A Thorough Review of Antimicrobial Agents Used in Food

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Abstract: Antibiotics are agents that have the ability to breakdown microorganisms or restrict their proliferation. These compounds are found in many chemical compositions, including intermediate-metabolite chemicals, chemotherapeutic and antibiotic compounds, non-antibiotic agents, antiseptics, preservatives, and disinfectants. Some of these compounds are naturally produced by bacteria, fungus, and plants. Furthermore, immunological products have been studied as agents with the ability to attack germs. Although there are thousands of antibiotics available, less than 1% of them are actually used in clinical settings to treat infectious. This is because certain antibiotics are unable to penetrate host cells or were toxic to the host. Recently, a wide range of antimicrobial ingredients and chemical additives have been employed in food preparation for both humans and animals, with the purpose of preserving the food. Certainly, using of chemical agents in food can have both pros and cons when utilized in small amounts. The problem of antibiotic resistance is a significant barrier in the food industry. In the development countries, breeders use antibiotics as substances that promote growth. As a result, antibiotics can easily be passed on to humans through the food chain, causing the emergence of antibiotic resistance in many microorganisms. This review emphasized the attributes and applications of substances that are created by fermentation, or other natural techniques utilized in the large-scale production of food.

Keywords: Antimicrobial, Chemical substances, Lysozyme, Preservatives and Lactoferrin.

1. Introduction

Since 1928, animals have been administered antimicrobials for a range of purposes, including disease treatment, disease control, and growth promotion through their diet. Antimicrobial growth promoters (AGPs) were first suggested in the mid-1950s due to the discovery that children were receiving small amounts of antibiotics, like procaine, penicillin, and tetracycline, at doses much lower than the recommended therapeutic dose (approximately 1/10 to 1/100 of the therapeutic dose). It has the capacity to improve the ratio of feed to weight in poultry, swine, and beef cattle [1]. The positive and negative effects of antibiotics have been thoroughly researched and observed over time, prompting microbiologists and infectious disease specialists to address the problem of antibiotic resistance [2, 3]. Finally, it will analyze the use of antimicrobials in food for both humans and animals in order to fill any current gaps in knowledge and provide definitive responses to any hanging questions.

1.1.Antimicrobials of Animal Origin

The animal's immune system contains various naturally occurring antimicrobial compounds, which are also found in animal food. Examples of these chemicals include Lysozyme and Lactoperoxidase. Numerous naturally occurring inhibitory molecules can be found in foods and food items, alongside artificial chemicals introduced by humans. These chemical compounds are classified as preventive or antibacterial inhibitors [4, 5].

1.1.1. Lysozyme

It affects the bacteria cell wall by catalyzing the hydrolysis of peptidoglycan layer. This enzyme is frequently found in food samples. Also it detected in milk and certain plant tissues in trace levels, while it is present in chicken eggs and is frequently found in human fluids including saliva and tears [6]. Gram-positive bacteria are more susceptible to lysozyme than Gram-negative bacteria due to the high abundance of peptidoglycan [7]. Lysozyme obtained from chicken eggs was tested against *Clostridium tyrobutyricum*, and represented as a natural inhibitor [8]. It is commonly employed as a potent preservative in alcoholic beverages, such as wine [9]. Recently, it has been used to inhibit the growth of *Listeria monocytogenes* in fish, and has also been utilized to inhibit undesirable lactic acid bacteria [4, 5].

1.1.2. Lactoperoxidase

It is a naturally occurring enzyme with a glycoprotein structure that is present in breast milk, raw milk, and tears. Milk contains naturally occurring oxidizing chemicals, including H_2O_2, and hypothiocyanate, which have antibacterial properties when combined with lactoperoxidase. Thus, lactoperoxidase is recognized for its ability to kill many harmful bacteria (such as *Escherichia coli* O157:H7, *Yersinia enterocolitica*, *Salmonella*, and *Listeria monocytogenes*) commonly present in milk and dairy products (including beef, fruit juices, and egg liquid) [4, 5].

1.1.3. Chitosan

It is approved by FAD at low levels in foods because it does not harm mammalian cells and has very low toxicity. It also has a broad spectrum effect against pathogenic bacteria, yeast and molds, and has even been widely used recently. It has obtained from arthropods and mollusca and is suitable for health for humans and animals [4, 5, 10]. Chitosan can be used to improve the quality and shelf life of foods. For example, after adding chitosan to freshly made noodles, the shelf life was increased by six days at 4℃ [11]. Moreover, it is responsible for preventing the proliferation of pathogenic *Escherichia coli* and *Listeria monocytogenes* strains on meat surfaces, and protects eggs from the development of *Escherichia coli* and *Salmonella* [12].

1.1.4. **Lactoferrin**

It is an endogenous glycoprotein that binds to iron and known a hemopexin. It is found in human and animal tissues, fluids, and milk. Due to it has high affinity to the Gram negative cell membrane and iron, can effectively inhibit bacterial reproductive by block iron metabolism, as it is not adequately absorbed by the bacterium. It disrupts the structural integrity of gram-negative bacteria by specifically attaching to the outer membrane. In the USA, beef and other meat products have seen widespread usage recently [13,14]. It exhibits antiviral and antibacterial properties. In addition, lactoferrin has a significant role in controlling the growth of human intestinal cells. Furthermore, its ability to regulate the immune system has been well-documented, which is why it has received approval from USDA-FSIS [5].

1.1.5. Pleurocidin

Pleurocidin is an antimicrobial polypeptide, present in the tissues of both vertebrate and invertebrate organisms. It exhibits a broad spectrum effect on bacteria, and also possesses antibacterial characteristics against pathogenic bacteria commonly found in food, such as *Listeria monocytogenes* and *Escherichia coli* O157:H7, as well as dangerous fungus [15]. In 1997, Cole and his colleagues discovered and extracted a polypeptide from the skin mucus discharge of fish [16].

1.1.6. Ovotransferrin

Ovotransferrin, also known as conalbumin, is a glycoprotein that binds to iron and is naturally present in the albumen of chicken eggs. Due to its great affinity for iron, it inhibits the utilization of iron by bacteria, leading to their eventual destruction. Egg albumin might induce allergies in certain individuals, therefore its use as a preservative in certain foods is restricted [4, 5, 17]. Ibrahim's 1997 research demonstrated bactericidal effects against *Escherichia coli* and *Staphylococcus aureus* [18]. It exhibits antibacterial properties against bacteria that cause food-borne illnesses and microorganisms that lead to food deterioration [7].

1.1.7. Protamine

Protamine is a positively charged peptide derived from salmon fish. It exhibits a wide-ranging antibacterial activity against both gram-positive and gram-negative bacteria. Due to its strong negative electrostatic charge, it exhibits diverse actions against spoilage bacteria (*Brochothrix thermosphacta*) and non-protolytic *Clostridium botulinum* [19, 20]. In their 2000 research, Hansen and Gill discovered that they were able to enhance the antibacterial activity of protamine in an alkaline environment. This caused an increase in the electrostatic attraction between protamine and the cell surface of *Escherichia coli* [21].

1.2. Antimicrobial substances of microbial origin

While the tissues of healthy animals, vegetables, and fruits may initially be free from microorganisms, they can become contaminated during food preparation. This contamination can occur through various means such as water, equipment, and tools used from harvest to consumption. As a result, these tissues can harbor hundreds of molds, yeasts, viruses, and bacteria [22]. Several microorganisms included in food generate intermediate metabolites that exhibit antibacterial properties. These metabolites can generate diverse by-products that stimulate the growth of microbes in food and improve the utilization of nutrients. However, these substances can have detrimental impacts on other microbes present in food. Gram-positive bacteria can harm gram-negative bacteria by producing bacteriocins. On the other hand, *Streptococcus thermophilus*, a bacteria commonly found in dairy products, releases proteinase enzymes into its environment to facilitate its normal functions and break down proteins [23].

1.2.1. Polylysine

Polylysine is a polypeptide composed of 25 to 35 L-Lysine residues [24, 25] and possesses inherent antibacterial properties. In Japan, an antibiotic derived from *Streptomyces albulus* was utilized in the naturally aerobinary fermentative process for food preservation [26]. This substance exhibits efficacy against both fungi and bacteria, making it a commonly employed preservative for inhibiting the proliferation of *Salmonella typhimurium*, *Escherichia coli* O157:H7, and *Listeria monocytogenes* in food products. Furthermore, it is generally accepted in Japan as a food preservative due to its ability to withstand temperatures of 100℃-120℃, its compatibility with a wide range of pH levels, and its high solubility in water [27]. Recently, the Food and Drug Administration has granted approval for the use of this substance in cooked or sushi rice in the United States, recognizing it as generally safe (GRAS) [28].

1.2.2. Tylosin

Belonging to the class of macrolide antibiotics, it produces from *Streptomyces* and has bactericidal properties. Tylosin, a macrolide antibiotic, is administered to pigs for therapeutic purposes. Tylosin phosphate or tylosin injections have been administered in two different manners. The European Union has prohibited its use as a growth booster, while it is effective in treating bacterial illnesses such as swine arthritis, ileitis, erysipelas, and most notably, pig dysentery [29]. Prior to 1999, tylosin was utilized in medicated feeds in the United States with the aim of enhancing feed efficiency and promoting weight growth in pigs [30]. It exhibits greater efficacy against gram-positive bacteria compared to gram-negative bacteria. Additionally, it inhibits spore germination, making it suitable for use at low doses in acidic canned products. Tylosin exerts a potent inhibitory effect on bacterial protein synthesis [31].

1.2.3. Reuterin

It is a compound with low-molecular-weight which has antibacterial properties. It is produced by some strains of *Lactobacillus* that are present in the intestinal tract of both humans and animals. It has antimicrobial activity by blocking crucial enzymes against a wide range of gram-positive and gram-negative bacteria. The application of reuterin for food preservation is restricted due to the necessity of glycerol in the environment for its formation. It inhibits the proliferation of *Staphylococcus*, *Listeria*, *Aeromonas*, *Salmonella*, *Yersinia*, and *Campylobacter*. It exhibits resistance to certain lipolytic and proteolytic enzymes commonly present in food [32].

1.2.4. Natamycin

Natamycin, a fungicidal compound derived from *Streptomyces natalensis*, has undergone extensive research in the field of food science. However, in comparison to bacteriocin, Natamycin has a low solubility in water. Nevertheless, Natamycin dry powder can maintain stability for an extended period without experiencing a major decrease in activity [33]. Natamycin, due to its several qualities, it has widely applied as an effective antifungal broad-spectrum bio preservative in various beverages and foods. Also it is safe for human consumption and has a potent effect even at low concentrations. It does not compromise the quality of food and its antimicrobial properties persist on the surface of the food for an extended period, particularly in cheese and sausage [34]. Due to its great affinity for ergosterol, a component present in the cell wall of fungus, it induces cell damage by causing excessive permeability [35]. Hondrodimou's research has shown that natamycin effectively prevents the growth of yeasts and fungi in black olives during the process of spontaneous fermentation [36].

1.2.5. Avoparcin Used in Livestock

In the European nations, the utilization of avoparcin as a substance to improve fertility and as an ingredient in feed for livestock has led to the frequent identification of vancomycin-resistant enterococci (VRE) in domestic animals and healthy individuals [37, 38]. Enterococci, which are known as a significant multidrug-resistant (MDR) pathogen, have led to the adoption of vancomycin as a crucial treatment option, typically reserved for cases when other drugs have failed. In the European nations, the utilization of avoparcin as a substance to improve fertility and as an ingredient in feed for livestock has led to the frequent identification of vancomycin-resistant enterococci (VRE) in domestic animals and healthy individuals [37, 38]. Enterococci, which are known as a significant multidrug-resistant (MDR) pathogen, have led to the adoption of vancomycin as a crucial treatment option, typically reserved for cases when other drugs have failed. After the avoparcin has been banned in 1995, various reports published and provided that the distribution of VRE in animal was decreased. While, the study was carried out in 1996/ Germany found that the effect of avoparcin was % 25 at high doses, both before and after it was forbidden [38]; in Denmark, the Poultry incidence from 73% to 80% and then declined to 5% to 6% after forbidden [39]. Also, the widespread of VRE in chicken body and bowel in Italy decline from 14.6% to 8% all over one year and half [40]. Moreover, other study carried out in Hungry explained the incidence of VRE was decreased among animals (which are including: cattle, pigs, and poultry, after the prevention of avoparcin, also the minimum inhibitory concentrations (MICs) of vancomycin was decreased in the same study [41].

1.2.6. Fluoroquinolones Used in Poultry

Fluoroquinolones, particularly the synthetic Enrofloxacin (ENR), are extensively applied in chicken farming as antibacterial agents for the treatment of bacterial sickness [42]. Fluoroquinolones are a class of antimicrobial drugs that are significant for both human and animal health. However, they have been extensively employed in veterinary medicine for the treatment of animals [43, 44]. ENR is commonly employed in the treatment of veterinary diseases and poultry infectious diseases due to its extensive range of activity. Furthermore, it exhibits potent activity against both gram-negative and gram-positive bacteria, with a particular emphasis on its efficacy against *Mycoplasma* in the intestinal tract of chickens [45, 43]. Due to its quick absorption through the mouth and extended duration of action, it has been utilized for treating mycoplasmal diseases including colibacillosis and pasteurellosis [46, 47]. Currently, the existence of antibiotic pollutants in animal-derived products is a significant concern in terms of ensuring food safety [48].

1.3.Antimicrobial agents produced by plants

Several classes of antimicrobial drugs, including macrolides, tetracyclines, lincomycins, and penicillins, have been approved for use in stimulating animal growth. However, the use of antimicrobial compounds in food has a negative impact on the treatment of human diseases [49]. To handle this problem, it is necessary to employ several natural substances, such as Allium, Artemisia, Clematis, Echium, and Euphorbia [50]. Local farmers have seen the use of various plant extracts, including *Dichrostachys cinerea* L., *Salvadora persica* L., and *Colophospermum mopane*, for animal therapy. Animals are administered these extracts by using herbal solutions or crude extracts [51]. Plants provide a wide range of natural substances that can kill bacteria. These substances might come from whole plants or specific parts of plants [20]. The growth of *Bacillus subtilis*, *Staphylococcus aureus, Klebsiella pneumoniae, Proteus mirabilis*, *Escherichia coli, Salmonella paratyphi* A, and *Salmonella paratyphi* B was inhibited by using of plant extracts from Aegle marmelos leaves [52]. The proliferation of *Bacillus cereus, Bacillus subtilis, Staphylococcus aureus*, and *Enterococcus faecalis* was inhibited by employing plant extracts from *Medicago arabica* roots, which are belonging to the Fabaceae family [53]. The leaf extracts of *Aloe barbadensis*, *Malus sylvestris*, and *Ocimum basilicum*, were tested against *Escherichia coli, Enterococcus fecalis*, and *Staphylococcus aureus* [54], *Enterococcus fecalis, Staphylococcus aureus* [55], and *Pseudomonas aeruginosa*, *Shigella* sp., *Listeria monocytogenes*, *Staphylococcus aureus*, and *Escherichia coli* [56], the results found that all mentioned above plants have antibacterial impacts. Furthermore, previous investigations tested the plant extracts of *Euphorbia tirucalli* (plant body) against *Bacillus subtilis*, *Escherichia coli, Proteus vulgaris,* and *Staphylococcus aureus* [57]. Also, the growth and proliferation of, *Pseudomonas fluorescens,* and *Bacillus megaterium* were stopped by employing *Pimenta dioica* leaves [58]. Other prior report revealed that the growth of *Bacillus subtilus, Enterococcus faecalis, Staphylococcus xylosus, Staphylococcus aureus, Staphylococcus epidermidis*, *Escherichia coli, Klebsiella pneumoniae,* and *Salmonella enteric* was prevented by using Piper nigrum [59]. Many other previous studies were done by using plant extracts as alternative antibiotic materials, for instance applying *Berberis vulgaris* against *Escherichia coli* [60], and *Momordica charantia* against *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus, Klebsiella pneumoniae*, and *Salmonella typhi* [61].

1.4. Chemical agents used in foods

Chemical agents are essential in the food industry as they serve important functions such as preservation, enhancing flavor, and modifying texture. Potassium sorbate and Sodium bezoate have been extensively applied in food sector as a preservaties. Both chemical materials have biological activity against microbes, and play crucial role in prolonging the shelf life of the food. Also, other chemical agents with antioxidant activity such as tocopherol (vitamin E) and ascorbic acid (vitamin C) were used as antioxidant agents in food production. Carrageenan and lecithin are used as emulsifiers in food production, which give the texture and consitency to food. Additionally, acids use in food production such as citric acid and tartaric acid that enhance the acidity of food environment and regulate the pH value. The using of these chemical agents has completely subjected to examine and monitor despite of they have demonstrated safe depending on the regulatory authorities. [62, 63].

1.4.1. EDTA (Ethylene diamine tetraacetic acid)

Ethylenediaminetetraacetic acid (EDTA) is a frequently employed chelating chemical in the food industry with the purpose of preserving metal ions and preventing enzymatic browning processes. EDTA inhibits the decomposition of food products by forming complexes with metal ions such calcium, magnesium, and iron, which act as catalysts for oxidation and enzymatic degradation reactions. EDTA preserves the color, flavor, and texture of foods, particularly in processed items such as canned fruits and vegetables, salad dressings, and beverages, by forming complexes with metal ions. Although EDTA is GRAS when used in compliance with good manufacturing standards, its utilization is dependent upon regulatory approval and stringent restrictions to guarantee consumer safety [64].

1.4.2.CO_2

Carbon dioxide (CO_2) is broadly used as a chemical factor in the food manufacture, generally for carbonation function and as a protective. Carbonation is the process of liquefaction CO_2 into liquids such as soda, beer, and sparkling water under pressure. This creates sparkle and improves sensory features such as taste and quality. Furthermore, CO_2 is used as a protective in modified atmosphere packaging (MAP) to extend the shelf life of spoilable foods by preventing the development of microbes and chemical reaction. The presence of CO_2 creates contained situation that conserve the quality and freshness of food while eliminating decomposition and decay. What is more, CO_2 is considered to be acceptable for employment in food-related function and is subject to regulation by food safety authorities in order to guarantee the well-being and safety of consumers [65, 66].

1.4.3. Parabens

Parabens are a group of chemical materials, which are extensivly applied as preservatives in food sector, cosmetic sector, and pharmaceutical sector in order to stop the growth of microbes. For instance methylparaben, ethylparaben, propylparaben, and butylparaben are considered important material and used to prevent the food deterioration by microbiological activity and to prolong the shelf life of nutrients such baked goods, dairy products, sauces, and dressings as well. Parabens function by interfering with the metabolic processes of bacteria, therefore inhibiting their growth in food matrices. Although regulatory agencies like the U.S. FDA and the European Food Safety Authority (EFSA) have declared parabens safe for use in foods, there are concerns about their potential estrogenic activity and endocrine-disrupting effects. This has led to ongoing research and monitoring [67, 68].

1.4.4. Organic acids

Organic acids, such as acetic acid, citric acid, lactic acid, and sorbic acid, are frequently employed as chemical agents in food products because of their antibacterial and preservation characteristics. These acids are essential for preserving food by preventing the growth of bacteria, yeast, and mold, hence prolonging the shelf life of certain food items. Acetic acid is commonly utilized in pickling and vinegar production to establish an acidic environment that inhibits deterioration. Citric acid is employed as a taste enhancer and preservative in beverages, jams, and canned fruits, whereas lactic acid is utilized in dairy products and fermented foods such as yogurt and sauerkraut. Sorbic acid, an organic acid, is frequently used as a food additive to inhibit the growth of mold, especially in bakery products and cheese. Food safety authorities control the use of organic acids in foods to guarantee consumer safety and compliance with approved limits [69, 70].

1.4.5. Diacetyl

Diacetyl, scientifically referred to as 2,3-butanedione, is a chemical molecule that is frequently employed in the food industry to give a buttery taste to many food items. It is commonly employed in butter-flavored microwave popcorn, bakery items, margarine, and snack foods to augment flavor and fragrance. Diacetyl is generated by fermentation processes, such as those used in the manufacturing of beer and wine, and can also be chemically manufactured for use in food applications. Although diacetyl is considered safe for use in food at low concentrations, there are concerns about its potential health effects, specifically its link to respiratory diseases like bronchiolitis obliterans, also known as "popcorn lung" among workers in microwave popcorn plants and flavoring production facilities [71, 72].

1.4.6. Epoxides (Propylene Oxide and Ethylene Oxide)

Propylene oxide and ethylene oxide are frequently employed as chemical agents in the food industry to fumigate and sanitize food products and surfaces that come into contact with food. Propylene oxide, a highly reactive molecule, is commonly used to sterilize spices, nuts, and dried fruits in order to eradicate germs and insects while preserving the quality of the products. Ethylene oxide is also used to sterilize heat-sensitive food items like herbs, spices, and cocoa powder. It is also used to sterilize food processing equipment and packaging materials. Both propylene oxide and ethylene oxide exhibit broad-spectrum antimicrobial activity, effectively targeting a diverse array of microorganisms such as bacteria, viruses, and molds. Nevertheless, the utilization of these substances in food processing is subject to stringent regulations, requiring the reduction of residues to a minimum level in order to adhere to safety requirements and safeguard the well-being of consumers [73, 74].

1.4.7. Nitrate and nitrites

Nitrate and nitrites are frequently employed in the food business as preservatives and color stabilizers, especially in processed meats like bacon, ham, hot dogs, and deli meats. These molecules have the ability to prevent the growth of hazardous bacteria like *Clostridium botulinum*, which is responsible for causing foodborne illness. Additionally, they also play a role in giving cured meats their distinct pink color and flavor. Nitrate undergoes conversion into nitrite through the activity of bacterial enzymes or chemical reactions that occur during the process of meat curing. Nitrites, in response, chemically interact with proteins found in meat to create a stable compound called nitrosylmyoglobin, which gives the meat its desired pink color. Although nitrate and nitrites are efficient preservatives, their utilization has sparked concerns due to the possible generation of nitrosamines, which are cancer-causing chemicals, under specific circumstances. Nevertheless, the inclusion of ascorbic acid (vitamin C) or erythorbic acid in cured meats can impede the creation of nitrosamines. The U.S. FDA and the EFSA carefully oversee the utilization of nitrate and nitrites in food products to guarantee adherence to safety regulations and safeguard the well-being of consumers [75, 76].

1.4.8. Sulfur dioxide (SO_2) and sulfites (SO_3)

Sulfur dioxide (SO_2) and sulfites (SO_3) are chemical compounds frequently employed in the food industry due to their antioxidant and antibacterial characteristics. Preservatives are used in a variety of food and beverage goods, such as dried fruits, wine, and processed meats. Sulfur dioxide and sulfites function as antimicrobial agents, effectively suppressing the growth of bacteria, yeasts, and molds, hence preventing oxidative browning and microbial spoilage. SO2 is used in dried fruits to preserve their color and inhibit the growth of microbes during storage and transit. Sulfites are used in winemaking to prevent the growth of undesirable microorganisms, oxidation, and enzymatic browning in grapes and wine. Although sulfur dioxide and sulfites are usually

GRAS when used within legal limits, they can provide health hazards, especially for persons with sulfite sensitivity or asthma. Regulatory agencies, such as the U.S. FDA and the EFSA, actively supervise the utilization of sulfur dioxide and sulfites in food products to guarantee the safety of consumers [77, 78].

1.4.9. Glycerol monolaurate (GML)

GML has attracted considerable interest in the food sector because of its powerful antibacterial capabilities and its capacity to prolong the shelf life of many food products. GML define as a monoester that consists of glycerol and lauric acid, has a various of antibacterial characteristics. GML can affect many types of bacteria such as *Listeria monocytogenes* and *S. aureus*, also it has antifungal and antiviruse properties. The mode of action of GML includes the disruption of cell membranes in microbes and the block the activity of enzyme that considered important for their survival. GML is demonstrated safe by regulatory bodies including the U.S. FDA, so that enhances its attractiveness as an option for food preservation. It has been applied in meat, dairy products, fish, and bakery products as antimicrobial agents in order to control the proliferation of microorganisms. However, additional studies are essential to test the extended consequences and ideal levels in various meal compositions [79, 80, 81].

1.4.10. H_2O_2

H_2O_2 is defined as a chemical agent that has extensively applied in food production since it has powerful antibacterial activity and its ability to decompose into water and oxygen without leaving behind any toxic material. It plays as a strong oxidizing factor, especially against various kinds of microbes for example yeast, molds, and bacteria. The antibacterial effectiveness of this substance is due to its ability to produce reactive oxygen species, which cause damage to the cell membranes and components of microorganisms, resulting in their deactivation. H_2O_2 has been applied in food production for many purposes, for example as disinfecting surfaces in food synthesis, sanitizing equipment, and treating fresh produce to prolong its shelf life and decline the presence of microbes. In addition, regulatory organizations such as the U.S.FDA and the EFSA have granted approval for the use of H_2O_2 during food processing. Nevertheless, the concentration and use of it must be meticulously regulated to guarantee food safety and adherence to regulatory norms [82, 83, 84].

1.5. Bacteriophages

Bacteriophages, often known as phages, are viral agents that selectively target and invade bacteria, rendering them highly suitable for utilization as natural preservatives within the food sector. Bacteriophage-based biocontrol provides a focused method for managing bacterial infections in food, without impacting the taste, texture, or nutritional composition of the food product. These viruses can be extracted and chosen to specifically attack particular bacterial strains that are recognized for causing foodborne diseases, such as *Escherichia coli*, *Salmonella* spp., and *Listeria monocytogenes*. Extensive research has been conducted on the use of phage-based therapies in several types of food, such as meats, dairy products, fruits, and vegetables. certain studies have yielded positive results in terms of lowering bacterial populations and prolonging the shelf life of certain food items. Nevertheless, in order to widely adopt bacteriophage preservatives in the food sector, it is necessary to tackle obstacles such as phage stability, host range, and regulatory approval [85, 86, 87].

1.6. Antimicrobial residues

Antimicrobial residues are small amounts of antimicrobial agents and their byproducts that remain in animal-based food products, environmental substances, and animal tissues after the use of antimicrobial therapies in veterinary medicine. Antimicrobial residues have the potential to build up in consumable tissues, milk, eggs, and honey, even with regulatory limitations and withdrawal times. This accumulation poses a threat to the health of consumers and the safety of food. Consuming food products contaminated with antimicrobial residues can result in allergic reactions, harmful consequences, and the development of AMR in disease-causing microorganisms that affect humans. Furthermore, the presence of antimicrobial residues in the environment and aquatic ecosystems can be attributed to environmental contamination caused by agricultural runoff, manure disposal, and aquaculture effluents. Also the environmental contamination may participate with the spread of antimicrobial resistance. The investigation programs, regulatory measures, and carrying out of dependable cultivation activities are indispensable for the observation and standard of antimicrobial substances in food production sectors. These techniques guarantee compliance with maximum residue limits (MRLs) and protect public health [88, 89, 90]. A previous inquiry determined the concentrations of Norfloxacin and Fleroxacin were respectively 225.45 and 99.43 mg/kg in chicken feces. Also, the concentrations of Ciprofloxacin were found 29.59 mg/kg in Cattle, 33.98 mg/kg in Swine, and 45.59 mg/kg in Chicken. Likewise, the residues of Enrofloxacin were respectively 46.70 , 1.42076, and 33.26 mg/kg in Cattle, Swine, and Chicken. Sulfonamides and Nitrofurans concentrations found in Swine, Chicken, and Cattle were respectively 0.085

mg/kg and 0.17 mg/kg. Furthermore, the antibiotic residues in swine were determined to be 59.06 for Oxytetracycline, 34.58 for Tetracyclines, 21.06 for Chlortetracycline, and 4.80 for Macrolides [91, 92, 93, 94].

1.7. The application of antimicrobial in Fish preservation

Various essential materials use in aquaculture for keep fish health and decreasing the harmful effects of microbial infections. However, the misuse of antimicrobial has demonstrated the main cause to the development of AMR in pathogens found in aquaculture, posing hazard to both public health and environmental stability. Among these materials are antifungus, antibacterial agents and disinfectants that have extensively applied to combat the deterioration in aquaculture system that causes by bacterial infections and control microbial development and sterilize facilities and equipment as well. While Iodine-depended compounds, H_2O_2, and formalin were extensively used as disinfectants for the aim of sterilizing equipment and water sanitizing, Florfenicol, Quinolones, Tetracycline, and sulfonamides are remarkably utilized as antibacterial in aquaculture to treat bacterial infections. While antimicrobial agents have been applied in the treatment and prosperity of aquaculture, it is imperative to exercise prudence in their usage and supply effective management to mitigate the risk of AMR appearance and environmental contamination. Increasingly, regulatory structures, surveillance programs, and alternative disease management methods are being used to promote the appropriate use of germicide in aquaculture and safeguard public health and environmental sustainability [95, 96, 97].

1.8. Preservatives

Preservative have crucial role in the food synthesis because they can stop the microbial proliferation as well as increase the life of biodegradable food materials. These compounds decelerate the oxidation process, and maintain the sensory qualities and safety of food products during storage and distribution [98]. It is typically used in diverse products include organic acids such as sorbic acid and benzoic acid, antibacterial agents like sodium nitrite and potassium sorbate, antioxidants such as tocopherols and ascorbic acid, and chelating agents like EDTA [99]. Preservatives are employed in a variety of food products, including baked goods, dairy products, beverages, and processed meats, to ensure microbiological safety and prevent economic losses resulting from spoilage [98]. However, regulatory authorities closely examine the use of these products to ensure consumer safety and adherence to accepted limits [99]. Furthermore, based on the FDA's published studies, it has been determined that antibacterial, additive, and preservative chemicals can be added to human foods in small and appropriate quantities without posing any harm. Benzoic acid and benzoate are derived from fruits, flowers, and margarine. They have the ability to block the growth of yeast and molds. Moreover, the proliferation of molds and yeast was inhibited through the use of parabens and sulfites found in fruit items, baked goods, and dried sausages. Some natural products have used in food production in order to inhibit the growth of *Clostridium botulinum* such as Nitrate, Nitrite, and Nisin, which are obtained from smoked foods, sausage casings, cooked pork, and cheese[100].

1.9. Study the Mechanisms of Preservatives utilized in Food Sector

The strategies of additives that are utilized in food are essential for keeping food safety; ameliorate quality, and guaranteeing nutritional content. Antioxidants, colorants, emulsifiers, preservatives, taste enhancers are chemical agents used for fulfilling specific functions in food systems. Potassium sorbate and Sodium benzoate are essential preservatives that prevent the development of microbes responsible for food spoiling. By inhibiting microorganism development, these additives effectively prolong the shelf life of food and prevent decomposition. Owing its effectiveness in acidic circumstances, it commonly used in beverages and sauces [101]. As mentioned above the Ascorbic acid and Tocopherols have been applied as antioxidants which prolong the shelf life of foods that include fats and oils by inhibiting the oxidation activities, hence protective the freshness of the products and preventing rancidity [102]. In addition to its antioxidant properties, Ascorbic acid participates in the nutritional composition by supplying vitamin C. Consumer preference for natural materials is driving the increasing usage of natural colorants such as curcumin over synthetic colors. The difficulty of guaranteeing the stability and consistency of these substances in food items persists [103]. In savory dishes, monosodium glutamate (MSG) is commonly employed as a flavor enhancer to augment the umami flavor. Its functionality in augmenting taste can result in decreased salt consumption, potentially promoting cardiovascular well-being [104]. Emulsifiers are crucial components in products that need the blending of liquids that cannot mix, such as Lecithin, a natural emulsifier employed to prevent separation and facilitate a consistent texture in products like mayonnaise and ice cream. Lecithin is also preferable in clean-label products but may be less efficient than synthetic alternatives in certain applications [105]. An in-depth investigation of the biochemical pathways by which these drugs function is essential to measure their safety and possible health effects. A modern survey has highlighted concerns with the prolonged utilization of particular artificial preservatives, which have the potential to disturb the gut flora and contribute to metabolic diseases [106]. Moreover, the combined impacts of several chemical components in processed foods are not sufficiently comprehended, thereby requiring extra investigation [107]. The safety of food additives is subject to ongoing evaluation by the Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA). However, the steady progression of original chemical materials necessitates constant examination and revised standards to tackle developing safety issues [108].Chromatography and mass spectrometry are demonstrated the advanced analytical technique that recently extensively applied in food production in order to determine and measure chemical components in complex food systems, thereby enabling more accurate safety assessing [109]. Furthermore, the increasing consumer desire for natural and clean-label products is challenging the improvement of alternative chemical factors created from natural origins. This requires a extensive knowledge of their mechanisms and effective [110]. A complete understanding of the technicians of chemical factors applied in food is important for the improvement of safe, high-quality, and aesthetically pleasing food items. Sustained research and cooperation among scientists, regulatory bodies, and the food sector are essential to tackle the issues and guarantee public health. Through precise exploration of these factors, scholars and industry experts can increase a more comprehensive understanding of the complex interplay and enduring consequences of chemical factors in food, so facilitating the development of safer and more influential food items.

2. Conclusion

Antibiotics are commonly used in poultry and cattle husbandry to treat infectious disorders and enhance reproduction, but this practice can lead to food contamination and resistance against various bacterial species. Natural molecules in food, such as avidin, ovoflavoprotein, lysozyme, conalbumin, biotin, and enzyme inhibitors found in eggs, serve as protective and inhibitory agents. These substances prevent the activity of proteolytic enzymes produced by bacteria and fungi in food and form complexes with Fe^{+}, preventing the growth of Gram-ve bacteria and yeasts. Milk and dairy products contain innate substances that hinder the growth of Gram-negative psychrotrophic bacteria. Animal products, such as meat, contain naturally occurring inhibitory compounds, while plant diets contain numerous natural inhibitory compounds. Certain plant-based foods, such as peels of fruits and vegetables, waxy coatings, and hard shells of nuts, have bioactive compounds that serve as natural defense mechanisms against pathogens. The development of these natural antibacterial compounds is economically valuable and has the potential to replace all current chemical food preservatives. Overall, not all antimicrobial agents suitable for using in food production since some of these materials have accumulation effects on human and animals life. Lastly, researchers focus on the side effects of preservatives in food production. Some of the aforementioned materials were appropriate to use as preservatives in food whereas the usage of other materials has been banned.

Generative AI

During the preparation of is work the authors used [QuillBot] in order to rephrase and increase clarity of some sections in introduction After using this tool, we reviewed and edited the content as needed and take full responsibility for the content of the publication.

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