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Enhancing Apoptosis Mediated Anti Breast Cancer Activity Employing Green Synthesis of Silver Nanoparticles

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ABSTRACT

Green synthesis of silver nanoparticles (AgNPs) using plant extracts has emerged as a sustainable and biocompatible approach in nanomedicine. Several medicinal plants have been employed to produce AgNPs with potent anticancer activity against breast cancer cell lines, particularly MCF-7 and MDA-MB-231. This review consolidates findings from recent studies on *Lonicera hypoglauca*, *Vitis vinifera*, *Artemisia monosperma, Fagonia indica, Astragalus fasciculifolius, Citrullus colocynthis, Centratherum anthelminticum*, Pumpkin peel, *Allium saralicum, and Eclipta alba*. We highlight synthesis protocols, characterization, cytotoxicity assays, mechanistic insights, and therapeutic potential of these AgNPs, emphasizing apoptosis induction, ROS generation, mitochondrial dysfunction, and selective toxicity towards breast cancer cells.

Keywords : Anti breast cancer activity, Silver nanoparticles, Green synthesis, Apoptosis induction, Nanotechnology

INTRODUCTION

Breast cancer develops when breast cells grow abnormally and uncontrollably, resulting in tumor formation and possible spread to other parts of the body. The most common type is ductal carcinoma, which begins in the lining of the milk ducts, while lobular carcinoma originates in the milk-producing lobules. When the cancer extends beyond the ducts or lobules into surrounding tissue, it is classified as invasive breast cancer. Although the disease can affect both women and men, male cases are relatively rare [1]. Human breast cancers are generally divided into three major subtypes: estrogen or progesterone receptor-positive (ER+ or PR+), HER2/neu-positive (HER2/neu+), and triple-negative breast cancer (TNBC), which lacks ER, PR, and HER2/neu expression . TNBC represents about 15% of all breast cancer cases and is distinguished by its aggressive nature, high metastatic potential, and poor response to chemotherapy compared to other breast cancer subtypes [2].

Breast cancer is the most commonly diagnosed cancer among women worldwide and continues to be a leading cause of death, with over 670,000 fatalities reported in 2022. The risk of developing breast cancer rises with age; however, early detection through screening combined with comprehensive treatment approaches plays a crucial role in reducing its burden and improving patient survival rates [3]. Based on GLOBOCAN (Global Burden of Cancer) statistics, in 2020 breast cancer ranked first globally in terms of new cases, with 2,261,419 reported incidences, accounting for 11.7% of all cancers. Treatment strategies for breast cancer may include chemotherapy, immunotherapy, targeted therapy, and radiation therapy [4].

In recent years, nanotechnology has been increasingly applied to biological systems, driving progress in translational and regenerative therapies. Among various nanoparticles, silver nanoparticles (AgNPs) synthesized through the bioreduction of silver ions have attracted significant research interest. Compared to other essential metals, silver offers abundant, safe and cost-effective material properties. As a result, AgNPs are now recognized for their wide-ranging applications, including anticancer, antimicrobial, larvicidal, catalytic, and anti-inflammatory uses. It have been demonstrated to disrupt tumor cell structures, induce DNA damage, generate reactive oxygen species, and regulate key signaling pathways. It can be synthesized through physical, chemical, or biological approaches. Among these, physical and chemical methods are generally more hazardous, whereas biological synthesis offers a safer, eco-friendly, and less toxic alternative. Plants are particularly effective in green synthesis because they contain phytochemicals that act as natural reducing and stabilizing agents. These phytochemicals not only facilitate nanoparticle formation but also enhance the biological activity of AgNPs [5].

Silver nanoparticles (AgNPs) are currently considered to have the highest level of commercialization among nanomaterials. They are emerging as one of the most promising nanoproducts in the field of nanomedicine. Their unique structural and functional

characteristics, along with their clear therapeutic potential, have attracted growing interest for the treatment of a wide range of diseases [6]. Nanoparticles are well recognized for their ability to interact with cellular molecular pathways. Numerous studies have reported on green-synthesized silver nanoparticles (AgNPs), both modified and unmodified with organic or inorganic compounds, showing their capacity to regulate diverse signaling mechanisms in breast cancer cells. The mechanism of action of AgNPs varies depending on surface modifications [7].

Why nanoparticle

Silver nanoparticles represent a significant advancement in nanotechnology because they exhibit greater stability and lower chemical reactivity compared to many other metals. Their distinctive physicochemical characteristics have made them highly attractive for biological applications. They are increasingly recognized for their potential in bioengineering and medical diagnostics. Their distinctive properties such as a high surface-to-volume ratio, enhanced magnetic behaviour, and strong surface plasmon resonance make them highly suitable for biological applications. In addition, they offer multifunctionality, chemical stability, large surface area, and ease of processing. These features underpin their promising role in biomedical fields, including biomaterials development, diagnostic platforms, pharmaceutical formulations, targeted drug delivery, and medical device coatings[8]. Nanotechnology is reshaping cancer treatment by improving drug delivery, reducing side effects, and enabling precision targeting. Conventional therapies like chemotherapy and radiotherapy suffer from toxicity and lack of specificity, but nanoparticles offer solutions through encapsulation, biofunctionalization, and theranostic applications. Their design (size, shape, surface chemistry, protein corona interactions) critically influences uptake and efficacy. It also enhance imaging, hyperthermia, and radiation sensitivity. Overall, they represent a promising frontier in oncology, merging therapy and diagnostics for safer, more effective cancer interventions [9]. Silver nanoparticles have been synthesized through a range of physical and chemical techniques, yet these conventional approaches typically depend on toxic chemical reducing agents. In recent years, significant attention has shifted toward green synthesis strategies aimed at minimizing the use of hazardous materials [1O].

Synthesis of silver nanoparticle (AgNPs) using plant extracts

Mani *et al*., investigates the green synthesis of AgNPs using aqueous leaf extract of Eclipta alba and evaluates their antioxidant, anticancer, and anti-leishmanial activities. Silver nanoparticles were synthesized using silver nitrate and plant extract as a reducing and capping agent. Formation of AgNPs was confirmed by color change and characterized by UV–Vis spectroscopy (peak at 437 nm), FTIR (functional groups responsible for reduction and stabilization), XRD (face-centered cubic crystalline silver structure), and SEM analysis, which showed spherical particles of 40–60 nm.In vitro antioxidant assays (DPPH and ABTS) demonstrated that AgNPs possessed significantly higher radical scavenging activity than the crude plant extract, with lower IC_{50} values.Cytotoxicity was evaluated using the MTT assay against triple-negative breast cancer cells (MDA-MB-231). The AgNPs showed dose-dependent cytotoxicity with an IC_{50} of 77.20 µg/ml, which was more potent than the aqueous extract (IC_{50} 105.80 µg/ml). Morphological and fluorescence staining studies confirmed apoptosis induction in treated cancer cells. Additionally, AgNPs exhibited strong anti-leishmanial activity against both promastigote and amastigote forms of Leishmania tropica, showing high percentage mortality at 400 µg/ml. Green synthesized silver nanoparticles from Eclipta alba demonstrated enhanced antioxidant, anticancer, and anti-leishmanial activities compared to the crude extract. The study suggests that plant-mediated AgNPs could serve as a promising nanotherapeutic agent for managing triple-negative breast cancer and parasitic infections [11].

Xu *et al*., reported on the green-synthesized silver nanoparticles (AgNPs) as an anticancer agent, specifically targeting breast cancer cells. The conventional chemotherapy drugs, which often damage healthy cells and cause severe side effects such as apoptosis, DNA breakage, and gastrointestinal issues. This has created a demand for natural bioactive compounds with lower toxicity profiles. Garlic (*Allium* species), particularly *Allium saralicum*, has long been recognized for its medicinal properties due to its rich content of sulfur and selenium compounds, which exhibit antioxidant, anti-inflammatory, and anticancer activities. The green synthesis of AgNPs using *Allium saralicum* extract, emphasizing the eco-friendly nature of this method compared to chemical synthesis. Silver nitrate ($AgNO_3$) was reduced using the plant extract, and the resulting nanoparticles were characterized through FT-IR spectroscopy, UV-Vis spectroscopy, TEM, and FE-SEM imaging. These analyses confirmed the successful formation of spherical nanoparticles ranging from 13.9 to 55.2 nm in size, with distinct Ag-O bond signatures and plasmonic resonance peaks. The green synthesis method not only minimized environmental pollution but also ensured biocompatibility, making the nanoparticles suitable for biomedical applications. The anticancer potential of these AgNPs was evaluated against four breast cancer cell lines: SK-BR-3, MDA-MB-231, AU565, and Hs 281.T, using the MTT assay. The results demonstrated dose-dependent cytotoxicity, with IC50 values of 208 µg/ml for SK-BR-3, 250 µg/ml for MDA-MB-231, 200 µg/ml for AU565, and 188 µg/ml for Hs 281.T. Importantly, the nanoparticles showed minimal toxicity toward normal endothelial cells (HUVEC), underscoring their selectivity for cancer cells. Among the tested lines, the MDA-MB-231 cell line exhibited the most significant reduction in viability, suggesting that these nanoparticles may be particularly effective against aggressive breast cancer subtypes. Mechanistically, the anticancer effects of AgNPs are attributed to both direct and indirect actions. Directly, the nanoparticles interact with cellular components such as DNA, RNA, proteins, and membranes, disrupting essential processes and inducing apoptosis. Indirectly, they generate reactive oxygen

species (ROS), which promote oxidative stress and further drive cancer cell death. The findings within the broader context of nanomedicine, where nanoparticles are increasingly used in drug delivery systems to improve efficacy and reduce side effects. The small size of AgNPs allows them to penetrate cells efficiently, making them ideal carriers for targeted therapies. Moreover, the green synthesis approach aligns with principles of sustainability and safety, avoiding toxic byproducts associated with chemical methods. The authors emphasize that combining nanotechnology with natural bioactive compounds represents a promising strategy for developing modern chemotherapeutic agents [12].

Husain *et al*., focuses on the synthesis of silver nanoparticles (AgNPs) using aqueous seed extract of Centratherum anthelminticum (kalijiri, bitter cumin) and their potential application against breast cancer cells. Nanotechnology has emerged as a promising field in oncology, offering targeted therapies with reduced side effects. Silver nanoparticles are especially attractive because of their antimicrobial, antioxidant, and anticancer properties. In this study, Centratherum anthelminticum seeds were extracted in distilled water, and phytochemical analysis revealed the presence of saponins, polyphenols, and steroids, which likely contributed to nanoparticle formation and stabilization. Silver nitrate was reduced to AgNPs, confirmed by a colour change from yellow to dark brown due to surface plasmon resonance. UV-Vis spectroscopy showed a peak at 428 nm, FTIR confirmed functional groups involved in reduction and stabilization, TEM revealed spherical nanoparticles with an average size of ~58 nm, DLS showed size distribution between 30–60 nm, and XRD confirmed a face-centered cubic crystalline structure. The nanoparticles remained stable for up to 55 days, demonstrating their robustness. The antioxidant activity was measured using the DPPH assay, showing strong free radical scavenging at 500 µg/mL concentration, indicating potential to reduce oxidative stress. Cytotoxicity was tested via MTT assay against breast cancer cells (MDA-MB-231) and normal Vero cells. The AgNPs exhibited dose-dependent cytotoxicity against cancer cells, with an IC50 of 35.06 ± 1.2 µg/mL, while showing no toxicity to normal cells, highlighting their selective anticancer potential. This selectivity is crucial, as it suggests the nanoparticles can target cancer cells without harming healthy tissue [13].

Rasool *et al.,* conducted a comprehensive study on the eco-friendly synthesis of silver nanoparticles (AgNPs) using fruit extract of *Citrullus colocynthis* (Cc) and their biomedical applications, particularly against multidrug-resistant bacteria and breast cancer cells. Nanotechnology has emerged as a transformative field in medicine, and silver nanoparticles are widely recognized for their antimicrobial and therapeutic properties. In this study, Cc extract, rich in phytochemicals such as flavonoids, glycosides, fatty acids, phenols, and alkaloids, was used as a reducing and stabilizing agent to convert silver ions into nanoparticles. The synthesis was confirmed by color change and characterized through UV-Vis spectroscopy, XRD, FTIR, SEM, TEM, and EDX analyses, which revealed spherical nanoparticles with sizes ranging from 17 to 40 nm, crystalline FCC structure, and phytochemical capping that enhanced stability and biological activity. Antibacterial assays demonstrated that Cc-AgNPs exhibited strong, dose-dependent bactericidal activity against *Escherichia coli* and *Pseudomonas aeruginosa*, with higher efficacy against *P. aeruginosa*, while chemically synthesized AgNPs showed weaker activity and silver nitrate solution had no effect. In cancer assays using MCF7 breast cancer cells, Cc-AgNPs displayed potent cytotoxicity with an LC50 of ~5 µg/mL, far lower than AgNO3, Chem-AgNPs, or native Cc extract, indicating superior antiproliferative potential. Colony formation, spheroid growth, and scratch assays confirmed that Cc-AgNPs significantly reduced clonogenicity, inhibited 3D tumor growth, and suppressed migration. Gene expression analysis revealed downregulation of tumor surface markers (CD24, CD29, CD44), suppression of proliferation genes (Ki67, Cyclin A, CDK2), and upregulation of pro-apoptotic genes (caspase-3, FAS) and tumor suppressors (p21, p53), confirming induction of apoptosis and cell cycle arrest. Additionally, Cc-AgNPs exhibited antilipidemic effects by lowering cholesterol and triglyceride levels and downregulating lipid metabolism genes (FASN, HMGCLL1, ELOVL6, ACSL1), with maximum downregulation observed in HMGCLL1 after 72 hours. These findings highlight the multifunctional therapeutic potential of Cc-AgNPs, which not only combat resistant pathogens but also inhibit cancer cell proliferation and regulate lipid metabolism [14].

Montazersaheb *et al*., explores the eco-friendly synthesis of silver nanoparticles (Ag-NPs) using pumpkin peel extract and their potential as radiosensitizers against triple-negative breast cancer (TNBC), a highly aggressive subtype lacking ER, PR, and HER2 receptors and therefore resistant to conventional hormonal and targeted therapies; the authors highlight that radiotherapy (RT) remains a cornerstone treatment but is limited by collateral damage to healthy tissues, and radiosensitizers can enhance tumor sensitivity while reducing side effects. Ag-NPs was prepared by mixing pumpkin peel extract with silver nitrate, confirmed nanoparticle formation through UV-vis spectroscopy, XRD, SEM, TEM, AFM, DLS, and FTIR analyses, and found spherical particles averaging 81 nm with a zeta potential of –9.96 mV that remained stable for six months; in vitro experiments on MDA-MB-231 TNBC cells showed that Ag-NPs reduced viability in a dose-dependent manner, and when combined with RT (4 or 8 Gy), they synergistically enhanced cytotoxicity with a combination index of 0.49, significantly increasing apoptosis as confirmed by flow cytometry, DAPI-TUNEL staining, and molecular assays. Mechanistic studies revealed upregulation of pro-apoptotic Bax and p53, downregulation of anti-apoptotic Bcl-2, increased PERK and CHOP protein levels indicating ER stress-mediated apoptosis, and suppression of cyclin D1 and phosphorylated ERK, which are critical for cell cycle progression and proliferation, while HIF-1α expression was reduced, suggesting improved radiosensitivity under hypoxic conditions. The green-synthesized Ag-NPs from pumpkin peel not only induce apoptosis and inhibit proliferation but also potentiate the effects of radiotherapy through multiple signaling pathways, offering a sustainable, low-toxicity, and cost-effective approach to enhance TNBC treatment outcomes, with broader implications for integrating plant-based nanotechnology into cancer therapy by valorizing agricultural waste and minimizing

environmental impact, thereby positioning pumpkin peel-derived Ag-NPs as promising adjuncts to radiotherapy that could lower required radiation doses, reduce damage to healthy tissues, and improve patient prognosis in one of the most challenging breast cancer subtypes [15].

Nosrati *et al.,* studied on *Astragalus fasciculifolius* Bioss, commonly known as Anzaroot, is a medicinal plant from the Fabaceae family rich in saponins, flavonoids, and polysaccharides, traditionally used to treat heart diseases, inhibit cancer cell growth, and alleviate chemotherapy side effects, and this study investigates its potential in the green synthesis of silver nanoparticles (AgNPs) and their cytotoxic effects on MCF-7 human breast cancer cells, highlighting the intersection of herbal medicine and nanotechnology. Aqueous extracts from Anzaroot and AgNO3 is used to prepare silver nanoparticles. Nanoparticle formation confirmed by colour change, UV-Vis spectroscopy showing a surface plasmon resonance peak at 443 nm, TEM revealing average particle size of ~16 nm, XRD confirming face-centered cubic crystalline structure, and FTIR identifying functional groups such as O-H, C-H, and C=O, indicating phytochemicals acted as reducing and stabilizing agents. Cytotoxicity was assessed using MTT assays on MCF-7 cells, showing dose-dependent inhibition of cell proliferation, with IC50 values demonstrating stronger anticancer activity for nanoparticles synthesized from root extract (21.73 µg/mL) compared to gum extract or aqueous extract alone (348.21 µg/mL), and fluorescent microscopy revealed morphological changes and reactive oxygen species generation, suggesting apoptosis induction; the study emphasizes that green synthesis is eco-friendly, cost-effective, and biocompatible compared to chemical methods, while also incorporating bioactive plant compounds that enhance therapeutic potential, and notes the dual functionality of AgNPs as both anticancer and antimicrobial agents, which is particularly beneficial for immunocompromised cancer patients; however, challenges remain in ensuring uniform nanoparticle size and shape due to variability in plant extracts and in scaling up production for clinical applications, requiring further research into mechanisms of action, testing across different cancer cell lines, and in vivo safety assessments; ultimately, the findings demonstrate that can serve as an effective reducing agent for AgNP synthesis, producing nanoparticles with significant cytotoxic effects against breast cancer cells, especially when derived from root extracts, thereby bridging traditional herbal medicine and modern nanotechnology, and offering promising avenues for developing novel, sustainable, and multifunctional anticancer therapies that address urgent health challenges such as antibiotic resistance and cancer proliferation, while also underscoring the importance of exploring lesser-known medicinal plants for innovative biomedical applications, making this study a foundational step toward integrating plant-derived nanomaterials into cancer treatment strategies and highlighting the potential of Anzaroot-based AgNPs as effective therapeutic agents in oncology [16].

Ullah *et al.,* studied on the ecofriendly biosynthesis of silver nanoparticles (AgNPs) using aqueous extracts of the medicinal plant *Fagonia indica* and their anticancer potential against human breast cancer MCF-7 cells. They emphasize the promise of nanobiotechnology, particularly AgNPs, which have unique physicochemical and biological properties. Unlike chemical and physical synthesis methods that generate toxic by-products, the green synthesis approach using plants offers a cost-effective, rapid, and biocompatible alternative. The study optimized biosynthesis conditions by varying precursor (AgNO3) concentrations, extract ratios, temperature, and reaction time, with successful nanoparticle formation confirmed by colour change and UV-vis spectroscopy showing a surface plasmon resonance peak at ~430 nm. XRD analysis revealed crystalline nanoparticles with an average size of 12.09 nm, while dynamic light scattering indicated a hydrodynamic size of 23.68 nm and zeta potential of -16.3 mV, confirming colloidal stability. SEM micrographs showed spherical, polydispersed nanoparticles with low agglomeration. Cytotoxicity assays demonstrated concentration-dependent inhibition of MCF-7 cell growth, with IC50 values of 12.35 µg/mL for AgNPs and 25.09 µg/mL for plant extract alone, establishing superior efficacy of AgNPs. Morphological studies using AO/EB staining revealed apoptotic features such as membrane blebbing, shrinkage, and nuclear fragmentation, while DAPI staining confirmed chromatin condensation and nuclear abnormalities. Annexin V/PI flow cytometry quantified apoptosis, showing early apoptotic populations of 43.05% and late apoptotic populations of 23.62% in AgNP-treated cells compared to controls. Mechanistically, AgNPs induced apoptosis by generating reactive oxygen species (ROS), as evidenced by DCFDA assays, which triggered oxidative stress and mitochondrial dysfunction. Furthermore, caspase assays revealed twofold enhancement of caspase 3 and 9 activities in treated cells, confirming activation of both initiator and effector caspases, thereby committing cells to programmed death. The authors conclude that *Fagonia indica*-mediated AgNPs exert potent anticancer effects through ROS generation, membrane and nuclear damage, and caspase activation, ultimately leading to apoptosis[17].

Al-Sheddi *et al*., explores the eco-friendly synthesis, characterization, and biological evaluation of silver nanoparticles (AgNPs) derived from *Artemisia monosperma* extract, with a focus on their anticancer potential against human breast carcinoma (MCF-7) cells. Traditional chemical and physical methods of nanoparticle synthesis, though effective, are costly and environmentally hazardous, prompting interest in bioinspired approaches using plant extracts that are inexpensive, biocompatible, and eco-friendly. Within this context, silver nanoparticles have attracted particular attention due to their broad applications in medicine, microbiology, and food technology. Study investigate that the AgNPs synthesized from *Artemisia monosperma*, a desert plant of the Asteraceae family known for its medicinal properties, against breast cancer cells. The methodology involved collection of *A. monosperma* from Riyadh, preparation of aqueous extracts, and synthesis of AgNPs by mixing the extract with silver nitrate solution, confirmed by colour change and spectrophotometric analysis. Characterization was performed using UV-vis spectroscopy (absorbance peak at 430 nm confirming AgNP formation), FTIR (identifying functional groups such as hydroxyl, alkyne, amine, sulfur, and aromatic

compounds involved in nanoparticle stabilization), XRD (revealing crystalline, face-centered cubic structure with average grain size of 24 nm), TEM and SEM (showing predominantly spherical nanoparticles of 40–60 nm with some aggregation), and EDX (confirming high purity with silver comprising 80.34% of elemental composition). Cytotoxicity was assessed using MTT and NRU assays, both showing dose-dependent inhibition of MCF-7 cell viability, with IC50 values around 32 µg/mL. Specifically, viability decreased to 87%, 76%, 21%, and 14% at 10, 25, 50, and 100 µg/mL in MTT, and to 91%, 80%, 29%, and 21% in NRU, respectively. Morphological assessment revealed membrane blebbing, cell shrinkage, and apoptotic body formation in treated cells, consistent with apoptosis. Mechanistic studies demonstrated that AM-AgNPs induced significant reactive oxygen species (ROS) generation, with increases of 29%, 56%, and 121% at 25, 50, and 100 µg/mL, respectively, suggesting oxidative stress as a key mediator of cytotoxicity. Additionally, mitochondrial membrane potential (MMP) analysis using Rhodamine-123 dye showed dose-dependent loss of MMP, indicating mitochondrial dysfunction as another mechanism of cell death. Together, these findings establish that AM-AgNPs exert potent anticancer effects on breast cancer cells through ROS generation and mitochondrial impairment, leading to apoptosis[18].

Alrudainy AM *et al.,* presents a comprehensive study on the green synthesis and multifunctional bioactivity of silver nanoparticles (AgNPs) mediated by *Vitis vinifera* (grape seed) extract, highlighting their potential applications against multidrug-resistant (MDR) uropathogens and breast cancer cells. Grape seeds, rich in phenolic compounds like catechins, gallic acid, and proanthocyanidins, serve as natural reducing and stabilizing agents, enhancing nanoparticle biocompatibility and bioactivity. The methodology involved preparing aqueous grape seed extract, mixing it with silver nitrate solution, and allowing nanoparticle formation, confirmed by a colour change and characterized using UV-Vis spectroscopy, FTIR, SEM, EDX, and XRD analyses. Results revealed spherical, well-dispersed nanoparticles averaging 46.6 nm in diameter, with strong absorption peaks at 430–480 nm, functional group involvement in reduction and stabilization, crystalline structure, and silver as the predominant element. Antibacterial assays demonstrated dose-dependent inhibition, with *E. coli* and *S. aureus* most sensitive, *K. pneumoniae* moderately inhibited, and *P. aeruginosa* largely resistant, attributed to differences in bacterial cell envelope structures and defense mechanisms. The anticancer activity was evaluated using MTT assays on MCF-7 breast cancer cells and normal fibroblasts, showing selective cytotoxicity toward cancer cells (IC50 = 157.3 µg/mL) while sparing normal cells, likely due to ROS generation, mitochondrial dysfunction, and apoptosis induction. Compared with other plant-derived AgNPs, VV-AgNPs exhibited higher IC50 values, suggesting milder but selective activity influenced by nanoparticle size, shape, and phytochemical capping. Anti-inflammatory assays revealed concentration-dependent effects on COX-2 enzyme expression: low to moderate concentrations maintained biocompatibility without significant upregulation, while high concentrations induced oxidative stress and COX-2 activation, reflecting a dual anti- and pro-inflammatory potential. Antioxidant activity measured by DPPH radical scavenging showed strong efficiency (73% at 500 µg/mL), comparable to ascorbic acid, confirming the synergistic role of phytochemicals in enhancing redox balance[19].

Jang SJ *et al.,* investigates the in-vitro anticancer activity of green-synthesized silver nanoparticles (AgNPs) using aqueous flower extract of *Lonicera hypoglauca* against MCF-7 human breast cancer cells, while assessing their selectivity toward normal immune cells (RAW 264.7 macrophages). *Lonicera hypoglauca* flower extract was prepared, mixed it with silver nitrate solution, and observed rapid nanoparticle formation within 25 minutes, confirmed by a colour change and characterized using UV-Vis spectroscopy (SPR peak at 437 nm), FTIR (functional groups such as hydroxyl, amines, nitro, and aromatic compounds involved in reduction and stabilization), SEM, TEM, EDX, and SAED analyses. TEM revealed predominantly spherical nanoparticles with some rod-like and hexagonal shapes, ranging from 4.99 to 25.83 nm, while SAED confirmed crystallinity. Stability tests showed the nanoparticles remained stable for six months before losing integrity. Biological assays demonstrated that AgNPs significantly reduced MCF-7 cell viability while sparing RAW 264.7 cells, underscoring selective cytotoxicity. Mechanistic studies revealed that AgNPs induced apoptosis through multiple pathways: upregulation of tumor suppressor p53 and pro-apoptotic Bax, downregulation of anti-apoptotic Bcl-2, activation of caspase-3 and caspase-9, and increased cytosolic cytochrome c release, all hallmarks of mitochondrial-mediated apoptosis. Furthermore, AgNPs inhibited JAK/STAT signaling, a pathway often constitutively active in cancer cells and associated with survival and proliferation, thereby enhancing apoptotic susceptibility. Comparative experiments confirmed that the anticancer effects were due to AgNPs rather than the flower extract alone, as nanoparticles consistently showed stronger activity. The study situates its findings within broader literature, noting similar anticancer effects of green-synthesized AgNPs against glioblastoma, lung carcinoma, and other breast cancer models, but emphasizes its novelty in using *Lonicera hypoglauca* flower extract, a plant traditionally used in Chinese medicine but not previously explored for nanoparticle synthesis. This work highlights the dual advantages of green synthesis—environmental nanoparticles for targeted cancer treatment[20].

Conclusion

Plant-mediated silver nanoparticles (AgNPs) exert their anticancer effects against breast cancer cells primarily through apoptosis induction, oxidative stress, and mitochondrial dysfunction, though the precise mechanisms vary depending on the phytochemicals present in each plant extract. *Eclipta alba*-derived AgNPs trigger apoptosis in triple-negative breast cancer cells by generating reactive oxygen species (ROS) and disrupting mitochondrial integrity, while *Allium saralicum* nanoparticles act both directly by interacting with DNA, RNA, and proteins and indirectly through ROS-mediated oxidative stress, showing selective toxicity toward

cancer cells. Similarly, *Centratherum anthelminticum* AgNPs demonstrate strong selectivity, inducing apoptosis in MDA-MB-231 cells without harming normal cells, whereas *Citrullus colocynthis* nanoparticles regulate gene expression by downregulating proliferation markers (Ki67, Cyclin A, CDK2) and upregulating pro-apoptotic genes such as caspase-3 and p53, leading to cell cycle arrest and apoptosis.

Other plant systems highlight additional mechanistic pathways: pumpkin peel AgNPs act as radiosensitizers, enhancing radiotherapy-induced apoptosis through Bax and p53 upregulation, Bcl-2 suppression, and ER stress-mediated signaling, while *Astragalus fasciculifolius* nanoparticles derived from root extracts show potent ROS-mediated cytotoxicity, outperforming gum extracts. Fagonia indica AgNPs induce apoptosis via ROS generation, mitochondrial damage, and caspase-3/9 activation, while *Artemisia monosperma* nanoparticles similarly promote oxidative stress and mitochondrial membrane potential loss, leading to programmed cell death. *Vitis vinifera* (grape seed) AgNPs exhibit selective cytotoxicity against MCF-7 cells through ROS and mitochondrial dysfunction, though with comparatively milder potency, while *Lonicera hypoglauca* nanoparticles activate mitochondrial-mediated apoptosis by upregulating p53 and Bax, downregulating Bcl-2, releasing cytochrome c, and inhibiting JAK/STAT signaling.

Across these studies, the unifying mechanisms involve ROS generation, mitochondrial impairment, and caspase activation, which converge on apoptosis induction. Many plant-derived AgNPs also modulate gene expression, suppress proliferation, and enhance therapeutic selectivity, sparing normal cells. Notably, some extracts confer multifunctionality such as radiosensitization (pumpkin peel), antimicrobial activity (grape seed, *Citrullus colocynthis*), or anti-inflammatory effects—underscoring the broad biomedical potential of green-synthesized AgNPs in breast cancer therapy.

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