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# Metallic Nanoparticles Playacting as Bactericidal Agent

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**ABSTRACT**

*Here, we present a review of the antibacterial effects of metal nanomaterial. Proposed antibacterial mechanisms and possible toxicity to bacterial cells. Nanoparticles (NPs) are increasingly used to target bacteria as an alternative to antibiotics. Nanotechnology may be particularly advantageous in treating bacterial infections. Currently accepted mechanisms include oxidative stress induction, metal ion release, and non-oxidative mechanisms. There is some evidence that nanoparticles can directly damage bacteria cell membranes, leakage of cellular content and disruption DNA replication. In this review, we discuss the antibacterial mechanisms of NPs against bacteria and the factors that are involved. We mainly emphasize on zinc, gold and cobalt material their synthesis and mechanism of bactericide.*

***Key words:*** *Antimicrobial activity, Nanoparticles, Metals, Bacteria, Oxidative stress.*

## INTRODUCTION

Bacterial infections are a major cause of chronic infections and mortality. Antibiotics have been the preferred treatment method for bacterial infections because of their cost-effectiveness and powerful outcomes[1,3]. However, several studies have provided direct evidence that the widespread use of antibiotics has led to the emergence of multidrug-resistant bacterial strains[4]. In fact, super-bacteria have the super resistance gene called NDM-1[5]. These bacteria are resistant to nearly all antibiotics have recently developed due to abuse of antibiotics[6]. The major groups of antibiotics that are currently in use have three bacterial targets: the cell wall synthesis, translational machinery, and DNA replication machinery[7]. Unfortunately, bacterial resistance can develop against each of these modes of action[8]. Most of the antibiotic resistance mechanisms are irrelevant for nanoparticles (NPs)[9].The mode of action of NPs is direct contact with the bacterial cell wall, without the need to penetrate the cell. For this hope that NPs would be less prone to promoting resistance in bacteria than antibiotics[10]. Now a day's attention has been focused on new and exciting NP-based materials with antibacterial activity.

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Antibacterial agents are very important in the textile industry, water disinfection, medicine, and food packaging[11]. Organic compounds used for disinfection have some disadvantages, including toxicity to the human body, therefore, to overcome the toxicity the interest in inorganic disinfectants such as metal oxide nanoparticles (NPs) is increasing[12]. This review focuses on the properties and mechanism of tuned nanostructured materials to the bacterial cells and their surface modifications, with good antimicrobial activity. Such improved antibacterial agents locally destroy bacteria, without being toxic to the surrounding tissue. We also provide an overview of opportunities and risks of using NPs as antibacterial agents. In particular, we discuss the role of different NP materials. As the field of Nano medicine emerges; there is a deficiency of research surrounding the topic of nanoparticle (NP) toxicity, particularly concerned with mechanisms of action. NPs have increasingly been used in industry over the past few decades with usages varying from food additives[13] to drug administration [14,15].

The continuous emergence of bacterial resistance has challenged the research community to develop novel antibiotic agents[16]. Among the most promising of these novel antibiotic agents are metal NPs, which have shown strong antibacterial activity in an overwhelming number of studies. Generally, antibiotic-resistant bacteria appear in a relatively short period of time even when new antibiotics are released into the market. However, it is hypothesized that NPs with antibacterial activities have the potential to reduce or eliminate the evolution of more resistant bacteria because NPs target multiple biomolecules at once avoiding, the development of resistant strains. In this review we discuss mechanisms of antibacterial action of different NPs. In addition, we discuss their involvement in the production of reactive oxygen species (ROS), biomolecule interaction and regulation, and membrane interaction. Several types of metal and metal oxide NPs such as CuO, CaO, Ag and Ag2O, Au, ZnO, and MgO have been investigated for their antibacterial effects.in this review we discuss on ZnO, Au and CO nanoparticles.

**ZnO Nanomaterials:**

Application of Zinc oxide nanoparticles in food system may effecting at inhibiting certain food borne pathogens[17]. ZnO NPs possess strong antibacterial activity against Listeria monocytogenes, Salmonella enteritidis and Escherichia coli(0157:H7)[18-19].ZnO NPs are toxic on mesophilic and halophilic bacteria like Enterobacter sp.,Marinobacter sp.,and Bacillus subtilis,.the nontoxicity is more pronounced on Gram negative bacteria[20]. Nanotoxicity towards Gram positive cells due to the thicker peptidoglycan layer toxicity is less from gram negative bacterial species[21]. Antibacterial activity of zinc based nanoparticles is enhanced by their morphological characteristics synthesis process size of nanoparticles in table-1(a),from different literature survey. Binding of nanoparticles to the bacterial cells mostly due to the positive surface charge of metal that binds to the negatively charged surface of tested bacteria[22]. Regardless of the used synthesis method, zinc oxide or cobalt doped ZnO nanostructures with low toxicity have shown an important antibacterial effect and can be used as a suitable alternative in pharmaceutical industries[23]. Researchers studied the contribution of the soluble zinc species regarding antimicrobial activity of ZnO on microbial cultures in broth medium[23]. The mechanism of tuning of ZnO with the bacterial cells still now not clear but main cause might be:1.Zn2+ released in the broth significantly contributed to the overall antibacterial effect of zinc oxide nanoparticle[24]. 2.Direct contact of ZnO with the bacterial cells walls[25]. The tuned nanoparticles causes destructing bacterial cell integrity[26], 2.liberation of antimicrobial ions mainly Zn2+ions[27] and ROS formation[28], Soluble zinc species and ZnO powders possessing larger specific area showed specificity with respect to the microbial strains[29]. In figure 1(b),there are certain mechanism of ZnO towards the gram positive and gram negative bacterial species. However,

the toxicity mechanism varies in various media as the species of dissolved Zn may change according to the medium components besides the physicochemical properties of ZnO-NPs.

**Gold nanoparticle:**

Gold nanoparticles present a higher stability when in contact with biological fluids[30]. AuNPs has antibacterial activity against both Gram positive and Gram negative bacteria. It shows antibacterial effect against Escherichia coli, Staphylococcus aureus, Bacillus subtilis and Klebsiella pneumonia[31]. Gold nanoparticles generating holes in bacterial cell walls thereby increasing permeability of cell wall ,resulting in the leakage of cell contents and also cell death[32]. Although the thickness of the bacterial wall, gold nanoparticles induce intracellular antibacterial activity against C.pseudotubercu-losis[33]. The size of AuNPs governs the properties of the nanoparticles and the applications for which they are used. Small size AuNPs (2 nm-15 nm) are used in applications such as immunohistochemistry, microscopy (light and high magnification TEM) and biomarkers. Medium size AuNPs (20 nm-60 nm) are used in environmental detection and purification, drug delivery, biomarkers, chemical sensors, DNA detection. Large size AuNPs (80 nm-250 nm) are used in forensic science, electronic device, manufacture, optical mammography etc. There are many synthesis process: Biosynthesis Polysaccharide, Chemical reduction, Green biosynthesis(plant Extract) describes in table 2(a). Chemically synthesized and stabilized gold nanocolloids are effective against most potent bacterial strain[34]. The antibacterial activity of the gold nanoparticles might be because of generation of Reactive Oxygen Species (ROS) which causes increase of the oxidative stress of microbial cells in form of vacuole formation as an indication of potent activity[35]. Au-NPs polarizes with opposite charges at the core and the surface which creates a dipole oscillation among several other modes of Plasmon resonances at other wavelengths and (2) excitation of Au-NPs at particular wavelengths leads to surface charge exchange with the fluorophore (FL). The mechanism behind the enhancement is due to the opposite charge dipole moment oscillation[36]. Au-NPs have the positive charge, and the E. coli cells have the negative charge on its outer membrane. Mechanism against bacteria Gold nanoparticles are reported to have weak antibacterial activity of varying degrees compared to the other metal nanoparticles mentioned[37]. AuNPs treated S. aureus had enhanced bactericidal effect when exposed to laser energy.

**Cobalt Antibacterial properties:**

More recently, the oxide nanoparticle cobalt (III) based ligand complexes have been found to possess both antiviral and antibacterial activities[38]. A large number of reports on the antibacterial properties of cobalt complexes have appeared in the literature, with Co (II) complexes being the most studied, presumably due to their aqueous stability, availability, and case of synthesis. As the small and ultra-small fractions of CoFe2O4 NPs possess especially strong antimicrobial activity against all tested microorganisms[39].There are several methods of fabrication of small size nanoparticles[40]. Cobalt ferrite nanoparticles (Nps) fabricated by co-precipitation approach in several average sizes, in particular, 15.0, 5.0, and 1.65 nm[41]. Green synthesis process employed to prepare cobalt /cellulose Nano composites with cubic structure cobalt. This nanocomposite cobalt shows antibacterial property towards gram positive and gram negative bacterial cells[43]. In table 3(a), there are some methods of synthesis and the antibacterial effect to some bacterial cells. Antibacterial activity was measured using simple zone inhibition techniques and activity was found to be less than the control antibiotics tetracycline and kanamycin (using μg of antibiotic per unit volume). However the same complex showed no activity towards Staphylococcus aureus or the Gram-negative bacteria Escherichia coli and Enterobacter fecalis. It has been reported that the antibacterial activity of a complex is influenced by its stability. The lower stability of the amino acid complex, the greater is the

antibacterial activity. This is probably because they have more free ions in the solution, which can enhance the cooperative interaction between the metal ions and the ligands. This can explain the different antibacterial activity of the copper and cobalt complexes depending on the amino acid type. Another possibility is linked to the fact that the activity in the chelated complex, the positive charge of the metal is partially shared with the donor atoms present in the ligands and there is π-electron delocalization over the whole chelate ring. This in turn increases the lipophilic character of the metal chelate and favors its permeation through the lipoid layers of the bacterial membranes. Apart from this, other factors such as solubility, conductivity and dipole moment may also be the possible reasons for increasing this activity in the case of Bacillus cereus that free salts.

## CONCLUSION

NPs are a viable alternative to antibiotics and appear to have high potential to solve the problem of the emergence of super bacterial strain. The current in-depth review of the antibacterial mechanisms may contribute to the development of efficient antibacterial NPs and to the prevention of NP cytotoxicity. The mechanism of antibacterial activity was found to be size- and dose-dependent. It was more influential against Gram-negative bacteria. In Conclusion, standardized technique in NP fabrication should be considered for binding to the bacterial cells, which should include a cytotoxicity analysis and an inflammatory response. Advanced quality research, dedicated efforts, successful application, and commercialization of antimicrobial nanomaterial will help fulfill the need to improve the quality of life.

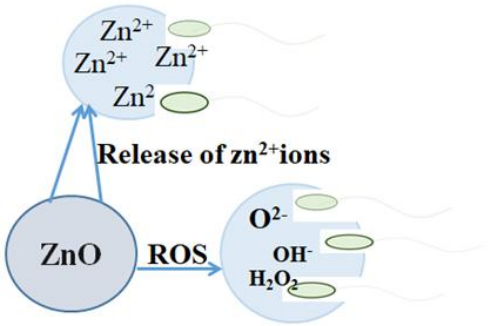


**Figure :1 (a) Mechanism of antimicrobial activity of ZnO nanoparticles**

**Table 1: Synthesis process and antimicrobial activity of ZnO nanoparticles**

| Type of ZnO, reference | Process of synthesis | Morphology | Bactericidal activity |
|---|---|---|---|
| ZnO[38] | sol-gel | Thorn like | Bacillus subtilis, Escherichia coli |
| ZnO[39] | hydrothermal method | nanorods | *Escherichia coli* |
| ZnO[23] | Biological method(plant extract) Chemical(Zinc nitrate based) | Nano-flowers | *S. aureus* , *S.marcescens, P. mirabilis, C. freundii* |
| ZnO[40] | Biological method(using plant) | Agglomeratised flower like structure | *S.aureus* ATCC 4163,*E.coli* ATCC 25922,*P.aeeruginosa* ATCC 6749 |
| ZnO nanoparticles[41] | Inframat Advanced Materials LLC (Manchester, CT) | Rod shape | *Salmonella enterica*, |

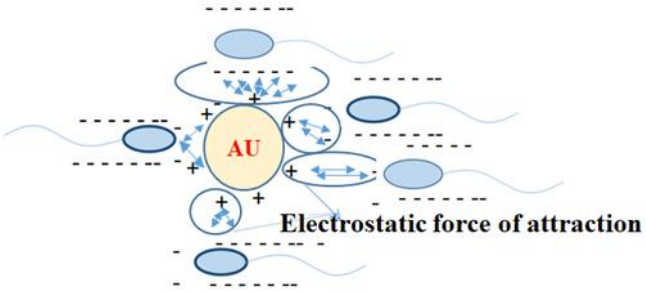


**Figure: 2(a) mechanisms of antimicrobial activity of AU-NP nanoparticles**

**Table 2. Synthesis process and antimicrobial activity of AU-NP nanoparticles**

| Type of AuNPs, reference | Process of synthesis | Morphology | Bactericidal activity |
|---|---|---|---|
| AuNPs[46] | co-precipitation protocol | spherical shape | *C. pseudotuberculosis* |
| AuNPs[28] | Green biosynthesis(plant Extract) | spherical in shape along with a few rod, triangular, truncated triangular and hexagonal shaped nanoparticles | *Escherichia coli, Klebsiella pneumoniae* |
| AuNPs[43] | Citrate stabilize | Spherical | *Bacillus Calmette-Guerin (BCG),Escherichia Coli(E.coli)* |

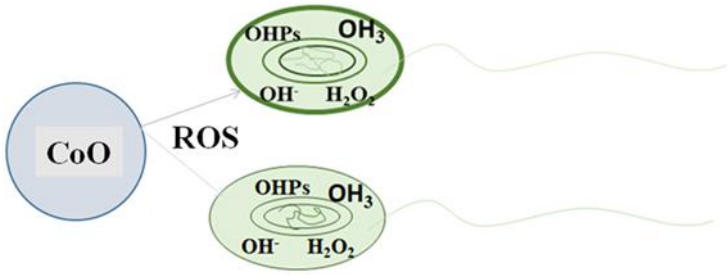


**Figure: 3(a) Mechanisms of antimicrobial activity of CoO nanoparticles**

**Table 3. Synthesis process and antimicrobial activity of Co nanoparticles**

| Type of AuNPs, reference | Process of synthesis | Morphology | Bactericidal activity |
|---|---|---|---|
| Co3O4-NPs[47] | microwave irradiation method | cubic phase | *Escherichia coli* |
| Co3O4-NPs[31] | urea-based thermal decomposition method | | *Escherichia coli* ATCC-35218, *Escherichia coli* ATCC-25922, *Enterococcus faecalis* ATCC-29212, and *Bacillus subtilis* NCTC-10400 and five Gram-negative bacteria *Staphylococcus aureus* ATCC-29213, *Pseudomonas aeruginosa* ATCC-27853, *Shigella sonnei* ATCC-11060, *Salmonella typhimurium* ATCC-13311, |

| | | | |
|---|---|---|---|
| | | | and *Proteus vulgaris* ATCC-6380)) |
| Cobalt nanoparticle[48] | Green synthesis | Cubic | *S.aureus,E.coli,A.baumannii, P.aeruginosa* |
| Co doped ZnO[36] | Chemical synthesis | wurtzite | *Escherichia coli, Vibrio cholerae* |
| Co-doped SnO2[31] | simple and cheap co-precipitation method | tetragonal shape | *Escherichia coli, Bacillus subtilis* |

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**Conflict of Interest**

The authors declare no conflict of interest.

## REFERENCES

1. Pranita D. Tamma, Sara E. Cosgrove, & Lisa L. Maragakis, Combination Therapy for Treatment of Infections with Gram-Negative Bacteria. *Clinical Microbiology Reviews* **25(3):** 450–470 (2012).
2. Capita, R. and Carlos Alonso-Calleja, Antibiotic-Resistant Bacteria: A Challenge for the Food Industry. *Critical Reviews in Food Science and Nutrition* **53(1):** 11-48 (2013).
3. Michael J. Mahan, John W. Tobias, James M. Slauch, Philip C. Hanna, R. John Collier, and John J. Mekalanos, Antibiotic-based selection for bacterial genes that are specifically induced during infection of a host.Proc. *Nat L Acad SC USA* **92:** (1995).
4. Iona K. Paterson1, Andy Hoyle1, Gabriela Ochoa1, Craig Baker-Austin2 & Nick G. H. Taylor, Optimizing Antibiotic Usage to Treat Bacterial Infections. *Scientific Reports* 6:37853: 1-10 (2016).
5. Shamsuzzaman, S.M., N.D.M.1. producing new superbug bacteria: a threat to control infection. *Bangladesh J Med Microbial* **05(01):** 1-2 (2011).
6. Peter A.L, Bacterial resistance to antibiotics: Modified target sites. *Advanced Drug Delivery Reviews* **57(10):** 1471-1485 (2005).
7. Michael A Kohanski, Daniel J Dwyer, and James J Collins, How antibiotics kill bacteria: from targets to networks. *Nat Rev Microbiol* **8(6):** 423–435 (2010).
8. Jamil, B. and Syed,M. A., Nano-antimicrobials: A Viable Approach to Tackle Multidrug-Resistant Pathogens. Springer International Publishing, Nanotechnology Applied To Pharmaceutical Technology (2017).
9. wang, L., Hu, C., Shao, L., The antimicrobial activity of nanoparticles: present situation and prospects for the future. *International Journal of Nanomedicine* **12:** 1227–1249 (2017).
10. Belousov, A.N., Nanotechnology as a New Direction in the Creation of Antimicrobial Drugs. *SAJ Pharmacy and Pharmacology*. **5(2):** (2018).
11. Ramesh, N., Prasanth, M., Shanthini, T., Gothandam, K.M., Karthikeyan S. and Bulent Bozdogan, Nano-antibiotics: A Therapeutic Future. *Nanoscience & Nanotechnology-Asia* **6:** 1-23 (2016).
12. NuritBeyth, YaelHouri-Haddad, AviDomb, WahidKhan, and Ronen Hazan, Alternative Antimicrobial Approach: Nano-Antimicrobial Materials. Hindawi Publishing Corporation Evidence-Based Complementary and Alternative Medicine 1-16 (2015).
13. Hajipour, Mohammad & Fromm, Katharina & Ashkarran, Ali Akbar & Aberasturi, Dorleta & Ruiz de Larramendi, Idoia & Rojo, Teofilo & Serpooshan, Vahid & Parak, Wolfgang & Mahmoudi, Morteza, Antibacterial properties of nanoparticles. Trends in Biotechnology 31:61-62 (2013)

14. Yael N. Slavin, Jason Asnis, Urs O. Häfeli and Horacio Bach, Metal nanoparticles: understanding the mechanisms behind antibacterial activity. *J Nanobiotechnol* **15:** 65:1-20 (2017).
15. Myths Ksenia S. Egorova and Val entine P. Ananikov, Toxicity of Metal Compounds. *Knowledge and Organometallics* **36(21):** 4071-4090 (2017).
16. Ameer Azam, Arham S Ahmed, Mohammad Oves, Mohammad S Khan, Sami S Habib1 Adnan Memic, Antimicrobial activity of metal oxide nanoparticles against Gram-positive and Gram-negative bacteria: a comparative study. *International Journal of Nanomedicine* **7:** 6003–6009 (2012).
17. Yanping Xie, Yiping He, Peter L. Irwin, Tony Jin, and Xianming Shi, Antibacterial Activity and Mechanism of Action of Zinc Oxide Nanoparticles against Campylobacter jejuni. *Applied And Environmental Microbiology* **77(7):** 2325–2331 (2011).
18. Guy Applerot Anat Lipovsky Rachel Dror Nina Perkas Yeshayahu Nitzan Rachel Lubart Aharon Gedanken, Enhanced Antibacterial Activity of Nanocrystalline ZnO Due to Increased ROS- Mediated Cell Injury **19(6):** 842-852 (2009).
19. Zarrindokht Emami-Karvani, Pegah Chehrazi, Antibacterial activity of ZnO nanoparticle on Gram-positive and Gram-negative bacteria. *African journal of microbiology research* **5(18):** 1368-1373 (2012)
20. A bdulrahman Syedahamed Haja Hameed, Chandrasekaran Karthikeyan, Abdulazees Parveez Ahamed, Nooruddin Thajuddin, Naiyf S. Alharbi, Sulaiman Ali Alharbi & Ganasan Ravi,In vitro antibacterial activity of ZnO and Nd doped ZnO nanoparticles against ESBL producing Escherichia coli and Klebsiella pneumonia.*Scientific Reports* **6:** 24312: 1-11 (2016).
21. Yunhong Jiang , Lingling Zhang, Dongsheng Wena, Yulong Ding, Role of physical and chemical interactions in the antibacterial behavior of ZnO nanoparticles against E. coli. Materials Science and Engineering C **69:** 1361–1366 (2016).
22. Ara Joea, Se-Ho Parka, Kyu-Dong Shima, Da-Jung Kima,Kwang-Hwan Jheea,Hyo-Won Leeb, Cheol-Ho Heob,Hwan-Myung Kimb,Eue-Soon Ara Joea,Se-Ho Parka, Kyu-Dong Shima, Da-Jung Kima, Kwang-Hwan Jheea,Hyo-Won Leeb, Cheol-Ho Heob, Hwan-Myung Kimb,Eue-Soon Janga, Antibacterial mechanism of ZnO nanoparticles under dark conditions. *Journal of Industrial and Engineering Chemistry* **45:** 430-439 (2017).
23. Mirzaeia, H., Darroudi, M., Zinc oxide nanoparticles: Biological synthesis and biomedical applications.*Ceramics International* **43:** 907–914 (2017).
24. Zawrah, M. F., and Sherein Abd El-Moez, Antimicrobial Activities of Gold Nanoparticles against Major Foodborne Pathogens. *Life Science Journal* **8(4):** 37-44 (2011).
25. Enrique Morales-Avila, GuillerminaFerro-Flores, BlancaE.Ocampo-García, GustavoLópez-Téllez,JohnnyLópez-Ortega,DianaG.Rogel-Ayala,andDiegoSánchez-Padilla,Antibacterial Efficacy of Gold and Silver Nanoparticles Functionalized with the Ubiquicidin Antimicrobial Peptide. *Journal of Nanomaterials* 29–41 (2017).
26. Shareena Dasari T.P., Zhang Y., Yu, H., Antibacterial Activity and Cytotoxicity of Gold (I) and (III) Ions and Gold Nanoparticles. *Biochem Pharmacol (Los Angel)* **4(6):** 1-5 (2015).
27. Jason N. Payne, Hitesh K. Waghwani, Michael G. Connor, William Hamilton, Sarah Tockstein, Harsh Moolani, Fenil Chavda, Vivek Badwaik, Matthew B. Lawrenz and Rajalingam Dakshinamurthy, NovelSynthesis of Kanamycin Conjugated Gold Nanoparticles with Potent Antibacterial Activity.Frontiers in Microbiology **7:** 1-10 (2016) .
28. MubarakAli, D., Thajuddin, N., Jeganathan, K., Gunasekaran, M., Plant

extract mediated synthesis of silver and gold nanoparticles and its antibacterial activity against clinically isolated pathogens. *Colloids and Surfaces B: Biointerfaces* **85(2):** 360-365 (2011).

29. Burygin, G. L., Khlebtsov, B. N., Shantrokha, A. N., Dykman, L. A., Bogatyrev, V. A., Khlebtsov, N. G., On the Enhanced Antibacterial Activity of Antibiotics Mixed with Gold Nanoparticles. *Nanoscale Res Lett* **4:** 794–801 (2009).
30. Enrique Lima, Roberto Guerra, Victor Lara and Ariel Guzmán, Gold nanoparticles as efficient antimicrobial agents for Escherichia coli and Salmonella typhi. *Chemistry Central Journal* **7(11):** 1-7 (2013).
31. Alireza Samavati, A.F. Ismail, Antibacterial properties of copper substitute edcobaltferritena noparticles synthesized byco-precipitation method. *Particuology* **30:** 158-163 (2017).
32. Subhasish Saha, Dharumadurai Dhanasekaran, Saravanan Chandraleka, Noorudin Thajuddin and Annamalai Panneerselvam, Synthesis, Characterization and Antimicrobial Activity of Cobalt Metal Complex Against Drug Resistant Bacterial and Fungal Pathogens. *Advances in Biological Research* **4(4):** 224-229 (2010).
33. Tomas Majtan, Frank E. Frerman, Jan P. Kraus, Effect of cobalt on Escherichia coli metabolism and metalloporphyrin formation.Biometals **24(2):** 335–347 (2011).
34. Khan, S., Ansari, A.A., Khan, A.A., Ahmad, R., Al-Obaid, O., Al-Kattan, W., In vitro evaluation of anticancer and antibacterial activities of cobalt oxide nanoparticles. *J Biol Inorg Chem* **20(8):** 1319-26 (2015).
35. Shahanavaj Khan, Anees A Ansari, Abdul Arif Khan, Rehan Ahmad, In vitro evaluation of anticancer and antibacterial activities of cobalt oxide nanoparticles. *European Journal of Biochemistry* **20(8):** (2015).
36. Alahmadi, N. S., Betts, J. W., Cheng, F. Francesconi, M. G., Kelly, S. M., Kornherr, A., Priora, T. J. and Wadhawan, J. D., Synthesis and antibacterial eff ects of cobalt–cellulose magnetic nanocomposites. *RSC Adv* **7:** 20020-20026 (2017).
37. Yanping Xie, Yiping He, Peter L. Irwin, Tony Jin, and Xianming Shi, Antibacterial Activity and Mechanism of Action of Zinc Oxide Nanoparticles against Campylobacter jejuni. *Applied And Environmental Microbiology* **77(7):** 2325–2331 (2011).
38. Mohd Farhan Khan, Akhter H. Ansari, M. Hameedullah, Ejaz Ahmad, Fohad Mabood Husain, Qamar Zia, Umair Baig, Mohd Rehan Zaheer, Mohammad Mezbaul Alam, Abu Mustafa Khan, Zeid A. AlOthman, Iqbal Ahmad, Ghulam Md Ashraf & Gjumrakch Aliev, Sol-gel synthesis of thorn-like ZnO nanoparticles endorsing mechanical stirring effect and their antimicrobial activities: Potential role as nano-antibiotics. *Scientific Reports* **6(27689):** 1-12 (2016).
39. Renata Dobrucka, Jolanta Dugaszewska, Biosynthesis and antibacterial activity of ZnO nanoparticles using Trifolium pratense flower extract. *Saudi Journal of Biological Sciences.* **23:** 517–523 ((2016).
40. Claire Bankier, Yuen Cheong, Suntharavathanan Mahalingam, Mohan Edirisinghe, Guogang Ren, Elaine Cloutman-Green, Lena Ciric. A comparison of methods to assess the antimicrobial activity of nanoparticle combinations on bacterial cells. *PLoS ONE* **13(2):** 1-13 (2018).
41. Nagarajan Padmavathy and Rajagopalan Vijayaraghavan. Enhanced bioactivity of ZnO nanoparticles, an antimicrobial study. Sci. Technol, Adv. *Mater* **9:** 1-7(2008).
42. Kumar, R., Shukla, S.K., Pandey, M., Pandey, A., Pathak,A., and Dikshit, A., Synthesis and antimicrobial effects of colloidal gold nanoparticles against prevalent waterborne bacterial pathogens. *Cogent Chemistry* **2:** 1-9 (2016).

43. Abalaka, M. E., Daniyan, S. Y., Adeyemo, S. O., Damisa, D., The Antibacterial Efficacy of Gold Nanoparticles Derived from Gomphrena celosioides and Prunus amygdalus (Almond) Leaves on Selected Bacterial Pathogens. *International Journal of Bioengineering and Life Sciences* **8(4):** 348-351 (2014).
44. Shamaila, S., Zafar, N., Riaz, S., Sharif, R., Nazir, J., and Naseem, S., Gold Nanoparticles: An Efficient Antimicrobial Agent against Enteric Bacterial Human Pathogen. *Nanomaterials* **6(71):** 1-10 (2016).
45. Justin P. Jahnke, Jose A. Cornejo, James J. Sumner, Andrew J. Schuler, Plamen Atanassov, and Linnea K. Ista, Conjugated gold nanoparticles as a tool for probing the bacterial cell envelope: The case of Shewanella oneidensis MR-1. *Biointerphases* **11(1):** 1-10 (2016).
46. Alaa A. A. Aljabali , Yazan Akkam , Mazhar Salim Al Zoubi , Khalid M. Al-Batayneh , Bahaa Al-Trad , Osama Abo Alrob , Alaaldin M. Alkilany , Mourad Benamara and David J. Evans, Synthesis of Gold Nanoparticles Using Leaf Extract of Ziziphus zizyphus and their Antimicrobial Activity. *Nanomaterials* **8(174):** 1- 15 (2018).
47. SyedKhadara, Y.A., Balamuruganb, A., Devarajana, V.P., Subramanianc, R., Kumar, S.D., Synthesis, characterization and anti bacterialactivity of cobaltdopedceriumoxide (CeO2:Co) nano particlesbyusing Hydrothermal method.*j Mater Res technol* 1-8 (2018).
48. Edreese Alsharaehn, Yasmin Mussa, Faheem Ahmed, Yazeed Aldawsari, Mohammed Al-Hindawi, Garwin Kim Sing, Novel route for the preparation of cobalt oxide nanoparticles reduced graphene oxide nanocomposites and their antibacterial activities. *Ceramics International* **42:** 3407–3410 (2016).
49. Emad Yousif, Ahmed Majeed, Khulood Al-Sammarrae, Nadia Salih, Jumat Salimon , Bashar Abdullah, Metal complexes of Schiff base, Preparation, characterization and antibacterial activity, *Arabian Journal of Chemistry* **10:** S1639–S1644 (2017) .
50. Kathryn R. Brocklehurst and Andrew P. Morby, Metal-ion tolerance in Escherichia coli: analysis of transcriptional profiles by gene-array technology. *Microbiology* **146:** 2277–2282 (2000).
51. Stanley Rosarin, F. and S Mirunalini; Rosarin and Mirunalini, Nobel Metallic Nanoparticles with Novel Biomedical Properties. *J Bioanal Biomed* **3(4):** 085-091 (2011).
52. Kumar, K.A., Meera, P., Selvi, M. A. and Dayalan, A., TRIS-(1, 10Phenanthroline) Cobalt(III)Bromidechloridehexahydrate:Synthesis,Characterization,Antimicrobial Screening And Xrd studies; *Int. J. Chem. Sci* **9(3):** 1421-1428 (2011).