IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 2, October 2025
Impact Factor: 7.67

+Herbal Drugs Used in the Treatment of Cancer

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Abstract: *Cancer remains one of the leading causes of morbidity and motility worldwide, posing significant challenges of to health care systems despite advanced in convention therapies such as chemotherapy, radio therapy and targeted drugs .how ever ,this treatment are often limited by severe side effects, drug resistance ,and high costs ,prompting increase interest in herbal drugs complimentary or alternative approaches. Herbal medicines, derive from medicinal plants ,contain diverse bioactive phytochemicals including alkaloids ,flavonoids,terpenoids,and polyphenols,many of which exhibit potent anticancer properties.this compound can modulate multiple molecular targets and pathways, such as apoptosis induction, angiogenesis innovation,oxidative stress reduction , and immune system inhancement. Notable examples include camptotheca acuminata (source of camptothecin), taxes brevifollia(pactaxel) catharanthus roseus (vincristine and vinblastine) , curcuma longa (curcumin). Clinical and preclinical studies suggest that this agents may act synergistically with conventional therapies , inproving efficacy while minimizing toxicity.further more ,certain herbal drugs possess chemopreventive potial ,reducing the risk of cancer intiation and progression through antioxidant and anti inflamantory mechanisms. despite promising outcomes changelles remain regarding standardization, quality control, dosages optimization ,and herb drug interaction ,which necessitate rigorous scientific validation and regulatory oversight. this review provides and overview of key herbal drugs with demonstrated anticancer potential, discussing their pharmacological mechanism, therapeutic application, current research status. By integrating traditional knowledge with modern phamacological insides, herbal drugs offers promising avenue for the development of novel, effective ,and saferan anti-cancer therapies*

Keywords: Herbal medicines, cancer treatment, phytochemicals chemoprevention, supplimentory therapies, drug discovery

I. INTRODUCTION

Cancer is one of the leading causes of death and illness worldwide. The number of cancer cases is increasing and could reach 21 million by 2030. Cancer is hard to treat because it can vary a lot – depending on the type, the organ affected, the genes involved, and how far the disease has spread. Although there are many treatment options available, their success depends on the type and stage of cancer.[1]

Common Cancer Treatments

Cancer is usually treated with:

Surgery – to remove the tumor

Radiotherapy – to kill cancer cells with radiation

Chemotherapy – to kill cancer cells using chemical drugs

Immunotherapy – to help the immune system fight cancer

Targeted Therapy – to attack specific molecules in cancer cell

Surgery and radiotherapy affect only the part of the body being treated, while chemotherapy and targeted therapy affect the whole body.[1]

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Chemotherapy

Chemotherapy uses drugs to kill fast-growing cells, like cancer cells. But it can also harm healthy cells, causing side effects like:

Nausea and vomiting
Hair loss
Fatigue
Mouth sores
Nerve damage
Weak immune system

Chemotherapy drugs fall into five main groups:

1. Alkylating agents (e.g., cisplatin)
2. Antimetabolites (e.g., 5-fluorouracil)
3. Antitumor antibiotics (e.g., doxorubicin)
4. Topoisomerase inhibitors (e.g., topotecan)
5. Tubulin-binding drugs (e.g., paclitaxel)

One major problem with chemotherapy is drug resistance – where cancer cells stop responding to treatment. This causes over 90% of cancer-related deaths during chemotherapy.[1]

Targeted Therapy

Unlike chemotherapy, small molecule targeted therapy (SMTT) focuses on specific changes in cancer cells. These drugs attack cancer-causing proteins that help tumors grow and survive. [1] Some examples include:

Imatinib
Carfilzomib
Ribociclib

These drugs usually have fewer side effects, but they can still cause problems like skin rash, diarrhea, and high blood pressure[1]. Resistance to these drugs can also develop over time.

The Role of Herbal Medicine

Because many synthetic (man-made) drugs have serious side effects and don't always pass clinical trials, researchers are looking into safer and more natural alternatives. Herbal medicine, used for centuries in many cultures, is gaining renewed interest[1]. In developing countries especially, herbal treatments are popular because they are believed to be safer[1].

Plants contain bioactive compounds that may:

Kill cancer cells by triggering cell death (apoptosis)
Stop the growth of blood vessels that feed tumors (anti-angiogenesis)
Block the spread of cancer cellsCommon Medicinal Plants with Anti-Cancer Effects

Ten herbs often used in the Middle East include:

Vinblastine and Vincristine – from the Madagascar periwinkle; used for blood cancers
Olive (Olea europaea)
Black cumin (Nigella sativa)
Saffron (Crocus sativus)
Pomegranate (Punica granatum)
Stinging nettle (Urtica dioica)
Garlic (Allium sativum)
Onion (Allium cepa)

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Turmeric (Curcuma longa)
Palestinian arum (Arum palaestinum)
Grapes (Vitis vinifera)
Successful Herbal Medicines
Some plant-based cancer drugs used in modern medicine include:
Paclitaxel (Taxol®) – from the Pacific yew tree; used for breast, lung, and ovarian cancer
Camptothecin – from a Chinese tree; led to drugs like topotecan and irinotecan
Etoposide and Teniposide – derived from the mayapple plant; used for lung and testicular cancer
Recent research focuses on herbal compounds like:
Curcumin (from turmeric)
Resveratrol (from grapes)
EGCG (from green tea)
These compounds show anti-cancer effects in lab studies by reducing inflammation, killing cancer cells, and stopping tumor growth.

Advances and Challenges

Many traditional healing systems, like Traditional Chinese Medicine and Ayurveda, have used herbs for cancer for centuries. In the past, herbal medicine was pushed aside by modern drug development, but new technologies now allow better research and use of plant-based treatments.
Modern science can:
Improve how herbal compounds are delivered (e.g., using nanoparticles) Increase their absorption and effectiveness Reduce side effects However, herbal medicines also face challenges:
The quality and strength of plant extracts can vary
Standard dosages are hard to establish They can interact with other drugsTheir exact working mechanisms are not always fully understood[1]
Cancer is a complicated disease that often needs different types of treatment. For cancers that have spread (metastatic cancers), doctors usually treat them with special drugs approved by the FDA. These are called systemic therapies, which means they affect the whole body.
One major problem with chemotherapy is the serious side effects it causes. This is because many chemotherapy drugs target the DNA of cells, and they can't tell the difference between cancer cells and healthy cells that grow quickly. As a result, healthy areas like the bone marrow, hair follicles, and the lining of the digestive system are also damaged.
These side effects can lower a patient's quality of life and may cause some people to stop taking their medication. When this happens, the cancer can become resistant to the drugs, making treatment even harder.
Many cancer patients choose to use herbal medicines (also called complementary or alternative medicine – CAM) along with chemotherapy. They do this for several reasons, such as:
To reduce the side effects of chemotherapy
To support overall health
To help with symptoms of the disease
To strengthen the immune system
Besides patients choosing to use herbs on their own, researchers are also studying how herbal medicine might be officially included in cancer treatments to help reduce the side effects of chemotherapy.[2]

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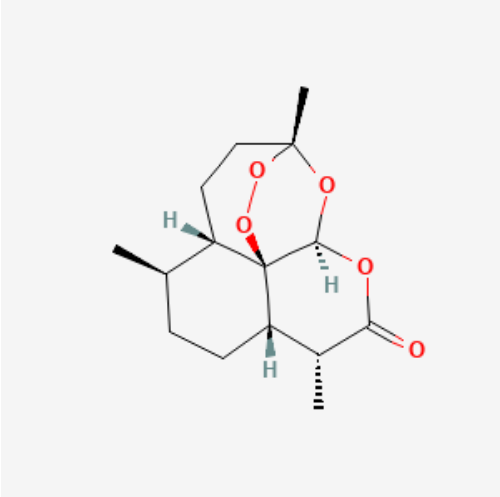
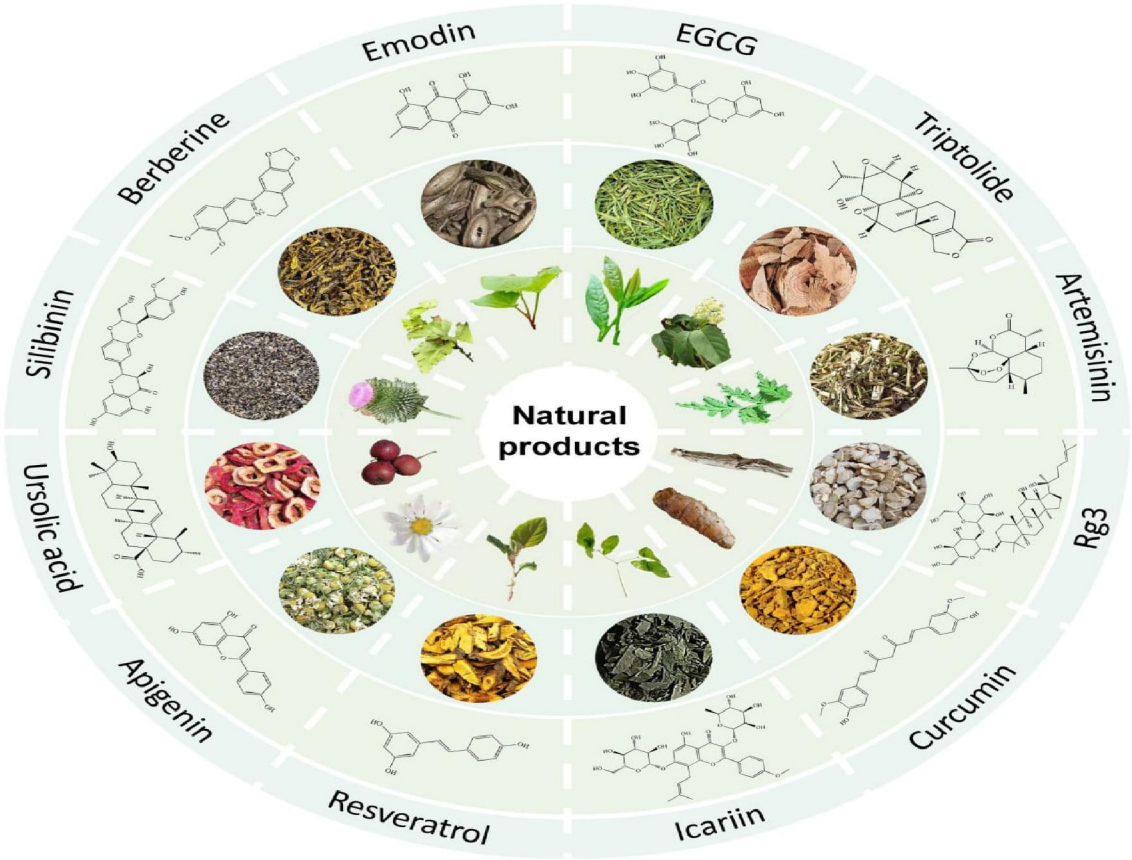
Artemisinin



Artemisinin is a sesquiterpene lactone compound derived from Artemisia annua L., a traditional Chinese medicinal herb (Qinghao in Chinese)[3]



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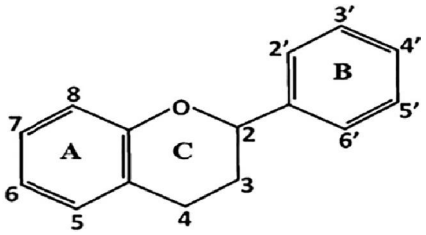
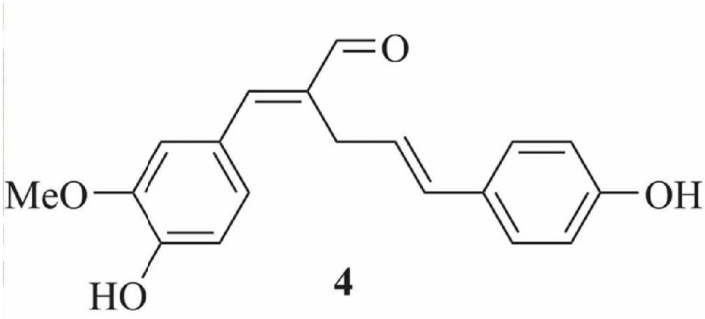
Flavonoid



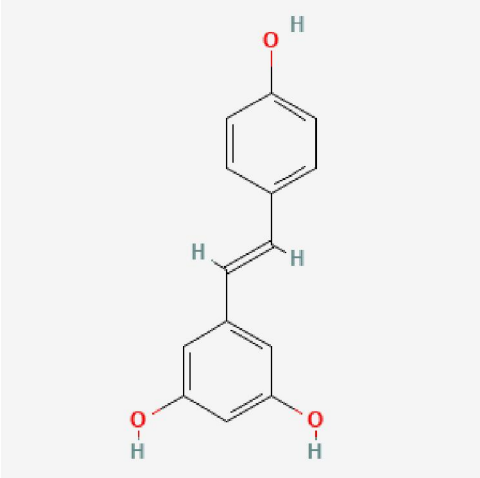
Early studies have shown that certain natural compounds called flavonoids, which are types of polyhydroxy phenols, may help lower the risk of colon and breast cancer[4] .Flavonoids are from the polyphenolic compounds and constitute a large family of plant secondary metabolites with 10,000 known structures 19. They are physiologically active agents in plants and becoming of high interest scientifically for their health benefits [5]

Alpinia galangal:



Acetoxy-chavicol-acetate(ACA), isolated from Alpinia galanga, possesses significant anticancer activity against cancers of breast, lung, stomach, colon, prostate, multipleyeloma and leukaemia. Pinocembrin isolated from Alpinia galanga inhibits growth and spread in colon cancer by arresting cell proliferation and inducing apoptosis. Galangin, a flavonoid isolated from Alpinia galanga, possesses strong anticancer, antioxidant, antimutagenic and anti-inflammatory properties. Galangin protects against breast and prostate cancers [6]

Resveratrol



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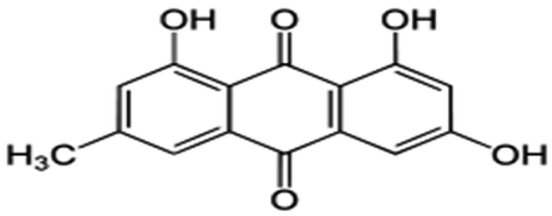
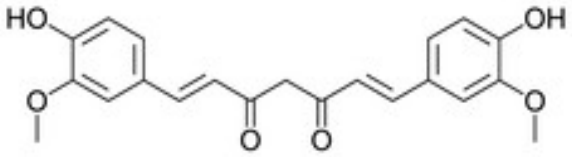
This natural polyphenol is a phytoalexin exhibiting very high antioxidant and an-timicrobial potential, acting against many pathogens, including bacteria and fungi. Othereffects, such as cardioprotective, phytoestrogenic, and neuroprotective, have also beenreported. Moreover, it could inhibit the growth of many cancers both in vitro and in vivo.At doses less than 1 g/d, resveratrol does not appear to cause side-effects. At doses of2.5 g/d or more, side-effects, such as nausea, vomiting, diarrhea, and liver dysfunction,could be observed. However, in long-term clinical trials, no significant side-effects were noticed[7]

Emodin



Emodin is a trihydroxyanthraquinone that is 9,10-anthraquinone which is substitutedby hydroxy groups at positions 1, 3, and 8, and by a methyl group at position 6. It is present in the roots and barks of numerous plants, moulds, and lichens. It derives from an emodin anthrone[8].

Curcuma longa



Turmeric is a plant with scientific name Curcuma longa from the Zingiberaceae family. This perennial plant usually requires humid and rainy environment. The main habitat of turmeric is hot areas of Asia such as India, Pakistan, Indonesia, and southern China, and it is native of Africa and South America. Turmeric has underground stem called rhizome. Several aerial shoots as high as 1 to 1.5 meters exit from these rhizomes.Edible part of turmeric is dried rhizomes.

The study of cytotoxic properties of turmeric on liver cancer cells (Hep-2) showed that the cytotoxicity mediated by curcumin in a dose-dependent manner leads to apoptosis of cancercells through mitochondrial pathway.The results of studying the effects of its extract on telomerase activity in breast cancer showed anti-proliferative and inhibitory effects of telomerase. In another study, it was found that turmeric imposes its cytotoxic effects on lung cancer cells through inhibition of telomerase activity in a dose-dependent manner. Curcumin, as an important ingredient of turmeric, plays a significant role in the prevention and treatment of primary ovarian cancer, and multiple clinical studies have proven its effectiveness. The anticancer potential of curcumin against cancers, including leukemia, lymphoma, digestive, urinary, reproductive, breast, uterus, ovary, lung, melanoma, colon cancers, and brain tumors have been shown. Free radicals and toxic products of oxidative stress play a significant role in the development of many diseases, including cancer, and curcumin has antioxidant effects that reduce or inhibit damage caused by free radicals. One study showed that treatment of human blood lymphocytes with curcumin significantly reduces genetic damage caused by radioactive iodine-131. Another study showed that curcumin induces apoptosis and inhibits proliferation of cancer cells. Apoptosis occurs due

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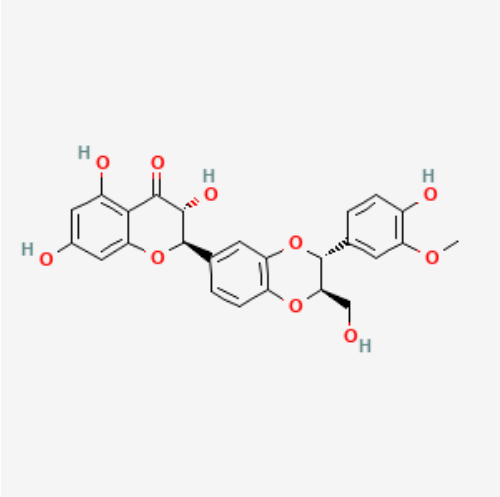
to release of cytochrome and its effect on P53 protein as well as the effect on intracellular signals is responsible for stopping cell growth. In fact, the mechanisms by which curcumin inhibits tumor formation are combination of properties including antioxidant[9]. It is cultivated all over Bangladesh. It is found that turmeric has been used in the Chinese and Indian pharmacopoeia from ancient time. It is known that turmeric's active ingredient is an extracted compound called curcumin. Some previous studies showed that that curcumin helps to prevent several forms of cancer including lung, breast, stomach, liver, and colon because of its anti-inflammatory as well as antioxidant properties. It stops the growth of cancer by interfering with the cellular signaling phases of cancer[10].

Silibinin



Silibinin, the principal bioactive compound of the silymarin extract from Silybum marianum (milk thistle), has long been recognized for its hepatoprotective and antioxidant properties, with established clinical use in liver disorders and mushroom poisoning. Beyond liver protection, silibinin exhibits diverse biological activities, including anti-inflammatory, antiviral, and anticancer effects. Preclinical and translational studies have highlighted its potential in lung cancer, where it can suppress tumor initiation, growth, and angiogenesis through the downregulation of VEGF, COX-2, and iNOS, largely mediated via inhibition of the STAT3 signaling pathway. Importantly, silibinin demonstrates a strong safety profile, making it an attractive candidate for long-term chemoprevention In therapeutic contexts, silibinin has been shown to inhibit proliferation, induce apoptosis, and overcome drug resistance in non-small cell lung cancer (NSCLC) models. It synergizes with chemotherapeutic agents and tyrosine kinase inhibitors (EGFR and ALK TKIs), reducing toxicity and resensitizing resistant tumors. Moreover, it counteracts metastasis by inhibiting epithelial-to-mesenchymal transition (EMT) and blocking key signaling pathways such as PI3K/AKT, MAPK, and STAT3. Clinical observations further support its ability to improve outcomes in patients with lung cancer brain metastases, particularly when administered in bioavailable formulations. These findings position silibinin as a promising natural compound for both prevention and treatment of lung cancer, with ongoing research focusing on optimized derivatives and combination strategies[11].

EGCG

Epigallocatechin gallate (EGCG), a major polyphenol in green tea and grapes, has gained attention for its strong antioxidant and anticancer properties. Cancer arises mainly from oxidative stress, DNA mutations, chronic inflammation, and dysregulated signaling pathways. EGCG helps counteract these processes by neutralizing reactive oxygen species, reducing pro-inflammatory markers, activating antioxidant enzymes, suppressing oncogenes, and enhancing tumor suppressor genes.

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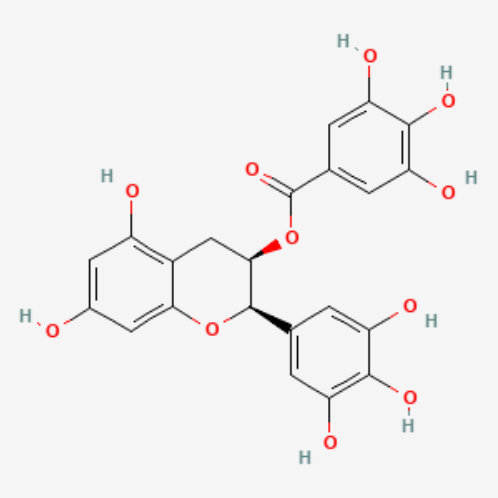
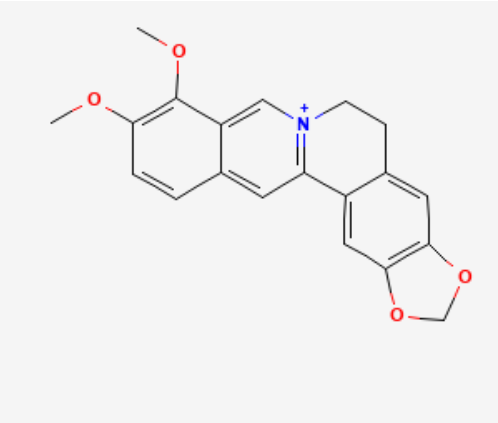


Although its natural bioavailability is low, strategies like nanoparticle delivery systems have significantly improved its stability and therapeutic impactExperimental studies show that EGCG can inhibit tumor growth, reduce metastasis, and induce apoptosis across many cancers including lung, breast, pancreatic, prostate, liver, kidney, bladder, colorectal, uterine, gastric, and bone cancers. It mainly works by modulating pathways such as PI3K/AKT, MAPK, NF-κB, and Wnt/β-catenin. Clinical trials in humans suggest EGCG and green tea extracts are safe and sometimes effective, but results are mixed, highlighting the need for larger, more standardized studies. Overall, EGCG represents a promising natural anticancer agent with potential for integration into future therapies[12].EGCG inhibits tumorigenesis and cancer progression by triggering apoptosis, suppressing proliferation, invasion, and migration, and altering tumor epigenetic modifications. It modulates the tumor microenvironment (TME) by suppressing tumor-associated macrophages (TAMs) infiltration and inflammatory chemokines, inhibits angiogenesis by downregulating VEGF and other proangiogenic factors, and prevents stromal cell activation and extracellular matrix remodeling. EGCG also impacts metabolic reprogramming by suppressing key metabolic pathways such as glucose uptake, aerobic glycolysis, and glutamine metabolism in tumor cells. Moreover, EGCG enhances antitumor immune responses, promoting cytotoxic lymphocytes and dendritic cell function while attenuating immunosuppressive cells like myeloid-derived suppressor cells and regulatory T cells[13].

Berberine



Skin cancers such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma remain a major health concern due to their high incidence, aggressive behavior, and treatment resistance. Research demonstrates that berberine can inhibit cell proliferation, trigger apoptosis, block metastasis, and suppress angiogenesis. Its mechanisms

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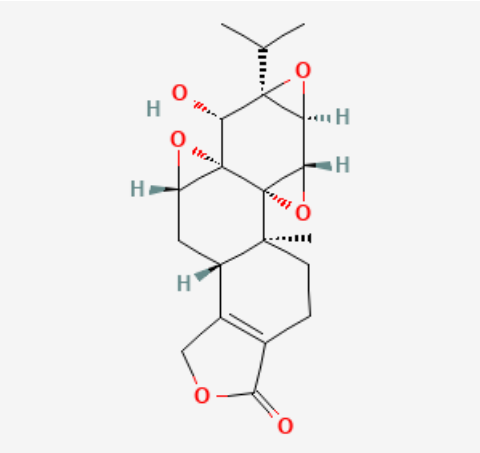
include modulation of the PI3K/AKT/mTOR pathway, activation of AMPK, accumulation of ROS, and regulation of transcription factors such as NF-κB and p53. In melanoma, berberine reduces epithelial–mesenchymal transition (EMT), inhibits migration through NF-κB/FAK/uPA signaling, and enhances apoptosis via ROS-caspase pathways. It also shows promise in combination therapies—for example, improving cisplatin sensitivity, synergizing with doxorubicin, or serving as a photosensitizer in photodynamic therapy. In SCC, berberine increases the Bax/Bcl-2 ratio, reduces Ezrin expression, and suppresses NF-κB–driven inflammation, thereby limiting tumor growth and invasion. Novel formulations such as nanoparticles and derivatives have further improved its bioavailability and anticancer potency[14].Berberine (BBR), an isoquinoline alkaloid mainly extracted from plants like Berberis and Coptis, has gained attention as a multifunctional compound with anticancer potential. Studies demonstrate that it suppresses tumor progression in cancers of the breast, colon, pancreas, liver, gastric system, bone, prostate, oral cavity, thyroid, skin, and brain. Its mechanisms involve inducing apoptosis, cell cycle arrest, and autophagy regulation, while also reducing invasion, metastasis, and drug resistance. Berberine influences several pathways such as PI3K/Akt/mTOR, MAPK, Wnt/β-catenin, NF-κB, and AMPK, in addition to modulating inflammatory cytokines and non-coding RNAs. Although berberine exhibits low oral bioavailability, strategies like nanotechnology and drug co-administration have been explored to enhance its absorption. Despite the absence of an approved clinical formulation, current evidence supports berberine as a strong candidate for future anticancer drug development[15].Berberine is a yellow alkaloid with poor solubility in most solvents and a structure of four rings where specific groups contribute to its anticancer and antibacterial effects. Structural modifications, especially in the C and D rings, enhance activities Like hypoglycem
ic, cytotoxic, and antiproliferative effects, while its fluorescence makes it useful for analytical detection[16].

Triptolide



Triptolide is a natural compound from Tripterygium wilfordii (“Thunder God Vine”) with strong anticancer, anti-inflammatory, and immunosuppressive effects. It works by stopping cancer cell growth, inducing apoptosis, blocking angiogenesis, and inhibiting DNA/RNA transcription, but its clinical use is limited due to poor solubility and high toxicity, especially to the liver and kidneys. Recent research focuses on nanotechnology-based delivery systems (like nanoparticles, liposomes, and micelles) to improve its safety and effectiveness, and combination therapies with other anticancer drugs are also being explored. Overall, Triptolide shows great promise as an anticancer agent, but more clinical studies are needed to overcome toxicity challenges and confirm its therapeutic potential[17].

Ursolic acid

Ursolic acid is a naturally occurring pentacyclic triterpenoid, abundantly present in apples, rosemary, basil, and other medicinal plants, and is well recognized for its broad spectrum of pharmacological effects [18].In recent years, it has gained significant attention for its ability to act against different types of cancers, especially gastrointestinal malignancies

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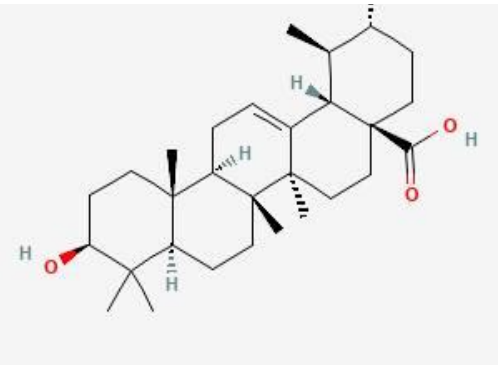
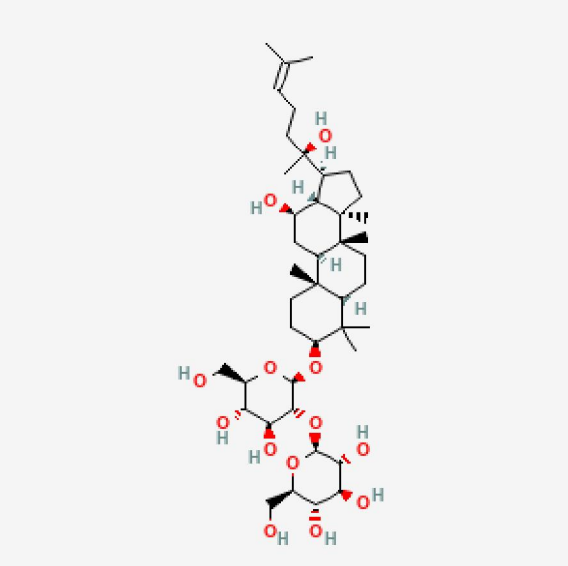


Mechanistically, ursolic acid can trigger programmed cell death (apoptosis) by activating caspase pathways and regulating the balance of pro- and anti-apoptotic proteins[19].It also inhibits uncontrolled proliferation of cancer cells, reduces tumor-induced angiogenesis, and modulates inflammatory cytokines, which together slow down tumor initiation and progression[19].At the molecular level, ursolic acid interferes with several key signaling cascades, including NF-κB, PI3K/Akt, MAPK, and STAT3, which are commonly deregulated in gastrointestinal cancers[19]. By targeting these pathways, it not only suppresses tumor growth but also helps in overcoming resistance mechanisms that make standard chemotherapy less effective[19]. Despite its therapeutic promise, native ursolic acid faces challenges such as poor water solubility, limited absorption, and rapid metabolism, which reduce its bioavailability[18]. To overcome these limitations, structural modifications and the development of derivatives have been explored, many of which show enhanced cytotoxicity and better pharmacokinetic properties compared to the parent compound[18].Additionally, advanced delivery systems like nanoparticles, liposomes, and polymer conjugates are being designed to improve drug stability, solubility, and targeted delivery[18]. Importantly, ursolic acid has also been shown to sensitize cancer cells to chemotherapeutic drugs, reduce multidrug resistance, and minimize treatment-associated side effects[19] These combined properties highlight its potential not only as a standalone therapeutic but also as an adjuvant in combination cancer therapies[18].

Rg3



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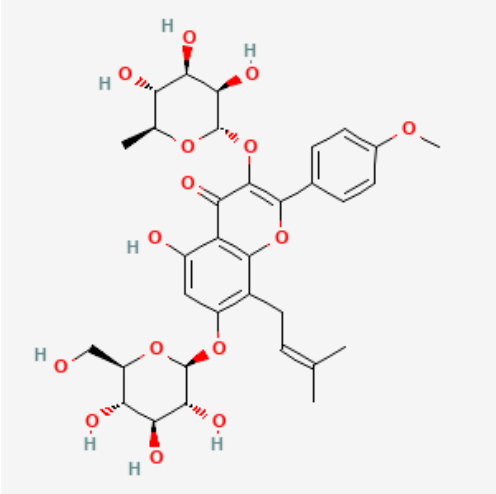
Ginsenoside Rg3 (GS-Rg3), a tetracyclic triterpene saponin derived from red ginseng, has been extensively studied for its anticancer potential [20]. It exists in two stereoisomers, 20(S) and 20(R), which differ in solubility and biological activity [21]. GS-Rg3 shows strong inhibitory effects on tumor growth by blocking cancer cell proliferation, migration, and metastasis [20].One of its major anticancer mechanisms is the suppression of angiogenesis, where GS-Rg3 prevents tumor vascular endothelial cell proliferation and reduces vascular endothelial growth factor (VEGF) expression through the PI3K/Akt and ERK1/2 pathways [21]. It also influences apoptosis by activating caspase signaling and regulating mitochondrial pathways, leading to cancer cell death[20].

Another important property of GS-Rg3 is its ability to overcome multidrug resistance and enhance the effectiveness of chemotherapeutic agents, thereby improving treatment response [20,21]. Recent advances include the development of nanomedicine formulations such as NpRg3, which combine GS-Rg3 with nanoparticles to improve solubility, stability, and targeted drug delivery, resulting in stronger anticancer effects in experimental models [21] . Additionally, GS-Rg3 has shown immune-modulating activities by enhancing antitumor immunity and reducing tumor-induced immunosuppression [20]. These properties highlight its potential not only as a direct anticancer compound but also as an adjuvant in modern cancer therapies [20,21].

Icariin



Icariin, a natural flavonoid derived from the traditional Chinese medicinal herb Herba Epimedium, possesses a wide range of pharmacological activities, including cardioprotective, anti-inflammatory, bone-regenerative, neuroprotective, antidepressant, and anticancer effects, with relatively low toxicity. One of its important features is the ability to cross the blood–brain barrier, allowing it to reach tumor cells more effectively. In glioblastoma models, icariin has been shown to inhibit the growth of U87 cells in a concentration-dependent manner. It also enhances the anticancer activity of temozolomide while reducing cell migration and invasion, likely through the suppression of NF-κB signaling[22].Apart from its traditional role, modern studies show that icariin has broad pharmacological activities, including anti-inflammatory, antioxidant, neuroprotective, cardioprotective, and bone-strengthening properties [23].

In recent years, increasing evidence has focused on its role in cancer therapy. Both in vitro and in vivo studies suggest that icariin can inhibit tumor cell proliferation, induce apoptosis, and suppress invasion and metastasis in multiple cancer types such as breast, lung, liver, prostate, and colorectal cancers [23,24].

Icariin also regulates important signaling pathways like PI3K/Akt, MAPK, NF-κB, and Wnt/β-catenin, which play a critical role in cancer progression and drug resistance [24].Furthermore, it has been reported to reduce angiogenesis, modulate tumor immune responses, and enhance the sensitivity of cancer cells to chemotherapy, suggesting its potential role as an adjuvant therapy [24].Taken together, these findings highlight icariin as a promising natural compound with multi-target anticancer effects, offering opportunities for future drug development and clinical application [24].

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II. CONCLUSION

Herbal medicines hold significant potential as anticancer agents because of their ability to target multiple signaling pathways, enhance the effects of conventional therapies, and reduce side effects. Compounds such as curcumin, resveratrol, berberine, icariin, silibinin, EGCG, ursolic acid, Rg3, and triptolide demonstrate wide-ranging activities including apoptosis induction, angiogenesis inhibition, immune modulation, and reversal of drug resistance. Despite these promising findings, challenges such as poor bioavailability, variability in extract quality, and lack of standardized clinical data must be resolved before herbal compounds can be fully integrated into modern oncology. Future research should focus on advanced delivery systems, well-designed clinical trials, and combination approaches that can improve efficacy and safety. By combining traditional knowledge with modern scientific advances, herbal medicines may contribute to the development of novel, affordable, and patient-friendly cancer therapies.

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International Journal of Advanced Research in Science, Communication and Technology
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ISSN: 2581-9429
Volume 5, Issue 2, October 2025
Impact Factor: 7.67

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International Journal of Advanced Research in Science, Communication and Technology
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ISSN: 2581-9429
Volume 5, Issue 2, October 2025
Impact Factor: 7.67

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ISSN: 2581-9429
Volume 5, Issue 2, October 2025
Impact Factor: 7.67

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