REVIEW PAPER

A Brief Review on the Synthesis of Zno Nanoparticles for Biomedical Applications

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Abstract: *The semiconducting Zinc Oxide (ZnO), particles have excellent biocompatibility, good chemical stability, selectivity, sensitivity, non-toxicity, and fast electron transfer characteristics. Thus, these nanoparticles are receiving increasing attention due to their potential performance in human body. The nanoparticles have become more promising in biomedical applications through the development of anticancer agents to recover different types of malignant cells in the human body. The ZnO nanoparticles can be the future materials for biomedical applications. The purpose of this paper is to review the cost-effective approaches to synthesize the ZnO nanoparticles. Moreover, the ideas developed, may be scaled-up for biomedical applications.*

Keywords: *Zinc oxide (ZnO); Nanoparticles; Biomedical applications; Cost-effective synthesis; Biomaterials.*

1. INTRODUCTION

ZnO nanoparticles are one of the low-cost materials. These nanoparticles have revolutionized major industrial sectors like drug delivery, agriculture, and the food industry [1]. It's also widely used in ethanol gas sensors, UV light-emitting devices, pharmaceuticals, photo-catalysts, and cosmetic industries [2–6]. These nanoparticles are also used in sunscreen because it absorbs ultraviolet light effectively [7]. Compared with other metal oxide nanoparticles, ZnO nanoparticles with comparatively less toxic properties can exhibit excellent biomedical applications, such as anticancer, drug delivery, antibacterial, and diabetes treatment [8–11]. The nanoparticles have acceptances to researchers because of these exceptional physical and chemical characteristics. In synthesis process to develop the ZnO nanoparticles are generally classified into three processes, first the physical, second the chemical, and third the green synthesis process. The physical and chemical synthesis processes of ZnO nanoparticles generally are involved in laser/vapor deposition, spray-pyrolysis, epitaxial, thermal evaporation, sol-gel, sonochemical, electro deposition, solvothermal, and hydrothermal [12–21]. The US FDA has enlisted generally recognized safe metal oxide of the ZnO. At ambient conditions, crystalline ZnO has a wurtzite crystal structure. It has two lattice parameters (a and c), with a hexagonal unit cell. It belongs to the C^4_{6V} or $P6_3mc$ space group. Fig. 1 shows the wurtzite crystalline structure of ZnO. Two tetrahedral show different configurations in this figure for the cations and anions. One shows the anion surrounded by four cations at the corners, and the other shows a cation in the central atom. It represents a typical sp^3 covalent bond to the coordination forms.

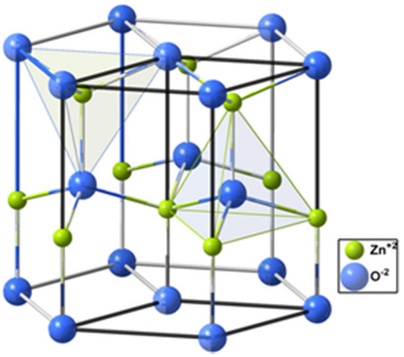

Fig. 1. Wurtzite hexagonal crystalline structure of ZnO [22].

It can be simply explained schematically as layer-by-layer along the c-axis direction. It is composed of a tetrahedral coordinated Zn^{2+} and O^{2-} inorganic compound semiconductor. The non-centrosymmetric structure founds rise by tetrahedral coordination. Some physical properties of ZnO are presented in Table 1.

Table 1. Some physical properties of ZnO for an ideal hexagonal structure [23].

Properties	**Zinc Oxide, ZnO**
Stable phase at 300 K	Wurtzite
Lattice parameters at 300 K, *a* and *c*	0.32495 nm and 0.52069 nm
Density	5.606 g/cm^3
Melting point	1975 ˚C
Thermal conductivity	0.6 W/cm.˚C, 1~ 1.2 W/cm.˚C
Static dielectric constant	8.656
Refractive index	2.008
Band-gap (Room Temperature)	3.370 eV
Band-gap (low Temperature)	3.437 eV
Exciton binding energy	60 meV
Electron Hall mobility at 300 K	200 cm^2/V.s
Hole Hall mobility at 300 K	5~50 cm^2/V.s
Electron effective mass	0.24
Hole effective mass	0.59

Already, discovered ZnO nanoparticles have been able to bind biological substances in nanotechnology. Its dimensions below 20 nm can display UV absorption behavior without light scattering. It can also be extensively employed as inorganic long-wave ultraviolet A (UVA) and short-wave ultraviolet B (UVB) filters. It is used to kill harmful microorganisms with its antibacterial and antifungal characteristics. It is a semiconductor material having a wide energy gap, and therefore, it is used as a UV photodetector. A considerable amount of research work is completed through different synthesis routes for ZnO nanostructures. One of the common processes to develop ZnO nanostructures is a chemical vapor deposition (CVD) method. It can also be obtained through an aqueous solution growth process. The effect of ZnO nanostructures on human cells has not clear to the researcher until now. They are thinking of the way it will dissolve the Zn ions into a human cell. The human cell must possess the following characteristics by antimicrobial substances:

- It must be nontoxic.
- It shouldn’t react with food.
- It has to a good taste or to be tasteless.
- It shouldn’t have a disagreeable smell.

The other synthesis process is a green synthesis that involves plants and herbal extracts [24–28]. There are various types of synthesis processes, which employed to develop ZnO nanostructures due to their vast areas of applications. It can easily prepare that performed an inexpensive, safe, and secure. It has drawn researcher interest due to its wide range of applicability in different fields of electronic, optic, and biomedical.

Recently, ZnO nanoparticles have taken more attention from scientists because of their prominent biological properties and biomedical applications. It shows the prospect and promise of a biomedical application field by developing a perfect size of nanomaterials. Zinc is an essential trace element that extensively exists in all body tissues, including the muscle, brain, skin, and bone marrow. It plays a crucial role in the nucleic acid synthesis, protein, neurogenesis, and hematopoiesis as prominent components of the different enzyme systems. It also takes part in the body’s metabolism [29–32]. Low dimensional ZnO nanoparticles can make zinc more easily absorbed by the human body. ZnO nanoparticle is a proficient platform for biomedical applications [33–37]. Nanoparticles exhibit the improved characteristics that are supported within particle size, distribution, and morphology. They consist of particles that have nanoscale dimensions. These small-sized particles can enhance catalytic reactivity, thermal conductivity, and non-linear optical performance [38–40]. These nanoparticles have received more consideration in biomedical applications for these characteristics. The ZnO nanoparticles can perform excellent biomedical applications compared to other metal oxide nanoparticles. Recently, in medical science, ZnO nanoparticles have started to be thought of in order to be used as nano antibiotics for their antimicrobial activities. One of the reasons behind the acute consent is a nanoparticle consisting of a particle size less than 100 nm. The typical diameter of many human cells is around 7 μm, so the nanoparticle is comparable to naturally occurring proteins and biomolecules of the cell. The contraction of particle size to the nanoscale formation can frequently change their structural, morphological, electrical, optical, magnetic, and chemical characteristics. The nanoscale particle has been making them for physical transport into the internal structures of cells and interacted with cell biomolecules in unique ways. The particles typically possess a large percentage of atoms on the main surface of a material that can easily lead to enhanced surface reactivity. It can also enlarge their capability to be loaded with therapeutic agents to deliver them to target bimolecular cells. These particles can acquire the capability of treatment to target selectively by proper mixing dilation. It has emerged a promising potential for antibacterial fields [41–45]. It has a very effective way to destroy the cancer cells of the human body [46–50]. The strain is the most important parameter in the biomedical sensing arena. Flexibility and incompatibility in the biomedical field are two major issues to used this biosensor [51–55]. The ZnO nanomaterial may be used for biosensor manufacturing purposes. Recently many researchers have shown that ZnO nanostructures are suitable materials for manufacturing a biosensor. There is ongoing research to observe the bio-imaging sensing purpose. It has shown positive results only on mice so far. The requirements of this sensor are non-allergenic, non-carcinogenic, high sensitivity, good reproducibility, and non-toxic characteristics. It can help in diagnosing the early stages of cancer germs. Moreover, sensing is important for monitoring and tracking the disease of a patient.

ZnO nanoparticle is one such inorganic metal oxide that would achieve all the above demand. It preserves an antibacterial and antimicrobial agent that can safely be used for drug delivery purposes [56, 57]. It can be applied to human cells, which open up a way to recovering some diseases. The preliminary advancement of this material is not adequate for biomedical applications. Until now, the efficient utilization of this material doesn't have sufficient influence on the biomedical sector. Recently, the ZnO nanoparticles exhibit tremendous semiconducting characteristics that have a wide range of biomedical applications. The development of appropriate particle dimensions is challenging research work for researchers. Systematic and intensive research work is necessary to develop and understand the process of this material to form nanostructure materials. This paper highlights which process would be suitable for developing ZnO nanoparticles. It also presents a new way for developing nanoparticles that would be impacted in biomedical applications. The discussion about the up-date situation about biomedical applications is the main objective of this review paper. Herein, we will try to summarize the cost-effective synthesis process for the development of ZnO nanoparticles. Moreover, this review paper also discussed ZnO nanoparticle prospects in biomedical applications.

2. SYNTHESIS OF ZNO NANOPARTICLES

ZnO nanoparticles have been developed by using several processes, such as physical, chemical, and biological synthesis processes. Physical and chemical processes are performed based on a thermodynamic and kinetic equilibrium approach. In physical and chemical synthesis processes, development rates of ZnO nanoparticles are very significant and mostly utilized for industrial advancement. Biological synthesis processes are performed through plants, fungi, algae, bacteria, etc. Large-scale productions of ZnO nanoparticles by plants show free additional impurities. The plant parts like fruits, seeds, stems, leaves, and roots have been used for nanoparticle development. Their extract is prosperous in photochemical, which can act as both stabilization and reducing agents.

2.1. Physical synthesis processes

Physical synthesis can be divided into high energy ball milling, physical/chemical vapor Physical synthesis can be divided into high energy ball milling, physical/chemical vapor deposition, and laser ablation processes. C. Prommalikit et al. [58] reduced the particle size from micron to nano scale of ultrafine ZnO powder by using a high energy ball milling process. The authors used the starting material of commercial grade ZnO powder with an average size of 0.8 μm. They investigated the crystalline structure, surface morphology, and particle size of milled samples by using the X-ray diffractometer (XRD), scanning electron microscopy (SEM), and particle analyzer, respectively. According to XRD results, the authors suggested that the XRD pattern had indicated the hexagonal crystalline structure. The SEM images indicated the particle size of ZnO nanopowders distinctly decreased due to the increase of milling time and speed. After a milling process, particle size was found in ultrafine nanopowers in the range between 200 and 400 nm. These results indicated the commercial ZnO powders minimized the particle size with specific milling speed and time. Finally, the authors recommended that the milling parameters (speed and time) of this process showed a significant influence on the reduction of particle size. S. Amirkhanlou et al. [59] also investigated how milling time had influenced the particle size in a high energy ball milling process. The authors obtained the particle size from 800 to 60 nm at 8 milling times. In this process, the other researcher [60] investigated the milling time duration from 02 to 50 hours to develop ZnO nanoparticles. The results showed that particle size decreased around 600 to ~30 nm with increased milling time duration. For other ball milling processes [61–63], researchers obtained the particle size between 10 and 58 nm at different parameters. The authors investigated the ball milling media, which also had an influence on the particle size.

Onur Tigli et al. [64] reported the synthesized ZnO nanowires onto the silicon (Si) substrates by using a vapor deposition process. They used the source material 1.38 grams of Zn powders and employed the measurements in a Lindberg horizontal multi-zone tuber furnace. The XRD and SEM characterization methods were used in the experiment. In experiments, the authors used variable reaction temperatures between 800 and 1200ºC, reaction time durations between 45 and 60 min. The experimental results indicated that prepared samples had very smooth surfaces having uniform diameters ranged between 50 and 120 nm. The SEM image shows aggregates of ZnO nanowires that accumulated sparsely onto the substrate. These experimental results indicate that it can occur a simple synthesize process to produce ZnO nanowires with eliminating all contamination. Finally, the authors reported that long time duration with high temperature, growth structure had a comb-like structure, which was not acceptable. The higher thermal condition from synthesized to vaporization zones accompanied by rapid change in the heat of self-catalysis mechanism might develop premature termination. For this reason, a comb-like structure can be developed on the grown nanowires. The authors concluded that the physical vapor deposition process is an inexpensive growth technique to synthesize ZnO nanowires.

O. Lupan et al. [65] synthesized the ZnO nanowires on silicon substrates by using a chemical vapor deposition process at 650ºC with low pressure. They used the starting reactants of the high purity metallic zinc and an oxygen–argon mixture (15 vol.% of oxygen). The XRD, Raman spectroscopy (RS), X-ray photoelectron spectroscopy (XPS), photoluminescence (PL), SEM, and transmission electron microscopy (TEM) characterization methods were employed in the experiment. The chemical and micro-structural quality of these prepared samples was justified through these experiments. According to JCPDS number 36-1451, the experimental results showed that nanowires had a hexagonal structure with diameters ranging from 50 to 200 nm. The authors recommended that obtained nanowires were transferable by pre-patterned external contacts to another substrate. They also fabricated a single ZnO nanosensor by using a focused ion beam. They contacted the metal electrodes pattern to every end of a single nanowire by using this lithography process. Finally, the authors conclude that nanowires can be used as a sensor having a higher response to the H_2 atmosphere in the room heat environment. Other researchers also developed the ZnO nanostructures by using these processes. In physical vapor deposition processes [66–68], other authors developed the ZnO nanowires and nanosheets onto the indium-tin-oxide glass substrate that was used in dye-synthesized solar cells with efficiency ranging between 0.1 to 0.5%. In conclusion, they recommended that its integration capability was proven for solar cell devices. Another researcher developed the ZnO nanowires in a hexagonal structure around 60 nm at 450ºC. It emitted ultraviolet light at room temperature conditions. In chemical vapor deposition processes [69, 70], other researchers developed the ZnO nanorods, nanotubes, nanowalls, and nanowires depending on different growth parameters. It showed the morphologically smooth surfaces with uniform diameters between 50 and 60 nm.

G. Al-Dahash et al. [71] prepared the ZnO nanoparticles by using laser ablation in NaOH aqueous solution. In this research, Q-switched Nd-YAG LASER use that operates at 532 nm wavelength, 50 pulses number, and 6 Hz pulse repetition rate. The laser beam was focused on the pure Zinc target surface with a diameter of 1 mm. The laser was placed at the bottom of a quartz cell and immersed at 8 mm depth in the 0.1 M NaOH solution. The UV-Visible spectroscopy, atomic force microscopy (AFM), SEM, and XRD characterization methods were used in the experiment. In optical characteristics, the UV-Visible spectroscopy had a part in the produced solution. It revealed red shifting in the peak position with the laser ablation energy that exhibited optical extinction. The surface topography by AFM measurement showed the wide distribution of the particle size that lay between 80.76 and 102.54

nm. The SEM image showed that nanoparticles had a spherical shape. The crystalline size was found at the range between 35 and 40 nm from the XRD result. In conclusion, the authors recommended that ZnO nanoparticles could be used as good insulating materials in reduction crystalline size by using the laser ablation process. In this process, other researchers [72–76] developed the ZnO nanoparticle characterized for morphology, structural, and optical properties. Most of the particles show the wurtzite hexagonal crystal structure with polycrystalline in nature. They can produce irregular shapes and different sizes of a particle by controlling pulse energies. For this process, other researchers can control the particle size between 10 and 60 nm at different conditions.

2.2. Chemical synthesis processes

A variety of chemical synthesis processes can be used for the development of ZnO nanoparticles. The chemical synthesis processes can be generally divided into two categories, such as gas and liquid phase. The gas phase process can be divided into processes as spray pyrolysis and gas condensation. The liquid phase process can be divided into processes as precipitation or co-precipitation, colloidal, sol-gel, oil microemulsion, hydrothermal, and solvothermal. G.J. Lee et al. [77] prepared the ZnO nanoparticles by using a spray pyrolysis process from zinc acetate dihydrate ($Zn(CH_3COOH)_2.2H_2O$) at a concentration of 0.5 M solution with distilled water. The solution was used as a precursor for spray by sonication into a vertical quartz reactor by being allowed to flow without a carrier gas in a 900ºC furnace. The authors studied the optical sensing characteristics conducted by temperature-dependent PL measurements. They observed the low-temperature PL spectra of the ZnO nanoparticles that displayed a strong exciton emission peak with multiple side band regions. This result attributed the bound exciton to optical phonon sidebands. The PL peak intensity was stronger, which revealed high optical sensing capabilities. In conclusion, the authors concluded that ZnO nanoparticles could be contributed to form a strong platform for the optical sensing device as biomaterials. In this process, other researchers [78–80] synthesized the ZnO particles/nanoparticles, depending on various reactor temperatures, solution concentrations, and atomizing pressures. The ultraviolet-visible spectroscopy, FTIR, XRD, SEM, and TEM characterization methods were used in their experiment. The authors recommended that all parameters showed a significant influence on particle sizes of synthesized materials. Their experimental results showed the particle size lay between 10 and 400 nm with uniform morphologies that indicated the wide distribution of particle size. In conclusion, the authors recommended that ZnO nanoparticles could enhance the photo catalytic efficiency and controlling the crystalline dimension by using this process.

M. Vaghayenegar et al. [81] synthesized the ZnO nanoparticles by using the one-step electromagnetic levitation gas condensation process with a relatively high production rate. In this process, a high temperature levitated Zn droplet was condensed and oxidized by considering both atmospheric and reduced pressures. The authors used XRD, SEM, and TEM measurements to characterize the prepared sample. They investigated the effects of temperature, carrier gas type, oxygen content, and reactor pressure on the morphology and particle dimension distribution of the sample. Finally, they recommended that all growth parameters showed a significant influence on the samples. In conclusion, the authors estimated the optimum O_2/He–0.2 for both atmospheric and reduced pressures, Ar molar gas ratio to produce fully oxidized samples to be found as 0.18 and 0.21 with the average length/width between 80/35 and 83/27 nm, respectively. In this process, other researchers [82, 83] synthesized ultrafine ZnO nanoparticles from the Zn droplet with a chamber filled by mixing the Ar, He, and O_2 gases under atmospheric and reduced pressure. In experimental results, the authors estimated the particle size between 30 and 40 nm with a web-like hexagonal crystalline structure.

Monalisha Goswami et al. [84] synthesized ZnO nanoparticles by using a chemical precipitation process at low temperatures. The authors used the zinc nitrate hexa hydrate [$Zn(NO_3)_2.6H_2O$] and sodium hydroxide (NaOH) as precursors at different annealing temperatures ranging between 200 and 600ºC for 2 hours. They observed the structural and optical properties by using XRD, SEM, FTIR, UV-Vis spectroscopy, and PL measurements. XRD results revealed that prepared samples exhibited hexagonal wurtzite crystalline structure, and the average crystalline dimension was proportional to the annealing temperatures. The SEM image revealed the formation of crystals, such as a spherical shape with slight agglomeration. All samples exhibited the peak corresponds to a Zn-O stretching band observed in FTIR spectra. The UV–Vis absorption spectra showed the optical band-gap changing from 3.56 to 3.84 eV with annealing temperature. The PL spectra showed excitation wavelength that increased in UV emission intensity at room temperature. In conclusion, the authors recommended that annealing temperatures could influence the improvement of the crystal quality and controlling the crystalline dimension of the prepared ZnO nanoparticles. R.E. Adam et al. [85] prepared the ZnO nanoparticles by using a co-precipitation process for solar driven photodegradation in low temperature conditions. The authors performed XRD, SEM, and photocatalytic measurements for produced samples. The experimental results revealed that the nanoparticles had indicated no impurity phases, and they had hexagonal wurtzite structures with uniform distribution. They investigated the sun driven photocatalytic activity under different pH values of the aqueous solutions. The authors saw that solar driven photocatalytic methods to abolish organic toxic from aqueous solutions were very prominent due to their environmental benefits. The ZnO nanoparticles were used as a catalyst to degrade Congo red dye from aqueous solutions at different pH values. Finally, the authors found higher photodegradation efficiency in the acidic medium solutions. In conclusion, the authors recommended that ZnO nanoparticles could perform considerable degradation efficiency after different usage cycles. In these processes, other researchers [86–90], prepared the ZnO nanoparticles at different temperatures ranging between 100 and 600ºC for 4 hours. For this preparation purpose, the authors used the Zinc acetate $ZnC_4H_6O_4$, Zinc nitrate $Zn(NO_3)_2$, Zinc sulphate $ZnSO_4$, Ammonium bicarbonate NH_4HCO_3, Potassium hydroxide KOH, and Oxalic acid $C_2H_2O_4$ in aqueous solution. Prepared ZnO nanoparticles were studied by XRD, FTIR, SEM, Energy Dispersive X-ray Spectroscopy (EDX), Electron Spin Resonance Spectroscopy (ESR), TEM, UV-Vis spectroscopy, Brunauer–Emmet–Teller (BET) analysis, and thermal analysis TG-DTA. The prepared samples possessed hexagonal wurtzite crystal structures with a crystal size between 3 and 45 nm.

H. Wang et al. [91] prepared the colloidal ZnO nanoparticles in ethanol solutions. Subsequently, the authors annealed the prepared samples at different temperatures ranging from 150 to 500ºC. They examined the structural and optical properties of these samples by using TEM, XRD, UV–vis absorption spectrum, and FTIR measurements. The TEM image indicated the samples had possessed a narrow size distribution fluctuating around 90 nm. These nanoparticles had a significantly higher surface-to-volume ratio in contrast to the bulk material. The morphologies of the samples mainly showed an irregular shape with aggregates to each other. The particle size was significantly affected by the annealing temperature, and it increased rapidly with a wide dimension distribution in nature. The average particle size increased from 10 to 90 nm with the annealing temperature. Finally, the authors recommended that photocatalytic activity and stability of these materials could be adjusted by utilizing the size effect.

A. Nagar et al. [92] synthesized ZnO nanoparticles by using a sol–gel process for a transparent element in transistors. In this synthesis process, the authors used $ZnC_4H_6O_4$ and distilled water as precursors. The experimental characterization was performed by using the field emission scanning electron microscope (FESEM), XRD, and high-resolution transmission electron microscope (HRTEM) for synthesized samples. The FESEM micrographs showed a nanoflower structure of morphology that was uniform and highly dense in nanoparticles. This behavior enhanced the field emission characteristics of a transistor. From XRD results, according to the JCPDS No 01–1136, the nanoflowers indicated a wurtzite hexagonal crystalline phase structure. The HRTEM micrographs revealed the ZnO nanoparticles had closely stacked with each other. The authors estimated the diameter distribution of these nanoparticles in a range between 30 and 60 nm. This flower-type nanoparticle had a high current density and significant field enhancement factor to conform to the field emission study. In conclusion, the authors recommended that ZnO nanoparticles might be effectively used in different liquid-crystal and field emission display devices. In this process, other researchers [93–96] synthesized these nanoparticles for antibacterial effect, dye-sensitized solar cells, and humidity sensing purposes. The synthesized samples were calcined at different temperatures ranging between 70 and 800ºC. The characterization of the developed samples was studied by using XRD, HRSEM, HRTEM, AFM, FT-IR, and UV-Vis spectroscopy with different calcinations temperatures. The authors recommended that temperature played a significant role in controlling the particle size and using the nanoparticles for different purposes. They estimated the particle size ranging between 10 and 40 nm having crystalline wurtzite hexagonal structure.

A.M. Pineda-Reyes et al. [97] synthesized the ZnO nanopowder by using an oil microemulsion which is a human and environmentally friendly process. This process consisted of water-in-oil (w/o) microemulsions, where continuous and discontinuous phases were emu oil and 0.5 M $ZnC_4H_6O_4$, respectively, in the aqueous solution that stabilized by a layer of surfactant molecules. After that, the precipitation was prepared by adding 1.0 M sodium hydroxide in this aqueous solution. Finally, the resultant precipitates were calcined at 800°C for 2h then dried at 100°C in air. The prepared nanopowders were characterized by using XRD, SEM, and TEM. The authors estimated average particle size around 31.2 nm with pseudo-spherical morphology in the wurtzite hexagonal structure. In this process, other researchers [98–100] synthesized ZnO nanoparticles of different shapes of particle dimension at the reaction (40 to 70°C) and calcination (300 to 500°C) temperatures. The reaction temperature did not considerably affect the average particle size, whereas the calcination temperature significantly affected the particle size. In order to prepare the Zn^{2+} source, the authors used the $Zn(NO_3)_2$, $ZnSO_4$, and Zinc chloride $ZnCl_2$. Finally, the authors recommended that in the synthesis process, the $Zn(NO_3)_2$ could perform the best activity. They estimated the average particle size ranging between 2.1 and 24 nm having a wurtzite hexagonal structure. The SEM and TEM images showed the particle like nanorods shape with diameter and length ranging between 22 and 28 nm, 66 and 72 nm, respectively.

S. Agarwal et al. [101] synthesized the ZnO nanostructures like flowers or rods by using a hydrothermal process. The authors investigated their morphology-dependent gas sensing characteristics. They used SEM, XRD, TEM, UV-Vis spectroscopy, and PL measurements for the prepared samples. The SEM images formed two kinds of floral structures, flower-like structures having a composition of nanoparticles formed at short time reaction, whereas at long time reaction floral assemblies of nanorods were formed. According to the JCPDS card no. 01-079-0205, the XRD spectra confirmed a hexagonal wurtzite crystal structure of the samples. The average crystalline dimensions were found to be 21 and 43 nm for nanoflowers and nanorods, respectively. The band-gap energy of the prepared specimen was found to be 3.0 and 3.19 eV for nanoflowers and nanorods, respectively, by using UV–Vis absorption spectra. The presence of oxygen vacancies was confirmed in both samples for the PL spectra. Finally, the authors investigated the gas sensing characteristic with morphology for different gases at operating temperatures. In conclusion, the authors recommended good sensitivity to nitrogen dioxide (NO_2) gas with the response of prepared samples. In this process, other researchers [102–105] synthesized the ZnO nanoparticles, nanopleates, nanorods, and nanoflowers for gas sensing and photoconductive applications. The authors used structural and optical measurements for the characterization of the developed samples. They observed gas sensing characteristics towards the ethanol at different operating temperatures. The authors estimated the average crystalline dimension ranging from 6 to 64 nm having a wurtzite hexagonal crystallographic structure.

Ankica Šarić et al. [106] developed ZnO nanoparticles from zinc acetylacetonate with the presence of alcoholic solvent and triethanolamine (TEA) at 170°C. The authors monitored the structural and optical properties with XRD, ultraviolet-visible spectroscopy, FT-IR, and FE-SEM investigations for the developed samples. In various alcoholic solvent and TEA systems, the authors proposed nucleation and mechanism formation of this nanoparticle. The experimental findings indicated that the alcoholic solvent, ethanol or octanol, and TEA could play a significant role in the particle size. The authors concluded that the impact of surface interactions between developed nanostructures and molecules of a solvent with TEA on the way of growth and aggregation could control structural characteristics. Finally, the authors estimated the particle size into 10 nm. In this process, other researchers [107–110] synthesized the ZnO nanoparticles in different solvents, temperatures, and time durations. The authors used zinc acetate dihydrate $Zn(CH_3COO)_2.2H_2O$ and KOH as a precursor to the develop samples. The authors recommended that the growth parameters had a significant influence on the controlling of particle size. The authors estimated the average crystalline dimension ranging from 10 to 76 nm having a wurtzite hexagonal structure in the different shapes.

2.3. Biological synthesis processes

A variety of biological synthesis processes have been used to develop ZnO nanoparticles. These processes have been performed through waste materials. The mediation of microbes such as fungi, algae, virus, actinomyces, bacteria and mediation of plants such as root, shoot, leave, stem. A. Deep et al. [111] proposed a simple process for the development of the pure ZnO nanoparticles from the waste electrode of used alkaline Zn–MnO_2 batteries. The authors collected used batteries to find out the waste electrode. After that, they were dismantled to collect Zn and Mn materials. In an aqueous solution, the authors added 5M HCl and 0.1M Cyanex 923 at 250°C for 30 minutes to form the Zn-Cyanex 923 complex. The authors used ethanol for centrifugation to separate the organic phase. Finally, pure ZnO nanoparticles were developed having about 5 nm particle diameter.

There is viable importance in developing environmentally friendly ZnO nanoparticles that don't produce toxic elements. The mediation of many microbes, including fungi, algae, viruses, actinomyces, and bacteria, can be used to synthesize ZnO nanoparticles by using the intracellular or extracellular process. This kind of synthesis process looks like an environmentally friendly green process which is a blessing to biological nature. Nowadays, the microbes' mediation is a simple and one of the most attractive sources of green synthesis processes for developing the ZnO nanoparticles. H.K. Abdelhakim et al. [112] successfully synthesized the ZnO nanoparticles by using an eco-friendly and cost-effective process of culture filtrate of the endophytic fungus Alternaria tenuissima. For this synthesis purpose, the authors used the Zinc sulfate $ZnSO_4.7H_2O$ and 100mL of the A. tenuissima cell-free culture filtrate (ATCF). To prepare the 2 mM concentration of an aqueous solution, a volume of 100 mL of ATCF was taken in a flask and mixed with 100 mL $ZnSO_4.7H_2O$. Then at room temperature, the reaction mixture was maintained under stirring for 20 min, and they observed the mixture looked like white precipitate. The precipitate was separated, washed, and then dried at 50°C in the air for preparing the ZnO nanoparticles. The prepared powder dissolved in ethanol for the ultrasonically treated dispersion, and finally, they developed the fine powders to be used for characterizations. The synthesized samples were characterized by UV–Vis spectroscopy, XRD, dynamic light scattering (DLS), TEM, and FT-IR measurements. The authors rapidly completed this synthesis process and confirmed surface plasmon resonance by UV–Vis spectroscopy. According to JCPDS card No. 361451, the XRD spectrum revealed the hexagonal crystal structure of ZnO nanoparticles having the lattice parameter 0.323420Å. The DLS analysis showed that the particle size distribution was in the range between 10 and 30 nm. This distribution confirmed by the TEM micrograph, and it also showed that the particles were mono-dispersed in a spherical shape. The FTIR spectra showed the main bands of asymmetric and symmetric vibrations of ATCF and ZnO nanoparticles. In conclusion, from experimental results, the authors found that low dimensional ZnO nanoparticles showed promising activities, which could be a better utilization for biomedical applications. Finally, the authors recommended that excellent biomedical potentiality could be performed with a new and alternate approach for the revelation of the ZnO nanoparticles by using microbial platforms. It could open up a new way for biomedical applications. In accordance with the other review and research article [113–117], the production of ZnO nanoparticles from microbes' mediation confirmed a promising utilization for biomedical applications. For this process, the authors used marine microbes and microorganisms to produce ultrafine, uniform, and well-dispersed ZnO nanoparticles for various biological and photocatalytic activities. Finally, the authors concluded that this process performed time saving, and it was eco-friendly to produce ZnO nanoparticles by using these sources. The 0verview of microbes' mediated extract for ZnO nanoparticles is summarized in Table 2.

The multifunctional inorganic ZnO nanoparticles have attained more interest for their vast applications in the biomedical sector. Due to their constructional view, potential applications of the ZnO nanoparticle can play a dominating role in this sector day by day. Using plant mediation is the green synthesis approach that a reliable, cost-effective, eco-friendly, and biocompatible process. Fig. 2 shows some of the fruits, flowers, roots, and plants for the synthesis of ZnO nanoparticles.

The plant mediation synthesis process has an easy step in the sequence for the development of eco-friendly nanoparticles. This process can minimize the hazards associated with the utilization of chemical and physical processes.

Table 2. Overview of microbes mediated extract for ZnO nanoparticles.

Microbe Part	Morphology	Size (nm)	Reference
Fungus alternaria tenuissima	Hexagonal, Spherical	10~30	112
Endophytic fungi	Hexagonal, Quasi-spherical	16~78	113
Fusarium keratoplasticum, Aspergillus niger	Hexagonal, Nanorods	8~42	114
Clonorchis sinensis, Candida albicans, Serratia ureilytica	Hexagonal	16~37	115
Saccharomyces cerevisiae	Quasi-spherical	~10	116
Aeromonas hydrophila	Spherical	~ 57.72	117

Syzygium cumini fruit
Cinnamomum verum fruit
Rhamnus virgata fruit
Punica granatum fruit
Star fruit
Couroupita guianensis leaf
Cinnamomum tamala leaf
Aloe barbadensis miller plant
Brassica oleracea
Radish root
Beta vulgaris root
Cassia fistula flower
Lagerstroemia speciosa flower
Achyranthes aspera flower
Pongamia pinnata flower
Medicago sativa flower
Andrographis paniculata plant
Caralluma fimbriata plant
Plectranthus amboinicus plant
Ocimum basilicum plant

Fig. 2. Some of the fruits, flowers, roots, and plants for the synthesis of ZnO nanoparticles.

The first step of washing the plants mediate is pursued by boiling in distilled water to achieve the extract. Then, a few subsequent steps followed that mixing of Zn salt with this extract and separation of liquid forwards to the aggregation of nanoparticles. Fig. 3 shows the symmetric diagram of the development of ZnO nanoparticles from plant mediation.

M. Rafique et al. [118] have synthesized the ZnO nanoparticles from Syzygium cumini (S. cumini) plants. The authors declared that their report was a facile and cost-effective green synthesis process to develop ZnO nanoparticles from this plant's leaves by using an extract. The authors prepared the aqueous solution with 5 mL S. cumini leaves extract. It was added drop wise to 0.05 M, 25 mL $ZnC_4H_6O_4$ under constant stirring at 60ºC for 2h. The reduction of $ZnC_4H_6O_4$ into ZnO nanoparticles showed a reaction to this mixture with a colour change after constant stirring. Then the prepared solution was centrifuged at 4500 rpm for 15 min, and the resulting sample was dried at 60ºC overnight. Finally, the synthesized sample was calcinated at 400ºC for 4h, and again a colour change occurred, meaning ZnO nanoparticles were ready for characterization. The authors observed their characteristics by varying the concentration of leaves' extract between 10 and 25 mL at constant molarity of 25 mL precursor solution. The synthesized samples were characterized by UV–Vis spectroscopy, XRD, SEM, and FT-IR measurements. The absorption spectra exhibited a well-defined exciton band at 320 to 350 nm that represented the robust absorption of a wurtzite hexagonal phase structure. There was no other peak identified in these spectra so that it would associate with impurities and structural defects of the prepared samples. It confirmed the formation of ultrafine pure crystalline ZnO nanoparticles. The extract concentration played a significant influence on band-gap energy that varies between 2.22 and 3.00 eV. The decrease of band-gap energy occurred with increases in extract concentrations in the prepared ZnO nanoparticles. According to JCPDS 76-0704 and 75-1533, the XRD pattern revealed the hexagonal crystal structure of the prepared sample having an average crystalline size of 16.40 nm. The SEM micrographs revealed uniformly dispersed spherical-like ZnO nanoparticles that particle size decreased from 78 to 64 nm with increases in extract concentration. The FTIR spectra indicated the oxidation occurrence and proved that the synthesized samples had pure form. The prepared samples were used to increase the germination of seeds and exhibited 60% germination enhancement in comparison to control the particle size. The ZnO nanoparticles were also used in water purification polluted by Rhodamine B dye. The effect of different growth parameters on dye removal visible light irradiation was analysed, and a maximum 98% performance was estimated. In conclusion, the authors concluded that ZnO nanoparticles had potential applications in technology enhancement. Other researchers have synthesized ZnO nanoparticles from other plants mediate [119–132], and they declared it can be used as antimicrobial agents in biomedical applications. The overview of plants mediated extract for ZnO nanoparticles is summarized in Table 3.

The authors used different plants' mediation to produce ultrafine, uniform, and well-dispersed ZnO nanoparticles for various biomedical applications.

The authors estimated average crystalline dimensions ranging from 5 to 120 nm having a wurtzite hexagonal structure in different shapes. Fig. 4 shows the different shapes of one-dimensional ZnO nanoparticles developed from plant mediation [119, 122, 124, 126, 131, 132]. Finally, the authors concluded that this process consisted of time-saving, eco-friendly, and a cost-effective role for produce the hexagonal ZnO nanoparticles by using these sources.

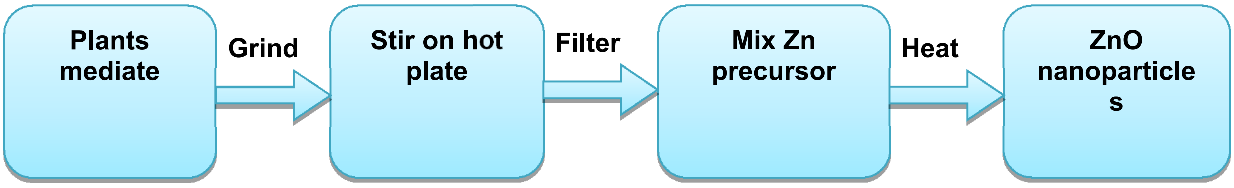

Fig. 3. Symmetric diagram of the development of ZnO nanoparticles from plant mediation.

Table 3. Overview of plants mediated extract for ZnO nanoparticles.

Plant Part	Morphology	Size (nm)	Reference
Syzygium cumini plant	Hexagonal, Spherical	16~78	118
Star fruit	Hexagonal, Nanoflakes	19.6	119
Beta vulgaris, Cinnamomum tamala, Cinnamomum verum, Brassica oleracea var. Italica	Hexagonal, Spherical, Nanotubes	14~30	120
Radish root	Hexagonal, Spherical, Nanorods	15~25	121
Punica granatum fruit	Spherical, Hexagonal	33~82	122
Rhamnus virgata	Hexagonal	~20	123
Achyranthes aspera and Couroupita guianensis leaf	Hexagonal, Spherical, Nanoflakes	5~40	124
Andrographis paniculata leaf	Hexagonal, Spherical	57~115	125
Lagerstroemia speciosa leaf	Hexagonal	~40	126
Caralluma fimbriata	Hexagonal, Spherical, Nanoflakes	~30	127
Pongamia pinnata leaf	Hexagonal, Nanorods	10~120	128
Plectranthus amboinicus leaf	Hexagonal, Nanorods	~88	129
Aspalathus linearis	Hexagonal, Quasi-spherical	~12.5	130
Cassia fistula plant	Hexagonal	5~15	131
Aloe barbadensis miller leaf	Spherical, Hexagonal	~35	132

In the above discussion, it is clear that physical and chemical synthesis process strategies are expensive to develop ZnO nanoparticles. The addition of the chemical agents for precipitation and reduction has required much source material that occurs in-depth labor and more time. Most of the chemicals are naturally poisonous, that synthesis by these products doesn't behave in an eco-friendly way. However, some physical and chemical processes have comparative and exceeding the short time period to synthesize more quantities of ZnO nanoparticles. Moreover, some of the chemical solution-based synthesis processes are also effective, such as chemical precipitation or co precipitation, sol-gel, solvothermal, and hydrothermal. In our previous reports [133–138], this process has been accepted for the development of nanoparticles compared to thin films for solar cells, optoelectronics, and thermoelectric applications. The biological synthesis process is used to make non-toxic, eco-friendly operations, and it secures reagents.

Nowadays, the fast universal advance of microorganism resistance with antibiotics is causing a serious hazard of worldwide public fitness. Nano-medicine is a promising research field that combines research knowledge about nanotechnology with medicine. It presents nano formed materials of antimicrobial agents utilized in biomedical applications. Recently, fast technology is the nanotechnology that low dimensional nano scale particle size can create advance characteristics for multifunction. The biological synthesis is significantly utilized in biomedical applications to emerging nanotechnology. The overview of these synthesis processes to prepare ZnO nanoparticles is shown in Table 4.

We recommend that the biological synthesis process mainly based on plant mediation is more advantages over the physical and chemical synthesis process for synthesized ZnO nanosize particles for biomedical uses. The advantages of the plant-mediated ZnO nanoparticles synthesis process are as given below:

In the plant mediation, the synthesis process can easily collect from plant material for its availability and presence of bio-component activity, which can act as the capping and reducing agent.

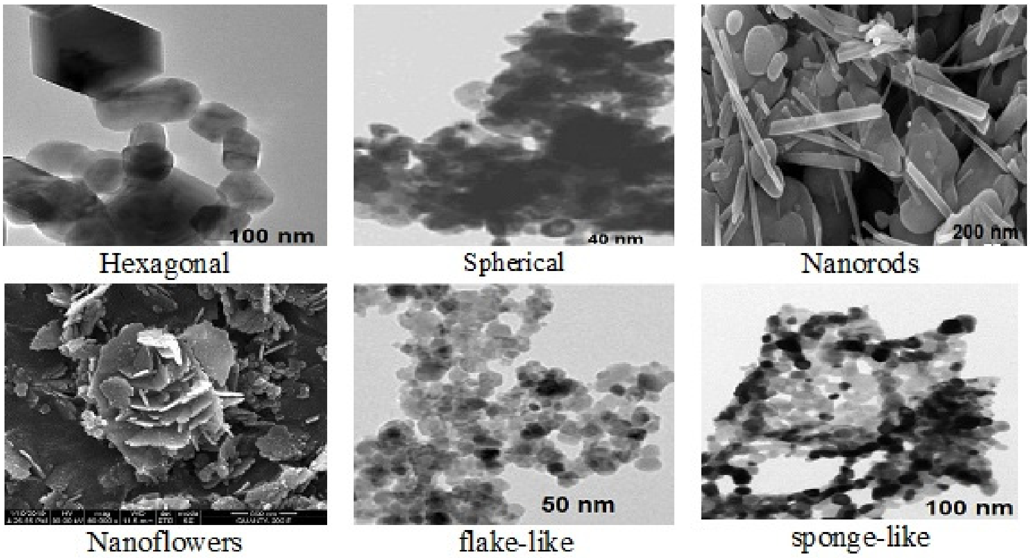

Fig. 4. The different shapes of one-dimensional ZnO nanoparticles developed from plants mediate [119, 122, 124, 126, 131, 132].

Table 4. Summarize of synthesis processes for ZnO nanoparticles.

Synthesis Process	Main morphology	Size (nm)	Reference
Physical synthesis process			
High energy ball milling	Hexagonal	10~400	58–63
Physical/chemical vapour deposition	Hexagonal	50~200	64–70
Laser ablation	Hexagonal	10~103	71–76
Chemical synthesis process			
Spray pyrolysis	Hexagonal	10~400	77–80
Gas condensation	Hexagonal	30~40	81–83
Precipitation or co precipitation	Hexagonal	03~45	84–90
Colloidal	Hexagonal	10~90	91
Sol-gel	Hexagonal	10~60	92–96
Oil microemulsion	Hexagonal	02~30	97–100
Hydrothermal	Hexagonal	06~64	101–105
Solvothermal	Hexagonal	10~76	106–110
Biological synthesis process			
Microbes mediated extract	Hexagonal	08~78	112–117
Plants mediated extract	Hexagonal	05~120	118–132

- Possible for developing a large-scale of nanoparticles by using plants’ mediation for biomedical applications.
- Nanoparticles synthesis by plants’ mediation would not require a well-designed laboratory room.
- It can synthesize at the normal pressure and room temperature conditions that not necessarily of the difficult energy processes.
- Producing a sample is mostly stable and safe due to the natural plant.

Finally, we can conclude that synthesize of ZnO nanoparticle from plants mediation are stable, safe, eco-friendly, and cost-effective for biomedical applications

3. BIOMEDICAL APPLICATIONS

Generally, ZnO nanoparticles are known as a safe material that is utilized in sunscreen products and food additives. Moreover, in this cause of luminescent characteristics of their, ZnO nanoparticles can be used in various biomedical applications. It is also well known as a semiconductor material, which has a potential activity for biomedical applications. For this circumstance, traditional Cd-related species used in biology landscapes can easily be replaced by ZnO nanoparticles. The ZnO nanoparticles have biomedical acceptance due to potential applications in bioimaging, antibacterial, antimicrobial, anticancer, drug delivery. Fig. 5 shows the summary of the synthesis process and principal utilization in the biomedical areas of ZnO nanoparticles.

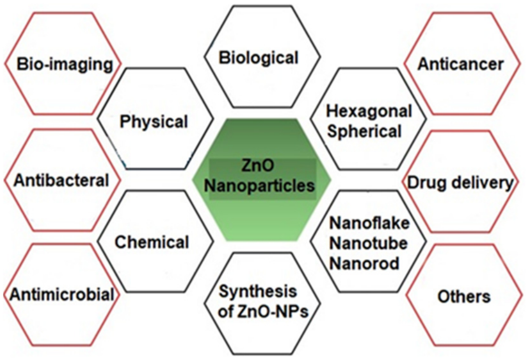

Fig. 5. Summarize the main synthesis process of ZnO nanoparticles in black hexagons and their utilization in biomedical areas in red hexagons.

3.1. Bioimaging

Recently, different shapes of ZnO nanoparticles have been recognized by the researcher to be utilized as bioimaging materials. G. Lei et al. [139] prepared the amphibious ZnO Quantum dots with blue fluorescence based on hyperbranched polymers and discussed their application for bioimaging purposes. The surfaces of ZnO nanoparticles can be modified conveniently, and they can stay stable in an aqueous solution, and their quantum dots (QDs) enhance around thirty percent after attentively the adjustment. Finally, the authors recommend that water-soluble ZnO with hyper-branched poly ethylenimine compounds has the best performance in bioimaging purposes. J.E. Eixenberger et al. [140] have investigated the pure n-type ZnO nanoparticles for bioimaging applications by using the traditional fluorescent microscopy methods. Generally, to produce emissions, most of the nanoparticles require UV excitation sources. Herein, the authors demonstrated that reducing the energy gap allows for a 405 nm laser to sufficiently excited the nanoparticles to detect their emissions during live-cell imaging experiments using a confocal microscope. The research lays the foundation for the utilization of these nanoparticles for different bioimaging purposes. It enables researchers to experiment with the interactions of pure n-type ZnO nanoparticles to human cells through fluorescence-based imaging methods. Fig. 6 shows their developing synthesis procedure that controls certain defects in pure n-type ZnO nanoparticles for bioimaging purposes.

Other research reports [141–145], the production of ZnO nanoparticles from different synthesis processes confirmed a promising utilization for bioimaging applications.

3.2. Antibacterial

Recent achievements will fulfil the future public health demand, which could help for biomedical areas by using the organic medicinal drug agents. We believe that the effectiveness of ZnO nanoparticles will escalate the biomedical applications for antibacterial activity in worldwide. In addition, we consequently observed that the crystalline dimension variation with surface area to volume ratio of ZnO nanoparticles had the cause of a promising antimicrobial function. I. Kim et al. [146] have discussed about strong antibacterial activity at a low concern of gram negative and positive bacteria. A large effect on their antibacterial activity is generated by the oxidative stress interacting with them by forming Zn^{2+} ions from ZnO nanoparticles. These inhibited the actions of respiratory enzymes. The authors demonstrated that the ability of these nanoparticles to damage the cell membrane and generate the reactive oxygen species (ROS). Thus, the bacterial cell membrane can damage by leading to ROS formation of free radicals to absorbing the Zn^{2+} ions. For this circumstance, oxidative stress and inhibit the action of respiratory enzymes to finally cell death. The authors recommend that ZnO nanoparticles can be prominently utilized in biomedical applications that will solve the next generation's public health issues. Fig. 7 shows the oxidative stress generated by ZnO nanoparticles that a large effect on their antibacterial activity. Other researchers [147–150] developed the ZnO nanoparticles by using different synthesis processes to confirm a promising application for antibacterial activity.

3.3. Antimicrobial

The substitute strategy to manage the advance of detrimental microorganisms in a human body can be introduced by ZnO nanoparticle as antimicrobial agents.

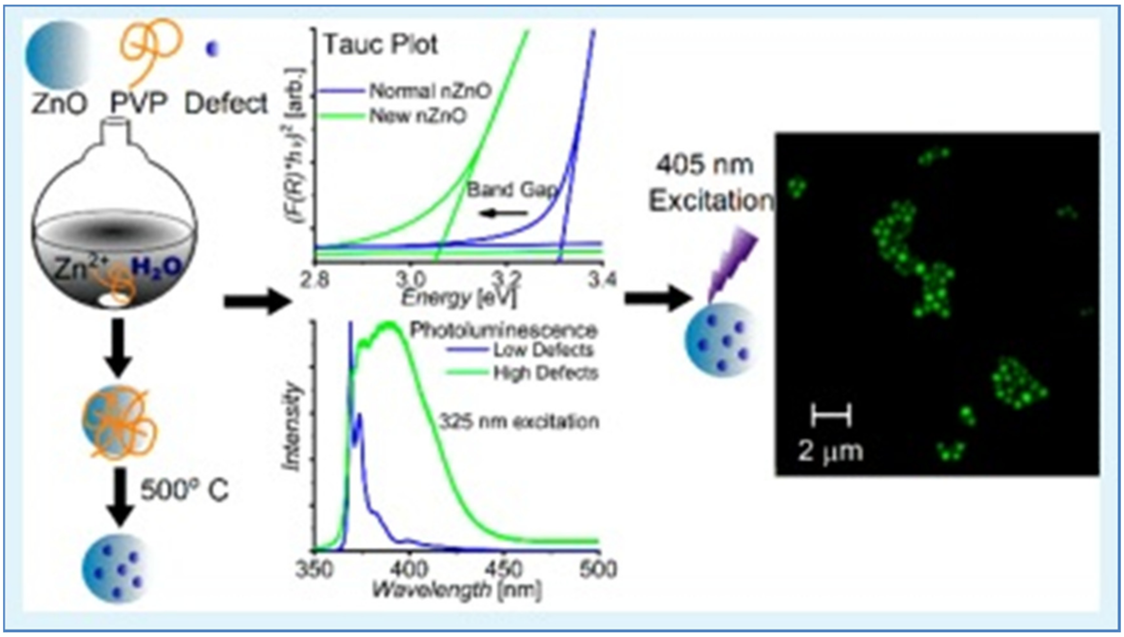

Fig. 6. A new chemical solution synthesis process to produce n-type ZnO nanoparticles for bioimaging applications [140].

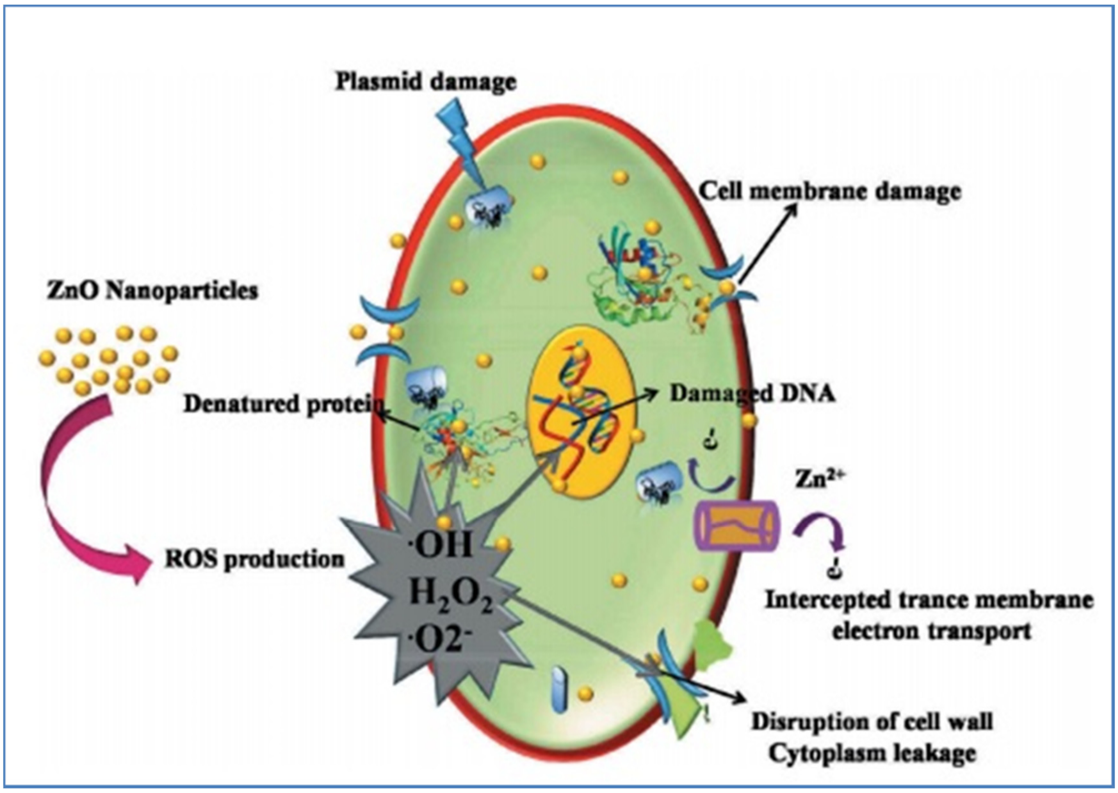

Fig. 7. A schematic representation of the destruction of bacteria by ZnO nanoparticle [146].

It has been investigated within microscale to nanoscale form as an associate medicament agent. The experimental results reveal that it has been indicated as an antimicrobial activity, whereas nano dimensional particles are involved within metal oxide materials. Although the actual structure of antimicrobial activity has not been consequently explained, yet it's been promptly comprehended that the major cause according to cell swelling depends on the surface and dimension of specimens, Zn ions, and nanoparticle acquisition position. S. Akbar et al. [151] have discussed about the antimicrobial potential of ZnO nanoparticles by synthesizing from the plants' mediation. In conclusion, the authors recommend that the chemical luminescence, oxygen electrode analysis, and electrical energy can be researched on the antimicrobial mechanism behavior of ZnO nanoparticals furthermore. M. Batool et al. [152] have synthesized and stabilized ZnO nanoparticles by using an eco-friendly method from plant extracts. This process is used as an antimicrobial active material to enhance mouse skin wound healing. Fig. 8 shows the schematic diagram of different steps of the synthesis and application of ZnO nanoparticles as antimicrobial activity.

The authors demonstrated that synthesized nanoparticles are a powerful antimicrobial activity against different types of bacterial strains of Bacillus subtilis, Klebsiella pneumonia, Bacillus licheniformis, and Escherichia coli. It is also antimicrobial activity against two types of fungi strains of Aspergillus niger and Candida albicans. Other researchers [153–155] developed the ZnO nanoparticles by using different synthesis processes to confirm a promising application for antimicrobial activity.

3.4. Anticancer

QDs encapsulates in bio-degradable polymers like Chitosan that are appropriate for the targeted delivery of anticancer drugs. Encapsulating within Chitosan is prevented drug release before attaching to the targeted cell membrane.

The effect of this size on emission spectra made it beneficial for simultaneous multi-color imaging of different parts of the body. Inorganic and organic materials can generally be used as a medicinal drug agent. The inorganic drug agent is more suitable than organic medicinal drug agents at high temperature conditions. For this reason, organic medicinal drug agents have more significant utilization at low temperature conditions. However, the precise phenomenon of medicinal drug activity has not been accurately identified. Recently, ZnO nanoparticles have been proved to be a prominent medicinal drug agent within microscale and nanoscale formation for therapeutic utilizations. The nano-dimension particle sizes between 5 and 100 nm have enormous exterior spaces that can be used to adjoining for diagnoses such as optical, radio isotopic, and therapies such as anticancer agents. Recent development can be performed in the cancer treatment to integrate the nano devices for early cancer detection and screening by bio affinity nanoparticle probes that molecular and

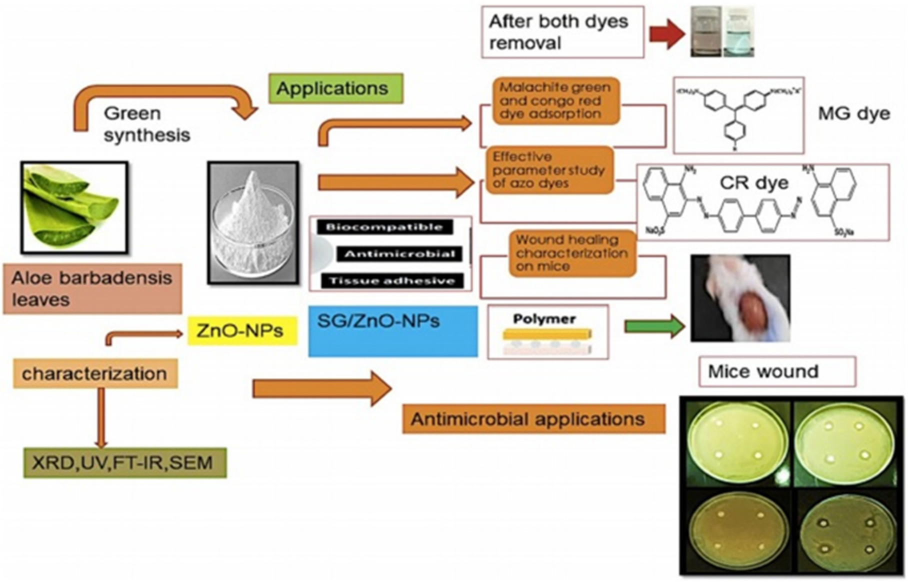

Fig. 8. Schematic diagram of different steps of the synthesis and application of ZnO nanoparticles [152].

cellular imaging can be related to a targeted nanoparticle. We recommend that this advancement can increase possibilities for generalized cancer treatment in biomedical applications. E.A. Elsayed et al. [156] have reported the anticancer potentials of ZnO nanoparticles against liver and breast cancer. The authors observed the experimental results that cancer cells might be affected by ZnO nanoparticles depending on applied concentration.

Authors declare that in cancer cells serious structural change can be the obstacle by nanoparticle exposure. Finally, ZnO nanoparticles can lead to cancer cells' death. The authors conclude that ZnO nanoparticles can be effectively utilized in different cancer cells to inhibit their development and generation. T.A. Singh et al. [157] discussed details about the anticancer activity of ZnO nanoparticles as well as health risks. Fig. 9 shows the possible anticancer mechanisms of ZnO nanoparticles.

Other literature reports [158–160] developed the ZnO nanoparticles by using different synthesis processes to confirm a promising application for anticancer activity.

3.5. Drug delivery

The main concern in cancer treatment minimizes the side effects of chemotherapy through localized drug delivery. For target drug delivery, there are many ways such as pH and temperature control, optical and ultrasonic wave's utilization through a magnetic field. Different nanoparticles as QDs have used for targeted drug delivery have been shown in Fig. 10, which represents a few targets for localized drug delivery.

Nanotechnology in cancer treatment is associated with medical science, technology, and drug delivery within deep utilizations for molecular imaging, recognition, and target for the specimen. The nanoscale particle size, such as metal oxide nanocrystals, and QDs has some prominent structural, optical, and electrical characteristics that can play the dominating role in biomedical applications. Drug delivery has appeared as an important appliance for nanomaterial advancement in the treatment of various diseases. B.A. Fahimmunisha et al. [162] have synthesized eco-friendly ZnO nanoparticles for approaching drug delivery. The authors provided an interesting explanation for the protection of bacterial infection.

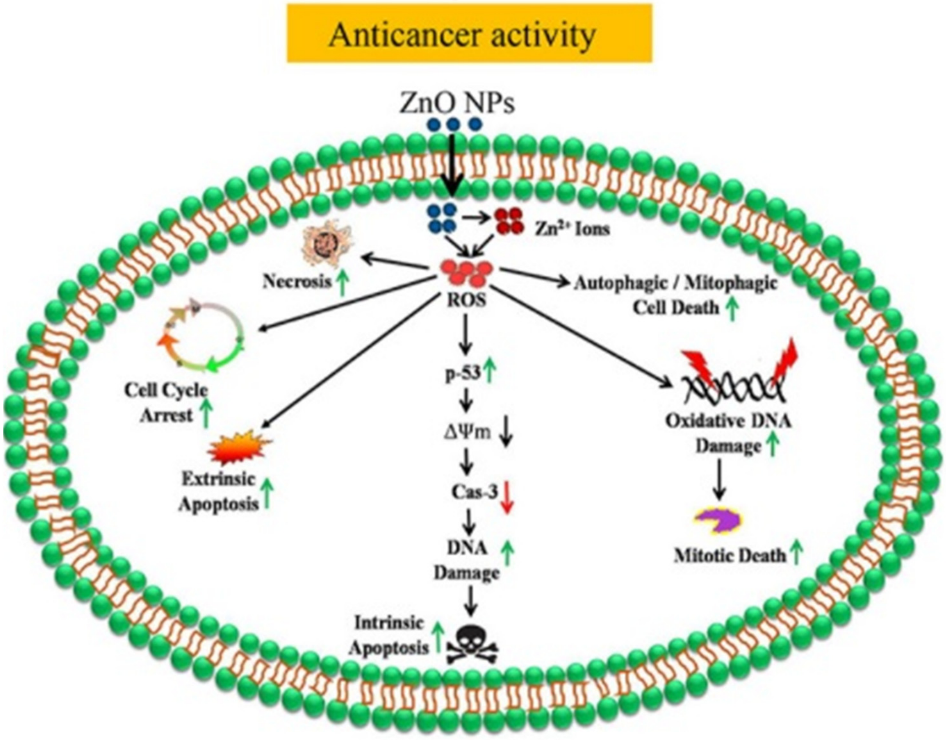

Fig. 9. Anticancer mechanisms of ZnO nanoparticles [157].

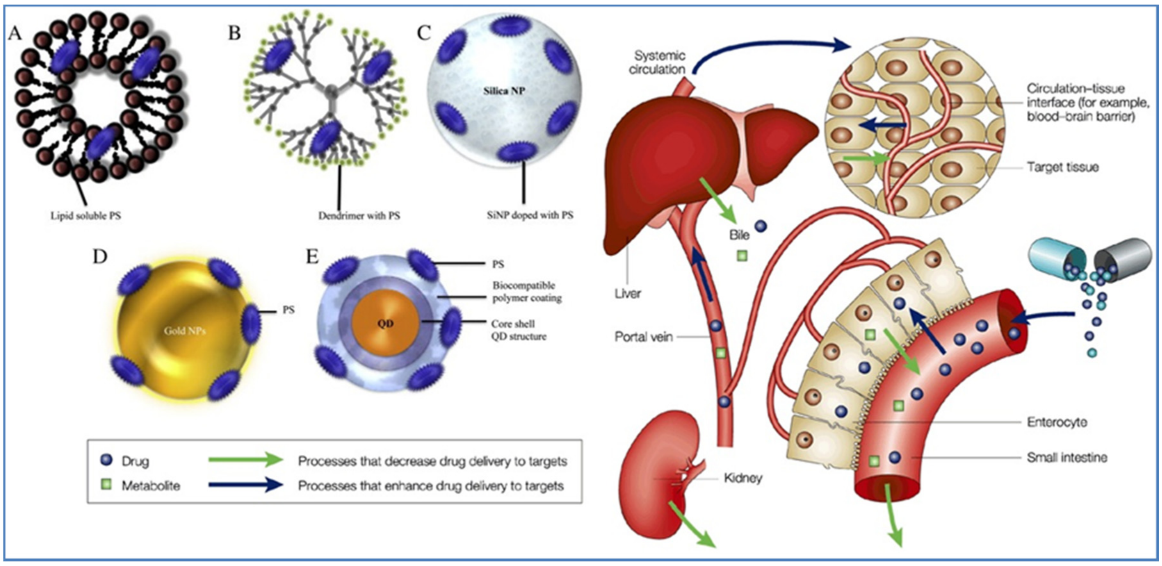

Fig. 10. Different nanoparticles as quantum dots for localized of targeted drug delivery process [161].

They also performed extensive experiments to understand the antibacterial activity of ZnO nanoparticles.

The advancement of nano-medicine from plant sources is a potential agent for biomedical utilizations. The authors conclude that the potent antibacterial performances of ZnO nanoparticles can be utilized as an effective bactericidal specimen for biomedical applications. In lots of studies, we can conclude that the ZnO nanoparticles can be used as a suitable vehicle for drug delivery and gene silencing. Other literature reports [163–165] discussed the ZnO nanoparticles as a smart drug delivery system.

4. CONCLUSIONS

Over the last several decades, ZnO nanoparticles have had a revolutionary impact in biomedical applications. Compared to bulk form, nanoparticles of ZnO have shown various characteristics due to nano-scale dimension. They offer unprecedented interactions with biomolecules both on the surface and inside cells. They can also act as smart weapons against multiple drug-resistant microorganisms and as a talented substitute for antibiotics. Moreover, ZnO biosensors and in vivo imaging are both critical for next generation by providing complementary information. The use of plants in the synthesis of these particles, is eco-friendly, cost-effective and can be easily scaled-up. This process is especially suitable in developing ZnO nanoparticles that can be free from contaminants for biomedical utilizations. The synthesis based on biological processes can easily control the particle dimension and structural morphology. In biomedical applications, these particles can be used as agents of antibacterial and antimicrobial for targeted drug delivery and clinical diagnostics in cancer cell treatment. From the review, it is concluded that, the green synthesis of ZnO nanoparticles is safer and more environmental friendly compared to the usual physical and chemical processes. It is expected that, the research on the ZnO nanomaterials in biomedical applications will continue to flourish over the next generation.

5. ACKNOWLEDGEMENT

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