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Analytical Study of Zinc-Oxide Nanoparticles for Human Health

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Abstract

Pure nanoparticles for medical applications more than 400 enzymes and hormones and play a curious part in the health of our skin, teeth, bones, hair, nails, muscles, nerves and brain function have attracted much attention due to their enhanced biocompatibility and multifunctional, antibacterial, antifungal, antiviral properties making them suitable for many applications such as prednisolone delivery systems and nanotherapy. Among Nanomaterials, zinc oxide nanoparticles (ZnO NPs) have been extensively studied due to their unique physical and chemical properties. High surface-to-volume ratio together with small size, antibacterial activity, photocatalytic and semiconductor properties make ZnO NPs a new generation of anticancer agents in physiotherapy, reactors Nano bioreactors and bone stimulants for bone tissue regeneration. However, ZnO NPs have limited stability and can be used in biological environments. ZnO NPs also exhibit unpredictable cytotoxic effects. To overcome the above limitations and further expand the use of ZnO NPs in nanomedicine, doping seems to be a promising solution. This theoretical review reveals important achievements in using ZnO-doped nanoparticles for applications in nanomedicine. Sol-gel, hydrothermal and combustion methods are commonly used to fabricate rare-earth and transition metal-doped ZnO NPs. The theoretical results indicate that the doping of ZnO NPs is a valuable tool to improve their biomedical properties compared with undoped NPs, opening up new possibilities for ZnO NPs in nanomedicine.

Keywords: Bioimaging, Antibacterial, Drug delivery, Doped ZnO, Photocatalytic, Rare-earth transition metals

1. Introduction

Nanoparticles may be synthetic or natural. Synthetic nanoparticles are classified into various types: such as metal nanoparticles, carbon nanoparticles, metal oxide nanoparticles (zinc oxide) and quantum dots (cadmium selenide [1, 2]. The melted and oxidized zinc at a high temperature can generate zine oxide nanoparticles that affect the growth of many bacteria and use in drugs. They are also used in various industries such as paints, pigments, dyes, electronics, cosmetics and personal care products. Consequently, human is more reveal to zinc oxide nanoparticles via several are routes such as dermal penetration, Intravenous, inhalational, In the last few years, the use of zinc oxide nanoparticles become

controversial [3]. Although zinc oxide nanoparticles can pass easily to the cell membrane and internet with cellular macro molecules leading to therapeutic effect on different again, they were found to exert oxidative stress causing cytotoxic effect on the organs [4, 5]. Zinc oxide nanoparticles were approved by food and drugs administration as a new and potent anticancer therapy, zinc oxide nanoparticle can produce selective cytotoxicity toward cancer cells via the induction of disequilibrium of zinc- dependent protein activity, in addition to the production of reactive oxygen species. Ability of zinc oxide nanoparticles to kill cancer cell through the induction of oxidative stress in the cancerous cells. Furthermore, zinc oxide nanoparticles are involved in all cellular protecting processes against cancer through the activation of DNA repair and hence preventing both apoptosis and cancer cell growth, Zinc oxide nanoparticles also play an important role to maintain the tumor suppressor gene activity that regulates apoptosis activity [6, 7]. Hence, zine oxide nanoparticles are considered potent therapy for many cancers. Zinc oxide nanoparticles were characterised by their increased penetration and by their retention inside the tumor cells. The small size and the surface properties of zinc oxide nanoparticles enabled them to diffuse easily through the blood vessels towards the tumor cells and to be localized inside these cells. Circumstantially and hence act on them. Zinc oxide nanoparticles could be used as a potent antioxidant and at an effective helpful treatment to chemotherapeutic drugs that course reproductive dysfunction in males [8, 9]. This was based upon the ability of zinc oxide nanoparticles to lead the therapeutic efficacy of doxorubicin. Furthermore, various theoretical studies revealed the capability of zinc to enhance the reproductive function and reported that zinc was found in high level in the male reproductive system and in the seminal fluid [10]. Therefore, zinc oxide. Nanoparticles it through to play an important role in spermatogenesis process. In recent years, a number Studies have shown the possibility of using zinc oxide nanoparticles as therapeutic agents and at gene carriers. At the same time many published research Studies showed the toxic effect of Zinc oxide nanoparticles on same specific body organs and cell lines [11]. These to Poisonous effect were attributed to high solubility of the particles resulting in oxidative stress and cytotoxicity. Therefore, an important exists to evaluate both of the toxicological hazards and the therapeutic benefits for the use of zinc oxide nanoparticles in drugs. Inhalation of zinc oxide nanoparticles induced inflammation and fibrosis in the alveolar and tracheobronchial tissues depending on the size and solubility of the particles. Intra-peritoneal injection of zinc oxide nanoparticles was found to cause neurotoxic effect in the form of attenuation of the learning ability and memory.

2. Synthesis of ZnO Nanoparticles on Nanostructure

Synthesizing Zinc Oxide nanostructure via sol gel technique in this research includes the use of several materials such as Zinc Acetate Dihydrate Zn $(CH_3COO)_2.2H2O$ ≥99% purity (HmbG Chemicals), Sodium hydroxide (NaOH) ≥98% (Sigma Aldrich), Ethanol (CH_2COOH) HmbG Chemicals and distilled water. Zinc Acetate Dihydrate was used as precursor and Ethanol was used as a reagent. Distilled water was used as a solvent medium. The biological activity of nanoparticles depends on factors including surface chemistry, size distribution particle morphology and particle reactivity in solution [12]. Therefore, the development of nanoparticles with controlled structures that are uniform in size, morphology and functionality is essential for various biomedical applications. The ZnO nanoparticles occurring in a very rich variety of size and shape will provide a wide range of properties. The methods for Stable ZnO nanoparticles preparation have been widely developed in recent years, which mainly include the chemical Precipitation method, sol-gel method, Sol-gel synthesis of ZnO NPs

has friendly environmentally aspects and various biomedical uses, and these techniques have rapidly evolved. Solid state pyrolytic. Method, solution-free mechanochemical method and bio synthesis method. Polysaccharides and biopolymer or plant extracts serve as modifying agents for the synthesis of biogenic ZnO NPs [13]. Among different modifiers, chitosan has gained attention for the synthesis of metal and metal oxide nanoparticles, including ZnO NPs. Chitosan is an aminated polysaccharide commonly found in nature in crustaceans and insects. The extraction of chitosan can be carried out by four different methods and under different conditions. The main method for obtaining chitosan is based the alkaline on deacetylation of chitin with a strongly alkaline solution [14]. Chitosan possesses functional groups, hydroxyl and amino groups, which are crucial for the chemical adsorption of metal ions. Therefore, it is widely reported as a green capping agent in the synthesis of metal and metal oxide nanoparticles [15]

3. Anticancer Cell Apoptosis and Activity.

Zinc-Oxide nanoparticles present certain cytotoxicity in cancer cells mainly by themselves based on a higher intracellular release of dissolved zinc ions, followed by increased ROS induction and induced cancer cell death via the apoptosis signaling pathway. The two common strategies for therapeutic targeting are stimulation of proapoptotic molecules and inhibition of antiapoptotic molecules. Cancer cells evade apoptosis through a variety of mechanisms. While not classified as such, prosurvival genes are potentially oncogenic and can have mutations that increase their expression. The proapoptotic genes may act as tumor suppressors. All of the inhibitors and activators have been found outside their normal range of expression in cancer cell lines.

Table.1 Anticancer effect of ZnO nanoparticles in different human cancer cell lines are

Cancer type	Effect and mechanism
Lung cancer	ZnO nanoparticles incorporated in liposomes not only rendered pH responsivity to the delivery carrier but also exhibited synergetic. Chemo-Photodynamic anti-cancer action. Human lung adenocarcinoma Cells with an EGFR mutation are sensitive to ZnO nanoparticle which resulted in non-autophagic Cell death
Human epidermal Cancer	Zno nanoparticles induced cell death at high concentrations, and at lower concentrations, they induce cell cycle arrest in the S and G 2/M phase by intercellular ROS generation in A431 cells.
Gastric cancer	PMMA-AA /ZnO nanoparticles and PMMA-PEG/ZnO nanoparticles were able to carry a large amount of the hydrophobic drug showing highly anti-gastric Cancer activity.
Ovarian cancer	ZnO nanoparticles are able to induce significant cytotoxicity apoptosis and autophagy in sk-ov-3 Cells through reactive oxygen species generation and oxidative Stress
Colon cancer	ZnO nanoparticles induced Caco-2 cell cytotoxicity associated with increased intercellular zn ions, ZnO nanoparticles conjugated with peptides had a higher antiproliferation in HT-29 colon cancer cells than other Au Nanoparticles and Fe_3O_4 Nanoparticles.

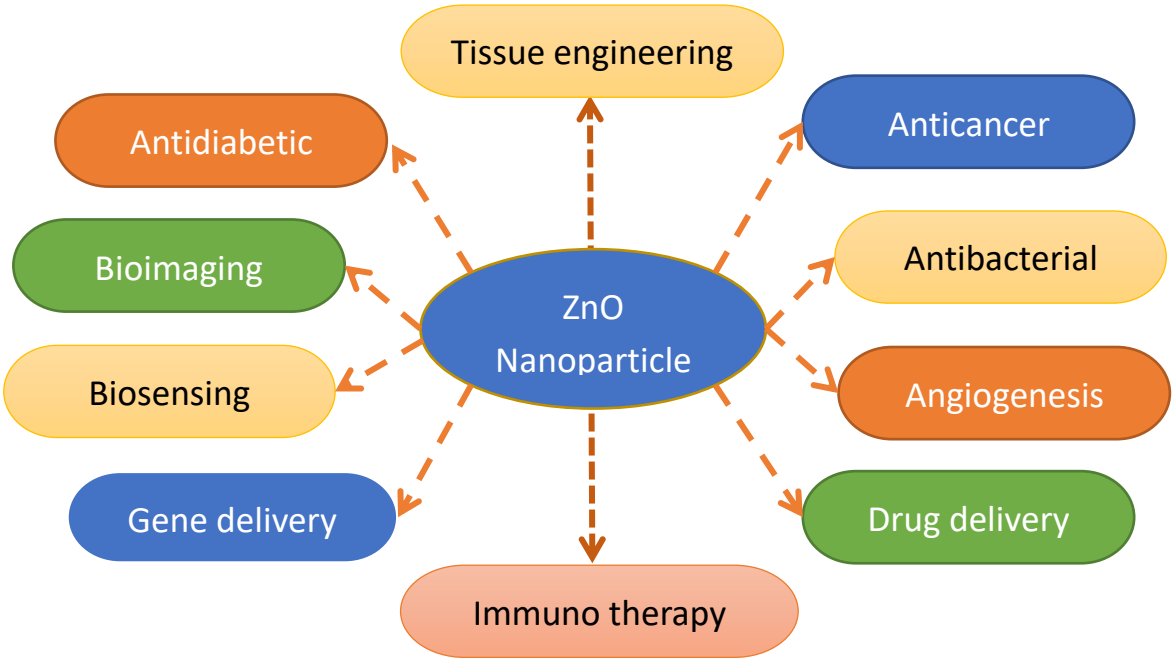

Fig.1 Applications of zinc oxide nanoparticles for Biophysics (Human health)

Table.2 Zno nanoparticles for diabetes treatment

Types of nanoparticles	Size	Drugs	Effects
ZnO nanoparticles	60-95nm spherical		mitigated the diabetic complications
ZnO nanoparticles	~ 20 nm spherical		Blood glucose and increase to high density lipoprotein levels
ZnO nanoparticles	10-30nm	Thiamine	ZnO nanoparticles in combination with thiamine-improved diabetes therapy. ZnO nanoparticle effectively reversed diabetes induced pancreatic injury
ZnO-RSW nanoparticles	~20nm	Conjugated red sandalwood (RSW)	ZnO-RSW-NPs Showed excellent activity against the crude murine Pancreatic individual. ZnO nanoparticles and the RSW extract.
ZnO nanoparticles	~10nm		ZnO-NPs presented Pleiotropic antidiabetic effects via improved enhanced glucose uptake decreased hepatic glucose output decreased lipolysis and enhanced pancreatic beta cell mass

3.1 Categorization of nanomaterials

Nanomaterials can be categorized into four shapes as zero-dimensional (0-D), one-dimensional (1-D), two-dimensional (2-D), and three-dimensional (3-D). Typical examples are carbon quantum dots (0-D), carbon nanotubes (1-D), graphene sheets (2-D), and zinc oxide nano flowers (3-D). Nanomaterials with

unique biological, chemical, and physical properties are promising for applications in energy, agricultural, biomedical, environmental, industrial, and pharmaceutical sectors. For applications in the biomedical field, nanomaterials are widely used in biosensing, bioimaging, antibacterial agents, drug delivery; Semiconducting oxide nanomaterials based on titanium dioxide and zinc oxide are very effective for water treatment and purification due to their large surface area and photocatalytic effect.

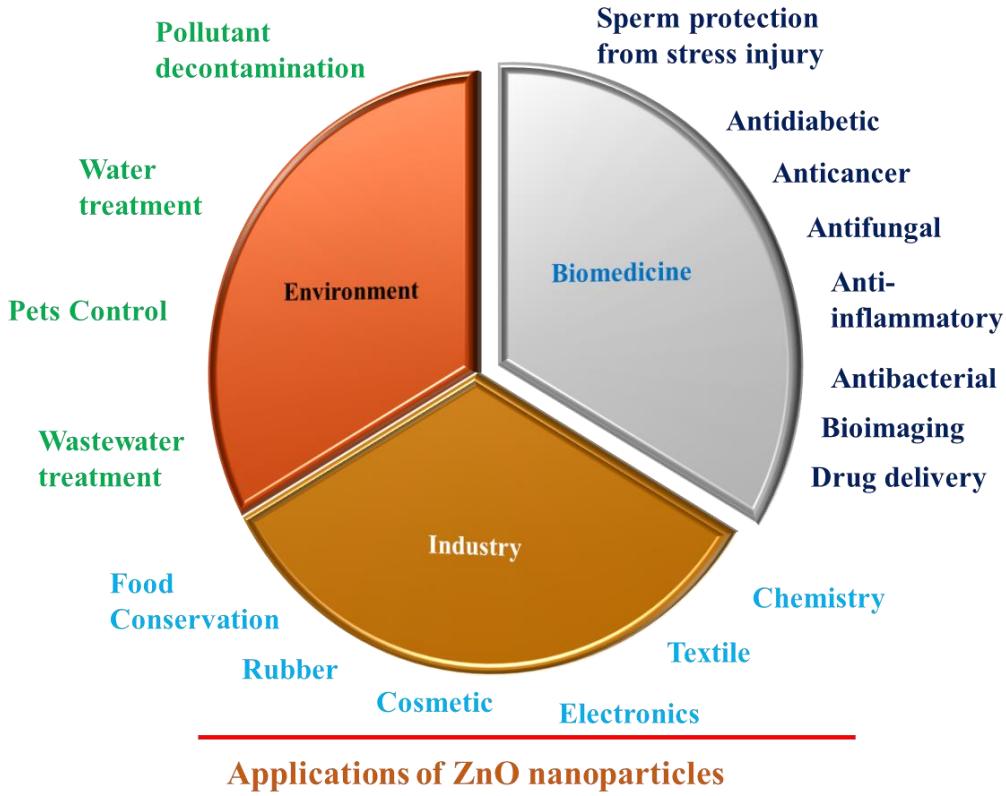

Fig.2. Applications of ZnO nanoparticles in biomedicine, industry, and environment.

Recently, studied the anticancer activity of ZnO NPs, Polyethylene glycol (PEG) coated zinc-oxide nanorods and AU-NP-Costed PEG-ZnO NPs against human cancer cell in the presence and absence of ultraviolet light. Some polyethylene glycol-ZnO NPs were further loaded with antioxidant/anticancer drug, Piperlongumine (PL) being designated as PL-PEG-ZnO NPs figure(a) shows the viability of cell treated with PL (0.5μm), PEG-ZnO NPs (20μg/mL) and PL-PEG-ZnO NPs (20 μg/mL) with or without UV irradiation for 7 min. comparing to PEG-ZnO NPs the cell viability declines markedly for PL-PEG ZnO NPs in the absence of UV light. The increased cytotoxicity is related to the improved cellular uptake of PL by PEG-ZnO NPs. Furthermore PL-PEG ZnO NPs also shows high toxicity than PEG-ZnO NPs toward cells under UV irradiation antioxidant PL contributes to a slightly higher Production of ROS. The modification of PEG-ZnO NPs with Au-NPs can further enhance the intracellular ROS level under UV irradiation figure (c). This results from the generation of photoexcited reactive species on ZnO NPs and Au-NPs under UV irradiation. Consequently, PL-Au/PEG-ZnO NPs selectively kill cells, but not normal human dermal fibroblast cells, especially under UV irradiation.

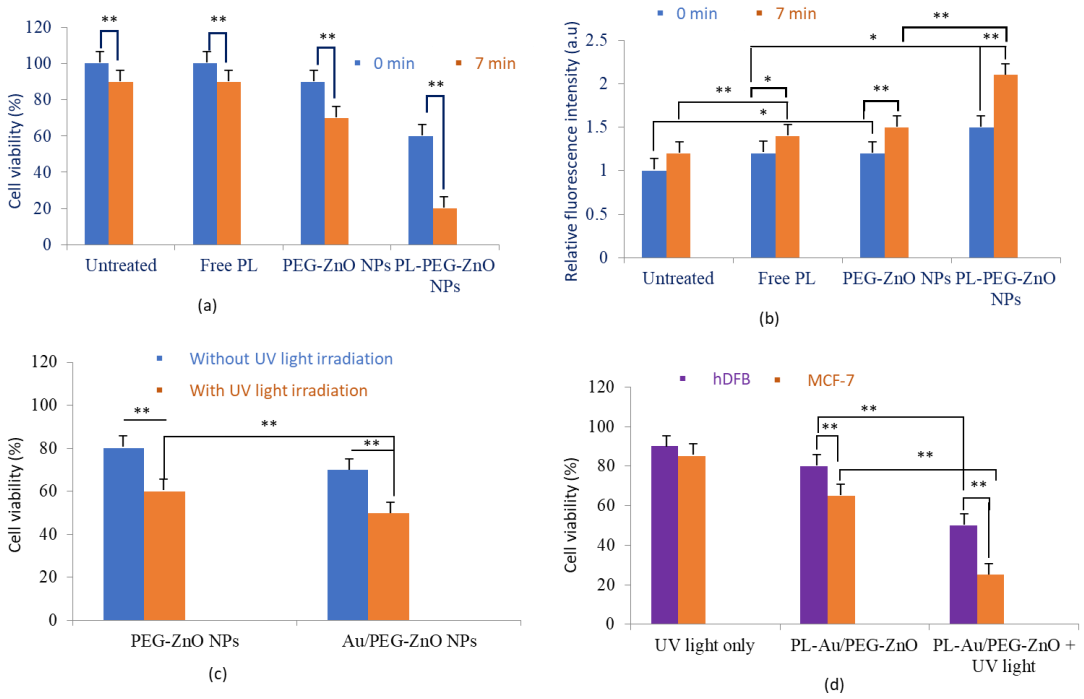

Fig.3. (a) Cell viability (b) Relative fluorescence intensity (c) Cell Viability of Without and with UVLI (d) Cell viability PL-Au/PEG-ZnO

4. Conclusion and future perspectives: -

ZnO nanoparticles were exhibited promising biomedical applications based on its anticancer, antibacterial, drug delivery as well as bioimaging activity. Due to inherent toxicity of ZnO nanoparticles they possess string inhibition effects against cancerous cell and bacteria by inducing intercellular RSW (Red sandalwood) generation and activating apoptotic signalling pathway which makes Zno nanoparticles a potential candidate as anticancer and antibacterial agents. In addition ZnO nanoparticles have also been well known to promote the bio availability of therapeutic drugs or biomolecules when functioning as drug carriers to achieve enhanced trophy efficiency, Moreover with the ability to decrease blood glucose and increase in insulin levels, ZnO nanoparticles have shown the promising potential in treating diabetes and attenuating its complications which can be further evaluated, ZnO nanoparticles are listed as a kind of safe substance by the MDA (malondialdehyde). However, some critical issues of ZnO nanoparticles still need to be further explored, which include the following:

- lack of comparative analysis of its biological advantages with other metal nanoparticles
- The limitation of ZnO nanoparticles toxicity toward biological system remains a controversial issue in recent research.
- lack of evidence-based randomized research specifically exp exploring therapeutic roles in improving anticancer, antibacterial activities
- Lack of insight into corresponding animals' study about its anticancer antibacterial and antidiabetic activities. Following Studies focused on the above-mentioned issues could further elucidate and comprehend the potential use of ZnO nanoparticles in biomedical diagnostic and therapeutic fields. We believe that nanomaterial would dramatically promote the development of medicine and ZnO nanoparticles are expected to massive more exciting contributions in these fields.

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