Cyanobacteria-Based Nanoparticles and Their Therapeutic Potential in Cancer Treatment

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Abstract

Cancer remains one of the leading causes of mortality worldwide, highlighting the urgent need for innovative and effective therapeutic approaches. In recent years, nanotechnology has emerged as a promising field in cancer research due to the unique physicochemical properties of nanoparticles (NPs). Among various biological systems, cyanobacteria have gained considerable attention as eco-friendly and efficient platforms for nanoparticle biosynthesis because of their rapid growth, metabolic diversity, and ability to produce bioactive compounds.

This review highlights the role of cyanobacteria-mediated nanoparticles in cancer therapy, with particular emphasis on zinc oxide (ZnO), gold (Au), and silver (Ag) nanoparticles. Cyanobacteria are capable of synthesizing nanoparticles through both intracellular and extracellular mechanisms, producing nanomaterials with significant biomedical potential. ZnO nanoparticles exhibit anticancer activity mainly through reactive oxygen species (ROS) generation, oxidative stress, and apoptosis induction in cancer cells. Gold nanoparticles have demonstrated promising applications in photodynamic and photothermal therapies by enhancing targeted tumor destruction while reducing damage to healthy tissues. Furthermore, silver nanoparticles have shown strong anticancer effects through selective tumor targeting, ROS generation, DNA damage, and apoptotic pathways.

Overall, cyanobacteria-based nanoparticles represent promising candidates for cancer treatment due to their targeted therapeutic potential and biological compatibility. However, additional studies are still required to assess their long-term safety, toxicity, and clinical applicability for future cancer therapies.

Keywords : *Cyanobacteria, Nanoparticles, Cancer Therapy, Anticancer Activity, Gold Nanoparticles, Silver Nanoparticles, Zinc Oxide Nanoparticles*

1. Introduction

Nanotechnology is an emerging field that includes synthesis, characterization, and development of various nanomaterials,[1][2] that have significant roles in daily life, providing valuable products that improve industrial production, agriculture, communication, and medicine .[3] The term “nano” denotes any particles or materials with at least one nanosized (1–100 nm) dimension. Nanoparticles (NPs) differ significantly from their bulk materials in terms of physical, chemical, and biological properties.[4] NPs have significant roles in bio-diagnostic and optical biosensing, nanophotonics, and imaging and treatment of many diseases affecting human health.[5] Quantum dot NPs have been used to detect the location of malignant cells inside the body . Iron oxide NPs are used in resonance imaging and diagnosis of tumors. hesis, applications of NPs in various areas as well as the toxicity strategies of NPs against living cells .

In the past few years, the synthesis of NPs using cyanobacteria has become an active research field.[6][7] Cyanobacteria (blue-green microalgae) are ubiquitous Gram-negative photoautotrophic prokaryotes, for which evidence they existed 3.3–3.5 billion years ago was found. They exist in the environment as unicellular, filamentous or colonial forms surrounded by a mucilaginous sheath. Owing to their ubiquitous nature and the vast diversity of their metabolites, they have several applications in the biomedical field.

During the last few decades, the emergence of new cancers and their developing resistance to available drugs has led to chemotherapeutic failure. In this regard, the medicinal properties of cyanobacteria have been explored.

Back in 1500 BC, *Nostoc* sp. was first used to treat gout, fistula and different types of cancers. Several cyanobacteria species are cultivated in commercial platforms to extract bioactive compounds, which have been shown to possess anticancer activity and potentially kill a variety of cancer cells via the induction of apoptosis or altering the activation of cell signaling .

The current paper comprehensively reviews work on cyanobacteria-mediated fabrication of NPs, their abiotic and biotic conditions used during biosynthesis process including illumination, pH, temperature, type of synthesis process (extracellular and intracellular), followed with the factors influence on the synthesis process of NPs, the corresponding mechanisms of the biological synthesis, applications of NPs in various areas as well as the toxicity strategies of NPs against living cells.

2. Biomedical application of cyanobacteria-based nanoformulations in cancer therapy

Cancer is among the leading causes of death in humans. [8] The incidence of cancer is increasing because of various factors, including aging, an increasing population, and lifestyles that predispose to individuals to the disease.[9] Advances in nanoscience have led to new methods to prevent tumor progression and metastasis. [10][11]

With the appreciation of the enhanced properties of metals at nanosizes, extensive research on different nanometals has been carried out in recent years for exploring their applications in cancer research. Emphasizing the biological synthesis, cyanobacteria are considered as one of the best biological systems for nanoparticle (NP) synthesis, both intra-cellularly as well as extra-cellularly . [12] However, there are only a few reports available on the biological synthesis of noble metal NPs utilizing cyanobacteria as the host system. Silver (Ag) is the most commonly reported NP synthesized .[12][13][14]

Besides this, gold (Au), palladium (Pd) and platinum (Pt) NPs of well-controlled size are also formed from cyanobacteria such as *Anabaena*, *Calothrix, Leptolyngbya*, etc. [14]
Very few studies on the above have suggested that these NPs could be used for the treatment of cancer . [15]

Recently, silver nanoparticles (AgNPs) synthesized from the aqueous extract of Oscillatoria limnetica have shown cytotoxic effects on human breast (MCF7) and colon (HCT-116) cancer cell lines.[16]

silver nanoparticles (20–50 nm size) synthesized from *L. majuscula* were screened against three leukemic cell lines, i.e., K562, MOLT-3, and REH, and showed dose- and time-dependent anticancer activity. The REH cells showed the maximum sensitivity to AgNPs .[17] These AgNPs exhibit in vitro antitumor activity against the human breast MCF-7 cancer cell line (IC50 = 27.79 ± 2.3 μg/mL), and were shown in vivo to inhibit tumor growth in Ehrlich ascites carcinoma-bearing mice .[12]

The Ag-NPs (100–1000 μg/mL) showed no effect on peripheral blood mononuclear cells. However, at the same concentrations of Ag-NPS, the Reh cell line was more sensitive to Ag-NPS than other leukemia cell lines, including myeloblastic leukemia and lymphoblastic leukemia.[19]

Also, the scholars studied the nuclear morphological changes of REH treated with Ag-NPs using DAPI staining assay and observed that Ag-NPs resulted in nuclear damage, shrinkage, chromatin condensation and chromatin margin.

A recent publication reported that *Anabaena sp*. could produce Ag-NPs with strong antitumor activities against *Dalton's lymphoma* and colo205 cancer cells.[20]
They found that low concentration of SNP was able to reduce the proliferation of both cell types via inducting the production of reactive oxygen species (ROS) and DNA damage led to cell death.

The antitumor properties of AgNPs biosynthesized by Nostoc sp. HKAR-2 were screened against the MCF-7 cell line . [21]

The Ag-NPs killed tumor cells effectively as their concentrations increased, suggesting potential applications in the treatment of cancerous cells.

Consequently, they showed notable effects as anticancer agents and could be used as nanomedicines in cancer research. Ag-NPs suppressed the proliferation of MCF-7 cancer cells seven-fold compared with normal human lung fibroblast (WI38) and human
amnion (WISH) cells. By contrast, the same concentration (13.07 ± 1.1 µg/mL) of a standard antitumor drug, 5-fluorouracil, had a greater cytotoxic effect against WI38 and WISH cells than against malignant cells .

ZnO NPs synthesized by using the cell extract of the Nostoc sp. EA03 exhibit less cytotoxicity when used in lower concentrations against the human adenocarcinoma alveolar basal epithelial cells (A549 cells) and human lung fibroblast (MRC-5 cells) cancer cell lines.[18] Cells and inhibited tumor growth.

Ebadi et al found that a 50 µg/mL concentration of ZnO NPs eliminated 50% of cancerous A549 lung cancer cell line, while the same concentration killed less than 50% of normal (MRC-5) cells . [22]

Similar studies could also be carried forward by conjugating cynobacterial metabolites with nanotags, or the nanovectorization of canonical anticancer drugs using cynobacteria to enhance the anticancer potential of the drug.
These could find future applicability, with a better shelf-life and stability as natural capping occurs .

3. Cyanobacteria –Mediated Biosynthesis of Nanoparticles

Due to their ease of cultivation under ambient conditions and rapid growth rate, cyanobacteria have attracted considerable attention in nanobiotechnology.[23] Their cellular components possess the ability to absorb heavy metal ions and convert them into biologically active compounds. As a result, cyanobacteria are considered an important biological platform for nanoparticle synthesis, enabling both extracellular and intracellular nanoparticle production.

Various studies have demonstrated the capability of cyanobacterial species to synthesize different types of nanoparticles, including metallic nanoparticles such as silver (Ag) and gold (Au), metal oxide nanoparticles such as zinc oxide (ZnO) and copper oxide (CuO), as well as bimetallic nanoparticles such as silver–gold (Ag–Au) alloys. [24]

4. Anticancer Effects of Zno Nanoparticles

Several studies have demonstrated that zinc oxide nanoparticles (ZnO NPs) can act as effective carriers with significant anticancer activity against various cancer cell types.[25][26] For instance, Ahamed et al. reported that zinc oxide nanorods exhibited antitumor effects against A549 lung cancer cells. These effects were shown to occur through concentration-dependent mechanisms, including the intracellular generation of reactive oxygen species (ROS), activation of the p53 protein, and caspase-mediated pathways.[27]

Furthermore, De Berardis et al. investigated the anticancer effects of ZnO nanoparticles on human colon cancer cells (LoVo) and reported that elevated intracellular ROS production plays a crucial role in their antitumor activity. [28] In another study, Akthar et al. evaluated the cytotoxic effects of ZnO nanoparticles on several cancer cell lines, including A549, HepG2, and BEAS-2B. Their findings demonstrated that ZnO nanoparticles induce cancer cell death through multiple molecular mechanisms, such as caspase activation, DNA fragmentation, and oxidative stress, while exhibiting minimal toxicity toward healthy cells.[29]
Additionally, the anticancer effects of ZnO nanoparticles have been reported against malignant head and neck cancer cell lines (HN5). The results indicated that a concentration of 300 µg/mL exerted the highest

impact on inducing cellular death in these cells. Overall, the concentration-dependent cytotoxic properties of zinc oxide nanoparticles highlight their promising potential as candidates for cancer chemotherapy.[30]

5. Anticancer Effects of Gold Nanoparticles

Gold nanoparticles (AuNPs), due to their unique optical and physicochemical properties, have emerged as promising candidates in cancer therapy. One of their most significant applications is in light-based therapeutic approaches, including photodynamic therapy (PDT) and photothermal therapy (PTT). In PDT, photosensitizing agents accumulate selectively within tumor tissues and are activated by light of a specific wavelength. This activation results in the generation of reactive oxygen species (ROS) and singlet oxygen, which induce oxidative stress, damage cellular structures, and ultimately promote apoptosis or necrosis in cancer cells.

In addition, gold nanoparticles play a crucial role in photothermal therapy. In this approach, light energy, particularly within the near-infrared (NIR) region, is absorbed by gold nanoparticles and converted into heat, leading to the targeted destruction of cancer cells. Gold nanoparticles, especially nanorods and nanoshells, exhibit high photothermal conversion efficiency and tunable optical properties, making them highly effective in enhancing therapeutic outcomes while reducing the need for high-intensity laser irradiation.

Several studies have demonstrated that the combination of gold nanoparticles with laser irradiation significantly enhances tumor destruction while minimizing damage to surrounding healthy tissues. Therefore, gold nanoparticles are considered effective tools for targeted cancer therapy and improving the efficiency of light-mediated therapeutic strategies.[31]

6. Anticancer Effects of Silver Nanoparticles

Silver nanoparticles (AgNPs) have gained considerable attention as promising nanomaterials for cancer therapy. Although their toxic properties share certain similarities with conventional chemotherapeutic agents, the nanoscale nature of AgNPs may contribute to reducing unwanted side effects while improving treatment specificity. One of the major advantages of AgNPs is their ability to accumulate in tumor tissues through both passive and active targeting mechanisms.

Passive targeting is primarily mediated through the enhanced permeability and retention (EPR) effect. In tumor tissues, abnormal angiogenesis and impaired lymphatic drainage result in porous vasculature, facilitating the penetration and accumulation of nanoparticles within the tumor microenvironment. Moreover, physicochemical properties such as particle size, morphology, surface charge, and coating materials can significantly influence nanoparticle accumulation and therapeutic efficiency.

In addition to passive targeting, active targeting strategies involve the use of ligands and specific molecules attached to the nanoparticle surface to enable selective recognition of cancer cell receptors. Several studies have demonstrated that incorporating AgNPs into transferrin-functionalized mesoporous silica or polymeric carriers linked to chlorotoxin peptides enhances selective delivery to cancer cells and contributes to tumor growth suppression.

Furthermore, AgNPs exert anticancer activity through multiple molecular pathways, including the induction of reactive oxygen species (ROS), oxidative stress, DNA damage, and activation of apoptotic signaling pathways, ultimately leading to cancer cell death. Therefore, due to their targeted delivery capability and cytotoxic effects, silver nanoparticles are considered valuable candidates for the development of advanced cancer therapeutic strategies.[32]

7. Conclusion

Cyanobacteria-based nanoparticle synthesis has emerged as a promising and environmentally friendly approach in nanobiotechnology, particularly in the field of cancer therapy. Due to their rich bioactive composition and ability to biosynthesize metallic nanoparticles, cyanobacteria provide an efficient biological platform for producing nanoparticles with potential biomedical applications.

Among the synthesized nanoparticles, zinc oxide (ZnO), gold (Au), and silver (Ag) nanoparticles have demonstrated significant anticancer properties through various molecular mechanisms. ZnO nanoparticles primarily induce cancer cell death through reactive oxygen species (ROS) generation, oxidative stress, and apoptosis. Gold nanoparticles have shown remarkable potential in photodynamic and photothermal therapies by enhancing targeted tumor destruction while minimizing damage to healthy tissues. Similarly, silver nanoparticles exhibit anticancer activity through targeted accumulation in tumor tissues, ROS production, DNA damage, and apoptosis induction.

Despite the promising therapeutic potential of these nanoparticles, further investigations are still required to evaluate their long-term safety, toxicity, biocompatibility, and clinical efficacy. Therefore, continued research may contribute to the development of safer and more effective nanoparticle-based strategies for cancer treatment in the future.

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