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MANAGEMENT OF MICROBIAL BIOFILM USING NANO PARTICLE: A REVIEW

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Abstract

Microorganisms create biofilms, which are surface adherent community structures. These biofilms are essential to the infection process mediated by microbes. Antibiotic resistance is another thing that biofilm spreads, which is a big worry these days. Diverse bacteria use diverse mechanisms to create biofilms, and these mechanisms often depend on the environment in which they grow as well as strain-specific characteristics. Many chemical compounds are discovered to be useful in investigating the biofilm management method. The usefulness of nanoparticles in preventing biofilm-mediated disease is the subject of the current review. Using nanoscale particles to fight microbial biofilm is one possible way to treat these persistent diseases. Recently, antibacterial agents have been delivered employing innovative nanotechnology-based antimicrobial activity in order to destroy planktonic bacteria and their biofilm structures. In the sphere of medicine, this technique is now considered developing. Antimicrobial-loaded nanoparticles alone or in combination with other materials could increase the bacterial activity of nanomaterials to prevent the formation of biofilms. These particles are reactive substances that readily penetrate the matrix, serving as a barrier to numerous antibodies. One type of nanoparticle, called AgNPs, exhibited antibacterial action by rupturing the integrity of the bacterial cell membrane, which resulted in the release of cellular content and eventual death. Additionally, polymeric-based formulations like hydrogel, polymeric microspheres, nanospheres, and smart olimer, as well as lipid-based nanoparticles like liposomes and solid lipid nanoparticles, have been used in the biofilm treatment. Additionally, research is ongoing with various metals like copper, zinc, and their

oxides. Here, we talked about the safety issues and the promise of metal oxide nanoparticles. The pathogens are effectively killed by NPs without endangering other cells or having any negative effects on living cells.

Key Words: Antimicrobial, colonize, nanoparticles, antibiofilm, antibacterial, nanospheres, microspheres**.**

Introduction

Any syntropic organization of microorganism that form at the surface of the microbial cells is referred to as a biofilm (Al-Wrafy et al. 2022). A thick layer of Extracellular Polymeric Substances (EPS), which is a polymeric combination of extracellular polysaccharides, proteins, lipids, and DNA and serves as a matrix to hold the cells together, surrounds microbial populations in biofilms. Biofilms are three-dimensional biopolymer structures with various heterogenous layers that resemble water and transport routes. Biofilm formation which is the primary cause of chronic infections and other illnesses connected to health care, is vitally associated to multidrug-resistant (MDR) bacteria (Morris and Cerceo et al. 2020). Furthermore, germs that are discharged from biofilms might result in a variety of infections in different locations. The main strategy for preventing medical equipment infection is to prevent biofilm formation [Tran et al. 2020]. In biofilm formation, there are five stages which are as follows:

1. Initial attachment [Attachment]
2. Irreversible attachment [Adhesion]
3. Maturation I [Proliferation]
4. Maturation II and
5. Dispersion.

Antibiotic concentration is typically required to eradicate floating types of bacteria. According to E. Paluch et al. (2020), the primary function of quorum sensing (QS) in cells is to reduce biofilm formation and hence prevent the synthesis of virulence factors. Compared to planktonic bacteria, biofilm bacteria—like E. Coli, Staphylococcus aureus, Enterococcus faecalis, and others—are hidden from the immune system and inflict local tissue damage before emerging as acute infections (Wright et al. 2022).

It is thought that using nanoparticles to cure bacterial biofilms is fortunate. It uses an effective method to break down the growth of biofilms. Nanoparticles' surface P light scattering gives them a clear advantage over the majority of materials. Thankfully, planktonic and biofilm-forming antibiotic-resistant bacteria can now be eliminated with the development and commercialization of antimicrobials based on nanoparticles. Copper nanoparticles, zinc oxide nanoparticles (ZnO NPs), titanium dioxide nanoparticles (TiO_2 NPs), iron oxide nanoparticles, and silicon oxide nanoparticles are a few examples of metal nanoparticles that may be used to produce antimicrobial activities and effects (Pan et al. 2021).

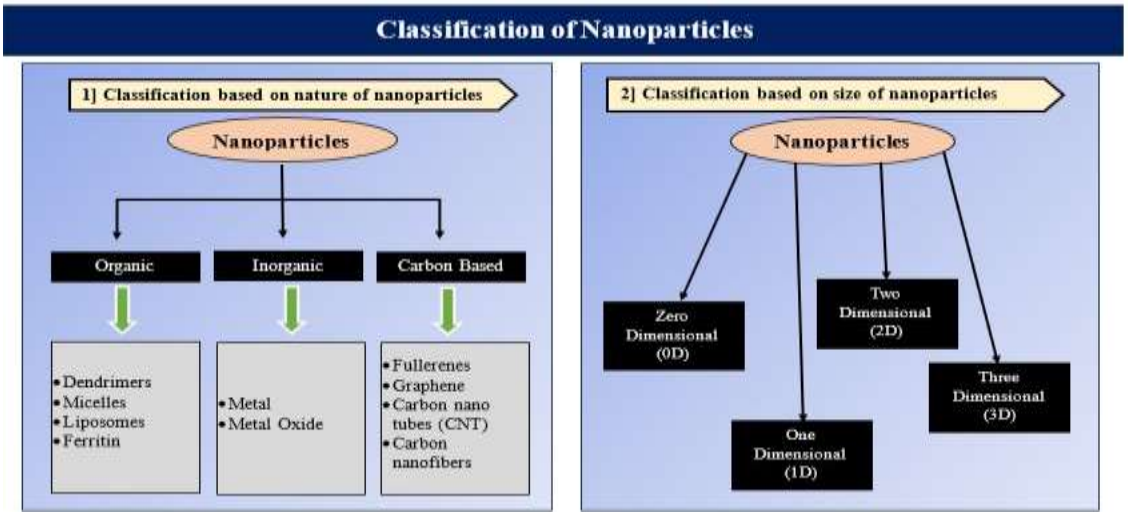

Figure 1: Classification of Nanoparticles

NPs are optimistic about the use of numerous medicinal treatments to treat bacterial infections brought on by various types of germs, as well as antibiotic resistance. As a result, interactions between NPs and antimicrobial agents can resolve medical treatments, maintain microbial agent concentrations, reduce cytotoxicity, and serve as a unique way to avoid biofilm formation.

Formation of Bacterial Biofilm

Biofilms can develop on living or nonliving surfaces and are frequently seen in the outdoors, in industry, and in healthcare facilities. Cellular identification of specific or general surface attachment sites is one of many processes that cause microbes to develop a biofilm. When the bacterial cell first touches the surface, it adheres and can readily separate itself from the surface, which is frequently reversible [Figure 2]. Over time, fimbriae and other adhesion components help the cells stick securely to the surface, making the connection irreversible (Al-Wrafy et al. 2022). For this reason, this process is known as the adhesion stage.

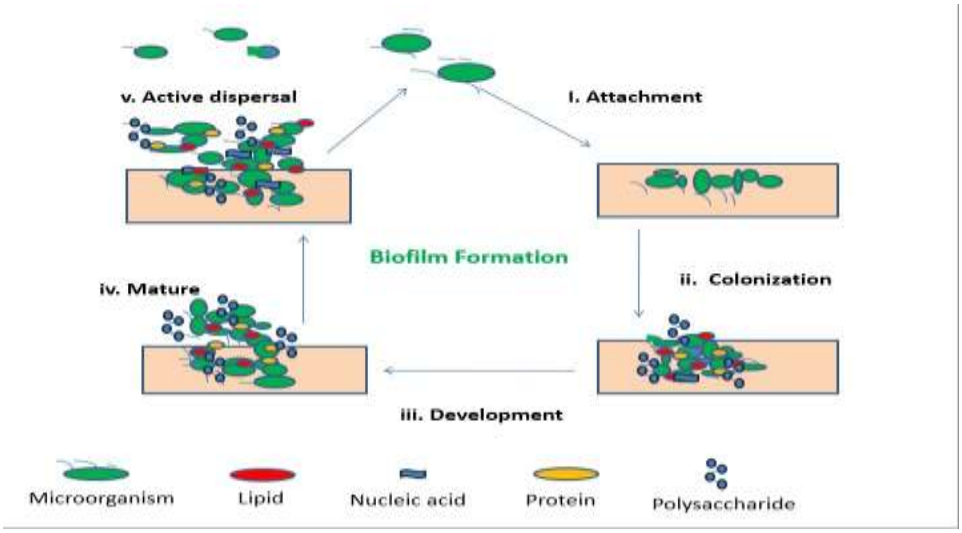

Figure 2: Formation of bacterial biofilm

(I) Bacterial cell attachment onto the surface
(ii) Cells become irreversibly attached.
(iii) Bacterial proliferation and EPS secretion
(iv) Biofilm formation and maturation
(v) Biofilm dispersal and mobility of planktonic cells.

Reversible attachment, which is sometimes aided by bacterial adhesive structures, is the first step in formation. The production of EPS leads to reversible attachment. In order to occupy new niches in the environment, the bacterial cells can eventually break loose from the mature biofilm (Muhammed et al. 2020). They finally develop into a captured organised structure. While Gram-negative bacteria, such as Escherichia coli and Pseudomonas aeruginosa, use AHL as an auto inducer, Gram-positive bacteria, such as Staphylococcus aureus and Bacillus anthracis, use processed oligopeptides for communication (Sahli et al. 2022). The intricate 3D biofilm structure of P. aeruginosa is supervised by rhamnolipid bio-surfactants.

Biofilms: An Infectious Agent or not

More than 80% of bacterial infections that are persistent and recurrent in humans are caused by bacterial biofilm. While they remain latent and unnoticed by the human immune system, they may cause local tissue damage and subsequently lead to an acute infection. These alterations also increase the bacteria's resistance to antimicrobial therapy by inactivating the antimicrobial targets or lessening the requirements for the cellular function that the antimicrobials interfere with. It is commonly known that biofilms play a role in infectious endocarditis (IE). Most of what we know about the patho-physiology of endocarditis including biofilms comes from research conducted on animals, mostly on rabbits (Vestby et al. 2020).

In hospital settings, biofilms assist bacterial cells in growing more resistant to various treatments. Antibiotic resistance among bacteria in biofilms exceeds that of planktonic bacteria by a factor of up to 1000. The existence of biofilm has been associated with disease prognosis and austerity, such as in chronic rhinosinusitis. Additionally, it has been established that these biofilm-mediated mechanisms play a role in the development and/or progression of some malignancies, including CRC (colorectal cancer or colon cancer), which originates from the rectum or colon. Biofilms may also serve as a habitat where several environmental problems that primarily affect human health arise (Schulze et al. 2021). These problems include the formation of numerous impediments collect various bacterial species and numbers of controlled settings. The majority of known human illnesses, according to the National Institutes of Health (NIH) in the USA, are caused by biofilms. Because they can corrode metal surfaces as well as those of tissue implants and prosthesis, biofilms are dangerous and an infectious agent. There are also some neutral biofilm phases in the environment. The environment and human health are not harmed or helped by such kind of biofilm.

Importance of Biofilm prevention

Humans should be concerned about biofilm formation in healthcare because it increases morbidity and death and costs in the healthcare system a lot of money. Microbe adherence is inhibited by extracellular polymeric compounds that biofilms secrete.

Biofilms are frequently more resistant to antibiotic treatment, which occasionally creates a severe health risk. The interaction of bacteria with the surface of biofilms has significant effects across a wide range of fields, including the transmission dynamics of numerous illnesses and disorders (Zheng et al. 2018).

In addition to causing financial losses, biofilms have also resulted in technical failures in the water system, cooling towers, heat exchangers, etc. Additionally, it raised the danger of infection in the medical industry. By expanding inside the mouth cavity, it can harm people's health. Regular disinfection may be used to prevent it. The saying "Prevention is better than cure" is well-known. Therefore, biofilm prevention is crucial in the environment and numerous fields today. Reduce the amount of bacterial contamination in the environment by inhibiting the production of biofilms.

Different strategies for harmful Biofilm prevention

There are several methods for preventing the production of biofilms, which are broken down into different categories. The formation of biofilms can also be avoided by coating with nanoparticles like silver nanoparticles, antioxidant nanoparticles, etc. The antibiotic used to treat biofilms should be ethically chosen based on its sensitivity and ability to effectively pass through the biofilm matrix (Wu et al. 2015).

Some strategies are as follows:

- **Changing abiotic surfectants:** The initial step in the creation of a biofilm is surface attachment. The most popular method for enhancing surface smoothness and preventing microbial adhesion is thermal cycling treatment. Another method to stop the growth of biofilms is ultraviolet radiation. When the surface free energy (SFE) of a material denatures it, also known as coating surfaces, can coat plasma proteins to change the SFE and prevent the attachment and formation of biofilm at a specific type of species. It is simple to synthesize and alter this procedure. It is the primary biofilm control system both now and in future (Yin et al. 2022).

- **Inhibition by Quorum Sensing**: One of the signalling pathways that regulates the formation of biofilms is quorum sensing (QS). N-acyl homo serine lactones (AHLs) are signalling chemicals that many bacteria, especially Gram-negative bacteria, use during quorum sensing to control their population density and to enhance swarming motility. These signaling molecules are created by LuxI synthase, a secondary metabolite product, and differ in length and acyl side chain substitutions. The Australian macroalga Dilseapulchra produces natural furanone, which is the source of the synthetic halogenated furanone molecule. This substance has the ability to hinder both bacterial signaling and swarm cell movement. By interacting in a competitive manner with the receptor, AHL molecules influence how potential regulatory proteins interact with it of its putative form (Mochado et al. 2020).

- **Inhibition of stringent response by Bacteria:** Guanosine tetraphosphate and guanosine penta phosphate, or (p)ppGpp, are alarmones that bacteria create in response to stress. The Re1A enzyme makes these compounds from GTP and GDP. By a particular mechanism, it can influence the production of biofilms. Two enzymes typically control

the metabolism of (p)ppGpp, and the concentration of (p)ppGpp can have a variety of impacts in biofilms. The following two enzymes are:

1. (p)ppGpp-synthetase/hydrolas**e**
2. RelA with dual function and the small alarmone synthetase.

- **Dispersion of extracellular polysaccharide substance of biofilm by enzymes:** The bacteria are protected against many antibiotic drugs by the Extracellular Polysaccharide Substance (EPS) present in the biofilm. Because of the EPS disruption, these chemicals would be exposed to the released and surviving biofilm cells. There are enzymes like polysaccharide lyases and DNAses that can harm exo polysaccharides. DNase I and dispersin B are the two primary enzymes that may act as anti-biofilm agents (Han et al. 2017).

- **Applying external forces**: The most crucial role in preventing the formation of the bacterial biofilm is played by a number of physical and metabolic effects. Some physical processes, such as ultrasonic elimination, provide forces that might cause biofilm dispersion at the dispersion stage of biofilm formation. According to Yin et al. (2022), high velocity spray and photothermal therapy are also utilized to destroy biofilm. Phage lysins, degradative enzymes, and microbial metabolites are some significant biochemical techniques that can eliminate EPS by separating the bacteria and eliminating the biofilm.

- **Uses of various Nanoparticles:** The best tool for preventing the development of biofilms is a nanoparticle. Conventional antibiotics along with different killing mechanisms are typically used in traditional methods of battling biofilms. Antibiotics' bioavailability and targeted administration can be enhanced by NPs. Different NP formulations are treated in order to either stop, disrupt**,** and suppress biofilm infections caused by bacteria, or to disperse them. The biofilm matrix may be damaged by magnetic iron oxide nanoparticles, which would eradicate the biofilm. It has been discovered that polymeric nanoparticles have natural anti-biofilm capabilities. Different organic and inorganic substances that have some inherent antibiofilm capabilities can be converted into nanoparticles (Benoit et al., 2015).

Mechanism of action of Nanoparticles for Biofilm prevention

The movement of NPs to the biofilm-fluid interface, adhesion to the biofilm surface, and migration inside the biofilm are some examples of the several stages of the interaction between NPs and biofilm. The NPs' physiological properties control how they interact with the biofilm components on the bacterial surface as well as in the EPS matrix. Only very brief time periods allow NPs to maintain their original state in any biological setting. The degree of particle uptake, the specificity of connection with the biofilm matrix, and the interactions with bacterial cells are all determined by these features and interactions. The surface characteristics of macromolecules are changed by a complicated combination. Once nanoparticles (NPs) cross the biofilm barrier, the Extracellular Polymer Matrix (EPM) controls their initial adhesion to the biofilm surface (Shkodenko et al. 2020). Different ion concentrations can be found in the water-containing pore region of the EPM. Organic and ion molecules pass via these pore spaces and diffusely enter the biofilm.

A deep invasion into the biofilm may result from NPs' association with EPM. Diffusion of NPs then took place inside the biofilm based on its size and pore structure. On the other hand, it is influenced by a variety of variables, including water channels, charges, hydrophobicity, ions, gradient, and many more. Reactive oxygen species (ROS) as well as hydroxyl, epoxy, and carbonyl functional groups are also present in the nanosheets of GO and its derivatives [Figure3].

Following completion of the GO connection with the bacterial cell membrane, GO permits phospholipid content has to be withdrawn through the membrane (Thambirajoo et al. 2021). After a specific number of hours, the effects of GO diminished and there was no longer any antibacterial action against the bacterial strains.

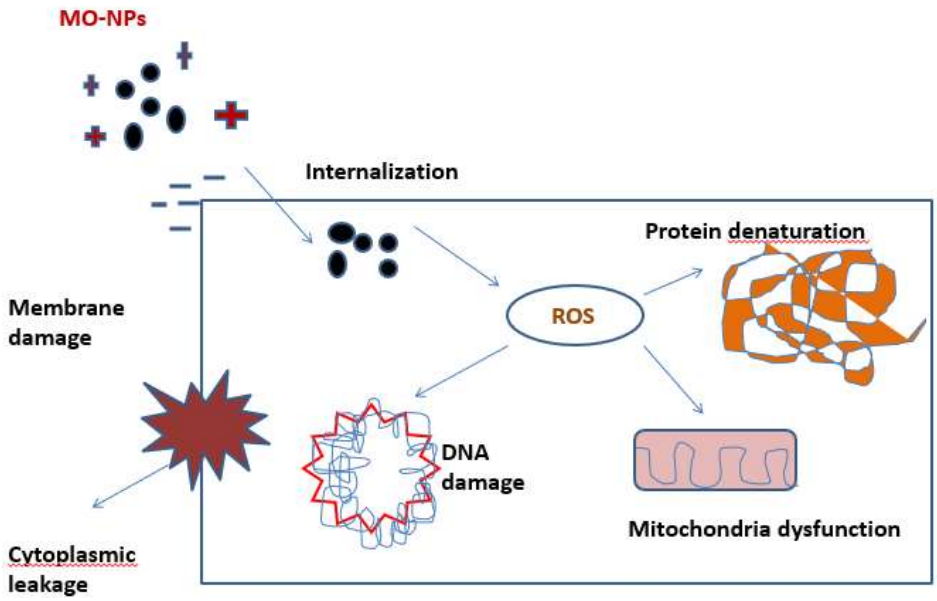

Figure 3: Antimicrobial activity of the metals and metal oxide Nanoparticles

Nanoparticles for the treatment of biofilms

Recent research demonstrates how effective nanoparticles are at treating biofilms. It is thought to be a useful tool for treating bacterial biofilms. Globally, chronic infections have placed a significant strain on healthcare systems. Metallic nanoparticles (NPs), which are comprised of lipids, silica, and polymers, have antibacterial properties. NPs are anticipated to shield antimicrobial drugs from enzymes that deactivate them, prevent NPs from attaching to EPS components, and do so in a controlled way to reduce the likelihood of systemic side effects improve the effectiveness of antimicrobials (Sondermann et al. 2014). It also aids in the treatment of oral biofilm. To increase a drug's water solubility inside bacterial cells, it can have a direct bactericidal effect. The complicated antimicrobial mechanism of action may defeat the most prevalent bacterial resistance mechanism through the interaction of the biofilm matrix (Benoit et al. 2015). Some metal oxide nanoparticles have various functions for preventing biofilm, including the following:

In S. aureus, ZnO-NPs aid in reducing the hydrophobicity of the cell surface, which is reported to have a negative impact on the ability of bacteria to form biofilms. In comparison to untreated control S. aureus, bacteria exposed to ZnO-NPs showed a substantial reduction in blood hemolysis (Abdelghafar et al. 2022).

TiO_2-NPs may lessen bacterial cell density and prevent the development of biofilms. The main method for destroying biofilms is a ROS attack (Mathur et al. 2017). A concentration-dependent

reduction in viability has been a key finding in studies on the toxicology of TiO_2-NPs towards anaerobic bacteria in prudential implants in a variety of animals.
Iron oxide nanoparticles are excellent at preventing the growth of biofilms on a variety of surfaces covered with biomaterials and polymers. These brush coatings can only stop adhesion; they cannot eradicate any existing bacteria. After reacting with hydrogen peroxide, Fe_3O_4-NPs release Fe^{2+} ions, which lead to the production of ROS (Shkodenko et al. 2020).
The following NPs can be grouped according to the decreasing strength of their antibacterial and antibiofilm properties: CuO-ZnO-MgO-TiO_2-Fe_3O_4-Al_2O_3.A nanomaterial has been activated into a more active species for dissolving bacterial biofilms by using a magnetic field, light, or the pH of the microenvironment.

Conclusion and Future perspectives

Clearly, biofilm infections are becoming a health concern. Since they are reactive substances, nanoparticles can easily penetrate the matrix, which serves as a barrier to many antibiotics. More information on the mechanism regulating biofilms can be gleaned from the interaction between NPs and biofilms. CuO and ZnO NPs are the most important NPs overall, and Fe_3O_4, TiO_2, and MgO NPs are less effective at removing biofilm. NPs have antimicrobial activity through a variety of mechanisms specific to each one, including their sizes, shapes, properties, morphologies, electric or magnetic charges, and surface coatings conjugated to intensify the antimicrobial effects against the growth of microbes and prevent the formation of biofilms. Studies on NPs could provide some light on how to minimize biofilm formation and manage infection prevention, diagnosis, and treatment.
This efficacy was dependent on the concentrations used in the trial as well as the individual or combination activity of the antibacterial drugs. Biological syntheis of AgNPs with strong antibacterial and antibiofilm activity is safer and more beneficial. Due to the presence of biofilm development, it has advanced to meet unmet clinical problems by infectious agents to cure. The development of novel antimicrobial medications has now been made possible thanks to the synthesis of NPs from a variety of sources. In order to reduce the cost of production, more research is being done on human cells, and environmentalists are assessing the toxicity of the impacts of using this nanotechnology over an extended period of time. As a result of information pointing to nanotechnology as a potential strategy is
carefully and successfully combating biofilm.

Conflict of Interest

Authors declare no competing interest.

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