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MINI REVIEW

Synthesis of Zinc Oxide, Titanium Dioxide and Magnesium Dioxide Nanoparticles and Their Prospective in Pharmaceutical and Biotechnological Applications

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ABSTRACT

The use of nanoparticles for the therapeutic purpose is gaining pronounced importance. In the last two decades, a number of nanomedicines received regulatory approval and several showed promises through clinical trials. In this content, it is important to synthesize nanoparticles from various sources and to check its efficiency, especially its antibacterial activity. In today's scenario number nanomedicines are proving useful to control multidrug resistance and since the mechanism of action of nanoparticles is totally different from the small molecules like antibiotics it obviates the chances of drug resistance. In this review, we discussed three metal-based nanoparticles prepared from various reducing sources namely Zinc Oxide Nanoparticle (ZnO NPs), Titanium Dioxide Nanoparticle (TiO_2 NPs) and Magnesium Dioxide Nanoparticle (MnO2 NPs). The focus also made towards the safety assessment of the several nanoparticles. In addition, the exact interaction of the nanoparticles with the bacterial cell surface and the resultant changes also been highlighted. The review put forward the sources, method, and antibacterial success of these nanoparticles so that future nanomedicines could be put forward.

SYNTHESIS OF NANOPARTICLES

ZnO nanoparticles

Green Synthesis and Characterization: An aqueous extract of orange peel was used as the biological reduction agent for the synthesis of ZnO NPs from zinc acetate dehydrate [1,2]. Shabaani, et al. [3] optimize the loquat (*Eriobutria japonica*) seed aqueous extract mediated green synthesis of Zinc Oxide Nanoparticles (ZnO NPs) through Response Surface Methodology (RSM). Nabi, et al. [4] the TiO_2 Nanoparticles (NPs) have been synthesised by the green synthesis method from lemon peel extract for the first time. Ullah, et al. [5] Bio-molecule capped α-MnO_2 nanoparticles have been successfully synthesized from the reduction of KMnO4 *via* a facile green synthesis route using an aqueous leaf extract of *Bryophyllum pinnatum* as a reducing and capping agent. ZnO nanoparticles able to control *Klebsiella pneumonia*, *Staphylococcus aureus*, *Penicillium notatum* and *Candida albicans* when tested in the well diffusion assay [6,7] when biosynthesized from

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Zingiber officinale rhizome. Efficiency reported with nano size of 23-26 nm when tested by Scanning Electron Microscopy (SEM), Energy Dispersive X-ray spectroscopy (EDX). Synthesized ZnO NPs particles using *Artocarpusgomezianus* extract and confirmed by using UV-Visible, XRD, SEM and Transmission Electron Microscopy (TEM) methods. As per X-Ray Powder Diffraction (XRD) ZnO NPs does showcase wurtzite structure and having maximum absorption at 370 nm. The NPs with photocatalytic activity able to degrade methylene blue dye. These NPs have also able to represent antioxidant activity against DPPH free radicals [8]. ZnO NPs from *Solanum nigrum* leaf extract confirmed as wurtzite hexagonal structure with average size of 20-30 nm as per FE-SEM study. As per TEM analysis, ZnO NPs appeared as quasi-spherical in shape and in diameter it was 29.79 nm. NP found to be better in antibacterial activities and useful in medicinal field [9]. Green synthesis of ZnO NPs are capable of reducing in methylene blue as studied in UV-Vis spectroscopy and found to be industrially useful [10]. The ZnO NPs synthesized by microwave assisted method by using *Vaccinium arctostaphylos L.* fruit extract and reported to be useful in antidiabetic activity [11]. Singh, et al. [12] reported novel method of ZnO NPs synthesis using Curcumin with ChGC@ZnO NPs showcase antioxidant and antibacterial activity. Tang, et al. [13] able to produce *Morusnigra*-loaded ZnO NPs bringing about apoptosis in gastric cancer cells. The nanoparticles further decreased antioxidants, and induced cell cycle arrest by altering gene expression of marker genes. Soliman, et al. [14] reported ZnO NPs synthesis using bravo-de-esmolfe apple extract able to form round lamina-like structures and useful in enhancing catalyst activity in apple waste.

Physical and chemical synthesis: ZnO-Ag heterostructure nanoparticles prepared by a precipitation method by involving cellulose nanocrystals as a stabilizer. ZnO-AgNPs showcased spherical shape with size diameter 9-35 nm range. Nanoparticles able to control Salmonella choleraesuis and Staphylococcus aureus [15]. Zinc Oxide Nanoparticles (ZnO NPs) is a bacteriostatic reagent but its small nanoparticles having better Nano dispersibility along with stability in aqueous solution possess a question with its use. Still, ZnO NPs successfully controlled S. aureus and *E. coli* and under *in vivo* studies, further its low toxicity and low cytotoxicity promising once tested in mice. As a product of 4 nm, ZnO NPs embeded with Poly (vinyl alcohol) gel was able to showcased antibacterial activity in rodent elyritis model put forward its use in disinfection [16]. Metal also expulsion from liquid alloys can be extended to a wide variety of molten metals for producing metallic and metallic compound nanostructures for advanced applications [17] The thermal decomposition for ZnO NPs found to be positive for antioxidant activity as determined by DPPH method and positive for cytotoxic activity when checked by haemolytic potentiality test along with antibacterial activity [18].

In recent time synthesis of ZnO NPs from microwave heating by using chitosan reported to be of 360 nm in size. As per EDXtesting, ZnO NPs recorded with 23.61% of zinc and 46.57% of oxygen. As per X-ray diffraction particle sizes recorded between 50 to 130 nm and ableto control S. aureus and E. coli in an application part [19]. The Silybummarinum based Zn -AgNPs along with Ag-ZnO heterostructures able to showcase better antioxidant and anti-leishmanial activity that finds its utility in pharmacological relevance [20]. The loading of spindle-shaped Graphene oxide with ZnO nanoparticles having length of ~ 1.0 μm and mean diameter of 100 nm registered MIC as 31.25 ± 0.25 μg/ml with Gram positive bacteria while it was 15.625 ± 0.5 μg/ml for gram negative bacteria [21]. Ali, et al. [22] synthesized ZnO NPs using co-precipitation method having size range of 15-25 nm able to control *P. aeruginosa* and *A. nigergrowth* with ability to showcase anti-inflammatory activity induced by bacterial and fungal strains.

Hussain, et al. [23] noted the ZnO NPs success once synthesized by precipitation method as an immunomodulatory and antimicrobial agent before using it in skin lotions and food products by involving in vivo evaluation of albino mice for potent toxicity. In a green synthesis Turbinariaconoides based ZnO NPs reported for anticancer activity and found to be useful in decreasing tumor volume. The treatment altered the haematological profile, antioxidant status and liver marker enzyme activities [24].

Shankar, et al. [25] prepared hybrid nanomaterial by one-pot synthesis of ZnO nanoparticles by involving regeneration of cellulose from cotton linker and microcrystalline cellulose. Results showcased better absorption of NPs on cellulose which increases thermal stability and antibacterial activity. Gupta and Srivastava [26] reported ZnO NPs synthesized from MSP assisted sonochemical flow loop reactor. Once coated on cotton fabric reported with high antibacterial activity especially against Staphylococcus aureus.

TiO_2 nanoparticles

Synthesis, functioning and safety of TiO_2 nanoparticles: Highly crystalized anatase TiO_2 NPs prepared at minimum temperature of 120°C by involving a glycothermal reaction using amorphous titanium hydrous gel as a precursor in a solvent used as 1, 4-butanediol and water. It is featured with excellent photocatalytic behaviour and its reaction conditions certainly controls the shape and dispersibility and that may change its function [27]. Pezzella, et al. [28] 2013 put forward the use of melanin- a wide class of natural pigments with 5, 6 Dihydroxyindole-2-Carboxylic Acid (DHICA) polymer and TiO_2 synthesis. TiO_2 hybrid nanoparticles which were involved in medicinal uses with number of techniques like Electron Paramagnetic Resonance, Fourier-Transform Infrared Spectroscopy (EPR, FTIR), Fluorescence spectroscopy, XRD, NPS reported with narrow size distribution with average particle of about

10 nm. Rapid and sensitive method of synthesis for TiO_2 NPs in aqueous solution by involving electro oxidation of titanium foil in tetrabutylammonium bromide aqueous solution, which functions as an electrolyte and a surfactant mentioned. After synthesis NPs recorded to be in size of 12nm. Further by diffuse reflectance measurement, the values of NPs were recorded as 2.95 and 3.10 eV and this suggested the successful production of TiO_2 nanoparticles in aqueous solution [29].

TiO_2 NPs are mostly used as metal oxide nanoparticles and having oxidative toxicity. TiO_2 NPs does able to bind to the catalase via electrostatic and hydrogen bonding forces. Upon interaction TiO_2 brings about destabilization in catalase with decrease in α-helical content and in addition solvent polarity of environment around the fluorescence chromophores on catalase also getting affected. It is observed that TiO_2 NPs activates catalase at a low concentration and act as an inhibitor at a higher molar concentration. This study related human toxicity of TiO_2 NPs in a better way [30] Besides number of positive aspects of TiO_2 NPs, worker reported the negative aspect of NPs when supplemented in food additives and coloring agent. The administration at low dose leads to persistent accumulation of nano- TiO_2 rise up inflammatory response, apoptosis and oxidative stress and sometimes lead to chronic gastritis which suggest its careful use in coming time [31]. As the TiO_2 NPs use are increasing in the society its effect on the environment has been better understood NPs applied for viability of mussel hemocytes and gill cells using neutral red and thiazolyl tetrazolium bromide assays. Results showed relatively low and close dependent toxicity for both cell models tested. As per size dependent toxicity, NPs produced by wet chemistry have higher toxicity at 10 nm, >40 nm and 60 nm. In bulk form TiO_2 NPs were more toxic except for plasma produced one [32].

With increased use of Titanium Oxide (TiO_2) nanoparticles since they possess features like small size, easy body penetration and less toxicological adverse effects. They recorded the actual effect of TiO_2 NPs on oral, dermal and respiratory system by involving TEM, ICP-OFS, histological studies and proposed that TiO_2 NPs having 10 days of half-life in body if given as an intravenous injection at concentration of 7.7 to 9.4 mg/Kg and it do not showcase any toxicological effects [33].

The possibility of synthesizing Zn Porphyrin (ZnPP) interacted with TiO_2 NPs as ZnPP- TiO_2 NPsreproted. The ZnPP- TiO_2 NPs able to preserve ZnPP's electrostatic properties within TiO_2 NPs and which makes NPs complex an excellent candidate for nanomedicine and related applications which could be applicable in localization of NPs in cells and tissues or in photodynamic therapy [34]. Effect of TiO_2 NPs on *E. coli* with the crystal size of 10-50 nm has reported and noted particles size dependent. Not only is that, TiO_2 NPs also involved in cell surface interaction, leading to membrane damage and internalization especially at smaller particle sizes which puts up a serious question over its use in ecosystem [35]. In one of the unique applications, NPs were involved to retrieve bioactive compound from living cells. They reported that Anatase TiO_2 NPs with 20 nm size able to form strong bond with enediol and especially with catechol group. They reported that NPs can enter plant cells and got attached to enediol and catechol group and comes out as flavonoid nanoparticle conjugate. This method could replace solvent based system of bioactive compound separation and opens the new avenues of separation [36]. The synthesis of Zn doped TiO2 nanoparticles reported by sologel method by using 5% Zn doping at 450 °C and reported with photocatalytic activity [37]. Irshad, et al. [38] involved plant extracts of *Trianthemaportulacastrum* and *Chenopodium quinoa* to synthesize TiO_2 NPs having average size of 15 nm. The NPs found to be promising antifungal agent especially against white rust.

Chemical synthesis of TiO_2 NPs: Hariharan, et al. [39] succeeded in doping titanium dioxide nanoparticles with silver NPs using hydrothermal method and capped by Aloe-vera. The NPs further able to produce excess ROS, resulting in complete cancer growth suppression and hence noted as promising anticancer agent. Sellschopp, et al. [40] put forward the concept of TiO_2 NPs synthesis in controlled shape and reproducible way by using hydrohalic and carboxylic acids since they influence shape under chemical synthesis mode. The method involved computational model system and thermodynamics to learn the concept in detail. Gahlot, et al. [41] reported the role of temperature to synthesize metal selenide nanoparticles (CuAgSe-TiO_2) which registered improved photocatalytic activity for the photodegradation of formic acid. Wei, et al. [42] reported the success of core-shell structured $CDsSiO_2$@TiO_2 nanoplatforms representing its potential photothermal effect and fluorescence resonance energy transfer. They also reported to be capable of inhibiting cancer cells *in vitro* and represented new avenue for clinic cancer therapy. Ma, et al. [43] noted the success of chemically synthesized TiO_2 NPs to increase the methane production by electrogenic bacteria and hence proposed TiO_2 NPs as bio-stimulation molecule. The need of sustainable manufacturing of nanoparticles especially of TiO_2 NPs has been put forward. Here synthesis of NPs via physical, chemical and biological route stands vital. The study noted the chemical route is the best way for TiO_2 NPs formation as compared to physical and biological route considering environmental impact [44]. The new approach to assemble NPs reported by using gas phase condensation of metal vapours in a He/O_2 atmosphere. The success noted with Fe-co/TiOx nanocomposite reported with features of catalyst and magnetic properties [45].

Lu, et al. [46] reported the success of $NaHoF_4$@TiO_2 NPs synthesis by involving low temperatures and by using sacrificial $Al(OH)_3$ template. The resultant formation of 60 nm $NaHoF_4$ core and a 5 nm anatase TiO_2 shell found to be individually useful. Montaser, et al. [47] noted the success of salicylaldehyde as a monoaldehyde cross linker once utilised with chitosan forming hydrogel membrane in presence of TiO_2 NPs via casting method. The membrane reported to be antibacterial. Alberti, et al. [48] noted crystallization of anatase TiO_2 nanoparticles by involving several ferrite nanoparticles under hydrothermal synthesis mode which catalyses hydrothermal reaction in presence of nucleation seeds. Shah, et al. [49] investigated doped and undoped TiO_2 NPs synthesized and stabilized by polyethylene glycol. The NPs are capable of phototoxicity activity. Resultant PEG-NPs brought about cytotoxicity towards human cervical cancer cells upon solar and ultraviolet radiations. Gaballah, et al. [50] reported chitosan-PVC conjugate improves antibacterial activity comprise of Ag/TiO_2 NPs once tested with *E. coli*, *S. typhimurium*, *S. aureus* and *L. monocytogenes* in reduced time period once used in biomedical application. El Mragui, et al. [51] reported the synthesis of pure TiO_2 and Fe-and Co-doped TiO_2 nanoparticles as photocatalysts once synthesized by sol-gel and precipitation method. The NPs in doped form reported to enhance photocatalytic degradation of carbamazepine in aqueous solution under UV-A light and visible light irradiations once compared with pure TiO_2. Locatelli, et al. [52] mentioned the success of titanium oxide octahedral composite ($Cu_2O@TiO_2$ $-NH_2$) decorated with amino functionalized cuprous oxide capable of quantitative detection of insulin by involving novel nanosheet-loaded gold nanoparticles.

MnO_2 nanoparticles

Green and chemical methods of synthesis: Successfully synthesized MnO_2 NPs by involving marine bacterium *Sacchrophagusdegradans* and Yeast *Sacchromyces cerevisiae* which was recorded to be having absorption maxima at 365 nm in UV-Visible spectrophotometry [53]. In a confirmation test, TEM found to contain NPs as uniformly dispersed hexagonal and spherical shaped particles with average size of 34.4 nm. In a comparative synthesis of MnO_2 NPs, yeast-based synthesis proving to be easy, cost effective, reliable and eco-friendly for nanoparticles production.

MnO_2 NPs was also synthesised by sonochemical reduction of $MnO_4(+)$ at pH 2.2 to 9.3 as per analysis done by XRD, NPs changed the shapes like aggregated sheet-like or needle like structure to spherical nanoparticles and finally it formed the cubic or polyhedron NPs [54]. Synthesized manganese dioxide nanoparticles by reduction of Potassium Permaganate ($KMnO_4$) using *Kalopanaxpictus* leaf extract [55]. As per UV-Vis data MnO_2 NPs formed an absorption peak at 404 nm. According to electron dispersive X-ray spectroscopy presence of Mn and O in the sample was detected. Further X-ray photoelectron spectroscopy revealed featured binding energies of MnO_2 nano particles. As per TEM analysis MnO_2 NPs appeared uniformly dispersed spherical shaped particles with a size of 19.2 nm. As per electron diffraction pattern crystalline nature of MnO_2 nanoparticles was revealed. In an FTIR analysis MnO_2 NPs shown O-Mn-O vibration mode at around 518 cm^{-1}. In an application part, MnO_2 NPs able to degrade dyes like Congo red and safranin O which make it eco-friendly and effective NPs prepared by plant extracts. In one of the researches, use of MnO_2 nanoparticles as a mimic to the enzyme has been demonstrated. As Inorganic nanomaterial like MnO_2 NPs has potential to act like enzyme and can tolerate extreme pH and temperature and remain less sensitive to protease action. In a success story, worker [56] prepared the Bovine Serum Albumin (BSA) stabilized MnO(2) nanoparticles which can showcase peroxidase-, oxidase-, and catalase- like activities. These NPs showcased good dispersion, biocompatibility and solubility and represented typical Michaelis-Menten kinetics with high affinity for H(2)O(2); 3,3',5,5'-Tetramethylbenzidine (TMB) and O- phenylenediamine. This suggested that BSA-MnO_2NPs can represent better enzyme mimic. Overall study highlighted that BSA-MnO_2NPs are having potential applications in medical, biochemical and biotechnological sectors. In another aspect of MnO_2 NPs use, researcher [57] reported the possibility of NPs use in degrading aqueous pharmaceutical chemicals. Here they synthesized MnO_2 NPs with Carboxymethyl Celluloses (CMC) as a stabilizer, and successfully demonstrated aqueous and soil sorbed estradiol. As per size, MnO_2 NPs measured to be of 39.5 nm with narrow size distribution. At a typical aquatic pH (6-7), CMC-stabilized MnO_2 NPs showcased increasing degradation kinetics for oxidation of 17 β-estradiol as compared to non-stabilized MnO_2. Hence CMC- stabilized MnO_2 NPs represents the success for facilitating *in situ* oxidative degradation of number emerging contaminants entering into soil and water.

Antibacterial activity of nanoparticles

Zinc oxide nanoparticles antibacterial activity: Nanoparticles are now routinely tested as an antibacterial agent to overcome the problem of antibiotic resistance. In a success stories, selenium doped ZnO nanoparticles synthesized through mechanochemical method of size 10.2 ± 3.4 nm, with concentration 0.45 mg/ml activity related to Reactive Oxygen Species (ROS) which is responsible for creation of oxygen vacancies making them potential antibacterial agent [58]. The success of silver doped ZnO NPs controlling the *E. coli* and *S. aureus* at 5.0 wt% of Ag as compared to only Ag and ZnO NPs reported. The real action of doped AgZnONP slinked with damage to plasmid [21]. The dry ginger rhizome (*Zingiber officinale*) based ZnO nanoparticles reported with size of 23-26 nm able to control the growth of *Klebsiella pneumonia*, *Staphylococcus aureus*, *Candida albicans* and *Penicillium notatum* [59].The increase or decrease in antibacterial activity of ZnO NPs reported to be dependent of type of target pathogens and also with the concentration used. The given capability used in the waste water treatment instead on chlorine disinfection, ultraviolet treatment and other methods [60]. The antibacterial activity of photo activated Zinc oxide nanoparticles against *E. coli O157:H7*, *Listeria monocytogenes ATCL3C* and plant pathogen

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Botrytis cinereal [61] reported promising and those remain dependent on increasing concentration and incubation period. ZnO NPs found to functioning by changing morphological structures of bacteria and fungi to register its antibacterial activity which could be useful in medicine and food industries of microbial control. ZnO NPs capping with Polyethylene Glycol (PEG), ascorbic acid, Mercaptoacetic Acid (MAA) and polysorbate 80 with ROS induced antibacterial activity. They found that MAA capped ZnO NPs and T-80 capped NPs exhibited 13% and 43% inhibition of growth of *E. coli*, respectively that leads to increase in ROS generation and resultant antibacterial activity [58].

Titanium dioxide nanoparticles antibacterial activity: In recent study effect of TiO_2 NPs as an antibacterial agent has been investigated. The antibacterial activity of graphite/TiO_2 nanocomposites linked with photocatalytic reaction with subsequent potential interaction of relative oxygen species with bacterial cells recorded. In a test, highest activity reported with MIC at 180 min of irradiation against *P. aeruginosa* [62]. In a different approach [63] prepared cover shell type Ag@TiO_2nanoparticles and found to be of size as 50 nm tested inhibitory against *E.coli* and *S. aureus.* The result directed that AgNPs are getting support from TiO_2 and SiO_2that does not allow bacterial aggregation and hence proved to be better antibacterial agent.TiO2 NPs synthesized with *A. hydrophila*rich in glycyl-L-proline which has acted as a capping agentable to control *E. coli, Pseudomonas aeruginosa, S. aureus, Streptococcus pyogenes* and *Enterococcus faecalis* with more than 33 mm of inhibition [64]. The antibacterial activity of As-annealed TiO_2 nanotubes doped with Ag nanoparticles when tested against *A. actinomycetemcomitans, T. forsythia,* and *C. rectus* [65]. The combined use of ZnO and Ag nanoparticles able to control *Staphylococcus epidermidis* by weakening cell adherence as tested with TiO_2 nanotubes. They reported that loading of nanotubes with ZnO nanoparticles diminishes *S. epidermidis* adhesion simply after 90 minutes. Here composite layer acts as future delivery system which can combat against post-operative infections especially in hard tissue replacement procedures has been reported [66]. TiO_2 nanoparticles formed in presence of enzyme alpha amylase able to control *S.aureus* and *E. coli*, at MIC value 62.50 µg/ml. The activity confers by NPs able to disrupts the bacterial cell wall [67].

The success of combined use of visible light to induce, antibacterial activity when used along with metal-oxide nanoparticles. ZnO and TiO_2 nanoparticles and both been able to increase antibacterial activity upon absorption of visible light without inducing damaging to tissue and cells [68]. Silver coating on an Anodic Oxidized Titanium (TiO_2) nanotube surface useful in preventing infections in dental implants. This treatment reduces *S. aureus* count as compared to control in an untreated surface. The preparation recorded with low cell cytotoxicity finds the feasibility to develop antibacterial Ag nanoparticle loaded titanium nanotube surfaces with magnetron sputtering [69]. The Anti-Quorum Sensing (QS) activity recorded with AgCl-TiO_2 Nanoparticles (ATNPs) and represented its potential in food preservation once tested with *Chromobacteriumviolaceum* [70]. Antibacterial activity against *MDR Acinetobacter baumannii* by using a combined therapy of pair of geometrical ferrocene-carborane derivatives (Fc SB1 and FcSB2) with nanoscale TiO_2 NPs linked with antibacterial activity by the Fc SB1/ or FcSB2 *MDR A. baumannii* [71]. The use of nanotopographical TiO_2 films implanted with Ag reported to inhibit effect of implant in an antibacterial mode and showcased *E. coli* and *S. aureus* successfully controlled by the Ag@TiO_2 system. The use of film acquired more potential to control growth on the surface to meet the clinical applications [72]. The combined use of electrospun-titanium dioxide nanofibers (TiO_2 NFs) along with photocatalytic effect of ultraviolet light reported enhanced antimicrobial activity of hierarchical antanase TiO_2 NFs against *S. aureus* ; further they recorded that with uniform deposition of Ag nanoparticles on the TiO_2NFs surface significantly increases antibacterial activity even without UV light or in dark condition [73].

Magnesium dioxide nanoparticles antibacterial activity: The use of palladium, ruthenium and silver doped MnO_2 nanoparticles found to be controlling *S. aureus, Bacillus subtilis, E. coli, Salmonella abony*and *K. pneumoniae* as per disc diffusion method. In a comparative study, Ag-doped MnO_2 NPs found to be better controlling all six isolates as compared to Ag-dope Mn_2O_3 [74]. The synthesis of silver loaded MnO_2 nanoparticles (Ag/MnO_2) including Ag/α-MnO_2, Ag/β-MnO_2, Ag/γ- MnO_2 and Ag/β-MnO_2 nanorods by involving hydrothermal and impregnation method able to control the *E. coli*, mechanisms involving Ag (+) and reactive oxygen species was recorded and among them Ag/β-MnO_2 reported with higher microbial activity. There was about 6 log decrease in *E. coli* colony number with Ag/β-MnO_2 after 120 minutes of treatment. Overall result confirmed that β-MnO_2 promotes ROS formation and disrupts the cell wall and cell membrane of *E. coli* [75]. The CNT-MnO_2 nanocomposite synthesized by microwave assisted processing able to bind with carbon nanotubes found to be effective to control Gram-positive and Gram-negative bacteria [76]. The success of eco-friendly production of manganese oxide nanoparticles in Chitosan (CS-MnO_2). This composite successfully evaluated to absorb Pb2+ ions from aqueous solution and found to be reusable even five times used consistently. In addition, CNT-MnO_2 reported antibacterial in nature when investigated with *Escherichia coli* and *Staphylococcus aureus* [77].

Wang, et al. [78] utilized the template and reductant feature of egg shell membrane to synthesize MnO_2 nanoparticles. The process gives an advantage of handy operation, low cost and easy purification. The ESM-templated MnO_2 recorded ability to decontaminate tetracycline hydrochloride. Nasrollahzadeh, et al. [79] noted the importance of MnO_2 to immobilize various nanoparticles especially copper nanoparticles and once reduced by the plant extract that further stabilizes the immobilization.

Interaction of nanoparticles with cell surface

In number of studies the ability to control bacterial growth when treated by nanoparticles were measured as changes recorded in membrane potential especially by flow cytometry. Now surface chemical properties of nanoparticles help us to understand their role in interaction with cells. This interaction always plays an important role to decide number of bio applications as given below:

Biofilm formation is common with medical device related infection. It is important to control the biofilm formation and bacterial growth and in requirement Poly Ethyleneimine (PEI) and PEI based nanoparticles (nano PEI) found to be controlling *S. aureus, S. epidermidis, A. baumannii*and *C.* albicans [80].

ZnO NPs with positive and negative surface potential are tested against different bacteria with varying surface potentials, ranging -14.7 to -23.6 mV. Chemically synthesized ZnO NPs with positive surface potential show very high antimicrobial propensity with minimum inhibitory concentration of 50 and 100 µg/mL for Gram negative and positive bacterium, respectively. ZnO NPs with positive surface potential when interacted with negative surface potential of bacterial membrane it results into reactive oxygen species and exerts mechanical stress on the membrane which resulted in membrane depolarization. Carried out the Study on Rose Bengal- Functionalized Chitosan Nanoparticles (CSRBNPs) for their interaction with mono species bacteria or biofilm to check its antibacterial efficiency on a multi species biofilm model *in vitro* [81]. Results showcased that CSRBNPs attached to bacteria, make cell surface rough, and later on disrupt the cell after photodynamic therapy. After CSRBNPs treatment, bacterial membrane undergoes significant damage ($p < 0.05$) and exhibited deeper penetration into the biofilm structure. This treatment is acted on most of the pathogen and eliminated clinically relevant multispecies bacterial biofilm especially in the root canal and act as an antibiofilm agent. Advocated the use of nanoscale material as an antibacterial agent specially to control drug-resistant pathogenic bacteria. They prepared water soluble gold nanoparticles polythiophene (AuNP-PTh) composite and found to be effective against common bacteria by exhibiting a membrane directed mode of action. As per study, it can easily breach the outer membrane defense barrier of Gram-negative pathogens for subsequent killing by using hydrophobic antibiotic which blocks its growth [82]. [83,84] reported the success story of Aluminium Oxide Nanoparticles (Al_2O_3 NPs) using leaf extract of lemongrass which can control extended-spectrum-β-lactamases and metallo-β-lactamases positive *P. aeruginosa.* The action of Al_2O_3 NPs when investigated by SEM it showcased that, clusters of nanoparticles getting attached to cell surface and that resulted in structural deformities in treated cells. According to high resolution transmission electron microscopy, nanoparticles found to be crossing the cell membrane to reach intracellular region and this insertion of Nanoparticles disrupts the cell membrane integrity and resulted in intracellular oxidative stress. Hence based on the results, Al_2O_3 NPs remained effective as a bactericidal agent especially against extended spectrum β-lactamases, non-extended-spectrum-β-lactamases, and metallo-β-lactamases strains of *P. Aeruginosa* and NPs found to be useful in pharmaceutical and biomedical applications [85]. demonstrated synthesis of stable copper nanoparticles (Cu-NPs) and which can control *E. coli* via NP- mediated dissipation of call membrane potential which was the main reason for the formation of cell filaments. It is also ascertained that Cu-NPs bring about multiple toxic effects such as generation of relative oxygen species, protein oxidation, lipid peroxidation in *E. coli.* Overall result highlighted that Cu-NPs acts on membrane to destabilise the structure and hence recognized as antibacterial agent. [86] involved Silver Nanoparticles (AgNPs) in antibacterial and antifungal activity in agriculture study and highlighted phytotoxic effect of AgNPs on *Oryza sativa* along with that results highlighted AgNPs treatment at 30 µg/ml accelerated root growth and at 60 µg/ml its restricts root growth ability. Further closeness of AgNPs to plants and soil induces reactive oxygen species and that lead to induction of controlling action against plant pathogens like *Bacillus thuringiensis* and inverse promotes *Bacillus amyloliquefaciens* further as per electron microscopy with AgNPs treatment bacteria was recorded with release of reducing sugar and protein through bacterial membrane and that hypothesized that AgNPs damages bacterial cell wall and further transform it into protoplasts. [87] investigated on Diamond Nanoparticles (DNPs) and put forward the possibility of antibacterial activity of DNPs and able to control *E. coli* and *S. subtilis*. They reported that DNPs activity was certainly influenced by its concentration and the morphology it possesses. According to TEM analysis, DNPs able to interact with bacterial surface and interferes with permeability of the cell functions by disturbing bacterial cell wall and/or cell membrane and that hinder *B. subtilis* growth for sure. [88,89] also put forward the success of immunological and antibacterial positive Zn nanoparticles (ZnO NPs) which was efficient in disrupting bacterial cell surface hydrophobicity and down regulating the transcription of oxidative stress resistant gene. This NPs used in study demonstrate properties of infection prevention and treatment facility and could act as future drug.

As per all these literatures it is suggested that metal oxide nanoparticles certainly been useful in antimicrobial activity and in relation present study also proposes the same to showcase few more features available with ZnO, TiO_2, and MnO_2 nanoparticles to control ever increasing multi drug resistant bacterial species.

CONCLUSION

The field of research is nanotechnology developing several nanoparticles which are proving promising in antibacterial activity. The synthesis of nanoparticles now very well understands which involves UV-visible spectrometry, XRD, and others. The synthesis of ZnO, TiO_2 and MnO_2 NPs successfully reported with plant extract and another nano-biological reducing agent. The addition of stabilizing agent like carboxymethyl celluloses reported to maintain its activity by obviating aggregation. The testing of these nanoparticles confirmed the antibacterial activity especially towards antibiotic resistance strains by producing reactive oxygen species, by damaging plasmid DNA, by changing cell morphology, and other factors. The application of ZnO. TiO_2 and MnO_2 NPs registered for better antibacterial activity in varied means such as in water purification, bandages, medical equipment surface coatings and in food preservation. Moreover, now increasing research also taking the safety and toxicity assessment of these nanoparticles via *in vivo* and *in vitro* studies.

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