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Anticancer potentials of medicinal plants: Phytochemicals, molecular mechanisms, and plant-mediated sulfur nanoparticles

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ABSTRACT: Despite advances in oncology, cancer treatment remains limited by therapeutic resistance, toxicity, and high treatment costs. Natural products, particularly plant-derived secondary metabolites, have historically contributed to the discovery of several clinically approved anticancer drugs and continue to represent an important source of new therapeutic leads. In many developing regions, particularly in African countries where access to advanced cancer care remains limited, medicinal plants play an important role in traditional healthcare systems, and numerous species have demonstrated anticancer activity in experimental studies. Phytochemicals such as alkaloids, terpenoids, polyphenols, and saponins exert anticancer effects through multiple mechanisms, including apoptosis induction, cell-cycle arrest, modulation of oxidative stress, and inhibition of angiogenesis and metastasis. However, the translation of plant extracts into clinically effective therapies remains challenging due to poor bioavailability, instability, and variability in phytochemical composition. Recent advances in nanotechnology provide promising strategies to overcome these limitations. In particular, plant-mediated synthesis of sulfur nanoparticles (SNPs) offers a sustainable and biologically compatible approach to overcome these limitations. These nanoparticles enhance drug delivery, improve cellular uptake, and potentiate anticancer activity through reactive oxygen species (ROS)-mediated mechanisms. This review provides a comprehensive overview of major anticancer phytochemicals, their molecular mechanisms of action, and the emerging role of plant-mediated sulfur nanoparticles as innovative nanotherapeutic agents in cancer treatment.

Keywords: Cancer, Medicinal plants, Molecular mechanisms, Phytochemicals, Sulfur nanoparticles, Apoptosis, and Nanotechnology.

INTRODUCTION

Cancer remains one of the leading causes of morbidity and mortality worldwide, posing a major public health challenge. Despite advances in conventional treatment strategies such as chemotherapy, radiotherapy, and targeted therapies, their effectiveness is often limited by drug resistance, adverse side effects, and high treatment costs. These limitations highlight the urgent need for alternative and more effective therapeutic approaches. Plant-derived natural products have played an essential role in anticancer drug discovery. Several widely used chemotherapeutic agents, including vincristine and paclitaxel, originate from plant metabolites, highlighting the therapeutic potential of phytochemicals in oncology (Greenwell and Rahman, 2015; Siddiqui *et al.,* 2022). Consequently, medicinal plants remain an important source of structurally diverse bioactive compounds that may serve as templates for the development of novel anticancer agents. In many African countries, traditional medicine continues to be an important component of healthcare systems.

Medicinal plants are widely used for the treatment of various diseases, including cancer-related conditions. Ethnobotanical investigations across Africa have documented numerous plant species traditionally used for tumour-related illnesses, and several of these plants have demonstrated cytotoxic and antiproliferative activities in experimental models (World Health Organisation 2013; James *et al.,* 2018). A comprehensive review of Nigerian medicinal plants reported more than fifty species with documented anticancer activity against various cancer cell lines, including breast, prostate, cervical, colon, and lung cancers (Ohiagu *et al.,* 2021). Despite encouraging preclinical evidence, translating plant-derived compounds into clinically effective anticancer therapies remains challenging.

Many phytochemicals exhibit poor aqueous solubility, limited bioavailability, and rapid metabolic degradation, which reduce their therapeutic effectiveness (Garcia-Oliveira *et al.,* 2021). In addition, variability in phytochemical composition due to plant species, environmental conditions, and extraction methods complicates standardisation and reproducibility. Nanotechnology-based drug delivery systems have recently emerged as promising strategies to address these limitations. Nanoparticles can enhance drug stability, improve cellular uptake, and facilitate targeted delivery to tumour tissues (Yap *et al.,* 2021; Karnwal *et al.,* 2024). Among emerging nanomaterials, sulfur nanoparticles have attracted attention due to their favourable redox properties, biological compatibility, and relatively low toxicity compared with many metal-based nanoparticles (Shukla *et al*., 2025; Kamyab *et al*., 2025). However, the integration of phytochemicals with nanotechnology, particularly plant-mediated sulfur nanoparticles, remains an emerging area that requires further exploration. Therefore, this review aims to provide a comprehensive overview of anticancer phytochemicals, their molecular mechanisms of action, and the emerging role of plant mediated sulfur nanoparticles as innovative nanotherapeutic agents.

ETHNOMEDICINAL USE OF PLANTS IN CANCER THERAPY

Medicinal plants in traditional cancer management

Traditional medicine plays a major role in healthcare systems in many developing regions, particularly in Africa, where medicinal plants are widely used for the treatment of numerous diseases, including inflammatory disorders, chronic illnesses, and tumour-related conditions (WHO, 2013; James *et al.,* 2018). Scientific investigations increasingly support the therapeutic potential of these plants. Ethnopharmacological studies have identified numerous plant species used in traditional medicine that demonstrate cytotoxic or antiproliferative activity against cancer cell lines. A comprehensive review focusing on Nigerian medicinal plants reported at least fifty-one species with documented anticancer activity in experimental models (Ohiagu *et al.,* 2021). Plant-derived compounds often exhibit multitarget mechanisms of action that influence multiple biological pathways involved in tumour development and progression. Unlike many synthetic drugs that act on a single molecular target, phytochemicals may simultaneously regulate pathways associated with cell proliferation, apoptosis, oxidative stress, and metastasis (Siddiqui *et al.,* 2022; Khan *et al.,* 2020). This multitarget activity may reduce the likelihood of drug resistance and contribute to improved therapeutic outcomes. Several medicinal plants commonly used in traditional medicine have demonstrated measurable anticancer activity in experimental studies. These plants contain diverse phytochemicals such as flavonoids, terpenoids, alkaloids, and organosulfur compounds that contribute to their biological effects.

BIOACTIVE PHYTOCHEMICALS RESPONSIBLE FOR ANTICANCER ACTIVITY

The anticancer activity of medicinal plants is largely attributed to their secondary metabolites, collectively known as phytochemicals. Major classes of phytochemicals with reported anticancer activity include alkaloids, terpenoids, polyphenols, and saponins. These compounds influence multiple molecular pathways involved in cancer development and progression. Some of these phytochemicals are discussed below.

Alkaloids

Alkaloids are nitrogen-containing secondary metabolites widely distributed in medicinal plants and are known for their diverse pharmacological activities. Many alkaloids exhibit significant anticancer properties through the regulation of cell proliferation, apoptosis, and metastatic signalling pathways (Tabakam and Makhafola, 2024; Olofinsan *et al*., 2023). Several alkaloids have demonstrated the ability to interfere with cancer cell survival and proliferation. For example, berberine has been reported to induce G_2/M cell-cycle arrest through the suppression of cyclins and cyclin-dependent kinases, while piperine inhibits cancer cell migration and metastasis by downregulating matrix metalloproteinases involved in epithelial–mesenchymal transition (Koochaki *et al.,* 2024; Chidananda *et al*., 2025). Other alkaloids, such as oxymatrine, promote mitochondrial-mediated apoptosis through increased reactive oxygen species production and activation of caspase signalling pathways (Ożarowski *et al.,* 2025).

Terpenoids

Terpenoids represent a structurally diverse group of natural compounds derived from isoprene units and are

widely distributed in medicinal plants. Numerous terpenoid compounds have demonstrated anticancer properties through mechanisms including apoptosis induction, inhibition of tumour growth, and modulation of inflammatory signalling pathways (Situmorang *et al.,* 2024). For example, triterpenoids such as ursolic acid inhibit nuclear factor-κB (NF-κB) signalling and reduce the expression of anti-apoptotic proteins, including Bcl-2 and survivin. In addition, several terpenoid compounds inhibit tumour angiogenesis by suppressing vascular endothelial growth factor signalling and endothelial cell migration (Barras *et al.,* 2024; Situmorang *et al.,* 2024).

Polyphenols

Polyphenols are widely distributed plant metabolites recognised for their antioxidant and anti-inflammatory properties. In cancer biology, these compounds can exhibit both antioxidant and pro-oxidant effects depending on the cellular environment (Mileo *et al.,* 2016). Polyphenolic compounds inhibit cancer cell proliferation by modulating signalling pathways such as PI3K/Akt and MAPK/ERK. Compounds including resveratrol and curcumin suppress nuclear factor-κB activation and reduce the expression of inflammatory and survival-related genes in cancer cells (Pavan *et al.,* 2016; Bakrim *et al.,* 2022). Through these mechanisms, polyphenols contribute to the inhibition of tumour growth and progression.

Saponins

Saponins are glycosylated secondary metabolites characterised by their amphiphilic structure and ability to interact with cell membranes. These compounds exert anticancer effects primarily through interactions with cholesterol-rich membranes, resulting in increased membrane permeability and cytotoxicity in cancer cells (Elekofehinti *et al.,* 2021). Several steroidal saponins have been reported to induce apoptosis through activation of caspase signalling pathways and modulation of pro- and anti-apoptotic proteins. In addition, saponins can inhibit tumour invasion and metastasis by suppressing matrix metalloproteinases involved in extracellular matrix degradation (Jiang *et al*., 2025; Wang *et al.,* 2025).

MOLECULAR MECHANISMS OF ACTION OF PLANTS WITH ANTICANCER POTENTIALS

Medicinal plant phytochemicals exert anticancer effects through multiple molecular mechanisms that influence tumour growth, survival, and metastasis. These mechanisms include induction of apoptosis, cell-cycle arrest, modulation of oxidative stress, inhibition of angiogenesis, and regulation of tumour microenvironment signalling pathways (Ahmed *et al.,* 2022; Verma *et al.,* 2023; Shahbaz *et al.,* 2026). Because cancer progression involves dysregulation of several cellular pathways, the multitarget nature of phytochemicals may provide therapeutic advantages compared with single-target synthetic drugs.

Induction of apoptosis

Apoptosis is a tightly regulated form of programmed cell death that plays a critical role in maintaining cellular homeostasis. Many anticancer therapies aim to trigger apoptosis in tumour cells, as cancer cells often evade apoptotic signalling through the overexpression of anti-apoptotic proteins and suppression of tumour suppressor pathways (Talib *et al*., 2022). Plant-derived phytochemicals have been widely reported to restore apoptotic signalling in cancer cells through both intrinsic and extrinsic pathways (Patra *et al.,* 2021; Rajabi *et al.,* 2021). In the intrinsic pathway, phytochemicals promote mitochondrial outer membrane permeabilisation, leading to the release of cytochrome c and subsequent activation of caspase-9 and caspase-3. These events ultimately result in the controlled destruction of cancer cells (Mustafa *et al.,* 2024).

Several phytochemicals also modulate the balance between pro-apoptotic and anti-apoptotic proteins. For example, increased expression of Bax and reduced expression of Bcl-2 have been observed in cancer cells treated with plant-derived compounds. Additionally, activation of tumour suppressor proteins such as p53 and upregulation of pro-apoptotic genes including PUMA and NOXA, further enhance apoptotic responses in cancer cells (Tat *et al.,* 2025). Recent studies also suggest that nanoparticle formulations synthesised using plant extracts may enhance apoptosis induction through reactive oxygen species–mediated mitochondrial damage and activation of caspase signalling pathways (Adetunji *et al.,* 2024).

Cell-cycle arrest and inhibition of proliferation

Uncontrolled cell proliferation is a hallmark of cancer and is primarily driven by dysregulation of cyclins and cyclin-dependent kinases that regulate the progression of cells through different phases of the cell cycle. Phytochemicals derived from medicinal plants can interfere with these regulatory mechanisms and induce cell-cycle arrest in cancer cells (Khan *et al.,* 2020; Song *et al.,* 2024). Many plant-derived compounds have been reported to arrest the cell cycle at either the G_0/G_1 or G_2/M checkpoint. Polyphenols and terpenoids frequently suppress cyclin D1 and CDK4 activity, resulting in G_0/G_1 arrest, whereas certain alkaloids inhibit cyclin B1/CDK1 complexes and induce G_2/M arrest (Garcia-Oliveira *et al.,* 2021; Olofinsan *et al.,* 2023).

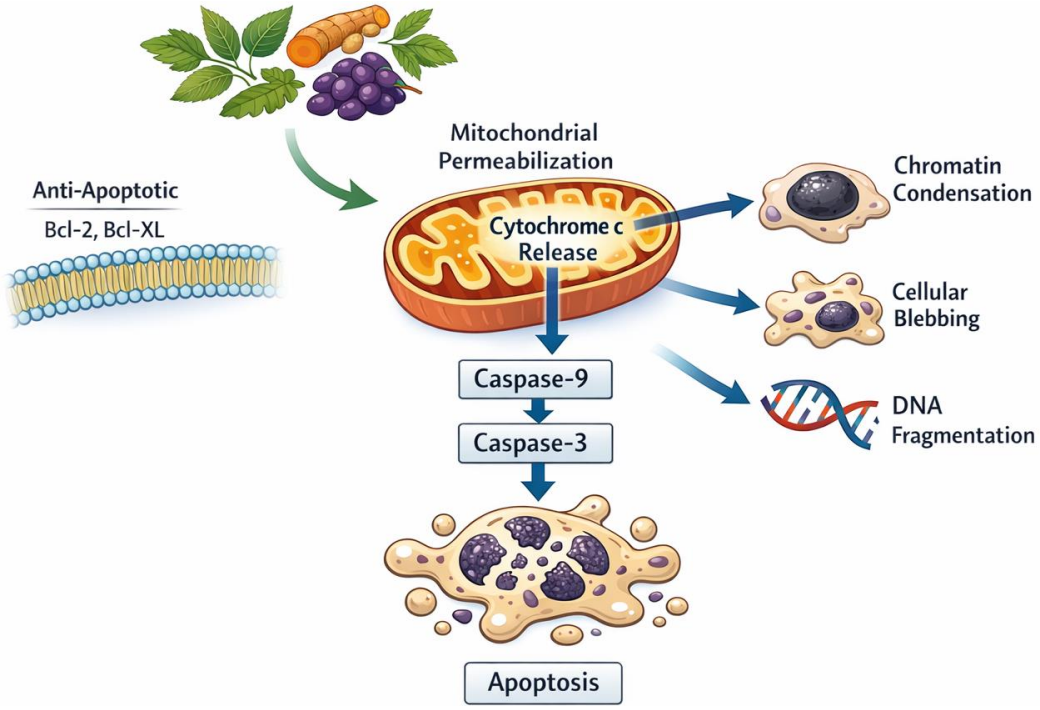

Figure 1. Apoptosis induction by anticancer phytochemicals [Created by the author based on well-established mechanisms reported in the literature by Mustafa *et al*. (2024) and Tat *et al*. (2025)].

In addition to regulating cyclins, phytochemicals can activate tumour suppressor pathways involved in cell-cycle control. Upregulation of cyclin-dependent kinase inhibitors such as p21 and p27 strengthens cell-cycle checkpoints and prevents uncontrolled proliferation. Furthermore, activation of checkpoint kinases such as Chk1 and Chk2 in response to DNA damage contributes to sustained growth arrest and increased sensitivity of cancer cells to apoptosis (Majrashi *et al.,* 2023; Carroll and Marangos, 2013).

Modulation of oxidative stress and reactive oxygen species

Reactive oxygen species (ROS) play a complex role in cancer biology. Cancer cells typically maintain elevated basal ROS levels as a result of metabolic reprogramming and mitochondrial dysfunction. This altered redox balance creates a vulnerability that can be exploited by anticancer therapies (NavaneethaKrishnan *et al.,* 2019). Phytochemicals can modulate oxidative stress in a context-dependent manner. During early stages of carcinogenesis, many polyphenols act as antioxidants by scavenging free radicals and enhancing endogenous antioxidant defences (Mileo *et al.,* 2016; Rajendran *et al.,* 2022). However, in established tumours, certain phytochemicals promote excessive ROS generation that exceeds the antioxidant capacity of cancer cells, resulting in oxidative damage and apoptosis (Chirumbolo *et al.,*

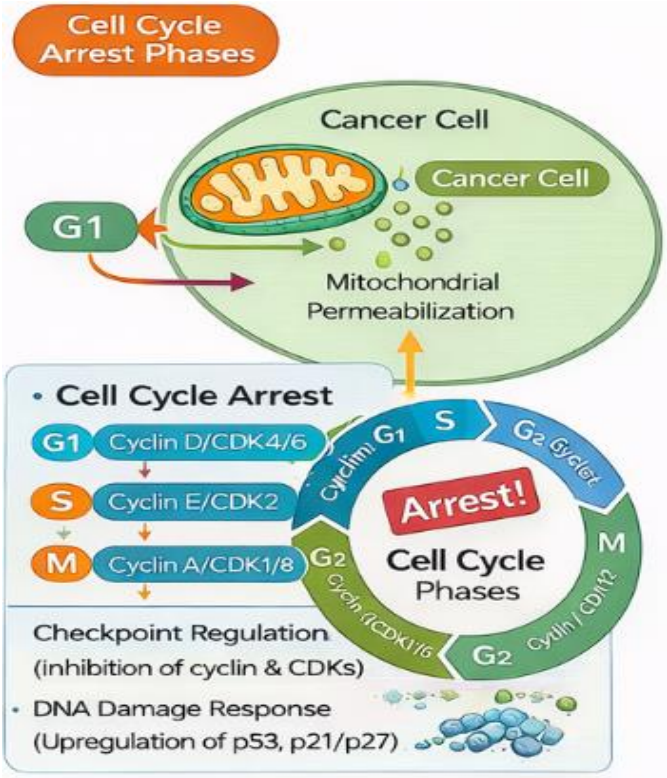

Figure 2. Cell cycle arrest induced by anticancer phytochemicals [Created by the author based on well-established mechanisms reported in the literature by Garcia-Oliveira *et al.* (2021) and Olofinsan et al. (2023)].

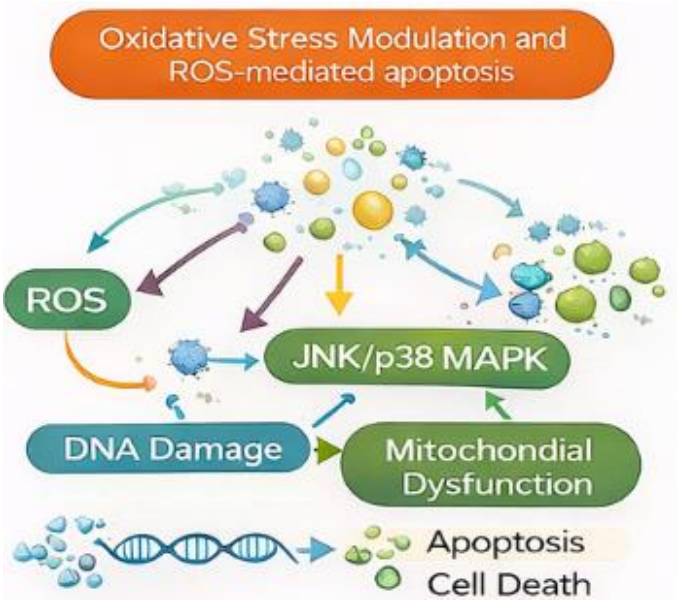

Figure 3. Oxidative stress modulation and reactive oxygen species (ROS)-mediated apoptosis in cancer cells (Created by the author, based on well-established mechanisms reported in the literature by Liu *et al.* (2025)).

2018).

Elevated ROS levels can activate stress-responsive signalling pathways such as c-Jun N-terminal kinase (JNK) and p38 MAPK, which contribute to mitochondrial dysfunction and apoptosis. In addition, ROS accumulation may promote ferroptosis, a form of regulated cell death characterised by lipid peroxidation and iron-dependent oxidative damage (Jiang *et al.,* 2025). These mechanisms contribute to the selective cytotoxic effects of phytochemicals in cancer cells (Fakhri *et al.,* 2025).

Inhibition of angiogenesis and metastasis

Tumour growth and progression require the formation of new blood vessels through a process known as angiogenesis. This process is primarily regulated by vascular endothelial growth factor (VEGF) and associated signalling pathways that stimulate endothelial cell proliferation and migration (Mahaki *et al.,* 2025). Several phytochemicals derived from medicinal plants inhibit angiogenesis by suppressing VEGF expression and interfering with downstream signalling pathways such as PI3K/Akt. These effects limit the formation of new blood vessels and restrict tumour growth (Ahmed *et al.,* 2022).

Phytochemicals also influence metastasis by regulating epithelial–mesenchymal transition (EMT), a process that enables cancer cells to acquire migratory and invasive properties. Downregulation of transcription factors such as Snail, Twist, and ZEB1, along with suppression of matrix metalloproteinases including MMP-2 and MMP-9, reduces cancer cell invasion and metastasis (Cui *et al.,* 2020). In addition to these mechanisms, plant-derived compounds can modulate the tumour microenvironment by regulating inflammatory mediators and immune cell signalling pathways, thereby reducing tumour progression and metastatic potential (Zubair *et al.,* 2020).

PLANT-MEDIATED SULFUR NANOPARTICLES AS EMERGING ANTICANCER AGENTS

The therapeutic application of plant-derived compounds is often limited by poor solubility, low bioavailability, and instability of many phytochemicals. These limitations have stimulated increasing interest in nanotechnology-based delivery systems that can improve the pharmacological properties of natural compounds (Garcia-Oliveira *et al.,* 2021; Siddiqui *et al.,* 2022). Nanoparticles can enhance drug stability, increase cellular uptake, and enable targeted delivery to tumour tissues, thereby improving therapeutic efficacy (Yap *et al.,* 2021). Among emerging nanomaterials, sulfur nanoparticles (SNPs) have gained considerable attention due to their favourable physicochemical properties, including high surface area, redox activity, and relatively low toxicity compared with many metal-based nanoparticles (Shukla *et al*., 2024). At the nanoscale, sulfur exhibits enhanced reactivity and improved interaction with cellular components, which may contribute to its biological activity (Ghotekar, 2019).

Green synthesis of nanoparticles using plant extracts has emerged as a sustainable alternative to conventional chemical synthesis methods. This approach avoids the use of toxic reducing agents and energy-intensive procedures while utilising naturally occurring phytochemicals as reducing and stabilising agents (Oza *et al.,* 2020; Kamyab *et al*., 2025). Plant-mediated synthesis, therefore, integrates phytochemistry with nanotechnology, providing environmentally friendly strategies for nanoparticle production.

Green synthesis of sulfur nanoparticles using plant materials

Green synthesis of sulfur nanoparticles typically involves the use of plant extracts rich in bioactive phytochemicals such as flavonoids, phenolics, alkaloids, and saponins. These compounds can function as both reducing agents and stabilising molecules during nanoparticle formation, facilitating the conversion of sulfur precursors into nanoscale particles while preventing aggregation (Paralikar *et al.,* 2017; Alqahtani *et al.,* 2025). Several plant sources have been successfully utilised for the biosynthesis of sulfur nanoparticles. For instance, sulfur nanoparticles synthesised using Cannabis sativa leaf extract exhibited controlled particle size and stable surface functionalization attributed to the presence of phenolic

compounds (Dasauni *et al.,* 2024). Similarly, Allium sativum (garlic) extract has been used to produce stable sulfur nanoparticles with well-defined morphology and enhanced biological activity (Khairan *et al.*, 2023).

Other plant materials have also demonstrated promising results in sulfur nanoparticle synthesis. For example, *Citrus limon* extract has been used to produce sulfur nanoparticles with particle sizes ranging from approximately 40 to 55 nm and moderate colloidal stability (Baloch *et al.,* 2023). Similarly, sulfur nanoparticles synthesised from *Citrus sinensis* peel extracts exhibited crystalline structures and functional surface groups as confirmed by spectroscopic and diffraction analyses (Usman *et al.,* 2026). The physicochemical properties of nanoparticles, including particle size, surface charge, morphology, and surface functionalization, play important roles in determining their biological behaviour. Smaller nanoparticles with optimised surface characteristics generally demonstrate enhanced cellular uptake through endocytic pathways, which may improve their therapeutic effectiveness (Zahran *et al.,* 2018; Kamyab *et al*., 2025).

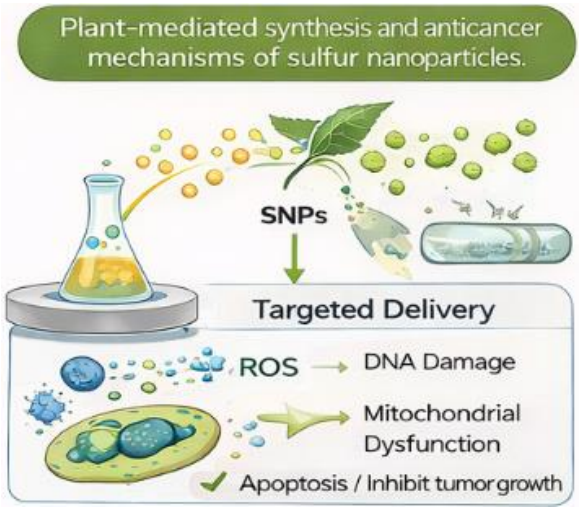

Figure 4. Plant-mediated synthesis and anticancer mechanisms of sulfur nanoparticles [Created by the author based on well- established mechanisms reported in the literature by Al-redha et al. (2026)].

ANTICANCER ACTIVITY AND MECHANISMS OF ACTION OF PLANT-MEDIATED SULFUR NANOPARTICLES

In vitro anticancer activity

A growing body of experimental evidence suggests that sulfur nanoparticles possess significant anticancer potential. *In vitro* studies have demonstrated that SNPs exhibit dose-dependent cytotoxic effects against various cancer cell lines, including breast, colon, and lung cancer models (Krishnappa *et al.,* 2021). Mechanistically, sulfur nanoparticles can induce apoptosis in cancer cells through several pathways. One of the primary mechanisms involves increased generation of reactive oxygen species, which disrupts mitochondrial membrane potential and activates caspase-dependent apoptotic pathways. Elevated ROS levels can also activate stress-responsive signalling pathways such as JNK and p38 MAPK, further promoting apoptosis (Liu *et al.,* 2025).

Recent investigations have reported that green-synthesised sulfur nanoparticles significantly reduce the viability of colon cancer cells, including HT-29 models, through ROS-mediated mitochondrial damage and activation of apoptotic signalling pathways (Al-Redha *et al.,* 2026). In addition, phytochemical molecules associated with the nanoparticle surface may enhance cytotoxic effects by modulating additional signalling pathways involved in cell proliferation and apoptosis (Dasauni *et al.,* 2024). Comparative studies have also indicated that nanoparticle formulations frequently demonstrate greater anticancer activity than crude plant extracts. This improvement is likely due to enhanced cellular uptake, improved stability, and prolonged retention of nanoparticles within tumour cells (Yap *et al.,* 2021).

In vivo evidence and biological relevance

In vivo studies further support the anticancer potential of sulfur nanoparticles. Experimental investigations in animal models have shown that SNP treatment can reduce tumour size and influence oxidative stress markers associated with cancer progression (Zahran *et al.,* 2018). These studies suggest that sulfur nanoparticles can modulate redox balance within tumour tissues, leading to increased oxidative stress and enhanced apoptosis in cancer cells. Changes in antioxidant enzyme activity and reductions in lipid peroxidation have also been reported following nanoparticle treatment.

Plant-mediated synthesis may offer additional advantages compared with chemically synthesised nanoparticles. Phytochemical molecules present on the nanoparticle surface can improve biocompatibility and potentially reduce systemic toxicity while enhancing biological activity (Karnwal *et al.,* 2024). Furthermore, the use of plant extracts provides sustainable and scalable approaches for nanoparticle production, supporting the development of environmentally friendly nanomedicine strategies (Shukla *et al*., 2024; Kamyab *et al*., 2025). Although these findings are promising, further research is required to evaluate the safety, pharmacokinetics, and long-term therapeutic potential of plant-mediated sulfur nanoparticles. Interdisciplinary collaboration between phytochemistry, nanotechnology, and oncology will be essential to translate these experimental findings into clinically applicable therapies (Yadav *et al.,* 2020).

CONCLUSION

Medicinal plants represent an important source of

structurally diverse bioactive compounds with significant potential for cancer therapy. Phytochemicals such as alkaloids, terpenoids, polyphenols, and saponins exert anticancer effects through multiple mechanisms, including apoptosis induction, cell-cycle arrest, modulation of oxidative stress, and inhibition of angiogenesis and metastasis. The multitarget nature of these compounds may provide advantages in overcoming drug resistance and improving therapeutic outcomes. Plant-mediated sulfur nanoparticles further enhance these effects by improving bioavailability, stability, and targeted delivery, while also exhibiting intrinsic anticancer activity. Despite these promising findings, challenges related to standardisation, safety, and clinical validation remain.

Future research directions

Future research should focus on the standardisation of plant extracts, identification of molecular targets using advanced omics technologies, development of targeted nanoparticle delivery systems, and comprehensive pharmacokinetic and toxicological evaluations. In addition, well-designed clinical studies will be necessary to determine the safety and therapeutic efficacy of plant-derived nanomaterials in cancer treatment.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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