

Review Article

Synthesis Approaches of Zinc Oxide Nanoparticles: The Dilemma of Ecotoxicity

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Human's quest for innovation, finding solutions of problems, and upgrading the industrial yield with energy efficient and cost-effective materials has opened the avenues of nanotechnology. Among a variety of nanoparticles, zinc oxide nanoparticles (ZnO) have advantages because of the extraordinary physical and chemical properties. It is one of the cheap materials in cosmetic industry, nanofertilizers, and electrical devices and also a suitable agent for bioimaging and targeted drug and gene delivery and an excellent sensor for detecting ecological pollutants and environmental remediation. Despite inherent toxicity of nanoparticles, synthetic routes are making use of large amount of chemical and stringent reactions conditions that are contributing as environmental contaminants in the form of high energy consumption, heat generation, water consumption, and chemical waste. Further, it is also adding to the innate toxicity of nanoparticles (NPs) that is either entirely ignored or poorly investigated. The current review illustrates a comparison between pollutants and hazards spawned from chemical, physical, and biological methods used for the synthesis of ZnO. Further, the emphasis is on devising eco-friendly techniques for the synthesis of ZnO especially biological methods which are comparatively less hazardous and need to be optimized by controlling the reaction conditions in order to get desired yield and characteristics.

1. Introduction

Nanoparticles (NPs) have revolutionized all major industrial areas, from drug delivery to agriculture and food industry [1]. Chemical synthesis methods for NPs include emulsion solvent extraction method, double emulsion and evaporation method, salting out method, emulsion diffusion method, and solvent displacement/precipitation method. But, industrial scale production of NPs has familiarized a new kind of pollution into environment. It is highly desirable to reduce the loads of chemical pollution on environment by developing new and convenient methods to overcome the drawbacks of chemical methods, improve the yield, and reduce the cost [2].

Bulk zinc oxide is cost-effective and shows a variety of applications in industry including nanoparticle synthesis [3, 4]. ZnO nanoparticles are II–VI semiconductor with wide

band gap energy, that is, 3.3 eV, and high excitation energy, that is, 60 eV. Thus, it can tolerate large electric fields, high temperature, and high power operations [5]. These properties make it highly applicable in solar cells, photo catalysis, and chemical sensors [6–12]. Moreover, it can also be made conductive by doping [13]. ZnO nanocrystals predominantly show wurtzite construction with lattice parameters $a = 0.3296$ nm and $c = 0.52065$ nm. ZnO in its simplest form shows tetrahedron geometry in which each ion is enclosed by four counter ions pointing towards corners of a tetrahedron (Table 1). This tetrahedron configuration is responsible for the piezoelectricity and pyroelectricity [14, 15]. Piezoelectricity of ZnO arises from its crystal structure and makes it applicable for acoustic wave resonators and acoustic-optic modulators. Also, because of its Centro symmetric structure, it is the highest tensor among all semiconductors and gives large electromechanical coupling [5].

TABLE 1: Physical properties of ZnO nanoparticles.

Physical appearance	White, colorless, odorless solid
Crystalline structure	Wurtzite
Molecular Weight	81.38 g/mol
Electron effective mass	60
Melting Point	1,975°C
Density	5.47 g/cm ³
Isoelectric point	9.5–10
Space group	$C_{6v}^4-P6_3mc$
Standard molar entropy	43.9 J·K ⁻¹ mol ⁻¹
Standard enthalpy of formation	-348.0 kJ/mol

2. Importance of ZnO for Industries

Ultraviolet A and Ultraviolet B radiations from the sun can cause injury by free radical mechanism on skin cells. ZnO nanoparticles of size less than 200 nm have high efficiency in scattering light and induce cosmetically desired whitening to the skin. It has also been used in foot care, ointments, and over-the-counter topical products [16–21]. Singh and Nanda performed a detailed comparative study between conventional zinc oxide and nanosized ZnO particles for their sun screen efficiency. Good texture, better spreadability, and enhanced in vitro sun protection factor (SPF) proved the advantageous role of nanoparticles in cosmetics [22]. Hypothesized hazards to human health due to these nanoparticles are still unexplored and it would be counterproductive to avoid them without any evidence.

Another astonishing property of ZnO is the green luminescence, related to the point defects, which makes it a useful agent for bioimaging. This can be further enhanced by doping with transition elements, for example, copper, cobalt, and nickel, for more desirable optical properties. Other application of ZnO includes gene delivery that is considered as an important milestone in therapeutics and has attained much attention of the researchers for the treatment of diseases like severe combined immune deficiency (ADA-SCID), chronic granulomatous disorder (CGD), hemophilia, genital blindness, lysosomal storage disease and muscular dystrophy, neurodegenerative diseases, viral infections (e.g., influenza, HIV, and hepatitis), heart disease, and diabetes. Quantum dots and tetrapod like structures of ZnO have been explored extensively for such applications [23–25]. Such quantum dots are also playing a vital role as sensors. ZnO is a semiconductor and its properties can be altered by a number of ways that has made it an exciting candidate for the sensor exploration. Such sensors have indispensable role, that is, from detecting environmental pollutants to epidemic diseases outbreaks. A number of authors have reported ZnO based biosensors for sensing cholesterol, biochemistry of enzymes, and other biosensing applications [26, 27]. Kazemi and coauthors have synthesized ZnO by sol-gel and hydrothermal method and devised a home-built apparatus which responded best at its “working temperature” to sense ethanol. Adsorbed oxygen species trapped the electron creating a charge depleted layer supposed to be responsible for sensing properties of the

created sensor [28]. In another study, Liu and colleagues reported a high performance ZnO based sensor for n-butanol sensing. Low temperature solvothermal method gave highly crystalline wurtzite NPs (spherical in shape with diameter of 8.4 ± 1.3 nm). The fabricated sample had the ability to sense n-butanol up to 500 ppm with a recovery time of 22 seconds. The designed sensor exhibited several advantages such as high and fast response, short recovery time, and good stability towards n-butanol gas [29].

Nowadays, ZnO has been widely investigated for plant protection products, fertilizers, soil improvement, water purification, and many other [3, 30–33]. Antimicrobially active packaging is a new generation of nano-food packaging based on metal nanocomposites which are made by incorporating ZnO into polymer films [34–38]. Espitia et al., has reviewed the utility of ZnO nanoparticles in food preservation and packaging industry when applied to biodegradable polymeric metrics. The NPs improved the quality of food and packaging mainly by three mechanisms, that is, release of antimicrobial ions, damaging the integrity of bacterial cell, and the formation of ROS by the effect of light radiation [39]. Elmer and White have reported the pesticidal properties of the ZnO. They sprayed synthesized ZnO on tomato and eggplant. It was noted that ZnO reduced disease estimate by 28% when compared to the control [40]. On the basis of thermodynamics, ZnO should dissolve faster and to a greater extent than bulk ZnO particles (equivalent spherical diameter > 100 nm). These novel solubility features of ZnO might be exploited to improve the efficiency of Zn fertilizers. Milani et al. found that urea and MAP granules coated with ZnO showed more thermodynamic dissolution may be due to pH difference; however kinetics of Zn dissolution remained unaffected [41].

3. Toxicity of ZnO in Mammalian Model

However, controversial results have been reported in the literature regarding toxicity of the ZnO in the living cells particularly in mammalian cells. Some of the reports have shown that ZnO are biocompatible and nontoxic [42–44], while some studies have recently reported both in vivo and in vitro toxicity of the ZnO on mammalian cells [45–48]. It can be elucidated from such studies that the toxicity of ZnO depends upon the concentration used. Vandebriel and Jong had reviewed the ZnO toxicity in mammalian model [48]. For more study, refer to reviews of [49–51]. Further, such toxicity is important in other aspects, for example, for the treatment of cancerous, pathogenic, and leukemic T cells [52–58]. Such nanoparticles are also important to overcome problems like drug resistance which is one of the major problem in the pharmaceutical industry [59]. This is because of the nonselectivity of ZnO.

4. Fabrication of ZnO Nanoparticles for Different Applications

A variety of synthetic techniques are used for the synthesis of ZnO. These techniques broadly can be divided into three types, that is, chemical, biological, and physical methods

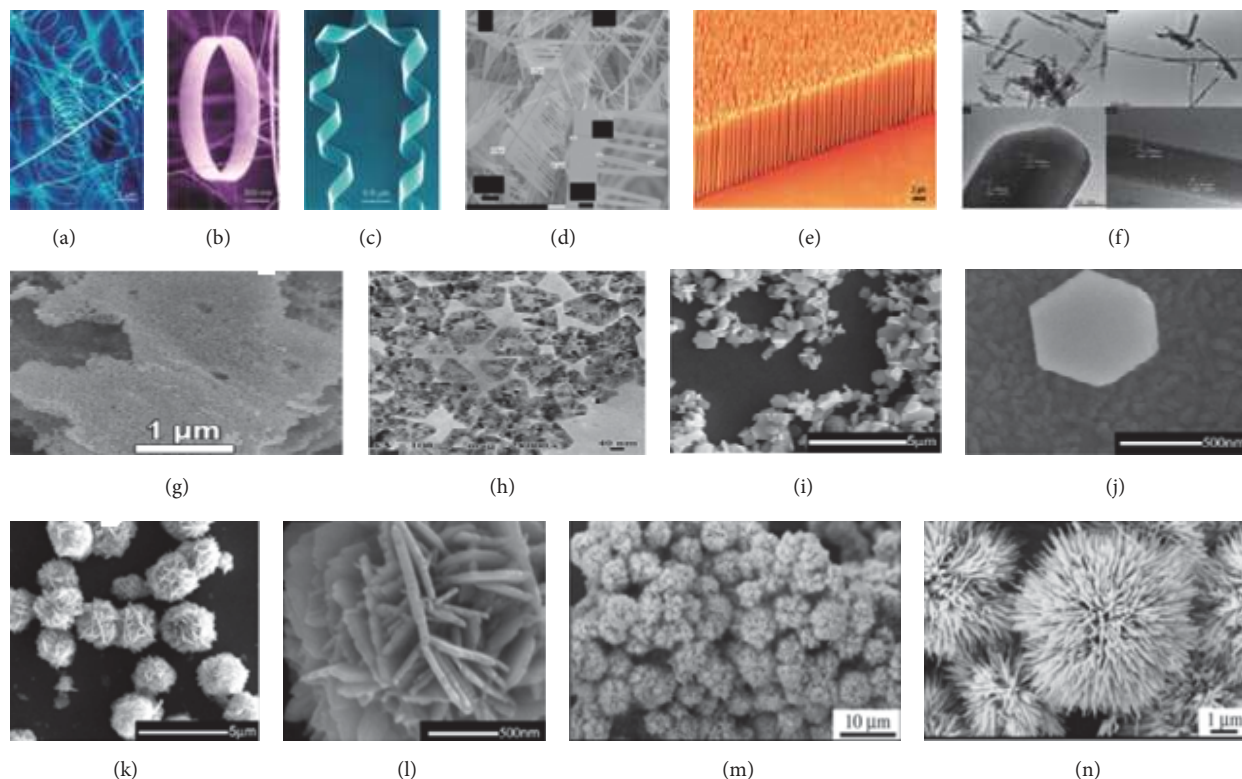


FIGURE 1: Different structures of ZnO; *one-dimensional ZnO*: (a) nanosprings, (b) nanorings, (c) nanohelix, (d) nanocombs, (e) nanowires, and (f) nanorods (adopted from [89, 90]). *Two-dimensional ZnO*: (g) nanosheets, (h) nanopellets, and (i) nanoplates (adopted from [91–93]). *Three-dimensional ZnO*: (k) & (l) nanoflowers. (m) Nanomesosphere. (n) Nanourchins (adopted from [91, 94]).

(Figures 1 and 2). Chemical synthesis can further be divided into liquid phase synthesis and gas phase synthesis. Liquid phase synthesis includes precipitation, coprecipitation method, colloidal methods, sol-gel processing, water–oil microemulsions method, hydrothermal synthesis, solvothermal, and sonochemical, and polyol method. And vapor phase fabrication includes pyrolysis and inert gas condensation methods.

4.1. Liquid Phase Synthesis. In a typical precipitation and coprecipitation method, a reducing agent (mostly inorganic alkalis) is allowed to react with the zinc salt. A resultant soluble or insoluble precipitate is produced that is afterwards washed and calcined at different temperatures to obtain the particular nanoparticles with desired morphology and characteristics. A range of nanoparticles and reaction conditions are used to control the size and shape of the ZnO by this method [60]. Colloidal methods rely on the simplest and well established chemistry since antiquity. However, in literature it was first reported by Faraday in 1857, who synthesized colloids of gold nanoparticles by the reduction of HAuCl_4 with phosphorus. Sol-gel techniques rely on colloidal chemistry. Sols are referred to the colloidal solution consisting of solid particles suspended in liquid phase having a diameter of a few hundred nanometers. Gels are mostly formed by polycondensation or polyesterification methods followed by aging to achieve phase transformations and Ostwald ripening. The gels are dehydrated at temperature as high as 8000°C

and finally densified at temperature greater than 8000°C to obtain metal oxide nanoparticles. An advantage of sol-gel methods is the insurance of highly pure and uniform structured ZnO [61]. Formation of thorn like ZnO in sol-gel method was reported by Khan and companions. The method was a little modified by mechanical stirring. Zinc acetate dihydrate $[\text{Zn}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}]$, sodium hydroxide (NaOH), and CTAB were used as precursors. Obtained nanoparticles were less than 50 nm which showed significant antimicrobial activity [61].

In solvothermal and hydrothermal processes, originators are dissolved in hot solvents (other than water) or water under moderate to high pressure (1–10,000 atm) and moderately high to high temperature ($100\text{--}1000^\circ\text{C}$). These processes are used to synthesize a variety of zinc nanostructures such as thin films, bulk powders, spheres (3D), rods (2D), and wires (1D). Further, this method is also useful for the synthesis of metastable and thermodynamically stable ZnO via manipulation of the reaction conditions [62]. In a study, the solvothermal synthesis of single layer ZnO was reported by Rai et al. They aimed to investigate the effect of zinc salts on the morphology of NPs. Formation of NPs in a range of 100–150 nm and 20–25 nm length occurred, respectively, whereas NPs were 20–25 nm in diameter. The synthesized nanorods also showed more sensitivity towards NO_2 [63].

4.2. Gas Phase Synthesis. One of the highly used techniques is spray pyrolysis method, in which aerosol droplets of the

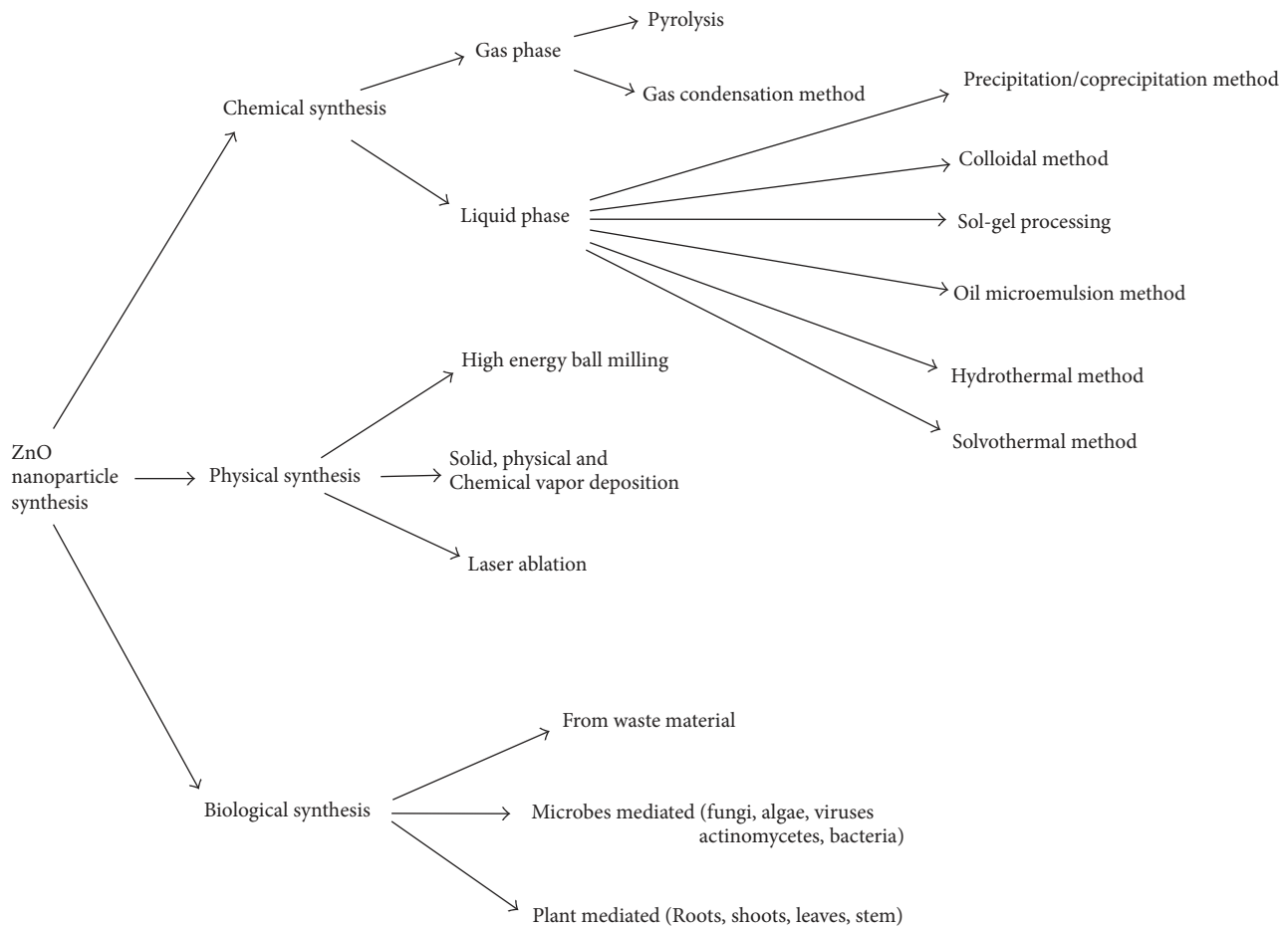


FIGURE 2: Major synthetic techniques used for ZnO nanoparticles synthesis.

precursor zinc salt are produced via flame heating. The droplets are dispersed in the gas and their size is reduced by dehydration. The last steps involve the decomposition and sintering of the required material [64]. Another method is inert gas condensation methods that is subdivided into physical vapor deposition (without catalytic interaction) and chemical vapor deposition (with catalytic interaction). Principally, these methods comprise evaporation of zinc source inside a chamber by resistive heat. Different sources of heat such as electron or laser beams or radio frequencies are also used. From the heat chamber, the vapors are forced to migrate into cooler chamber having inert gas, from where they are collected for further consolidation. The major disadvantage of this method is the coalesces and agglomeration of ZnO nanoparticles. Another important method is the one-step levitational gas condensation method that was reported by Uhm and coworkers for ZnO. Apparatus consisted of 2.5 kW induction generator levitation and evaporation chamber and oxygen concentration control unit. Obtained nanoparticles showed very good morphology with diameter of 30 nm [65].

4.3. Physical Methods. Physical methods of ZnO nanoparticles synthesis include high energy ball milling, melt mixing, physical vapor deposition, laser ablation, sputter deposition, electric arc deposition, and ion implantation. In most

physical/mechanical processes, the production rates of ZnO nanoparticles are very high and are mostly used for the industrial processes. High energy ball milling is a nonequilibrium process developed by Salah and coworkers in 1961. In this method powdered material placed inside a ball mill is subjected to high energy collision from balls [66]. Amirkhanlou and coworkers reported high energy ball milling processes as very efficient, cost-effective, and simple techniques for the preparation of ZnO nanostructures. They used 15 balls with diameter of 20 mm confined in a 500 ml bowl. XRD and field emission scanning electron microscopy (FESEM) showed ZnO nanopowder particles with crystallite size of 15 nm, particle size of about 60 nm, and lattice strain of 0.67%. Similar methodology was reported by Salah et al. and used such ZnO in antimicrobial activity [66]. Laser ablation technique utilizes a laser beam to remove particle from a solid or a liquid surface. Spherical ZnO with average diameter of 35 nm was reported by Ismail and companions. They used pulsed laser ablation in double distilled water [67]. At lower reflux, materials are heated by the energy absorbed through laser and evaporates, while, at higher refluxes, materials may convert into plasma. Other frequently and studied methods used are vapor solid liquid (VLS), physical vapor deposition (PVD), and chemical vapor deposition (CVD) [68]. Physical vapor deposition (PVD) methods are used

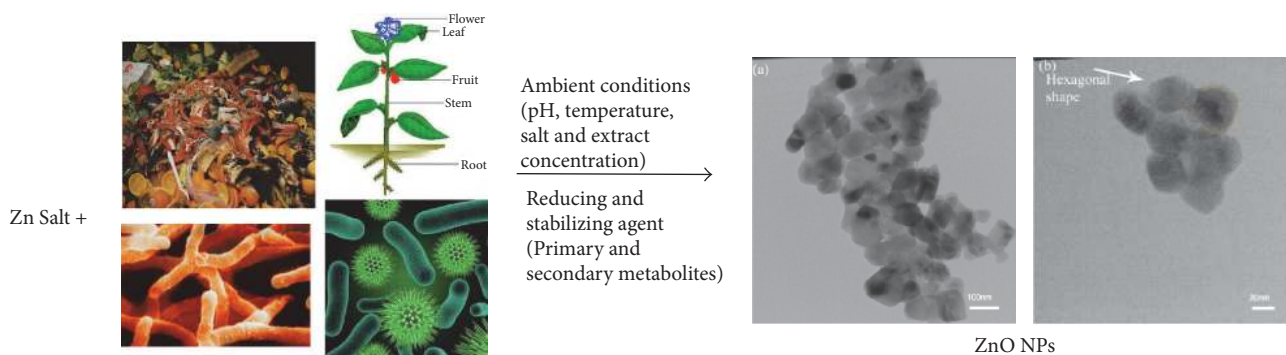


FIGURE 3: Green synthesis of ZnO via plants, microbes, and other routes.

to coat the surfaces by depositing the metals. Two types of techniques, namely, evaporation and sputtering, are used in PVD. Sputtering refers to the mechanism of particle escape from the surface by striking high energy particles. The ions for sputtering process are supplied from plasma [39].

4.4. Green Synthesis of Nanoparticles. Green routes are used for the synthesis of ZnO because of the least possible number of chemicals utilized that produces least amount of pollutants and are energy efficient as well as cost-effective. A number of natural moieties such as plants, fungi, algae, bacteria, and viruses are used to synthesize the ZnO (Figure 3).

4.4.1. Plant Mediated Synthesis. Plants and plant extracts as a machinery for metal nanoparticles synthesis are fascinating as they eliminate the need of using hazardous materials as well as the tedious process of culturing and downstream processing. However, plant extracts are more attractive because the methodology is much simpler and cost-effective [69, 70]. Nanoparticles synthesis driven by plant extracts is perhaps the most explored biological source. Plants have the ability to synthesize the nanoparticles both via in vivo and in vitro methods. The mechanism of synthesis of such nanoparticles by plants is their capability to uptake metals from the soil and water, hyperaccumulation, and further reduction to recoverable nanoparticles. Such techniques are extensively used in phytoremediation and phytomining. However, the focus is majorly on silver and gold nanoparticles on using plants. Literature is limited in the synthesis of ZnO by plant and plant extract based routes.

In vitro approaches make use of plant extracts to bioreduce a particular zinc salt (zinc nitrate, sulphate, chloride, and many other) and provide a control over size and shape of the nanoparticles. Basically, plants contain a number of primary and secondary metabolites, for example, tannins, terpenoids, saponins, starches, polypeptides, flavonoids, and phenolic, that act as an excellent reducing as well as capping agents. Mild solvents like water, ethanol, or methanol are used for the extraction of the plant metabolites, which are allowed to react with zinc salt solution under different conditions to obtain a maximum yield [71–73].

4.4.2. Microorganisms Facilitated Synthesis of Nanoparticles. Microbes are considered as eco-friendly factories of nanoparticles synthesis. Interactions between metals and microbes have been exploited for various biological applications in the fields of bioremediation, biomineralization, bioleaching, and biocorrosion [74]. It is one of the most sustainable, eco-friendly techniques so far in spite of its few limitations. Both prokaryotes and eukaryotes are used for the synthesis of metal/metal oxide especially ZnO. Further, the synthesis may be intracellular or extracellular.

Fungi are decomposers as well as parasite in nature. In intracellular synthesis, fungal biomass is incubated for a particular time period in dark along with a zinc salt solution, while in extracellular synthesis fungal filtrates are treated with the precursor solution and synthesis is assessed [75]. A number of studies are available on using fungi as ZnO synthesizer. Jain et al. isolated 19 fungal cultures from rhizospheric soil. Among those cultures, *Aspergillus aeneus* isolate NJP12 showed highest potential for extracellular synthesis of ZnO under ambient conditions. The resultant nanoparticles were coated with protein which acted as a stabilizer [76]. In another study, fungal filtrate of *Aspergillus niger* was used by Jacob and coscientists for the production of the ZnO. The synthesized nanoparticles were spherical in shape with an average diameter of 39.4–114.6 nm [77]. Baskar and coworkers extracellularly prepared ZnO by *Aspergillus terreus* filtrate. The synthesized ZnO particles were spherical in shape with a size range of 54.8 to 82.6 nm [78].

However, a number of studies are also available on using bacteria as green synthesizer for ZnO; for example, bacterial strain *Aeromonas hydrophila* formed spherical and oval shaped nanoparticles with an average diameter of 57.72 nm [79]. Synthetic pathways of nanoparticles by microbes may involve basic combinations of cellular biochemistry, metal ions transportations in and out of the cells, microbial resistance towards toxic metal mechanism and activated metal-binding sites, intracellular metal ions accumulation, and metal oxide nucleation [80]. *Lactobacillus sporogenes* was reported to produce ZnO of diameter of 5–15 nm. The authors proposed the mechanism of synthesis that depends upon reduction of metals by oxidoreductases which were activated by the nutritional media contents and pH variations [81]. Actinomycetes, having properties of both prokaryotes

(fungi) and bacteria, are also used for the synthesis of ZnO particles. Scientists are attempting to develop an eco-friendly and cost-effective method, for example, by using brown marine macroalgae *Sargassum muticum* aqueous extract. The resulting nanoparticles had diameter ranging from 30 to 57 nm and hexagonal wurtzite in structure [82].

4.4.3. Other Green Synthesis Methods. A number of other green means are used for the synthesis of ZnO. Jha and Prasad have reported the formation of ZnO by slaughtered goat waste (mainly intestine). Simple distillation method by methanol followed by boiling with zinc chloride salt was adopted. This resulted in agglomerates of nanoparticles as smaller as 3–11 nm. His work is an important contribution in getting rid of waste which subsequently may cause disease dispersal [83]. Researchers have also explored the ZnO synthetic capability of the peels obtained from different fruits and vegetables. Mishra and Sharma used fresh peels extract powder of *Punica granatum*. Distilled water was used to prepare the extract, which was mixed with zinc nitrate solution at 60–80°C under constant stirring. In another study, filtrate of *Musa balbisiana* peels and zinc nitrate dihydrate was used to obtain ZnO NPs by Tamuly and coworkers. Nanoflowers of less than 2 nm in diameter were obtained which were used as catalyst for the synthesis of chalcone derivatives [84–88].

5. Environmental Implications of Physical, Chemical, and Green Synthesis

5.1. Capping Agents, Surfactants, and Stabilizers. Three major factors should be kept in view while devising an industrial scale synthesis of the nanoparticles. These factors are solvent choice, the use of an environmentally benign reducing agent, and the use of a nontoxic material for nanoparticle stabilization [95]. In chemical synthesis, capping agents and stabilizers are extensively used in order to control the size and to avoid agglomeration [96]. Owing to the wide application of the ZnO nanoparticles and their large production, potential of capping agents and stabilizers are investigated by many researchers. Despite inherent toxicity, organic and polymeric capping agents are majorly contributing in environmental pollution. Toxicity of the surface modified and unmodified ZnO on zebra fish were comprehensively studied by the Zhou and his colleagues. Their experiment showed a significant difference in toxicity level of surface modified and unmodified ZnO NPs [97]. Toxicity of some of the frequently used capping and stabilizing agents is mentioned in Table 2.

5.2. Reducing Agents and pH. Most of the synthetic techniques for ZnO utilize a reducing agent to reduce a respective zinc salt and vigorous synthetic environment that involves either highly acidic or basic conditions. Precipitation/coprecipitation is the easiest and widely employed method for the ZnO synthesis. This method mainly employs sodium hydroxide (NaOH) as reducing agent, which is highly corrosive and degrades all kinds of protein. Dissolution of NaOH in water is exothermic and may cause heat burns or may ignite. On contact with metals it produces flammable

hydrogen. In the synthesis of ZnO, excessive amounts of NaOH with higher molar concentrations are used to ensure the reaction completion. Upon filtration of reaction mixture, supernatant is discarded that might directly go to waste water and ultimately in water bodies. It not only may degrade the metallic parts of the sewage system but also alters the pH of water bodies causing hazards to aquatic flora and fauna.

Another highly used chemical for ZnO synthesis is hydrazine, which is a highly reactive alkali and reducing agent extensively used in industry and military. Strict protective instrument utilization is recommended while working with hydrazine. It may cause burns to skin and severely damages the respiratory track while overexposure may cause death. Due to its corrosive potential and its reactivity with oxidant, it is of great ecological concern. Metabolites of hydrazine have more ability to damage than the parent compound [98, 99]. Ethanol is known to be therapeutic in low to moderate dosage; however, high dosage or chronic exposures may lead to dehydration, central nervous system suppression, impaired sensory and motor function, slowed cognition, unconsciousness, and possible death [100–102]. Ethylene glycol shares a number of characteristics. In earlier stage of metabolism, it is responsible for the metabolic acidosis of intoxication. In late stages, lactate may also accumulate, mainly due to formate inhibition of the respiratory chain. However, toxicity of ethylene glycol is complex and not fully understood yet [103]. High concentrations of 1,3 propanediol in lab rats have shown significant toxicity [81].

5.3. Sonication. Sonicators use ultrasonic or sound energy to agitate the particles in the mixture. Typical lab sonicators employ 20 kHz of ultrasonic frequency. The major hazards associated with the use of sonicator are the creation of hearing impairment and generation of aerosols [104]. Sonochemical synthesis of ZnO nanoparticles has been recently reported by many groups [105–111]. Two types of aerosols are produced by the sonochemical method, namely, chemical aerosols produced by the reagents used in the method and aerosols of nanoparticles. Moreover, the aerosols produced by the chemicals often go unattended in the labs. Furthermore, there is no such report to understand the mechanism of NP aerosols. However, Taurozzi's groups emphasized on the optimization and standardization of sonological parameters. They recommended the rational use of the sonicator and comprehending the unattended side effects [112].

5.4. Temperature. Anthropogenic accomplishments using high temperature processes are altering the overall heat balance of the earth; that is, it is increasing the entropy. The major disadvantage of the high temperature processes is the consumption of the energy. Majorly, heat evolving from high temperature processes may cause heat edema, heat rashes, heat cramps, heat exhaustion, heat syncope, and heat strokes [113]. A number of methods in synthesis of ZnO NP involve high temperatures, for example, hybrid electrochemical thermal method (60–700°C) [114], gas condensation method (595°C) [115], direct thermal decomposition method (600°C) [116], spray pyrolysis method (1200°C) [117], and high

TABLE 2: Frequently employed capping agents and stabilizers.

Capping agents/stabilizers	Inherent toxicity	Toxicity reported by	Reference of utility in ZnO NP synthesis
Triethyl amine	Reversible ocular effects including corneal swelling and halo vision in humans	[119]	[120] [121] [122]
Oleic acid	Promote apoptosis and necrosis, mitochondrial depolarization, lipid accumulation, and overexpression of C-MYC and P53	[123]	[124] [125] [126]
Thioglycerol	Irritant for skin, eye and inhalation; Hazardous in case of ingestion	[127]	[128] [129] [130]
EDTA	Cytotoxic and genotoxic	[131] [132]	[133] [134] [135]
Tetraethyl ammoniumbromide	Tremors, incoordination, flaccid prostration, and death from respiratory failure in animals	[136]	[137] [138] [139]
Tetraethyl orthosilicate	Highly damaging to eyes	[140]	[141] [142] [143]
Polyethylene glycol (PEG)	Immunogenic	[144]	[11] [145] [137]
Polyethylene phthalate (PEP)	Endocrine disruptor	[146]	[147] [148] [149]
Ethylene glycol	Adversely affects reproduction and development	[150]	[11] [151] [152]
Gelatin	Toxic	[153]	[154] [155]
Polyvinyl alcohol (PVA)	Toxic	[156] [157]	[158] [159] [160]
Polyvinyl pyrrolidone (PVP)	Weight increase in lab mice	[161]	[162] [163] [164]

temperature mixing hydrothermal processes (160–200°C) [118], that might be lethal.

5.5. Toxicological Implications of Green Synthesis of ZnO. Instability of biologically synthesized nanoparticles is worth consideration. Physical instability of nanoparticles may alter their arrangement/confirmations due to different conditions like temperature pressure, light, medium, pH, and so on, which may lead to the creation of the different unwanted chemical moieties. Moreover, potential hazards of these chemical metabolites are very poorly investigated.

Inherent toxicity of ZnO nanoparticles is linked to dissolution and ROS generation. Dissolution is the leading phenomenon in chemical and biological instability of ZnO. Metal solubility and concentration gradient between particle surface and the bulk solution phase acts as a driving force.

Dissolution of the ZnO nanoparticles may lead to the Zn^{2+} and $Zn(OH)^+$ that are highly toxic [165]. However, it is possible to control the dissolution phenomenon by coating the nanoparticles, doping, surface area effect, additional factors such as size-dependent changes of the surface curvature, and roughness of the particles. Also, the crystalline nature of the nanoparticles may be changed by redox reaction taking place on the surface of NPs, which may occur at the same time or simultaneously. Electronic transfers taking place during these processes lead to the generation of the reactive oxygen species (ROS) and oxidative stress inducing toxicological injury [166]. Chemically synthesized NPs are considerably stable; still they pose both type of hazards, whereas green synthesized nanoparticles are relatively less stable. Thus, the problem of dissolution of ions and ROS augments which may act as potential threat to the surrounding environment.

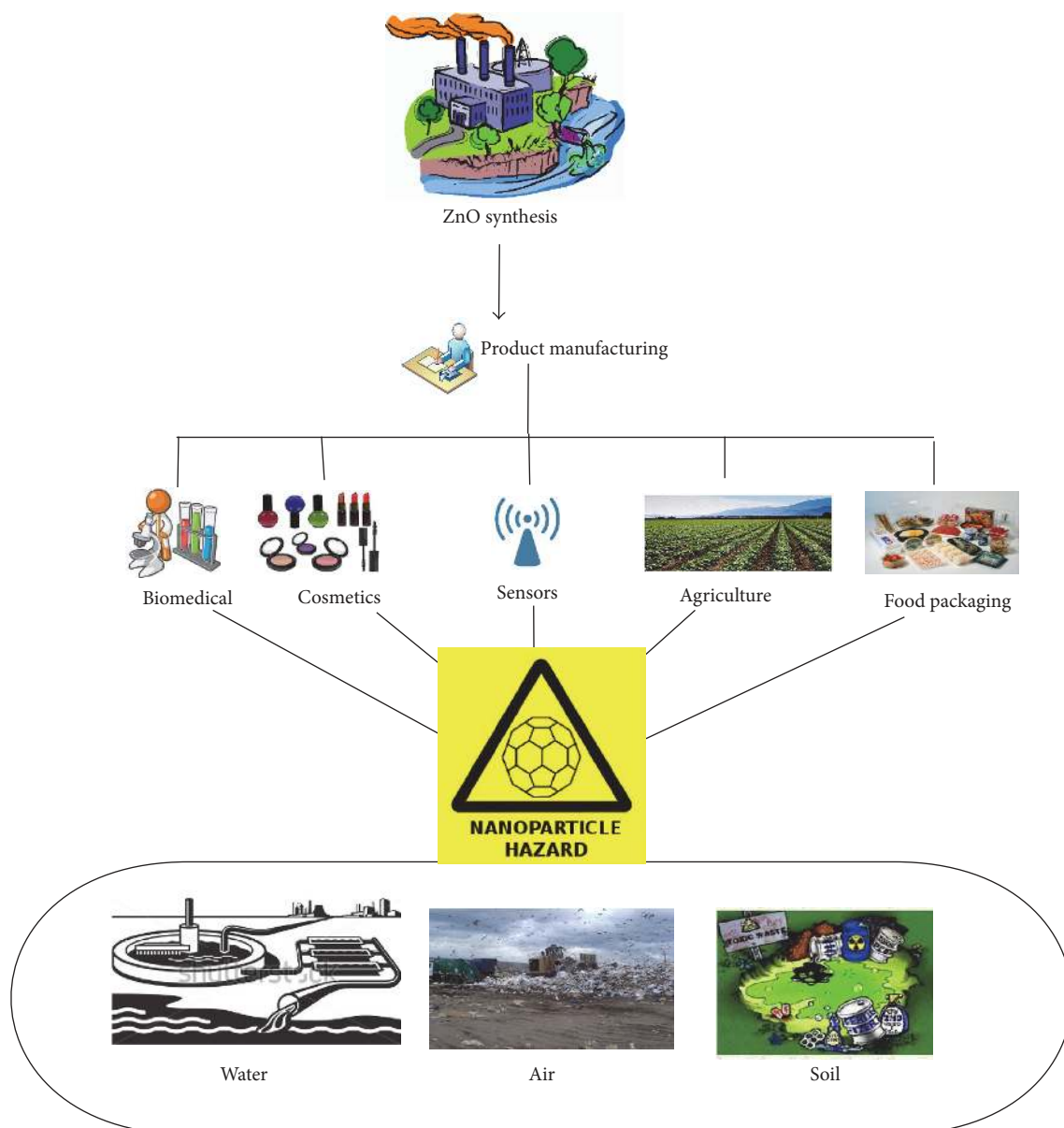


FIGURE 4: Environmental pollution from industrial scale production of ZnO nanoparticles.

6. Conclusion and Future Prospects

Referring to the varied and widespread use of ZnO in research and industry, it is inevitable to clearly understand the whole life cycle of the ZnO, from raw materials, synthesis, and applications because of lack of data. Further, these particles have altogether different properties from their parent bulk materials. Despite their proven utilities and benefits, still, there are apprehensions about their environmental impacts (Figure 4), as we are still coping with the outcomes of the industrial revolution, although, with a delay of almost fifty years, scientists are able to comprehend the environmental implications of the traditional pollutants created by anthropogenic activities. However, full understanding does not mean that we have successfully dealt with them. Nowadays, with the advancement of science and technology, we are

entering in an era of nanomaterials that have rendered unlimited services due to their unique size and shape. Like industrial revolution, the environmental impacts and perils of these synthetic nanoparticles, pollutants emerging from their whole life cycle and potential hazards to biological systems (animals and plants), are least bothering. So far, the fate and distribution of ZnO pollution have been studied in mammalian models [167, 168]. However, the question of whether nanoparticles could have a negative/positive biological impact on exposed plants and other organisms is unclear as only few studies are published till date that have revealed variable and, in some cases, conflicting results. Also, there is a lack of regulations for the synthesis, manipulation, and disposal of engineered NPs and as a result these NPs in the environment are being accumulated. Nanoindustry has established itself as a viable substitute of traditional industrial

processes. A large number of synthetic techniques have been used to get cheaper raw materials (ZnO NP) and to get maximum yield. Thus, that it may provide a milestone to the researchers to overcome the loop holes of the process.

Chemical synthesis as evident from the name relies on intensive consumption of the chemicals, which are exhausted to the environment as waste material contributing to anthropogenic waste. Techniques employed for the chemical synthesis have their own limitations and drawbacks which can be dealt with green synthesis (plants, microbes, and waste) of ZnO, which offers a relatively pollution free mechanism but optimization of reaction conditions to get higher yield, desired characteristics, and instability put a limitation on its use. It is unpredictable to gauge stability of biosynthesized ZnO which may otherwise cause serious damage to biological systems. Thus, there is a need to devise and optimize reaction mechanism and techniques for both chemical and green synthesis.

Further, most of the chemicals used in synthetic processes of ZnO are present in hazardous chemical list and maximum exhaustible limits in environment is well defined in most countries. However, we still need to define these limitations in case of nanopollutants exhausted from the nanoindustry. There is an utter requirement to perform environmental risk assessment in order to estimate the threat posed by ZnO. Also, simulation models should be developed to sketch an analogy between the increasing utility, amount of ZnO synthesized, and pollutants exhausted during these activities.

Conflicts of Interest

The authors declare no conflicts of interest.

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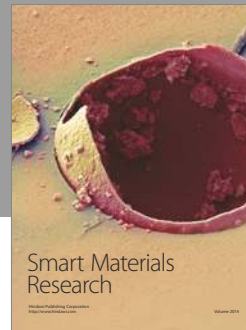
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