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Mechanistic study on antibacterial action of zinc oxide nanoparticles synthesized using green route

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ABSTRACT

A large array of diseases caused by bacterial pathogens and origination of multidrug resistance in their gene provokes the need of developing new vectors or novel drug molecules for effective drug delivery and thus, better treatment of disease. The nanoparticle has emerged as a novel drug molecule in last decade and has been used in various industrial fields like cosmetics, healthcare, agricultural, pharmaceuticals due to their high optical, electronic, medicinal properties. Use of nanoparticles as an antibacterial agent remain in current studies with metal nanoparticles like silver, gold, copper, iron and metal oxide nanoparticles like zinc oxide, copper oxide, titanium oxide and iron oxide nanoparticles. The high anti-bacterial activity of nanoparticles is due to their large surface area to volume ratio which allows binding of a large number of ligands on nanoparticle surface and hence, its complexation with receptors present on the bacterial surface. Green synthesis of Zinc Oxide Nanoparticle (ZnO NP) and its anti-bacterial application has been particularly discussed in the review literature. The present study highlights differential nanoparticle attachment to gram + and gram - bacterial surface and different mechanism adopted by nanoparticle for bacterial control. Pharmacokinetics and applications of ZnO NP are also discussed briefly.

1. Introduction

Nanotechnology manipulates material at an atomic or molecular level and makes them gain novel properties not exhibited by bulk matter [1]. The field is dedicated to the application of nanosciences and nano-based structure for advanced biotechnology [2]. Uses of physical and chemical means for the synthesis of nanostructures have been greatly replaced by green methods employing the use of various plant parts, bacteria, fungi, and algae. Biosynthesis of the Nano-based structure is particularly very useful for medical applications as they provide us non-toxic, eco-friendly and cheap nanomaterials [3]. Organic sources are employed for biosynthesis of nanomaterials which eliminates the need for using toxic chemicals as reducing agent. Plants are considered as one of the most useful sources for the green synthesis of the nanoparticle as they host a wide range of metabolites which act as both reducing and stabilizing agent. Fig. 1 represents the green synthesis procedure of ZnO nanoparticle and different tools employed for its characterization.

Besides the development of a plethora of drug molecule, bacterial infections are still a major cause of mortality. The origination of multidrug-resistant gene in bacteria is a matter of pressing concern thus, the development of novel drug molecules or vectors which can target bacterial genes more specifically is need of the hour [4]. Development of nanotechnology opens a new horizon for control of multidrug-resistant bacteria and related diseases and infections. Green synthesized nanoparticles surround themselves with a large group of organic phytochemicals which helps in ligand-based complexation with various receptors like proteins, lipid, phospholipid, lipoteichoic acid at the microbial surface. This complexation of nanoparticle with bacteria prevents biofilm formation and their growth [5].

The present study focusses on different antibacterial mechanism or pathways adopted by zinc oxide nanoparticle. It includes a concise literature review highlighting the use of different plant source for the synthesis of differently shaped and sized Zinc oxide nanoparticle. Biomolecules commonly involved in reduction and stabilization of nanoparticles has also been reported in the literature survey. Bacteria used and mechanism assumed or referred is properly formulated in Table 1. Present work also demonstrates the impact of different physiological parameters of nanoparticles like its shape, size, surface charge, concentration on bacterial growth inhibition. The impact of different working conditions like pH and Temperature on the antibacterial activity of nanoparticles has also been demonstrated.

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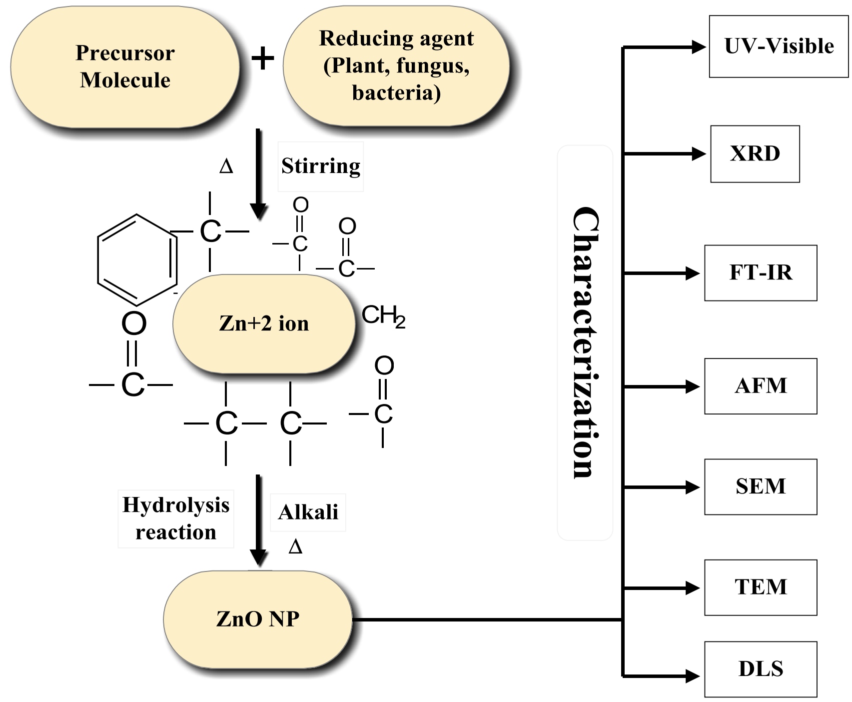

Fig. 1. Green synthesis of Zinc Oxide Nanoparticles and commonly employed characterization tools. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

1.1. Synthesis of zinc oxide nanoparticles using green chemistry and traditional approaches

Traditional route employs the use of physical and chemical methods for the synthesis of nanoparticles. Physical methods of nanoparticle synthesis like vapor condensation, Interferometric lithography, physical fragmentation and amorphous crystallization require a great deal of space for machine set-up, use of costly equipment and high temperature and pressure conditions for the nanoparticle synthesis process [6–9]. The chemical approach of nanoparticle synthesis includes sol-gel method, solution evaporation method, reduction of precursor molecules like silver nitrate ($AgNO_3$), Gold chloride ($HAuCl_4$), and Zinc acetate dihydrate ($C_4H_6O_4Zn \cdot 2H_2O$) by using non eco-friendly toxic chemicals [10]. Some volume of the chemical may reside in the final nanoparticle product which may interfere with the biological applications and the additional stabilizing agent is also needed to cap the nanoparticle in case of physical and chemical synthesis [11–14]. Thus, use of green chemistry for the synthesis of the nanoparticle is a boon for healthcare industries as it eliminates the need of using toxic chemicals and help in large-scale synthesis of extra pure nanoparticles.

Green synthesis employs the use of plant parts, bacteria, fungus, algae and organic products for the synthesis of nanoparticles [15]. There is no need to add any separate stabilizing agent as plant metabolites itself act as both reducing and stabilizing agent [16]. Phytochemicals may aid to provide specific medical applications to the nanoparticles and they are easy to manipulate at laboratory scale. For instance, nanoparticles synthesized by green route tend to exhibit better anti-bacterial activity than physical or chemical method derived nanoparticles due to the coating of various pharmacologically active biomolecules on their surface which allows multiple ligands based conjugation of nanoparticle with receptors on bacterial membranes. These biomolecules are mainly organic acids, flavones, aldehyde, ketone, amides, polysaccharides, and quinones and known to have significant therapeutic effect against a wide range of human pathogen [17]. Recently, An experiment conducted by K. Gudikandula and S.C Maringanti demonstrated better zone of inhibition obtained through biologically synthesized silver nanoparticle (AgNP) than the chemically synthesized one against bacterial sp. *E.coli*, *S. aureus*, *B. subtillis* and *K. pneumonia* [18]. Similar results were demonstrated for lemon synthesized silver nanoparticle and tri-sodium synthesized silver nanoparticle as lemon synthesized AgNP depicted better antibacterial activity against both gram-positive and gram-negative bacteria [19].

Shape, size, surface properties and other physiological features can be carefully monitored using characterization tools like UV–Visible spectroscopy (UV–Vis), X-ray diffraction spectroscopy (XRD), Scanning electron microscope (SEM), atomic force microscopy (AFM), Fourier transform infrared spectroscopy (FT-IR), elemental dispersive analysis of X-ray (EDAX), Transmission electron microscopy (TEM), Dynamic light scattering (DLS).

1.2. Anti-bacterial activity of zinc oxide nanoparticle

Nanoparticles have widely emerged as an anti-bacterial agent in the last decade. The nanoparticle can be used as a personalized medicine because it shows specific targeting and minimum toxicity [20]. They have proven useful for inhibiting antibiotic-resistant bacteria particularly [21,22]. Nanoparticles exhibit their bacteriostatic or bactericidal effect by either blocking their food source or by disrupting their cell membrane. The nanoparticle can accommodate a large number of ligands for better targeting of pathogenic microbes owing to its large surface area to volume ratio. Several types of metal and metal oxide nanoparticles have been already reported to possess anti-microbial property like Silver [23], gold [24], copper [25], Iron [26], Zinc Oxide, titanium oxide [27], copper oxide [28], Iron oxide [29] nanoparticles. ZnO NP has gained considerable attention out of all other nanoparticles because of its unique electronic, optical and medicinal properties [30]. Zinc oxide nanoparticle is highly biocompatible and its electron transport kinetics rate is fast so, it's suitable to use it as a biological membrane or for other biological applications [31]. Review literature clearly illustrates the antimicrobial activity of ZnO NPs against a broad spectrum of pathogenic bacteria like *Staphylococcus aureus, Streptococcus pyogenes*, *Escherichia coli*, *Klebsiella aerogenes*, *Pseudomonas aeruginosa, Proteus mirabilis, Mycobacterium tuberculosis* and *Bacillus subtilis*. Despite the great anti-bacterial property reflected by nanoparticles, its toxicity