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Review

A review on biogenic mediated synthesis of zinc oxide nanoparticles and their biological application

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ABSTRACT

In current science, nanotechnology is an important area for material science researchers due to their diversify applications in the field of material engineering, medical science, pharmaceutical science, etc. The biomedical applications of nanomaterials have been usage with the nanoscale dimension range of 1-100 nm. Recently, the zinc oxide nanoparticles (ZnO NPs) had been reported large band gap energy and binding energy which important physicochemical feature has potential applicable for various biological applications like anticancer, anti-diabetic, antibacterial, antifungal, wound healing, anti-inflammatory, antioxidant and optic, etc. Generally, the conventional method synthesis of ZnO NPs has involved toxic hazardous chemicals and afterwards which leads to myriad health risks as well as environment. However, the advantages of biogenic method synthesis of ZnO NPs is free chemical, eco-friendly and cost-effectively. The biological methods have been employed various resources of plants, bacteria, fungi and algae, etc. In this review is focused on the biogenic synthesis of ZnO NPs and their biomedical applications.

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1. Introduction

Nanomaterials are new emerging field of research and that nanoscale dimension of materials dealing with various biological applications such as sensors, catalysis, electrochemistry, optics, space industry, textile industries, pharmaceutics, biomedicals, cosmetics, health care, agriculture and food technology, (Ayelen Velez et al., 2017; Fernandes et al., 2017; Sharif et al., 2017; Syedmoradi et al., 2017; Bera et al., 2016) etc. The metal oxide nanoparticles are promising materials as use biomedical applications due to their exhibit unique physicochemical and biological properties. In generally, nanoparticles synthesis have been use chemical method, which process is involving toxic chemicals for reducing and capping agent its leads to side effects in aquatic environment as well as human health care applications. Several methods have been proposed the synthesis of zinc oxide nanoparticles (ZnO NPs) such as precipitation, hydrothermal, vapor deposition, thermal decomposition, microwave, sol-gel, electrochemical depositions and laser ablation, (Kahouli et al., 2015; Mirzaei et al., 2017; Pulit-Prociak et al., 2016) etc. According to the literature survey have been reported, the toxic chemicals are used through the physical and chemical synthesis of ZnO NPs, which techniques are required high energy, and more expensive its leads hazardous to health risk (Vijayan et al., 2016). Thus, reasons recently several researchers have been focused on green chemistry method synthesis of ZnO NPs, because of their eco-friendly, less toxic chemical and one step synthesis of nanoparticles. The biogenic synthesis method use of plants, microorganisms like bacteria, fungi, algae, yeast and natural raw materials of vegetable and fruits are used for synthesis of nanoparticles (Rajendran et al., 2021; . In this biogenic method presence of some biomolecules or phytochemicals that react as both capping or stabilizing and reducing of metal oxide nanoparticles (Stankic et al., 2016; Khan et al., 2016). Fig. 1, shows graphical abstract of biogenic synthesis of ZnO NPs. In currently more researchers have been clearly reported, the highly considerable potential antimicrobial activity of green synthesized metal oxide NPs like SiO_2, MgO, TiO_2, CaO, CuO, Iron oxide and ZnO NPs. In this review is focused on the biogenic synthesis of ZnO NPs and their biomedical applications.

2. 0. Biogenic synthesis of ZnO NPs using plant

Plant mediated synthesis of ZnO NPs have been using of leaf, fruit, stem and root because of they are exclusive presence of phytocompound that at act as capping and reducing or stabilizing agent of ZnO NPs. In this alternative method of plant parts mediated synthesis is a very less cost effective, ecofriendly and an easily to handling procedure. In moreover, the less involve of costly equipment as well as chemical precursor. Generally plant mediated synthesis of metal oxide or ZnO nanoparticles are most preferred because of highly purities, less toxic effect, stable and possible to large scale production. The phytochemicals of polyphenolic compounds, polysaccharides, terpenoids, alkaloids, vitamins, amino acids are secreted from plant parts which involve bio-reduction conversion reaction of metal oxide or metal ions to 0 valence ZnO NPs (Qu et al., 2011; Heinlaan et al., 2008).

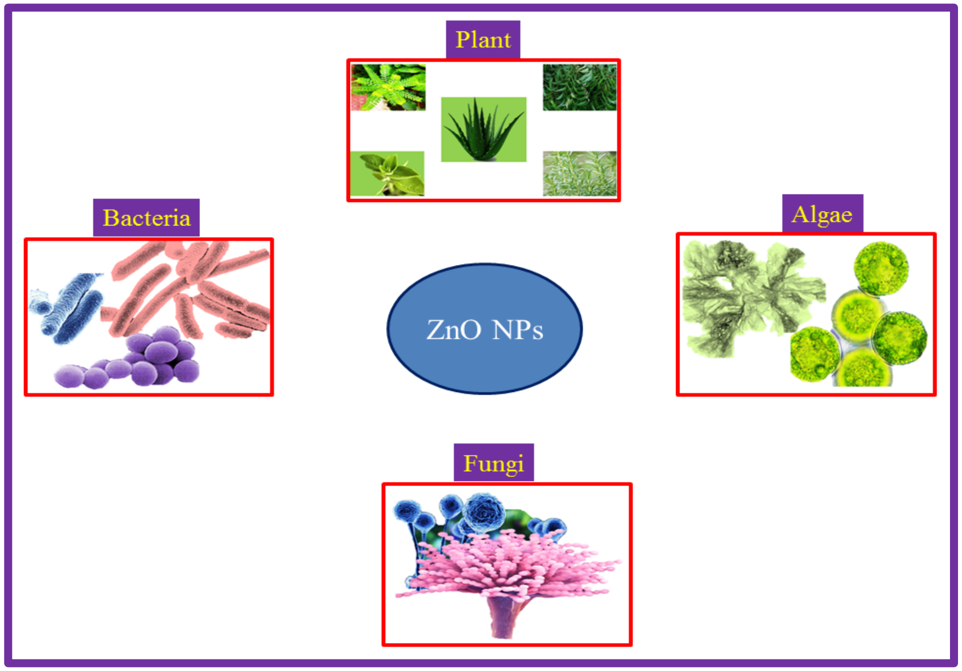

Fig 1. Graphical abstract of biogenic mediated synthesis of Zno NPs

A very commonly applicable method for the green synthesis of ZnO NPs from plant parts such as leaves, stem, root and flowers, etc. are collected and washed thoroughly washed with running tap water, its help to removal of unwanted materials and debris particles and then finally washed with deionized water. The plant parts were air dried at room temperature followed weighing and chopped into small pieces then crushing in a mortar pestle. Milli-Q water (or different solvents ethanol, methanol, etc.) is directly added to plant parts as desired concentration and then mixture solution was boiled under the continuous magnetic stirring. The solution is filtered and desired volume of plant parts extract is mixed with desired Mm concentration of zinc sulfate or zinc nitrate solution and then the mixture is boiled at desired temperature and time to achieve formation of ZnO NPs. After that incubation time the mixture solution turned into yellow color which is primarily conformation of the synthesized ZnO NPs. UV-Vis spectrophotometry is performed to confirmation of synthesized ZnO NPs and followed to mixture solution is centrifuged then collected pellet is air dried in hot air oven. In moreover, synthesized ZnO NPs are additionally characterized using of Fourier Transform Infrared Spectroscopy (FTIR), X-ray diffractometer (XRD), Field Emission Scanning Electron Microscopy (FESEM) with Energy Dispersion Analysis of X-ray (EDAX), High-Resolution Transmission Electron Microscopy (HRTEM), Thermal-gravimetric Differential Thermal Analysis (TG-DTA), Photoluminescence Analysis (PL), Raman Spectroscopy, Attenuated total reflection (ATR), Dynamic Light Scattering (DLS), and Thermal-gravimetric Differential Thermal Analysis (TG-DTA) (Rajeshkumar et al., 2016; Ochieng et al., 2015; Qu et al., 2011).

Waseem Ahmad and Divya Kalra, have been reported the green synthesis of ZnO NPs using of *Euphorbia hirta* leaf extract. The ethanolic extraction of phytocompounds is clear revealed that presence of flavonoid, alkaloid, sponins, terpenoids and carbohydrate obtained from *Euphorbia hirta* extract. The X-ray diffraction pattern and SEM images are also revealed hexagonal structure and spherical aggregation observed. The synthesized ZnO NPs is potential against Gram positive bacteria of *Staphylococcus aureus* and fungi of *Aspergillus niger*, *Cuboida*, the result is suggested *Euphorbia hirta* mediated synthesized ZnO NPs is possible material for biological related applications. Another similar reported Sharma et al. using *Carica papaya* mediated synthesis of ZnO NPs surface morphology is revealed nanoflowers structure. The ZnO NPs was excellent biodegradation properties and exhibited good antibacterial activity against of *Staphylococcus aureus* and *Pseudomonas aeruginosa* (Ahmad, W and Kalra, D, 2020). Table. 1 showed recent reports of plant mediated synthesis of ZnO NPs.

2. 2. Biogenic synthesis of ZnO NPs using bacteria

Bacteria mediated synthesis of ZnO NPs is another important green synthesis approach but it has various disadvantages like broth culture careful monitoring from the contamination, difficult of microbial screening process, bacterial culture medium is also Very costly and production of nanoparticles undesirable size and shape.

Table 1 Zinc oxide nanoparticles (ZnO NPs) biogenic synthesis using by plant part

Plant family	**Plant part**	**Application**	**Reference**
Prunus dulcis	Almond gum	Antimicrobial activity	Anand et al., 2019
Phoenix dactylifera	Date Pulp waste	Dye degradation	Rambabu et al., 2021
Ziziphus jujuba	Leaves	Dye degradation	Alharthi et al., 2021
Musaceae	Anana peel	Anti-bacterial and anti-cancer activity	Ruangtong et al., 2020
Ruellia tuberosa	Leaves	Photocatalytic activity and anti-bacterial activity	Vasantharaj et al., 2021
Syzygium cumini	Leaf	antioxidants, cytotoxic and as nanonutrient	Rumugam et al., 2021
Eriobotrya japonica	Seed	Photocatalytic activity	Shabaani et al., 2020
Knoxia sumatrensis	Leaf	Anti-proliferative and larvicidal	Loganathan et al., 2021
Syzygium Cumini	Leaves	Photocatalytic activity	Sadiq et al.2021
Citrus sinensis	Peel	Photocatalytic activity	Yashni et al., 2012
Dysphania ambrosioides	Leaves	Antibacterial activity	Álvarez-Chimal et al., 2021
Azadirachta indica and Cymbopogon citratus	Leaves	Anti-ticks	Zaheer et al., 2021
Solanum nigrum	Leaf	photocatalytic, antibacterial and antioxidant activity	Muthuvel et al., 2020
Selaginella convolute	Leaf	Pain management	Xua ey al., 2020
Nilgiriantusciliantus	Leaf	Antibacterial and anticancer activity	Resmi et al., 2021

Acacia concinna	Fruit	Dye degradation	Palai et al., 2021
Lantana Camara	Flower	Photocatalytic and anti-inflammatory	Mahadeva et al., 2021
Aristolochia indica	Leaf	Antibacterial activity	Steffy et al., 2018
Camellia sinensis L	Leaf	Anticancer activity	Akbarian et al., 2020
Cynodon Dactylon	Leaf	Antibacterial activity	Meenatchi et al., 2021
Acalypha fruticosa L	Leaf	Antibacterial activity	Vijayakumar et al., 2020
Amygdalus scoparia	stem bark	Antimicrobial activity	Jobie et al., 2021
Ocimum americanum	Leaf	antimicrobial and anticancer activity	Vidhya et al., 2020
Eucalyptus spp.	Leaves	Wastewater treatment	Chauhan et al., 2020
Psidium guajava	Leaf	Antibacterial activity	Saha et al., 2018
Amomum longiligulare	Fruit	Photocatalytic activity	Liu et al., 2020
Codonopsis lanceolata	Roots	photocatalytic activity	Lu et al., 2019

The screened or selected bacterial culture is inoculated into an Erlenmeyer flask containing bacterial culture medium. After that incubation, various concentration of ZnO precursor (Zinc nitrate or zinc sulfate) is added and incubated at 37°C for 24hrs, until white precipitation deposit at bottom of conical flask that the conformed to formation of ZnO NPs. Then visual conformation followed to initial NPs bio-reduction can be monitored by using UV-Vis spectrophotometer. Separation of NPs, the bacterial culture medium is transferred into centrifuge tubes and centrifuged at 3000 rpm for 15 min, after that process pellets were collected and washed with distilled water for the further application process (Ahmed et al., 2017).

ZnO NPs is synthesized from *Aeromonas hydrophila* through the biogenic approach method. In this rout of synthesized ZnO NPs surface morphologies were revealed smooth and spherical in shape which performed antimicrobial activity against both bacteria and fungi. ZnO NPs maximum zone of inhibition was showed against *Pseudomonas aeruginosa* and *Aspergillus flavus* which proved potential antimicrobial properties of synthesized ZnO NPs (Jayaseelan et al., 2012). In furthermore, similar research report the synthesis of ZnO NPs using by *B. licheniformis* through an eco-friendly method which is revealed nanoflowers ZnO NPs and it showed potential photocatalytic activity the degradation of Methylene blue dye (Raliya et al., 2013). Another researcher has been reported through the biosynthesis of ZnO NPs using of *Lactobacillus plantarum* TA4, which HR-TEM images of biosynthesized ZnO NPs showed irregular flower like pattern of ZnO NPs supernatant (CFS) and cell-biomass (CB) with particles size ranges between 291.1 and 191.8 respectively. Biosynthesized ZnO NPs was potential bactericidal activity against pathogenic bacteria of *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Helicobacter pylori*. Biocompatibility experiment was performed the synthesized ZnO NPs by using of Vero cell line (Yusof et al., 2020). Recent reports are showed in Table. 2.

Table 2 Bacterial mediated biogenic synthesis of zinc oxide nanoparticles (ZnO NPs)

Bacterial strain	Application	Reference
Lactobacillus spp	Antimicrobial activity	Suba et al., 2021
Bacillus subtillis	Photocatalytic activity	Dhandapani et al., 2020
Serratia ureilytica (HM475278)	Antibacterial activity	Dhandapani et al., 2014
Lactobacillus paracasei LB3	Antimicrobial activity	Krol et al., 2018
Lactobacillus johnsonii	-	Al-Zahrani et al., 2018
Bacillus megaterium	Antibacterial activity	Saravanan et al., 2018
Sphingobacterium thalpophilum	Antibacterial activity	Rajabairavi et al., 2017
Staphylococcus aureus	Antibacterial activity	Rauf et al., 2017
Pseudomonas aeruginosa rhamnolipids	Antioxidants activity	Singh et al., 2014
Streptomyces sp	Anticancer and antibacterial activity	Balraj et al., 2017

2. 3. Biogenic synthesis of ZnO NPs using algae

Photosynthetic organism of marine algae unicellular forms (ex. Brown algae). Marine algae can be classified based on the pigment present like chlorophytes presence of green pigment, Phaeophyta with brown pigment and Rhodophyta containing red pigment. Algae extract solution presence of proteins, carbohydrates, oil, minerals, fats, bioactive compounds like antioxidants (tocopherols, polyphenols) and pigments such as chlorophylls, phycobilins, and carotenoids which bioactive compounds potentially capping and reducing or stabilizing agents of biosynthesized NPs (Sharma et al., 2016; Michalak and Chojnacka, 2015; Thema et al., 2015). Marine algae mediated synthesis of ZnO NPs has been reported very limit of research papers. In this method, algae mediated synthesis of ZnO NPs is involves steps such as metal precursor, algae extract and desired time incubation of algal extract solution with precursor. After that process color change is visually observed it's to be conformed the formation ZnO NPs. Rajiv et al., have been reported, the green synthesis of ZnO NPs using of *Sargassum muticum* and *S. myriocystum* under to the family of Sargassaceae. Biosynthesized ZnO NPs results of XRD and FESEM are revealed hexagonal wurtzite structure with presence of sulfated polysaccharides and hydroxyl group. Yung et al., have been reported green synthesis of ZnO NPs using of freshwater algae *C. reinhardtii* (FACHB-479), *C. pyrenoidosa* (FACHB-9) and *P. subcapitata* (FACHB-271) (Rajiv et al., 2013). Table 3 illustrates algae mediated synthesis of ZnO NPs.

Table 3 Algae mediated Biogenic synthesis of zinc oxide nanoparticles (ZnO NPs)

Algal strain	Application	Reference
Arthrospira platensis	Antibacterial activity	El-Belely et al., 2021
Sargassum muticum	Antiangiogenic and antiapoptotic	Sanaeimehr et al., 2018
Chlamydomonas reinhardtii	Photocatalytic activity	Rao et al., 2016
***Anabaena* strain L31**	UV-B absorbance	Singh et al., 2014
Sargassum muticum	-	Azizi et al., 2014
Sargassum myriocystum	Antibacterial activity	Nagarajan et al., 2013

2. 4. Biogenic synthesis of ZnO NPs using fungus

Fungal extracellular mediated synthesis of ZnO NPs is highly preference because of their metal bioaccumulation, high metal tolerance, large scale production, downstream process and low cost effective (Pati et al., 2014). Bacterial strain compared to fungal culture mediated synthesis of ZnO NPs is easy to maintain and can be culturing, fast growth in the laboratory at room temperature conditions. Moreover, biologically mediated synthesized ZnO NPs has been gained more importance due to their non-toxic and biocompatibility.

Table 4 Mycological mediated synthesis of zinc oxide nanoparticles (ZnO NPs)

Fungal strain	Application	Reference
Periconium sp	Antimicrobial and Antioxidant activity	Ganesan et al. 2021
Cochliobolus geniculatus	-	Kadam et al., 2019
Aspergillus niger:	Antimicrobial and photocatalytic activity	Kalpana et al., 2018
Candida albicans	Photocatalytic activity	Shamsuzzaman et al., 2017
Aspergillus fumigatus	Antibacterial activity	Rajan et al., 2016
Aspergillus terreus	Antifungal activity	Baskar et al., 2013
Aspergillus fumigatus TFR-8	Agriculture	Raliya et al., 2013
Fusarium spp	-	Velmurugan et al., 2010

Pavani et al., have been reported, fungal mediated synthesized of ZnO NPs using *Aspergillus fumigatus* that DLS analysis exhibited the size range of 1.2 to 6.8 and with the average particles size of 3.8 nm. Another similar report have been using of *Aspergillus fumigatus* for the synthesis of ZnO NPs. The NPs size range of 54.8–82.6 nm were evaluated by SEM analysis and XRD analysis to be calculated average particle size of 29 nm through followed Debye-Sherrer equation method. Primary and secondary compounds such as alcohol, amine, and aromatic nitro and also to be confirmed the NPs formation by FTIR analysis (Pavani et al., 2012). Table 4 represents the recent reports of fungal mediated synthesis of ZnO NPs.

3. Conclusion

In this review mainly summarized on the eco-friendly biosynthesis approach of ZnO NPs by using of plants and microbes source in the last decade. Green route of biosynthesis NPs has containing the bioactive compounds that can be act as reducing and stabilizing agents and also size and shape control manner. Among different biological pattern synthesis of ZnO NPs which through the microorganism mediated synthesis is not an ease industrial scale production because of their highly requirements of aseptic conditions and high cost effective of culture medium as well as maintenance. Therefore, generally plant extract mediated synthesis of NPs has been possessing several advantageous over compared to microorganisms due to the less biohazard, ease handling and single step process. Phytosynthesis of ZnO NPs needs to be more research due to the huge availability of plant species and become potential candidate as phytonanofabication. In further more research needs to be exploring actual mechanism of phytosynthesis of ZnO NPs and their biological applications.

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