Medical Sains : Jurnal Ilmiah Kefarmasian
Vol. 10 No. 3, July - September 2025
https:/ojs.ummada.ac.id/index.php/iojs


# THE EFFECTIVENESS OF BIOSYNTHESIZED ZnO NANOPARTICLES AS ANTIBACTERIALS: A LITERATURE REVIEW

**Selly Nopriyanti[1*], Yani Mulyani[1]**
[1]*Faculty of Pharmacy, Bhakti Kencana University, Indonesia*
**Email Corresponding: sellyarsyid@gmail.com*

***Submitted: February 2, 2025 Revised: August 28, 2025 Accepted: September 22, 2025***

**ABSTRACT**
One of the human infections caused by bacteria is digestive tract infection, some of these bacteria include S.typhi, E.coli, S.dysenteriae. Antibiotics are required to treat infectious diseases caused by microbes; however, most antibiotics cause resistance to these microbes. To avoid this, researchers are interested in developing plant-derived antibiotics. This review aims to evaluate the antibacterial effectiveness of ZnO nanoparticles synthesized from plant extracts or microorganisms and their antibacterial activity against gram-positive bacteria (B. Cereus & S. Aureus) and gram-negative bacteria (E. Coli, K. Pneumonia & S. Thypi). From this review, it can be concluded that ZnO nanoparticles have significant antibacterial activity against gram-negative bacteria. This antibacterial effectiveness is influenced by the particle size, ZnO-NPs concentration, and environmental conditions, such as pH and temperature. However, further studies are needed to determine the effectiveness of biosynthesized ZnO nanoparticles and their activities other than antibacterials.

**Keywords**: Zinc Oxide Nanoparticles, Nanoparticles, Antibacterial, Biosynthesis, Green Synthesi

## INTRODUCTION

Infection is a disease caused by the proliferation of microorganisms, a broad group of microscopic organisms consisting of bacteria, parasites, fungi, and viruses. One of the human infections caused by bacteria is digestive tract infection, some of these bacteria include S.typhi, E.coli, S.dysenteriae, and V. cholerae. Antibiotics are required to treat infectious diseases caused by microbes; however, most antibiotics cause resistance to these microbes. Resistance can occur due to the delivery of antibiotics without a doctor's prescription and lack of patient compliance in taking them. To avoid this, researchers are interested in developing new plant-derived antibiotics (Rusli, 2016).

Advances in science and technology have led to the emergence of nanotechnology, which is a rapidly growing field of research in modern materials science. Nanoparticles play an important role as a foundation for various nanotechnology applications (Ajitha et al., 2015). Nanoparticles are nanoscale materials with sizes ranging from 1-100 nm (Fagier, 2021). Metal oxide nanoparticles are interesting to study because they exhibit physical properties such as dimensions, uniform size distribution, morphology, crystallinity, and better chemical physics compared to bulk materials (Saravanadevi et al., 2020). Among other metal oxide nanoparticles, ZnO nanoparticles are preferred because of their non-toxic nature, thus providing high mobility and good thermal stability (Preethi et al., 2020). ZnO nanoparticles are n-type inorganic semiconductors that have a hexagonal phase and wurtzite structure with a wide band gap of

3.37 eV, and due to the high binding energy of excitons, ZnO has a strong ultraviolet (UV) light emission of 60 MeV (Mydeen et al., 2020). The advantage of using ZnO is its abundant availability in nature, making it inexpensive and easy to synthesize (Yurestira et al., 2021).

The synthesis of ZnO nanoparticles using physical (top-down) and chemical (bottom-up) methods has the disadvantages of high costs and equipment, high temperatures, large energy consumption, and the use of toxic chemicals as reducing agents and stabilizers, such as polyetherimide (PEI), polyethylene glycol (PEG), and polyacrylic acid (PAA), which have the potential to become pollutants in the environment (Alamdari et al., 2020). Therefore, an environmentally friendly biosynthesis method was used, which still produced ZnO nanoparticles with good characteristics (Nurbayasari et al., 2017). ZnO nanoparticles synthesized using plant extracts and their derivatives are more stable than those synthesized using other organisms (Rajakumar et al., 2018). Plant extracts, such as kingkilaban stems (Jayappa et al., 2020), dafnah leaf (Chemingui et al., 2019), and pineapple fruit (Ahmad et al., 2019) extracts, have been used in the biosynthesis of ZnO nanoparticles. Plant parts, including sap, seeds, fruits, flowers, leaves, and roots, are rich in phytochemical compounds that can reduce metal salts to nanosized metal oxides (Singh et al., 2016). This is because the protein content and secondary metabolites in plant extracts act as reducing agents, stabilizers, and capping agents in the biosynthesis of ZnO nanoparticles (Chatterjee et al. & Ovais et al., 2020). The mechanism of stabilizing and preventing the agglomeration of ZnO nanoparticles is by creating steric hindrance, controlling particle growth by reducing the particle surface energy to prevent aggregation, and forming coordination compounds with stable metal (II) ions (Yunita et al., 2020).

ZnO is currently being investigated as an antibacterial agent in both micro- and nano-scale formulations. ZnO exhibits significant antimicrobial activity when the particle size is reduced to the nanometer range. Nano-sized ZnO can interact with the bacterial surface or with the bacterial nucleus as it enters the cell, and further exhibits different bactericidal mechanisms (Brayner, 2016). The interaction between these unique materials and bacteria is mostly toxic, and has been utilized for antimicrobial applications, such as in the food industry. Research related to Zinc Oxide Nanoparticles as antibacterials has been widely conducted, but there have not been many reviews or discussions related to the effectiveness of ZnO Nanoparticles synthesized from various natural materials as antibacterials. This study aimed to determine the effectiveness of ZnO Nanoparticles from various natural materials in inhibiting bacterial development.

## RESEARCH METHOD

This article uses a narrative review evaluates the antibacterial effectiveness of plant-based biosynthesized ZnO nanoparticles. Literature searches were conducted through Google Scholar, PubMed, Scimago, and ScienceDirect using the keywords: “ZnO Nanoparticle Biosynthesis”, “ZnO Nanoparticles”, “Antibacterial”, “Plant Extracts”, and “Nanoparticles”. The screening process was performed in several stages. First, duplicate articles were removed. The titles and abstracts were then screened for relevance to the topic. Finally, the full texts were reviewed to assess methodological quality. The inclusion criteria were original research articles discussing ZnO nanoparticle biosynthesis using plant extracts, studies evaluating antibacterial activity (in vitro or in vivo), articles published in English or Indonesian full text available, and published between 2015–2025. The exclusion criteria were unclear methods, reviews, and studies with unrepresentative samples. From an initial search of 35 articles, 22 articles remained after title and abstract screening. After applying the inclusion and exclusion criteria, 8 articles were included in this review. The data were analyzed narratively to identify key findings, trends, and relationships between ZnO nanoparticles and their antibacterial effectiveness.

## RESULTS AND DISCUSSION

ZnO nanoparticles exhibit significant antibacterial activity when their particle size is reduced to the nanometer range. Here are some research results on the antibacterial activity of ZnO obtained through biosynthesis. **(Table I)**

**Table I. Antibacterial activity of biosynthesized ZnO nanoparticles**

| Journal Citation | Plants Extract | Materials | Physical Characteristics (Size) | Method of Antibacterial Test | Results |
|---|---|---|---|---|---|
| Arinjoy et al., 2017 | *Parthenium Histeroforus Extract* | Plantphytochemicals (not specified) | 12–36 nm | Agar well diffusion method Bakteri : *Stafilokokus aureus, Subtilis,klebsiella pneumonia* dan *Eschericia coli.* | The maximum zone of inhibition (36 mm) was observed to be higher against Enterobacter aerogenes bacteria while the least activity was observed against S. aureus and B. Subtili. |
| M. Awwad et al., 2020 | *Ailanthus altissima Extract* | Plantflavonoids Terpenoids | 20–40 nm | Methods: Disc diffusion method Bacteria. Eschericia coli And Staphylococcus aureus | ZnO Nanoparticles have a significant growth inhibitory effect on S. Aureus and E. Coli bacteria. |
| Ravinder et al., 2018 | *Aloevera peel extract* | Aloe polysaccharides | 30–70 nm | Methods : Agar well diffusion method Bacteria : *Staphylococcus epidermidis and Eschericia coli* | ZnO nanoparticles showed no antibacterial effect against S. Epidermidis (gram positive) due to the presence of a thick peptidoglycan layer on the cell membrane.. |
| Huzaifa et al., 2019 | *Albizia lebbeck stem bark extract* | Tannins, alkaloids | 25–60 nm | Methods : Diffusion Method Bacteria : 2 gram positive *(B. Cereus and S. Aureus)* And 3 gram negative *(E.* | There is no significant inhibition on gram-positive bacteria. Because gram-positive bacteria have a thick peptidoglycan layer on their cell walls. |

| | | | | | |
|---|---|---|---|---|---|
| | | | | *Coli, K. Pneumonia and S. Thypi)* | |
| Rajeshkumar et al., 2019 | *Cassia alata extract* | Phenolics,flavonoids | 20 nm (IC50 = 20 µg/mL), | Methods : Agar Diffusion Method Bacteria : *Eschericia coli* | The excellent antibacterial potential of ZnO NPs through growth curve analysis and nanoparticle bactericidal activity testing. Treatment of ZnO NPs with bacteria showed the IC50 value to be 20 µg/mL. |
| Ahmad Fatoni et al., 2020 | *Psidium guajava.L extract* | Chitosan stabilizer | ~40 nm, rough surface | Methods: Disc Diffusion Method Bacteria : Gram negative *(Eschericia Coli)* | The higher the concentration of ZnO nanoparticles, the greater the inhibition diameter produced in inhibiting bacterial growth with an inhibition of 20.23 mm. |
| Rafael et al., 2022 | *Dysphania ambrosioides extract* | Secondary metabolites | 4–10 nm | Methods : Disc Diffusion Test Bacteria : *Staphylococus aureus, Staphylococus epidermidis, Streptococus mutans, E. Coli, Pseudomonas Aeruginosa* | The influence of ZnO-NP size on the inhibition of bacterial strains was demonstrated by higher inhibition or elimination of strains with smaller ZnO NPs (4-10 nm). This was mainly observed with Staphylococcus aureus and Escherichia colistrain bacteria, although all strains evaluated were sensitive to ZnO-NPs. |

| | | | | | |
|---|---|---|---|---|---|
| Suzan et al., 2016 | *Anchusa italica(A.Ital i ca)* | Alkaloids, flavonoids | ~18–30 nm | Methods : Disc Diffusion Test Bacteria : Gram positive Bacteria *(Bacteria megaterium and Staphylococcus aureus)* and Gram negative Bacteria *(Escherichia coli and Salmonella typhimurium).* | Gram-positive bacteria are more susceptible to the toxicity of ZnO nanoparticles compared to Gram-negative bacteria which may be due to the different structure of the bacterial cell membrane that controls the access of the toxin to its site of action. |

Various herbal plants synthesized with ZnO nanoparticles have shown excellent antibacterial activity. *Parthenium hysterophorus* is a weed of the Asteraceae group that has traditionally been used to treat fever and diarrhea in humans and systemic toxicity in livestock (Patel, 2011). Arinjoy et al. synthesized *P. hysteroforus* extract with ZnO nanoparticles and tested its antibacterial activity against gram-positive *Staphylococcus aureus* and gram-negative *Klebsiella pneumoniae*, *Escherichia coli*, and *Enterobacter aerogenes*. The results showed an inhibition zone of 36 mm for gram-negative bacteria, while the lowest antibacterial activity was found for gram-positive bacteria, with an inhibition zone of 11 mm for *Staphylococcus aureus* and 10 mm for *B. subtilis*. ZnO synthesis with white oyster mushrooms also showed a significant inhibition zone against both bacteria. This is due to the high surface area of ZnO-NPs and their small size of 12 nm. (Vijayakumar et al., 2019). Ravinder et al (2018) synthesized ZnO with aloe vera plant extract and conducted activity tests against *Stapylococcus aures*, *Stapylococcus epidermidis*, *K. pneumonida* and *E.coli* bacteria. The diameter of the inhibition zone was measured and expressed in millimeters. The results showed that ZnO NPs had no antibacterial activity against gram-positive bacteria. This is due to the thick peptidoglycan layer on the cell membranes (Salar, 2015). The same results were also observed in ZnO biosynthesis with *Alibizia lebbec* plants, where gram-negative bacteria were less resistant to ZnO NPs than gram-positive bacteria. Elham et al. also found strong antibacterial potential against gram-negative bacteria using ZnO NPs synthesized from caraway seeds and concluded that the resistance in gram-positive bacteria is due to the presence of a thick peptidoglycan layer in their cell walls, which is similar to the results achieved in Huzaifa et al.'s study. The binding of $Zn^{+}$ ions to the cell membrane and the production of reactive oxygen species (ROS) in the cell result in cell disruption (Zare, 2017).

ZnO synthesized with cassia flower extract showed good antibacterial activity against *Eschericia coli* bacteria. The positively charged ZnO NPs interact with the negatively charged bacterial membrane, thereby causing loss of membrane integrity and leakage of intracellular proteins, resulting in delayed growth (Rajeskumar, 2019). Ahmad et al (2020) also synthesized ZnO with *guava leaf* extract. ZnO NPs have an uneven and rough surface texture, which allows them to break the bacterial cell wall and cause cell wall decomposition, followed by cell membrane decomposition, resulting in good antibacterial activity against *E. coli* (Padmavathy, 2018). The antibacterial activity of ZnO is attributed to the release of $Zn^{2+}$ ions and reactive oxygen species (ROS) (Chemingui et al., 2019). The resulting ROS species, namely hydroxyl radical $OH^-$ and peroxide $O^{2-}$, damage DNA and denature proteins from cells. ZnO nanoparticles will dissolve in aqueous media and release $Zn^{2+}$ ions. The mechanism of $Zn^{2+}$ ion release is as follows :

$$\mathbf{ZnO + H_2O \rightarrow Zn^{2+} + 2OH^-}$$

$Zn^{2+}$ ions bind to the negative charge on the outer surface of the cell membrane. This interaction causes cell disorders, such as inhibition of bacterial cell activities, including active transport, bacterial metabolism, and enzyme activity, followed by leakage of cell contents, which results in damage and death of bacterial cells due to the toxicity of $Zn^{2+}$ ions (Demissie et al., 2020).

## CONCLUSION

ZnO nanoparticles synthesized using living organisms or plant extracts have the advantage of being more environmentally friendly than conventional synthesis methods because they do not involve hazardous chemicals. ZnO nanoparticles synthesized using plant extracts or microorganisms have great potential as effective antibacterial agents, especially against Gram-negative bacteria such as *Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*. This antibacterial effectiveness is influenced by the particle size, ZnO-NPs concentration, and environmental conditions, such as pH and temperature. The mechanism of action involves the formation of ROS, interaction with the cell membrane, and release of $Zn^{2+}$ ions, which damage bacterial cell structures.

## REFERENCES


Ahmad, F., Hilma, Ade, A., Selly, N., Nulisa, H (2020). Biosynthesis of ZnO Nanoparticles from Water Extract of Guava Leaf (Psidium guajava L) and Zn2+ Ion and its interaction with chitosan as Antibacterial Escherichia coli. Journal of Pharmaceutical & Clinical Science. ISSN : 2407-7062 e-ISSN : 2424-5435. https://doi.org/10.25077/jsfk.7.2.151-157.2020.

Ahmad, R. A. R., Harun, Z., Othman, M. H. D., Basri (2019). Biosynthesis of Zinc Oxide Nanoparticles by Using Fruits Extracts of Ananas Comosus and Its Antibacterial Activity. *Malaysian Journal of Fundamental and Applied Sciences*. *15*(2):268–273. https://doi.org/10.11113/mjfas.v15n2.1217.

Ajitha, B., Ashok, K., Reddy, Y & Sreedara, R (2015). Green Synthesis and Characterization of Silver Nanoparticles using Lantana camara Leaf Extract. *Materials Science and Engineering* C. 49 : 373-381. https://doi.org/10.1016/j.msec.2015.01.035.

Alamdari, S., Ghamsari, M., Lee, H., & Ara, M (2020). Preparation and Characterization of Zinc Oxide Nanoparticles Using Leaf Extract of Sambucus Ebulus. Applied Sciences (Switszerland), 10 : 1-19. https://doi.org/10.3390/app10103620.

Arinjoy, D., Chandi, P., Himani, B., Sukhjeet, K (2017). Green Synthesis of Zinc Oxide Nanoparticles Using Parthenium Hysterophorus Leaf Extract and Evaluation of their Antibacterial Properties. Journal of Biothecnology and Biomaterials. Phagwara. India. https://doi.org.10.4172/2155-952x.1000271.

Awwad, A., Amer, M., Nida, M., Salem (2020). Green synthesis of zinc oxide nanoparticles (ZnO-NP) using Alianthus altissima fruit extract and antibacterial activities. Internasional Scintific Organization. Jordan.

Chatterjee, A., Kwatra, N., & Abraham, J (2020). Chapter 8 Nanoparticles Fabrication by Plant Extracts. In *Phytonanotechnology*. Elsevier Inc. https://doi.org/10.1016/b978-0-12-822348-2.00008-5.

Chemingui, H., Missaoui, T., Mzali, J. C., Yildiz, T., Konyar, M., Smiri, M., Saidi, N., Hafiane,A., & Yatmaz, H. C. 2019. Facile Green Synthesis of Zinc Oxide Nanoparticles (ZnO NPs): Antibacterial and Photocatalytic Activities. *Material Research Express*, 1–33.

Demissie, M., Sabir., Edossa, G & Gonfa, B. (2020). Synthesis of Zinc Oxide Nanoparticles Using Leaf Extract of Lippia adoensis (Koseret) and Evaluation of Its Antibacterial Activity. *Journal of Chemistry*, *2020*: 1–9.

Fagier, M (2021). Plant-Mediated Biosynthesis and Photocatalys Activities of Zinc Oxide Nanoparticles : A Prospect toward Dyes Mineralization. Journal of Nanothecnology. 2021. 1-15. https://doi.org/10.1155/2021/6629180.

Huzaifa, U., Doga, K., Nahit, R (2019). Biosynthesis of Zinc Oxide Nanoparticles using Albizia lebbeck stem bark adn evaluation of its antimicrobial, antioxidant and cytotoxic activities on human breast cancer cell lines. *Internasional Journal of nanomedicine.* University Mercine Turkey.

Jayappa, M., Ramaiah, C., Kumar, M., & Sheikh, S (2020). Green Synthesis of Zinc Oxide Nanoparticles from The Leaf Stem and In Vitro Grown Callus of Mussaenda Frondosa L:Characterization and Their Applications. *Apllied Nanoscience*. Switzerland. 10(8):3057-3074. https://doi.org/10.1007/s13204-020-01382-2.

Mydeen, S., Kumar, R., Kottaisamy, M., & Isaabadi, Z (2020). Biosynthesis of ZnO Nanoparticles Through Extract from Prospois Juliflora Plant Leaf : Antibacterial Activities and A New Approach by Rust-Induced Photocatalysis. *Journal of saudi Chemical Society*. 24 (5) : 393-406. https://doi.org/10.1016/j/jscs.2020.03.003.

Nurbayari, R., Saridewi, N & Shofwatunnisa (2017). Biosynthesis and Characterization of ZnO Nanoparticles with Extract of Green Seaweed Caulerpa sp. *Jurnal Perikanan Universitas Gajah Mada*. 19(1):17-28. https://doi.org/10.22146/jfs.24488.

Ovais, M., Khalil, A. T., Ayaz, M., & Ahmad, I. 2020. Metal Oxide Nanoparticles and Plants.*InPhytonanotechnology*.ElsevierInc.https://doi.org/10.1016/b978-0-12-8223 48-2.00007-3.

Padmawathy, N., Vijayaraghavan, R (2018). Enchanced bioactivity of ZnO nanoparticles an antimicrobial studi. Sci Technol Adv Mater. (3):035004. https://doi.org/10.1088/1468-6996/9/2/035004.

Patel, S (2011). Harmfull and benefical aspect of Parthenium hysterophorus. Biotech. 1 : 1-9.

Preethi, S., Abarna, K., Nithyasari, M., Kishore, P., Deepika, K., Ranjithkumar, r., Bhuvaneshwari, V & Bharathi, D (2020). Synthesis and Characterization of Chitosan/Zinc Oxide Nanocomposite for Antibacterial Activity Onto Cotton Fabrics and Dye Degradation Applications. *Internasional Journal of Biological Macromolecules.* 164 : 2779-2787. https://doi.org/10.1016/j.ijbiomac.2020.08.047.

Ravinder, K., Asha, C., Naresh, K (2018). Antimicrobial activity of zinc oxide nanopaticles synthesized from Aloe vera peel extract. *Springer Nature Science Journal*. Switzerland. Salar, R.,K., Sucitra (2015). Evaluation of antimicrobial potential of different extract of salanum xanthocarphum schrad. Afr Journal Microbial. Res 3 : 97-100.

Rajeshkumar, S., Agarwal, H., Menon, S., David, S (2019). Phyto-assited synthesis of zinc oxide nanoparticles using *Cassia alata* and its antibacterial activity agains *Eschericia coli.* Biochemistry and Biophysics Report. https://doi.org/10.1016/j.bbrep.2019.01.002

Rajakumar, G., Thiruvengadam, M., Mydhili, G., Gomathi, T., & Chung, I. M. 2018. Green Approach for Synthesis of Zinc Oxide Nanoparticles from Andrographis paniculata Leaf Extract and Evaluation of Their Antioxidant, Anti-Diabetic, and Anti-Inflammatory Activities. *Bioprocess and Biosystems Engineering*, *41*(1): 21–30. https://doi.org/10.1007/s00449-017-1840.

Saravandevi, K., Kavitha, M., Karpagavinagayam, P., Saminathan, K (2020). Biosynthesis of ZnO and Ag doped ZnO Nanoparticles from vitis vinifera Leaf of Antibacterial Photocatalytic Application. *Material Today : Proceedings*. https://doi.org/10.1016/j/lwt.2020.110133.

Singh, P., Kim, Y. J., Zhang, D., & Yang, D. C (2016). Biological Synthesis of Nanoparticles from Plants and Microorganisms. *Trends in Biotechnology*, *34*(7): 588–599. https://doi.org/10.1016/j.tibtech.2016.02.006.

Vijayakumar, S., Arulmozhi, P., Kumar, N., Sakhtibel, B. (2019). Axalypha fruticosa. L leaf extract mediated synthesis of ZnO nanoparticles : characterization and antimicrobial activities.Materialsscienceinsemiconductorprocessing. https://doi.org/10/1016/j/matpr.

Yunita, Nurlina, & Syahbanu, I. 2020. Sintesis Nanopartikel Zink Oksida (ZnO) dengan Penambahan Ekstrak Klorofil sebagai Capping Agent. *Positron*. *10*(2): 44. https://doi.org/10.26418/positron.v10i2.42136.

Yurestira, I., Aji, A., Desfri, M., Rini, S., Rati, Y (2021). Potential of ZnO/Zns as Electron Transport Materials on Perosvskite Solar Cells. *Journal of Aceh Physics Society*. 10 (2) :41-47. https://doi.org/10/24815/jacps.v10i2.18383.

Zare, E., Pourseyedi, S., Khatami, M (2017). Simple Biosynthesis of zinc oxide nanoparticles using nature source and its in vitro bio activity. Journal Medicine struct. Vol : 1146. 96-103