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Green Synthesis of Zinc Oxide Nanoparticles and Their Pharmacokinetic Properties

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Abstract: *In recent decades, the use of nanoparticles across various industries, including biomedical, cosmetics, and food, has gained significant global attention due to their nanoscale dimensions and exceptional properties. This has made nanotechnology a highly sought-after research field. Among the different synthesis approaches, green chemistry-based methods have emerged as a sustainable alternative, leveraging natural biological reduction processes to minimize the use of hazardous chemicals, unlike conventional physical and chemical techniques. Among inorganic nanoparticles, zinc oxide (ZnO) nanoparticles have garnered considerable interest due to their wide bandgap, high exciton binding energy, ease of fabrication, biocompatibility, non-toxic nature, and eco-friendly characteristics. ZnO nanoparticles readily dissolve in biological fluids and have a tendency to aggregate under varying physiological conditions. However, their physicochemical properties play a crucial role in determining bioavailability. This review aims to explore and summarize the green synthesis of zinc oxide nanoparticles and their pharmacokinetic properties..*

Keywords: nanoparticles, zinc oxide, biocompatibility, green synthesis, pharmacokinetics, bioavailability

I. INTRODUCTION

Over the past few decades, nanotechnology has revolutionized various industries, including engineering, environmental science, agriculture, medicine, electronics, pharmaceuticals, biotechnology, food processing, and pharmacology. The widespread adoption of nanotechnology is primarily due to its nanoscale dimensions, high surface area-to-volume ratio, and unique properties such as electronic, magnetic, mechanical, optical, thermal conductivity, and enhanced catalytic activity. Research and development in this field focus on modifying atomic, molecular, and supramolecular structures to enhance physicochemical properties for targeted applications.

Inorganic nanoparticles are synthesized by integrating organic and inorganic materials, forming hybrid structures with distinct characteristics. Several types of inorganic nanoparticles, including quantum dots, magnetic nanoparticles, and metal-based nanoparticles like silver, gold, silicon dioxide (SiO_2), titanium dioxide (TiO_2), copper oxide (CuO), and zinc oxide (ZnO), have been extensively studied for their diverse applications. Among these, ZnO nanoparticles have attracted considerable attention due to their wide bandgap, high exciton binding energy, and broad application potential. ZnO nanoparticles rank as the third most widely produced and utilized nanoparticles worldwide.

Nanoparticle Synthesis

Various physical and chemical techniques have been developed for the synthesis of inorganic nanoparticles, including:

Physical Methods:

- Vapor transport and condensation
- Amorphous crystallization
- Physical fragmentation
- Pulsed laser deposition
- Molecular beam epitaxy
- Thermal evaporation and decomposition

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Chemical Methods:

- Chemical microemulsion
- Wet chemical synthesis
- Spray pyrolysis
- Electrodeposition
- Direct and homogeneous precipitation
- Microwave-assisted combustion
- Solvothermal and sonochemical methods
- Reverse micelle synthesis
- Sol-gel method
- Microwave irradiation
- Zinc-alcohol reaction
- Hydrothermal synthesis
- Microemulsion synthesis
- Spray drying

Despite their efficiency, physical methods often require high pressure and temperature, making them energy-intensive, while chemical methods involve toxic reagents and the need for capping and stabilizing agents.

Green Synthesis of Nanoparticles

To address these limitations, researchers have turned to eco-friendly, green synthesis approaches using biological sources such as bacteria, algae, fungi, yeast, and plant-derived materials, including leaves, fruits, seeds, roots, and stems. Nanoparticles synthesized from plant extracts exhibit improved stability, diverse morphologies, and controlled size distribution compared to those derived from other biological sources. The green synthesis method not only enhances catalytic efficiency but also minimizes the use of hazardous chemicals, reducing environmental and health risks.

Green Synthesis of Zinc Oxide Nanoparticles

Zinc oxide nanoparticles can be synthesized using an eco-friendly approach by dissolving zinc-based precursors such as zinc oxide, zinc nitrate, zinc acetate, or zinc sulfate in distilled water. A specific volume of plant extract is then added to this solution and stirred continuously using a magnetic stirrer. To achieve a pH of 12, sodium hydroxide (NaOH) solution is introduced dropwise while stirring the mixture for one hour. A noticeable color change in the reaction mixture indicates nanoparticle formation. The synthesized ZnO nanoparticles are confirmed using UV-Vis spectroscopy based on their surface plasmon resonance (SPR) effect. The resulting white crystalline ZnO nanoparticles are separated through centrifugation and then dried at 60–80°C in a hot air oven for two hours.

During this process, plant-derived phytochemicals such as amino acids, vitamins, terpenoids, alkaloids, polyphenols, and polysaccharides act as reducing, capping, and stabilizing agents, eliminating the need for additional chemical stabilizers. This green synthesis method is cost-effective, non-toxic, biocompatible, and environmentally sustainable. The U.S. Food and Drug Administration (FDA) has classified ZnO, along with other zinc compounds, as Generally Recognized as Safe (GRAS).

The successful formation of ZnO nanoparticles depends on factors such as temperature, pH, reaction time, and the concentration of the plant extract. Various ZnO nanoparticle morphologies, including nanoflowers, nanoflakes, nanorods, nanowires, and nanobelts, have been reported.

Characterization of Zinc Oxide Nanoparticles

The synthesized ZnO nanoparticles are characterized using multiple analytical techniques:

Fourier Transform Infrared Spectroscopy (FT-IR): Determines the functional groups involved in nanoparticle formation and their binding properties.

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Scanning Electron Microscopy (SEM): Analyzes the surface morphology, shape, and size of the nanoparticles.
X-ray Diffraction (XRD): Evaluates the crystalline structure of the nanoparticles.
Atomic Force Microscopy (AFM): Assesses the topography and surface roughness of the nanoparticles.
Pharmacokinetic Properties of Zinc Oxide Nanoparticles

Absorption

Zinc oxide nanoparticles are highly soluble in biological fluids, leading to the release of zinc ions. When administered orally, their bioavailability is reduced due to factors such as the first-pass metabolism, gastrointestinal barriers, and liver processing. However, intravenous administration ensures 100% bioavailability. Several factors, including pH, particle size, concentration, and the presence of organic compounds, influence ZnO nanoparticle solubility. Negatively charged particles exhibit better absorption than positively charged ones. The dissolution, absorption, and distribution of ZnO nanoparticles depend on the exposure dose rather than the particle size.

Distribution

Following oral administration, ZnO nanoparticles primarily accumulate in the kidneys, liver, and spleen, while intraperitoneal administration leads to their distribution in the lungs, kidneys, spleen, heart, and liver. The kidneys and liver are the primary target organs in both cases. The distribution pattern is influenced by factors such as the type of experimental model, route of exposure, and physicochemical properties of the nanoparticles.

Excretion

Zinc oxide nanoparticles with a hydrodynamic diameter smaller than 6 nm are eliminated through urine via glomerular filtration. Both absorbed and unabsorbed nanoparticles are excreted through feces, while metabolites are primarily eliminated via bile. Although physicochemical properties and exposure routes influence excretion, biliary and fecal elimination play a dominant role, regardless of nanoparticle size, surface charge, or administration method. The excretion kinetics of ZnO nanoparticles are more dependent on particle size than surface charge.

Protein Interaction with Nanoparticles

When nanoparticles enter the systemic circulation and come into contact with biological fluids, they rapidly interact with plasma proteins, leading to protein adsorption on their surface. The extent of protein adsorption is primarily influenced by the nanoparticle's surface charge and particle size. Key plasma proteins such as fibrinogen, lipoproteins, albumin, and immunoglobulins are commonly used to evaluate nanoparticle-protein interactions, including binding efficiency, adsorption patterns, and potential structural changes in the proteins. Additionally, plasma proteins play a significant role in the deposition, distribution, and transportation of nanoparticles within the body.

S. No	Name of the plant (Parts)	Application
1	Trifolium pratense (flower)	antibacterial activity[33]
2	Catharanthus roseus (leaf)	Antibacterial activity[34]
3	Murraya koenigii (seed)	Antimicrobial activity[35]
4	Nyctanthes arbortristis (flower)	Anti-fungal[18]
5	Passiflora caerulea (Leaf)	Urinary tract infection[8]
6	Hibiscus subdariffa (leaf)	Anti diabetic[36]
7	Polygala tenuifolia (root)	Anti-inflammatory[37]
8	Eucalyptus globulus (leaf)	Antioxidant[38]

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II. CONCLUSION

The green synthesis of zinc oxide nanoparticles has gained significant attention due to its biocompatibility and environmentally friendly nature. Phytochemicals derived from natural sources serve as both reducing and stabilizing agents, facilitating the formation of nanoparticles within a controlled size range of 1–100 nm. This method minimizes the reliance on conventional physical and chemical synthesis techniques. Zinc ions play a crucial role in maintaining cellular function and structural integrity. However, further in-depth research is required to scale up this synthesis process for large-scale commercial applications. Additionally, more studies are needed to fully understand the pharmacokinetics and bioavailability of zinc oxide nanoparticles in humans to establish their precise mechanism of action.

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