Chapter 7

Algal Nanoparticles: Synthesis and Biotechnological Potentials

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Abstract

A nanoparticle can be defined as a small object that behaves as a whole unit in terms of its transport and properties. Nanoparticles are sized between 1 and 100 nm in diameter. Nanoparticles can act against the microbes in multiple ways, and the microbes are less likely to develop resistance against nanoparticles because it requires multiple gene mutations. The large surface-to-volume ratio of nanoparticles, their ability to easily interact with other particles, and several other features make them attractive tools in various fields. Nanoparticles are widely used various fields such as electronics, cosmetics, biomedical, and biotechnology. Nanoparticles can be synthesized by physical methods such as attrition, pyrolysis, and using some wet chemical methods. The physical and chemical methods have various drawbacks such as high cost of production, require high energy input and generation of toxic by-products. To overcome this, several biological methods are employed in the synthesis of nanoparticles. The biological methods are generally cost effective, nontoxic, and ecofriendly. This chapter focuses on the methods involved in algal-synthesized nanoparticles and its applications.

Keywords: Nanoparticles, Green synthesis, Antibiotic activity, Antitumor, Antibiofilm

1. Introduction

Nanotechnology is a vibrant and developing area of science, engineering, and technology accomplished at the nanoscale level. The products of nanotechnology are nanoparticles or

nanomaterials (NPs), lying in the range of 10^{-9} m and having dimensions of 1–100 nm. NPs are categorized into three types: natural nanoparticles, incidental nanoparticles, and engineered nanoparticles [1]. The large surface-to-volume ratio of nanoparticles, their ability of easy interaction with other particles, and several other features make them as an attractive tool in various fields. NPs are widely used in electronic, cosmetic, biomedical, and biotechnological applications. The efficient crystallographic and physiochemical properties of NPs make nanotechnology as an excellent area to focus. The synthesis of NPs can be achieved by some physical methods and chemical methods. The traditional and commonly used method for nanoparticles synthesis is wet method. In chemical synthesis, nanoparticles are grown in a liquid medium containing various reactants particularly reducing agents such as sodium borohydride [2], potassium bitartartarate [3], methoxypolyethylene glycol [4], or hydrazine [5]. Some stabilizing agents such as sodium dodecyl benzyl sulfate [5] or polyvinyl pyrrolidone [3] are added to the reaction mixture to prevent the agglomeration of metallic nanoparticles. Most commonly used chemical methods are chemical reduction [6], electrochemical techniques [7], and photochemical reactions in reverse micelles [8]. Commonly used physical methods are attrition and pyrolysis. Attrition involves grinding of the particles by a size-reducing mechanism. The particles are then air-classified, and oxidized nanoparticles are recovered. Pyrolysis involves burning of the precursor by passing them through an orifice at high pressure. The ash obtained is air classified to recover the oxidized nanoparticles [9]. Chemical methods are of low cost for high volume, and their major drawbacks include contamination from precursor chemicals, use of toxic solvents, and generation of hazardous by products, and the demerits of physical methods are low production rate, high cost of production, and high energy consumption [5]. There is need for replacing the toxic ingredients with environmentally safe method for synthesizing NPs. To overcome this, researchers are focusing on employing biological method for the synthesis of nanoparticles. They are generally cost effective, nontoxic, and ecofriendly [10]. So far, several plant extract [11], bacteria [12], fungi [13], enzymes [14], and algae [15] have been used for the synthesis of NPs. To our surprise, an emerging trend of synthesizing NPs using algae is developing in the recent years.

Algae are economically and ecologically important group of photosynthetic organism. They are unicellular or multicellular organisms dwelling in different environment such as freshwater, marine water, or surface of moist rocks [16–18]. Algae are categorized as microalgae (microscopic) and macroalgae (macroscopic). They play a key role in medical, pharmaceutical, agriculture, aquaculture, cosmetics applications. Algae are valuable source for various commercial products such as natural dyes and biofuels [19–22]. Till now, for the biosynthesis of metallic NPs, different group of algae such as Chlorophyceae, Phaeophyceae, Cyanophyceae, Rhodophyceae, and others (diatoms and euglenoids) have been used [23]. The ability of algae to accumulate metals and reduce metal ions makes them the superior contender for the biosynthesis of nanoparticles. Furthermore, algae are relatively convenient and easy to handle, along with several other advantages such as synthesis at low temperature with greater energy efficiency, less toxicity, and risk to the environment. In physical and chemical method, different commercially available surfactants were used as templates and capping agents in NPs synthesis with different morphologies. Removal of the residual components becomes a major issue. Considering this utilization of naturally eco-friendly methods having been developed

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which involves the synthesis of NP using different biological sources which could naturally modify the shape or size of a crystal with superior quality [24].

Among the biological materials, algae are called as ―bionanofactories‖ because both the live and dead dried biomasses were used for the synthesis of metallic nanoparticles [25]. Several algae such as *Lyngbya majuscule*, *Spirulina platensis*, and *Chlorella vulgaris* were used as a cost effective method for silver nanoparticles synthesis [26, 27]. The synthesis of silver nanoparticles using *Ulva fasciata* extract as a reducing agent and this nanoparticles inhibited the growth of *Xanthomonas campestris* pv. *malvacearum* [28]. In addition to seaweeds, microalgae such as diatoms (*Navicula atomus* and *Diadesmis gallica*) have the ability to synthesize gold nanoparticles, gold, and silica–gold bionanocomposites [29]. Comparing with other organism such as fungi, yeast, and bacteria, algae is equally an important organism in the synthesis of NPs; therefore, the study of algae-mediated biosynthesis of nanometals can be taken towards a newer branch and it has been termed as phyconanotechnology [10, 23, 30]. Thus, this work explains the potential and beneficial application of algal-mediated synthesized nanoparticles for present and future perspectives.

2. Types of nanoparticles

There are two different types of NPs, inorganic NPs and organic NPs. The inorganic NPs include metal and metal oxides, which are potent antibacterial agents [31] (**Figure 1**). Metal

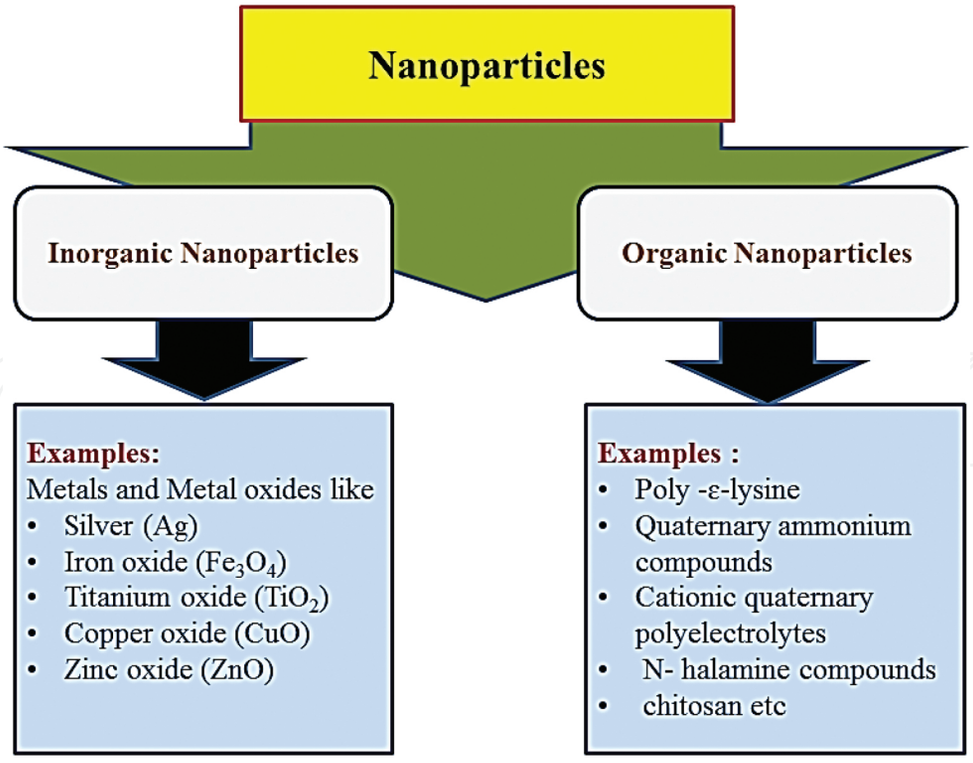

Figure 1. Different types of nanoparticles.

oxide nanoparticles such as silver (Ag), iron oxide (Fe_3O_4), titanium oxide (TiO_2), copper oxide (CuO), and zinc oxide (ZnO) are certain examples of inorganic NPs. Organic NPs includes poly-◎-lysine, quaternary ammonium compounds, cationic quaternary polyelectrolytes, N-halamine compounds, and chitosan . Organic nanoparticles are generally less stable at high temperatures. Due this reason, inorganic nanoparticles are more preferred as antimicrobial polymers [32].

2.1. Inorganic nanoparticles

So far, there are different types of inorganic metals and metal oxide NPs, which have been studied. Some important examples are detailed (**Figure 2**)

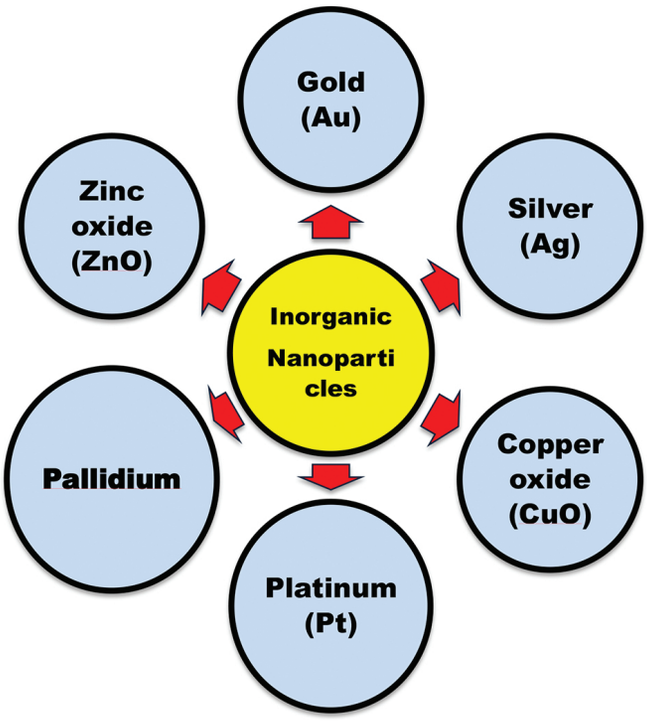

Figure 2. Types of inorganic nanoparticles.

2.1.1. Silver

Silver nanoparticle (AgNP) is the most widely used antimicrobial agent against many bacteria, fungi, and viruses [33]. The antimicrobial activity AgNP was found to be size dependent, and larger particles are less active than smaller one against many pathogens in both *in vitro* and *in vivo* analysis [34–36]. The resistance of bacteria towards antibiotics has made AgNPs more effective than antibiotics [37, 38]. Though there is plenty of research in AgNPs, the actual mode of action of AgNPs is still unclear [39]. In *E. coli*, the AgNPs create holes in the cell wall and increase the membrane permeability, thereby inactivating the cell activity [40, 41]. Some reports revealed that the Ag ions disrupt the protein structure by binding to thiol and amino groups [42]. AgNPs are photocatalytic [43], and they can generate reactive oxygenic species

(ROS) [44, 45]. AgNPs are effective against both Gram-positive and Gram-negative bacteria [46, 47].

2.1.2. Titanium oxide

Titanium oxide (TiO_2) is found to be effective against both Gram-positive/Gram-negative bacteria, viral, and parasitic infections [48, 49]. They are photocatalytic; their toxicity can be induced by visible light, or UV light, generates ROS [50]. TiO_2 is an effective bactericidal agent and a potent sporicidal agent against wide range of bacteria [51].

2.1.3. Zinc oxide

ZnO nanoparticles (ZnONPs) are another broad spectrum antibacterial agent, based on concentration and size of the NPs, and they are effective against methicillin-sensitive *Staphylococcus aureus* (MSSA), methicillin-resistant *S. aureus* (MRSA), and methicillin-resistant *Streptococcus epidermis* (MSSE) [52]. They are of low cost and found to inhibit the growth of a wide range of pathogenic bacteria (*Klebsiella pneumoniae*, *Listeria monocytogenes*, *Salmonella enteritidis*) [53], *S. mutants*, *Lactobacillus* sp., and *E. coli* [53, 54], with less toxicity to human cells. Their UV blocking and anti-biofilm activity makes them as a suitable coating material for medical and other devices, and it is approved by the Food and Drug Administration (FDA) in the treatment of disease and ingredients in food additives [50, 55].

2.1.4. Iron oxide

Iron oxide is generally inactive in their bulk form. Reducing their size to nanoscale makes them a potential antimicrobial agent. Iron oxide nanoparticles-coated surfaces prevent the adhesion and colonization of Gram-positive and Gram-negative bacteria [56].

2.1.5. Gold

As compared to Ag, Au nanoparticles are less effective and lack antimicrobial properties when used alone but found to be effective when used in combination with antibiotics such as ampicillin [57, 58], vancomycin [59], and lysozyme (an antibacterial enzyme) [60]. The Au nanoparticles can also be used in combination with nonantibiotic molecules such as amino substituted pyrimidines [61] and citrate, which induces the generation of ROS and mutations, hence used in cancer therapy [62].

2.1.6. Copper oxide

Despite copper oxide (CuO) nanoparticles are used as antibacterial agents, they are less effective than that of Ag and ZnO. So a comparatively higher concentration is required to get desired results. But some bacteria are more susceptible to CuO than Ag. For example, *E. coli* and *S. aureus* were more sensitive to silver but *B. subtilis* and *B. anthracis* were more sensitive to Cu [63, 64]. The cell wall composition of *B. subtilis* and *B. anthracis* is rich in amine and carboxyl groups, which allow the strong affinity of CuO towards the bacteria [65, 66]. CuO NPs exhibit antibacterial activity by membrane disruption and ROS production [65].

2.1.7. Magnesium oxide

Magnesium oxide (MgO) nanoparticles are efficient antimicrobial agent exhibiting bactericidal activity against both Gram-positive and Gram-negative bacteria, spores and viruses. The MgO NPs can be prepared from available and economical precursors. Along with membrane disruption and ROS generation, it also inhibits the essential enzymes of bacteria [50, 67].

2.1.8. Nitric oxide

Nitric oxide (NO) nanoparticles are highly reactive antibacterial agent. Similar to other nanoparticles, the activity of NO is also size dependent [68, 69]. The mode of inhibition is by the production of reactive nitrogen species (RNS) rather than ROS. They are effective against MRSA and various biofilm forming bacterial species [70, 71].

2.1.9. Aluminium oxide

Aluminium oxide is a mild antibacterial agent effective only at higher concentrations [65]. There mode of inhibition is by pit formation, perforation, and membrane disruption leading to cell death [66].

2.2. Organic nanoparticles

Some of the well-known examples of organic NPs are discussed below (**Figure 3**).

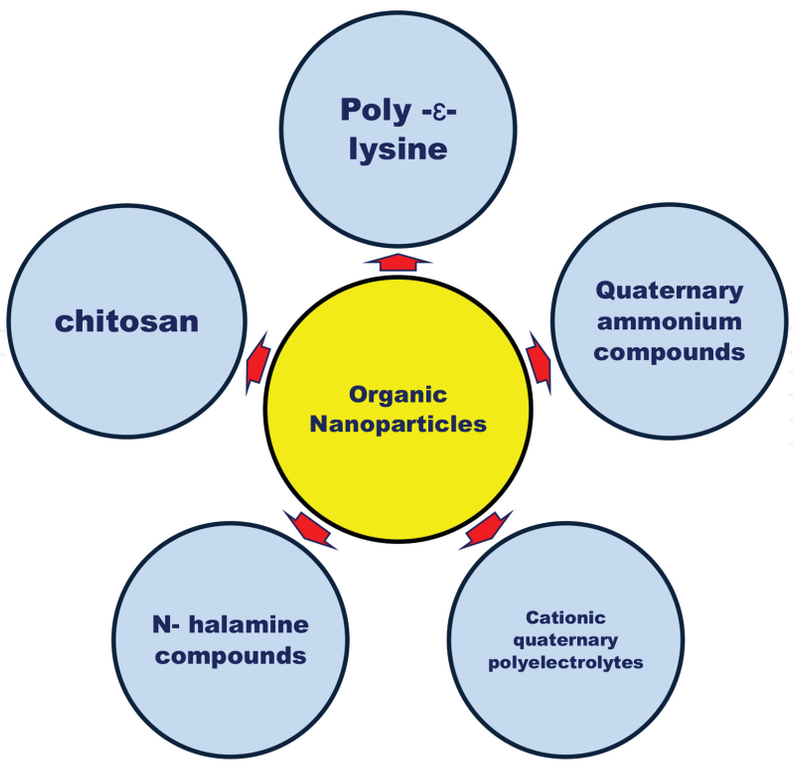

Figure 3. Types of organic nanoparticles.

2.2.1. Poly-ε-lysine

Poly-ε-lysine, a cationic homopeptide of L-lysine is effective against Gram-positive bacteria and spores of *B. coagulans*, *B. subtilis*, *and B. stearothermophilus* [72].

2.2.2. Quaternary ammonium compounds

Quaternary ammonium compounds are well known disinfectants and their antimicrobial property dependents on the chain length. The positively charged moieties of the compounds are attached to the negatively charged bacterial membrane by weak electrostatic interaction, followed by the insertion of hydrophobic tail of the compound in to the bacterial hydrophobic membrane core leading to the denaturation of structural proteins and enzymes [73].

2.2.3. Cationic quaternary polyelectrolytes

They are synthesized from methacrylic monomers such as 2-(dimethylamino) ethyl methacrylate and majority of them are derivatives of acrylic and methacrylic compounds. These molecules possess a wide range of biological applications due to their structural flexibility through the alteration of hydrophobicity, molecular weight, surface charge and other factors [74].

2.2.4. N-halamine compounds

N-halamine compounds are formed by the halogenation of imide amide or amine groups with one or more nitrogen–halogen covalent bonds. These are high stable compounds releasing free active halogen groups slowly in to the environment leading to the inhibition or inactivation of the microbial cells [75].

2.2.5. Chitosan

Chitosan NPs are biocompatible, nontoxic, and have the ability to act as absorption enhancer. These characteristics make the chitosan nanoparticles as an effective antimicrobial agent with broad spectrum activity against a wide range of bacteria, fungi and viruses. The antibacterial activity of chitosan nanoparticles depends on several factors such as pH and the nature of solvent [76, 77]. The use of chitosan along with metal nanoparticles is not feasible since chitosan reduced the activity of metal nanoparticles such as Zn. It can be used in combination with antibiotics [76, 78]. Even though some studies state that the interaction of cells with chitosan lead to membrane destabilization, followed by lysis and cell death, the detailed mode of action is unclear [79].

2.3. Synthesis of NPs using algae

The abundance and ease of availability of algae make them good and worthwhile sources for the synthesis of metallic nanoparticles [80]. Synthesis of nanoparticles using algae can be performed in three important steps, (i) preparation of algal extract in water or in an organic solvent by heating or boiling it for a certain duration, (ii) preparation of molar solutions of

ionic metallic compounds and (iii) incubation of algal solutions and molar solutions of ionic metallic compounds followed either by continuous stirring or without stirring for a certain duration under controlled conditions [10, 30]. The synthesis of NPs is dose dependent and it is also related to the type of algae used. There are a variety of biomolecules responsible for the reduction of metals which include polysaccharides, peptides, and pigments. Stabilizing and capping the metal nanoparticles in aqueous solutions is done by proteins through amino groups or cysteine residues and sulfated polysaccharides [81]. Synthesis of nanoparticles using algae takes comparatively shorter time period than the other biosynthesizing methods [10, 30]. So far, several seaweeds (*Sargassum wightii* and *Fucus vesiculosus*) have been used for the synthesizing AgNPs of different sizes and shapes [81, 82]. Marine algae are meagerly explored for the synthesis of NPs. *C. vulgaris* has strong binding ability towards tetrachloroaurate ions to form algal-bound gold reducing into Au(O). Approximately 88% of algal-bound gold attained metallic state, and the crystals of gold were accumulated in the inner and outer parts of cell surfaces with tetrahedral, decahedral, and icosahedral structures [83]. *S. platensis* has been for the extracellular synthesis of gold, silver, and Au/Ag bimetallic NPs [26]. Senapati et al. [84] reported the intracellular production of gold nanoparticles using *Tetraselmis kochinensis*. The biomass of the brown alga *F. vesiculosus* was reported for the reduction of Au(III)–Au(O) [82]. In addition to seaweeds, microalgae such as diatoms (*N. atomus* and *D. gallica*) have the ability to synthesize gold nanoparticles, gold, and silica–gold bionanocomposites [15].

2.4. Application of algal-synthesized NPs

The biomedical application of algal-synthesized NPs is significantly becoming more important due to their antibacterial, antifungal, anti-cancer, and wound healing activity. They are given (**Figure 4**).

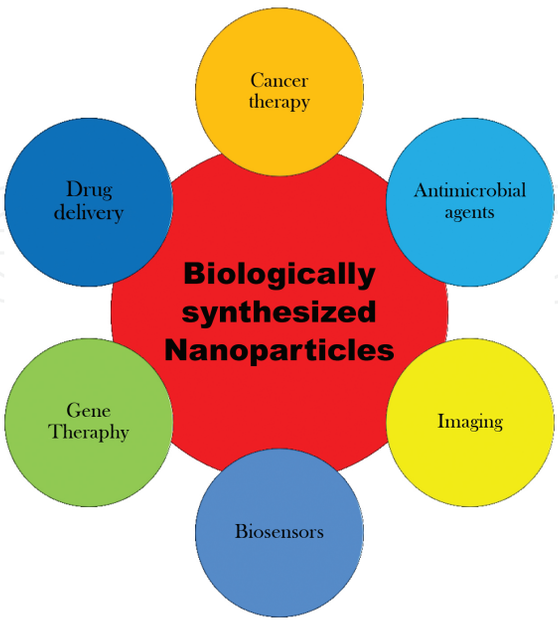

Figure 4. Applications of algal-synthesized nanoparticles.

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2.4.1. Antibacterial activity

Algal-synthesized NPs are known to possess efficient antibacterial activity (**Figure 5**; **Table 1**). Brown alga (*Bifurcaria bifurcate*) is reported for the synthesis of copper oxide nanoparticle (5–45 nm) exhibiting antibacterial activity against *Enterobacter aerogenes* (Gram-negative) and *S. aureus* (Gram-positive) [85]. Gold nanoparticles synthesized using *Galaxaura elongata* (powder or extract) were evaluated for their antibacterial activities which showed better antibacterial effects against *E. coli*, *K. pneumoniae*, MRSA, *S. aureus*, and *Pseudomonas aeruginosa* [86]. In another work, silver chloride (AgCl) NPs synthesized using marine alga *Sargassum plagiophyllum* were analyzed using fluorescence and electron microscopy showed bactericidal activity against *E. coli* [87]. Synthesis of AgNPs using fresh extract and whole cell of microalga *Chlorococcum humicola* inhibited the growth of Gram-negative bacteria *E. coli* (ATCC 1105) [88]. In a recent report, the aqueous extract of a diatom *Amphora*-46 was used for the light-induced biosynthesis of polycrystalline AgNPs, in which fucoxanthin a photosynthetic pigment was responsible for the reduction of Ag ion. Furthermore, the synthesized AgNPs were tested against Gram-positive and Gram-negative bacteria for its antibacterial activity [89].

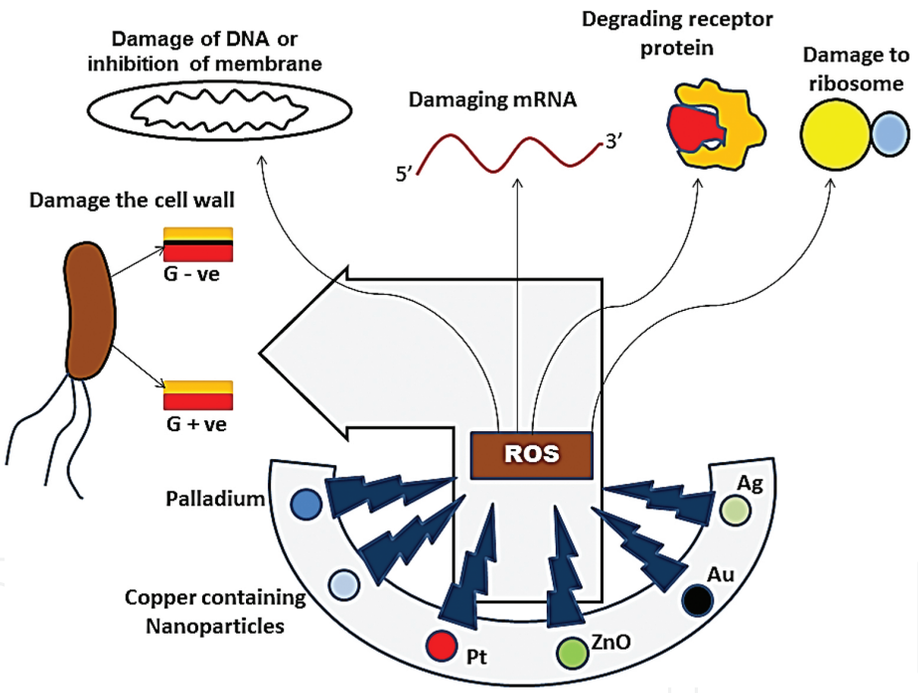

Figure 5. Different nanoparticles and their mode of inhibition against bacteria.

AgNPs synthesized using *Caulerpa racemose*, a marine algae, exhibited antibacterial activity against human pathogens such as *S. aureus* and *Proteus mirabilis* [90]. The cellular metabolites of *Microcoleus* sp. used to synthesize AgNPs, and it enhanced the antibacterial activity of antibiotics against *Proteus vulgaris*, *Salmonella typhi*, *Vibrio cholera*, *Streptococcus* sp., *Bacillus subtilis*, *S. aureus*, and *E. coli* [91]. In a work done by Merin et al. [92], he used marine microalgae *C. calcitrans*, *C. salina*, *I. galbana*, and *T. gracilis* were used for the synthesis of AgNPs and tested the antibacterial activity of AgNPs against *E. coli*, *Klebsiella* sp., *Proteus* sp., and *Pseudomonas*

sp. were tested high inhibitions over the growth of *E. aerogenes*, *S. typhi*, and *P. vulgaris* was exhibited by AgNPs synthesized using seaweed extracts of *Sargassum cinereum* [93]. In addition to antibacterial activity, the nanoparticles synthesized by seaweed extracts do have stabilizing effect on cotton fabrics [94].

Algae	NPs	Size	Shape	Intracellular (IC) or extracellular (EC)	Pathogens	References
Bifurcaria bifurcate	CuO	5–45 nm	Spherical and elongated	IC	*E. aerogenes* *S. aureus*	[85]
Galaxaura elongata	Au	3.85–77.13 nm	Spherical	IC	*E. coli* *K. pneumoniae* MRSA *S. aureus* *P. aeruginosa*	[86]
Sargassum plagiophyllum	AgCl	18–42 nm	Spherical	IC	*E. coli*	[87]
Chlorococcum humicola	Ag	4 and 6 nm	Spherical	IC	*E. coli* (ATCC 1105)	[88]
Amphora-46	Ag	5–70 nm	Spherical	IC		[89]
Caulerpa racemose	Ag	5–25 nm	Spherical and triangle		*S. aureus* and *P. mirabilis*	[90]
Microcoleus sp.	Ag	–	–		*P. vulgaris*, *S. typhi*, *V. cholera*, *Streptococcus* sp., *B. subtilis*, *S. aureus*, *E. coli*	[91]
Ulva fasciata	Ag	28–41 nm	Spherical	IC	*Xanthomonas campestris* pv. *malvacearum*	[96]
Turbinaria conoides	Au	60 nm	Triangle, rectangle & square	IC	*Streptococcus* sp., *B. subtilis* and *K. pneumoniae*	[97]
Padina pavonica	Ag	10–72 nm	Spherical	IC	*Fusarium oxysporum* f. sp. *vas* infectum *Xanthomonas campestris pv. malvacearum*	[99]
Gracilaria dura	Ag	6 nm	Spherical	IC	*B. pumilus* (accession number HQ318731)	[100]
Spirulina platensis	Au	5 nm	–	IC	*B. subtilis* and *S. aureus*	[101]

Table 1. Different types of algal-synthesized NPs and its antibacterial activity.

The aqueous extract of red marine algae *Gracilaria corticata* as the reducing agent was explored for its antibacterial activity against Gram-positive and Gram-negative bacteria [95]. *U. fasciata*-based AgNPs were synthesized and used to inhibit the growth of *Xanthomonas campestris* pv. *malvacearum* [96]. Another work shows the antibacterial activity of AuNPs synthesized using marine brown algae *Turbinaria conoides*, against *Streptococcus* sp., *B. subtilis*, and *K. pneumoniae* [97]. Ag, Au, and bimetallic alloy Ag–Au nanoparticles were synthesized from marine red alga, *Gracilaria* sp., exhibited good antibacterial activity against Gram-positive bacteria *S. aureus* and Gram-negative bacteria *K. pneumoniae* [98]. Extracellular synthesis of AgNPs from the thallus broth of marine algae *Padina pavonica* (Linn.) inhibited the growth of cotton Fusarium wilts (*Fusarium oxysporum* f. sp. *vasinfectum*) and bacterial leaf blight (*Xanthomonas campestris* pv. *malvacearum*) [99]. Bactericidal activity of AgNPs and nanocomposite material synthesized using agar extracted from the red alga *Gracilaria dura* was tested against *B. pumilus* (accession number HQ318731) [100]. In a work done by Suganya et al. [101] blue green alga *S. platensis* protein mediated synthesis of AuNPs was performed; further, it showed efficient antibacterial activity against Gram-positive bacteria (*B. subtilis* and *S. aureus*) (**Table 2**)

Nanoparticle	Target organism	References
Silver nanoparticles	*S. paratyphi*, *P. aeruginosa*, *S. epidermidis*	[112, 113]
Bismuth oxide aqueous colloidal nanoparticles	*C. albicans*, *S. mutans*	[114, 115]
Nano-oil formulation from *Mentha piperita* L	*Staphylococcus* sp.	[116]
Nano-emulsion (detergent, oil, and water) in combination with cetylpyridinium chloride	*A. baumannii*	[117]
Silver- and gold-incorporated polyurethane, polycaprolactam, polycarbonate, and polymethylmethacrylate	*E. coli*	[118]
Silver nanoparticles in combination with nystatin and chlorhexidine	*C. albicans*, *C. glabrata*	[119]
Silver nanoparticle and 12-methacryloyloxydodecylpyridinium bromide (MDPB)	Dental plaque microcosm biofilms	[120, 121]
Copper	*P. aeruginosa*	[108]
Zinc	*Actinobacillus pleuropneumoniae*, *S. Typhimurium*, *Haemophilus parasuis*, *E. coli*, *S. aureus*, *S. suis*	[122]
Magnetite nanoparticles	*C. albicans*	[56]
Eugenia carryophyllata essential oil stabilized by iron oxide/oleic acid core/shell nanostructures	*S. aureus*	[123, 124]
Zinc and copper oxide nanoparticles	*S. mutans*	[125]
Zerovalent bismuth nanoparticle	*S. mutans*	[114]

Nanoparticle	Target organism	References
Dextran sulfate nanoparticle complex containing ofloxacin and levofloxacin	*P. aeruginosa*	[126]
PEG-stabilized lipid nanoparticles loaded with terpinen-4-ol	*C. albicans*	[127]
Magnesium fluoride nanoparticles	*S. aureus*, *E. coli*	[128–130]
Yttrium fluoride nanoparticles	*S. aureus*, *E. coli*	[131]
Iron oxide/oleic acid in combination with essential oil from *Rosmarinus officinalis*	*C. albicans*, *C. tropicalis*	[132]
Gold nanoparticles and methylene blue	*C. albicans*	[133]
Starch-stabilized silver nanoparticles	*S. aureus*, *P. aeruginosa*	[134]
Iron oxide–oleic acid nanofluid	*S. aureus*	[124]
Quaternary ammonium polyethylenimine nanoparticles	Oral biofilms	[41]
Zinc oxide nanoparticles, chitosan nanoparticles, and combination of both	*E. faecalis*	[135]
Polyurethane nanocomposite	*S. epidermidis*	[136]

Table 2. Antibiofilm activity of different NPs against microbial pathogen.

2.4.2. Antifungal activity

Algal-synthesized NPs were used as efficient antifungal agents. Only countable number of work has been carried out in this aspect. This includes the synthesis AgNPs using the aqueous extract of red seaweed *Gelidiella acerosa* as the reducing agent exhibited antifungal property against *Humicola insolens* (MTCC 4520), *Fusarium dimerum* (MTCC 6583), *Mucor indicus* (MTCC 3318), and *Trichoderma reesei* (MTCC 3929) [102]. In another report, the effect of the algal (*Sargassum longifolium*)-mediated AgNPs against the pathogenic fungi *Aspergillus fumigatus*, *Candida albicans*, and *Fusarium* sp. was determined [103].

2.4.3. Anticancer activity

In a work done by Boca et al. [104] synthesized chitosan-coated silver nano-triangles (Chit-AgNPs) were used as a photothermal agents against a line of human nonsmall lung cancer cells (NCI-H460) [104]. In another work, AgNPs (10 nm) were synthesized using *Sargassum vulgare* and its ability to kill cancerous human myeloblastic leukemic cells HL60 and cervical cancer cells HeLa was tested [105].

2.4.4. Other applications

Algal-synthesized NPs are explored in certain other area of applications, which include the synthesis of spherical palladium nanocrystals via aqueous Na_2 $[PdCl_4]$ solution using the photosynthetic reaction within *C. vulgaris*, which can be used as a material for recycling as a catalyst for the Mizoroki–Heck cross-coupling reaction [106]. The antioxidant potentials of

AgNPs synthesized using *G. corticata* was also determined [95]. In another work, AuNPs were synthesized using the dried biomass of an edible freshwater epilithic red alga, *Lemanea fluviatilis* (L.) C. Ag., as both reductant and stabilizer; further, its antioxidant property was determined using DPPH assay [107].

2.5. Future application of algal-synthesized NPs

2.5.1. Antibiofilm agents

The use of nanoparticles as antibiofilm agents is an emerging area of research. Due to the extensive use and misuse of antibiotics, many of the pathogens acquired resistance toward multiple drugs. As the bacteria are less likely to develop resistance against nanoparticles, they can be used as a promising therapeutic agent against biofilms. Nanoparticles have the ability to penetrate EPS and the cell membranes (**Figure 6**). Silver nanoparticles were found to be more prevalent than the other ones, and they exhibit antibiofilm activity against both Gram-positive and Gram-negative pathogens. In a work done by LewisOscar et al. [108]. Chemical synthesis of CuNPs was performed by one-pot synthesized method and used for biofilm inhibition against *P. aeruginosa* PA14, *P. aeruginosa* ATCC10145 and some clinical isolated of *P. aeruginosa*. Along with the biofilm, CuNPs also weakened the extracellular polymeric substance and cell surface hydrophobicity of *P. aeruginosa*.

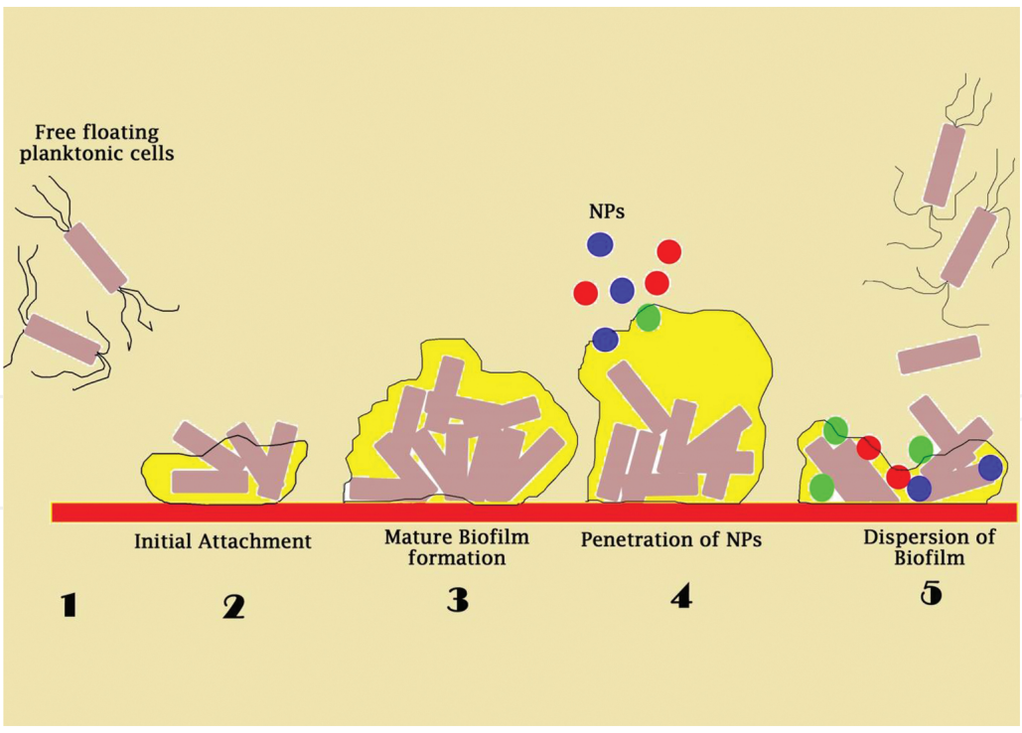

Figure 6. Antibiofilm activity of different nanoparticles.

The zero-valent selenium and tellurium NPs synthesized using *Stenotrophomonas maltophilia* and *Ochrobacterium* sp. were found to be effective against biofilms of *E. coli*, *P. aeruginosa*, and

S. aureus [109]. Similarly, AgNP synthesized from *E. faecalis*, when used in the form of nanocolloids, inhibited the biofilm of multidrug resistant pathogens [110]. Green-synthesized AgNP coated on medical devices inhibited the *S. aureus* biofilms [111]. Some other potential NPs against biofilm of different Gram-negative and Gram-positive bacteria are given below in **Table 2**.

2.5.2. Nanocomposite

The diatom *Stauroneis* sp. was used for the preparation of silicon–germanium nanocomposite, and this method of nanocomposite preparation has great importance for possible future applications due to its accessibility, simplicity, and effectiveness [137].

2.5.3. Lipid nanoparticles

There are possibilities for the production of lipid nanoparticles with the help of lipid-rich marine organisms such as algae, fungi, and bacteria [138]. Lipid nanoparticles can be synthesized from the organisms through heating to liquefy fatty acids; incorporating active agents of pharmacological and cosmetics importance; adding a hot surfactant; and stirring or homogenized under high pressure by ultrasound. These can be used in the production of food stuffs, cosmetics, and medicines [139].

2.5.4. Biosensing

Algal-synthesized NPs can be explored in biosensing applications. Such as, AuNPs has been proved as an important tool for hormone (HCG) detection in pregnant women urine sample [140]. Platinum (Pt) NPs act as a novel biosensor with high sensitivity for the determination of adrenaline for the treatment of allergies, heart attack, asthma, and cardiac surgery [141]. Synthesis of nanoscale Au–Ag alloy prepared using chloroplasts exhibited high electrocatalytic activity for 2-butanone at room temperature which can be developed as a tool for detecting cancer at early stages [142].

2.6. Conclusion

The developing era of nanoscience is a renowned gift for the development of science all over the world. Despite numerous studies conducted over the last decade, there are still considerable gaps in our knowledge about the biotechnological potential of green-synthesized nanoparticles. Furthermore, the precise basis of their antibiotic and antibiofilm activity has yet to be defined. However, the toxicity of nanoparticles to eukaryotic cells is a legitimate concern and still remains uncharacterized. One way of avoiding this potential drawback might be to target green-synthesized nanoparticles to the specific site of an infection so that toxic nanoparticles concentrations are localized. In addition, improvements in the way that green-synthesized nanoparticles are incorporated into medical devices could increase their efficacy and diminish any side effects, but considerable research effort is still required to perfect this technology.

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