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SHORT REVIEW

A Review on Green Synthesis of Metallic Nanoparticles by Using Plant Extracts and Their Role in Cancer

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Abstract

Cancer is one of the deadliest diseases that have a significant negative impact on the world's enormous population. The chemotherapeutic medicines used in the treatment of cancer spread throughout the body causing general toxicity, poor patient compliance and even treatment cessation. This makes it difficult to deliver therapeutic agents to tumour cells with precision. Advancements in the field of medical science are being uplifted by the development of nanotechnology, which provides tremendous solutions to deal with such life-threatening diseases. Nanoparticles (NP) synthesised for medical purposes need to be biocompatible and low- or non-toxic. Therefore, the green generation of NPs is emerging as an alternative approach to physical and chemical methods. This study reviews the use of plants to synthesise these NPs. These are more stable than those synthesised from other biological sources. These NPs can be synthesised by using different metals such as gold (Au), silver (Ag), zinc (Zn), platinum (Pt), etc. Plant-derived green-manufactured Metallic Nanoparticles (MNPs) are extensively utilised in medicine as antibacterial, anti-inflammatory, anti-angiogenic and anti-cancer agents. Therefore, this review aims to study different green synthesised MNPs, their synthesis method, characterisation and their role in cancer therapy.

Keywords: Anti-angiogenic, Anti-bacterial, Anti-inflammatory, Cancer, Nanoparticles

1. Introduction

Cancer is one of the deadliest diseases that has a significant negative impact on the world's population[1]. Most chemotherapy drugs disperse throughout the body, leading to widespread toxicity, low patient adherence and even treatment discontinuation. This makes it challenging to administer therapeutic medicines to tumour cells precisely. The invention of nanotechnology has greatly advanced medical research by offering remarkable options for treating life-threatening illnesses. Many materials at the nanoscale level (between 1 and 100 nm) have been produced by nanotechnology[2,3].

Based on the origin of the NPs, they are classified as natural and synthetic. Natural NPs are produced by volcanic explosions, combustion of materials, straightforward erosion, plants and animals, or even bacteria[4,5]. NPs created artificially are crucial to nanotechnology. They serve as the basis for a wide range of currently prevalent applications and offer significant potential for the development of innovative materials. They differ in size, chemical makeup, shape, surface properties and method of their synthesis[6]. Based on their size- and shape-dependent tuneable optoelectronic capabilities, the most well-known anti-cancer NP are silver (Ag), gold (Au), zinc (Zn) and platinum (Pt)[7].

For medicinal use, NP synthesis must be low or non-toxic and biocompatible[8]. Silver, gold and platinum NPs, among other MNPs, have all passed rigorous human testing. These NPs exhibit a variety of features in the realm of nanotechnology and this has opened

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up numerous new avenues, particularly for drug delivery carriers[8]. Other well-known uses of MNPs in medicine besides drug delivery include diagnostics, the creation of improved biocompatible materials and nutraceuticals[9].

Several advantages have been observed by using nanoparticle (NP)-based drug delivery systems in the treatment of cancer, including improved pharmacokinetics, precise targeting of tumour cells, decreased side effects and decreased drug resistance[9-11].

In the field of bio-nanotechnology, the green method of generation of NPs is emerging as an alternative approach to physical and chemical method[9,10,12]. The advantages of using green methods for NP generation include lower failure rates, lower costs and simpler characterisation[12]. This technique is extremely appealing nowadays, due to its potential to lessen the toxicity of NPs[13]. Green synthesised MNPs are widely used as antibacterial, anti-inflammatory, anti-angiogenic and as an anti-cancer medicine.

Therefore, this review aims to study the Green synthesised different MNPs, their method of synthesis, characterisation and their applications in medicine.

2. Biogenic/ Green Synthesis of Nanoparticles

There are several methods for creating nanoparticles biologically or biogenically from salts of the relevant metals[14-27]. Many plant components (peel, leaves, bark, fruits, stem, etc.) and microorganisms (bacteria, fungus and algae) are employed in the biological synthesis of MNPs[28,29]. The procedures for making NPs using plant extracts are easily scalable and may be less expensive than the very costly technologies based on microbiological processes[30]. Plants are the finest biological source to employ for NP manufacturing because they provide a more favourable platform than both chemical and biological processes. They don't contain any harmful compounds, can be produced at a reasonable price, synthesise more quickly, offer protection and secondary metabolites can act as a capping agent and a natural reducing agent. Furthermore, compared to nanoparticles from other biological sources, those produced by plants are more stable[30-32].

Research on green synthesis is currently gaining popularity. Green synthesis principles are compatible with the use of bio-organisms in synthesis, particularly plants that exude the functional molecules for the process. The manufacture of NPs necessitates the selection of three essential components: a safe stabilising substance, an effective reducing agent and an environmentally compatible solvent[33,34]. Typically, the green chemistry-based strategy uses either pure phytochemicals with potential medical value or medicinally useful plants. These phytochemicals aid in the stabilising and chelating of NPs[35,36].

Metallic ions are reduced by the phytocompounds present in plant extracts, which include alkaloids, terpenoids and polyphenols[28,37]. The function of reductases and reducing equivalents in characterising the elements of live organisms involved in such nanoparticle formation has been revealed.

Various plants including *Aloe barbadensis*, *Phyllanthus reticulatus*, *Medicago sativa*, *Osimum sanctum*, *Citrus limon*, *Azadirachta indica*), *Coriandrum sativum*, *Syzigium cumini, Curcuma longa*, *Brassica juncea* and *Cymbopogon flexuosus* have been utilised to synthesise various NPs[38-43].

3. Synthesis of MNPs from Plants

The process of synthesising metallic nanoparticles from plant extracts involves three steps: (1) The activation phase, involving the nucleation of the reduced metal ions and the bio-reduction of salts and metal ions; (2) The growth phase involves the spontaneous aggregation of smaller particles into larger ones through a process called Ostwald ripening; (3) The termination phase involves the determination of the ultimate shape of the NP.

To prepare the plant extract various plant parts, including the fruit, leaf, peel, etc., are used to prepare the extract as fresh or dry material. The plant material is typically extracted by soaking it in a green solvent with or without stirring. It is then followed by filtration and centrifugation. The reducing and capping agents necessary for the bio-reduction of metallic ions are abundant in the filtered extract. While employing dried plants has the benefit of having a lengthy shelf life at room temperature, it's crucial to store fresh plants at a temperature of -20°C to prevent any deterioration

(Figure. 1). Additionally, the use of dry plant material avoids the seasonal fluctuations that could change the composition of plants[44,45].

4. Factors Affecting the MNPs Synthesised by Plant Extracts

Plant-based MNP production can be influenced by several variables. Among them are a few of these elements: (1) The type and concentration of plant extract utilized: Quantities of phytochemicals in various plant extracts can alter the production process and the characteristics of the NPs[46]. (2) The pH, temperature and reaction time: These variables can impact the size, stability and rate of production of NPs[47]. (3) The concentration of metal precursor: The production and size of the NPs can be impacted by the quantity of metal precursor added to the plant extract[48]. (4) The existence of any additional capping agents or additives: Variations in the synthesis process's chemical composition may have an impact on the NP's shape, stability and size[49].

5. Characterisation of MNPs

Biogenic NPs are usually characterised by their physicochemical properties, such as size, shape, distribution, stability, purity and the presence of functional groups. There are various techniques to characterize NPs[46]. The produced nanoparticles are verified using UV-Vis spectroscopy. Atomic Force Microscopy (AFM), Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM) are used to analyse the morphology of the NPs. The crystal structure and chemical makeup of the nanoparticles are ascertained using Fourier-Transform Infrared (FTIR) spectroscopy, Energy-Dispersive X-ray Spectroscopy (EDS or EDX) and X-ray Diffraction (XRD). To describe the functional groups that are on their surfaces, FTIR spectroscopy is used. NP size and dispersion in a liquid solution are measured using Zeta Potential (ZP) and Dynamic Light Scattering (DLS) methods[47,48] (Figure 2).

6. Nanoparticles in Cancer Therapy

For targeted drug delivery several nanoformulations such as dendrimers, liposomes, micelles, carbon nanotubes, gold nanoparticles (AuNPs) and silver nanoparticles (AgNPs) are frequently utilised as delivery vehicles[49]. Liposomes are tiny, aqueous-cored nanovesicles that are generated by lipid bilayer[50]. Anticancer medications have been delivered using liposomes, which can change the biodistribution and

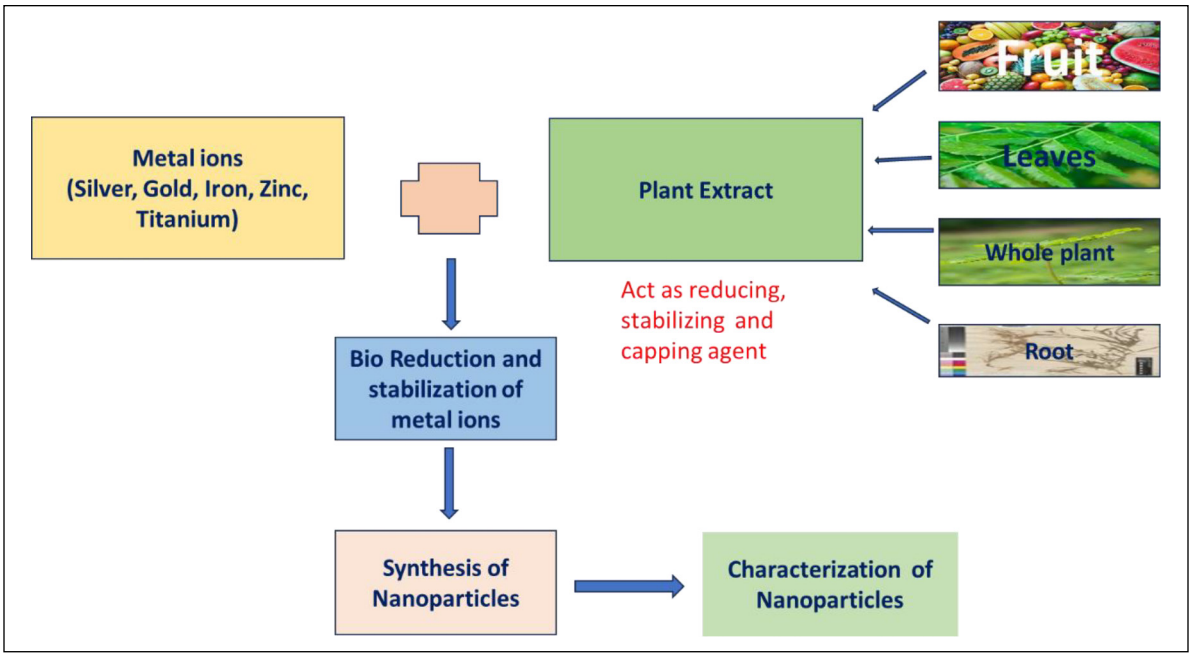

Figure 1. Flow chart of the synthesis of metallic nanoparticles by plant extract.

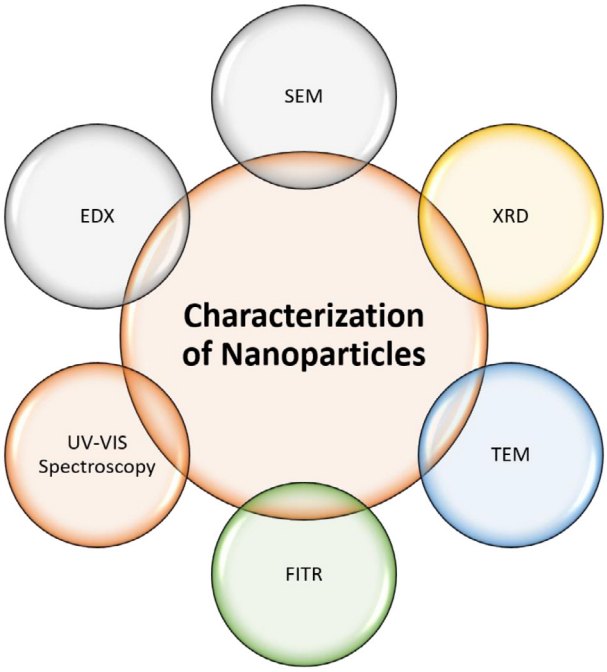

Figure 2. Techniques of characterisation of nanoparticles.

clearance of drug molecule[51,52]. The drug transport efficacy of these nanostructures depends on their size, morphology and other physical/chemical features[53]. Among all the NPs, metal NPs have drawn particular attention due to their ability to function as versatile agents[54]. Here we discuss some metal NPs and their therapeutic potential.

6.1 Silver Nanoparticles

Silver NPs created through green synthesis have drawn considerable interest in the biomedical, drug delivery, cosmetics and cellular imaging fields because of their unique biological and physicochemical properties[54]. In the current research setting, it is expected that the production of MNPs by biogenesis will prove to be a more economical and environmentally sustainable option[55].

The process of creating nanoparticles involves heating plant extract to 70C for three minutes while adding 2mm $AgNO_3$. When the NPs are formed, the extract's colour shifts from yellowish to reddish-brown[56]. AgNps synthesised with *Nelumbo nucifera* extract are produced in different shapes such as spherical, triangular, etc. The particle size varies from 25 to 80 mm[57,58] (Table 1). Fitri *et al.* demonstrated the anti-proliferative activity on breast cancer cells[58]. It has been reported that *Skimmia laureola* can produce spherical AgNPs with a size of 38+ 0.27nm[57] (Table 1). According to Roshni *et al.*, the AgNPs produced from *Murraya koenigii* leaf were homogenous and spherical, with diameters of 80.62 to 100.50nm. They studied the effect of these NPs against the HT-29 colon cancer cell line[59] (Table 1).

In another study, aqueous extracts of fresh *Lantana camara* and *Impatiens balsamina* leaves were used to create AgNPs. Visual inspection and UV-Vis spectra revealed that the leaf extracts of *L. camara* turned greyish brown and those of *I. balsamina* turned brownish yellow. TEM analysis confirmed the size of AgNps, was less than 24nm[32] (Table 1). AgNps synthesised from *L. camara* showed a cytotoxic effect against the Adenocarcinomic Human Alveolar Basal Epithelial (A549) cell line and the Michigan Cancer Foundation (MCF7) cell lines[60] (Table 1). AgNPs made from *I. balsamina* flower extract showed anti-cancer potential against several cancer cell lines[61].

In a different investigation, AgNPs were made using the seed exudates of *Medicago sativa*. 90% of the Ag+ was decreased at 30°C in around 50 minutes, and NPs were observed to form within one minute of metal salt contact. The resulting NPs had a heterogeneous size distribution and had spherical shape and size varied from 5 to 50nm[62,63] (Table 1).

The anticancer impact of AgNPs has received a lot of attention recently. AgNPs are effective in combating a range of cancers, including cervical cancer, breast cancer, lung cancer, etc[64,65]. Pei *et al.*, synthesised the biogenic AgNPs by *Coptis chinensis* and studied their anticancer activity in A549 cells[65]. These NPs induce apoptosis in A549 cells by interfering with a mitochondria-mediated mechanism[65].

Archana Chakravarty *et al.*, evaluated the antioxidant, antibacterial and anti-inflammatory properties of the silver nanoparticles synthesised by *Syzygium cumini* fruit extract[55]. Several studies suggested that AgNPs are known to impede metastasis and invasion in a dose-dependent way[66-68].

The cellular electron transport system is disrupted by silver NP interaction with the mitochondria, which leads to a rise in ROS. AgNPs were therefore thought to be toxic to the cells primarily through the oxidative

stress caused by ROS. AgNPs' large surface area may therefore make it easy for them to enter cells and interact with their contents, disrupting the cellular signalling cascade[69].

6.2 Gold Nanoparticles (AuNPs)

The medicinal applications of AuNPs are widely recognised and have been the topic of much research. AuNPs are very attractive in the field of nanomaterial research because of their excellent adsorption capacity, stability, size controllability and biocompatibility.

Typically, plant extracts are used as reducing agents to reduce gold ions during the green production of Au NPs. To obtain the extracts, the ground plants are often soaked in solvents (such as water or ethanol) under favourable environmental circumstances (various green substances have different ideal conditions). The extracts are then combined with a gold ion solution and when the solution turns red, Au NPs start to form[70-73].

Biosynthesised AuNPs reportedly displayed anticancer efficacy by causing cellular death in renal carcinoma A498 cells, according to Liu *et al*[74]. Biogenic NPs synthesised from *Taxus baccata* exhibited spherical, hexagonal and triangular morphologies, with a diameter of under 20nm. Researchers investigated the anti-cancer activity of AuNPs synthesised by *Taxus baccata* on cell lines, such as Caov-4, MCF-7 and HeLa. The anti-cancer mechanism of AuNPs generated by *T. baccata* is confirmed by this investigation to be the caspase-independent death[75]. Yang *et al*., synthesised the AuNPs from the leaf of *Catharanthus roseus* (CR). TEM verified that the produced AuNPs were in the 50–200 nm particle size range (Table 1). They studied the effect of conjugated AuNPs with CR leaf extract on human cervical cancer (HeLa) cells in terms of ROS-mediated apoptotic effects[76]. Human cervical carcinoma (HeLa) cells showed cytotoxic effects by enhanced apoptosis when exposed to biologically produced CR-AuNPs. Caspase-3 was cleaved after being exposed to CR-AuNPs for 24 hours. These results demonstrate that in human cervical carcinoma (HeLa) cells, CR-AuNPs contribute to apoptotic cell death[76].

TEM images revealed the spherical shape of NPs and their average size was 20nm synthesised from *Murraya koenigii* leaf extract[77]. A dose-dependent increase in the anti-cancer activity of gold nanoparticles synthesised from *Mentha longifolia* leaf extract was seen against various breast cancer cell lines (MCF7, Hs 578Bst, Hs 319.T and UACC-3133) (Table 1). These NPs had spherical shapes with an average diameter of 36.4nm[78]. AuNPs synthesised from *Cassia roxburghii* leaf extract had a diameter of 25-35nm and showed promising anticancer activity against HepG2, MCF7 and HeLa cell lines[79] (Table 1).

Raghunandan *et al*., reported the anti-cancer efficacy of biofunctionalised gold nanoparticles synthesised from guava and clove extract against distinct cancer cell lines, human colorectal adenocarcinoma, human kidney, human chronic myelogenous leukaemia, bone marrow and human cervix. At a dosage of 20g/mL, AuNP produced with clove bud extract inhibits 50% growth of HeLa, HEK-293 and HT-29 cancer cells. Conversely, AuNP generated from guava extract had anti-cancer action against HEK-293, although the IC_{50} value was more than 30µg/mL[80] (Table 1).

Ismail *et al*. reported the anticancer effects of AuNPs synthesised by *Corchorus olitorius* leaves extract against many cancer cell lines (colon cancer HCT-116, breast adenocarcinoma MCF-7 and hepatocellular cancer HepG-2)[81]. *C. olitorius* extract at low concentrations produced both triangular and hexagonal geometries, whereas at higher concentrations quasi-spherical morphologies of Au NPs were produced with an average size of 37–50 nm[81] (Table 1).

Researchers showed that green AuNPs produced from a variety of plants, including *Camellia sinensis, Coriandrum sativum, Mentha arvensis, Phyllanthus amarus, Artabotrys hexapetalus, Mimusops elengi* and *Syzygium aromaticum*, have anticancer potential against the MCF7 human breast cancer cell line. They found that AuNPs are just as effective as conventional medications for treating cancer at the lowest dose (2µg/mL)[82].

The anticancer effect of gold NPs is caused by several mechanisms such as; altering the permeability of the cell, which causes mitochondrial dysfunction[83,140], producing Reactive Oxygen Species (ROS), which results in oxidative stress and DNA fragmentation and ultimately activates caspase-dependent or independent apoptotic pathways, altering the chemical structure of proteins/DNA and cell cycle arrest[75].

According to Chowdhury *et al*., AuNPs are particularly selective against malignant cells among the various NPs because of their increased permeability and

Table 1. Size and shape of different metallic nanoparticles synthesised from various plant extracts and their effect on cell lines

S. No.	Metal	Shape	Size	Plant	Plant Part	Cell Lines (Anti-cancer effect on)	IC50	References
1	Ag	Spherical, Triangular, Truncated Triangular, and Decahedral	25 to 80 mm	*Nelumbo nucifera*	Leaves	T47D and 4T1 cell lines	12.10±0.08 µg/mL in T47D and 98.77±1.27 µg/mL in 4T1	[57,58]
2	Ag	Spherical	80.62 - 100.50 nm	*Murraya koenigii*	Leaves	HT-29	26.05 µg/mL.	[59,77]
3	Ag	Spherical	3.2-12 nm	*Lantana camara*	Leaves	A549 and MCF-7	49.52 g/mL and 46.67 g/mL	[32,60]
4	Ag	Spherical	5-40 nm	*Impatiens balsamina*	Flower	U937	84.17 ± 2.13	[61]
						Colo205	65.40 ± 2.41	
						B16F10	196.5 ± 4.19	
						HepG2	95.52 ± 4.08	
						HeLa	93.27 ± 2.53	
5	Ag	Spherical	5-50 nm	*Medicago sativa*	Seed	Human Fibroblasts	8.22 µg/mL	[62,63]
6	Au	Spherical	50-200 nm	*Catharanthus roseus*	Leaves	HeLa Cells	5 µg/ml	[76,86]
7	Au	Spherical	36.4 nm	*Mentha longifolia*	Leaves	MCF7	74 µg/mL	[78]
						Hs 578Bst	279 µg/mL	
						Hs 319.T	274 µg/mL	
						UACC-3133	201 µg/mL	
8	Au	Spherical	25–35 nm	*Cassia roxburghii*	Leaves	HepG2	30 µg/ml	[79]
						MCF7	50 µg/ml	
						HeLa	50 µg/ml	
9	Au	Triangular, hexagonal and quasi-spherical	37-50 nm	*Corchorus olitorius*	Leaves	MCF-7	11.2-12.2 µg/mL	[81]
						HCT-11	12.2 µg/mL	
						HepG-2	10.3 µg/mL	
10	Au	Irregular	5-100 nm	Clove	Bud	HeLa, HEK-293, and HT-29	20 µg/mL	[80,87]
						K-562	30 µg/mL	
11	Zno_2	spherical or elliptical shape	41.23 nm	*M. fragrans*	Fruit	HepG2	20 and 22 µg/ml (After 48 and 24 h)	[88,89]
12	Zno_2	ribbon or strip-shaped	30-40 nm	*Azadirachta indica*	Leaves	A549	125.64 (L5) and 115.63 (L 10) µg/mL	[90]
13	Zno_2	Hexagonal	9.26 to 31.18 nm	*Deverra tortuosa*	Leaves	Caco-2	0.81 µg/mL	[91]
						A549	83.47 µg/mL	

Table 1. Continued...

14	ZnO_2	spherical, hexagonal	209 nm	*Raphanus sativus*	Leaves	A549	40 µg/ ml	[92]
15	ZnO_2	elongated and rod-like, hexagonal	66.25 nm to 112.87 nm	*Albizia lebbeck*	stem bark	MDA-MB 231 and MCF-7	48.5-60.2 µg/ ml	[93]
16	Fe	Cuboidal and irregular	50 nm	*Ricinus communis*	Leaves	MDA-MB 231	7.103 µg/mL	[94,95]
17	Fe	Spherical	32-100 nm	*Albizia adianthifolia*	Leaves	AMJ-13 and MCF-7	1.8 µg/ ml and 7.7 µg ml	[96]

retention (EPR) effects[84,85]. Nano-based approaches are thought to be a crucial component of medication design and delivery.

6.3 Zinc Oxide Nanoparticles (ZnO NPs)

The unique qualities and potential uses of Zinc oxide NPs have gained significant attention in the field of medicine. The United States Food and Drug Administration (FDA) has also classified them as "Generally Recognised as Safe" (GRAS) (21CFR182.8991)[47].

These are made by mixing plant extract with zinc-nitrate hexahydrate ($Zn(NO_3)26H_2O$). Furthermore, the mixture is heated to 60 °C continuously for two hours. After 40 minutes, the solution's colour changes to a yellowish-black, indicating the synthesis of ZnONPs[48,97]. Zinc oxide NPs made by plants are produced in a variety of sizes and shapes and have a wide range of characteristics[98].

Systemic toxicity caused by ZnO NPs has been seen in mouse models. On the other hand, combining antioxidants with zinc oxide nanoparticles may reduce the negative effects and increase their anticancer potential.[88]. Fruit extracts of *Myristica fragrans* were used for the production of zinc oxide nanoparticles[99]. ZnO-NPs are produced when $Zn(NO_3)22H_2O$ and *M. fragrans* react, as seen by the mixture's colour changing from light brown to dark grey. The synthesised NPs' spherical or elliptical shape was confirmed by SEM and TEM studies of the crystallites, which had an average diameter of 41.23nm[88] (Table 1).

ZnO NPs synthesised with leaf extract of *Azadirachta indica* have proven cytotoxic activity against human lung cancer cell lines (A549)[90]. Field-Emission Scanning Spectroscopy (FE-SEM) confirmed the ribbon or strip-shaped NPs. The sheet was 20–30nm thick 600nm long, and 30 to 40 nm wide[90] (Table 1).

Selim *et al*., investigated ZnONPs synthesised from the *Deverra tortuosa* extract showed promising anti-cancer activity against CaCo-2 and A549 cell lines. TEM analysis showed the hexagonal structure of particles and their size in a range of 9.26 to 31.18 nm[91] (Table 1). Anti-cancer potential of zinc oxide NPs against astrocytes and hepatocytes of rats and different cancer cell lines (HepG2, A549, and BEAS-2B) was also demonstrated by Akhtar *et al*[100]. Data from this study revealed that ZnO NPs specifically cause programmed cell death in cancer cells, with no discernible effect on normal cells. This effect is probably mediated by the upregulation of p53, caspase, and bax genes[100].

Biogenic synthesis of ZnO NPs from *Raphanus sativus* leaves was done by Uma Maheshwari *et al*. These particles had a size of 209nm and they were spherical to hexagonal (Table 1). The cytotoxicity studies were carried out against A549 cell lines, which suggests the toxic effect exerted by the synthesized NPs on cancer cells[92].

Umar *et al*., generated ZnO nanoparticles from the stem bark extract of *Albizia lebbeck*. Some of the NPs have an appearance of being elongated and rod-like, while others show a small aggregation of zinc oxides and are hexagonal. Their diameter at different concentrations ranges from 66.25nm to 112.87nm[93]. The cytotoxic effect of these nanoparticles on MDA-MB 231 and MCF-7 was studied. These nanoparticles have promising cytotoxic activity on MDA-MB 231 and MCF-7[93] (Table 1).

There are various studies where Green ZnO NPs were made using various plant extracts such as *Trifolium pretence* flower extracts[101], the flower of *Nyctanthes arbor-tristis*[102], the leaf extract from *Passiflora caerulea*[103], leaflets of *Catharanthus roseus*[104], leaf extract of *Murraya koenigii*[105], *Lathyrus sativus* root[106] and *Aloe vera* leaf extract[107].

6.4 Iron Nanoparticles

Iron nanoparticles (FeNPs) are toxic to a wide range of pathogenic bacteria and fungi and have been widely and frequently employed in drug delivery and medicinal applications[108]. These NPs are synthesised by combining the plant extract in a 1:1 ratio with a 0.1 M $FeCl_36H_2O$ solution. At room temperature, an equal amount of leaf extract was added gradually dropwise to the ferric chloride solution and stirred with a stirrer. FeNPs were produced, as evidenced by the solution's appearance of a hue change from pale yellow to black[94].

Dharshini *et al*., synthesised the FeNPs combined with leaf extract of *Phyllanthus reticulatus*. The SEM results revealed that FeNPs were irregularly shaped spheres with rough surfaces and an area with a high concentration of FeNPs was seen in the EDX spectrum. The FeNPs created ranged in size from 185.6nm[108] (Table 1). The *Ricinus communis* leaf extract was used to create cuboidal and irregularly shaped nanoparticles[105], whereas the leaf extract from *Albizia adianthifolia* generated spherical NPs with a size range of 32–100 nm[96] (Table 1).

FeNPs synthesised by *Coriandrum sativum* leaf extract were examined for cytotoxicity against the HeLa cancer cell line and the results indicated that cytotoxicity increased with increasing concentration of nanoparticles[109].

Sulaiman *et al*., synthesised Magnetic Nanoparticles (MNPs) by combining them with *Albizia adianthifolia* leaf extract. They documented MNPs' anti-proliferative potential against human breast (AMJ-13 and MCF-7) cancer cells[96]. Ahmadi *et al*., studied the anti-tumour properties of FeNPs synthesised using *Satureja hortensis* essential oil against human cancer cell lines K-562, and MCF-7[110].

7. Future Direction

The future direction of herbal metallic nanoparticles in cancer holds great promise for targeted therapy, minimal side effects and improved patient outcomes. These nanoparticles can be synthesised using medicinal herbs, which are known for their therapeutic properties. By combining the medicinal properties of these herbs with the unique properties of MNPs, researchers are exploring the potential for enhanced anticancer activity. These herbal metallic nanoparticles have shown potential in suppressing the growth of neoplasm, inducing programmed cell death in cancer cells, and reducing the risk of drug resistance. Furthermore, the use of herbal metallic nanoparticles may provide a more sustainable and eco-friendly approach to cancer treatment compared to traditional methods.

8. Conclusion

NPs could be used to treat a variety of ailments because of their distinctive properties. This review focuses on MNP, synthesised from a plant source and their role in cancer therapies. Due to the usage of a variety of phytochemicals found in plants, these NPs can be produced using environmentally friendly ways as an alternative to traditional chemical processes, which reduces hazardous effects. Therefore, in this scenario, exploiting plant sources for the production of biogenic NPs could lead to new opportunities. Herbal nanoformulations have generally been shown to be safer, more bioavailable and have better therapeutic value when compared to traditional herbal and synthetic pharmaceuticals[107]. Despite the promising results of MNPs as a novel therapy approach, they have not yet been used in clinical settings, primarily because of a lack of understanding regarding their toxicity and behaviour in humans. Overall, it is well established that compared to traditional herbal and synthetic pharmaceuticals, herbal nanoformulations are safer, have a higher bioavailability, and have improved therapeutic value[111]. Despite the positive outcome of MNPs as a novel therapy method, they have not yet been used in clinical settings, mostly due to a lack of knowledge about their human behaviour and toxicity. Thus, these green MNPs may serve as the biomedical industry's future catalyst for developing a drug delivery system.

9. References

1. Pradhan D, Biswasroy P, Sahu A, Sahu DK, Ghosh G, Rath G. Recent advances in herbal nanomedicines for cancer treatment. Curr Mol Pharmacol. 2021; 14(3):292-305. https://doi.org/10.2174/1874467213666200525010624 PMid:32448111.

2. Jeevanandam J, Barhoum A, Chan YS, Dufresne A, Danquah MK. Review on nanoparticles and nanostructured materials: History, sources, toxicity and regulations. Beilstein J Nanotechnol. 2018; 9:1050-74. https://doi.org/10.3762/bjnano.9.98 PMid:29719757 PMCid: PMC5905289.
3. Gupta R, Xie H. Nanoparticles in daily life: Applications, toxicity and regulations. J Environ Pathol Toxicol Oncol. 2018; 37(3):209-30. https://doi.org/10.1615/JEnvironPatholToxicolOncol.2018026009 PMid:30317972 PMCid: PMC6192267.
4. Love JC, Estroff LA, Kriebel JK, Nuzzo RG, Whitesides GM. Self-assembled monolayers of thiolates on metals as a form of nanotechnology. Chem Rev. 2005; 105(4):1103-69. https://doi.org/10.1021/cr0300789 PMid:15826011.
5. Dahoumane SA, Jeffryes C, Mechouet M, Agathos SN. Biosynthesis of inorganic nanoparticles: A fresh look at the control of shape, size and composition. Bioengineering (Basel). 2017; 4(1):14 https://doi.org/10.3390/bioengineering4010014 PMid:28952493 PMCid:PMC55 90428.
6. Raab CS, Myrtill S, Gazsó A, Fiedeler U, Nentwich M. What are synthetic nanoparticles? 2011.
7. Vlamidis Y, Voliani V. Bringing again noble metal nanoparticles to the forefront of cancer therapy. Front Bioeng Biotechnol. 2018; 6:143. https://doi.org/10.3389/fbioe.2018.00143 PMid:30349817 PMCid: PMC6186777.
8. Cooper ER. Nanoparticles: A personal experience for formulating poorly water-soluble drugs. J Control Release. 2010; 141(3):300-2. https://doi.org/10.1016/j.jconrel.2009.10.006 PMid:19822177.
9. Chandrakala V, Aruna V, Angajala G. Review on metal nanoparticles as nanocarriers: current challenges and perspectives in drug delivery systems. Emergent Mater. 2022; 5(6):1593-615. https://doi.org/10.1007/s42247-021-00335-x PMid:35005431 PMCid: PMC8724657.
10. Palazzolo S, Bayda S, Hadla M, Caligiuri I, Corona G, Toffoli G, *et al*. The clinical translation of organic nanomaterials for cancer therapy: A focus on polymeric nanoparticles, micelles, liposomes and exosomes. Curr Med Chem. 2018; 25(34):4224-68. https://doi.org/10.2174/0929867324666170830113755 PMid:28875844.
11. Dadwal A, Baldi A, Kumar Narang R. Nanoparticles as carriers for drug delivery in cancer. Artif Cells Nanomed Biotechnol. 2018; 46(sup2):295-305. https://doi.org/10.1080/21691401.2018.1457039 PMid:30043651.
12. Gour A, Jain NK. Advances in green synthesis of nanoparticles. Artif Cells Nanomed Biotechnol. 2019; 47(1):844-51. https://doi.org/10.1080/21691401.2019.1577878 PMid:30879351.
13. Baruwati B, Polshettiwar V, Varma RS. Glutathione promoted expeditious green synthesis of silver nanoparticles in water using microwaves. Green Chem. 2009; 11(7):926-30. https://doi.org/10.1039/b902184a
14. Bar H, Bhui DK, Sahoo GP, Sarkar P, De SP, Misra AJC, *et al*. Green synthesis of silver nanoparticles using latex of *Jatropha curcas*. 2009; 339(1-3):134-9. https://doi.org/10.1016/j.colsurfa.2009.02.008
15. Dhillon GS, Brar SK, Kaur S, Verma MJCrib. Green approach for nanoparticle biosynthesis by fungi: Current trends and applications. 2012; 32(1):49-73. https://doi.org/10.3109/07388551.2010.550568 PMid:21696293.
16. De Lima R, Seabra AB, Durán. Silver nanoparticles: A brief review of cytotoxicity and genotoxicity of chemically and biogenically synthesised nanoparticles. Journal of Applied Toxicology 2012; 32(11):867-79. https://doi.org/10.1002/jat.2780 PMid:22696476.
17. Cui C, Gan L, Li H-H, Yu S-H, Heggen M, Strasser. Octahedral PtNi nanoparticle catalysts: Exceptional oxygen reduction activity by tuning the alloy particle surface composition. Nano Letters 2012; 12(11):5885-9. https://doi.org/10.1021/nl3032795 PMid:23062102.
18. Gericke M, Pinches A. Biological synthesis of metal nanoparticles. J Hydrometallurgy 2006; 83(1-4):132-40. https://doi.org/10.1016/j.hydromet.2006.03.019
19. Korbekandi H, Iravani S, Abbasi S. Production of nanoparticles using organisms. Critical Reviews in Biotechnology 2009; 29(4):279-306. https://doi.org/10.3109/07388550903062462 PMid:199293 19.
20. Luangpipat T, Beattie IR, Chisti Y, Haverkamp RG. Gold nanoparticles produced in a microalga. Journal of Nanoparticle Research 2011; 13:6439-45. https://doi.org/10.1007/s11051-011-0397-9
21. Mohanpuria P, Rana NK, Yadav SK. Biosynthesis of nanoparticles: technological concepts and future applications. Journal of Nanoparticle Research 2008; 10:507-17. https://doi.org/10.1007/s11051-007-9275-x
22. Mukherjee P, Ahmad A, Mandal D, Senapati S, Sainkar SR, Khan MI, *et al*. Fungus-mediated synthesis of silver nanoparticles and their immobilization in the mycelial matrix: a novel biological approach to nanoparticle synthesis. 2001; 1(10):515-9. https://doi.org/10.1021/nl0155274
23. Wood LD, Parsons DW, Jones S, Lin J, Sjoblom T, Leary RJ, *et al*. The genomic landscapes of human breast and colorectal cancers. 2007; 318(5853):1108-13. https://doi.org/10.1126/science.1145720 PMid:17932254.
24. Shankar SS, Ahmad A, Sastry M. Geranium leaf assisted biosynthesis of silver nanoparticles. Biotechnology Progress 2003; 19(6):1627-31. https://doi.org/10.1021/bp034070w PMid:14656132.
25. Shankar SS, Rai A, Ahmad A, Sastry M. Rapid synthesis of Au, Ag, and bimetallic Au core-Ag shell nanoparticles using Neem (*Azadirachta indica*) leaf broth. Journal of Colloid and Interface Science 2004; 275(2):496-502. https://doi.org/10.1016/j.jcis.2004.03.003 PMid:15178278.

26. Singaravelu G, Arockiamary J, Kumar VG, Govindaraju K, Biointerfaces sB. A novel extracellular synthesis of monodisperse gold nanoparticles using marine alga, *Sargassum wightii* Greville. Colloids and Surfaces B: Biointerfaces. 2007; 57(1):97-101. https://doi.org/10.1016/j.colsurfb.2007.01.010 PMid:17350236.
27. Thakkar KN, Mhatre SS, Parikh RY. Biological synthesis of metallic nanoparticles. Nanomed Nanotechnol Bio Med. 2010; 6(2):257-62. https://doi.org/10.1016/j.nano.2009.07.002 PMid:19616126.
28. Pantidos N, Horsfall EL. Biological synthesis of metallic nanoparticles by bacteria, fungi and plants. J Nanomed Nanotechnol. 2014; 5(5). https://doi.org/10.4172/2157-7439.1000233
29. Luangpipat T, Beattie IR, Chisti Y, Haverkamp RG. Gold nanoparticles produced in a microalga. J Nanopart Res. 2011; 13(12):6439-45. https://doi.org/10.1007/s11051-011-0397-9
30. Ahmed S, Ahmad M, Swami BL, Ikram S. A review on plants extract mediated synthesis of silver nanoparticles for antimicrobial applications: A green expertise. J Adv Res. 2016; 7(1):17-28. https://doi.org/10.1016/j.jare.2015.02.007 PMid:26843966 PMCid: PMC4703479.
31. Jain S, Mehata MS. Medicinal plant leaf extract and pure flavonoid mediated green synthesis of silver nanoparticles and their enhanced antibacterial property. Sci Rep. 2017; 7(1):15867. https://doi.org/10.1038/s41598-017-15724-8 PMid:29158537 PMCid: PMC5696514.
32. Aritonang HF, Koleangan H, Wuntu AD. Synthesis of silver nanoparticles using aqueous extract of medicinal plants (*Impatiens balsamina* and *Lantana camara*) fresh leaves and analysis of antimicrobial activity. Int J Microbiol. 2019; 2019:8642303. https://doi.org/10.1155/2019/8642303 PMid:31354833 PMCid: PMC6636566.
33. Nande A, Raut S, Michalska-Domanska M, Dhoble SJ. Green synthesis of nanomaterials using plant extract: A review. Curr Pharm Biotechnol. 2021; 22(13):1794-811. https://doi.org/10.2174/1389201021666201117121452 PMid:33208069.
34. Ahmad N, Sharma S, Alam MK, Singh VN, Shamsi SF, Mehta BR, *et al*. Rapid synthesis of silver nanoparticles using the dried medicinal plant of basil. Colloids Surf B Biointerfaces. 2010; 81(1):81-6. https://doi.org/10.1016/j.colsurfb.2010.06.029 PMid:20656463.
35. Barabadi H, Honary S, Ali Mohammadi M, Ahmadpour E, Rahimi MT, Alizadeh A, *et al*. Green chemical synthesis of gold nanoparticles by using *Penicillium aculeatum* and their scolicidal activity against hydatid cyst protoscolices of *Echinococcus granulosus*. Environ Sci Pollut Res Int. 2017; 24(6):5800-10. https://doi.org/10.1007/s11356-016-8291-8 PMid:28054267.
36. Ovais M, Khalil AT, Raza A, Khan MA, Ahmad I, Islam NU, *et al*. Green synthesis of silver nanoparticles via plant extracts: Beginning a new era in cancer theranostics. Nanomedicine (Lond). 2016; 11(23):3157-77. https://doi.org/10.2217/nnm-2016-0279 PMid:27809668.
37. De Morais MG, Vaz Bda S, De Morais EG, Costa JA. Biologically active metabolites synthesized by microalgae. Biomed Res Int. 2015; 2015:835761. https://doi.org/10.1155/2015/835761 PMid:26339647 PMCid: PMC4538420.
38. Singh J, Dutta T, Kim KH, Rawat M, Samddar P, Kumar P. "Green' synthesis of metals and their oxide nanoparticles: applications for environmental remediation. J Nanobiotechnol. 2018; 16. https://doi.org/10.1186/s12951-018-0408-4 PMid:30373622 PMCid: PMC6206834.
39. Hettiarachchi SS, Dunuweera SP, Dunuweera AN, Rajapakse RGJAo. Synthesis of curcumin nanoparticles from raw turmeric rhizome. ACS Omega. 2021; 6(12):8246-52. https://doi.org/10.1021/acsomega.0c06314 PMid:33817483 PMCid: PMC8015141.
40. Danawala TM, Trivedi KA, Lad UM, Desai BN, Singh SK, Suthar DH, *et al*. Luminescent carbon quantum dots derived from *Syzygium cumini* seeds with endogenous anti-oxidant and cytotoxic potency including *in vitro* photoluminescence and live cell imaging. New J Chem. 2024. https://doi.org/10.1039/D4NJ00040D
41. Velidandi A, Sarvepalli M, Gandam PK, Pabbathi NPP, Baadhe RR. Characterization, catalytic and recyclability studies of nano-sized spherical palladium particles synthesized using aqueous poly-extract (turmeric, neem and tulasi). Environmental Research 2023; 228:115821. https://doi.org/10.1016/j.envres.2023.115821 PMid:37019298.
42. Nisha SN, Aysha O, Rahaman JSN, Kumar PV, Valli S, Nirmala P, *et al*. Lemon peels mediated synthesis of silver nanoparticles and its antidermatophytic activity. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2014; 124:194-8. https://doi.org/10.1016/j.saa.2013.12.019 PMid: 24486863.
43. Rao KG, Ashok CH, Rao KV, Chakra CS, Tambur P. Green synthesis of TiO_2 nanoparticles using *Aloe vera extract*. Int J Adv Res Phys Sci. 2015; 2(1A):28-34.
44. Altemimi A, Lakhssassi N, Baharlouei A, Watson DG, Lightfoot DA. Phytochemicals: extraction, isolation and identification of bioactive compounds from plant extracts. Plants (Basel). 2017; 6(4):42 https://doi.org/10.3390/plants6040042 PMid:28937585 PMCid: PMC5750618.
45. Ingle KP, Deshmukh AG, Padole DA, Dudhare MS, Moharil MP, Khelurkar VC. Phytochemicals: Extraction methods, identification and detection of bioactive compounds from plant extracts. Journal of Pharmacognosy and Phytochemistry 2017; 6(1):32-6.

46. Karmous I, Pandey A, Haj KB, Chaoui A. Efficiency of the green synthesized nanoparticles as new tools in cancer therapy: Insights on plant-based bioengineered nanoparticles, biophysical properties and anticancer roles. Biol Trace Elem Res. 2020; 196(1):330-42. https://doi.org/10.1007/s12011-019-01895-0 PMid:31512171.
47. Murali M, Kalegowda N, Gowtham HG, Ansari MA, Alomary MN, Alghamdi S, *et al*. Plant-mediated zinc oxide nanoparticles: Advances in the new millennium towards understanding their therapeutic role in biomedical applications. Pharmaceutics. 2021; 13(10). https://doi.org/10.3390/pharmaceutics13101662 PMid:34683954 PMCid: PMC8540056.
48. Khan ZUH, Sadiq HM, Shah NS, Khan AU, Muhammad N, Hassan SU, *et al*. Greener synthesis of zinc oxide nanoparticles using *Trianthema portulacastrum* extract and evaluation of its photocatalytic and biological applications. J Photochem Photobiol B. 2019; 192:147-57. https://doi.org/10.1016/j.jphotobiol.2019.01.013 PMid:30738346.
49. Pippa N, Chronopoulos DD, Stellas D, Fernandez-Pacheco R, Arenal R, Demetzos C, *et al*. Design and development of multi-walled carbon nanotube-liposome drug delivery platforms. Int J Pharm. 2017; 528(1-2):429-39. https://doi.org/10.1016/j.ijpharm.2017.06.043 PMid:28627453.
50. Amreddy N, Babu A, Muralidharan R, Panneerselvam J, Srivastava A, Ahmed R, *et al*. Recent advances in nanoparticle-based cancer drug and gene delivery. Adv Cancer Res. 2018; 137:115-70. https://doi.org/10.1016/bs.acr.2017.11.003 PMid:29405974 PMCid: PMC6550462.
51. Bingham RJ, Olmsted PD, Smye SW. Undulation instability in a bilayer lipid membrane due to electric field interaction with lipid dipoles. Phys Rev E Stat Nonlin Soft Matter Phys. 2010; 81(5Pt1):051909. https://doi.org/10.1103/PhysRevE.81.051909 PMid:20866263.
52. Wang XY, Ishida T, Ichihara M, Kiwada H. Influence of the physicochemical properties of liposomes on the accelerated blood clearance phenomenon in rats. J Control Release. 2005; 104(1):91-102. https://doi.org/10.1016/j.jconrel.2005.01.008 PMid:15866337.
53. Senapati S, Mahanta AK, Kumar S, Maiti P. Controlled drug delivery vehicles for cancer treatment and their performance. Signal Transduct Target Ther. 2018; 3:7. https://doi.org/10.1038/s41392-017-0004-3 PMid:29560283 PMCid: PMC5854578
54. Jain AS, Pawar PS, Sarkar A, Junnuthula V, Dyawanapelly S. Bionanofactories for green synthesis of silver nanoparticles: Toward antimicrobial applications. Int J Mol Sci. 2021; 22(21). https://doi.org/10.3390/ijms222111993 PMid:34769419 PMCid: PMC8584914.
55. Chakravarty A, Ahmad I, Singh P, Sheikh MUD, Aalam G, Sagadevan S, *et al*. Green synthesis of silver nanoparticles using fruits extracts of *Syzygium cumini* and their bioactivity. Chemical Physics Letters. 2022; 795:139493. https://doi.org/10.1016/j.cplett.2022.139493
56. Al-Shmgani HSA, Mohammed WH, Sulaiman GM, Saadoon AH. Biosynthesis of silver nanoparticles from *Catharanthus roseus* leaf extract and assessing their antioxidant, antimicrobial, and wound-healing activities. Artif Cells Nanomed Biotechnol. 2017; 45(6):1-7. https://doi.org/10.1080/21691401.2016.1220950 PMid:27534756.
57. Santhoshkumar T, Rahuman AA, Rajakumar G, Marimuthu S, Bagavan A, Jayaseelan C, *et al*. Synthesis of silver nanoparticles using *Nelumbo nucifera* leaf extract and its larvicidal activity against malaria and filariasis vectors. Parasitol Res. 2011; 108(3):693-702. https://doi.org/10.1007/s00436-010-2115-4 PMid:20978795.
58. Fitri K, Andry M, Khairani T, Winata H, Violenta A, Lubis N, *et al*. Synthesis of silver nanoparticles using ethanolic extract of *Nelumbo nucifera* Gaertn. leaf and its cytotoxic activity against T47D and 4T1 cell lines. Rasayan Journal of Chemistrymistry 2023; 16(1):104-10. https://doi.org/10.31788/RJC.2023.1618000
59. Roshni K, Younis M, Ilakkiyapavai D, Basavaraju P, Puthamohan VMJ. Anticancer activity of biosynthesized silver nanoparticles using *Murraya koenigii* leaf extract against HT-29 colon cancer cell line. J Cancer Sci Ther 2018; 10(04):72-5. https://doi.org/10.4172/1948-5956.1000521
60. Hublikar LV, Ganachari SV, Patil VB, Nandi S, Honnad A. Anticancer potential of biologically synthesized silver nanoparticles using *Lantana camara* leaf extract. Progress in Biomaterials 2023; 12(2):155-69. https://doi.org/10.1007/s40204-023-00219-9 PMid:37093445 PMCid: PMC10154448.
61. Raju Nalavothula, Jahnavi Alwala, Nagati V, Manthurpadigya P. Biosynthesis of silver nanoparticles using *Impatiens balsamina* leaf extracts and its characterization and cytotoxic studies using human cell lines. International Journal of ChemTech Research 2015; 7(5):974-4290.
62. Lukman AI, Gong B, Marjo CE, Roessner U, Harris AT. Facile synthesis, stabilization, and anti-bacterial performance of discrete Ag nanoparticles using *Medicago sativa* seed exudates. J Colloid Interface Sci. 2011; 353(2):433-44. https://doi.org/10.1016/j.jcis.2010.09.088 PMid:20974473.
63. Zare-Bidaki M, Aramjoo H, Mizwari ZM, Mohammadparast-Tabas P, Javanshir R, Mortazavi-Derazkola S. Cytotoxicity, antifungal, antioxidant, antibacterial and photodegradation potential of silver nanoparticles mediated via *Medicago sativa* extract. Arabian Journal of Chemistry. 2022; 15(6):103842. https://doi.org/10.1016/j.arabjc.2022.103842
64. Lin J, Huang Z, Wu H, Zhou W, Jin P, Wei P, *et al*. Inhibition of autophagy enhances the anticancer activity of silver nanoparticles. Autophagy. 2014; 10(11):2006-20. https://

doi.org/10.4161/auto.36293 PMid:25484080 PMCid: PMC4502813.

65. Pei J, Fu B, Jiang L, Sun T. Biosynthesis, characterization, and anticancer effect of plant-mediated silver nanoparticles using *Coptis chinensis*. Int J Nanomedicine. 2019; 14:1969-78. https://doi.org/10.2147/IJN.S188235 PMid:30936697 PMCid: PMC6421896.
66. Meenakshisundaram S, Krishnamoorthy V, Jagadeesan Y, Vilwanathan R, Balaiah AJBC. *Annona muricata* assisted biogenic synthesis of silver nanoparticles regulates cell cycle arrest in NSCLC cell lines. 2020; 95:103451. https://doi.org/10.1016/j.bioorg.2019.103451 PMid:31927333.
67. Lu W, Kang YJDC. Epithelial-mesenchymal plasticity in cancer progression and metastasis. 2019; 49(3):361-74. https://doi.org/10.1016/j.devcel.2019.04.010 PMid:31063755 PMCid: PMC6506183.
68. Komai K, Niwa Y, Sasazawa Y, Simizu SJFl. Pirin regulates epithelial to mesenchymal transition independently of Bcl3-Slug signalling. 2015; 589(6):738-43. https://doi.org/10.1016/j.febslet.2015.01.040 PMid:25680527.
69. Habeeb Rahuman HB, Dhandapani R, Narayanan S, Palanivel V, Paramasivam R, Subbarayalu R, *et al*. Medicinal plants mediated the green synthesis of silver nanoparticles and their biomedical applications. IET Nanobiotechnol. 2022; 16(4):115-44. https://doi.org/10.1049/nbt2.12078 PMid:35426251 PMCid: PMC9114445.
70. Priya Tharishini P, Saraswathy N, Smila K, Yuvaraj D, Chandran M, Vivek PJIJCR. Green synthesis of gold nanoparticles from *Cassia auriculata* leaf aqueous extract and its cytotoxicity effect on in vitro cell line. 2014; 6(9):4241-50.
71. Smitha S, Philip D, Gopchandran KJSAPAM, Spectroscopy B. Green synthesis of gold nanoparticles using *Cinnamomum zeylanicum* leaf broth. 2009; 74(3):735-9. https://doi.org/10.1016/j.saa.2009.08.007 PMid:19744880.
72. Jafarizad A, Safaee K, Gharibian S, Omidi Y, Ekinci DJPMS. Biosynthesis and *in-vitro* study of gold nanoparticles using Mentha and Pelargonium extracts. 2015; 11:224-30. https://doi.org/10.1016/j.mspro.2015.11.113
73. Ying S, Guan Z, Ofoegbu PC, Clubb P, Rico C, He F, *et al*. Green synthesis of nanoparticles: Current developments and limitations. 2022; 26:102336. https://doi.org/10.1016/j.eti.2022.102336
74. Liu R, Pei Q, Shou T, Zhang W, Hu J, Li W. Apoptotic effect of green synthesized gold nanoparticles from *Curcuma wenyujin* extract against human renal cell carcinoma A498 cells. Int J Nanomedicine. 2019; 14:4091-103. https://doi.org/10.2147/IJN.S203222 PMid:31239669 PMCid: PMC6556565.
75. Bharadwaj KK, Rabha B, Pati S, Sarkar T, Choudhury BK, Barman A, *et al*. Green synthesis of gold nanoparticles using plant extracts as beneficial prospect for cancer theranostics. Molecules. 2021; 26(21). https://doi.org/10.3390/molecules26216389 PMid:34770796 PMCid: PMC8586976.
76. Ke Y, Al Aboody MS, Alturaiki W, Alsagaby SA, Alfaiz FA, Veeraraghavan VP, *et al*. Photosynthesized gold nanoparticles from *Catharanthus roseus* induces caspase-mediated apoptosis in cervical cancer cells (HeLa). Artif Cells Nanomed Biotechnol. 2019; 47(1):1938-46. https://doi.org/10.1080/21691401.2019.1614017 PMid:31099261.
77. Philip D, Unni C, Aromal SA, Vidhu VK. *Murraya Koenigii* leaf-assisted rapid green synthesis of silver and gold nanoparticles. Spectrochim Acta A Mol Biomol Spectrosc. 2011; 78(2):899-904. https://doi.org/10.1016/j.saa.2010.12.060 PMid:21215687.
78. Li S, Al-Misned FA, El-Serehy HA, Yang LJAJoC. Green synthesis of gold nanoparticles using aqueous extract of *Mentha Longifolia* leaf and investigation of its anti-human breast carcinoma properties in the in vitro condition. 2021;14(2):102931. https://doi.org/10.1016/j.arabjc.2020.102931
79. Balashanmugam P, Durai P, Balakumaran MD, Kalaichelvan PTJJoP, Biology PB. Phytosynthesized gold nanoparticles from *C. roxburghii* DC. leaf and their toxic effects on normal and cancer cell lines. 2016; 165:163-73. https://doi.org/10.1016/j.jphotobiol.2016.10.013 PMid:27855358.
80. Raghunandan D, Ravishankar B, Sharanbasava G, Mahesh DB, Harsoor V, Yalagatti MS, *et al*. Anti-cancer studies of noble metal nanoparticles synthesized using different plant extracts. Cancer Nanotechnol. 2011; 2(1-6):57-65. https://doi.org/10.1007/s12645-011-0014-8 PMid:26069485 PMCid: PMC4451508.
81. Ismail EH, Saqer AMA, Assirey E, Naqvi A, Okasha RM. Successful green synthesis of gold nanoparticles using a *Corchorus olitorius* extract and their antiproliferative effect in cancer cells. Int J Mol Sci. 2018;19(9). https://doi.org/10.3390/ijms19092612 PMid:30177647 PMCid:PMC6163711.
82. Kamala Priya M, Iyer PRJAN. Anticancer studies of the synthesized gold nanoparticles against MCF 7 breast cancer cell lines. 2015; 5(4):443-8. https://doi.org/10.1007/s13204-014-0336-z
83. Jain N, Jain P, Rajput D, Patil UKJM, Letters NS. Green synthesized plant-based silver nanoparticles: Therapeutic prospective for anticancer and antiviral activity. 2021; 9(1):5. https://doi.org/10.1186/s40486-021-00131-6 PMCid:PMC8091155.
84. Jiao PF, Zhou HY, Chen LX, Yan B. Cancer-targeting multifunctionalized gold nanoparticles in imaging and therapy. Curr Med Chem. 2011; 18(14):2086-102. https://doi.org/10.2174/092986711795656199 PMid:21517767.

85. Chowdhury A, Kunjiappan S, Panneerselvam T, Somasundaram B, Bhattacharjee CJInl. Nanotechnology and nanocarrier-based approaches on treatment of degenerative diseases. 2017; 7:91-122. https://doi.org/10.1007/s40089-017-0208-0
86. Ke Y, Al Aboody MS, Alturaiki W, Alsagaby SA, Alfaiz FA, Veeraraghavan VP, *et al*. Photosynthesized gold nanoparticles from *Catharanthus roseus induces* caspase-mediated apoptosis in cervical cancer cells (HeLa). Artificial Cells, Nanomedicine, and Biotechnology. 2019; 47(1):1938-46. https://doi.org/10.1080/21691401.2019.1614017 PMid:31099261.
87. Raghunandan D, Bedre MD, Basavaraja S, Sawle B, Manjunath S, Venkataraman AJC, et al. Rapid biosynthesis of irregular shaped gold nanoparticles from macerated aqueous extracellular dried clove buds (*Syzygium aromaticum*) solution. Colloids and Surfaces B: Biointerfaces. 2010; 79(1):235-40. https://doi.org/10.1016/j.colsurfb.2010.04.003 PMid:20451362.
88. Faisal S, Jan H, Shah SA, Shah S, Khan A, Akbar MT, *et al*. Green synthesis of Zinc Oxide (ZnO) nanoparticles using aqueous fruit extracts of *Myristica fragrans*: Their characterizations and biological and environmental applications. ACS Omega. 2021; 6(14):9709-22. https://doi.org/10.1021/acsomega.1c00310 PMid:33869951 PMCid: PMC8047667.
89. Ashokan AP, Paulpandi M, Dinesh D, Murugan K, Vadivalagan C, Benelli GJJoCS. Toxicity on dengue mosquito vectors through *Myristica fragrans*-synthesized zinc oxide nanorods, and their cytotoxic effects on liver cancer cells (HepG2). Journal of Cluster Science. 2017; 28:205-26. https://doi.org/10.1007/s10876-016-1075-y
90. Rani N, Rawat K, Shrivastava A, Yadav S, Gupta K, Saini KJMTP. *In vitro* study of green synthesized ZnO nanoparticles on human lung cancer cell lines. 2022; 49:1436-42. https://doi.org/10.1016/j.matpr.2021.07.203
91. Selim YA, Azb MA, Ragab I, HM Abd El-Azim M. Green synthesis of zinc oxide nanoparticles using aqueous extract of *Deverra tortuosa* and their cytotoxic activities. Sci Rep. 2020; 10(1):3445. https://doi.org/10.1038/s41598-020-60541-1 PMid:32103090 PMCid: PMC7044426.
92. Umamaheswari A, Prabu SL, John SA, Puratchikody A. Green synthesis of zinc oxide nanoparticles using leaf extracts of *Raphanus sativus* var. *longipinnatus* and evaluation of their anticancer property in A549 cell lines. Biotechnol Rep (Amst). 2021; 29:e00595. https://doi.org/10.1016/j.btre.2021.e00595 PMid:33659193 PMCid: PMC7896141.
93. Umar H, Kavaz D, Rizaner N. Biosynthesis of zinc oxide nanoparticles using *Albizia lebbeck* stem bark, and evaluation of its antimicrobial, antioxidant, and cytotoxic activities on human breast cancer cell lines. Int J Nanomedicine. 2019; 14:87-100. https://doi.org/10.2147/IJN.S186888 PMid:30587987 PMCid: PMC6304255.
94. Linima VK, Ragunathan R, Johney J. Biogenic synthesis of *Ricinus communis* mediated iron and silver nanoparticles and its antibacterial and antifungal activity. Heliyon. 2023; 9(5):e15743. https://doi.org/10.1016/j.heliyon.2023.e15743 PMid:37305504 PMCid: PMC10256862.
95. Shobha N, Nanda N, Giresha AS, Manjappa P, Sophiya P, Dharmappa K, *et al*. Synthesis and characterization of zinc oxide nanoparticles utilizing seed source of *Ricinus communis* and study of its antioxidant, antifungal and anticancer activity. 2019; 97:842-50. https://doi.org/10.1016/j.msec.2018.12.023 PMid:30678976.
96. Sulaiman GM, Tawfeeq AT, Naji AS. Biosynthesis, characterization of magnetic iron oxide nanoparticles and evaluations of the cytotoxicity and DNA damage of human breast carcinoma cell lines. Artif Cells Nanomed Biotechnol. 2018; 46(6):1215-29. https://doi.org/10.1080/21691401.2017.1366335 PMid:28826240.
97. Iqbal J, Abbasi BA, Yaseen T, Zahra SA, Shahbaz A, Shah SA, *et al*. Green synthesis of zinc oxide nanoparticles using *Elaeagnus angustifolia* L. leaf extracts and their multiple *in vitro* biological applications. Sci Rep. 2021; 11(1):20988. https://doi.org/10.1038/s41598-021-99839-z PMid:34697404 PMCid: PMC8545962.
98. Jiang J, Pi J, Cai J. The advancing of zinc oxide nanoparticles for biomedical applications. Bioinorg Chem Appl. 2018; 2018:1062562. https://doi.org/10.1155/2018/1062562 PMid:30073019 PMCid: PMC6057429.
99. Barzinjy AA, Hamad SM, Abdulrahman AF, Biro SJ, Ghafor AA. Biosynthesis, characterization and mechanism of formation of ZnO nanoparticles using *Petroselinum crispum* leaf extract. Curr Org Synth. 2020; 17(7):558-66. https://doi.org/10.2174/1570179417666200628140547 PMid:32598261.
100. Akhtar MJ, Ahamed M, Kumar S, Khan MM, Ahmad J, Alrokayan SA. Zinc oxide nanoparticles selectively induce apoptosis in human cancer cells through reactive oxygen species. Int J Nanomedicine. 2012; 7:845-57. https://doi.org/10.2147/IJN.S29129 PMid:22393286 PMCid: PMC3289443.
101. Dobrucka R, Dlugaszewska J. Biosynthesis and antibacterial activity of ZnO nanoparticles using *Trifolium pratense* flower extract. Saudi J Biol Sci. 2016; 23(4):517-23. https://doi.org/10.1016/j.sjbs.2015.05.016 PMid:27298586 PMCid: PMC4890195.
102. Jamdagni P, Khatri P, Rana J. Green synthesis of zinc oxide nanoparticles using flower extract of *Nyctanthes arbor-tristis* and their antifungal activity. Journal of King Saud University-Science. 2018; 30(2):168-75. https://doi.org/10.1016/j.jksus.2016.10.002

103. Santhoshkumar J, Kumar SV, Rajeshkumar. Synthesis of zinc oxide nanoparticles using plant leaf extract against urinary tract infection pathogen. Resource-Efficient Technologies. 2017; 3(4):459-65. https://doi.org/10.1016/j.reffit.2017.05.001
104. Bhumi G, Savithramma. Biological synthesis of zinc oxide nanoparticles from *Catharanthus roseus* (L.) G. don. leaf extract and validation for antibacterial activity. Int J Drug Dev Res. 2014; 6(1):208-14.
105. Sundaraselvan G, Quine SD. Green synthesis of zinc oxide nanoparticles using seed extract of *Murraya koenigii* and their antimicrobial activity against some human pathogens. J Nanosci Nanotechnol. 2017. p. 289-92.
106. Panda KK, Golari D, Venugopal A, Achary VMM, Phaomei G, Parinandi NL, *et al*. Green synthesized zinc oxide (ZnO) nanoparticles induce oxidative stress and DNA damage in *Lathyrus sativus* L. root bioassay system. Antioxidants (Basel). 2017; 6(2). https://doi.org/10.3390/antiox6020035 PMid:28524089 PMCid: PMC5488015.
107. Ali K, Dwivedi S, Azam A, Saquib Q, Al-Said MS, Alkhedhairy AA, *et al*. *Aloe vera* extract functionalized zinc oxide nanoparticles as nanoantibiotics against multi-drug resistant clinical bacterial isolates. J Colloid Interface Sci. 2016; 472:145-56. https://doi.org/10.1016/j.jcis.2016.03.021 PMid:27031596.
108. Dharshini RS, Poonkothai M, Srinivasan P, Mythili R, Syed A, Elgorban AM, *et al*. Nano-decolorization of methylene blue by *Phyllanthus reticulatus* iron nanoparticles: an eco-friendly synthesis and its antimicrobial, phytotoxicity study. Appl Nanosci. 2023; 13(3):2527-37. https://doi.org/10.1007/s13204-021-02002-3 PMid:34367863 PMCid: PMC8325042.
109. Sathya K, Saravanathamizhan R, Baskar G. Ultrasonic assisted green synthesis of Fe and Fe/Zn bimetallic nanoparticles for invitro cytotoxicity study against HeLa cancer cell line. Mol Biol Rep. 2018; 45(5):1397-404. https://doi.org/10.1007/s11033-018-4302-9 PMid:30128625.
110. Ahmadi S, Fazilati M, Nazem H, Mousavi SM. Green synthesis of magnetic nanoparticles using *Satureja hortensis* essential oil toward superior antibacterial/fungal and anticancer performance. Biomed Res Int. 2021; 2021:8822645. https://doi.org/10.1155/2021/8822645 PMid:33542927 PMCid: PMC7840253.
111. Teja PK, Mithiya J, Kate AS, Bairwa K, Chauthe SK. Herbal nanomedicines: Recent advancements, challenges, opportunities and regulatory overview. Phytomedicine. 2022; 96:153890. https://doi.org/10.1016/j.phymed.2021.153890 PMid:35026510.