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Biosynthesis of silver and gold nanoparticles using cyanobacteria, their pharmaceutical and industrial applications

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Nanotechnology has become a fast-growing field, and to prepare metallic nanoparticles for clinics or chemical establishments, it is mandatory that a cost-effective, eco-friendly technique be developed, using all nontoxic and renewable resources. This review presents biogenesis of silver and gold nanoparticles based on the utilization of natural metabolic routes leading to the synthesis of these nanoparticles mediated by cyanobacteria. These photosynthetic microorganisms become highly efficient 'bio-factories', for metal ion reduction and stabilization on the resulting biosynthesis of nanoparticles in a one-step manner. Significant attention has been directed towards the potent antimicrobial potential of these biogenic nanoparticles against numerous pathogenic multidrug resistant bacteria and fungi, as well. Furthermore, this review also provides a summary of recent understanding on mechanisms of their activities, as well as their huge potentialities for use in a variety of industrial/medical sectors, such as cleansing uses, wastewater remediation and industrial utilities as advanced materials. Indeed, the laboratory-scale biosynthesis with an oxygen-evolving photosynthetic prokaryote, the cyanobacterium, is user-friendly, but it could be scaled up for several industrial processes.

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1 Introduction

Cyanobacteria (blue–green algae) are a ubiquitous set of Gram-negative prokaryotes which are able to perform oxygenic photosynthesis. Those provide clear benefits compared to eukaryotic algae as biotechnology models; the high surface-

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volume ratio allows such algae to absorb nutrients efficiently, and certain strains have specialized heterocysts used to fix nitrogen.[1,2] Importantly to nanotechnology, cyanobacteria contain bioactive metabolites such as phycocyanin, phycoerythrin, proteins and several secondary metabolites namely, alkaloids, flavonoids, phenols, ethers; and such compounds are important in reducing and stabilizing metal ions, during the formation of nanoparticles (NPs).[3,4] Blithely, their adaptation to different environmental factors and adaptability to pigment change by chromatic adaptation renders them strong biofactories of producing bioactive compounds.[5–7] Significant bioactivity including antifungal, antiviral and anticancer properties had been demonstrated by species of *Lyngbya*,[8] *Oscillitoria*,[9] *Nostoc*,[10] *Anabaena*,[11] and *Spirulina*,[12] making cyanobacteria useful for the synthesis of NPs as newer medicinal molecules.

Although metal nanoparticles have unique physicochemical characteristics, including high surface area and increased reactivity, their synthesis had historically been based on physical and chemical processes.[13] Those traditional methods tend to be energy expensive and use hazardous reducing agents that release toxic effects on the environment.[14] Eventually, this creates an urgent need of green chemistry alternatives. Microorganism-based biosynthesis of NPs provides a long-term solution, as the cellular machinery can reduce metal precursors to nanoparticles without the use of external sources of energy or toxic solvents.[15] By the by, cyanobacteria are photo-autotrophic, facilitating the product gets synthesized directly through the

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use of atmospheric CO_2, light and water, unlike heterotrophic bacteria, in which the synthesis of the product is metabolically costly, because it requires the usage of expensive organic carbon sources.[16] Thus, cyanobacteria stand out to be the superior source to other biological materials, hence should be promoted for biosynthesis.

AgNPs (silver nanoparticles) and AuNPs (gold nanoparticles) are among the examples of nanoparticles that have attracted a lot of attention. AgNPs are famously known because those have a wide spectrum of antimicrobial efficacy especially against multidrug resistant (MDR) pathogens, which make them useful in wound management and in medical devices.[17,18] On the other hand, AuNPs are highly valued due to their surface plasmon resonance (SPR), which is unparalleled in biocompatibility, enabling their use in diagnostics, imaging and photothermal therapy.[19] Cyanobacteria such as *Spirulina* sp., *Lyngbya* sp. and *Oscillatoria* sp. Had been used for biosynthesis of AgNPs that exhibit antibacterial activity against human pathogens like, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Acinetobacter baumannii* and *Escherichia coli*.[9,12,20] AgNPs, green-synthesized from *Nostoc* sp. exhibited antibacterial, antifungal and anticancer properties, by efficiently inhibiting fungal strains such as *Aspergillus niger*, *Trichoderma harzianum*, *Ralstonia solanacearum* and *Xanthomonas campestris* and cancer cell lines were too documented.[21] Similarly, AuNPs prepared using green alga *Chlorella* sp. showed antifungal activity against human fungal pathogens, *Candida tropicalis*, *C. glabrata* and *C. albicans*. AuNPs synthesized from *Anabaena* sp. exerted antibacterial activity against *Klebsiella oxytoca*, methicillin-resistant *Staphylococcus aureus* (MRSA), and *Streptococcus pyogenes*.[22] Additionally, nanoparticles from *Oscillatoria* sp. and *Spirulina plantensis* showed impressive antiviral effects, especially on Herpes Simplex Virus (HSV-1), with approximately 90% reduction in cytopathic effects by inhibiting viral replication.[23] Although bacteria and fungi had been studied in terms of extracellular and intracellular synthesis pathways, cyanobacteria provide a clean synthesis route with nanoparticles being crowned by secondary metabolites, proteins and fatty acids for stability of these products.[24] Borophycin from the cyanobacterium *Nostoc* sp. was seen having good activity against human cancer cell lines *in vitro*, while extracts of the filamentous cyanobacterium *Calothrix* sp. had reduced the growth of HeLa cells *in vitro* and chloroquine-resistant strains of, the malaria parasite *Plasmodium falciparum*. Extracts from *Lyngbya lagerhaimanni* had anti-HIV properties, while lyngbyatoxin A isolated from the cyanobacterium *Lyngbya majuscula* was known for its strong inflammatory effects.[25] Additionally, intracellularly produced polyhydroxyalkanoates (PHA) of cyanobacteria are currently engineered to be biodegradable polymeric equivalents of polyethylene/polypropylene. Carotenoids such as canthaxanthin, beta-carotene, zeaxanthin and nostoxanthin, from cyanobacteria are widely used as food additives, dietary supplements and colourants in livestock diets. Astaxanthin extracted from the green alga *Haematococcus pluvialis* had shown a strong antioxidant and has confirmed therapeutic value in managing AIDS related conditions resulting from protease inhibition. Additionally, AgNPs produced by cyanobacteria are embedded in food packaging materials to enhance microbiological security and extend product shelf life.[26] Health products, obtained from cyanobacteria, are currently commercially available in pill, powdered and tablet forms, making those an affordable resource for food and health benefits. Unlike heterotrophic bacteria, which require expensive carbon sources for fermentation, cyanobacteria perform photosynthesis and can grow using atmospheric CO_2, light, water, and minimal nutrients. This makes economic and carbon-neutral production of biofuels, fine chemicals and bioplastics feasible, avoiding land consumption and environmental side effects.[16] Additionally, the ability of the bacterial strains to oxidize hydrocarbons and degrade organic pollutants made them interesting tools for environmental remediation.

Numerous studies have reported green synthesis of nanomaterials, a consolidated analysis focusing specifically on the efficiency of cyanobacterial platforms remains necessary. Thus, the main aim of this review could be considered to evaluate critically the current situation of cyanobacteria-mediated biosynthesis of AgNPs and AuNPs. This methodically assesses mechanistic pathways of reduction; differentiating between intracellular and extracellular processes and examines the decisive role of parameters of optimization that include light intensity, pH and concentration ratio of precursor on morphology of the cyanobacterial synthesized nanoparticle. Furthermore, to bridge the gap between laboratory production and practice with the strict analysis of antimicrobial, anticancer, antioxidant properties and industrial implementation of these biogenic nanoparticles attempts were taken. Lastly, this review deals with the existing barriers to toxicity, reproducibility and scalability and provides an outlook on how these challenges will be circumvented. The review is meant to be a general reference to nanobiotechnology, pharmaceutical chemistry and environmental science researchers to enable the transfer of cyanobacterial nanotechnology laboratory technology to commercial use.

2 Methodology

A systematic literature review was conducted following established protocols to ensure a comprehensive and transparent evaluation of the biosynthesis of AgNPs and AuNPs utilizing cyanobacteria. Through large scientific databases such as Google Scholar, Scopus, PubMed and Web of Science articles were searched; mostly at books and articles published between 2000 to October 2025 were seen. Several keywords such as, cyanobacteria, blue–green algae, silver nanoparticles, AgNPs, gold nanoparticles, AuNPs, NP-biosynthesis and industrial applications of NPs were used. The screening process had used some 'inclusion and exclusion criteria' to make sure that the data was useful. Downloads included original research and review articles, brief communications published in peer-reviewed SCOPUS indexed journals; and studies specifically utilizing cyanobacterial strains for the synthesis of AgNPs or AuNPs and papers presenting characterization data such as, UV-vis, TEM/SEM, XRD and discussing pharmaceutical, antimicrobial, anticancer, antioxidant or industrial applications were

included for the study. Studies concentrating exclusively on eukaryotic algae, bacteria, or plant-mediated synthesis without a cyanobacterial counterpart; conference abstracts, and editorials; articles deficient in methodological specifics concerning synthesis conditions or characterization were excluded. Firstly, titles and abstracts were screened to find studies that were not needed or were the same as others. After that, the full-text articles were checked to see if they met the standards for inclusion. Analysis of the cyanobacterial species, the amounts of precursor salts, the best conditions for the nanoparticle synthesis such as, pH, temperature and light intensity, their size and shape, and the quantitative bioactivity metrics like MIC, IC_{50}, and zone of Inhibition were done. This methodical approach led to the selection of about 300 studies, which were the basis for the literature, tables and critical analysis embodied in this review.

3 Botanical descriptions

Cyanobacteria belong to the empire prokaryote, kingdom eubacteria, phylum cyanobacteria and the cyanophycean class. According to the morphological characteristics and 16s rRNA analysis, 5185 sp. have been identified and placed under 7 orders, namely, Chroococcales, Gloeobacterales, Nostocales, Oscillatoriales, Pleurocapsales, Spirulinales, and Synechococcales.[27] Chroococcales, comprising the famous freshwater blooming unicellular cyanobacterium *Microcystis aeruginosa* is an order of unicellular and colonial cyanobacteria embedded in a mucilaginous sheath.[28] Members of the order Gloeobacterales lack thylakoids and are unicellular or irregularly rod-shaped.[29] Nostocales are prominent due to their excellent nitrogen-fixing capabilities and the filamentous shape of their species, including of *Nostoc* and *Anabaena*.[30,31] The highest number of benthic linear filamentous species are associated with Oscillatoriales, consisting of species like *Oscillatoria*, *Phormidium* and Pleurocapsales, including the genus *Pleurocapsa* sp., which can be coccoid cells or resemble filaments or pseudo-filaments, forming complex colonies characterized by their ability to divide by binary fission. Members of the order Spirulinales have open helix screw like coiled filaments, while species of the order Synechococcales, comprising *Synechocystis* sp. contain both unicellular and filamentous forms.[21]

4 Morphology

Cyanobacteria showcase a diversity of morphological traits, essential for their ecological succession and identification. They exist as unicellular, colonial, or multicellular filamentous forms, with specific characteristics such as cell shape, size, and the arrangement of specialized cells like heterocysts and akinetes, crucial for taxonomy. Some taxa exhibit polymorphism with cells of different shapes occurring within the same species. Unicellular forms typically range in size from 0.2 μm to around 40 μm in diameter, with some filamentous forms reaching up to 100 μm in cell diameter. The small cyanobacteria, often termed picocyanobacteria, measure between 0.2 and 2 μm and are significant components of the picoplankton in both marine and freshwater ecosystems. Cyanobacteria grow in different habitats, such as aquatic, planktonic, benthic and periphytic, attached to pteridophyte-plant like *Azolla* and other submerged objects; in polar regions and deserts.[31]

The cell wall of cyanobacteria is Gram-negative type, which consists of an outer membrane made of a lipopolysaccharide layer and a peptidoglycan layer that is superior, and these can help in maintaining structural integrity and motility.[32] Studies published have shown differences in the thickness of the cell wall in terms of different filamentous cyanobacteria, such as *Aphanizomenon gracile*, depending on consideration of its filament's density, which is correlated with resistance to grazing from planktonic protozoan crustacean *Daphnia* sp. because of greater stiffness.[33] Cell walls of cyanobacteria are also important about the ability to become symbiotic with other organisms. Specialized structures of cyanobacteria, including heterocysts and hormogonia, help in nitrogen-fixing ability and survival of the bacteria in their host environment.[34,35] Their cell walls contain large amounts of extracellular polymeric substances, which give them resistance against several environmental stresses and help in bioremediation by capturing the pollutants.[36]

However, the peptidoglycan layer in cyanobacteria is thicker, 10–700 nm than that in most of Gram-negative bacteria which is 2–6 nm. Unicellular strains such as *Synechococcus* had been demonstrated to have a thin 15 nm layer of peptidoglycan,[37] whereas filamentous strains have been reported to have a layer thickness of more than 700 nm for *O. princeps*. The cell membrane primarily transfers nutrients and metabolites to and from the cell and prevents environmental stress.[38] Certain cyanobacteria, like Gram-negative bacteria, contain external non-flagellar appendages termed pili or fimbriae that are involved in adhesion, movement, DNA absorption, and biofilm formation.[39,40]

5 Secondary metabolites

Cyanobacteria produce a wide range of secondary metabolites, including alkaloids, flavonoids, phenols, peptides, *trans*-fatty acids, amino acids, vitamins, carotenes, chlorophylls, phycocyanin and minerals, providing antibacterial, antifungal, antioxidant, and anti-cancerous properties.[40] Additionally, those were seen to produce various kinds of cyanotoxins like microcystin, saxitoxin, and anatoxin, which display hepatotoxicity and neurotoxicity.[41,42] The methanolic extract of *Microcystis* sp. demonstrated strong antialgal action against the green alga *Bracteacoccus* and anticyanobacterial activity against *Anabaena* BT2 and *Nostoc* pbr01.[43] Furthermore, humans, fish, birds, mammals, and invertebrates are all poisoned by some of the secondary metabolites.[44] Therefore, various nations, including Europe, the USA, Canada, Brazil, Australia, South Africa, China, and Japan, have set guidelines and values to protect the population from exposure to cyanotoxins[45] (Table 1).

5.1 Alkaloids from cyanobacteria

Cyanobacterial alkaloids are a chemically heterogeneous group of nitrogenous secondary metabolite, with indole, indoline or

Table 1 Chemical structure of some prominent secondary metabolites

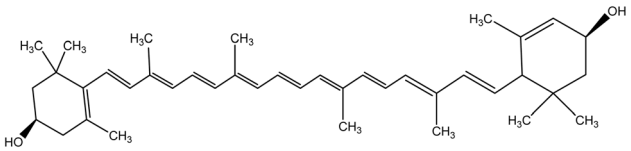
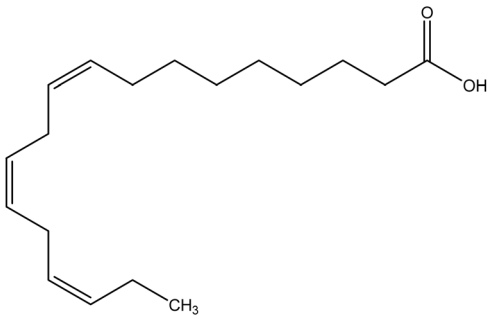
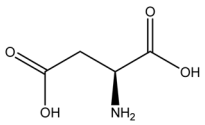
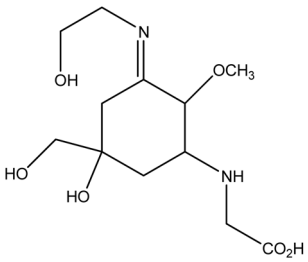
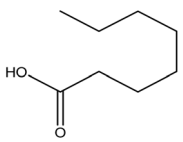
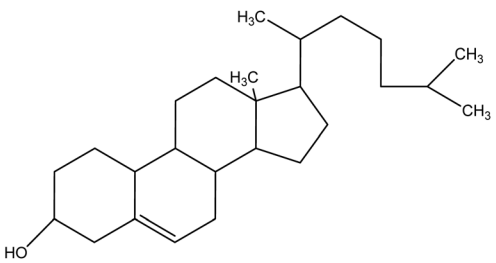
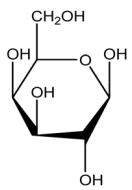
Sl no.	Phycocompound	PubChem ID	Chemical formula	Chemical structure	Activity	Ref.
1	Lutein	5281243	$C_{40}H_{56}O_2$		Antioxidant, protects eye tissues from sunlight damage	46
2	Alpha-linoelic acid	5280934	$C_{18}H_{30}O_2$		Essential omega-3 fatty acid, anti-inflammatory properties	47
3	Aspartic acid	594	$C_4H_7NO_4$		Building block for proteins, neurotransmitter	48
4	Asterina-330	102293881	$C_{15}H_{24}N_2O_7$		Mycosporine-like amino acid (MAA) that acts as a natural UV sunscreen	49
5	Capric acid	2969	$C_{10}H_{20}O_2$		Saturated fatty acid with antimicrobial and anti-inflammatory properties	47
6	Caprylic acid	379	$C_8H_{16}O_2$		Saturated fatty acid with antifungal properties	47
7	Cholesterol	5997	$C_{27}H_{46}O$		Essential component of animal cell membranes; precursor for steroid hormones	48

Table 1 (*Contd.*)

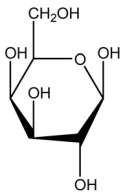
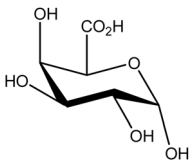
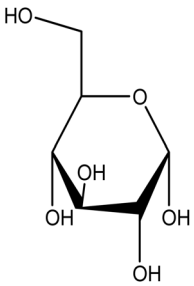
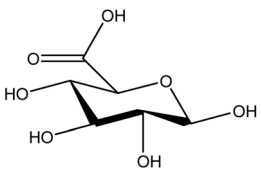
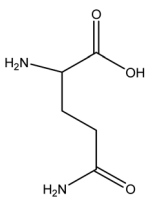
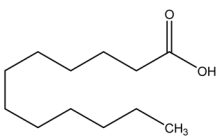
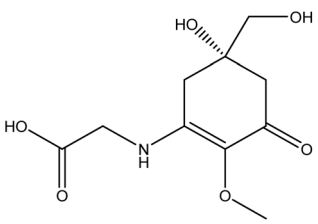
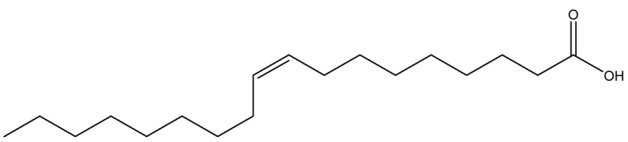
Sl no.	Phycocompound	PubChem ID	Chemical formula	Chemical structure	Activity	Ref.
8	Galactose	6036	$C_6H_{12}O_6$		Monosaccharide used as an energy source; component of glycolipids	48
9	Galacturonic acid	5460395	$C_6H_{10}O_7$		Main component of pectin in plant and algal cell walls	50
10	Glucose	5793	$C_6H_{12}O_6$		Primary source of energy for most living organisms	48
11	Glucouronic acid	959	$C_6H_{10}O_7$		Involved in detoxification processes by conjugating with other molecules	52
12	Glutamic acid	33032	$C_5H_9NO_4$		Building block for proteins, important excitatory neurotransmitter	48
13	Lauric acid	3893	$C_{12}H_{24}O_2$		Saturated fatty acid with strong antiviral and antibacterial properties	47
14	Mycrosprine amino acids		Variable		A class of compounds that absorb UV radiation, acting as natural sunscreens	49
15	Oleic acids	445639	$C_{18}H_{34}O_2$		Monounsaturated fatty acid; a primary component of olive oil	47

Table 1 (*Contd.*)

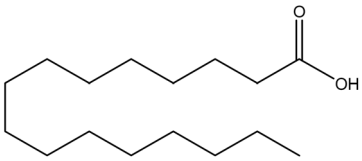
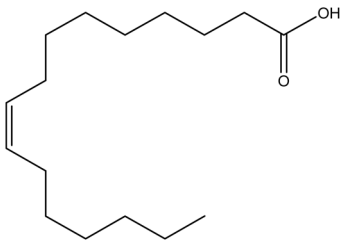
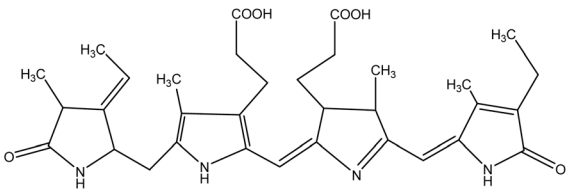
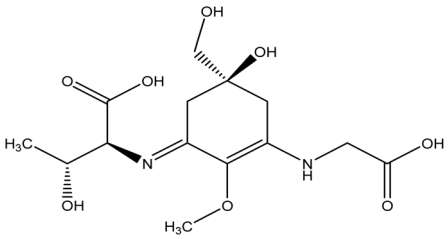
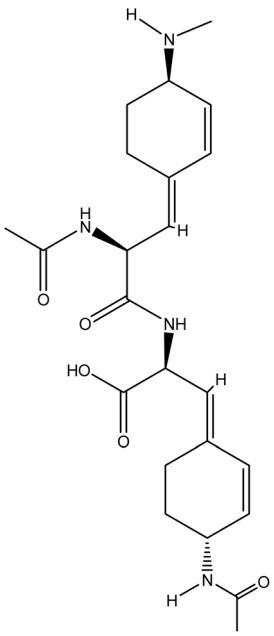
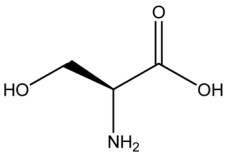
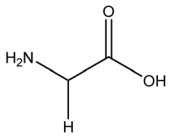
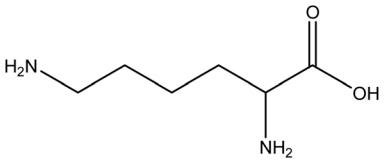
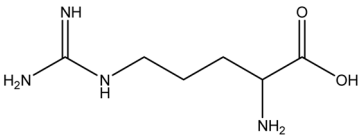
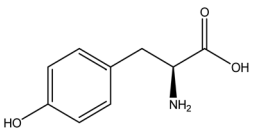
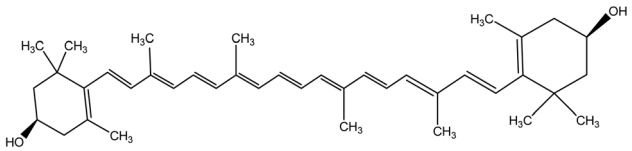
Sl no.	Phycocompound	PubChem ID	Chemical formula	Chemical structure	Activity	Ref.
16	Palmitic acid	985	$C_{16}H_{32}O_2$		The most common saturated fatty acid in animals and plants	47
17	Palmitoleic acid	445638	$C_{16}H_{30}O_2$		Omega-7 monounsaturated fatty acid with potential metabolic benefits	47
18	Phycocyanin	53837743	$C_{33}H_{38}N_4O_6$		Pigment-protein complex with antioxidant and anti-inflammatory activity	51
19	Porphyra 334	10255390	$C_{19}H_{28}N_2O_8$		A potent UV-absorbing MAA found in red algae	49
20	Radiosumin B	10812638	$C_{25}H_{30}O_7$		Diarylheptanoid with antioxidant properties	53

Table 1 (*Contd.*)

Sl no.	Phycocompound	PubChem ID	Chemical formula	Chemical structure	Activity	Ref.
21	Serine	5951	$C_3H_7NO_3$		Building block for proteins; involved in the biosynthesis of other metabolites	48
22	Glycine	750	$C_2H_5NO_2$		Simplest amino acid; building block for proteins and an inhibitory neurotransmitter	48
23	Lysine	5962	$C_6H_{14}N_2O_2$		Essential amino acid required for protein synthesis and calcium absorption	48
24	Arginine	6322	$C_6H_{14}N_4O_2$		Semi-essential amino acid; precursor for nitric oxide synthesis	48
25	Tyrosine	6057	$C_9H_{11}NO_3$		Amino acid precursor to key neurotransmitters (dopamine) and hormones	48
26	Zeaxanthin	5280899	$C_{40}H_{56}O_2$		Carotenoid pigment important for eye health; protects against light-induced damage	46

guanidines remnants that are produced through complex NRPS and PKS pathways.[54,55] Anatoxins are type of neurotoxins produced by some species of cyanobacteria, such as, *Oscillatoria* and *Anabaena*. These compounds are potent inhibitors of both pre- and post-synaptic neuromuscular transmission and are highly toxic to mammals. Anatoxin-a and homoanatoxin-a are produced *via* a PKS pathway initiated by L-proline.[56] Saxitoxins are also, a class of neurotoxins that are found in species of *Anabaena* and *Aphanizomenon*. These are sodium channel blockers and cause paralytic shellfish poisoning. Saxitoxins possess a tetrodotoxin structure and are tricyclic.[54] Nostocarboline produced by *Nostoc* sp. is an acetylcholinesterase inhibitor, which is a promising lead in the treatment of Alzheimer disease therapy.[57] In infectious disease contexts, the aerucyclamides of *Microcystis aeruginosa* are antiplasmodial active with an IC_{50} of less than 1 μg mL^{-1} against *P. falciparum*,[58] whereas ambiguine isonitrile displays very strong antifungal activity with an MIC of 0.312 μg mL^{-1} and 0.39 μg mL^{-1} against *S. cerevisiae* and *C. albicans* respectively.[59,60] Moreover, *Fischerella* sp. and *Hapalosiphon* sp. hapalindoles possess cytotoxic and antiviral effects[55,61] and drugs, such as dolastatin 10 and lyngbyastatins, are crucial structurals leading in antiviral and cancer treatments as approved antibody-drug conjugates.[8,62,63]

5.2 Peptides from cyanobacteria

Its peptide profile, which is also linear, cyclic, and depsipeptides, provides a further pharmaceutical potential through ribosomal and non-ribosomal biosynthetic machineries.[64] Lipopeptides (hassallidins A and B) of *Hassallia* sp. are antifungal against candida sp. with MIC of 4.8 μg mL^{-1},[65] but hassallidin D of *Anabaena* sp. is active at a concentration of 2.8 μg mL^{-1} or below.[66] Inhibitors of particular enzymes have also been discovered; brunsvicamides B and C of *Tychonema* sp. like *M. tuberculosis* inositol monophosphatase with IC_{50} of 7.3 and 8.0 mM, respectively, and scyptolin A of *Scytonema hofmanni* of bacterial transpeptidases[67] have also been identified.

Cryptophycin-1 is a cyclic depsipeptide produced by *Nostoc* sp. and is reported to cause disruption of the assembly of the microtubules in multidrug-resistant cancer cell lines[42,68] in the field of oncology. Although promising, the clinical translation of these peptides is hampered by poor yields of purification and complicated scale up needs.[69]

5.3 Terpenoids cyclophanes, aromatics and phenols from cyanobacteria

In addition to alkaloids and peptides, cyanobacteria also synthesize bioactive terpenoids, phenolics and fatty acids, which destroy microbial cell membranes. Terpenoids like comnostins and scytoscalarol cause depolarization of the membrane of the pathogenic bacteria.[70] Noscomin, which is isolated from *Nostoc commune* is active against Gram-positive bacteria such as *Bacillus cereus* and *Streptomyces epidermidis* with a MIC concentration within 8 and 128 mg mL^{-1},[71] and tetraterpene terscytoscalarol is presented by *Scytotema* sp. against *S. aureus* with a MIC of 1.7 mM.[72] Out of the exracted lipid products, majusculic acid of *Lyngbya majuscula* exhibits antifungal effects using *C. albicans* at an MIC of 8 mM.[73] There are also aromatic compounds containing 4,4′-dihydroxybiphenyl by *Nostoc insulare* and polychlorinated phenolic ethers like ambigols which are a part of the broad-spectrum antimicrobial defense mechanism of these organisms.[74]

6 Cyanobacteria-mediated synthesis

6.1 AgNP synthesis

Even though biosynthesis of AgNPs with cyanobacteria is mediated through various mechanism, but mainly bioactive compounds such as polysaccharides, proteins, or other biological molecules were involved in the reduction process, acting as reducing and stabilizing agents to convert Ag^+ to Ag^0.[75] The biosynthesis mechanism was based on the reduction of the Ag^+ ions by electron transfer, O–H, and C=O functional groups that was confirmed using the Fourier transform infrared spectroscopy.[76] Nanoparticles, especially AgNPs, have been synthesized in either top-down method or bottom-up method. Such methods have been extensively studied in biological systems for the product of nanoparticles with desired properties and functions. In the top-down approach, lithography, for instance, is used to pinch off larger materials into nanoparticles. This results in the particles being broken down in size to a small nano size material. Furthermore, this technique is employed at high temperature tube furnaces to produce nanoparticles of materials, such as silver, gold or lead, scouting the limitation and growth processes. The surface structures and physical properties of the nanoparticles obtained by these means are much more sensitive to room temperature and surroundings. On the other hand, bottom-top strategies are more common in nanoparticle production, specifically when using biological systems. Microbes accomplish such a bio reduction by a construction inside-out manner, where the cells are self-reducing bioreactors. Three crucial processes form the basis of the synthesis process: activation, growth, and termination. To create larger particles, metal ions are first reduced in the activation step, and then they are nucleated and grown. Proteins and polysaccharides are utilized for capping, stabilizing, and other purposes involving metal nanoparticles. The protein aqueous solution acts as a capping agent and stabilizer for the metal nanoparticles through the action of amino groups, particularly cysteine. There is a growing interest in sustainable nanotechnology where toxic by-product can be reduced to a minimum and bottom to top approach is a green, sustainable and cost-effective strategy. In this method, the pH, temperature, incubation time and the concentration of the substrate significantly influence the size, shape and properties of the synthesized nanoparticles.[77] The biosynthesis process of AgNPs mediated by cyanobacteria is mainly subdivided into the biosorption on the EPS molecules and the complex formation mechanism of Ag particle through the nucleation/aggregation–reduction processes. EPS adsorbs Ag^+ from stock solution initially and the main process is not dependent on light. Then under light, EPS gives electrons to reduce Ag^+ to Ag^0, and the better the light, the more efficient this reaction is. Furthermore, the end equilibrated EPS concentration is directly proportional to the size and stability of the produced AgNPs, illustrating that EPS plays a role as a protection matrix of the AgNPs against agglomeration.[78] Furthermore, the huge diversity in EPS composition, particularly proteins and polysaccharides, have a strong influence on both reduction and stabilization in the biosynthesis of NPs, thus giving them such a multi-functional character.[79]

Cyanobacteria, such as *Oscillatoria* sp., *Spirulina platensis,* and *Nostoc* sp., have been used effectively in AgNPs biosynthesis. They have a tremendous capacity to yield bioactive compounds with antibacterial, antioxidant, and anticancer activity. For example, AgNPs generated with *Oscillatoria limnetica* not only demonstrated high anticancer activity against breast MCF-7 and colon HCT-116 cancer cell lines but also had significant antibacterial activity. Likewise, the nanoparticles synthesized using *Spirulina platensis* were also found to possess a range of 7–16 nm in size, exhibiting a high ability to reduce biologically and effective antimicrobial potential. For example, AgNPs, mainly 12–15.3 nm in size and with significant cytotoxicity against cancer cells, were produced with the use of polysaccharides obtained from *S. platensis* to reduce silver ions.[80]

6.2 AuNP synthesis

Cyanobacterial AuNPs are mainly formed through bottom-up approach. In extracellular synthesis method, the enzymes, proteins and pigments entrapped in the cell membrane display ability to reduce metal ions on the available sites on the cell surface of cyanobacterial cells. The reduction of Au^+ to Au^0 nucleates and stabilizes AuNPs and is mediated by a series of enzymes, such as NADH-dependent reductase. For instance, oval-shaped AuNPs secreted by *Plectonema boryanum* are said to facilitate purification. This demonstrates the advantage of extracellular synthesis in minimizing downstream processes.[81]

In intracellular biosynthesis nitrate reductase and nitrogenase are a few of the intracellular enzymes that are being exploited by cyanobacterial cells to synthesize AuNPs. These enzymes reduce gold ions entering the cells. Thylakoid membranes, critical for photosynthesis-1 and the electron transfer chains are involved in the reduction process in these membranes. Here, synthesized NPs were often entrapped in an organic-matrix system and additional extraction procedures were needed, which might be viewed as a drawback. Examples of reagents that serve as capping and reducing agents include cyanobacterial proteins, peptides and polysaccharides. These biomolecules contain some functional groups like, amino (–NH_2), hydroxyl (–OH), and carboxyl (–COOH) groups, which may act as stabilizing agents and prevent the aggregation of AuNPs.[60]

7 Challenges in synthesis process reproducibility and scalability

7.1 Interplay of strain specificity and culture variability

Cyanobacteria exhibit substantial metabolic and genetic diversity across taxa, leading to significant interspecific variability in nanoparticle synthesis mechanisms and efficiency (Table 2). For example, unicellular strains like *Synechocystis* sp. primarily utilize photo-catalytic reduction *via* photosynthetic electron transport, while filamentous, nitrogen-fixing strains such as *Anabaena* sp. may also employ exopolysaccharides and nitrogenase enzymes for metal reduction. This strain-dependent variability is further compounded by high sensitivity to culture conditions—light intensity, temperature, pH, and nutrient availability all critically influence metabolic pathways and nanoparticle synthesis outcomes. Even within the same strain, shifts from exponential to stationary growth phases can drastically alter secreted metabolite profiles and redox states, resulting in inconsistent nanoparticle characteristics when identical protocols are applied under slightly different conditions.[94–96]

7.2 Batch-to-batch variability and polydispersity

Cyanobacterial metabolism is dynamic and growth-phase dependent, causing fluctuations in the types and concentrations of reducing agents such as proteins, pigments, enzymes available for nanoparticle synthesis. Minor deviations in environmental parameters such as illumination, temperature, or pH can lead to highly polydisperse nanoparticle samples, with significant variability in size and morphology. This heterogeneity complicates downstream applications, especially in clinical contexts where uniformity is essential for safety and efficacy.[96,97]

7.3 Maintenance of axenic cultures and contamination

Large-scale cultivation of axenic (pure) cyanobacterial cultures is challenging. Open-pond or bioreactor systems are susceptible to contamination by heterotrophic bacteria or fungi, which can introduce foreign metabolites, compete for metal ions, or alter nanoparticle capping mechanisms. Such contamination increases batch variability and operational complexity, raising costs compared to abiotic chemical synthesis.[94,96]

7.4 Scalability and the "self-shading" effect

Scaling up from flask-level to industrial photobioreactors introduces unique engineering challenges. As biomass density increases, self-shading limits light penetration, causing non-uniform illumination and uneven reduction rates throughout

Table 2 Comparative summary of optimization parameters (pH, temperature, light) and characterization profiles (size, morphology) for silver and gold nanoparticles synthesized by various cyanobacterial species and comparative organisms

Organism/species	Category	Metal NP	pH	Temp (°C)	Light/cond.	Size (nm)	Morphology	Ref.
Comparision between different cyanobacterial species								
Khargia iranica KH.T.2 (biomass)	Cyanobacteria	Ag	7	25	Light	11–13	Spherical	82
Khargia iranica KH.T.2 (supernatant)		Ag	7	25	Light	11–13	Spherical	
Khargia iranica KH.T.2 (biomass)		Au	7	80	Light	—	Spherical	
Khargia iranica KH.T.2 (supernatant)		Au	7	100	Light	—	Spherical	
Microchaete NCCU-342		Ag	5.5	60	UV (60 min)	60–80	Spherical (polydisp.)	83
Oscillatoria limnetica		Ag	6.7	—	—	3.3–18	Quasi-spherical	81
Phormidium ambiguum		Ag	—	—	Light	6.5–12.2	Spherical (fcc)	84
Desertifilum tharense		Ag	—	—	Light	6.2–11.4	Spherical (fcc)	84
Nostoc linckia (phycocyanin)		Ag	10	—	—	9.4–25.9	Spherical	85
Spirulina platensis		Ag	—	—	—	~28.7	Spherical	86
Synechocystis sp.		Ag	—	—	—	10–35	Spherical	87
Nostoc muscorum 2/91		Ag	7.4	25	Light	11.8 ± 0.5	Cubic to oval	82
Comparison with different organisms								
Noctiluca scintillans	Algae	Ag	7	80	—	4.1–4.5	Spherical	88
Aconitum violaceum	Plant	Ag	8	60	—	<100	Spherical/triangular	89
Aconitum violaceum	Plant	Au	8	60	—	<100	Spherical/triangular	
Bacillus cereus	Bacteria	Ag	9	48.5	—	5–7.1	Spherical	90
Leclercia adecarboxylata	Bacteria	Ag	7	40	Light	17.4	Spherical	91
Antigonon leptopus	Plant	Ag	10	—	—	93.5 ± 1.9	Spherical	92
Hibiscus leaves	Plant	Ag	6	70	—	12–17	Spherical	93

the reactor. Since many synthesis pathways are photo-activated, this effect leads to inconsistent nanoparticle yields and quality, impeding reliable industrial-scale production.[95,97,98]

8 Characterization of AgNPs and AuNPs synthesized by cyanobacteria

8.1 Ultraviolet-visible spectrophotometry

The UV-visible spectrophotometry approach is a quick and cheap way to be sure that metal NPs have been made. The surface plasmon resonance (SPR) peaks of gold and silver nanoparticles are found in the visible range and have distinct values. This is because free conduction band electrons move about on their surfaces. For gold nanoparticles, the absorption would usually be in the high wavelength range of 510–560 nm, depending on the size, shape, and location of the localized SPR peak. For AgNPs, it would be about 400–450 nm. Characterization tests indicated that the produced *S. platensis*-derived AuNPs had a λ max at 530 nm, hence validating the synthesis. The produced AuNPs from *Lyngbya majuscula* exhibited a particle with peak absorbance at a wavelength of 540 nm, thereby validating the stability and monodispersity of the nanoparticles.[99] The SPR peak for the AgNPs of *Nostoc muscorum* was found at 420 nm.[100] A further surface plasmon resonance band at 528 nm was identified for gold nanoparticles of *Oscillatoria limnetica*. The plasmonic nature of the SPR shift may also help us understand how nanosomes stick together, how they look, and how their surfaces can be changed[101,102].

8.2 Fourier transform infrared spectroscopy (FTIR) and XRD

Functional groups on the surface of the nanoparticle, namely reduction and capping groups, are traced by FTIR. This is important for understanding how cyanobacterial biomolecules can interact with metal ions. Amide (–NH), hydroxyl (–OH), and carboxylic (–COOH) groups in the *Spirulina*-mediated AuNPs, indicated the role of proteins and polysaccharides in stabilization of nanoparticles.[103] The phenolic and carbonyl groups like leads 12–15 on the AgNPs synthesized from *Phormidium* sp. was observed.[104] Notable absorption bands at 3400 cm^{-1} (–OH), 1650 cm^{-1} (–C═O), and 1540 cm^{-1} (amide II) provided strong evidence for the presence of cyanobacterial proteins and flavonoids on the surface of AuNPs synthesized using *Oscillatoria limnetica*.[105] The FTIR analysis of Os-AgNPs showed a strong and broad peak at 3352 cm^{-1} corresponding to the –OH stretching vibration of alcohol due to intermolecular bonding[106] (Fig. 1).

XRD is commonly used to determine the crystal size and phase purity of nanoparticles. It is well known that the typical AuNPs and AgNPs are face-centered cubic (FCC), and characteristic peaks appearing at 38.1°, 44.3°, 64.5° and 77.4° can be assigned to the (111), (200), (220), and (311) lattice planes, respectively.[107] AuNPs synthesized with *Anabaena flos-aquae* had characteristic FCC structure and significant peaks indicating high degree of crystallinity.[108] Significant diffraction peaks of *Spirulina*-mediated AuNPs were reported, thus confirming crystallinity of gold.[103] XRD confirms crystallinity of the AgNPs obtained from *Phormidium* sp. which estimated the crystallite size to about 18 nm by Debye–Scherrer formula.[104]

8.3 FESEM (field emission scanning electron microscopy) and EDS (energy dispersive spectrometry)

FESEM offers detailed surface images that are especially useful to reveal face structure and to monitor aggregation on hard surfaces. When combined with energy-dispersive X-ray (EDS), it is used to analyze the chemical composition of a sample containing a nanoparticle. FESEM microstructural analysis of *Nostoc muscorum* mediated AgNPs, observed that the particles were spherical in shape with a slight aggregation.[100] EDS analysis showed a strong peak of silver at 3 keV thus confirming the elemental composition. Furthermore, AuNPs are distributed uniformly on exposed surfaces of *Oscillatoria*-prepared samples by FESEM, and elemental gold was confirmed by EDS.[101] FESEM analysis of *Anabaena flos-aquae*-induced AuNPs had spherical shaped particles arranged in group of nanoclusters. EDS analysis showed elemental peaks at 2.1 keV and 9.7 keV confirming the presence of metallic gold[109] (Fig. 2).

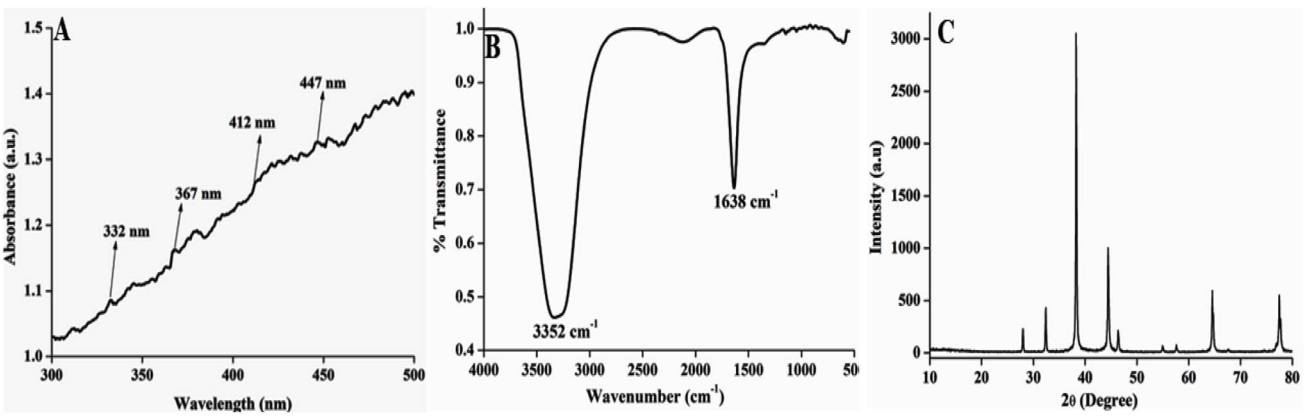


Fig. 1 The biosynthesized Os-AgNPs UV-vis (A), FTIR (B), and XRD (C) spectra analysis adapted/reproduced from (Bishoyi *et al.*,2025)[106] with permission from Wiley, copyright 2025.

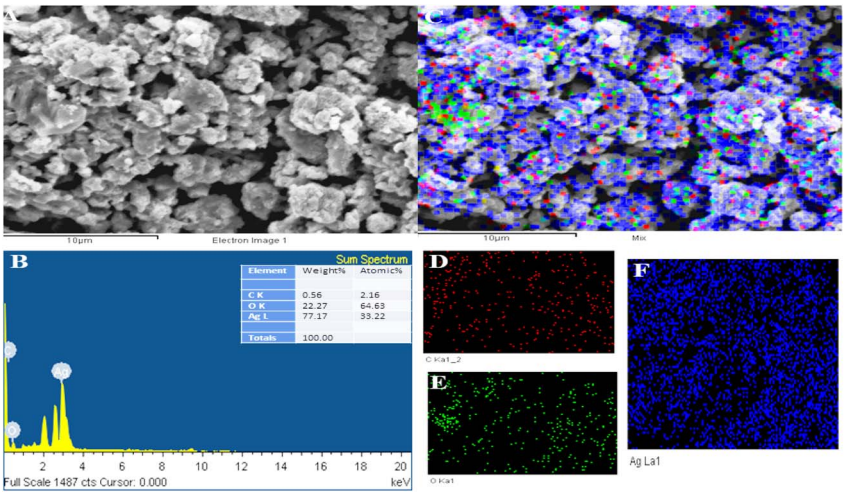


Fig. 2 The biosynthesized Os-AgNPs FESEM image (A), EDS spectrum (B), and surface colour image (C). The presence of carbon spotted crimson red colour (D), oxygen spotted neon green colour (E), and silver spotted navy-blue colour (F) of Os-AgNPs. adapted/reproduced from (Bishoyi *et al.*,2025)[106] with permission from Wiley, copyright 2025.

8.4 Dynamic light scattering (DLS) and zeta potential assessment

Nanoparticles in colloidal dispersions are characterized by DLS which provides their hydrodynamic size and polydispersity Index (PDI). It often shows a slightly bigger size than TEM on account of solvation layers or surface-bound biomolecules. The hydrodynamic size for the AuNPs synthesized is around approximately 45 nm with PDI< 0.3 indicating a narrow size distribution.[99] AgNPs from *Phormidium* sp. showed an average hydrodynamic diameter of 38 nm and high stability in solution.[104] Additionally, average diameters of 35–50 nm and a width of AgNP size distributions are shown on DLS analysis for *Anabaena variabilis*-synthesized silver nanoparticles.[109] Further, doxorubicin functionalized AuNPs for drug delivery showed low polydispersity index, PDI is ~0.2 which is clinically relevant, AuNPs can also be characterized for their stability and homogeneity using DLS.[110]

Zeta potential measures surface charge and predicts colloidal stability. Values above ±30 mV indicate strong electrostatic repulsion and stable dispersions. A zeta potential of −32 mV for *Oscillatoria*synthesized AuNPs, indicated high colloidal stability.[105] Zeta potential of −35 mV was observed in their green-synthesized *Lyngbya* AuNPs, suggesting that it remained stable with no sign of aggregation[99] (Fig. 3).

8.5 Transmission electron microscopy

TEM is a strong imaging method that lets you see the form and size distribution of the nanoparticle directly. It can tell the difference between spherical, rod-shaped, filler-triangle, and unispheric particles, as well as give an idea of the size of the degree of dispersion or agitation level. The AuNPs made by *O. limnetica* are mostly round and have a diameter of 5 to 25 nm.[105] The synthesized AuNPs exhibited a nearly perfect spherical morphology, as indicated by prior findings on *Spirulina-*

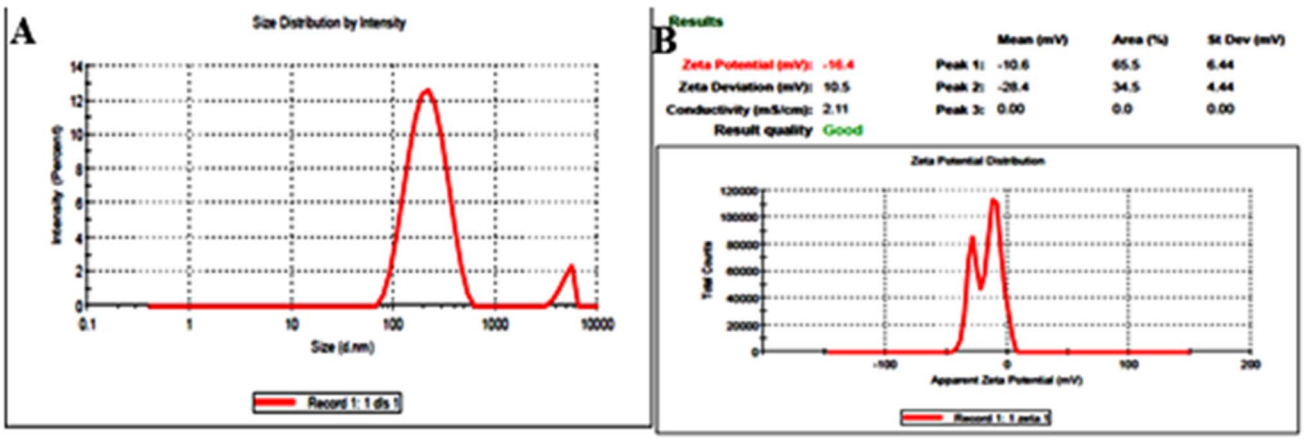


Fig. 3 Intensity distribution (A) and zeta potential (B) of biosynthesized Os-AgNPs by DLS. adapted/reproduced from (Bishoyi *et al.*,2025)[106] with permission from Wiley, copyright 2025.

mediated nanoparticles with an average dimension ranging from 10 to 30 nm.[103] TEM showed that the AgNPs made by *Anabaena variabilis* were crystalline and had lattices and fringes at the atomic level.[109] AuNPs obtained from *Phormidium valderianum* were synthesized by HR-TEM, revealing a crystalline structure with a spherical morphology, predominantly consisting of particles measuring less than 20 nm[110] (Fig. 4).

8.5.1 Antimicrobial properties exhibited by AgNPs

8.5.1.1 Antibacterial activities of AgNPs. AgNPs produced from *Synechococcus* showed strong antibacterial activity with maximum inhibition zones of 24 nm and 11 nm for the *S. aureus* and *E. coli.* Both Gram positive as well as Gram negative bacteria were significantly inhibited.[111,112] Mechanistically, these AgNPs directly interfere with metabolic energy and membrane functions, making them a viable substitute for current antibiotics. Moreover, compared to chemically synthesized AgNPs, *Spirulina platensis*-AgNPs display better antibacterial capacity and stability. They show good bactericidal effects on Gram positive bacteria such as *Enterococcus hirae*, *E. faecalis* and *S. aureus*, as well as synthetic stability against Gram negative bacteria, *P. aeruginosa* and *Staphylococcus typhimurium*.[113] AgNPs generated with the cyanobacterium *Pseudanabaena*/*Limnothrix* sp. showed strong inhibitory effects on both Gram positive and negative bacteria, such as *Corynebacterium glutamicum* and *E. coli*.[114] Additionally, *Chroococcus* sp. Ag NPs as spherical shaped, 11 nm to 13 nm particles displayed significant antibacterial activity against the pathogenic bacteria *Micococcus luteus*, *Bacillus subtilis* and *Pseudomonas aeruginosa*.[115]

(a) *Factors affecting antibacterial activity*: the biosynthetic process can be optimized by varying parameters such as the concentration of silver nitrate/gold, pH, temperature, and incubation period. Ag NP synthesis by *Chroococcus* sp., reported that the extract ratio of 3 : 1 v/v corresponds to maximum $AgNO_3$ reduction to silver nitrate (10 mM) at pH 7, 60 °C, at 30 minutes.[115] Similarly, *Synechococcus* sp. was used to synthesize AgNPs using different biological approaches like the direct strain powder method, the ethanolic extract of pellet method and the ethanol extract method, producing a higher inhibition zone of 24 mm against Gram-positive bacteria *S. aureus*.[112] AgNPs exhibit antibacterial activity, resulting from their interaction with bacterial cell membranes, which in turn causes membrane disruption and DNA damage, leading to bacterial cell death.[87] Moreover, multiple parameters including overall shape, size, concentration, and surface charge of Ag NPs, play a role in their antibacterial effects. Nanoparticles with smaller sizes have demonstrated enhanced antibacterial activity due to their higher surface area to volume ratio that facilitates increased interaction with bacterial cells.[84] AgNPs synthesized with the cyanobacterium *Desertifilum* sp. exhibited a larger range of antibacterial activity against MDR bacteria, with inhibition zones between 9–25 mm.[116] The antibacterial activity of AgNPs is also significantly dependent on their concentration. AgNPs show a stronger antibacterial activity at higher concentrations; however, an over-concentration of Ag NPs can lead to agglomeration, which can compromise their action.[117]

8.6 AgNPs as antifungal agents. Subsequently, the broad antifungal activities of cyanobacteria-synthesized AgNPs have been reported, highlighting the potential of AgNPs as a new antifungal agent against pathogenic fungi. These nanoparticles have demonstrated exceptional inhibitory activity against fungi such as *Candida albicans*, *Aspergillus* sp., *Fusarium oxysporum*, and others. AgNPs produced using *Synechocystis* sp. had a diameter of 10–35 nm, whereas nanomaterials from *Phormidium ambiguum* were spherical and found with sizes of 6.46–12.2 nm.[84,116] AgNPs synthesized by cyanobacterial species such as *Desertifilum* sp. and *Nostoc* sp. display potent antifungal activity, affecting cell membranes, blocking several enzymes that are vital for cell function, and inducing oxidative stress. AgNPs in *Desertifilum* sp. exhibited as such prominent inhibition of *C. albicans* (ZOI: 15–20 mm) growth, while also downregulating the expression of virulence-linked genes like Hwp1 and CDR1 known to support biofilm development and drug resistance Likewise, cyanobacteria-derived AgNPs exhibit strong antifungal activity, especially towards phytopathogenic fungi including *Fusarium oxysporum* and *Bipolaris maydis* with inhibition zones of 13–17 mm.[11,118]

AgNPs synthesized from cyanobacteria exhibit antifungal activity through the generation of reactive oxygen species, damaging plasma membranes, and disturbing the metabolic

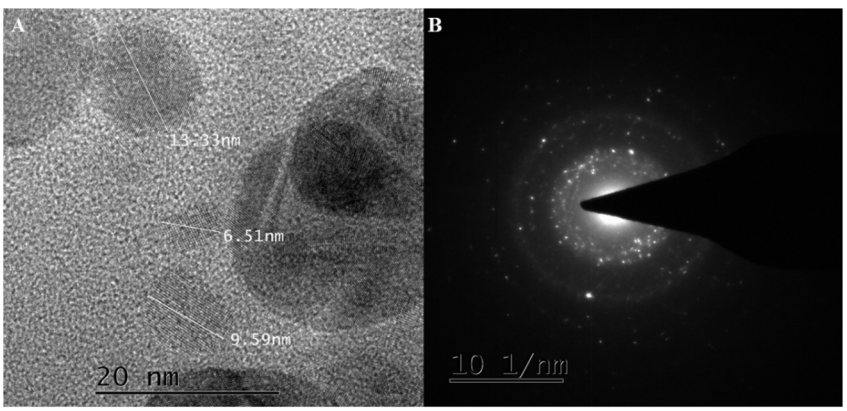


Fig. 4 TEM image (A) and the selected area electron diffraction (SAED) pattern (B) of synthesized Os-AgNPs, adapted/reproduced from (Bishoyi *et al.*,2025)[106] with permission from Wiley, copyright 2025.

process of the cell by adsorption on the cell membrane. Additionally, nanoparticles disrupt the cell wall and pierce the fungal cell wall, which leads to lysis of the cells and death due to the leakage of cell contents. These mechanisms also are evidenced in two studies where inhibition of critical expression of enzymes such as lactate dehydrogenase and glutathione peroxidase in fungal cell after exposure to AgNPs were found.[119] Chitosan-stabilized AgNPs were more stable and demonstrated antifungal activity against pathogenic fungi, such as *Candida* sp., *Aspergillus fumigatus* and *Cladosporium* sp., than other AgNPs.[120] For example, endophytic fungus with ability of producing chitosan capped AgNPs from *Curvularia kusanoi* exhibited highly potential in antifungal action toward *Aspergillus fumigatus* along with 83% thread growth inhibition at doses of 50 mg L^{-1}.[106] Ag NPs produced using *Oscillatoria salina* were found to be effective against *Trichophyton rubrum* and *Candida tropicalis* pathogenic fungi, with inhibition zones ranging 20–30 mm.[121] *Spirulina platensis* and *Nostoc linckia* have been characterized as aggressive reducers of AgNPs. These organisms biosynthesize and produce phycobiliproteins, which can act as a reducing and stabilizing agent. The TEM results revealed that AgNPs produced from *S. platensis* had a particle size distribution between 15.1 and 27.4 nm in size with a mean size of 21.211 nm. The AgNPs produced by *N. linckia* have average particle sizes ranging from 16.3 to 25.8 nm and an average particle size of 21.052 nm. Moreover, the antifungal activity of SPI-AgNPs has been demonstrated to be potent against *Candida albicans*.[122] *Anabaena variabilis*-mediated AgNPs has prevented growth of biofilm formation of *C. albicans* (62.5% inhibition of biofilm after 25 μg mL^{-1} concentrations).[123] Similarly, AgNPs synthesized with *Synechocystis* sp. have wound healing effect in diabetic animal model that manifests as the potential biomedical applications.[84] (Table 3).

8.7 Antiviral activity

AgNPs prepared from *Spirulina platensis* demonstrated that AgNPs have an inhibition rate of 48.334% of hepatitis C virus (HCV) compared with the standard drug of hepatitis, ribavirin.[135] The antiviral activities of Ag NPs derived from cyanobacteria were assigned to their interaction with viral proteins, which disrupt key steps in the virus life cycle. It has been reported that the viral entry of host cells can be inhibited by Ag NPs, which affects viral glycoproteins from binding to receptors of host cells. This mechanism was evident in an experiment where Ag NPs prevented IBV from entering the centrosome by inhibiting the formation of viral RNA genome.[136,137] Ag NPs also has the ability to act against both tropic forms of HIV-1 by preventing the protease activity of this virus (having wider spectrum of antiviral action) may classify this as a broad-spectrum antiviral.[13] In the case of SARS-CoV-2, the cyanobacterial metabolites involved in the Ag NPs synthesis inhibit viral replication by interacting with the key proteases, that are required for viral polyprotein cleavage, such as, Mpro and PLpro.[138] Likewise, the Ag-NPs of *Phormidium ambiguum* exhibited the highest scavenging activity of 48.7% comparing with that of the cyanobacterium *Desertifilum tharense,* which displayed 43.753%[116] (Fig. 5).

8.8 Anticancer activity

Silver Nanoparticles synthesized using *O. salina* show immense lethality towards human derived cancer cell lines, HeLa, the cervical adenocarcinoma and MDAMB-231 the breast adenocarcinoma, which reflects their possible employment as anticancer capability.[121] Similarly, AgNPs prepared from *Desertifilum* sp. showed cytotoxic effects on MCF-7, HepG2, and Caco-2 cancer cell lines, with IC_{50} values of 58, 32, and 90 μg mL^{-1}, respectively.[118] Studies demonstrated an unprecedented approach for the bio synthesis of AgNPs, using the polysaccharide of *Spirulina platensis* as reducing and capping agents, with superior anticancer activity against a hepatocellular carcinoma cell line. The IC_{50} for polysaccharides isolated from *Spirulina platensis* (PSP) and Ag-NPs were 65.4 and 24.5 μg mL^{-1}, respectively. Moreover, cell apoptosis assays for PSP and Ag-NPs against the growth of Hep-G2 cells revealed superior growth inhibitory effects of the bio synthesized Ag-NPs that encouraged tracing the apoptotic signaling pathway.[80] Silver nanoparticles produced by *Nostoc* sp. *Bahar* M induce oxidative stress and apoptosis leading to significant inhibition of growth of ehrlich ascites carcinoma tumour in the organs of tumour-bearing mice.[118] Similarly, in breast cancer cells (T47D) cell line, treated by *Anabaena flos-aquae*-synthesized Ag NPs, apoptosis was observed due to the induction of ROS and DNA fragmentation.[138] Silver nanoparticles (AgNPs) prepared by *Desertifilum* sp. displayed substantial cytotoxicity against MCF-7, HepG2 and Caco-2 cancer cell lines with IC_{50} values of 58, 32 and 90 μg mL^{-1}, respectively.[118,119]

8.9 Antioxidant property of AgNPs

The antioxidant property of AgNPs is related to its potential in scavenging free radicals and reducing oxidative stress and enhancing that of antioxidant enzymes as catalase, superoxide dismutase and glutathione peroxidase. Silver NPs prepared using cyanobacterial extracts of *Spirulina platensis* and *Nostoc linckia*, showed notable DPPH radical scavenging and total antioxidant capacity tests showing IC_{50} values of 45.2 μg mL^{-1} and 38.5 μg mL^{-1}, respectively.[135] The antioxidant potential is correlated with the content of phenolic compounds and other metabolites, which could be involved in free radicals scavenging and thus in the cellular protection against oxidative damage.[139,140] The scavenging activity was noted to be highly significant in the case of AgNPs synthesized by *O. salina* which showed IC_{50} 32.4 μg mL^{-1}.[121] Size, shape and surface charge of AgNPs also affect their antioxidant performance. Smaller NPs with higher surface area are often more efficient in being reactive and passing through cellular barriers in their potential role as antioxidant agents. *Chroococcus* sp. produces AgNPs ranging in size from 5–50 nm, and *Bacillus cereus* generates AgNPs in a smaller size range of 1–5 nm.[115]

9 Gold nanoparticles

9.1 Antibacterial activity

Over the past decade, cyanobacteria biofabricated AuNPs have been synthesized that are nontoxic, green and show potential antibacterial activity against several bacterial pathogens.

Table 3 Comprehensive analysis of cyanobacteria-mediated nanoparticles: synthesis mechanisms, physicochemical characterization, and quantitative pharmaceutical efficacy against pathogens and cancer cell lines

Nanoparticle type & source	Synthesis mechanism	Key metabolites/ reducing agents	Characterization methods	Pathogen/cancer target	Antimicrobial efficacy (MIC/ ZOI)	Anticancer/cytotoxic potency (IC_{50})	Ref.
AgNPs (*Nostoc linckia*)	Extracellular	*C*-phycocyanin (pigment)	UV-vis, TEM, XRD, FTIR, DLS	*S. aureus*, *P. aeruginosa*, *E. coli*, *K. pneumoniae*, MCF-7	ZOI: significant	27.79 μg mL^{-1} (MCF-7)	85
AgNPs (*Oscillatoria limnetica*)	Enzymatic/ metabolic	Proteins (amine/ carboxyl groups)	UV-vis, FTIR, TEM, SEM, XRD	*E. coli*, *B. cereus*, MCF-7, HCT-116	Not specified	6.15 μg mL^{-1} (MCF-7); 5.37 μg mL^{-1} (HCT-116)	81
ZnO-NPs (*Arthrospira platensis*)	Extracellular	Phycobiliproteins & polysaccharides	UV-vis, XRD, TXRF, TEM	*B. subtilis*, *S. aureus*, *P. aeruginosa*, *C. albicans*, Caco-2	MIC: 12.5–50 ppm; ZOI: 19.1–24.1 mm	9.95 μg mL^{-1} (Caco-2); 53.34 μg mL^{-1} (WI38)	124
AgNPs (*Desertifilum* sp.)	Intracellular	Phycoerythrin & phycocyanin	UV-vis, TEM, XRD, FTIR	5 pathogenic bacteria, MCF-7, HepG2, Caco-2	Not specified	58 μg mL^{-1} (MCF-7); 32 μg mL^{-1} (HepG2); 90 μg mL^{-1} (Caco-2)	117
AuNPs (*Nostoc calcicola*)	Extracellular	Phenolic compounds & proteins	UV-vis, FTIR, TEM, EDX, XRD	5 bacteria, 2 fungi, breast/cervical cancer	MIC: 11–18 μg mL; ZOI: 11–18 mm	37.3 μg mL^{-1} (breast); 44.5 μg mL^{-1} (cervical)	125
AgNPs (*Anabaena variabilis*)	Intracellular	Exopolysaccharides (EPS)	UV-vis, FTIR, TEM, SEM, XRD	HeLa, SiHa, HepG2, HEK-293	Not specified	23.76 μg mL^{-1} (HeLa); 11.21 μg mL^{-1} (SiHa)	126
AgNPs (*Oscillatoria princeps*)	Biomimetic	Nitrate reductase (enzyme)	UV-vis, FESEM, EDX	Not specified	ZOI: 10.6–14.6 mm	Not specified	127
AgNPs (*Chroococcus*/ *Characium*)	Extracellular	Extracellular proteins	UV-vis, XRD, TEM, TGA	MCF-7, HepG2	ZOI: 2–6.9 mm	40.9 μg mL^{-1} (MCF-7); 20.8 μg mL^{-1} (HepG2)	128
SeNPs (gamma irradiation)	Enzymatic	(Gamma ray induced reduction)	UV-vis, FTIR, SEM, EDX	HepG2, others	MIC: 0.313 μg mL; ZOI: 36.33 mm	8.87 μg mL^{-1} (HepG2)	125
CuO-Se BNPs (*L. siceraria*)	Extracellular	Flavonoids & phenolics	UV-vis, XRD, FTIR, SEM	MCF-7, Hep-G2, Wi-38	MIC: 7.8–250 μg mL; ZOI: 10–21 mm	31.1 μg mL^{-1} (MCF-7); 83.4 μg mL^{-1} (HepG2)	129
CMC-AuNPs (carboxymethyl cellulose)	Photo-catalytic	CMC polymer (stabilizer)	UV-vis, TEM, FTIR, DLS	*S. aureus*, *B. cereus*, *K. oxytoca*, MCF-7	MIC: 25–100 μg mL; ZOI: 13–26 mm	2.56 μg mL^{-1} (MCF-7)	130
GA@Ag-CuO Nanocomposite	Intracellular	Gum Arabic (polysaccharide)	UV-vis, TEM, FTIR, EDX	*S. epidermis*, *S. aureus*, *L. plantrum*, MCF-7	MIC: 15.6–125 μg mL^{-1}	26.11 μg mL^{-1} (MCF-7); 59.5 μg mL^{-1} (HepG2)	131
AgNPs (*Pseudanabaena*/ *Limnothrix*)	Biomimetic	*C*-phycocyanin & *C*-phycoerythrin	UV-vis, XRD, TEM, SEM	*E. coli*, *C. glutamicum*	Not specified	Not specified	132
MgO-NPs (*Cystoseira crinita*)	Nanocomposite	Fucoidan (polysaccharide)	UV-vis, FTIR, XRD, DLS	Bacteria, Caco-2, Vero cell	MIC: 12.5–50 μg mL^{-1}	113.4 μg mL^{-1} (Caco-2); 141.2 μg mL^{-1} (Vero)	133
AgNPs (actinobacteria)	Polymer-stabilized	Extracellular enzymes	UV-vis, FTIR, TEM, zeta	*E. coli*, *K. pneumoniae*, *P. aeruginosa*, MCF-7	MIC: 8–128 μg mL^{-1}	16.3 μg mL^{-1} (MCF-7)	134
AgNPs (*Streptomyces*/ *Bacillus*)	Extracellular	Microbial proteins	UV-vis, FTIR, TEM, XPS	MCF-7, DU-145	Not specified	<3.5 μg mL^{-1} (MCF-7); <2.5 μg mL^{-1} (DU-145)	129

Biosynthesized nanoparticles are being used as antibacterial mediated agents based on their geometrically designed extremely large surface area that originates from their nano-scale. It can attach to the bacterial peptidoglycan cell wall by electrostatic forces to degrade it. Membrane potential is altered, and ATPase activity is inhibited, which leads to a decrease in ATP content in the bacterial cell. Additionally, AuNP exposures cause a pore formation on the cell walls, which results in the leaking of the cell contents and interferes with tRNA binding to the ribosomal subunit inhibiting thus the transcription process. The accumulation of AuNPs in biofilms induces a higher cell wall tension, leading into nano-toxicity and metabolic interruption, subsequently leading to bacterial cell death. The deformation of the cell membrane due to nanoparticle clustering could then shorten treatment duration and reduce the side-effects of the nanomedicine.[22] Studies demonstrated AuNPs biosynthesized using *Oscillatoria* sp. and *S. platensis* showed antibacterial activity against Gram-positive bacteria, *B. subtilis* ATCC 19,659, and *S. aureus* ATCC 25,923, MRSA ATCC MP-3 and Gram-negative bacteria, *Salmonella typhi*

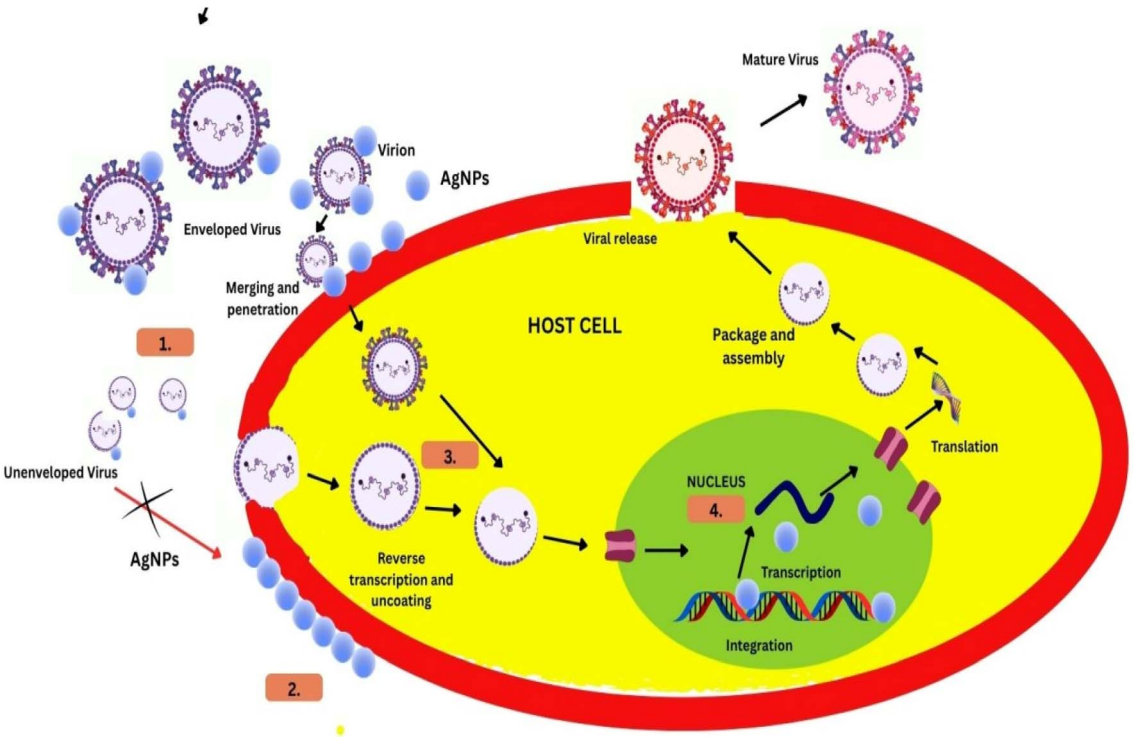


Fig. 5 NPs interrelate with the viral surface protein (gp120) in envelope and unenveloped virus. (2) AgNPs inhibits the host cell penetration by the virus. (3) AgNPs bars the viral entry of the cell to nucleus. (4) AgNPs prevent viral replication by inhibiting viral genome.

ATCC 14,028, *Klebsiella pneumoniae* ATCC 70,063 and *Pseudomonas aeruginosa* ATCC 9027.[140] *Spirulina subsalsa* synthesized spherical AuNPs exhibited excellent activity against *Staphylococcus aureus*, *S. pyogenes*, *Escherichia coli* and *A. baumannii*.[141] *Anabaena spiroides* synthesized AuNPs exhibited antibacterial activity against *K. oxytoca,* MRSA, and *S. pyogenes*[22] (Fig. 6).

9.2 Antifungal activity

The cyanobacterium, *Hassallia* sp. produced a variety of cyclic lipopeptides, such as, hassallidins and puwainaphycins, which target cell membranes of pathogenic fungi such as, Aspergillus *fumigatus* and *Candida albicans,* by binding to cholesterol and ergosterol, and ultimately inducing cell death.[142] Some phytochemicals found to have a positive relationship with antifungal effectiveness against infections by *Fusarium solani* and *Botryodiplodia theobromae* include phenolics, flavonoids and enzymes such as xylanase and *glucanase*.[143] The antifungal properties of AuNPs are size-dependent. In the case of *Candida* sp., fungal inhibition by 25 nm particles was higher as compared to 30 nm particles.[144] AuNPs may possibly interact with fungal proteins. Interaction of AuNPs with biologically active fungal H^+-ATPase enzyme in cells leads to deviation from the natural orientation of enzyme, hence loss of the fungal function. This disturbance leads to the detriment of metabolism, with reduced nutrition adsorption, eventually leading to death of the fungal cell. Additionally, the possible interaction between the shapes and sizes of the AuNPs and some components of the plasma membrane like sulfur containing protein or phosphorus of the DNA base can result in improved antifungal activity.[145] *Oscillatoria* sp. was used in bio synthesis of gold nanoparticles (AuNPs), which exhibited anti-fungal activities against *C. albicans* ATCC 24,423, *A. favus* ATCC 9643 and *C. tropicalis* ATCC 13,80 with ith inhibition zones ranging from 10 to 15 mm. Polysaccharides from *S. maxima* cyanobacterium were successfully employed for synthesis of AuNPs that further showed anticandidal activity toward *C. albicans*.[140]

9.3 Antiviral activity

The antiviral activity of gold nanoparticles (AuNPs) against several viruses such as, H3N2, H1N1, the herpes simplex virus, and the foot-and-mouth disease virus have been reported. The absorbance of nanoparticles on the virus surface was investigated using microscopic methods which induced modifications that further restrains viral entry into cells. Phosphates or thiols from amino acids and nucleic acids are the electron donor groups. The electron donor groups thus formed complexes with Au ions, inhibiting proviral transcription or reverse transcription by attaching directly to DNA or RNA molecules. It can also be assumed that AuNPs denatured inherent disulfide bonds to modify the viral protein. *In vitro* anti-HIV activity was shown by C-60-based AuNP and AgNPs. Thus, nanotechnology is highly anticipated to bring excessive benefits as an aid for the HIV/AIDS patients for years to come. Proteins from blue–green algae, namely scytovirin (SVN) and griffithsin (GRFT) contain unique structural organizations that facilitate simultaneous attachment to multiple carbohydrate moieties as well as flexible

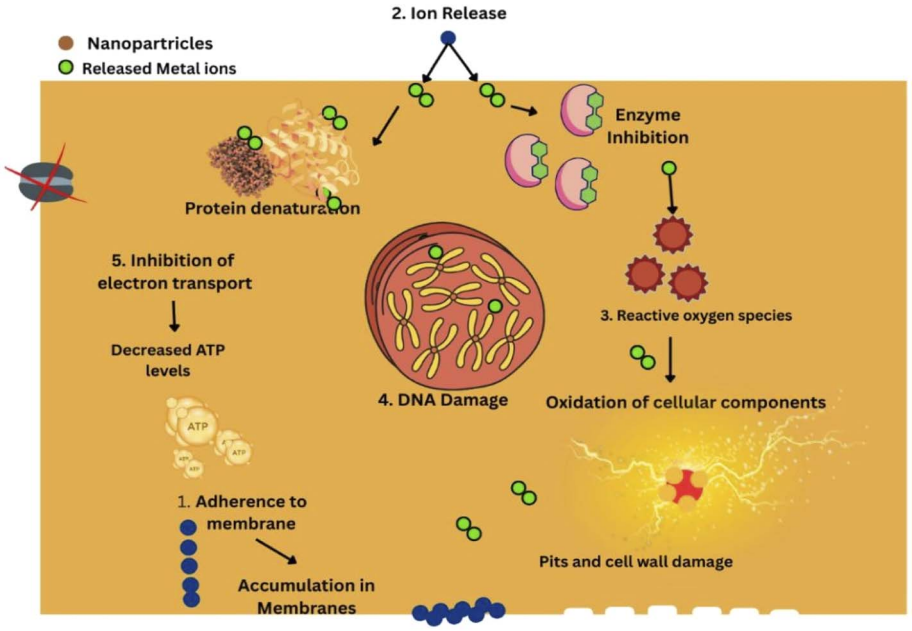


Fig. 6 Antibacterial mechanism of nanoparticles (1). Adherence to membrane: the nanoparticles bind to the bacterial cell wall, disrupting it, and accumulating in the membrane, destabilizing the membrane and damaging vital cells, causing membrane pits and cell wall rupture. (2) Ion release and enzyme Inhibition: the released metal ions (Ag^{+}) enter the cell and disrupts its structure and accumulates in the membrane, thereby damaging the membrane and essential cellular components (3). Reactive Oxygen Species (ROS) generation: metal ions trigger the production of ROS, which oxidize and damage proteins, lipids, and other essential cellular components, leading to membrane pits and cell wall damage. (4) DNA and energy damage: the released ions damage bacterial DNA, stopping replication, while also interfering with the electron transport chain, lowering ATP production and leading to energy depletion and cell death.

loop regions in their structures that harbour anti-HCV activity. SVN and GRFT both efficiently inhibit HCV envelope glycoproteins.[22]

9.4 Anticancer activity of AuNPs

Gold nanoparticles because of their ability to be shaped, sized, and surface chemistry are extensively used in anticancer drug delivery for targeting, internalization, and improved cytotoxicity of drugs. They are integrated into different types of delivery systems, including light-responsive, pH-sensitive and glutathione-responsive systems. For instance, gum karaya-stabilized AuNPs loaded with gemcitabine hydrochloride exhibited 19.2% of drug-loading efficiency and remarkably conferred the cytotoxicity upon A549 lung cancer cells to 10% more than that with the free drug, with marked suppression of colony formation along with intracellular ROS generation. The size and shape of AuNPs have a substantial impact on the efficiency of delivery of drugs. The study showed that the nano stars had the most systemic cytotoxicity compared with the nanospheres and nanorods; the results also demonstrated antiosogenesis of the bone cancer cells. Gelatin coated AuNPs which are spherical 50/100 nm; nanorods 20/50/100 nm applied in methotrexate delivery in the treatment of breast cancer were also used to study the influence of size on methotrexate release, in which the smaller NPs were barreling faster at acidic pH (5.4), and the efficiency at drug delivery was higher in the case of nanorods, which has also showed higher intrinsic toxicity. AuNPs also have a promising potential for PTT, which irradiates the tumor with a laser to trigger release or uptake of drugs by the cells. The doxorubicin-loaded AuNP vesicles killed 50% of HeLa cells upon laser irradiation compared to non-irradiated groups. Similarly, fabricated paclitaxel-loaded PEGylated aptamer-conjugated AuNPs that featured 86% encapsulation efficiency and the maximum release of drug at pH5.5 upon near-infrared (NIR) irradiation (160 mW cm^{-2}), almost 10% greater release in response to NIR exposure than under dark conditions. These NPs considerably reduced cell viability and increased apoptosis from 12.8% to 41.49% specifically targeting MUC-1-positive cells, accumulating almost twice as much as in MUC-1-negative cells.[18]

AuNPs derived from cyanobacteria have recently gained momentum in cancer therapeutics due to their exceptional physiochemical features and eco-friendly preparation. Cyanobacterial species like *S. platensis*, *A. variabilis*, *O. limnetica* and *N. muscorum* served as biological factories to generate AuNPs using cellular reducing and stabilizing metabolites such as proteins, flavonoids and polysaccharides. These biomolecules not only promote the reduction of gold ions into particles, but also cap and stabilize the particles, giving biocompatible and functional surface groups. This bio synthetic method is free from toxic reagents and the AuNPs produced are safer for biomedical applications and in oncology.

The anticancer action of cyanobacteria-mediated AuNPs is largely due to selective induction of cytotoxicity in cancer cells without causing damage to normal healthy cells. These NPs are taken up into cancer cells *via* endocytosis and accumulate into

organelles, such as mitochondria, to produce reactive oxygen species (ROS). Increase in ROS levels caused oxidative stress, loss of mitochondrial membrane potential and release of pro-apoptotic factors such as cytochrome c leading to activation of caspase-3 and caspase-9 and ensuing apoptosis. Further, AuNPs can disrupt the cell cycle, resulting in arrest at the G2/M phase that suppresses cellular growth. They also influence the major regulatory pathways such as PI3K/Akt, p53 in tumor cells to actively promote the apoptotic events.[146]

The anticancer effectiveness of these NPs has been proved through many recent studies. For example, AuNPs successfully synthesized with *Lyngbya majuscula* showed higher cytotoxicity with A549 lung carcinoma cells, although normal fibroblasts were not influenced.[99]

N. muscorum generated AuNPs showed cytotoxicity in-7 breast and liver HepG2 cancer cells; apoptosis was mediated by increased ROS formation and mitochondrial depolarization by nanoparticles.[101] Studies reported that *O. limnetica*-induced AuNPs were effective at inhibitingthe growth of the HeLa cervical cancer cells and they caused fragmentation of the DNA.[147] The AuNPs from *S. platensis* showed anticancer activity against, HepG-2 and A549 cell lines which were successfully killed by apoptosis, as identified by nuclear condensation and caspase activation.[148] Some decapeptides such as cryptophycins have shown potential antitumor properties. For example, cryptophycin A and B are reported active against KB cells which are effective against drug-resistant and drug-sensitive tumor cells. It has been well documented that several species of *Lyngbya*, *Nostoc*, *Oscillatoria*, and *Phormidium* produce bioactive compounds, which were proved to be having effective anti-cancer effect. A cyanobacterium *Gloeocapsa* sp. acted as a reducing and capping agent, in a successfully synthesized AuNPs of spherical and triangular shapes intracellularly; and its anticancer activity was seen against human cervical cancer cell line. AuNPs bioreduced by cyanobacterial extracts of *Oscillatoria* sp. and *S. platensis* showed control activity against human colon CaCo-2 and cervical HeLa cancer cells with IC_{50} value of 311.00, and 382.90 μg mL^{-1} (Fig. 7).[149]

9.5 Antioxidant activity AuNPs

AuNPs synthesized by cyanobacteria are employed for biomedical applications in various fields including antioxidants therapy, and diseases associated with oxidative stress. For instance, AuNPs prepared from *Cyanothece* sp. have previously

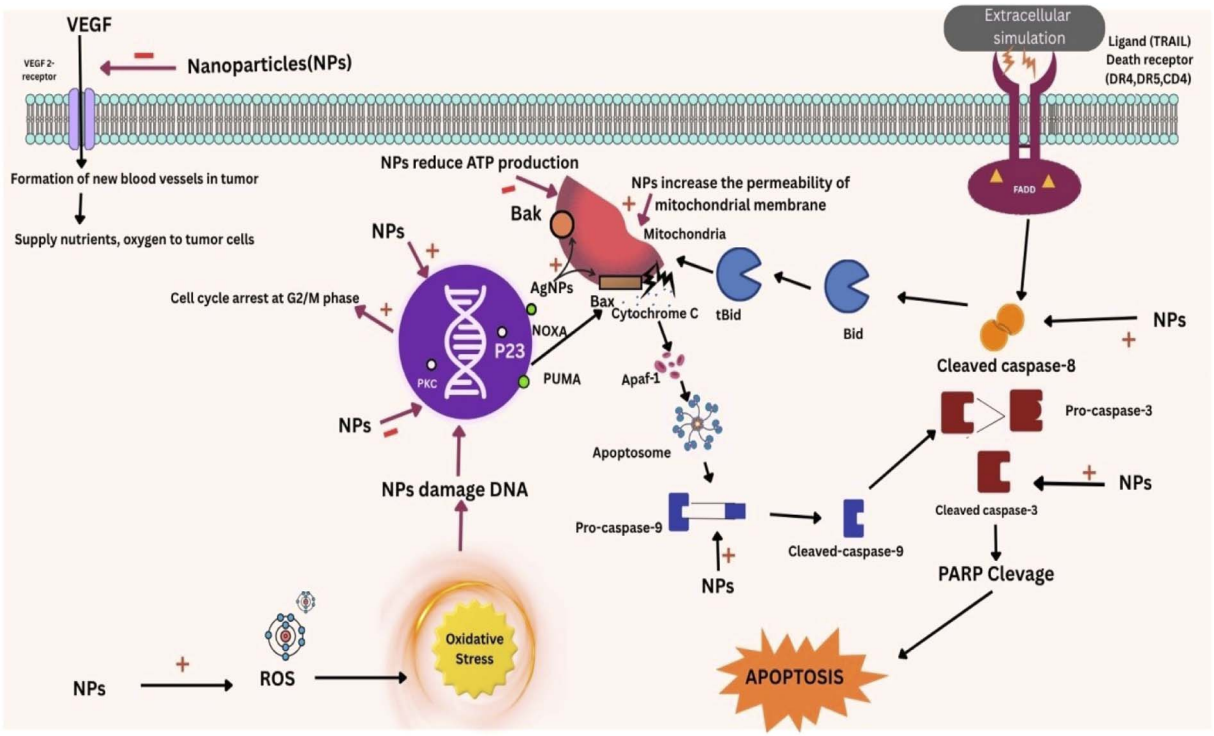


Fig. 7 Anticancer activity of NPs: NPs upregulated caspase-8 induces stimulation and activation of the pro-apoptotic proteins-Bid, *t*Bid, and an addition of cytochrome C. Further Apaf-1 release leading to the formation of apoptosome. After apoptosome is formed, caspases get activated leading to apoptosis. The upregulation of cleaved caspase-3 by NPs directly as well enhances the process of apoptosis. NPs leads to the enhancement of the release of cytochrome C based on the growth of apoptotic protein- Bak and Bax, which leads to the destruction of the mitochondrial membrane and damages the DNA because of oxidative stress (genetic damage). These NPs prevent the formation of protein kinases (PKC) as well as at G2/M phase of the cell cycle. NPs increases the expression of P-23 protein that activates the apoptosis process through activating the expression of other pro-apoptotic proteins. The caspases can be activated with intracellular pro-apoptotic proteins released into the cell that leads to cel death following the DNA damage. Vascular endothelial growth factor (VEGF) which is the pro-angiogenic factor that is involved in the stimulation of the signalling pathways that promote cell proliferation and migration, by tyrosine kinase receptor (VEGf Rz), and incurs angiogenesis in tumor cells. NPs suppress VEGF induced cell proliferation in the mechanism.

been used as drugs in a model of reversal of cardiomyopathy caused by systemic administration of isoproterenol in the experimental rat,[150] that may have clinical applications for cardiac therapy. As natural antioxidant AuNPs originated from cyanobacteria have also been reported for treating neurodegenerative diseases because oxidative stress is one of the major factors of these diseases.[150]

10 Applications for cyanobacteria AgNPs

Cyanobacteria-produced AgNPs have also been investigated in the context of wound healing, notably in diabetic wounds. Blithely, due to their antioxidant and anti-inflammatory properties, these nanoparticles can promote wound closure, collagen synthesis, and angiogenesis, making them suitable candidates for therapeutic applications as well.[150] Besides, AgNPs also appear to possess an antioxidant activity that would offer protection against heavy metal induced oxidative stress, as shown in its efficacy in sequestering and minimizing the effect of mercury ions[151] (Table 4).

10.1 Agriculture

Cyanobacterial AgNPs have been also employed in the agricultural sector for increasing crop yield and plant pathogen control. The potential of these nano nutrients and pesticides is mediated either through enhancement of nutrients uptake by the plants and their growth, or as nano-pesticides controlling the plant pathogens and pests.[171] Additionally, AgNPs have been documented to stimulate the production of EPS in cyanobacteria, an important biopolymer used in food, pharmaceuticals, and cosmetics industries.[172] Additionally, silver nanoparticles from cyanobacterium are sustainable to different sectors of agriculture like plant protection, promotion of plant growth and post-harvest management of plants. Cyanobacterial like species of *Nostoc*, *Anabaena* and *Oscillatoria* mediated cyanogenic AgNPs were found to have strong antifungal activity against *Alternaria alternata*, *Pseudomonas syringae* and *F. oxysporum*. They exert their mode of action by attacking the microbe membrane, leaking cell contents and oxidative stress causes cell proliferation inhibition of the pathogen.[173] Additionally, cyanobacteria-assisted AgNPs improve the seed germination, root length, and overall vigour of the plant. These NPs, if applied at low doses, enable phytohormone signaling and nutrient uptake thus enhancing biomass and chlorophyll content of the treated plants. Enhanced yield and disease control of rice, tomato, and wheat have been reported when treated with biosynthesized AgNPs. Furthermore, these nanoparticles can form part of antimicrobial coverings for fruit and vegetables, thereby prolonging their duration and contentment during refrigerated storage systems and transportation.[19]

From an industrial standpoint, agrochemical companies are beginning to adopt cyanobacteria-derived AgNPs for use in nano-fertilizers, nano-pesticides, and bio-formulated sprays. These formulations offer prolonged effectiveness and some reduced environmental impact compared to conventional agrochemicals. However, while the benefits are substantial, ongoing research is addressing concerns related to nanoparticle accumulation in soil and crops, as well as potential toxicity to beneficial soil microbiota. Regulatory frameworks are being developed to guide the safe use of nanomaterials in agriculture, with biosynthesized nanoparticles receiving particular interest due to their natural origins and lower ecological footprint.[174]

10.2 Environmental applications

These nanoparticles have been employed for the degradation of organic contaminants like methylene blue by photocatalysis, which is practical in wastewater treatment, as microbial disinfections. These have shown a strong bactericidal and virucidal efficacy towards a broad range of pathogens, like, *E. coli*, *Salmonella* sp. and *Vibrio cholerae* found in the contaminated water systems. They act by disrupting bacterial membranes, causing oxidative stress by ROS and disrupt enzymatic systems, finally causing the lysis of pathogenic cells. Thus, cyanobacteria-fabricated AgNPs are promising to use in water treatment equipment, filter coatings, and sterilization spray.[175] Additionally, AgNPs based cyanobacteria have been used for heavy metal biosorption from industrial effluents, effectively participating in a circular economy process, including recovery and reuse of metals.[176] The cyanobacterial AgNPs have also been used for producing bioplastics, since polyhydroxyalkanoates (PHA) is biodegradable and therefore any application in producing PHA would pave way for more sustainable alternatives to conventional plastics.[177] Silver nanoparticles synthesized using cyanobacteria offer considerable promise in environmental remediation, due to their potent antimicrobial activity, catalytic potential, and sustainable synthesis makes those popular. As concerns about pollution, waterborne pathogens, and industrial waste intensify, the use of biologically synthesized nanomaterials is emerging as a sustainable solution.[173]

Heavy metal removal is just one of the important applications of these AgNPs. Cyanobacteria synthesized AgNPs have been found to reduce and sequester toxic heavy metal pollutants such as, cadmium, lead, mercury that are involving in redox reactions as well as, nanoparticle adsorption. Biomolecules on nanoparticle surfaces, originated from the cyanobacteria extract increase the binding affinity towards metal ions and therefore effectively remove them from alkali solutions.[178] These characteristics render them appropriate for nanoadsorbents, bioreactors and industrial effluent treatment devices. Those have been demonstrated for the degradation of many organic pollutants including dyes, *e.g.*, methylene blue, rhodamine B, and pesticides *via* photo or catalytic oxidation. Due to their high surface area and electron exchange ability, those rapidly transform toxic substances to less toxic intermediates, thus contributing to environmental detoxification.[99] This renders those useful for applications like textiles, tanning and agrochemicals that often generate dye-laden or pesticide-contaminated wastewater. AgNPs prepared through cyanobacteria have been included in antimicrobial paints, coatings and packages that allow inhibiting of biofouling and microbial

Table 4 Industrial applications of Ag and Au nanoparticles

Sl. no.	Nanoparticle type	Application area	Specific use	Mechanism/ function	Examples	Benefits	Challenges	Ref.
1	Silver (ag NPs)	Textiles	Antimicrobial fabrics	Releases Ag^+ ions to inhibit microbial growth	Sportswear, socks, hospital linens	Durable, odour-resistant	Leaching during washing	152
2		Water treatment	Pathogen removal	Adsorption and inactivation of bacteria on nanoparticle surfaces	Nanocomposite filters (*e.g.*, LG NanoH_2O)	High efficiency, low energy use	Environmental accumulation	153
3		Medical implants	Antimicrobial coatings	Prevents biofilm formation on implants by releasing Ag^+ ions	Silver-coated catheters, orthopedic implants, bone cement	Reduces risk of post-operative infections	Long-term cytotoxicity, ion leaching	154
4		Cosmetics	Preservative in creams	Prevents microbial spoilage, extending product life	AgNP-infused creams provide better skin permeabilit y	Long shelf life, non-irritating	Regulatory restrictions in some regions	155
5		Air purification	Antibacterial air filters	Captures and inactivates airborne pathogens through silver ion release	HEPA filters with silver coating	Improved air quality, potential health benefits	Long-term effectiveness, ion release rate	156
6		Wound dressing	Infection prevention & healing	Releases Ag^+ ions to kill bacteria and reduce inflammation	Acticoat™, Aquacel® Ag dressings	Reduces infection risk, promotes faster healing	Potential cytotoxicity, bacterial resistance	157
7		Agriculture	Crop protection	Acts as a broad-spectrum fungicide and pesticide	AgNP-coated seeds, foliar sprays	Increased yield, disease resistance	Soil and water ecotoxicity	158
8		Electronics	Conductive inks	Sintered nanoparticles form conductive traces for circuits	Printed flexible electronics, RFID antennas	Low-cost fabrication, flexibility	Oxidation (tarnishing), electromigration	159
9		Food packagin g	Antimicrobial packaging	Inhibits the growth of spoilage microbes on the packaging surface	Food packaging films and wrappers	Prolonged shelf life, improved food safety	Risk of nanoparticles leaching into food	152
10	Gold (au NPs)	Medicine & theranostics	Cancer therapy & imaging	Generates localized heat (photothermal therapy) when exposed to NIR light to kill tumor cells	AuroLase® therapy, targeted contrast agents	Targeted, non-invasive treatment; combines diagnosis with therapy	Precise targeting, long-term clearance	160
11		Sensors	Pathogen & biomolecule detection	Surface plasmon resonance (SPR) shifts colorimetrically upon binding to a target molecule	COVID-19 lateral flow tests, glucose biosensors	High sensitivity, rapid results, visual detection	Requires precise surface functionalization	161
12		Pharmaceuticals	Targeted drug delivery	Act as carriers to transport drugs directly to diseased cells, enhancing absorption	AuNP-doxorubicin conjugates for cancer treatment	Targeted therapy, improved drug stability, controlled release	Biocompatibility, high cost	162
13		Electronics	Conductive inks & transparent films	Provides high electrical conductivity and stability for printing circuits on various substrates	Printed flexible circuits, components in OLEDs	Miniaturization, flexibility, enhanced performance	Cost, long-term stability of printed components	163
14		Catalysis	Industrial synthesis & hydrogen production	High surface area and unique electronic properties	Catalytic converters, catalysts for producing hydrogen fuel	High efficiency, selectivity, works under mild condition s	Cost, deactivation over time	164

Table 4 (*Contd.*)

Sl. no.	Nanoparticle type	Application area	Specific use	Mechanism/ function	Examples	Benefits	Challenges	Ref.
				accelerate chemical reactions				
15		Data storage	High-density optical storage	Encodes data in 5 dimensions (3D position + orientation + wavelength) using lasers on nanorods in glass	"Superman memory crystal" prototypes	Extremely high data density and longevity	Slow writing/ reading speeds, complex tech	165
16		Solar energy	Photovoltaic cells	Plasmonic effects enhance light absorption across the solar spectrum	AuNP-enhanced thin-film or dye-sensitized solar cells	Increased light-harvesting efficienc y	High production cost, stability issues	166
17		Cosmetics	Anti-aging & skin products	Claimed antioxidant properties; reflect light to give skin a radiant glow	Snail slime based cosmetics, luxury anti-wrinkle creams	Immediate glow effect, perceived luxury	Scientific evidence is debated, high cost	167
18		Anti-counterfeiting	Security labels	Creates a unique, unclonable optical signature ("plasmonic fingerprint")	Security tags for luxury goods, pharmaceuticals	Extremely high level of security	Cost of implementation, specialized readers	168
19		Environmental remediation	Water purification	Catalyze the degradation of persistent organic pollutants (*e.g.*, dyes, pesticides)	Lab-scale systems for degrading industrial wastewater	High catalytic efficiency for breaking down pollutants	Catalyst recovery, potential for leaching	169
20		Biotechnology	DNA/RNA detection	Binds to nucleic acids, enabling detection through electrochemical or optical signals	AuNP-based biosensors for genetic analysis	High specificity and sensitivity for diagnostics	Sample preparation complexity	170

adhesion on surfaces. This would be especially beneficial in lowering microbiological contamination in public places, health care centers and food industries. Biosynthesized nanoparticles are less toxic and biodegradable in the environment compared with chemically synthesized AgNPs, meeting the global objectives of sustainable environmental technologies.[174] However, despite these benefits, environmental implications of cyanogenic AgNPs should be strictly controlled in terms of their toxicological consequences. Issues concerning nanoparticle accumulation in aquatic biospheres as well as, disruption in microbe diversity and long-term presence in soil and water are all currently being explored. However, available evidence indicates that biosynthesized AgNPs from cyanobacteria with biocompatible coatings and a smaller synthesis footprint have a safer and cleaner status compared with those of traditional nanomaterials in pollution control technology applications.

10.3 Food packaging and preservation

Cyanobacteria mediated silver nanoparticles is incorporated into biodegradable polymers or cellulose films, which function as antimicrobial agents to improve the shelf-life of perishable food products by inhibiting microorganism contamination and spoilage, imparting antioxidant properties to the packaging films. These cyanobacteria AgNP-containing film packaging had been reported to be effective against the food borne pathogens such as *Listeria monocytogenes*, *Salmonella typhimuriam*, *Aspergillus niger* on meat, dairy and fruit surfaces.[179] These bi-functionalities inhibit lipid oxidation or retards discoloration and thus preserving the organoleptic and nutritional quality of food stuffs.[172] Meanwhile, for commercial food companies the prospect of using nano-packaging is attractive as a means of meeting clean-label and eco-friendly packaging trends and responding to the demands of expanded exports of fresh produce, seafood and dairy. Use of green-synthesized nanoparticles lessens the possibility of regulatory rebuttal for synthetic chemical residues and are advantageous for international food safety regulations.

10.4 Cosmetics and personal care

Biosynthesized silver nanoparticles are now widely used in cosmetics and personal care applications, because of their antimicrobial, anti-inflammatory, and anti-aging effects. Cyanobacteria mediated synthesis of AgNPs show better skin-compatibility properties attributable to the organic capping

agents derived from the metabolites of cyanobacteria such as polysaccharides, flavonoids and peptides. There are also nanoparticles in creams, lotions, face masks, deodorants and sunscreens that inhibit microbial growth, calm inflamed skin and protect from oxidative damage. In contrast to their synthetic counterparts, cyanogenic AgNPs represent a clean-label and environmentally friendly alternative to what current consumers are seeking for: natural and sustainable products. Furthermore, their diminutive size is suited for cutaneous penetration which increases the efficacy of the active agents without irritating the skin. AgNPs are also used in some of the formulations for the whitening and anti-pigmentation, as it inhibits synthesis of the melanin, leading to a decrease in the oxidative stress. Consequently, cosmetic industries are now getting inclined toward cyanobacterial nanoparticles to fulfil the demand for green and efficacious multifunctional ingredients.[180]

10.5 Ammonia sensing

Recently, cyanobacterium *Haloleptolyngbya alkalis* KR2005/106 had been reported for the photo-biochemical synthesis of silver nanoparticles (approx. 50 nm). This cyanobacterium was isolated from a saline-alkaline habitat, a soda lake. The considerable decrease in the blue absorption observed is attributed to the interaction between silver nanoparticles and ammonia. The increased sensitivity of this transition was previously observed between 50 and 500 ppm ammonia.[181]

10.6 Degradation of carcinogenic dyes

Silver nanoparticles were bio synthesized with a cyanobacterial extract, and the photocatalytic degradation of methylene blue dye was studied. Silver nanoparticles can act as catalysts for the decomposition of methylene blue dye under UV-H_2O_2 (20 mg L^{-1}) to less than 4 h, with dye removal of 18% in this time span.[175] *A. variabilis* and *S. platensis* were used for the synthesis of silver nanoparticles and as bio-sorbents to removal of malachite green dye. The dye concentration was reduced when the removal efficiency increased to 93% and 82% for *S. platensis* and *A. variabilis*-AgNPs, respectively. Results indicate that when compared with *A. variabilis*, larger specific surface area and lower particle size of *S. platensis*-AgNPs led to its superior catalytic activity in dye degradation. After dye treatment, Ag NPs were re-inoculated in growth of *Triticum aestivum* L., Giza 171 seedlings to compare the apparent non-toxicity of Ag NPs toward environmental system with its safety for agricultural purposes.[122] AgNPs with cell free aqueous cyanobacterial extract *Microchaete* NCCU 342 were prepared and used for the degradation of azo-dye, Methyl Red (MR).[182] MR dye (50 mg L^{-1}) was decolorized by 84.60% at 2 h and the extract alone without nanoparticles could remove 49.80% of the dye.[183]

10.7 Biosensing and diagnostics

Cyanobacteria-mediated silver nanoparticles are being widely employed in sensors and diagnostic devices due to their efficient surface plasmon resonance (SPR), electronic conductivity and high surface area-to-volume ratio. These nanoparticles can be used to increase the sensitivity and selectivity of detection platforms for pathogens, toxins, heavy metals and disease markers.[184] As examples, AgNPs prepared with species of non-nitrogen-fixing *Oscillatoria* or nitrogen-fixing *Nostoc* have been functionalized with bio-probes to diagnose glucose, DNA fragments or cancer bio-markers at some ultra trace level. The biocompatible, non-toxic surface of cyanobacterial AgNPs enhances the immobilization of probes, signal transduction, and minimizes background noise in electrochemical and colorimetric assays. These AgNPs are being incorporated into lateral flow test strips, electrochemical biosensors and lab-on-chip devices for medical, environmental and agricultural diagnostics. Thus, the use of bio synthesis approach drives these biosensing platforms to be earth-conscious.[179]

10.8 Dentistry and oral care

In dental sciences, these have applications on oral hygiene products, restorative materials, and endodontics. Additionally, these are ideal candidates for toothpastes, mouth rinses, composites and implants *etc.*, having their antimicrobial activity against dental and oral pathogens such as, *Streptococcus mutans*, *Lactobacillus acidophilus* and *Candida albicans*. Cyanobacteria mediated synthesized AgNPs are potential candidates, as they offer nontoxic and mucosal compatibility especially those synthesized from *A. cylindrica*. Those also are being explored for biofilm control on dental prosthetics, and root canal disinfection in a manner that would obviate the use of harsh chemical irritants such as sodium hypochlorite. The slow liberation of ionic silver from the naturally derived capping protein matrix leads to long-term anti-microbial activity without staining or irritation. Dental products businesses are starting to spend on these types of green nano materials to satisfy elevated requirements from clients who need less risky and natural oral care products[19].

10.9 Textile industry

The use of silver nanoparticles is growing in the textile industry, as those are natural antimicrobial and are applied to produce antimicrobial textiles in paper and polymer materials, where a good standard of hygiene and long lifetime are critical. Notably, AgNPs have been incorporated into medical textiles to provide antimicrobial protection, which is an essential aspect in health care, that is able to prevent infections, and the spreading of nosocomial infections. Products for an actual industrial application of textiles with cyanobacteria made AgNPs are still in part pending.[118]

11 Applications of gold nanoparticles

Synthesis of AuNPs, particularly with cyanobacteria, has attracted considerable attention for its eco-compatibility, cost-effectiveness, and amenability from energy saving, for mass production. By secretion of extracellular molecules such as peptides, polysaccharides, and proteins, cyanobacteria are effective biological synthesizing agents of nanoparticles. Due to the biologically capped layer, these AuNPs show improved

biocompatibility and stability; and therefore, are suitable for several applications in industry.

11.1 Pharmaceutical and biomedical applications

Cyanobacteria-fabricated AuNPs have great potential in biomedicine, because its non-toxic synthesis and the natural capping agents on the surface improve biological interaction. Their drug delivery applications have been reported, where the biomolecules immobilized on AuNPs can be employed to assist desired delivery and release of anticancer drugs. Additionally, they are promising in the field of photothermal therapy of cancer being able to absorb near-infrared (NIR) light effectively and convert it into heat and kill cancer cells selectively without affecting the adjacent tissues. These nanoparticles are also highly antimicrobial that is suiting as wound healing dressings and surgical instruments coating too. The growth suppressive abilities are due to the cooperative effects of gold along with bioactive cyanobacterial compounds on pathogenic bacteria such as, *E. coli* and *S. aureus*.[18]

11.2 Targeted drug delivery

Naturally coated with biomolecules like peptides and polysaccharides, these nanoparticles serve as perfect surfaces for the conjugation of ligands, such as antibodies, nucleic acids, or chemotherapeutics. These nanoparticles can passively accumulate in tumor tissues exploiting the enhanced permeability and retention (EPR) effect. In addition, the delivery of drugs can be only induced by certain stimuli like, pH, enzymes, or light, which enable a target therapy and any systemic side effect is avoided.[185]

11.3 Diagnostic imaging

Gold nanoparticles synthesized by cyanobacteria are also useful contrast agents for CT, as well as photoacoustic imaging. They are appealing because of their large atomic numbers that enhance X-ray absorption and SPR properties leading to enhanced photoacoustic signals. Cyanobacteria-capped AuNPs show higher biocompatibility in comparison with iodine-based agents and may be tailored for actively targeting specific disease indicators, which makes diagnoses more accurate.[186,187]

11.4 Self-cleaning and antimicrobial coatings

Coatings generated with cyanobacteria-assembled AuNPs were found to be effective in self-cleaning, anti-fouling and antimicrobial applications. These coatings are useful in marine applications, electronic platforms, and biomedical surfaces by preventing the colonization of microorganisms or the collecting of dirt. The biocompatibility and chemical inertness of such AuNPs provide long-term stability, and their optical behaviour provides aesthetic or functional features.[188,189]

11.5 Diagnostic devices

Biosynthesized AuNPs have been utilized in diagnostic devices, for detecting biomolecules or pathogens. AuNPs prepared from cyanobacteria maintain the surface plasmon resonance features that are critical for use in colorimetric and lateral flow assays. Functionalization with antibodies or nucleic acids can offer further specificity for detection of disease biomarkers in point-of-care diagnostic kits Their own naturally occurring capping agents provide for an excellent bioconjugation and stability in biological media.[190]

11.6 Catalysis in the environment

Cyanobacteria-mediated gold nanoparticles have great potential in environmental catalysis, since they are green-synthesized and high surface-area-to-volume nanostructures. These AuNPs can also be used to catalyze different oxidation reactions of interest such as degradation of VOCs and CO, even at low temperatures. Their efficiency in decomposing harmful industrial gases renders them suitable for incorporation in catalytic converters and gas treatment systems. These particles are stabilized by biological capping agents derived from cyanobacteria, thereby enhancing catalytic turnover as well as being sustainable for the environment. Furthermore, these biogenic NPs avoid the use of toxic chemical stabilizing and reducing agents that are used in traditional synthesis, thus, following the principles of green chemistry.[191]

11.7 Chemical synthesis catalysis

Moreover, biogenic AuNPs are highly active catalysts in a wide range of redox reactions, which are applied in fine chemical and pharmaceutical industries. AuNPs made by cyanobacteria were reported to catalyze the reduction of nitroarenes to amines and the oxidation of alcohols to aldehydes or ketones at room temperature. These reactions are important for the synthesis of dyes, agrochemicals and pharmaceuticals. These biosynthesized AuNPs are, therefore, considered ideal for green chemical synthesis, as the reaction is carried out under mild conditions and with high selectivity. Moreover, these nanoparticles are also recyclable and can be utilized repeatedly for several cycles of MCNPs toward their economic and environmental efficiency.[192]

11.8 Electronics and sensor technology

The high conductivity and biocompatibility of cyanobacteria AuNPs make those interesting candidates for electronic and biosensor systems. When used in electrochemical sensors, those serve as a signal enhancer to sense pollutants or biomolecules with high sensitivity. Through bio-reduction, unique shapes and surface functionalities are typically added that can act as a fingerprint resulting in improved sensor performance. These attributes make them attractive building blocks for flexible electronics, wearable sensors, and nanocircuit construction as well.[193]

11.9 Environmental applications

Cyanobacteria synthesized-AuNPs are being actively used for environmental monitoring as well as remediation. Their surface can be modified for heavy metal detection of lead, arsenic, and cadmium in water. Besides that, those are used as catalysts in

degradation reactions to eliminate organic pollutants as dyes, pesticides, and pharmaceutical residues from industrial effluents.[194]

11.10 Agricultural and veterinary applications

In agriculture, biocomponent AuNPs–fertilizer–pesticide combination can be used as a smart delivery system. Their biofunctional nature enhances their ability to interact with plant tissues, which can help increase nutrient uptake and utilization. They play a role in lowering the misuse of agrochemicals, which leads to avoid the pollution of the environment.[194] Cyanobacteria-mediated AuNPs also appeared to enhance seed germination and promote growth of the plant, because of potential modulation of stress responsive genes. In veterinary medicine, these NPs are employed in lateral flow assays to enable the rapid diagnosis of diseases in farm animals. Due to their bio-safety profile, they have a great potential for food-producing animal applications.

11.11 Photonics and electronics

Cyanobacteria-mediated AuNPs exhibit distinct plasmonic characteristics, which are crucial for emerging next-generation photonic and nano-optoelectronic architectures. These nanoparticles display what is known as surface plasmon resonance (SPR) in which light is absorbed and scattered very strongly at certain wavelengths. It has been widely used in the design of optical switches, waveguides and photonic crystals. As biosynthesized pathways frequently give shape to monodisperse, spherical, anisotropic NP with stable capping of cyanobacterial biomolecular networks, the optical responses of these can be custom tuned for a specific device need.[179]

12 Barriers to clinical and industrial translation

It would not be out of place to cite, an old work of this laboratory, monitoring cyto-toxicity of AgNPs biosynthesized with the higher timber-yielding plant, *Anogeisus acuminata* against lymphocytes culturing *in vitro* from human umbilical cord blood, as an offal.[195] Such work of monitoring cytotoxicity and nuclear toxicity of cyanobacterial nanoparticles with human lymphocytes are in progress and gaining much more attention now a days. Despite the promising *in vitro* antimicrobial and anticancer properties of silver and gold nanoparticles synthesized by cyanobacteria reported in recent literature, several significant barriers hinder their clinical and industrial translation.

12.1 Standardization and reproducibility

A major challenge is the lack of standardized protocols for nanoparticle synthesis. The physicochemical properties of nanoparticles—such as size, shape, and surface charge—are highly sensitive to variations in cyanobacterial strains, culture conditions, and synthesis parameters. This leads to batch-to-batch variability and polydispersity, complicating reproducibility and making it difficult to ensure consistent efficacy and safety in clinical or industrial settings.[82,196,197]

12.2 Scalability and process control

Scaling up biosynthesis from laboratory to industrial levels introduces further complexity. Factors such as light distribution, nutrient supply, and contamination risk become more difficult to control in large-scale photobioreactors, often resulting in inconsistent nanoparticle yields and quality. Maintaining axenic (pure) cultures at scale is also challenging and increases operational costs.[196]

12.3 Regulatory and safety concerns

There is a lack of comprehensive toxicological data for cyanobacteria-derived nanoparticles. While *in vitro* studies show low toxicity to healthy cells at certain concentrations, *in vivo* biosafety, long-term effects, and environmental impacts remain underexplored. Regulatory agencies require robust, standardized data on nanoparticle characterization, safety, and efficacy, which is currently insufficient for clinical approval[196,197]

12.4 Quality control and good manufacturing practice (GMP)

Industrial translation demands strict quality control and compliance with GMP standards. The biological variability inherent in cyanobacterial systems makes it difficult to meet these requirements, especially regarding nanoparticle uniformity, purity, and stability.[196,197]

13 Conclusion and future perspectives

Biosynthesis of AgNPs and AuNPs using cyanobacteria appears to be attractive and sustainable, in comparison to the traditional physicochemical methods. This clean technology is at the same time convenient, inexpensive and meeting the demand of green technology around the world without using any hazardous reagents. Current situation has rendered it quite obvious that the outcome of laboratory findings and the clinical preparedness differ significantly. It has already been demonstrated that these nanoparticles possess a powerful antimicrobial activity; numerous studies have consistently revealed a high bactericidal efficacy with regard to the MDR pathogens which is a pointer that in the days of age it could substitute the conventional antibiotics. On the other hand, application of nanocrystals as far as clinical cancer therapy and targeted drug delivery is seriously a conjecture. Despite the perceived presence of reported cytotoxicity on specific cell lines, *in vitro* observations are yet to be converted into clinical efficacy since adequate *in vivo* pharmacokinetic data of nanotoxicity of its prospective off targets have not been investigated in detail. Not only that, the existing impediment in bench-top synthesis to manufacturing is the economies of scale as a technological aspect in the form of scalability and repeatability. This means that biological synthesis may be dynamic and hence change in

size and shape of nanoparticles batch to batch, making it quite challenging to standardize it in case it is utilized as a pharmaceutical. However, biosynthesis of cyanobacterials is field of genomics is currently developing. The futures of synthetic biology and genetic engineering development give hope to enable the control of the morphology of a nanoparticle at a molecular level because of manipulation of biosynthetic pathways. To sum up, despite the fact that the chemical variety of cyanobacteria offers a great channel towards the new therapeutic options, the potential has to be brought into reality by turning simple record of synthesis of various compounds into tangible form of standardization. The future work should put into consideration the mechanisms of fine formation, biosafety profile and scalable bioreactors. Only once these and other types of engineering and regulatory-level bottlenecks are overcome, the massive therapeutic promise of cyanobacteria be translated into practical solutions to problems of world health.

Author contributions

S Sabat: writing – original draft, writing review & editing, visualization. S Patra: formatting and editing. S Swain: formatting and editing., S Bej: formatting and editing. AK Bishoyi: writing – original draft & editing, visualization. G Sabat: formal analysis. RN Padhy: writing – review & editing, supervision & fund acquisition.

Conflicts of interest

The authors declare no competing interests.

Data availability

No primary research results and no new data were generated or analysed as part of this review.

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