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Conjugated silver nanoparticles as antibacterial: A mini review

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Abstract

This review discusses the antibacterial activity of silver nanoparticles and their composites. In this study, a comparative study of silver nanoparticles and conjugated silver nanoparticles was done. During this study, literature of many years was surveyed. The literature survey gave information that silver nanoparticles can be a great technology for antibacterial activity, but due to their high cost and some changes should be made to them to increase the antibacterial activity, so many types of conjugated silver nanoparticles were made. These silver nanoparticles were obtained from the interaction between two components. One can be a polymer or an organic compound that has been interacted with silver nanoparticles. The comparative study also showed that conjugated silver nanoparticles may be cheaper and better antibiotics than many commercial drugs and virgin silver nanoparticles. Looking at the future of silver-based drug in the medical world this review could be a better document for researcher or scientists.

Keywords: Bacterial; Disease; Drug; Nanoparticles; Conjugated nanoparticles; Silver.

1. Introduction

Pathogenic microbes in this source water or food may cause short-term effects, such as diarrhea, cramps, nausea, headaches or other symptoms, as well as potentially pose long-term health effects **(NRC-US, 1977; Suzzi and Corsetti, 2020).** They may pose a special health risk for infants, young children, some of the elderly and people with severely compromised immune systems. Heterotrophic bacteria are noncoliform species of bacteria that utilize an organic substance for development. Heterotrophic bacteria can be

widespread throughout a water system **(Cabral, 2010)**. The presence of heterotrophic bacteria in drinking water is not an indication that the water presents a health risk. The bacterial gastrointestinal diseases transmitted through water are cholera, salmonellosis and shigellosis. These diseases are mainly transmitted through water and food. Drinking water can be contaminated with these pathogenic bacteria, and this is an issue of great concern. However, the presence of pathogenic bacteria in water is sporadic and erratic, levels are low, and the isolation and culture of these bacteria is not straightforward. For these reasons, routine water microbiological analysis does not include the detection of pathogenic bacteria. However, safe water demands that water is free from pathogenic bacteria **(NRC-US, 1977)**.

2. Inhibition of growth of bacterial cells

The process of prohibiting, restraining, or hindering the growth of bacteria, including the inhibition of enzyme activity within the bacteria. Agents which kill cells are called cidal agents; agents which inhibit the growth of cells (without killing them) are referred to as static agents. Thus, the term bactericidal refers to killing bacteria, and bacteriostatic refers to inhibiting the growth of bacterial cells. If an antibiotic stops the bacteria from growing or kills the bacteria, there will be an area around the wafer where the bacteria have not grown enough to be visible. This is called a zone of inhibition **(Abdulla et al., 2021)**.

3. Silver nanoparticles as antibacterial agents

Silver nanoparticles (Ag NPs) are widely used for antibacterial actions. Ag NPs are less toxic towards the human cells. These NPs were synthesized by either biological method using plant extract or chemical methods. The prepared Ag NPs are characterized by the several characterization methods such as UV–Vis spectroscopy, Fourier transform infra-red spectroscopy (FTIR), X-ray diffraction (XRD), high resolution transmission electron microscopy HRTEM, and energy dispersive X-ray analysis (EDX) techniques.

For instance: **Senthil et al. (2017)** have synthesize Ag NPs using ethanolic extract of fenugreek leaves. The UV-Vis analysis at regular intervals of 1, 3, 6, 12, 24, 48 and 96 h showed a gradual increase in the absorbance values, the peak becomes intense and sharper suggested the gradual increased in the reduction of $AgNO_3$ and thus preparation of the Ag NPs. The surface plasma resonance (SPR) of Ag was indicated by the optical absorption band at 410 nm. This might be due to the stimulation of free electron in the outermost orbitals of Ag NPs **(Senthil et al. 2017)**. The color of Ag solution changes from colorless ($AgNO_3$) to green

(plant extract + $AgNO_3$) and finally to dark brown color (Ag NPs). The FTIR analysis was suggested the formation of Ag NPs having various functional groups. These functional groups might be due to the constituent phytochemical of the leave extract.

XRD analysis have shown the characteristic peaks corresponding to the planes of the FCC crystal lattice structure of Ag particles (JCPDS NO: 87-0720). XRD analysis have given the size of the particles around the 18 nm. The shape of synthesized Ag NPs was spherical ranging size from 20 to 30 nm. There is no agglomeration of the Ag NPs might be due to the encapsulation of the NPs with extract. The SAED pattern shows the well agreement to the XRD analysis. EDX analysis shows the elemental composition of Ag NPs. The prepared Ag NPs showed a significant susceptibility against E. coli as well as S. aureus. The enhancement of antibacterial activity using prepared Ag NPs can be seen from the **Table 1**.

Test organism	Crude extract (1 µL)	Silver nitrate (1 µL)	Silver NPs (1 µL)	Streptomycin (1 µL)
Staphylococcus aureus	–	5.97 ± 0.15	12.47 ± 0.31	9.47 ± 0.21
Escherichia coli	–	6.67 ± 0.25	16.27 ± 0.51	10.12 ± 0.10

Table 1: Antibacterial activity of synthesized Ag NPs against S. aureus and E. coli. ZOI was measured as millimeter ± standard deviation for three independent experiments; (–) shows no activity **(Senthil et al. 2017)**.

This activity can also be confirmed from the morphological changes in the bacterial cell membrane using SEM image. The MTT assay method was used to investigate the cytotoxicity of Ag NPs against human skin cell (HaCaT). The results of MTT assay suggested the less toxicity of Ag NPs to HaCaT cells as compared to bacteria cells. This referred the prepared Ag NPs as eco-friendly in nature.

Similarly, Ag NPs were prepared by using fruit extract of Garcinia indica, popularly known as Kokum under the optimum conditions: 1.5 mM $AgNO_3$, 1:1 ratio of $AgNO_3$ to Kokum fruit extract, pH 10, incubation of reaction mixtures at 37 °C for 24 h **(Sangaonkar et al. 2018)**. Prepared NPs have shown the antibacterial property against bacterial samples along with antioxidant property. **Kora and Sashidhar (2018)** have synthesized the Ag NPs using Gum Kondagogu (5 nm) which also showed an excellent antibacterial action by

various modes. **He et al. (2017)** has utilized sericin obtained from silkworm cocoon as a reductant for facile biosynthesis of Ag NPs. The synthesis had involved the reduction of $AgNO_3$ by the phenolic hydroxyl group of tyrosine residues of sericin. The synthesized Ag NPs had good crystalline, size distribution, and long-term stability at room temperature. Synthesized Ag NPs was efficient for the bacterial growth inhibition of S. aureus. Similarly, Ag NPs was synthesized using Phenerochaete chrysosporium (MTCC-787). Prepared Ag NPs showed the substantial antibacterial activity against Pseudomonas aeruginosa, Klebsiella pneumoniae, S. aureus and Staphylococcus epidermidis at a high dose. The synthesized Ag NPs were spherical and oval shaped and particles size were ranging between 34 and 90 nm. At 12.5 µg/ml concentration, it was non-toxic towards fibroblast cells (**Saravanan et al. 38).** Several other biologically synthesized NPs are discussed in the Literature **Ahmed et al. (2016).**

These NPs showed a remarkable antibacterial property against gram positive as well as gram negative bacterial cells. Recent research suggested that the medicinal properties of Ag NPs largely depend on the conjugated compounds and its size **(Sofi et al., 2022; Vishwanath et al. 2021)**. Several medicinal studies are available to devise behaviour of AgNPs by tuning conjugated compounds and its size **(Sofi et al., 2022; Vishwanath et al. 2021)**. Ag NPs have also been used to increase the efficiency and application of pre-existing drugs (**Sadiqa et al., 2021**). Many commercial drugs have been shown to have medicinal properties by conjugating them with Ag NPs, which exhibited better results than conventional drugs **(Sadiqa et al., 2021**; **Siddiqui and Chaudhry, 2019)**. Although, several antibacterial studies of Ag modified drugs are reported, but very rare literature review on antibacterial activities is available. This review reports the various Ag based conjugated compounds as an antibacterial material.

4. Ag conjugated compounds as an antibacterial agent

Several Ag modified compounds were utilized for the inhibition of bacterial growth. These were prepared by several methods. Some of them are discussed here.

For instance: **Delgado-Beleño et al. (2018)** have synthesized Ag selenoid NPs (Ag_2S and Ag_2Se) which shows antibacterial property against both gram-positive and gram-negative bacteria along with optical properties. The particles were loaded on the synthetic zeolite A4. NPs of Ag, Ag_2S, and Ag_2Se were shaped hexagonally, monoclinically, and orthorhombic respectively with size of around 9 nm and surface plasmon

resonance of 415 nm. The maximum adsorption spectrum for NPs were around 330 and 375 nm. **Mohammadi (2018)** has used Ag NPs to make antibacterial cotton clothes with addition of different concentrations (2, 4, and 6 g/L) of bio degradable gum tragacanth (GT) in 5% of Ag. The synthesized NPs antibacterial potency was investigated against E. coli and S. aureus. **Wu et al. (2018)** devised a technique to synthesize Ag NPs in controlled size of average sizes 2, 12, and 32 nm which showed an excellent antibacterial activity. For the synthesis of controlled size Ag NPs, reaction condition- especially pH of the system, played a vital role. The antibacterial property of synthesized NPs was determined by broth dilution and disk diffusion. **Jung et al. (2018)** has synthesized the starch coated antibacterial Ag NPs which is gaining its roots in antibacterial paper packaging. Mixture of starch which is biodegradable and acts as reducing agent, $AgNO_3$, and distilled water were ultrasonicated to make this NPs. **Shao et al. (2018)** devised a green technique for synthesis of Ag NPs which has excellent antimicrobial potential against S. aureus and E. coli. This technique requires Sodium alginate (Na-Alg) as stabilizing agent and ascorbic acid (AA) as reducing agent. This synthesis was affected was by various reaction conditions such as pH, the addition of $AgNO_3$ and AA, ultrasonication treatments on the synthesis of Ag NPs for the formation of various sized NPs. **Jalali et al. (2017)** synthesized silver magnetite nanocomposite $Co_{0.7}Zn_{0.3}Fe_2O_4$/PET/Ag which showed high antimicrobial activity and being magnetic, it can be easily separated after being used. In this technique, $Co_{0.7}Zn_{0.3}Fe_2O_4$ NPs were synthesized first and coated by the PET polymer which was later embedded with Ag NPs. The FTIR spectra of synthesized nanocomposites indicated that $Co_{0.7}Zn_{0.3}Fe_2O_4$ nanocomposite was firstly composed and functional groups appearance including carbonyl and ester groups' emphasis to covering core magnetic with PET. The synthesized Ag NPs possessed FCC symmetry.

Volova et al. (2018) synthesized bacterial cellulose (BC) composites using the strain of acetic acid bacterium Komagataeibacter xylinus VKPM B-12068 with Ag NPs which showed the wide range of antibacterial activity with utmost susceptibility to S. aureus, without causing any harm to the eukaryotic cells. The average atomic number of Ag particles in composite samples increase with increasing concentration of $AgNO_3$. BC antibacterial composites was also prepared with amikacin and ceftriaxone which showed more antibacterial activity than BC/Ag NP.

Similarly, **Zhang et al. (2018)** modified the polyester (PET) fibre using quaternary ammonium compound 2-dimethyl-2-hexadecyl-1-methacryloxyethyl ammonium bromide (DEHMA) via electron-beam (EB) irradiation process along with adsorption of $AgNO_3$.The modified sample inactivated all the S. aureus and E. coli in 10 min.

Liu et al. (2017) have prepared nano-Ag-coated polyetheretherketone (PEEK) through magnetron sputtering at varying thickness which enhanced the antibacterial activity of PEEK without causing any cytotoxicity to the mouse fibroblast cells (L929). The coated PEEK had a significant increase in surface roughness ($P < 0.05$) as the thickness of their nano-Ag coating increased. Nano-Ag coating modification had increased the water contact angle of modified samples.

Asha et al. (2017) used a facile hydrothermal method for the synthesis of Europium doped hydroxyapatite (EDA) nanorods embedded with various concentrations of ionic Ag on its surface. Its antibacterial activity was directly proportional to the concentration of Ag ions. The synthesized nanorods were found highly biocompatible to L929 fibroblast cells but were toxic to MCF-7 breast cancer cells. **Sharma (2017)** have enhanced the antibacterial activity of Ag NP by loaded onto chitosan nanocarriers which was synthesized by ionotropic gelation of Ag NP-chitosan with tripolyphosphate. The NCs posses an excellent antibacterial efficacy against both Gram negative and Gram positive bacteria causing irreparable membrane damage to bacterial cell.

Similarly, **Mokhena and Luyt (2017)** have synthesized Ag NPs using chitosan as reducing and stabilizing agent whose shapes were determined heating condition of the reaction system. The chitosan/Ag NPs was coated onto an electrospun alginate membrane to produce stable polyelectrolyte complex (PEC) nanofibre composites which showed the high antibacterial property against both gram positive and negative bacteria. **Brobbey et al. (2017)** have devised a novel method for incorporating Ag NPs into paper surface precoated with mineral pigments and plastics, using a flame pyrolysis procedure known as Liquid Flame Spray without producing any effluent. Plastic precoated paper showed comparatively more antibacterial activity than Ag NPs. The modified paper exhibit antibacterial properties against E. coli.

The mechanism of bacterial resistant properties of these conjugated materials can be understood by the **Fig. 1**. The development of these materials with anti-microbial utility is obtained through synergistic properties of the two combining materials **(Malwal and Gopinath, 2017)**.

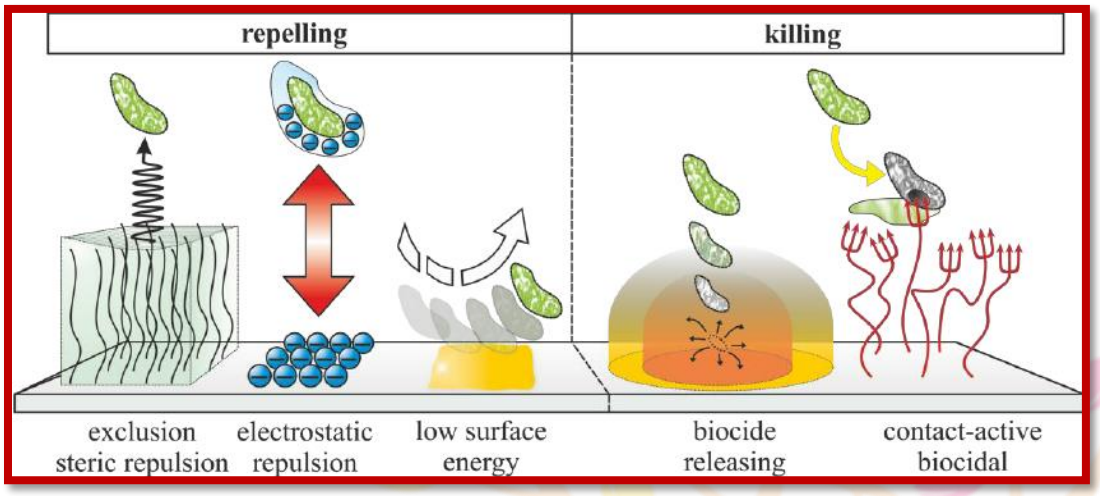

Fig. 1. General principles of antimicrobial surfaces (Adapted from **Siedenbiedel and Tiller, 2012**).

By following same idea, Abdulla et al., have prepared the economic and eco-friendly material $Ag/Ag_2O/ZrO_2/GL$ using simple preparative steps such as coprecipitation. In this method $Ag\text{-}Ag_2O\text{-}ZrO_2$ was incorporated on the Guava leave (GL) **(Abdulla et al., 2021)**. Prepared composite was characterized by several characterization techniques. In the FTIR spectrum of $Ag/Ag_2O/ZrO_2/GL$ peaks from 3560-1161 cm^{-1} were assigned for the GL and peaks 820-475 cm^{-1} which indicated for the $Ag\text{-}Ag_2O\text{-}ZrO_2$ **(Abdulla et al., 2021)**. This analysis revealed the growth of $Ag\text{-}Ag_2O\text{-}ZrO_2$ onto the GL as well as the functionalization of $Ag\text{-}Ag_2O\text{-}ZrO_2$ with by functional groups of GL. Powder-XRD spectra has confirmed the crystalline nature of prepared composite having the peaks corresponding to the Ag-Ag2O-ZrO_2/GL **(Abdulla et al., 2021).** The irregular and polygons shaped crystalline particles of various sizes were assigned by SEM image. The aggregation in the particles can also be seen from the SEM image which might be due to van der Waal forces of attraction between the NPs.

The outer layer of the particles is smooth, show some amorphously and porosity, this might be due to the organic parts of the composite. The growth of nano-sized particles of $Ag\text{-}ZrO_2$ onto the cellulosic structure of the GL can be seen from the TEM image**.** The average diameter range of the $Ag\text{-}ZrO_2$ was observed from 55 to 80 nm. Furthermore, the TEM image also indicated the presence of vacuoles of GL cell which confirmed

the cellulosic structure of the leaf. These cellular structures can be attractive sites for MB. SEAD pattern connected to the TEM image of Ag-ZrO_2/GL shows clearly visible spots which suggested that the prepared sample was nanocrystalline **(Abdulla et al., 2021)**.

The bacterial cells, *S. aureus* and *E. coli*, associated with medical infections, were used to investigate the antibacterial activities of Ag/Ag_2O/ZrO_2/GL. The agar diffusion method was adopted for examining the antibacterial activities through measuring the inhibition zone. Ag/Ag_2O/ZrO_2/GL had shown higher inhibition zone for both *S. aureus* and *E. coli* in comparison to the *Gentamycin* **(Table 2)**. The efficient antibacterial activities of Ag/Ag_2O/ZrO_2/GL might be the results of presence of Ag in the composite. The incorporation of Ag-Ag_2O-ZrO_2 enhanced the antibacterial activity of GL and stability of composite materials **(Abdulla et al., 2021).**

Table 2. Antibacterial activity of Ag/Ag_2O/ZrO_2/GL **(Abdulla et al. 2021)**.

Order	**Drug**	**Bacterial cell**	**Drug dose (µg)**	**Diameter of zone of inhibition (mm)**
1.	Gentamicin	*S. aureus*	10.0	5.0
2.		*E. coli*	10.0	5.0
3.	Ag/Ag_2O/ZrO_2/GL	*S. aureus*	40.0	7.0
4.			80.0	8.0
5.			120.0	9.0
6.		*E. coli*	40.0	3.0
7.			80.0	4.0
8.			120.0	6.0

The findings supported the greater antibacterial activity of Ag/Ag_2O/ZrO_2 incorporated GL than the essential oils of Guava leaves and its various extracts **(Abdulla et al. 2021)**. Therefore, Ag/Ag_2O/ZrO_2/GL is better antibacterial than the previously reported materials and can be good choice for economic anti-bacterial agent.

Conclusion

This study reports the study of preparation, characterization and antibacterial application of the silver and conjugated silver nanoparticles. This study suggests that silver nanoparticles are a better technology for antibacterial activity, but due to its high cost, it needed modification, so this study explains the modification in silver nanoparticles. Conjugated silver nanoparticles exhibited better antibacterial activity than virgin silver nanoparticles and their cost was also lower than virgin. The result of the study of several spectroscopic

analysis suggests that conjugated silver nanoparticles can be developed from the interaction between the functional group present in the organic surface and the silver nanoparticle, which has been proved to be an improved technology for antibacterial activity.

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