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Opinion

Pharmaceutical Applications of Zinc Oxide Nanoparticles- A Review

Balasubramanian Malaikozhundan*

Young Scientist, Nanobiosciences and Nanopharmacology Division, Biomaterials and Biotechnology in Animal Health Lab, Department of Animal Health and Management, Alagappa University, Karaikudi, Tamil Nadu, India

***Corresponding Author:** Balasubramanian Malaikozhundan, Young Scientist, Nanobiosciences and Nanopharmacology Division, Biomaterials and Biotechnology in Animal Health Lab, Department of Animal Health and Management, Alagappa University, Karaikudi, Tamil Nadu, India.

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The synthesis of nanoparticles using microorganisms and plants has been reported to possess biomedical applications. Biological synthesis of nanoparticles is an eco-friendly, cost-effective, biocompatible and safer approach [1]. Recently different types of metallic nanoparticles are synthesized by green approach. Among the metal oxide nanoparticles, zinc oxide is very interesting because it has vast applications such as optical, piezoelectric, magnetic, and gas sensing. Besides these properties, ZnO nanostructure exhibits high catalytic efficiency, strong adsorption ability and are used more frequently in the manufacture of sunscreens, ceramics and rubber processing, wastewater treatment, and as a fungicide [2]. It has a wide range of biomedical applications like drug delivery, anti-cancer, anti-diabetic, anti-bacterial, anti-fungal and agricultural properties [3-6]. Although ZnO is used for targeted drug delivery, it has the limitation of cytotoxicity which is yet to be resolved [7]. ZnO NPs have a very strong antibacterial effect against Gram negative and Gram positive bacteria at a very low concentration. Further, they have shown strong anti-bacterial effect than the chemically synthesized ZnO NPs [8-10].

ZnO nanoparticles have gained interest in biomedical applications based on their high stability, inherent photoluminescence properties which can be useful in biosensing applications, and wide band-gap semiconductor properties useful in photocatalytic systems and promotion of reactive oxygen species generation. ZnO nanoparticles have recently been used in cholesterol biosensors, dietary modulators for hydrolase activity relevant to controlling diabetes and hyperlipaemia, as well as cell imaging [11,12]. Additionally, ZnO nanoparticles shown promise in modulating allergic reactions via inhibition of mast cell degranulation [13]. The diversity of these activities has popularized ZnO nanomaterials in interdisciplinary research communities involving physicists, chemists, and biologists. One of the primary advantages for considering ZnO nanoparticles for use in cancer is the inherent preferential cytotoxicity against cancer cells *in vitro* [14,15]. It is suggested that their cancer cell selectivity may be even further improved by engineering design to minimize harmful effects to normal body cells, which has been observed to occur at very high concentrations of ZnO nanoparticles, particularly those in the smaller size range of 4 - 20 nm [12]. In this regard, the surface chemistry of ZnO nanoparticles readily lends them to functionalization with targeting proteins or chemical groups, and may be a key to rendering them benign to normal cells while still retaining their cancer targeting and killing properties.

Another feature of ZnO nanoparticles, as stated earlier, is their ability to induce reactive oxygen species (ROS) generation, which can lead to cell death when the antioxidative capacity of the cell is exceeded [16,17]. The ability of ZnO nanoparticles to generate ROS is related to their semiconductor properties. Several studies have suggested an increase in *in vitro* cytotoxicity with nanophase ZnO compared to micron-sized ZnO for several types of cancers including glioma, breast, bone, colon, and leukemias and lymphomas [14,15]. ZnO nanoparticle exposure has been shown to induce the production of a variety of pro-inflammatory cytokines, including TNF-α, IFN-γ and IL-12, in *in vitro* and *in vivo* pulmonary inhalation studies [12,18]. The ability of ZnO nanoparticles to induce pro-inflammatory cytokines at nanoparticle concentrations below those causing appreciable cell death suggests that, when used at appropriate concentrations, they could enhance tumor cell killing through the production of TNF-α (tumor necrosis factor), a cytokine named for its potent anti-tumor activities [19]. Nanoparticle-induced cytokines could also facilitate effective anti-cancer actions by eliciting a cytokine profile crucial for directing the development of Th1-mediated immunity [20]. The Th1 lymphocyte subset plays an essential role in enhancing the natural cytotoxic potential of natural killer cells and T cytotoxic cells against cancer cells. Recently, the anti-bacterial activity of *Laurus nobilis* leaf extract coated ZnO nanoparticles (Ln-ZnO NPs) has been reported against Gram positive (*Staphylococcus aureus*) and Gram negative (*Pseudomonas aeruginosa*) bacterial. In addition, the anti- cancer activity of Ln-ZnO NPs against human A549 lung cancer cells has been reported [21]. The therapeutic applications of *Pongamia pinnata* coated zinc oxide nanoparticles (Pp-ZnO NPs) against clinically important pathogenic bacteria, fungi, and human breast cancer (MCF-7) cells have been reported [22]. It was demonstrated that *Plectranthus barbatus* leaf extract mediated zinc oxide nanoparticles effectively controlled the clinically important biofilm forming Gram positive (*Bacillus subtilis*) and Gram negative (*Vibrio parahaemolyticus* and *Proteus vulgaris*) bacteria [23].

The development of tumor-specific nanoparticles as vehicles for drug delivery is currently an area of intensive research with the potential to revolutionize therapeutics against cancer. The use of nanoparticles as drug delivery for anti-cancer agents has significant advantages such as the ability to target specific locations in the body, reduce the overall amount of drug used, and the potential to reduce drug concentrations at non-target sites resulting

in fewer side effects. This review has focused on the pharamaceutical applications of ZnO nanoparticles, including anti-bacterial, anti-biofilm and anti- cancer properties. The green synthesized ZnO NPs has potential benefits compared to that of chemically synthesized one. This review concludes that the green synthesized ZnO NPs could be synthesized in large scale for pharmaceutical applications to mitigate human health associated diseases.

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