Frontiers in Life Sciences and Related Technologies 5(3) (2024) 231-243

Contents lists available at Dergipark

Frontiers in Life Sciences and Related Technologies

Journal homepage: http://dergipark.org.tr/en/pub/flsrt

Review article

Effect of metallic nanoparticles on cancer cell lines: A review on plant-based biosynthesis

Beyzanur Cakar*[1], Ozlem Darcansoy Iseri[2,3]

[1] *Baskent University, Faculty of Engineering, Department of Biomedical Engineering, 06790, Ankara, Türkiye*
[2] *Baskent University, Faculty of Science and Letters, Department of Molecular Biology and Genetics, 06790, Ankara, Türkiye*
[3] *Baskent University, Institute of Food, Agriculture and Livestock Development, 06790, Ankara, Türkiye*

Abstract

The green synthesis method is an environmentally friendly, cost-efficient, and safe method for the production of metallic nanoparticles (MNPs). This method mainly relies on the use of plants and microorganisms as well. While plant-based MNPs are produced via the green synthesis method, the secondary metabolites of plants have the ability to enrich some functional properties of these MNPs. As a result of this, plant-based MNPs can be cytotoxic to some cancer cell lines. This review regarding the effect of plant-based MNPs anticancer activities on various cancer cell lines provides a summary of research articles in this area. Additionally, this review reports secondary metabolites of the plants used to synthesize MNPs. The present article offers a survey of plant species used with metallic nanoparticles, focusing on their anti-cancer properties in specific cancer cell lines. The objective is to provide researchers with a broad overview, facilitating exploration of plant–metal combinations.

Keywords: *Anti-cancer; anti-proliferation; cell line; green synthesis; nanoparticles; metal*

1. Introduction

Metallic nanoparticles (MNPs) are synthesized from salts of metals in a size range of 1-100 nm. Metal and metal oxide nanoparticles have unique physical and chemical functionalities. Given their small size, MNPs can cross biological membranes and biological barriers to influence cell metabolism. They can also be used in many biomedical applications as antimicrobial or therapeutic agents for diagnostic purpose and cancer treatments. (Khan et al., 2019; Franco et al., 2022; Khursheed et al., 2022). In the literature, zinc oxide (ZnO), iron oxide (Fe_3O_4NPs), and copper oxide nanoparticles (CuONPs) are commonly used for drug and gene delivery, biosensor design, cancer diagnosis, and treatment (Sharma et al., 2014). Although many types of metals are used in biomedical fields, silver nanoparticles (AgNP) are mostly preferred (Patra et al., 2018; Akhter et al., 2024). Since AgNPs have anti-angiogenic, antimicrobial, antiviral, antioxidant, and anti-cancer properties, their use in various nanoparticle applications in biomedicine is quite common (Iqbal et al., 2019). AgNPs have cytotoxic properties on cancer cells, arrest the cell cycle, and cause DNA damage and cell death by inducing oxidative stress (Liu et al., 2016). FeNPs can be used for many purposes, such as disease diagnosis and treatment, water decontamination, and cancer treatment (Montiel Schneider et al., 2022). Gold (Au) is a naturally inert material that is spontaneously resistant to bacteria, so it is widely used in biomedical applications (Ghobashy et al., 2024). ZnO nanoparticles have proven to be anti-fungal, anti-bacterial, and anti-cancer properties, and they have been used in various drug release systems (Ozcelik, 2023; Yalcin et al., 2023). Considering these properties, the use of nanoparticles in cancer treatment stands out due to their superior properties, such as high efficiency, selectivity, sensitivity, low toxicity, biosafety, and stability. Physical and chemical methods frequently used in

* Corresponding author.
E-mail address: beyzacakar005@gmail.com (B Cakar).
https://doi.org/10.51753/flsrt.1498193 Author contributions
Received 10 June 2024; Accepted 29 October 2024
Available online 30 December 2024

nanoparticle production may require the use of high radiation, stabilizing agents, and toxic substances. Chemicals used to capture and reduce metal salts in particle formation increase free radical formation (Balmuri et al., 2017), thus increasing the toxicity of the nanoparticle. The green synthesis method has emerged as an eco-friendly alternative synthesis to existing chemical and physical methods. This method is easy to apply, cheap, fast, simple, eco-friendly, and safe since it does not contain stabilizing agents (Carrapico et al., 2023). Environmentally friendly synthesis is achieved by minimizing waste generation in green synthesis. It is also possible to produce particles with variable morphology and size by changing synthesis parameters (Gour et al., 2019). NPs can be produced by using various plants and microorganisms. However, the use of plants is more advantageous as they allow larger-scale production with faster NP synthesis. In addition, secondary metabolites of plants cover the particle during NP synthesis and provide various functions for the particle depending on the nature of the secondary metabolites. Given the fact that different plants contain different phytochemicals, the effect of the NP produced may vary, although the same metal salt is used. Concordantly, the cellular effects of synthesized MNPs can be modified and enriched.

In this review, nanoparticle production methods with a particular focus on plant-based green synthesis are explained, and the studies of the last decade examining the effects of Ag, Au, Fe, PbO, Pt, MgO, ZnO, and CeO nanoparticles, which are produced from plants by green synthesis, on cancer lines are compiled. In this context, the important contributions using plant-based synthesis are stated in detail, and their developmental aspects are presented as future perspectives in the field.

2. Production methods of metallic nanoparticles

There are top-down and bottom-up methods for MNP production. Bottom-up synthesis of NPs can be divided into three main groups: physical, chemical, and green synthesis (Fig. 1).

2.1. Physical methods

Evaporation-condensation, laser ablation, and mechanical milling are examples of physical techniques employed in synthesizing metallic nanoparticles. These physical methods typically aim to reduce bulk metals into nanoscale particles by applying high energy or mechanical forces. The evaporation-condensation process involves the application of a highly controlled vacuum to a metallic material, facilitating the evaporation of small particles that subsequently condense onto a target substrate. This method is preferred for the production of thin metallic layers (Pandey et al., 2011).

Another method is laser ablation, which is based on Cu or Ti vapor laser exposure on the metals (Al, Ag) in a liquid medium (Simakin et al., 2004). When these metal plates emit laser energy, small particles from metals break off and turn into nanoparticles (Sadrolhosseini et al., 2019). Depending on the laser parameters, the size of the nanoparticles can be changed. In addition, during long-term laser ablation, the rate of formation of new nanoparticles in the liquid medium may be reduced by saturation in the medium (Ghorbani et al., 2014).

The other method of metal nanoparticle production is the milling method. In this method, metal powders are made to be smaller particles through the use of rotating balls (Rajput et al., 2015). Although this method is cost-efficient for large-scale production, it has many disadvantages, such as high energy consumption and long processing time (Ullah et al., 2014).

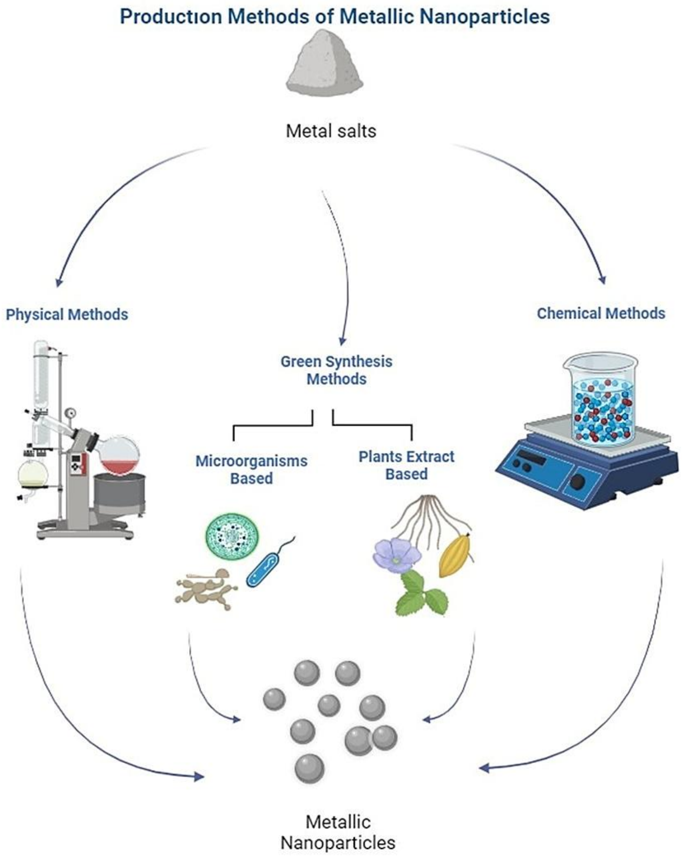

Fig. 1. Production methods of metallic nanoparticles (Created with Biorender).

In bottom-up nanoparticle production, the aforementioned methods are suitable, but these methods have some limitations such as the great deal of energy needed, high pressure, and temperature. In addition, these methods are rarely preferred for the large-scale formation of MNPs due to low production yields, high energy consumption, and cost (Dikshit et al., 2021).

2.2. Chemical methods

The most common methods to synthesize MNPs are chemical methods. In chemical methods, metal salts are reduced to metal nanoparticles by the use of some chemical agents for capping and stabilizing. In general, metal salts and chemical agents are mixed in a solvent that is toxic and corrosive during the generation of MNPs (Herlekar et al., 2014). Due to this, many chemical agents are used as reducing and capping agents, such as sodium borohydride ($NaBH_4$) (Banne et al., 2017), sodium citrate, Tollen’s reagent, N, N-dimethylformamide (DMF), and formaldehyde (Norris et al., 2010). Compared to physical methods, chemical methods are mostly used for the industrial-scale production of MNPs due to their higher production yields. However chemical methods have some limitations such as toxicity problems, environmental hazards and unsustainability. Moreover, MNPs can lead to toxic nanoparticles depending on the use of some chemicals during their production. Thus, these methods are not safe MNP synthesis methods for clinical applications (Pal et al., 2007).

2.3. Green synthesis (biosynthesis)

Nanoparticles can be used in many applications in biomedical fields. There are also some concerns about toxicity. Despite the many advantages of physical and chemical methods, there is a need for safer and more environmentally friendly methods. Green synthesis methods have a huge potential to synthesize MNPs that are safe, environmentally friendly, sustainable, thermodynamically favorable, and cost-efficient (Razavi et al., 2015). Similar to other methods, many types of metal nanoparticles, such as Au, Ag, and Fe, can be produced via green synthesis methods (Singh et al., 2018). In this method, microorganisms or plant extracts provide some biomolecules. These molecules act as reducing, capping, and stabilizing agents. The green synthesis method has many advantages, such as the minimization of waste production throughout the process and the use of non-toxic solvents. Moreover, the preparation of metallic nanoparticles by green synthesis is cheap, fast, easy, and suitable for mass production. In addition, it is possible to produce metallic nanoparticles of different sizes by optimizing some parameters (temperature, pH, and pressure). Green synthesis metal nanoparticles can be used in many different applications, such as the use of antimicrobial agents, molecular detection, labeling, and optical imaging for diagnostic or therapeutic purposes (Gade et al., 2014). Although these methods do not include toxic chemicals for green synthesis, MNPs can have cytotoxic activity on various cancer cells. Thus, depending on the inclusion of biomolecules, some green synthesis-based MNPs can be used as anticancer agents on some cancer cell lines.

2.3.1. Microorganism-based synthesis

The microorganism-based green synthesis method includes the use of bacteria, fungi, or algae in metallic nanoparticle generation. In this method, metal salts are reduced to metal ions through electron transfer by enzymes or supernatants derived from microorganisms. When metal salts become metal ions, these small molecules begin to aggregate to form metallic nanoparticles. This method is a more environmentally friendly production method compared to chemical and physical methods. However, microorganism-based methods require the culturing of microorganisms, isolation of supernatant or enzyme, and filtration of extracts. Although the production of MNPs with microorganisms is a long-term process, microorganism culture is essential for this purpose. Similar to other methods, the microorganism-based method is suitable for the production of different types of metallic nanoparticles such as Ag, Au, Fe, Ti, PbO, Pt, MgO, ZnO, and CeO, (Gade et al., 2014; Molnár et al., 2018). In this method, metal salt can directly or indirectly interact with microorganisms. Microorganisms release a special biopolymer called extracellular polymeric substances (EPS). EPSs have some functional chemical groups, such as carboxylate (-COOH), amino (-NH_2), thiol (-SH), and alcohol (-OH). During the indirect interactions, biomolecules extracted from the microorganism are added to the medium for metal salts to be reduced to metallic nanoparticles (Escárcega-González et al., 2018). These chemical groups also make metallic nanoparticles biocompatible (Jeevanandam et al., 2022). However, the direct interaction method is based on real-time interaction with metal salts and microorganisms. During these interactions, some enzymes, such as nicotinamide adenine dinucleotide (NADH), play critical roles in the formation of MNPs. Despite the advantages of this method, the mechanism of generation of MNPs may vary because of the diversity of microorganisms. Thus, it is a great challenge to optimize the size, quantity, and morphology of MNPs. For these reasons, microorganism-based synthesis methods are not suitable for large-scale production or standardized synthesis of magnetic nanoparticles (Mittal et al., 2013).

In the literature, there are various studies of the microorganism-based MNPs. Haji et al. (2022) prepared AgNPs by using silver nitrate ($AgNO_3$) and extracts of *Acinetobacter baumannii* (Haji et al., 2022). In another study, AuNPs were produced by using ($HAuCl_4{\cdot}3H_2O$). ZnONPs were also prepared by using [$Zn(CH_3COO)_2{\cdot}2H_2O$] and the supernatant of *Leuconostoc* sp. The antibacterial activity of these MNPs was investigated against biofilms formed by *Staphylococcus aureus* and *Pseudomonas aeruginosa* (Kabiri et al., 2023). Lahiri et al. (2021) prepared copper oxide nanoparticles (CuONPs) from $CuSO_4$ and *Streptomyces* sp. and evaluated their antimicrobial activity.

2.3.2. Plant extract-based synthesis

Plant-based green synthesis methods are simpler, easier, cheaper, and more useful than the other methods to produce MNPs on a large scale. Additionally, plants have various secondary metabolites for reducing metal salts to metal nanoparticles. These metabolites, such as steroids, saponins, carbohydrates, and flavonoids, which are called phytochemical molecules, act as reducing and capping agents during the formation of MNPs. Plant-based green synthesis methods also have more advantages than microorganism-based methods. The microorganism-based methods additionally require cell culture and cell extraction compared to the plant-based methods. As a result of this, whole extracts from plants (leaf, fruit, roots, etc.) can be used directly and are easier and cheaper to produce compared to the other methods. In the literature, many researches have been reported on the generation of MNPs using plant extracts. Similar to microorganism-based methods, particle size can be optimized by controlling parameters such as temperature and pH (Pal et al., 2019). Although both methods are environmentally friendly, plant-based methods require less energy and are faster to produce MNPs. In plant-based methods, the plant extracts and metal salts are mixed directly, and metal salts are reduced to MNPs during the process. MNPs gain functionality by phytochemicals from plants. Thus, it is possible to produce MNPs in one step. In the production of green synthesis of MNPs, plant tissues such as roots, leaves, fruits, and flowers are homogenized and mixed with metal precursor solutions (Mittal et al., 2013). The plant tissue to be used for nanoparticle synthesis is sequentially cleaned, mixed, boiled, and filtered to prepare the plant extract. This extract is then added to a solution containing metal salts (Nguyen et al., 2023). The most important feature of MNP production from plant extract is the reduction of metal salts of secondary metabolites (ketones, aldehydes, flavones, phenolic acids, amides, sugars, ketones, carboxylic acids, terpenoids, etc.) in plant extracts to MNPs while giving particles unique properties at the same time (Ovais et al., 2018). When plant extract is used in NP production, the secondary metabolites and plant-derived phytochemical agents surround the nanoparticle and give it various functions, such as anti-microbial and anti-cancer activities.

The percentage distribution of studies on AgNP, CuONP, PtNP, ZnONP, AuNP, PbO NP, and CeO_2 MNPs, based on 20 articles sourced from Scopus, PUBMED, Springer, and MDPI databases can be seen in Fig. 2. These studies were selected according to the inclusion and exclusion criteria considered during the preparation of this review. The graph aims to provide readers with a projection of the distribution of green-synthesized MNPs, produced from plant extracts and investigated for their anticancer activity over the last 10 years. Categorizing nanoparticle types offers a broad projection of the relevant literature (Vijayakumar et al., 2023; Batool et al., 2024; Muslim and Naji, 2024; Ullah et al., 2024).

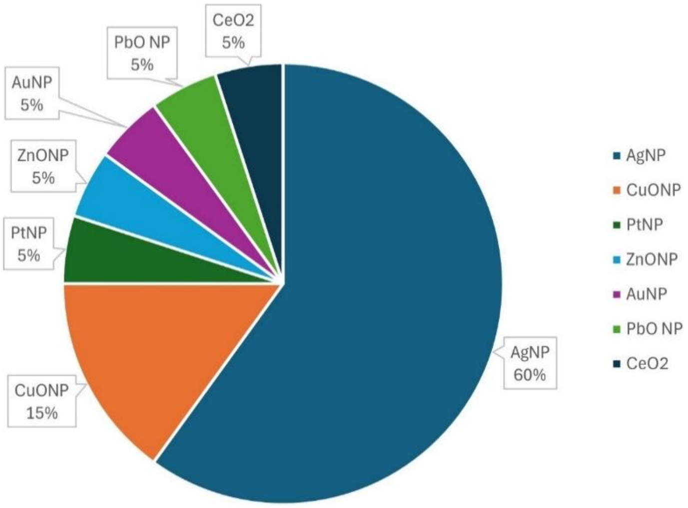

Fig. 2. The distribution of metal nanoparticles prepared by the green synthesis method in the literature. It was prepared on the basis of metal and metal oxide nanoparticles listed in Table 2. In accordance, the corresponding references are listed in Table 2.

The plants used for particle production, the secondary metabolites contained in these plants, and the studied biological effects are summarized in Table 1. Plant-based MNPs can acquire anticancer, antibacterial, antimicrobial, anti-arthritic, or antioxidant activities through the functional molecules derived from the plants they interact with during synthesis. These molecules enhance the properties and functionality of the nanoparticles, enabling them to exhibit various biological effects. The phytochemicals present in plant extracts are essential components that support the potential applications of these nanoparticles. Given this, plant-based MNPs can play a promising role in the treatment and prevention of various diseases (Demir et al., 2024; Grancharova et al., 2024; Revathi et ai., 2024).

According to Table 1, walnut fruit is especially rich in polyphenols, and it has been shown that polyphenol has a selective cytotoxic effect on cancer cells (Arulvasu et al., 2010; Dai and Mumper, 2010). In the literature, it has been reported that in research on *Punica granatum,* which contains flavonoids and tannins, these molecules' anti-cancer activities were shown on breast cancer cell lines (Moga et al., 2021). Another study reported the antimicrobial, anticancer, antidiabetic, and anti-inflammatory activities of *Saussurea costus,* which contains tannin and alkaloid derivatives (Singh et al., 2018). Salehi et al. (2016) demonstrated the induction of apoptotic pathways of cancer cell lines by using an extract that contains phenolic acid and flavonoids. In another research, the anti-inflammatory, anti-microbial, anti-fungal, anti-cancer, anti-arthritic, and anti-proliferative activities of *Curcuma wenyujin*, which contains terpenoid derivatives, were investigated. Its anti-cancer activities on many cancer cell lines, such as gastritis, prostate, ovarian, and uterine were also evaluated. *C. wenyujin* extract showed cytotoxic activity when applied to various cancer cell lines (Manzan et al., 2003; Zhou et al., 2014). Takemoto et al. (1983) demonstrated the anti-viral, anti-cancer, anti-diabetic, and anti-allergenic activities of *Glycyrrhiza glabra* (Liquorice), which is rich in flavonoid chalcone, isoflavone, and flavonols. In the literature, there is much research on ginseng extract. Ginseng's anti-proliferative activities have been shown on myeloma and HeLa cell lines (Davydov and Krikorian, 2000; Yesil-Celiktas et al., 2010). *Camellia sinensis* has anti-cancer, anxiolytic, anti-diabetic, anti-obesity, anti-inflammatory, analgesic, antipyretic, cytotoxic, and apoptogenic activities (Johnson 2011). It has many secondary metabolites, which are terpenoids, proanthocyanidins, and other phenolic compounds, flavones, and catechins. In another study, researchers evaluated the anti-proliferative and anti-cancer activities of rosemary extract on colon, pancreatic, and breast cancer cell lines. It is enriched in flavonoids, carnocytic acid, rosmarinic acid, and ursolic acid (Gutiérrez and Perez 2004; Movahedi et al., 2014).

In another study, *Raphanus sativus* (Longipinnatus), rich in flavonoids, and phenolics was reported to have anti-tumor activity (Gutiérrez and Perez 2004). The extract of *Teucrium polium*, which contains high levels of diterpenoids, flavonoids, iridoids, sterols, and terpenoids, was applied to cancer cell lines and displayed anti-cancer activity (Nematollahi-Mahani et al., 2007; Movahedi et al., 2014). Another plant, *Commiphora wightii* also has anti-microbial, anti-cancer, and anti-inflammatory activities due to the fact that it contains terpenoids and flavonoids. *C. wightii* has been confirmed to have anti-cancer activities. (Bhardwaj and Alia, 2019). *Mangifera indica* is rich in mangiferin and acts as an anti-oxidant, anti-bacterial, anti-fungal, anti-inflammatory, anti-allergic, and anti-cancer (Pattanayak 2013). *Rehmanniae radix* also has anti-inflammatory, anti-arthritic, anti-apoptotic, anti-cancer, and antioxidant activities. Its anti-cancer activities were shown on cervical cancer cells (Kim et al., 2006; Xia et al., 2019). Additionally, *Curcumae kwangsiensis* consists of steroids, saponin, tannin, terpenoids, alkaloids, glycoside, phenolic compounds, and flavonoids. *C. kwangsiensis* has anti-parasitic, anti-fungal, anti-viral, anti-bacterial, antioxidant, hypoglycemic, anti-diabetic, neuroprotective, and analgesic properties (Chen et al., 2021). In Chinese traditional medicine, *C. kwangsiensis* folium has been used in the treatment of ovarian cancer (Ebell et al., 2016). Anti-diabetic, anti-spasmodic, and anti-inflammatory properties of *Prosopis farcta* extracts, which mainly contain tannin, tryptamine, quercetin, and apigenin, have been described in studies (Asadollahi et al., 2010). Interestingly, *Scutellaria barbata* has been known as the magic herb that protects life in Asian societies. The cytotoxicity of *S. barbata* extract on various cancer cell lines has been studied so far (Lee et al., 2017; Suh et al., 2007; Marconett, et al., 2010; Chen et al., 2017; Kan et al., 2017; Yang et al., 2017; Zhang et al., 2017).

3. Effects of metallic nanoparticles on cancer cell lines

Cancer cell lines originate from cancerous tissue and are considered *in vitro* experimental models to test the cellular effects of natural and synthetic compounds as well as biomaterials. Anti-carcinogenic activity of any test agent depends on its ability to inhibit cancer cell proliferation, cancer cell migration, invasion, and angiogenesis, induce apoptosis and/or autophagy, and modulate the cell cycle and metabolism

Table 1
Plants used in the green synthesis of metallic nanoparticles and their bioactive compounds.

Plants	Plant Part	Bioactive compounds	Bioactivity	Reference
Adansonia digitata	fruit	terpenoids, flavonoids, sterol	*A. digitata* has analgesic and antipyretic, anti-inflammatory, antioxidant activity and antiviral activities.	(Kamatou et al., 2011)
Artemisia turcomanica	leaves	phenolic acid, flavonoid, alkaloid, terpenoid	*Artemisia turcomanica* has been shown to have a cytotoxic effect by inducing apoptosis in AGS cell line.	(Salehi et al., 2016)
Barleria buxifolia	leaves	alkaloids, terpenoids, triterpenoids, esters, aliphatic ketones, β-carotene	*B. buxifolia* extract demonstrates antioxidant, anti-bacterial, and anti-biofilm activities. These properties indicate its potential for protecting against oxidative stress, combating bacterial infections, and inhibiting the formation of biofilms.	(Sekar et al., 2022)
Camellia sinensis	leaves	terpenoid, phenolic compound, purine and alkaloid	*Camellia sinensis* has proven anti-cancer, anti-diabetic, anti-inflammatory and apoptogenic properties.	(Sharangi, 2009)
Centratherum anthelminticum	seed	phytochemicals, tetrahydroxy chalcone, tetrahydroxy flavone	*C. anthelminticum* has shown antioxidant and anti-proliferative effects in cancer cells.	(Lambertini et al., 2004; Qureshi et al., 2016)
Commiphora wightii	leaves	terpenoids, flavonoids, steroids, carbohydrates, sterols,	The anti-cancer and anti-inflammatory activities of *C. wightii* extract has been proven.	(Bhardwa and Alia, 2019)
Curcumae kwangsiensis	leaves	saponin, tannin, terpenoid, alkaloids, phenolic compound flavonoid	The successful effect of *C. kwangsiensis* extract in the treatment of ovarian cancer has been demonstrated.	(Sacchetti et al., 2005; Ebell et al., 2016)
Curcuma wenyujin	rhizome, stem	terpenoids and sesquiterpene derivatives	The anti-cancer properties of C. *wenyujin* have previously been demonstrated in gastritis, prostate, ovarian and uterine cancers.	(Zhou et al., 2014; Manzan et al., 2003)
Eclipta alba	leaves	coumestan, wedelolactone, desmethylwedelolactone, sitosterol	*E. alba* has anti-fungal, anti-bacterial, analgesic, anti-hepatotoxic, immunomodulatory, and antioxidant activities.	(Gupta et al., 2011)
Eleutherococcus senticosus (Siberian ginseng*)*	stem	Triterpenoidal saponins and phenylpropane derivatives	Ginseng extract has been shown to inhibit cancer cell growth when applied directly to myeloma (B-16) and Hela (S-3) cell lines.	(Takemoto et al., 1983; Davydov and Krikorian, 2000)
Glycyrrhzia glabra (Liquorice)	roots	flavonoid chalcon, isoflavone, flavonol,	Liquorice extract is antiviral, anti-cancer, anti-diabetic and has anti-allergenic activity.	(Pandian et al., 2017)
Jacobaea maritima	leaves	flavonoids, triterpenoids	*J. maritima* exhibits anti-cancer and anti-bacterial effects, highlighting its potential as a therapeutic agent in inhibiting cancer cell growth and combating bacterial infections.	(Grace and Khattab 1998; Althubiti et al.,2023)
Juglans regia (Walnut)	peeled walnut	polyphenol	Many studies have proven that polyphenol is safe against healthy cells and shows cytotoxicity against cancer cells.	(Dai and Mumper, 2010; Pandian et al., 2017)
Mangifera indica	leaves	mangiferin	*Mangifera indica* has been shown that high magniferin content of *M. indica* has anti-bacterial, anti-fungal, anti-viral, anti-inflammatory, and anti-cancer properties.	(Pattanayak and Nayak, 2013)
Moringa peregrina	leaves	flavonoids	*M. peregrina* has antioxidant, anti-microbial, anti-diabetic, anti-spasmodic, hypertension, hepatotoxicity, anti-inflammatory, anti-cancer properties	(Senthilkumar et al., 2018)
Ocimum sanctum	leaves	saponins, flavonoids, triterpenoids, and tannins	*O. sanctum* demonstrates anti-cancer activity by reducing tumor volume in fibrosarcoma tumors.	(Jaggi et al.,2003; Pattanayak et al.,2010)
Prosopis farcta	fruits	tannin, tryptamine, quercetin and apigenin	The anti-diabetic, anti-spasmodic and anti-inflammatory properties of *P. farcta* have been demonstrated.	(Asadollahi et al., 2010)
Punica granatum	crusts	flavonoid, tannin	*P. granatum* has been shown to have cytotoxic activity in the human breast cancer cell line.	(Arulvasu et al., 2010)
Raphanus sativus var. longipinnatus	leaves	flavanoid, phenol, alkaloid	Anti-tumor activity of *R. sativus var. longipinnatus* extract has been demonstrated.	(Gutiérrez and Perez, 2004)
Rehmanniae radix	roots	iridoid glycosides, phenylethanoid glycosides, monoterpenoidand triterpenes	In Hela cells, it was observed that *R. radix* extract increased apoptosis by increasing *Fas* expression.	(Xia et al., 2019; Kim et al., 2006)
Rhus coriaria	fruit	phenolic acids, favonoids, and tannins	*R. coriaria has* anti-cancer, antioxidant, anti-microbial, anti-infamматory, anti-fungal, hypoglycemic,	(Sakhr and El Khatib 2020; Elagbar et al.,

			hypolipidemic, neuroprotective, and anti-atherogenic properties	2020; Alsamri et al., 2021)
Rosmarinus officinalis (Rosemary)	leaves	flavonoid compounds carnosic acid, rosmarinic acid, and ursolic acid	Rosemary extract has been shown to have anti-proliferative properties on colon pancreatic and breast cancer cell lines. Carnasol causes the release of apoptosis-related proteins in cancer cells.	(Yesil-Celiktas et al., 2010; Gutiérrez and Perez, 2004)
Saussurea costus	roots	sesquiterpens, alkaloids, triterpenes, lignans, tannins	The anti-microbial, anti-cancer, anti-diabetic and anti-inflammatory properties of *S. costus* have been described in previous studies.	(Singh et al., 2018)
Scutellaria barbata	aqueous extract of the whole plant	flavonoid, alkaloid and saccharide	*S. barbata* extract has been shown to have anti-tumor activity on breast cancer, colorectal cancer, hepatocarcinoma, skin cancer, and ovarian and lung cancer.	(Marconett et al., 2010; Liu et al.,2015; Zhang et al., 2017)
Solanum lycopersicum	fruit	flavonoids	*S. lycopersicum* has anti-cancer, anti-microbial, anti-mutagenic, anti-inflammatory, anti-neurodegeneration, anti-platelet activities.	(Mousa et al., 2023).
Tectona grandis	leaves	terpenoids, apocarotenoids, phenolic compounds, flavonoids steroids/saponin	*T. grandis* exhibits significant antioxidant, anti-inflammatory, cytotoxic, analgesic, hypoglycemic, wound healing, and anti-plasmodial activities. These properties suggest its potential for therapeutic applications in managing oxidative stress, inflammation, cancer, pain, diabetes, wound healing, and malaria.	(Vyas et al., 2019)
Teucrium polium	leaves	diterpenoids, flavonoids, iridoids, sterols, and terpenoids	*T. polium* extract showed anti-tumor activity by inhibiting proliferation and colonization in BT20 breast cancer, DU145 prostate and A549 lung cancer cell line and MCF-7 cell line.	(Movahedi et al., 2014; Nematollahi-Mahani; 2007).
Zingiber officinale (Ginger)	roots	polyphenols, flavones, isoflavones, flavonoids, anthocyanins, coumarins, lignans, catechins, and isocatechins	Ginger has been confirmed to have anticancer activity against many types of cancer.	(Mukjerjee and Karati, 2022; Alkhathlan et al., 2021; Plengsuriyakarn et al., 2012; Khdary et al., 2023; Osman et al., 2020; Nachvak et al., 2023)

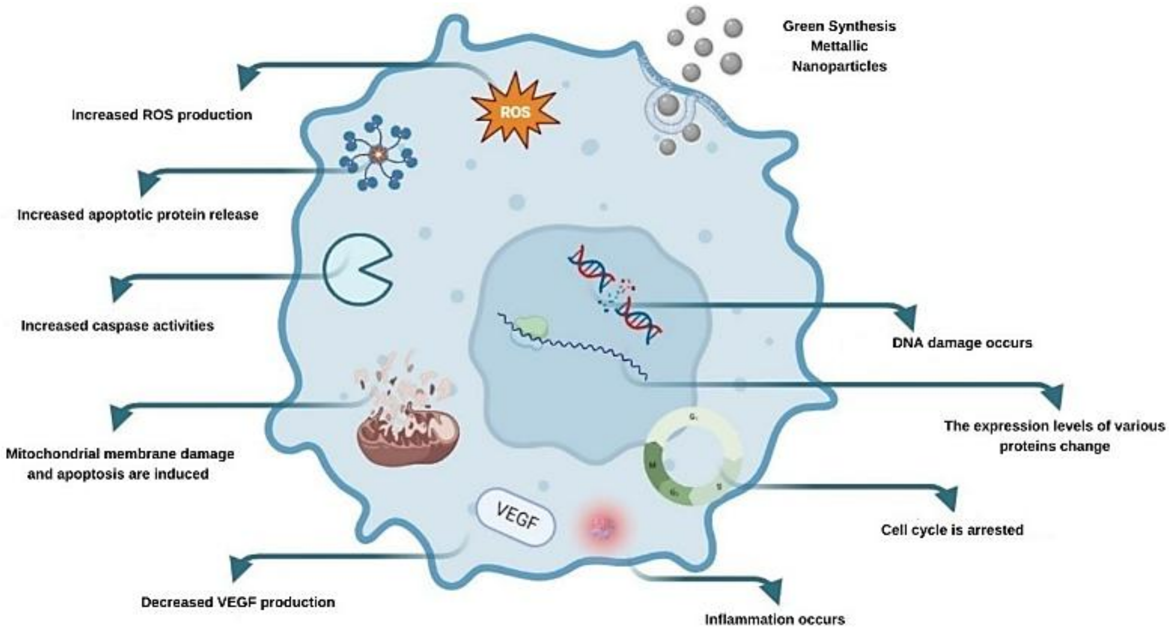

Fig. 3. The mechanism of actions of green-synthesized metal nanoparticles on cancer cells (Created with Biorender).

and ECM remodeling (Mehrotra et al., 2024; Perumal et al., 2024; Ramya et al., 2024). These effects are caused by direct interaction of the agent with cellular components and biomolecules, which inhibit biomolecule function or deregulate critical survival and apoptotic pathways, epigenetic gene regulatory effects, formation of free radicals inducing oxidative damage, or altered membrane fluidity. However, conclusions for therapeutic potentials should be drawn based on comparative studies on normal cells (Gharari et al., 2023; Ullah et al., 2024). In this context, if a nanoparticle is claimed to have anti-cancer activity, cancer cell lines serve as good, fast, and easy models to test cellular effects at molecular and biochemical levels upon direct application, which is also concordant with recent regulations on animal testing. 947 human cancer cell lines of 36

Table 2
Use of metallic nanoparticles produced by green synthesis method on various cancer cell lines.

MNP	Cell Line Tested	Plant	Bioactivity	Reference
AgNP	MCF-7 (breast cancer cells), L-929 (fibroblast cell line)	*Juglans regia*	AgNP showed cytotoxic effects in cancer cells compared to normal cells.	(Khorrami et al., 2018)
AgNP	MDA-MB-2 (Triple-negative breast cancer)	*Eclipta alba*	AgNPs exhibited higher anti-cancer activity on MDA-MB-2	(Mani et al., 2023).
AgNP	MCF-7, HeLa (cervical), HepG2 (liver), cell lines and L-929 (fibroblast cell line)	*Barleria buxifolia*	AgNPs exhibited anti-cancer activity on cancer cell lines but did not show cytotoxic effects against normal human cells	(Sekar et al., 2022)
AgNP	HTC116, HT29 cell line (human colon cancer cell lines**)**	*Zingiber officinale* (Ginger)	AgNPs demonstrated anti-cancer activity.	(Shanmugam et al., 2022; Alkhathlan et al., 2021;)
AgNP	HepG2 (human liver cancer cell lines)	*Tectona grandis*	AgNPs exhibited cytotoxic effects on cancer cell line.	(Younis et al., 2023)
AgNP	MCF-7, Caco-2 (colorectal cancer cell lines)	*Moringa peregrina*	AgNPs showed potential as a good anti-cancer agent.	(Al Baloushi et al., 2024)
AgNP	MCF-7, A-549) (lung cancer cell lines.	*Jacobaea maritima*	AgNPs exhibited cytotoxic effects on cancer cells.	(Althubiti et al., 2023)
AgNP	SW480 and HCT116 cell lines	*Adansonia digitata*	AgNPs exhibited cytotoxic effects on cancer cells.	(Almukaynizi et al., 2022)
AgNP	MDA-MB-231 (triple-negative breast cancer cell line)	*Centratherum anthelminticum*	AgNPs demonstrated anti-cancer activity by increasing cell death.	(Husain et al., 2020)
AgNP	AGS (gastric cancer cell line), L-929 (fibroblast cell line)	*Artemisia turcomanica*	AgNP plant-derived anti-proliferation property was concentration dependent. Apoptosis was induced rather than necrosis in AGS cells.	(Mousavi et al., 2018)
AgNP	MNK45 (human gastric cancer cell line)	*Teucrium polium*	AgNPs induced mitochondrial apoptosis in cancer cells by generating ROS.	(Hashemi et al., 2020)
AgNP	MCF-7, 3T3-L1 (embryonic cells)	*Commiphora wightii*	AgNPs induced apoptosis through DNA fragmentation by arresting the cell cycle in the G2M phase in the MCF-7 cell line.	(Malik et al., 2020)
AgNP AuNP	MCF-7, HaCaT (human keratinocyte cell line)	*Eleutherococcus senticosus* (*Siberian ginseng*)	AuNPs did not have any cytotoxic effect on cell lines. Therefore, AgNPs could be used therapeutically in breast cancer given their cytotoxic effect.	(Abbai et al., 2016)
AuNP	A498 (renal cancer cell lines), Sw-156	*Curcuma wenyujin*	AuNPs increased mitochondrial membrane permeability by generating ROS in A-498 cell line. AuNPs activated pro-apoptotic proteins and inhibited anti-apoptotic proteins.	(Liu et al., 2019)
AuNP	MCF-7, HEP-G2 (human liver cancer cell line)	*Glycyrrhzia glabra*	In the morphological analyzes, it was determined that AuNPs led cancer cells to apoptosis.	(Al-Radadi, 2021)
AuNP	HUVEC, Human HL60/vcr, 32D-FLT3-ITD, Murine C1498	*Camellia sinensis*	AuNPs did not show cytotoxic effect in HUVECs. AuNPs could be used in the treatment of acute myeloid leukemia.	(Ahmeda et al., 2020)
AuNP	PA-1, SW-626, SK-OV-3, HUVEC	*Curcumae kwangsiensis*	Dose-dependently, AuNPs inhibited growth in cancer cell lines.	(Chen et al., 2021)
AuNP	PANC-1 (pancreatic cancer cell)	*Scutellaria barbata*	Nps showed anti-cancer activity by increasing intracellular ROS production in PANC-1 cell line.	(Wang et al., 2019)
AgNP CuNP	human T-cell lymphoma (Jurkat) cell line.	*Ocimum sanctum*	AgNPs and CuNPs had anti-cancer activity.	(Ashokkumar et al., 2024)
CuONP	MCF-7, HCT-116, and HEK-293 cell lines	*Juglans regia* (*walnut*)	CuONPs demonstrated anti-cancer activity against breast and colon cancers.	(Abdollahzadeh et al., 2024)
CuONP	MCF-7 and normal NIH/3T3 cells.	*Moringa peregrina*	CuONPs exhibited cytotoxic activity against the MCF-7 cell line.	(Barani et al., 2024)
FeNP	4T1 (breast cancer cell line), C26 (colon carcinoma cell lines)	*Rosmarinus officinalis* (Rosemary)	The cytotoxicity of Rosemary-FeNP was higher than that of rosemary extract. Rosemary-FeNPs induced mitochondrial pathway apoptosis by down-regulating the anti-apoptotic protein BCL-2.	(Ahmeda et al., 2020)
MgO	MCF-7	*Saussurea costus*	MgONPs increased ROS generation and induced apoptosis by creating oxidative stress in MCF-7 cells.	(Malik et al., 2020)
CeO_2NP PbONP	HT-29 (colon cancer cell lines)	*Prosopis farcta*	PbO NPs were more cytotoxic than CeO_2 NPs. CeO_2 NPs could be used as a potential agent, especially for drug delivery systems.	(Nazaripour et al., 2021)
PtNP	MCF-7	*Punica granatum*	PtNPs induced apoptosis by arresting the cell cycle in the G0/G1 phase, increased oxidative stress and caused DNA damage.	(Sahin et al., 2018)

ZnONP	MCF-7, MDA-MB-231 cell lines	*Rhus coriaria*	ZnO NPs exhibited dose-dependent anti-cancer activity in both cancer cell lines.	(Mongy and Shalaby 2024)
ZnONP	A549 (lung cancer cells)	*Raphanus sativus var. longipinnatus*	Compounds in *R. sativus var. longipinnatus* extract increased the anti-cancer properties of ZnONP by targeting cancer-related proteins in the cell.	(Umamaheswari et al., 2021)
ZnONP	A549 (lung cancer cells)	*Mangifera indica*	NPs penetrated the membrane through ion channels and interacted with intracellular proteins.	(Rajeshkumar et al., 2018)
ZnONP	MG-63 (bone cancer cells)	*Rehmanniae radix*	Increased ROS caused apoptosis via the mitochondrial pathway.	(Cruz et al., 2020)

tumor types (Cancer Cell Line Encyclopedia (CCLE)) having the genomic diversity of their respective cancers and demonstrating the metabolic profiling and hormonal response status of the tumor microenvironment from which they were derived served as useful systems for medical research (Mirabelli et al., 2019). Additionally, HUVEC (human endothelial cell line), L-929 (normal fibroblast cell line), and 3T3-L1 (embryonic cell line) were used to evaluate the effect of particles on normal cells compared to cancer cells.

Various metal salts are selected due to their properties and reduced to MNPs with the determined plant extract. The mechanism of action of green-synthesized MNPs on cancer cells varies (Fig. 3). Nanoparticles tend to accumulate in cancer cells more than in healthy cells. Considering the side effects of traditional chemotherapy applications, the use of NPs with anti-cancer activity for therapeutic purposes has many advantages. MNPs can cross the cell membrane, induce free radical formation, conjugate with DNA, or cause cell death by affecting cell enzymes and transcription processes (Moghaddam et al., 2024; Shochah et al., 2024). In this context, both the anti-cancer activity of the metals selected for NP production and the plant-derived cytotoxic activity used in the production of green synthesis become critical. For example, AgNP are quite unique due to their diverse bioactivity spectrum with antioxidant, anti-fungal, anti-inflammatory, anti-viral, anti-angiogenic, and anti-microbial properties. Moreover, many studies have shown that MgONP have a cytotoxic effect on cancer cells. Studies on gold nanoparticles have demonstrated anti-cancer properties, and it has been stated that AuNPs can be used as a potential therapeutic agent in cancer treatment. Similarly, ZnONP have been shown to have anti-fungal, anti-bacterial, and anti-cancer activities and have been studied on various cancer cell lines due to their cytotoxic effects (Yalcin et al., 2020; Karahan et al., 2023; Genc and Celik, 2024).

Table 2 summarizes the MNPs produced, plants used for the biosynthesis process, and the test cell lines. Studies of the last decade are exemplified in this review. In a study conducted by Abdollahzadeh et al. (2024) copper(II) nitrate hexahydrate [$(Cu(NO_3)_2 \cdot 6H_2O)$] was mixed with walnut shell powder to synthesize CuONPs. These nanoparticles were then applied to different concentrations in MCF-7, HCT-116, and HEK-293 cell lines. According to the results, the anti-cancer activities of CuONPs are dependent on the particle size and have been reported anti-cancer activities on breast and colon cancer. Mongy and Shalaby prepared ZnONPs using *Rhus coriaria* fruit extract and zinc acetate dihydrate [$Zn(C_2H_3O_2)_2 \cdot 2H_2O$] and they investigated the anti-cancer activity of the particles on MCF-7 and MDA-MB-231 cell lines. They demonstrated that ZnONPs have dose-dependent anticancer activity through cell cycle arrest in the S phase (Mongy and Shalaby, 2024). In a similar study, AgNPs were prepared by mixing them with $AgNO_3$ and the plant *Eclipta alba*. When comparing between direct *plant* extract and AgNPs application, nanoparticles have been reported to have higher anti-cancer activities on triple-negative breast cancer (MDA-MB-2) cell lines (Mani et al., 2023). In another study, AgNPs were synthesized by using leaves of *Barleria buxifolia*, and nanoparticles were treated on human breast cancer (MCF-7), cervical (HeLa), and liver (HepG2) cell lines and fibroblast cells (L929). AgNPs showed selective anticancer activity on cancer cell lines (Sekar et al., 2022). Mousa et al. (2023) prepared ZnO nanoparticles using *Solanum lycopersicum* (tomato) extract and nanoparticles exhibited anti-cancer activity on ovarian cancer cell line (SKOV3). In another study, CuOMNPs were synthesized using *Moringa peregrina* leaf extracts and have been investigated for their anti-cancer activities on MCF-7 cell lines and normal NIH/3T3 cells. According to the results, nanoparticles have anti-cancer activities on cancer cells selectively (Barani et al., 2024). Ginger's anti-cancer activities have been demonstrated in previous studies so ginger-based green synthesis of AgNPs showed cytotoxicity on cancer cell lines (Alkhathlan et al., 2021; Shanmugam et al., 2022). Younis et al. (2023) prepared AgNPs from *Tectona grandis* leaf extract and reported cytotoxicity on the HepG2 cancer cell line via the induction of reactive oxygen species (ROS) generation. In another research, the anti-cancer activities of AgNPs produced from *Moringa peregrina* leaf extract were investigated on breast (MCF-7) and colon (Caco-2) cancer cell lines and demonstrated anti-cancer activities on cancer cells (Al Baloushi et al., 2024). Similarly, AgNPs synthesized from *Jacobaea maritima* leaves have been utilized in the treatment of breast cancer (MCF-7) and lung cancer (A-549) cell lines. According to the result, AgNPs exhibited cytotoxic activities on both cell lines with different inhibitory concentrations (IC_{50}) values, which were 1.37 $\mu g\ mL^{-1}$ for the MCF-7 cell line and 1.98 $\mu g\ mL^{-1}$ for the A-549 cell line (Althubiti et al., 2023). Almukaynizi et al. (2022) applied AgNPs produced from *Adansonia digitata* fruit via green synthesis on SW480 and HCT116 cell lines and demonstrated the effects of cell inhibition on cancer cells. AgNPs were also synthesized using *Centratherum anthelminticum* seed extract, and the resulting nanoparticles exhibited anti-cancer activity on the MDA-MB-231cell line by inducing apoptosis (Husain et al., 2020). Ashokkumar et al. (2024) prepared AgNPs and CuNPs using *Ocimum sanctum* leaves. AgNPs and CuNPs were applied at different concentrations on the human T-cell lymphoma (Jurkat) cell line, and synthesized nanoparticles showed anti-cancer activity at all concentrations.

In another study, Khorrami et al. (2018) prepared AgNPs using walnut extract and they applied AgNPs and direct walnut extract to MCF-7 breast cancer and L-929 fibroblast cell lines. When AgNPs and walnut extract at different concentrations (10-60 $\mu g\ mL^{-1}$) were treated on cancer cell lines, AgNPs were found to be more cytotoxic on MCF-7 cells than direct walnut extract. Additionally, green synthesized platinum nanoparticles (PtNPs) prepared from *Punica granutum* extract were applied to MCF-7 cells at different concentrations (2.5, 5, 10, 20, 40, and 50 µg mL^{-1}), and cell death was induced by PtNPs (Sahin et al., 2018). Amina et al. synthesized MgONPs using *Saussurea costus* extract and they compared the cytotoxic activities of MgONPs and paclitaxel on MCF-7 cells. The results demonstrated that MgONP applied cell death rate was 84.3% compared to the 65.4% cell death rate of the paclitaxel-applied group at the same concentration (Amina et al., 2020). In another study, the anti-cancer activities of green synthesized AgNPs from *Artemisia turcomanica* and commercial AgNPs were compared on AGS (human gastritis adenocarcinoma cell line) and L-929 at different concentrations (3,5, 12.5, 25, 50, and 100 µg mL^{-1}). When comparing the cytotoxic effects of green synthesized AgNPs at different concentrations, the AGS cell line showed higher anti-cancer activity compared to L-929 cells (Mousavi et al., 2018).

AuNPs were produced from *Curcuma wenyujin* extract and tested on A498 renal cancer and SW-156 human kidney-derived cell lines. AuNPs were applied to cell lines at concentrations of 5, 10, 25, 30, 40, and 50 µg mL^{-1}. AuNPs activated pro-apoptotic proteins and inhibited anti-apoptotic proteins in the A498 cell line. Mitochondrial membrane damage increased 2-fold at 50 µg mL^{-1} AuNP application in comparison to 25 µg mL^{-1}. In addition, caspase9 and caspase3 activities also increased when AuNP application was increased to 50 µg mL^{-1} from 25 µg mL^{-1}. In another study, AuNPs were produced from *Glycyrrhiza glabra* extract (Al-Radadi, 2021). AuNPs' anti-cancer activity was evaluated on MCF-7 and HepG2 human liver cancer cell line at a concentration range of 0-500 µg mL^{-1}. AuNP application caused concentration-dependent inhibition of cell growth, and IC_{50} of the AuNPs were found to be 50 µg mL^{-1} and 23 µg mL^{-1} on MCF-7 and HepG2 cells, respectively.

In a study, both AgNP and AuNP were produced using *Siberian Ginseng*, and their bioactivities were tested on MCF-7 and HaCa-T human keratinocyte cell lines. Interestingly, AuNPs did not exert cytotoxic effects on both cell lines, even at 100 µg mL^{-1} concentration. On the other hand, the concentration-dependent cytotoxic effect of AgNPs on both cell lines was demonstrated. 100 µg mL^{-1} AgNP reduced the cell viability of MCF-7 cells by 50%, whereas it caused a 30% reduction in cell viability of HecaT cells. The possiblee application of AuNPs in the drug release of anti-cancer agents was further discussed (Abbai et al., 2016). In another study by which AuNP was produced from *Camellia sinensis* extract, the effectiveness of the particles was tested on C1498 murine acute myeloid leukemia cell line, incristine resistant acute promyleocytic leukemia (HL-60/VCR), 32D-FLT3-ITD (32D cells with FMS-like tyrosine kinase 3-internal tandem duplication mutation), and human normal endothelial (HUVEC) cell lines. Gold salt, daunorubicin, green synthesized AuNP, and *C. sinesis* extract were applied to cells separately in 1-1000 µg mL^{-1}. Each treatment decreased cell viability in a concentration-dependent manner. IC_{50} values of gold salt, plant extract, AuNP, and daunorubicin on the murine C1498 cell line were determined as 698, 389, 158, and 129 µg mL^{-1}, respectively. The cytotoxic effect of green synthesized AuNP was comparable to the chemotherapeutic drug daunorubicin. AuNPs also exerted concentration-dependent cytotoxicity on HL-60/VCR and 32D-FLT-ITD cell lines whereas they did not show any effect on the HUVEC cell line. The bioactivities of the FeNPs synthesized from rosemary plant extract, the rosemary extract, and the green synthesis FeNPs were investigated on 4T1 breast and C26 colon carcinoma cell lines in a concentration range of 3-200 µg mL^{-1}. 90% growth inhibition was achieved at 200 µg mL^{-1} of FeNPs. The IC_{50} of rosemary-FeNPs was 21 µg mL^{-1}, whereas it was 48 µg mL^{-1} for the extract, indicating a higher cytotoxic effect of green synthesized FeNPs in comparison to plant extract (Ahmeda et al., 2020). ZnONPs produced with *Raphanus sativus* extract were applied to the cells at a concentration of 5, 10, 15, 20, 25, 30, 35, 40, 45, and 50 µg mL^{-1} and incubated for 48 hours. It was observed that the cell viability was reduced by 50% when 40 µg mL^{-1} was applied (Umamaheswari et al., 2021).

In another study, AgNPs derived from *Teucrium polium* were applied to MNK45 gastric cancer cells within the concentration range of 12.5 µg mL^{-1} to 130 µg mL^{-1}. The ratio of cell death was elevated to 74% at the concentration of 130 µg mL^{-1}, which correlates with the fact that cell death increases with higher concentration (Hashemi et al., 2020). AgNPs were prepared from *Commiphora wightii* extract and treated for MCF-7 breast cancer and 3T3-L1 embryonic cells. It has also been reported that AgNPs induced more selective cell death in MCF-7 breast cancer cells compared to 3T3-L1 embryonic cells. For example, when AgNPs were applied at a concentration of 67 µg mL^{-1}, cell viability decreased by 50% in MCF-7 cells (Malik et al., 2020).

Similarly, ZnONPs prepared using *Magnifera indica* and ZnONPs and direct plant extract were applied to the A549 human lung cancer cell line. The increased ROS generation in cancer cells was dependent on the increasing concentration of ZnONPs. Compared with the direct application of plant extract, the anti-cancer activity of ZnONPs was found to be higher (Rajeshkumar et al., 2018). In another study, ZnONPs produced using *Rehmanniae radix* and treated on MG-63 human bone cancer cell line demonstrated a correlation between the concentration of ZnONPs and the induction of cytotoxic activity by the formation of ROS in the cells. It is also hypothesized that ZnONPs induce apoptosis in cancer cells (Chen et al., 2021).

AuNP produced using *Curcumae kwangsienis* extract were applied to 3 different human ovarian cancer lines which are PA-1 (human ovarian teratocarcinoma cell line), SW-626 (human ovarian metastatic cell line), and SK-OV-3 (human ovarian carcinoma cell line), and a normal human cell line (HUVEC) in the range of 0-1000 µg mL^{-1}. The particles did not exhibit any cytotoxic effects on HUVEC cells at any concentration. However, IC_{50} of AuNPs was found to be 153 µg mL^{-1} in PA-1 cells, 166 µg mL^{-1} in SW-626 cells, and 204 µg mL^{-1} in the SK-OV-3 cell line (Chen et al., 2021). A recent study showed that *Scutellaria barbata* extract was used in AuNP synthesis, and its anti-cancer activity on the PANC-1 human pancreatic cancer cell line was evaluated. NPs were applied at a concentration of 0-100 µg mL^{-1}, and an IC_{50} of 52 µg mL^{-1} has been determined (Wang et al., 2019).

Both lead oxide (PbONP) and selenium oxide (CeO_2NPs) nanoparticles were produced from *Prosopis farcta* extracts. HT-29 particles (human colon cancer cell line) were exposed to concentrations of PbONPs in the range of 1-500 µg mL^{-1}. The results showed that PbONPs did not exhibit any cytotoxic effects at concentrations below 30 µg mL^{-1}. The IC_{50} of PbONPs was determined to be 60 µg mL^{-1}. In contrast, CeO_2NPs exhibited a cell viability of 58% even at a concentration of 500 µg mL^{-1}. Therefore, PbO NPs have greater anti-cancer activity in cancer cells compared to CeO_2NPs (Nazaripour et al., 2021).

4. Conclusion

The examined articles here summarized the effects of metallic nanoparticles from plant sources, including Ag, Au, Fe, PbO, Pt, MgO, ZnO, and CeO. It is worth noting that Ag and Au nanoparticles appear to be particularly common and effective in this context. This review suggests that metal nanoparticles produced from plants using green synthesis have cytotoxic properties on cancer cells through the functional phytochemicals derived from the plants they interact with during synthesis. Enhanced biological effects with reduced toxicity achieved through green biosynthesis increase the potential for healthcare applications. While physical and chemical production methods are also utilized for MNP synthesis, the green synthesis method is preferred due to its eco-friendly, practical, inexpensive, and reliable nature. Sources for green synthesis in the literature vary between plants and microorganisms, with plant-based sources being prominent due to their numerous advantages.

It is worth noting that the toxicity of nanoparticles on cell lines can vary depending on the concentration applied, the cell line used, and the combination of plant and metal. Additionally, compounds from plants used in MNP synthesis have been found to support the cytotoxic properties of MNPs. Optimization and standardization of cell line-based biological assays using different 2D and 3D *in vitro* experimental models are required in particular for the determination of the anti-carcinogenic potential of NPs.

Conflict of interest: The authors declare that they have no conflict of interests.

Informed consent: The authors declare that this manuscript did not involve human or animal participants and informed consent was not collected.

References

Abbai, R., Mathiyalagan, R., Markus, J., Kim, Y. J., Wang, C., Singh, P., ... & Yang, D. C. (2016). Green synthesis of multifunctional silver and gold nanoparticles from the oriental herbal adaptogen: Siberian ginseng. *International Journal of Nanomedicine*, 3131-3143.

Abdollahzadeh, H., Pazhang, Y., Zamani, A., & Sharafi, Y. (2024). Green synthesis of copper oxide nanoparticles using walnut shell and their size dependent anticancer effects on breast and colorectal cancer cell lines. *Scientific Reports*, *14*(1), 20323.

Ahmeda, A., Zangeneh, A., & Zangeneh, M. M. (2020). Green synthesis and chemical characterization of gold nanoparticle synthesized using *Camellia sinensis* leaf aqueous extract for the treatment of acute myeloid leukemia in comparison to daunorubicin in a leukemic mouse model. *Applied Organometallic Chemistry*, *34*(3), e5290.

Akhter, M. S., Rahman, M. A., Ripon, R., Mubarak, M., Akter, M., Mahbub, S., ... & Sikder, M. T. (2024). A systematic review on green synthesis of silver nanoparticles using plants extract and their bio-medical applications. *Heliyon*, *10*(11), e29766.

Al Baloushi, K. S. Y., Senthilkumar, A., Kandhan, K., Subramanian, R., Kizhakkayil, J., Ramachandran, T., ... & Jaleel, A. (2024). Green synthesis and characterization of silver nanoparticles using *Moringa peregrina* and their toxicity on MCF-7 and Caco-2 Human Cancer Cells. *International Journal of Nanomedicine*, 3891-3905.

Alkhathlan, A. H., Al-Abdulkarim, H. A., Khan, M., Khan, M., Alkholief, M., Alshamsan, A., ... & Siddiqui, M. R. H. (2021). Evaluation of the anticancer activity of phytomolecules conjugated gold nanoparticles synthesized by aqueous extracts of *Zingiber officinale* (ginger) and *Nigella sativa* L. seeds (black cumin). *Materials*, *14*(12), 3368.

Almukaynizi, F. B., Daghestani, M. H., Awad, M. A., Althomali, A., Merghani, N. M., Bukhari, W. I., ... & Bhat, R. S. (2022). Cytotoxicity of green-synthesized silver nanoparticles by *Adansonia digitata* fruit extract against HTC116 and SW480 human colon cancer cell lines. *Green Processing and Synthesis*, *11*(1), 411-422.

Al-Radadi, N. S. (2021). Facile one-step green synthesis of gold nanoparticles (AuNp) using licorice root extract: Antimicrobial and anticancer study against HepG2 cell line. *Arabian Journal of Chemistry*, *14*(2), 102956.

Alsamri, H., Athamneh, K., Pintus, G., Eid, A. H., & Iratni, R. (2021). Pharmacological and antioxidant activities of *Rhus coriaria* L.(Sumac). *Antioxidants*, *10*(1), 73.

Althubiti, A. A., Alsudir, S. A., Alfahad, A. J., Alshehri, A. A., Bakr, A. A., Alamer, A. A., ... & Tawfik, E. A. (2023). Green synthesis of silver nanoparticles using *Jacobaea maritima* and the evaluation of their antibacterial and anticancer activities. *International Journal of Molecular Sciences*, *24*(22), 16512.

Amina, M., Al Musayeib, N. M., Alarfaj, N. A., El-Tohamy, M. F., Oraby, H. F., Al Hamoud, G. A., ... & Moubayed, N. M. (2020). Biogenic green synthesis of MgO nanoparticles using *Saussurea costus* biomasses for a comprehensive detection of their antimicrobial, cytotoxicity against MCF-7 breast cancer cells and photocatalysis potentials. *PLoS One*, *15*(8), e0237567.

Arulvasu, C., Prabhu, D., Manikandan, R., Srinivasan, P., Dinesh, D., Babu, G., & Sellamuthu, S. (2010). Induction of apoptosis by the aqueous and ethanolic leaf extract of *Vitex negundo* L. in MCF-7 human breast cancer cells. *International Journal of Drug Discovery*, *2*(1), 1-7.

Asadollahi, K., Abassi, N., Afshar, N., Alipour, M., & Asadollahi, P. (2010). Investigation of the effects of *Prosopis farcta* plant extract on rat's aorta. *Journal of Medicinal Plants Research*, *4*(2), 142-7.

Ashokkumar, M., Palanisamy, K., Ganesh Kumar, A., Muthusamy, C., & Senthil Kumar, K. J. (2024). Green synthesis of silver and copper nanoparticles and their composites using *Ocimum sanctum* leaf extract displayed enhanced antibacterial, antioxidant and anticancer potentials. *Artificial Cells, Nanomedicine, and Biotechnology*, *52*(1), 438-448.

Balmuri, S. R., Selvaraj, U., Kumar, V. V., Anthony, S. P., Tsatsakis, A. M., Golokhvast, K. S., & Raman, T. (2017). Effect of surfactant in mitigating cadmium oxide nanoparticle toxicity: implications for mitigating cadmium toxicity in environment. *Environmental Research*, *152*, 141-149.

Banne, S. V., Patil, M. S., Kulkarni, R. M., & Patil, S. J. (2017). Synthesis and characterization of silver nano particles for EDM applications. *Materials Today: Proceedings*, *4*(11), 12054-12060.

Barani, M., Mir, A., Roostaee, M., Sargazi, G., & Adeli-Sardou, M. (2024). Green synthesis of copper oxide nanoparticles via *Moringa peregrina* extract incorporated in graphene oxide: evaluation of antibacterial and anticancer efficacy. *Bioprocess and Biosystems Engineering*, *47*(11), 1915-1928.

Batool, A., Azizullah, A., Ullah, K., Shad, S., Khan, F. U., Seleiman, M. F., ... & Zeb, U. (2024). Green synthesis of Zn-doped TIO2 nanoparticles from *Zanthoxylum armatum*. *BMC Plant Biology*, *24*(1), 820.

Bhardwaj, M., & Alia, A. (2019). Commiphora wightii (Arn.) Bhandari. Review of its botany, medicinal uses, pharmacological activities and phytochemistry. *Journal of Drug Delivery and Therapeutics*, *9*(4-s), 613-621.

Carrapico, A., Martins, M. R., Caldeira, A. T., Mirão, J., & Dias, L. (2023). Biosynthesis of metal and metal oxide nanoparticles using microbial cultures: Mechanisms, antimicrobial activity and applications to cultural heritage. *Microorganisms*, *11*(2), 378.

Chen, C. C., Kao, C. P., Chiu, M. M., & Wang, S. H. (2017). The anti-cancer effects and mechanisms of *Scutellaria barbata* D. Don on CL1-5 lung cancer cells. *Oncotarget*, *8*(65), 109340.

Chen, J., Li, Y., Fang, G., Cao, Z., Shang, Y., Alfarraj, S., ... & Duan, X. (2021). Green synthesis, characterization, cytotoxicity, antioxidant, and anti-human ovarian cancer activities of *Curcumae kwangsiensis* leaf aqueous extract green-synthesized gold nanoparticles. *Arabian Journal of Chemistry*, *14*(3), 103000.

Cruz, D. M., Mostafavi, E., Vernet-Crua, A., Barabadi, H., Shah, V., Cholula-Díaz, J. L., ... & Webster, T. J. (2020). Green nanotechnology-based zinc oxide (ZnO) nanomaterials for biomedical applications: a review. *Journal of Physics: Materials*, *3*(3), 034005.

Dai, J., & Mumper, R. J. (2010). Plant phenolics: extraction, analysis and their antioxidant and anticancer properties. *Molecules*, *15*(10), 7313-7352.

Davydov, M., & Krikorian, A. D. (2000). *Eleutherococcus senticosus* (Rupr. & Maxim.) Maxim. (Araliaceae) as an adaptogen: a closer look.

Journal of Ethnopharmacology, *72*(3), 345-393.

Demir, C., Aygun, A., Gunduz, M. K., Altınok, B. Y., Karahan, T., Meydan, I., ... & Sen, F. (2024). Production of plant-based ZnO NPs by green synthesis; anticancer activities and photodegradation of methylene red dye under sunlight. *Biomass Conversion and Biorefinery*, 1-16.

Dikshit, P. K., Kumar, J., Das, A. K., Sadhu, S., Sharma, S., Singh, S., ... & Kim, B. S. (2021). Green synthesis of metallic nanoparticles: Applications and limitations. *Catalysts*, *11*(8), 902.

Ebell, M. H., Culp, M. B., & Radke, T. J. (2016). A systematic review of symptoms for the diagnosis of ovarian cancer. *American Journal of Preventive Medicine*, *50*(3), 384-394

Elagbar, Z. A., Shakya, A. K., Barhoumi, L. M., & Al-Jaber, H. I. (2020). Phytochemical diversity and pharmacological properties of *Rhus coriaria*. *Chemistry & Biodiversity*, *17*(4), e1900561.

Escárcega-González, C. E., Garza-Cervantes, J. A., Vázquez-Rodríguez, A., & Morones-Ramírez, J. R. (2018). Bacterial exopolysaccharides as reducing and/or stabilizing agents during synthesis of metal nanoparticles with biomedical applications. *International Journal of Polymer Science*, *2018*(1), 7045852.

Franco, D., Calabrese, G., Guglielmino, S. P. P., & Conoci, S. (2022). Metal-based nanoparticles: Antibacterial mechanisms and biomedical application. *Microorganisms*, *10*(9), 1778.

Gade, A., Gaikwad, S., Duran, N., & Rai, M. (2014). Green synthesis of silver nanoparticles by *Phoma glomerata*. *Micron*, *59*, 52-59.

Genc, D., & Celik, I. (2024). Investigation of the effects of *Eremurus spectabilis* Bieb. lyophilized and nanoparticle extracts on the cellular and enzymatic immune system in experimentally-induced hepatocellular carcinogenesis in rats. *Frontiers in Life Sciences and Related Technologies*, *5*(2), 95-100.

Gharari, Z., Hanachi, P., Sadeghinia, H., & Walker, T. R. (2023). Eco-friendly green synthesis and characterization of silver nanoparticles by *Scutellaria multicaulis* leaf extract and its biological activities. *Pharmaceuticals*, *16*(7), 992.

Ghobashy, M. M., Alkhursani, S. A., Alqahtani, H. A., El-damhougy, T. K., & Madani, M. (2024). Gold nanoparticles in microelectronics advancements and biomedical applications. *Materials Science and Engineering: B*, *301*, 117191.

Ghorbani, H. R. (2014). A review of methods for synthesis of Al nanoparticles. *Oriental Journal of Chemistry*, *30*(4), 1941-1949.

Gour, A., & Jain, N. K. (2019). Advances in green synthesis of nanoparticles. *Artificial Cells, Nanomedicine, and Biotechnology*, *47*(1), 844-851.

Grace, M. H., & Khattab, A. M. (1998). Chemical constituents and molluscicidal activity of *Senecio cineraria* DC.

Grancharova, T., Simeonova, S., Pilicheva, B., & Zagorchev, P. (2024). Gold nanoparticles in Parkinson's disease therapy: A focus on plant-based green synthesis. *Cureus*, *16*(2).

Gupta, R., Sharma, A. K., Dobhal, M. P., Sharma, M. C., & Gupta, R. S. (2011). Antidiabetic and antioxidant potential of β-sitosterol in streptozotocin-induced experimental hyperglycemia. *Journal of Diabetes*, *3*(1), 29-37.

Gutiérrez, R. M. P., & Perez, R. L. (2004). *Raphanus sativus* (Radish): Their chemistry and biology. *The Scientific World Journal*, *4*(1), 811-837.

Haji, S. H., Ali, F. A., & Aka, S. T. H. (2022). Synergistic antibacterial activity of silver nanoparticles biosynthesized by carbapenem-resistant Gram-negative bacilli. *Scientific Reports*, *12*(1), 15254.

Hashemi, S. F., Tasharrofi, N., & Saber, M. M. (2020). Green synthesis of silver nanoparticles using *Teucrium polium* leaf extract and assessment of their antitumor effects against MNK45 human gastric cancer cell line. *Journal of Molecular Structure*, *1208*, 127889.

Herlekar, M., Barve, S., & Kumar, R. (2014). Plant-mediated green synthesis of iron nanoparticles. *Journal of Nanoparticles*, *2014*(1), 140614.

Husain, J. H., Arumugam, D., Nawabjohn, M. S., Kumaran, S., & Pandurangan, A. K. (2024). Green synthesis of silver nanoparticles using *Centratherum anthelminticum* extract against breast cancer cells. *Asian Pacific Journal of Cancer Prevention: APJCP*, *25*(8), 2711.

Iqbal, S., Fakhar-e-Alam, M., Akbar, F., Shafiq, M., Atif, M., Amin, N., ... & Farooq, W. A. (2019). Application of silver oxide nanoparticles for the treatment of cancer. *Journal of Molecular Structure*, *1189*, 203-209.

Jaggi, R. K., Madaan, R., & Singh, B. (2003). Anticonvulsant potential of holy basil, *Ocimum sanctum* Linn., and its cultures. *Indian Journal of Experimental Biology*, *41*, 1329-1333.

Jeevanandam, J., Kiew, S. F., Boakye-Ansah, S., Lau, S. Y., Barhoum, A., Danquah, M. K., & Rodrigues, J. (2022). Green approaches for the synthesis of metal and metal oxide nanoparticles using microbial and plant extracts. *Nanoscale*, *14*(7), 2534-2571.

Johnson, J. J. (2011). Carnosol: a promising anti-cancer and anti-inflammatory agent. *Cancer Letters*, *305*(1), 1-7.

Kabiri, F., Aghaei, S. S., Pourbabaee, A. A., Soleimani, M., & Komeili Movahhed, T. (2023). Antibiofilm and cytotoxic potential of extracellular biosynthesized gold nanoparticles using actinobacteria *Amycolatopsis* sp. KMN. *Preparative Biochemistry & Biotechnology*, *53*(3), 265-278.

Kamatou, G. P. P., Vermaak, I., & Viljoen, A. M. (2011). An updated review of Adansonia digitata: A commercially important African tree. *South African Journal of Botany*, *77*(4), 908-919.

Kan, X., Zhang, W., You, R., Niu, Y., Guo, J., & Xue, J. (2017). *Scutellaria barbata* D. Don extract inhibits the tumor growth through down-regulating of Treg cells and manipulating Th1/Th17 immune response in hepatoma H22-bearing mice. *BMC Complementary and Alternative Medicine*, *17*, 1-10.

Karahan, H., Tetik, N., & Colgecen, H. (2023). Phytofabrication of silver nanoparticles using callus extracts of natural tetraploid *Trifolium pratense* L. and its bioactivities. *Frontiers in Life Sciences and Related Technologies*, 18-28.

Khan, I., Saeed, K., & Khan, I. (2019). Nanoparticles: Properties, applications and toxicities. *Arabian journal of chemistry*, *12*(7), 908-931.

Khdary, N. H., Alangari, A. A., Katubi, K. M., Alanazi, M., Alhassan, A., Alzahrani, S. D., ... & Alanazi, I. O. (2023). Synthesis of Gingerol-Metals Complex and *in-vitro* Cytotoxic Activity on Human Colon Cancer Cell Line. *Cancer Management and Research*, 87-98.

Khorrami, S., Zarrabi, A., Khaleghi, M., Danaei, M., & Mozafari, M. R. (2018). Selective cytotoxicity of green synthesized silver nanoparticles against the MCF-7 tumor cell line and their enhanced antioxidant and antimicrobial properties. *International Journal of Nanomedicine*, 8013-8024.

Khursheed, R., Dua, K., Vishwas, S., Gulati, M., Jha, N. K., Aldhafeeri, G. M., ... & Singh, S. K. (2022). Biomedical applications of metallic nanoparticles in cancer: Current status and future perspectives. *Biomedicine & Pharmacotherapy*, *150*, 112951.

Kim, J. Y., Jo, O. H., Choe, C. M., & Cho, H. B. (2006). Rhizoma *Rehmanniae* induced apoptosis in human cervical carcinoma HeLa cells. *The Journal of Korean Obstetrics and Gynecology*, *19*(1), 69-80.

Lahiri, D., Nag, M., Sheikh, H. I., Sarkar, T., Edinur, H. A., Pati, S., & Ray, R. R. (2021). Microbiologically-synthesized nanoparticles and their role in silencing the biofilm signaling cascade. *Frontiers in Microbiology*, *12*, 636588.

Lambertini, E., Piva, R., Khan, M. T. H., Lampronti, I., Bianchi, N., Borgatti, M., & Gambari, R. (2004). Effects of extracts from Bangladeshi medicinal plants on *in vitro* proliferation of human breast cancer cell lines and expression of estrogen receptor α gene. *International Journal of Oncology*, *24*(2), 419-423.

Lee, S. R., Kim, M. S., Kim, S., Hwang, K. W., & Park, S. Y. (2017). Constituents from *Scutellaria barbata* inhibiting nitric oxide production in LPS-stimulated microglial cells. *Chemistry & Biodiversity*, *14*(11), e1700231.

Liu, P., Jin, H., Guo, Z., Ma, J., Zhao, J., Li, D., ... & Gu, N. (2016). Silver nanoparticles outperform gold nanoparticles in radiosensitizing U251 cells *in vitro* and in an intracranial mouse model of glioma. *International Journal of Nanomedicine*, 5003-5014.

Liu, R., Pei, Q., Shou, T., Zhang, W., Hu, J., & Li, W. (2019). Apoptotic effect of green synthesized gold nanoparticles from *Curcuma wenyujin* extract against human renal cell carcinoma A498 cells. *International Journal of Nanomedicine*, 4091-4103.

Liu, Y., Deng, A. J., Ma, L., Zhang, H. J., Zhang, Z. H., Wu, L. Q., ... & Qin, H. L. (2015). Chemical constituents of the roots of *Macleaya microcarpa* and activation efficacy of benzophenanthridine alkaloids for the transcription of xbp1 gene. *Yao xue xue bao=Acta Pharmaceutica Sinica*, *50*(2), 207-210.

Malik, U. U., Siddiqui, I. A., Ilyas, A., Hashim, Z., Staunton, L., Kwasnik, A., ... & Zarina, S. (2020). Identification of differentially expressed proteins from smokeless tobacco addicted patients suffering from Oral squamous cell carcinoma. *Pathology & Oncology Research*, *26*, 1489-1497.

Mani, S. T., Jayakumar, P., Pavithra, M. E., Saranya, K., Rathinavel, T., & Ammashi, S. (2023). Green synthesis and characterization of silver nanoparticles from *Eclipta alba* and its activity against triple-negative breast cancer cell line (MDA-MB-231). *Molecular Biotechnology*, 1-11.

Manzan, A. C. C., Toniolo, F. S., Bredow, E., & Povh, N. P. (2003). Extraction of essential oil and pigments from *Curcuma longa* [L.] by steam distillation and extraction with volatile solvents. *Journal of Agricultural and Food Chemistry*, *51*(23), 6802-6807.

Marconett, C. N., Morgenstern, T. J., San Roman, A. K., Sundar, S. N., Singhal, A. K., & Firestone, G. L. (2010). BZL101, a phytochemical extract from the *Scutellaria barbata* plant, disrupts proliferation of human breast and prostate cancer cells through distinct mechanisms dependent on the cancer cell phenotype. *Cancer Biology & Therapy*, *10*(4), 397-405.

Mehrotra, S., Goyal, V., Dimkpa, C. O., & Chhokar, V. (2024). Green synthesis and characterization of ginger-derived silver nanoparticles and evaluation of their antioxidant, antibacterial, and anticancer activities. *Plants*, *13*(9), 1255.

Mirabelli, P., Coppola, L., & Salvatore, M. (2019). Cancer cell lines are useful model systems for medical research. *Cancers*, *11*(8), 1098.

Mittal, A. K., Chisti, Y., & Banerjee, U. C. (2013). Synthesis of metallic nanoparticles using plant extracts. *Biotechnology Advances*, *31*(2), 346-356.

Moga, M. A., Dimienescu, O. G., Bălan, A., Dima, L., Toma, S. I., Bîgiu, N. F., & Blidaru, A. (2021). Pharmacological and therapeutic properties of *Punica granatum* phytochemicals: possible roles in breast cancer. *Molecules*, *26*(4), 1054.

Moghaddam, N. A., Eskandari, A., Khodadadi, B., Hafezi, Y., Paduvilan, J. K., & Yaraki, M. T. (2024). Green synthesis of bimetallic AgZnO Nanoparticles: Synergistic anticancer effects through regulation of gene expression for lung cancer treatment. *Results in Engineering*, 102329.

Molnár, Z., Bódai, V., Szakacs, G., Erdélyi, B., Fogarassy, Z., Sáfrán, G., ... & Lagzi, I. (2018). Green synthesis of gold nanoparticles by thermophilic filamentous fungi. *Scientific Reports*, *8*(1), 3943.

Mongy, Y., & Shalaby, T. (2024). Green synthesis of zinc oxide nanoparticles using *Rhus coriaria* extract and their anticancer activity against triple-negative breast cancer cells. *Scientific Reports*, *14*(1), 13470.

Montiel Schneider, M. G., Martín, M. J., Otarola, J., Vakarelska, E., Simeonov, V., Lassalle, V., & Nedyalkova, M. (2022). Biomedical applications of iron oxide nanoparticles: Current insights progress and perspectives. *Pharmaceutics*, *14*(1), 204.

Mousa, A. B., Moawad, R., Abdallah, Y., Abdel-Rasheed, M., & Zaher, A. M. A. (2023). Zinc oxide nanoparticles promise anticancer and antibacterial activity in ovarian cancer. *Pharmaceutical Research*, *40*(10), 2281-2290.

Mousavi, B., Tafvizi, F., & Zaker Bostanabad, S. (2018). Green synthesis of silver nanoparticles using *Artemisia turcomanica* leaf extract and the study of anti-cancer effect and apoptosis induction on gastric cancer cell line (AGS). *Artificial Cells, Nanomedicine, and Biotechnology*, *46*(sup1), 499-510.

Movahedi, A., Basir, R., Rahmat, A., Charaffedine, M., & Othman, F. (2014). Remarkable anticancer activity of *Teucrium polium* on hepatocellular carcinogenic rats. *Evidence-Based Complementary and Alternative Medicine*, *2014*(1), 726724.

Mukjerjee, S., & Karati, D. (2022). A mechanistic view on phytochemistry, pharmacognostic properties, and pharmacological activities of phytocompounds present in *Zingiber officinale*: A comprehensive review. *Pharmacological Research-Modern Chinese Medicine*, *5*, 100173.

Muslim, A. M., & Naji, I. S. (2024). Green synthesis of CuO nanoparticles mediated *Rhazya stricta* plant leaves extract characterization and evaluation of their antibacterial and anticancer activity (*in vitro* study). *Iraqi Journal of Physics*, *22*(3), 93-105.

Nachvak, S. M., Soleimani, D., Rahimi, M., Azizi, A., Moradinazar, M., Rouhani, M. H., ... & Miryan, M. (2023). Ginger as an anticolorectal cancer spice: A systematic review of *in vitro* to clinical evidence. *Food Science & Nutrition*, *11*(2), 651-660.

Nazaripour, E., Mousazadeh, F., Moghadam, M. D., Najafi, K., Borhani, F., Sarani, M., ... & Khatami, M. (2021). Biosynthesis of lead oxide and cerium oxide nanoparticles and their cytotoxic activities against colon cancer cell line. *Inorganic Chemistry Communications*, *131*, 108800.

Nematollahi-Mahani, S. N., Rezazadeh-Kermani, M., Mehrabani, M., & Nakhaee, N. (2007). Cytotoxic effects of *Teucrium polium*. On some established cell lines. *Pharmaceutical Biology*, *45*(4), 295-298.

Nguyen, N. T. T., Nguyen, T. T. T., Nguyen, D. T. C., & Van Tran, T. (2023). Green synthesis of $ZnFe_2O_4$ nanoparticles using plant extracts and their applications: A review. *Science of The Total Environment*, *872*, 162212.

Norris, C. B., Joseph, P. R., Mackiewicz, M. R., & Reed, S. M. (2010). Minimizing formaldehyde use in the synthesis of gold−silver core−shell nanoparticles. *Chemistry of Materials*, *22*(12), 3637-3645.

Osman, A. M. E., Taj Eldin, I. M., Elhag, A. M., Elhassan, M. M. A., & Ahmed, E. M. M. (2020). *In-vitro* anticancer and cytotoxic activity of ginger extract on human breast cell lines. *Khartoum Journal of Pharmaceutical Sciences*, *1*(1), 26-29.

Ovais, M., Khalil, A. T., Islam, N. U., Ahmad, I., Ayaz, M., Saravanan, M., ... & Mukherjee, S. (2018). Role of plant phytochemicals and microbial enzymes in biosynthesis of metallic nanoparticles. *Applied Microbiology and Biotechnology*, *102*, 6799-6814.

Ozcelik, S. (2023). Investigation of antimicrobial effects of zinc-based nanoparticles on food-borne pathogens. *Frontiers in Life Sciences and Related Technologies*, *4*(3), 132-137.

Pal, G., Rai, P., & Pandey, A. (2019). Green synthesis of nanoparticles: A greener approach for a cleaner future. In *Green Synthesis, Characterization and Applications of Nanoparticles* (pp. 1-26). Elsevier.

Pal, S., Tak, Y. K., & Song, J. M. (2007). Does the antibacterial activity of silver nanoparticles depend on the shape of the nanoparticle? A study of the gram-negative bacterium *Escherichia coli*. *Applied and Environmental Microbiology*, *73*(6), 1712-1720.

Pandey, P. A., Bell, G. R., Rourke, J. P., Sanchez, A. M., Elkin, M. D., Hickey, B. J., & Wilson, N. R. (2011). Physical vapor deposition of metal nanoparticles on chemically modified graphene: observations on metal-graphene interactions. *Small*, *7*(22), 3202-3210.

Pandian, N., & Chidambaram, S. (2017). Antimicrobial, cytotoxicty and anti cancer activity of silver nanoparticles from *Glycyrrhiza glabra*. *International Journal of Pharmaceutical Sciences and Research*, *8*(4), 1633.

Patra, J. K., Das, G., Fraceto, L. F., Campos, E. V. R., Rodriguez-Torres, M. D. P., Acosta-Torres, L. S., ... & Shin, H. S. (2018). Nano based drug delivery systems: recent developments and future prospects. *Journal of Nanobiotechnology*, *16*, 1-33.

Pattanayak, M., & Nayak, P. L. (2013). Ecofriendly green synthesis of iron nanoparticles from various plants and spices extract. *International Journal of Plant, Animal and Environmental Sciences*, *3*(1), 68-78.

Pattanayak, P., Behera, P., Das, D., & Panda, S. K. (2010). *Ocimum sanctum* Linn. A reservoir plant for therapeutic applications: An overview. *Pharmacognosy reviews*, *4*(7), 95.

Perumal, P., Sathakkathulla, N. A., Kumaran, K., Ravikumar, R., Selvaraj, J. J., Nagendran, V., ... & Rathinasamy, S. (2024). Green synthesis of zinc oxide nanoparticles using aqueous extract of shilajit and their anticancer activity against HeLa cells. *Scientific Reports*, *14*(1), 2204.

Plengsuriyakarn, T., Viyanant, V., Eursitthichai, V., Tesana, S., Chaijaroenkul, W., Itharat, A., & Na-Bangchang, K. (2012). Cytotoxicity, toxicity, and anticancer activity of *Zingiber officinale* Roscoe against cholangiocarcinoma. *Asian Pacific Journal of Cancer Prevention*, *13*(9), 4597-4606.

Qureshi, S. A., Rais, S., Usmani, R., Zaidi, S. S. M., Jehan, M., Lateef, T., & Azmi, M. B. (2016). *Centratherum anthelminticum* seeds reverse the carbon tetrachloride-induced hepatotoxicity in rats. *African journal of Pharmacy and Pharmacology*, *10*(26), 533-539.

Rajeshkumar, S., Kumar, S. V., Ramaiah, A., Agarwal, H., Lakshmi, T., & Roopan, S. M. (2018). Biosynthesis of zinc oxide nanoparticles using *Mangifera indica* leaves and evaluation of their antioxidant and cytotoxic properties in lung cancer (A549) cells. *Enzyme and microbial technology*, *117*, 91-95.

Rajput, N. (2015). Methods of preparation of nanoparticles-a review. *International Journal of Advances in Engineering & Technology*, *7*(6), 1806.

Ramya, B., Khusro, A., Indra, V., Agastian, P., Almutairi, M. H., & Almutairi, B. O. (2024). Green synthesis of silver nanoparticles using *Justicia adhatoda* leaves extract and its anticancer effect on human lung carcinoma via induced apoptosis mechanism. *Results in Chemistry*, *7*, 101472.

Razavi, M., Salahinejad, E., Fahmy, M., Yazdimamaghani, M., Vashaee, D., & Tayebi, L. (2015). Green chemical and biological synthesis of nanoparticles and their biomedical applications. *Green processes for nanotechnology: From Inorganic to Bioinspired Nanomaterials*, 207-235.

Revathi, S., Sutikno, S., Hasan, A. F., Altemimi, A. B., ALKaisy, Q. H., Phillips, A. J., ... & Abedelmaksoud, T. G. (2024). Green synthesis and characterization of silver nanoparticles (AgNP) using *Acacia nilotica* plant extract and their anti-bacterial activity. *Food Chemistry Advances*, *4*, 100680.

Sacchetti, G., Maietti, S., Muzzoli, M., Scaglianti, M., Manfredini, S., Radice, M., & Bruni, R. (2005). Comparative evaluation of 11 essential oils of different origin as functional antioxidants, antiradicals and antimicrobials in foods. *Food Chemistry*, *91*(4), 621-632.

Sadrolhosseini, A. R., Mahdi, M. A., Alizadeh, F., & Rashid, S. A. (2019). Laser ablation technique for synthesis of metal nanoparticle in liquid. *Laser Technology and its Applications*, 63-83.

Sahin, B., Aygun, A., Gunduz, H., Sahin, K., Demir, E., Akocak, S., & Sen, F. (2018). Cytotoxic effects of platinum nanoparticles obtained from pomegranate extract by the green synthesis method on the MCF-7 cell line. *Colloids and Surfaces B: Biointerfaces*, *163*, 119-124.

Sakhr, K., & El Khatib, S. (2020). Physiochemical properties and medicinal, nutritional and industrial applications of Lebanese Sumac (Syrian Sumac-*Rhus coriaria*): A review. *Heliyon*, *6*(1).

Salehi, S., Shandiz, S. A. S., Ghanbar, F., Darvish, M. R., Ardestani, M. S., Mirzaie, A., & Jafari, M. (2016). Phytosynthesis of silver nanoparticles using *Artemisia marschalliana* Sprengel aerial part extract and assessment of their antioxidant, anticancer, and antibacterial properties. *International Journal of Nanomedicine*, 1835-1846.

Sekar, V., Balakrishnan, C., Kathirvel, P., Swamiappan, S., Alshehri, M. A., Sayed, S., & Panneerselvam, C. (2022). Ultra-sonication-enhanced green synthesis of silver nanoparticles using *Barleria buxifolia* leaf extract and their possible application. *Artificial Cells, Nanomedicine, and Biotechnology*, *50*(1), 177-187.

Senthilkumar, A., Karuvantevida, N., Rastrelli, L., Kurup, S. S., & Cheruth, A. J. (2018). Traditional uses, pharmacological efficacy, and phytochemistry of *Moringa peregrina* (Forssk.) Fiori. -a review. *Frontiers in Pharmacology*, *9*, 465.

Shanmugam, K. R., Shanmugam, B., Venkatasubbaiah, G., Ravi, S., & Reddy, K. S. (2022). Recent Updates on the Bioactive Compounds of Ginger (Zingiber officinale) on Cancer: A Study with Special Emphasis of Gingerol and Its Anticancer Potential: Effect of Ginger and Its Compounds in Cancer Subjects. In *Handbook of Oxidative Stress in Cancer: Therapeutic Aspects* (pp. 1-18). Singapore: Springer Nature Singapore.

Sharangi, A. B. (2009). Medicinal and therapeutic potentialities of tea (*Camellia sinensis* L.)–A review. *Food Research International*, *42*(5-6), 529-535.

Sharma, B., Purkayastha, D. D., Hazra, S., Gogoi, L., Bhattacharjee, C. R., Ghosh, N. N., & Rout, J. (2014). Biosynthesis of gold nanoparticles using a freshwater green alga, *Prasiola crispa*. *Materials Letters*, *116*, 94-97.

Shochah, Q. R., & Jabir, F. A. (2024). Green synthesis of Au/ZnO nanoparticles for anticancer activity and oxidative stress against MCF-7 cell lines. *Biomass Conversion and Biorefinery*, *14*(14), 15283-15296.

Simakin, A. V., Voronov, V. V., Kirichenko, N. A., & Shafeev, G. A. (2004). Nanoparticles produced by laser ablation of solids in liquid environment. *Applied Physics A*, *79*, 1127-1132.

Singh, J., Dutta, T., Kim, K. H., Rawat, M., Samddar, P., & Kumar, P. (2018). 'Green' synthesis of metals and their oxide nanoparticles: applications for environmental remediation. *Journal of Nanobiotechnology*, *16*, 1-24.

Takemoto, T., Nishimoto, N., Nakai, S., Takagi, N., Hayashi, S., Odashima, S., & Wada, Y. (1983). Pfaffic acid, a novel nortriterpene from *Pfaffia paniculata* Kuntze. *Tetrahedron Letters*, *24*(10), 1057-1060.

Ullah, I., Khalil, A. T., Zia, A., Hassan, I., & Shinwari, Z. K. (2024). Insight into the molecular mechanism, cytotoxic, and anticancer activities of phyto-reduced silver nanoparticles in MCF-7 breast cancer cell lines. *Microscopy Research and Technique*, *87*(7), 1627-1639.

Ullah, I., Rauf, A., Khalil, A. A., Luqman, M., Islam, M. R., Hemeg, H. A., ... & Quradha, M. M. (2024). Peganum harmala L. extract-based Gold (Au) and Silver (Ag) nanoparticles (NPs): Green synthesis, characterization, and assessment of antibacterial and antifungal properties. *Food Science & Nutrition*.

Ullah, M., Ali, M. E., & Abd Hamid, S. B. (2014). Surfactant-assisted ball milling: a novel route to novel materials with controlled nanostructure-a review. *Reviews on Advanced Materials Science*, *37*.

Umamaheswari, A., Prabu, S. L., John, S. A., & Puratchikody, A. (2021). Green synthesis of zinc oxide nanoparticles using leaf extracts of *Raphanus sativus* var. Longipinnatus and evaluation of their anticancer property in A549 cell lines. *Biotechnology Reports*, *29*, e00595.

Vijayakumar, S., Chen, J., Sánchez, Z. I. G., Tungare, K., Bhori, M., Durán-Lara, E. F., & Anbu, P. (2023). *Moringa oleifera* gum capped MgO nanoparticles: Synthesis, characterization, cyto-and ecotoxicity assessment. *Int J Biol Macromol, 233*, 123514.

Vyas, P., Yadav, D. K., & Khandelwal, P. (2019). *Tectona grandis* (teak)–A review on its phytochemical and therapeutic potential. *Natural Product Research*, *33*(16), 2338-2354.

Wang, L., Xu, J., Yan, Y., Liu, H., Karunakaran, T., & Li, F. (2019). Green synthesis of gold nanoparticles from *Scutellaria barbata* and its anticancer activity in pancreatic cancer cell (PANC-1). *Artificial Cells, Nanomedicine, and Biotechnology*, *47*(1), 1617-1627.

Xia, T., Dong, X., Jiang, Y., Lin, L., Dong, Z., Shen, Y., ... & Qin, L. (2019). Metabolomics profiling reveals rehmanniae radix preparata extract protects against glucocorticoid-induced osteoporosis mainly via intervening steroid hormone biosynthesis. *Molecules*, *24*(2), 253.

Yalcin, B., Akcan, D., Yalcin, I. E., Alphan, M. C., Senturk, K., Ozyigit, I. I., & Arda, L. (2020). Effect of Mg doping on morphology, photocatalytic activity and related biological properties of $Zn_{1-x}Mg_xO$ nanoparticles. *Turkish Journal of Chemistry*, *44*(4), 1177-1199.

Yalcin, B., Arda, L., Yalcin, I. E., Senturk, K., Alphan, M. C., Akcan, D., & Ozyigit, I. I. (2023). Exploration of the improving effect of Cd-doping on structural, photocatalytic, and biological properties of ZnO nanoparticles. *Journal of Nanoparticle Research*, *25*(7), 146.

Yang, N., Zhao, Y., Wang, Z., Liu, Y., & Zhang, Y. (2017). Scutellarin suppresses growth and causes apoptosis of human colorectal cancer cells by regulating the p53 pathway. *Molecular Medicine Reports*, *15*(2), 929-935.

Yesil-Celiktas, O., Sevimli, C., Bedir, E., & Vardar-Sukan, F. (2010). Inhibitory effects of rosemary extracts, carnosic acid and rosmarinic acid on the growth of various human cancer cell lines. *Plant Foods for Human Nutrition*, *65*, 158-163.

Younis, H. M., Hussein, H. A., Khaphi, F. L., & Saeed, Z. K. (2023). Green biosynthesis of silver and gold nanoparticles using Teak (*Tectona grandis*) leaf extract and its anticancer and antimicrobial activity. *Heliyon*, *9*(11).

Zhang, L., Ren, B., Zhang, J., Liu, L., Liu, J., Jiang, G., ... & Li, W. (2017). Anti-tumor effect of *Scutellaria barbata* D. Don extracts on ovarian cancer and its phytochemicals characterisation. *Journal of Ethnopharmacology*, *206*, 184-192.

Zhou, R., Xu, L., Ye, M., Liao, M., Du, H., & Chen, H. (2014). Formononetin inhibits migration and invasion of MDA-MB-231 and 4T1 breast cancer cells by suppressing MMP-2 and MMP-9 through PI3K/AKT signaling pathways. *Hormone and Metabolic Research*, *46*(11), 753-760.

Cite as: Cakar, B., & Darcansoy Iseri, O. (2024). Effect of metallic nanoparticles on cancer cell lines: A review on plant-based biosynthesis. *Front Life Sci RT*, *5*(3), 231-243.