Green Nanoparticles as Antibiofilm: A Review

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Abstract: Biofilms formation is one of the main reasons for bacterial infections. Microorganisms protect themselves from antibiotics by creating a biofilm barrier. Recent studies have proved that nanoparticles, because of its distinct properties, gained a tremendous medical science approach. Nanoparticles are very promising for drug delivery because of their size having less than 100nm. The main reason for antibiotics delivery to the respected site is their bulk size. This problem can be solved with the help of nanoparticles. Since nanoparticles’ chemical synthesis is a hazardous and highly energy consuming process, now a day’s environment-friendly approach, that biological synthesis of nanoparticles is given more importance. In this review, it was provided an overview of biofilm-mediated infections and nanoparticle application towards biofilm-mediated infections.

Keywords: antibiotic; bacteria; biofilms; nanoparticle.

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1. Introduction

Biofilms are groups of microbes surrounded by a matrix secreted by residing microbes to protect themselves from harsh environmental conditions [1]. Several studies reported that more than 80% of bacterial infections are caused by biofilm formation [2]. When biofilms are synthesized on microbes, it gets changed physiologically; it increases microorganisms’ lifespan and microbial growth [3]. These biofilms interfere with antibiotics with a microorganism; it protects microorganisms from antibiotics as it doesn’t allow antibiotics to reach the microbial surface [4]. The management of biofilm-mediated infections is a big challenge for scientific groups. Hence, several research has been done to develop effective antibiotics and regulate biofilm-mediated infections. In recent years importance is given to nanotechnology because of its solubility [5], highly reactive, and easy penetration into the matrix, which is the main barrier for many antibiotics [6]. Apart from antibiofilm activity, nanoparticles also have many medical applications, such as the delivery of drugs [7], for dental and medical implants [8], for cancer therapy [9], treatment of burn wound infections [10], antibacterial [11], tissue repair [12], cell labeling [13], cell targeting immunoassays[14], detoxification of biological fluids[15], magnetic resonance imaging [16]. To be called a particle as Nano, the particles must be less than 100nm in one dimension [7]; in atmospheric science, particles less than 100 nm are called ultrafine particles. Most of the atmospheric nanoparticles are usually less than 50 nm [17]. Numerous studies on Nanoparticles report that nanoparticles have been recognized as an excellent contender to fight against biofilms with their proven toxicity against microorganisms [10,11]. Synthesis of nanoparticles from chemicals is toxic, hence biological synthesis of nanoparticles is preferred as they are cost-effective, environmentally friendly, and have the least maintaining cell culture [18].
2. Biosynthesis of nanoparticles

Nanoparticles can be synthesized by various chemical, physical and biological methods. In chemical synthesis of nanoparticles, hazardous solvents, chemicals, and toxic reagents are used, and they are highly energy-consuming processes [19]. Hence, in recent years, importance is given to nanoparticle synthesis's biological method because they are simple, clean, low-cost, environmentally friendly, non-toxic, reliable, safe approach [20], and act as both stabilizing and reducing agent [21]. Biological synthesis of nanoparticles can be achieved using bacteria, fungi, viruses, algae, and plants [22].

3. Synthesis of nanoparticles by bacteria

Many procedures are available for bacterial intracellular and extracellular biosynthesis of nanoparticles; some of the nanoparticles synthesized from bacterial organisms are listed in Table-1. among these, much importance is given to the extracellular bacterial synthesis of nanoparticles because it eliminates the downstream processing steps that are required for the recovery of nanoparticles in intracellular methodologies, it also prevents aggregation of nanoparticles. It helps them to stay stable for a long time [23].

<table>
<thead>
<tr>
<th>Bacterial organism</th>
<th>Nanoparticles synthesized</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em> [24]</td>
<td>Silver</td>
</tr>
<tr>
<td><em>Pseudomonas debctionensis</em> [25]</td>
<td>Silver</td>
</tr>
<tr>
<td><em>Bacillus methylotrophic</em> [26]</td>
<td>Silver</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em> [27]</td>
<td>Gold</td>
</tr>
<tr>
<td><em>Pseudomonas stutzeri AG259</em> [28]</td>
<td>Silver</td>
</tr>
<tr>
<td><em>Lactobacillus</em> [29,30]</td>
<td>Titanium, silver</td>
</tr>
<tr>
<td><em>Bacillus subtilis</em> [31]</td>
<td>Silver</td>
</tr>
<tr>
<td><em>Enterobacter cloacae</em> [32]</td>
<td>Silver</td>
</tr>
<tr>
<td><em>Klebsiella pneumonia</em> [33]</td>
<td>Selenium</td>
</tr>
</tbody>
</table>

4. Synthesis of nanoparticles by algae

Algaes are a rich source of biologically active compounds and antioxidants like polyphenols, bromophenols, polysaccharides, photosynthetic pigments, proteins, vitamins, fatty acids glycolipids. [34]. Since polyphenols and biomolecules are present in the algae acting as a reducing agent, they are an excellent biological system for synthesizing nanoparticles. In Table-2, we can see examples of some algae synthesized from nanoparticles.

<table>
<thead>
<tr>
<th>Algae</th>
<th>NPs Synthesized</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Sargassum wightii</em> [35, 36]</td>
<td>Gold, silver</td>
</tr>
<tr>
<td><em>Turbinaria conoides</em> [37]</td>
<td>Gold, Silver</td>
</tr>
<tr>
<td><em>Laminaria japonica</em> [38]</td>
<td>Silver</td>
</tr>
<tr>
<td><em>Stoechospermum marginatum</em> [39]</td>
<td>Gold</td>
</tr>
<tr>
<td><em>Sargassum muticum</em> [40, 41]</td>
<td>Iron, Zinc oxide</td>
</tr>
<tr>
<td><em>Padina pavonia</em> [42]</td>
<td>Silver</td>
</tr>
</tbody>
</table>

5. Nanoparticle synthesis by plants

Many nanoparticles synthesized using plant extracts [Table-3]. Because plant extracts are one of the best biological methods over other biological processes. It eliminates the elaborate process of maintaining cell cultures, and plant systems are also suitable for large-scale nanoparticle synthesis [43]. During secondary metabolism, active compounds secreted by plants helps to heal infectious disease. Ethanol and Methanol extracted from plants are
potent organic compounds in treating biofilm. [44]. Nanoparticles are synthesized using different parts of the plant. Examples of the plants used for the synthesis of nanoparticles can be seen in Table 3.

<table>
<thead>
<tr>
<th>Plants</th>
<th>Nanoparticles synthesized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panax ginseng [45]</td>
<td>Gold and silver</td>
</tr>
<tr>
<td>Cinnamomum camphora [46]</td>
<td>Gold and Silver</td>
</tr>
<tr>
<td>Helianthus annuus [47]</td>
<td>Gold</td>
</tr>
<tr>
<td>Tamarindus indicus [48]</td>
<td>Gold</td>
</tr>
<tr>
<td>Aloe vera [49]</td>
<td>Gold and Silver</td>
</tr>
<tr>
<td>Ulva lactuca [21]</td>
<td>Zno</td>
</tr>
<tr>
<td>Dioscorea bulbifera [50]</td>
<td>Ag</td>
</tr>
<tr>
<td>Drosera binata [51]</td>
<td>Silver</td>
</tr>
</tbody>
</table>

6. Nanoparticles as antibiofilm

Biofilms are aggregates of bacteria growing together in a community surrounded by a protective and adhesive extracellular matrix of exopolysaccharides, extracellular DNA [eDNA], and proteins [52]. These are a thick layer of organisms that aggregate to form a colony. This colony formation is the survival strategy employed by bacteria in the environment to develop resistance to antibiotic treatment [53]. Biofilms are often associated with plant disease and responsible for bacterial infections; biofilms’ formation appears to be an essential factor in the disease cycle of bacterial pathogens in plants [54]. In plants, biofilm forms on different tissues, including leaves, stems, vasculature, seeds, and roots [55]. Symptoms produced by vascular pathogens because of biofilm formation are wilting and scorching of leaves [56]. It also contributes to the virulence of phytopathogenic bacteria through blockage of xylem vessels [57]. Biofilm formation in a particular host depends on developing plant immune response upon contact with the bacterial pathogen. In some plants, it also depends on key molecules responsible for the enhancement of immune response. [58]. Hence the number of research has been done towards the development of antibiofilm treatment. The essential strategies being developed against biofilms are quorum sensing inhibitors [QSIs], bacteriophages, enzymes, surfactants, nanoparticles [NPs], antimicrobial photodynamic therapy [APT], ethnopharmacology, and diguanylatecyclase [DGC] inhibitors [59]. Nanoparticles showed novel antibiofilm activity over other organic antibiofilm agents because of its unique chemical and physical properties, which are different from their bulk particles [59]. They disturb biofilm integrity by interacting with EPS proteins and lipids biofilms [60].

Since nanoparticles are smaller and reactive, they easily penetrate the biofilm matrix and cell membrane. When these particles penetrate the biofilm cell membrane, it damages cell structure and alters its physiology; this protein enzyme, polysaccharides, and lipids present in the matrix get rupture. On interaction with microbes, nanoparticles generate Reactive oxygen species that damage cell envelope cell membranes and biomolecules [61]. There is evidence that many natural elements from plants [62] and nanoparticles extracted from plants have antimicrobial and antibiofilm activity [63]. There are different strategies to prevent each stage of biofilm formation like Anti-adhesion agents, which is used to prevent the attachment of bacteria onto the surface. [64-67]. Nanoparticles also help to prevent the formation of biofilm at the initial stage itself [21]. Microcolony formation and biofilm maturation, lytic phages, EPS-degrading enzymes, and nanoparticles help prevent biofilm formation [21,68,69]. Nanoparticles extracted from plant sources showed toxicity against bacterial biofilms both during light [95%] and dark conditions [80%] [21]. As plant extract is also one of the strategies in eliminating biofilm activity, its reduction activity on biofilms is lesser than nanoparticles.
extracted from the same plant source [21]. For example, the extract from *U. lactuca*, which is edible green seaweed widely present in marine environments worldwide, shows the antibiofilm activity. However, it shows less reduction in activity when compared to nanoparticles extracted from it. In recent years, NPs [71-74] have become a noble antibiofilm tool because commercially available antibiotics [75-79] are losing their efficacy to treat biofilm-mediated infections.

2. Conclusion

Biofilms reside on microbes is the main reason for the cause of infectious disease. Biofilms protect microorganisms by preventing the entry of antibiotics into microorganisms. Further, it also increases microorganisms’ life span and increases the microorganism's persistence period inside the host. A nanoparticle, because of its small size and high reactivity, helps penetrate the matrix, which is the main barrier for many antibiotics. Since commercially available antibiotics are losing their efficacy, Nanoparticles has become an efficient antibiofilm tool for treating biofilm mediated infections. Hence in recent years, green synthesized nanoparticles have opened a new site in the synthesis of the antibiofilm agent.

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Conflicts of Interest

The authors declare no conflict of interest.

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