Letters in Applied NanoBioScience
Open-Access Journal (ISSN: 2284-6808)

Review
Volume 12, Issue 4, 2023, 119
https://doi.org/10.33263/LIANBS124.119

Natural Antimicrobial as an Alternative Food Preservatives in the Dietary Systems of Human and Livestock

Arka Karmakar [1], Sweta Ghosh [1], Rofiqul Islam [1], Prakash Rajak [1,*]

[1] Department of Pharmaceutical Sciences, Dibrugarh University, Dibrugarh, Assam-786004
* Correspondence: prakash@dibru.ac.in (P.R.);
Scopus Author ID AAAAAAAAA
Received: 24.03.2022; Accepted: 29.04.2022; Published: 18.09.2022

Abstract: Natural antimicrobials have gained immense importance for researchers in the food industries in preserving food and increasing its shelf life by inhibiting the growth of microbial cells or by killing them. It can be an alternative to the critical complications of microbial resistance and combat various side effects of some synthetic compounds, alongside fulfilling the food safety requirements. In contrast to the benefits imparted by the natural preservatives, the emerging negative impacts exerted by synthetic preservatives on the health and safety of consumers are leading to the obligation for more systematic research to assess the toxicity and mechanism of action of bio preservatives. This review summarizes the natural antimicrobials that can be utilized in dietary systems of humans and livestock, their mechanism of action, various factors affecting their antimicrobial activity, and their incorporation into nano-system to ensure their safety and efficacy.

Keywords: natural antimicrobials; bio-preservatives; chitosan; bacteriocins; lactic acid bacteria; nanotechnology.

1. Introduction

Consumption of food contaminated with pathogens results in several foodborne diseases in humans and cattle [1]. Foodborne pathogens are bacteria, viruses, fungi, and parasites that contaminate food during the production, storage, and transportation stages. This is the main cause of foodborne diseases either directly by infectious agents or indirectly due to a toxic metabolite. Their symptoms may not be just mild but can range from mild to severe and even lead to death. To improve the shelf-life and retain the quality of the food product, various synthetic preservatives, antibiotics, and conventional applied food processing and preservation techniques are being popularly used, and synthetic food packaging is done, which adds to the health risk [2]. According to a report by the World Bank, unsafe and contaminated foods still cost India up to $15 billion a year, despite the continuous effort by the Food Safety and Standards Authority of India (FSSAI) to ensure the quality of food in India [3].

Natural preservatives or bio-preservatives are antimicrobial agents that find their application in preserving the food and extending its shelf life by inhibiting the growth of microbial cells or killing them. They are an alternative to the critical complications of microbial resistance and combat various side effects of some synthetic compounds, alongside fulfilling the food safety requirements [4]. The use of natural preservatives is focused on the sources obtained from plants, animals, bacteria, and fungi, potentially ensuring food safety because of their antimicrobial activity extended against a wide range of foodborne pathogens (fig. 1). If bacteria contaminate food, natural antimicrobials are becoming a viable option for reducing or eliminating health risks and financial losses. Seeds, spices, herbs, fruits, vegetables, milk, animal tissues, and microorganisms such as bacteria and fungus produce secondary metabolites with antibacterial action.

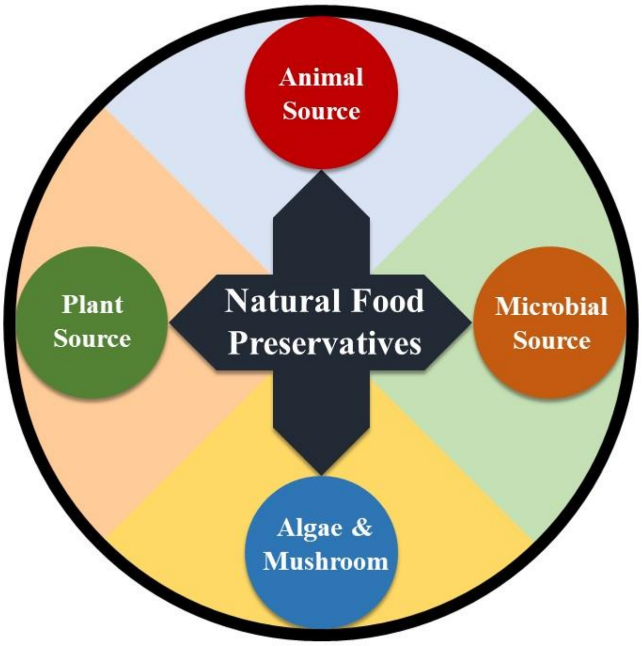

Figure 1. Natural sources of food preservatives.

The use of natural antimicrobials as preservatives for food can help prevent excessive physical processing of food from certifying microbial safety, which frequently alters the organoleptic properties of food. In the last few years, we have been at the forefront of a growing need for natural antibacterial bio-preservatives. Therefore, identifying and using natural antimicrobials and their design in terms of safety and efficacy are important goals in food and medicine research and development. This review summarizes the natural antimicrobials that can be utilized in the dietary systems of livestock, their mechanism of action, various factors affecting their antimicrobial activity, along various physical treatments to process food to ensure their safety.

2. Animals Derived Compounds

Several animal defense systems are reported to have antimicrobial properties. Some natural animal products, like milk, eggs, etc., manifest powerful antimicrobial properties because of their well-characterized compounds, such as lactoperoxidase, lactoferrin, and lysozyme. A number of polypeptides of animal origin, like pleurocidin, chitosan, curvacin A, megainin, and spheniscin have been reported to exhibit prominent preservative actions against microbes [5-9]. These peptides are being explored as a viable option to the growing threat of antibiotic resistance, as some of them may be able to swiftly breakdown cellular lipid bilayer membranes (fig. 2), even in fast-developing microbes. In addition to their effective antibacterial activity against gram-positive and gram-negative bacteria, they also demonstrate antifungal and antiviral activity [10,11].

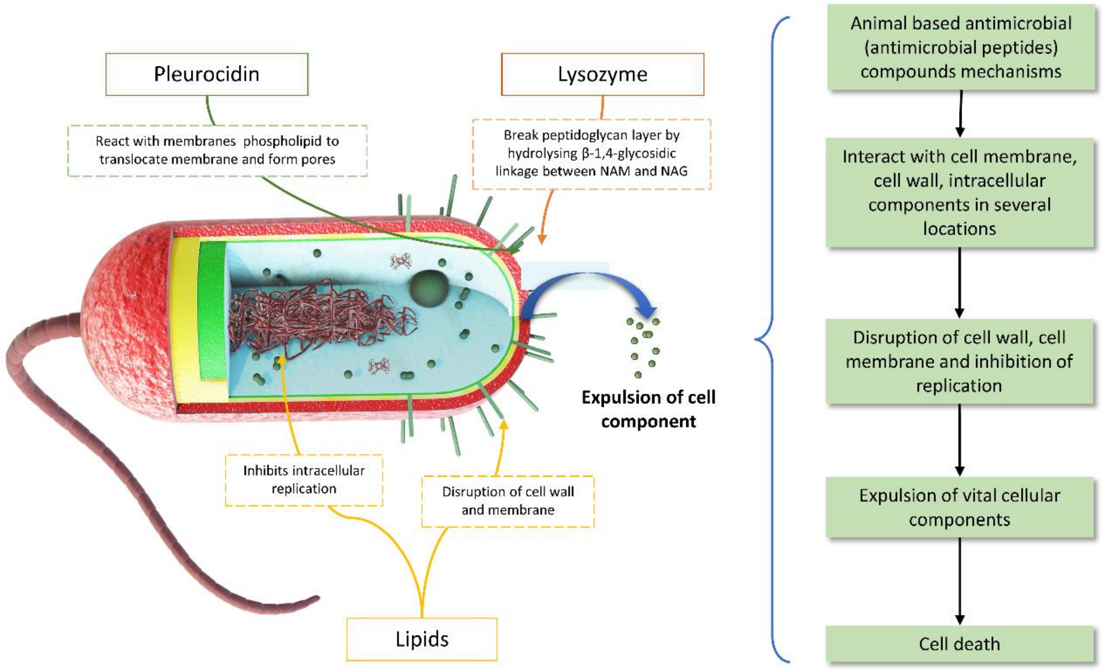

Figure 2. Mechanism of action antimicrobial peptides (NAG: *N*-acetyl glucosamine; NAM: *N*- acetylmuramic acid).

2.1. Pleurocidin.

Pleurocidin is a 25 amino acid polypeptide obtained from the skin secretions of *Pleuronectes americanus* (winter flounder) by Cole *et al*. in 1997 [5]. Pleurocidin is found in myeloid cells and mucosal tissues of several vertebrates and invertebrates and provides a natural system of defense that lowers the mortality of fish infected with pathogenic microorganisms [12]. It has also been reported to be effective against many foodborne bacteria such as *E.coli*, *L. monocytogenes*, *Saccharomyces cerevisiae*, *Penicillium expansum*, and *Vibrio parahemolyticus* [13]. It is thermostable, non-cytotoxic, and salt-tolerant, but it is destroyed by an optimum concentration of magnesium and calcium. Though antimicrobial activity of pleurocidin does not affect on the human red blood cells, and the potent activity is well below the legal limit of nisin (10,000 IU/g) [14], the high expense of chemical pleurocidin production or winter flounder purification might be viewed as a barrier to extensive use. According to Burrowes *et al*., recombinant pleurocidin gene expression can be used for large-scale manufacturing and purification [15].

2.2. Chitosan.

Chitosan is a polycationic biopolymer obtained from the exoskeletons of arthropods and crustaceans. Chitosan consists of polymer sequences with different ratios of N-acetylglucosamine and glucosamine connected by β 1-4 glycosidic linkage and is the most copious naturally occurring polymer after cellulose [16,17].

Chitosan exhibits a broad-spectrum antimicrobial activity against several foodborne microorganisms; it is more efficient against Gram-negative bacteria and makes it a preferable choice because of its low toxicity and safety against mammalian cells for antimicrobial applications [18].

There was a problem of solubility of chitosan in its application as food preservatives at alkaline and neutral pH, which, however, was lately overcome by its N-alkylated disaccharide chitosan derivatives [13]. Maillard reactions were used to prepare water-soluble chitosan derivatives, demonstrating specific antibacterial activity against *S. aureus*, *E. coli*, *Shigella dysenteriae*, *L. monocytogenes*, *B. cereus*, and *Salmonella typhimurium* and can be a good commercial replacement for acid-soluble chitosan [19]. It was reported that chitosan-treated food samples in the form of a solution, nanoparticle, or chitosan-based films under refrigerated conditions showed bacteriostatic effect 6 times greater. Xing *et al*. observed that after 8°C storage, coating treatment with chitosan solution decreased sweet pepper degradation by 20%. Meng *et al*. modified chitosan-coated grapes using pre-harvest and post-harvest sprays of 0.1 percent and 1% chitosan solution, respectively, which considerably d the decay index for 16 days to 42 days at 8˚C [20].

Chitosan's antifungal action and the mechanical barrier produced by a chitosan coating most likely contributes to the lower decay incidence by limiting the development of indigenous microorganisms and protecting samples from foreign infection.

Chitosan significantly reduces the color alteration in pork meat, seafood, sausages, and white pacific shrimp and also retard the rate of lipid oxidation in food product either by scavenging the reactive radicle or by forming a barrier for oxygen diffusion [21]. Chitosan solution-treated eggs also improved egg storability by reducing the passage of carbon dioxide and water vapor via the eggshell pores and enhancing commercial value.

2.3. Conalbumin.

Conalbumin, also known as ovotransferrin, comprises 10% to 13% of the total protein content in an egg, i.e., an iron-chelating protein. Ovotransferrin acts as a good antimicrobial agent showing broad-spectrum activity; however, it has been reported to be more sensitive against gram-positive compared to gram-negative species [22].

2.4. Lysozyme.

It is one of the primary bacteriolytic enzymes of egg white and is usually acknowledged as safe (GRAS) in direct food application. Major foodborne pathogens, including *Clostridium botulinum* and *Listeria monocytogenes* have been reported to create significant problems during food storage, which can be suppressed using lysozyme. Even though lysozyme is easily obtained from eggs and makes up 3.5% of total egg white, human lysozyme has three times the antibacterial effect and thermal stability [21,23]. Additionally, human lysozyme is more therapeutically potent for a broad range of human diseases without creating side effects or modifying immunogenicity, but its usage is restricted due to its scarcity. Lysozyme successfully preserves fish, poultry, meat, and some vegetables against various microbial pathogens, and its antibacterial effects are improved when lysozyme is chemically and thermally modified. The combination of lysozyme and chitosan was found to be effective in preserving the internal quality of fresh eggs over time research [24]. Another research concluded that lysozyme embedded in carboxymethyl cellulose-containing paper was the most efficient in preventing *Listeria innocua* from growing on meat slices. The antibacterial and antifungal activity of lysozyme is enhanced against typical strains of *E. coli*, *A. niger*, *S. aureus*, and *Candida albicans* when conjugated with nanocellulose. Many countries, including the World Health Organization, authorize the use of lysozyme as a preservative in food, and it is now used in kimuchi pickles, sushi, Chinese noodles, cheese, and wine manufacturing [25].

2.5. Lactoferrin.

This is another antimicrobial peptide that has proven efficacy against Gram-negative and Gram-positive bacteria, parasites, and fungi. This iron chelating protein can be found to occur naturally in milk, physiological fluids, colostrum, and polymorphonuclear leukocytes. Chelation of iron and even direct interaction between target microorganisms and the protein are the possible mechanisms of the functioning of lactoferrin [1,26]. It is primarily used in meat products as an antimicrobial agent.

The effectiveness of lactoferrin alone and in combination with nisin improves the microbiological quality of meatballs, resulting in a considerable decrease in the total number of aerobic bacteria, coliforms, *Escherichia coli*, Pseudomonas species, yeast, and mold [27].

2.6. Lactoperoxidase.

Lactoperoxidase is a glycoprotein enzyme found in cows' milk, goats, buffalo, colostrum, saliva, and other secretions, and it has antimicrobial action against bacteria, fungi, and viruses. Lactoperoxidase has a greater effect on Gram-negative bacteria than Gram-positive bacteria. Adding lactoperoxidase to milk increases the product's quality. It functions by oxidizing thiocyanate (-SCN) in the presence of hydrogen peroxide (H_2O_2) to produce antimicrobial active compounds [28,29].

2.7. Protamine.

Protamine, as a cationic antimicrobial peptide, has wide antibacterial action against both Gram-negative and Gram-positive bacteria and fungi. An increase in its electrostatic affinity for the cell surface of target cells may be responsible for the rise in antibacterial action against *Escherichia coli* [30].

The antibacterial effect of Protamine is probably due to its electrostatic affinity for negatively charged bacterial cell envelopes. However, decreased charge protamine may better suppress the multiplication of L. monocytogenes in milk and bacteria in beef than native protamine [31]. Alkaline pH improves protamine antibacterial action against *E. coli*, possibly due to increased electrostatic affinity for target cell surface cells. Protamine shows activity against many foodborne pathogens such as *Actinomyces naeslundii*, *Enterococcus faecalis, Lactobacillus acidophilus*, *Candida albicans*, *Fusobacterium nucleatum* [13,30].

2.8. Magainin.

Magainin, a polycationic peptide obtained from the frog *Xenopus laevis*, destroys gram-positive bacteria that reduce bacterial adhesion to surfaces. There are 23 amino acids in Magainin, and they create an amphipathic helical shape that is likely to be responsible for the creation of transmembrane holes, resulting in a modification in membrane permeability that causes cell death. They have a broad range of antibacterial actions such as *Staphylococcus aureus*, *Klebsiella pneumonia*, *Staphylococcus epidermidis*, *Escherichia coli*, and fungi like *Saccharomyces cerevisiae*, *Cryptococcus neoformans*, and *Candida albicans* and are not harmful to normal eukaryotic cells. As a food preservative, its activity against a variety of foodborne diseases is already proven, and it has been employed during the production of meat and cheese [32].

2.9. Casocidin.

Bovine milk contains another peptide, namely Casocidin, which has antimicrobial properties against foodborne pathogens such as *E. coli*, *Staphylococcus carnosus*, *B. subtilis*, *Diplococcus pneumonia*, *Streptococcus pyogenes*. The peptide consists of 32 amino acids, and it is hydrolyzed product of - casein by the enzyme chymosin [33,34].

2.10. Defensins.

Another broad-spectrum antimicrobial peptide, also a cationic peptide and is naturally available in many animals. It provides defense action against enveloped viruses, fungi, and both gram-positive and gram-negative bacteria due to its unique amino acid sequence. The application of antimicrobial peptides is growing due to their potential for the control of biofilm formation and the killing of microorganisms, which are highly tolerant of antibiotics [35,36].

2.11. Lipids.

Lipids from animal sources, such as free fatty acids derived from animal mucosal surfaces and milk lipids, have inherent antibacterial action against a wide spectrum of bacteria and fungi. Lipids in food can limit microbial multiplication and food development, and spoiling. For example, bovine milk and breast milk contain an 8-carbon fatty acid, i.e., caprylic acid, that is considered GRAS by the U.S. FDA, which can potentially inactivate *Enterobacter sakazakii* in reconstituted infant formula [37].

S. aureus, *Clostridium botulinum*, *Bacillus subtilis*, *Bacillus cereus*, *Listeria monocytogenes*, and other gram-positive bacteria, along with gram-negative bacteria like *E. coli*, *Salmonella enteritidis*, and *Aspergillus niger*, *S. cerevisiae*, and *C. albicans*, can all be inhibited by the lipids in milk. The oxidative phosphorylation of fatty acids, including Eicosapentaenoic and Docosahexaenoic acids, found in many animal tissues, including fish and shellfish, inhibits a wide range of gram-negative and gram-positive bacteria, including *B. subtilis*, *L. monocytogenes*, *S. aureus* ATCC6538, *S. aureus* KCTC1916, *E. coli* O157:H7, *P. aeruginosa*, *S. typhimurium*, and *S. enteritidis* [38].

3. Microbial Derived Compounds

Many microbial metabolic products act as microbial inhibitors. Several gram-positive bacteria often produce amphiphilic, cationic, membrane-permeabilizing peptides that have broad-spectrum antimicrobial properties. For instance, *Lactobacillus spp*. produce a category of antimicrobial peptides known as bacteriocins which can manifest potent antimicrobial activity. Their application in food preservation shows a promising perspective, provided suitable strains are chosen scientifically and an appropriate delivery system is applied.

3.1. Lactic acid bacteria.

Lactic acid bacteria (LAB) have significant antagonistic properties, due to which they are used as bio-preservatives [23]. When they compete for nutrients, they produce certain useful antimicrobials, including acetic acid, bacteriocin, peptide bacteriocins, hydrogen peroxide, and metabolites with low-molecular and antifungal compounds like phenyl lactate, propionate [1,6]. LAB, when used along with other preservatives, can mainly prevent the spoilage of fermented food and control the growth of pathogens [39].

Lactic acid bacteria are a group of the non-spore-forming, gram-positive, catalase-negative, aerotolerant, rod or coccus-shaped fastidious organisms with a high tolerance for high acidic pH [40-42]. Their antimicrobial property is exhibited by producing lactic acid as the principal product from glucose and a few others, such as bacteriocins, diacetyl, acetic acid, reuterin, hydrogen peroxide, ethanol, and ammonia, which help in the control of foodborne diseases by restricting the growth of pathogenic and food spoiling organisms along with their contribution to the development of aroma and flavor in food and beverages [43].

They are extensively studied for their efficacy in controlling food spoilage due to yeast and molds [23]. Lactic Acid Bacteriocin includes the genera of *Streptococcus*, *Lactobacillus*, *Lactococcus*, *Pediococcus*, *Leuconostoc*, *Enterococcus*, *Carnobacterium*, *Aerococcus*, *Oenocovvus*, *Tetragenococcus*, *Vagonococcus* and *Weisella* [40,42]. They obtain energy by fermentation carbohydrates, using endogenous carbon sources instead of oxygen. In accordance with the products of fermented carbohydrates, LAB can be classified into homofermentative and heterofermentative microorganisms. Homofermentative LAB (e.g., *Streptococcus* and *Lactococcus*) mainly produces lactic acid from sugars by the process of glycolysis (fig. 3), whereas heterofermentative (e.g., *Weisella*, *Leuconostoc*) produces lactic acid from acetic acid, ethanol and carbon dioxide [43].

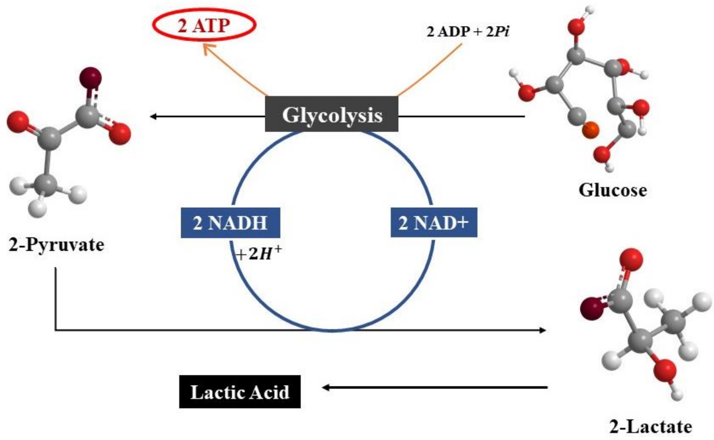

Figure 3. Formation of lactic acid by homofermentative LAB.

LAB is considered GRAS (generally regarded as safe) and non-pathogenic microorganisms, due to which they have been used as probiotics in humans and other animals. According to FAO (Food and Agriculture Organisation) and WHO (World Health Organisation), probiotics are described as preparations containing viable products and microorganisms in sufficient numbers that can alter the microbiota and exert beneficial effects on the host. They help strengthen the immune system and protect the host body against harmful microorganisms [41]. Furthermore, bacteriocinogenic LAB can be used as dairy starting cultures in food processing.

3.2. Bacteriocins.

Bacteriocins are naturally occurring antimicrobial peptides with optimal potential as bio preservatives, especially against closely related bacteria [44]. When they are applied in combination with physicochemical treatments and low concentrations of traditional and natural or chemical preservatives, they allow the pathogens and other spoilage bacteria to be controlled, and they extend the inhibitory action even to gram-negative bacteria [43].

Those bacteriocins, which are GRAS (Generally Recognized As Safe) specified and Qualitative Presumption of Safety (QPS) microorganisms, are utilized as food preservatives in the food industry [45]. Bacteriocins are produced by a heterogeneous group of ribosomally synthesized antimicrobial peptides that can kill closely related (narrow spectrum) or a diverse range of (broad-spectrum) microorganisms. They contain cationic molecules with 30-60 amino acids [23,46].

They are regarded as safe since they are easily degraded by the gastrointestinal tract and produce no harmful effects for human consumption. They have increased human well-being due to their increased potential to regulate gut microbiota [44]. Bacteriocins are mainly used as a preservative in dairy products by incorporating the bacteriocins as food packaging coatings, improving their stability in food complexes. They also find their applications by incorporating food matrixes, which, however, get degraded easily. They can be added to food as pure preparation, fermentates, and bacteriocins-producing culture [40].

Bacteriocins can be classified mainly into three major classes:

i) Class I: small post-translationally modified peptides or lantibiotics with heat-stable property, for example, nisin; sub-divided into class Ia/Ib/Ic (Table 1).

ii) Class II: unmodified bacteriocins or non-lantibiotics with heat stable and containing amino acids like glycine and pediocin; Sub-divided into class IIa/IIb/IIc (Table 1)

iii) Class III: larger and thermolabile peptides, for example, Enterolysin.

Table 1. Classification of bacteriocins.

Class		Typical Producing Species	Attributes	Examples	References
I	Ia	*Lactobacillus lactis* subsp.	Lantibiotics (< 5 kDa peptides containing lanthionine and β-methyl lanthionine)	Nisin	[47-50]
	Ib	*Actinomadura namibiensis*	Carbocyclic lantibiotics containing labyrinthine and labionin	Labyrinthopeptin A1	[51]
	Ic	*Bacillus thuringiensis*	Sactibiotics (sulphur to alpha carbon-containing antibiotics)	Thuricin CD	[52]
II	IIa	*Leuconostoc gelidum*	Low molecular weight (<10 kDa); thermostable; pediocin-like, non-modified, hydrophobic peptides;	Pediocin PA-1 leucocin A, and, sakacin A	[53-55]
	IIb	*Enterococcus faecium*	two complementary peptides required;	plantaricin A, enterocin X, lactococcin G	[56]
	IIc	*Lactobacillus acidophilus*	Affect membrane permeability and cell wall formation; Circular bacteriocins	Gassericin A, entereocin P, reuterin 6	[57]
III		*Lactobacillus helveticus*	Thermo-labile; large peptides; >30 kDa	Lysostaphin, Enterolysin A, Helveticin M	[58-60]

The bacteriocins produced by LAB target the cell envelope association mechanisms. Certain bacteriocins kill the target cell by inhibiting the gene expression, while others can kill the target cell by binding to the cell envelope association mannose phosphotransferase system.

3.2.1. Nisin.

It belongs to the class of cationic antimicrobial peptides known as Type A (I) lantibiotics, and it is the only bacteriocin that is utilized commercially as a food preservative. Nisin is considered Generally Recognized as Safe (GRAS) by FAO/WHO and is also approved by Food and Drug Administration (FDA). It is approved as a food preservative under the European number E234 [59]. Nisin was first discovered in 1928 in fermented milk cultures and was merchandised in England in 1953 as an antibacterial agent, and it gained U.S Food and Drug approval in 1988. It has been used as food bio-preservatives since the 1990s [10,61].

Nisin was produced commercially by fermenting milk with numerous nisin-producing *Lactococcus lactis* strains [40]. According to WHO in 2013, nisin can also be produced from non-fat milk or non-milk-based fermented products, yeast extract, and carbohydrate solids. Nisin was applied as a preservative in various products like cheese, salad dressing, pudding, vegetables, meat, juices, and other beverages [44,62]. It was studied that nisin has antimicrobial potency against gram-positive bacteria like *Listeria monocytogenes*, *Clostridium botulinum*, and *Staphylococcus aureus* but less towards gram-negative bacteria like *E. coli*, *P.aeruginosa*, and *S. etyphimurium* because of the bacterial cell membrane which restricts the entry of hydrophobic compounds like nisin (fig. 4) [63]. Eight types of variants are found, namely: nisin A, nisin Z, nisin Q, nisin U, and U2, nisin F, nisin P, and nisin H. nisin A, Z, F, and Q are produced by L. lactis. Nisin A and Z are obtained from milk and dairy products, nisin Q are isolated from river water, and nisin F is isolated from catfish. Nisin U, U2 are produced from *Streptococcus uberis* and nisin H from *Streptococcus hyointestinalis*. Nisin U and U2 are found in lips, skin, raw milk, and nisin H from gut-derived strain [23,44]. Nisin is usually considered a bacteriocin because of the following reasons [64]: (a) The peptide present in nisin can be degraded by intestinal proteases; (b) There is no change in the organoleptic profile and sensory properties.

The antimicrobial action of nisin depends on the aqueous solubility, structural stability, and also on pH. Nisin is stable and soluble in acidic conditions. Low pH and low temperature are the two most important conditions that need to be considered for the optimum antimicrobial activity of nisin [42,44]. Mechanisms by which nisin exerts antibacterial activity are pore formation in the membrane and inhibition of cell wall biosynthesis by binding to lipid II. It also prevents spore germination, hence preventing spore outgrowth.

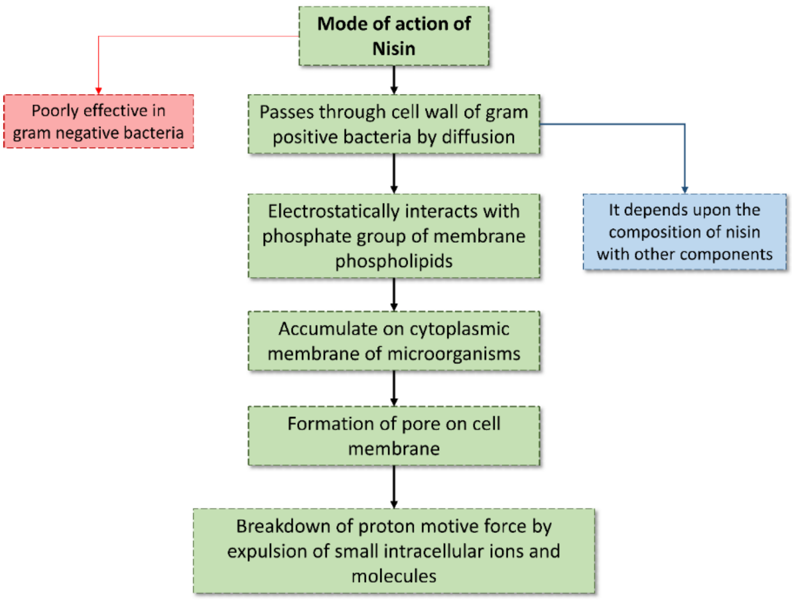

Figure 4. Mechanism of action of nisin.

In more than 50 countries, nisin has been used as a food biopreservative [13]. However, nisin as a broad-spectrum lantibiotic has been confined due to its ineffectiveness in fungi and gram-negative bacteria.

3.2.2. Pediocin.

Pediocin is class IIa bacteriocin produced by *Pediococcus* species and is commonly accessible under the name Alta 2341TM and MicrogardTM [13,44]. It is included as GRAS (Generally Regarded as Safe) in food applications. Most of the lactic acid bacteria produced by class IIa bacteriocins have anti-listerial activity because they are produced by GRAS organisms [15]. They have great potency as antimicrobial preservatives in food. The pediocin producing strains are *Pediococcus acidilactici*, *Pediococcus pentosaceus*, and *Pediococcus damnosus*. These strains are either used as pure cultures or as a mixture to restrict the growth of foodborne pathogens and improve food quality. They are both thermostable peptides and antimicrobial compounds over a broad range of pH [44].

Class II bacteriocins are divided into many subgroups, out of which Class IIa is one of the major subgroups, and it is termed as “pediocin family”, after the first and most extensively studied representant of this class, pediocin PA- 1 [65]. The pediocin PA-1 containing fermented Alta 2341TM is a commercially available food ingredient. It has been reported to extend the shelf life of many foods and, most importantly, inhibit the growth of *Listeria monocytogenes*, a gram-positive bacterium. Pediocin has been reported to show lesser antimicrobial potency against gram-negative bacteria like *Pseudomonas* and *Escherichia coli* due to the structural framework of the outer membrane of gram-negative bacteria, which does not allow pediocin to access its target, the cytoplasmic membrane [66].

Listeria monocytogenes, microorganisms have shown the highest mortality rate in foodborne pathogens in countries of Western Europe and North America. Pediocin displays a wide spectrum against a broad range of gram-positive bacteria, out of which many are responsible for food spoilage due to foodborne pathogens [67].

The purified strain of pediocin PA- 1/Ach has antimicrobial activity against many pathogenic and harmful food brone bacteria [12]. PA-1/Ach pediocin strain, when combined with nisin A, organic acids, lysozyme, ethylenediaminetetraacetic acid EDTA enhances the activity spectrum of gram-positive and gram-negative bacteria and the bactericidal potency [67,68].

The bactericidal mode of action of pediocin PA -1 involves three steps: (i) pediocin binding to the cytoplasmic membranes, (ii) insertion of bacteriocin molecules in the membrane, and (iii) the formation of poration complex. This process ultimately results in cells' death, which may occur with or without cell lysis [66].

Pediocin PA-1 provides an antimicrobial effect to meat-based products. It was observed that beef meat samples when inoculated with *Clostridium laramiae, Lactobacillus* spp., and Leuconostoc and after that packed in a vacuum and stored in a refrigerator, showed no contamination and the sample remained unaltered after storage for 12 weeks. The spoilage of the sample containing the bacteriocin was comparatively lowered than the sample without bacteriocin. The antimicrobial activity was also found in milk and dairy products, including cheese, cream, and cheese sauce. The viable count of *L. monocytogenes* decreased rapidly in the pH range of 5.5-7.0. The addition of the bacteriocin during the fermentation of vegetables also decreased the growth of *L.monocytogenes* and inhibited its growth for about 16 days [69,70].

3.2.3. Enteriocins.

Enterocins are produced by Enterococcus species, a member of Lactic Acid Bacteria. The enteriocins have been firmly divided into four major classes: class I consisting of post-translationally modified lantibiotic enterocins, Class II comprising linear, unmodified peptides having molecular mass less than 10kDa, Class III comprising of cyclic peptides, and Class IV consisting of the large, heat liable proteins. Out of all these categories, Class II and Class III have attended considerable attention because they are suitable for use as a food preservative and have antimicrobial activity against foodborne pathogens and gram-positive bacteria. They also have anti-listerial activity, a promising candidate for antimicrobial activity. Lactic acid bacteria are usually approved as GRAS and can be safely used in food preservatives, but bacteriocinogenic enterococci raise certain concerns. Worldwide, more than 25 numbers of species belonging to the genus Enterococcus were found, but most importantly, *Enterococcus faecium* and *Enterococcus faecalis* have been major discoveries [71]. The intestine of humans and animals is common where these bacteria could be found. They are also associated with causing infections in humans. In addition, some of the enterococci may result in determinants of virulence. However, the food enterococci have fewer virulence determinants than clinical strains. The purified bacteriocins are more suitable in food applications than the bacteriocinogenic enterococci, considering the safety concerns [69].

Enterocin AS-48 is produced by *Enterococcus faecalis* and belongs to class IIc bacteriocin having inhibitory potency against Bacillus and Clostridium sp. This particular bacteriocin has great stability to pH and heat, which finds application in food [44].

Listeria monocytogenes is a very pathogenic microorganism, and it is found to be present in many dairy products, especially milk and cheese. Many strains of enteriocins can be used in cheese starters since they are found to be effective against *L. monocytogenes*. They are beneficial because they provide anti-listerial activity in cheese without any additional preservatives. *E.faecium* F58, a strain that produces enterocin, was isolated from goat's milk and used as a starting culture to produce Jben, a fresh Moroccan cheese. It was found to reduce the pathogen *L. monocytogenes* to a huge amount when added as co-culture along with enteriocin producing strains at the beginning of cheese preparations. The AS-48 strain provides good stability to fruits and vegetables [71]. Enteriocin also has good preservative action in meat, poultry and fish products. As nisin is not an effective preservative in meat products, enteriocin serves the preservative's purpose. The use of broad-spectrum enteriocins of AS-48 or strongly anti-listerial enteriocins A and B have potential in meat preservatives. The anti-listerial effect of enteriocins A and B was effective at 7ºC in meat products, e.g., cooked ham and deboned chicken breast [68].

The use of bacteriocins and/or bacteriocin-producing strains of LAB are of significant interest as they are generally recognized as safe organisms and their antimicrobial products as bio preservatives. Nevertheless, it is essential to carry on with the research to expand our understanding of the influences of several factors and to quantify the efficiency and effectiveness of future applications in food systems.

4. Natural Antimicrobials from Algae and Mushrooms

The search in the marine environment has led to the discovery of several bioactive compounds with prominent pharmaceutical and industrial applications. Both seaweeds and diatoms (marine algae) contain bioactive compounds that can potentially combat bacterial invasion in the ocean environment (Table 2). The antimicrobial potential of the micro and macroalgae has led to their introduction into the food industry. However, the identification and validation of algal antimicrobial activity are still in the growing stage.

Table 2. Some efficient algal species and their extracts have antimicrobial activity against foodborne pathogens.

Algal species	Extraction Solvents	Antimicrobial activity against the foodborne pathogen	References
Scenedesmus obliquus; Chlorella vulgaris; Pithophora oedogonium; Nostoc sp.; Microcystis sp.; Scenedesmus sp.; Oscillatoria geminate; Chlorella vulgaris; Turbinaria conoides; Dunaliella salina; Enteromorpha linza.	Ethanolic extract; Methanolic extract; Ethylacetate Extracts; Diethyl ether extract	*Staphylococcus aureus*	[72-74]
Spirulina maxima; Laurencia okamurae; Dictyopteris undulata; Chaetomorpha linum	Methanolic extract	*Bacillus cereus*	[75,76]
Ecklonia cava; Dunaliella salina; Myagropsis myagroides; Himanthalia elongate.	Ethanolic extract; Methanolic extract; Diethyl ether extract; n-hexane; and chloroform	*Listeria monocytogenes*	[77,78]
Ascophyllum nodosum; Chaetomorpha linum; Enteromorpha linza; Ulva rigida; Dunaliella salina; Padina gymnospora.	Phlorotannins (PT); Ethanolic extract; Methanolic extract; Diethyl ether extract;	*Escherichia coli O157:H7*	[73-75,77]
Dictyota dichotoma; Turbinaria conoides; Padina gymnospora; Pithophora oedogonium; Dunaliella salina	Ethanolic extract; Methanolic extract; Diethyl ether extract; and chloroform	*Salmonella spp.*	[74,79]
Turbinaria ornate; T. decurrens; T. conoides; Sargassum polycystum; S. incisifolium; S. ilicifolium; Hormophysa cuneiformis	Heat-assisted extraction; Ethyl acetatete extract; Methanolic extract.	*Staphylococcus aureus and Streptococcus pneumoniae*	[80]
Ulva reticulata	Methanolic extract; chloroform extract; Water extract	*E. cloace and E. coli*	[81]
C. racemosa/ C. sertularioides/ K. alvarezii	Methanolic extract; chloroform extract; Water extract; Ethanolic extract; Ethyl acetatete extract;	*B. cereus; S. aureus; E. coli; K. pneumoniae; P. aeruginosa; C. albicans; C. parapsilosis*	[82]

Herrero and his team researched this direction to identify antimicrobial compounds in macroalgae (i.e., *Himanthalia elongata*) and microalgae (*Synechocystis* spp.,); observed that the extracts from both exhibited antioxidant and antimicrobial activities against /*E. coli* and *S. aureus*. Devi and her co-worker found out about similar activities against *S. aureus* from the extracts of *Haligra* spp. [83,84]. *H. elongata*, *Laminaria digitate*, Padina, *Saccharina latissima*, and Dictyota were reported to have antimicrobial activity against *L. monocytogenes*, *P. aeruginosa*, *B. cereus*, *Salmonella* sp., *Enterococcus faecalis*, and *E. coli* [85,86].

Methanolic extracts of *Oscillatoria sancta* and *Lyngbya birgei* by Prakash *et al*. in 2011 and Methanolic extracts from *Nostoc* spp., *Scenedesmus* spp., *Microcystis* spp., *Oscillatoria geminata*, and *Chlorella vulgaris* by Salem *et al*. in 2014 found similar results concerning the antimicrobial potential against this foodborne pathogen such as *S. aureus* and *B. subtilis* [87].

Edible food coatings can be formulated using algae-derived carrageenan and alginates. Their applications in food industries can be expanded by combining them with other suitable natural extracts/derivatives. Broad-spectrum antimicrobial activity was observed in the ethanolic extracts of *Laetiporus sulphureus* (Bull.) when investigated against *Candida parapsilopsis* CBS604, *C. albicans* ATCC10321, *E. coli* ATCC8739, *S. aureus* ATCC6538, *S. epidermidis* ATCC12228 and *Enterococcus faecalis*.

Among fungi, mushrooms exhibit antimicrobial and antioxidant properties. Extracts of wild *Laetiporus sulphureus* (Bull.) have exhibited antimicrobial activity *in vitro* against bacteria such as *C. albicans*, *C. parapsilopsis*, *E. coli*, *S. aureus*, *E. faecalis*, and *S. epidermidis*. The extracts of the edible mushrooms such as Agaricus, *Meripilus giganteus*, *Morchella costata*, *Armillaria mellea*, *M. elata*, *M. esculenta* var. vulgaris, *M. hortensis*, *M. rotunda*, *Paxillus involutus*, and *Pleurotus eryngii* and *P. ostreatus* showed antimicrobial activity [88,89].

Ramesh and his research team isolated methanolic extracts of *Cantharellus cibarius*, *Clavaria vermiculris*, *Lycoperdon perlatum*, *Marasmius oreades*, *Pleurotus pulmonarius*, and *Ramaria formosa*, which they found to be rich in flavonoids and phenol contents with antimicrobial properties against *E. coli*, *B. subtilis*, *P. aeruginosa*, *S. aureus*, and *Candida albicans* [88]. Crude extracts of lignicolous mushroom species revealed that the antibacterial activity was mostly because of Fomes fomentarius extract [90]. Marijana *et al*. examined and found out that methanolic and acetonic extracts of the mushrooms *Boletus aestivalis, B. edulis,* and *Leccinum carpini* demonstrated a strong antioxidant and antimicrobial activity.

5. Different Biopreservation Techniques Used to Entrap Food Antimicrobials

Many of the antimicrobial agents are sensitive to the production process and storage conditions, i.e., physical pressures and high temperatures can degrade the antimicrobial agents which will lead to the loss of their antimicrobial features [91].

Therefore, nanotechnology has come up with an alternative to delivering natural preservatives in food, showing better possibilities than free antimicrobials. When delivered in encapsulated form, the antimicrobials ensured protection against chemical reactions and unappealing interactions with other food compounds. Furthermore, encapsulation controls delivery and improves absorption and bioavailability. Microencapsulation systems also provide protection, but there are certain disadvantages like microencapsulates when undergoes degradation and can get evaporated, whereas nanoencapsulation system can increase the concentrations of antimicrobials in those areas of food where microorganisms are located due to their high surface area to volume ratio. Encapsulation in nanocarriers protects antimicrobials from adverse conditions like improving their stability and site of action. Certain characteristic properties of nano-capsulation make them one of the widely used encapsulated methods, firstly efficient release properties, secondly nucleolus size, and thereafter biocompatibility with tissues and cells, which enhances pharmacokinetic profile. The rate of release of the antimicrobials from the encapsulated form is an important parameter; thus, the controlled release from nanostructures is as advantageous as ensuring a constant release of antimicrobials into the food [92].

5.1. Nanoemulsions.

Nanoemulsions are colloidal particulate systems with a nanometric size range of 100nm or less. They are optically transparent and provide better shelf stability. Food antimicrobials that are poorly soluble in water are delivered in an O/W type of nanoemulsion, thereby improving the physical stability form of the active compound and increasing its distribution [93].

Eugenol nanoemulsion was stable for about two months and showed antibacterial activity against *Staphylococcus aureus*. Carvacrol, limonene, and cinnamaldehyde were encapsulated in sunflower oil-based nanoemulsions and different emulsifiers. Basil oil was encapsulated in nanoemulsion formulated with Tween 80 and water, showing antimicrobial activities [94].

Bovine lactoferrin is an iron-binding protein that kills iron-dependent pathogenic bacteria. It gets trapped within the W/O/W type of nanoemulsion with lecithin and poloxamers by homogenization. Encapsulated lactoferrin showed inhibition against *S. aureus*, *L. innocua, Candida albicans* [91,95].

5.2. Nanoparticle.

Nanoparticles include both nanocapsules and nanospheres. Nanocapsules are structurally vesicular systems where the moiety is confined to the inner liquid core. The nanospheres are polymetric matrixes where the moiety can be absorbed in the sphere surface or encapsulated within the particle [96].

Nisin is loaded in solid lipid nanoparticles (SLN) which protect prolonged biological activity and the food environment. SLN is comprised of a solid lipid shell. They have the advantage of providing enhanced encapsulation efficiencies and need no organic solvents for preparation, enabling slow release. Nisin ensures the sustained release rate from nanoparticles and inhibits the growth of *Listeria monocytogenes* and *Lactobacillus plantarum* compared to free nisin in solution. When loaded with nisin nanocapsules, chitosan showed sustained release of food preservatives. Chitosan and alginate combination also showed great efficiency and inhibited *S. aureus* more likely than its free form.

Zein nanocapsules were encapsulated with thymol and carvacrol. They both inhibited pathogenic *E. coli*. Thymol nanoparticles showed more coherent growth inhibition of *S. aureus* than free thymol [97].

Nanoparticles of eugenol are loaded with PLGA (Poly Lactic-co-Glycolic Acid), and trans-cinnamaldehyde inhibits the growth of *Listeria* spp. and Salmonella spp. Thus, the water solubility of eugenol increases and sustained or continuous release of antimicrobials was observed over 72 hours. Some antimicrobials are used to build these nanoparticles. Zinc oxide (ZnO) is one example. ZnO is used to build up the body. It is GRAS approved by FDA. ZnO nanospheres are effective against *S. aureus* and *S. typhimurium*. ZnO nanoparticles were also used to study poultry and meat challenge study, which thereby showed antimicrobial activity against some pathogens [91].

5.3. Nanoliposomes.

Nanoliposome structures are encapsulated deliverable, water-soluble, lipid-soluble, and amphiphilic materials. They have nanometric bilayer vesicles mainly composed of phospholipid molecules where hydrophobic hydrocarbon tails are associated inside the bilayer, and the polar part is directed in the aqueous phases of the inner and outer layer.

The mode of action by which liposomes interact with the target cell surface is either adsorption or fusion on the cell surface and cell membrane. Pediocin encapsulated in nanoliposomes showed enhanced stability and efficiency (approx. 90%) and maintained antimicrobial activity in food [98].

5.4. Nanofibers.

Nanofibers have a very thin and narrow diameter, approximately less than 100 nm. Nanofibers are produced in the presence of an external magnetic field on the solution, producing continuous polymeric fibers. They are immensely used in the food industry due to their huge area-to-volume ratio.

One such example is the incorporation of nisin into the gelatin nanofibers, which showed inhibition against pathogens. The antimicrobial activity of nisin nanofiber showed its activity for 5 to 6 months at a stable temperature of 25°C [99]. Nanofiber cellulose is another example that showed good antimicrobial properties, hydrophilicity, and biodegradability. Nisin, when grafted into nanofibers, carboxylated cellulose inhibited the growth of pathogens like *Bacillus subtilis* and *Staphylococcus aureus* [95].

6. Impact on Health of Natural Antimicrobial Preservatives

Since penicillin was discovered, antimicrobial drugs and their derivatives have been widely utilized in the medical field to prevent the growth of a wide variety of microbes and bacteria. Natural antimicrobials have gained popularity in recent years due to their effectiveness in disease prevention, treatment, and food preservation. However, some health concerns or effects have been associated with this use as a preservative.

During the preservation process, antimicrobials can accumulate in the tissues of fish and other animal products as residue, which, after consumed by people, can lead to various health problems. Interfering harmful microbes with natural antimicrobials and/or their antibacterial biological end products may affect human health. In fermented foods and other foods, lactic acid bacteria (LAB) can occur naturally as part of the microflora or be added as starter cultures, where they outcompete other microorganisms after fermentation and home freezing, e.g., vacuum-packaged meat. When LAB grows, it reduces nutrition and oxygen availability and produces inhibitory metabolic chemicals such as acetoin, lactic and acetic acid, hydrogen peroxide, diacetate, reuterin, and bacteriocins, which may affect the normal physiological system.

Natural antimicrobials have not yet been shown to significantly negatively influence human health or the digestive system compared to synthetic preservatives. Toxicity tests on antimicrobials have been conducted and reported in recent years, which indicates that employing natural antimicrobials as a preservative has a lower health risk. Though few natural antimicrobials have been certified by the WHO (World Health Organization) for direct use as food preservatives due to a better understanding of antimicrobial processes and modes of action, their stability and optimal potency remain uncertain.

7. Conclusions

With the emerging negative impacts exerted by synthetic preservatives on the health and safety of consumers and their increasing demand for food free of synthetic chemicals, there is a need to find and substitute safe alternatives without compromising the quality of the food. Preservatives from natural sources show promising perspectives as an appropriate alternative to ascertain safety from foodborne pathogens and enhance shelf-life.

With further research in this direction, proper characterization and validation of the optimum number of antimicrobials and the possible combination of two or more natural antimicrobials that can be safely incorporated for food safety and storage can lead to complete substitution of the synthetic methods. Another possibility is that the bioactive compounds may bind to hydrophobic moieties of proteins or lipids in complex food matrices, which can ultimately inactivate the preservative action, can be countered by nanoparticle incorporation. Moreover, algae and mushrooms have promising prospects and immense potential as rich sources of natural antimicrobial agents for application in the food industries. Therefore, sufficient progress is yet to be achieved in understanding their profiles, potencies, efficient extraction methods, and toxicities.

With their immense potential, more in-depth phytochemical, pharmacological, and toxicological studies need to be assessed before they become the first choice of preservatives in the food processing and packaging industries.

Funding

Declared none.

Acknowledgments

This research has no acknowledgment.

Conflicts of Interest

The authors have no conflict of interest of any nature to disclose.

References

1. Lee, N.-K.; Paik, H.-D. Status, antimicrobial mechanism, and regulation of natural preservatives in livestock food systems. *Korean J. Food Sci. Animal Resour.* **2016**, *36*, https://doi.org/10.5851/kosfa.2016.36.4.547.
2. Gyawali, R.; Ibrahim, S.A. Natural products as antimicrobial agents. *Food control* **2014**, *46*, 412-429, http://dx.doi.org/10.1016/j.foodcont.2014.05.047.
3. India, T.t.o. Study: Foodborne diseases cost India $15 billion a year. Available online: https://timesofindia.indiatimes.com/india/study-food-borne-diseases-cost-india-15-billion-a-year/articleshow/68176718.cms (accessed on 10th December, **2021**).
4. Ananou, S.; Maqueda, M.; Martínez-Bueno, M.; Valdivia, E. Biopreservation, an ecological approach to improve the safety and shelf-life of foods. *Communicating Current Research And Educational Topics And Trends In Applied Microbiology* **2007**, *1*, 475-487.
5. Cole, A.M.; Weis, P.; Diamond, G. Isolation and characterization of pleurocidin, an antimicrobial peptide in the skin secretions of winter flounder. *J. Biol. Chem.* **1997**, *272*, 12008-12013, http://dx.doi.org/10.1074/jbc.272.18.12008.
6. Zasloff, M.; Martin, B.; Chen, H.-C. Antimicrobial activity of synthetic magainin peptides and several analogues. *Proc. Natl. Acad. Sci.* **1988**, *85*, 910-913, https://doi.org/10.1073/pnas.85.3.910.
7. Gänzle, M.G.; Hertel, C.; Hammes, W.P. Resistance of Escherichia coli and Salmonella against nisin and curvacin A. *Int. J. Food Microbiol.* **1999**, *48*, 37-50, https://doi.org/10.1016/s0168-1605(99)00026-4.
8. Tikhonov, V.E.; Stepnova, E.A.; Babak, V.G.; Yamskov, I.A.; Palma-Guerrero, J.; Jansson, H.-B.; Lopez-Llorca, L.V.; Salinas, J.; Gerasimenko, D.V.; Avdienko, I.D. Bactericidal and antifungal activities of a low molecular weight chitosan and its N-/2 (3)-(dodec-2-enyl) succinoyl/-derivatives. *Carbohydr. Polym.* **2006**, *64*, 66-72, https://doi.org/10.1016/j.carbpol.2005.10.021.
9. Tiwari, B.K.; Valdramidis, V.P.; O'Donnell, C.P.; Muthukumarappan, K.; Bourke, P.; Cullen, P. Application of natural antimicrobials for food preservation. *J. Agric. Food Chem.* **2009**, *57*, 5987-6000, https://doi.org/10.1021/jf900668n.
10. Fattouch, S.; Caboni, P.; Coroneo, V.; Tuberoso, C.I.; Angioni, A.; Dessi, S.; Marzouki, N.; Cabras, P. Antimicrobial activity of Tunisian quince (Cydonia oblonga Miller) pulp and peel polyphenolic extracts. *J. Agric. Food Chem.* **2007**, *55*, 963-969, https://doi.org/10.1021/jf062614e.
11. Aires, A.; Mota, V.; Saavedra, M.; Rosa, E.; Bennett, R. The antimicrobial effects of glucosinolates and their respective enzymatic hydrolysis products on bacteria isolated from the human intestinal tract. *J. Appl.Microbiol.* **2009**, *106*, 2086-2095, https://doi.org/10.1111/j.1365-2672.2009.04180.x.

12. Jia, X.; Patrzykat, A.; Devlin, R.; Ackerman, P.; Iwama, G.; Hancock, R. Antimicrobial peptides protect coho salmon from Vibrio anguillarum infections. *Appl. Environ. Microbiol.* **2000**, *66*, 1928-1932, https://doi.org/10.1128/aem.66.5.1928-1932.2000.
13. Pisoschi, A.M.; Pop, A.; Georgescu, C.; Turcuş, V.; Olah, N.K.; Mathe, E. An overview of natural antimicrobials role in food. *Eur. J. Med. Chem.* **2018**, *143*, 922-935, https://doi.org/10.1016/j.ejmech.2017.11.095.
14. Burrowes, O.; Hadjicharalambous, C.; Diamond, G.; LEE, T.C. Evaluation of antimicrobial spectrum and cytotoxic activity of pleurocidin for food applications. *J. Food Sci.* **2004**, *69*, FMS66-FMS71, https://doi.org/10.1111/j.1365-2621.2004.tb13373.x.
15. Burrowes, O.-J.; Diamond, G.; Lee, T.-C. Recombinant expression of pleurocidin cDNA using the Pichia pastoris expression system. *J. Biomed. Biotechnol.* **2005**, *2005*, 374-384, https://doi.org/10.1155/JBB.2005.374.
16. Cacciatore, F.A.; Brandelli, A.; Malheiros, P.d.S. Combining natural antimicrobials and nanotechnology for disinfecting food surfaces and control microbial biofilm formation. *Crit. Rev. Food Sci. Nutr.* **2021**, *61*, 3771-3782, https://doi.org/10.1080/10408398.2020.1806782.
17. Mesgari, M.; Aalami, A.H.; Sahebkar, A. Antimicrobial activities of chitosan/titanium dioxide composites as a biological nanolayer for food preservation: A review. *Int. J. Biolo. Macromol.* **2021**, *176*, 530-539, https://doi.org/10.1016/j.ijbiomac.2021.02.099.
18. Kong, M.; Chen, X.G.; Xing, K.; Park, H.J. Antimicrobial properties of chitosan and mode of action: a state of the art review. *Int. J. Food Microbiol.* **2010**, *144*, 51-63, http://dx.doi.org/10.1016/j.ijfoodmicro.2010.09.012.
19. Chung, Y.-C.; Yeh, J.-Y.; Tsai, C.-F. Antibacterial characteristics and activity of water-soluble chitosan derivatives prepared by the Maillard reaction. *Molecules* **2011**, *16*, 8504-8514, https://doi.org/10.3390/molecules16108504.
20. Torlak, E.; Sert, D. Antibacterial effectiveness of chitosan–propolis coated polypropylene films against foodborne pathogens. *Int. J. Biol. Macromol.* **2013**, *60*, 52-55, https://doi.org/10.1016/j.ijbiomac.2013.05.013.
21. Davidson, P.M.; Critzer, F.J.; Taylor, T.M. Naturally occurring antimicrobials for minimally processed foods. *Annu. Rev. Food Sci. Technol.* **2013**, *4*, 163-190, https://doi.org/10.1146/annurev-food-030212-182535.
22. Abeyrathne, E.N.S.; Lee, H.; Ahn, D.U. Egg white proteins and their potential use in food processing or as nutraceutical and pharmaceutical agents—A review. *Poult. Sci.* **2013**, *92*, 3292-3299, https://doi.org/10.3382/ps.2013-03391.
23. Mei, J.; Ma, X.; Xie, J. Review on natural preservatives for extending fish shelf life. *Foods* **2019**, *8*, 490, https://doi.org/10.3390/foods8100490.
24. Yuceer, M.; Caner, C. Antimicrobial lysozyme–chitosan coatings affect functional properties and shelf life of chicken eggs during storage. *J. Sci. Food Agric.* **2014**, *94*, 153-162, https://doi.org/10.1002/jsfa.6322.
25. Mine, Y.; Ma, F.; Lauriau, S. Antimicrobial peptides released by enzymatic hydrolysis of hen egg white lysozyme. *J. Agric. Food Chem.* **2004**, *52*, 1088-1094, https://doi.org/10.1021/jf0345752.
26. Farnaud, S.; Evans, R.W. Lactoferrin—a multifunctional protein with antimicrobial properties. *Mol. Immunol.* **2003**, *40*, 395-405, https://doi.org/10.1016/S0161-5890(03)00152-4.
27. Colak, H.; Hampikyan, H.; Bingol, E.B.; Aksu, H. The effect of nisin and bovine lactoferrin on the microbiological quality of turkish-style meatball (TEKIRDAĞ KÖFTE). *J. Food Saf.* **2008**, *28*, 355-375, https://doi.org/10.1111/j.1745-4565.2008.00105.x.
28. Magacz, M.; Kędziora, K.; Sapa, J.; Krzyściak, W. The significance of lactoperoxidase system in oral health: application and efficacy in oral hygiene products. *Int. J. Mol. Sci.* **2019**, *20*, https://www.mdpi.com/1422-0067/20/6/1443.
29. Batiha, G.E.-S.; Hussein, D.E.; Algammal, A.M.; George, T.T.; Jeandet, P.; Al-Snafi, A.E.; Tiwari, A.; Pagnossa, J.P.; Lima, C.M.; Thorat, N.D. Application of natural antimicrobials in food preservation: Recent views. *Food Control* **2021**, *126*, https://doi.org/10.1016/j.foodcont.2021.108066.
30. Hansen, L.T.; Gill, T.A. Solubility and antimicrobial efficacy of protamine on Listeria monocytogenes and Escherichia coli as influenced by pH. *J. Appl. Microbiol.* **2000**, *88*, 1049-1055, https://doi.org/10.1046/j.1365-2672.2000.01074.x.
31. Potter, R.; Hansen, L.T.; Gill, T.A. Inhibition of foodborne bacteria by native and modified protamine: Importance of electrostatic interactions. *Int. J. Food Microbiol.* **2005**, *103*, 23-34, https://doi.org/10.1016/j.ijfoodmicro.2004.12.019.
32. Villalobos-Delgado, L.H.; Nevárez-Moorillon, G.; Caro, I.; Quinto, E.J.; Mateo, J. Chapter 4-Natural antimicrobial agents to improve foods shelf life. In: *Food quality and shelf life*. Elsevier: **2019**; pp. 125-157, https://doi.org/10.1016/b978-0-12-817190-5.00004-5.
33. Mohanty, D.; Mohapatra, S.; Misra, S.; Sahu, P. Milk derived bioactive peptides and their impact on human health–A review. *Saudi J. Biol. Sci.* **2016**, *23*, 577-583, http://dx.doi.org/10.1016/j.sjbs.2015.06.005.
34. Sah, B.N.P.; Vasiljevic, T.; McKechnie, S.; Donkor, O. Antioxidative and antibacterial peptides derived from bovine milk proteins. *Crit. Rev. Food Sci. Nutr.* **2018**, *58*, 726-740, https://doi.org/10.1080/10408398.2016.1217825.

35. Ganz, T. Defensins: antimicrobial peptides of innate immunity. *Nat. Rev. Immunol.* **2003**, *3*, 710-720, https://doi.org/10.1038/nri1180.
36. Rai, M.; Pandit, R.; Gaikwad, S.; Kövics, G. Antimicrobial peptides as natural bio-preservative to enhance the shelf-life of food. *J. Food Sci. Technol.* **2016**, *53*, 3381-3394, https://doi.org/10.1007/s13197-016-2318-5.
37. Amalaradjou, M.A.R.; Hoagland, T.A.; Venkitanarayanan, K. Inactivation of Enterobacter sakazakii in reconstituted infant formula by trans-cinnamaldehyde. *Int. J. Food Microbiol.* **2009**, *129*, 146-149, https://doi.org/10.1016/j.ijfoodmicro.2008.11.016.
38. Shin, S.Y.; Bajpai, V.K.; Kim, H.R.; Kang, S.C. Antibacterial activity of bioconverted eicosapentaenoic (EPA) and docosahexaenoic acid (DHA) against foodborne pathogenic bacteria. *Int. J. Food Microbiol.* **2007**, *113*, 233-236, https://doi.org/10.1016/j.ijfoodmicro.2006.05.020.
39. Ouiddir, M.; Bettache, G.; Salas, M.L.; Pawtowski, A.; Donot, C.; Brahimi, S.; Mabrouk, K.; Coton, E.; Mounier, J. Selection of Algerian lactic acid bacteria for use as antifungal bioprotective cultures and application in dairy and bakery products. *Food Microbiol.* **2019**, *82*, 160-170, https://doi.org/10.1016/j.fm.2019.01.020.
40. O'Connor, P.M.; Kuniyoshi, T.M.; Oliveira, R.P.; Hill, C.; Ross, R.P.; Cotter, P.D. Antimicrobials for food and feed; a bacteriocin perspective. *Curr. Opin. Biotechnol.* **2020**, *61*, 160-167, https://doi.org/10.1016/j.copbio.2019.12.023,
41. Zielińska, D.; Kolożyn-Krajewska, D. Food-origin lactic acid bacteria may exhibit probiotic properties. *BioMed Res. Int.* **2018**, *2018*, https://doi.org/10.1155/2018/5063185.
42. Gharsallaoui, A.; Oulahal, N.; Joly, C.; Degraeve, P. Nisin as a food preservative: part 1: physicochemical properties, antimicrobial activity, and main uses. *Crit. Rev. Food Sci. Nutr.* **2016**, *56*, 1262-1274, https://doi.org/10.1080/10408398.2013.763765.
43. Mokoena, M.P. Lactic acid bacteria and their bacteriocins: classification, biosynthesis and applications against uropathogens: a mini-review. *Molecules* **2017**, *22*, https://doi.org/10.3390/molecules22081255.
44. Silva, C.C.; Silva, S.P.; Ribeiro, S.C. Application of bacteriocins and protective cultures in dairy food preservation. *Front. Microbiol.* **2018**, *9*, https://doi.org/10.3389/fmicb.2018.00594.
45. Pereira, B.C.; Isreb, A.; Forbes, R.T.; Dores, F.; Habashy, R.; Petit, J.-B.; Alhnan, M.A.; Oga, E.F. 'Temporary Plasticiser': A novel solution to fabricate 3D printed patient-centred cardiovascular 'Polypill'architectures. *Eur. J. Pharm. Biopharm.* **2019**, *135*, 94-103, https://doi.org/10.1016/j.ejpb.2018.12.009.
46. Soltani, S.; Hammami, R.; Cotter, P.D.; Rebuffat, S.; Said, L.B.; Gaudreau, H.; Bédard, F.; Biron, E.; Drider, D.; Fliss, I. Bacteriocins as a new generation of antimicrobials: Toxicity aspects and regulations. *FEMS Microbiol. Rev.* **2021**, *45*, https://doi.org/10.1093/femsre/fuaa039.
47. Szabo, E.; Cahill, M. Nisin and ALTATM 2341 inhibit the growth of Listeria monocytogenes on smoked salmon packaged under vacuum or 100% CO2. *Lett. Appl. Microbiol.* **1999**, *28*, 373-377, https://doi.org/10.1046/j.1365-2672.1999.00547.x.
48. Le Lay, C.; Dridi, L.; Bergeron, M.G.; Ouellette, M. Nisin is an effective inhibitor of Clostridium difficile vegetative cells and spore germination. *J. Med. Microbiol.* **2016**, *65*, 169-175, https://doi.org/10.1099/jmm.0.000202.
49. Harris, L.J.; Fleming, H.P.; Klaenhammer, T.R. Sensitivity and resistance of Listeria monocytogenes ATCC 19115, Scott A, and UAL500 to nisin. *J. Food Prot.* **1991**, *54*, 836-840, https://doi.org/10.4315/0362-028X-54.11.836.
50. Małaczewska, J.; Kaczorek-Łukowska, E. Nisin—A lantibiotic with immunomodulatory properties: A review. *Peptides* **2021**, *137*, https://doi.org/10.1016/j.peptides.2020.170479.
51. Férir, G.; Petrova, M.I.; Andrei, G.; Huskens, D.; Hoorelbeke, B.; Snoeck, R.; Vanderleyden, J.; Balzarini, J.; Bartoschek, S.; Brönstrup, M. The lantibiotic peptide labyrinthopeptin A1 demonstrates broad anti-HIV and anti-HSV activity with potential for microbicidal applications. *PloS One* **2013**, *8*, https://dx.plos.org/10.1371/journal.pone.0064010.
52. Mathur, H.; Fallico, V.; O'Connor, P.M.; Rea, M.C.; Cotter, P.D.; Hill, C.; Ross, R.P. Insights into the mode of action of the sactibiotic thuricin CD. *Front. Microbiol.* **2017**, *8*, https://doi.org/10.3389/fmicb.2017.00696.
53. Balay, D.R.; Dangeti, R.V.; Kaur, K.; McMullen, L.M. Purification of leucocin A for use on wieners to inhibit Listeria monocytogenes in the presence of spoilage organisms. *Int. J. Food Microbiol.* **2017**, *255*, 25-31, http://dx.doi.org/10.1016/j.ijfoodmicro.2017.05.016.
54. Trinetta, V.; Morleo, A.; Sessa, F.; Iametti, S.; Bonomi, F.; Ferranti, P. Purified sakacin A shows a dual mechanism of action against Listeria spp: proton motive force dissipation and cell wall breakdown. *FEMS Microbiol. Lett.* **2012**, *334*, 143-149, https://doi.org/10.1111/j.1574-6968.2012.02630.x.
55. Chen, H.; Tian, F.; Li, S.; Xie, Y.; Zhang, H.; Chen, W. Cloning and heterologous expression of a bacteriocin sakacin P from Lactobacillus sakei in Escherichia coli. *Appl. Microbiol. Biotechnol.* **2012**, *94*, 1061-1068, https://doi.org/10.1007/s00253-012-3872-z.
56. Hu, C.-B.; Malaphan, W.; Zendo, T.; Nakayama, J.; Sonomoto, K. Enterocin X, a novel two-peptide bacteriocin from Enterococcus faecium KU-B5, has an antibacterial spectrum entirely different from those of

its component peptides. *Appl. Environ. Microbiol.* **2010**, *76*, 4542-4545, https://doi.org/10.1128/AEM.02264-09.
57. Pandey, N.; Malik, R.; Kaushik, J.; Singroha, G. Gassericin A: a circular bacteriocin produced by lactic acid bacteria Lactobacillus gasseri. *World J. Microbiol. Biotechnol.* **2013**, *29*, 1977-1987, https://doi.org/10.1007/s11274-013-1368-3
58. Parada, J.L.; Caron, C.R.; Medeiros, A.B.P.; Soccol, C.R. Bacteriocins from lactic acid bacteria: purification, properties and use as biopreservatives. *Braz. Arch. Biol. Technol.* **2007**, *50*, 512-542.
59. Özel, B.; Şimşek, Ö.; Akçelik, M.; Saris, P.E. Innovative approaches to nisin production. *Appl. Microbiol. Biotechnol.* **2018**, *102*, 6299-6307, https://doi.org/10.1007/s00253-018-9098-y.
60. Kirtonia, K.; Salauddin, M.; Bharadwaj, K.K.; Pati, S.; Dey, A.; Shariati, M.A.; Tilak, V.K.; Kuznetsova, E.; Sarkar, T. Bacteriocin: A new strategic antibiofilm agent in food industries. *Biocatal. Agric. Biotechnol.* **2021**, *36*, https://doi.org/10.1016/j.bcab.2021.102141.
61. Khelissa, S.; Chihib, N.-E.; Gharsallaoui, A. Conditions of nisin production by Lactococcus lactis subsp. lactis and its main uses as a food preservative. *Arch. Microbiol.* **2021**, *203*, 465-480, https://doi.org/10.1007/s00203-020-02054-z.
62. Amiri, S.; Moghanjougi, Z.M.; Bari, M.R.; Khaneghah, A.M. Natural protective agents and their applications as bio-preservatives in the food industry: An overview of current and future applications. *Ital. J. Food Sci.* **2021**, *33*, 55-68, https://doi.org/10.15586/ijfs.v33iSP1.2045.
63. de Freitas, L.L.; Dos Santos, C.I.A.; Carneiro, D.G.; Vanetti, M.C.D. Nisin and acid resistance in Salmonella is enhanced by N-dodecanoyl-homoserine lactone. *Microb. Pathog.* **2020**, *147*, https://doi.org/10.1016/j.micpath.2020.104320.
64. Ko, K.Y.; Park, S.R.; Lee, C.A.; Kim, M. Analysis method for determination of nisin A and nisin Z in cow milk by using liquid chromatography-tandem mass spectrometry. *J. Dairy Sci.* **2015**, *98*, 1435-1442, http://dx.doi.org/10.3168/jds.2014-8452.
65. Balandin, S.; Sheremeteva, E.; Ovchinnikova, T. Pediocin-like antimicrobial peptides of bacteria. *Biochem.(Mosc.)* **2019**, *84*, 464-478, https://doi.org/10.1134/S000629791905002X.
66. Rodríguez, J.M.; Martínez, M.I.; Kok, J. Pediocin PA-1, a wide-spectrum bacteriocin from lactic acid bacteria. *Crit. Rev. Food Sci. Nutr.* **2002**, *42*, 91-121, https://doi.org/10.1080/10408690290825475.
67. Porto, M.C.W.; Kuniyoshi, T.M.; Azevedo, P.; Vitolo, M.; Oliveira, R.S. Pediococcus spp.: An important genus of lactic acid bacteria and pediocin producers. *Biotechnol. Adv.* **2017**, *35*, 361-374, http://dx.doi.org/10.1016/j.biotechadv.2017.03.004.
68. Ríos Colombo, N.S.; Chalón, M.C.; Navarro, S.A.; Bellomio, A. Pediocin-like bacteriocins: new perspectives on mechanism of action and immunity. *Curr. Genet.* **2018**, *64*, 345-351, https://doi.org/10.1007/s00294-017-0757-9.
69. Bali, V.; Panesar, P.S.; Bera, M.B.; Kennedy, J.F. Bacteriocins: recent trends and potential applications. *Crit. Rev. Food Sci. Nutr.* **2016**, *56*, 817-834, https://doi.org/10.1080/10408398.2012.729231.
70. Yu, H.H.; Chin, Y.-W.; Paik, H.-D. Application of Natural Preservatives for Meat and Meat Products against Foodborne Pathogens and Spoilage Bacteria: A Review. *Foods* **2021**, *10*, https://doi.org/10.3390/foods10102418.
71. Hugas, M.; Garriga, M.; Aymerich, M. Functionalty of enterococci in meat products. *Int. J. Food Microbiol.* **2003**, *88*, 223-233, https://doi.org/10.1016/s0168-1605(03)00184-3.
72. Najdenski, H.M.; Gigova, L.G.; Iliev, I.I.; Pilarski, P.S.; Lukavský, J.; Tsvetkova, I.V.; Ninova, M.S.; Kussovski, V.K. Antibacterial and antifungal activities of selected microalgae and cyanobacteria. *Int. J. Food Sci. Technol.* **2013**, *48*, 1533-1540, https://doi.org/10.1111/ijfs.12122.
73. Danyal, A.; Mubeen, U.; Malik, K.A. Investigating two native algal species to determine antibiotic susceptibility against some pathogens. *Curr. Res. J. Biol. Sci.* **2013**, *5*, 70-74, https://doi.org/10.19026/crjbs.5.5476.
74. Manivannan, K.; Anantharaman, P.; Balasubramanian, T. Antimicrobial potential of selected brown seaweeds from Vedalai coastal waters, Gulf of Mannar. *Asian Pac. J. Trop. Biomed.* **2011**, *1*, 114-120, https://doi.org/10.1016/S2221-1691(11)60007-5.
75. Abd El-Baky, H.H.; El Baz, F.K.; El-Baroty, G.S. Characterization of nutraceutical compounds in blue green alga Spirulina maxima. *J. Med. Plants Res.* **2008**, *2*, 292-300.
76. Senthilkumar, P.; Sudha, S. Antioxidant and antibacterial properties of methanolic extract of green seaweed Chaetomorpha linum from Gulf of Mannar: Southeast coast of India. *Jundishapur J. Microbiol.* **2012**, *5*, 411-415, https://doi.org/10.5812/jjm.3400.
77. Lee, S.-Y.; Lim, S.-I.; Ahn, D.-H. Antibacterial mechanism of Myagropsis myagroides extract on Listeria monocytogenes. *Food Control* **2014**, *42*, 23-28, http://dx.doi.org/10.1016/j.foodcont.2014.01.030.
78. Rodrigo, D.; Palop, A. Applications of Natural Antimicrobials in Food Packaging and Preservation. *Foods* **2021**, *10*, https://doi.org/10.3390/foods10030568.
79. Swapnil, S.; Bruno, B.; Udhaya, R.; Krishna, K.; Sandhya, S.; Waman, P. Bioactive compounds derived from microalgae showing antimicrobial activities. *J. Aquac. Res. Dev.* **2014**, *5*, 3-6, https://doi.org/10.4172/2155-9546.1000224.

80. Rahelivao, M.P.; Gruner, M.; Andriamanantoanina, H.; Bauer, I.; Knölker, H.-J. Brown algae (Phaeophyceae) from the coast of Madagascar: Preliminary bioactivity studies and isolation of natural products. *Nat. Prod. Bioprospect.* **2015**, *5*, 223-235, https://doi.org/10.1007/s13659-015-0068-0.
81. Vijayavel, K.; Martinez, J.A. In vitro antioxidant and antimicrobial activities of two Hawaiian marine Limu: Ulva fasciata (Chlorophyta) and Gracilaria salicornia (Rhodophyta). *J. Med. Food* **2010**, *13*, 1494-1499, https://doi.org/10.1089/jmf.2009.0287.
82. Chan, Y.S.; Ong, C.W.; Chuah, B.L.; Khoo, K.S.; Chye, F.Y.; Sit, N.W. Antimicrobial, antiviral and cytotoxic activities of selected marine organisms collected from the coastal areas of Malaysia. *J. Mar. Sci. Technol.* **2018**, *26*, https://doi.org/10.6119/JMST.2018.02_(1).0012.
83. Plaza, M.; Santoyo, S.; Jaime, L.; Reina, G.G.-B.; Herrero, M.; Señoráns, F.J.; Ibáñez, E. Screening for bioactive compounds from algae. *J.Pharm. Biomed. Anal.* **2010**, *51*, 450-455, https://doi.org/10.1016/j.jpba.2009.03.016.
84. Devi, K.P.; Suganthy, N.; Kesika, P.; Pandian, S.K. Bioprotective properties of seaweeds: in vitro evaluation of antioxidant activity and antimicrobial activity against food borne bacteria in relation to polyphenolic content. *BMC Complement. Altern. Med.* **2008**, *8*, 1-11, https://doi.org/10.1186/1472-6882-8-38.
85. Gupta, S.; Rajauria, G.; Abu-Ghannam, N. Study of the microbial diversity and antimicrobial properties of Irish edible brown seaweeds. *Int. J. Food Sci. Technol.* **2010**, *45*, 482-489, https://doi.org/10.1111/j.1365-2621.2009.02149.x.
86. Dussault, D.; Vu, K.D.; Vansach, T.; Horgen, F.D.; Lacroix, M. Antimicrobial effects of marine algal extracts and cyanobacterial pure compounds against five foodborne pathogens. *Food Chem.* **2016**, *199*, 114-118, http://dx.doi.org/10.1016/j.foodchem.2015.11.119.
87. Prakash, J.W.; Marimuthu, J.; Jeeva, S. Antimicrobial activity of certain fresh water microalgae from Thamirabarani River, Tamil Nadu, South India. *Asian Pac. J. Trop. Biomed.* **2011**, *1*, S170-S173, http://dx.doi.org/10.1016/S2221-1691(11)60149-4.
88. Öztürk, M.; Duru, M.E.; Kivrak, Ş.; Mercan-Doğan, N.; Türkoglu, A.; Özler, M.A. In vitro antioxidant, anticholinesterase and antimicrobial activity studies on three Agaricus species with fatty acid compositions and iron contents: A comparative study on the three most edible mushrooms. *Food Chem. Toxicol.* **2011**, *49*, 1353-1360, https://doi.org/10.1016/j.fct.2011.03.019.
89. Kalyoncu, F.; Oskay, M.; Sağlam, H.; Erdoğan, T.F.; Tamer, A.Ü. Antimicrobial and antioxidant activities of mycelia of 10 wild mushroom species. *J. Med. Food* **2010**, *13*, 415-419, https://doi.org/10.1089/jmf.2009.0090.
90. Karaman, M.; Stahl, M.; Vulić, J.; Vesić, M.; Čanadanović-Brunet, J. Wild-growing lignicolous mushroom species as sources of novel agents with antioxidative and antibacterial potentials. *Int. J. Food Sci. Nutr.* **2014**, *65*, 311-319, https://doi.org/10.3109/09637486.2013.860584.
91. Lopes, N.A.; Brandelli, A. Nanostructures for delivery of natural antimicrobials in food. *Crit. Rev. Food Sci. Nutr.* **2018**, *58*, 2202-2212, https://doi.org/10.1080/10408398.2017.1308915.
92. Rai, M.; Ingle, A.P.; Paralikar, P. Sulfur and sulfur nanoparticles as potential antimicrobials: from traditional medicine to nanomedicine. *Expert Rev. Anti-Infect. Ther.* **2016**, *14*, 969-978, https://doi.org/10.1080/14787210.2016.1221340.
93. Yazgan, H.; Ozogul, Y.; Kuley, E. Antimicrobial influence of nanoemulsified lemon essential oil and pure lemon essential oil on foodborne pathogens and fish spoilage bacteria. *Int. J. Food Microbiol.* **2019**, *306*, https://doi.org/10.1016/j.ijfoodmicro.2019.108266.
94. Jamali, S.N.; Assadpour, E.; Feng, J.; Jafari, S.M. Natural antimicrobial-loaded nanoemulsions for the control of food spoilage/pathogenic microorganisms. *Adv. Colloid Interface Sci.* **2021**, *295*, https://doi.org/10.1016/j.cis.2021.102504.
95. Cao, Y.; Gu, W.; Zhang, J.; Chu, Y.; Ye, X.; Hu, Y.; Chen, J. Effects of chitosan, aqueous extract of ginger, onion and garlic on quality and shelf life of stewed-pork during refrigerated storage. *Food Chem.* **2013**, *141*, 1655-1660, http://dx.doi.org/10.1016/j.foodchem.2013.04.084.
96. Makabenta, J.M.V.; Nabawy, A.; Li, C.-H.; Schmidt-Malan, S.; Patel, R.; Rotello, V.M. Nanomaterial-based therapeutics for antibiotic-resistant bacterial infections. *Nat. Rev. Microbiol.* **2021**, *19*, 23-36, http://dx.doi.org/10.1038/s41579-020-0420-1.
97. Sridhar, A.; Ponnuchamy, M.; Kumar, P.S.; Kapoor, A. Food preservation techniques and nanotechnology for increased shelf life of fruits, vegetables, beverages and spices: a review. *Environ. Chem. Lett.* **2021**, *19*, 1715-1735, https://doi.org/10.1007/s10311-020-01126-2.
98. Pinilla, C.M.B.; Lopes, N.A.; Brandelli, A. Lipid-Based Nanostructures for the Delivery of Natural Antimicrobials. *Molecules* **2021**, *26*, https://doi.org/10.3390/molecules26123587.
99. Coelho, S.C.; Estevinho, B.N.; Rocha, F. Encapsulation in food industry with emerging electrohydrodynamic techniques: Electrospinning and electrospraying–A review. *Food Chem.* **2021**, *339*, https://doi.org/10.1016/j.foodchem.2020.127850.