A review of zinc oxide nanoparticles: an evaluation of their synthesis, characterization and ameliorative properties for use in the food, pharmaceutical and cosmetic industries.

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Received: August 29, 2020*; Accepted:* December 8, 2020

Review Article

ABSTRACT

Nanoscale materials and structures, usually ranging from 1 to 100 nanometers (nm) are of great significance in nanoscience and nanotechnology. Inorganic metal oxide nanoparticles are already used in many different products and there is an increasing demand for them. Amongst these, zinc oxide nanoparticles (ZnO NPs) are commonly used in various products because of their unusual physical and chemical properties. The U.S. Food and Drug Administration (FDA) has listed zinc oxide as a generally recognized as safe (GRAS) material. It has wide applications as a food additive, as excipients in pharmaceutical formulations, cosmetics, and implant materials. Several methods have been employed in the synthesis of ZnO NPs. These nanoparticles have been characterized by modern analytical tools such as X-ray diffraction (XRD) spectroscopy, Scanning Electron Microscopy (SEM), Fourier transformed infrared spectroscopy (FTIR), and transmission electron microscopy (TEM). The effect of ZnO NPs on biological systems has been established through studies carried out by several researchers. This review focuses on the synthesis, characterization, and pharmacological activity of zinc oxide nanoparticles.

KEY WORDS: Zinc oxide nanoparticles, ZnO, phytosynthetic route, bioimaging, surface plasmon resonance, near-hexagonal, biopersistent

INTRODUCTION

Nanoparticles (NPs) encompass a wide array of particles of matter defined as being less than 100 nm in diameter (1). Such particles can exist as nanocapsules or nanospheres (2-4). They exhibit size-associated properties that are significantly different from bulk materials (5). These particles can be synthesized by physical, chemical, and biological processes (6). Due to their small size, NPs have a larger surface area in comparison with their unprocessed counterparts. This discrete property permits their possible applications in many fields such as biosensors, nanomedicine, and bionanotechnology (7-9). NPs have gained prominence in anti-microbial therapy because of their potential to disrupt the bacterial cell membrane, as well as, cause the destruction of biofilms (10). NPs of Zinc oxide (ZnO NPs) have been recognized by several researchers for their unique morphology dependent, optical, and chemical attributes allowing for the development of many useful products (11, 12). In addition to existing conventional electronic, cosmetic, and biosensing products, ZnO NPs have been approved for use as shelf-life enhancing food additives, drug carriers, anti-bacterial, anti-fungal, and anti-oxidant agents by the US Food and Drug Administration (FDA) (13-

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21). For this paper, the authors selected ZnO NPs as model nanoparticles for review of NPs from source to characterization and applications. The objective was to highlight their importance and provide an extensive assessment of their usefulness.

A review of existing studies show that ZnO NPs have been prepared by many different methods such as chemical vapor deposition (22), hydro (solve) thermal (23), direct deposition (24), sol-gel (2), ultrasound (26), microwave-assisted combustion method (27), two-step mechanochemical-thermal synthesis (28), anodization (29), co-precipitation (30) and spray pyrolysis (31). Most of these synthetic methods use organic solvents and toxic reducing agents such as thiophenol, mercapto acetate, and sodium borohydride. These chemicals are highly reactive and pose potential environmental and biological risks. To minimize, or eliminate such risks, biological, biomimetic, and biochemical approaches have been attempted (13, 32). ZnO NPs can be characterized using X-Ray Diffractometry, Scanning Electron Microscopy, Transmission Electron Microscopy, Fourier Transform Infrared spectrometry, and Photoluminescence spectrofluorophotometry (24, 28, 33). To study the transparency and absorptivity of synthesized ZnO nanoparticles, UV-visible spectrophotometry has been used previously (34).

In this review, several key techniques used in the synthesis and characterization of zinc oxide nanoparticles have been summarized. Valuable properties, as well as, toxicity produced by ZnO NPs on biological systems are presented.

METHOD OF SYNTHESIS

Sol-gel synthesis

The sol-gel method is of interest as it offers controlled synthesis, shape variation, and patterning of the nanostructures at low processing temperatures (35-37). ZnO sols are prepared by dissolving zinc acetate dihydrate in methanol at room temperature. The pH is increased using a sodium hydroxide solution. These modified sols are then stirred ultrasonically for 60 minutes at room temperature and filtered. The resulting filtrate is allowed to stand for 48 hours to complete gelation and hydrolysis. Precipitation of white crystals of ZnO were observed. This white precipitate is filtered and washed with excess methanol to remove the starting materials and dried at 120°C for 2 hours. The investigation of the underlying mechanism showed that zinc acetate dihydrates dissolve in methanol. With an increase in the availability of hydroxyl ions at pH values above 7, acetate ions are hydrolyzed to yield zinc hydroxide. Zinc hydroxide ionizes into Zn^{+} cations and OH^{-} anions. The hydroxyl complex is then polymerized to form Zn-O-Zn bridges that are finally transformed to ZnO. Crystallinity and particle size of the ZnO powder are influenced by the pH of the starting solution (38-40). As the pH of the reaction solution increases from 6 to 9, ZnO particles gradually increase in size. However, as the pH increases above 9, these particles dissolve and recrystallize as ZnO nanocrystallites (41). Figure 1 illustrates the sol-gel route of synthesis.

Phytosynthetic route

Plant extracts have been used in the synthesis of several nanoparticles. This method takes advantage of the reducing activity of phytoconstituents on the starting materials. ZnO NPs have been synthesized using *Citrus aurantifolia* fruit extract (42). Briefly, the fruit

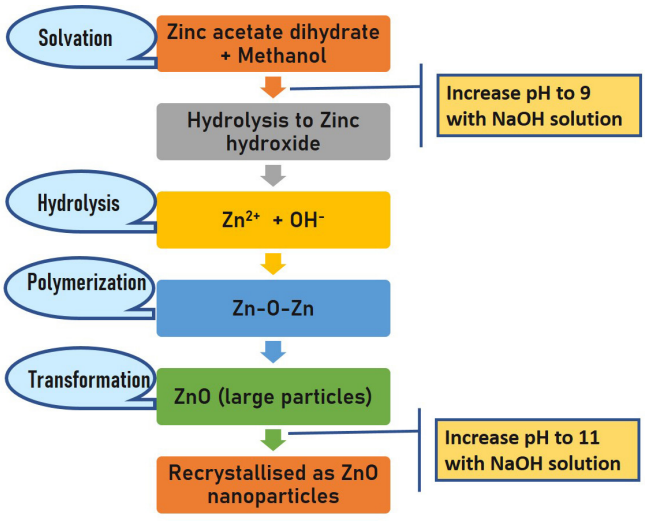

Figure 1 Sol-gel synthesis of ZnO NPs.

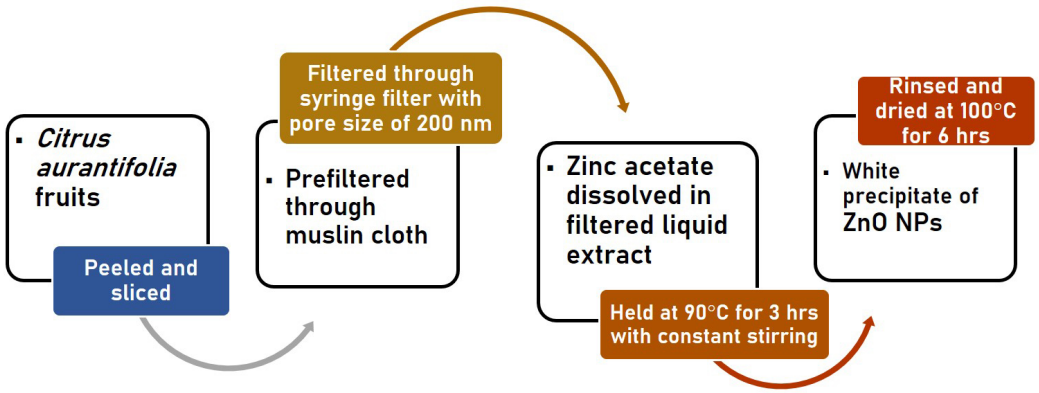

Figure 2 Phytosynthesis of ZnO NPs

pulp was pre-filtered to remove solid particles. The pulp was then passed through a syringe filter having a pore size of 200 nm. Zinc acetate was dissolved in 100 mL of the filtered *Citrus aurantifolia* liquid extract at concentrations of 0.05 M, 0.10 M, 0.15 M, and 0.20 M. The mixture was held at 90°C for 3 hours. ZnO NPs were formed by the reduction of Zinc acetate. Figure 2 illustrates this biosynthetic method. This method has the advantage of being environmentally friendly, as well as, of taking advantage of commonly available starting materials.

Solvothermal synthesis

Solvothermal synthesis involves the use of a non-toxic solvent to facilitate the reaction between precursors under conditions of moderately high pressure and temperature (43). When water is used as the solvent, the hydrothermal synthesis is carried out below the supercritical temperature of water (374°C).

It has been reported that ZnO NPs could be synthesized by reacting methanolic zinc acetate hexahydrate with NaOH solution (44). A surfactant was added to the mixture and sonicated. The mixture was transferred to a tightly closed container and held at 180°C for 3 hours. The mixture was then allowed to cool, washed with water, and centrifuged. The precipitate of ZnO was dried at 70-80°C in a vacuum oven to obtain ZnO NP in free-flowing form. Figure 3 illustrates the solvothermal synthesis of ZnO NPs.

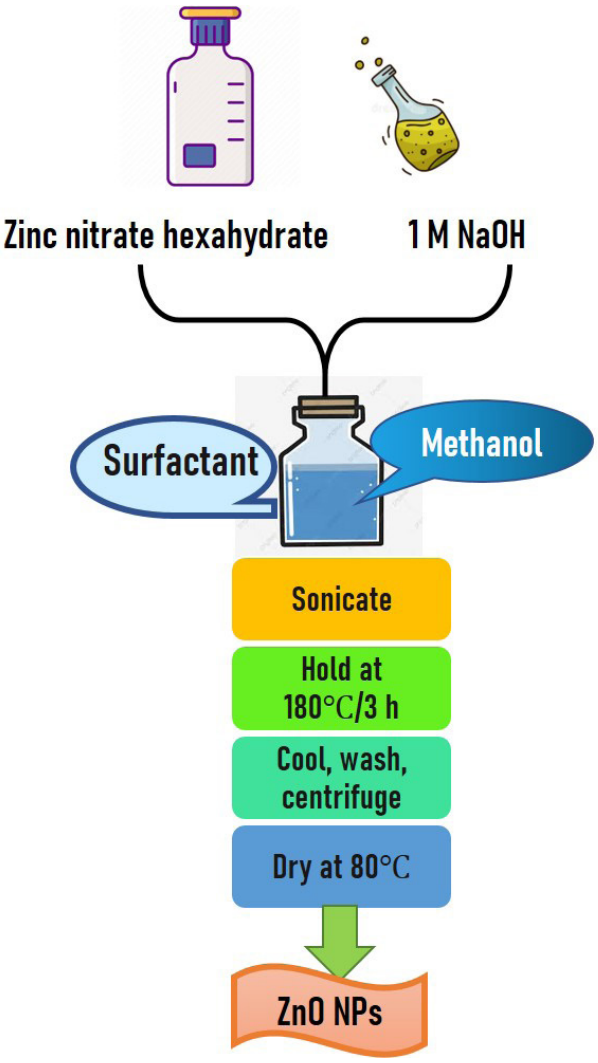

Figure 3 Solvothermal synthesis of ZnO NPs

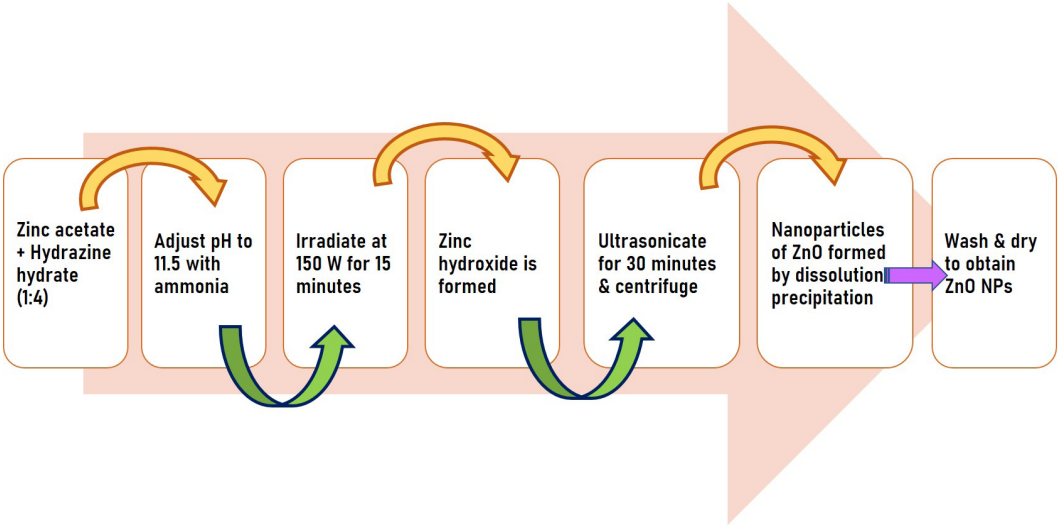

Figure 4 Microwave-assisted synthesis of ZnO NPs

Zinc precursors can also be formed through the interaction of zinc acetate and dimethyl sulfone with KOH, resulting in the formation of zinc oxide crystal nucleus. ZnO NPs disperse well in aqueous solutions because of the hydrophilic property of dimethyl sulfone (45). Some studies have shown the benefits of using ethanol, triethanolamine (TEA) or diethanolamine (DEA) as starting materials (46, 47). Here alcohol plays a very important role as it contributes its oxygen to Zn^{2+} to form ZnO (48). Due to the presence of an ionic-dipolar interaction between the hydrogen atoms in the polymer and oxygen in the ZnO, the formed ZnO seeds attract to some of the TEA or DEA chains. These chains arrest further increase in particle size as they prevent the ZnO seeds from interacting with each other (46, 47, 49).

Microwave-assisted synthesis

Microwave-assisted synthesis has been widely used to produce oxide, hydroxide, and sulfide nanoparticles because it is simple, clean, and does not pose problems due to thermal gradient effects (50). Microwave heating works on the principle of converting electromagnetic radiation into heat energy. Since different compounds have different microwave absorbing properties, selective heating of compounds in the reaction mixture takes place, resulting in the formation of products (51). Compared to the hydrothermal method, this method is advantageous due to (a) lesser reaction time, (b) inexpensive medium (c) rapid and selective heating, and (d) controlled morphology of the particles (52-56). Hasanpoora *et. al.,* successfully synthesized zinc oxide nanoparticles with different morphologies by using a microwave-assisted hydrothermal method. This experimental procedure is illustrated in Figure 4. Aqueous solutions of zinc acetate dihydrate and hydrazine hydrate in the ratio 1:4 and ammonia (NH_3) were used for this method (53). Ammonia was added to aqueous solutions of zinc precursors to adjust the pH to 11.5. A zinc hydroxide complex was formed when the reaction mixture was irradiated at 150 W for 15 minutes. The resulting complex was ultra-sonicated for 30 minutes and then centrifuged. ZnO NPs were formed through dissolution-precipitation. These were recovered by washing with deionized water and anhydrous methanol and then dried at 100°C for 2 hours.

Krishnakumar *et. al.,* have reported a quick and additive-free microwave-assisted synthesis of nanocrystalline ZnO using 1,3-propanediol as the solvent and zinc acetate as the precursor (57). ZnO nanostructures can also be synthesized in presence of polyvinyl pyrrolidone (PVP) as a 'shape modifier' (58).

Precipitation method

The precipitation method is a well-established technique that is controllable and reproducible. In this process, a capping agent is used to prevent the

agglomeration between the NPs (59). Temperature and calcination processes also influence the formation of ZnO NPs (60, 61). Kahouli *et. al.,* synthesized successfully ZnO NPs using a direct precipitation method including zinc sulfate, adipic acid, sodium hydroxide, and distilled water. The reactants were stirred to form the precipitate, and then filtered and washed with distilled water and acetone to remove the residues of adipic acid. The finished powder was dried under ambient conditions for several hours (61).

Lanje *et. al.,* prepared ZnO NPs using the precipitation method including zinc nitrate and sodium hydroxide as precursors and soluble starch as the stabilizing agent (62). In this process the starch was dissolved in distilled water at 27°C, and then 0.1 M zinc nitrate was added to the starch solution while stirring. Subsequently, 0.2 M NaOH was added drop by drop to the solution and the reaction was allowed to proceed for 2 hours after the complete addition of NaOH solution. The solution was allowed to settle for 24 hours. The supernatant solution was discarded and the sediment was centrifuged. ZnO NPs were obtained after drying at 100°C for 2 hours. This process is illustrated in Figure 5.

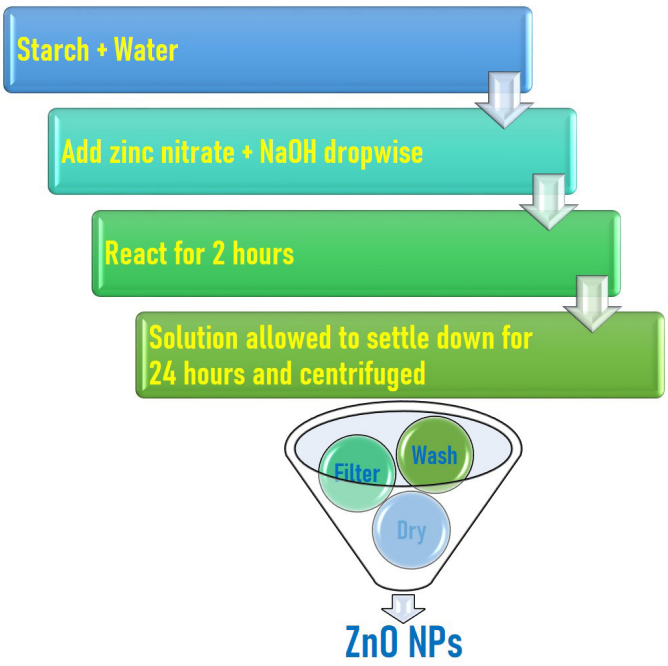

Figure 5 Precipitation method for preparation of ZnO NPs

CHARACTERIZATION

Characterizing synthesized nanoparticles is necessary to optimize the reaction conditions. The transparency and absorptivity of synthesized ZnO NPs can be measured using UV visible spectrophotometry, X-Ray Diffraction (XRD) can be used to show the structural properties of ZnO NPs while their morphological characteristics can be examined under the Scanning Electron Microscope (SEM) (63, 64).

UV visible absorption spectroscopy

UV-visible spectroscopy is widely used to determine particle formation and properties. The surface plasmon resonance of nanoparticles is influenced by their size, shape, interparticle interactions, free electron density, and the nature of the surrounding medium (65). UV absorption spectra can be used for the characterization of optical properties of ZnO NPs in the wavelength range of 300-500 nm. At a certain wavelength range, the oscillation of conducting electrons occurs due to the surface plasmon resonance (SPR) effect (66, 67). Yedurkar *et. al.*, confirmed the formation of ZnO NPs manufactured by the phytosynthetic route, wherein the SPR and absorption maxima were elicited at 340 nm (shown in Figure 6) (68).

X-ray diffraction

X-ray diffraction (XRD) is a rapid analytical technique

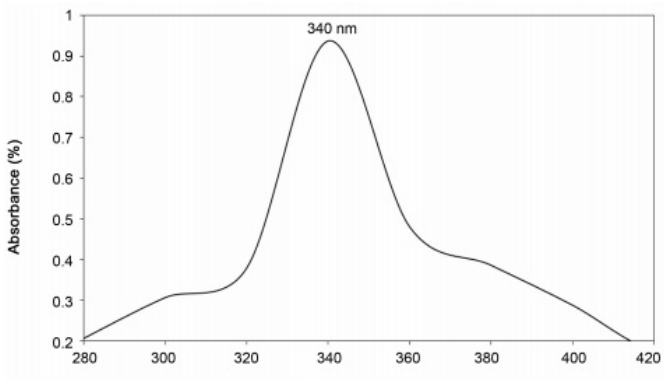

Figure 6 UV-visible spectrum of ZnO NPs (Source: Open Journal of Synthesis Theory and Applications, 5: 1-14, 2016)

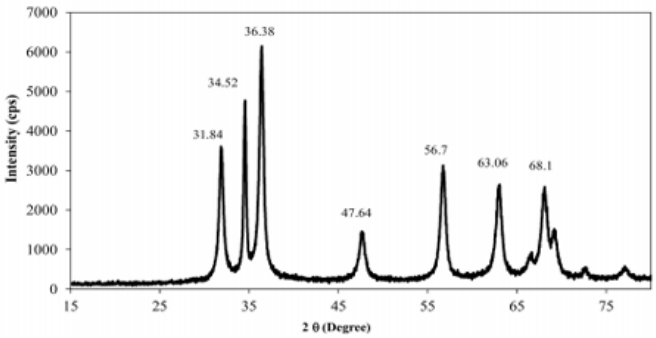

Figure 7 XRD pattern of ZnO NPs (Source: Open Journal of Synthesis Theory and Applications, 5: 1-14, 2016)

primarily used for phase identification of a crystalline material and can provide information on unit cell dimensions. The phenomenon of diffraction involves the scattering of x-rays by the atoms of a crystal and the reinforcement of scattered rays in definite directions away from the crystal (64). An X-Ray diffraction spectrum of ZnO NPs synthesized by the sol-gel method is shown in Figure 7, confirming the hexagonal wurtzite structure of the nanoparticles. The average size of the nanoparticles was in the range of 80 to 130 nm (68). The XRD pattern of ZnO-NPs prepared by the solvothermal process at 150°C for 18 hours presented with detectable peaks that could be attributed to a ZnO wurtzite structure. The crystal size was measured at 33 ± 2 nm (46).

Scanning Electron Microscopy and Transmission Electron Microscopy

Due to a high resolution and imaging speed, scanning electron microscopy (SEM) and transmission electron microscopy (TEM) are the standard methods for direct imaging and dimensional measurements of micro- and nano-structures. SEM uses a focused beam of high-energy electrons to generate a variety of signals at the surface of solid specimens. Due to the electron sample interactions, signals are produced showing information about the external morphology (texture), chemical composition, and crystalline structure, as well as, orientation (33). TEM micrographs are important tools to investigate nanoparticle sizes and shapes. When a prepared ZnO NP sample was studied with the help of TEM micrographs, an average diameter of 20 ± 2 nm was measured (69). The scattered electrons showed a characteristic diffraction pattern of the nanostructure samples, which helped in analyzing their crystal structure (33). Figures 8 A and B represent TEM and SEM images respectively of ZnO NPs prepared by the solvothermal method. The TEM in Figure 8 A shows that the ZnO NPs have crystallized in a near-hexagonal shape, which demonstrates certain favorable characteristics of the ZnO NPs. The SEM in Figure 8 B shows that the ZnO NPs are homogeneous and well dispersed (68).

APPLICATIONS

The application of ZnO NPs range from ingredients in cosmetic formulations, biosensing activities, shelf-life enhancing food additives, drug carriers, antibacterial, antifungal, and antioxidant agents because they have a favorable biocompatibility profile, are low cost, and exhibit low toxicity. They have superior antibacterial, antimicrobial, and UV blocking properties and therefore they are used extensively in the textile industries, concrete production, photocatalysis, electronics, and various other industries (70, 71). ZnO NPs have been studied for potential applications for treatments for cancer, infections and the control of diabetes. Due to their luminescent properties, ZnO NPs have been studied for use in bioimaging (72). They have been classified as Generally recognized as safe by the US FDA (GRAS) (7, 18, 72, 73). Due to their ability to absorb and scatter UV rays, they are widely used as sunscreen agents (74, 75).

BIOACTIVITY GUIDED STUDIES PERFORMED ON ZnO NPs

ZnO NPs are known for their growth inhibition properties against gram-positive and gram-negative bacteria. Food pathogens such as *Staphylococcus aureus*, *Escherichia coli*, *Salmonella typhimurium*, and *Klebsiella pneumoniae* were studied and the extent of inhibition was measured using ZnO NP enhanced nutrient broth.

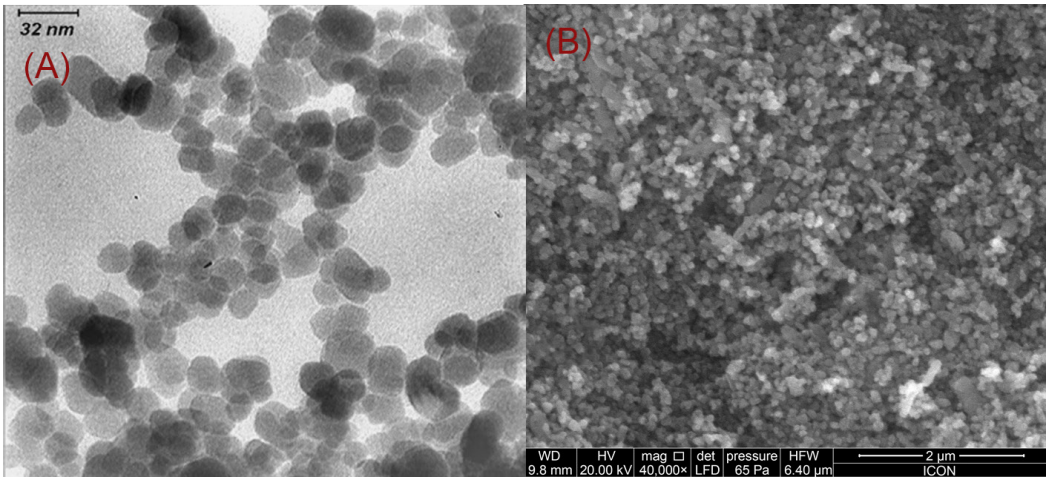

Figure 8 (A) TEM morphology image of ZnO NPs (Source: Mater Chem Phys, 121:198–201, 2010) (B) SEM of the ZnO NPs (Source: Open Journal of Synthesis Theory and Applications, 5: 1-14, 2016)

One study found that ZnO NPs have considerable anti-bacterial action against the test pathogens. This study showed that the minimum inhibitory concentration (MIC) of ZnO NPs responsible for controlling the growth of bacterial strains was 15 µg/ml for *Staphylococcus aureus*, *Salmonella typhimurium*, and *Escherichia coli*, whereas for the *Klebsiella pneumoniae* it was 5 µg/ml. In both gram-positive as well as gram-negative bacteria, damage to cell membranes leading to the leakage of cell contents and cell death was the underlying mechanism (76).

ZnO NPs have also been investigated against a panel of human pathogens and drug-resistant clinical isolates representing gram-positive, gram-negative, and acid-fast bacteria. Concurrently, the mechanism of antibacterial activity and potential to treat skin infections caused by *Staphylococcus aureus* in a murine model was explored. The results showed an improvement in skin architecture, reduced bacterial burden, and lowering of inflammation induced by *Staphylococcus aureus* infection in mice indicating that ZnO NPs could be used as a topical anti-infective agent. An important conclusion of the study was that gram-positive bacteria are more susceptible to ZnO NPs compared to gram-negative and acid-fast bacteria. However, *M. Bovis* BCG was effectively eliminated only when ZnO NPs were administered in conjunction with the anti-tubercular drug rifampicin. The study reported that ZnO NPs killed bacteria by disrupting the cell membrane and by down-regulating the expression of oxidative-stress resistance genes thereby making bacteria prone to oxidative stress. ZnO NPs significantly inhibited the intracellular survival of *Mycobacterium smegmatis* in infected macrophages by increasing the production of reactive oxygen species (ROS) (77). In another study, ZnO NPs were investigated for their effect on cultured osteosarcoma cells. The ZnO NPs reduced the proliferation of MG63 osteoblast-like cells in a concentration-dependent manner. This was confirmed by a 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) assay method and by Fluorescein diacetate hydrolysis (FDA) staining (78).

Semiconductor nanocrystals have shown promise in the area of bioimaging because of their photoluminescent properties which include a broad absorption, narrow and symmetric emission band, large Stokes shifts, and weak self-absorption and tunable emission wavelength based on quantum size effects, and high stability against photo-bleaching (79-82). However, the luminescence elicited by ZnO NPs in a murine model was unstable (83). On the other hand, ZnO quantum dots (QDs) which are coated with a silica shell and silane groups have shown more stable luminescence in cell culture and animal blood (84-87).

ZnO NPs have demonstrated biocidal activity and cellular internalization when tested *in-vitro* against *E. coli* (88). A study carried out by Jones *et. al.,* confirmed the versatility of ZnO NPs as anti-bacterial agents of choice by demonstrating their bactericidal effects against *S. aureus, S. epidermidis, S. pyogenes, B. subtilis* and *E. faecalis* (89). He *et. al.*, investigated the anti-fungal activity of ZnO NPs against two important plant pathogenic fungi, *B. cinerea* and *P. expansum.* The ZnO NPs possessed significant anti-fungal properties against both fungal species, and the inhibitory effects were concentration-dependent (90). Additionally, the concentration of ZnO NPs required to inhibit *A. hydrophila, E. coli, S. aureus, P. aeruginosa, E. faecalis, S. pyogenes, A. flavus, A. niger* and *C. albicans* was experimentally determined and reported (91).

In a study carried out by Olbert *et. al.,* ZnO NPs, when injected intraperitoneally demonstrated anti-inflammatory activity and enhanced the effect of ketoprofen, an established anti-inflammatory drug (92). The underlying mechanism was correlated to the anti-oxidative property of zinc and inhibition of NF-β pathway with a concomitant decrease in the production of IL-1 and IL-6 as well as COX and NO synthetase (pro-inflammatory cytokines). The same study showed that ZnO NPs could protect gastric mucosa from ketoprofen induced gastric ulcer. ZnO NPs improved the microcirculation in the ulcerogenic area. Zinc also caused an increase in plasma gastrin level which enhances the process of ulcer healing (93, 94).

Zinc, an essential trace element has been reported to be responsible for maintaining the structural integrity of insulin and plays an important role in its secretion from pancreatic cells. It also participates in insulin synthesis and storage. The role of ZnO NPs as an anti-diabetic has been reported in the literature (95-97). ZnO NPs elicit anti-inflammatory activity by suppressing nitric oxide production and by the secretion of iNOS, COX-2, IL-β, Il-6 and TNF-α (pro-inflammatory markers) (98). ZnO NPs elicited immunomodulatory effects wherein they enhanced the immune response by increasing antibody production and activating cell-mediated immune response via T-cells. They also increased the production and activation of cytokines associated with immunomodulatory responses (99). The anti-cancer activity of ZnO NPs has been evaluated in several cancer cell lines (15, 100-105). ZnO NPs have been also been reported to have anxiolytic effects (106, 107). As a component of pharmaceutical drug delivery systems and personal care products for external use, ZnO NPs are tested for their sensitization properties and allergenic potential using standardized tests. When used as a component of functional foods, anti-microbial, and sunscreen agents, such agents can enter the human system accidentally or otherwise, albeit in small quantities.

TOXICITY PROFILING OF ZINC OXIDE NANOPARTICLES

Two facets of the toxicity elicited by ZnO NPs (direct and indirect) were reviewed in detail by McClements and Xiao (108). Although the particle size of ZnO NPs is small, these nanoparticles exist as large aggregates in the gastrointestinal tract and hence it is difficult to predict their GI fate and toxicity. Further, these aggregates encounter huge variations in pH ranging from 7.4 (oral cavity) to 2 to 3 (gastric fluid) to 5 to 7 (small intestine) to 8 in the colon. This may alter the electrostatic interactions of these nanoparticles leading to changes in their aggregation state. Additionally, during transit, they are also exposed to digestive enzymes, electrolytes, bile salts, lipids, colonic bacteria, and undigested food. The properties of these ZnO NPs and their aggregates are appreciably altered by the gastrointestinal environment and hence their undesirable effects on the gastrointestinal system need to be studied on a case-by-case basis.

Ingested nanoparticles are known to interfere with the normal functioning of the gastrointestinal tract (GI) thus manifesting toxicity. Due to the large surface area of these nanoparticles, they may adsorb digestive and metabolic enzymes, as well as, starches, lipids, and proteins on their surface, leading to denaturation and/or inadequate absorption. However, this is not a major cause of concern for ZnO NPs as these are not consumed in large quantities. However, ZnO NPs may be able to physically disrupt important structures such as tight junctions or microvilli within the GI tract

thereby affecting nutrient absorption. The immune response to these particles also needs to be considered (109). Furthermore, inorganic nanoparticles being biopersistent may accumulate in the tissues on chronic exposure resulting in toxicity.

Nanoparticles used for the encapsulation of bioactive agents may indirectly manifest toxicity by altering the location of the release of the bioactive. Thus, a bioactive agent that is normally absorbed from the stomach may, upon the combination with a ZnO NP carrier, be released only in the colon thereby altering its metabolism leading to toxicity (110). Such effects are system-specific and difficult to predict. Nanoparticles have been known to enhance the stability, as well as, bioavailability of hydrophobic molecules thereby impacting the safety profile of such moieties. A fallout of this tendency is enhanced uptake of pesticides and hormones (111-114).

Several preclinical studies have been carried out to understand the toxicity traits of ZnO NPs. Xiao *et. al.*, studied the influence of ZnO NPs on cell viability of mouse podocytes using an MTT assay (115). Parameters such as apoptosis of cells, the concentration of reactive oxygen species generated, superoxide dismutase, and malondialdehyde levels were measured. The results showed that ZnO NPs, when cultured in the medium with the podocytes, were responsible for decreasing cell viability, inducing apoptosis, and increasing the levels of reactive oxygen species and malondialdehyde levels with a concurrent decrease in levels of superoxide dismutase. Acute toxicity studies were performed in rats to gather supporting evidence. A decrease in body weight and kidney index verified the toxicity of ZnO NPs.

The toxicity potential of ZnO NPs was further confirmed by Liu *et. al.,* in an *in vitro* study where the effect of ZnO NPs on human neuroblastoma cells were examined (116). ZnO NP induced the formation of reactive oxygen species. The subsequent oxidative stress was identified as the main causative factor for the initiation of the apoptotic mechanism in the cells. It is noteworthy that ZnO NPs dissolved rapidly in the acidic vesicular organelles releasing zinc ions which were also responsible for inducing toxicity. The cytotoxicity of ZnO NPs was evaluated using three mouse myoblast cell lines (117). A significant decrease in cell viability was recorded in all three cell lines. Microscopic studies revealed that cells exposed to ZnO NPs developed abnormality in shape and cellular contraction. Reduction in cytoplasm and the absence of cellular adhesion was also evident.

There are a few reports of ZnO NPs eliciting toxicity after penetrating through the skin. However, a study by Mohammed *et. al.*, conclusively proved that ZnO NPs do not penetrate the viable epidermis or cause toxicity on epidermal surfaces (118). This and several other studies were condensed by Wright (119).

Inhalation of ZnO NPs has been shown to result in the inflammation and fibrosis in alveoli and bronchioles (120). Administration of ZnO NPs has also been observed to elevate levels of liver enzymes and blood glucose levels. Also, severe anemia and undesirable histopathological changes were perceived in the liver and heart of rats (121, 122). This was in addition to an altered hematological profile (123). Maternal and developmental toxicity has also been reported in a preclinical study performed in rats (124).

CONCLUSIONS

Zinc oxide is a multi-faceted material with interesting properties such as absorptivity of UV rays, high photostability, biocompatibility, and biodegradability. As nanoparticles, ZnO elucidates unique morphology dependent optical and chemical attributes, which are responsible for its applications in several functionalized products in various fields such as biosensors, nanomedicine, and bionanotechnology. It is imperative to weigh the beneficial effects of these promising nanoparticles against their toxicity. The immunological and inflammatory responses elicited by the body when faced with these foreign particles need to be understood better. There are several contrasting reports of the role of ZnO NPs in ROS formation and cell apoptosis. Most of the studies reported so far have been carried out using cell lines and therefore warrant extensive preclinical and clinical studies before

these promising moieties can be exploited for their health benefits. This review aims to spark an interest in further research into the lesser-explored aspects of ZnO NPs such as their mechanism of action, clinical studies, and commercial applications.

ACKNOWLEDGEMENTS

The authors wish to thank the Management of the Gahlot Institute of Pharmacy for supporting this work.

CONFLICT OF INTEREST

The Authors hereby declare no conflict of interest.

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