REVIEW ARTICLE

Plant-Mediated Green Synthesis of Gold Nanoparticles and their Anticancer Applications: An Updated Review

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Abstract

Due to the wide range of applications in the field of medicine, gold nanoparticles are the most promising agents in nanotechnology with a variety of physical, chemical, optical, and mechanical properties. Researchers have been interested in the green synthesis of gold nanoparticles in recent years because of their wide range of applications and low toxicity. The synthesis of gold nanoparticles using plant-mediated extracts has shown the fastest reduction due to the presence of phytoconstituents like phenolic compounds, flavonoids, alkaloids, terpenoids, polyphenols, polysaccharides, etc. Proteins, vitamins, and minerals are included in the extracts and act as stabilizing and capping agents. Gold nanoparticles are made from plant extracts and are of natural origin; they are thought to be safer for biomedical uses. In this review, we elaborate on the plant-mediated biosynthesis of gold nanoparticles and their biological applications, emphasizing cancer therapeutics.

Keywords: Anticancer Activity, Gold Nanoparticles, Green Synthesis, Nanotechnology, Plant Extracts.

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Introduction

In the past decades, one of the important and widely used in the research was nanotechnology, which has been used in various fields like chemistry, physics, biology, material science, engineering, medicine, etc. This paid much attention due to their enormous biological and biomedical applications. It was termed that the particles prepared by this technology were found to be 1-100 nm in various shapes.[1,2] Nanotechnology, based on the size and shape of nanoparticles, has shown better potential for early-stage cancer detection, as well as boosted their abundance in diagnostics and treatment due to its distinctive surface plasmon resonance.[3,4] The nanoparticles come in a variety of sizes and shapes, and they could be used in a variety of industries. Compared to conventional methods, plant-derived nanoparticle synthesis has the cost efficiency, safety, non-toxic, eco-friendliness properties, etc. These types of particles are developed for targeted drug delivery, especially in cancers. It was used not only for enhancing conventional cancer chemotherapy but also used in various fields like electronics, optronics, sensing, etc.[5] These nanoparticles can be made using a top-down strategy (physical method), in which the nanoparticles are made by breaking down the bulk materials, or a bottom-up approach (chemical and biological methods), in which the nanoparticles are made by breaking down the bulk materials. The drawback in the bottom-up approach is that it produces internal stress due to increased contaminants.[6] Various synthetic approaches for the generation of nanoparticles are presented in Figure 1.

Metallic nanoparticles were crucial in green chemistry because they attracted more attention than traditional approaches. Due to the characteristic properties, the metallic nanoparticles exhibited their better role in biomedical, optronics, and magnetic fields.[7,8] Gold nanoparticles are

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one of the most extensively utilized particles in theranostics among the numerous metallic nanoparticles. This had wide applications on gene delivery, controlled release, photothermal cancer therapy, sensing, imaging, immune assays, and catalysis.[3,7] In the historical Indian system, gold was used to diagnose various diseases like cold, tuberculosis, anemia, and also due to the reactive oxygen species caused cell damage, DNA injuries, etc. It induced necrosis, apoptosis,

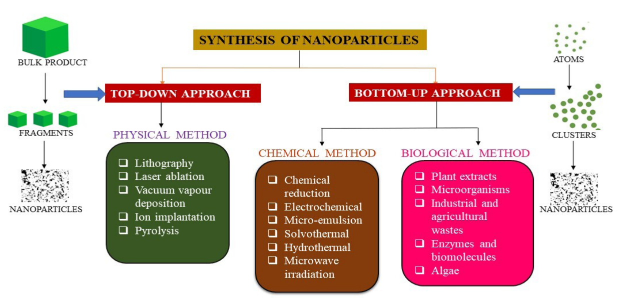

Figure 1: Synthetic approach of nanoparticles

and gene modification in the case of cancer chemotherapy.[9] Because of their smaller size, non-toxic and stable qualities, gold nanoparticles were widely used for cancer therapy. When compared to other metallic nanoparticles, the gold nanoparticles showed a shorter synthetic period with better beneficial effects on human health. The gold nanoparticles were synthesized using different methods such as citrate reduction, sodium borohydride reduction, soft-gel, ion sputtering, thermal, hydrothermal, sonochemical, microwave irradiation, etc. Most of these different methods utilize hazardous chemicals and induced toxicity. Plant-mediated or biological synthesis was preferred to overcome the harmful effects of hazardous chemicals.[10,11] The applications of gold nanoparticles are illustrated in Figure 2.

The use of green chemistry to make gold nanoparticles was well-established, and it had a stronger impact on biological applications. Plant extracts, fruit wastes, and microbial organisms are used in the most common environmental friendly green chemistry strategy to manufacture metallic nanoparticles. The plant extracts themselves act as reducing and stabilizing agents.[12,13] The plant-mediated extracts contain various bioactive or phytochemical constituents which are responsible for reduction, such as alkaloids, flavonoids, phenolics, proteins, vitamins, etc. The gold nanoparticles synthesized using a plant-mediated approach exhibited biocompatibility with wide therapeutic applications like anticancer, antimicrobial, antioxidant, antiangiogenic, antidiabetic, analgesic properties, etc. It also exhibited a better role in cosmetics, medical devices, and food industries.[14] The advantages of plant-mediated synthesis of gold nanoparticles is illustrated in Figure 3.

The gold nanoparticles using the green chemistry approach include various techniques like microwave-assisted synthesis,[15] one-pot synthesis,[16] facile one-step synthesis,[14], etc. In recent years, bacteria, fungi, yeast and algae have also been used to synthesize nanoparticles.[17] In cancer research, the green mediated gold nanoparticles had enhanced efficiency in drug delivery and target specificity than other metallic nanoparticles. Polyphenols play a vital role in cancer therapy and possess activity against various types of cancer cell lines, i.e., polyphenol mediated or polyphenol coated gold nanoparticles had better anticancer efficiency.[18] This review focused on the various plant-mediated synthesis of gold nanoparticles along with their mechanism, reaction conditions, characterization parameters, and anticancer efficiency against various cancer cells.

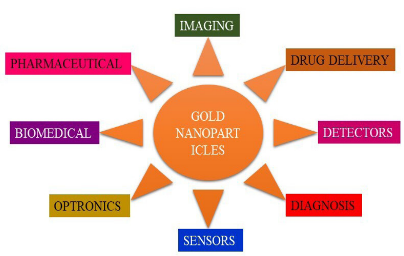

Figure 2: Applications of gold nanoparticles

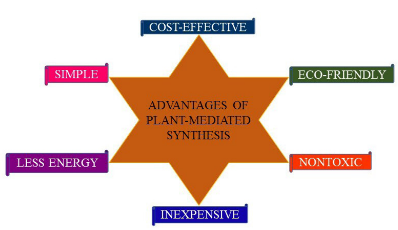

Figure 3: Advantages of plant-mediated synthesis of nanoparticles

Plant-Mediated Synthesis of Gold Nanoparticles

The green synthesis of nanoparticles was in high demand among researchers due to their numerous uses. For the production of simple, non-toxic, eco-friendly, facile, and renewable gold nanoparticles, the plant-mediated method showed greater interest than other conventional methods.[4] The synthesis of gold nanoparticles using plant extracts was found to be one of the most successful techniques for generating nanoparticles with various advantages over other techniques like enzymatic and microbial synthesis.[4,19] Plant-mediated synthesis of gold nanoparticles was a non-tedious and cost-effective method in which they can act as a catalyst, sensor, etc. with controlled crystal growth and stability. Plants include a variety of phytoconstituents that serve as stabilizers and reductants. Plant-mediated gold nanoparticles have better stability and substantially increase their anticancer therapy application. The size of most of the gold nanoparticles prepared from plant extracts were from 1-100 nm, majorly with spherical shape. Some of the particles were triangular, oval, hexagonal, polygonal, irregular, or rods. Due to their smaller size and increased applications paid attention to nanotechnology and nanomedicine.[21,22]

The gold nanoparticles have been prepared using different types of greener-mediated sources like *Linum usitatissimum*,[5] *Rosa damascena*,[12] *Musa acuminata*,[20] *Lotus Leguminosae*,[23] *Pistacia Atlantica*,[24] *Padina tetrastromatica*,[25] *Dracacephalum kotschyi*,[26] *Curcuma wenyujin*,[2] *Justicia adhatoda*,[27] *Eupharosia officinalis*,[28] etc. The amount of plant extract used in the production of gold nanoparticles has a significant impact on the yield of gold nanoparticles hence raising the amount/percent of extract used improves the output of gold nanoparticles. Colour changes also indicate the production of nanoparticles. The aqueous extract of *Lawsonia inermis*, the purple color of gold nanoparticles was appeared at the employment of 8% extract, while at 4 and 6% resulted in dull and pale red wine colour.[29] A colour change can confirm the formation of gold nanoparticles to red wine, purple and dark pinkish colour. Surface Plasmon Resonance (SPR) was another essential factor in the creation of gold nanoparticles. The SPR band for gold nanoparticles usually occurs between 510 and 560 nm in an aqueous medium.[30] Bioreduction and stabilization were important step in the synthesis and stability of gold nanoparticles. Plant secondary metabolites work as both a reducing and a stabilizing agent. Phytoconstituents such as phenolic compounds, flavonoids, terpenoids, alkaloids, polysaccharides, reducing sugars, tannins, amino acids, steroids and saponins played a major role in this reduction.[27,30] For the synthesis of gold nanoparticles using *Mangifera indica* seed extract, the chloroaurate ($AuCl_4$) ions were produced, which promotes the reduction of gold ions. Thus, the gold atoms got agglomerated and the formation of gold nanoparticles.[34] The plant-mediated biogenic synthesis of gold nanoparticles and their synthetic parameters are given in Figure 4 and Table 1.

Mechanism for the Plant-Mediated Synthesis of Gold Nanoparticles

Plant extracts operate as reducing and stabilizing agents in the plant-mediated production of gold nanoparticles. Bioreduction is aided by phytoconstituents such as phenolic compounds, flavonoids, terpenoids, alkaloids, steroids, saponins, polysaccharides, proteins, reducing sugars, vitamins, and minerals, which cause the Au^{3+} in gold salts like $HAuCl_4$ to be reduced to Au^0.[36] Based on the reduction and surface plasmon resonance, the gold nanoparticles with various morphologies were obtained. The surface plasmon resonance is the important factor for the formation of gold nanoparticles. This phenomenon increases the concentration of nanoparticles by increasing the reduction

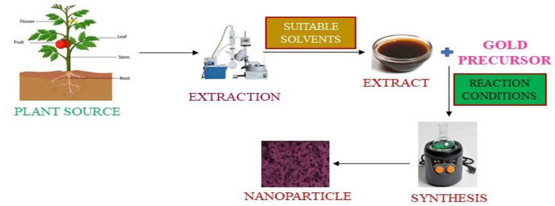

Figure 4: Schematic representation of the plant-mediated synthesis of gold nanoparticles

Table 1: Plant-mediated synthesis of gold nanoparticles with their synthetic parameters

Material used	*Part used*	*Phytoconstituents involved in the reduction*	*Precursor salt*	*Reaction condition*	*Colour produced*	*Reference*
Persicaria salicifolia	Leaf	Phenolic compounds, flavonoids, glycosides	$HAuCl_4.H_2O$	RT	Violet	[1]
Curcuma wenyujin	Rhizome	Phenolic compounds, flavonoids, alkaloids, tannins	$NaAuCl_4$	Stirring, RT	Purple-red	[2]
Tasmannia lanceolata	Leaf	Alkaloids, proteins, phenolic acids, terpenoids, polyphenols	$HAuCl_4.3H_2O$	Stirring, 15 min	Ruby red	[3]
Corchorus olitorius	Leaf	Phenolic compounds, vitamins, fatty acids	$HAuCl_4.3H_2O$	Stirring, 1 min	Dark red	[4]
Linum usitatissimum	Seed	Alkaloids, flavonoids, phenols, proteins, vitamins	$HAuCl_4.3H_2O$	RT, 6h	Ruby red	[5]
Garcinia mangostana	Pericarp	Phenolic acids, xanthones, tannins	$HAuCl_4.3H_2O$	Incubated, RT, 5 min	Purple	[7]
Cibotium barometz	Root	Phenolic acids, flavonoids	$HAuCl_4$	80°C, 1 min	Ruby red	[8]
Pituranthos tortuosus	Aerial parts	Flavonoids, tannins, carbohydrates, glycosides, alkaloids, terpenoids, proteins	$HAuCl_4.4H_2O$	RT, 40 min	Pink	[9]
Solanum xanthocarpum	Leaf	Flavonoids, saponins, alkaloids, glycosides	$HAuCl_4$	Stirring, RT	Purple	[10]
Nigella sativa	Seed	Terpenoids, thymoquinone, polyphenols	$HAuCl_4.3H_2O$	pH 6-10, 0-48h	Purple	[11]
Rosa damascena	Flower	Flavonoids, polyphenols, terpenoids	$HAuCl_4$	Stirring, 40 °C, 3 min	Pink	[12]
Azadirachta indica	Fruit	Phenolic compounds, alkaloids	$AuCl_3$	Stirring, 1-2h	Pink ruby	[13]
Glycyrrhiza glabra	Root	Flavonoids, chalcones, phenolic compounds	$HAuCl_4.3H_2O$	RT	Dark violet	[14]
Trachyspermum Ammi	Seed	Phenolic compounds, terpenoids, flavonoids, proteins	$HAuCl_4$	Stirring, 30 min and microwave irradiation, 2 min	Ruby red	[15]
Genipa Americana	Fruit	Genipin, geniposide, phenolic compounds	$AuCl_4$	22-25 °C, 15 min	Ruby red	[16]
Indigofera tinctoria	Leaf	Flavonoids, saponins, carbohydrates, steroids, alkaloids, phenolic compounds, glycosides	$HAuCl_4.3H_2O$	Microwave irradiation, 800 W, 1 min	Violet	[17]

Material used	*Part used*	*Phytoconstituents involved in the reduction*	*Precursor salt*	*Reaction condition*	*Colour produced*	*Reference*
Triphala (Terminalia chebula, Terminalia belerica, Phyllanthus Emblica)	Aerial parts (Triphala tablet/ powder)	Polyphenols, alkaloids, flavonoids	$HAuCl_4.3H_2O$	Stirring, 40 °C, 5 minutes	Ruby red	[18]
Carassocephalum Rubens	Leaf	Carbohydrates, vitamins, minerals, proteins	$HAuCl_4.4H_2O$	Stirring, 50 °C, 20 minutes	Purple	[19]
Musa acuminata	Flower	Polyphenols, carotenoids, vitamins, proteins, minerals	$HAuCl_4.3H_2O$	RT	Ruby red	[20]
Aegle marmelos Eugenia jambolana Annona muricata	Fruit	Alkaloids, phenolic compounds, flavonoids, proteins, tannins, reducing sugars	$HAuCl_4.4H_2O$	Boil, 5 min	Wine red	[21]
Juglans regia	Husk	Phenolic compounds, especially juglone	$HAuCl_4.3H_2O$	RT/Moderate temp (45 °C), 1-hour	Dark purple	[22]
Lotus Leguminosae	Aerial parts	Glycosides (Kaempferol), flavonoids	$HAuCl_4.3H_2O$	Stirring, RT, 15 minutes	Wine red	[23]
Pistacia Atlantica	Leaf and fruit	Flavonoids, phenolic compounds, fatty acids, phytosterols	$HAuCl_4.H_2O$	Stirring, 1-hour	Dark red	[24]
Dracocephalum kotschyi	Leaf	Flavonoids, proteins, carbohydrates	$HAuCl_4.H_2O$	Stirring, 2 min	Stable violet	[26]
Justica adhatoda	Leaf	Phenolic compounds, alkaloids, flavonoids, tannins, terpenoids	$HAuCl_4.3H_2O$	Autoclave, 120 °C, 24 hours	Yellowish-brown	[27]
Euphrasia Officinalis	Leaf	Phenolic compounds, flavonoids	Gold salt	37 °C, 24 hours	Deep purple	[28]
Lawsonia inermis	Leaf	Phenolic compounds, flavonoids, terpenoids, saponins, proteins	$HAuCl_4.3H_2O$	Rotary shaking, dark	Dull red wine	[29]
Commiphora wightii	Leaf	Flavonoids, steroids, terpenoids, carbohydrates	$HAuCl_4$	RT, 5 minutes	Purple wine	[30]
Vitis vinifera	Peel	Polyphenols, phenolic compounds	$HAuCl_4.3H_2O$	Incubation, 10 minutes	Purple-red	[32]
Aspalathus lineraris	Leaves	Phenolic compounds, volatile compounds, flavonoid (quercetin)	Gold salt	45 °C, 2 minutes	Wine red	[33]
Mangifera indica	Seed	Phenolic compounds, flavonoids, alkaloids, reducing sugars, terpenoids	$HAuCl_4.4H_2O$	Incubation, RT	Ruby red	[34]
Glycyrrhiza uralensis	Root	Flavonoids, glycyrrhizin	$HAuCl_4.3H_2O$	Oil bath, 80 °C	Dark purple	[35]
Petroselinum crispum	Leaf	Flavonoids, terpenoids, vitamins, minerals	$HAuCl_4.H_2O$	Stirring, 2 minutes	Purple	[36]
Allium sativum	Leaf	Phenolic compounds, flavonoids	$HAuCl_4$	Stirring, RT, 12 hours	Dark yellow	[37]
Panax ginseng	Berries powder	Phenolics, reducing sugars, polysaccharides, ginsenosides	$HAuCl_4.3H_2O$	40-90 °C	Purple	[38]
Catharanthus roseus	Leaf	Vincristine, vinblastine, alkaloids	$HAuCl_4$	Darkroom, 24 hours	Ruby red	[39]
Curcumae kwangsiensis	Leaf	Alkaloids, flavonoids, phenolic compounds, essential oils	$HAuCl_4.H_2O$	25 °C, 1h	Dark yellow	[40]
Turnera diffusa	Leaf	Phenolic compounds, alkaloids, flavonoids	$HAuCl_4$	Stirring, 60 °C, 4 hours	Reddish-brown	[41]
Mentha longifolia	Leaf	Polyphenols, alkaloids, organic acids, terpenoids, carbohydrates	$HAuCl_4$	Heat, 80 °C, 30 minutes	Wine red	[42]
Elettaria cardamomum	Seed	Phenolic compounds, terpenoids, sterols, flavonoids, proteins, tannins, starch	$HAuCl_4$ boiling solution	Boil, 2 minutes	Violet shade to purple	[43]
Vitex negundo	Leaf	Phenolic compounds, terpenoids, alkaloids, glycosidic iridoids	$HAuCl_4$	Overnight, 25 °C	Ruby red	[44]

Material used	*Part used*	*Phytoconstituents involved in the reduction*	*Precursor salt*	*Reaction condition*	*Colour produced*	*Reference*
Curcuma longa	Rhizome	Curcumin	$HAuCl_4$ Functionalized with INH	Stirring	Wine red	[45]
Crocus sativus	Flower	Crocin	$HAuCl_4$	50 °C, 24 hours	Purple	[46]
Vigna radiata	Seed	Phenolic compounds, steroids, organic acids	Gold solution	Stirring, 4-6 hours	Purple	[47]
Hippophae rhamnoids	Leaf	Phenolic compounds, flavonoids, terpenoids	$HAuCl_4.3H_2O$	RT, 2 minutes	Ruby red	[48]
	Berries			RT, 15 minutes	Purple	
Ananas comosus Passiflora edulis	Waste peel	Phenolic compounds, flavonoids, vitamins, proteins, carotenoids	$HAuCl_4.3H_2O$	Stirring, 1-hour	Dark brown, purple	[49]
Cannabis sativa	Leaf	Phenolic compounds, terpenoids, flavonoids	$HAuCl_4.H_2O$	RT	Purple	[50]
Anacardium occidentale	Leaf	Flavonoids, terpenoids, polyphenols	$HAuCl_4$	Stirring, incubation overnight	Ruby red	[51]
Rabdosia rubescens	Leaf	Phenolic acids, flavonoids, triterpenoids, volatile oils	$HAuCl_4.3H_2O$	Incubation, RT, 15 minutes	Ruby red	[52]
Maclura tricuspidate	Aerial parts	Phenolic compounds, flavonoids	$HAuCl_4$	Incubation, 25 °C, 15 minutes	Violet	[53]
Crescentia cujete	Leaf	Phenols, flavonoids, terpenoids, proteins, carbohydrates	$HAuCl_4$	60 °C, 25 minutes	Pinkish violet	[54]
Annona muricata	Leaf	Phenolic compounds, flavonoids, terpenoids, alkaloids, glycosides, tannins, vitamins, proteins	Gold solution	Stirring, 100 rpm, 6 hours	Deep purple	[55]
Curcuma longa	Rhizome powder	Curcumin, turmeric, quercetin, paclitaxel	$HAuCl_4$	50 °C, 15 minutes	Intensely red	[56]
Dracocephalum kotschyi	Leaf	Phenolic compounds, flavonoids, terpenoids	$HAuCl_4$	Stirring, RT, 15 minutes	Dark purple	[57]
Alternanthera bettzickiana	Leaf	Alkaloids, carbohydrates, saponins, phenolic compounds, flavonoids, terpenoids	$HAuCl_4$	80 °C, 10 minutes	Cherry red	[58]
Lonicera japonica	Flower	Flavonoids, phenolic compounds	$HAuCl_4.3H_2O$	Water bath, 60 °C, 2 min	Ruby red	[59]
Coleus forskohlii	Root	Phenolic acids, flavonoids, alkaloids, terpenoids	$HAuCl_4$	pH 7.0, RT	Wine red	[60]
Lycium chinense	Fruit	Alkaloids, flavonoids, polyphenols, terpenoids, glycosides, tannins	$HAuCl_4.3H_2O$	80 °C, 1-2 min	Deep purple	[61]
Thymus vulgaris	Aerial parts	Phenolic compounds, flavonoids, glycosides	$HAuCl_4.H_2O$	Stirring, RT, 1h	Dark red	[62]
Coleus aromaticus	Leaf	Flavonoids, polyphenols, terpenoids, alkaloids	$HAuCl_4.3H_2O$	Stirring, pH 7.0, 250 rpm, 30 min	Blackish brown	[63]
Muntingia calabura	Fruit	Polyphenolic compounds, terpenoids, flavonoids	$HAuCl_4$	Stirring, 50 °C, 2h	Stable violet	[64]
Cassia roxburghii	Leaf	Phenolic compounds, alkaloids, terpenoids, flavonoids	$HAuCl_4$	Dark, RT, 24h	Ruby red	[65]
Jasminum auriculatum	Leaf	Alkaloids, terpenoids, glycosides, phenolic compounds	$HAuCl_4.3H_2O$	RT, 1h	Violet	[66]
Rivea hypocrateriformis	Aerial parts	Alkaloids, glycosides, phenolic compounds, steroids, flavonoids	$HAuCl_4$	Microwave irradiation, 700 W	Purple	[67]
Musa paradisiaca	Peel	Flavonoids, polyphenols, alkaloids	$HAuCl_4$	353K, 20 min	Wine red	[68]
Actinidia deliciosa	Fruit	Polyphenolic compounds, flavonoids, terpenoids, vitamins	$HAuCl_4$	80 °C, 5 min	Ruby red	[69]

Material used	*Part used*	*Phytoconstituents involved in the reduction*	*Precursor salt*	*Reaction condition*	*Colour produced*	*Reference*
Hygrophila Spinosa	Aerial parts	Flavonoids, phenolic compounds, carbohydrates, proteins	$HAuCl_4.3H_2O$	pH 2.0, 80 °C, 45 min	Ruby red	[70]
Guazuma ulmifolia	Bark	Terpenoids, phenolic compounds, flavonoids, sterols	$HAuCl_4.3H_2O$	RT, 1h	Purple	[71]
Marsdenia tenacissima	Aerial parts	Phenolic compounds, flavonoids, vitamins, terpenoids	$HAuCl_4$	Incubation, 25 °C, overnight	Ruby red	[72]
Panax notoginseng	Leaf	Amino acids, polyphenolic acids, polysaccharides	$HAuCl_4$	138 °C, 2 min	Ruby red	[73]
Sasa Borealis	Leaf	Glycosides, alkaloids, phenolic compounds, flavonoids	$HAuCl_4$	Stirring, 50 °C, 20 min	Violet	[74]
Abies spectabilis	Aerial parts	Flavonoids, polyphenols, saponins, steroids	$HAuCl_4.3H_2O$	Incubation, 29 °C, 24h	Ruby red	[75]
Commelina nudiflora	Aerial parts	Phenolic compounds, flavonoids, glycosides, alkaloids, vitamins	$HAuCl_4$	Stirring, 37 °C, 150 rpm, 3h	Pink	[76]
Pleuropterus multiflorus	Root	Alkaloids, glycosides, phenolic compounds, flavonoids	$HAuCl_4.3H_2O$	80 °C, 10 min	Deep purple	[77]
Hylocereus undalus	Fruit	Betanin, hylourecenin, phenolic compounds	$HAuCl_4$	Stirring, 10 min	Deep reddish-purple	[78]
Siberian ginseng	Leaf	Chalcones, coumarins, flavonoids, triterpenoids, polyacetylenes	$HAuCl_4$	Incubation, 28 °C	Dark red	[79]
StigmaPhyllon ovatum	Leaf	Polyphenolic compounds, flavonoids, glycosides, alkaloids	$HAuCl_4$	80-85 °C, 1h	Purple	[80]
Nerium oleander	Bark	Polyphenolic compounds, steroids, terpenoids, flavonoids, glycosides	$HAuCl_4$	RT, 7h	Purple	[81]
Hibiscus sabdariffa	Flower	Polyphenolic compounds, flavonoids, terpenoids, steroids	$HAuCl_4.H_2O$	RT, 30 min	Dark brown	[82]
Scutellaria barbata	Aerial parts	Flavonoids, polyphenols, alkaloids, tannins, steroids	$HAuCl_4$	Stirring, 15-20 min	Reddish yellow	[83]
Camellia sinensis	Leaf	Polysaccharides, polyphenolic acids, flavonoids, reducing sugars	$HAuCl_4.3H_2O$	Oven incubation, 80 °C, 2h	Deep burgundy	[84]
Combretum erythrophyllum	Leaf	Flavonoids, alkaloids, tannins, carbohydrates, polyphenolic compounds, vitamins	$HAuCl_4$	Stirring, 750 rpm, RT	Light brown	[85]
Curcuma manga	Rhizome	Curcumin, terpenoids, flavonoids, alkaloids, polyphenols	$HAuCl_4.3H_2O$	Incubation, RT	Reddish violet	[86]
Moringa olifera	Leaf	Vitamins, proteins, polyphenols, flavonoids	$HAuCl_4$	RT	Purple	[87]
Bauhinia tomentosa	Leaf	Alkaloids, flavonoids, glycosides, polyphenols	$HAuCl_4.3H_2O$	RT	Ruby red	[88]
Eclipta prostrata	Leaf	Organic acids, phenolic compounds, flavonoids	$HAuCl_4$	Incubation, RT, 30 min	Dark brown	[89]
Ricinus communis	Leaf	Flavonoids, polysaccharides, phenolic compounds, reducing sugars	$HAuCl_4.3H_2O$	Stirring upto colour change, RT	Dark brown	[90]
Euphrasia Officinalis	Rhizome	Flavonoids, phenolic acids, iridoids	$HAuCl_4$	Stirring, 90 min	Ruby red	[91]
Thymus vulgaris	Leaf	Polyphenols, flavonoids, alkaloids, glycosides	$HAuCl_4.H_2O$	Stirring, RT, 30 min	Dark red	[92]
Tussilago farfara	Flower bud	Sesquiterpenoids, polyphenols	$KAuCl_4$	Dry oven, 80 °C, 2h	violet	[93]

rate.[4,9] The mechanism of the plant-mediated synthesis of gold nanoparticles is given in Figure 5.

Characterization of the Synthesized Gold Nanoparticles

After the synthesis of nanoparticles, the primary step in characterization is to determine their morphology, crystalline nature, and elemental composition. The various analytical and spectral techniques were used to determine the size, shape, crystalline structure, surface plasmon resonance peak, and elemental composition. Scanning electron microscopy (SEM), field-emission scanning electron microscopy (FESEM), transmission electron microscopy (TEM), and high-resolution transmission electron microscopy (HRTEM) were used to examine the morphology of the produced gold nanoparticles initially. The elemental composition was determined using a combination of techniques, including selected area electron diffraction (SAED) and an energy-dispersive X-Ray spectrometer (EDX). Dynamic light scattering (DLS) and a particle size analyzer (PSA) were used to determine the size and dispersive nature of the produced nanoparticles. Along with these properties, the surface charge of the synthesized gold nanoparticles was measured using a zeta potential analyzer or zeta sizer (ZP).[3,11] Surface plasmon resonance is an important characteristic in gold nanoparticles. A UV-Visible spectrophotometer (UV-Vis) was used to observe the surface plasmon resonance peak of the synthesized gold nanoparticles in the wavelength range of 200-800 nm. Surface plasmon resonance occurs in the range of 510-560 nm for these particles.[10,13]

The crystalline nature and structure of the gold nanoparticles synthesized using plant extracts were performed using X-ray diffraction (XRD), crystallography, or X-ray photoelectron spectroscopy (XPS). Gold nanoparticles obtained from *Persicaria salicifolia* exhibited the face-centered cubic crystalline structure with four distinct peaks at 38.1 ^{0}, 44.6 ^{0}, 64.7 ^{0}, and 78.3 ^{0} on XRD and to investigate its elemental composition, XPS analysis was performed and showed the presence of three elements viz. oxygen (O), carbon (C) and nitrogen (N) other than gold (Au). For the three different elements, five distinct peaks were observed at 531.3 eV (O), 532.6 eV (S=O), 284.6 eV (C-C), 286.3 eV (C=C) and 287.5 eV (C-O).[1]

The chemical composition and presence of functional groups were examined using Fourier transform infrared spectroscopy (FTIR) at 400-4000 cm^{-1} as the next crucial parameter to describe the plant-mediated produced nanoparticles. The presence of various functional groups shows the presence of gold nanoparticles and represents the reduction process. The presence of alkaloids, amino acids, flavonoids, terpenoids, phenolics, saponins, steroids, tannins, carbohydrates, and glycosides were identified as the functional groups involved in *Indigofera tinctoria* leaf extract mediated gold nanoparticles. The formation and stabilization of gold nanoparticles are may be due to these phytoconstituents. Peaks at 3206 cm^{-1} (O-H), 2909 cm^{-1} (C-H), 1587 cm^{-1}, 1393 cm^{-1} (C-O), 1017 cm^{-1} (C-N), 739, 708 and 523 cm^{-1} (=C-H) proved the existence of these phytoconstituents.[17,36] Other studies like polydispersity index (PDI), atomic force microscopy (AFM), and several thermal and spectral techniques were used. All the gold nanoparticles synthesized using plant extracts were approximately 1-100 nm in size with spherical, oval, hexagonal, triangular, and irregular shapes. The various characterization parameters are given in Table 2.

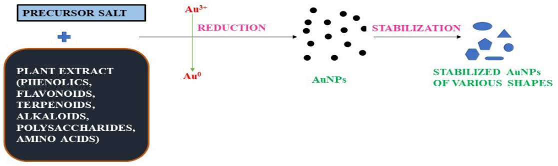

Figure 5: Diagrammatic representation of the mechanism of gold nanoparticles

Anticancer Activity of the Plant-Mediated Gold Nanoparticles

The gold nanoparticles from a wide range of plant extracts showed the anticancer efficiency against various types of cancers like liver,[9] lung,[17] breast,[18] colorectal,[36] colon,[37] skin,[38] cervical,[39] ovarian,[40] etc. To determine the anticancer efficiency of the synthesized gold nanoparticles, the MTT, MTS, SRB and other colorimetric and staining techniques were used. The chemotherapy or other synthetic sources used for the treatment of cancer comprises the use of toxic chemicals and artificial reducing agents. This disadvantage was solved by using plant-mediated gold nanoparticle production instead. Plant extracts contain phytoconstituents that are biocompatible and can act as reductants.[41]

Breast cancer is the most frequent cancer in women and the second most common cancer worldwide. Since there are numerous chemotherapeutic drugs, targeted therapies, immunotherapies, radiation therapies, and other treatments available to treat cancer, the plant-mediated target-oriented drug delivery held greater and promising treatment for cancer due to their higher risk effects. *In vitro* cytotoxicity of the gold nanoparticles synthesized using *Commiphora wightii* against MCF-7 cells using MTT assay demonstrated the better activity with an IC_{50} value of 66.11 µg/ml and the activity got increased by increasing the concentration of the gold nanoparticles. The flow cytometry results revealed that the earlier apoptosis was taken within the cells. Thus, apoptosis was induced with significant DNA damage at higher concentrations.[30,42]

Rajan et al. looked into the effects of gold nanoparticles on human cervical cancer (HeLa) cell lines. These types of gold nanoparticles prepared using plant-mediated sources has the ability to cross physiological barriers and are used as a potential targeted drug delivery system. More than 65 % of cell death was observed by using *Elettaria cardamomum*

Table 2: Characterization studies of synthesized gold nanoparticles

Plant material	*SPR peak (nm)*	*Size (nm) and shape*	*Crystalline nature/ Elemental composition*	*Functional group present*	*Reference*
Persicaria salicifolia	535	5-23 Rod, triangle, irregular, rhomboid	FCC/C,O,Au	C–H, C=O, C=C, C=N, C–O, C≡C	[1]
Curcuma wenyujin	530	127 Spherical	Au, Cu(weak)	C–N, N–H	[2]
Tasmannia lanceolata	525	7.1 Spherical	FCC/Au	O–H, N–H, C–H, C=O, C=C	[3]
Corchorus olitorius	535	37-50 Triangular, hexagonal	FCC/Au	O–H, C=O	[4]
Linum usitatissimum	525	3.4-6.9 Spherical, triangular	Moderate crystalline/ Ca, K, Al, Au	C–H, O–H, C–O, C=O	[5]
Garcinia mangostana	544	27.73 Spherical	FCC/Au	O–H, C–H, C=O, C=C, C–O	[7]
Cibotium barometz	540	5-20 Spherical	FCC/Au	O–H, C–H, C–O, C=O	[8]
Pituranthos tortuosus	535	12 Spherical, triangular, hexagonal	Crystalline gold, FCC/ Au	C–H, N–H, O–H, C–O, C=O	[9]
Solanum xanthocarpum	525	100 Spherical	FCC/Au	C–H, C–O, =CH–H, C=O, =C–H	[10]
Nigella sativa	535	20-50 Elliptical	FCC/Au	O–H, N–H, C=O, C=C	[11]
Rosa damascene	520	10 Spherical, monodispersed	FCC/Au	O–H, C–H, C–O, C=O, C=C, C–O–C	[12]
Azadirachta indica	531	20-25 Prism, rod, hexagonal	FCC/Au	C–H, C–N, C=C, =C–H	[13]
Glycyrrhiza glabra	549	2-16 Circular	FCC/Au, Ca, Fe, Cl, P, C, N, O	O–H, C–H, C–O, C–N, N–H, C=O	[14]
Trachyspermum Ammi	522	11.11 Spherical and spheroidal	FCC/Au	O–H, C–H, C–O, C=O	[15]
Genipa Americana	535	15-40 Spherical	FCC/Au	O–H, C–H, C–O, C=O, C=C, C–O–C	[16]
Indigofera tinctoria	545	19.73 Spherical	FCC/Au	O–H, C–H, C–N, C=C, =C–H	[17]
Triphala (Terminalia chebula, Terminalia belerica, Phyllanthus Emblica)	524	25 Spherical	Au	O–H, C–H, C–O, N–H, C=C	[18]
Carassocephalum Rubens	538	20±5 Spherical	FCC/Au	O–H, C–H, C–O, C=C	[19]
Musa acuminata	540	10.1-15.6 Spherical	FCC/Au	C–H, O–H, N–H, C–N, C–O, C=O, C=C	[20]
Aegle marmelos *Eugenia jambolana* *Annona muricata*	519 523 526	18 28 16 Spherical	FCC/Au	O–H, N–H, C–N, C=O	[21]
Juglans regia	531 (m.t) 550 (r.t)	14.32 19.19 Spherical	FCC/Au	C–C, C–O, O–H, C=C, C=C	[22]
Lotus Leguminosae	528	37 Spherical	-	C–H, C–O, C=O	[23]
Pistacia Atlantica	530	40-50 Spherical	FCC/Au, C, O, N	C–H, C–C, C–N, C=O	[24]

Plant material	*SPR peak (nm)*	*Size (nm) and shape*	*Crystalline nature/ Elemental composition*	*Functional group present*	*Reference*
Dracocephalum kotschyi	536	11 Triangular, pentagonal, hexagonal	FCC/Au, P, Fe, K, Cl, S	O–H, N–H, C–N, C–C, C=O, C–O–C, C–O–H	[26]
Justica adhatoda	-	Nanoflakes	FCC/Au, K, O	O–H, C–H, C–Cl, C=O	[27]
Euphrasia Officinalis	540	5-30 Spherical, hexagonal	FCC/Au	O–H, C–H, C–C, C–O, C=C, C=O	[28]
Lawsonia inermis	532	10-60 Spherical	-	O–H, C–H, N–H, C–C, C=O, C–O–C, C–O–H	[29]
Commiphora wightii	533	20.2±6.6 Spherical, triangular, hexagonal	FCC/Au	O–H, C–O	[30]
Vitis vinifera	540	20-40 spherical	FCC/Au	O–H, C–H, C–O, N–O, C=C, C=O	[32]
Aspalathus lineraris	535	4-37 Triangular, hexagonal	FCC/Au	O–H, C–H, C=O	[33]
Mangifera indica	528	46.8 Spherical	FCC/Au	O–H, N–H, C–H, C–O, C=O, C–O–C	[34]
Glycyrrhiza uralensis	540	10-15 Spherical	Polycrystalline/ C, Au	O–H, C–H, C–O, C=C	[35]
Petroselinum crispum	547	17 Spherical	C, O, N, K, Au	C–H, C–C, C–N, C=O	[36]
Allium sativum L.	523	19 Spherical	-	O–H, C–O, Au–O, C=O, C=C	[37]
Panax ginseng	540	5-10 Spherical	FCC/Au	O–H, C–H, C–C, C–O, C–O–C, C–O–H	[38]
Catharanthus roseus	540	55 Spherical	FCC/Au	C–H, C–O, O–H, C=O	[39]
Curcumae kwangsiensis	539	8-25 Spherical	C, O, Au	O–H, C–H, C–O, Au–O, =C–H	[40]
Turnera diffusa	530-540	24±4 Spherical	-	O–H, C–O, C=O, C–O–H	[41]
Mentha longifolia	512	36.4 Spherical	FCC/Au	O–H, C=O, C=C, ≡C–H	[42]
Elettaria cardamomum	527	2-15 Spherical	FCC/Au, C, O	O–H, N–H, C–H, C–N, C=O, C–O–C	[43]
Vitex negundo	538	30 Spherical	Circular pattern Crystalline gold FCC/Au	C–H, N–H, C=O, =C–H	[44]
Curcuma longa	524	52 Spherical	-	O–H, C–O, C–H, C=O	[45]
Crocus sativus	520	5 Spherical	FCC/Au	O–H, C–O, C=O	[46]
Vigna radiata	548	4-10 Spherical	FCC/Au	C–H, C–Cl, C=C, C=O, C≡C	[47]
Hippophae rhamnoids	546	27±3.2 Spherical	FCC/ Au, C, Cu (weak)	O–H, C–H, =C–H, C=O, C–O–H	[48]
Ananas comosus *Passiflora edulis*	545.5	20.71±7.44 18.68±5.55 Spherical	FCC/ Au	O–H, C–O, C–C	[49]
Cannabis sativa	538	18.6 Spherical	-	O–H, C–H, C–O, Au–O, C=C, C=O, C–O–C	[50]
Anacardium occidentale	540	40 Spherical	FCC/C, O, Au	O–H, C–O, C=C	[51]

Plant material	SPR peak (nm)	Size (nm) and shape	Crystalline nature/ Elemental composition	Functional group present	Reference
Rabdosia rubescens	550	130 Spherical, polydispersed	Au, Cu (weak)	O–H, C–H, C–O, N–H, C=O	[52]
Maclura tricuspidata	525	23-26 Spherical, hexagonal	FCC/Au	O–H, C–H, C–C, C–N	[53]
Crescentia cujete	560	32.89 anisotropic	FCC/Au	O–H, C–N, N–H, C=O	[54]
Annona muricata	538	89.34±2.76 Spherical	-	O–H, N–H, C=O, C=C, C–O–C	
Curcuma longa	530-540	5-25 Spherical, monodispersed	-	-	[56]
Dracocephalum kotschyi	537	5-21 Spherical	FCC/Au	O–H, C–H, N–H, C=O, C=C	[57]
Alternanthera bettzickiana	530	80-120 Spherical	FCC/Au, Cl	O–H, C–H, N–H, N–O, C–C	[58]
Lonicera japonica	535	10-20 Spherical	FCC/Au	O–H, C–H, N–H, C–C, C–N, C–O	[59]
Coleus forskohlii	530	10-30 Spherical	FCC/Au	O–H, C–H, N–H, C–O	[60]
Lycium Chinese	536	20-80 Spherical	FCC/Au	O–H, C–H, N–H, C–C, C–O, C–N, N–O	[61]
Thymus vulgaris	530	35 Spherical	FCC/Au	O–H, C–H, C–C, C–N, C=O	[62]
Coleus aromaticus	544	80 Spherical, needle, triangular	FCC/Au	O–H, C–N, C=O	[63]
Muntingia calabura	531	27 Spherical, oval	-	O–H, C–H, C–O, C=C	[64]
Cassia roxburghii	530	25-35 Spherical	FCC/Au, O	O–H, C–H, N–H, C–O, C–N, C=C	[65]
Jasminum auriculatum	547	8-37 Spherical	FCC/Au	O–H, N–H, C–O, C=O, C≡C	[66]
Rivea hypocrateriformis	550	20-30 Spherical narrow	FCC/Au	O–H, C–H, C–O, C–O–H	[67]
Musa paradisiaca	541	50 Spherical, triangular	FCC/Au	O–H, C–H, C–N, C=C, C=O	[68]
Actinidia deliciosa	538	7-20 Spherical	FCC/Au	N–H, C=C	[69]
Hygrophila Spinosa.	540	68 Spherical, polygonal	FCC/ Au, O, Al, Cu (weak)	O–H, C–H, C–O, C=O, Si–O–Si	[70]
Guazuma ulmifolia	522	20-25 Spherical	FCC/Au	N–H, C–H, C–O	[71]
Marsdenia tenacissima	535	40-50 Spherical	FCC/Au, Cu (weak)	O–H, C–H, C–O–C	[72]
Panax notoginseng	540	8-12 Spherical, oval, polygonal, triangular	Au	O–H, C–H, C–O	[73]
Sasa Borealis	542	10-30 Spherical, oval	FCC/Au	O–H, N–H, C–H, N–O, C–N	[74]
Abies spectabilis	530	108.6 Spherical	FCC/Au	O–H, C–H, S=O, C=C	[75]
Commelina nudiflora.	540	50 Spherical	-	O–H, N–H, C=O	[76]

Plant material	*SPR peak (nm)*	*Size (nm) and shape*	*Crystalline nature/ Elemental composition*	*Functional group present*	*Reference*
Pleuropterus multiflorus	540	104.8 Spherical	FCC/Au	O–H, N–H, C–O, C–H, C=C	[77]
Hylocereus undalus	560	10-20 Spherical, oval, triangular	FCC/Au, C, O, N	O–H, C–H, C–C, C–N, C=O	[78]
Siberian ginseng	538	200 Spherical	FCC/Au	O–H, N–H, C–O	[79]
Stigmaphyllon ovatum	534	78 Triangular	FCC/Au, Cl	-	[80]
Nerium oleander	534-553	20-40 Spherical	FCC/Au	-	[81]
Hibiscus sabdariffa	532	30 Spherical	FCC/Au	O–H, C–H, C=C, C=O	[82]
Scutellaria barbata	525	154 Spherical	Au, Cu (weak)	O–H, C–H, C=O	[83]
Camellia sinensis	532	8.7±1.7 Spherical	-	O–H, C=O	[84]
Combretum erythrophyllum	530	11.18±4.5 Spherical, monodispersed	FCC/Au, C, N, O	O–H, C–H, C–N, C–O, C=O, S=O	[85]
Curcuma manga	535	15.6 Spherical	-	O–H, C–H, C–O	[86]
Moringa olifera	544	10-20 Spherical	-	-	[87]
Bauhinia tomentosa	563	31.32 Spherical	FCC/Au, O, C	O–H, C–H, N–H, P–H, C–O, C=O, C≡C	[88]
Eclipta prostrata	534	32±1.1 Spherical	FCC/Au, P, O	O–H, N–H, P–H, C=O	[89]
Ricinus communis	536	40-80 Spherical	FCC/Au	O–H, C–H, N–H, C=O	[90]
Euphrasia Officinalis	558	49.72±1.2 Quasi-spherical	FCC/Au, C, Cu (weak)	O–H, C–H, N–H, C–F, C=O, C=C, C=N	[91]
Thymus vulgaris	532	10-30 Spherical	FCC/Au, C, O, P, Cl	O–H, C–H, C–O, C=C, C=O, C–O–C	[92]
Tussilago farfara	538	13.57±3.26 Spherical	FCC/Au, Cl	-	[93]

The presence of functional groups shows numerous phytoconstituents responsible for reduction, such as phenolic compounds, flavonoids, alkaloids, terpenoids, tannins, etc. The presence of organic components such as C, N, and O indicates that they are also involved in the capping of gold nanoparticles. All of the particles had an SPR peak around 520-560 nm, were about 1-100 nm in size and were mostly spherical in form.

mediated gold nanoparticles against HeLa cells. The ability of the produced gold nanoparticles to penetrate cells was responsible for the increased activity. This study also revealed apoptosis induction and cell death by ROS accumulation.[45] On focusing on colorectal cancers, the *Allium sativum* L. derived gold nanoparticles were examined against various colorectal cancer cell lines using MTT assay. It showed that the cell viability of colon cancer cell lines decreased in the presence of gold salt dose-dependently. The cell viability was analyzed against HT-29, HCT116, and Ramo.2G6.4C10 cell lines. The better cytotoxicity was observed against the HCT116 cell line with an IC_{50} value of 225 µg/ml. It also confirmed the non-toxic effect against normal cell line (HUVEC).[37]

For tumor growth, angiogenesis is the necessary step. The treatment by blocking angiogenesis has now become a widely used approach. *M.indica* mediated gold nanoparticles significantly affected human gastric adenocarcinoma cells, and it does not exert cytotoxicity towards the normal healthy cells. The chick embryo angiogenesis approach was used to investigate the antiangiogenic role. By increasing the concentration of gold nanoparticles, the fold of blood vessel size, length and junctions was reduced, as was the down-regulation of the Ang-1/Tie2 pathway. Thus, inhibiting/blocking angiogenesis could be used as a therapeutic option for the treatment of cancer, tumor or cancer progression.[34]

Apoptosis is an important thing in various types of cancer management. Cell apoptosis was activated through the stimulation of apoptosis using external signals or by using internal pathways like mitochondrial apoptotic pathway or death receptor pathway. The ROS accumulation initiated the cell apoptosis, thus the cellular MMP level got decreased.

When the ROS was accumulated, the cytochrome C got liberated and combined with apoptotic protein, thereby inducing apoptosis by activating caspase-3 and caspase-9. Programmed cell death in human lung fibroblast (TIG-120) and human lung squamous carcinoma (LK-2) cells against curcumin-mediated gold nanoparticles was observed.[44,45] The schematic illustration of the cell apoptosis is given in Figure 6.

Higher ROS generation promotes apoptosis via the Mitochondrial-mediated pathway. The major biochemical alterations that triggered apoptosis were intracellular ROS modifications. *Catharanthus roseus* mediated gold nanoparticles induced apoptosis against HeLa cells and were quantified using Ao/EtBr staining technique. It induced apoptosis at 5 µg/mL concentration. i.e., the cell shrinkage, nuclear condensation, fragmentation, and formation of apoptotic bodies happen. The protein levels of pro-apoptotic Bax, Bid, and anti-apoptotic Bcl-2 were determined by Western blotting analysis. Increased Bax and Bid proteins expression occurred after treatment with plant-mediated gold nanoparticles (*C.roseus*-Gold nanoparticles), followed by suppression/down-regulation of Bcl-2 proteins. Thus, the intracellular modulation and apoptosis induction of the plant-mediated gold nanoparticles against cancer cells was illustrated.[39] The schematic representation of the intracellular modulation and cell apoptosis induction is given in Figure 7**,** along with the various plant-mediated sources against various cancer cells in Table 3.

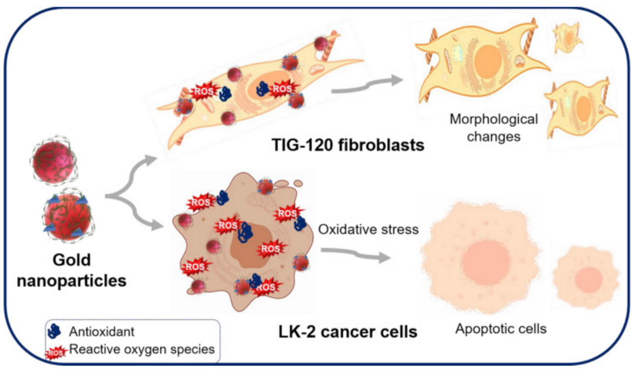

Figure 6: Schematic illustration of programmed cell death. It represents the apoptosis in human lung fibroblast (TIG-120) and human lung squamous carcinoma (LK-2) against curcumin-mediated gold nanoparticles. The cell apoptosis was initiated by ROS accumulation thus the cytochrome-C got liberated. Apoptosis happened by the interaction with apoptotic proteins.[45]

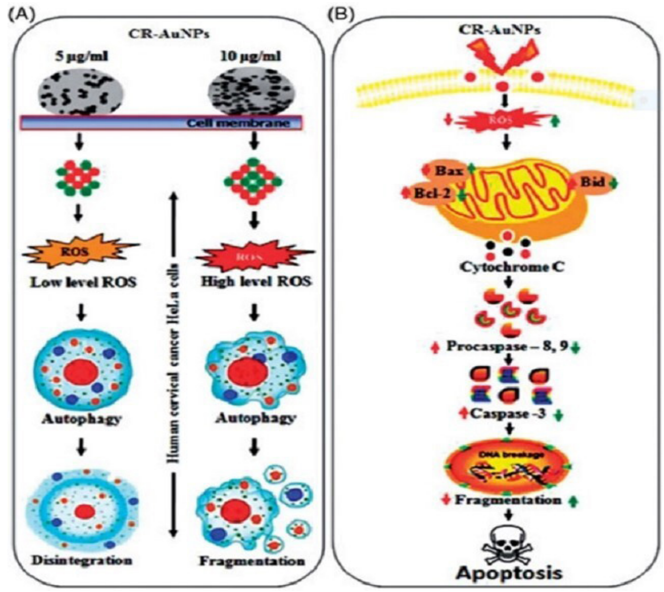

Figure 7: Illustration of apoptosis induction against HeLa cells. Schematic representation of the intracellular modulation and apoptosis induction of the plant-mediated gold nanoparticles against cancer cells by Ke et al., 2019. Apoptosis is triggered by increased ROS generation in the mitochondrial pathway. The enhanced expression of Bax and Bid proteins and the down-regulation of Bcl-2 proteins resulted in substantial apoptosis in HeLa cells when CR-AuNPs were used at 5 g/ml. It then interacts with caspases 9 and 3, triggering apoptosis to occur.[39]

Table 3: Anticancer efficiency of synthesized plant-mediated gold nanoparticles

Plant material	*Tested cells*	*Method used*	*Reference*
Persicaria salicifolia	MCF-7	SRB	[1]
Curcuma wenyujin	MDA-MB-231	MTT	[2]
Tasmannia lanceolata	HePG2, MM418, MCF-7	MTT	[3]
Corchorus olitorius	MCF-7, HCT-11, HepG2	MTT	[4]
Linum usitatissimum	MCF-7, HepG2, HCT-116	MTT	[5]
Garcinia mangostana	A549, NIH373	WST	[7]
Cibotium barometz	RAW 264.7, MCF-7	MTT	[8]
Pituranthos tortuosus	HepG2, HCT-116	MTT	[9]
Solanum xanthocarpum	C666-1	MTT	[10]
Nigella sativa	RAW 264.7, AGS, HaCaT	MTT	[11]
Rosa damascena	P13ML, HL60, A549	Celltiter-blue cell viability assay	[12]
Azadirachta indica	TNBC, NIH373	MTT	[13]
Glycyrrhiza glabra	HepG2, MCF-7	MTT	[14]
Trachyspermum Ammi	HepG2	MTT	[15]

Plant material	*Tested cells*	*Method used*	*Reference*
Genipa Americana	A549, HeLa	MTT	[16]
Indigofera tinctoria	A549	MTT	[17]
Triphala (Terminalia chebula, Terminalia belerica, Phyllanthus Emblica)	MDA-MB-231	MTT	[18]
Carassocephalum Rubens	MCF-7, CaCo2	MTT	[19]
Musa acuminata	MCF-7, Vero	MTT	[20]
Aegle marmelos Eugenia jambolana Annona muricata	MCF-7	MTT	[21]
Juglans regia	3T3, HT29	MTT	[22]
Lotus Leguminosae	MCF-7	MTT	[23]
Pistacia Atlantica	HeLa	MTT	[24]
Dracocephalum kotschyi	K562, HeLa	MTT	[26]
Justica adhatoda	HeLa	MTT	[27]
Euphrasia Officinalis	RAW 264.7	MTT	[28]
Lawsonia inermis	L132	MTT	[29]
Commiphora wightii	MCF-7	MTT	[30]
Vitis vinifera	A431	MTT	[32]
Aspalathus lineraris	NHM	Fluorescence using presto blue reagent	[33]
Mangifera indica	AGS	MTT, LDH	[34]
Glycyrrhiza uralensis	RAW 264.7, MCF-7	MTT	[35]
Petroselinum crispum	COLO-201	MTT	[36]
Allium sativum	HUVEC, HT29, HCT116, HCT8, Ramos.2G6.4C10	MTT	[37]
Panax ginseng	HDF, B16	MTT	[38]
Catharanthus roseus	HeLa	MTT	[39]
Curcumae kwangsiensis	HUVEC, PA-1, SW-626, SKOV-3	MTT	[40]
Turnera diffusa	Head kidney leukocytes	Alamar blue	[41]
Mentha longifolia	MCF-7, Hs578Bst, Hs 319.T, UACC-3133	MTT	[42]
Elettaria cardamomum	HeLa	MTT	[43]
Vitex negundo	AGS	MTT	[44]
Curcuma longa	LK-2, TIG-120	DCFH-DA	[45]
Crocus sativus	MCF-7	MTT, LDH, Neutral red	[46]
Vigna radiata	MCF-7, MDA-MB-231, MDA-MB-453, MDA-MB-435S, MDA-MB-468	MTT, Alamar blue	[47]
Hippophae rhamnoids	MCF-7, Jurkat, HepG2, SSC-40,SK-UV-3	SRB	[48]
Ananas comosus Passiflora edulis	MCF-7	MTS	[49]
Cannabis sativa	HUVEC, MOLT-3, TACC-104, J.RT3-T3.5	MTT	[50]
Anacardium occidentale	MCF-7, PMBC	MTT	[51]
Rabdosia rubescens	A549	MTT	[52]
Maclura tricuspidata	HepG2, SK-Hep-1	CCK-8	[53]
Crescentia cujete	HeLa	MTT	[54]
Annona muricata	MCF-7, MM-138, FM-55	MTT	[55]
Curcuma longa	MCF-7, MDA-MB-231, HEK293	MTT	[56]
Dracocephalum kotschyi	MCF-7, H1299	MTT	[57]

Plant material	*Tested cells*	*Method used*	*Reference*
Alternanthera bettzickiana	A549	MTT	[58]
Lonicera japonica	HeLa, HEK293	WST-1	[59]
Coleus forskohlii	HepG2	MTT	[60]
Lycium chinense	RAW264.7, MCF-7	MTT	[61]
Thymus vulgaris	HeLa	MTT	[62]
Coleus aromaticus	HepG2	MTT	[63]
Muntingia calabura	HepG2, Vero	MTT	[64]
Cassia roxburghii	Vero, HepG2, HeLa, MCF-7	MTT	[65]
Jasminum auriculatum	HeLa	MTT	[66]
Rivea hypocrateriformis	Vero, MCF-7, SF-9	MTT	[67]
Musa paradisiaca	A549	MTT	[68]
Actinidia deliciosa	HCT116	MTT	[69]
Hygrophila Spinosa	MCF-7, MDA-MB-231, SKOV-3, U-87	MTT	[70]
Guazuma ulmifolia	HeLa	MTT	[71]
Marsdenia tenacissima	A549	MTT	[72]
Panax notoginseng	PANC-1	MTT	[73]
Sasa Borealis	HEK293, AGS	WST-1	[74]
Abies spectabilis	T24	MTT	[75]
Commelina nudiflora	HCT116	MTT	[76]
Pleuropterus multiflorus	A549	MTT	[77]
Hylocereus undalus	MCF-7, MDA-MB-231	Alamar blue	[78]
Siberian ginseng	B16	MTT	[79]
Stigmaphyllon ovatum	HeLa	MTT	[80]
Nerium oleander	MCF-7	MTT	[81]
Hibiscus sabdariffa	Mice (*in vivo*)	-	[82]
Scutellaria barbata	PANC-1	MTT	[83]
Camellia sinensis	AGS, HeLa, HepG2, HT29	MTT	[84]
Combretum erythrophyllum	BHK21, HeLa, A549	MTS	[85]
Curcuma manga	CCD-18Co, MRC-5	SRB	[86]
Moringa olifera	A549, SNO	MTT	[87]
Bauhinia tomentosa	Vero, A549, HepG2, MCF-7	MTT	[88]
Eclipta prostrata	HepG2	MTT	[89]
Ricinus communis	HeLa, HepG2	Vybrant MTT	[90]
Euphrasia Officinalis	RAW264.7, A549, HeLa	MTT	[91]
Thymus vulgaris	HUVEC, HL-60/ver, 32D-FLT3-ITD, Muraine C1498	MTT	[92]
Tussilago farfara	AGS, HT29, PANC-1	MTT	[93]

List of Abbreviations

°C- Degree Celsius
3T3- Embryonic fibroblasts
A549- Human alveolar epithelial cells
AGS- Adenocarcinoma gastric cell line
CCK-8- cell counting kit-8
COLO201- Colorectal cell line
DCFH-DA- 2′,7′-dichlorofluorescein diacetate
FCC- Face centered cubic
FLT3-ITD- Myeloid leukemia.
HaCaT- Cultured human keratinocyte
HCT116- human colorectal carcinoma
Hek293- Human embryonic kidney 293
HepG2- Liver hepatocellular carcinoma
HL60- Human acute myeloid leukemia 60
HT-29- Human adenocarcinoma colorectal cell line
HUVEC- Human umbilical endothelial cells

IC_{50}- Half-maximal inhibitory concentration
K562- Human leukemic cell line
L132- Nontomorigenic human lung epithelial cells
LDH- Lactic acid dehydrogenase
LK-2- Lung cancer cell line
MCF-7- Michigan cancer foundation-7
MDA-MB-231- human breast adenocarcinoma
MM418- Melanoma cell line
MMP- Matrix metalloproteinase
MTS- 3-(4,5-dimethylthiazol-2-yl)-5-(3-carbmethoxyoxy phenyl)-2-(4-sulfophenyl)-2H-tetrazolium
MTT- 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide N- Nitrogen
NIH- National Institute of health
PA-1- Human ovarian teratocarcinoma cell line
PANC-1- Human pancreatic cell line
PMBC- Peripheral blood mononuclear cell
PMBL- Primary mediastinal large B-cell lymphoma
Raw264.7- Macrophage cell line
ROS- reactive oxygen species
RT- Room temperature
SK-Hep-1- Human hepatic adenocarcinoma
SKOV-3- Human ovarian cancer cell line
SPR-Surface plasmon resonance
SRB- Sulforhodanine B
SW-620- adenocarcinoma cell
TIG-120- Tokyo Institute of Gerontology
TNBC- Triple-negative breast cancer
WST-1- Water-soluble tetrazolium salts

Conclusion

In recent years, the synthesis of gold nanoparticles using a plant-mediated approach is increased and explored successfully due to its eco-friendly, non-toxic, low cost, and clean properties. The reaction time is based on the reducing agents used for the bioreduction. The phytoconstituents present in the plant extracts act as both reducing and capping agents, which provided the fastest reaction ranging from minutes to hours with improved stability. The gold nanoparticles with different sizes and shapes were synthesized using plant extracts with anticancer activity and vast applications. The surface plasmon resonance peak was observed in gold nanoparticles produced employing a plant-mediated greener method in the region of 520-560 nm. The greener-mediated gold nanoparticles had achieved great potential and prospects as future drug molecules. Especially in targeted therapies like cancer, the greener technology using plant extracts/resources is very bright, and it will be further developed in the pharmaceutical field.

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References

1. Hosny M, Fawzy M. Instantaneous photosynthesis of gold nanoparticles via *Persicaria salicifolia* leaf extract and their medical applications. *Adv Powder Technol*. 2021; 32(8):2891-2904. https://doi.org/10.1016/j.apt.2021.06.004.
2. Zhang N, Yu J, Liu P, Chang J, Ali D, Tian X. Gold nanoparticles synthesized from *Curcuma wenyujin* inhibits HER-2/neu transcription in breast cancer cells (MDA-MB-231/HER2). *Arab J Chem*. 2020;13(10):7264-7273. https://doi.org/10.1016/j.arabjc.2020.08.007.
3. Khandanlou R, Murthy V, Wang H. Gold nanoparticle-assisted enhancement in bioactive properties of Australian native plant extracts, *Tasmannia lanceolata and Backhousia citriodora*. *Mater Sci Eng C*. 2020;112:110922. https://doi.org/10.1016/j.msec.2020.110922.
4. 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):2612. https://doi.org/10.3390/ijms19092612.
5. Al-Radadi NS. Green Biosynthesis of Flaxseed Gold Nanoparticles (Au-NPs) as Potent Anti-cancer Agent Against Breast Cancer Cells. *J Saudi Chem Soc*. 2021;25(6):101243. https://doi.org/10.1016/j.jscs.2021.101243.
6. Lee KX, Shameli K, Yew YP, Teow SY, Jahangirian H, Rafiee-Moghaddam R, Webster TJ. Recent Developments in the Facile Bio-Synthesis of Gold Nanoparticles (AuNPs) and Their Biomedical Applications. *Int J Nanomedicine*. 2020;15:275-300. https://doi.org/10.2147/IJN.S233789.
7. Park JS, Ahn EY, Park Y. Asymmetric dumbbell-shaped silver nanoparticles and spherical gold nanoparticles green-synthesized by mangosteen (*Garcinia mangostana*) pericarp waste extracts. *Int J Nanomedicine*. 2017;12:6895-6908. https://doi.org/10.2147/IJN.S140190.
8. Wang D, Markus J, Wang C, Kim YJ, Mathiyalagan R, Aceituno VC, Ahn S, Yang DC. Green synthesis of gold and silver nanoparticles using aqueous extract of *Cibotium barometz* root. *Artif Cells Nanomed Biotechnol*. 2016;45(8):1548-1555. https://dx.doi.org/10.1080/21691401.2016.1260580.
9. Abd El-Moaty HI, Soliman NA, Hamad RS, Ismail EH, Sabry DY, Khalil MMH. Comparative therapeutic effects of *Pituranthos tortuous* aqueous extract and Phyto-synthesized gold nanoparticles on Helicobacter pylori, diabetic and cancer proliferation. *S Afr J Bot*. 2021;139:167-174. https://doi.org/10.1016/j.sajb.2021.02.009.
10. Zhang P, Wang P, Yan L, Liu L. Synthesis of gold nanoparticles with *Solanum xanthocarpum* extract and their *in vitro* anticancer potential on nasopharyngeal carcinoma cells. *Int J Nanomedicine*. 2018;13:7047-7059. https://doi.org/10.2147/IJN.S180138.
11. Dhandapani S, Xu X, Wang R, Puja AM, Kim H, Perumalsamy H, Balusamy SR, Kim YJ. Biosynthesis of gold nanoparticles using *Nigella sativa* and *Curtobacterium proimmune K3*

and evaluation of their anticancer activity. *Mater Sci Eng C Mater Biol Appl*. 2021;127:112214. https://doi.org/10.1016/j.msec.2021.112214.

12. Kyzioł A, Łukasiewicz S, Sebastian V, Kuśtrowski P, Kozieł M, Majda D, Cierniak A. Towards plant-mediated chemistry - Au nanoparticles obtained using aqueous extract of *Rosa damascena* and their biological activity *in vitro*. *J Inorg Biochem*. 2021;214:111300. https://doi.org/10.1016/j.jinorgbio.2020.111300.
13. Siddiq MA, Thangam R, Madhan B, Alam MDS. Green (Gemini) surfactant mediated gold nanoparticles green synthesis: Effect on triple-negative breast cancer cells. *Nano-Struct Nano-Objects*. 2019;1:100373. https://doi.org/10.1016/j.nanoso.2019.100373.
14. Al-Radadi NS. Facile one-step green synthesis of gold nanoparticles (AuNp) using licorice root extract: Antimicrobial and anticancer study against HepG2 cell line. *Arab J Chem*. 2021;14(2):102956. https://doi.org/10.1016/j.arabjc.2020.102956.
15. Perveen K, Husain FM, Qais FA, et al. Microwave-Assisted Rapid Green Synthesis of Gold Nanoparticles Using Seed Extract of *Trachyspermum Ammi*: ROS Mediated Biofilm Inhibition and Anticancer Activity. *Biomolecules*. 2021;11(2):197. https://doi.org/10.3390/biom11020197.
16. Kumar B, Smita K, Cumbal L, Camacho J, Hernández-Gallegos E, de Guadalupe Chávez-López M, Grijalva M, Andrade K. One pot phytosynthesis of gold nanoparticles using *Genipa americana* fruit extract and its biological applications. *Mater Sci Eng C Mater Biol Appl*. 2016;62:725-31. https://doi.org/10.1016/j.msec.2016.02.029.
17. Vijayan R, Joseph S, Mathew B. *Indigofera tinctoria* leaf extract mediated green synthesis of silver and gold nanoparticles and assessment of their anticancer, antimicrobial, antioxidant and catalytic properties. *Artif Cells Nanomed Biotechnol*. 2018;46(4):861-871. https://doi.org/10.1080/21691401.2017.1345930.
18. Nirmala JG, Rachineni K, Choudhary S, Hosur RV, Lopus M. Triphala polyphenols-functionalized gold nanoparticles impair cancer cell survival through induction of tubulin dysfunction. *J Drug Deliv Sci Technol*. 2021;61:102167. https://doi.org/10.1016/j.jddst.2020.102167.
19. Adewale OB, Anadozie SO, Potts-Johnson SS, Onwuelu JO, Obafemi TO, Osukoya OA, Fadaka AO, Davids H, Roux S. Investigation of bioactive compounds in *Crassocephalum rubens* leaf and in vitro anticancer activity of its biosynthesized gold nanoparticles. Biotechnol Rep. 2020;28:e00560. https://doi.org/10.1016/j.btre.2020.e00560.
20. Valsalam S, Agastian P, Esmail GA, Ghilan AKM, Al-Dhabi NA, Arasu MV. Biosynthesis of silver and gold nanoparticles using *Musa acuminata* Colla flower and its pharmaceutical activity against bacteria and anticancer efficacy. *J Photochem Photobiol B: Biol*. 2019;201:111670. https://doi.org/10.1016/j.jphotobiol.2019.111670.
21. Vijayakumar S. Eco-friendly synthesis of gold nanoparticles using fruit extracts and *in vitro* anticancer studies. *J Saudi Chem Soc*. 2019;23(6):753-761. https://doi.org/10.1016/j.jscs.2018.12.002.
22. Izadiyan Z, Shameli K, Hara H, Taib SHM. Cytotoxicity assay of biosynthesis gold nanoparticles mediated by walnut (*Juglans regia*) green husk extract. *J Mol Struct*. 2018;151:97-105. https://doi.org/10.1016/j.molstruc.2017.09.039.
23. Oueslati MH, Tahar LB, Harrath AH. Catalytic, antioxidant and anticancer activities of gold nanoparticles synthesized by kaempferol glucoside from *Lotus Leguminosae*. *Arab J Chem*. 2020;13(1):3112-3122. https://doi.org/10.1016/j.arabjc.2018.09.003.
24. Hamelin M, Hemmati S, Varmira K, Veisi H. Green synthesis, antibacterial, antioxidant and cytotoxic effect of gold nanoparticles using *Pistacia Atlantica* extract. *J Taiwan Inst Chem Eng*. 2018;93:21-30. https://doi.org/10.1016/j.jtice.2018.07.018.
25. Rajeshkumar S, Sherif MH, Malarkodi C, Ponnanikajamideen M, Arasu MV, Al-Dhabi NA, Roopan SM. Cytotoxicity behaviour of response surface model optimized gold nanoparticles by utilizing fucoidan extracted from *padina tetrastromatica*. *J Mol Struct*. 2021;1228:129440. https://doi.org/10.1016/j.molstruc.2020.129440.
26. Dosti N, Jamshidi F. Plant-mediated gold nanoparticles by *Dracocephalum kotschyi* as anticholinesterase agent: Synthesis, characterization and evaluation of anticancer and antibacterial activity. *J Appl Biomed*. 2016;14(3):235-245. https://doi.org/10.1016/j.jab.2016.03.001.
27. Pandiyan N, Murugesan B, Arumugam M, Chinnaalagu D, Samayanan S, Mahalingam S. Ionic liquid mediated green synthesis of Ag-Au/Y2O3 nanoparticles using leaves extracts of *Justicia adhatoda*: Structural characterization and its biological applications. *Adv Powder Technol*. 2021;32(7):2213-2225. https://doi.org/10.1016/j.apt.2021.04.030.
28. Liu Y, Kim S, Kim YJ, Perumalsamy H, Lee S, Hwang E, Yi TH. Green synthesis of gold nanoparticles using *Euphrasia officinalis*leaf extract to inhibit lipopolysaccharide-induced inflammation through NF-κB and JAK/STAT pathways in RAW 264.7 macrophages. *Int J Nanomedicine*. 2019;14:2945-2959. https://doi.org/10.2147/IJN.S199781.
29. Kumari P, Meena A. Green synthesis of gold nanoparticles from *Lawsonia inermis* and its catalytic activities following the Langmuir-Hinshelwood mechanism. *Colloids Surf A: Physicochem Eng Asp*. 2020;606:125447. https://doi.org/10.1016/j.colsurfa.2020.125447.
30. Uzma M, Sunayana N, Raghavendra VB, Madhu CS, Shanmuganathan R, Brindhadevi K. Biogenic synthesis of gold nanoparticles using *Commiphora wightii* and their cytotoxic effects on breast cancer cell line (MCF-7). *Process Biochem*. 2020;92:269-276. https://doi.org/10.1016/j.procbio.2020.01.019.
31. Jeyarani S, Vinita NM, Puja P, Senthamilselvi S, Devan U, Velangani AJ, Biruntha M, Pugazhendhi A, Kumar P. Biomimetic gold nanoparticles for its cytotoxicity and biocompatibility evidenced by fluorescence-based assays in cancer (MDA-MB-231) and non-cancerous (HEK-293)

cells. *J Photochem Photobiol B*. 2020;202:111715. https://doi.org/10.1016/j.jphotobiol.2019.111715.

32. Nirmala JG, Akila S, Narendhirakannan RT, Chatterjee S. *Vitis vinifera* peel polyphenols stabilized gold nanoparticles induce cytotoxicity and apoptotic cell death in A431 skin cancer cell lines. *Adv Powder Technol*. 2017;28(4):1170-1184. https://doi.org/10.1016/j.apt.2017.02.003.
33. Blom van Staden A, Kovacs D, Cardinali G, Picardo M, Lebeko M, Khumalo NC, Ray SS, Lall N. Synthesis and characterization of gold nanoparticles biosynthesised from *Aspalathus linearis* (Burm.f.) R.Dahlgren For progressive macular hypomelanosis. *J Herb Med*. 2021;29:100481. https://doi.org/10.1016/j.hermed.2021.100481.
34. Vimalraj S, Ashokkumar T, Saravanan S. Biogenic gold nanoparticles synthesis mediated by *Mangifera indica* seed aqueous extracts exhibits antibacterial, anticancer and antiangiogenic properties. *Biomed Pharmacother*. 2018;105:440-448. https://doi.org/10.1016/j.biopha.2018.05.151.
35. Huo Y, Singh P, Kim YJ, Soshnikova V, Kang J, Markus J, Ahn S, Castro-Aceituno V, Mathiyalagan R, Chokkalingam M, Bae K, Yang DC. Biological synthesis of gold and silver chloride nanoparticles by *Glycyrrhiza uralensis* and *in vitro* applications. *Artif Cells Nanomed Biotechnol*. 2018;46(2):303-312. https://doi.org/10.1080/21691401.2017.1307213.
36. El-Borady OM, Ayat MS, Shabrawy MA, Millet P. Green synthesis of gold nanoparticles using Parsley leaves extract and their applications as an alternative catalytic, antioxidant, anticancer and antibacterial agents. *Adv Powder Technol*. 2020;31(10):4390-4400. https://doi.org/10.1016/j.apt.2020.09.017.
37. Liu Q, Wu F, Chen Y, Alrashood ST, Alharbi SA. Anti-human colon cancer properties of a novel chemotherapeutic supplement formulated by gold nanoparticles containing *Allium sativum* L. leaf aqueous extract and investigation of its cytotoxicity and antioxidant activities. *Arab J Chem*. 2021;14(4):103039. https://doi.org/10.1016/j.arabjc.2021.103039.
38. Jiménez Pérez ZE, Mathiyalagan R, Markus J, Kim YJ, Kang HM, Abbai R, Seo KH, Wang D, Soshnikova V, Yang DC. Ginseng-berry-mediated gold and silver nanoparticle synthesis and evaluation of their *in vitro* antioxidant, antimicrobial and cytotoxicity effects on human dermal fibroblast and murine melanoma skin cell lines. *Int J Nanomedicine*. 2017;12:709-723. https://doi.org/10.2147/IJN.S118373.
39. Ke Y, Al Aboody MS, Alturaiki W, Alsagaby SA, Alfaiz FA, Veeraraghavan VP, Mickymaray S. Photosynthesized gold nanoparticles from *Catharanthus roseus* induces caspase-mediated apoptosis in cervical cancer cells (HeLa). *Artif Cells Nanomed Biotechnol*. 2019;47(1):1938-1946. https://doi.org/10.1080/21691401.2019.1614017.
40. Chen J, Li Y, Fang G, Cao Z, Shang Y, Alfarraj S, Alharbi SA, Li J, Yang S, Duan X. Green synthesis, characterization, cytotoxicity, antioxidant and anti-human ovarian cancer activities of *Curcumae kwangsiensis* leaf aqueous extract green-synthesized gold nanoparticles. *Arab J Chem*. 2021;14(3):103000. https://doi.org/10.1016/j.arabjc.2021.103000.
41. Reyes-Becerril M, Ruvalcaba F, Sanchez V, López MG, Silva-Jara J, Hernandez-Adame L, Angulo C. Green synthesis of gold nanoparticles using *Turnera diffusa* Willd enhanced antimicrobial properties and immune response in Longfin yellowtail leukocytes. *Aquac Res*. 2021;52:3391-3402. https://doi.org/10.1111/are.15184.
42. Li. S, Al-Misned FA, El-Serehy HA, Yang L. 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. *Arab J Chem*. 2021;14(2):102931. https://doi.org/10.1016/j.arabjc.2020.102931.
43. Rajan A, Rajan AR, Philip D. *Elettaria cardamomum* seed-mediated rapid synthesis of gold nanoparticles and its biological activities. *OpenNano*. 2017;2:1-8. https://doi.org/10.1016/j.onano.2016.11.002.
44. Yun Z, Chinnathambi A, Alharbi SA, Jin Z. Biosynthesis of gold nanoparticles using *Vitex negundo* and evaluation of pro-apoptotic effect on human gastric cancer cell lines. *J Photochem Photobiol B: Biol*. 2020;203:111749. https://doi.org/10.1016/j.jphotobiol.2019.111749.
45. Umapathi A, Navya PN, Madhyastha H, Singh M, Madhyastha R, Maruyama M, Daima HK. Curcumin and isonicotinic acid hydrazide functionalized gold nanoparticles for selective anticancer action. *Colloids Surf A: Physicochem Eng Asp*. 2020;607:125484. https://doi.org/10.1016/j.colsurfa.2020.125484.
46. Hoshyar R, Khayati GR, Poorgholami M, Kaykhaii M. A novel green one-step synthesis of gold nanoparticles using crocin and their anticancer activities. *J Photochem Photobiol B*. 2016;159:237-42. https://doi.org/10.1016/j.jphotobiol.2016.03.056.
47. Singh N, Das MK, Ansari A, Mohanta D, Rajamani P. Biogenic nanosized gold particles: Physico-chemical characterization and its anticancer response against breast cancer. *Biotechnol Rep*. 2021;30:e00612. https://doi.org/10.1016/j.btre.2021.e00612.
48. Sharma B, Deswal R. Single pot synthesized gold nanoparticles using *Hippophae rhamnoides* leaf and berry extract showed shape-dependent differential nanobiotechnological applications. *Artif Cells Nanomed Biotechnol*. 2018;46(sup2):408-418. https://doi.org/10.1080/21691401.2018.1458034.
49. Pechyen C, Ponsanti K, Tangnorawich B, Ngernyuang N. Waste fruit peel – Mediated green synthesis of biocompatible gold nanoparticles. *J Mater Res Technol*. 2021;14:2982-2991. https://doi.org/10.1016/j.jmrt.2021.08.111.
50. Chang Y, Zheng C, Chinnathambi A, Alahmadi TA, Alharbi SA. Cytotoxicity, anti-acute leukemia and antioxidant properties of gold nanoparticles green-synthesized using *Cannabis sativa* L leaf aqueous extract. *Arab*

J Chem. 2021;14(4):103060. https://doi.org/10.1016/j.arabjc.2021.103060.

51. Sunderam V, Thiyagarajan D, Lawrence AV, Mohammed SSS, Selvaraj A. *In-vitro* antimicrobial and anticancer properties of green synthesized gold nanoparticles using *Anacardium occidentale* leaves extract. *Saudi J Biol Sci*. 2019;26(3):455-459. https://doi.org/10.1016/j.sjbs.2018.12.001.
52. Zhang X, Tan Z, Jia K, Zhang W, Dang M. *Rabdosia rubescens* Linn: green synthesis of gold nanoparticles and their anticancer effects against human lung cancer cells A549. *Artif Cells Nanomed Biotechnol*. 2019;47(1):2171-2178. https://doi.org/10.1080/21691401.2019.1620249.
53. Park SY, Kim B, Cui Z, Park G, Choi YW. Anti-Metastatic Effect of Gold Nanoparticle-Conjugated *Maclura tricuspidata* Extract on Human Hepatocellular Carcinoma Cells. *Int J Nanomedicine*. 2020;15:5317-5331. https://doi.org/10.2147/IJN.S246724.
54. Seetharaman P, Chandrasekaran R, Gnanasekar S, Mani I, Sivaperumal S. Biogenic gold nanoparticles synthesized using *Crescentia cujete* L. and evaluation of their different biological activities. *Biocatal Agric Biotechnol*. 2017;11:75-82. https://doi.org/10.1016/j.bcab.2017.06.004.
55. Imran M, Husseini G, Awad N, Paul V, El-Haj BM, Ali HS. An Effective Anticancer Nano-approach for Melanoma and Breast Cancers Using *Annona muricata* Gold Nanoparticles. *Acta Sci Pharm Sci*. 2021;5(9):46-54. https://doi.org/10.31080/ASPS.2021.05.0782.
56. Vemuri SK, Bangla RR, Mukherjee S, Uppula P, Gpv S, A V GR, T M. Novel biosynthesized gold nanoparticles as anticancer agents against breast cancer: Synthesis, biological evaluation, molecular modelling studies. *Mater Sci Eng C Mater Biol Appl*. 2019;99:417-429. https://doi.org/10.1016/j.msec.2019.01.123.
57. Chahardoli A, Karimi N, Fattahi A, Salimikia I. Biological applications of photosynthesized gold nanoparticles using leaf extract of *Dracocephalum kotschyi*. *J Biomed Mater Res A*. 2019;107(3):621-630. https://doi.org/10.1002/jbm.a.36578.
58. Nagalingam M, Kalpana VN, Rajeswari VD, Panneerselvam A. Biosynthesis, characterization and evaluation of bioactivities of leaf extract-mediated biocompatible gold nanoparticles from *Alternanthera bettzickiana*. *Biotechnol Rep*. 2018;19:e00268. https://doi.org/10.1016/j.btre.2018.e00268.
59. Patil MP, Bayaraa E, Subedi P, Piad LLA, Tarte NH, Kim GD. Biogenic synthesis, characterization of gold nanoparticles using *Lonicera japonica* and their anticancer activity on HeLa cells. *J Drug Deliv Sci Technol*. 2019;51:83-90. https://doi.org/10.1016/j.jddst.2019.02.021.
60. Dhayalan M, Denison MIJ, Ayyar M, Gandhi NN, Krishnan K, Abdulhadi B. Biogenic synthesis, characterization of gold and silver nanoparticles from *Coleus forskohlii* and their clinical importance. *J Photochem Photobiol B: Biol*. 2018;183:251-257. https://doi.org/10.1016/j.jphotobiol.2018.04.042.
61. Chokkalingam M, Singh P, Huo Y, Soshnikova V, Ahn S, Kang J, Mathiyalagan R, Kim YJ, Yang DC. Facile synthesis of Au and Ag nanoparticles using fruit extract of *Lycium chinense* and their anticancer activity. *J Drug Deliv Sci Technol*. 2019;49:308-315. https://doi.org/10.1016/j.jddst.2018.11.025.
62. Hamelin M, Varmira K, Veisi H. Green synthesis and characterizations of gold nanoparticles using Thyme and survey cytotoxic effect, antibacterial and antioxidant potential. *J Photochem Photobiol B*. 2018;184:71-79. https://doi.org/10.1016/j.jphotobiol.2018.05.016.
63. Boomi P, Ganesan RM, Poorani G, Gurumallesh Prabu H, Ravikumar S, Jeyakanthan J. Biological synergy of greener gold nanoparticles by using *Coleus aromaticus* leaf extract. *Mater Sci Eng C Mater Biol Appl*. 2019;99:202-210. https://doi.org/10.1016/j.msec.2019.01.105.
64. Kumar PS, Jeyalatha MV, Malathi J, Ignacimuthu S. Anticancer effects of one-pot synthesized biogenic gold nanoparticles (Mc-AuNps) against laryngeal carcinoma. *J Drug Deliv Sci Technol*. 2018;44:118-128. https://doi.org/10.1016/j.jddst.2017.12.008.
65. Balashanmugam P, Durai P, Balakumaran MD, Kalaichelvan PT. Phytosynthesized gold nanoparticles from *C. roxburghii* DC. leaf and their toxic effects on normal and cancer cell lines. *J Photochem Photobiol B: Biol*. 2016;165:163-173. https://doi.org/10.1016/j.jphotobiol.2016.10.013.
66. Balasubramanian S, Kala SMJ, Pushparaj TL. Biogenic synthesis of gold nanoparticles using *Jasminum auriculatum* leaf extract and their catalytic, antimicrobial and anticancer activities. *J Drug Deliv Sci Technol*. 2020;57:101620. https://doi.org/10.1016/j.jddst.2020.101620.
67. Godipurge SS, Yallappa S, Biradar NJ, Biradar JS, Dhananjaya BL, Hegde G, Jagadish K, Hegde G. A facile and green strategy for the synthesis of Au, Ag and Au–Ag alloy nanoparticles using aerial parts of *R. hypocrateriformis* extract and their biological evaluation. *Enzyme Microb Technol*. 2016;95:174-184. https://doi.org/10.1016/j.enzmictec.2016.08.006.
68. Vijayakumar S, Vaseeharan B, Malaikozhundan B, Gopi N, Ekambaram P, Pachaiappan R, Velusamy P, Murugan K, Benelli G, Suresh Kumar R, Suriyanarayanamoorthy M. Therapeutic effects of gold nanoparticles synthesized using *Musa paradisiaca* peel extract against multiple antibiotic-resistant Enterococcus faecalis biofilms and human lung cancer cells (A549). *Microb Pathog*. 2017;102:173-183. https://doi.org/10.1016/j.micpath.2016.11.029.
69. Naraginti S, Li Y. Preliminary investigation of catalytic, antioxidant, anticancer and bactericidal activity of green synthesized silver and gold nanoparticles using *Actinidia deliciosa*. *J Photochem Photobiol B: Biol*. 2017;170:225-234. https://doi.org/10.1016/j.jphotobiol.2017.03.023.
70. Satpathy S, Patra A, Ahirwar B, Hussain MD. Process optimization for green synthesis of gold nanoparticles mediated by extract of *Hygrophila Spinosa* T. Anders

and their biological applications. *Phys E: Low-dimens Syst Nanostructures*. 2020;121:113830. https://doi.org/10.1016/j.physe.2019.113830.

71. Karthika V, Arumugam A, Gopinath K, Kaleeswarran P, Govindarajan M, Alharbi NS, Kadaikunnan S, Khaled JM, Benelli G. *Guazuma ulmifolia* bark-synthesized Ag, Au and Ag/Au alloy nanoparticles: Photocatalytic potential, DNA/protein interactions, anticancer activity and toxicity against 14 species of microbial pathogens. *J Photochem Photobiol B: Biol*. 2017;167:189-199. https://doi.org/10.1016/j.jphotobiol.2017.01.008.
72. Sun B, Hu N, Han L, Pi Y, Gao Y, Chen K. Anticancer activity of green synthesised gold nanoparticles from *Marsdenia tenacissima* inhibits A549 cell proliferation through the apoptotic pathway. *Artif Cells Nanomed Biotechnol*. 2019;47(1):4012-4019. https://doi.org/10.1080/21691401.2019.1575844.
73. Wang L, Xu J, Yan Y, Liu H, Li F. Synthesis of gold nanoparticles from leaf *Panax notoginseng* and its anticancer activity in pancreatic cancer PANC-1 cell lines. *Artif Cells Nanomed Biotechnol*. 2019;47(1):1216-1223. https://doi.org/10.1080/21691401.2019.1593852.
74. Patil MP, Jin X, Simeon NC, Palma J, Kim D, Ngabire D, Kim NH, Tarte NH, Kim GD. Anticancer activity of *Sasa Borealis* leaf extract-mediated gold nanoparticles. *Artif Cells Nanomed Biotechnol*. 2017;46(1):82-88. https://doi.org/10.1080/21691401.2017.1293675.
75. Wu T, Duan X, Hu C, Wu C, Chen X, Huang J, Liu J, Cui S. Synthesis and characterization of gold nanoparticles from *Abies spectabilis* extract and its anticancer activity on bladder cancer T24 cells. *Artif Cells Nanomed Biotechnol*. 2019;47(1):512-523. https://doi.org/10.1080/21691401.2018.1560305.
76. Kuppusamy P, Ichwan SJA, Al-Zikri PNH, Suriyah WH Soundharrajan I, Govindan N, Maniam GP, Yusoff MM. *In Vitro* Anticancer Activity of Au, Ag Nanoparticles Synthesized Using *Commelina nudiflora* L. Aqueous Extract Against HCT-116 Colon Cancer Cells. *Biol Trace Elem Res*. 2016;173:297–305. https://doi.org/10.1007/s12011-016-0666-7.
77. Castro-Aceituno V, Abbai R, Moon SS, Ahn S, Mathiyalagan R, Kim YJ, Kim YJ, Yang DC. *Pleuropterus multiflorus* (Hasuo) mediated straightforward eco-friendly synthesis of silver, gold nanoparticles and evaluation of their anticancer activity on A549 lung cancer cell line. *Biomed Pharmacother*. 2017;93:995-1003. https://doi.org/10.1016/j.biopha.2017.07.040.
78. Divakaran D, Lakkakula JR, Thakur M, Kumawat MK, Srivastava R. Dragon fruit extract capped gold nanoparticles: Synthesis and their differential cytotoxicity effect on breast cancer cells. *Mater Lett*.2019;236:498-502. https://doi.org/10.1016/j.matlet.2018.10.156.
79. Wu F, Zhu J, Li G, Wang L, Veeraraghavan VP, Mohan SK, Zhang Q. Biologically synthesized green gold nanoparticles from *Siberian ginseng* induce growth-inhibitory effect on melanoma cells (B16). *Artif Cells Nanomed Biotechnol*. 2019;47(1):3297-3305, https://doi.org/10.1080/21691401.2019.1647224.
80. Elemike EE, Onwudiwe DC, Nundkumar N, Singh M, Iyekowa O. Green synthesis of Ag, Au and Ag-Au bimetallic nanoparticles using *Stigmaphyllon ovatum* leaf extract and their *in vitro* anticancer potential. *Mater Lett*. 2019;243:148-152. https://doi.org/10.1016/j.matlet.2019.02.049.
81. Barai AC, Paul K, Dey A, et al. Green synthesis of *Nerium oleander*-conjugated gold nanoparticles and study of its *in vitro* anticancer activity on MCF-7 cell lines and catalytic activity. *Nano Converg*. 2018;5(1):10. https://doi.org/10.1186/s40580-018-0142-5.
82. Zangeneh MM, Zangeneh A. Novel green synthesis of *Hibiscus sabdariffa* flower extract conjugated gold nanoparticles with excellent anti-acute myeloid leukemia effect in comparison to daunorubicin in a leukemic rodent model. *Appl Organometal Chem*. 2020;34:e5271. https://doi.org/10.1002/aoc.5271.
83. Wang L, Xu J, Yan Y, Liu H, Karunakaran T, Li F. Green synthesis of gold nanoparticles from *Scutellaria barbata* and its anticancer activity in pancreatic cancer cell (PANC-1). *Artif Cells Nanomed Biotechnol*. 2019;47(1):1617-1627. https://doi.org/10.1080/21691401.2019.1594862.
84. Lee YJ, Ahn EY, Park Y. Shape-dependent cytotoxicity and cellular uptake of gold nanoparticles synthesized using green tea extract. *Nanoscale Res Lett*. 2019;14:129. https://doi.org/10.1186/s11671-019-2967-1.
85. Fanoro OT, Parani S, Maluleke R, Lebepe TC, Varghese JR, Mavumengwana V, Oluwafemi OS. Facile Green, Room-Temperature Synthesis of Gold Nanoparticles Using *Combretum erythrophyllum* Leaf Extract: Antibacterial and Cell Viability Studies against Normal and Cancerous Cells. *Antibiotics.2021;10*:893. https://doi.org/10.3390/antibiotics10080893.
86. Foo YY, Periasamy V, Kiew LV, Kumar GG, Malek SNA. *Curcuma mangga*-Mediated Synthesis of Gold Nanoparticles: Characterization, Stability, Cytotoxicity and Blood Compatibility. *Nanomaterials*. 2017; 7(6):123. https://doi.org/10.3390/nano7060123.
87. Tiloke C, Phulukdaree A, Anand K, Gengan RM, Chuturgoon AA. *Moringa oleifera* Gold Nanoparticles Modulate Oncogenes, Tumor Suppressor Genes and Caspase-9 Splice Variants in A549 Cells. *J Cell Biochem*. 2016;117:2302-2314. https://doi.org/10.1002/jcb.25528.
88. Mukundan D, Mohankumar R, Vasanthakumari R. Comparative study of synthesized silver and gold nanoparticles using leaves extract of *Bauhinia tomentosa* Linn and their anticancer efficacy. *Bull Mater Sci*. 2017;40:335–344. https://doi.org/10.1007/s12034-017-1376-2.
89. Rajakumar G, Gomathi T, Abdul Rahuman A, Thiruvengadam M, Mydhili G, Kim S-H, Lee T-J, Chung I-M. Biosynthesis and Biomedical Applications of Gold Nanoparticles Using *Eclipta prostrata* Leaf Extract. *Appl Sci*. 2016;6(8):222. https://doi.org/10.3390/app6080222.

90. Ghramh HA, Khan KA, Ibrahim EH, Setzer WN. Synthesis of Gold Nanoparticles (AuNPs) Using *Ricinus communis* Leaf Ethanol Extract, Their Characterization and Biological Applications. *Nanomaterials*. 2019;9(5):765. https://doi.org/10.3390/nano9050765.
91. Singh H, Du J, Singh P, Yi TH. Ecofriendly synthesis of silver and gold nanoparticles by *Euphrasia Officinalis* leaf extract and its biomedical applications. *Artif Cells Nanomed Biotechnol*. 2017;46(6):1163-1170. https://doi.org/10.1080/21691401.2017.1362417.
92. Hemmati S, Joshi Z, Zangeneh A, Zangeneh MM. Green synthesis and chemical characterization of *Thymus vulgaris* leaf aqueous extract conjugated gold nanoparticles for the treatment of acute myeloid leukemia in comparison to doxorubicin in a leukemic mouse model. *Appl Organometal Chem*. 2020;34:e5267. https://doi.org/10.1002/aoc.5267.
93. Lee YJ, Song K, Cha S-H, Cho S, Kim YS, Park Y. Sesquiterpenoids from *Tussilago farfara* Flower Bud Extract for the Eco-Friendly Synthesis of Silver and Gold Nanoparticles Possessing Antibacterial and Anticancer Activities. *Nanomaterials*. 2019;9(6):819. https://doi.org/10.3390/nano9060819.