GREEN SYNTHESIZED METALLIC NANOPARTICLES AS PROSPECTIVE THERAPEUTICS IN FIGHT AGAINST LISTERIA MONOCYTOGENES

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Abstract: *Listeria monocytogenes* is a gram-positive facultative foodborne pathogen that causes a disease called human listeriosis. Elderly people, children, immunocompromised people, and pregnant women are most affected by listeriosis. Some strains of *Listeria* have developed resistance to several conventionally used antibiotics. Thus, the search for antibacterial agents against such emerging drug-resistant bacteria is currently an area of research worldwide. Metallic nanoparticles derived from various metals have been extensively investigated for their microbicidal properties. The outstanding bactericidal properties exhibited by these metallic nanoparticles have backed their merit as future antimicrobial agents. The present review aims to present an overview of listeriosis, available therapy against *Listeria,* and gaps in the existing anti-listerial treatment. Further, green synthesized metallic nanoparticles, their merits, and antimicrobial potential against *L.monocytogenes* have been summarized. The synthesis of nanoparticles using plant extracts has more benefits than any other nanoparticle synthesis method. This is because the method of green synthesis employs minimal steps, is eco-friendly, cost-effective, relatively safer, compatible with pharmaceutical applications, and easy to upscale. Many plants' secondary metabolites serve as reducing and stabilizing agents to synthesize these metallic nanoparticles. Several thus synthesized plant-mediated nanoparticles have exhibited good antibacterial activity against *L.monocytogenes*.

Keywords: Synthesis; listeriosis; nanoparticles; antimicrobial; *Listeria monocytogenes*.

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INTRODUCTION

Listeria monocytogenes(*L. monocytogenes*) is a gram-positive facultative anaerobic intracellular bacterium inhabits almost every (e.g., in water, soil, sewage, and food items like soft cheeses) zone(Gandhi & Chikindas, 2007, p. 1). *L. monocytogenes* can withstand harsh environmental conditions like desiccation, high salt concentration (up to 14%), a very acidic (4.3) to basic (9.4) pH, and a temperature gradient of 0 to 45°C(Bouymajane et al., 2021). Such properties of Listeria make it quite ubiquitous. Listeria abundantly grows on various foodstuffs, including dairy and meat products and surfaces of industrial food processing and packaging units (Hyden et al., 2016; Oloketuyi & Khan, 2017).*L. monocytogenes* causes listeriosis disease in human beings, characterized by septicaemia, gastroenteritis, spontaneous abortions, and central nervous system infections characterized by septicaemia, gastroenteritis, spontaneous abortions, and central nervous system infections such as meningitis, encephalitis, or both meningoencephalitis(Goldenberg & Thompson, 2003; Souza, Franceschini, Martinez, Ratti, & De Martinis, 2008).The high fatality rate of 20-30% associated with listeriosis owing to the cerebral damage caused by the bacteria makes it a risk to human health(Santos, Viala, Chambon, Esbelin, & Hebraud, 2019).The disease can be life-threatening, particularly in the case of pregnant women, newborns, elderly people, and or individuals who are immunocompromised, such as those who are already suffering from HIV or some respiratory infections(Bekondi et al., 2006; David & Cossart, 2017; Ferreira, Wiedmann, Teixeira, & Stasiewicz, 2014; Gandra et al., 2019; Liu et al., 2020; H. H. Yu, Song, Song, Lee, & Paik, 2019).The listeriosis disease may result in miscarriage or premature birth in pregnant women(ELEFTHERIOS MYLONAKIS, 2002; Lamont et al., 2011).Although infection and development of disease by Listeria is not much common, due to the high rate of mortality associated with the disease, the human listeriosis is considered one of the major foodborne illnesses, a fact that is well supported by World Health Organization (WHO) as well(WHO, 2018).

Development of Biofilm in *L. Monocytogenes* as a Factor for Drug Resistance

L. monocytogenes either exist as planktonic cells (or free-floating cells), form as planktonic cells (or free-floating cells), or form cell communities by attaching to a substrate. Cell communities adsorbed onto either biotic or abiotic surfaces and enclosed inside an extracellular polymeric substance (EPS) are known to be biofilms(O'Toole, 2001).The fact that *L.monocytogenes* is capable of forming biofilms complicates its control. Microorganisms form biofilms to resist extreme environmental conditions and trap nutrients(Poulsen, 1999).Compared to free-living cells, cells in the biofilms are relatively more resistant to drying, heat, salinity, acidic environments, food preservatives, and antimicrobials (Chen et al., 2019; Jolivet-Gougeon &

Bonnaure-Mallet, 2014; Pang, Wong, Chung, & Yuk, 2019; Xu, Lee, & Ahn, 2011). embedded cells from these toxic agents, thereby contributing to the development of resistance(J. W. COSTERTON, 1994; Song, Yu, Kim, Lee, & Paik, 2019).The penetration power of antimicrobials into the interior of a biofilm can be prevented by an extracellular matrix that increases the antimicrobial tolerance by 100–1000 folds compared to planktonic cells(Huang et al., 2019; Olsen, 2015).Further, enzymes produced by bacterial colonies in a biofilm may degrade antimicrobials. In addition to this, physiological changes in biofilm cells may also enhance resistance to membrane-perturbing or oxidizing compounds. The development of tolerance to variations in nutrient concentration is another factor that allows enhanced resistance in biofilms(Djordjevic, Wiedmann, & McLandsborough, 2002).Biofilm development is a five-step process that includes reversible or initial adsorption; irreversible attachment; proliferation of microcolonies by growth and division of bacteria; maturation of biofilm; and dispersion of cells to release free-floating bacteria(Davey & O'Toole G, 2000; McLandsborough, Rodriguez, Pérez-Conesa, & Weiss, 2006).Initially, the biofilm is attached to the surface, biotic or abiotic. The surface proteins in bacteria facilitate the adhesion to the surface. The extracellular DNA also regulates the early attachment of biofilm, forming the biofilm cellular matrix component, enabling bacteria to aggregate and create micro-colonies. The internalin protein synthesized by the inlL gene plays a crucial role in the adhesion of the bacterial cells to the surface. The microcolonies develop into the monolayer and then into themulti-layer colonies. The bacteria within the colonies are arranged as per the metabolic rate and aero tolerance. The formation of a multi-layer colony is the maturation stage of the biofilm. The biofilm is disrupted and detached from the surface while it is matured. Biofilm formation is dependent on several physiological, environmental, and biochemical factors. Cell-to-cell communication, temperature, nutrients, sugar level, salinity, pH, flow velocity, contact duration, and surface textures are important factors that determine the adsorption and formation of biofilms in bacteria (Crespo Tapia, den Besten, & Abee, 2018; da Silva & De Martinis, 2013; Dhowlaghar et al., 2018; Keeney, Trmcic, Zhu, Delaquis, & Wang, 2018; Simões, Simões, & Vieira, 2010; Valderrama & Cutter, 2013). *L. monocytogenes* can form biofilms in food processing environments (on abiotic surfaces), causing huge economic losses by contaminating food (F. Khan, Jeong, Park, Kim, & Kim, 2019; R. Li, Du, Yang, Liu, & Yousef, 2018).The ability of *L.monocytogenes* is the main reason for its stress resistance and persistence in food processing environments(Pagán, 2015).In L. monocytogenes, initial cell attachment to the substrate is mediated by flagellar motility (Lemon, Higgins, & Kolter, 2007; O'Neil, Marquis, & immunity, 2006; Todhanakasem & Young, 2008; Vatanyoopaisarn, Nazli, Dodd, Rees, & Waites, 2000).In fact, reduction in flagellar motility diminishes biofilm formation(Donlan, 2002).*L. monocytogene* genes used for flagella synthesis and motility Flagellin A (FlaA), Flagellar biosynthesis protein (fliP), Flagellar motor switch protein (fliG), Flagellar hook protein(flgE), Flagellar motor protein (motA), Flagellar motor protein(motB), Motility gene repressor (mogR) and Transcriptional regulatory protein (DegU) are involved in cell attachment during biofilm formation(Chang, Gu, Fischer, & McLandsborough, 2012; Chang, Gu, & McLandsborough, 2012; Gründling, Burrack, Bouwer, & Higgins, 2004; Williams, Joseph, Beier, Goebel, & Kuhn, 2005).Nature of the surface also plays a key role in cell attachment, as the loss in cell surface hydrophobicity decreases the adhesion of the bacterial cell to the substrate(Donlan, 2002).After cell attachment, biofilm formation is initiated and mediated by the production of molecules used for cell-to-cell communication. These molecules bring changes in gene expression within the bacterial communities (Richards & Melander, 2009; Simões et al., 2010).The accessory gene regulator (Agr) quorum sensing genes, agrA, agrB and agrD, play important roles in biofilm development by *L. monocytogenes(Chang, Gu, Fischer, et al., 2012; C. U. Riedel et al., 2009).*Mutations in agrD have been associated with a lower tendency to form biofilms(Christian U Riedel et al., 2009).In addition, the key transcriptional activator of virulence genes PrfA(Positive regulatory factor A and a class I heat-shock response protein involved in stress resistance in *L.monocytogenes* plays a major role in the formation of biofilm(Lemon, Freitag, & Kolter, 2010).

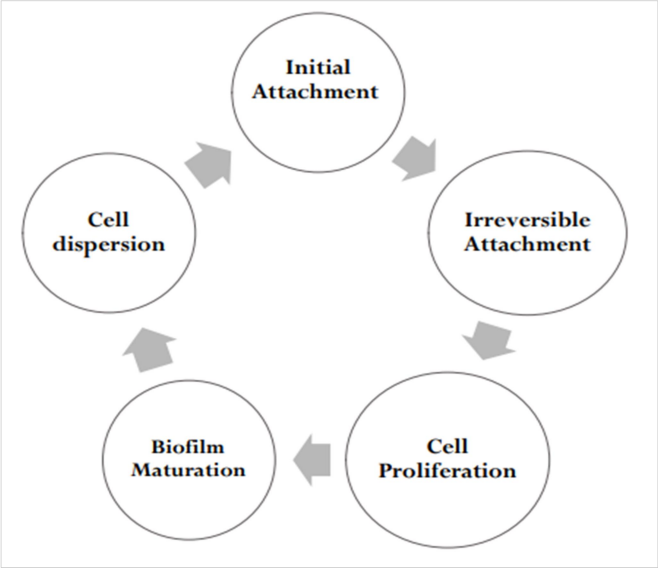

Figure 1.Biofilm formation and development steps in L. monocytogenes

Available chemotherapies against human listeriosis and antibiotic resistance

Ampicillin and Penicillin alone or in combination with gentamicin can be used to treat human listeriosis (Alonso-Hernando, Prieto, García-Fernández, Alonso-Calleja, & Capita, 2012; Dortet et al., 2011).The majority of antimicrobial drugs target specific bacterial cell properties such as synthesis of a bacterial cell wall, membrane of the bacteria, specific protein synthesis stages, nucleic acid (DNA and RNA) synthesis, metabolism of folic acid, and based on the drug; these might cause the death of bacterial cell or inhibition of growth(Wright, 2010).B-lactam antibiotics like Penicillin and ampicillin inhibit cell wall synthesis by targeting penicillin-binding sites of gram-positive bacteria. Other antibiotics, such as vancomycin, are applied to bacteremia treatment, and erythromycin is used to treat pregnant women with listeriosis(Alonso-Hernando et al., 2012).Antibiotics such as chloramphenicol, tetracycline, rifampicin, and fluoroquinolones are also used for treating human listeriosis (Allerberger, Wagner, & Infection, 2010; Conter et al., 2009; D. Walsh1, 2001).Penicillin or ampicillin, combined with aminoglycosides, is currently the most popular therapeutic option for treating listeriosis(W. Yu et al., 2021).Fluoroquinolones inhibit DNA synthesis by acting on topoisomerase II (DNA gyrase) or topoisomerase IV enzymes. Similarly, rifampicin inhibits RNA synthesis by affecting DNA-dependent RNA polymerase. Tetracycline, streptomycin, erythromycin, and chloramphenicol abrogate protein synthesis in bacteria. Streptomycin disrupts translation by binding to 30S ribosome, and tetracycline inhibits aminoacyl t-RNA binding to 30S ribosome, blocking polypeptide synthesis. In the same way, erythromycin affects protein synthesis in bacteria by stimulating peptidyl-tRNA dissociation from the 50 S ribosomes during elongation, whereas chloramphenicol inhibits the elongation step of the 50S ribosome (Etebu & Arikekpar, 2016; Khan*, 2018; Peach, Bray, Winslow, Linington, & Linington, 2013).However, despite the availability of standard antibiotics, control of *L. monocytogenes* infections is becoming difficult as the bacteria have developed resistance against many antimicrobials (Alonso-Hernando et al., 2012; Gomez et al., 2014; Zhang et al., 2007).Antibiotic misuse and abuse in humans and animals significantly contribute to antibiotic resistance in foodborne bacteria like *L. monocytogenes*. The use of antibiotics in low-dose or incomplete treatment processes is the primary cause of widespread antimicrobial resistance. Some foodborne pathogens are resistant to antibiotics due to their entire physiology, whereas others gain drug resistancedue to mutations or other genetic alterations. Bacterial resistance can be classified into intrinsic resistance (naturally occurring) and acquired resistance (acquired by chromosomal gene alterations and horizontal gene transfer)(Blair, Webber, Baylay, Ogbolu, & Piddock, 2015).The intrinsic structural or functional features of the microbe produce intrinsic resistance. In *L. monocytogenes*, inherent resistance may develop due to the lack of affinity of an antimicrobial drug for its target inside the bacterial cell. This is the case with two β-lactam-based compounds, broad-spectrum cephalosporins, and monobactams. Low affinities of these drugs cause inherent resistance for Penicillin-Binding Protein 3 (PBP3), an enzyme that catalyzes the final stage in cell wall synthesis. Despite a few intrinsic resistance mechanisms in Listeria species, most antimicrobial resistance in this bacteria is due to acquired mechanisms via mobile genetic components such as self-transferable plasmids and conjugative transposons(Charpentier, Gerbaud, & Courvalin, 1999; Godreuil et al., 2003).DNA elements that can migrate between genomes or from one genome to another are mobile genetic elements. In Listeria species, transposons and plasmids are two of the most frequently identified mobile genetic components. They have been recognized as one of the most fundamental driving forces underlying the species' evolution(Kuenne et al., 2013).Transposons have a crucial function in providing bacterial populations with resistant characteristics. Conjugation is genetic material being transferred from one bacterial cell to another by direct cell-to-cell contact or a bridge-like connection. One incidence of such transmission is conjugation between streptomycin-resistant *L.monocytogenes* LM35(donor) and streptomycin-sensitive *L.monocytogenes* LM65 (recipient strain)(Purwati, Radu, Hassan, Ling, & Rahim, 2001).Through conjugation, plasmid pIP501 was transferred from *Streptococcus agalactiae* to *L. monocytogenes*(Perez-Diaz, Vicente, & Baquero, 1982).Chloramphenicol, macrolides, lincosamide, and streptogramin resistance are all imparted on this plasmid. Other plasmids, such as pAM1 from *Streptococcus faecalis*, impart erythromycin resistance(Flamm, Hinrichs, Thomashow, & immunity, 1984),and pIP823 from *E. faecalis* and *E. coli* that dissemination of trimethoprim resistance can be transmitted to *L. monocytogenes*(Charpentier et al., 1999).Various species of Listeria have acquired target gene mutations and resistance-encoding genes on mobile genetic elements because of selective pressure exerted in the past following the use of different antimicrobial drugs(Morvan et al., 2010).Transmission of drug resistance genes across Listeria species and other bacteria, like Streptococcus and Enterococcus, has also been demonstrated(Lungu et al., 2011).The presence of self-transferable plasmids or Enterococcus and Streptococcus originated conjugative transposons may have contributed to the development of multidrug resistance in *L. monocytogenes*(Doucet-Populaire et al., 1991; Poyart-Salmeron, Carlier, Trieu-Cuot, Courvalin, & Courtieu, 1990).Several studies have presented resistance in Listeria strains. *L. innocua*, *L.monocytogenes*, *L. welshimeri*, *L. ivanovii* , *L. grayi* and *L. seeligeri* were observed to be moderately resistant to carbapenems, aminoglycosides, cefoperazone, chloramphenicol, macrolides, cefotiam, first- and second-generation cephalosporins (cefazolin, cefaclor, cefaclor, and loracarbef),glycopeptides,dalfopristin/quinupristin,lincosamides, penicillins (except oxacillin), oxacillin) and tetracyclines, although natural resistance between members of the genus(Troxler et al., 2000).Listeria strains isolated from food and clinical samples have shown antibiotic resistance to erythromycin, gentamicin, kanamycin, rifampin, streptomycin, sulfamethoxazole, and tetracycline (F. Khan et al., 2019; Kumar, 2016).*L. monocytogenes* was also discovered to be naturally resistant to fosfomycin and fusidic acid(Troxler et al., 2000).On the other hand, efflux pumps (EPS) are linked to *L. monocytogenes* antibiotic resistance(Navratilova et al., 2004).E.P.S are membrane proteins found in Gram-positive and Gram-negative bacteria that aid in detoxifying cells from within, including antibiotics, to the outside environment(Lungu et al., 2011).Efflux pumps transport various chemically and structurally different substrate molecules from the bacterial cell to the extracellular matrix, including antibiotics(Piddock, 2006).The five families of bacterial EPS are the ATP-binding cassette (ABC) superfamily, the multidrug and toxic compound extrusion family (MATE),

the major facilitator superfamily (MFS), and the small multidrug resistance (SMR) family, and the resistance nodulation division superfamily(RND)(X.-Z. Li & Nikaido, 2004).These systems employ the proton motive force as an energy source, except ABC transporters, which use direct ATP hydrolysis to drive substrate transport(Livermore, 2003).In recent years, several efflux pumps have been found in *L. monocytogenes*. CadAC was the first efflux pump found in *L. monocytogenes*. Shortly after, multidrug resistance Listeria (MdrL) was discovered. An MFS efflux pump was found in *L.monocytogenes*, which helped detoxify bacterial cells by exporting cefotaxime, ethidium bromide, heavy metals, and macrolides out of the cell(Lismond et al., 2008).MdrL's significance in *L. monocytogenes'* adaptation to benzalkonium chloride B.C. has been described in various research studies(Mereghetti, Quentin, Marquet-Van Der Mee, Audurier, & Microbiology, 2000; Tamburro et al., 2015).MdrT and MdrM are two Listeria-coded discharge pumps nearly identical to the quaternary ammonium compounds QacA of *Staphylococcus aureus*. Both major facilitator superfamily MFS efflux pumps confer Cholic acid resistance(Crimmins et al., 2008; Zeevi et al., 2013).MrdT and MdrM also play a role in bacterial reproduction in the cytosol of infected cells by secreting cyclic-di-AMP(c-di-AMP), which stimulates the manufacture of type I interferons, including beta interferon(IFN-β), promote *L. monocytogenes* virulence(Schwartz et al., 2012).In *L. monocytogenes*, two efflux pumps that confer fluoroquinolone resistance have been identified: Lde and FepA. The Lde gene encodes the former, which results in a 12-segment transmembrane spanning putative MFS efflux pump that shares 44 percent of its amino acid sequence with *S. pneumonia*'s PmrA. The Listeria drug efflux(Lde) pump detoxifies fluoroquinolone antibiotics(Mata, Baquero, & Perez-Diaz, 2000).The research findings suggest that this pump confers ciprofloxacin and norfloxacin resistance and decreases sensitivity to the dyes acridine orange and ethidium bromide(Godreuil et al., 2003; Marquez et al., 2014).Other research has revealed that Lde may be involved in B.C. resistance(Romanova, Wolffs, Brovko, Griffiths, & microbiology, 2006).Lde interacts with excretory transporters such as eukaryotic multidrug resistance-related proteins (MRPs) in *L.monocytogenes*-infected J774 macrophages and is the substrate for both ciprofloxacin pumps. The expression of Lde and MRP transporters has distinct but additive negative effects on ciprofloxacin (common substrate) activity. The addition of transport inhibitors allows restoration of the activity of ciprofloxacin to an extent essentially commensurate with the increases of (i) its cellular accumulation (through modulation of the MRP activity) and (ii) it's antibacterial potency (through impairment of Lde)(Lismond et al., 2008).In addition, *L. monocytogenes* in vivo-induced pathogenic factor hexose phosphate transporter Hpt facilitates phosphomycin uptake into *L. monocytogenes*, imparting a resistant phenotype in vitro. Because the bacterium is resistant in vitro yet vulnerable to the antibiotic in vivo, generating an in vitro-in vivo antibacterial paradox(X.-Z. Li & Nikaido, 2004; Scortti et al., 2006).Further, overexpression of FepA, an extrusion pump for numerous medicines and hazardous substances, is linked to fluoroquinolone resistance in *L. monocytogenes*. Single-point mutations in the FepA transcription factor fepR, which belongs to the TetR family, have been demonstrated to cause frame shift mutations, resulting in inactive truncated proteins with premature stop codons. This single point mutation produced overexpression of fepA, which conferred resistance to ciprofloxacin, ethidium bromide, and norfloxacin, supporting the role of Fluoroquinolone Efflux Protein Regulator (FepR)as a local regulator of Fluoroquinolone Efflux Protein A (FepA)(Guérin, Galimand, Tuambilangana, Courvalin, & Cattoir, 2014).AnrB function was discovered through non-polar deletion mutations in the lmo2115 gene, and the absence of this multidrug transporter enhanced vulnerability to bacitracin, -lactams, galidermin, and nisin(Collins et al., 2010).efflux-multidrug resistanceE (EmrE) (324 bp), a new estimated discharge pump found in *L. monocytogenes*, was reported in 2015(Kovacevic et al., 2016).The efflux-multidrug resistance E(EmrE) deletion mutant increased sensitivity to benzalkonium chloride(B.C.) and quaternary ammonium compounds(QACs)-based disinfectants, but not to acriflavine, chloramphenicol, ciprofloxacin, erythromycin, gentamicin, tetracycline, or triclosan MICs(Kovacevic et al., 2016).Membrane fluidity can also affect *L.monocytogenes* antibacterial resistance. The susceptibility of *L.monocytogenes* to antibacterial drugs was altered when the lipid content of the bacterial membrane was altered by growing in the presence of extra fatty acids. *L. monocytogenes* cells cultured with carbon chain fatty acids (C14: 0 or C18: 0) have faster phase transitions and higher antibiotic levels than cells cultured with carbon chain fatty acids (C18: 1)(Juneja & Davidson, 1993).Branched-chain fatty acids are abundant in *L. monocytogenes*. It is possible to maintain consistent membrane fluidity at low temperatures by adding fatty acids with lower phase transition temperatures(Kapoor, Saigal, & Elongavan, 2017).The fatty acid composition of the membrane has the most significant impact on the fluidity of the lipid bilayer. Changes in fatty acid chain length or the production of branched-chain fatty acids are expected to cause changes in *L. monocytogenes* membrane fluidity(Yoon, Lee, Lee, Kim, & Choi, 2015).The primary types of membrane fatty acids, branched-chain fatty acids, have been identified as significant factors of *L.monocytogenes* resistance.Lastly, structural or conformational modification(s) in target molecules that antibiotics bind inside a bacterial cell can induce resistance. Bacterial resistance is most commonly caused by a molecular alteration of the bacterial surface that changes the nature of the drug-target interaction(Ndieyira et al., 2017).Because an antibiotic's interaction with a target molecule is usually quite precise, even the tiniest alteration in the target molecule can significantly impact the antibiotic's binding.Antibiotics are meant to attack and destroy specific components of the bacterium; however, resistant bacteria can alter the target's appearance, rendering the antibiotic ineffective. As a result, bacteria can evolve antibiotic resistance by changing the medication's target adheres and works(Kapoor et al., 2017).For instance, if the structure of PBPs in bacteria changes, Penicillin will no longer be able to bind to it and will be rendered ineffective.

Nanoparticles as an alternative to overcome multidrug resistance in *L. monocytogenes*

Antibiotic resistance, especially multi-resistance, is a public health issue since it might result in treatment failure. Despite being susceptible to a wide range of antibiotics, *L. monocytogenes* is resistant to first-generation Quinolones, Fosfomycin, Monobactams, and broad-spectrum Cephalosporins(Hof & Microbiology, 2003).Antibiotic resistance has been seen in several Listeria strains isolated from food and clinical samples. Thus, alternative Therapeutics that can either complement or replace antibiotics is highly desired to resolve the issue of multidrug

resistance. In this regard, several nanoparticles have been known to exhibit vigorous antibacterial activity and, therefore, may aid in alleviating the problem of bacterial resistance in *L.monocytogenes*.

Therefore, the development of antibacterial resistance against nanoparticles is less when compared to conventional antibiotics.Nanoparticles are materials whose three-dimensional size lies in the nanometre range (1-100 nm) (1-100 nm). These minuscule particles offer vast applications in almost every field of science(Laurent et al., 2008).Nanoparticles are used in a variety of biological and physicochemical applications. They could be employed in biomedical research for medication delivery, biosensing, bioimaging, and biomolecule recognition. Because of their antimicrobial capabilities, such nanoparticles are used in various daily items such as cosmetics, toothpaste, deodorants, water purification systems, and humidifiers(Baker, Pradhan, Paktis, Pochan, & Shah, 2005).They play a vital role in agricultural technology, such as detecting and eradicating plant diseases and reducing nutrient leaching to boost crop output. They are also utilized to store energy in solar and oxide batteries. Nano medicine is a burgeoning topic of study with many perspectives on enhancingthe diagnosis and treatment of human illnesses(Fadeel & Garcia-Bennett, 2010).Nanoparticles are used as fluorescent biological markers(Fadeel & Garcia-Bennett, 2010),geneanddrugdeliveryfactors(Tian et al., 2008),pathogenbio-detection(Pantarotto et al., 2003),tissueengineering(De La Isla et al., 2003),tumourdestructionbyheating (hyperthermia)(Yoshida & Kobayashi, 1999),MRIcontrastenhancement(Weissleder et al., 1990),and phagokinetic studies(Parak et al., 2002).There are different synthetic routes through which nanoparticles can be synthesized, amongst which the most common are physical, chemical, and biosynthetic routes. Chemical-based methods are generally costly and involve dangerous and poisonous compounds that pose various environmental hazards(Nath, Banerjee, & pharmacology, 2013).On the other hand, nanoparticle preparation using the biosynthetic technique is a biocompatible, safe, and environmentally friendly method of synthesizing nanoparticles utilizing plants and microbes(Razavi et al., 2015)Fungi, algae, bacteria, and plants, among other things, can be used to carry out this synthesis. Plant components like leaves, fruits, roots, stems, and seeds have been utilized to synthesize different nanoparticles due to phytochemicals in their extract, which function as a stabilizing and reducing agent(Narayanan, Sakthivel, & science, 2011).Nanoparticles vary in their morphology and size depending on their chemical properties. Nanoparticles can be carbon-based, where the two most common forms are fullerenes and carbon nanotubes. Nanoparticles can also be derived from inorganic non-metallic solids named ceramic nanoparticles. The appearance of the nanoparticle can be amorphous, polycrystalline, dense, porous, or hollow. Semiconductor nanoparticles are also extremely researched as they possess intermediate properties between metals and non-metals and can revolutionize the field of photo catalysis, electronic devices, and photo-optics. Next, the common nanoparticles that have been extensively investigated in the biomedical field are polymeric nanoparticles. These nanoparticles are synthesized from polymeric organic compounds and can be observed most commonly as Nano spheres or Nano capsules. Polymeric nanoparticles are mostpopular for their role in drug or vaccine delivery and or as gene therapy vehicles. Lipid-based nanoparticles are also fairly common and are used the same as polymeric nanoparticles to carry drugs or vaccines to a defined target site. Last in the category are metallic and metallic oxide nanoparticles. Metal and metal oxide nanoparticles are studied as antimicrobial, ant parasitic, anticancer, and antifungal agents(Gahlawat & Choudhury, 2019).Metallic nanoparticles such as zinc and zinc oxide nanoparticles, titanium nanoparticles, copper and copper oxide nanoparticles, silver nanoparticles, , and aluminium nanoparticles have been shown to possess antimicrobial action against various bacteria, implying that metal and metaloxide N.P.s can be utilized to kill microbes and prevent biofilm development(Kanematsu, Ikigai, & Yoshitake, 2009; Sadiq, Chowdhury, Chandrasekaran, & Mukherjee, 2009).Gold nanoparticles (AuNPs), silver nanoparticles (AgNPs), zinc oxide nanoparticles (ZnONPs), copper oxide nanoparticles (CuONPs), and iron oxide nanoparticles (Fe_3O_4NPs) are examples of N.P.s that can prevent biofilm formation and growth (Chifiriuc et al., 2012; Hajipour et al., 2012; Markowska, Grudniak, & Wolska, 2013; Miao et al., 2016; Q. Yu et al., 2016).Different nanoparticles vary in their antibacterial activities because of their different mechanism of action against the target microbe. The antibacterial actions of nanoparticles against the target bacterial cell are mediated by damage to the bacterial cell membrane, the generation of reactive oxygen species (ROS), penetration of the bacterial cell membrane, and induction of intracellular antibacterial effects(Wang, Hu, & Shao, 2017).Their smaller size, which results in a high surface area, helps metallic nanoparticles improve antimicrobial activity.

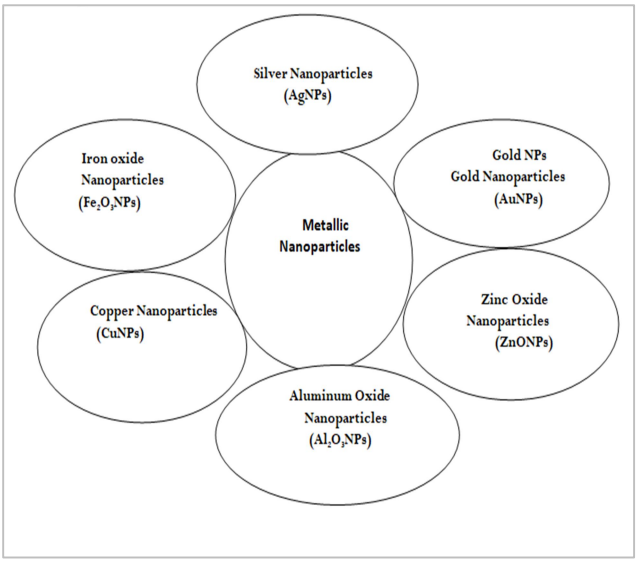

Figure 2.Metallic nanoparticles

Green Synthesized Metallic and Metallic Oxide Nanoparticles against *L.monocytogenes*

Of late, bio-fabrication of metallic nanoparticles has been considerably promoted as it is eco-friendly and thus avoids the use of chemicals that can be extremely toxic and or recalcitrant.Green synthesis of nanoparticles is an environmentally friendly research area in which plants, bacteria, and fungus are involved. It is preferable to other physicochemical methods. It is economical, eco-friendly, can be scaled up easily, and produces highly stable nanoparticles. In addition, applying high pressure and high temperatureand using toxic chemicals are not required during the process(Gokulakrishnan, Ravikumar, & Raj, 2012).It is an environmentally benign process that uses proteins, enzymes, polysaccharides, vitamins, and amino acids found in extracts to reduce metal ions. Gold, silver, iron, palladium, copper, zinc, and platinum nanoparticles have been prepared using various plant extracts from whole plants or plant leaves, roots, stems, bark, flowers, etc. Using plant extracts, bio fabricated AuNPs, AgNPs, Fe_3O_4NPs, and ZnONPs have displayed powerful inhibitory properties against innumerable pathogenic bacterial species. In the following sections, we specifically discuss the inhibitory potential of various metallic nanoparticles against *L. monocytogenes*.

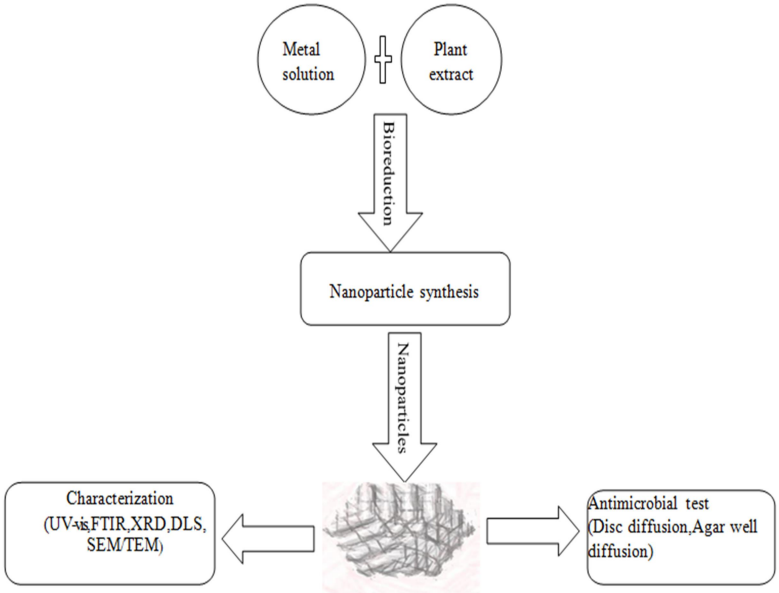

Figure 3. Green synthesis of nanoparticles

Silver nanoparticles (AgNPs): AgNPs are already a focus of extensive research since they have many applications in biological and other non-biological fields(Gokulakrishnan et al., 2012).They are also referred to as one of the strongest antimicrobial agents. The antimicrobial activity of AgNPs against microorganisms depends on their size and morphology and is largely mediated by the production of ROS. Flow cytometric detection has shown that AgNPs enhanced ROS generation by 85.68% and 89.36% in E. coli and S. aureus, respectively(B. Das et al., 2017).It is believed that elevated intracellular ROS levels contribute to the oxidation of cellular macromolecules like DNA and proteins(B. Das et al., 2017).As more and more physiological damage is imparted to the bacterial cell, the

cell loses its homeostasis. It becomes genetically unstable, ultimately leading to metabolic arrest and cell death. AgNPs also impact signal transduction in bacterial cells, preventing biofilm formation. AgNPs also alter membrane permeability leading to loss of membrane potential of the bacterial cell membrane. Once inside the bacterial cell, AgNPs get converted into silver ions. These silver ions interact rapidly with cell membrane proteins and DNA after conversion, and abrupt DNA replicates. Silver ions interact rapidly with cell membrane proteins and DNA and abrupt DNA replication. Table 1 below summarizes the antimicrobial property of different green synthesized silver nanoparticles against *L.monocytogenes*.

Table 1. Green synthesized silver nanoparticles (AgNPs) against L. monocytogenes

S. No.	Plant used	MNPs	Size (nm)	*L. monocytogenes* strain	MIC	Mechanism of action	Ref.
1	*Berberis vulgaris*	AgNPs	75.7 ± 17.1	*Listeria monocytogenes CCM 4699*	2 mM	-	(Salayova et al., 2021)
2	*Brassica nigra*	AgNPs	14.7 ± 7.9	*Listeria monocytogenes CCM 4699*	2 mM	-	(Salayova et al., 2021)
3	*Capsella bursa-pastoris leaves*	AgNPs	16.2 ± 8.4	*Listeria monocytogenes CCM 4699*	2 mM	-	(Salayova et al., 2021)
4	*Lavandula angustifolia leaves*	AgNPs	37.8 ± 10.7	*Listeria monocytogenesCCM 4699*	2 mM	-	(Salayova et al., 2021)
5	*Origanum vulgare leaves*	AgNPs	46.1 ± 19.7	*Listeria monocytogenes CCM 4699*	2 mM	-	(Salayova et al., 2021)
6	*Dicranum majus (Dm) Turner*	AgNPs	268.6±8.86	*Listeria monocytogenes (ATCC 7644)*	0.078 µg mL^{-1}	Cleave plasmid DNA.	(O. Tonguc Yayintasa*, 2021)
7	*Punica granatum*	AgNPs	20	*Listeria monocytogenes (ATCC 19114)*	15.62 mg mL^{-1}	.	(A. A. Khan, Alanazi, Alsaif, Wani, & Bhat, 2021)
8	*Securidaca inappendiculata*	AgNPs	10–15	*Listeria monocytogenes F2365,*	2 µg mL^{-1}	-	(T. J. Jayeoye et al., 2021)
9	*Chromolaena odorata*	AgNPs	20- 25	*Listeria monocytogenes F2365*	4 µg mL^{-1}	-	(Jayeoye, Eze, Olatunde, Benjakul, & Rujiralai, 2021)
10	*Ephedra sinica*	AgNPs	10	*L. monocytogenes(ATCC19118)*	6.25 mg mL^{-1}	-	(Bahman Fazeli-Nasab 1* 2021)
11	*Citrus Sinensis*	AgNPs	14-60	*L. monocytogenes (MTCC 657)*	34.6/46.8 µg mL^{-1}	Pit formation in the bacterial cell wall and membrane leads to cellular component leakage (proteins and reducing sugars), bacterial enzyme deactivation, and respiratory enzyme deactivation, contributing to bacterial cell death.	(Sinha, Manjhi, & Nanotechnology-Asia, 2020)
12	*Punica granatum*	AgNPs	14-60	*L. monocytogenes (MTCC 657)*	36.0/52.0 µg mL^{-1}	Pit formation in the bacterial cell wall and membrane leads to cellular component leakage, leading to bacterial cell death.	(Sinha et al., 2020)
13	*Carya illinoinensis*	AgNPs	12–30	*L. monocytogenes (ATCC 7644)*	64 µg mL^{-1}	-	(bakht Dalir, Djahaniani, Nabati, & Hekmati, 2020)
14	*Phyla dulcis*	AgNPs	63-76	*L. monocytogenes (ATCC 19115)*	1.88 x 10-4M	-	(Laura Carson et al., 2020)
15	*Garcinia mangostana*	AgNPs	93.50	*L. monocytogenes ATCC 19114*	5 mg mL^{-1}	-	(Alkhuriji et al., 2020)
16	*salvia officinalis*	AgNPs	30 – 50	*L. monocytogenes (ATCC 7644)*	6.25 µg mL^{-1}	-	(Yanuar et al., 2020)

17	*Z. officinale*	AgNPs	25-30	*Listeria monocytogenes*	0.625 µg mL^{-1}	-	(Mohammed, Lawrance, Sampath, Sunderam, & Madhavan, 2020)
18	*C. amada*	AgNPs	25-30	*Listeria monocytogenes*	0.625 µg mL^{-1}	-	(Mohammed et al., 2020)
19	*Ocimum campechianum*	AgNPs	5-50	*L. monocytogenes*		-	(Manjula Bomma1, 2020)
20	*Citrus Sinensis*	AgNPs	14-60	*L. monocytogenes (MTCC 657)*	34.6 µg mL^{-1}	Pit formation in the bacterial cell wall and membrane results in cellular component leakage and bacterial enzyme deactivation.	(Manjhi, 2020)
21	*Punica granatum*	AgNPs	14-60	*L. monocytogenes (MTCC 657)*	36.0 µg mL^{-1}	-	(Manjhi, 2020)
22	*Carya illinoinensis*	AgNPs	12–30	*Listeria monocytogenes (ATCC 7644)*	64 µg mL^{-1}	-	(Javan Bakht Dalir, Djahaniani, Nabati, & Hekmati, 2020)
23	*Phyla dulcis Trev. (verbenaceae)*	AgNPs	63-76	*Listeria monocytogenes (4b; ATCC 19115)*	1.88 · 10-4M	-	(L. Carson et al., 2020)
24	*Madhuca latifoliaL.*	AgNPs	2–30	*L. Monocytogenes*		-	(Biswal & Misra, 2020)
25	*amarix nilotica*	AgNPs	93–121	*Listeria monocytogenes ATCC 19114*	16 mg mL^{-1}	Excessive ROS production induces cell death.	(Nasser A. Al-Shabib et al., 2020)
26	*Stachys lavandulifolia*	AgNPs	20–40	*Listeria monocytogenes (ATCC No. 13932)*	4± 0b mg mL^{-1}	-	(Zangeneh, Joshani, Zangeneh, & Miri, 2019)
27	*Morus alba L.*	AgNPs	150	*L. monocytogenes ATCC 19115*	5000 µg mL^{-1}	-	(Yordshahi, 2019)
28	*Adiantum lunulatum Burm.f.*	AgNPs	28±2	*L. monocytogenesMTCCCode657*	25µg mL^{-1}	-	(Chatterjee, Khatua, Acharya, & Sarkar, 2019)
29	*Forsythia suspense*	AgNPs	47.3±2.6	*L. monocytogenes*	1.25 mg mL^{-1}	-	(Du, Hu, Yu, et al., 2019)
30	*Angelia keiskei*	AgNPs	130.1±2.1	*L. monocytogenes*	12.5 µg mL^{-1}	Damage the membrane integrity and induce the release of nucleic acids from the cells, thereby disrupting cell reproduction	(Du, Hu, Dong, et al., 2019)
31	*Fritillaria*	AgNPs	10	*L. monocytogenesATCCNo.13932*	8 mg mL^{-1}	-	(Hemmati et al., 2019)
32	*Vitis vinifera*	AgNPs	3-14	*L. monocytogenes (ATCC35152)*	100 µg mL^{-1}	-	(Soto et al., 2019)
33	Orange residues	AgNPs	5-50	*L. monocytogenes (ATCC35152)*	100 µg mL^{-1}	-	(Soto et al., 2019)
34	*Ananas comosus*	AgNPs	-	*L. monocytogenes ATCC 19111*	50 µg mL^{-1}	-	(G. Das, Patra, Debnath, Ansari, & Shin, 2019)
35	*Fumaria officinalis L.*	AgNPs	20 ± 1-18 ± 1	*Listeria monocytogenes ATCC 15313*		-	(Milorad et al., 2019)
36	*Ceriops decandra*	AgNPs	28	*Listeria monocytogenesATCC® 19111™ (MTCC 657)*	62.77±11.74 µg mL^{-1}	-	(Gajendra Nath, Joy, Somanjana, Soumitra, & Krishnendu, 2019)
37	*Verbena officinalis*	AgNP	42.57 ±	*Listeria monocytogenes (1298)*	1.25 mg mL^{-}	-	(Narjes Sanchooli1*

		s	5.34		$^{1-1}$		1 2018)
38	*Eucomis autumnalis*	AgNPs	112	*Listeria monocytogenes (ATCC 19111)*	0.06 mg mL^{-1}	-	(Lediga, Malatjie, Olivier, Ndinteh, & van Vuuren, 2018)
39	*Sclerocarya birrea*	AgNPs	56	*Listeria monocytogenes (ATCC 19111)*	0.03 mg mL^{-1}	-	(Lediga et al., 2018)
40	turmeric powder	AgNPs	18±0.5	*L. monocytogenes*	6 µg mL^{-1}	Leakage of bacterial internal contents due to disruption of the bacterial cell wall and cell membrane permeability.	(Alsammarraie et al., 2018)
41	*Verbena officinalis*	AgNPs	42.57	*L. monocytogenes*	0.62 mg mL^{-1}	-	(Sanchooli, Saeidi, Barani, & Sanchooli, 2018) ,
42	*Zea mays*	AgNPs	45.26	*Listeria monocytogenes ATCC 19115*	25 µg mL^{-1}		(Patra & Baek, 2017)
43	*Cymbopogon citratus*	AgNPs	45 ± 1.8	*L. monocytogenes (MTCC 1143)*	40 ± 1.0 µg mL^{-1}	-	(Pandit, Rai, & Santos, 2017)
44	*Jatropha curcas*	AgNPs	43.67	*L. monocytogenes*	0.01 mg mL^{-1}	Membrane pits,intracellular AgNPs accumulation and cell damage in treated cells	(N. Chauhan, A. K. Tyagi, P. Kumar, & A. J. F. i. m. Malik, 2016)
45	*Cucurbita pepo* root	AgNPs	5–40	*Listeria monocy-togenes (KCCM 40307)-*		-	(Krishnaraj, Ji, Harper, & Yun, 2016)
46	*Jatropha curcas*	AgNPs	50–100	*Listeria monocytogenes (SCOTT-A)*	0.010 mg mL^{-1}	-	(N. Chauhan, A. K. Tyagi, P. Kumar, & A. Malik, 2016)
47	*Euphorbia amygdaloides*	AgNPs	7–20	*Listeria monocytogenes*		-	(Cicek, Gungor, Adiguzel, & Nadaroglu, 2015)
48	*Acacia leucophloea*	AgNPs	17–29	*Listeria monocytogenes (MTCC 657)*		-	(K. Murugan, B. Senthilkumar, D. Senbagam, & S. Al-Sohaibani, 2014)
49	oak bark	AgNPs		*Listeria monocytogenes ATCC 19111*		-	
50	*juniper berries*	AgNPs		*Listeria monocytogenes ATCC 19111*		-	(Judita Puišo1, 2014)
51	*Acacia leucophloea*	AgNPs	17–29	*L. monocytogenes (MTCC657)*	5µg mL^{-1}		(K. Murugan, B. Senthilkumar, D. Senbagam, & S. J. I. J. o. N. Al-Sohaibani, 2014)
52	*Zingiber officinale*	AgNPs	15	*L. monocytogenes*	20 ± 12.8 µg mL^{-1}		(Velmurugan et al., 2014)
53	*Fumaria officinalis L.*	AgNPs	18-20	*L.monocytogenesATCC15313*	0.5 mg mL^{-1}		(Annamalai et al., 2013)
54	*Olea europaea*	AgNPs	10	*L.monocytogenes*	-		(Awwad, Salem, Abdeen, & Nanotechnology, 2012)
55	*Sesuvium portulacastrum L. Callus*	AgNPs	5-20	*L. monocytogenes*	-	-	(Nabikhan, Kandasamy, Raj, Alikunhi, & Biointerfaces, 2010)

"-" indicates not mentioned; MNPs= metallic nanoparticles

Gold nanoparticles (AuNPs): Gold has been used for treating many types of diseases such as smallpox, syphilis, measles, and skin ulcers in ancient cultures in different countries like India, Egypt, and China. Because of their smaller size, AuNPs have other properties than bulk gold. AuNPs have been used to deliver drugs into cells for a long time.The molecules of drugs are first attached to the surface of AuNPs, followed by insertion into the cells using different techniques like gene guns or particle ingestion. Then, molecules detach themselves from AuNPs inside the cells. AuNPs are also used to deliver peptides, proteins, DNA, or RNA(S. Tikariha, 2012).AuNPs can be used alone or combined with some other bioactive compounds or drugs or pathogen-specific antibodies regarding their antimicrobial property. Better bactericidal results have been observed in the case of conjugated AuNPs.

Nonetheless, AuNPs exert variable course of action in bacterial cells. First, they can disrupt bacterial membrane potential by inhibiting the enzyme ATP synthase leading to depletion of ATP levels. AuNPs are known to kill MDR bacteria in this non-ROS-dependent manner. The generation of ROS might also be attributed to the antibacterial activity of AuNPs. The ROS contributes to enhancing oxidative stress in microbial cells leading to cell mortality(Mohamed, Fouad, Elshoky, Mohammed, & Salaheldin, 2017).The green synthesized AuNPs have also shown good antimicrobial activity against *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumonia*, and *Clostridiumsupergenes*(Folorunso et al., 2019).Different sized AuNPs were synthesized from *Trachyspermum ammi*, *Citrus limonum*, *Satureja hortensis*, *Cucurbita pepo*, *Malva crispa*, and *Garcinia cambogia*, and all have antibacterial activities against *L.monocytogenes* at different concentrations (Table 2.).

Table 2. Green synthesized gold nanoparticles (AuNPs) against L. monocytogenes.

S.No.	Plant used	MNPs	Size (nm)	L. monocytogenes strain	MIC	Mechanism of action	Ref.
1	*Trachyspermum ammi seed extract*	AuNPs	16.63	*Listeria monocytogenes ATCC 19,114*	32 µg mL^{-1}	A proposed mechanism of antibiofilm activity is increased ROS generation.	(Perveen et al., 2021)
2	*Citrus limonum*	AuNPs	30 ± 6	*Listeria monocytogenes.*		-	(Mahmood et al., 2021)
3	*Satureja hortensis*	AuNPs	22.26	*L. monocytogenes (ATCC 19118)*		-	(Sepideh Gharehyakheh1 | Ahmad Ahmeda2 | Amir Haddadi3 | Morteza Jamshidi4 | Masoumeh Nowrozi5 | Mohammad Mahdi Zangeneh5, 2020)
4	*Cucurbita pepo*	AuNPs	1-100	*Listeria monocytogenes (KCCM 40307)*	400 µg mL^{-1}	Disruption of bacterial cell membranes	(Chandran, Song, & Yun, 2019)
5	*Malva crispa*	AuNPs	1-100	*Listeria monocytogenes (KCCM 40307)*	400 µg mL^{-1}	Disruption of bacterial cell membranes	(Chandran et al., 2019)
6	*Garcinia cambogia*	AuNPs	40–50	*L. monocytogenes*		-	(Nithya, 2016)

"-" indicates not mentioned; MNPs= metallic nanoparticles

Zinc oxide nanoparticles (ZnONPs): ZnOPs are special in that they are considered biosafe and are already a component of several commercial ointments and creams. Their strong antimicrobial potential results from their unique Physico-chemical properties and high surface area to volume ratio. ZnONPs enter the bacterial cell through electrostatic interaction with the bacterial cell membrane, and once inside the cytoplasm, they release zinc ions (Zn2+). These Zn2+ ions interact with cellular components and produce genotoxic damage and oxidative stress. ROS generated by ZnONPs affects the microbial cell membrane and causes the cell contents to leak out, resulting in cell mortality. Thus, the antibacterial effect of ROS is associated with the high reactivity and oxidizing property of ZnONPs(Abbasi, Anjum, & Hano, 2017).One such study supporting the statementsmentioned above is where ZnONPs synthesized from *Punica granatum* extract produced ROS when attached to the cell membrane of bacteria, as discussed in Table 3.

Table 3. Green synthesized zinc oxide nanoparticles (ZnONPs) against L. monocytogenes

S.No.	Plant used	MNPs	Size (nm)	*L. monocytogenes*	MIC	Mechanism of action	Ref.
1	*Punica granatum*	ZnONPs	52.50	*Listeria monocytogenes ATCC 19115*	1250 µg mL^{-1}	ROS Production upon attachment to the cellmembrane damages the cell membrane and causes protein dysfunction.	(Ifeanyichukwu, Fayemi, & Ateba, 2020)
2	*Cinnamomum verum)*	ZnONPs	60	*L. monocytogenes (ATCC 7644*	----	-	(Osaili et al., 2019)

3	*Peganum harmala*	ZnONPs	39.94	*Listeria monocytogenes*		-	(Mehar et al., 2019)
4	*Ochradenus baccatus*	ZnONPs	< 50	*Listeria monocytogenes*	100 µg mL^{-1}	Binding with HSA protein.	(Nasser A. Al-Shabib et al., 2018)
5	*Lagenaria siceraria*	ZnONPs	48.6	*L. monocytogenes MTCCNo.657*	-	-	(Kalpana, Payel, & Rajeswari, 2017)
6	*Allium sativum*	ZnO NPs	14	*Listeria monocytogenes ATCC-19115*	0.78 µgmL^{-1}	-	(Vodnar2, 2016)
7	*Nigella sativa*	ZnONPs	24	*L. monocytogenes*	512 µg mL^{-1}		(Nasser A Al-Shabib et al., 2016)
8	*Rosmarinus officinalis*	ZnONPs	54	*L. monocytogenes ATCC-19115*	6.25 µg mL^{-1}	-	(Stan, Popa, Toloman, Silipas, & Vodnar, 2016)
9	*Ocimum basilicum*	ZnONPs	25	*L. monocytogenes ATCC-19115*	6.25 µg mL^{-1}	-	(Stan et al., 2016)
10	*Rosa canina*	ZnONPs	<50	*L. monocytogenes*		-	(Jafarirad, Mehrabi, Divband, Kosari-Nasab, & C, 2016)
11	*Petroselinum crispum*	ZnONPs	12	*L. monocytogenes ATCC-19115*	6.25 µgmL^{-1}		(Stan et al., 2015)

"-" indicates not mentioned; MNPs= metallic nanoparticles

Aluminium oxide nanoparticles (Al_2O_3NPs): The antimicrobial properties of aluminium oxide nanoparticles may be associated with electrostatic interactions between Al_2O_3NPs and the surface of the bacterial cell. The positively charged surface of Al_2O_3NPs gets adsorbed onto the negatively charged bacterial surface, and bacterial cell death is finally potentiated (Pakrashi et al., 2011).Lemongrass-mediated Al_2O_3NPs has shown antibacterial properties against *P. aeruginosa*(Ansari et al., 2015).whereas Al_2O_3NPs synthesized from *Prunus xyedonesis* has antibacterial activity against *S.aureus* and *E. coli*(Manikandan et al., 2019).

Copper nanoparticles (CuNPs): Currently, CuNPs are obtaining special emphasis due to their increased demand as antimicrobials(Cioffi et al., 2005).Essential ions exchange, enzyme inactivation, the release of H_2O_2 by copper, and the breaking of plasma membrane integrity are some of the mechanisms that prevent microbes' normal growth (Ibrahim, Yang, & Seo, 2008).*Stachys lavandulifolia Vahl* and *Morus albaL*. were used to prepare plant-mediated CuNPs. In contrast, *Capsicum frutescens*, *walnut shells*, *Cinnamomum verum*, *Syzigium aromaticum*, *Rosmarinus officinalis L*, and Lemon Extract were used to synthesize CuONPs against *L.monocytogenes* (Table 4.).

Table 4. Green synthesized copper nanoparticles against L. monocytogenes

S. No.	Plant used	MNPs	Size (nm)	*L. monocytogenes* strain	MIC	Mechanism of action	Reference
1	*Lemon Extract*	CuONPs	50	*L. monocytogenes (ATCC 19115*	25 µg mL^{-1}	-	(Tshireletso, Ateba, & Fayemi, 2021)
2	*Capsicum frutescens*	CuONPs	20 - 40	*Listeria monocytogenes (MTCC 657).*	150 µg mL^{-1}	-	(K, S, P, S, & S, 2021)
3	*Stachys lavandulifolia Vahl*	CuNPs	10–25	*Listeria monocytogenes*	2 mg mL^{-1}	-	(Saba Hemmati1Sheida Ahany Kamangar1Ahmad Ahmeda2Mohammad Mahdi Zangeneh3, 2020)
4	*walnut shells*	CuONPs	15–22	*Listeria monocytogenes*	500 ppm	-	(Mehdizadeh, Zamani, & Abtahi Froushani, 2020)

				(ATCC19115)			
5	*Morus alba L.*	CuNPs	101.2	*L. monocytogenes ATCC 19115*	2500 µg mL^{-1}	-	(Yordshahi, 2019)
6	*Cinnamomum verum*	CuONPs	171–204	*L. monocytogenes (ATCC 7644*	400 µg mL^{-1}	-	(Osaili et al., 2019)
7	*Syzigium aromaticum*	CuONPs	171–204	*L. monocytogenes (ATCC 7644*	>400 µg mL^{-1}	-	(Osaili et al., 2019)
8	*Rosmarinus officinalis L.*	CuONPs	171–204	*L. monocytogenes (ATCC 7644*	400 µg mL^{-1}	-	(Osaili et al., 2019)

"-" indicates not mentioned; MNPs= metallic nanoparticles

Iron oxide nanoparticles (Fe_2O_3NPs): An organic compound containing multiple hydroxyl groups (polyol) components found in plant extracts has been used to reduce iron to produce Fe_2O_3NPs. Mango, clove, green tea, coffee, rose, cumin, oregano, and thyme are some plants utilized so far for Fe_2O_3NPs synthesis(Pattanayak, Nayak, & Sciences, 2013).Green synthesized Fe_2O_3NPs have shown growth inhibitory activity against *Bacillus subtilis* and *E. Coli*(Pal, 2014).Those Fe_3O_4NPs generated ROS, singlet oxygen, and superoxide radicals that could cause the inhibition of *E. coli*(Gabrielyan, Hovhannisyan, Gevorgyan, Ananyan, & Trchounian, 2019).Fe_2O_3NPs were prepared from plant extracts of *Leucasaspera*, *Solanumtuberosum*, and *Laurus nobilis* and have shown an antimicrobial effect on *L.monocytogenes* (Table 5.).

Table 5. Green synthesized iron oxide nanoparticles (Fe2O3NPs) against L. monocytogenes

S. No.	Plant used	MNPs	Size (nm)	*L. monocytogenes* strain	MIC	Mechanism of action	Reference
1	*Laurus nobilis*	Fe_2O_3NPs	8.03 ± 8.99	*Listeria monocytogenes (PTCC 1294)*		-	(Jamzad & Kamari Bidkorpeh, 2020)
2	*Solanum tuberosum*	Fe_3O_4NPs	105-145	*L. monocytogenes (NCIM 5277)*	1500 µg mL^{-1}	-	(Madhu et al., 2019)
3	*Leucasaspera*	Fe_3O_4 NPs	<20	*L. monocytogenes NCIM 5277*	150 µg mL^{-1}	-	(Veeramanikandan et al., 2017)

"-" indicates not mentioned; MNPs= metallic nanoparticles

CONCLUSION

Plants have emerged as efficient candidates for synthesizing nanoparticles. Nanoparticles synthesis using plant extracts has more benefits than other synthesis methods. This uses a single step, is eco-friendly, cost-effective, safe, compatible with pharmaceutical applications, and easily scaled. Since they have a multitarget mechanism of action, nanoparticles are preferable to other commercially available antibiotics to treat multidrug-resistant bacteria. Plants are sources of reducing and stabilizing agents to synthesize nanoparticles, and several plant-mediated nanoparticles exhibit antibacterial activities against L.monocytogenes. In this review, many plant-mediated nanoparticles have promising effects in treating diseases caused by these pathogens. Although significant advances have been made in studying the antibacterial activity of green synthetic metals and metal oxide nanoparticles against Listeria monocytogenes, the exact mechanism of their action on target microorganisms needs to be investigated. In addition to this, further research is needed to synthesize more stable toxic-free nanoparticles.

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