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A REVIEW ON NANOPARTICLES – ZINC OXIDE NANOPARTICLES CHARACTERIZATION, APPLICATIONS AND EVALUATIONS

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ABSTRACT

Nanoparticles are defined as particulate dispersions or solid particles drug carrier that may or may not be biodegradable. As per International organization for standardization (ISO) and American society for testing and materials (ASTM) standards, nanoparticles sizes ranges from 1 to 100nm with one or more dimensions. Among metal nanoparticles, Zinc oxide nanoparticles are given much importance due to their utilization in gas sensors, biosensors, cosmetics, drug-delivery systems. Zinc oxide nanoparticles are synthesized by several different methods. Zinc oxide nanoparticles exhibit broad and potential applications in different fields with their specific characteristics such as surface area, shape, low toxicity, optical properties, high binding energy and large band gap. In this review paper an attempt has been made to elaborate the types, preparation methods, applications, evaluation parameters and different characterization techniques of Zinc oxide nanoparticles.

INTRODUCTION

Nanotechnology is a modern field of science which plays a dominant role in day to day life aspects. The fundamental component of nanotechnology is nanoparticles. Nanoparticles are made up of carbon, metal, metal oxides or organic matter. Numerous synthesis methods are either being developed or improved to enhance the properties and reduce the production costs. A vast development in the instrumentation has led to an improved nanoparticle characterisation and subsequent application. Recently, the scientific community has shown interest to synthesis of metal and metal oxides nanoparticles. Among these nanoparticles Zinc oxide nanoparticles exhibits most significance and wide range of applications. Zinc oxide is an inorganic compound with the molecular formula ZnO. ZnO appears as a white powder and nearly insoluble in water. Zinc oxide nanoparticles are synthesised by Means of numerous conventional approaches. Nano-sized Zinc oxide exhibits varying morphologies and shows significant antibacterial activity over a wide spectrum of bacterial species explored by a large body of researchers. In the present review, the synthesis of Zinc oxide nanoparticles using numerous approaches and the characterization of Zinc oxide nanoparticles using X-ray diffraction, scanning electron microscopy (SEM), transmission electron microscopy (TEM), UV-visible absorption spectroscopy is discussed. This paper presents a review on types of nanoparticles present. Different methods used for the preparation and application of Zinc oxide nanoparticles. Finally, general evaluation parameters and significant characterization techniques used in Zinc oxide nanoparticles are discussed.

LITERATURE REVIEW

RESEARCH ARTICLES:

Asmaa H. Hammadi et al., (2020) this study presents the synthesis, characterization and biological activity of zinc oxide nanoparticles (ZnO NPs). Zinc nitrate hexahydrate and potassium hydroxide materials have been utilized without a purifying process. Here thermal precipitation technique is used in KOH (pH=8) as alkaline media 60-70°C to provide thermal factor undergoing synthesis process and resulted in white precipitation. The prepared powder was characterized by scanning electron microscopy image which illustrated the homogeneity and agglomeration. It was also characterized for energy dispersive x-ray analysis spectrum which displays four peaks that could be identified as zinc and oxygen. At last X-ray diffraction analysis diffracting peaks indicates that the material falls within the nanometer span. (1)

Neha Silas et al., (2020) the author evaluated anti-diabetic property of green synthesized Zinc oxide nanoparticles from leaf extract of Chrysanthemum indicum plant. Here Zinc oxide was synthesized using the Chrysanthemum indicum plant extract then the prepared Zinc oxide nanoparticles were tested for its antidiabetic activity on animals (Wister rats). Determination of oral acute toxicity was done. And it was found that Zinc oxide nanoparticles of Chrysanthemum indicum may prevent hyperglycaemia in streptozotocin induced rats. (57)

Nagaraj Govindan et al., (2020) this study presents, green synthesis of Zinc-doped Catharanthus roseus nanoparticles for enhanced anti- diabetic activity. Green synthesis of zinc oxide nanoparticles is done using Catharanthus roseus plant extract. Then it was characterized by X-ray diffraction, Transmission electron microscopy, Scanning electron microscopy, zeta potential, dynamic light scattering and UV-diffuse reflectance spectroscopy techniques. Antidiabetic activity of prepared nanoparticles were tested using alpha-amylase assay. It was found that zinc- doped catharanthus roseus nanoparticles showed can elicit potent anti-diabetic activity. (58)

Shirin Hajiashrafi et al., (2019) this article gives information about preparation and evaluation of Zinc oxide nanoparticles by thermal decomposition of MOF-5 (metal organic frame). The materials used for synthesis are Zinc acetate dehydrate as the zinc precursor, terephthalic acid as ligand, tri-ethylamine as capping agent, dimethylformamide as solvent. Zinc oxide nanoparticles were prepared by simple and repeated method with thermal decomposition. MOF were synthesized by solution and solvothermal methods in dimethylformamide. Then the Fourier transform infrared results were recorded in range of 400-4000 cm. The X-ray diffraction was measured from 10-100° which represented the crystalline structure. Scanning electron microscopy, Energy-dispersive X-ray spectroscopy, Diffuse reflection spectroscopy were characterized and antibacterial activity was found. (2)

Wali Muhammad et al., (2019) in this paper optical, morphological and biological analysis of zinc oxide nanoparticles (ZnO NPs) using Papaver somniferum L were studied. Green synthesis of Zinc oxide nanoparticles were done using plant extract. The obtained Zinc oxide nanoparticles were characterized by UV- visible absorption spectroscopy, X- ray diffraction, Fourier transform infrared analysis, transmission electron microscopy and scanning electron microscopy techniques. Anti- diabetic activity by inhibition of alpha amylase and antibacterial activity of plant mediated Zinc oxide nanoparticles were done. The results showed Zinc oxide nanoparticles prepared from plant extract can be used in diabetes and also for infectious diseases. (55)

Abolfazl Bayrami et al., (2019) this article presents information on a facile ultrasonic-aided biosynthesis of Zinc oxide nanoparticles using Vaccinium arctostaphylos L. leaf extract and its antidiabetic, antibacterial, and oxidative activity evaluation. An aqueous extract of

Vaccinium arctostaphylos leaf was obtained via ultrasonic-assisted extraction method and used to produce Zinc oxide nanoparticles. Antidiabetic activities on wistar rats and antibacterial activities against both gram negative and gram positive bacteria were studied. The results showed great efficiencies against microbial and organic pollutants. The resulted Zinc oxide nanoparticles were found effective towards antidiabetic, antibacterial and oxidative performances. [56]

Anup A Teragundi et al., (2018) the author gave a literature review on synthesis of Zinc oxide nanoparticles using natural and synthetic methods. It demonstrated that Zinc oxide nanoparticles have advantage because of its physical, chemical properties, and manufacturing methods. The methods mentioned here are micro emulsions, molecular beamepitaxcy, spray pyrolysis, and chemical vapour method. This zinc oxide leads to increase in pollution and environmental hazardous, both natural and artificial synthesis of Zinc oxide using different method are discussed. Application on nanoparticles have been discussed about various industrial, health, food, feed, space, and chemical and cosmetics industry of consumers which calls for a green and environment-friendly approach to their synthesis.[3]

Kalakotla Shanker et al., (2017) this research presents a sub-acute oral toxicity analysis and comparative in vivo anti-diabetic activity of Zinc oxide(ZnO), Cerium oxide(CeO_2), Silver nanoparticles(Ag Nps) and Momordica charantia in Streptozotocin-induced diabetic wistar rats. Here plant extraction was done by soxhlet extraction technique and biosynthesis of ZnO, CeO_2 and Ag Nps were done and fused with plant extract. The obtained green synthesized nanoparticles were characterized by in vivo sub- acute oral toxicity study in mice, induction of diabetes and insulin assay and hypoglycaemic activity in non- diabetic fasted rats were tested. Results show that crude extract green synthesis nanoparticles can be perfect alternative for treatment in diabetes mellitus. [54]

Avnish Kumar Arora et al., (2014) evaluated synthesis and characterization of Zinc oxide nanoparticles. Chemicals used in these research are analytic reagent grade as Zinc chloride, ammonium hydroxide. Here Zinc oxide nanoparticles are prepared by precipitation method using ammonia as precipitating agent. And nanoparticles characterization has shown X-ray diffraction studies giving a hexagonal structure. Surface area of nanoparticles is 4.3737 m/g was found. From Transmission electron microscopy images, it is found that nanoparticles with average size of 27-82nm are formed. Magnetic measurements show that Zinc oxide is diamagnetic in nature. [4]

Awodugba Ayodeji Oladiran et al., (2013) presented a research article on synthesis and characterization of Zinc oxide nanoparticles with zinc chloride as zinc source. Here Zinc oxide nanoparticles were prepared by wet chemical method using Zinc chloride and sodium hydroxide as precursors. The prepared Zinc oxide nanoparticles were characterized for their optical properties and Nano structural properties. X-ray diffraction pattern were recorded using X-ray diffractometer and UV-Visible spectroscopy were recorded using UV-Visible spectrophotometer. This study reveals the hexagonal structure with crystal size of ~5.3689nm and excitonic absorption peak at 277nm and 235nm wavelength. [5]

Varsha Srivastava et al., (2013) in present study, synthesis, characterization and application of Zinc oxide nanoparticles are studied. Nanoparticles of Zinc oxide has been prepared by the sol-gel method, a simple solution based approach. Then Characterization of nanoparticles was carried out by Transmission electron microscopy image which ranged nanoparticles from 17-50nm, X-ray diffraction of Zinc oxide nanoparticles were done where no peaks were found, Scanning electron microscopy which ranged nanoparticles of 95-450nm was found. Fourier transform infrared results of nanoparticles confirmed presence of specific absorption peak of Zinc oxide bond. The resulted Zinc oxide particles displayed significant efficiency of removal (~92%) of

Cadmium (II) from aqueous solutions. It was found that the zinc oxide particles can serve as an excellent material for the removal of Cadmium (II) from effluents. (6)

Satyanarayana Talam et al., (2012) this research article presents a review on synthesis, characterization, and spectroscopic properties of Zinc oxide nanoparticles. Material methods such as Zinc nitrate, sodium hydroxide, and ethanol are used without purification. Zinc oxide nanoparticles were prepared by wet chemical method using zinc nitrate and sodium hydroxide precursors. Then powder was characterized by X-ray diffraction whose peaks indicates that the material consist of particles in nanoscale range, Scanning electron microscopy/Transmission electron microscopy images confirm the formation of Zinc oxide nanoparticles, these powder was also characterized for UV-Visible absorption spectrum, photoluminescence spectrum. Nanoparticles prepared by this method has industrial applications namely luminescent material for fluorescent tubes, active medium for lasers, sensors and many more. (7)

B. Akbari et al., (2011) the author evaluated particle size characterization of nanoparticles. There are two basic methods of defining particle size firstly microscopic technique and second method utilizes the relationship between particle behaviour and its size. Particle size in Transmission electron microscopy was found in range of 5-95nm which reveals that particles are spherical in shape and loosely agglomerated. X-ray diffraction, High resolution transmission electron microscopy results shows the particles are single-crystal. It was also found that, there is a good correlation between the Surface area analysis, X-ray diffraction and Transmission electron microscopy measurements other than Photon correlation spectroscopy that is sensitive to the presence of the agglomerates.(8)

N. Singh et al., (2011) in this paper, we report the synthesis and characterization of Zinc oxide nanoparticles. Here two methods are used for preparation of Zinc oxide nanoparticles they are sol-gel and solid state reaction methods. The Zinc oxide nanoparticles prepared by sol-gel route were highly crystalline and bears smaller crystallite size (~24nm) as compared to the one prepared by solid state reaction method (~37nm). The crystallanity and the crystallite size were characterized by X-ray diffraction and Transmission electron microscopy. Photoluminescence (PL) was also recorded in the visible region for the two types of particles and results have been analysed. (9)

A Khorsand Zak et al., (2011) published an article on synthesis and characterization of a narrow size distribution of Zinc oxide nanoparticles. Here Zinc oxide nanoparticles were synthesized by solvothermal method in Triethanolamine (TEA) media. TEA was utilized as a polymer agent to terminate the growth of Zinc oxide nanoparticles. The X-ray diffraction and Transmission electron microscopy results show Zinc oxide nanoparticles were formed in a hexagonal structure. A sharp absorption peak (370nm) was detected in the UV-Visible region which was found to be 3.3 eV. The Fourier transform infrared results show the high purity of the obtained Zinc oxide nanoparticles. The results confirm the quality of the Zinc oxide nanoparticles, which found them suitable for medical applications. (10

REVIEW ARTICLES:

Rajat Sharma et al., (2020) reviewed biogenic synthesis, applications and toxicity aspects of Zinc oxide nanoparticles. In this method of nanoparticles synthesis it doesn’t make use of high energy, temperature, costly instruments and environmentally hazardous chemicals. In comparison to the expensive and toxic methods, the green synthesis of nanoparticles is less expensive and eco-friendly. (34) Biogenic synthesis, photocatalytic activity, antimicrobial activity, toxicity issues of green synthesis of nanoparticles on human beings and animals were reviewed. The morphological and physico-chemical properties of obtained nanoparticles determined by various characterization techniques have been discoursed.

Aaron C. Anselmo et al., (2019) have given an update on nanoparticles in the clinical trials.Newer generation of nanoparticles have emerged that can enable treatment via new therapeutic modalities. In the current clinical landscape, many of these new generation nanoparticles have reached clinical trials and have been approved for various indications. Over 75 new trials have begun and 5 new nanoparticles technologies have entered clinical trials. In new approval first clinically approved nanoparticles to deliver a synergistic combination of free drug were studied. It provides an update on previous clinical trials and new technologies that have recently entered the clinic. (11)

Beena Kumara et al., (2018) studied nanoparticles preparation method and their applications. Nanoparticles are size ranges from 1 to 100 nanometers similar to the ultrafine particles hence their ability to absorb and carry other compounds such as drugs, probes and proteins as is well suitable for permitting the catalytic promotion of reactions.(12) Here nanoparticles different types such as gold, silver, alloy were studied. Usage of nanoparticles in the field of medicines in vaccine delivery, diagnostics, gene silencing and also for the treatment of cancer was shown. As nanoparticles shows high solubility and fast penetration hence they are used in almost all formulation now days. (12)

Bryan Calderon-Jimenez et al., (2017) presented silver nanoparticles: technological advances, societal implants, and metrological challenges. It showed that silver nanoparticles show different physical and chemical properties compared to their macro scale analogues. This article defines nanomaterials and nanoparticles their importance in nanoscience, and nanotechnology. The impacts of nanoparticles and silver nanoparticles on commerce, technology and society were shown. Silver nanoparticles possible impacts on environment, health and safety and development of nanoparticle reference materials (RMs) in the nanoscale their outlooks and perspectives were reviewed. (13)

Anu Mary Ealias et al., (2017) this article presents a review on classification, characterization, synthesis of nanoparticles and their applications. Generally nanoparticles are classified into organic, inorganic and carbon based on particles in their nanometric scale that has improved properties. Nanoparticles prepared showed enhanced properties such as high reactivity, strength, surface area, sensitivity. (14) Based on various methods for research and commercial uses they are also classified into three main type's namely physical, chemical and mechanical processes.

NANOPARTICLES

Nanoparticles are defined as particulate dispersions or solid particles with a size ranges from 10-100nm. The major goals in designing nanoparticles as a delivery system are to control particle size, surface properties and release of pharmacologically active agents in order to achieve the site-specific action of the drug at the therapeutically optimal rate and dose regimen.

CLASSIFICATION OF NANOPARTICLES:

The nanoparticles were generally classified into the organic, inorganic and carbon based.

a) Organic nanoparticles:

Dendrimers, Micelles, liposomes and ferritin etc. are commonly known as organic nanoparticles. These nanoparticles are generally biodegradable, non-toxic. There drug carrying capacity, its stability and delivery systems, either entrapped drug or absorbed drug system determines their field of applications and their efficiency. The organic nanoparticles are most widely used in the biomedical field for example drug delivery system as they are efficient and can be injected on specific parts of the body that is also known as targeted drug delivery.(14)

b) Inorganic nanoparticles:

Metal and metal oxide based nanoparticles are generally categorised as inorganic nanoparticles.

i. Metal based:

Nanoparticles that are prepared from metals to Nanometric sizes either by destructive or constructive methods are metal based nanoparticles. The commonly used metals for nanoparticle synthesis are aluminium (AI), cadmium (Cd), cobalt (Co), gold (Au), iron (Fe), lead (Pb), silver (Ag) and zinc

(Zn). These nanoparticles have distinctive properties such sizes as low as 10 to 100nm, surface characteristics like high surface are to volume ratio, pore size, surface charge etc.

ii. Metal oxides based:

Metal oxide based nanoparticles are prepared to modify the properties of their respective metal based nanoparticles. For example nanoparticles of iron instantly oxides to iron oxide in the presence of oxygen at room temperature that increases its reactivity compared to iron nanoparticles. Metal oxide nanoparticles are synthesized mainly due to their increased reactivity and efficiency. (15) The commonly synthesized are aluminium oxide, cerium oxide, iron oxide, zinc oxide. These nanoparticles possess exceptional properties when compared to their metal counterparts.

c) Carbon based:

The nanoparticles made completely of carbon are known as carbon based. (16) They can be classified into fullerenes, graphene, carbon Nano tubes (CNT), carbon nanofibers and carbon black and sometimes activated carbon in Nano size.

ZINC OXIDE NANOPARTICLES:

Zinc oxide is a member of II-VI semiconducting compounds and occurs naturally as the mineral zincite. It is a hexagonal wurtzite type crystal exhibiting anisotropy. ZnO is a well-known n-type semiconductor and has got a wide band gap of 3.3 eV at 300K. Due to its vast industrial applications such as electrophotography, electroluminescence phosphorus, pigment in paints, flux in ceramic glazes, filler for rubber products, coatings for paper, sunscreens, medicines and cosmetics. ZnO is attracting considerable attention in powder as well as thin film form. Zinc oxide nanoparticles resistance to radiation damages makes it useful for space applications. The fabrication of ZnO nanostructures have attracted intensive research interests as these materials have found uses as transparent conducting oxides (TCO). Since Zinc, the main constituent is cheap, non-toxic and abundant, ZnO has become commercially available.

SYNTHESIS OF ZINC OXIDE NANOPARTICLES: Metal Nanoparticles can be synthesized by two main approaches top down and bottom up.

Conventional methods: Zinc oxide nanoparticles are synthesized by means of numerous conventional approaches; such as: Co-precipitation, sol-gel method, high energy ball milling, electrochemical and electrophoretic depositions, chemical vapour deposition, chemical vapour and microwave-assisted combustion methods. (17)

Co-precipitation method:

Precipitation/co-precipitation is a standard synthesis technique to prepare metal oxide nanoparticles. In a typical co-precipitation reaction, a salt precursor, generally a nitrate, chloride, or oxychloride, is dissolved in aqueous solution and then the corresponding hydroxides are precipitated by the addition of a base as ammonium hydroxide or sodium hydroxide. After washing the produced ammonium or sodium salt, the hydroxides are calcined results in metal oxide powders. If more than one precursor salt is used in the starting solution, pure metal oxides can be obtained by co-precipitation of the corresponding hydroxides. (18)

Sol-gel: Sol-gel is the most preferred bottom-up method to its simplicity and as most of the nanoparticles can be synthesized from this method. In sol-gel technique discrete particles are integrated network precursor involved in chemical solution that is mainly used for the fabrication of metal oxides hence it is a chemical technique. The precursor sol can be either deposited on the substrate to form or used to synthesize powders.

High energy ball milling: High energy ball milling process is a ball milling process in which a powder mixture placed in a ball mill is subjected to high-energy collisions from the balls. High-energy ball milling is also called mechanical alloying, can successfully produce fine, uniform dispersions of oxide particles in nickel-base super alloys that cannot be made by conventional powder metallurgy methods. High energy ball milling is a way of modifying the conditions in which chemical reactions usually take place, either by changing the reactivity of asmilled solids or by inducing chemical reactions during milling. [19]

Electrophoretic depositions (EPD):
EPD is used to deposit a variety of materials including borides, carbides, metals, organics, oxides, and phosphors. EPD techniques allow preparation of films with thickness varying from less than 10 nm up to several 100μm.Under an applied DC electric field, a colloidal solution consisting of charged particles is directed onto a conductive substrate. The substrate could be of any shape. Particle coagulation on the substrate leads to the formation of film. EPD could be performed at either constant potential or constant current. The second approach is often preferred because at constant voltage the current decreases significantly once a thick layer is obtained. Often, post treatment is required to remove trapped solvent and/or anneal the green film [20]

Chemical vapour deposition (CVD): Chemical vapour deposition is the deposition of a thin film of gaseous reactants onto a substrate. The deposition is carried out in a reaction chamber at ambient temperature by combining gas molecules. A chemical reaction occurs when a heated substrate comes in contact with combined gas. This reaction produces a thin film of product on the substrate surface that is recovered and used. Substrate temperature is the influencing factor in CVD. The advantage of CVD are highly pure, uniform, hard and strong nanoparticles. The disadvantage of CVD are the requirements of special equipment and the gaseous by-products are highly toxic. [21]

Microwave assisted combustion method: Zinc oxide nanoparticles were prepared by mixing of Zn $(NO_3)_2 \cdot 6H_2O$ (zinc nitrate hexahydrate) and glycine in the molar ratio of 1: 2, respectively. These two starting materials were thoroughly mixed and grounded and the obtained white liquid after grinding was transferred into a porcelain crucible. The mixture was then heated in a microwave oven for 2 minutes with 80% power. After evaporation, the crystallization water the mix ignited and released a great deal of foams yielding a fluffy grey white product in the container. Finally, the obtained fine solid was washed with deionized water several times and then with ethanol to remove unreacted materials. The solid zinc oxide nanoparticles were dried in an oven at 100°C for 3 hours. [22]

Biological methods: Nowadays, Zinc oxide nanoparticles are also synthesized by biogenic methods using plants, yeast, fungi, bacteria and algae. Although, various biological species such as microorganism including fungi and bacteria can be used for green synthesis yet plants are the most common biological substrate used for green synthesis of metal nanoparticles due to the reason that plants are more cost-effective, easier to handle and non-toxic.

Synthesis by bacteria: A low-cost green and reproducible probiotic microbe (Lactobacillus sporogenes) mediated biosynthesis of Zinc oxide nanoparticles is reported. The synthesis is performed to room temperature in five replicate samples. X-ray and transmission electron microscopy analysis are performed to ascertain the formation of Zinc oxide nanoparticles. [23] The X-ray data indicated that Zinc oxide nanoparticles have hexagonal unit cell structure. Individual nanoparticles having the size of 5-15 nm are found. A possible involved mechanism for the synthesis of Zinc oxide nanoparticles has been proposed. [24]

Green Synthesis of Zinc Oxide Nanoparticles:

By using leaf extract of Calotropis gigantean; the plant Calotropis gigantean has potential to be utilized for synthesis of Zinc oxide nanoparticles. 50ml of Calotropis gigantean leaves extract is taken and boiled to 60-80 degree temperature by using a stirrer heater or hot plate. Then 5 grams of zinc nitrate is added to the solution as the temperature reaches 60° C. [25]. This whole mixture is then boiled till it reduces to a deep yellow colour paste. This paste is then collected in a ceramic crucible and heated in furnace at 400 degree Celsius for 2 hours. A light yellow color powder will be obtained and this is carefully collected and packed further characterization purposes. The material grounded in a mortar-pestle so as to get a finer nature product fir characterization purposes. [26]

Synthesis by algae: Algae samples were washed with distilled water to remove the adhering particles. Dried in shaded place then powdered, weighed and stored in clean container. In synthesis of zinc oxide nanoparticles, about 100 ml of ethanol algal extract heated at 50° C for (5,10 and 15 min) was added drop wise in 500 ml of 0.01,0, g\ml of zinc nitrate solution (0.297, g of zinc nitrate dissolved in 100 ml of distilled water). This was then put in a PH-controlled magnetic stirrer for 15min. Then sodium hydroxide up to 3, 4 and 6ml was added to change the PH 10. Then the precipitate was formed at 16000 rpm for 15min. Further Purification and characterization of synthesized Zinc oxides are done. [27] Biological synthesis using microbes offers an advantage over plants since microbes are easily reproduced. Also there are many drawbacks pertaining to the isolation and screening of potential microbes. The main drawback includes cost-effective of the synthesis processes as it is time-consuming and involves the use of chemical for growth medium.

Microbial growth of zinc oxide nanoparticles: Microbes such as bacteria, fungi, and yeast play an important role in the biological synthesis of metal and metal oxide nanoparticles. [28] Microbial synthesis of zinc oxide nanoparticles requires the selection of microbes, optimal conditions for cell growth, and route of biosynthesis (intra- or extracellular). The Zinc oxide nanoparticles precipitates are washed repeatedly with distilled water followed by ethanol and afterwards dried at 60 °C overnight to obtain a white powder of Zinc oxide nanoparticles. Various physicochemical techniques are used to characterize the properties of nanoparticles, including size, shape, surface charge, functional groups, and purity, by using ultraviolet–visible spectroscopy (UV–Vis), Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), transmission electron microscopy (TEM), and dynamic light scattering (DLS).

APPLICATIONS OF ZINC OXIDE NANOPARTICLES: Zinc oxide Nanoparticles have attracted intensive research efforts for their unique properties and versatile applications in different fields.

a) Antidiabetic activity:

Zinc, an essential metal, is an activator for more than three hundred enzymes in the body and plays a key role in different metabolic pathways including glucose metabolism. Zinc promotes hepatic glycogenesis through its actions on the insulin pathways and thus improves glucose utilization.[29] Zinc is also known to keep the structure of insulin[30] and has a role in insulin biosynthesis, storage and secretion.[31] Oral administration of zinc oxide nanoparticles resulted in significant antidiabetic effects-that is improved glucose tolerance, higher serum insulin (70%), reduced blood glucose (29%), reduced non-esterified fatty acids (40%), and reduced triglycerides (48%).

a) Zinc oxide nanoparticles as a biomaker in cancer treatment:

The size of nanoparticles can facilitate their entry into tumour tissues, and their subsequent retention, by a process recognized as the enhanced permeation and retention (EPR). Zinc oxide and other metal oxide nonmaterial are used as biomarkers for cancer diagnosis, screening and imaging. Recent studies have shown that zinc oxide nanoparticles cores capped with polymethyl methacrylate are useful in the detection of low abundant biomarkers. [32]

b) Use for Biomedical Applications:

Zinc oxide Nano powders are available as dispersions and powders. These nanoparticles, exhibit antifungal, anti-corrosive, antibacterial and anti-corrosive properties.

c) Cosmetics and Sunscreens:

The conventional ultraviolet (UV) protection sunscreen lacks long-term stability during usage. The sunscreen including nanoparticles such as titanium dioxide provides numerous advantages. The UV protection property of titanium oxide and zinc oxide nanoparticles as they are transparent to visible light as well as absorb and reflect UV rays found their way to be used in some sunscreens. [33]

Most of the bacteria and pathogenic fungi are harmful for environment, agriculture and living organisms. The antibacterial character of zinc oxide nanoparticles against pathogenic fungi and bacteria is due to change in the cell permeability when the plasma membrane of bacterial cell comes in contact with zinc oxide nanoparticles. This is due to the reason that zinc oxide nanoparticles move to the cytoplasm and affect the normal functioning of cell resulting in the formation of zone of inhibition against the microbes. Further, zinc oxide nanoparticles damage the cell membrane which results in the death of bacteria. [34]

a) **Role of zinc oxide nanoparticles in agriculture:**

Zinc oxide nanoparticles play a significant role in agriculture, where colloidal solution of zinc oxide nanoparticles is used in Nano fertilizers. Zinc oxide nanoscale treatment at 1000ppm concentration was used which promoted seed germination, seedling vigor and plant growth and these zinc oxide nanoparticles also proved to be effective in increasing stem and root growth in peanuts.[35]

Medicinal uses of zinc oxide nanoparticles: Some studies have indicated that zinc oxide nanoparticles affected functions of different cells or tissues, biocompatibility and neural tissue engineering. Zinc oxide nanoparticles have been suggested to modulate synaptic transmission in vitro and to change the spatial cognition capability via enhancing long-term potential in rats. It is also suggested that exposure to zinc oxide nanoparticles led to a genotoxic potential mediated by lipid peroxidation and oxidative stress. Due to its targeting potential zinc oxide nanoparticles have potential utility in the treatment of cancer and/or autoimmunity.

Electronics: The higher necessity for large size and high brightness displays in recent days that are used in the computer monitors and television is encouraging the use of nanoparticles in the display technology. [36]

Photocatalytic activity of zinc oxide nanoparticles: Waste water as well as organic wastage from many industries such as textile industries, paints and dye industries contains non-biodegradable dyes that accumulate in ground water, and environment. The researches and scientist community have been developing various new biodegradable methods which are simple, efficient, cost-effective, non-toxic and eco-friendly. Their photocatalytic activity is a function of size, shape, surface and optical activity. In this context, Zinc oxide nanoparticles have been synthesized by green route that show better photocatalytic activity. [37]

Zinc oxide application as biosensors: Zinc oxide provided good chemical stability, wonderful biocompatibility, easy surface modification, and various types of nanostructures which make it promising material for DNA biosensor. A simple method for the immobilization of oligonucleotides onto Zinc oxide surface by electrochemical ovalent grafting of diazonium salts were reported.

EVALUATION PARAMETERS OF NANOPARTICLES:

I. **Yield of nanoparticles:** The yield of nanoparticles was determined by comparing the total weight of nanoparticles formed against the combined weight of the copolymer and drug used in preparation. [38]

$$\%\text{yield} = \frac{\text{amount of nanoparticle}}{\text{amount of drug+polymer}} \times 100$$

Drug content/ surface entrapment/ drug entrapment: After centrifugation, the amount of drug present in supernatant (w) is determined by UV spectrophotometry. After that standard calibration curve is plotted. Then the amount of drug present in supernatant is subtracted from the total amount used in the preparation of nanoparticles (W). (W-w) is the amount of drug entrapped. % drug entrapment is calculated by;[39]

$$\%\text{ drug entrapment} = \frac{W-w}{W} \times 100$$

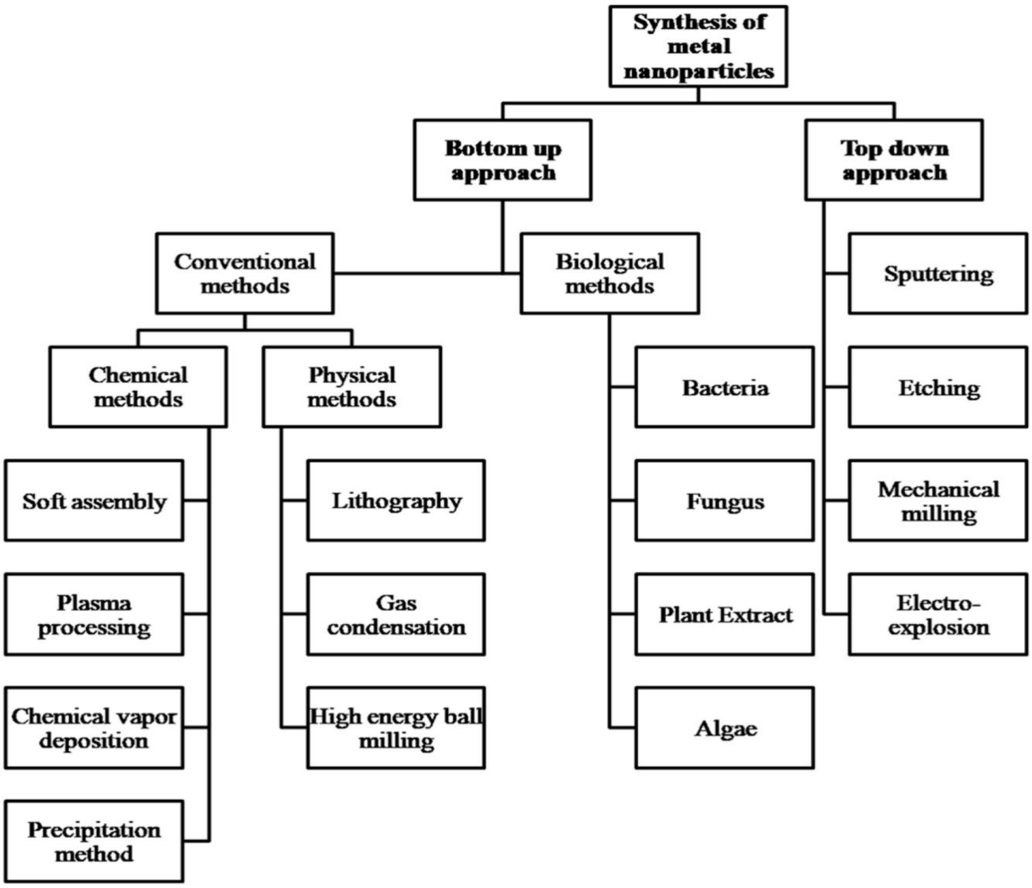

Fig no 1: Synthesis of metal nanoparticles.

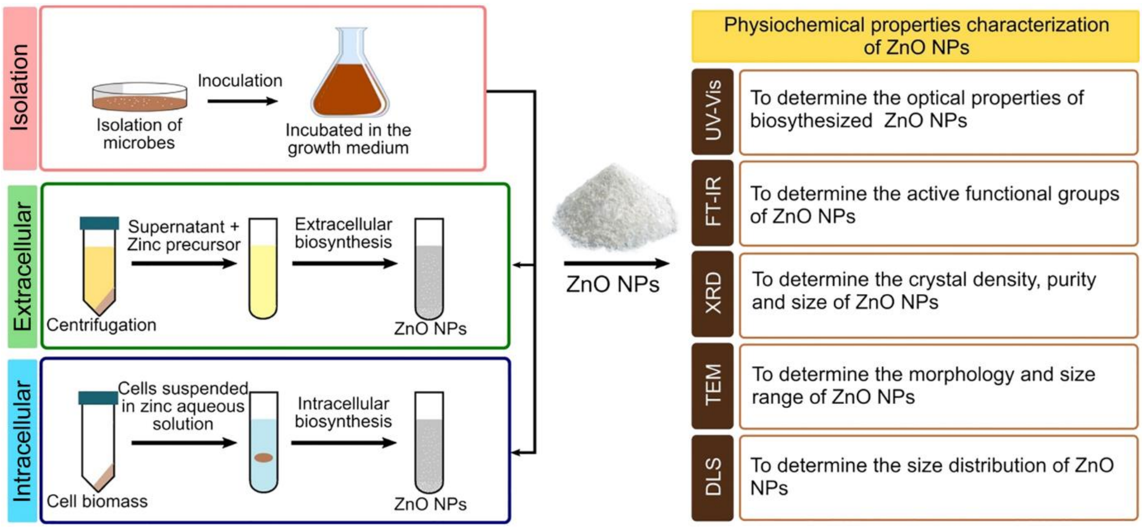

Fig 2: Microbe-mediated synthesis of metal and metal oxide nanoparticles.

I. **Particle size and zeta potential:** Value of particle size and zeta potential of prepared nanoparticles can be determined by using Malvern Zetasizer [40]

II. **Surface morphology:** Surface morphology study is carried out by scanning electron microscopy (SEM) of prepared nanoparticles.[41]

III. **Polydispersity index:** Polydispersity index of prepared nanoparticles was carried out by using Malvern Zetasizer [42]

IV. **In-vitro release study:** In-vitro release studies were performed in USP type II dissolution apparatus at rotation speed of 50 rpm. The prepared nanoparticles were immersed in 900ml of phosphate buffer solution in a vessel, and temperature was maintained at 37±0.20°C. Required quantity of 5ml medium was withdrawn at specific time periods and the same volume of dissolution medium was replaced in the flask to maintain a constant volume. The withdrawn samples were analysed using UV spectrophotometer.[43]

V. Kinetic study: For estimation of the kinetic and mechanism of drug release, the result of in vitro drug release study of nanoparticles were fitted with various kinetic equation like zero order (cumulative % release vs. time), first order (log % drug remaining vs time), Higuchis model (cumulative % drug release vs square root of time).r2 and k values were calculated for the linear curve obtained by regression analysis of the above plots.[44]

VI. Stability of nanoparticles: Stability studies of prepared nanoparticles determined by storing optimized formulation at 4°C ±1°C and 30°C ±2°C in stability chamber for 90 days. The samples were analysed after a time period like at 0, 1, 2, and 3 months for their drug content, drug release rate (t50%) as well as any changes in their physical appearance.[45]

CHARACTERIZATION TECHNIQUES OF NANOPARTICLES:

The quantity and homogeneity of the product for ensuing materials performance can be characterized by a number of simple measures, the most common of which are the mean pore size, porosity, surface area, and the more complex pore size distribution. The values of these measures are obtained by fitting experimental data to one of many models and reporting the corresponding property of the model.

i. Particle size:

Particle size distribution and morphology are the most important parameters that are seen in characterization of nanoparticles. Morphology and size are measured by electron microscopy. The major application of nanoparticles is seen in drug release and drug targeting. It has found that particle size affects the drug release. Smaller particles offer larger surface area. As a result, most of the drug loaded onto them will be exposed to the particle surface leading to fast drug release. On the contrary, drugs slowly diffuse inside larger particles. As a drawback, smaller particles tend to aggregate during storage and transportation of nanoparticles dispersion. Hence, there is a compromise between a small size and maximum stability of nanoparticles. [46]

ii. Surface charge:

The nature and intensity of the surface charge of nanoparticles is very important as it determines their interaction with the biological environment as well as their electrostatic interaction with bioactive compounds. The colloidal stability is analysed through zeta potential of nanoparticles. This potential is indirect measure of the surface charge. It corresponds to potential difference between the outer Helmholtz plane and the surface of shear. The measurement of the zeta potential allows predictions about the storage stability of colloidal dispersion. High zeta potential values, either positive or negative, should be achieved in order to ensure stability and avoid aggregation of the particles. [47]

iii. Surface hydrophobicity:

Surface hydrophobicity can be determined by several techniques such as hydrophobic interaction chromatography, biphasic partitioning, adsorption of probes, contact angle measurements etc. Recently, several sophisticated analytical techniques are reported in literature for surface analysis of nanoparticles. X – Ray photon correlation spectroscopy permits the identification of specific chemical groups on surface of nanoparticles.

iv. Zeta potential:

The zeta potential of a system is a measure of charge stability and controls all particles-particle interactions within a suspension. Understanding zeta potential is of critical importance in controlling dispersion and determining stability of a nanoparticles suspension, i.e. to what degree aggregation will occur over time. The zeta potential is the measure of the electric potential at the slip plane between the bound layer of diluents molecules surrounding the particle, and the bulk solution. (48) This can be closely linked to the particle's surface charge in simple systems but is also heavily dependent on the properties of the diluents solution. The level of zeta potential between -30 mV and +30 mV results in greater electro-static repulsion between the particles, minimizing aggregation/flocculation.

v. Transmission electron microscope (TEM):

TEM is a microscopy technique whereby a beam of electrons is transmitted through a specimen, interacting with the specimen as it passes through. An image is formed from the interaction of the electrons transmitted through the specimen the image is magnified and focused onto an imaging device, such as a fluorescent screen, on a layer of photographic film, or to be detected by a sensor. (49) TEMs are capable of imaging at a significantly higher resolution than light microscopes, owing to the small de Broglie wavelength of electrons. This enables the instrument's user to examine fine detail even as small as a single column of atoms, which is tens of thousands times smaller than the smallest resolvable object in a light microscope. For the confirmation of nanoparticle size and shape TEM measurements can be carried out using drop coating method in which a drop of solution containing nanoparticles was placed on the carbon coated copper grids and kept under vacuum desiccation for overnight before, loading them onto a specimen holder. (50)

vi. Scanning Electron Microscopy (SEM):

Scanning electron microscopy (SEM) was extremely useful for the determination of topology and observations of surfaces as they offer better resolution and depth of field than optical microscope. SEM is a type of electron microscope that images the sample surface by scanning it with a high-energy beam of electrons in a raster scan pattern. The electrons interact with the atoms that make up the sample producing signals that contain information about the sample's surface topography, composition and other properties such as electrical conductivity. The types of signals produced by an SEM include secondary electrons (SE), back-scattered electrons (BSE), characteristic X-rays, light (cathodoluminescence), specimen current and transmitted electrons. (51)

vii. Atomic Force Microscope (AFM):

The AFM is one of the tools used for imaging, measuring, and manipulating matter at the nanoscale. The atomic force microscope (AFM) is ideally suited for characterizing nanoparticles. It offers the capability of 3D visualization and both qualitative and quantitative information on many physical properties including size, morphology, surface texture and roughness. Statistical information, including size, surface area, and volume distributions, can be determined as well. (52) A wide range of particle sizes can be characterized in the same scan, from 1 nanometre to 8 micrometres.

viii. X-Ray Diffraction:

X-ray diffraction or crystallography is a method of determining the arrangement of atoms within a crystal, in which a beam of X-rays strikes a crystal and diffracts into many specific directions. From the angles and intensities of these diffracted beams, three-dimensional picture of the density of electrons within the crystals can be produced. (53)

CONCLUSION:

Nanotechnology is the emerging technology of present century operating in all fields of science. Zinc oxide nanoparticles stand out as one of the most versatile materials, due to their diverse properties, functionalities, and applications. Zinc oxide nanoparticles (ZnO) have advantage because of its physical, chemical properties, its usage and manufacturing methods. The green synthesis of zinc oxide nanoparticles is much safer and environment friendly than physical and chemical methods. It provides a clean environment by providing safer air and water, and clean renewable energy for a sustainable future. Zinc oxide has a novel approach for drug delivery as in cancer therapy where we can achieve better therapeutic action, better bioavailability, reduce toxicity. Zinc oxide nanoparticles can be characterized by their size, morphology and surface charge using advanced microscopic techniques as Scanning electron microscopy (SEM), Transmission electron microscopy (TEM), Atomic force microscope (AFM), and X-ray diffraction (XRD).This review provides an overview of zinc oxide nanoparticles based upon the characterization methods, types, protocols based upon strategies used to synthesize zinc oxide nanoparticles and wide range of applications. Zinc oxide nanoparticles has a wide range of opportunities and tremendous growth in recent years due to their eco-friendly nature, drug targeting action and cost effectiveness.

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