

Comparative Evaluation of Antimicrobial Effects of Silver Nanoparticles with Antimicrobial Properties of Copper and Zinc

AllourVaishnavi , Keerthi Sasanka, A.K.Anjali

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Allour Vaishnavi

Saveetha Dental College and Hospitals,
Saveetha Institute Of Medical and Technical Sciences,
Saveetha University,
Chennai, India.

Email ID: 151801005.sdc@saveetha.com

Keerthi Sasanka

Lecturer,
Department of Prosthodontics,
Saveetha Dental College and Hospitals,
Saveetha Institute Of Medical and Technical Sciences,
Saveetha University,
Chennai 77 ,India.

Email ID: keerthis.sdc@saveetha.com

A.K.Anjali

Lecturer,
Department of General Pathology,
Saveetha Dental College and Hospitals,
Saveetha Institute Of Medical and Technical Sciences,
Saveetha University,
Chennai 77 ,India.

Email ID: anjaliak.sdc@saveetha.com

Corresponding author:

Dr. Keerthi Sasanka

Lecturer,
Department of Prosthodontics,
Saveetha Dental College,
Saveetha University,

162, Poonamallee High Road,
Chennai-600077, Tamilnadu.India
Email ID: keerthis.sdc@saveetha.com
Contact number: 837469110

ABSTRACT

The era of associate antibiotic resistance may be a cause for increasing concern as microorganisms still develop adaptive countermeasures against current antibiotics at an atrocious rate. In recent years, studies have reported nanoparticles as a promising difference to medical reagents owing to their exhibited activity in many medical specialty applications, as well as drug and cistron delivery, tissue engineering, and imaging. Moreover, nanomaterial analysis has diodes to report a potential relationship between the morphological characteristics of a nanomaterial and therefore the magnitude of its delivered toxicity. However, the conventional synthesis of nanoparticles requires harsh chemicals and costly energy consumption. In our research, we reviewed a total of 45 articles. The sampling data collection was done by search engines such as PubMed, Google Scholar, Cochrane, Elsevier, and various journals of Prosthodontics. The published articles were collected from the year 2005 -2020. Here, we tend to review the recent advancements in synthesis techniques for silver, copper, zinc metal nanomaterials with a spotlight on the toxicity exhibited by nanomaterials of multidimensions. The ever-increasing resistance of pathogens towards antibiotics has caused serious health issues within recent years. It's been shown that by combining trendy technologies like technology and material science with intrinsic antimicrobial activity of the metals, novel applications for these substances may well be known. per the reports, metal and metal compound nanoparticles represent a gaggle of materials that were investigated in regard to their antimicrobial effects. This review highlights the advantages of choosing every material or metal-based composite for sure applications whereas conjointly addressing attainable setbacks and also the harmful effects of the nanomaterials on the setting.

Keywords: antibacterial reagents; antibiotic resistance; drug delivery; metals; nanomaterials; nanoscale; nanostructure; synthesis; toxicity.

INTRODUCTION

Microorganisms are serious and potentially life-threatening agents, capable of promoting infectious diseases [1]. The bubonic/pneumonic plague pandemic of the ordinal century and also the transmission of virulent Asiatic cholera [2] were each sample of bacteria acting as motivativating agents for infection. The bubonic/pneumonic plague, or the Black Death, was one in all the foremost devastating illness outbreaks in human history, killing ~50 million individuals worldwide[3]. Though the etiology of the illness remained extremely arguable till recently, the gram-negative Bacilli was confirmed to cause the Black Death and later epidemics over the course of 4 centuries[4]. Pandemics of cholera, a disease caused by *Vibrio cholera*, have affected millions of people since the early 1800s. Second cholera [5] pandemic (1832) alone claimed the

lives of over 15,000 people throughout Asia and Europe. The magnitude and severity of such outbreaks left local governments ill-equipped to supply necessary aid, eventually leading to the establishment of the World Health Organization (WHO) in 1945. The WHO worked to provide local governments with vaccines, laboratory personnel training, and equipment² to mitigate the effects of outbreaks. Despite programs from the United Nations agency set in situ, outbreaks of diseases like enteric fever and scarlatina junction rectifiers lead to forceful fluctuations in morbidity and mortality rates within the twentieth century. The invention of the role of microorganism as infectious agents propelled the scientific community toward the event of artificial medicament agents.

Introduced in 1910, Salvarsan was the first antimicrobial agent to be synthesized as a remedy for syphilis. The era of antibiotics soon followed, and antimicrobial agents such as chloramphenicol, nalidixic acid, and macrolides were introduced into clinics. The introduction of antibiotics in the 20th century provided temporary relief to infectious bacterial pathogens. The emergence of antibiotic-resistant bacteria has been traced to several dynamic mechanisms of action consistent with bacterial roles against antimicrobial host defense. [6]Moreover, bacterial pathogens have also significantly evolved effective countermeasures against antibacterial agents stemming from overexposure to antibiotics, such as efflux pumps that remove the antibacterial agent before it can reach its target site and exert its effect. [7]

Methods for overcoming the emergence of these resistant strains have delved into the development of new antibiotic drugs boasting chemical diversity, such as the antibiotic daptomycin found in soil actinomycetes. [8] Additionally, identification of antibiotic-producing bacteria such as that found on the European beewolf [9] (a hunting wasp) has proven the existence of additional antibiotics from natural, previously unexplored sources. Developments in these areas, however, have not produced sufficient advancement against the rapidly increasing number of resistant bacterial strains.[10][11] Non-traditional antimicrobial agents have now been identified as promising tools against bacteria resistant to traditional antibiotic drugs. [12]

One type of nontraditional antimicrobials recently introduced was nanomaterials. Nanomaterials have been proven to demonstrate toxic effects against several bacterial strains during in vitro studies. Because of these results, nanomaterials could be promising in several biomedical applications, including drug and gene delivery, tissue engineering, and imaging techniques. [13] Additionally, these materials could be used as a vehicle for delivering a range of therapeutic agents, including drugs, pharmaceuticals, and antibodies. Paul Ehrlich first sparked the idea of developing drug delivery systems, pioneering the development of drug targeting nanoparticles, and introducing nanomaterials for possible use in the medical field.[14] This review focuses on the recent advancements made in metallic nanomaterials as antibacterial-trial agents, with a focus on their antibacterial activity based on the structure, dimension, and size of nanomaterials. Our team has rich experience in research and we have collaborated with numerous authors over various topics in the past decade [15–39].

Furthermore, the benefits of using nanomaterials of silver, copper, as well as zinc, will be discussed.

LIMITATIONS OF THE MATERIALS

Despite the massive use of AgNPs, CuNPs, and ZnNPs in commercial applications and the numerous studies regarding their bactericidal properties, there is still a significant level of controversy/uncertainty. In the following text, such points were discussed, giving particular attention to the drawbacks and limits of some methods and providing some suggestions to overcome them.

MATERIALS AND METHODS

The study setting of this research is a scoping review. The approval from the research committee was not required since it is a review. The minimum number of articles required are 20. In our research, we reviewed a total of 45 articles. The sampling data collection was done by search engines such as PubMed, Google Scholar, Cochrane, Elsevier, and various journals of Prosthodontics. The published articles were collected from the year 2005 -2020. These articles were chosen by using some keywords such as Antimicrobial effect, Nanoparticles, Metals, Antibiotic resistance, etc. After Collecting the information from the chosen articles the analysis was done and reported.[40][41][42][43][44][45]

DISCUSSION

Antimicrobial effect of Silver Nanoparticles

Silver as an antibacterial reagent can be traced back thousands of years to early civilizations when it was utilized for food preservation and production of potable water. [46][47][48] Silver was introduced into the medical field for use in wound healing and burn treatment when its antibacterial properties were discovered. [49] In the early 1940s, the era of antibiotics emerged, and silver was largely replaced by penicillin. Now as antibiotic-resistant microorganism strains still emerge and rise in variety, silver has been reintroduced as a promising material within the development of the latest bactericides.

In recent years, several studies have established the ability of silver nanomaterials to exhibit unique electronic, optical, and chemical properties.[50] Studies square measure exploring the likelihood of a relationship between chemical science characteristics of silver nanomaterials and their delivered magnitude of toxicity.[51] Shapes such as beads, rods, mats, sheets, and nanoprisms are being developed and investigated for their specific antibacterial effects. Recent studies have reported that the size and surface coating of silver nanoparticles (AGNPs) play a large role in antibacterial activity, with smaller nanoparticles observed to deliver a higher magnitude of toxicity. [52] Furthermore, a study using gene deletion mutants to identify the physiological pathways involved in the antibacterial response of gram-negative bacteria *Escherichia coli* to AgNPs techniques reported from its findings that the mechanism, in addition to the magnitude, of delivered toxicity may be strongly influenced by the physicochemical properties of the nanoparticle.[53]

Many studies have sought to establish a mechanism of action of antibacterial activity exhibited by silver in both its colloidal and ionic form. Two leading theories on the proposed mechanism

suggest 1) a disruption of membrane functionality from an interaction between released Ag^+ ions and the cell membrane and 2) extensive cell membrane damage caused by the formation of reactive oxygen species (ROS) ultimately causing damage to the cell due to oxidative stress. In brief, the first mechanism suggests that Ag^+ ions released from AgNPs can bind with thiol groups ($-\text{SH}$) of proteins and enzymes found on the cellular surface, causing destabilization of the cellular membrane and a breakdown of the ATP synthesis pathway. AgNPs may then adhere to the membrane wall, causing holes through which they can later penetrate the bacteria and interact with intracellular components or proteins containing sulfur. The second mechanism suggests that ROS, such as singlet oxygen, can be produced at the cell membrane and lead to irreversible damage to DNA replication affecting metabolic processes and cell division. As a better understanding is gained on both mechanisms, several reports suggest the first as causing the most significant damage to bacteria. This section will examine advancements in the antibacterial properties of silver nanomaterials due to different structures and their toxicity activities. [54]

Antimicrobial property of Copper Nanoparticle

The element copper has been used in ornaments, weaponry, and coinage since early into the 14th century. Copper coinage was originally developed in what is now known as Turkey and Iraq, and soon spread to Spain, Europe, and Sweden. Symbolically, copper was used to mark the beginning of womanhood, consecrate kings, and propitiate ancestors or gods. After the 1850s, copper began its use in electrical wiring. For example, copper was laid across the Atlantic as a telegraph cable in 1866 and used as telephone wire that allowed for communication across larger distances. [55] At the turn of the 20th century, copper began to be used in applications within the service activities. Since then, copper has been important in research because of its role in living organisms. A copper deficiency in the human body can lead to anemia and improper fetal development during pregnancy. On a smaller scale, it plays an important role in the transportation of oxygen during the electron transport chain and iron homeostasis. Shortly after reports identified copper as an antibacterial reagent, synthesis techniques for producing nanosized copper were developed. It has been reported that the antibacterial characteristics displayed by copper are a result of cellular damage after contact between released Cu^{2+} ions and bacteria membrane.

This section analyzes different synthesis, antibacterial properties of the structure nanoparticle, comparison of different shapes and sizes, promising composites, and toxicity properties of copper nanoparticles. Copper nanoparticles (CuNPs) were very excellent bactericide reagents because of their heat resistance and chemical stability. This could be attributed to an oversized area to volume magnitude relation, that permits CuNPs to penetrate microorganism membranes. CuNPs can be synthesized through several techniques including chemical reduction, laser ablation, sol-gel processing, and thermal reduction each resulting in CuNPs displaying varying antibacterial properties. [56]

Antimicrobial Effect of Zinc Oxide nanoparticle

Zinc (Zn) and its alloys have been used extensively in biomedical applications due to their abundance and low toxicity. These materials have shown promise in biosensing, imaging, and drug delivery due to their electrical, optical, and photocatalytic properties. Recently, the incorporation of Zn into biomedical devices and bioceramics has increased. [57] One reason for the addition of zinc into biomedical devices is its importance in several biological functions including DNA synthesis and nucleic acid metabolism and because it is known to be an important trace element in human bone. Additionally, Zn-containing nanomaterials have been reported to exhibit excellent antibacterial qualities. Although zinc has been successfully incorporated into materials using techniques, such as plasma electrolytic oxidation, the most commonly studied zinc-containing nanomaterial is zinc oxide nanoparticles.

Zinc oxide (ZnO) nanomaterials are unique in possessing semiconducting and piezoelectric properties, in addition to exhibiting biocompatible and biodegradable features. Although the mechanism through which more complex Zn-containing nanomaterials produce antibacterial effects remains largely unknown, the most supported toxicity mechanisms of zinc oxide nanoparticles (ZnONPs) are thought to result from ROS generation and Zn²⁺ release. ROS, such as superoxide anion, hydrogen peroxide, and hydroxide, can damage lipids and proteins once inside the bacterial cell membrane, while the release of Zn²⁺ from ZnONPs can disrupt important metabolic pathways. [58] Because synthesis techniques and resulting morphology of ZnO nanomaterials can impact their antibacterial properties, current research efforts are focused equally on developing novel synthesis methods and applications.[59]

Advancements in synthesizing techniques of ZnONPs include using precursors (coordination polymers and biological extracts). Using ultrasound radiation, [60]synthesized ZnONPs from two zinc (II) color-dination polymers. The simple and controlled method resulted in ZnONPs while not vital impurities and sensible crystallinity, however with nonhomogeneity in nanoparticle size.[61] Meanwhile, Thatoiet al synthesized ZnONPs mistreatment Rhizophora mangle plant extracts. The nanoparticles made from the Sonneratia apetala Rhizophora mangle plant exhibited comparatively higher bactericide capabilities, likewise as anti-inflammatory drug properties. [62]

Reports of antibacterial activity in nanomaterials have stemmed from observed biophysical interactions occurring between nanoparticles and bacteria, including cellular uptake and nanoparticle aggregation, leading to membrane damage and toxicity. In particular, metallic nanomaterials (such as silver, zinc, copper,) exhibit favorable physicochemical characteristics resulting in significant levels of antibacterial activity.

Investigations into discovering extra applications for ZnONPs have progressed considerably in dental medicine and antitumor treatments. Ciereh et al recommend ZnONP-modified acrylic glass as a promising material for dentures. By combining ZnONPs and acrylic glass or polymethyl methacrylate (PMMA), the group observed inhibition of fungal biofilm formation that could treat conditions such as denture stomatitis.[63] After several reports of ZnONPs exhibiting selective toxicity toward cancer cells surfaced, Akhtar et al, report the selective killing

of cancer cells to induce apoptosis after exposure to ZnONPs. [64–69]The group suggests induced apoptosis of human cancer cells to result from the production of the tumor suppressor protein p53. [70]

FUTURE SCOPE

This study gives a better understanding and knowledge about nanoparticles and their antimicrobial properties. Clinical trials can be conducted using Nanomaterials included in drug therapies which may help in managing several diseases with more effective medical therapies that actively work against several microorganisms. Our institution is passionate about high quality evidence based research and has excelled in various fields ([71–81]

CONCLUSION

This review has focused on the recent advancements made in metallic nanomaterials as antibacterial agents, with a focus on their toxicity and antibacterial activity based on the structure, dimension, and size of nanomaterial. Many studies on the antibacterial effects mentioned nanomaterials suggest that manipulating the physicochemical properties of the nanomaterials affects their resulting antibacterial activity. However, there is a large gap in the information on the exact mechanisms leading to these changes in antibacterial activity.

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AUTHORS CONTRIBUTION:

The authors have carried out the study by collecting data from search engines and drafted the manuscript by necessary information. They have aided in the conception of the topic, have participated in the review, and have supervised in preparation of the manuscript. The authors have participated in the study design and have coordinated in developing the manuscript. All authors have discussed the study details among themselves and contribute to the final manuscript.

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