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Research Article

"Anticancer properties of Natural products" – A Review

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A B S T R A C T

The challenge of cancer remains one of the significant challenges for the health of the world; millions suffer every year. Despite the significant improvements in conventional approaches like chemotherapy and radiation and their continued inclusion in modern treatment protocols, the potential for toxic side effects and treatment resistance has led to a growing interest in alternative therapies. Natural products extracted from plants, marine organisms, and microorganisms constitute a major portion of traditional medicines. Researchers are now discovering these compounds for their anticancer activity. Researchers assert curcumin, resveratrol, and EGCG, among other important compounds, can prevent the proliferation of cancer cells, induce apoptosis, and suppress metastasis by activating a variety of pathways inside the cells. We discuss here the mechanisms through which these natural compounds cause apoptosis, control the cycle of a cell, possess anti-metastatic properties, and regulate redox. A major area of controversy remains the ability of natural products to complement traditional treatments—that is, their ability to enhance treatment results with synergistic effects. The review also considers the challenges posed by the low solubility and poor bioavailability of compounds like curcumin and explores strategies to modify their structure for improved efficacy. Therefore, this review has advocated for additional research on natural products as complementary or alternative cancer treatments, with a focus on clinical applications and the identification of molecular mechanisms that could enhance therapeutic strategies. The results showed the potential of natural compounds in providing safer and more effective treatment options for cancer and encouraged further research on the integration of such natural compounds into mainstream oncology practices.

Keywords: Apoptosis, Curcumin, EGCG, Metastasis, Natural products, Resveratrol

Introduction

Cancer still is a global health challenge for the millions of people it affects each year. Conventional cancer therapy, with its advances in chemotherapy, radiation, and surgery, still faces numerous obstacles.[1] Patients usually suffer from harsh side effects, and cancer cells gradually become resistant, reducing the effectiveness of such treatments. Recently, the use of natural products has generated interest in alternative or complementary therapies. Use of natural products derived from the flora, sea, and microorganisms in traditional medicine dates back for many centuries. Over the past two decades, interest in these natural products with anticancer potential has been increasing. These compounds include curcumin from turmeric, resveratrol from grapes, and EGCG from green tea, which show inhibition of proliferation, apoptosis induction, and blockade of metastatic processes.[2] These natural compounds induce a multi-pathway blockade, which appears promising in drug-resistance and in reduction or alleviation of the side effects so often accompanying synthetic drugs.[3]

One of the most significant mechanisms by which natural products express their anticancer activities is through the induction of apoptosis, or programmed cell death.[4] Some natural products, like paclitaxel from the yew tree and berberine from goldenseal, have been found to cause pathways that kill cancer cells through a process called apoptosis. Other compounds studied in this regard demonstrated anticancer activity by inhibiting the metastasis of cancer through genistein and silibinin. They demonstrated the ability to impede the invasion and migration of cancer cells, as well as hinder the creation of new blood vessels from preexisting ones, a feature of the angiogenesis process.[5] Despite these challenges, the goal of this review will be to analyze the anticancer properties of natural products and provide their mechanisms of action, key compound classes, and their potential in both treatment and prevention. Examining recent studies and clinical trials, this review offers insight into how such compounds complement conventional therapies, enhance patient outcomes, and contribute to safer and more effective alternatives. This will eventually lead to more research and innovation in this area, fill the existing gaps, and pave the way for their more widespread clinical utilization.

Natural Products as Anticancer Agents

Curcumin

Curcumin is the principal constituent of the rhizomes of Curcuma longa L. (turmeric)[6] and was first isolated in pure crystalline form from the turmeric plant in 1870. Curcumin and its derivatives have garnered significant attention over the past two decades owing to their biofunctional properties, including anti-tumor, antioxidant, and anti-inflammatory activities.[7,8] The properties are ascribed to the fundamental components of the curcumin structure. Consequently, extensive scientific research has elucidated the structure-activity relationship (SAR) of curcumin to enhance its physicochemical and biological properties. This review primarily examines the anticancer efficacy of curcumin, given the significance of cancer as a predominant cause of mortality and the continuous pursuit of more effective and less toxic anticancer agents. The applications of curcumin in other diseases exceed the parameters of this review and have been examined in other sources.[9]

Curcumin's unique anticancer activity primarily operates through mechanisms that induce apoptosis and inhibit tumor proliferation and invasion by suppressing various cellular signaling pathways.[10] Numerous studies have documented curcumin's antitumor efficacy against breast cancer, lung cancer, head and neck squamous cell carcinoma, prostate cancer, and brain tumors[11], demonstrating its ability to target various cancer cell lines. Despite the advantages, curcumin's applications are constrained by its low water solubility, leading to poor oral bioavailability and diminished chemical stability.[7] A further challenge is the limited cellular absorption of curcumin. The hydrophobic nature of the curcumin molecule facilitates its penetration into the cell membrane, where it binds to the fatty acyl chains of membrane lipids via hydrogen bonding and hydrophobic interactions, leading to reduced availability of curcumin within the cytoplasm.[12] To address these challenges and augment the overall anticancer efficacy of curcumin, various structural modifications have been proposed to improve selective toxicity towards particular cancer cells, increase bioavailability, or enhance stability. An alternative method involves employing various delivery systems to enhance the physicochemical properties and anticancer efficacy of curcumin. This review examines the contemporary literature regarding the structure-activity relationship (SAR) of curcumin and its analogues, alongside their anticancer efficacy in various cancer cell lines, animal models, and human clinical trials, as well as the diverse curcumin delivery systems employed in cancer therapy.

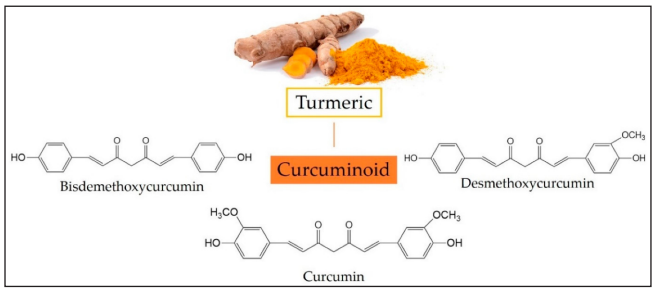

Figure 1.Structure of Curcumin

Resveratrol

Resveratrol, a polyphenolic stilbene derivative found naturally in grapes, red wine, and various plant sources,

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has garnered considerable attention for its anti-neoplastic properties.[13] These properties encompass various cellular and molecular mechanisms, positioning resveratrol as a potentially significant candidate for the prevention and treatment of breast, prostate, lung, pancreatic, liver, colorectal, and other cancers. Furthermore, resveratrol demonstrates antioxidant, anti-inflammatory, and neuroprotective properties.[14] The anti-carcinogenic effects of resveratrol are mediated by its various interactions with cellular signaling pathways involved in multiple biological processes, including apoptosis, cell cycle regulation, inflammation, angiogenesis, and metastasis. Moreover, resveratrol has been noted to inhibit the expression of oncogenes, activate genes that suppress tumor growth, and modulate the activity of transcription factors. Recent studies have increasingly demonstrated resveratrol's ability to specifically target cancer stem cells, which often contribute to resistance against conventional therapies and disease recurrence.[15] Furthermore, resveratrol can affect the tumor microenvironment, an essential, albeit occasionally overlooked, factor in cancer progression and treatment response.[12] Resveratrol demonstrates potential in enhancing the sensitivity of cancer cells to conventional chemotherapeutic agents, suggesting possible synergistic effects that could augment treatment efficacy and mitigate side effects.[9]

The anti-cancer properties of resveratrol are primarily ascribed to its effects on mitochondria, the organelles known as the "powerhouses" of the cell, due to their essential roles in energy production, cellular signaling, and apoptosis. These functions are closely linked to the initiation and advancement of cancer. Resveratrol exerts diverse effects on mitochondria, offering a compelling avenue for research into its potential therapeutic applications in oncology.[16] The interactions involving resveratrol and mitochondrial activity provide a thorough strategy for cancer suppression, applicable either independently or in conjunction with other methods.[17] Identifying specific molecular targets and clarifying the mechanisms of action of resveratrol are critical areas of current research. These insights may enhance the clinical application of resveratrol for chemoprevention, cancer therapies, and neuroprotection.

Epigallocatechin-3-gallate (EGCG)

Epigallocatechin-3-gallate (EGCG) is a catechin present in green tea. EGCG demonstrates diverse activities, including anti-inflammatory, antidiabetic, antiobesity, and antitumor properties. The onset and advancement of cancer are associated with epigenetic modifications, such as abnormal DNA methylation and acetylation. EGCG impedes tumorigenesis in the lungs, oral-digestive tract, and prostate. In A/J mice, EGCG suppresses lung tumorigenesis induced by the tobacco-specific nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone through the inhibition of 8-hydroxydeoxyguanosine formation via its antioxidant properties.[18] Furthermore, EGCG suppresses lung tumorigenesis induced by cisplatin or dimethylarsinic acid, as well as liver tumorigenesis induced by diethylnitrosamine, by inhibiting insulin-like growth factor signaling in obese and diabetic C57BL/KsJ-db/db mice. EGCG treatment also inhibits N-methyl-N'-nitro-N-nitrosoguanidine-induced carcinogenesis in the glandular stomach. The oral administration of EGCG suppresses the proliferation of prostate cancer cells in xenograft models through the enhancement of apoptosis.[19] While the mechanisms by which EGCG exerts its anticarcinogenic and antitumorigenic effects remain unclear, its anticancer efficacy has been documented across various cancers.

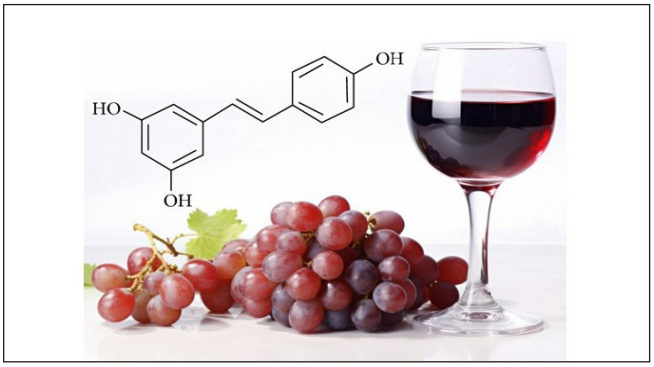

Figure 2.Structure of Resveratrol

Figure 3.Structure of EGCG

Paclitaxel

Paclitaxel is a member of the cytoskeletal drug class that targets tubulin. Consequently, paclitaxel treatment induces abnormalities in mitotic spindle assembly, chromosome segregation, and subsequently results in defects in cell division. Paclitaxel stabilizes microtubule polymers and inhibits their disassembly, thereby arresting the cell cycle in the G0/G1 and G2/M phases and inducing apoptosis in cancer cells (Figure 3). The inhibition of the mitotic spindle by paclitaxel is typically contingent upon its suppression of microtubule dynamics.[20] Recent studies, however, indicated that only low-dose paclitaxel is effective, whereas high-dose paclitaxel may inhibit microtubule detachment from the centrosomes. The paclitaxel binding site has

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been identified as the beta-tubulin subunit. Paclitaxel possesses mechanisms of action beyond microtubule targeting. Panis et al.[21] discovered that breast cancer patients post-acute paclitaxel treatment displayed an immunosuppressive condition characterized by a pronounced type 2 helper T-cell (Th2) profile, evidenced by elevated interleukin (IL)-10 levels. Alexandre et al.[22] and Hadzic et al.[23] reported that paclitaxel induces the generation of reactive oxygen species by augmenting the activity of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, thereby contributing to the drug's potent anticancer efficacy. The antineoplastic mechanisms associated with the non-chemotherapeutic application of paclitaxel were identified. Sevko et al.[24] reported that paclitaxel augmented the efficacy of chemotherapy by inhibiting the immunosuppressive capabilities of myeloid-derived suppressor cells. Gan et al. (2023)[25] discovered that paclitaxel inhibits the androgen receptor by promoting the nuclear accumulation of FOXO1 (forkhead box protein O1) as one of its anticancer mechanisms (Figure 3). The anticancer mechanisms and specific cancer types addressed by natural products are detailed in Table 1.

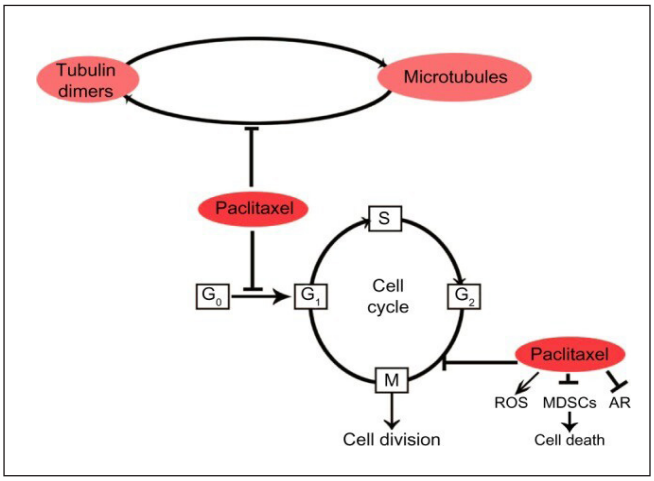

Figure 4.Anti-cancer actions of paclitaxel

Table 1.Anticancer mechanisms and specific cancer types targeted by natural products

Natural Product	Source	Primary Mechanism	Cancer Types Targeted
Curcumin	Turmeric	Induces apoptosis, anti-inflammatory	Breast, colon, prostate
Resveratrol	Grapes	Modulates epigenetics, inhibits angiogenesis	Lung, breast, colorectal
EGCG	Green tea	Regulates oxidative stress, anti-angiogenic	Prostate, skin, breast
Paclitaxel	Yew tree	Inhibits cell proliferation	Ovarian, breast, lung
Berberine	Goldenseal	Disrupts cell cycle, reduces proliferation	Colorectal, breast, liver
Genistein	Soy	Inhibits metastasis, MMP downregulation	Breast, prostate
Quercetin	Fruits, vegetables	Modulates oxidative stress, induces apoptosis	Lung, liver, leukemia
Silibinin	Milk thistle	Inhibits angiogenesis, reduces metastasis	Liver, colon, prostate

Mechanism of action of Natural Products

Induction of Apoptosis

Apoptosis, or programmed cell death, is crucial for cell degradation and forms a part of the process of degrading cancer cells.[26] Natural products interact with intrinsic as well as extrinsic pathways initiating apoptosis. The intrinsic pathway starts the sequence by inducing mitochondrial damage, which causes the release of cytochrome c to activate the caspases in breaking down the cancer cell. For instance, the extrinsic pathway starts through death receptors, Fas and TNF, from outside the cell to cause caspase cascades.[27] Some constituents have isolated compounds that activate both pathways selectively killing the cancer cells with minimal or no damage to normal tissues. Grapes' Resveratrol and green tea's EGCG trigger apoptosis by activating proteins such as p53 and Bcl-2, which lead to cancer cell death.[28] Natural products induce apoptosis, which serves as a mechanism to control the uncontrollably proliferation of harmful cells before they grow into tumor masses. For instance, curcumin demonstrates its effectiveness in targeting proteins involved in apoptosis in cancers resistant to conventional therapy. Resveratrol can target multiple pathways, providing a multitude of ways to overcome the survival mechanisms of the cancer cell.[29]The apoptotic effects of these compounds show the immense potential of natural products as alternatives or complements to standard cancer therapies.

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Inhibition of Proliferation

Cancer involves the unconstrained proliferation of cells, and one of the major goals of treatment is the inhibition of this proliferation. Natural products include paclitaxel and berberine, which interfere with the cell cycle, thus preventing cancer cells from dividing and multiplying. Paclitaxel, extracted from the bark of the yew tree, stabilizes microtubules during the mitotic phase, thereby blocking the cell cycle at the G2/M transition point and preventing the completion of cell division.[30] The unique phytochemicals in goldenseal act on the AMPK/mTOR pathways, critical for cell growth and metabolism, so that cancer cell proliferation is slowed. As these compounds interfere with new tumor formation, they also interfere with the cycle of cancer cells, thus making other effective treatments for cancer.[31] A prime example is paclitaxel-it is the chemotherapeutic drug known by quite a long duration in the clinic, and cell division inhibition presents features useful for the management of fast proliferative cancers such as breast and ovarian cancer. Such activity across many pathways by berberine holds a promising approach against the proliferation of cancer cells and makes it an attractive candidate for further research and clinical application.

Anti-metastatic Properties

Metastasis is the spread or dispersal of cancer from its native place to other sites within the body. It is the most important cause of death in cancer patients.[32] Effective prevention of metastasis determines survival improvement. Natural products such as genistein from soy and silibinin from milk thistle have been shown to exhibit anti-metastatic activity by inhibiting invasion, migration, and angiogenesis that is triggered by cancer cells. Genistein works through the downregulation of matrix metalloproteinases, an enzyme that degrades the extracellular matrix, allowing cancerous cells to migrate into other tissues.[33] Silibinin also suppresses the VEGF signaling process that is crucial for blood vessel formation in tumors, thus starving it of the nutrient supply.[34] These anti-metastatic effects are very critical in the control of cancer at its primary site, making it manageable and easier to treat. The capability of genistein to inhibit tissue barriers breakdown reduces the possibilities of cancer cells' invasion towards far-off organs, whereas silibinin inhibits angiogenesis, which cuts out the resources required for tumor growth and spread. Together, these characteristics make natural products promising leads for treatments targeting metastatic cancers with aggressive behaviors, such as melanoma and breast cancer.

Oxidative Stress Modulation

Cancer cells typically contain increased oxidative levels that include reactive oxygen species (ROS) and antioxidants. Oxidative stress might be unbalancing and can damage cells but is actually known to be used by cancer cells for survival and growth. The natural products such as quercetin and catechins, from the green tea, may selectively modulate oxidative stress in cancer cells.[35] While the compound works as an antioxidant by inhibiting oxidative damage in normal cells, it also acts as a pro-oxidant in cancerous cells, enhancing levels of ROS to induce cell death. Like catechins, normal tissues are protected from oxidative stress, while the accumulation of ROS is stimulated in cancer cells leading to apoptosis. In a way, this dual function of natural substances in regulating oxidative stress will prove highly valuable because they can penetrate cancerous cells but avoid normal tissues. Compounds such as quercetin and catechins induce oxidative-stress-induced cell death through elevated ROS levels within cancer cells above the tolerance threshold. Simultaneously, their antioxidant property preserves normal cells from oxidative damage, thus ensuring minimal side effects associated with conventional cancer therapies.[36] Selective activity against cell targets makes modulation of oxidative stress an essential mechanism in the anticancer potential of natural products.

Targeting Inflammatory Pathways

Chronic inflammation is very strongly associated with the development and progression of cancer. Inflammatory pathways create a tumor-friendly environment through survival, proliferation, and metastasis. Anti-inflammatory natural products with curcumin are effective in disrupting these pathways. Curcumin inhibits NF-κB, which is a transcription factor controlling the expression of many pro-inflammatory cytokines and proteins that are involved in cell survival and proliferation.[37] Curcumin inhibits NF-κB and other inflammatory mediators, that affect not only the inflammation but also the environment on which the cancer cells depend for their growth and spread. Natural compounds can limit the progression of cancer at the source by targeting inflammation. Chronic inflammation precedes tumorigenesis, and by inhibiting the pathways of inflammatory pathways, compounds such as curcumin effectively cut off one of cancer's prime survival mechanisms [38]. This has made anti-inflammatory natural products particularly useful in cancers resulting from inflammatory diseases, for instance, colon and liver cancer, by controlling the inflammation to prevent the formation of cancer and therefore improving treatment outcomes.

Regulation of Angiogenesis

Tumor growth and metastasis are significantly dependent on angiogenesis, the process of new blood vessel formation, which provides the basic nutrients to cancer cells. Anti-angiogenesis is an important strategy in anticancer therapy, and several natural products, such as those derived

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from green tea EGCG and grapes resveratrol, have been demonstrated to possess significant anti-angiogenic activity. These compounds can bind to the VEGF pathway, whose function plays a pivotal role in the formation of blood vessels. The EGCG and resveratrol inhibit the VEGF signaling, hence inhibiting the growing blood vessels required to fuel tumor growth and spread. Controlling angiogenesis through natural products represents an inherently safe approach to depriving tumors of resources they need to grow. This positions these compounds in high demand for cancers in which angiogenesis plays a central role in the pathogenesis, such as cancers like breast, prostate, and colorectal cancers. Both EGCG and resveratrol have proven to be capable of suppressing blood vessel formation without causing damage to the normal tissue, thus representing a much safer alternative compared to the conventional inhibitors of angiogenesis which often come with serious side effects.[39]

Modulation of Immune Responses

This involves primarily the immune system responding to the presence and destruction of cancer cells. Cancer cells evade this immune detection. Polysaccharides from medicinal mushrooms such as Reishi and ginsenosides from ginseng work in modulating immune responses to increase the body's ability to fight cancer. These substances stimulate the activity of natural killer (NK) cells, increase the production of immune-cytokines, and enhance the activity of macrophages that, collectively, play significant roles in the recognition and eradication of cancer cells. Through simply stimulating the immune system, natural products restore the natural defense mechanisms of the body against the development of cancer. For these immunomodulatory effects, natural products may potentially be useful in combinatory therapies with conventional immunotherapy and other treatments. While immune enhancement indeed allows the body to target these cells better, it also decreases the rate of recurrence. Immune modulation thus stands as a core strategy both in the treatment and prevention of cancer.[40]

Epigenetic Modifications

Epigenetic alterations in cancer have been known to include DNA methylation and histone modifications. They are known to be able to silence tumor suppressor genes and promote oncogenes, which help drive the disease forward. Some of the well-known natural products that reverse epigenetic changes include resveratrol and curcumin through blockade of the enzymes DNA methyltransferases (DNMTs) and histone deacetylases (HDACs).[41] These compounds bring about a state of resensitization of the tumor suppressor gene so that its expression is restored again. The oncogenes are further blocked by such compounds and show reduced levels and the process of cancer development is slowed down. Targeting epigenetic modifications opens new avenues in the cancer treatment approaches. Since reversal of aberrant gene expression is a step that naturally inhibits cancer at the molecular level, natural products may present long-term therapeutic efficacy. This epigenetic regulation makes resveratrol and curcumin particularly promising in cancers driven by genetic and epigenetic changes, such as colorectal and breast cancers, where gene silencing plays a pivotal role in tumor growth.[42]

Enhancing Conventional Therapies

In addition to showing independent anticancer effects, natural products have the potency to enhance the effectiveness of traditional anticancer therapies. For instance, some curcumin derivatives are reported to enhance the sensitivity of cancer cells to chemotherapeutic agents such as cisplatin and doxorubicin, thereby lowering their toxicity but increasing the efficiency of the treatment. Similarly, EGCG potentiation of radiotherapy results from sensitizing cancer cells to the action of the radiations. These synergistic interactions enhance treatment outcome, reduce the required dosage of toxic drugs, and minimize side effects. The clinicians could formulate more effective regimens using less adverse effect by combining natural products with conventional therapies. This type of synergy would best associate with the aggressive cancers for which standard treatments may be insufficient.[43] The argument for their inclusion in strategies of integrative cancer therapy is thus strong with the possibility of maximizing the potency of known treatments while lowering their toxicity.

Table 2. Key mechanisms by which natural products exert their anticancer effects.

Mechanism of Action	Natural Product	Description
Apoptosis Induction	Curcumin, Resveratrol	Triggers programmed cell death via intrinsic/extrinsic pathways
Cell Cycle Inhibition	Paclitaxel, Berberine	Halts cancer cell division by disrupting mitosis and cell cycle
Angiogenesis Inhibition	EGCG, Silibinin	Prevents blood vessel formation, starving tumors of nutrients

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Oxidative Stress Modulation	Quercetin, Catechins	Balances ROS levels, inducing apoptosis in cancer cells
Anti-metastatic Activity	Genistein, Silibinin	Inhibits cancer cell invasion and migration
Inflammation Suppression	Curcumin	Reduces pro-inflammatory signaling, weakening tumor growth
Epigenetic Modulation	Resveratrol, Curcumin	Reverses abnormal DNA methylation and histone modifications
Immune System Enhancement	Ginsenosides, Polysaccharides	Boosts NK cells, cytokine production, and macrophage activity

Key classes of natural compounds

Alkaloids

Alkaloids, a type of natural chemical compound, inhibit cell division with good anticancer action; one such mechanism involves interfering with the formation of microtubules during mitosis, thereby preventing the proliferation of cancerous cells. A good source of alkaloids used as cancer drugs are vincristine and vinblastine, obtained from the Catharanthus roseus, which is the periwinkle plant. These drugs inhibit the normal separation of chromosomes during mitosis, and cell cycle arrest eventually leads to apoptosis.[44] Vincristine primarily treats leukemia, lymphomas, and sarcomas, while vinblastine effectively combats diseases like Hodgkin's disease and testicular cancer. These alkaloids are particularly useful in the treatment of rapidly proliferating tumors in which the cell cycle occurs at a faster pace. These alkaloids were successful in disrupting the foundation of cancer cell replication by targeting the mitotic spindle apparatus. The efficacy of alkaloids such as vincristine and vinblastine in chemotherapy regimens highlights their significance in formulation with anticancer drugs. These two alkaloids select and target only the dividing cells; they are necessary drugs used in chemotherapy treatment for cancers that have developed resistance to other types of chemotherapy.[45]

Flavonoids

Flavonoids are polyphenolic compounds commonly found in fruits, vegetables, and herbs. They exhibit anti-inflammatory and anticancer properties. Mainly, they inhibit inflammatory pathways associated with cancer. Quercetin is present in apples and onions and suppresses the generation of pro-inflammatory cytokines and enzymes such as COX-2 responsible for chronic inflammation in cancers.[46] Flavonoids decrease inflammation and thus make the microenvironment less favorable for tumor progression and metastasis. In addition to their anti-inflammatory activity, some flavonoids, like apigenin present in parsley, have direct anticancer effects by induction of apoptosis as well as inhibition of angiogenesis. Apigenin inhibits pathways involved in the survival and proliferation of tumor cells, in this case the PI3K/AKT and MAPK pathways. It is through this multi-level mechanism that flavonoids have become promising anticancer agents, especially against inflammation-driven cancers such as colon and breast cancers. The same flavonoids that could act on inflammation may be suggested as acting on tumor growth, and it is this dual activity that might increase their therapeutic potential.[47]

Terpenoids

Terpenoids are a vast class of natural compounds notable for their activities on cancer cells: forcing apoptosis and inhibiting angiogenesis. Apoptosis is programmed cell death; it is always central to therapies in cancer. Terpenoids, such as paclitaxel, also known as Taxol, play a crucial role in inducing this pathway [48]. The Pacific yew tree contains paclitaxel, which binds to microtubules to keep them persistent in their polymerized state rather than disassembling. It prevents the cell cycle from moving forward while inducing apoptosis in cancer cells. Paclitaxel's ability to inhibit cell growth has led to its application in the treatment of ovarian, breast, and lung cancers. Limonene, a constituent of citrus fruits, shares another mode of action: it inhibits apoptosis. Besides apoptosis, limonene, among other limonoids present in citrus fruits, has shown strong anti-angiogenic activity. Angiogenesis, the process of developing new blood vessels, primarily drives the growth and metastasis of a tumor [49]. Because it stops the VEGF pathway from working, limonene stops the growth of new blood vessel networks that feed the tumor. This starves the tumor and stops it from spreading. The combination of cell death promotion along with the prevention of blood vessel growth makes terpenoids one of the most valuable assets in cancer treatment strategies. These natural products vary widely in mechanisms whereby plant-derived compounds act against cancer, offering multiple entry points into therapeutic intervention. Their potential as integral components of cancer therapy relates to the disruption of critical cell processes such as cell division, inflammation, apoptosis, and angiogenesis.

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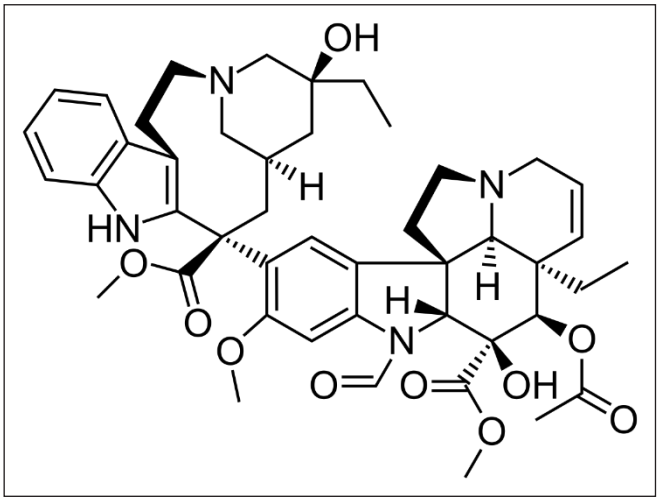

Figure 5.Chemical structure of vinca alkaloids

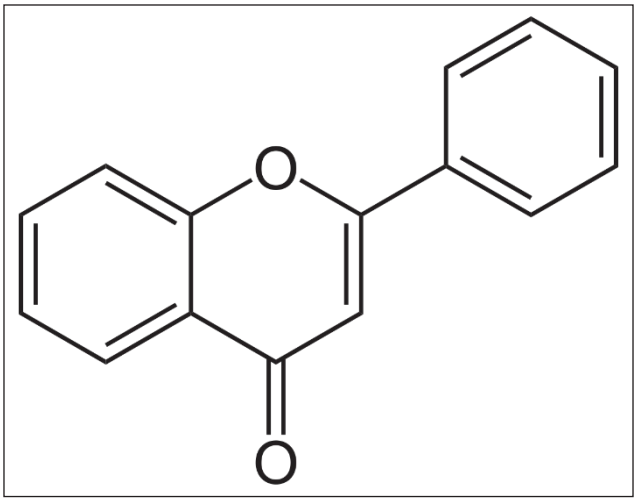

Figure 6.Chemical structure of flavonoids

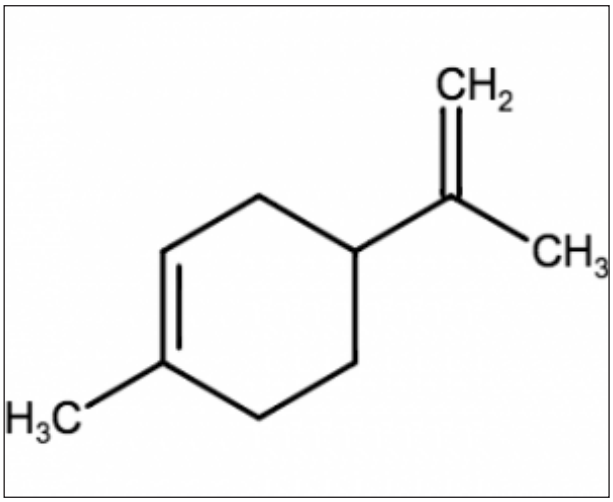

Figure 7.Chemical structure of Terpenoids

Polyphenols

Polyphenols in the form of curcumin and resveratrol have demonstrated huge bioactive potential in modulating cellular signaling pathways, which are relevant to the progression of cancer cells. These natural compounds impact several pathways such as NF-κB, PI3K/Akt, MAPK, and Wnt/β-catenin pathways, which are known to mediate anti-cancer effects. Curcumin has been well established

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for its potent inhibition of NF-κB signaling pathway, thus preventing inflammation and inhibiting proliferation of cancer cells. It also suppresses the Akt/mTOR pathway and triggers apoptosis of cancer cells and reduces tumor growth.[50] Resveratrol, which is present in grapes and berries, similarly blocks the PI3K/Akt pathway and upregulates the p53 tumor suppressor gene, which leads to cell death in cancer and forecloses metastasis. These polyphenols not only hit the cancerous cells but also render the drugs sensitive to chemotherapy and radiotherapy; they are invaluable in integrated approaches of cancer treatment. In addition, polyphenols have antioxidant properties, where they mop up ROS that cause DNA damage leading to initiation of the cancer process, providing additional prevention against cancer.[51] The modulation of oxidative stress and associated signaling pathways by polyphenols provides cellular homeostasis and decreases the cancerous process. Due to their significant roles in inhibiting the proliferation of cancer cells, inducing apoptosis, and attenuating inflammation, multifunctional curcumin and resveratrol hold much promise for the development of natural anti-cancer therapy.

Saponins and Glycosides

Plant-derived molecules such as saponins and glycosides have also been shown to inhibit cancer cell membranes as well as modulate the immune system. Potent anticancer effects can be induced by ginsenosides, a class of saponin in ginseng, through the disruption of the membranes of cancer cells, enhancing permeability and inducing apoptosis.[52] These compounds further enhance immunological responses through the induction of natural killer (NK) cell activity as well as macrophage function to allow for effective targeting and elimination of cancer cells. Similarly, the steroidal glycoside Diosgenin, a yam extract, has shown similar properties through interference in the proliferation of cancerous cells while inducing apoptosis through caspase activation.[53] Saponins and glycosides further prevent damage to cell membrane integrity and thus invoke an immune system response against such cancers, hence considered crucial natural anticancer agents. In addition to their direct cell cytotoxicity to cancerous cells, saponins and glycosides also interfere with important signaling pathways of the immune system in which the body is programmed to recognize and lyse the tumor cells. For example, ginsenosides activate some of the pathways, such as the NF-κB and JAK/STAT pathways, which involve immune cell differentiation and functions. These compounds therefore suppress inflammation-related processes that involve the development of tumors and thus are suitable for the therapy of early and advanced cancers. Saponins and glycosides, in their ability to target cancerous cells while boosting the immunity system, provide an approach for a unique strategy towards the strategy of natural cancer treatment.

Future directions

Elucidation of their molecular mechanisms of action from the bioactive compounds including curcumin, resveratrol, EGCG, and paclitaxel could be the prime focus of future research for anticancer properties of natural products. The major concern needs to be in resolving synergistic interactions between the natural compounds and conventional chemotherapy or targeted therapies meant to increase the efficacy of treatment. Advanced drug delivery systems, including nanoparticle-based formulations, can improve the bioavailability and targeted action of the natural compound. It will be crucial to conduct clinical studies for the authentication of preclinical observations, especially in terms of dosing, toxicity, and long-term safety. Investigating therapeutic strategies based on genetic and epigenetic profiles would also be a must for optimizing the outcomes of therapy. Such an expansion of research into natural products with the hope of overcoming drug resistance in cancer cells could usher in new therapeutic doors. An integration of metabolomics and proteomics would supply critical depth to understanding how these compounds modulate cancer cell metabolism and immune responses. Collaboration by the academia, industries, and clinicians can accelerate the translation of natural product-based research into effective and accessible therapies for human cancer.

Conclusion

Natural compounds exhibit promising anticancer activities, selectively targeting specific cell pathways such as apoptosis, cell cycle regulation, and metastasis inhibition. This makes them valuable adjuncts or even alternatives to conventional cancer treatments. Compounds such as curcumin, resveratrol, and EGCG have demonstrated potent anticancer activity by inhibiting cancer cell proliferation and enhancing chemotherapy and radiation therapies, all while posing minimal harm to patients. Derived from plants and other natural sources, these bioactive compounds modulate oxidative stress and inflammation, influence epigenetic alterations, and indicate potential for an anticancer therapy with numerous therapeutic benefits. To get lab results used in the real world, more detailed research needs to be done on how different drugs work together and how to deliver them more effectively. This could help beat drug resistance and make things better for patients.

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