	https://webs.iiitd.edu.in/raghava/hemopi/index.php	Chaudhary et al. (2016)
	HAPPENN	Hemolytic activity prediction	https://research.timmons.eu/happenn	Timmons and Hewage (2020)
	IgPred	Predicts antigenicty of peptides	https://webs.iiitd.edu.in/raghava/igpred/	Gupta et al. (2013a)
	ToxinPred	Predicts toxic and non-toxic peptides	https://webs.iiitd.edu.in/raghava/toxinpred/	Gupta et al. (2013b)
	Protscale	Hydrophilicty and hydrophobicity prediction	https://web.expasy.org/protscale/	Gasteiger et al. (2005)
	HLP	Peptide half-life prediction in intestinal environment	http://crdd.osdd.net/raghava/hlp/pep_both.htm	Sharma et al. (2014)
	AMP-toxicity-predictor	Predicts cytoxicity of peptides	https://github.com/h-khabbaz/amp-toxicity-predictor	Khabbaz et al. (2021)

electrospinning, self-assembly, laser spinning, and melt spinning, of which electrospinning is the most common. AMP-loaded nanoparticles, when electrospun into nanofibers such as polyethylene oxide, have demonstrated increased effectiveness against foodborne bacteria without producing any effect on sensory characteristics (Cui et al. 2017). AMP-conjugated nanotubes or nanocomposites have also been studied with promising results (Hemmati et al. 2021).

Liposomes are spherical nanocarriers based on lipids that are frequently utilized in delivery systems due to their biocompatibility, stability, and ease of synthesis. Liposome-encapsulated AMPs are also widely used in the food industry. AMPs such as Nisin have shown higher antimicrobial activity when loaded into liposomes as compared to when directly applied to the food (Malheiros et al. 2012). Furthermore, liposomes have demonstrated stabilization of the trapped materials against different environments and chemical changes such as pH, temperature, enzymatic modifications. (Mozafari et al. 2008).

Nano-emulsions are also one of the lipid-based nanoencapsulation systems that have been employed in active food packaging. A variety of biopolymers are employed to create emulsions for the inclusion of AMPs (Imran et al. 2012).

Biopolymeric AMPs

Another approach to using AMPs in food preservation is their integration into biopolymers for increased effectiveness. Biopolymers can be synthesized in vitro in cell-free systems, e.g., dextran, or derived from nature, e.g., alginate or hyaluronic acid. Being biocompatible and biodegradable in nature, they can be used as edible films or for packaging food materials (Baranwal et al. 2022). One of the most commonly used biopolymers is chitosan. Its antifungal, antibacterial, and antioxidant qualities are widely recognized. It has shown a synergistic effect in combination with AMPs against the pathogens, along with other characteristics such as decreased moisture content and higher oxygen barrier effectiveness (Luo et al. 2023). Many approaches have been used for the incorporation of AMPs into biopolymers. One of them involves mixing polymer with AMP using click chemistry and then embedding it into another polymer (Chiloeches et al. 2023). It creates a robust packaging material that would prevent leaching out of the components. Combining biopolymer derivatives with antimicrobial peptide dendrimers (AMPDs) is another strategy that targets both the inner and outer membranes of bacteria (Jordan et al. 2024). Controlled release due to retention of the antimicrobial compounds in polymer matrices is also achieved by the use of nanofillers (Jamróz et al. 2019).

Casting films

The fabrication of antimicrobial films integrating AMPs using the casting approach has been documented (Meira et al. 2017). The use of nanofillers results in films being mechanically resistant, with enhanced thermal performance and good water-resistant qualities. AMP encapsulation has also been combined with techniques like biopolymer immobilization to form biodegradable films that showed improved barrier properties against food-borne pathogens (Imran et al. 2012). Jamróz et al. (2021) demonstrated the effectiveness of active double-layered furcellaran/gelatin hydrolysate films containing Ala-Tyr peptide for fish preservation.

Cold plasma technology

Cold plasma technology is a novel environmental-friendly approach for activating polymers that employs the use of naturally or laboratory-produced plasma, which contains a mixture of ions, photons, reactive species for synthesizing polymers or modifying their surface for conjugating AMPs (Jordá-Vilaplana et al. 2014). This technology has been used for the immobilization of biologically active functional substances such as Nisin, Lysozyme, and Vanillin into the packaging material. Polymers used in food packaging, such as polyethylene terephthalate, effectively prevented the formation of biofilms when they were surface-plasma activated and subsequently conjugated to immobilized peptides (Agrillo et al. 2019).

Conclusion and future perspectives

Although antimicrobial peptides offer themselves as an ideal substitute to chemical additives for preventing food spoilage and foodborne infections, their application in this sector is not without limitations. Ideally AMPs to be used for food preservation should be chemically well designed for high effectiveness, nontoxic to native host cells and normal microbiota, stable and cost-effective. As a result, biocompatibility testing is required prior to employing AMPs as food preservatives. Furthermore, a comprehensive approach is required to establish particular conditions that must replicate those present during food processing and storage to determine AMPs applicability, stability, safety, biocompatibility, and potential interactions with food components. Numerous online tools including those based on ML can be utilized to investigate the various properties required for an effective and safe AMP. These are quite fast and accurate, potentially saving time and money as compared to lengthy experimental studies for AMP discovery and prediction. With the addition of new AMPs to the database, ML predictions are constantly improving, which will pave the way for the discovery of more effective and safe peptides in the future.

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Declarations

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