# PROPERTY OF ZINC OXIDE NANOPARTICLE - A REVIEW

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**Abstract:**

Nanoparticles are smaller in size and can easily penetrate the cell line and can cause cell lysis. They possess outstanding properties like antiseptic and antimicrobial and phototoxicity on budding flora. Therefore with the recent advancement nanoparticles are broadly used in various fields either as coating medical devices, as drug delivery system. NPs are broadly divided into various categories depending on their morphology, size and chemical properties. There are various techniques for producing nanoparticles and for deposition of nanoparticles some are magnetic spluttering, physical vapour deposition, chemical vapour deposition, electrospinning etc. Among various inorganic nanoparticles zinc oxide nanoparticle is readily available, all human bodily tissues contain zinc and are cheaper to synthesis. ZnO NPs exhibit tremendous wound healing, catalytic, bio-imaging, anti-bacterial, anti-inflammatory properties making it the most suitable candidate for biomedical applications among other metal and metal oxide nanoparticles. ZnO NPs is used as a potential drug delivery vehicle for standard drugs as it provides synergistic effects for the treatment. In this study we exhibit on the anti-inflammatory and antioxidant property of ZnO nanoparticle.

**Keywords:** Nanoparticles, Anti-inflammatory, Antioxidant.

## Background:

The evolving of nanotechnology in an eco-friendly manner has become a part of greenery biotechnology with crucial study of dimension and their shape and structure [1,2]. The ultimate intention of the nano medicine domain is to develop drugs with precise targets and these nanoparticles can be manufactured by means of physical, chemical and natural

process [3]. Among these, the opting of biosynthesis is an ideal way in the terms of ecological friendly [4], which possess outstanding properties of antiseptic and antimicrobial and further are supposed to reveal substantial phototoxicity on budding flora [5].

Nanotechnology and its implication in various pharmaceutical field is the area of focus in modern material science. In the International System of Units (Système international d'unités, SI), a nanometer (nm) is a unit that corresponds to 109 metres in length. In theory, NMs are materials with at least one dimension having a length of 1-1000 nm; however, in practise, NMs are typically characterised as having a diameter between 1 and 100 nm. It explores the synthesis, manipulation, and fabrication of surface atoms with particle diameter in the nanometer range of 1-100 nm [6]. One of the two primary methods—bottom-up approach or top-down approach—is commonly used to create nanomaterials. Among all the techniques, the production of nanomaterials through physical vapour deposition, chemical vapour deposition, electrospinning, 3D printing, biological synthesis, and supercritical fluid has recently gained prominence. These techniques are combined with others to increase the effectiveness of the synthesis process. Nanomaterials exhibit superior physicochemical properties unlike their bulk counterparts like enhanced electronic, optical, catalytic and pharmaceutical properties. Metal oxide nanoparticles demonstrate far-ranging prospects in the biomedical fields like biosensor development, cell imaging technique and as a vehicle for drug delivery [7].

NPs are broadly divided into various categories depending on their morphology, size and chemical properties

- Carbon-based NPs
- Metal NPs
- Ceramics NPs
- Semiconductor NPs
- Polymeric NPs
- Lipid-based NPs

The advantages of using nanoparticles include the following:

- Particle size and surface characteristics of nanoparticles can be easily changed to achieve both passive and active drug targeting after parenteral administration.
- They control and sustain release of the drug during the transportation and at the site of localization, altering organ distribution of the drug and subsequent clearance of the drug so as to achieve increase in drug therapeutic efficacy and reduction in side effects.
- Controlled release and particle degradation characteristics can be readily modulated by the choice of matrix constituents. Drug loading is relatively high and drugs can be incorporated into the systems without any chemical reaction; this is an important factor for [9] preserving the drug activity.
- Site-specific targeting can be achieved by attaching targeting ligands to surface of particles or use of magnetic guidance.
- The system can be used for various routes of administration including oral, nasal, parenteral,intraocular etc.

Among the various inorganic nanoparticles available, Zinc (Zn) and its oxide are among the metals with biological effects that have been extensively investigated (ZnO). Since it has significant reduction characteristics, zinc is an active element. It is readily oxidizable and produces zinc oxide. Since zinc is one of the most vital trace elements, it plays a significant function in the human body. All human bodily tissues contain zinc, but myocytes have the largest quantity (85% of the body's total zinc content) [8]. It has been demonstrated that zinc is essential for the normal operation of a significant number of macromolecules and enzymes, where it serves as both a structural and catalytic component (coenzyme). In response, Zincfinger structures offer a special framework that enables protein subdomains to bind with DNA or other proteins [9].

Zinc Oxide (ZnO) has easy processing methods, is inexpensive, has wide range of applications and is a safe material. The special qualities and adaptability of ZnO make it possible to create different ZnO nanostructures using a variety of techniques. By adjusting the synthesis settings, ZnO-NPs can be made in a variety of ways. The properties are adaptable in terms of size and shape, leading to renewable applications according to their structural characteristics. The chosen technique largely relies on the intended application because various techniques result in ZnO particles with various morphologies and sizes. As a result, factors including the kind of solvent, the precursors, the pH, and the temperature were carefully taken into account. Due to these properties, Zn O pulls a particular interest among researchers. Zinc Oxide nanoparticles (ZnO NPs) play a vital role in diagnostics, biomolecular detection, microelectronics. ZnO NPs has drawn considerable attention as compared to other metal and metal oxide nanoparticles owing to its excellent biomedical properties. Zn plays an important role in maintaining the metabolism of the body through hematopoiesis, enzyme regulation, maintaining cell redox balance and DNA and protein synthesis machinery regulation. ZnO NPs have been recognized as generally recognized as safe (GRAS) material by Food and drug administration (FDA) U.S.A [10]. ZnO NPs exhibit tremendous wound healing, catalytic, bio-imaging, anti-bacterial, anti-inflammatory properties making it the most suitable candidate for biomedical applications among other metal and metal oxide nanoparticles. ZnO NPs is used as a potential drug delivery vehicle for standard drugs as it provides synergistic effects for the treatment [11]. This review also provides a synopsis of anti-inflammatory and antioxidant property of ZnO NPs.

**ANTI-INFLAMMATORY AND ANTIOXIDANT PROPERTY**

Inflammation is an adaptive immune response that is induced by pathogen, irritants, and damaged cells, and tissue injury (Majno and Joris, 2004; Kumar and Cotran, 2003). The aims of inflammation are to delete the initial cause of cell injury, tissues damaged from the original insult, and clear out death cells. At a basic level, the primary inflammatory response induced by tissue injury or infection involves the infiltration of neutrophils, eosinophils, basophils, mast cells, ma

Anti-inflammatory activity of zinc oxide nanoparticle have widely emerged as an anti-inflammatory agent in the last several decades. The large surface area to volume ratio confers them high surface reactive properties and thus facilitates their interaction with the biological membrane and their physical transport inside the membrane. ZnO NPs allows Zn to be easily

absorbed through the biological membranes due to its size in the nano-scale range. Previous literature suggests potent anti-inflammatory activity of zinc oxide nanoparticles. Common anti-inflammatory mechanisms adopted by zinc oxide nanoparticles include inhibition of inducible nitric oxide synthase (iNOS) enzyme expression [12], inhibition of pro-inflammatory cytokines release [13], myeloperoxidase inhibition [14], inhibition of the NF-κβ pathway and inhibition of mast cell degranulation.

Suppressing the expression of inflammatory marker genes like IL-6, IL-1β, IL-10, and TNF-α is the most common mechanism adopted by ZnO NPs for showcasing antiinflammatory activity. Expression of COX-2 enzyme; which is the major contributor for cardinal signs development of inflammation is also downregulated. ZnO NPs alters protein release and expression of inflammatory mediators by inhibiting NF-kB pathway. TNF-α assists in the activation of nuclear factor-kappa B (NF-κβ) pathway. Previous studies suggest Zn+2 mediated inhibition of TNF- α, IL-1β and IL-6 release in LPS induced endotoxemia model [13]. Another study also reports the dose-dependent downregulation of IL-6 upon administration of 4 µg/mL ZnO NPs to HepG2 cells. It has also been shown that ZnO NPs inhibit the release of TNF-α from human lymphocytes against inflammation and cytotoxicity caused by chlorpyrifos, an acetylcholinesterase inhibitor. These findings suggest the probable mechanism of Zn+2 release from ZnO NPs and subsequent inhibition of proinflammatory cytokines [15].

The antiinflammatory mechanism of ZnO NPs has been investigated using a variety of models. In LPS-stimulated RAW 264.7 macrophages, P.C. Nagajyothi et al. reported that ZnO NPs have anti-inflammatory effect by inhibiting the gene and protein production of pro-inflammatory mediators such IL-6, IL-1b, iNOS, COX-2, and TNF [16]. By inhibiting the NF-B pathway, which further reduced the release of pro-inflammatory cytokines like IL-1, IL-6, COX enzyme, and nitric oxide synthase activity, In the study by Mohapatra S et al., it was seen that at 5 µL concentration there was a death of 20% of nauplii, at 10 and 20 µL there was a death of 30% of nauplii, at 30 µL there was a death of 40% of nauplii and at 50 µL there was a death of 50% of nauplii. Percentage of inhibition of protein denaturation (antiinflammatory activity) was 68.2% at 10 µL concentration, 89.8% at 20 µL, 88.5% at 30 µL and highest at 40 µL (91.1%) and 50 µL (90.5%). Percentage of inhibition of DPPH free radicals (antioxidant activity) was 83.9% at 10 µL concentration, 86.2% at 20 µL, 85.3% at 30 µL, 85.2% at 40 µL (85.2%) and 84.9% at 50 µL [17].

Many studies have been conducted to assess the cytotoxicity of Zinc Oxide nanoparticles, clove and cinnamon [18,19]. The mechanisms of cytotoxicity from Zinc Oxide nanoparticles are not yet entirely understood, but the generation of hydroxyl radicals (OH•), superoxide anion, and perhydroxyl radicals from the surface of Zinc Oxide are believed to be major components [20]. High eugenol content in clove makes it cytotoxic. Hence they can be used against cancer cells. Studies have also revealed that Zinc Oxide nanoparticles, clove and cinnamon have anti-inflammatory and antioxidant properties [21]. Zinc Oxide nanoparticles are known to have anti-inflammatory properties by blocking pro-inflammatory cytokines, inhibiting mast cell proliferation and suppressing LPS induced COX-2 expression. Antioxidant Zinc Oxide nanoparticles is due to release of hydrogen which reduces DPPH free radical easily [22]. Anti-inflammatory and antioxidant of clove is due to its high eugenol content. Eugenol is a natural phenolic compound which reduces DPPH free radical by easily donating hydrogen.

Different flavonoids isolated from cinnamon have anti-inflammatory free-radical-scavenging activities [23].

In the mouse AD model, Ilves et al. looked at whether various-sized ZnO NPs could penetrate wounded skin and harmed allergic skin. Their research amply shown that bulk-sized ZnO (bZnO) remained in the surface layers of both injured and allergic skin, but only nanosized ZnO (nZnO) was able to penetrate into the deep layers of allergic skin. In the animal model of AD, nZnO exerted more anti-inflammatory effects than bZnO by significantly lowering proinflammatory cytokines (IL-10, IL-13, IFN-, and Th2 cytokines). These findings showed that in AD models, tiny ZnO NPs had a significant impact on decreasing skin inflammation .

**ANTIOXIDANT PROPERTY**

Antioxidants play an important role in the functioning of all bio-systems. In biological systems, free radicals are generated due to interaction of biomolecules with molecular oxygen [24]. Nanoparticles of a number of metal oxides lead to the production of ROS upon interaction with bacteria. The metal ions released by the nanoparticles affect the respiratory chain and inhibit some enzymes. This leads to the formation and accumulation of singlet oxygen, hydroxyl radical, hydrogen peroxide, superoxide anions, and other ROS. ROS can cause damage to the internal components of bacteria, such as proteins and DNA. These free radicals are responsible for degradation of biomolecules. Oxidation is also accountable for nutritional quality deterioration and discoloration of food. Consumption of oxidized foods generates lipid peroxides and low molecular weight compounds which causes serious diseases like hepatomegaly or necrosis of epithelial tissues. In the biological systems, antioxidant plays an important role for scavenging of these toxic free radicals [25]. Many kinds of natural and synthetic antioxidants have been investigated to inhibit these oxidation reactions to date.

Mohanan and co-workers synthesized and studied the effect of ZnO nanoparticles on cellular oxidative stress and antioxidant defense mechanisms in mouse liver. They have found that when ZnO nanoparticles were exposed to mouse liver tissue homogenate,there was a concentration-dependent decrease in cell viability and rise in antioxidant enzyme levels occurs [26]. Wang and co-workers studied the synergistic cytotoxic effect of different sized ZnO nanoparticles with the accompanying anticancer drug of daunorubicin on leukemia cell lines and found efficient to exert the synergistic cytotoxicity suppression on both leukemia cell lines under UV irradiation [27].

In a study by Das et al., Antioxidant efficiency of ZnO nanoparticles increases with increasing concentration. The particles show free radical scavenging capacity upto 91% in 90 min, which gives good evidence toward antioxidant activity. The ZnO nanoparticles also show a permissible limit of hemolysis activity at its lower concentration and hence, this can be considered as biocompatible. Therefore, this nanoparticle can be applied as a promising antioxidant in the biological system. This study might lead us to a new insight into the activity of ZnO nanoparticles in biological system [28].

ZnO NPs were created by Arakha et al. using the chemical precipitation method, and their anticancer efficacy was then assessed [64]. It was discovered that ZnO NPs of various sizes could clearly inhibit the proliferation of fibrosarcoma HT1080 cells. The findings demonstrated a connection between intracellular ROS production and the incidence of autophagy in cancer cells. Following treatment with ZnO NPs, HT1080 cells stained with

acridine orange dye showed striking orange and red fluorescence, indicating the presence of autophagic cells with acidic vesicular organelles. Additionally, ZnO NPs-treated cells had a relative amount of LC3 II that was noticeably higher than untreated cells, indicating a greater degree of autophagy. The formation of ROS when ZnO NPs interact with HT1080 cells is substantially higher. DNA damage was one of the biomolecular damages caused by excessive ROS.

Although previous research has suggested that ROS and autophagy have a role in ZnO NPs' cytotoxicity, the regulating mechanisms between autophagy and ROS have not yet been fully understood. In lung epithelial cells treated with ZnO NPs, Zhang et al. looked at the control of autophagy and the relationship between autophagy and ROS [29]. The findings showed that ZnO NPs could cause A549 cells to accumulate autophagosomes and have impaired autophagic flux. This ZnO NP dissolution in lysosomes to release zinc ions was positively connected with the induction of autophagy, and the zinc ions that were released could harm lysosomes and disrupt autophagic flux and mitochondria.

The drawbacks of nanoparticles

Despite these benefits, there are certain restrictions with nanoparticles.

Physical handling of nanoparticles in liquid and dry forms can be challenging because to, among other things, their small size and huge surface area, which can also easily result in limited drug loading and burst release.

Before nanoparticles may be sold commercially, several practical issues must be solved. The newest advancements in nanoparticulate drug delivery systems, surface modification difficulties, drug loading techniques, release control, and future applications of nanoparticles are all covered in this study.

Based on their anticancer, antibacterial, antidiabetic, anti-inflammatory, drug delivery, and bioimaging properties, ZnO NPs have demonstrated promising biological uses. Due to their inherent toxicity, ZnO NPs have the potential to be used as anticancer and antibacterial treatments since they have substantial inhibitory effects against bacteria and malignant cells by causing intracellular ROS generation and activating the apoptotic signalling pathway.

## CONCLUSION

Based on the findings of the review we can say that reinforcing zinc oxide nanoparticles has a synergistic effect and can be used as an alternative to commercially available anti-inflammatory and antioxidant agents.

ZnO NPs have a promising future in biomedicine due to their innate capacity to trigger the formation of ROS and trigger apoptosis. ZnO NPs are well suited as anticancer, antibacterial, and antifungal agents due to their characteristics. When loaded and delivered with additional therapeutic drugs, ZnO NPs have also been observed to have synergistic effects. Although the FDA has allowed ZnO for use in cosmetic preparations and it is thought to be a relatively harmless metal oxide, the toxicity of ZnO NPs is still a worry due to its huge surface area and metallic makeup. While ZnO NPs' biological potential is currently being investigated, in-depth research are necessary to examine their toxicity profile in order to get the most out of this intriguing metal oxide.

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