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Review Paper

Natural Agents Used for Cancer Management

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ABSTRACT

The increasing global burden of cancer and the limitations of conventional treatments, such as toxicity and drug resistance, have encouraged the exploration of natural agents as alternative and supportive therapeutic options [1,4,18]. Natural compounds obtained from medicinal plants, dietary sources, and microbial origins contain diverse bioactive constituents that exhibit significant anticancer potential [1,5,7,9]. This review discusses various natural agents, including polyphenols, flavonoids, alkaloids, and organosulfur compounds, with emphasis on their anticancer mechanisms and therapeutic relevance [1,6,8]. These agents have been reported to inhibit tumor initiation and progression [1,25] by regulating cell cycle arrest, promoting programmed cell death, reducing inflammation, controlling oxidative stress, and interfering with key molecular signaling pathways involved in cancer development [1,5,11]. Furthermore, several natural compounds demonstrate the ability to enhance the effectiveness of standard chemotherapy while minimizing associated side effects [2,10]. Despite encouraging experimental and early clinical findings, issues related to bioavailability, formulation, and large-scale clinical validation remain unresolved [2,11]. This review aims to summarize current knowledge on natural anticancer agents, highlight their mechanistic roles, and outline future research directions for their integration into effective cancer management strategies [1,5,9].

INTRODUCTION

Cancer is a complex group of diseases characterized by uncontrolled cell growth, disruption of normal cellular regulation, and the ability to invade surrounding tissues and metastasize to distant organs [18]. Despite significant advancements in early diagnosis and treatment, cancer continues to pose a major global health challenge [18]. Conventional treatment strategies such as chemotherapy, radiotherapy, and

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surgery have improved patient survival; however, their clinical use is often associated with severe side effects, toxicity to normal cells, high treatment costs, and the development of drug resistance [1,4]. These limitations highlight the urgent need for safer and more effective therapeutic approaches. Natural agents derived from plants, dietary sources, and microorganisms have long been utilized in traditional medicine and are now gaining renewed scientific interest for their potential role in cancer prevention and treatment [1,7,12]. Many of these agents contain bioactive compounds, including flavonoids, polyphenols, terpenoids, alkaloids, and organo sulfur compounds, which have a wide range of pharmacological activities [5,8,12]. Unlike single-target synthetic drugs, natural compounds often act on multiple molecular pathways, allowing them to interfere with various stages of cancer development [1,5,11] and progression. Accumulating experimental evidence suggests that natural anticancer agents exert their effects through modulation of key biological processes such as inhibition of cell proliferation, induction of apoptosis, regulation of the cell cycle, suppression of angiogenesis, and prevention of metastasis [1,5,11]. Additionally, these agents can influence oxidative stress, inflammation, and immune responses, which play critical roles in tumor initiation and progression [1,25]. Importantly, several natural compounds have been shown to enhance the efficacy of conventional anticancer therapies while reducing their adverse effects [2,26], making them promising candidates for combination treatment strategies. Although numerous natural agents have demonstrated strong anticancer potential in preclinical studies, challenges related to bioavailability, standardization, and clinical validation remain significant barriers to their widespread application [2,11]. Therefore, a comprehensive understanding of their sources, mechanisms of action, and therapeutic limitations is essential. This review aims to provide an updated overview of natural agents used in cancer, focusing on their mechanistic pathways, therapeutic potential, and future prospects in the development of effective and safer cancer management strategies [1,5,9].

Classification of Natural Anticancer Agents

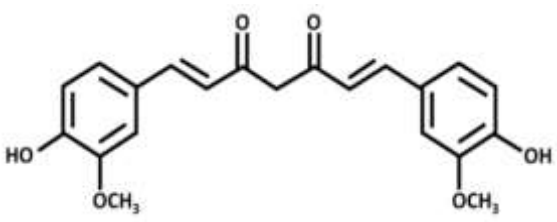
Natural anticancer agents can be classified based on their source as follows:

1. Plant-derived agents: Plant-derived compounds represent the largest group of natural anticancer agents and include polyphenols, flavonoids, alkaloids, terpenoids, and organosulfur compounds. These compounds exhibit antioxidant, anti-inflammatory, and pro-apoptotic properties.
2. Marine-derived agents: Marine organisms such as sponges, algae, and microorganisms are rich sources of bioactive compounds with potent anticancer activity. Several marine-derived agents have entered clinical trials due to their unique chemical structures.
3. Microbial-derived agents: Microorganisms produce a variety of secondary metabolites with anticancer properties, including antibiotics and enzyme inhibitors that interfere with DNA synthesis and cell division.

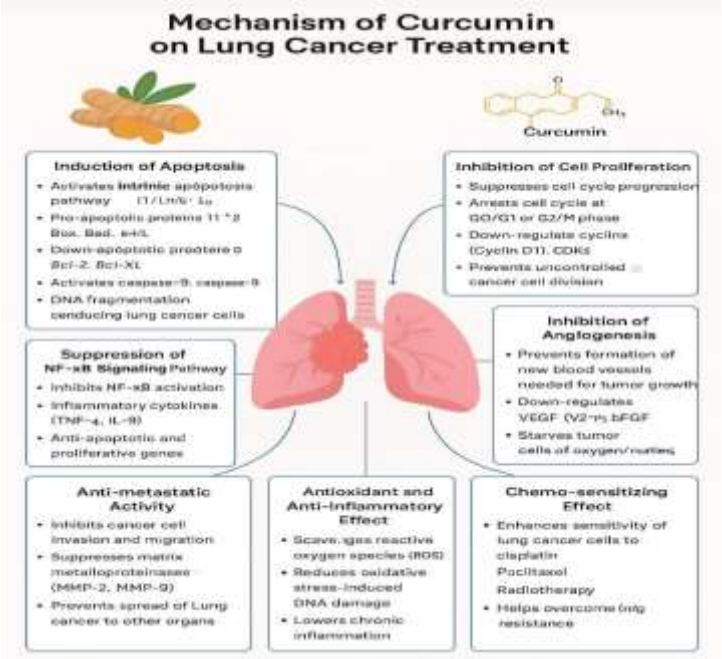
Natural Agents:

1. Curcumin

Source: Curcuma longa (Turmeric)
Chemical class: Polyphenol



Mechanism of action: It induces apoptosis predominantly via the intrinsic mitochondrial pathway by up-regulating pro-apoptotic proteins such as Bax, Bad, and Bid, while down-regulating anti-apoptotic proteins including Bcl-2 and Bcl-xL, leading to activation of caspase-9 and subsequent DNA fragmentation. Curcumin also inhibits lung cancer cell proliferation by suppressing cell cycle progression and inducing arrest at the G0/G1 or G2/M phases through down-regulation of cyclins (such as cyclin D1) and cyclin-dependent kinases (CDKs). Furthermore, it suppresses the NF-κB signaling pathway, resulting in reduced expression of inflammatory cytokines like TNF-α and IL-6, as well as inhibition of genes involved in cell survival and proliferation. Curcumin exhibits potent anti-angiogenic effects by downwards vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF), thereby inhibiting tumor-associated neovascularization and limiting nutrient and oxygen supply to tumor cells. Its anti-metastatic activity is mediated through inhibition of cancer cell invasion and migration by suppressing matrix metalloproteinases such as MMP-2 and MMP-9. Additionally, curcumin acts as a strong antioxidant and anti-inflammatory agent by scavenging reactive oxygen species (ROS), reducing oxidative stress-induced DNA damage, and lowering chronic inflammation. Importantly, curcumin enhances chemosensitivity of lung cancer cells to conventional therapies including cisplatin, paclitaxel, and radiotherapy, thereby helping to overcome drug resistance and improve therapeutic efficacy [19,25].



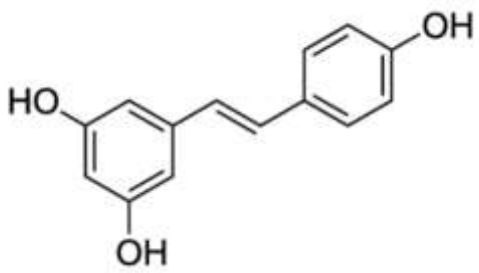
Cancer types studied: Breast, lung, colorectal, prostate

Source: Grapes, berries, peanuts

Chemical class: Stilbene polyphenol

Limitations: Poor bioavailability and rapid metabolism

2. Resveratrol



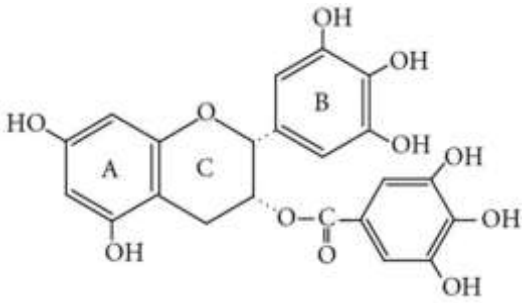
Mechanism of action: Resveratrol also causes cell-cycle arrest at the G_0/G_1 or G_2/M phase by down-regulating cyclins (Cyclin D1, Cyclin B1) and cyclin-dependent kinases while up-regulating cell-cycle inhibitors such as p21 and p27. This effect is closely related with stabilization and activation of the tumor suppressor protein p53, leading to suppressed uncontrolled cell proliferation. Another critical mechanism involves the inhibition of pro-survival and inflammatory signaling pathways, including PI3K/Akt/mTOR, NF-κB, and STAT3. By suppressing these pathways, resveratrol reduces cancer cell survival, inflammation-driven tumor promotion, and resistance to chemotherapy. Additionally, resveratrol interferes with vasculogenesis by down regulating vascular endothelial growth factor (VEGF) and hypoxia-inducible factor-1α (HIF-1α), thereby limiting tumor blood supply and nutrient availability. Resveratrol further exerts anti-metastatic effects by inhibiting epithelial–mesenchymal transition (EMT), reducing matrix metalloproteinases (MMP-2 and MMP-9), and impairing cancer cell migration and invasion. Its antioxidant and pro-oxidant dual role allow it to protect normal cells from oxidative damage while selectively increasing reactive oxygen species in cancer cells, leading to oxidative stress-mediated apoptosis. Through this multi-targeted mode of action, resveratrol acts as a promising chemopreventive and therapeutic agent in cancer management [1,5,9]. Cancer types studied: Breast, colon, prostate, skin

Additional benefit: Cardioprotective and antioxidant effects

3. Epigallocatechin-3-gallate (EGCG)

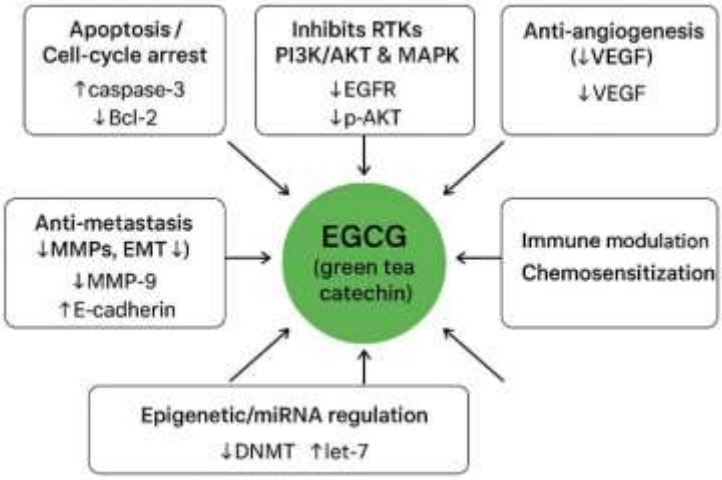
Source: Green tea (Camellia sinensis)

Chemical class: Catechin (flavonoid)



Mechanism of action: Induction of apoptosis and cell-cycle arrest EGCG activates intrinsic (mitochondrial) apoptotic pathways: ↑Bax, ↓Bcl-2/Bcl-XL, mitochondrial membrane depolarization, cytochrome-c release and caspase-3/9 activation. It also modulates extrinsic apoptosis (death receptors) in some models and induces G0/G1 or G2/M cell-cycle arrest via upregulation of p21/p27 and downregulation of cyclins/CDKs. Inhibition of pro-survival signaling pathways (proliferation) EGCG inhibits receptor tyrosine kinase pathways important in lung cancer (EGFR, IGF-1R) and downstream cascades: PI3K/AKT/mTOR, RAS/RAF/MEK/ERK (MAPK), JAK/STAT3. Inhibition of these nodes reduces proliferation and promotes apoptosis. Anti-angiogenic effects EGCG reduces VEGF expression and VEGFR signaling and suppresses angiogenesis in tumor models (reduced micro vessel density and VEGF transcription via STAT3/NF-κB suppression). This limits tumor nutrient supply and metastasis potential. Anti-metastatic and anti-invasive actions EGCG downregulates matrix metalloproteinases (MMP-2, MMP-9), inhibits epithelial-to-mesenchymal transition (EMT) markers (↓vimentin, ↑E-

cadherin), and reduces migration/invasion in NSCLC cell lines and animal models. Oxidative stress modulation: antioxidant and context-dependent pro-oxidant EGCG is a strong radical scavenger (antioxidant), lowering oxidative DNA damage and mutation risk. Paradoxically, at higher doses in cancer cells EGCG can act pro-oxidant (↑ROS) and produce oxidative stress that triggers apoptosis this duality is dose- and context-dependent. Epigenetic regulation & miRNA modulation EGCG alters DNA methylation (inhibits DNMTs), histone acetylation, and modulates tumor-suppressor/oncogenic miRNAs (e.g., upregulates let-7, miR-16; downregulates some oncogenic miRNAs), thereby reprogramming gene expression toward growth suppression [1,5,26].

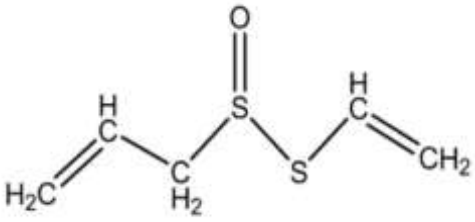


Cancer types studied: Lung, breast, liver, prostate

4. Allicin

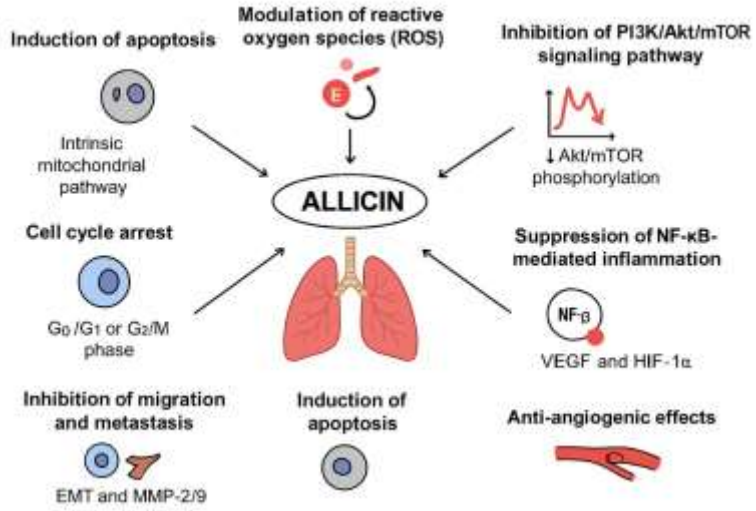
Source: Garlic (Allium sativum)

Chemical class: Organosulfur compound



Mechanism of action: Allicin also promotes the generation of reactive oxygen species (ROS) within tumor cells. Elevated ROS levels cause oxidative stress, damaging cellular macromolecules such as DNA, proteins, and lipids. Cancer cells, which already maintain a higher basal oxidative state, are particularly susceptible to reactive oxygen species mediated cytotoxicity, making allicin selectively toxic to malignant cells while sparing normal cells. Another important anticancer mechanism of allicin involves cell cycle arrest. Allicin modulates the expression of key regulatory proteins, including cyclins and cyclin-dependent kinases (CDKs), leading to arrest at the G0/G1 or G2/M phase of the cell cycle. This inhibition prevents uncontrolled proliferation and limits tumor growth. Furthermore, allicin suppresses pro-survival and inflammatory signaling pathways, such as NF-κB, PI3K/Akt, and MAPK pathways, which are commonly overactivated in cancer. Inhibition of these pathways reduces cancer cell survival, angiogenesis, invasion, and metastasis. Allicin has also been shown to downregulate anti-apoptotic proteins (Bcl-2) while upregulating pro-apoptotic proteins (Bax), further shifting the

balance toward cell death. In addition, allicin exhibits anti-metastatic and anti-angiogenic effects by inhibiting matrix metalloproteinases (MMPs) and reducing vascular endothelial growth factor (VEGF) expression. These actions limit tumor invasion and new blood vessel formation, thereby restricting tumor progression. Overall, the multitargeted nature of allicin combining apoptosis induction, oxidative stress generation, cell cycle inhibition, and suppression of oncogenic signaling pathways highlights its potential as a promising natural anticancer agent for both chemoprevention and adjunct cancer therapy [6,7,8].

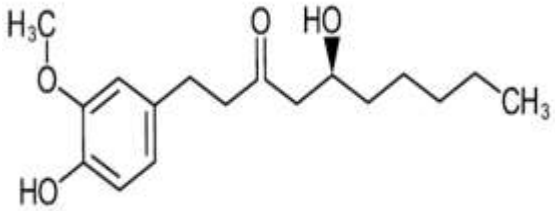


Cancer types studied: Gastric, colorectal, lung

5. Gingerol

Source: Ginger (Zingiber officinale)

Chemical class: Phenolic compound



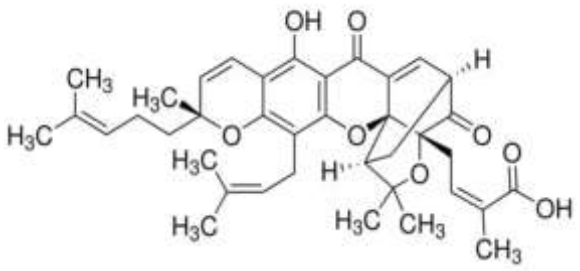
Mechanism of action: gingerol suppresses tumor progression by inhibiting key oncogenic signaling pathways, including NF-κB, PI3K/Akt, and MAPK pathways, leading to reduced expression of survival proteins and inflammatory mediators. Its potent anti-inflammatory effect is mediated through downregulation of COX-2, TNF-α, and interleukins, thereby limiting chronic inflammation associated carcinogenesis. Gingerol also exerts antioxidant activity by scavenging reactive oxygen species (ROS), which helps prevent DNA damage and oxidative stress–induced mutations. gingerol inhibits angiogenesis and metastasis by decreasing vascular endothelial growth factor (VEGF) expression and suppressing matrix metalloproteinases (MMP-2 and MMP-9), thereby restricting tumor invasion and spread. Collectively, these mechanisms highlight gingerol as a promising natural chemopreventive and therapeutic agent against various cancers [6,8].

Cancer types studied: Colon, breast, ovarian

6. Gambogenic Acid

Source: Garcinia hanburyi

Chemical class: Xanthone derivative



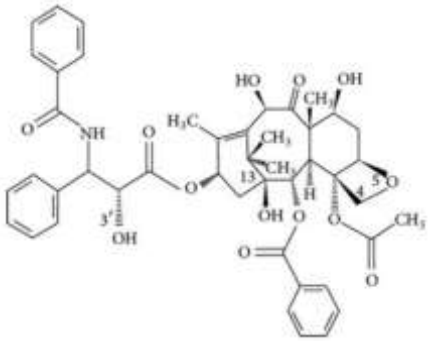
Mechanism of action: induction of apoptosis via the intrinsic (mitochondrial) pathway. Gambogenic acid disrupts mitochondrial membrane potential, leading to the release of cytochrome-c into the cytosol. This event subsequently activates initiator caspase-9 followed by executioner caspase-3, resulting in programmed cell death. Additionally, gambogenic acid alters the balance of Bcl-2 family proteins by downregulating anti-apoptotic proteins such as Bcl-2 and Bcl-xL, while upregulating pro-apoptotic proteins including Bax and Bak, thereby favoring apoptosis. Gambogenic acid also inhibits cancer cell proliferation by inducing cell cycle arrest, commonly at the G0/G1 or G2/M phase. This effect is mediated through suppression of cyclins and cyclin-dependent kinases (CDKs), along with upregulation of CDK inhibitors such as p21 and p27. Furthermore, gambogenic acid interferes with key oncogenic signaling pathways, particularly the PI3K/Akt and NF-κB pathways, which are crucial for tumor cell survival, growth, and resistance to apoptosis. Inhibition of these pathways leads to reduced phosphorylation of downstream targets, thereby suppressing cell survival signals. Another important mechanism of gambogenic acid is the induction of oxidative stress within cancer cells. Gambogenic acid promotes excessive generation of reactive oxygen species (ROS), which causes oxidative damage to cellular components including DNA, proteins, and lipids. Elevated ROS levels further enhance mitochondrial dysfunction and activate stress-related signaling pathways, amplifying apoptotic cell death. In addition, gambogenic acid has been reported to inhibit tumor angiogenesis and metastasis by downregulating vascular endothelial growth factor (VEGF) and matrix metalloproteinases (MMPs), thereby limiting tumor growth and spread. Gambogenic acid exerts its anticancer effects through a multi-targeted mechanism involving apoptosis induction, cell cycle arrest, inhibition of survival signaling pathways, oxidative stress generation, and suppression of angiogenesis and metastasis, highlighting its potential as a promising natural anticancer agent [6,7].

Cancer types studied: Lung, liver, leukemia

7. Paclitaxel [Natural origin]

Source: Taxus brevifolia (Pacific yew tree)

Chemical class: Diterpenoid



Mechanism of action: Paclitaxel is a diterpenoid anticancer agent originally derived from the bark of Taxus species and is widely used in the treatment of various solid tumors. Its primary mechanism of action involves disruption of microtubule dynamics, which are essential for mitotic spindle formation and successful cell division. Unlike vinca alkaloids that inhibit microtubule polymerization, paclitaxel selectively binds to the β-tubulin subunit of microtubules and promotes their polymerization while simultaneously preventing depolymerization. This

results in the formation of abnormally stable and nonfunctional microtubules. Stabilization of microtubules by paclitaxel leads to arrest of the cell cycle at the G2/M phase, as cancer cells are unable to complete mitosis. Prolonged mitotic arrest triggers activation of cell death pathways, ultimately resulting in apoptosis. Paclitaxel-induced apoptosis is primarily mediated through the intrinsic mitochondrial pathway. The drug alters mitochondrial membrane permeability, leading to the release of cytochrome-c and subsequent activation of caspase-9 and caspase-3. Additionally, paclitaxel modulates the expression of Bcl-2 family proteins by downregulating anti-apoptotic proteins such as Bcl-2 and Bcl-xL, while enhancing pro-apoptotic proteins like Bax. In addition to its effects on mitosis, paclitaxel has been shown to influence multiple signaling pathways involved in cancer cell survival and proliferation. It can inhibit the Akt signaling pathway, enhance reactive oxygen species (ROS) generation, and activate stress-related kinases, further promoting apoptotic cell death. Paclitaxel also exhibits anti-angiogenic activity by suppressing endothelial cell proliferation and reducing vascular endothelial growth factor (VEGF) expression, thereby limiting tumor blood supply. Overall, paclitaxel exerts its anticancer activity through microtubule stabilization–mediated mitotic arrest, induction of mitochondrial apoptosis, modulation of survival signaling pathways, and inhibition of tumor angiogenesis. These multifaceted mechanisms contribute to its broad clinical efficacy against a wide range of malignancies [4,7].

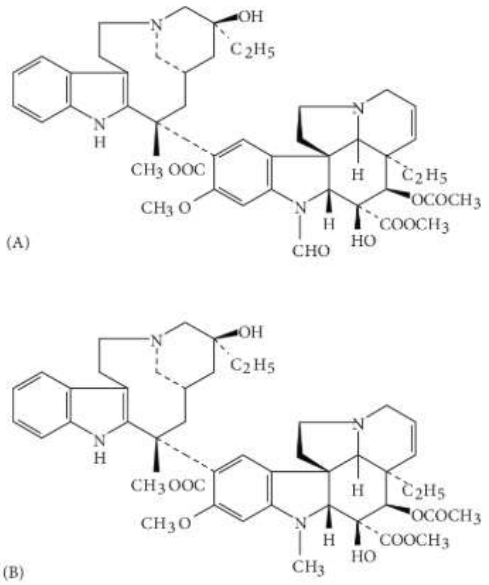
Cancer types treated: Breast, ovarian, lung

Clinical status: Approved anticancer drug

8. Vincristine and Vinblastine

Source: Catharanthus roseus

Chemical class: Alkaloids



Mechanism of action: Vincristine and vinblastine bind specifically to the β-tubulin subunit of tubulin dimers, thereby inhibiting microtubule polymerization. This binding prevents the assembly of the mitotic spindle apparatus, leading to destabilization of microtubules. As a result, cancer cells are unable to progress through mitosis, causing cell cycle arrest predominantly at the metaphase of the G2/M phase. Prolonged mitotic arrest ultimately triggers apoptotic cell death. The induction of apoptosis by vincristine and vinblastine is mainly mediated through the intrinsic mitochondrial pathway. Disruption of microtubules activates stress signaling pathways that alter mitochondrial membrane integrity, leading to the release of cytochrome-c into the cytoplasm. This event initiates the caspase cascade, particularly activation of caspase-9 and caspase-3, resulting in DNA fragmentation and programmed cell death. Additionally, these agents modulate the expression of Bcl-2 family proteins by reducing anti-apoptotic proteins and enhancing pro-apoptotic factors. Beyond mitotic inhibition, vincristine and vinblastine interfere with intracellular transport, signal transduction, and

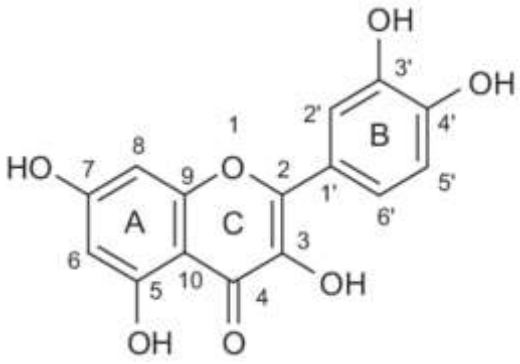
angiogenesis. Vinblastine, in particular, exhibits anti-angiogenic activity by inhibiting endothelial cell proliferation and reducing tumor vascularization. Vincristine shows a higher affinity for neuronal microtubules, which accounts for its prominent neurotoxic effects but also contributes to its potent antimitotic activity [4,7].

Cancer types treated: Leukemia, lymphoma, solid tumors

9. Quercetin

Source: Fruits, vegetables, onions

Chemical class: Flavonoid



Mechanism of action: the primary mechanisms of quercetin involve the induction of apoptosis in cancer cells. Quercetin activates the intrinsic mitochondrial apoptotic pathway by disrupting mitochondrial membrane potential, leading to the release of cytochrome-c into the cytosol and subsequent activation of caspase-9 and caspase-3. This process is accompanied by downregulation of anti-apoptotic proteins such as Bcl-2 and Bcl-xL, along with upregulation of pro-apoptotic proteins including Bax and Bad. Quercetin also suppresses cancer cell proliferation by inducing cell cycle arrest at various checkpoints, particularly the G1/S and G2/M phases. This effect is mediated through inhibition of cyclins and cyclin-dependent kinases (CDKs), as well as enhanced expression of CDK inhibitors such as p21 and p27. In addition, quercetin interferes with key oncogenic signaling pathways, including PI3K/Akt, MAPK/ERK, and NF-κB, which play crucial roles in cell survival, inflammation, and resistance to apoptosis. Inhibition of these pathways results in reduced tumor cell growth and increased sensitivity to apoptotic stimuli [5,8,9]. Another important anticancer mechanism of quercetin is its ability to modulate oxidative stress. Quercetin exhibits a dual redox behavior; at higher concentrations in cancer cells, it promotes the generation of reactive oxygen species (ROS), leading to oxidative damage to DNA and mitochondria, thereby enhancing apoptotic cell death. Furthermore, quercetin inhibits angiogenesis and metastasis by downregulating vascular endothelial growth factor (VEGF), matrix metalloproteinases (MMPs), and epithelial–mesenchymal transition (EMT) markers, thus restricting tumor invasion and spread. Overall, quercetin exerts its anticancer effects through a multi-targeted mechanism involving induction of apoptosis, cell cycle arrest, modulation of survival signaling pathways, oxidative stress-mediated cytotoxicity, and inhibition of angiogenesis and metastasis. These pleiotropic actions highlight quercetin's potential as a promising natural compound for cancer prevention and therapy [5,8,9].

Cancer types studied: Lung, breast, colon

10. Berberine

Source: Berberis species

Chemical class: Isoquinoline alkaloid

Mechanism of action: Berberine activates the intrinsic mitochondrial apoptotic pathway by disrupting mitochondrial membrane potential, which leads to the release of cytochrome-c into the cytoplasm. This event initiates the activation of caspase-9 and caspase-3, culminating in programmed cell death. Concurrently, berberine alters the expression of Bcl-2 family proteins by downregulating anti-apoptotic members (Bcl-2, Bcl-xL) and upregulating pro-apoptotic proteins such as Bax and Bad. Berberine also inhibits cancer cell proliferation by inducing cell cycle arrest at the G0/G1 or G2/M phases. This effect is mediated through suppression of cyclins and cyclin-dependent kinases (CDKs), along with increased expression of CDK inhibitors including p21 and p27. Additionally, berberine interferes with key oncogenic signaling pathways such as PI3K/Akt, MAPK, and NF-κB, which play critical roles in tumor cell survival, inflammation, and resistance to apoptosis [5,8]. Inhibition of these pathways reduces proliferative signaling and enhances apoptotic sensitivity in cancer cells. Another important mechanism of berberine is activation of AMP-activated protein kinase (AMPK), a central regulator of cellular energy homeostasis. AMPK activation by berberine leads to inhibition of the mTOR pathway, thereby suppressing protein synthesis and tumor growth. Berberine also promotes the generation of reactive oxygen species (ROS) in cancer cells, resulting in oxidative stress–mediated DNA damage and mitochondrial dysfunction, further amplifying apoptotic cell death. Furthermore, berberine exhibits anti-angiogenic and anti-metastatic effects by downregulating vascular endothelial growth factor (VEGF), matrix metalloproteinases (MMPs), and epithelial mesenchymal transition (EMT) markers. These actions limit tumor vascularization, invasion, and metastatic spread [5,8].

Cancer types studied: Liver, colorectal, breast

Mechanism of action: catechins [epigallocatechin-3-gallate, EGCG)

Market-Available Natural Agent Based Formulations in Cancer:

Natural phytochemicals and extracts have long been studied for their anticancer activity, and many have been formulated into nutraceuticals, dietary supplements, or adjunct therapies that patients often use alongside conventional cancer treatment. While most are not approved as standalone cancer drugs, several products are commercially available that contain plant-derived agents shown to have potential anticancer or chemopreventive properties.

1. Curcumin-Based Formulations

Curcumin, a polyphenol from Curcuma longa, is one of the most widely marketed natural compounds with supported anticancer mechanisms such as apoptosis induction, inhibition of proliferation, and modulation of oncogenic pathways. Many nutraceutical and nano-enhanced curcumin products are available commercially to improve bioavailability and deliver higher systemic concentrations. These include curcumin extracts, phospholipid complexes, and nanoparticle-enhanced forms that are promoted for health support and adjunctive use in cancer care.

2. Green Tea Extract Products (EGCG)

Products containing concentrated green tea polyphenol especially (−) epigallocatechin-3-gallate (EGCG) are widely sold as dietary supplements and functional foods. Green tea extracts are studied for their potential to inhibit tumor cell proliferation and modulate signaling pathways involved in carcinogenesis. Although oral supplement products do not carry formal cancer treatment indications, they are marketed for antioxidant, health support, and wellness benefits that may complement cancer prevention strategies.

3. Mushroom Extract Supplements (e.g., AHCC)

AHCC (Active Hexose Correlated Compound) derived from shiitake mushroom mycelia is commercially available and widely used as an immunomodulatory supplement, particularly in Japan. It is promoted to support immune function in cancer patients and enhance overall well-being, though formal clinical evidence for direct cancer treatment efficacy is still under investigation.

4. Resveratrol and Flavonoid Supplements

Resveratrol (from grapes and berries), quercetin, and other flavonoid-based supplements are available on the market with claims of supporting antioxidant defense and cellular health. These products are generally positioned as health-promoting nutraceuticals rather than cancer therapeutics; however, extensive research explores their ability to regulate apoptosis, growth signaling, and oxidative stress in cancer models.

5. Combination Herbal Blends

Some multi-herbal products combine several botanical extracts (e.g., turmeric, green tea, milk thistle, ashwagandha) and are marketed for overall health or immune support. Important note: regulatory agencies (e.g., FDA) have issued warnings when companies make explicit claims that such products can treat or cure cancer, as robust clinical evidence is lacking. Therefore, these products remain in the supplement category, not approved cancer drugs.

RESULT AND DISCUSSION

Natural products derived from plants, marine organisms, microorganisms, and fungi have historically played a foundational role in the discovery of anticancer agentsand continue to be a rich source of therapeutic compounds [4,7]. Many of the most effective anticancer drugs in clinical use today, such as vinca alkaloids, paclitaxel, etoposide, and topotecan, are either directly extracted from natural sources or synthetically derived analogues of natural molecules, reflecting the enduring value of nature in oncology pharmacotherapy [4]. Research over the past decade has highlighted secondary metabolites including flavonoids, terpenoids, alkaloids, and polyphenols as promising anticancer bioactives with diverse mechanisms such as apoptosis induction, cell cycle arrest, inhibition of angiogenesis, immunomodulation, and reduction in metastatic potential [1,5,8]. These agents often exhibit lower toxicity compared to conventional chemotherapeutics, and when formulated with modern delivery systems (e.g., nano formulations), they show improved stability, bioavailability, and targeted action against tumor cells. Despite their therapeutic promise, challenges remain including variability in extract composition, limited clinical efficacy data, standardization issues, and poor pharmacokinetic properties for some compounds [2,11]. Continued multidisciplinary research, rigorous clinical evaluation, and integration of novel delivery technologies are essential to realize the full potential of natural agents in cancer treatment. Overall, natural products represent a valuable and

expanding source of anticancer agents that may augment existing therapies and contribute to more effective and less toxic cancer management strategies [1,5,9].

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