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Research Paper

Synthesis of Nanoparticles and their Application Potential for Pharmaceutical Applications

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Abstract
Nanotechnology has significantly influenced modern pharmaceutical research, particularly in the development of advanced drug delivery systems. Nanoparticles, typically ranging from 1–100 nm in size, exhibit unique physicochemical properties such as high surface area, improved solubility, enhanced bioavailability, and the ability to target specific tissues. These characteristics make nanoparticles valuable carriers for therapeutic agents. Various synthesis strategies including physical, chemical, and biological methods have been developed to produce nanoparticles with controlled size, morphology, and surface properties. This paper discusses the major synthesis methods for nanoparticles and their application potential.

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I. Introduction

Nanotechnology has emerged as a transformative field in pharmaceutical sciences, offering innovative approaches for drug delivery, diagnostics, and therapeutic interventions. Conventional drug delivery systems often suffer from limitations such as poor solubility, low bioavailability, and non-specific distribution. Nanoparticles provide solutions to these challenges by enabling targeted and controlled drug delivery (Sahoo and Labhasetwar 2003).

Nanoparticles are defined as particulate dispersions or solid particles with a size in the range of 10-1000 nm (Langer 2000). Nanoparticles are considered as building blocks of the next generation of optoelectronics and various chemical and biochemical sensors (Wong and Schwaneberg 2003). Nanoparticles are becoming a part in human medical applications (Cai and Chen 2007; kim et al. 2010; Del burgo et al. 2013). Drug loaded nanoparticles interact organ and tissues and are taken up by cells (Alexiou et al. 2000; Groneberg et al. 2006). Several studies have shown that the tissue, cell and even cell organelle distribution of drugs may be controlled and improved by their entrapment in colloidal nanomaterials, mainly of the micellar structure, such as nanocontainer (Savic et al. 2003). More applications are expected in new areas such as biosensing, cell labelling, drug targeting, gene delivery, hyperthermia therapy, microelectronics, solar cells, electroluminescent devices, phagokinetic studies, photocatalysis, detergent, cosmetics and antimicrobials (Kong et al. 2000; Parak et al. 2002**;** Ball 2001; Wasan and Nikolov 2003; Mallin 2006, Brayner et al. 2006; Venkatasubramanian and Sundaraj 2014).

2.1 Synthesis of Nanoparticles: Materials Scientists are conducting research to develop novel materials with better properties, more functionality and lower cost than the existing ones. Several chemical and biological synthesis methods have been developed to enhance the performance of nanomaterials displaying improved properties with the aim to have a better control over the particle size, distribution and morphology (Granqvist and Bhurman 1976; Shibata et al. 1998; Shankar et al. 2003; Mohanpuria et al. 2008**).** Synthesis of nanoparticles to have a better control over particles size, distribution, morphology, purity, quantity and quality, by employing efficient economical processes has always been a challenge for the researchers (Hahn 1997). Various chemical and biological methods used for synthesis of nanoparticles are discussed as follows:

2.1.1 Chemical synthesis of nanoparticles: Synthesis methods for nanoparticles are typically grouped into two categories: “top-down” and “bottom-up”. The first involves division of a massive solid into smaller portions. This approach may involve milling or attrition, chemical methods and volatilization of a solid followed by condensation of the volatilized components. The second, bottom-up, method of nanoparticles fabrication

involves condensation of atoms or molecular entities in a gas phase or in solution (Gopalakrishnan 1995); (Tsuzuki. 2009; Betke and Kikelbick. 2014).

Various chemical and physical methods like general template-based method (Hulteen et al. 1997; Huczko 2000; Liu et al. 2008; Wang et al. 2010; Jiang et al. 2011), supercritical hydrothermal synthesis (Polarz et al. 2005; Zhou et al. 2012), solid vapour process (Singh et al. 2007; Chang et al. 2008; Gao et al. 2014), co-precipitation method (Moghaddam et al. 2009; Kandpal et al. 2014) and many other methods have been used so far for the synthesis of nanoparticles (Lin et al. 1998; Xu et al. 2007; betke and kikelbick. 2014).

2.1.1.1 Solvent evaporation method: In this process, the polymer is dissolved in an organic solvent which is also used to dissolve the water repellant drug. The mixture containing the drug solution and polymer is then emulsified in a solution containing an emulsification agent to form an emulsion of oil in water. The organic solvent is then evaporated after the formation of emulsion by continuously stirring the solution or by reducing the pressure. Particle size is influenced by homogenizer speed, the type and concentrations of stabilizer and polymer concentration (Spanhel et al. 1991; Hwisa et al. 2013). Mainardes and Evangelista (2005) reported the preparation of spherical drug-loaded systems of biodegradable PLGA [poly (d,l-lactide-*co*-glycolide) acid] nanoparticles containing an anti-schistosoma drug (praziquantel), incorporated in the polymeric matrix. Various workers have synthesized Poly-(D, L-lactide-co-glycolide) (PLGA) nanoparticles (Xiong et al. 2011: Ghasemian et al. 2013) and polymeric nanoparticles (Nava-Arzaluz et al. 2012; Bhatt et al. 2013) by this method.

2.1.1.2 Solvent diffusion method: This is a modified version of the solvent evaporation method. The water miscible solvent together with a small quantity of the organic solvent serves as the oil phase. An interfacial turbulence is generated between the two phases due to the diffusion of solvents which in turn leads to the formation of small sized particles. As the quantity of solvent increases, a further decrease in the particle size can be achieved (Meulenkamp 1998). It has been reported that solvent diffusion technique for encapsulating hydrophilic molecules in PLGA [poly (d,l-lactide-*co*-glycolide) acid] nanoparticles is advantageous in terms of smaller size, lower size distribution, higher encapsulation yield and more biocompatible ingredients with unaltered bioactivity (Cohen et al. 2009; Singh and Mishra 2013). The solid lipid nanoparticles of water soluble drug (Ciprofloxacin Hydrochloride) are synthesized by this method (Shah et al. 2012). The synthesis of repaglinide loaded ethylcellulose nanoparticles were also reported by this method as an effective drug for the manangement of type II diabetes mellitus (Lokhande et al. 2013).

2.1.1.3 Sol-gel method: Sol-gel synthesis method has been used for the production of nanoparticles with high purity and good homogenicity (Brinker et al. 1996). A sol is a dispersion of the particles (0.1-1 μm) in a liquid where only the Brownian motions suspend the particles. A gel is a state where both liquid and solid are dispersed in each other, which presents a solid network containing liquid components.

In sol-gel coating process, the desired particles once dispersed in a liquid to form a sol and the deposition of sol solution produces the coatings on the substrates by spraying, dipping or spinning. The particles in sol are then polymerized through the removal of the stabilizing components and produce a gel in a state of a continuous network. The final heat treatments pyrolyze the remaining organic or inorganic components and form an amorphous or crystalline coating (Olding et al. 2001; Troczynski and Yang 2001). The effects of pH variation as well as ageing on structural properties of ZnO nanoparticles were also investigated (Singh et al. 2007). The synthesis of silica nanoparticles and tin oxide (Aziz et al. 2013) by sol-gel method was also reported in literature (Rahman and Padavettan 2012; Olfat et al. 2013).

2.1.1.4 Polymerization method: In this method, monomers are polymerized to form nanomaterials in an aqueous solution. Drug is incorporated by adsorption onto the nanoparticles or by dissolving in the polymerization medium after polymerization has been completed. The suspension is then purified to remove stabilizers and surfactants which were used for polymerization by ultracentrifugation and then resuspending the particles in a medium free of isotonic surfactants. This technique is suitable for making polyalkylcyanoacrylate or polybutylcyanoacrylate nanoparticles (Zhang et al. 2001; Boudad et al. 2001; Yoradanov. 2012). The particle size depends on the concentration of the stabilizers and surfactants used during synthesis (Mohanraj and Chen 2006; Mahapatro and Mahapatro 2011). The synthesis of magnetite (Fe_3O_4) nanoparticles by polymerization method has also been repoted (Jadhav and Bongiovanni 2012; Muthia et al. 2013).

2.1.1.5 Ionic gelation method or Coacervation: Much research has focussed on the preparation of nanoparticles from biodegradable hydrophilic polymers such as gelatin, chitosan and sodium alginate. A method for preparing hydrophilic chitosan nanoparticles by ionic gelation has been developed (Calvo et al. 1997; Sailja et al. 2011). The method involves a mixture of two aqueous phases one is the polymer chitosan and the other is

the polyanion sodium tripolyphosphate. In this technique, amino group of chitosan combines with tripolyphosphate to form coacervates with a size in the range of 350 nanometer. These are formed due to electrostatic interaction between the two phases, while ionic gelation involves transition from liquid phase to the gel phase due to ionic interaction which takes place at room temperature (Mohanraj and Chen 2006). This technique was also used for the synthesis of chitosan nanoparticles (Malhotra et al. 2011; Masalova et al. 2013) and PEGylated chitosan nanoparticles (Fan et al. 2012; Malhotra et al. 2013).

2.1.1.6 Supercritical fluid technology: Conventional methods such as solvent diffusion, solvent evaporation and organic phase separation methods require organic solvents which are harmful to the environment. Therefore, the supercritical fluid technology is generally used as an alternative for preparing biodegradable micro and nanoparticles because supercritical fluids are considered to be environmentally safe. A supercritical fluid can be generally defined as a solvent at a value higher than its critical temperature, at which it remains in a single phase irrespective of pressure. Supercritical CO_2 is the most widely used super critical fluid because of its relatively mild critical conditions, non-flammability, non toxicity and lesser cost.

The most common processing techniques involving supercritical fluids are Rapid Expansion of Critical Solution (RESS) and Supercritical Anti-Solvent (SAS). This method employs a liquid solvent like methanol, which is miscible with the supercritical fluid to dissolve the solute to be nano-material. This is because the solute is not soluble in the supercritical fluid. The extract of the liquid solvent by supercritical fluid results in instantaneous precipitation of the solute, thus leading to the formation of nanoparticles (Jung and Perrut 2001; Caputo et al. 2013). Thote and Gupta (2005) reported the use of a modified SAS method for formation of hydrophilic drug dexamethasone phosphate drug nanoparticles for microencapsulation purpose. The glucose-assisted continuous flow system was used for the synthesis of Bi_2Te_3 (Bismuth Tellurides) nanoparticles by supercritical fluid technique (Li et al. 2012).

2.1.1.7 Precipitation method: Precipitation method also called solvent displacement method was developed by (Fessi et al. 1989). It is one of the easiest, most economic and reproducible routes to produce nanoparticles using preformed polymers instead of monomers. This method is based on the interfacial deposition of a polymer after displacement of a semi polar solvent, miscible with water from a lipophilic solution. Three ingredients are required to achieve the process: the polymer, the polymer solvent, and the non-solvent of the polymer. The nanoparticles are generated by a rapid diffusion of the polymer solvent in the non-solvent phase by mixing the polymer solution with the latter one. This results in a drop of the interfacial tension between the two phases causing an increase of the surface area and the instantaneous precipitation of polymeric nanoparticles. Some other workers have also used this method for synthesis of cobalt doped hexagonal zinc oxide nanoparticles (Udayakumar et al. 2012) and ferric chloride doped zinc sulphide nanoparticles (Theivasanthi et al. 2013).

2.1.1.8 Solvothermal method: The solvothermal process, is employed to synthesise ZnO nanostructures. The technique is based on the thermal decomposition at 80° C of organnometallic compound in organic solvent and has been successfully applied for synthesis of various types of nanosized metal oxides with large surface area, high crystallinity and high thermal stability (Yiamsawas et al. 2009). In this process alcohol plays a very important role in contributing the unoccupied oxygen to Zn^{2+} in order to form zinc oxide (ZnO). The formed zinc oxide seeds are attracted to some of the Triethanolamine (TEA) chains because of the ionic–dipolar interaction between the hydrogen atoms in the polymer and oxygen in the zinc oxide. The zinc oxide nanoparticles will grow with the association of the zinc oxide seeds. On the other hand, some of the TEA chains are attracted to each other by hydrogen-bonding forces. So, the growth of the particles will be eliminated, because the polymer chains do not permit the zinc oxide seeds to reach each other easily (Niederberger and Pinna 2009). This mehod is also used for the synthesis of various other nanoparticles like cobalt triantimonide (Kumari et al. 2010), silver telluride (Zhou et al. 2012) and cadmium selenide nanoparticles (Suresh and Arunseshan 2013).

2.1.1.9 Wet chemical method: The simplest and the most commonly used method for metal nanoparticles is the chemical reduction of metal salts (Chaudhari et al. 2007; Pal et al. 2007). This method involves reduction of anionic salt in an appropriate medium in the presence of surfactant using various reducing agents and result in the production of nanosized metal particles with different morphologies and sizes (Chen et al. 2007). Among all the techniques, wet chemical method have been considered to be most attractive due to its robust and reliable control of the shape and size of the nanoparticles without requiring the expensive and complex equipments. The chemicals required for this method are easily available and cheap (Arabi et al. 2012).

The synthesis of yellowish-brown colored stable arsenic (As) nanoparticles is done by simple chemical reduction method (Pal et al. 2012). The zinc oxide nanoparticles with the average particle size of about 30 nm

were synthesized by the chemical technique and their properties were studied with the help of scanning electron microscope and X-ray diffraction (Arefi et al. 2012). The antimicrobial properties of zinc oxide nanoparticles produced by chemical method were investigated using *Listeria monocytogenes* (Arabi et al. 2012). Cadmium sulfide (CdS) nanoparticles were synthesized by simple one step wet chemical synthesis with an average size of 15 nm (Ramesh and Narayanan 2013).

2.1.2 Biological synthesis of nanoparticles: Biology is considered as the master of so-called bottom-up fabrication which includes building up nanostructures starting from basic atoms or molecules (Naik and Stone 2005). A number of single-celled organisms also produce inorganic materials of nanometer range intracellularly or extracellulary. Common examples include magneto tactic bacteria which synthesize magnetite (Lovley et al. 1987; Alphandery. 2014), diatoms which synthesize siliceous materials (Kroger et al. 1999) and S-layer forming bacteria (Pum and Sleytr 1999; Mulani and Mujumdar. 2013). These structures are highly controlled, range from macroscopic to nanometer scale, and result in intricate architectures that provide multifunctional properties. Taking inspiration from these natural biological systems, biologists were able to develop an alternative strategy for nanoparticle synthesis using microorganisms (Jain et al. 2012; Huang et al. 2014)

A landmark study by Klaus et al. (1999) established an interface between material science and biological systems. They reported the synthesis of crystalline silver nanoparticles of well-defined composition and shapes using *Pseudomonas stutzeri* isolated from silver mine. Labrenz et al. (2000) had shown the synthesis of spherical aggregates of sphalerite particles (2–5 nm) within the natural biofilms dominated by sulfate-reducing bacteria of the family *Desulfobacteraceae.* Bansal et al. (2004) reported the synthesis of spherical shape zirconium oxide nanoparticles from *Fusarium oxysporum* with an average size of 3 to 11 nm.

The use of biological entities in the synthesis of nanoparticles has been investigated like Ribosome's for biosynthesis of gold nanoparticle (Pavel 2005; Huang et al. 2014), bacteria for production of cadmium sulfide (Smith et al. 1998; Kowshik et al. 2002; Malarkodi et al. 2014), zinc sulfide (Labrenz et al. 2000; Mirhendi et al. 2013), iron sulfide (Watson et al. 2000; Bharde et al. 2008) and silver nanoparticles (Klaus et al. 1999; Kowshik et al. 2002; Naik et al. 2002; Shivakrishana et al. 2013) and yeasts for production of lead sulfide and cadmium sulfide nanoparticles (Kowshik et al. 2002; Li et al. 2011; Seshadri et al. 2011). The leaves of different plants, sprouts, roots (Shankar et al. 2003; Marchiol et al. 2014) and stems of live alfalfa plants (Gardea et al. 2003) were also used for synthesis of nanoparticles of variable morphology. The production of gold nanoparticles using lemongrass extract (Shankar et al. 2004; Pandey et al. 2012) and production of silver nanoparticles using *Emblica Officinalis* herbal fruit extract has also been reported (Balaprasad et al. 2005; Ankamwar et al. 2005).

Different microorganisms have different mechanisms for synthesis of nanoparticles. Synthesis of various nanoparticles by microbes is due to their defense mechanism which is responsible for its nanoparticles synthesis. The ions in nature are highly toxic for the bacterial cells and the cellular machinery of the microbes helps in the conversion of reactive and toxic ions into stable silver atoms (Kumar et al. 2007). A proposed a mechanism of nanoparticle production suggests the involvement of a NADPH-dependent enzyme that reduces Au^{3+} to Au^0 through an electron shuttle pathway for the synthesis of gold nanoparticles (Nangia et al. 2009; Li et al. 2011). In contrast, Prasad and Jha (2009) hypothesized the role of pH dependent membrane-localized oxidoreductases for synthesis of zinc oxide nanoparticles using *Lactobacillus sporogenes*. Some workers have also postulated that synthesis of metal nanoparticles is a two step procedure which involves the following steps i.e. metal ions are first trapped on the surface or inside of the microbial cells and then trapped metal ions are reduced to nanoparticles in the presence of enzymes (Benzerara et al. 2010).

Senapati et al. (2005) reported the synthesis of bimetallic Au-Ag alloy by *Fusarium oxysporum* and argued that the secreted cofactor NADH plays an important role in determining the composition of Au-Ag alloy nanoparticles. Some stable metal sulfide nanoparticles such as cadmium sulphide (CdS), zinc sulphide (ZnS) and lead sulphide (PbS) can be produced extracellularly by the fungus *Fusarium oxysporum* when exposed to aqueous solution of metal sulfate. The quantum dots were formed by the reaction of Cd^{2+} ions with sulfide ions which were produced by the enzymatic reduction of sulfate ions to sulfide ions (Bai et al. 2006). Nangia et al. (2009) reported the intracellular synthesis of gold nanoparticles by *Stenotrophomonas maltophilia* isolated from soil samples of the Singhbhum gold mines, India. Biocompatible magnetic nanoparticles like Fe_3O_4 (magnetite) and Fe_2O_3 (maghemite) have been actively investigated for targeted cancer treatment (magnetic hyperthermia), stem cell sorting and manipulation, guided drug delivery, gene therapy, DNA analysis and magnetic resonance imaging (MRI) (Fan et al. 2009; Avram et al. 2013)

Jha et al. (2009) reported the production of titanium oxide by incubating the *Lactobacillus sp.* at 25°C having size of 20 to 80 nm. Zinc phosphate nanopowders were synthesized with yeasts as biotemplates (Pandian et al. 2009). Yan et al. (2009) demonstrated the synthesis of $Zn_3(PO_4)_2$ powders with butterfly-like microstructure with a size range of 10–80 nm in width and 80–200 nm in length.

Ramanathan et al. (2011) investigated that *Morganella sp.* (*M. morganii* and *M. psychrotolerans*) when exposed to Cu^{+2} ions results in formation of ultra-small spherical copper oxide (CuO) nanoparticles of 7-15 nm diameters. Dhoondia and Chakraborty (2012) reported the *Lactobacillus* mediated synthesis of silver oxide (AgO) nanoparticles. Mousavi et al. (2012) reported the synthesis of cadmium sulphide nanoparticles using the bacteria of *Enterobacteriaceae* (*Escherichia coli* PTCC 1533 and *Klebsiella pneumonia* PTCC 1053). The synthesis of silver sulfide (Ag_2S) nanoparticles from metal reducing bacterium (*Shewanella oneidensis* MR-1) with an average size of 2-16 nm was investigated by Debabov et al. (2013). The synthesis of spherical shape titanium oxide nanoparticles from *Planomicrobium sp.* has been reported by Malarkodi et al. (2013).

2.2 Doping of Various Nanoparticles: Currently, modification of metal oxide properties by impurities/dopant incorporation has become topic of interest in nanomaterial synthesis. For example, doping ions in zinc oxide will make scientists to tailor its optical, electrical and magnetic properties through altering its electronic structure (Udayakumar et al. 2012). There are some reports on the effect of doping of various transition metals on the structural and electrical conductivity of zinc oxide prepared by several methods (Sedky et al. 2007; Wang et al. 2009). One of the most widely used nanomaterials in the bioanalysis field is gold doped nanoparticles, which are already available in the form of commercial products. One well-known example is the lateral flow strip developed for fast pathogen detection and point of care diagnosis (Daniel and Astruc 2004). The presence of a plasmon absorbance band, and their shape and size dependent optical properties, make gold nanoparticles suitable as colorimetric probes (Schultz 2003; West and Halas 2003).

Nanometer sized gold nanoparticles supported on substrates such as oxides carbides or hydroxides have proven to possess noticeable active reaction rates (Burygin et al. 2009). Gold doped zinc oxide nanocomposites are studied for their excellent coating properties that can be used as metal protective coating, owing to their superior glass, durability, tint strength, particle uniformity and brightness (Jones et al. 2008). Doping of nanoparticles with silver has been known to have unique antimicrobial activity that may be useful in the construction of antibacterial materials to aid in the fight against bacteria-related infections (Cadar et al. 2007). The silver-doped zinc oxide nanopowders were proven to have antibacterial capabilities that render them potentially useful as antibacterial agents for a variety of applications (Burygin et al. 2009).

It has been established that doped zinc oxide has maximum effect against pathogenic organisms as compared to zinc oxide (Jones et al. 2008). Surface defects play an important role in the photocatalytic activities of metal oxides as they increase the number of active sites (Ullah et al. 2008; Rekha et al. 2010). It has been found through mechanochemical synthesis method that cobalt-doping in zinc oxide progressively decreased the photocatalytic activity while the manganese-doping in zinc oxide initially increased photocatalytic activity (Dodd et al. (2009). The influence of copper dopant in zinc oxide powders and thin films has been investigated by Fu et al. (2011).

2.3 Applications of Nanoparticles: Nanoparticles offer many new developments in various fields like biomedicine, bionanotechnology especially in area of drug delivery, medical diagnostic, biosensing, bioimaging, cosmetics etc. Zinc oxide nanoparticles are used in number of applications due to their unique properties. Zinc oxide, a metal oxide, is much more stable and has longer life than organic-based disinfectants or antimicrobial agents. This is particularly important for harsh conditions such as high temperatures or pressures occurring during product manufacturing, storage and transportation (Utamapanya et al. 1991; Wang et al. 1998; Hewitt et al. 2001; Stoimenov et al. 2002; Sawai 2003; Fu et al. 2005; Makhluf et al. 2005; Brayner et al. 2006). Although there are numerous reports in the literature on the biocidal effects of metal oxide nanoparticles such as silicon dioxide, aluminium oxide, iron oxide, titanium dioxide, magnesium oxide and calcium oxide, but zinc oxide is of particular interest due to extensive applications of the material in the personal care and home care products (Schumacher et al. 2004; Axtell et al. 2005; Li et al. 2005).

2.3.1 Nanoparticles in biosensors: The sensing of biological agents, diseases and toxic materials is an important goal for biomedical diagnosis, forensic analysis and environmental monitoring (Diamond 1998). The unique physicochemical property of nanoparticles coupled with the inherent increase in signal-to-noise ratio provided by miniaturization makes these systems promising candidates for sensing applications (Daniel and Astruc 2004). Gas sensors based on zinc oxide nanoparticles has already been developed for detection and control of gases such as CO, H_2, H_2S, NH_3 etc (Zhu et al. 2005). Nanosized semiconductor crystals can increase efficiency of photochemical reactions and greatly improve the catalytic activity of enzymes to generate novel photoelectrochemical systems. Hence, zinc oxide nanoparticles/glucose oxidase photoelectrochemical system is used for the fabrication of novel biosensors (Ren et al. 2009). A novel tyrosinase biosensor based on biofunctional zinc oxide nanorod microarrays on the nanocrystalline diamond electrode is used for detection of phenolic compounds (Zhao et al. 2009). Photoelectrochemistry of free-base-porphyrin-functionalized zinc oxide nanoparticles have applications in biosensing (Tu et al. 2011). Zinc oxide nanoparticles have sensing applications for electrochemical monitoring of nucleic acid hybridization (Yumak et al. 2011). An amperometric xanthine biosensor based on zinc oxide nanoparticles-polypyrrole composite film has been reported by Devi et

al. (2011). A biosensor is designed based on catalase and modified carbon paste electrode with zinc oxide nanoparticles for determination of dopamine level (Fooladsaz et al. 2012).

2.3.2 Antimicrobial potential of nanoparticles: A number of mechanisms have also been proposed to interpret the mechanism of antimicrobial potential. These include production of active oxygen species due to the presence of nanoparticles (Sawai et al. 1996; Makhluf et al. 2005), damage of membrane cell wall through adhesion on the cell membrane (Stoimenov et al. 2002), penetration through the membrane cell wall (Makhluf et al. 2005) and cellular internalisation of nanoparticles (Brayner et al. 2006). Sawai et al. (1996) suggested that the electrostatic interaction between the bacteria surface and nanoparticles was a probable reason for the antibacterial activity. Nair et al. (2002) suggested the mechanism of antibacterial activity that the increase in Reactive Oxygen Species (ROS), membrane dysfunction and internalization of nanoparticles are the main cause of cell swelling and cell death.

A study by Yamamoto (2001), to evaluate the antibacterial activity of zinc oxide with different particle sizes showed that zinc oxide nanoparticles (10-50 nm) exhibit better antimicrobial properties than bulk zinc oxide (2 μm). The antibacterial activity of zinc oxide nanoparticles is due in part to their electrostatic interaction with cell surfaces (Sawai et al. 1996). Zinc is an essential element and zinc oxide nanoparticles are considered to be non-toxic. Toxicity studies have shown that zinc ions do not cause any damage to the DNA of human cells (Yamada et al. 2007). Zinc oxide nanoparticles have been shown to be useful antibacterial and antifungal agents when used as a surface coating on materials and textiles (Abramov et al. 2009). Zinc oxide nanoparticles could potentially be used as an effective antibacterial agent to protect agricultural and food safety from foodborne pathogens, especially *E. coli* O157:H7 (Thill et al. 2006). Zinc oxide powder is an active ingredient for dermatological applications in creams, lotions and ointments on account of its antibacterial properties. Zinc oxide nanoparticles are used in the wallpapers in hospitals as antimicrobials (Brayner et al. 2006). The antimicrobial activity of zinc oxide nanoparticles have been studied against the food related bacteria *Bacillus subtilis* and *Pseudomonas fluorescens* (Jiang et al. 2009). Wang et al. (2012) evaluate the antibacterial effects of zinc oxide nanoparticles against *Esherichia coli* K88 because it cause diarrhea in both children and in early weaned piglets. Antimicrobial activity of spherical shaped zinc oxide nanoparticles was examined against food borne pathogens (*Escherichia coli, Pseudomonas aeruginosa* and *Aspergillus niger*) which may lead to the proficient application in food packaging and preservation process (Chitra and Annadurai et al. 2013).

2.3.3 Drug delivery through nanoparticles: Delivering the drugs precisely and safely to their target sites at the right time to have a controlled release and achieve the maximum therapeutic effect is a key issue in the design and development of novel drug delivery systems. The last decade has seen significant achievements in biomedical diagnosis and therapy at the levels of cells and molecules (Fadeel and Garcia-Bennett 2010). The ability to synthesize zinc oxide into hollow nanotube-type structures also makes them reasonable choices for drug delivery, particularly slow drug release applications (Wang et al. 2003; Wu et al. 2004).

Zinc oxide nanomaterials are used as biomarkers for cancer diagnosis and screening. Recent studies have shown that zinc oxide nanoparticles cores capped with polymethyl methacrylate are useful in the detection of low abundant biomarkers (Shen et al. 2008). These nanobeads work by facilitating surface absorption of peptide/proteins from cell extracts enabling increased sensitivity and accuracy of cancer biomarker detection using mass spectrometry. Using another approach, a zinc oxide nanorod-based cancer biomarker assay has been developed for high-throughput detection of ultralow levels of the telomerase activity for cancer diagnosis and screening (Dorfman et al. 2008). Recently, the use of zinc oxide quantum dots loaded with doxorubicin has proved to be an effective drug carrier characterized by an initial rapid drug release followed by a controlled release *in vitro* (Yuan et al. 2010). Nanoparticles with luminescent or magnetic properties are used as detection probes and drug carriers, both *in vitro* and *in vivo.* Zinc oxide nanoparticles, due to their good biocompatibility and low cost, have shown promising potential in drug delivery (Xiong 2013).

2.3.4 Nanoparticles in bioimaging and biomedicine: Zinc oxide nanoparticles are a newer type of promising candidate for bioimaging because of its high safety, low price, lack of polluting effects and good stability against air and sunlight (Tang et al. 2009). Zinc oxide nanoparticles coated with polymer shell that contains an internal layer of hydrophobic polyester and external layer of hydrophilic polyether exhibited very stable luminescence and used for cell imaging (Xiong et al. 2008).

Various nanoparticles are usually employed in nanobiomedicine as fluorescent biological labels (Chan and Nie 1998; Tian et al. 2008), gene delivery agents (Pantarotto et al. 2003; Cui et al. 2007) and in applications such as biodetection of pathogens (Edelstein et al. 2000), tissue engineering (Isla et al. 2003; Ma et al. 2003), tumor destruction via heating (hyperthermia) (Shinkai et al. 1999), MRI (Magnetic resonance imaging) contrast enhancement (Weissleder et al. 1990) and phagokinetic studies (Parak et al. 2002). Zinc oxide nanowires have been shown to be biodegradable and to eventually dissolve into ions that can be absorbed by the body and become part of the nutritional cycle, and thereby proposed for in vivo biosensing and biodetection applications (Zhou et al. 2006). Zinc oxide nanoparticles have gained interest in biomedical applications based on their high

stability, inherent photoluminescence properties useful in photocatalytic systems and promotion of reactive oxygen species generation (Dhobale et al. 2008). Additionally, zinc oxide nanoparticles show promising results in modulating allergic reactions via inhibition of mast cell degranulation (Yamaki and Yoshino 2009). It has been established that highly luminescent silica-coated zinc oxide nanoparticle quantum dots with biotin show better stability in cell culture and have applications in bioimaging of various biological samples (Moussodia et al. 2010; Matsuyama et al. 2013).

In conclusion, the synthesis of nanoparticles represents a transformative approach to combating bacterial infections in pharmaceutical applications. Their unique physicochemical properties such as small size, high surface area, and tunable functionality enable multiple antibacterial mechanisms that surpass traditional antibiotics. Among various types, silver and zinc oxide nanoparticles stand out for their potent activity, while green synthesis methods offer sustainable and biocompatible production routes.

However, challenges related to toxicity, environmental safety, and regulatory approval must be carefully addressed to ensure responsible integration into clinical practice. With continued research and innovation, nanoparticles hold immense promise as next-generation antibacterial agents, potentially revolutionizing drug delivery systems, wound healing, and infection control in modern medicine.

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