Application of green synthesized silver nanoparticles in cancer treatment—a critical review

Shazina Jabeen 1, Rahmatullah Qureshi 1, Mehmooda Munazir 2, Muhammad Maqsood 1, Mubashrah Munir 3, Syed Sabir Hussain Shah 1 and Bakht Zareen Rahim 1

1 Department of Botany, Pir Mehr Ali Shah Arid Agriculture University, Rawalpindi, Punjab 46300, Pakistan
2 Department of Botany, Government College, Women University, 51040 Sialkot, Punjab, Pakistan
3 Department of Botany, University of Animal & Plant Sciences, Ravi Campus, Pattoki, Punjab, Pakistan
4 Department of Botany, Baluchistan University, 87500 Quetta, Baluchistan, Pakistan

E-mail: Shazinasheraz95@gmail.com

Keywords: green synthesis, nanomedicine, anticancer, reactive oxygen species, silver nanoparticles, nanotechnology, nanoparticles

Abstract

With the breakthrough in advance technologies, researchers are looking to devise novel approaches to control different types of deadly cancers. Progress in medicinal plants research and nanotechnology has drawn scientist’s attention toward green synthesis of metallic nanoparticles by exploiting plants secondary metabolites owing to its advantage over routinely used physical and chemical synthesis (simple, one step approach to reduce and stabilize bulk silver into silver nanoparticles (AgNPs), cost effectiveness, energy efficient, biocompatibility and therapeutic significance). Owing to control size, shape and functional surface corona, AgNPs hold considerable potentiality for therapeutic applications by opting different mechanistic pathways such as mitochondrial disruption, DNA fragmentation, cell membrane disruption, interruption of cellular signaling pathways, altered enzyme activity and reactive oxygen species (ROS) production leading to apoptosis etc. In this review, we discussed the green synthesized AgNPs in the possible cancer treatment by harnessing phytochemicals present in plant extract. In addition, this review also provides recent advances and achievements in utilization of green synthesized AgNPs in cancer treatment and proposes mechanistic action for their anticancer and cytotoxic potential. By understanding the mechanistic action of AgNPs responsible for their therapeutic efficacy will help to devise customized therapies and treatment against cancer as a potential cancer therapeutic tool.

1. Introduction

Silver, being a noble metal, has been extensively harnessed since ancient times. Hippocrates suggested the use of silver to treat disease and for wound healing [1]. Silver is naturally occurring abundant metal possessing numerous physical, chemical and biological fascinating properties like electrical conductivity, optical activities, nonlinear catalytic effect, surface enhanced Raman scattering, elevated thermal response and various biochemical characteristics making silver most appropriate candidate having diverse biomedical potential i.e. as an antiseptic, integral component of medical and surgical devices, constituents of medicines, antimicrobial potential, significance in drug delivery, cosmetic products, biolabelling, optical properties, larvicidal applications and food preservation usage. Silver nitrate is applied on microbial infections in hospitals. Antimicrobial agents having silver ions are reported to disrupt the outer membrane of targeted cell. Silver ions react with thiol group of proteins and leads to bacterial inactivation. Application of silver results into impaired DNA replication owing to uncoupling of electron transport from oxidative phosphorylation. As a result it inhibits the enzymes of respiratory chain and disrupts the membrane permeability. However, this activity is found at concentrations which are 10 fold higher than those used for AgNPs. Hence, AgNPs are reported to have antimicrobial activities at low concentrations [2, 3]. Moreover, silver ions in the form of silver salts, displayed considerably higher toxicity than AgNPs of any size [4]. Silver in ionic form such as AgCl and AgNO3 have
shown some cardiac changes such as left ventricular hypertrophy, induced hypersensitivity, and repressed normal function of fibroblast in rats [5]. AgNPs are safe and harmless in biomedical implants as compared to silver ions [6].

Any change in size, shape and biochemical surface characteristics of material alters its properties [7, 8]. Nano-silver possesses much advantage over bulk materials in terms of its distinctive physical, chemical, magnetic, optical, biological and electronic properties [9, 10]. Matter exploitation at nanoscale offers unprecedented way to get targeted idea by modifying boiling point, melting point, solubility, permeability and storage life of material [11]. Nanoscience and nanotechnology offer key disciplines for society advancement particularly perpetual endeavor leading to preeminent success in nano-based therapies [12]. A significant concern developed toward reassessment and biofunctional investigation of metallic nanoparticles in biomedicine owing to their exclusive physical, chemical and biological properties [13, 14]. Biologically compatible nanoparticles, especially with supreme physiochemical actions, standard biomechanical potential and robust therapeutic potency can be devised [15]. Nanoparticles owing to their size related magnificent properties are renowned as excellent candidate for biomedical applications, being acknowledged as star technology of the 21st century [16].

Out of zero dimensional nanoparticles, AgNPs are most investigated agents for their unusual and unprecedented applications in pharmaceutical science, anti-infection coatings, wound dressing, antimicrobial textiles, food packaging and cosmetics industry [17]. Biosynthesized AgNPs for last few decades exhibited several applications like larvicidal, antioxidant and anticancer potential [8]. There are about 383 nano silver based commercial products worldwide, accounting for 24% of all nano products in markets [18]. Table 1 shows the anticancer drugs coupled AgNPs along their synthesis methods.

### 2. Trends on the application of Green Synthesized Silver Nanoparticles in Cancer Treatment

Silver nanoparticles are holding preeminent role in biomedical applications such as antimicrobial, antiviral, antidiabetic, antioxidant and anticancer. Presence of phytochemicals on the surface of green synthesized AgNPs is attributed to their antimicrobial and anticancer activities [24]. By keeping in view the expanding burden of cancer globally, several research groups have synthesized variety of metallic nanoparticles via green approach. Plant mediated AgNPs have been exhibiting potential anticancer activities against various types of carcinoma cells [25]. Such as banana leaf mediated AgNPs exhibited anticancer potential against A549 and MCF7 cell lines [26], Mangifera indica seed mediated AgNPs against Hela and MCF7 [27]. AgNPs formulated by Heliotropium bacciferum showed anticancer potential against HCT-116 [28] and AgNPs using Zingiber officinale displayed anticancer potential against AsPC-1, PANC-1 and MIA PaCa-2 cell line [29].

AgNPs are reported to exhibit effective anticancer activity with great selectivity toward the cancer cells in dose dependent manner. The magnificent selectivity of AgNPs is due to biocompatibility of Ag0 and phytochemicals from plant source that attached on their source. Moreover, recent researches have revealed that plant mediated AgNPs shown their anticancer activity by decreasing the proliferation rate of cancerous cell via cell cycle arrest [30].

The physiochemical properties of AgNPs have been confirmed by the immense and constantly increasing amount of literature data availability regarding synthesis of AgNPs (figure 1(A)) and their application in cancer treatment (figure 1(B)). By keeping in view these critical concerns and growing applications of AgNPs in cancer treatment, this review article highlights the anticancer activities of AgNPs synthesized via green route.

### 3. Methods of AgNPs Synthesis

There are different techniques used for synthesis of nanoparticles such as 'top-down' and 'bottom up'. Top-down approach involves the synthesis of nanoparticles from bulk whereas bottom-up starts synthesis from

| Anticancer drug | Synthesis method | Used Reagents | References |
|-----------------|-----------------|---------------|------------|
| Methotrexate    | Conventional heating | NaBH₄, Tri sodium citrate, AgNO₃, NaOH | [19] |
| Doxorubicin     | Biosynthesis    | Azadirachta indica, AgNO₃, Graphene oxide dispersion | [20] |
| Epirubicin      | One-pot synthesis | Epirubicin, AgNO₃ | [21] |
| Imatinib        | Biosynthesis    | Eucalyptus protera, AgNO₃ | [22] |
| Doxurubicin Alendronate | Microwave | AgNO₃, N-Hydroxy Succinimide | [23] |
nanoscaled material at atomic level (Figure 2). Top-down approach is generally used during physical method of nanoparticles synthesis while the bottom-up approach is manipulated in chemical or plant mediated synthesis. Bottom up approach is useful to get monodispersed nanostructure with lesser flaws [31]. Physical method facilitates the nanoparticles synthesis without solvent and suitable for AgNPs of uniform size formation in contrast to chemical method [32]. Physical route and chemical synthesis of AgNPs includes various different procedures [33] as illustrated in (Figure 2).

Chemical reduction process of AgNPs in the solution typically comprises of three main stages such as (1) metal precursors (2) reducing agents and (stabilizing or capping agents). There are various commonly used reducing agents such as N2H4, NaBH4, tri-sodium citrate (TSC), sodium citrate, polyols and N,N-dimethylformamide (DMF). Ascorbic acid as a reducing agent advocates the synthesis of flower like silver nano architecture with average size of 20nm at room temperature. There are some capping agents use to stabilize and prevent the AgNPs from agglomeration include sodium dodecyl sulfate (SDS), polyvinyl pyrrolidone (PVP), polymethacrylic acid and polymethyl methacrylate. PVP not only reported to prevent nano materials from
agglomeration but also favor the process of nucleation. In order to synthesize AgNps of uniform size, the simultaneous formation of nuclei is necessary for growth/capping of nanoparticles [34].

Nanomaterials synthesis by using physical and chemical method restricts their usage to limited zone and their therapeutic applications also confined due to toxicity produced and noxious to environment [35]. However, now researchers focus is diverted toward cost effective and eco-friendly synthesis of AgNPs which can be of plant source or of microbial origin [36, 37]. Biosynthesis of AgNPs can be carried out using microorganisms such as bacteria, fungi, yeast, viruses’ DNA, diatoms and plants (figure 3) [38].

Green synthesis, commonly referred as biogenic synthesis is another method for AgNPs synthesis and lead to emergence of novel domain of ‘phytonanotechnology’ involving green synthesis of metallic nanoparticles by utilizing plant resources followed by their optimization and characterization. The size and shape of AgNPs is determined by type of solvent, reduction and stabilization [39]. Green synthesis comprises the manipulation of natural constituents and environment friendly elements with handling safety which results in product formulation that is nontoxic to human and environment [40].

Table 2 Presents the phytochemicals associated with AgNPs formulation in particular plants. Plants being excellent source of secondary metabolites possess various activities and reduce the bulk metals into metal nanoparticles. In plants, naturally occurring potential to interact with metals and their conversion into innocuous form directed the scientists and nanotechnologists’ attention toward the utilization of secondary metabolites in plants as a stabilizing and reducing agent [7, 8]. The phytochemical constituents i.e. alkaloids, phenols, ketones, amines and enzymes are not only responsible for plant routine activities but also act as an outstanding deposit of chemicals which is employed to reduce metal in bulk to metal ions. The synthesis of nanoparticles can be optimized by adjusting the physiochemical parameters such as pH, temperature, salt concentration, amount of reducing agents and capping agents [41]. The biological materials utilization has supremacy over physical and chemical method in several ways such as biomass accessibility in excess, cost efficient, handling safety and nontoxicity. Physical method demands for high energy and force which increase the cost value of product and harmful to environment. Whereas chemical method demands costly chemicals which may be hazardous to workers and environment as well [42]. Green synthesis of nanostructures not only restrains the demand of dangerous chemicals but also leads to one step synthesis of nanomaterial [43]. In this review, we have thoroughly discussed the exploitation of plant resources in synthesis of AgNPs, synthesis mechanism and their therapeutic efficacy with respect to anticancer potential.
| Plant                        | Phytochemical                                           | AgNO₃ (mM) | Size (nm) | Shape       | Incubation Time | References |
|-----------------------------|--------------------------------------------------------|------------|-----------|-------------|-----------------|------------|
| Punica granatum             | Flavonoid and aromatic acids                           | 1          | 48        | Spherical   | 20 min          | [44]       |
| Nepeta deflersiana          | Flavonoids and terpenoids                              | 0.1M       | 33        | Spherical   | 24h             | [45]       |
| Detarium microcarpum        | Polyphenol and flavonoids                              | 5          | 81        | Cubical     | 12h             | [46]       |
| Chrysanthemum indicum       | Tannins, flavonoids and glycosides                     | 1          | 37.71–71.9| Spherical   | 2 min           | [47]       |
| Eucalyptus hybrid           | Flavonoids and terpenoids                              | 1          | 50–150    | Cubical     | 3h              | [48]       |
| Putranjiva roxburgi         | Alkaloids, flavonoids and saponins                     | 0.1        | 25.68     | Spherical   |                 | [49]       |
| Boswellia dalzielii         | Aromatic compounds, ether and alkynes                  | 5          | 12–10     | Rod, Circular, Spherical | 1.5h       | [50]       |
| Eranthermum pulchellum      | Reducing sugars and flavonoids                          | 10         | 10–100    | Spherical   | 90 min          | [51]       |
| Matricaria chamomilla       | Flavonoids (Quercetin & luteolin), terpenoids and sugar | 0.5–2      | 26        | Spherical   | 10 min          | [52]       |
| Musa paradisiaca            | Polyphenol and alkaloids                               | 0.0001M    | 80–100    | Bead        | 5 min           | [53]       |
| Ajuga bracteosa             | Flavonol glycosides, neo-clerodane and diterpenoids    | 1          | 50        | Spherical   | 24h             | [54]       |
| Muntingia calabura          | Polyphenols, flavonoids and terpenoids                 | 0.01–0.03M | 22–37     | Spherical   | 24h             | [55]       |
| Boerhavia procumbens        | Phenols, alcohols and ketones                          | 0.001M     | 20–80     | Spherical   | 3h              | [56]       |
| Calotropis procera          | Phenols, alcoholic aromatics and amines                 | 1          | 22        | Spherical   | 5–10 min        | [57]       |
| Vitis vinifera              | Polyphenols and proteins                               | 1          | 20–35     | Spherical   | 20 min          | [58]       |
3.1. Chemical mechanism of green synthesis of AgNPs

Large number of studies is performed to explore the potential of plants to produce nanoparticles of various sizes and shapes and to reveal their significant job in biological domain. Although physiological analysis of secondary metabolites which take part in nanoparticles synthesis need to be explored. The investigation of exact mechanism responsible for reducing bulk material into nanomaterial is critical to frame protocol for nanoparticles formulation of required size and shape. Different secondary metabolites present in plants are classified by various functional groups and these function groups confer surface modifications and functional capabilities to green synthesized nanoparticles and provide biomedical potential to nanoparticles (figure 3).

Various studies reported that hydroxyl, carboxylic and amines group are involved in reduction of silver salt [41]. Biogenesis of silver nanoparticles can be described by chemical mechanism proposed (figure 4). During synthesis the first step involves the oxidation of bioactive compound of plant source and release of electrons. These electrons lead of Ag\(^+\) to Ag\(^0\). After reduction, Ag\(^0\) undergoes sequence of agglomeration known as nucleation (I) and (II) to form a nanoparticle. Nucleation of silver zero atoms lead to formation of nanoparticles i.e. AgNPs as shown in figure [58]. Presence of various significant bioactive compounds and bonding of their function groups with metallic salt provides stabilization to nanoparticles. Presence of phenolic compounds on the surface of nanoparticles is attributed to prevent their coalescence [59].

4. Cancer: A Global Threat

Cancer is reported as leading cause of death globally, 10 million people are estimated to have died from cancer and about 19.3 million fresh cancer cases reported in 2020 [60]. The global cancer burden will upsurge to 27 million fresh cancer cases by 2040 [61]. Onset of cancer and metastasis is due to uncontrolled cell division and its invasion into surrounding healthy cells and tissues [62]. Any mutation in proto oncogenes and tumor suppressor genes results into cancer [63]. It is estimated that 1 out of 6 deaths is caused by cancer and approximately 70% of all cancer deaths reported from middle and low income countries [64]. It is estimated that 1 out of 5 people develops cancer before age of 75 years and one out of ten would die in this age range suffering from cancer [65]. Higher growth rate of cancer is denoting that cancer occurrence will 60% increase by 2030 [66]. The cause of cancer can be categorized as external and internal factors. Viruses, radiations and chemical exposure are external cause while mutations, hormones and internal conditions are internal factors which can stimulate carcinogenesis [67, 68].

Lung, thyroid, cervical, liver, stomach, colorectal, prostate and breast cancers are most common types of cancer diagnosed in humans. Most frequently occurring cancer among women and men are breast and prostate.
cancer respectively [63]. Surgical excision of tumor or cancerous part, chemotherapy to kill cancer cells, endocrine and radioactive therapy is used to treat cancer traditionally [69]. Hormone therapy and immunotherapy are lesser used secondary approaches for cancer treatment as they may cause abnormalities and side effects inside patient’s body including damage to healthy cells and different organs due to decline in life quality [70]. Nonspecificity, less bioavailability, rapid clearance and toxicity are some other side effects [71]. Manipulation of chemotherapeutic agents may cause various types of toxicities. 5- fluorouracil is a common used therapeutic agent which results into myelotoxicity, cardiotoxicity and blood vessels constriction [72]. Moreover, cyclophosphamide and bleomycin are associated with bladder toxicity and cutaneous toxicity respectively [73]. Keeping in view the scenario, there is needed to investigate novel approaches and develop promising and systematic vehicle for effective cancer therapy with limited side effects.

5. The Interface of Phyto-Nanotechnology and Cancer

There is novel emerging technology utilizing cost effective therapeutic entities from natural resources i.e. plants, opposing to established approaches for cancer treatment [74]. Medicinal plants have open up new prospects and possibilities for cancer treatment. They are not only source of new compounds upon phytochemical screening but also help to develop novel approaches to treat cancer such as green synthesis of AgNPs [75]. In the recent years, paradigm shift in methodologies and approaches found concerning cancer treatment. Progress in medicinal plants research and nanotechnology developed a variety of new strategies toward various types of cancer treatment [76]. This coalescence of nanotechnology and plants for green synthesis of nanoparticles has drawn the attention of researchers for cancer treatment [77, 78]. These green synthesized nanoparticles may overthrow the obstacles and complications of conventional diagnosis and treatment therapies [79]. Table 3 presents the anticaner results of green synthesized AgNPs from recently conducted studies.

The cancer cells differentiate from normal healthy cells in the context of blood vessels proliferation (angiogenesis), reduced permeability of capillaries and lymphatic drainage system. This altered microenvironment of cancerous cells provides a platform to nanotechnologists to device suitable nanodrug having selective advantage to precisely target cancer cells [111]. Currently, research studies are paying focus on the synthesis of anticancer drugs and to device a tool which can specifically and precisely target cancer cells with optimized drug concentration and less adverse effects [112]. Cancer nanobiotechnology has promising capacity to improve the detection, diagnosis and treatment of cancer [113]. At present, AgNPs have been widely explored for cancer diagnosis and cancer therapy. Green synthesized AgNPs featured with phytochemicals coating furnish them increased biological actions than AgNPs synthesized via chemical method. Apart from potential application of green synthesized AgNPs in cancer treatment, AgNPs reported to have various other biomedical applications such as antimicrobial, antileishmanial, antiviral, wound healing, targeted drug delivery, antitubercular and antidiabetic potential [114, 115].

Several studies have reported the anticancer property of plant mediated AgNPs against various cancer cell lines such as HEPG2 (human liver cancer cells), Hep-G2 (liver cancer), COLO 205 (colon cancer), MCF-7 (human breast cancer), PC3 (human prostate cancer), HCT-116, HCT-15 (human colon adenocarcinoma), VCaP (prostate cancer), AGS (human gastric carcinoma), SiHa (cervical cancer), Caco-2 (intestinal adenocarcinoma), HeLa (cervical cancer), Hek-293 (kidney cancer), H1299, A549 (lung cancer), PA1 (ovarian cancer), HL-60 (human promyelocytic leukemia cells), B16 (mouse melanoma cell line), A431 (epidermoid carcinoma) and BxPC-3 (pancreas cancer) [106, 116, 117].

Nanoparticles possess site specific and targeted action which enhances the drug efficiency as nanoparticles move across impermeable membrane and could tackle the immune system response, so suitable for cancer treatment [118]. Green synthesized AgNPs revealed their efficacy against several cancers such as breast cancer, colon adenocarcinoma, Ehrlich ascites carcinoma and liver cancer. Green synthesized AgNPs application in different concentrations showcased the promising anticancer potential against lung cancer, liver cancer, cervical and carcinoma. However, there is need to explore the anticancer mechanism of green synthesized AgNPs. AgNPs synthesized from mint extract exhibited notable activity against HCT116 colon cancer cells in human. These green synthesized AgNPs delayed the cell division in G1 phase revealing that the AgNPs can control the cell cycle and reduce their proliferation [119]. AgNPs sythesized from leaf extract of *Piper nigrum* shown efficacy against MCF-7 and Hella cancer cell lines [120]. The green synthesized AgNPs have shown change in morphological parameters when applied against MCF-7. Significant disruption in plasma membrane integrity and inhibition in cell growth was found. Moreover, there was shrinkage of cytoplasm and cells aggregation was recorded as compared to healthy cell with AgNPs treatment. AgNPs synthesized from *Prosopis cineraria* and *Coriandrum sativum* indicated potent anticancer activity against MCF-7 cancer cells [121].

Green synthesized AgNPs have shown promising toxic effects against A549 (human lung carcinoma cell) as compared to non-cancerous lung cells, revealing that AgNPs could induce toxicity specifically in target cells.
Table 3. Green synthesized silver nanoparticles (AgNPs) against human cancer cell line.

| Plant name               | Part used | Cancer cell line | IC₅₀ value | Size (nm) and shape of AgNPs | References |
|--------------------------|-----------|------------------|------------|----------------------------|------------|
| Elephantopus scaber      | Leaf      | MCF-7, A-549 and SCC-40 | 10 μg ml⁻¹ (GI₁₅₀) | 59nm (spherical) | [80] |
| Litchi chinensis         | Leaf      | MCF-7            | 40.9 μg ml⁻¹ | 41–55 (Spherical) | [81] |
| Fagonia indica           | Whole     | MCF-7            | 12.35 μg ml⁻¹ | 10–60 (spherical) | [82] |
| Ganoderma neo-japonicum  | Whole     | MDA-MB-231       | 6.0 μg ml⁻¹  | 5–8nm (spherical) | [83] |
| Putranjiva roxburgii     | Seed      | MDA-MB-231, HCT-116 and PANC-1 | 0.26mg ml⁻¹, 0.54mg ml⁻¹ and 0.00025 mg ml⁻¹ | 8nm spherical | [84] |
| Jasminum officinale.     | Leaf      | MCF-7, Bladder (S637) | 9.3 μg ml⁻¹, 13.0 μg ml⁻¹ | 9.2nm (spherical) | [85] |
| Noctiluca scintillans    | Whole     | MDA-MB-231       | 30% (reduction) | 4.5nm (spherical) | [86] |
| Espenolepis procera      | Leaf      | MCF-7            | 1.6μM       | 60nm (spherical) | [87] |
| Nostoc linckia           | Whole     | MCF-7            | 27.79 μg ml⁻¹ | 9.39–25.89nm (spherical) | [88] |
| Solanum trifolatum       | Fruit     | MCF-7            | 30 μg ml⁻¹   | 41.90nm (Spherical, polygonal) | [89] |
| Elephantopus scaber      | Leaf      | COLO-205         | 17.4 μg ml⁻¹ (GI₁₅₀) | 59nm (spherical) | [81] |
| Zingiber officinale      | Rhizome   | HT-29            | 150.8 μg ml⁻¹ | 20–51 (spherical) | [90] |
| Chlorophytopic sp.       | Leaf      | HT-29            | 7% (viability) | 52nm (spherical) | [91] |
| Olea chrysophylla, Lavandula dentata | Leaf | HCT116         | 99.35 μg ml⁻¹, 59.79 μg ml⁻¹ | 328.6nm,284.5nm (crystalline) | [92] |
| Menthe arvensis          | Whole     | HCT116          | 1.7 μg ml⁻¹ | <100nm (spherical) | [93] |
| Zanthoxylum rhetsa       | Seed coat | A549           | 65.17 μg ml⁻¹ | 10–68nm (spherical) | [94] |
| Punica granatum          | Peel      | A549            | 5 μg ml⁻¹   | 6–45nm (spherical) | [95] |
| Derris trifoliote        | Seed      | A549            | 86.23 μg ml⁻¹ | 16.92nm (spherical) | [96] |
| Dimocarpus longan Lour.  | Peel      | H1299           | 5.33 μg ml⁻¹ | 8–22nm (spherical) | [97] |
| Nepeta deflersiana       | Aerial parts | HeLa              | 23% (viability) | 33nm (cubical) | [98] |
| Detarium microcarpum     | Leaf      | HeLa, PANC-1    | 31.5 μg ml⁻¹, 84 μg ml⁻¹ | 312nm (cubical) | [99] |
| Ginkgo biloba            | Leaf      | HeLa, SiHa      | Dose dependent | 40nm (Spherical) | [100] |
| Rhizophora apiculata     | Leaf      | HEK-293, HeLa   | 0.062 μg ml⁻¹, 1.98μg ml⁻¹ | >100nm (Spherical) | [101] |
| Punica granatum          | Leaf      | HeLa            | 100 μg ml⁻¹  | 46.1nm | [102] |
| Punica granatum          | Leaf      | HepG2           | 70 μg ml⁻¹  | 35–69nm (Spherical) | [103] |
| Allium sativum           | Whole plant | HepG2           | 31.25 μg ml⁻¹ (LD₅₀) | 100–800nm (Spherical) | [104] |
| Boerhavia erecta         | Leaf      | HepG2          | 25 μg ml⁻¹  | 15.9nm | [105] |
| Alternanthera sessilis    | Leaf      | PC3           | 6.8 μg ml⁻¹ | 30–50nm (Spherical) | [106] |
| Dimocarpus longan Lour.  | Peel      | PC3           | 10 μg ml⁻¹ | 9–32nm (Cubical) | [107] |
| Perilla frutescens       | Leaf      | COLO205, LNCaP  | 39.28 μg ml⁻¹, 24.33 μg ml⁻¹ | 25.71nm (Spherical, Cubical) | [108] |
| Salvia miltiorrhiza      | Leaf      | LNCaP          | 50 μg ml⁻¹ | 100nm (Spherical, Hexagonal) | [109] |
| Zingiber officinale      | Leaf      | AsoPC-1, PANC-1 | 312 μg ml⁻¹, 295 μg ml⁻¹ | 18.93nm (Spherical) | [110] |

* cancer cell lines: MCF-7; human breast cancer, A-549; lung cancer, SCC-40; oral cancer, MDA-MB-231; human breast cancer cells, HCT-116; human colon cancer, PANC-1; pancreatic cancer cells, Bladder (S637); bladder cancer cells, HT-29; human colon carcinoma, HCT116; human colon cancer, A549; lung cancer cell line, H1299; human lung cancer, HeLa; human cervical cancer, HeLa & SiHa; cervical cancer cell lines, HEK-293; human embryonic kidney cells, HepG2; human liver cancer cells, PA-1; human ovarian teratocarcinoma cell line, PC3; prostate cancer cells, LNCaP; human prostate adenocarcinoma.
This site specificity toxicity might be due to particular acidic pH of cancer cells [122]. Zureberek et al also provided evidence about engrossing capability of AgNPs to affect the cell viability specifically. They explored the status of respiration in oxidative stress induced by AgNPs. By keeping in view that cancer cell’s key source of energy is glucose, researcher associated the glucose availability with nanoparticles toxicity. The production of H2O2 by AgNPs application in dose dependent manner was observed [123]. Furthermore, less AgNPs induced toxicity found in cell with little glucose supply than cell with high glucose availability. This finding suggested that limited supply of glucose lead to upregulation of antioxidant defense system which ultimately regulated ROS production and AgNPs induced toxicity [124]. Kovacs et al reported the significant tumor killing activity of AgNPs in osteosarcoma cancer cells with tumor suppressing deficiency. They observed that AgNPs resulted into apoptosis in U2Os (wild type p53) and SOAS-2 cells with deficiency of p53, exhibiting their chemotherapeutic potential [125]. Similarly, in a comparative study AgNPs synthesized by using extract of 30 medicinal plants demonstrated pronounced cytotoxicity against lung cancer cells. Increased toxic effects observed on AgNPs incubation in culture media supplied with bovine serum albumin as it regulated the protein corona interactions [126]. AgNPs synthesized from tamarind fruit shell resulted into apoptosis in human breast cancer cells. Anticancer activity was observed in dose dependent manner as augmented ROS generation resulted into mitochondrial damage and DNA impairment [127]. In another study AgNPs synthesized from Nepeta deflersiana exhibited potent cytotoxicity against human cervical cancer cells. AgNPs induced oxidative stress which leads to mitochondrial impairment and cell cycle arrest followed by death of tumor cells [128]. AgNPs obtained from lotus extract exhibited cytotoxic effects against liver, gastric and prostate cancer cells [129]. AgNPs synthesized from fruit of Crataegus microphylla also showed significant impairment of gastric adenocarcinoma cells.74 Kanipandian and kannan, reported the mitochondrial dependent death of lung adenocarcinoma cells upon exposure to nanosilver synthesized from cotton leaf [130].

AgNPs apart from their effects on cellular and subcellular structures, also remarkably work against tumor angiogenesis which is behind altered expression of growth factor and inhibited migration and proliferation of endothelial cells [131]. AgNPs not only cause apoptotic death in breast cancer but also restricted the transcription of hypoxia inducible factor-1 (HIF-1) and induced the expression of vascular endothelial growth factor-A (VEGF). Antiangiogenic activity of AgNPs reported by protection from tube formation in normal endothelial cells [132]. Similarly, the significant role of AgNPs reported in enhanced expression of caspase-3 and caspase-8 genes upon inoculation in chorioallantic membrane which leads to cellular apoptosis. AgNPs synthesized from red amaranth, reduced the number and length of blood vessels and demonstrated cytotoxicity against breast cancer cells [133].

Beside their magnificent anticancer efficacy, special focus was oriented toward development and analysis of novel silver based nanotechnology for improved chemotherapy and radiotherapy. A study in this context performed on silver-gold nanoparticles coated by dopamine and exposed to near infrared radiation, evaluated for their photothermal induced cytotoxicity against colon cancer cells. In vitro and in vivo study provided evidence about nanoparticles induced photothermal therapy (PTT) via apoptotic and necrotic pathways [134]. He et al investigated the AgNPs core based multifunctional core–shell nanosystems and molecules with aggregation induced emissions. This complex nanosystem significantly improved the radiotherapy and regulated PTT and photo acoustic effect. They also showed more pronounce role as contrasting agent in tomography imaging and as a fluorescent [135].

Silver/magnetite nanoparticles along with PEG coating and folic acid, loaded with chemotherapeutic drug; Doxorubicin reported to have outstanding potentiality for PTT of cervical cancer. Apart from their chemotherapeutic as well as photothermal effect, this nanosystem also showed high selectivity for targeted cancer cells and imaging properties owing to their fluorescence and magnetic resonance [136]. Dual chemotherapeutic and photothermal effect resulted from laser irradiation of nanosystem based on Methotrexate conjugated graphene oxide (GO) and AgNPs lead to high cytotoxicity against malignant cells [137]. Similar results reported by using 5-fluourouracil loaded silver–gold nanoparticles coated with mesoporous SiO2 [138].

5.1. Phytonanotechnology and cancer treatment: a mechanistic approach

AgNPs due to their small size and potentiality to prompt cell death by various mechanisms are considered as phenomenal candidate for cancer treatment. AgNPs cause cell death by breaking double stranded DNA, chromosomal instability and oxidative stress. AgNPs of larger size (∼100 nm) produce these results more effectively than smaller size but AgNPs of smaller size (∼10 nm) induce cellular toxicity at greater level because they enter the cell and get localized inside nucleus smoothly. AgNPs are reported to induce cytotoxicity in mammalian cells via various mechanisms such as (a) disturbance in energy dependent cellular processes and impaired DNA replication induced by uptake of free silver ions (b) generation of reactive oxygen species (ROS) and free radicals (c) cell membrane damage owing to direct interconnection with AgNPs [139, 140]. Avalos et al
explored AgNPs of two different sizes i.e. 4.7nm and 42nm for their induced cytotoxicity in normal human dermal fibroblasts. Nanoparticles of smaller size were found to be more toxic than larger size particles observed through (3-(4, 5-dimethylthiazol-2-5-diphenyletrazolium bromide) (MTT) and lactate dehydrogenase assays [141].

Green synthesized AgNPs induce production of reactive oxygen species (ROS) which leads to cell death. ROS generation adversely strike the signal transduction pathways followed by cell apoptosis. Hydrogen peroxide generation affects the membrane potential of mitochondria resulting into uncoupling of respiration [142]. AgNPs after entry into the cell induce ROS generation and reduction of glutathione (SGH) level, activation of nuclear factor b (NF- b) and tumor necrosis factor-alpha (TNF-). The elevated superoxide radicals’ level alters the mitochondrial transmembrane potential and disturbs the signal transduction pathway which triggers apoptosis and cell death [143, 144]. The increased ROS production and decreased GSH evokes cellular components damage such as DNA fragmentation, peroxidation of lipid membrane and protein carbonylation (protein harmful oxidation). Figure 5 shows the possible mechanism for anticancer potential of green synthesized AgNPs. Furthermore, altered mitochondrial membrane potential lead to activation of caspases 3 and 9 leading to cellular apoptosis. Subsequently, it activates c-Jun NH2 terminal kinase (JNK) which triggers formation of apoptotic bodies and DNA breaks results into cell cycle arrest [145]. New blood vessels formation (angiogenesis) is responsible for tumor formation as suggested by Folkman’s hypothesis. According to this hypothesis, blood supply is essential for growth and spread of tumor. These new blood vessels supply nutrients and oxygen to cancer cells helping them to invade surrounding tissues. Green synthesized AgNPs demonstrated efficacy against retinal neovascularization (RNV) like disease. AgNPs inhibited the RNV induced by vascular endothelial growth factor and blocked the activation of extracellular signal related kinase (ERK1/2) by regulating vascular endothelial growth factor receptor –2 phosphorylation. AgNPs due to these anti-angiogenic properties have been utilized in cancer treatment [146].

Apoptosis induced by caspase dependent and mitochondrial dependent pathways, cell cycle arrest in sub-G1 phase, generation of ROS and disturbance of cellular equilibrium, activation of p53 protein and caspase 3 upregulation, pH dependent release of silver ions and selective killing of cancerous cells and VEGF induced activities inhibition are proposed mechanism for anticancer action of green synthesized AgNPs [147]. Furthermore, green synthesized AgNPs induced p53 protein upregulation which leads to cellular toxicity or death is another suggested mechanistic pathway by nanotechnologists [148]. Similarly, another study reported the AgNPs induced p53 upregulation via Western blotting in PB16 cells. Furthermore, activation of apoptosis proposed to be responsible for upregulation of p53. Green synthesized AgNPs exposure induce oxidative stress and activates caspase-3 which are considered as key reason of cell death [149]. AgNPs treatment triggers the activation of caspase-3 expression. Now, it is experimentally proven that green synthesized AgNPs stimulates P53 upregulation by activation of apoptosis followed by cell death [150]. Gurunthan et al demonstrated that
silver ions released by AgNPs were responsible for upregulation of caspase-3 leading to cell death [122]. Furthermore, acidic environment of cancerous cell attributed for release of phytochemicals from green synthesized AgNPs which boosts the anticancer effect of AgNPs [71].

AgNPs synthesized from Mentha arvensis demonstrated the activation of caspase-9 dependent apoptosis in MCF-7 cells and resulting into toxicity against breast cancer cells. These nanoparticles also exhibited cytotoxicity against Hep2 cells via activation of caspase-9 dependent apoptosis [151]. Green synthesized AgNPs also showed potent cytotoxicity during cell cycle analysis by exhibiting significant increase in sub-G1 cell proliferation. Mao et al reported the relation between enhanced populations of cancer cells in sub-G1 phase and activation of caspase-3, which lead to apoptosis [152]. Similarly, Chang et al reported the connection between sub-G1 phase arrest of cancer cells and apoptosis by showing sub-G1 arrest in cancer cells treated by curcumin [153]. So, this suggests that green synthesized AgNPs induced death of cancer cells might be caused by increased sub-G1 arrest of cancer cells which is interrelated with apoptosis stimulation.

Death of cancer cells is displayed by release of silver ions from green synthesized AgNPs. Hence, selective killing of cancerous cells is direct by concentration of silver ions released inside cells. Release of silver ions in normal cell lines differ from cancer cell lines in different pH. Electrostatic interaction between normal cells and cancer cells also determines the silver ions release [154]. Selective killing of cancer cells also depends on wide ranging electrostatic interaction between normal and cancer cells [155]. Exorbitant release of silver ions strikingly found at acidic pH. AgNPs on incubation in buffers with pH 5 and pH 7.4, reported to release more silver ions at low pH that proves the selective killing of cancer cells at acidic pH. Green synthesized AgNPs are also proposed as anti-angiogenic agent by some analysts [156]. Biosynthesized AgNPs demonstrated their anti-angiogenic properties by hampering cell proliferation induced by vascular endothelial growth factor (VEGF). AgNPs after entering cell inhibited the VEGF and IL-1β induced vascular permeability through Src-dependent pathway [121]. Green synthesized AgNPs owing to their anti-angiogenic efficacy suggested as could provide a new gateway for cancer treatment. Autophagy induced cell degradation which leads to cell death are reported as another mechanism proposed for anticancer potential of AgNPs. Additionally, green synthesized AgNPs promotes autophagy because of autophagolysosomes accumulation in cancer cells and their increased level subsequently leading to cell death [85].

6. Toxicity of Green Synthesized AgNPs

Nano biotechnology has been flourishing with wide range applications of their commercialized products globally. However, there is need to investigate the consequences of increased exposure of animals, human and environment to nanoparticles particularly AgNPs and their potential hazards in terms of acute and chronic toxicity [157]. In vivo and in vitro potential hazards of green synthesized AgNPs to cells and their possible risks are reviewed here. Various studies have reported acute as well as chronic in vivo toxicity of different nanomaterials containing silver also [158, 159]. Bioavailable silver ions reported as toxicity inducing agent in zebrafish embryos [160]. However, more in vivo cytotoxicity and genotoxicity of chemically produced AgNPs found than green synthesized AgNPs which suggests green synthesized AgNPs are less toxic and biologically compatible than chemically synthesized one [161]. Undetectable level of toxicity observed in healthy volunteers upon oral administration of AgNPs prepared commercially [162].

Overdose of AgNPs was found toxic and resulted into various health issues in animals and humans [163, 164]. Furthermore, latest studies demonstrated the neurotoxicity, hepatotoxicity, cytotoxicity, pulmonary inflammation and genotoxicity which are outcome of over dosage of AgNPs of different shapes and sizes [165]. AgNPs application resulted into impaired mitochondria function and leakage via cell membrane in vitro which induce toxicity in mouse germ line stem cells. It was also demonstrated that AgNPs resulted into toxic response on expression of cytokines and proliferation through peripheral blood mononuclear cells (PBMC) production. Overdose of AgNPs reported to induce toxic effects on reproductive system in males. A research study reported the cytotoxicity of AgNPs on rats in vivo. Histopathological studies revealed the more frequent bile duct hyperplasia, pigmentation and fibrosis associated with excessive use of AgNPs [166].

Various studies reported that green synthesized AgNPs induce ROS generation and oxygen species (OS) which results into cytotoxicity and genotoxicity [148]. There is relation between ROS production and cytotoxicity. Exorbitant production of ROS leads to enhanced toxicity of green synthesized AgNPs which in turn conferring them more toxic effects [167]. Over production of ROS cause oxidative stress and in turn cell becomes unable to carry out routine physiological activities. The critical damage to physiological functioning and cell development result into protein oxidation which produce protein radicals and initiates lipid peroxidation, DNA’s strand breakage, inflammatory response regulation via multiple pathways, regulation of gene expression by activating different transcription factors, cytotoxicity, genotoxicity, cell membrane disruption by increased ion permeability and subsequently inducing cell death through apoptosis [168]. The
adverse effects induced by ROS generation from green synthesized AgNPs can be reduced. In the given context, a study reported that alkaloids, tannins and polyphenols are potent ROS scavengers, thus nanoparticles with their coating can inhibit the ROS generation and avoid cellular damage \[169\]. Additionally, AgNPs synthesized from leaf extract of *Butea monosperma* exhibited effective cytotoxic response against cancer cells as compared to non-cancer cells. This response is attributed to the phytochemicals found in plant extract i.e. aldehydes, ketones, flavones, terpenoids, amides, quinones and carboxylic acid that are involved in reduction, capping and stabilization of AgNPs.\[174\]. These findings from latest studies provide a new way for AgNPs utilization in clinical trials for cancer treatment in near future \[98, 99, 144\]. However, there is need to explore toxicological attributes together with pharmacodynamics and pharmacokinetics of metal nanoparticles apart from strengthening them as potent anticancer tool. Taking into account the less toxicity of green synthesized AgNPs, plant mediated AgNPs could be advocated as potent futuristic candidate for potential biomedical application owing to their significant specificity and lesser toxicity.

7. Future Perspective

In spite of recent advancements in the treatment of cancer, cancer is still the leading cause of deaths worldwide. At the same time we are also familiar with side effects of traditional treatment approaches. While at present AgNPs have attained much attention in pharmaceutical sector due to their non-toxicity, cheap and environment friendly approach. AgNPs owing to their clearance potential and high biodegradability nature prevents from the effects of long term toxicity. Green synthesized AgNPs displayed outstanding efficacy as an anticancer agent *in vitro*. However, clinical trials of green synthesized AgNPs based nanomedicines are needed to find the future direction of their application. Currently, biodegradability, dose and AgNPs route of administration involving studies are most significant concerns to be tackled out in clinical trials. Keeping in view the excellent anticancer activities of these AgNPs it is believed that green synthesized AgNPs will be applied as potential anticancer agent in upcoming arena of cancer treatment. Moreover, business experts have anticipated that global market of nanotechnology has bright future.

8. Conclusions

The biogenesis of nanomedicine possess a considerable scope in 21st century to treat various diseases by devising dynamic drug delivery tools to deliver drugs effectively to selective targeted sites. After looking at the outstanding and significant research outcomes of green synthesized AgNPs it is anticipated that AgNPs have therapeutic efficacy to treat different deadly diseases owing to their pharmaceutical applications. AgNPs have physical as well as chemical advantage of ROS production, fine absorption and smooth penetration inside cell’s cytoplasm and entry to nucleus to produce their deleterious result on cancerous cells.

The significant anticancer potential of green synthesized AgNPs come up with breakthrough in metastatic cancer treatment. We also reviewed the most recent research studies about toxicology activity of AgNPs at cellular level which presents it as effective anticancer agent with pronounced therapeutic efficacy. By keeping in view the excellent potential of AgNPs and biocompatibility at the same time, it is expected that green synthesized AgNPs could be used for development of commercialized nanomedicine for cancer treatment in near future. However, this advance silver nanoapproach is facing hurdles in usage as therapeutic agent *in vivo* in term of toxicity. To resolve this issue and for their preclinical in human beings, the green synthesized AgNPs should be nontoxic and free from side effects. There is also need to understand the various physiochemical parameters such as pH, temperature, concentration of silver salt to that of plant extract and incubation time to optimize the synthesis of nanoparticles of controlled size, shape and biochemical nature. Green synthesis of silver nanoparticles is still in its beginning and such efforts will refine the nanoparticles synthesis at massive level to produce nanoparticles of potential biomedical applications effective for customized cancer therapies.

Data availability statement

No new data were created or analysed in this study.

Declarations
Funding

There is no funding to report.

Conflict of Interest

The authors declare no competing interests.

Availability of data and material

Not applicable.

Code availability

Not applicable.

ORCID iDs

Shazina Jabeen @ https://orcid.org/0000-0002-8533-942X
Mehmooda Munazir @ https://orcid.org/0000-0002-5905-9440

References

[1] Russell A and Hugo W 1994 Antimicrobial activity and action of silver Prog. Med. Chem. 31 551–70
[2] Durán N, Durán M, de Jesus M R, Seabra A B, Fávaro W J and Nakazato G 2016 Silver nanoparticles: a new view on mechanistic aspects on antimicrobial activity Nanomed. Nanotechnol. Biol. Med. 12 789–99
[3] Du J, Tang J and Xu S 2018 A review on silver nanoparticles-induced ecotoxicity and the underlying toxicity mechanisms Regul Toxicol Pharmacol. 98 231–9
[4] Rezvani E, Rafferty A, McGuinness C and Kennedy J 2019 Adverse effects of nanosilver on human health and the environment Acta Biomater. 94 145–59
[5] Jamieson W R E, Fradet G J, Abol J G, Janusz M T, Lichtenstein S V, McNab J S, Stanford E A and Chan F 2009 Seven-year results with the St Jude Medical Silzone mechanical prosthesis 1 Thorac. Cardiovasc. Surg. 137 1109–15
[6] Ge L, Li Q, Wang M, Ouyang J, Li X and Xing M M Q 2014 Nanosilver particles in medical applications: Synthesis, performance, and toxicity Int. J. Nanomed. 9 2399–407
[7] Javed B, Nadhmam A and Mashwani Z R 2020 Phytosynthesis of Ag nanoparticles from Mentha longifolia: their structural evaluation and therapeutic potential against HTCT16 colon cancer, Leishmanial and bacterial cells Appl. Nanosci. 10 3503–15
[8] Javed B, Nadhmam A, Razzaq A and Mashwani Z 2020 One-pot phytosynthesis of nano-silver from mentha longifolia L.: their characterization and evaluation of photodynamic potential Mater. Res. Express 7 1–9
[9] Chen L Q, Fang L, Ling L, Ding C Z, Kang B and Huang C Z 2015 Nanotoxicity of silver nanoparticles to red blood cells: size dependent adsorption, uptake, and hemolytic activity Chem. Res. Toxicol. 28 501–9
[10] Kędziora A, Speruda M, Krzyżewska E, Rybka J, Łukowiak A and Buglałapośkońska G 2018 Similarities and differences between silver ions and silver in nanoforms as antibacterial agents Int. J. Mol. Sci. 19 2
[11] Lestrill E, Patolsky F, Voelcker N H and El Nathan R 2019 Engineered nano-bio interfaces for intracellular delivery and sampling: applications, agency and artefacts Mater. Today 33 87–104
[12] Feldman D 2018 Polymer nanocomposites for tissue engineering, antimicrobials and drug delivery Biointerface Res. Appl. Chem 8 3153–60
[13] Keshtvadi M, Karimi F, Valizadhe S and Valizadeh A 2019 Comparative study of antibacterial inhibitory effect of silver nanoparticles and garlic oil nanomulsion with their combination Biointerface Res. Appl. Chem 9 [CrossRef]
[14] Kang T, Kim Y G, Kim D and Hyeon T 2020 Inorganic nanoparticles with enzyme-mimetic activities for biomedical applications Coord. Chem. Rev. 403 213092 [CrossRef]
[15] Gaafar M, El-Zawahy L, El-Temsahy M, Shalaby T I and Hassan A 2019 Silver nanoparticles as a therapeutic agent in experimental cyclosporiasis Exp. Parasitol 207 107772
[16] Bayda S, Aedd M, Tuccinardi T, Cordeni M and Rizzollo F 2019 The History of Nanoscience and Nanotechnology: From Chemical-Physical Applications to Nanomedicine Molecules 25 112 [CrossRef]
[17] Rafique M, Rafique M S, Kalsoom U, Afzal A, Butt S H and Usman A 2019 Laser ablation synthesis of silver nanoparticles in water and dependence on laser nature Opt. Quantum Electron. 51 6 [CrossRef]
[18] Bhattacharya S, Zhang Q, Carmichael P L, Boekelheide K and Andersen M E 2011 Toxicity testing in the 21 century: defining new risk assessment approaches based on perturbation of intracellular toxicity pathways PLoS One 6 e20887 [CrossRef]
[19] Rozañ M, Sánchez-Polo M, Fernández-Perales M, Widmann T J and Rivera-Utrilla J 2020 Synthesis of controlled-size silver nanoparticles for the administration of methotrexate drug and its activity in colon and lung cancer cells RSC Adv. 10 10646–60
[20] Palai P K, Mondal A, Chakraborti C K, Banerjee I and Pal K 2019 Green synthesized amino-PEGylated silver decorated graphene nanoplatfrom as a tumor-targeted controlled drug delivery system SN Appl. Sci. 1 269
[21] Ding I, Chen G L, Chen G F and Guo M Q 2019 One-pot synthesis of epiurubicin-capped silver nanoparticles and their anticancer activity against hep G2 cells Pharmaceutics. 11 123
Mater. Res. Express 8 (2021) 092001

Shandize S A S, Ardestani M S, Shahbazzadeh D, Assadi A, Cohan R A, Asgary V and Salehi S 2017 Novel imatinib-loaded silver nanoparticles for enhanced apoptosis of human breast cancer MCF-7 cells Artif. Cells Nanomed. Biotechnol. 45 1–10

Benyeftou F, Rezgui R, Ravaux F, Jaber T, Blumber K, Jouaid M, Motte L, Olsen J C, Platas-Iglesias C and Magzoub M 2015 Synthesis of silver nanoparticles for the dual delivery of doxorubicin and alendronate to cancer cells J. Mater. Chem. 3 7237–45

Tadale K T, Abire T O and Feyissa T Y 2021 Green synthesized silver nanoparticles using plant extracts as promising prospect for cancer therapy: a review of recent findings J Nanomed. 4 1040

Jha M and Shimpri N G 2018 Green synthesis of zero valent colloidal nanosilver targeting AS49 lung cancer cell: in vitro cytotoxicity J Genet Eng Biotechnol. 16 115–24

Raghavendra N, Hublikar L V, Patil S M and Bhat P 2021 Microwave assisted biosynthesis of silver nanoparticles using banana leaves extract: Phytochemical, spectral characterization, and anticancer activity studies J Water Environ Nanotechnol. 6 49–61

Donga S and Chanda S 2021 Facile green synthesis of silver nanoparticles using Mangifera indica seed aqueous extract and its antimicrobial, antioxidant and cytotoxic potential (3-in-1 system) Artif. Cells Nanomed. Biotechnol. 49 292–302

Mohd S H K, Alya A, Shams T, Iftekhar H and Rizwan W 2021 Anticancer potential of biogenic silver nanoparticles: a mechanistic study Pharmaceuticals. 13 707

Wang Y, Chinnathambi O, Nasif O and Ali A 2021 Green synthesis and chemical characterization of a novel anti-human pancreatic cancer supplement by silver nanoparticles containing Zinger officinalis leaf aqueous extract Artif. J. Chem. 14 103081

Niika K, Zielinska E, Radomski M W and Inkleiewska-Stejnler I 2018 Metal nanoparticles in dermatology and cosmetology: Interactions with human skin cells Chem. Biol. Interact. 295 38–51

Irvani S, KorbeKandi H, Mirmohammadi S V and Zolfaghar B 2014 Synthesis of silver nanoparticles: chemical, physical and biological methods Res. Pharm. Sci. 9 385–406 [PubMed]

Gurav A S, Kodas T T, Wang I M, Kaupinnen E I and Joutsensaaari J 1994 Generation of nanometer–size fullerene particles via vapor condensation Chem. Phys. Lett. 218 304–8 [CrossRef]

De Matteis V, Cascione M, Toma C C and Leporatti S 2018 Silver nanoparticles: synthetic routes, in vitro toxicity and theranostic applications for cancer disease Nanomaterials 8 319

Yasu M 2020 Silver nanoparticles: synthesis and applications Handbook of Ecomaterials 20 2343

Abbasi B A, Iqbal J and Nasir J A 2020 Environmentally friendly green approach for the fabrication of silver oxide nanoparticles: characterization and diverse biomedical applications Microres. Tech. 83 1–13

Ali G W, Abd El-Moez S H and Abdel-Fattah W A 2019 Synthesis and characterization of nontoxic silver nano-particles with preferential bactericidal activity Biointerface Res. Appl. Chem. 9 4617–23 [CrossRef]

Kuntiyi I, Kytoya A R and Mertsalo I P 2019 Electrochemical synthesis of silver nanoparticles by reversible current in solutions of sodium polycrylate Colloid. Polym. Sci. 297 689–95 [CrossRef]

Rafique M, Saddal I, Rafique M S and Tahir M B 2017 A review on green synthesis of silver nanoparticles and their applications Artif. Cells Nanomed. Biotechnol. 45 1272–91 [CrossRef] [PubMed]

Duan H, Wang D and Li Y 2015 Green chemistry for nanoparticle synthesis Chem. Soc. Rev. 44 5778–92

Ghoyavand S, Madani M and Karimi J 2020 Green synthesis, characterization and antifungal activity of silver nanoparticles using stems and flowers of felfy germander J. Inorg. Organomet. Polym. Mater. 30 2987–97

Ulaeto S B, Mathew G M and Pancerecious J K 2019 Biogenic Ag nanoparticles from neem extract: their structural evaluation and diverse biomedical applications for cancer disease J Mater. Chem. 37 9

Vennila K, Chitra L, Balagurunathan R and Palvannan T 2018 Comparison of biological activities of selenium and silver nanoparticles attached with bioactive phytoconstituents: green synthesized using Spermacoce hispida extract Adv. Nat. Sci.: Nanosci. Nanotechnol. 9 9

Ping Y, Zhang J, Xing T, Chen G, Tao R and Choo K H 2018 Green synthesis of silver nanoparticles using grape seed extract and their appl microbil biotechnol application for reductive catalysis of direct orange 26 J. Ind. Eng. Chem. 58 74–9

Saratale R G, Shin H S, Kumar G, Benelli G, Kim D S and Saratale G D 2018 Exploiting antidiabetic activity of silver nanoparticles synthesized using Punicia granatum leaves and anticancer potential against human liver cancer cells (HepG2) Artif. Cells, Nanomed. Biotechnol. 46 211–22

Al-Sheddi E S, Farshori N N, Al-Oqail M M, Al-Massarani S M, Saquib Q, Wahab R and Siddiqui M A 2018 Anticancer potential of green synthesized silver nanoparticles using extract of Nepeta sibirica against MCF-7 breast cancer cells (HeLa) Bioinorg Chem Appl 2018

Adebayo I A, Arsal H, Giggan H A, Ismail N Z and Samian M 2020 Inhibitory effect of eco-friendly naturally synthesized silver nanoparticles from the leaf extract of medicinal Detarium microcarpus plant on pancreatic and cervical cancer cells APJCP. 21 1247

Arokijarai S, Arasu M V, Vincent S, Prakash N U, Choi S H, Oh Y K and Kim K H 2014 Rapid green synthesis of silver nanoparticles from chrysanthemum indicum l. and its antibacterial and cytotoxic effects: an in vitro study Inter J Nanomed. 9 379

Dubey M, Bhadouria S and Kushwah B S 2009 Green synthesis of nanosilver particles from extract of Eucalyptus hybrida (safeda) leaf Dig J Nanomater Biostruct. 4 537–43

Nayaka S, Bhat M P, Chakraborty B, Pallavi SS, Airodagi D, Muthuraj R and Pukanshi C 2020 Seed extract-mediated synthesis of silver nanoparticles from putranjiva roxburghii wall., phytochemical characterization, antibacterial activity and anticancer activity against MCF-7 cell line Indian J Pharm Sci. 82 60–9

Adebayo I A, Usman A I, Shittu F B, Ismail N Z, Arsalad H, Muftaudeen T K and Samian M 2020 Boswellia dalzielii-mediated silver nanoparticles inhibited acute myeloid leukemia (AML) K562 cells by inducing cell cycle arrest Bioinorg chem appl. 2020 11

Prakash J, Shekhar H, Yadav S R, Dwivedy A K, Patel V K, Tiwari S and Vishwakarma N K 2021 Green synthesis of silver nanoparticles using Eranthum Pulchellum (Blue Sage) aqueous leaves extract: Characterization, evaluation of antifungal and antitussive properties BBNN. 5 222

Alshoheri A A and Malik M A 2020 Phyto-mediated photo-induced green synthesis of silver nanoparticles using Matricaria chamomilla L. and its catalytic activity against rhodamine B Bimoleculars. 10 1604

Afreen A, Ahmed R, Mehboob S, Tariq M, Alghamdi A H, Zahid A A and Hasain A A 2020 Phytochemical-assisted biosynthesis of silver nanoparticles from Ajuga bracteosa for biomedical applications Mater. Res. Express 7 075704

Ahmad M A, Salmati S, Marpongntun M, Salim M R, Lolo J A and Syaufiuddin A 2020 Green synthesis of silver nanoparticles using muntingia calabura leaf extract and evaluation of antibacterial activities Biointerface Res. Appl. Chem 10 6253–61

Rizwan M, Amin S and Malikova B K 2020 Green synthesis and antimicrobial potential of silver nanoparticles with Boerhavia procumbens extract J Pure Appl Microbiol. 14 1437–51

Sagadevan S, Vennila S, Muthukrishnan L, Guruswathan K, Oh W C, Pissam S and Obulapuram P K 2020 Exploring the therapeutic potentials of phyto-mediated silver nanoparticles formed via Calotrops procera (Ait.) R. Br. root extract J. Exp. Nanosci. 15 217–31
[57] Saratale G D, Saratale R G, Kim D S, Kim D Y and Shin H S 2020 Exploiting fruit waste grape pomace for silver nanoparticles synthesis, assessing their antioxidant, antidiabetic potential and antibacterial activity against human pathogens: A novel approach Nanomater. 10 1457
[58] de Meo A P Z, Maciel MV D O B, Sganzerla W G, da Rosa Almeida A, de Armas R D, Machado M H and Barreto P L M 2020 Antibacterial activity, morphology, and physicochemical stability of biosynthesized silver nanoparticles using thyme (Thymus vulgaris) essential oil Mater. Res. Express 7 105087
[59] Sganzerla W G, Longo M, de Oliveira J L, da Rosa C G, de Lima Veec A P, de Aquino R S and Nunes M 2020 Nanocomposite poly (ethylene oxide) films functionalized with silver nanoparticles synthesized with Acca sellowiana extracts Colloids Surf. A: Physicochem Eng. Asp. 602 125125
[60] Ferlay J, Ervik M and Lam F 2020 Global Cancer Observatory: Cancer Today. (Lyon: International Agency for Research on Cancer) 2020 (https://gco.iarc.fr/ today)
[61] Wild C P, Weiderpass E and Stewart B W 2022 IARC world cancer report 2020(cancer research for cancer prevention)
[62] Hollstein M, Alexandrov L, Wild C, Ardin M and Zavadil J 2016 Base changes in tumour DNA have the power to reveal the causes and evolution of cancer Oncogene. 199 512 (Epub ahead of print)
[63] Javed B, Nadhman A and Mashwani Z R 2020b Optimization, characterization and antimicrobial activity of silver nanoparticles against plant bacterial pathogens phyto-synthesized by Mentha longifolia Mater. Res. Express 7 085406
[64] Sener S F and Grey N 2005 The global burden of cancer J. Surg. Oncol 92 1–3
[65] Ferlay J, Soerjomataram I and Dikshit R 2015 Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012 Int. J. Cancer 136 E395–86
[66] Jemal A, Center M M, Desantis C and Ward E M 2010 Global patterns of cancer incidence and mortality rates and trends Cancer Epidemiol. Biomarkers Prev. 19 1893–907
[67] Anand P, Kunnunmakara A K and Sundaram C 2008 Cancer is a preventable disease that requires major lifestyle changes Pharm. Res. 25 1097–116
[68] Manzoor M, Khan A H A, Ullah R, Khan M Z and Ahmad I 2016 Environmental epidemiology of cancer in South Asian population: risk assessment against exposure to polycyclic aromatic hydrocarbons and volatile organic compounds Arab. J. Sci. Eng. 41 2031–43
[69] Sharma P, Mehta M and Dhanjal D S 2019 Emerging trends in the novel drug delivery approaches for the treatment of lung cancer Chem. Biol. Interact. 309 108720
[70] Han H J, Ekeremadu C and Patel N 2019 Advanced drug delivery system with nanomaterials for personalised medicine to treat breast cancer J Drug Deliv Sci Technol 52 1051–60
[71] Mukherjee S and Patra C R 2016 Therapeutic application of antiangiogenic nanomaterials in cancers Nanoscale 8 12444–70
[72] Macdonald J S 1999 Toxicity of 5-fluorouracil Oncology (Williston Park, NY) 13 35–44
[73] Fraser I H, Kanekal S and Kheere J P 1991 Cyclophosphamide toxicity Drugs 42 781–95
[74] Kumar V and Yadav S K 2009 Plant-mediated synthesis of silver and gold nanoparticles and their applications J. Chem. Technol. Biotechnol. 84 151–7
[75] Klefenz H 2004 Nanobiotechnology: from molecules to systems Eng. Life Sci. 4 211–8
[76] Shinwari Z, Khan A and Nakaikv T 2003 Medicinal and other Useful Plants of District Swat, Pakistan. (Peshawar, Pakistan: Al-Aziz Communications) 97–8
[77] Bhaumik J, Thakur N S, Ali P K, Ghanghoriya A, Mittal A K and Banerjee U C 2015 Bioinspired nanotheranostic agents: synthesis, surface functionalization, and antioxidant potential ACS Biomaterials Science & Engineering 1 382–92
[78] Chung I M, Park I, Seung-Hyun K, Thiruvengadam M and Rajakumar G 2016 Plant-mediated synthesis of silver nanoparticles: their characteristic properties and therapeutic applications Nanoscale Res. Lett. 11 1
[79] Oberdörster G, Oberdörster E and Oberdörster J 2005 Nanotoxicology: an emerging discipline evolving from studies of ultrafine particles. Environ Health Perspect. 823–39
[80] Poussel B K, Soe Z C, Ruttala H B, Gupta B, Ramasamy T, Thapa R K, Gautam M, Ou W, Nguyen H T and Jeong J H 2018 In situ fabrication of mesoporous silica-coated silver-gold hollow nanoshell for remotely controllable chemo-photothermal therapy via phase-change molecule as gatekeepers Int. J. Pharm. 548 92–103 [CrossRef]
[81] Shinde A and Dendukullar V 2020 Antiproliferative Activity Of Elephantopus Scaber Mediated Silver Nanoparticles Against MCF-7, A-549, SCC-40, And Colo-205 Human Cancer Cell Lines Asian J Pharm Clin Res 13 163–7
[82] Iqbal M J, Ali S and Rashid U 2018 Biosynthesis of silver nanoparticles from leaf extract of Litchi chinesis and its dynamic biological impact on microbial cells and human cancer cell lines Cell. Mol. Biol. 64 42–7
[83] Ullah I, Khalil A T and Ali M 2020 Green-synthesized silver nanoparticles induced apoptotic cell death in mcf-7 breast cancer cells by generating reactive oxygen species and activating caspase 3 and 9 enzyme activities Oxidative Medicine and Cellular Longevity 2020
[84] Gurunathan S, Raman J, Abd Malek S N, John P A and Vikineswary S 2013 Green synthesis of silver nanoparticles using ganoderma neo-japonicum Imazeki: a potential cytotoxic agent against breast cancer cells Int. J. Nanomed. 8 4399
[85] Balkrishna A, Sharma V K and Das S K 2020 Characterization and anti-cancerous effect of putrajinva roxburghii seed extract mediated silver nanoparticles on human colon (HCT–116), pancreatic (PANC-1) and breast (MDA-MB-231) cancer cell lines: a comparative study Int. J. Nanomed. 15 573
[86] Elhawary S, Hala E H, Mokhtar F A, Mansour Soheb E M, Osman S and El-Raey M 2020 Green synthesis of silver nanoparticles using extract of jasminum officinal L. leaves and evaluation of cytotoxic activity towards bladder (5637) and breast cancer (MCF-7) cell lines Int. J. Nanomed. 15 9771
[87] Elgamouz A, Idriss H and Nassab C 2020 Green synthesis, characterization, antimicrobial, anti-cancer, and optimization of colorimetric sensing of hydrogen peroxide of algae extract capped silver nanoparticles Nanomaterials 10 1861
[88] Sadat Shandiz S A, Shafiee Ardestani M and Shahbaazaar D 2017 Novel imatinib-loaded silver nanoparticles for enhanced apoptosis (ethylenox) films Mater. Res. Express 4 085117
[89] El-Naggar N E, Hussein M H and El-Sawah A A 2017 Bio-fabrication of silver nanoparticles by phycocyanin, characterization, in vitro antiangiogenic activity against breast cancer cell line and in vivo cytotoxicity Sci. Rep. 7 1–20
[90] Raman M, Manikandan B and Marimuthu P N 2015 Synthesis of silver nanoparticles using Solanum trilobatum fruits extract and its antibacterial, cytotoxic activity against human breast cancer cell line MCF 7 Spectroch Acta A Mol. Biomol. Spectros 140 223–8
[91] Venkatadri B, Shanparvish E and Ramesh Kumar M 2020 Green synthesis of silver nanoparticles using aqueous rhizome extract of Zingiber officinale and curcuma longa. In-vitro anti-cancer potential on human colon carcinoma HT-29 cells Saudi J. Biol. Sci 27 2980–6
[92] Huang F, Long Y, Liang Q, Purushotham B, Swamy M K and Duan Y 2019 Safed musli (Chlorophyllum borivilianum L.) callus-mediated biosynthesis of silver nanoparticles and evaluation of their antimicrobial activity and cytotoxicity against human colon cancer cells J. Nanomater. 2019

[93] Sufyan I, Moslah N, Hussien N A and Hawsawi Y M 2019 Characterization and anticancer potential of silver nanoparticles biosynthesized from olea chrysophylla and lavandula dentata leaf extracts on hct116 colon cancer cells J. Nanomater. 19 9

[94] Javed B 2020 Synergistic effects of physicochemical parameters on bio-fabrication of mint silver nanoparticles: structural evaluation and action against HCT116 colon cancer cells Int. J. Nanomed. 15 3621

[95] Nayaka S R, Chakraborty B I, Pallavi S S, Bhat M P, Shakiraj K N and Ghasti R B 2020 Synthesis of biogenic silver nanoparticles using zanthoxyllum rheta (Roxb.) DC seed coat extract as reducing agent and in-vitro assessment of anticancer effect on A549 lung cancer cell line Int. J. Pharm. Res. 12 302–14

[96] Annu M, Ahmed S, Kaur G, Sharma P, Singh S and Ikrarn S 2018 Evaluation of the antioxidant, antibacterial and anticancer (lung cancer cell line A549) activity of Punica granatum mediated silver nanoparticles Toxicol. Res. 7 923–30

[97] Cyril N, George J B, Joseph L, Raghavamoven A C and Assessment V P S 2019 of antioxidant, antibacterial and anti-proliferative (lung cancer cell line A549) activities of green synthesized silver nanoparticles from Derris trifoliata Toxicol. Res. 8 297–308

[98] He Y, Du Z and Ma S 2016 Effects of green-synthesized silver nanoparticles on lung cancer cells in vitro and grown as xenograﬁ tum tumors in vivo Int. J. Nanomed. 11 1879

[99] Al-Sheddi E S, Farshori N N and Al-Oqail M M 2018 Anticancer potential of green synthesized silver nanoparticles using extract of Nepeta delersianna against human cervical cancer cells (HeLa) Bioinorg Chem Appl. 2018 12

[100] Adebayo I A, Arsal H, Gagman H A, Ismail N Z and Samian M 2020 Inhibitory effect of eco-friendly synthesized silver nanoparticles from the leaf extract of medicinal Detarium microcarpum plant on pancreatic and cervical cancer cells Asian Pacific journal of Cancer Prevention: APJCP 21 1247

[101] Xu Z, Feng Q, Wang M, Zhao H, Lin Y and Zhou S 2020 Green biosynthesized silver nanoparticles with aqueous extracts of ginkgo biloba induce apoptosis via mitochondrial pathway in cervical cancer cells Front Oncol. 10 2282

[102] Liu X, Shan K and Shao X 2021 Nanotoxic effects of silver nanoparticles on normal HEK-293 cells in comparison to cancerous HeLa cell line Int. J. Nanomed. 16 753

[103] Sarkar S and Kotteeswaran V 2018 Green synthesis of silver nanoparticles from aqueous leaf extract of Pomegranate (Punica granatum) and their anticancer activity on human cervical cancer cells Adv Nat Sci: Nanoscale 9 025014

[104] Saratate R G, Shin H S, Kumar G, Benelli G, Kim D S and Saratate G D 2018 Exploiting antiadipic activity of silver nanoparticles synthesized using Punica granatum leaves and anticancer potential against human liver cancer cells (HepG2) Artif Cells, Nanomed Biotechnol. 46 211–22

[105] Pandian A M K, Karthikeyan C, Rajasimman M and Dinesh M 2015 Synthesis of silver nanoparticle and its application Ecotoxicol. Environm. Saf. 121 211–7

[106] Firdhouse M J and Lalitha P 2013 Biosynthesis of silver nanoparticles using the extract of Alternanthera sessilis—intraproliferative effect against prostate cancer cells Cancer Nanotechnol. 4 137–43

[107] Palle S R, Penchalaneni J, Lavudi K, Gaddam S A, Kotakadi V S and Challagundla V N 2020 Green synthesis of silver nanoparticles by leaf extracts of boerhavia erecta and spectral characterization and their antimicrobial, antioxidant ad cytotoxic studies on ovarian cancer cell lines Letters in Applied Nano Bio Science 9 1165–76

[108] He Y, Du Z and Ma S 2018, 2016 Nano synthesis, antibacterial activity and anticancer effects against prostate cancer (PC-3) cells of silver nanoparticles using Dimocarpus Longan fruit peel extract Nanoscale Res. Lett. 11 1–9

[109] Reddy N V, Li H, Hou T, Bethu M S, Ren Z and Zhang Z 2021 Phytosynthesis of Silver Nanoparticles Using Perilla frutescens Leaf Extract: Characterization and Evaluation of Antibacterial, Antioxidant, and Anticancer Activities Int. J. Nanomed. 16 15

[110] Zhang K, Liu X and Samuel Ravi S 2019 Synthesis of silver nanoparticles (AgNPs) from leaf extract of Salvia miltiorrhiza and its anticancer potential in human prostate cancer LNCaP cell lines. Artif cells, nanomed biotechnol. 47 2846–54

[111] Gulzar A, Xu J and Wang C 2019 Tumour microenvironment responsive nanoconstructs for cancer theranostic Nano Today 26 16–56

[112] Lim E K, Kim T, Paik S, Haam S, Huh Y M and Lee K 2017 Nano materials for theranostics: Recent advances and future challenges Chem. Rev. 115 327–94 [CrossRef] [PubMed]

[113] Farokhzad O C and Langer R 2009 Impact of nanotechnology on drug delivery ACS Nano 3 16–20

[114] Ashraf M, Ansari M A, Khan H M, Ahloowalia B S and Choi J 2016 Green synthesis of silver nanoparticles and characterization of their inhibitory effects on biological techniques Sci. Rep. 6 20414

[115] Sreekanth T, Pandurangam M, Kim D H and Lee Y R 2016 Green synthesis: in-vitro anticancer activity of silver nanoparticles on human cervical cancer cells J. Cluster Sci. 27 671–81

[116] Mukherjee S, Chowdhury D and Kotcherlakota R 2014 Potential theranostics application of bio-synthesized silver nanoparticles (4-in-1 system) Theranostics 4 316–35

[117] Du J, Singh H and Yi T H 2016 Antibacterial, anti-biofilm and anticancer potentials of green synthesized silver nanoparticles using benzoin gum (Styrax benzoin) extract Bioprocess. Biostyr. Eng. 39 1923–31 (Epub ahead of print)

[118] Singh R, Shelbalkar U U, Wadhwani S A and Chopard A B 2015 Bacteriogenic silver nanoparticles: synthesis, mechanism, and applications Appl. Microbiol. Biotechnol. 99 4579–93 [CrossRef] [PubMed]

[119] Javed B and Mashwani Z R 2020a Synergistic effects of physicochemical parameters on bio-fabrication of mint silver nanoparticles: structural evaluation and action against HCT116 colon cancer cells Int. J. Nanomed. 15 3621–37

[120] Venugopal K, Rather H A and Rajagopal K 2017 Synthesis of silver nanoparticles (Ag NPs) for anticancer activities (MCF7 breast and A549 lung cell lines) of the crude extract of Syzygium aromaticum J. Photochem Photobiol B Biol 167 282–9

[121] Hembram K G, Kumar R, Kandla L, Parhi P K, Kundu C N and Bindhani B K 2018 Therapeutic prospective of plant-induced silver nanoparticles: application as antimicrobial and anticancer agent Artif Cells, Nanomed Biotechnol. 46 538–51

[122] Narayanan S, Jeong J K, Han W, Zhang X F, Park H J and Kim H J 2015 Multidimensional effects of biologically synthesized silver nanoparticles in helicobacter pylori, helicobacter felis, and human lung (H132) and lung carcinoma A549 cells. Nanoscale Res. Lett. 10 35 [CrossRef] [PubMed]

[123] Zuberek M, Wojciechowski D, Krzyzanowski D, Meczyńska-Wielgosz S, Kruzewski M and Grzelak A 2015 Glucose availability determines silver nanoparticles toxicity in HEpG2 cells Nano biotechnol. 13 72 [CrossRef] [PubMed]

[124] Hallibell B, Clement M V, Ramalingam J and Long L H 2000 Hydrogen peroxide. ubiquitous in cell culture and in vivo Int J UMB L 50 251–7 [CrossRef] [PubMed]

[125] Kovacs D, Igor N and Keskeeny C 2016 Silver nanoparticles defeat p53-positive and p53-negative osteosarcoma cells by triggering mitochondrial stress and apoptosis Sci. Rep. 6 27902
[126] Ahn E Y, Jin H and Park Y 2019 Assessing the antioxidant, cytotoxic, apoptotic and wound healing properties of silver nanoparticles green-synthesized by plant extracts Mater. Sci. Eng. C Mater. Biol. Appl. 101 204–16 [CrossRef]

[127] Gomathi A C, Xavier Rajarathnam S R, Mohammed Sadiq A and Rajeshkumar S 2020 Anticancer activity of silver nanoparticles synthesized using aqueous fruit shell extract of Tamarindus indica on MCF-7 human breast cancer cell line J. Drug Deliv. Sci. Technol. 55 101376 [CrossRef]

[128] Al-Sheddi E S, Farshori N N and Al-Qoaili M M 2018 Anticancer potential of green synthesized silver nanoparticles using extract of Nepeta delphsiana against human cervical cancer cells (HeLa) Biomorg. Chem. Appl. 18 9399784 [PubMed]

[129] He Y, Li X and Zheng Y 2018 A green approach of synthesizing of silver nanoparticles and their antibacterial and cytotoxicity activities New J. Chem. 42 2882–2886 [CrossRef]

[130] Mortazavi-Derazkola S, Ebrahimpazeh M A and Amir O 2020 Facile green synthesis and characterization of Crapeagius microphylla extract-capped silver nanoparticles (CME@Ag-NPs) and its potential antibacterial and anticancer activities against AGS and MCF-7 human cancer cells J. Alloys Compd. 820 153186 [CrossRef]

[131] Kanipandian N, Li D and Kannan S 2019 Induction of intrinsic apoptotic signaling pathway in A549 lung cancer cells using Silver nanoparticles from Gossypium hirsutum and evaluation of in vitro toxicity Biotechnol. Rep. 23 e00339 [CrossRef]

[132] Yesilot S and Aydin C 2019 Silver nanoparticles; a new hope in cancer therapy ! East J. Med. 24 111–6

[133] Yang S, Yao Q, Cao F, Liu Q, Liu B and Wang X H 2016 Silver nanoparticles inhibit the function of hypoxia-inducible factor-1 and target genes: Insight into the cytotoxicity and antiangiogenesis Int. J. Nanomed. 11 6679–92 [CrossRef]

[134] Baghani M and Es-haghi A 2020 Characterization of silver nanoparticles biosynthesized using Amaranthus cruentus Bioinspir. Biomim. Nanobiomater. 9 129–36 [CrossRef]

[135] Hao M, Kong C and Jiang C 2019 Polydopamine-coated Au–Ag nanoparticle-guided photothermal colorectal cancer therapy through multiple cell death pathways Acta Biomater. 83 414–24 [CrossRef]

[136] He X, Peng C and Qiang S 2020 Less is more: Silver-AIE core@shell nanoparticles for multimodality cancer imaging and synergistic therapy Biomaterials 238 119834 [CrossRef]

[137] Wang M, Liang Y and Zhang Z 2019 AgTeO4 nanoparticles for multi-modal imaging-guided chemo-photothermal synergistic targeting for cancer therapy Anal. Chem. 1086 122–32 [CrossRef]

[138] Thapa R K, Kim J H, Jeong J H, Shin B S, Choi H G, Yong C S and Kim J O 2017 Silver nanoparticle-embedded graphene oxide-methotrexate for targeted cancer treatment Colloids Surf. B Biointerfaces 153 95–103 [CrossRef]

[139] Wang Y, Chinmathamba A, Nasif O and Alharbi S A 2021 Green synthesis and characterization of a novel anti-human pancreatic cancer supplement by silver nanoparticles containing Zingiber officinale leaf aqueous extract Arab. J. Chem. 14 103081

[140] Mei L, Xu Z and Shi Y 2020 Multivalent and synergistic chitosan oligosaccharide–Ag nanoparticles for the treatment of bacterial infection Sci. Rep. 10 10101 [CrossRef]

[141] Tortella G R, Rubilar O and Duran N 2020 Silver nanoparticles: toxicity in model organisms as an overview of its hazard for human health and the environment J. Hazard. Mater. 390 121974 [CrossRef]

[142] Avalos A, Haza A I, Mateo D and Morales P 2016 Interactions of manufactured silver nanoparticles of different sizes with normal human dermal fibroblasts Int. Wound J 13 101–9 [CrossRef]

[143] Fani S, Kamalideghban B and Lo K M 2016 Anticancer activity of a monobenzyltin complex C1 against MDA-MB-231 cells through induction of apoptosis and inhibition of breast cancer stem cells Sci. Rep. 6 38992

[144] Nishamath R P, Jyotsna R G, Schlager J J, Hussain S M and Reddanna P 2011 Inflammatory responses of raw 264.7 macrophages upon exposure to nanoparticles: Role of ROS-NFKB pathway Nanotoxicology 5 502–16 [CrossRef] [PubMed]

[145] Verano-Braga T, Mietlhling-Grall R and Woydyla K 2014 Insights into the cellular response triggered by silver nanoparticles using quantitative proteomics ACS Nano 8 2161–75 [CrossRef] [PubMed]

[146] Ratan Z A, Haideere M F, Nurunnabi M, Ahammad A J, Shim Y Y and Cho J Y 2020 Green chemistry synthesis of silver nanoparticles in jurkat t cells and their potential anticancer effects Cancers 12 855

[147] Eom H J and Choi J 2010 P38 mapk activation, DNA damage, cell cycle arrest and apoptosis as mechanisms of toxicity of silver nanoparticles in Jurkat t cells Environ. Sci. Technol. 44 8337–42 [CrossRef] [PubMed]

[148] Ovais M, Khalid A T and Raza A 2016 Green synthesis of silver nanoparticles via plant extracts: beginning a new era in cancer theranostics Nanomedicine 12 3157–77

[149] Halawani E M, Hassan A M and El Rab S M F G 2020 Nanof ormulation of biogenic cetoxafamine-conjugated silver nanoparticles for enhanced antibacterial efficacy against multidrug-resistant bacteria and anticancer studies Int. J. Nanomedicine 15 1889–901

[150] Lee B and Lee D G 2019 Synergistic antibacterial activity of gold nanoparticles caused by apoptosis-like death J. Appl. Microbiol. 127 701–12

[151] Amaral JD, Xavier M J, Steer C J and Rodrigues C M 2010 The role of p53 in apoptosis Discov. Med. 9 145–52

[152] Banjerjee P P, Bandopadhyay A and Harsha S 2017 Mentha arvensis (Linn.)-mediated green silver nanoparticles trigger caspase 9-dependent cell death in MCF7 and MDA-MB-231 cells Breast Cancer Targets Ther. 9 265–78

[153] Nadeem M, Khan R and Afridi K 2020 Green synthesis of cerium oxide nanoparticles (CeO2 nps) and their antimicrobial applications: a review Int J. Nanomedicine 15 3951–61

[154] Shi J, Kantof PW, Wooster R and Farokhzad O C 2017 Cancer nanomedicine: progress, challenges and opportunities Nat. Rev. Cancer 17 20–37

[155] Haggag E G, Elshamy A M and Rabeh M A 2019 Antiviral potential of green synthesized silver nanoparticles of Lampranthus cocineus and Malephora lutea Int J. Nanomedicine 14 6217–29

[156] Aalapati S, Ganapathy S, Manapuram S, Anumolu G and Prakya B M 2014 Toxicity and bio-accumulation of inhaled cerium oxide nanoparticles in CD1 mice Nanotoxicology 8 786–98

[157] Triboulet S, Aude-Garcia C and Armand L 2015 Comparative proteomic analysis of the molecular responses of mouse macrophages to titanium dioxide and copper oxide nanoparticles unravels some toxic mechanisms for copper oxide nanoparticles in macrophages PLoS One 10 e0124496

[158] Van Aarle R, Lange A and Moorhouse A 2013 Molecular mechanisms of toxicity of silver nanoparticles in zebrafish embryos Environ. Sci. Technol. 47 8005–14

[159] Lima R, Seabra A B and Duran N 2012 Silver nanoparticles: a brief review of cytotoxicity and genotoxicity of chemically and biogenically synthesized nanoparticles J. Appl. Toxicol. 32 867–79

[160] Munger M A, Radwanski P and Hadlock G C 2014 In vivo human time–exposure study of orally dosed commercial silver nanoparticles Nanomedicine 10 1–9

[161] Asidu S O, Ugwu K and Akpa P A 2019 Biogenic synthesis and antibacterial activity of controlled silver nanoparticles using an extract of Gongronema latifolium Mater. Chem. Phys. 237 237
[162] Madivoli E S, Kareru P G and Gachanja A N 2020 Facile synthesis of silver nanoparticles using Lantana trifolia aqueous extracts and their antibacterial activity J. Inorg. Organomet. Polym. Mater. 30 2842–50

[163] Abdelsalam N R, Abdel-megeed A and Ali H M 2018 Ecotoxicology and environmental safety genotoxicity effects of silver nanoparticles on wheat (Triticum aestivum L.) root tip cells Ecotoxicol. Environ. Saf. 155 76–85

[164] Bapat R A, Chaubal T V and Joshi C P 2018 An overview of application of silver Appl Microbiol Biotechnol nanoparticles for biomaterials in dentistry Mater. Sci. Eng. C 91 881–98

[165] Li Y, Ke Y and Zou H 2019 Gold nanoparticles synthesized from Strychni semen and its anticancer activity in cholangiocarcinoma cell (KMCH-1) ArtifCells, Nanomed Biotechnol 47 1610–6

[166] Dormont F, Varna M and Couvreur P 2018 Nanoplumbers: biomaterials to fight cardiovascular diseases Mater. Today 21 122–43

[167] Marcelo G A, Lodeiro C, Capelo J L, Lorenzo J and Oliveira E 2020 Magnetic, fluorescent and hybrid nanoparticles: from synthesis to application in biosystems Mater. Sci. Eng. C 106 110104

[168] Ajitha B, Reddy Y A K, Lee Y, Kim M J and Ahn CW 2019 Biomimetic synthesis of silver nanoparticles using Syzygium aromaticum (clove) extract: catalytic and antimicrobial effects Appl. Organomet. Chem. 33 1–13

[169] Elder A, Yang H and Gwiazda R 2007 Testing nanomaterials of unknown toxicity: an example based on platinum nanoparticles of different shapes Adv. Mater. 19 3124–9