Use of Nutritional Components for the Control of Zoonotic Listeriosis

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ABSTRACT

Listeriosis is a disease of animal origin caused by L. monocytogenes. The disease affects humans, animals, poultry, and marine life also. Humans get infection with the consumption of contaminated foods mainly foods from animals such as milk and meat. The outbreaks of the disease are sporadic, but mortality rate is high in humans. The disease is controlled by antibiotics in humans, animals and poultry. But the L. monocytogenes have attained resistance against the antibiotics. The novel and alternative control strategies to overcome this problem are the nutritional and biological methods. The objective of this study was to review and conclude all the possible nutritional control methods for listeriosis. They consist of use of probiotics, bacteriophages, peptides, herbal use, essential oils and nanoparticles. The use of nutritional treatments is specific and safe for public health as they do not have any toxicity. These methods stop the growth of L. monocytogenes by causing cell death of bacteria through different mechanisms. Their important mechanism of action is the pore formation in cell membranes and outflow of components from bacterial cell. Most of the studies have been conducted to control L. monocytogenes by these methods in food industry. Further research needs to be conducted to control listeriosis in animals and humans.

Keywords: L. monocytogenes, animals, humans, treatments, foods, meat

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1. INTRODUCTION

Listeria (L.) monocytogenes, a gram-positive bacterium, causes the zoonotic disease known as listeriosis. The pathogen is cellular in nature and capable of intercellular movement, allowing it to traverse the blood-brain and placental barriers (Janakiraman 2008). According to Dhama et al. (2015), the condition is also known as meningoencephalitis, silage disease, and circular disease. This disease is transmissible to animals, livestock, fish, birds, crustaceans, and humans. Dhama et al. (2013) reported that *L. monocytogenes*-contaminated food can transmit the disease to humans. Direct contact with the environment and diseased animals can also infect humans (Matle et al. 2020). This disease is more likely to be contracted by pregnant women, young infants, old persons, and those with compromised immune systems. If animals consume contaminated silage, they may acquire this disease (Chen et al. 2020). The disease's signs and symptoms manifest infrequently but in extreme cases. The disease causes encephalitis, septicemia, meningitis, rhombencephalitis, meningoencephalitis, miscarriage, abortion, perinatal infections, and GIT infections in animals (Mateus et al. 2013).

Food handling and processing can lead to sporadic and epidemic outbreaks of listeriosis by contaminating commodities with the bacterium. The disease affects animals and humans globally (Dhama et al. 2013). According to Salama et al. (2018) and Jensen et al. (2014), the South African (2017) and Danish (2014) listeriosis epidemics resulted in 204 and 37 fatalities, respectively. In 2008, the disease caused 23 deaths in Canada, which is also a significant burden in industrialized nations such as the United States and Europe (Thomas et al. 2015). The disease has an incidence rate of 0.3% and a mortality rate of 21% in the United States (Tack et al. 2019). Between 2011 and 2017, China recorded 562 cases with a fatality rate of 32.68 % (Fan et al. 2019). It also causes substantial economic losses for the cattle industry, food contamination, and abortions in both humans and animals (Li et al. 2014).

A wide range of techniques are used for handling and caring for people, animals, and food. Standard interventions for both humans and animals include antibiotics and food-borne disinfectants (Guerrero-Navarro et al. 2019). This bacterium develops resistance to antibiotics and disinfectants due to their wide and frequent use. Second, because the bacteria are intracellular, the medications must enter the cells and accumulate there for the organism to be eradicated (Pagliano et al. 2017). Various remedies are required to prevent these complications and treat listeriosis (Dhama et al. 2015). Nutritional therapies are among the most cutting-edge and modern methods for controlling *L. monocytogenes*. The use of bacteriophages to control *L. monocytogenes* during the processing of meat, meat products, and poultry is an efficient method (Klumpp and Loessner 2013). As antibacterial agents, essential oils and plant extracts play a crucial role in the treatment of *L. monocytogenes*. Probiotics are essential dietary components that eliminate this pathogen and strengthen the immune system. To treat and manage *L. monocytogenes* in humans, animals, and food, cytokines, chicken eggs, prebiotics, enzybiotics, medicinal compounds, and nanoparticles are required (Dhama et al. 2015). The use of nutritional and biological control measures has increased over the past few years. In consideration of this, the objective of this book chapter is to identify and summarize all the prospective nutritional management strategies that have been used or may be used to control *L. monocytogenes*.

2. TRANSMISSION BY ANIMALS

Animal feed is a common source of *L. monocytogenes*. The majority of bacterial reservoirs consist of infected animals that excrete the pathogen via their feaces. Without adequate sanitation precautions during lactation, feaces are the primary source of pathogen contamination in milk (Rodriguez et al. 2021). Inadequately constructed silage serves as a source of bacteria for animals. *L. monocytogenes* is unable to flourish in silage with a pH between 3.7 and 4.7. In addition, it strengthens the animal's immune system by providing microorganisms (Limin et al. 2018). 7.5% of silage samples tested positive for *L. monocytogenes*, according to research done by Nucera et al. (2016). Small ruminants, such as sheep, are more susceptible to listeriosis due to their fodder and grass forage consumption. 2.5% to 5.9% *L. monocytogenes* positive clamp silage samples were discovered (Rodriguez et al. 2021). Antibiotic-resistant microorganisms are posing a threat to public health and facilitating the development of novel management strategies. Consequently, there has been an increase in the adoption of nutritional and biological management techniques over the past few decades (Rothrock et al. 2017).

Other food sources such as crops, and pasture are also capable of transmitting bacteria to animals (Locatelli et al. 2013). Cats considerably contribute to the spread of bacteria through grazing animals' manure (Mohammed et al. 2010). According to Matto et al. (2017), the infection was acquired by a two-year-old heifer browsing on bovine manure-contaminated ground. According to a research, *L. monocytogenes* is spread by high-velocity winds and heavy precipitation, which contaminate pasture vegetation and infect animals (Pang et al. 2017). In agricultural contexts, water is the primary source of bacteria, and all sediment contaminations eventually contaminate water with this bacterium. It was reported that the prevalence of microorganisms in animal colonies was 6.5% (Mohammed et al. 2010). Farm surfaces are usually contaminated with the pathogen, so farm workers' and veterinarians' shoes can disseminate the bacterium (Schoder et al. 2011).

Listeria affects both domestic and wild animals, including sheep, goats, and livestock, with ewes being the most susceptible. Initial observations of the bacteria were made in guinea pigs and rabbits (Malakar et al. 2019). The intestines and milk of these animals contaminate humans. According to a study, 42.5 % of meat and meat products obtained by restaurants contained *L. monocytogenes* (Ng et al. 1995). In another study conducted in China, it was determined that the prevalence of microorganisms in beef and pork was 9.1% and 11.4%, respectively (Cavalcanti et al. 2022). According to Schoder et al. (2023), the prevalence of the bacteria in milk from cattle and small animals (sheep and goats) was 13% and 17%, respectively.

3. TRANSMISSION BY POULTRY AND SEAFOOD

Infectious variants of listeriosis in poultry are uncommon and frequently asymptomatic (Wesley 2007). In China (2014) and Washington (2013), sporadic infectious epidemics of listeriosis affected poultry which were raised at home (Crespo et al. 2013; Gu et al. 2015). Two of the primary risk factors for *L. monocytogenes* transmission in poultry are the hatchery and the development conditions of the farms (where live fowl are maintained). Incubation of fertilized eggs derived from reproductive progenitors precedes the hatching of birds in a hatchery. Consequently, the pathogen may spread to the egg surface, embryo, and neonatal birds as described in Fig. 1 (Rothrock et al. 2017). Only a few studies have demonstrated bacterial transmission at this time. Cox et al. (1997) of the United States discovered *L. monocytogenes* in only 1% of chicken napkins and 6% of eggshells. Another study conducted in Thailand discovered no evidence of *L. monocytogenes* in hatchery conditions (Kanarat et al. 2011).

The second place in which pathogens may be transmitted to poultry is agricultural and growing conditions. The chicks are relocated to the location of the farm's expansion. *L. monocytogenes* can be found in numerous environments and production sites, including vegetation, water, soil, enclosures, feed, and excretion (Dhama et al. 2013). Based on 2012 research conducted in the United States, the prevalence of the bacteria in ambient samples varied between 1.45% and 53.3% (Jones et al. 2012). *L. monocytogenes* was nevertheless more prevalent than anticipated in 2010 samples of broiler litters, nutrients, water, and soil from U.S. poultry farms (Milillo et al. 2012; Rothrock et al. 2017). Some poultry farms allow access to other animals, including dogs, goats, sheep, cattle, pigs, and other livestock that serve as bacterial reservoirs and can disseminate pathogens to fowl (Aury et al. 2011). Consequently, these are a few sites where *L. monocytogenes* could potentially spread to poultry.

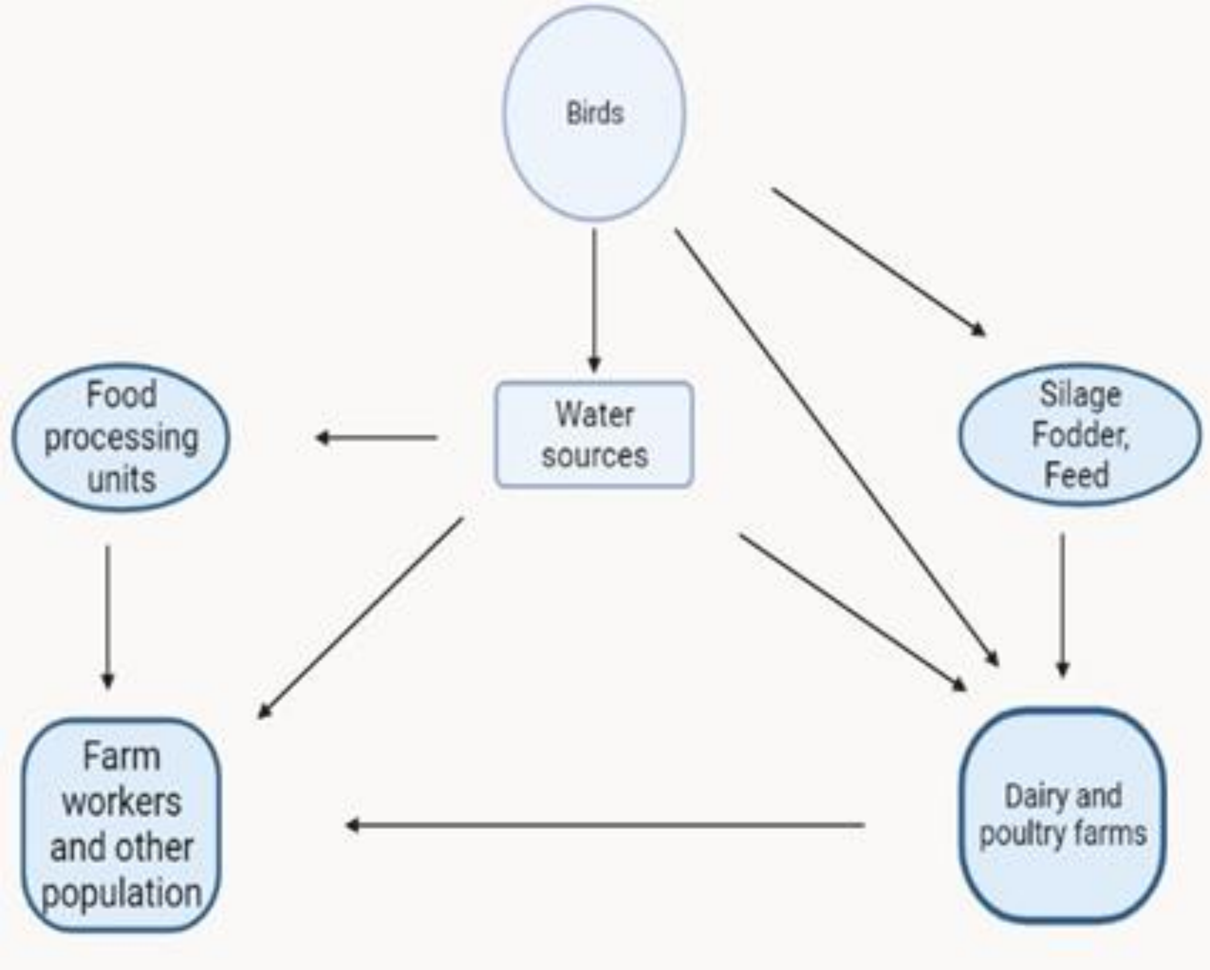

Fig. 1: Different possible routes for the transimission of L. monocytogenes.

4. NUTRITIONAL CONTROL OF LISTERIOSIS

4.1. *PROBIOTICS*

Probiotics are beneficial microorganisms that are given to the host in moderate amounts. Common sources of probiotics include milk and dairy products like yogurt and cheese (Zielinska et al. 2018). They are safe to use and can be used to eradicate pathogenic microorganisms in food to preserve it. Probiotics assist in food preservation by preventing the proliferation of *L. monocytogenes* in food. According to Rios-Covian et al. (2018), the most commonly used probiotics to treat *L. monocytogenes* are Bifidobacterium, lactic acid bacteria (LAB), and yeasts. Probiotics inhibit *L. monocytogenes* growth by preventing biofilm formation, reducing the availability of nutrients and energy for bacterial cells, interfering with quorum sensing mechanisms, and decreasing *L. monocytogenes'* environmental tolerance (Martín et al. 2022).

Bacteriocins such as nisin, which are generated by LAB and secreted by probiotics, inhibit the proliferation of *L. monocytogenes* in food. Three hours of nisin treatment inhibited *L. monocytogenes* growth by six log10 CFU/g (Zhao et al. 2020). Combining bacteriocins with other compounds increases their efficacy. Nisin and fatty acids were utilized in a study, and the outcomes demonstrated a 5 log10 CFU/ml reduction in *L. monocytogenes* as well as an inhibition of biofilm formation (Zhou et al. 2020). Biofilms are bacterial microcolonies that adhere to surfaces and are encased in polymeric substances that are extraordinarily resistant to external stimuli (Nwaiwu et al. 2021).

L. monocytogenes and probiotics compete for the energy source (ATP). The overproduction of metabolites by LAB increases energy consumption and decreases the ability of *L. monocytogenes* to produce energy. Probiotics emit acetic and lactic acids, which prevent electron transfer and decrease energy generation similar to how probiotics and *L. monocytogenes* compete for essential nutrients (Aljewicz and Cichosz 2017). Due to their accelerated growth, probiotics deplete *L. monocytogenes* of nutrients, resulting in their eventual demise (Wu et al. 2022). In numerous foods, *L. monocytogenes* is inhibited by probiotics. *L. monocytogenes* in beef samples decreased by 2.57 log10 CFU/g when probiotics such as *Lactobacillus plantarum* and *Lactobacillus reuteri* were administered (Khalili Sadaghiani et al. 2019). LAB also decreased the amount of *L. monocytogenes* in chicken breast meat (Costa et al. 2018). When probiotics (LAB) are introduced to cheese, they decrease the temperature, pH, and water activities of *L. monocytogenes*, thus decreasing its concentration (Gonzalez-Fandos et al. 2020).

4.2. *PLANT EXTRACTS*

L. monocytogenes in various foods is now controlled and treated with plant extracts, such as essential oils (EOs) and herbal remedies. EOs are utilized for antiliteral purposes (Bajpai et al. 2019). EOs are derived from the leaves, roots, seeds, blossoms, blooming, and bark of various plants. Rosemary, thyme, and oregano are examples of essential oils employed for nonliteral purposes (Dhama et al. 2015). The oils of *Cinnamomum crassinervium* and *Cinnamomum cuspidatum* were utilized to limit the development and decrease the quantity of *L. monocytogenes* (Calo et al. 2015). EOs are used in foods as flavoring and preservation agents in addition to their antibacterial properties. The principal antibacterial components of EOs that eliminate pathogenic microorganisms are phenols and terpenes (Pietrysiak et al. 2019).

Because EOs are made up of a variety of chemical components, they have a variety of methods to eradicate pathogens. They can penetrate the bacterial cell wall and inhibit the functioning of the bacterial cell as shown in Fig. 2. Due to their hydrophobic nature, they cause the lipid bilayer of mitochondrial and bacterial cell membranes to rupture. Changes in the permeability of the cell membrane result in the loss of essential ions and other cell components, ultimately leading to cell death (Calo et al. 2015). Phenolic components of EOs alter intracellular proton transport, cell permeability, cytoplasmic membrane integrity, and energy synthesis, ultimately leading to cell death (Bajpai et al. 2019).

The impact of EOs on the growth of *L. monocytogenes* in a variety of foods has been analyzed. El Abed et al. (2014) discovered that beef treated with various concentrations of EOs derived from *Thymus capitata* enhanced the beef's activity against *L. monocytogenes*. According to another study by Giarratana et al. (2016), three genotypes of *L. monocytogenes* grew more slowly in the presence of rosemary and thyme essential oils at concentrations of 0.25% and 0.50%. When the effects of clove EOs (1% and 2%) on chicken were tested in the laboratory on seven strains of *L. monocytogenes*, a significant reduction in the number of bacteria was observed (Mytle et al. 2006). Likewise, steak containing 10% clove essential oil was completely delayed (Khaleque et al. 2016). Storage conditions, such as temperature and time, do not affect the proliferation of *L. monocytogenes*. The use of EOs from savory, cinnamon, *Satureja horvatii*, qysoom, nutmeg, and oregano inhibited the proliferation of *L. monocytogene*s (Yousefi et al. 2020). In contrast, it has been discovered that plant extracts may aid in the control of *L. monocytogenes*. It has been demonstrated that white tea, almond skin, and coffee extracts inhibit *L. monocytogenes* proliferation (Zamuz et al. 2021). It has also been determined that plant products (EOs) have no negative impact on fish or animals. There have been no reports of cancer-causing effects when consumed orally in large quantities.

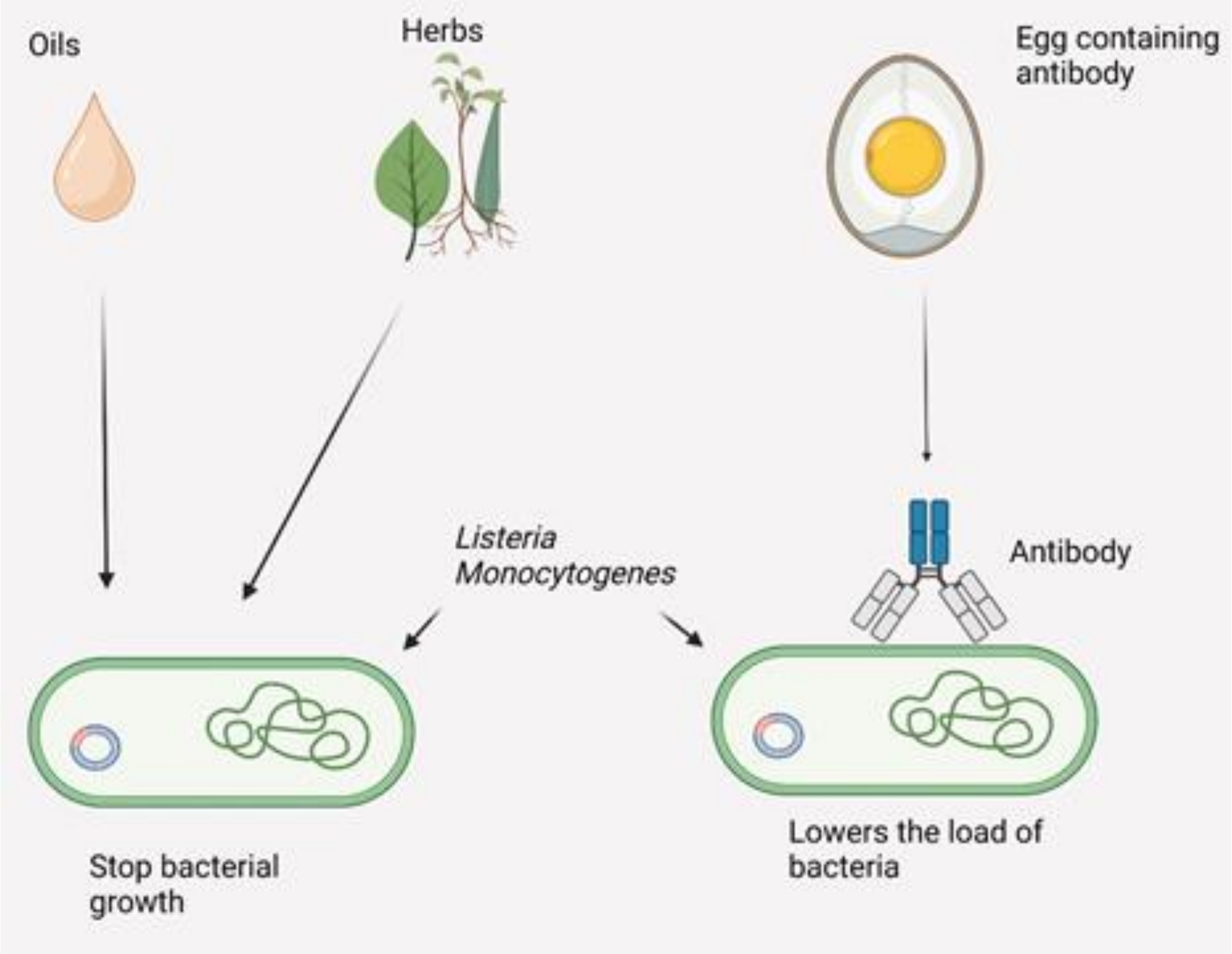

Fig. 2: Use of oils, herbs, and egg yolk antibodies to control *L. monocytogenes*.

However, they have disadvantages and, when used in large quantities, modify the flavor and aroma of food. Numerous strategies, such as the use of EOs in edible coatings, EO combinations, and microencapsulation, have been devised to address this problem (Yousefi et al. 2020).

4.3. *BACTERIOPHAGES*

Bacterial pathogens are responsible for the onset of severe and sometimes fatal illnesses, posing significant challenges in terms of their management and treatment. Bacteriophages have significant attention from researchers due to their potential to eradicate antibiotic-resistant bacteria while preserving the natural gut microbiota (Gandham 2015). Bacteriophages are viral agents that induce infection and undergo replication inside bacterial cells, ultimately leading to the lysis of the affected bacterial cell. Phages possess two fundamental mechanisms for bactericidal activity, namely lytic and lysogenic pathways. In the lytic mechanism, viral particles introduce their genetic material into the host bacterial cell and exert control over its metabolic processes. According to Batinovic et al. (2019), recently developed bacteriophages undergo replication inside the host cell and subsequently exit the cell, resulting in the demise of the bacterial cell. This process also has the potential to infect more cells. The lysogenic process entails the integration of phage genetic material into the chromosomal material of the host bacterial cell, resulting in the formation of a prophage. Subsequently, the prophage undergoes reproduction inside the host cell (Wernicki et al. 2017). The conversion of this process into a lytic mechanism may occur at any given moment as a result of both internal and external cell-triggering signals (O'Sullivan et al. 2019).

A total of around 500 phages of the Listeria genus have been identified, with the majority exhibiting a lysogenic lifecycle. It is worth noting that these lysogenic phages have limited use in the field of biocontrol (Hagens and Loessner 2014). A limited number of listeria phages have been discovered as having virulent properties for managing listeria. The use of Listeria phages has been employed to manage *L. monocytogenes* in several contexts, including animals, milk, meat, fish, cheese, fruits, and vegetables (Kawacka et al. 2020). ListSheildTM (LMP-102) and ListexTM (P100) are the phages most often used to control *L. monocytogenes* in food products. In an experimental investigation, mice were administered a daily oral dose of 2x1012 phage concentrations per kg for five consecutive days. In this investigation, the researchers used a total of 100 P100 phages, which have been previously established as safe for usage and have shown a lack of adverse effects (Carlton et al. 2005). Soni et al. (2010) reported a significant decrease in the population of *L. monocytogenes* in catfish after the application of P100 phages. In a similar vein, the lytic effects of phages were examined by using LMP7 and LMP1 phages in soy broth and pasteurized milk samples obtained from commercial establishments. The use of these phages resulted in a notable decrease in the proliferation of *L. monocytogenes*, as seen in the study conducted by Lee et al. (2017). According to Bigot et al. (2011), the application of phages on packaged chicken meat resulted in a reduction in bacterial count and subsequent inhibition of bacterial growth over 21 days. An alternative strategy involves the use of a phage cocktail including many phages inside a unified assemblage. A solution consisting of a combination of six phages was administered to various food samples, resulting in a significant decrease in the proliferation of *L. monocytogenes* (Moye et al. 2018). Utilizing a cocktail of phages as opposed to a single phage is a potentially advantageous strategy, as it enables the targeting of a wider range of bacterial strains and mitigates the likelihood of bacterial resistance development towards therapy. This phenomenon might be attributed to the presence of many phages inside the cocktail, which ensures that if a particular bacterium develops resistance to one phage, it remains susceptible to other phages (Moye et al. 2018).

The effectiveness of phages might be modified by several circumstances. Multiple variables affect the functioning abilities of phages in complicated matrices of food and their interactions with phage-host systems. The elements included in this study are resistance, pH levels, phage concentrations, bonding properties, temperature, stability of phage form, and content of foods (Kawacka et al. 2020).

4.4. *PEPTIDES AND POLYPEPTIDES*

Peptides and polypeptides are becoming more common to be used in therapeutic contexts. Due to their high specificity and low toxicity, peptides are essential in medicine (Sato et al. 2006). Some dietary peptides are produced by the enzymatic proteolysis of proteins derived from other species, and they play a crucial role in the fight against microorganisms. Proline, arginine, and glycine are peptides that inhibit the development of *L. monocytogenes*. Moreover, barbel peptides derived from the enzymatic hydrolysis of barbel muscle proteins are employed to control *L. monocytogenes* (Falardeau et al. 2021). Bacterial ribosomes produce bacteriocins such as nisin, pediocins, enterocins, and lacticins, similar to peptides and polypeptides (Slozilova et al. 2014).

Peptides regulate the proliferation of *L. monocytogenes* in several distinct methods. Electrostatic forces adhere to the cell walls and membranes of microorganisms. The positively charged end of peptides interacts with mannose receptors and negatively charged lipids on the bacterial cell membrane (Kumariya et al. 2019). As a result of the flux of potassium ions outside the bacterial cell, these interactions halt the production of peptidoglycans in the cell wall and modify polarization. As a result, the propelling force of the protons and the equilibrium of the water are disturbed, resulting in an energy deficit. According to Egan et al. (2016), the metabolites and nutrients of a bacterial cell exit through the cell's apertures and cause cell death. LAB produces peptides/bacteriocins via both pore-formation and peptidoglycan synthesis inhibition pathways (Bizani et al. 2008).

Numerous studies have investigated the effect of peptides on *L. monocytogenes* proliferation. The administration of Cerein 8A peptides at 4°C and 160 AU/ml concentrations slowed *L. monocytogenes* proliferation in milk by a factor of three (Kiran and Osmanagaglu 2014). When chicken flesh was stored at 4°C for 14 days, pediocin inhibited the growth of the target bacteria by 3.8 log (Renye et al. 2009). *L. monocytogenes* proliferation in salami was inhibited by 1.6 logs using Enterocin (Yap et al. 2021). Chicken and other avian eggs are an abundant source of peptides (antibodies) that inhibit *L. monocytogenes* development (Dhama et al. 2015). The interactions of peptides with dietary components, peptide-degrading enzymes, variations in the viscosity, fatty acid content, and fluid content of bacterial cell membranes, and peptide-degrading enzymes may all reduce their antibacterial effects. All of these factors reduce the ability of peptides to attach to the bacterial cell of interest and, consequently, their efficacy. To circumvent this issue, the peptides are microencapsulated and combined with additional preservatives (Chugh et al. 2021).

4.5. *NANOPARTICLES*

Nanoparticles (NPs) with medical significance are inorganic substances between 1 and 100 nm in size (Al-Shabib et al. 2020). Nanoparticles are increasingly used to inhibit the proliferation of microorganisms. Chemical synthesis and plant extraction are both viable options (Khezerlou et al. 2018). The use of NPs can be used to control *L. monocytogenes*. The most commonly used nanoparticles (NPs) to inhibit *L. monocytogenes* in various foods are ZnO, MgO, CuO, Ag, and sulfur (Ahmadi et al. 2016; Kumar et al. 2021; Priyadarshi et al. 2022). Different processes are used by NPs as part of their action mechanism to regulate *L. monocytogenes*. Due to their small size, they can more easily enter bacterial cells, where they can disrupt the respiratory system and genome, thereby eradicating the bacterium. Moreover, they impact the expression of the virulence gene in bacterial cells (Zakarienė et al. 2018). Other processes include the formation of oxygen-reactive species, the release of ions from nanoparticles, and the production of free radicals. When these particles adhere to the membranes of bacterial cells, they create holes that kill the bacteria (Rai et al. 2009). For NPs to effectively regulate microorganisms, their size is crucial. Research indicates that smaller NPs are more effective against *L. monocytogenes* than larger NPs (Firouzabadi et al. 2014). This is because smaller NPs have a greater surface area and a greater potential for cell interaction. Silver nanoparticles may inhibit the formation of listeria biofilm (Sani et al. 2022). Similar research demonstrated that Silver and CuO can eradicate *L. monocytogenes* (Milillo et al. 2012).

5. CONCLUSION

As a consequence of frequent and extensive use of antibiotics, the microorganisms that cause listeriosis have developed drug resistance. New approaches to control bacteria are being implemented to address this issue. Utilizing biological techniques and nutritional components is one of the most widespread new approaches. Probiotics, plant extracts, peptides, essential oils, bacteriophages, and nanoparticles are among the methods. Before destroying *L. monocytogenes,* bacteriophages modulate bacterial development by introducing their genetic material into bacterial cells. Before causing cell death, probiotics release substances such as acids and bacteriocins that inhibit bacterial growth. Nanoparticles, peptides, and essential oils are all capable of permeating a cell and rupturing bacterial cell membranes, thereby interfering with normal cell activity and resulting in cell mortality. These are effective methods for preventing the spread of *L. monocytogenes*. To fully comprehend how these strategies function, additional research is necessary. The majority of labor is performed in the food industry, and data on listeria in humans and animals is scarce. Evaluating the effects of dietary approaches for managing *L. monocytogenes* in animals and, eventually, humans will necessitate future research.

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