Anti-cancer green bionanomaterials: present status and future prospects

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ABSTRACT
Cancer is one of the most common health problems responsible for outnumbered deaths worldwide. Nanomedicine plays an important role in developing alternative and more effective treatment strategies for cancer theranostics. However, the toxicity, high cost and nanoparticles (NPs) production complexity are some of the major issues that obstruct the use of existing nanomedicine. Recently, the green synthesis of biogenic NPs from plants and microbial sources has become an emerging field due to their safer, eco-friendly, simple, fast, energy efficient, low-cost and less toxic nature. Interestingly, NPs play a key role in diagnosis of tumor at the initial stage by allowing cellular visualization. Furthermore, prospective applications of green NPs include magnetically responsive drug delivery, anti-cancer activity, photo-thermal therapy and bio-imaging. The present review provides perspective on the use of anti-cancer green bionanomaterials with a focus on their present status and future prospects in the theranostics of cancer.

1. Cancer: a global menace
According to the National Cancer Institute (NCI), United States (U.S), cancer contains over more than 100 types of Institute (1). Besides, it is anticipated that the incidence of cancer by 2030 will reach around 21.7 million and there would be about 13 million deaths owing to aging and population growth. The latest report published in June 2016 by iMSHealth (Institute for Healthcare Informatics) anticipates the global cancer treatment market to reach $150 Billion by 2020 Informatics (2). Nevertheless, the tumor load in the future is likely to be considerably larger due to lifestyle adoption, leading to an increased risk of developing tumor, such as physical inactivity, cigarette smoking and unhealthy diet in the economically developing countries' society (3). Notably, cancer causes one in seven deaths globally, causing more deaths than malaria, tuberculosis and AIDS Society (3, 4). Impressively, the largest proportion of cancer cases is in developing countries, accounting for around 57% of new cases and 65% of cancer-related
deaths. In 2012, cancer caused premature deaths of about 4.3 million people and the number of premature cancer deaths are presumed to increase by 44% between 2012 and 2030 Organization (5). By 2025, it is estimated that in the industrialized world only 20–25% of the people will be aged over 65 years, and of those 50–60% who die of tumor will be aged over 75 years (6). On 1 January 2016, over 15.5 million of the population of the United States had a previous history of cancer disease. By 1 January, 2026, this number is estimated to increase to 20.3 million. Moreover, the high prevalent cancers in 2016 that affects women are uterine corpus (757,190), breast (3,560,570), and colon and rectum cancer (727,350). For men, prostate (3,306,760), melanoma (614,460), and colon and rectum (724,690) cancers are most common (7). Additionally, nearly 189,910 new cancer patients and about 69,410 cancer-related deaths were estimated among black people in 2016 in the United States, involving 95,920 cases among women and 93,990 cases in men. Although black people have higher death rates due to cancer than whites, the discrepancy has lessened for all types of cancer combined and for prostate and lung cancers (in males only).

Radiotherapy, chemotherapy and surgery are some of the cancer treatments which are used to improve a patient’s life. Besides, one of the major problems in the cancer treatment process is the side-effects owing to conventional treatment strategies (8–10). Recent cancer research findings have enhanced understanding about carcinogenesis, the metastatic cascade and genetic factors that influence tumor growth and development. Overall, despite some progress in cancer control, incidence and death rates are increasing for cancer types. Recently, the applications of nanobiotechnology have revealed novel strategies for the treatment and diagnosis of cancer. Thereby, the current review article aims to highlight significant applications of biosynthesized green nanomaterials in cancer theranostics and the hurdles in their way to clinical trials.

2. Green bionanomaterials: an insight

Green bionanomaterials involving metals such as gold, silver, copper, titanium, zinc and iron prepared from different bio-sources, and have been reported for various biomedical applications (11). In addition, metal NPs are used in drug delivery, gene delivery, medicine, cell labeling, sensors, food packaging, wound dressings, etc. However, some applications of metal NPs are still under development such as magnetically responsive drug delivery, photo-thermal therapy and photo-imaging (Figure 1) (12–14). Although fabrication of NPs has attracted great interest for various physical and chemical processes, but there is an urgent need to explore alternative routes owing to some unsatisfying conditions of these methods such as the need for high temperature in the thermo-reductive process or intensive energy in the laser ablation process (15). Moreover, the fabrication of NPs by a chemical process may require toxic substrates, generates harmful wastes or requires large amounts of energy and even has low productivity (16). Hence, natural products and resources may ultimately prove to be more efficient and cost-effective. Remarkably, many plant extracts, algae and an extensive range of microorganisms containing bacteria, actinomycetes, fungi and yeast are reported to be proficient in synthesizing bionanomaterials, Priester et al. (17), Barabadi et al. (18), Honary et al. (19), Rahimi et al. (20), Salunke et al. (11), Ovais et al. (21), Mukherjee et al. (22), Patra et al. (23) and Ovais et al. (24). Interestingly, isolated chloroplasts were reported to be able to catalyze the biosynthesis of bionanomaterials. More interestingly, microalgae were designed for ecofriendly, scalable and permanent photobioreactors for sustainable and continuous fabrication of valuable bionanomaterials (15). Notably, the exact mechanism of biosynthesis of metal NPs is not well understood yet (25). However, it is believed that some enzymes play a role in bio-reducing metal ions to form metal NPs (26, 27). Figure 2 shows the schematic mechanism of microbial-mediated synthesis of metal NPs (11). The negatively charged bacterial cell wall interacts electrostatically with metal ions having positive charge. In addition, the bioreduction process may be catalyzed by enzymes inside the cells or on the cell surface. Salunke et al. (28) suggested the role of Saccharomyces cerevisiae cell wall components, some proteins and alcoholic compounds in the synthesis and stabilization of MnO2 NPs (28). The mechanism of extracellular microbial-mediated biofabrication of metal NPs is basically due to microbial nitrate reductase responsible for reduction of metal ions into metallic NPs (11). All the mentioned mechanisms lead to extracellular or intracellular fabrication of metal NPs. In case of phytosynthesis of metal NPs, it is believed that phytochemicals such as proteins, flavonoids, polyphenols, alkaloids, saponins, phenols, essential oils and polyols which are present in the plants extract play a main role in bio-reducing the metal ions, converting them to metal NPs and also capping of the synthesized NPs for stabilization (13, 29–31). The plant-mediated mechanism of biogenic silver NPs’ (AgNPs’) production is illustrated in Figure 3.
2.1. Anti-cancer activity of green nanomaterials: A mechanistic approach

*In vitro* anti-cancer activity of metal bionanoparticles has been confirmed against different cancer cell lines, i.e. MDA-MB-231 and MCF-7 (human breast adenocarcinoma) (32, 33), A549 (human lung adenocarcinoma) (34, 35), HCT116 (human colon colorectal carcinoma) (36), HeLa (human cervical cancer) (37, 10, 38), NCI-H460 (non-small cell lung cancer) (39), U87 (glioblastoma multiforme cell) (40), PANC-1 (pancreatic adenocarcinoma) (41), MG-63 (osteosarcoma cell) (42, 43), AGS (human gastric carcinoma) (44, 45), SMMC-7721 (human hepatoma cells) (46), LS174T (human colon adenocarcinoma cell) (46), HT-29 (human colorectal adenocarcinoma) (47), Varsha B (48), Caco-2 (human epithelial colorectal adenocarcinoma) (47, 49), HCT 15 (human colon adenocarcinoma) (50, 51), PC-3 (human prostate carcinoma) (52, 53), U937 (human histiocytic lymphoma cell) (54), COLO205 (human colon adenocarcinoma) (41, 54), B16F10 (mouse melanoma) (54, 55), 4T1 (mouse breast cancer) (56), CRL-1451 (mouse lung adenocarcinoma) (56), EAC (ehrlich ascites carcinoma) (57), CT-26 (mouse colon adenocarcinoma) (56), WEHI-3B (mouse leukemia) (56), CEM-ss (human T acute lymphoblastic leukemia) (58), CaOV-3 (ovarian adenocarcinoma) (41), Jurkat (human T acute lymphoblastic leukemia) (58, 59), HL-60 (human acute myeloid leukemia) (41, 60), K562 (human chronic myelogenous leukemia) (58, 61), A431 (human vulvar squamous cell carcinoma) (62), HNGC-2 (human adult glioma tissue) (55), ECV-304 (human urinary bladder carcinoma) (55), RAW254.7 (mouse leukemia) (49), SiHa (human cervical squamous cell carcinoma) (63), DL (dalton’s lymphoma) (64), HepG2 (hepatic cancer) (65–67), HEp-2 (human larynx carcinoma) (68, 69), ZR-75-1 (human caucasian breast carcinoma) (70), DAUDI (human burkitt’s lymphoma) (70), T47D (human breast cancer) (71), KB (human oral cancer) (72, 73), C26 (murine colon carcinoma) (74), LoVo (human colon adenocarcinoma) (75), LoVo/DX (multidrug resistance human colon adenocarcinoma sub-line) (75). The anticancer activity of various metal bionanoparticles from different bio-sources has been listed in Tables 1 and 2 from studies conducted in recent years by several research groups. Based on the enlisted studies, metal NPs exhibit a dose-dependent cytotoxic activity on various cancer cell lines. Moreover, biocompatibility testing of metal NPs has been done on different normal cell lines such as HaCaT (human keratinocyte) (76, 77), HMEC (human mammary epithelial cell) (33), HDFa (human normal skin dermal fibroblast) (39), HEK 293 (normal human embryonic kidney cell) (40, 78), Vero (african green monkey kidney cell) (79, 80), RWPE-1 (non-malignant human prostate epithelial cell) (81),...
PBMC (human peripheral blood mononuclear cell) (82), HL-7702 (normal human liver cell) (46), 3T3 (normal mouse fibroblast cell) (83, 84), HUVEC (human umbilical vein endothelial cell) (55), Rat L6 (rat skeletal muscle cell) (85), MDCK (canine cocker spaniel kidney cell) (86), CV-1 (monkey African green kidney fibroblast) (87), WI-38 (human caucasian fetal lung) (87), HEK-293 (human embryo kidney) (88), BHK21 (hamster syrian kidney) (89), MRC-5 (normal human lung fibroblast cell) (41, 45), Raw 264.7 (Murine macrophage cell lines) (35), 3T3-L1 (mouse embryo) (90), PLs (human normal peripheral lymphocytes) (34), hFOB (human fetal osteoblast progenitor cell) (91), MCF10A (human breast epithelial cell) (71), H9c2 (rat cardiac myoblast) (92), NIH3T3 (mouse fibroblast) (93) and C2C12 (mouse muscle myoblast) (94).

According to the literature, several studies reported nontoxicity and biocompatibility of some metal NPs in normal cell lines, but high toxicity in cancer cell lines. For instance, Anand et al. (95) reported notable antitumor activity of phyto-synthesized palladium NPs against A549, but no toxicity was found in human normal peripheral lymphocytes cells (95). Besides, Du et al. (96) reported plant-mediated synthesis and anticancer activity of AgNPs against Hela and A549 in the range of 1–5 μg/mL, but no significant cytotoxic effect was observed up to 10 μg/mL in normal HaCaT and also ≤2 μg/mL in Raw 264.7 (96). Similarly, Uma Suganya et al. (33) reported substantial in vitro anticancer activity of biosynthesized AuNPs (2–10 μg/mL) against MDA-MB-231, but no significant toxicity was found in normal HMEC in the range of 5–80 μg/mL, indicating considerable biocompatibility of NPs in normal cells (33). Also, Kummara et al. (97) showed very high cytotoxicity of green synthesized AgNPs against NCI-H460 at 240 ppm, but no cytotoxicity was found in normal HDFa (97). Furthermore, Singh et al. (98) reported not only remarkable cytotoxicity of phyto-fabricated AgNPs against A549 and HeLa above 5 μg/mL, but also no significant toxicity in normal RAW 264.7 (98). Further work showed antitumor effects of bio-fabricated AgNPs (0.02–50 μg/mL) against MCF-7; however, no cytotoxic effect was found in normal human blood mononuclear cells (99). In addition, Namvar et al. (58) reported biocompatibility of biological AuNPs in normal human blood mononuclear cells up to 100 μg/mL, but substantial cytotoxicity against cancer cell lines including CEM-ss, Jurkat, HL-60 and K562 (58). Likewise, Venkatesan et al. (76) showed biocompatibility of biosynthesized AuNPs in

**Figure 2.** Schematic mechanism of microbial-mediated synthesis of metal nanoparticles (Adapted with permission from Salunke et al. (11)).
normal HaCaT in the range of 10–50 μg/mL (76). Furthermore, Yang et al. (87) reported no cytotoxicity of plant-mediated synthesized AuNPs (10–160 μg/mL) in normal CV-1, WI-38 (87). Although these studies depicted biocompatibility of metal NPs, some studies are not in agreement. Specifically, Majeed et al. (100) reported fungus-mediated synthesis of AgNPs by using *Penicillium decumbens* (MTCC-2494) and assessed significant cytotoxic effects by MTT assay in the range of 20–120 μg/mL against A-549 while 50% survival was demonstrated in the normal Vero cell line (100). In other study reported by Baharara et al. (101), as evidenced by MTT assay, biosynthesized AuNPs inhibit proliferation of HeLa cells (IC50:100 μg/mL) and normal bone marrow mesenchymal stem cells (IC50:300 μg/mL). However, cytotoxicity of AuNPs in bone marrow were lower than cancerous Hela cells (101). Likewise, Xia et al. (46) affirmed stronger cytotoxic effects of biogenic AgNPs (IC50: 27.75 μg/mL) against human cancerous hepatoma SMMC-7721 cells but showed lower cytotoxic against human normal liver (HL-7702) cells (IC50: 81.39 μg/mL) (46). Furthermore, Ma et al. (102) reported that the biosynthesized AgNPs, using a cell-free filtrate of the fungus strain *Penicillium aculeatum* Su1 as a reducing agent, presented higher biocompatibility toward human bronchial epithelial cells and high cytotoxicity in a dose-dependent manner with an IC50 of 48.73 μg/mL toward A549 cells. Additionally, Kasithevar (13) reported a simple and rapid synthesis of AgNPs using aqueous leaf extract of *Alysicarpus monilifer* mostly spherical in shape with a mean size of 15 ± 2 nm. Their study showed no cytotoxicity of AgNPs against Vero cell lines at the concentration of 200 μg/mL after 72 h of incubation. In contrast, Valli Nachiyar et al. (103) reported microbial-mediated synthesis of titanium dioxide (TiO2) NPs. In their study, TiO2 NPs were found to be more toxic against normal HaCaT (IC50: 55 μg/mL) than cancerous HEp2 cell lines (IC50:172 μg/mL) (103). Moreover, Lima et al. (104) reported genotoxic effects of microbial biosynthesized spherical AgNPs (Average size: 40.3 ± 3.5 nm) at concentrations of 5.0 and 10.0 μg/mL (104). In a study, natural anti-cancer flavone Chrysin (ChR), (5, 7-Dihydroxyflavone ChR), was used to synthesize AgNPs and AuNPs in a greener route without toxic additives. ChR strongly reduces Ag+ and Au3+ into their nano-forms with uniform size, shape and surface chemistry. In vitro anti-cancer results revealed that the prepared NPs exhibit enhanced cytotoxicity than ChR against treated two
## Table 1. Phyto-sources for synthesis of bionanoparticles and their anticancer activity in various cell lines for the past 5 years.

| Plant                          | Part used | Nanoparticle type | Size (nm) | Morphology               | Anticancer activity (in vitro model)* | Dose (µg/well) | Exposure time | Major outcome | Reference |
|--------------------------------|-----------|-------------------|-----------|--------------------------|---------------------------------------|----------------|---------------|---------------|-----------|
| Acalypha indica                | Leaf      | CuO               | 26–30 nm  | Spherical                | MCF-7                                 | 6.5–100 µg/mL  | 48 h          | IC50: 56.16 µg/mL | Sivaraj and colleagues (32) |
| Achillea biebersteinii         | Leaf      | Ag                | 10–40 nm  | Spherical and pentagonal | MCF-7                                 | 15–100 µg/mL   | 24 h          | IC50: 20 µg/mL  | Baharara et al. (153) |
| Adenium obesum                | Leaf      | Ag                | 10–30 nm  | Spherical                | MCF-7                                 | 100–600 µg/mL  | 24 h          | IC50: 217 µg/mL | Farah et al. (154) |
| Alianthus excelsa             | Leaf      | Ag                | 22–30 nm  | Spherical                | MCF-7                                 | 50–150 µg/mL   | 24 h          | IC50:265.579 µg/mL | Vinmathi and JACOB (155) |
| Albizia adianthifolia         | Leaf      | Ag                | 4–35 nm   | Spherical                | A549 and PLs                          | 10 and 50 µg/mL | 6 h           | Low toxicity at 10µg/mL, but significant toxicity at 50µg/mL in A549 | Gengan and colleagues (34) |
| Aloe vera                     | Leaf      | Ag                | 70.7–192.02 nm | Spherical               | PBMCs                                 | 0.0025–0.04 mg/mL | 48 h         | IC50: ≤0.0025 mg/mL | Tippayawat and colleagues (82) |
| Alternanthera sessilis        | Leaf      | Ag                | 30–50 nm  | Spherical                | PC3                                    | 1.56–25µl/mL   | 48 h          | IC50: 6.85 µg/mL | Firdhouse and Lalitha (156) |
| Alternanthera tenella         | Leaf      | Ag                | ~48 nm    | Spherical                | MCF-7                                 | 25–100 µg/mL   | 24 h          | IC50: 42.5 µg/mL | Sathishkumar et al. (157) |
| Andean Mora (Rubus glaucus Benth.) | Leaf   | Ag                | 12–50 nm  | Quasi-spherical          | HepG2                                  | 0.01–1.0 µM    | 2 h           | No toxicity observed | Kumar and colleagues (65) |
| Annona squamosa               | Peel      | SnO2              | Average size: 27.5 nm | Spherical | HepG2                                 | 1–500 µg/mL    | 2 h           | IC50: 148 µg/mL | Roopan and colleagues (66) |
| Antigone letopus Hook. and Arn. | Aerial part | Au             | 13–28 nm  | Spherical with few triangular shapes | MCF-7                                 | 31.25–1000 µg/mL | 48 h         | IC50: 257.8 µg/mL | Balasubraman et al. (158) |
| Apple (Malus domestica)       | Fruit     | Ag                | 10–40 nm  | Spherical                | MCF-7                                 | 10–100 µg/mL   | 24 and 48 h | No toxicity at ≤ 70 µg/mL after 24 h of incubation Significant toxicity at ≥ 10 µg/mL after 48 h of incubation | Lokina and colleagues (9) |
| Areca catechu                 | Nut       | Au                | 22.2 nm   | Spherical                | HeLa                                   | 6.25–100 µg/mL | 24 h          | IC50: 25.17 µg/mL | Rajan and colleagues (37) |
| Argemon maxicana              | Leaf      | Ag                | 2–6 nm    | Spherical                | SiHa                                   | 25–100 µg/mL   | 72 h          | IC50: >50 µg/mL | Jha and Prasad (63) |
| Artemisia marschalliana Sprengel | Aerial part | Ag             | 5–50 nm   | Spherical                | AGS                                    | 3.125–100 µg/mL | 24 h         | IC50: 21.05 µg/mL in AGS | Salehi and colleagues (44) |
| Azadirachta indica            | Leaf      | Au                | ≤121.7 nm | Spherical, hexagonal and triangular shapes | HeLa and MDCK | 0.1–0.25 mM | 48 h | No toxicity | Dharmatti and colleagues (86) |
| Azadirachta indica (neem)     | Leaf      | Ag                | 94 nm     | Spherical                | HDFa and NCI-H460                      | 0–240ppm       | 24 h          | Very high toxicity at 240 ppm in NCI-H460, but no toxicity in normal HDFa | Kummara and colleagues (39) |
| Bambusa arundinacea (Ba) and Bambusa nutans (Bn) | Leaf | Ag | 30–90 nm | Spherical | PC3 and Vero cells | 0–100 µg/mL | 48 h | IC50: 73.57 µg/mL for BaAgNP in PC3 | Kalaarasi et al. (159) |
|                               |           |                   |           |                          |                                       |                |               | IC50: 84.88 µg/mL for BnAgNP in PC3 | |
|                               |           |                   |           |                          |                                       |                |               | IC50: 93.58 µg/mL for BaAgNP in Vero | |
| Common Name                  | Part                | Material | Size (nm) | Morphology                                      | Cells/Line/Plant          | IC50/IC90/EC50 (µg/mL) | Description                                                                 |
|------------------------------|---------------------|----------|-----------|------------------------------------------------|---------------------------|------------------------|-----------------------------------------------------------------------------|
| Borago officinalis          | Leaf                | Ag       | 30–80     | Spherical, hexagonal, and irregular             | RAW 264.7, A549 and HeLa | 1–10                   | 24 h No significant toxicity in RAW 264.7. Significant toxicity in A549 at 10 µg/mL and HeLa at 5 µg/mL                |
| Broccoli                    | Whole plant         | Cu       | ~4.8      | Spherical                                      | PC-3                      | 0.5–1.5µM             | 2 h No toxicity                                                            |
| Broccoli florets (Brassica Oleracea L.var. Italica) | Aerial part         | Ag       | 40–50     | Spherical                                      | MCF-7                     | 50–150                 | 24 h IC50: 121.56µg/mL                                                     |
| Bruguiera cylinlica         | Leaf                | Ag       | 9–24      | Hexagonal                                      | MCF-7                     | 50, 100 µg/mL          | 12, 24, 36 h IC50: 100 µg/mL after 12 h of incubation 90% toxicity at 100 µg/mL after 36 h of incubation               |
| Butea monosperma            | Leaf                | Ag and Au| 20–80     | Mainly spherical but few rods, irregular and hexagonal | B16F10, MCF-7, HNGC2, A549, HUVEC and ECV-304 | 0.3–2.5µM             | 24, 48 h No toxicity                                                        |
| Cajanus cajan               | Seed coat           | Au       | 9–41      | Spherical                                      | HepG2 and vero cells      | 2–10 µg/mL in HepG2 10–320 µg/mL in vero cells | 24 h IC50:6 µg/mL in HepG2                                               |
| Calotropis procera L.       | Latex               | Cu       | 5–30      | Spherical                                      | HeLa, A549 and BHK21      | 20–160 µM             | 24 h No toxicity                                                            |
| Cassia fistula              | Flower              | Ag       | 21–30     | Spherical                                      | MCF-7 and Vero cells      | 7.8–1000 µg/mL         | 24 h IC50: 7.19 µg/mL in MCF-7 IC50: 66.34 µg/mL in Vero cell line          |
| Cassytha filiformis         | Whole plant         | Ag       | 16–66     | Spherical                                      | HCT116                    | 0.1–10 µg/mL           | 24 h IC50:0.5 mg/mL                                                        |
| Cauliflower floret (Brassica Oleracea var. botrytis. l) | Aerial part         | Ag       | 40–50     | Spherical                                      | MCF-7                     | 50–150 µg/mL           | 24 h Moderate (40.24%) toxicity at 150 µg/mL IC50: 190.501 µg/mL ≥4.7 µg/mL significant toxicity after 24 h and 48 h No toxicity at 25 µg/mL but toxic at 50 µg/mL IC50: 40.365 µg/mL |
| Chlorella vulgaris (Algae)  | Whole cell          | Ag       | 6.5–13.5  | Spherical                                      | HepG2                     | 2.35–300 µg/mL         | 24 and 48 h IC50:64µg in Hep 2 IC50:90g in Vero IC50–40 µg/mL              |
| Chrysanthemum indicum       | Flower              | Ag       | 37.71–71.99 | Spherical                                      | 3T3                      | 25 and 50 µg/mL        | 24 h IC50:42.9± 3.1 µg/mL in AgNPs synthesized from C. maxima              |
| Chrysophyllum oliviforme (Satin leaf) | Leaf               | Ag       | 25        | Flower                                         | HeLa                      | 6.25–100 µg/mL         | 48 h IC50:82.39 ± 3.1 µg/mL in AgNPs synthesized from C. maxima             |
| Cissus quadrangularis       | Stem                | Ag       | 5–30      | Spherical                                      | HEP 2 and Vero cells      | 20–160 µg             | 4 h IC50:64 µg in Hep 2 IC50:90g in Vero IC50–40 µg/mL                      |
| Clerodendron serratum       | Leaf                | Ag       | 5–30      | Spherical                                      | EAC                       | 5–60 µg/mL            | 24 h IC50:83.57 ± 3.9 µg/mL in AgNPs synthesized from M. oleifera          |
| Cucurbita maxima, Moringa oleifera and Acorus calamus | C. maxima (petal), M. oleifera (leaf) and A. calamus (rhizome) | Ag       | 30–70     | Spherical and cuboidal                          | A431                      | 10–150 µg/mL             | IC50: 78.58 ± 2.7 µg/mL in Vero cell line                                  |

(Continued)
| Plant                        | Part used | Nanoparticle type | Size (nm) | Morphology | Anticancer activity (in vitro model) | Dose (µg/well) | Exposure time | Major outcome                                                                 | Reference                          |
|-----------------------------|-----------|-------------------|-----------|------------|-------------------------------------|----------------|---------------|-----------------------------------------------------------------------------|-----------------------------------|
| Cymodocea serrulata         | Aerial part | Ag                | 17–29 nm  | Spherical  | HeLa and Vero cells                 | 10–100 µg/mL  | 48 h          | IC50: 34.5 µg/mL in Hela cell IC50: 61.24 µg/mL in Vero cell ICS0: 100 µg/mL | Chanthini et al. (167)             |
|                            | Leaf      | Ag                | 5–25 nm   | Spherical  | A549                                | 10–250 µg/mL  | 36 h          | IC50: 100 µg/mL in HepG2                                                   | Palaniappan et al. (168)          |
| Datura inoxia Leaf         | Leaf      | Ag                | 30–60 nm  | –          | MCF-7                               | 10–80 µg/mL   | 24 h          | IC50: 20 µg/mL                                                          | Gajendran et al. (169)             |
| Delonix regia Petal        | Petal     | ZnO               | 65–184 nm | Spherical  | A549                                | 5–20 µg/mL    | 1–5 days      | Very low toxicity after 1 day IC50: 20 µg/mL after 2 day Low toxicity at <10 µg/mL | Abbasi et al. (170)                |
| Dendropanax morbifera Leaf| Leaf      | Ag and Au         | Ag 100–150 nm and Au 10–20 nm | Polygon and hexagon | HaCaT and A549 | 1–100 µg/mL | 48 h          | No toxicity of AgNPs at 100 µg/mL in HepG2, No toxicity of AgNPs at 10 µg/mL, but significant toxicity at 100 µg/mL in A549 | Wang and colleagues (77)          |
| Dimocarpus Longan Lour.    | Peel      | Ag                | 9–32 nm   | Spherical  | PC-3                                | 2–30 µg/mL    | 72 h          | He and colleagues (53)                                                  | Ghosh et al. (171)                |
| Dioscorea bulbifera Tuber  | Pt, Pd, Pt–Pd | Pt, Pd | PtNPs:2–5 nm PdNPs:10–20 nm Pt–PdNPs:20–25 nm | Spherical and blunt ended cubes | Pt–PdNPs: spherical | 10 µg/mL    | 48 h          | Cytoxic effect at 10 µg/mL: PtNPs (12.6%), PdNPs (33.15%), and Pt–PdNPs (74.25%) | Venkatesan and colleagues (76)     |
| Dracocephalum kotschyi Leaf| Leaf      | Au                | 11 nm     | Spherical  | K562 and HeLa                       | 62.5–500 µg/mL| 24, 48 and 72 h | IC50: 196.32 µg/mL in K562 and IC50: 152.16 µg/mL in HeLa | Dorosti and Jamshidi (61)          |
| Ecklonia cava (marine brown alga) Seaweed | Au | 20–50 nm | Spherical and triangular | HaCaT | RAW254.7, MCF-7 and Caco-2 | 0.5–50 µM | 48 h          | IC50: 5 µM in MCF-7 IC50: 7 µM in RAW254.7 | Premasudha and colleagues (49)     |
| Eclipta alba Leaf          | Leaf      | Ag                | 310–400 nm| Cubic      | RAW254.7, MCF-7 and Caco-2          | 0.5–50 µM | 48 h          | IC50: 10 µM in Caco-2                                                      | Prema et al. (76)                  |
| Erythrina indica lam Root | Root      | Ag                | 20–118 nm | Spherical  | MCF-7 and HepG2                     | 0.625–25 µg/mL| 24 h          | IC50: 5.25 µg/mL in HepG2                                                  | Sre et al. (172)                   |
| Eucalyptus Leaf            | Leaf      | Ag                | 30–70 nm  | –          | AGS, MRC-S                          | 3–100 µg/mL  | 24,48,72 h    | IC50: 9.01, 6.31, 3.99 µg/mL in AGS after 24, 48 and 72 h of incubation, respectively. | Rashmeezad and colleagues (45)     |
| Ficus benghalensis Bark    | Bark      | Ag                | ~40 nm and ~50 nm | Spherical | MG-63                                | 20–200 µg/mL | 48 h          | IC50: 81.8 ± 2.6 µg/mL for Ag from A. indica IC50: 75.5 ± 2.4 µg/mL for Ag from F. benghalensis | Nayak and colleagues (42)          |
| Ficus religiosa Bark       | Bark      | Au                | 20–30 nm  | Spherical  | HEK 293                             | 10–200 µM | 24 h          | No toxicity                                                             | Wani K (78)                       |
| Plant or Animal | Part | Material | Size | Shape | Cell Line/Location | Concentration | Effect | IC50 |
|----------------|------|----------|------|-------|-------------------|---------------|--------|------|
| Genipa americana L. | Fruit | Au | 30.4 ± 14.9 nm | Spherical | A-549 and Hela | 0.01–20µM | 48 h | No toxicity observed | Kumar et al. (173) |
| Haliclona exigua | Sponge | Ag | 0.078–5 µg/mL | Flower like | KB | 100 to 120 nm | 48 h | IC50: 0.6 µg/mL | Inbakandan and colleagues (72) |
| Helianthus annuus L. | Sunflower oil | Ag | 10–100 µg/mL | Spherical | KB | 0–200 µg/mL | 24 h | IC50: 70 µg/mL | Bhakya and colleagues (73) |
| Helicteres isora | Stem bark | Ag | 16–95 nm | Spherical | KB | 0–200 µg/mL | 24 h | IC50: 70 µg/mL | Mishra and colleagues (40) |
| Hibiscus sabdariffa | Leaf and stem | Au | 10–60 nm | Near spherical | U87 and HEK 293 | 0–2.5 ng/mL | 48 h | IC50–1.5 ng/mL and high toxicity at 2 ng/mL in U87 and little toxicity in HEK 293 | Nalavothula R (54) |
| Impatiens balsamina | Flower | Ag | Average size: 15 nm | Spherical | U937, COLO205, B16F10, HepG2, HeLa | 25–200 µg/mL | 24 h | IC50:84.17 ± 2.13 µg/mL in U-87, IC50:65.40 ± 2.41 µg/mL in COLO205, IC50:196.5 ± 4.19 µg/mL in B16F10, IC50:95.52 ± 4.08 µg/mL in HepG2, IC50:93.27 ± 2.53 µg/mL in HeLa | Thakore et al. (174) |
| Iresine herbstii | Leaf | Ag | 44–64 nm | Cubical | HeLa | 25–300 µg/mL | 3 h | IC50:51 µg/mL | Dipankar and Murugan (175) |
| Justicia adhatoda | Leaf | Ag | 11–20 nm | Spherical | HeLa, A549, MCF-7, HT-29, and Caco-2 | 10–80 µg/mL | 4 h | IC50:55 µg/mL | Salari and colleagues (47) |
| Lavandula vera | Leaf | Zn | 30–80 nm | Spherical | HeLa, A549, MCF-7, HT-29, and Caco-2 | 10–160 µg/mL | 24 h | IC50:22.3 ± 1.1 µg/mL in A549, IC50:86 ± 3.7 µg/mL in MCF-7, IC50:10.9 ± 0.5 µg/mL in HT-29, IC50:56.2 ± 2.8 µg/mL in Caco-2 | Salari and colleagues (47) |
| Mangifera indica Linn | Peel | Au | 6.03 ± 2.77–18.01 ± 3.67 nm | Quasi-spherical | CV-1 and WI-38 | 10–160 µg/mL | 24 h | No toxicity | Yang and colleagues (87) |
| Mimosa pudica | Leaf | Au | 12 nm | Spherical | MDA-MB-231, MCF-7, and HMEC | 2–10 µg/mL for MDA-MB-231, MCF-7, and HMEC | 24 and 48 h | IC50:4 µg/mL in MDA-MB-231 after 48 h of incubation, IC50:0.6 µg/mL in MCF-7 after 48 h of incubation IC50 did not observed after 24 h no significant toxicity in HMEC | KS and colleagues (33) |
| Momordica charantia | Leaf | Ag | ~91.63 nm | Spherical | MCF-7 | 12–100 µg/mL | 24 h | IC50:20 µg/mL | Gandhiraj V (177) |
| Momordica cymbalaria | Fruit | Ag | Average size: 15.5 nm | Spherical | Rat L6 | 20–100 µg/mL | 24–48 h | IC50:20 µg/mL | Swamy and colleagues (85) |
| Morinda citrifolia | Root | Ag | 30–55 nm | Spherical | HeLa | 0.1–100 µg/mL | 24 h | IC50:20 µg/mL | Suman et al. (178) |
| Moringa oleifera | Flower | Pd | 10–50 nm and 2–18 nm | Spherical | A549 and human normal peripheral lymphocytes | 10 µg/mL and 50 µg/mL | 6 h | Significantly cytotoxic to A549 cells and no toxicity in normal peripheral lymphocytes | Anand and colleagues (95) |

(Continued)
| Plant                         | Part used             | Nanoparticle type      | Size (nm)       | Morphology          | Anticancer activity (In vitro model) | Dose (µg/well) | Exposure time | Major outcome                                                                 | Reference |
|------------------------------|-----------------------|------------------------|-----------------|---------------------|--------------------------------------|----------------|---------------|--------------------------------------------------------------------------------|-----------|
| **Musa paradisiaca** (banana) | Stem of banana        | Au                     | Average size: 30 nm | Spherical           | MCF-7 and HEK-293                    | 10–100 nM      | 24 h          | IC50 > 80 nM in MCF-7; No toxicity at 60 nM in HEK-293, but low toxicity above 60 nM | Arunkumar and colleagues (88) |
| **Oak fruit hull (Jaft)**    | Fruit                 | Ag                     | Average size: 40 nm | Spherical           | MCF-7 and human blood mononuclear cells | 0.02–50 µg/mL  | 24 h          | IC50: 50 µg/mL (AgNPs in purified water) in MCF-7; IC50: 0.04 µg/mL (AgNPs in plant extract) in MCF-7; No toxicity in human blood mononuclear cells | Heydari and Rashidipour (99) |
| **Origanum vulgare** (Oregano) | Leaf                  | Ag                     | 63–85 nm         | Spherical           | AS49                                 | 10–500 µg/mL   | 36 h          | IC50: 51.9 nM in HepG2; IC50: 76.40 nM in AS49; No toxicity in 3T3                | Sankar et al. (179) |
| **Padina gymnospora** (marine Macroalgae) | Leaf                  | gold-reduced graphene oxide (Au-rGO) nanocomposite | 8–15 nm | Pentagonal, hexagonal and spherical | PC3 and RWPE-1 | 10–50 µg/mL | – | IC50: 12.02 µg/mL in PC3; IC50: 25.1 µg/mL in RWPE-1 | Saikia and colleagues (81) |
| **Plumbago zeylanica, Semecarpus anacardium and Terminalia arjuna** | Bark, root bark and nut, for P. zeylanica, S. anacardium and T. arjuna, respectively | Ag | 80–98 nm, 60–95 nm and 34–70 nm for P. zeylanica, S. anacardium and T. arjuna, respectively | Spherical for P. zeylanica and T. arjuna; Cubic for S. anacardium | HepG2, PC3 and Vero cells | 1–100 µg/mL | 48 h | IC50 of HepG2, PC3 and Vero cells: 70.97, 58.61, 96.41 µg/mL, respectively for P. zeylanica; IC50 of HepG2, PC3 and Vero cells: 83.86, 42.77, 10.04 µg/mL, respectively for S. anacardium; IC50 of HepG2, PC3 and Vero cells: 28.42, 41.78, 69.48 µg/mL, respectively for T. arjuna | Prasannaraj and colleagues (79) |
| **Potentilla fulgens**       | Root                  | Ag                     | 10–15 nm         | Spherical           | MCF-7 and U-87                      | 0–12 µg/mL     | 24 h          | IC50: 4.91 µg/mL in MCF-7; IC50: 8.23 µg/mL in U-87; Significant antitumor effect to improve biochemical plasma factors to reach normal levels | Mittal et al. (180) |
| **Premna serratifolia L.**   | Leaf                  | Ag                     | 16–32 nm, (Average size: 22.97 nm) | Cubic               | Hepatocancerous Swiss albino mice | 500 mg/Kg in vivo study in mice | 15 days | IC50: 28.5 µg/mL in MCF-7; IC50: 8.23 µg/mL in U-87 | Patra and colleagues (55) |
| **Rheum rhabarbarum**        | Stem                  | Ag                     | 60–80 nm ≤ 50 nm | Spherical           | HeLa                                 | 10–500 µg/mL   | 72 h          | IC50: 28.5 µg/mL; 0.05 mg/mL; 0.5 mg/mL | Reddy et al. (181) |
| **Rosa canina**              | Fruit                 | ZnO                    | 23.52–60.83 nm   | Spherical           | HCT 15                               | 5–60 µg/mL     | 24 h          | IC50: 0.25 mg/mL; 30 µg/mL; ~ 30 µg/mL | Jafarirad et al. (182) |
| **Rosa indica**              | Petal                 | Ag                     | 23.52–60.83 nm   | Spherical           | HCT 15                               | 5–60 µg/mL     | 24 h          | IC50: 30 µg/mL; 0.25 mg/mL; 30 µg/mL | Manikandan and colleagues (50) |
| **Rosmarinus officinalis**   | Leaf                  | Ag                     | Average size: 60 nm | Cubical             | HL-60                                | 1 mM, 2 mM     | 6, 12, 24 h | No IC50 after 6 h IC50: < 2 mM after 12 h 80% toxicity at 2 mM after 24 h | Sulaiman and colleagues (60) |
| **Sargassum Muticum** (algae) | Whole cell | hyaluronan/zinc oxide (HA/ZnO) nanocomposite | 3–8 nm | Polygonal | PANC-1, CaOV-3, COLO205, and HL-60 and MRC-5 | 0–100 μg/mL | 72 h | Namvar and colleagues (41) |
| **Sargassum Longifolium** | Seaweed | Ag | Average size: 30 nm | Cubical | HEP-2 | 3.9–1000 μg/mL | 48 h | No toxicity observed in MRC-5 |
| **Sargassum muticum** | Seaweed | ZnO | 50–100 nm | Hexagonal | 4T1, CRL-1451, CT-26, WEHI-3B and 3T3 | 0–100 μg/mL | 72 h | IC50: 21.7 ± 1.3 μg/mL in 4T1 |
| **Sargassum muticum** | Seaweed | Au | 5.42 ± 1.18 nm | Spherical | CEM-ss, Jurkat, HL-60, K562 and normal human blood mononuclear cells | 0–100 μg/mL | 72 h | IC50: 62.5 μg/mL in Jurkat |
| **Sargassum swartzii** | Seaweed | Fe3O4 | 18 ± 4 nm | Cubic | Jurkat, MCF-7, HeLa and HepG2 | – | 72 h | Namvar and colleagues (59) |
| **Sesbania grandiflora** | Leaf | Ag | 10–45 nm | Spherical and few hexagonal | HeLa | 15.63–500 μg/mL | 24 h | Dhas et al. (183) |
| **Solanum muricatum** | Leaf | Ag | 20–80 nm | Spherical and irregular | HeLa | 0–50 μg/mL | 24 and 48 h | ICS0: 20 μg/mL in Jurkat |
| **Solanum trilobatum** | Fruit | Ag | 12.50–41.90 nm | Spherical and polygonal | MCF-7 | 5–50 μg/mL | 24 h | IC50: 12.5 ± 1.7 μg/mL in Jurkat |
| **star anise (Illicium verum)** | Pod | Au | 20–150 nm | Triangular and hexagonal | AS49 | 10–200 nM | 48 h | Sathishkumar et al. (187) |
| **Styra x benzoin** | Benzoin gum | Ag | 12–38 nm | Spherical | Raw 264.7, Hela, A549 and HaCaT | 1–5 μg/mL in Raw 264.7, Hela and AS49, 1–10 μg/mL in HaCaT | 24 h | Rajasekharreddy and Rani (188) |
| **Syzygium cumini** | Fruit | Ag | 5–20 nm | Spherical | DL | 50–500 μg/mL | 48 h | Mittal and colleagues (64) |

(Continued)
**Table 1.** Continued.

| Plant                        | Part used | Nanoparticle type | Size (nm)                        | Morphology | Anticancer activity (in vitro model)* | Dose (µg/well) | Exposure time | Major outcome                                                                 | Reference                  |
|------------------------------|-----------|-------------------|----------------------------------|------------|--------------------------------------|----------------|---------------|--------------------------------------------------------------------------------|-----------------------------|
| *Syzygium samarangense*      | Leaf      | Ag                | –                                | Spherical  | A549                                 | 50–200 µg/mL  | 24 h          | IC50: 87.37 µg/mL                                                                 | Thampi and Shalini (189)    |
| *Tabernaemontana divaricata* | Flower    | Au                | 100 nm                           | Nearly spherical | MCF-7 and Vero cells                 | 25–75 µg/mL  | 24 h          | 75 µg/mL moderate toxicity in MCF-7 but little toxicity in Vero cell line      | Raj and Khusro (80)         |
| *Taxus yunnanensis*          | Callus    | Ag                | 6.4–27.2 nm                      | Spherical  | SMMC-7721, LS174T, A549, MCF-7 and HL-7702 | 10–50 µg/mL  | 24 h          | IC50: 27.75 µg/mL in SMMC-7721 IC50: 40.3 µg/mL in A549 IC50: 42.2 µg/mL in MCF-7 IC50: 27.75 µg/mL in LS174T | Xia and colleagues (46)    |
| *Torreya nucifera*           | Leaf      | Ag                | 8–42 nm, 4 35 nm, 4–38 nm        | Spherical, pentagonal | 3T3-L1                                 | 0.1 ng/mL–10 µg/mL | 24 h      | Low toxicity in AgNPs from *T. nucifera* and *N. indica* but moderate toxicity in AgNPs from *C. japonicum* | Kalpana and colleagues (90) |
| *Cinnamomum japonicum*, and *Nerium indicum* (marine algae) | Whole cell | Ag                | 8–16 nm                          | Spherical  | EAC                                  | 42–98 µg/mL  | –            | 99% toxicity at 98 µg/mL                                                      | Khalifa et al. (190)        |
| *Turbinaria turbinata*       | Seed      | Lanthanum         | –                                | Spherical  | Mg-63                                | 12.5–200 µg/mL | 48 h      | IC50: 200 µg/mL                                                               | Chatterjee A (43)           |
| *Vigna radiata* (green gram) | Seed      | Titanium dioxide  | –                                | –          | Mg-63                                | 12.5–200 µg/mL | 48 h      | IC50: 200 µg/mL                                                               | Chatterjee et al. (191)    |
| *Vitex negundo L.*           | Leaf      | Ag                | 5–49 nm                          | Spherical  | HCT15                                | 10–100 µg/mL  | 48 h      | IC50: 20 µg/mL                                                                | Prabhu and colleagues (51) |
| *Zataria multiflora*         | Leaf      | Au                | 10–50 nm (Average size: 20.52 nm)| Different shapes; pentagon, triangular, undefined shapes | HeLa and BMSCs | 0–400 µg/mL | 48 h      | Significant toxicity at 400 µg/mL in Hela cell line (IC50:100 µg/mL). IC50: 300 µg/mL in BMSCs: | Baharara and colleagues (101) |
| *Zingiber zerumbet*          | Rhizome   | ZnO–Ag nanocomposite | 23 nm                           | Spherical  | Vero cells                           | 0–300 µg/mL  | 24 h      | No toxicity at <100 µg/mL but at higher concentration toxicity gradually increased | Azizi et al. (192)         |

*Cancer and normal Cell Lines: HeLa (human cervical cancer), HepG2 (hepatic cancer), MDA-MB-231 and MCF-7 (human breast adenocarcinoma), PC-3 (human prostate carcinoma), KB (human oral cancer), A549 (human lung adenocarcinoma), HCT116 (human colon colorectal carcinoma), EAC, NCI-H460 (non-small cell lung cancer), U87 (glioblastoma multiforme cell), Panc-1 (pancreatic adenocarcinoma), CaOV-3 (ovarian adenocarcinoma), COL0205 (colonic adenocarcinoma), HL-60 (acute promyelocytic leukemia), MG-63 (osteosarcoma cell), AGS (human gastric carcinoma), SMMC-7721 (human hepatoma cells), LS174T (human colon adenocarcinoma cell), HT-29 (human colorectal adenocarcinoma), Caco-2 (human epithelial colorectal adenocarcinoma), HCT 15 (human colon adenocarcinoma), U937 (human histiocytic lymphoma cell), B16F10 (mouse melanoma), 4T1 (mouse breast cancer), CRL-1451 (mouse lung adenocarcinoma), WEHI-3B (Mouse leukemia), CEM-ss (human T acute lymphoblastic leukemia), Jurkat (human T acute lymphoblastic leukemia), K562 (human chronic myelogenous leukemia), A431 (human vulvar squamous cell carcinoma), HN5-2 (human adult glioma tissue), ECV-304 (human urinary bladder carcinoma), RAW264.7 (mouse leukemia), SiHa (human cervical squamous cell carcinoma), DL, HaCaT (aneuploid immortal keratinocyte cell line), RAW 264.7 (murine Macrophage), PBMC (peripheral blood mononuclear cell).*
| Microbial species                  | Microbe type | Nanoparticle type | Size (nm) | Morphology     | Anticancer activity (in vitro model)* | Dose (µg/well) | Exposure time | Major outcome                                                                 | Reference                  |
|-----------------------------------|--------------|-------------------|-----------|----------------|--------------------------------------|----------------|---------------|---------------------------------------------------------------------------------|----------------------------|
| Aspergillus deflectus and Penicillium pinophilum | Fungus       |Ag/CS              | 15–40 nm  | –              | MCF 7, PC3 and A549                   | 12.5–100 µg/mL | 24 h          | IC50:27.9 and 53µg/mL in MCF 7 and PC3 for AgNPs synthesized from A. deflectus under optimized conditions and no toxicity in A549 No toxicity of AgNPs synthesized from P. pinophilum under optimized conditions in MCF 7 and PC3 and low toxicity in A549 | Osman et al. (193)          |
| A. flavus | Fungus |Ag | Average size: 33.5 nm | – | HL-60 | 5 and 10 µg/mL | 6, 12 and 24 h | High toxicity at 10 µg/mL after 6 h IC50: ∼5µg/mL after 12 h. Very high toxicity at 10µg/mL after 12h | Sulaikam et al. (194) |
| A. flavus SP-3 | Fungus |Ag | 20–60 nm | Spherical | HEP2 | 0–1000 µg/mL | 24 h | IC50: 23µg/ml for T. gamsii SP-4, 100 µg/ml for A. flavus SP-3, 39 µg/ml for T. flavus SP-5, and 36 µg/ml for A. oryzae SP-6 | Anand et al. (195) |
| Aspergillus foetidus | Fungus |Au | 30–50 nm | Spherical | A549 | 10–100µM | 24 h | No toxicity IC50: ∼20, ≥20, ≥60 µg/ml in hFOB, HaCat, Vero, and different shapes for both bacteria | Roy et al. (196) |
| Bacillus cereus | Bacterium |Cu | Average size: 20 nm | Different shapes (irregular, spherical, triangular) | MCF-7 | 25–200 µM/mL | 24 h | No toxicity IC50: ∼100µM for both | Tiwari and colleagues (91) |
| Bacillus cereus (ATCC 14579) and Escherichia fergusonii (ATCC 35409) | Bacterium |Ag | 10–20 nm for both of bacteria | Spherical and hexagonal for both of bacteria | NIH3T3 D4 | 0.008–0.5 mg/mL | 4 h | IC50: ≤0.25 mg/100 µL is nontoxic and 1 mg/100 µL is toxic for AgNPs from B. cereus | Pourali and Yahyaei (198) |
| Bacillus flexus | Bacterium |Au | Average size: 20 nm | – | MCF-7 | 25–200 µM/mL | 24 h | No toxicity IC50: ∼100µM for both | Murugan et al. (199) |
| Bacillus sp. MSh-1 | Bacterium |Se | 80–220 nm | Spherical | MCF-7 | 0–200 µg/mL | 24 h | IC50: 41.5 ± 0.9µg/mL for | Forootanfar et al. (200) |

(Continued)
| Microbial species            | Microbe type | Nanoparticle type | Size (nm) | Morphology         | Anticancer activity (in vitro model) | Dose (µg/well) | Exposure time | Major outcome                                                                 | Reference |
|-----------------------------|--------------|-------------------|-----------|--------------------|-------------------------------------|----------------|--------------|-----------------------------------------------------------------------------|-----------|
| Beauveria bassiana          | Fungus       | Ag                | 4–50 nm   | Spherical          | HeLa                                | 3.125–50 µg/mL | 24 h         | At 50 µL (1 mL) the viability of HEK 293 cells was 83.5 ± 1.66%             | Kanakahskii et al. (2019) |
| Cryptococcus laurentii (BNM 0525) | Yeast        | Ag                | 20.44 – 34.16 nm | Spherical          | MCF-7, T47D and MCF10-A              | 0–5 µg/mL     | 12 h         | Significant toxicity above 2.5 µg/mL in MCF-7 and T47D but slight toxicity in MCF10-A | Prabakaran and colleagues (38) |
| Endophytic Fungus           | Fungus       | Au                | 15–35 nm  | Spherical          | HEp2 and Vero cells                 | 1.17–75 µg/mL  | 4 h          | IC50: 23 µg/mL in Hep2                                                     | Nichiyar et al. (202) |
| Enterococcus sp.            | Bacterium    | Au                | 6–13 nm   | Spherical          | HepG2 and A549                      | 1–100 µg/mL    | 24 h         | IC50: 100 µg/mL in Hep2                                                     | Rajeshkumar (203) |
| Fusarium oxysporum          | Fungus       | Au                | 10–40 nm  | Spherical          | ZR-75-1, Daudi and PBMC             | 5–500 µg/mL    | 24 h         | Moderate toxicity in ZR-75-1 and Daudi, but no toxicity in PBMC            | Ahmad Siddiqui and colleagues (70) |
| Fusarium oxysporum          | Fungus       | Ag                | 5–13 nm   | Spherical          | MCF-7 C26 and HaCaT                 | 0–220 µg/cm³  | –           | IC50:121.23 µg/cm³                                                        | Husseiny et al. (206) |
| Fusarium oxysporum          | Fungus       | Ag                | 5–15 nm   | Spherical          | HeLa and HaCat                      | 10–150 µg/mL   | 24 h         | IC50: 50 µg/mL in HeLa, No toxicity in HaCa                                | Srivastava et al. (207) |
| Halococcus salifodinae BK18 | Bacterium    | Se                | Average size: 28 nm | Rod and hexagonal | NIH3T3 and MDA-MB-231              | 50–1000 µg/mL | 24 h         | Very low toxicity at 250 µg/mL in both cell line Significant toxicity at 1000 µg/mL in both cell line | Syed and colleagues (93) |
| Humicola spp.               | Fungus       | Au                | 18–24 nm  | Spherical          | NIH3T3 and MDA-MB-231              | 50–1000 µg/mL | 24 h         | No toxicity at 50 µg/mL in both cell line Significant toxicity at ≥250 µg/mL in both cell line | Syed et al. (208) |
| Klebsiella pneumoniae (KACC 11402) | Bacterium    | Au                | 16–36 and 24–50 nm | Spherical          | T3L1, H9c2 and HepG2               | 0.01–1000 µg/mL | 24 and 48 h | No toxicity                                                                     | Kalpana and colleagues (92) |
| Moraxella osloensis         | Bacterium    | Titanium dioxide  | 60–150 nm | Irregular          | HaCaT and Hep2                      | 8–100 µg/mL    | –           | IC50: 55 µg/mL in HaCaT                                                     | Vahili Nachiyar and colleagues (103) |
| Nocardiopsis sp.            | Marine       | Ag                | 11.57 ± 1.24 nm | Spherical          | HeLa                                | 50–400 µg/mL   | 24 h         | IC50: 172 µg/mL in Hep2                                                     | Manivasagan et al. (209) |
| Nocardiopsis sp.            | Marine       | Ag                | 10–50 nm  | Spherical          | HepG2 and A549                      | 50–500 µg/mL   | 24, 48 h      | IC50: 350 and 250 µg/mL in 24 and 48 h of incubation                     | Manivasagan and Oh (210) |
| Nocardiopsis sp.            | Marine       | Ag                | 45 ± 0.15 nm | Spherical          | HeLa                                | 50–250 µg/mL   | 24 h         | IC50: 200 µg/mL                                                            | Manivasagan et al. (211) |
| Nocardiopsis                | Alkaliphilic  | Ag                | 5–50 nm   | Spherical          | HeLa                                | 25–100 µg/mL   | 48 h         | IC50: 100 µg/mL                                                            | Rathod et al. (212) |
| Vallisporis OT1 strain      | Bacterium    |                              |           |                   |                                     |                |              |                                                                            |                       |
| Penicillium brevicompactum   | Fungus       | Au                | 10–120 nm | Spherical          | C2C12                                | 200–2000 ng/mL | 24, 48, 72 h | IC50: >1000 ng/mL after 24h Significant toxicity after 72 h at any range of concentration | Mishra and colleagues (94) |
| **Fungus** | **Ag** | **Size** | **Sphericity** | **Cancer and normal Cell Lines:** |
|------------|--------|----------|---------------|---------------------------------|
| *Penicillium decumbens* (MTCC-2494) | Fungus | Ag | 30–60 nm | Spherical | A-549 and Vero cells | 20–120 μg/mL | 24 and 48 h | A-549 IC50:80 and 60 μg/mL after 24 h and 48 h of incubation, respectively. Vero cell IC50: 100μg/ml after 24 h of incubation | Majeed and colleagues (100) |
| *Pleurotus djamor var. roseus* | Fungus | Ag | 5–50 nm | Spherical | PC3 | 1–6 μg/mL | 24 h | IC50: 10 μg/mL | Raman et al. (213) |
| *Pleurotus ostreatus* | Fungus | Ag | 4–15 nm | Spherical | MCF-7 | 10–640 μg/mL | 24 h | IC50~160 μg/mL | Yehia and Al-Sheikh (214) |
| *Pseudomonas aeruginosa* (JQ989348) | Bacterium | Ag | 13–76 nm | Spherical | Human carcinoma cervical cell line | 5–100 μg/mL | 24 h | 100% toxicity at 40μg/mL | Ramalingam et al. (215) |
| *Schizophyllum commune* | Fungus | Ag | 51–93 nm | Spherical | HEP -2 | 10–100 μg/mL | 24 h | IC50:53 μg/mL | Arun et al. (216) |
| *Stenotrophomonas maltophilia* | Bacterium | Ag | Average size: ~93 nm | Cuboidal | HeLa and Splenocyte cells | 0–500 μg/mL | 48 h | IC50: >31.25 μg/mL in HeLa IC50: >250 μg/mL in Splenocyte cells | Oves et al. (217) |
| *Streptomyces naganishii* (MA7) | Actinobacteria | Ag | 5–50 nm | Spherical | HeLa | 0.1–300 μg/mL | 48 h | IC50: 1.53 μg/mL. LD50:24.39 μg/mL | Shanmugasundaram et al. (218) |
| *Streptomyces rochei* MHM13 | Actinomycetes | Ag | 22–85 nm | Spherical | HepG2, HCT-116, MCF-7, PC-3, A-549, CACO, HEP-2 and HeLa | 1.56–50 μg/well | 24 h | IC50:32.90 μg/Well in HepG2 IC50:9.05 μg/Well in HCT-116 IC50:40.00 μg/Well in MCF-7 IC50: 48.50 μg/Well in PC-3 IC50: 42.10 μg/Well in A-549 IC50: >50 μg/Well in CACO IC50: >50 μg/Well in HEP-2 IC50: >50 μg/Well in HeLa | Abd-Elnaby et al. (219) |
| *Trichoderma koningii* | Fungus | Au | 10–14 nm | Spherical | LoVo and LoVo/DX | 1–1000 μg/mL | 24 h | IC50:33.04 ± 4.9 μg/mL in LoVo IC50:28.88 ± 2.9 μg/mL in LoVo/DX | Maliszewska (75) |
| *Trichoderma viride* | Fungus | Ag | 5–40 nm | – | MCF-7 | 1–100 μg/mL | 24 h | Low toxicity ≤10 μg/mL, but toxicity gradually increased over 10 μg/mL | Kulandaivelu and Gothandam (220) |
| *Xylarious* | Fungus | Ag | – | Spherical | HT-29 | 7.8–1000 μg/mL | 48 h | IC50:62.5 μg/mL | Varsha B (48) |

*Cancer and normal Cell Lines:* HeLa (human cervical cancer), A549 (human lung adenocarcinoma), HepG2 (hepatic cancer), MDA-MB-231 and MCF-7 (human breast adenocarcinoma), PC-3 (human prostate carcinoma), MG-63 (osteosarcoma cell), HT-29 (human colorectal adenocarcinoma), Caco-2 (human epithelial colorectal adenocarcinoma), HL-60 (human acute myeloid leukemia), HEP-2 (human larynx carcinoma), ZR-75-1 (human caucassian breast carcinoma), Daudi (human burkitt’s lymphoma), T47D (human breast cancer), LoVo (human colon adenocarcinoma), LoVo/DX (multidrug resistance human colon adenocarcinoma sub-line), HaCat (aneuploid immortal keratinocyte cell line), hFOB (homo sapiens bone), Neuro-2a (mus musculus brain neuroblastoma), HCT 116 (homo sapiens colon colorectal carcinc), RAW 264.7 (murine Macrophage), NIH3T3 (mouse fibroblast), Saos-2 (homo sapiens bone osteosarcoma), PBMC (peripheral blood mononuclear cell).
different breast carcinoma cell lines (MDA-MB-231 and MDA-MB-468) (105). Besides, Rajendran et al. (106) reported the highly stable flavonoid apigenin conjugated to gold nanoparticles (ap-AuNPs) are formed when apigenin reacts with Au^{3+} under appropriate conditions. The ap-AuNPs are also found to exhibit toxicity toward cancerous A431 cell lines, while being nontoxic toward normal epidermoid cells (HaCat). Additionally, Sahu et al. (107) investigated the role of pure aqueous solution of plant secondary metabolites, namely hesperidin, naringin and diosmin, in the biosynthesis of AgNPs. The secondary metabolites have the polyhydroxy group which may be responsible for their role in the reduction of metal ions into NPs. In this study, the cytotoxicity of the synthesized AgNPs was investigated on the cancerous HL-60 cell line. The result represented that AgNPs synthesized using naringin as reducing agent had higher stability and better cytotoxic activity (107). Interestingly, a fish-intestine-associated bacterial strain was a potential source of exopolysaccharide (EPS) production reported with a significant ability to reduce iron-based materials and convert them to iron oxide nanoparticles (FeONPs). EPS was extracted from a spore-forming strain of *Bacillus subtilis* isolated from the gut microbiome of the freshwater fish *Oreochromis mossambicus*. In this study, the *in vitro* cytotoxicity effects of free EPS and EPS-stabilized FeONPs were probed in the human epidermoid carcinoma cell line A431. The IC50 values of EPS and EPS-stabilized FeONPs were found to be 350.18 and 62.946 mg/mL, respectively (108). In a study, AgNPs were biosynthesized by an aqueous leaf extract of *Erythrina suberosa* (Roxb.). Following that, the cytotoxicity of AgNPs was compared with plant extract and AgNO3 against the A-431 osteosarcoma cell line. The IC50 values were determined to be around 106.15, 74.02 and 136.73 μg/mL for leaf extract, AgNPs and AgNO3, respectively, indicating excellent cytotoxicity of AgNPs among all (109). Notably, the exact mechanism of metal NPs’ anti-cancer activity is not fully understood yet. However, it is believed that reactive oxygen species (ROS) generation, Sub-G1 arrest in cell, up-regulation of p53 protein and caspase-3 expression, inhibition of VEGF-induced activities are the major proposed anti-cancer mechanisms (21, 110). Recent advances in the proposed mechanisms for anticancer activity shown by colloidal biogenic AgNPs are shown in Figure 4. Importantly, the ROS leads to activation of caspase-3 which is responsible for cell apoptosis by arresting the cell cycle at the G2/M phase (111). Besides, increased oxidative stress leads to oxidation of glutathione (GSH) to glutathione disulfide (GSSG) through the oxidation process. Notably, GSH is known as an antioxidant that prevents cells from ROS damages, consequently resulting in remarkably much MNPs’ cytotoxicity and loss of GSH (24). Furthermore, AgNPs were shown to downregulate the activity of a recognized enzyme involved in DNA damage repair named DNA-dependent protein kinase (112). Coccini et al. (113) showed that the AgNP-induced oxidative stress genes involved Gpx1, SOD, FMO2 and GAPDH in different organs indicating AgNP-induced toxicity. Jeyaraj et al. (114) evaluated the caspase-mediated apoptotic cell death on treatment of biosynthesized AgNPs in the HeLa cell line. AgNPs exhibited the downregulation of Bcl-2 gene and, conversely, upregulation of the Bax gene. This regulation triggered the cascade and regulates the caspases 3, 8 and 9 which are responsible for apoptotic cell death (114). More interestingly, some studies reported neither cancerous nor normal cells showed metal NPs’ mediated cytotoxicity. Specifically, Patra et al. (55) reported phytosynthesis of AuNPs and AgNPs and assessed their lack of cytotoxic effect in the range of 0.3–2.5 μM on different cancer and normal cell lines. In another study, the *in vitro* cytotoxicity of microbial biosynthesized AuNPs (0.01–1000 μg/mL) on normal 3T3-L1, H9c2 and cancerous HepG2 cell lines showed the nontoxic and biocompatible nature of biosynthesized AuNPs (92).

The cytotoxicity of NPs may depend on parameters such as particle size, surface area and surface reactivity (115). Upon understanding the mechanism of metallic NPs’ synthesis from plants and microbes, strategies can be designed for optimum synthesis of NPs of the desired shape and size. Eventually, based on heterogeneity of bio-sources, various factors such as temperature, synthesis conditions, reaction time, substrate concentrations and pH can have significant impacts on the rate of synthesis reaction.

### 2.2. Biocompatible nanomaterials for cancer diagnosis

Recent nano-medical developments helped the progress of NPs for diagnostic and therapeutic (theranostics) applications. Notably, NPs can play a vital role in cancer diagnosis at an early stage by allowing visualization of cancer cells. Cancer diagnostic instruments used routinely in preclinical research and clinical practice involve MRI, CT, ultrasound, optical imaging, positron emission tomography, photo-acoustic imaging and single-photon emission CT (SPECT). In this regard, these instruments differ based on their underlying physical principles, sensitivity and specificity to contrast agents, tissue contrast, spatial resolution, quantitative-ness and tissue penetration (116). Remarkably, alpha fetal protein (AFP) is a cancer biomarker in clinical
diagnosis associated with the disease progression and therapeutic responses of liver cancer. Xuan et al. (117) reported a plasmonic ELISA strategy by means of alkaline phosphatase-mediated growth of AgNPs for the colorimetric detection of serum AFP. This plasmonic ELISA provided high sensitivity displaying high performance in cancer diagnosis and therapeutic monitoring. This plasmonic assay is based on the in situ generation of AgNPs, leading to rapid color with various degrees of yellow, which can be easily performed on currently available instruments in clinical laboratories. Surprisingly, cancer detection has been widely investigated by applying metal NPs for marking tumor cells to find tumor-target fluorescence bio-imaging as an excellent fluorescent probe (118). Specifically, Ge et al., (118) reported biosynthesis of fluorescent Au/Ce nanoclusters (NCs) (1.2–2.2 nm) as highly sensitive bio-imaging agents. As demonstrated in Figure 5, the Au/Ce NCs show significant fluorescence in the HeLa cancer cells (Figure 5A–C). Moreover, Figure 5D depicted the variations of fluorescence intensity between cancerous and normal cell types. Besides, the same results were obtained in HepG2 in the same situation. In contrast, the control group including L02 cells showed almost no intracellular fluorescence. Furthermore, according to the acceptable in vitro results, Au/Ce NCs were also investigated for in vivo bio-imaging in a tumor mice model of cervical carcinoma. As shown in Figure 6, fluorescence was observed around the tumor after 24 h of subcutaneous Au/Ce NCs injection (118). This is in agreement with the study of Wang et al., 2013, which demonstrated green synthesis of silver NCs employing glutathione and showed in vivo fluorescent tumor imaging through living animal tumors (119). Furthermore, Mukherjee et al. (120) reported green synthesis of monodispersed AgNPs (20–60 nm) by using Olax scandens leaf extract, with spherical shape and high stability for several days. In this study the fluorescence properties of biogenic AgNPs were observed through two cell lines (A549 & B16F10) employing a fluorescence microscopy. The untreated cells used as control and those treated with chemically fabricated AgNPs did not exhibit fluorescence, while those cancerous cells that were treated with biological synthesized AgNPs exhibited very strong fluorescence indicating the internalization of AgNPs by A549 & B16F10 cells (120). Overall, based on the aforementioned, the use of nanotechnology will be the best strategy for cancer diagnosis due to their self-fluorescence ability. One of the major drawbacks of current cancer treatment strategies is the lack of targeted drug delivery, resulting in systemic toxicity (8,121). Recently, magnetically targeted NPs have overcome this significant disadvantage of non-specificity as carriers for FDA-approved anti-cancer drugs. The basic principle is the loading of a particular anticancer drug on to a magnetic NP carrier like biocompatible super-paramagnetic iron oxide nanoparticles followed by injecting into the blood stream. Thereupon, with the application of external magnetic fields (high-gradient), the particular drug delivery system (DDS) is targeted specifically at cancerous cells via changes in physiological conditions (osmolality, enzymatic activity

![Figure 4. Recent advances in proposed mechanisms for anticancer activity shown by colloidal biogenic silver nanoparticles (AgNPs) (Adapted with permission from Ovais et al. (21)).](image-url)
and temperature). Indeed, by applying this strategy the associated side-effects along with the amount of the drug delivered are reduced, ultimately leading to reduced systemic toxicity \((122,123)\). Seo et al. \((124)\) have reported a novel study of biosynthesizing AuNPs via employing heavy metal binding proteins (HMBPs) of genetically engineered \(Escherichia\ coi\ acting\ as\ reducing,\ stabilizing\ and\ capping\ agent.\ The\ synthesized\ NPs\ were\ spherical\ in\ nature\ having\ a\ size\ of\ 5\textendash20\ nm\ in\ diameter.\ Furthermore,\ the\ group\ loaded\ doxorubicin\ (Dox)\ on\ the\ AuNPs@HMBPs\ DDS\ for\ treating\ the\ cancerous\ HeLa\ cells.\ The\ process\ of\ AuNPs@HMBPs’\ preparation\ along\ with\ Dox-loaded\ AuNPs@HMBPs’\ cytotoxic\ evaluation\ are\ illustrated\ in\ Figure\ 7\ (124).

### 3. Hurdles for green nanomaterials as future cancer nanomedicine

A wide range of applications of metal nanoparticle therapeutics in the future is doubtless though there are still many challenges to be overcome and eventually routine clinical practice. If we talk about phytosynthesis, many amino acids, polysaccharides, flavonoids, alkaloids, vitamins, etc. exist in the metal NPs’ medium method, which play a role in NPs’ function, even if their surfaces are washed and purified since the residuals would stick to the NPs’ surface. Likewise, in microbial synthesis, there are a number of microorganisms involving saprophytes and even pathogenic microbes such as \(E.\ coli\ introduced\ as\ a\ bio-source\ for\ preparation\ of\ metal\ NPs\ which\ would\ cause\ some\ hazards\ according\ to\ clinical\ studies.\ As\ an\ example,\ Aspergillus\ niger,\ Aspergillus\ flavus,\ Fusarium\ solani,\ etc.\ have\ been\ employed\ to\ biosynthesize\ metal\ NPs\ (26,\ 125\textendash129).\ Importantly,\ another\ limitation\ is\ the\ protein\ corona\ effect,\ which\ occurs\ via\ adsorption\ of\ proteins\ on\ the\ colloidal\ NPs’\ surfaces\ when\ the\ nanoparticle\ enters\ the\ biological\ system\ (130).\ This\ adsorption\ actually\ compromises\ the\ ultimate\ dependability\ of\ NPs\ in\ the\ in\ vivo\ system\ (131).\ Overall,\ nanotechnology-based\ products\ are
highly expensive probably due to difficulties in the manu-
ufacturing and preserving process; thereby its progress
would cost a high amount of money. The key hurdles
faced by researchers for entrance of biosynthesized
NPs into the clinical phase have been graphically illus-
trated in Figure 8 (132–134).

By and large, many challenges and issues came in the
way of scaling up nanoparticles/nanoconjugates’
production to industrial scale. NPs produced using routine top-down or bottom-up approaches in the lab vary greatly from those obtained from commercial producers. These approaches include sonication, emulsification, organic solvents evaporation and use, homogenization, centrifugation, elevated temperature, crosslinking and lyophilization \(^{(35)}\). Practically, a slight change in the optimized conditions of NPs’ synthesis can render the NPs biologically inactive, less stable and highly impure. Hence, a robust production process should be used at the lab-scale for NPs with an extraordinary reproducibility rate to be viable for large-scale commercial production.

### 3.1. Diffusion and penetration

In general, diffusive resistance of various tissues (intestine, vagina, nose mucosal membranes and lungs) poses a major barrier in nanomedicine delivery. Researchers have scientifically proved that the sedimentation and diffusion velocities of NPs highly affect their penetration and cellular uptake. Specifically, it is also reported that the cellular uptake and penetration are independent of surface coating, size, density, initial dose concentration and morphology of NPs \(^{(136)}\). In addition, Cho et al. \(^{(137)}\) reported that the shape dependency of AuNPs for their penetration through the cells could vary depending on their surface functional group. Wang et al. \(^{(138)}\) studied endocytosis of AuNPs with different sizes (45, 70 and 110 nm) in the human cancerous cell lines (CL1-0 and HeLa). This study revealed that the optimal size for the penetration into cells was around 45 nm. Interestingly, Chithrani et al. \(^{(139)}\) evaluated the effect of spherical and rod-shaped AuNPs on cellular uptake in the HeLa cell line. This study depicted that spherical-shaped AuNPs had a higher cellular uptake in comparison to rod-shaped AuNPs because of variable biophysical properties such as receptor diffusion kinetics. More interestingly, it was suggested that the surface coating of NPs impact on rate of uptake \(^{(140)}\). For instance, Sur et al. \(^{(141)}\) investigated cytotoxicity and cellular penetration of modified AgNPs with glucose, lactose, etc. in normal (L929) and cancerous (A549) cell lines. In this study, no differences were revealed in the cellular penetration of lactose- and glucose-modified AgNPs in L929, though there was a substantial growth in the cellular internalization of lactose-modified AgNPs into the A549, could be explained by the role of the chemical nature of the ligand in cellular uptake.

### 3.2. Toxicological and immunological aspect

Mukherjee and coworkers experimentally proved the nontoxic nature of these biogenic NPs in C57BL6/J female mice via various biochemical parameters along
with a histopathology study of different organs. Even after successive injections of biogenic AuNPs (1 or 10 mg/kg/day) for seven days in healthy mice, no toxicity was observed (142). Moreover, it is interesting to note that in another study the same group reported that mice treated with chemically synthesized AuNPs showed broken alveolar walls with hyperplasic sinusoids as compared to the untreated or green synthesized AuNPs-treated mice (143). On the other hand, various chronic and acute toxicities of liver and nephrons were reported to be associated with zinc, platinum and cerium oxide NPs (144–146). Hence, it is very crucial to screen the potential nanoparticles/nanomaterials for various toxicity studies including their pharmacokinetics, pharmacodynamics and responses to immune system before moving on to clinical trials (147–149).

3.3. Biodegradability, metabolic kinetics and clearance

Biodegradability is a very vital aspect to be considered before exploiting AuNPs in vivo. Polymeric NPs are naturally biodegradable and are cleared from the body. However, in case of metallic NPs biodegradability is slow and poses serious challenges in terms of toxicity (50, 147, 151). Although detailed knowledge regarding the mechanism of metallic NPs’ biodegradability and clearance is still unclear, few recent studies validate the gradual excretion of metal NPs in feces and urine even up to 14 days (147, 152). Furthermore, the studies shed light on the positively charged AuNPs, which may encounter a negative charge repulsion from the glomerular basement membrane in nephrons and pass out via urine. In another study reported by Rengan and coworkers, liposomal AuNPs were demonstrated for their biodegradability and as a potential DDS for cancer therapy. Moreover, metabolic degradation of the delivery system was noticed in liver and hepatocytes followed by its easy excretion via the renal route (147). All the studies discussed in detail that in vivo biodistribution, metabolic kinetics, clearance and ultimate dependability of NPs are determined by their shape, size and morphology.

4. Conclusions and future prospects

Green nanomaterials are currently in a highly investigative phase for the treatment and diagnosis of cancer but the ultimate dependability is yet to be decided in clinical trials. A number of new possibilities have come into account in relation to the use of green nanomaterials, owing to their biocompatibility and effectiveness. Moreover, many types of cancers that do not have cures today may be cured by these green nanomaterials in the future. Additionally, thorough understanding of key physiological barriers in vivo is the key to effectively deliver NPs into the tumor. Furthermore, the knowledge regarding the safety of nanomaterials is not sufficient and comprehensive acute and chronic toxicity in clinical studies should be observed to identify the hazards associated with the use of NPs. Considering the above discussion, it is expected that green nanomaterials could emerge as future cancer therapeutics and diagnostics agents in the near future.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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