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Management of Foodborne Disease Using Silver Nanoparticles: A perspective

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ABSTRACT

The rising incidence of foodborne diseases caused by pathogenic bacteria represents a significant global public health challenge. Microbial spoilage not only reduces the shelf life of food products but also exacerbates the risk of foodborne diseases. According to the World Health Organization, one in ten individuals worldwide suffers from foodborne diseases annually. Despite being largely preventable, the effective management and prevention of these diseases continue to pose critical challenges on a global scale. The distinctive properties of both organic and inorganic nanoparticles have garnered considerable interest in the food industry due to their potential to improve the nutritional, safety, and quality aspects of food products. A substantial proportion of foodborne infections are caused by pathogens such as *Salmonella*, *Listeria*, *Escherichia coli*, *Clostridium*, and *Campylobacter*. Among the various antimicrobial agents, silver and its compounds have demonstrated potent activity against a wide range of bacterial species. The expanding body of research on the application of silver nanoparticles for controlling foodborne pathogens offers new insights into their mechanisms of action, benefits, and limitations. This analysis seeks to explore innovative strategies for mitigating the burden of foodborne diseases by critically assessing the potential of silver nanoparticles. Additionally, the possible health implications of silver nanoparticles for human consumption will be examined to guide the formulation of effective public health policies.

Keywords: silver nanoparticles, foodborne pathogens, antimicrobial activity, food safety, food packaging, human health

INTRODUCTION

Every year worldwide, unsafe food causes 600 million illnesses and 420,000 deaths. Statistics show that about 30% of foodborne deaths occur in children under 5 years of age. The World Health Organization estimates that 33 million healthy life years are lost globally each year due to the consumption of unsafe food. World Health Assembly resolution 73.5 mandates the World Health Organization to regularly monitor the global burden of foodborne diseases and zoonotic diseases at the national, regional, and international levels, and to report to Member States. The Organization is also required to produce a new report by 2025 on the global burden of foodborne diseases based on updated estimates of the incidence of foodborne diseases, mortality, and disease burden in terms of Disability-Adjusted Life Years (DALYs) (1). Foodborne illness impose significant costs on society, with the most important being economic. At the individual level, treatment costs are incurred, and at the macro-industrial level, food production factories suffer financial and reputational losses. Additionally, imposing insurance costs for treating affected patients, along with the possibility of issuing national and international rulings such as food export bans, can cause significant financial damage to the economic system (2). Foodborne diseases are preventable, and with this approach, the management of foodborne diseases by any scientific means is one of the major and important goals of health systems in different countries. To the extent that the use of new knowledge and technologies for their control has become a global effort.

METHOD

This perspective was developed based on a comprehensive review of relevant literature, including reports from the World Health Organization (WHO) and recent studies published in peer-reviewed journals. The selection of sources focused on research related to foodborne diseases, the application of nanotechnology in food safety, and the health impacts of silver nanoparticles. Key findings from these sources were synthesized to provide an overview of the current state of knowledge, identify gaps in research, and propose areas for future investigation. The perspective aims to contribute to the ongoing discussion on food safety by highlighting the potential benefits and risks of using silver nanoparticles in food-related applications.

RESULT

The following section presents the critical findings related to foodborne diseases, the application of nanoparticles, and the impact of silver nanoparticles on food safety and human health.

Foodborne diseases

Over 200 types of diseases have been identified that are caused by foodborne pathogens in humans. These agents include various viruses, bacteria, and parasites, and the diseases that occur following the consumption of foods contaminated with these agents are called foodborne diseases. According to the World Health Organization, foodborne disease is defined as any diseases, whether of an infectious or toxic nature, caused by the consumption of contaminated food or drink (3). Therefore, foodborne diseases are classified into two main categories: 1) those mediated by pathogens or infectious agents, and 2) those mediated by various chemicals and toxins. Every foodborne disease has three main components. First, the host, which is a human. Second, the causative agent, and third, the transmission route, which is food and water.

Foodborne pathogens can cause food poisoning in three ways. Intoxication is a condition in which a food containing a microbial toxin is consumed by a human. The toxin has entered the food, multiplied, and has been metabolically active. In this case, the presence of the pathogen is not very important, and the causative agent is the microorganism's toxin. The second method is toxic infection, in which the microbe enters the food and is consumed by humans. The microorganism then multiplies in the gastrointestinal tract and, as a result of its biological activities, produces a substance that is toxic to humans. In this case, the causative agent is the fresh toxin of the microorganism present in the gastrointestinal tract. The third type of food poisoning is food infection, in which the microbe itself is present in the gastrointestinal tract and invades the tissues, causing disease (2).

Microbial contamination in food occurs at various stages of food processing and preparation; from the time of harvesting or slaughtering animals, cleaning and preparation, packaging and distribution, purchasing and home preparation, until the time of consumption by humans, which encompasses the well-known process from farm to fork, and can be due to environmental contamination such as water, soil, or air (4). One of the most common symptoms of foodborne illnesses is gastrointestinal upset and disorders such as diarrhea and vomiting, which are present in most people who suffer from these diseases and improve with simple treatments. However, foodborne diseases have other important consequences that are often overlooked or less studied; kidney and liver failure, neurological disorders, reactive arthritis, and more are among these consequences and occur with greater severity in vulnerable groups such as children, pregnant women, the elderly, and immunocompromised individuals (5). Therefore, given the importance and impact of foodborne diseases on human health, the use of various methods to control and prevent the occurrence of these diseases has long been considered a common and important practice. The use of traditional methods such as salting food, fermentation, freezing, pasteurization, drying, and the like are all aimed at reducing the occurrence of foodborne diseases and managing the burden of these diseases in health systems (6). Today, with the same approach, the use of new methods and technologies to increase food safety has attracted attention. The application of biotechnology, nanotechnology, omics technologies, and the like seems to be a new and growing trend (7).

Nanoparticles

In recent years, the application of nanotechnology as a beneficial and easily accessible technology has experienced significant growth in various industries; from agricultural products to biotechnology, engineering, cosmetics, textiles, food, and even medical and pharmaceutical industries (8). The application of this type of technology in various fields is considered a technological revolution; especially with a focus on food and health, nanotechnology is finding increasingly widespread use in drug delivery processes and nutrient release (nanoencapsulation), increasing the speed of disease symptom detection, and providing rapid treatments (9). Nanomaterials exist naturally, and randomly, and are man-made. These materials consist of various particles, including loose particles, agglomerated particles, or granular particles, and exist in the form of nanoparticles, nanowires, nanotubes, nanofibers, and more. Among these, nanoparticles with dimensions of 1 to 100 nanometers have attracted the most attention for use in various industrial and technological fields, especially in the food industry, due to their greater diversity in terms of shape and size (10). Nanoparticles can be classified into two main categories: organic and inorganic. Organic nanoparticles are based on natural compounds and organic molecules that contain carbon. Protein grains, lipid bodies, milk emulsions, or more complex compounds of this type are examples of organic nanoparticles. One of the characteristics of these nanoparticles is that their separation and encapsulation methods are relatively simple and often biodegradable. Another important feature of these nanoparticles is their dynamism and activity, which is due to the interaction between their atoms. Such characteristics have led to an increasing tendency to use them in biological structures, especially targeted drug delivery and the food industry (11). Inorganic nanoparticles usually form as a result of the precipitation of inorganic salts in a related matrix. These particles have metallic components (gold, silver, copper), magnetic components (nickel, iron, cobalt), or semiconductor components (zinc oxide, zinc sulfide, cadmium sulfide) (12).

Among the many properties of nanoparticles, four properties, shape, size, charge, and surface, have been the focus of particular attention by researchers because slight changes in any of these properties change the properties of nanoparticles and alter their efficiency. One of these changes is the emergence of antimicrobial properties and the fight against the infectivity of microbial agents in various media, especially in the field of foodborne diseases. Changing the shape of nanoparticles from shapes such as triangular, decahedral, spherical, cubic, flat plate, and the like has a significant effect on antimicrobial activity, to the extent that studies have shown that changing the shape of nanoparticles to spherical or triangular increases antimicrobial properties (13). The surface of nanoparticles can be modified and their applications can be specialized by adding coating agents such as polymers (chitosan, polyethyleneimine, polyethylene glycol, poly-gamma-glutamic acid), proteins (milk casein, bovine serum albumin, human serum albumin), antioxidants (glutathione), or multivalent anion salts (14).

Silver Nanoparticles

The use of various inorganic metal nanoparticles in the biomedical, biopharmaceutical, and food industries is rapidly expanding. Low toxicity, high affinity for target molecules, and their specificity are among the characteristics that have made metal nanoparticles popular among researchers (15). Among these, silver and silver salts are being studied worldwide to eliminate pathogenic bacteria. The use of potent antimicrobial agents such as silver nanoparticles (Ag-NPs) has introduced a new approach to combating microbes, to the extent that it is well known that silver and silver-based compounds are highly toxic to 16 major bacterial species. Silver is commonly used in the form of nitrate, which enhances antimicrobial effects (16). Many studies have shown the size-dependent antibacterial activity of Ag-NPs, so that a size range of 1 to 100 nanometers is the most commonly used range for these particles, and it is attributed a large surface area (9). Additionally, the charge of silver nanoparticles determines their interaction with biological environments and cellular uptake, which leads to the modulation of their antibacterial activity. Furthermore, the antimicrobial activity of silver nanoparticles is related to the type and strain of bacteria and the structure of its cell wall (13).

The antimicrobial property of silver is attributed to silver ions released from silver-containing compounds in a matrix and combining with enzymes and proteins with thiol groups in cells. Most of these proteins play a vital role in the life of cells, especially bacteria, and any disruption in their function prevents cellular respiration processes, which leads to cell death. The cell walls of Gram-positive and Gram-negative bacteria differ physiologically. In general, peptidoglycan is a thick, net-like layer in the plasma membrane of Gram-positive bacteria and creates a thicker cell wall than Gram-negative bacteria. Such a thicker wall plays a vital protective role for the bacterial cell against the penetration of silver into the cytoplasmic membrane. In Gram-negative bacteria, silver ions can easily penetrate the cell wall and consequently interfere with the thiol groups of bacterial proteins and facilitate the release of reactive oxygen species. The long-term interaction of silver ions with bacterial thiol groups causes DNA to lose its ability to replicate and proteins to become inactive. Therefore, respiratory enzymes are inhibited by silver nanoparticles and lead to the formation of reactive oxygen species such as hydroxyl radicals, superoxide, and hydrogen peroxide, which through the oxidative degradation process of cellular components leads to the destruction of proteins and cell death (18, 17).

Silver Nanoparticles and Food Safety

Unsafe food poses a threat to human health and national economies, affecting all individuals, especially vulnerable groups such as those at risk of food deprivation or restriction, migrants, populations involved in war or conflict zones, populations affected by natural disasters like floods and earthquakes, and poor populations in various countries. Microbial food spoilage is a major global concern that can reduce the shelf life of food and increase the risk of foodborne diseases. Most foodborne infectious diseases are caused by pathogenic bacteria of the genera Salmonella, Listeria, Escherichia coli, Clostridium, and Campylobacter in consumed food. Numerous research studies have confirmed the effectiveness of Ag-NPs in inhibiting the growth of pathogenic bacteria such as Staphylococcus aureus, Streptococcus mutans, Streptococcus pyogenes, Escherichia coli, and Proteus vulgaris (19). The antibacterial effect of Ag-NPs against multidrug-resistant Campylobacter strains isolated from poultry food chains and patients with food poisoning has been demonstrated (20). On the other hand, extracts from various foods to create silver nanoparticle carrier molecules have created a new approach to research in this field. Silver nanoparticles synthesized from jackfruit seeds have shown significant antibacterial properties against Escherichia coli and Salmonella typhimurium (21). Also, nanoparticles synthesized through Forsythia suspensa fruit juice extract have shown antibacterial activity against the most common food pathogens, including Listeria monocytogenes, Vibrio parahaemolyticus, Escherichia coli O157:H7, and Salmonella typhimurium (22). The use of plant extracts for the green synthesis of silver nanoparticles is relatively easy and cost-effective method for producing large quantities of silver nanoparticles tailored to the type of bacteria to be controlled in specific foods (23). In the same vein, studies have shown that nanoparticles with a diameter of less than 10 nanometers have a higher bactericidal capability and therefore exhibit better effectiveness in the final product (24).

Two main hypotheses have been proposed for the antimicrobial mechanism of silver nanoparticles: Hypothesis (1): Direct interaction of the nanoparticle with the cell membrane; silver nanoparticles adhere to the cell membrane through electrostatic attractions between the positive charges of the nanoparticles and the negative charges of the cells, or through the interaction of nanoparticles with sulfur and phosphorylated proteins present in the cell wall. In both cases, the interaction of silver nanoparticles with the cell membrane causes its partial dissolution (25 and 26). Hypothesis (2): Release of silver ions; silver nanoparticles enter the cell and lead to the release of silver ions and consequently, an increase in reactive oxygen species, which damages the enzymes involved in the redox process of cellular respiration and ultimately leads to cell death (27). Studies have shown that for most food microorganisms (both Gram-positive and Gram-negative), these two stages occur simultaneously or sequentially and are usually affected by the charge of the silver nanoparticle (28). Despite the acceptable antimicrobial effectiveness of silver nanoparticles for many microorganisms, bacterial resistance to silver nanoparticles has been reported for some microbes, for which mechanisms such as the downregulation of purines, chromosomal resistance genes, or plasmids with resistance genes have been proposed (29).

Food packaging is one of the important areas that has received special attention for the use of nanoparticles because of factors such as the need for protection against foodborne diseases, consumer demand for an increased shelf life of food products, development and diversity in antimicrobial food packaging, and many other reasons have increased the desire to use new methods. Therefore, in the past decade, many diverse and numerous studies have been conducted in this area, and various combinations of nanoparticles, especially silver nanoparticles, have been investigated and proposed for different food packaging (30). In the same vein, a group of studies has focused on the preparation of food packaging materials based on natural materials. The use of packaging materials of natural origin such as extracts from green tea containing various types of health-promoting bio-substances (phytochemicals) has long been of interest, but silver nanoparticles seem to have a stronger antimicrobial effect than these substances. Therefore, the effort to combine silver nanoparticles with phytochemicals has become a new approach in this field. From this perspective, recently, the potential migration of nanoparticles from the packaging matrix to the food and beverage matrix has been raised as an important issue in the field of food safety and consumer health. Studies have shown that there is a significant correlation between silver migration and time and temperature in food simulants such as water, 20% ethanol, n-hexane, and 4% acetic acid, which is as follows: water < 20% ethanol < n-hexane < 4% acetic acid. This order shows that in the composition of real foods exposed to silver nanoparticles, the order of silver migration occurs as follows: acidic food > fatty food > alcoholic food > aqueous food. In particular, silver dissolves rapidly in 4% acetic acid, and increasing the temperature increases solubility. Therefore, the amount of silver in acidic solutions is much higher than in other solutions. Since water and ethanol are polar solvents, the solubility of silver in them is relatively low. The solubility in n-hexane is also reported to be relatively high (31, 32).

Today, most studies focusing on the use of silver nanoparticles in food packaging are at the laboratory level, and their use is not permitted in most countries. Therefore, it is necessary to investigate the use of nanoparticles as part of food additives that enter food in various ways and to evaluate their impact on consumer health, as there are no long-term studies that have examined their side effects. The European Food Safety Authority (EFSA) Panel on Food Additives has stated that the acceptable migration limits for silver from nanoparticle-containing packaging are less than 0.05 mg/L for water and 0.05 mg/kg for food. The organization has also obliged food producers to use silver nanoparticle-based packaging for food products only by providing documentation containing assessments of migration, genotoxicity, absorption, distribution, and metabolism (33,34).

Nutritional Value of Silver Nanoparticles

The use of nanoparticles in the food industry to improve food safety and make healthy and fresh food available is increasingly gaining attention. On the other hand, these particles have been investigated for their effective delivery of nutrients due to their potential effects in enhancing thermal resistance, water solubility, and oral bioavailability (35). The use of nanoparticles to introduce various vitamins, minerals, prebiotics, probiotics, and peptides to an extent that ensures adequate absorption is a process that is undergoing animal and human studies as it significantly contributes to improving the health and nutritional status of individuals, especially vulnerable groups such as the elderly and children. Using nanoparticles to deliver nutrients and non-essential nutrients reliably and efficiently, while ensuring health, can prevent the occurrence and exacerbation of chronic diseases such as high blood lipids, bone and skeletal disorders, cardiovascular diseases, dental problems, mental disturbances, and the like (36).

In studies, the average level of human exposure to silver nanoparticles has been estimated to be approximately 70 to 90 grams per day (37). After eating foods containing silver nanoparticles, these materials come into direct contact with the mucous membranes of the mouth and esophagus, and therefore, the primary site of exposure to these particles is the mouth and gastrointestinal tract (38). One of the most important effects and limitations of the application and effectiveness of silver nanoparticles is the possibility of various side effects and toxicity in humans, which can endanger people's health (39).

The Impact of Silver Nanoparticles on Human Health

Growing research into the application of nanotechnology in food is leading to the broader use of nanoparticles in the food industry, resulting in increased human exposure to these materials. The effects of such exposure are being studied in numerous in vitro laboratory and animal studies across various fields worldwide

Studies have shown that the absorption of silver nanoparticles occurs through transcellular, paracellular, and phagocytic transport in the gastrointestinal epithelium. Nanoparticles that escape the absorption process reach the large intestine and can alter the composition or activity of the gut microbiota, thereby affecting the production and toxicity of bacterial metabolites (37). On the other hand, the physical and chemical changes of silver nanoparticles during gastrointestinal digestion can alter their toxicity effect, which is related to the specific characteristics of these particles and the differences between them and the close relationship between their physicochemical reactivity and bioavailability in the gastrointestinal tract (40). A group of recent studies has shown that silver nanoparticles, due to their oxidative properties, can pass through many biological membranes, including cell membranes, and by releasing silver ions, can affect intracellular activities, interfere with intracellular molecules, and lead to cytotoxicity, genotoxicity, and even cell death (41-43). Also, silver ions can increase oxidative stress processes within cells by activating reactive oxygen species and cause DNA damage, inducing apoptosis, and chromosomal abnormalities (44). The entry of silver nanoparticles into the bloodstream and crossing the blood-brain barrier of animals and humans has been investigated in several studies, and thus their involvement in some mental disorders has been controversial (45). Inflammation in various brain cells and other body cells, especially liver cells, is one of the issues that has been considered in studies (46).

The sum of studies on human cells shows that silver nanoparticles, depending on their size, shape, concentration, and carrier, have various effects that can adversely affect overall individual health. Therefore, more extensive and accurate studies are necessary to achieve a practical result.

DISCUSSION AND CONCLUSION

Nanotechnology, particularly silver nanoparticles, has opened a new and global gateway in the field of food and nutrition, offering a promising outlook for controlling the burden of foodborne diseases. For centuries, humans have been seeking a solution to eliminate microorganisms that contaminate various foods and cause foodborne infections in humans. Silver nanoparticles have attracted the attention of researchers in this field for over a decade and have shown remarkable results. Controlling a variety of the most important, potent, and common foodborne microbes using a wide and diverse range of silver nanoparticles in various food matrices has become possible in a significant and cost-effective manner. Moreover, the use of carriers extracted from natural compounds, especially plant-based foods, which contain various phytochemicals and antioxidants, facilitates the delivery and success of these nanoparticles. The application of silver nanoparticles in various types of food packaging has provided innovative approaches to making healthy and fresh food available. However, the ability of silver ions to migrate into food matrices has challenged food safety and hygiene, making it undeniable and highly necessary to conduct more accurate tests and studies and develop stricter standards. Therefore, conducting extensive research in the field of food safety and its effects on various aspects of human health should be on the agenda of researchers and food and health experts.

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