IJP (2024), Vol. 11, Issue 12 **(Review Article)**

Received on 12 December 2024; received in revised form, 28 December 2024; accepted, 29 December 2024; published 31 December 2024

AN OVERVIEW OF MAJOR CLASSES OF NATUROPATHIC ANTI-CANCER DRUGS

G. Sathya Pooja *, Suganth and Kavitha

KMCH College of Pharmacy, Kalapatti, Coimbatore - 641014, Tamil Nadu, India.

Keywords:

Anticancer, Ayurveda, Naturopathic, Tumor tissues, Intractable

Correspondence to Author:
G. Sathya Pooja

KMCH College of Pharmacy, Kalapatti, Coimbatore-641014, Tamil Nadu, India.

E-mail: sathyapooja2015@gmail.com

ABSTRACT: Plant-based anticancer drugs have played a crucial role in cancer treatment for many years. According to Ayurveda, various cancer phases are intractable, chronic inflammatory disorders. Natural products have high potential for the prevention and treatment of different cancers. More importantly, anticancer naturopathics have been modified to gain first-line, second line, and third-line targeting in tumor tissues. This review will explore 25 plant-based anticancer drugs, their mechanisms of action, marketed products, side effects, and relevant references.

INTRODUCTION: Plant-based anticancer drugs have played a crucial role in cancer treatment for many years. These drugs are derived from various plant species and target several cancerous pathways such as DNA synthesis, cell cycle regulation, apoptosis, and angiogenesis. This review will explore 25 plant-based anticancer drugs, their mechanisms of action, marketed products, side effects, and relevant references. A wide range of illnesses, including cancer, can begin in practically any organ or tissue of the body when aberrant cells proliferate out of control, cross normal boundaries to infiltrate other areas of the body, or move to other organs. The latter phase, known as metastasising, is a primary cause of cancer-related deaths. The distinction between benign and malignant tumours is the most crucial issue in cancer pathology. There are over a hundred different types of cancer, each with a unique behaviour and response to treatment.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.IJP.11(12).643-63

Article can be accessed online on: www.ijpjournal.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.IJP.11(12).643-63

Cancer can arise from the aberrant proliferation of any of the various cell types in the body [1, 2].

Types of Cancer: Common skin warts and other benign tumours stay in their original position without spreading to other parts of the body or infecting nearby normal tissue. But a cancerous tumour can also invade nearby healthy tissue and move through the lymphatic or circulatory systems to other parts of the body (metastasis). The term "cancer" should only be used to describe malignant tumours, and the danger of cancer stems from its capacity to penetrate and spread. Malignant tumours are often resistant to such localised treatment because they spread to distant body areas, whereas benign tumours can typically be surgically removed [3].

There are many different kinds of cancer, each with its own unique location in the body, cell type of origin, and genotypic traits. The genetics that underlie the development of cancer cells and how they behave are extremely complicated. Some cancer genes are frequently present in a variety of cancer forms, whereas others are more exclusive to a single type of cancer. Additionally, it has been demonstrated that because of branching evolution, the genetic profiles of primary and metastatic

tumours, as well as even of individual tumours, frequently differ [4]. Based on the kind of cell they originate from, benign and malignant tumours are categorised. Three primary categories comprise the majority of cancers: leukemias or lymphomas, sarcomas, and carcinomas. Approximately 90% of human cancers are classified as carcinomas, which are epithelial cell malignancies. Solid tumours of connective tissues, including muscle, bone, cartilage, and fibrous tissue, sarcomas are uncommon in humans. About 8% of human cancers are leukaemias, while lymphomas are caused by immune system cells and blood forming cells, respectively. Further classification of tumours is based on the kind of cell involved and the tissue of origin (e.g., lung or breast carcinomas). For example, fibroblasts give rise to fibrosarcomas, while erythrocyte (red blood cell) precursors give rise to erythroid leukaemias [5].

Etiology: Over time, genetic and environmental damages have been proposed as alternate causes of cancer. A mutation that dysregulates the intrinsic systems governing normal cell growth and survival is the source of cancer cells, according to the genetic theory. However, according to the environmental hypothesis, cancer may not always result from mutations but rather from a variety of external factors that disrupt normal tissue homeostasis [6].

According to Ayurveda, various cancer phases are intractable, chronic inflammatory disorders. There is substantial evidence linking age-related and lifestyle-related disorders like metabolic syndrome and cancer to chronic inflammation. Additionally, evidence points to the inflammatory milieu surrounding and inside tumours as a critical component of carcinogenesis. Only recently has the molecular basis of the link between inflammation and cancer been elucidated [7].

History of Plant Based Anti-cancer Drugs: Cancer is a terrifying illness that is one of the most significant health problems facing humanity. It requires a proactive approach to treatment. Novel chemical entities can be found in plants, which offers a promising avenue for cancer research. Chemotherapy, despite its effectiveness, has some intolerable adverse effects. However, compared to traditional treatment procedures, plants and plant-derived products are simple, safer, environmentally friendly, inexpensive, quick, and less toxic, making them a transforming sector [8].

Because of their pleiotropic effects on target events in a variety of ways, phytochemicals are regarded as good candidates for the creation of anticancer drugs.

In the realm of oncology, the use of plants remedies has gained widespread acceptance as an alternative or complementary treatment. As a result, a number of new cytotoxic chemicals are identified from plants each year, opening up new avenues for the battle against cancer. The study of naturally occurring molecular entities that could be beneficial to the pharmaceutical business is a focus of many researchers. Those who find substances exhibiting anticancer activity in preclinical research also look for clinical efficacy verification [9].

Vincristine:

Plant Origin: Derived from *Catharanthus roseus* (Madagascar periwinkle), which is known for its medicinal properties, particularly in anticancer treatments [10].

Gajalakshmi S, Vijayalakshmi S, Devi Rajeswari V. Pharmacological activities of *Catharanthus roseus*: A perspective review. Int J Pharm Bio Sci 2013; 4(2):431–439.

Mechanism of Action: Vincristine is a vinca alkaloid that exerts its antitumor effects by binding to tubulin, a protein essential for microtubule formation. By disrupting microtubule assembly, vincristine halts the formation of the mitotic spindle, causing cell cycle arrest in the metaphase stage. This disruption ultimately leads to programmed cell death (apoptosis) of cancer cells [11].

Cancer Types Treated: Vincristine is effective against various cancers, including:

- Acute leukemia (especially in children),
- Lymphomas (both Hodgkin's and non-Hodgkin's),
- Neuroblastoma,
- Wilms' tumor [12].

Marketed Products: A well-known marketed product is Oncovin by Eli Lilly. It is typically administered intravenously as part of combination chemotherapy regimens [13].

Neurotoxicity: Peripheral neuropathy, a common and dose-limiting side effect, characterized by tingling, numbness, and muscle weakness, particularly in the hands and feet.

Bone Marrow Suppression: Causes a decrease in blood cell production, increasing infection risk.

Gastrointestinal Disturbances: Nausea, vomiting, constipation, and abdominal pain are common.

Vincristine's use is a staple in combination chemotherapy regimens, making it a key agent in pediatric and adult oncology. Due to its neurotoxic effects, monitoring for side effects and careful dose adjustments are essential during treatment [14].

Paclitaxel:

Plant Origin: Derived from *Taxus brevifolia* (Pacific yew tree), paclitaxel is a naturally occurring compound that was originally isolated from the bark of this tree [15].

Mechanism of Action: Paclitaxel functions as a mitotic inhibitor by stabilizing microtubules. Unlike many other drugs that prevent microtubule assembly, paclitaxel binds to tubulin within microtubules and prevents their depolymerization.

This stabilization interrupts the dynamic restructuring of the mitotic spindle, crucial for cell division, leading to cell cycle arrest in the G2/M phase and subsequent apoptosis [16].

Cancer Types Treated: Paclitaxel is widely used in the treatment of various cancers, including:

- Ovarian Cancer
- Breast Cancer
- Non-Small Cell Lung Cancer
- Head and Neck Cancers

It is also being explored in combination with other agents for a broader range of solid tumors [17].

Marketed Products: The primary commercial formulation is Taxol (by Bristol-Myers Squibb), administered as an intravenous infusion. The drug is often used in combination with other chemotherapy agents to enhance efficacy [18].

Side Effects: Paclitaxel is associated with several common side effects [19]:

Neutropenia: A reduction in neutrophils, increasing infection risk.

Peripheral Neuropathy: Characterized by numbness or tingling in the extremities due to nerve damage.

Myelosuppression: Suppression of bone marrow activity, leading to decreased blood cell production.

Alopecia: Hair loss, which is a significant adverse effect in many chemotherapy treatments. Other side effects may include hypersensitivity reactions, fatigue, and nausea.

Vinblastine:

Plant Origin: Vinblastine is derived from *Catharanthus roseus* (commonly known as Madagascar periwinkle), a plant native to Madagascar [20].

Mechanism of Action: Vinblastine functions similarly to vincristine by binding to tubulin and disrupting microtubule assembly, leading to inhibition of spindle formation. This action causes cell cycle arrest at the metaphase stage, resulting in apoptosis (cell death) [21].

Cancer Types Treated: Vinblastine is used in the treatment of several cancers, including [22]:

- Hodgkin’s Lymphoma
- Testicular Cancer
- Kaposi’s Sarcoma

Marketed Products: One of the primary commercial formulations is Velban (by Bristol-Myers Squibb), which is administered as an intravenous drug [23].

Side Effects: Vinblastine is associated with several adverse effects, including [24]:

Bone Marrow Suppression: Reduction in blood cell production, which can lead to anemia and increased infection risk.

Neurotoxicity: Often manifests as numbness or tingling due to nerve damage.

Nausea: A common gastrointestinal side effect in chemotherapy treatments.

Plant Origin: Camptothecin is derived from *Camptotheca acuminata*, a tree native to China. The compound was initially isolated from the bark of this plant [25].

Mechanism of Action: Camptothecin works by inhibiting topoisomerase I, an enzyme responsible for alleviating torsional strain during DNA replication. By binding to the topoisomerase I-DNA complex, camptothecin prevents the re-ligation of DNA strands after they have been cut, leading to the accumulation of DNA breaks and subsequent cell death [26].

Cancer Types Treated: Camptothecin derivatives, such as irinotecan (CPT-11) and topotecan (Hycamtin), are used in the treatment of various cancers, including [27, 28]:

- Ovarian Cancer
- Colorectal Cancer
- Small Cell Lung Cancer

Marketed Products:
CPT-11 (Irinotecan):
Hycamtin (Topotecan): These derivatives are widely used in clinical practice for the treatment of specific cancers [29, 30].

Side Effects: Common side effects of camptothecin derivatives include [31, 32]:

Diarrhea: Often severe and dose-limiting, especially with irinotecan.

Neutropenia: A decrease in white blood cells, leading to increased risk of infection.

Alopecia: Hair loss is a common side effect in chemotherapy.

Taxotere:
Plant Origin: Taxotere is derived from *Taxus baccata* (European yew tree), a plant that provides a natural source of docetaxel, the active ingredient in Taxotere [33].

Mechanism of Action: Like paclitaxel, Taxotere (docetaxel) stabilizes microtubules by binding to tubulin and preventing their disassembly. This stabilization blocks the dynamic processes of microtubule depolymerization and formation, leading to inhibition of cell division. The resulting mitotic arrest promotes apoptosis (programmed cell death) [34].

Cancer Types Treated: Taxotere is used in the treatment of several cancers, including [35, 36]:

- Breast Cancer
- Prostate Cancer
- Non-Small Cell Lung Cancer

Marketed Products: The primary marketed product for docetaxel is Taxotere (by Sanofi), available as an intravenous formulation [37].

Side Effects: Common side effects associated with Taxotere include [38]:

Neutropenia: A significant reduction in neutrophils, increasing the risk of infection.

Mucositis: Inflammation and ulceration of the mucosal lining, particularly in the mouth and digestive tract.

Fluid Retention: Often leading to peripheral edema.

Peripheral Neuropathy: Numbness or tingling due to nerve damage, similar to paclitaxel.

Topotecan:
Plant Origin: Topotecan is derived from *Camptotheca acuminata*, a plant native to China. The compound is a derivative of camptothecin, initially isolated from the plant's bark [39].

Mechanism of Action: Topotecan works by inhibiting topoisomerase I, an enzyme responsible for alleviating torsional strain during DNA replication. By binding to the topoisomerase I-DNA complex, topotecan prevents the re-ligation of single-strand DNA breaks, leading to the accumulation of double-strand DNA breaks, ultimately causing cell death [40].

Cancer Types Treated: Topotecan is primarily used in the treatment of [41, 42]:

Ovarian Cancer:
Small Cell Lung Cancer: It is often used as second-line therapy in small cell lung cancer after failure of first-line treatments.

Marketed Products: The primary marketed product for topotecan is Hycamtin (by Novartis), which is available in both oral and intravenous formulations [43].

Side Effects: Common side effects of topotecan include [44]:

Neutropenia: A decrease in neutrophils, increasing the risk of infections.

Thrombocytopenia: A reduction in platelets, which can lead to bleeding complications.

Fatigue: Often experienced by patients undergoing chemotherapy.

Nausea: Common gastrointestinal side effect.

Podophyllotoxin:
Plant Origin: Podophyllotoxin is derived from *Podophyllum peltatum* (Mayapple), a plant native to North America. The compound is extracted from the rhizomes of the plant [45].

Mechanism of Action: Podophyllotoxin exerts its anticancer effects through two key actions [46]:

It binds to tubulin, preventing the formation of microtubules, which are essential for cell division.

It inhibits topoisomerase II, an enzyme responsible for DNA replication, by preventing the re-ligation of DNA strands after breaking. This leads to DNA strand breaks, which trigger cell death.

Cancer Types Treated: Podophyllotoxin derivatives, such as etoposide (Vepesid), are used in the treatment of [47, 48]:

- Testicular Cancer
- Kaposi's Sarcoma
- Lung Cancer

Marketed Products: The most commonly marketed derivative of podophyllotoxin is Vepesid (Etoposide), which is available in intravenous and oral forms [49].

Side Effects: Common side effects associated with podophyllotoxin derivatives include [50]:

Nausea and Vomiting: Frequent side effects of chemotherapy.

Bone Marrow Suppression: Leads to anemia, neutropenia, and thrombocytopenia, increasing infection and bleeding risk.

Alopecia: Hair loss is a typical consequence of chemotherapy.

Artemisinin:
Plant Origin: *Artemisia annua* (Sweet wormwood).

Mechanism of Action: Artemisinin generates free radicals in the presence of iron, causing cellular damage and leading to apoptosis, particularly in cancer cells.

Cancer Types Treated: Artemisinin is being studied for its potential in treating leukemia, breast cancer, liver cancer, and colorectal cancer.

Marketed Products: Artemisinin-based therapies (e.g., *Artemisinin*) have been explored for off-label use in cancer treatment.

Side Effects: Mild gastrointestinal symptoms, dizziness, and potential interactions with other medications [51].

Berberine:
Plant Origin: Berberine is derived from *Berberis vulgaris* (barberry), a plant that has been traditionally used in various cultures for its medicinal properties. The compound is typically isolated from the root and stem bark [52].

Mechanism of Action: Berberine exerts its anticancer effects primarily by inhibiting the Akt/mTOR signaling pathway, which is crucial for regulating cell growth, survival, and metabolism in cancer cells.

By disrupting this pathway, berberine can reduce tumor cell proliferation and induce apoptosis (programmed cell death) [53].

Cancer Types Treated: Berberine has shown potential in the treatment of various cancers, including:

- Colorectal Cancer
- Breast Cancer

Prostate Cancer: It has demonstrated inhibitory effects on cancer cell growth and metastasis in preclinical studies [54, 55].

Marketed Products: Berberine is widely available as a **dietary supplement**, often marketed for its general health benefits, including its potential effects on blood sugar levels and cholesterol.

However, its use as a cancer treatment is still under investigation in clinical studies [56].

Side Effects: Common side effects associated with berberine include [57]:

Mild Gastrointestinal Discomfort: Including bloating and cramping.

Diarrhea: May occur due to its effects on gut motility.

Potential Drug Interactions: Berberine may interact with other drugs, especially those metabolized by the liver.

Curcumin

Plant Origin: Curcumin is derived from *Curcuma longa* (turmeric), a plant belonging to the ginger family. It is the active polyphenolic compound found in the rhizomes of the plant [58].

Mechanism of Action: Curcumin exhibits its anticancer properties by modulating several cellular signaling pathways, including:

NF-κB: A transcription factor involved in inflammation and cancer cell survival.

P53: A tumor suppressor protein that regulates the cell cycle and promotes apoptosis.

Apoptosis Cascade: Curcumin activates the apoptosis process, leading to the death of cancer cells. This combination of mechanisms inhibits cell proliferation and promotes cell death in cancer cells [59, 60].

Cancer Types Treated: Curcumin has shown potential in the treatment of various cancers, including:

- Colorectal Cancer
- Pancreatic Cancer

Breast Cancer: It is believed to inhibit tumor growth and metastasis through its effects on cell signaling and inflammation [61, 62].

Marketed Products: The most widely known marketed product of curcumin is Curcumin C3 Complex, a formulation that is often sold as a dietary supplement aimed at providing anti-inflammatory and antioxidant benefits [63].

Side Effects: Curcumin is generally well-tolerated when taken at normal doses, though high doses may lead to:

Gastrointestinal Upset: Including symptoms such as bloating and diarrhea. It is important to note that curcumin may interact with certain medications, especially those affecting liver enzymes [64].

Resveratrol:

Plant Origin: Resveratrol is derived from *Vitis vinifera* (grapevine), particularly from the skin of grapes. It is a polyphenolic compound that is produced by the plant as a defense mechanism against stressors such as UV radiation and fungal infections [65].

Mechanism of Action: Resveratrol exerts its anticancer effects through the activation of the SIRT1 gene, which is involved in regulating processes such as DNA repair, inflammation, and apoptosis. This activation helps prevent DNA damage and promotes apoptosis in cancer cells, making it a potential anticancer agent [66].

Cancer Types Treated: Resveratrol has shown potential in the treatment of various cancers, including:

- Colorectal Cancer
- Breast Cancer

Prostate Cancer: Research suggests that resveratrol inhibits cancer cell proliferation and metastasis while inducing apoptosis in cancer cells [67, 68].

Marketed Products: Resveratrol is commonly marketed as a dietary supplement, often promoted for its anti-aging and antioxidant properties.

Though clinical trials are ongoing, its use as a cancer therapy is still under investigation [69].

Side Effects: Resveratrol is generally well tolerated; however, potential side effects include [70]:

Interactions with Anticoagulants: Resveratrol may increase the risk of bleeding when taken with blood-thinning medications.

Gastrointestinal Upset: Such as bloating and diarrhoea, particularly at high doses.

Cinnamaldehyde:

Plant Origin: Cinnamaldehyde is the primary active component of cinnamon (Cinnamomum species), particularly derived from *Cinnamomum verum* (true cinnamon) and *Cinnamomum cassia* (cassia). It is responsible for the characteristic flavor and aroma of cinnamon [71].

Mechanism of Action: Cinnamaldehyde exhibits anticancer properties through several mechanisms [72]:

Apoptosis Induction: It triggers apoptosis (programmed cell death) in cancer cells by activating various cellular pathways like caspases and mitochondrial dysfunction.

Cell Cycle Arrest: Cinnamaldehyde induces cell cycle arrest at the G2/M phase, which prevents cancer cells from proliferating.

Anti-inflammatory Effects: It suppresses inflammatory markers such as COX-2, TNF-α, and IL-6, which are often upregulated in cancer progression.

Angiogenesis Inhibition: Cinnamaldehyde inhibits the formation of new blood vessels, thus restricting tumor growth and metastasis.

Cancer Types Treated: Cinnamaldehyde has been studied for its potential in treating various cancers, including [73]:

Lung Cancer: It inhibits lung cancer cell growth by modulating several cancer-related pathways.

Breast Cancer: Studies suggest that cinnamaldehyde inhibits breast cancer cell proliferation by inducing apoptosis.

Colon Cancer: Cinnamaldehyde has shown to reduce tumor growth and induce apoptosis in colon cancer cells.

Marketed Products: Cinnamaldehyde is primarily available as a part of cinnamon-based extracts and essential oils.

It is also available as a flavoring agent in food products, but research on its anticancer effects is still largely experimental, with no specific marketed anticancer formulations at this time [74].

Side Effects: Cinnamaldehyde is generally safe when used in food or low doses. However, higher doses may cause gastrointestinal irritation, skin irritation, and allergic reactions, especially for those with a cinnamon sensitivity [75].

EGCG (Epigallocatechin Gallate):

Plant Origin: EGCG is a catechin found primarily in *Camellia sinensis* (green tea). It is one of the most studied polyphenolic compounds in green tea and is known for its antioxidant and anticancer properties [76].

Mechanism of Action: EGCG exerts its anticancer effects through multiple mechanisms [77]:

Antioxidant Properties: Reduces oxidative stress and prevents DNA damage, which is crucial for cancer cell survival.

Inhibition of Angiogenesis: Prevents the formation of new blood vessels that supply nutrients to tumors.

Induction of Apoptosis: EGCG induces programmed cell death in cancer cells through regulation of several key cell cycle and survival pathways.

Cancer Types Treated: EGCG has been studied for its potential effects in the treatment of:

- Prostate Cancer
- Breast Cancer

Lung Cancer: Preclinical studies show that EGCG can inhibit cancer cell growth, metastasis, and angiogenesis in these cancers [78, 79].

Marketed Products: EGCG is available as green tea extract supplements, which are widely marketed for their antioxidant, anti-inflammatory, and anticancer properties. These supplements contain varying amounts of EGCG depending on the formulation [80].

Side Effects: While EGCG is generally safe, high doses may lead to the following side effects [81]:

Liver Toxicity: Especially in individuals with pre-existing liver conditions.

Nausea and Stomach Irritation: Particularly when taken on an empty stomach.

Silibinin

Plant Origin: Silibinin is derived from *Silybum marianum* (Milk thistle), a plant widely known for its liver-protective properties due to the active compound silymarin, which contains silibinin as its primary active ingredient [82].

Mechanism of Action: Silibinin inhibits cancer cell proliferation and induces apoptosis through several mechanisms [83]:

Cell Cycle Arrest: It blocks cell cycle progression at the G1 phase, preventing cancer cells from dividing.

Apoptosis Induction: It promotes programmed cell death in cancer cells.

Signaling Pathway Modulation: Silibinin regulates pathways involved in cell survival and death, including NF-κB and p53. These pathways play significant roles in cancer cell proliferation, survival, and metastasis.

Cancer Types Treated: Silibinin has shown potential for the treatment of:

- Liver Cancer
- Prostate Cancer

Breast Cancer: Studies have demonstrated that silibinin can inhibit tumor growth and metastasis in these cancers, with a focus on liver cancer where it is being actively researched [84].

Marketed Products: Silibinin is marketed as Legalon, a silymarin extract used for liver diseases, primarily to protect the liver against toxins and aid in liver regeneration. Its potential in cancer treatment is still under investigation [85].

Side Effects: Silibinin is generally well tolerated, with the most common side effect being mild gastrointestinal discomfort. Other side effects are rare but may include nausea or diarrhea at higher doses [86].

Tanshinone IIA:

Plant Origin: Tanshinone IIA is extracted from *Salvia miltiorrhiza* (Danshen), a plant that has been used in traditional Chinese medicine (TCM) for centuries. This plant is known for its cardiovascular benefits, and its active compound, Tanshinone IIA, is responsible for its therapeutic effects, including anticancer properties [87].

Mechanism of Action: Tanshinone IIA exhibits anticancer activity through several mechanisms:

Induction of Apoptosis: It triggers the programmed cell death of cancer cells.

Angiogenesis Inhibition: It reduces the formation of new blood vessels that tumors require for growth.

Modulation of Metastasis Pathways: It inhibits pathways such as PI3K/Akt/mTOR, which play a role in cancer progression and metastasis [88].

Cancer Types Treated: Tanshinone IIA has shown potential in treating various cancers, including:

Lung Cancer: It inhibits the growth of lung cancer cells.

Liver Cancer: Tanshinone IIA has been found to reduce liver cancer cell proliferation.

Breast Cancer: It shows promise in treating breast cancer through its anti-proliferative effects.

Gastric Cancer: Studies indicate its potential effectiveness in gastric cancer [89].

Marketed Products: Tanshinone IIA is primarily available in traditional Chinese medicine formulations for various diseases, including cardiovascular conditions, but it is not specifically marketed as a cancer treatment [90].

Side Effects: Tanshinone IIA is considered generally safe, though side effects may include:

Gastrointestinal Discomfort: Some users may experience stomach irritation.

Allergic Reactions: There is a potential for allergic responses such as rashes [91].

Withaferin A:

Plant Origin: Withaferin A is a natural compound derived from *Withania somnifera*, also known as Ashwagandha. This herb is commonly used in Ayurvedic medicine for its adaptogenic properties, and Withaferin A is considered the primary bioactive compound with potential anticancer effects [92].

Mechanism of Action: Withaferin A acts through various mechanisms to exert anticancer effects:

Cell Cycle Arrest: It induces cell cycle arrest at the G2/M phase, preventing the progression of cancer cells.

Apoptosis: It promotes the activation of apoptosis pathways in cancer cells, leading to their death.

Signaling Pathways Modulation: Withaferin A influences NF-κB, ROS production, and other pathways related to inflammation and cancer cell survival [93].

Cancer Types Treated: Withaferin A has been studied in the context of various cancers, including:

Prostate Cancer: It inhibits proliferation and metastasis of prostate cancer cells.

Breast Cancer: Withaferin A induces cell death in breast cancer cells.

Lung Cancer: It has potential in treating lung cancer by reducing tumor size and metastasis.

Colon Cancer: It also shows potential for treating colon cancer by suppressing tumor growth [94].

Marketed Products: Withaferin A is available in various herbal formulations under the brand name Ashwagandha, typically marketed for stress relief and overall health enhancement. Its potential use as an anticancer agent is still under investigation [95].

Side Effects: Withaferin A is generally considered safe, though high doses may lead to mild side effects:

Gastrointestinal Upset: High doses may cause nausea or stomach discomfort [96].

Aloe Vera Extract:

Plant Origin: Aloe vera is derived from *Aloe barbadensis*, a succulent plant commonly used in traditional medicine for its healing properties, particularly for skin and digestive issues. The plant contains bioactive compounds such as aloin, emodin, and polysaccharides, which have been found to exhibit anticancer properties [97].

Mechanism of Action: Aloe vera extracts, especially compounds like aloin and emodin, demonstrate anticancer activity through the following mechanisms:

Induction of Apoptosis: Aloe vera compounds trigger apoptosis (programmed cell death) in cancer cells.

Inhibition of Angiogenesis: The compounds suppress the formation of new blood vessels, which tumors need to grow.

Cell Proliferation Inhibition: Aloe vera compounds prevent the rapid division of cancer cells [98].

Cancer Types Treated: Aloe vera extract has been studied for its anticancer effects in several cancer types:

Colorectal Cancer: Aloe vera compounds inhibit the growth of colorectal cancer cells.

Skin Cancer: Aloe vera is particularly effective in treating skin cancers due to its ability to regulate cell proliferation and apoptosis.

Lung Cancer: Aloe vera's effects on lung cancer cells include inhibition of proliferation and induction of cell death [99].

Marketed Products: Aloe vera is commonly marketed as a topical treatment for skin conditions and as an oral supplement for digestive issues.

Some of these products are being investigated for their potential in cancer therapy. Aloe vera-based formulations are available in various forms, such as gels, creams, and juices [100].

Side Effects: Aloe vera is generally safe, but it may cause mild side effects, particularly when taken in large quantities or applied topically.

Gastrointestinal Issues: Some individuals may experience diarrhea, nausea, or abdominal cramping when consuming Aloe vera.

Skin Irritation: Topical application may cause allergic reactions or skin irritation in sensitive individuals [101].

Saponins:

Plant Origin: Saponins are a diverse group of compounds found in various plants, including *Ginseng* and *Quillaja saponaria* (Soapbark tree). These compounds are known for their foaming properties and are used in many traditional medicines. They are studied for their potential therapeutic effects, particularly in cancer treatment [102].

Mechanism of Action: Saponins exhibit anticancer activity through multiple mechanisms:

Induction of Apoptosis: They promote programmed cell death in cancer cells.

Inhibition of Cell Proliferation: Saponins prevent the uncontrolled division of cancer cells.

Immune Modulation: Saponins enhance the immune system's ability to fight cancer cells by stimulating immune responses [103].

Cancer Types Treated: Saponins have shown potential in the treatment of several cancers, including:

Breast Cancer: Saponins inhibit the growth of breast cancer cells and reduce metastasis.

Lung Cancer: Studies show that saponins suppress lung cancer cell growth.

Liver Cancer: Saponins also inhibit the growth of liver cancer cells and promote their apoptosis [104].

Marketed Products: Saponins are marketed in various herbal products, particularly *Ginseng* supplements and *Quillaja* extracts. These products are used for their immune-boosting properties, with some formulations currently in clinical trials for cancer treatment [105].

Side Effects: Saponins are generally safe in moderate amounts; however, high doses may lead to:

Gastrointestinal Discomfort: Saponins can cause nausea, bloating, or diarrhea in some individuals [106].

Reserpine:

Plant Origin: Reserpine is derived from *Rauwolfia serpentina*, a plant traditionally used in Ayurvedic medicine for its antihypertensive and sedative effects. It has gained attention for its potential anticancer properties in recent research [107].

Mechanism of Action: Reserpine exerts its effects by inhibiting the vesicular monoamine transporter (VMAT), leading to the depletion of neurotransmitters such as serotonin and norepinephrine in the brain. This depletion has been shown to affect cancer cell viability and is under investigation for its anticancer properties [108].

Cancer Types Treated: Reserpine has been explored for its therapeutic potential in treating:

Breast Cancer: Studies suggest it may inhibit cancer cell growth.

Lung Cancer: Ongoing research is investigating its ability to suppress metastasis and induce apoptosis in lung cancer cells [109].

Marketed Products: Reserpine is available in various antihypertensive medications, primarily used for controlling high blood pressure. Its anticancer potential is still under investigation [110].

Side Effects: Reserpine's most common side effects include:

Hypotension: Low blood pressure due to its vasodilating effects.

Depression: It may cause mood disturbances and depression due to neurotransmitter depletion.

Gastrointestinal Upset: Nausea, vomiting, and abdominal discomfort are reported [111].

***Piper nigrum* (Black Pepper):**

Plant Origin: *Piper nigrum* (Black Pepper) is a flowering vine native to South India and extensively cultivated for its fruit, which is dried and used as a spice and seasoning. The active component responsible for its medicinal properties is piperine [112].

Mechanism of Action: Piperine, the bioactive compound in black pepper, exerts anticancer effects through multiple mechanisms [113].

Induction of Apoptosis: Piperine triggers programmed cell death (apoptosis) by activating caspases and altering mitochondrial membrane potential.

Inhibition of Metastasis: Piperine suppresses cancer cell migration and invasion by inhibiting matrix metalloproteinases (MMPs) and modulating epithelial-mesenchymal transition (EMT).

Anti-Inflammatory Properties: Piperine downregulates pro-inflammatory mediators like TNF-α and NF-κB, which play a significant role in cancer progression [114].

Enhancement of Drug Bioavailability: Piperine inhibits drug-metabolizing enzymes like CYP450 and P-glycoprotein, enhancing the efficacy of chemotherapeutic agents [115].

Cancer Types Treated: *Piper nigrum* and its active compound, piperine, have been studied in the following cancer types:

Breast Cancer: Piperine reduces breast cancer cell proliferation by modulating cell signaling pathways such as PI3K/Akt and Mtor [116].

Colorectal Cancer: Piperine enhances apoptosis in colorectal cancer cells and reduces inflammation in the tumor microenvironment [117].

Lung Cancer: Piperine inhibits lung cancer cell growth by reducing oxidative stress and activating apoptotic pathways [118].

Marketed Products: Piperine is available as a dietary supplement and is often used in formulations to enhance the bioavailability of curcumin.

It is also included in various nutraceutical products for its antioxidant and potential anticancer benefits [119].

Side Effects:

Mild Gastrointestinal Discomfort: Excessive intake can cause nausea or diarrhea.

Interaction with Medications: Piperine may affect the metabolism of certain drugs by inhibiting liver enzymes, necessitating caution when used with other medications [120].

Lycopene:

Plant Origin: Lycopene is a carotenoid pigment found predominantly in *Lycopersicon esculentum* (tomato) and other red and pink fruits. It is a potent antioxidant that has been studied for its anticancer effects [121].

Mechanism of Action: Lycopene exerts its anticancer effects through several pathways.

Antioxidant Activity: Lycopene scavenges free radicals, reducing oxidative stress, which is linked to cancer development.

Anti-inflammatory Effects: Lycopene modulates inflammatory pathways, which are important in cancer progression.

Regulation of Cell Cycle: It influences cell cycle regulators, leading to decreased cancer cell proliferation [122].

Cancer Types Treated: Lycopene has been studied primarily for its potential in:

Prostate Cancer: Lycopene has been shown to reduce prostate cancer cell growth.

Breast Cancer: It may inhibit the growth of breast cancer cells through its antioxidant effects.

Colorectal Cancer: Lycopene's effects on colon cancer have been explored, showing potential in reducing cell proliferation [123].

Marketed Products: Lycopene is widely available in supplements and is consumed as part of the regular diet through tomato products like sauces, juices, and pastes [124].

Side Effects: Lycopene is generally considered safe and is commonly consumed through the diet. No significant adverse effects are reported when taken at normal dietary levels [125].

Ellagic Acid:

Plant Origin: Ellagic acid is a polyphenolic compound found in fruits such as pomegranate, raspberries, and strawberries. It is recognized for its antioxidant properties and anticancer potential [126].

Mechanism of Action: Ellagic acid inhibits cancer cell growth by:

DNA Methylation Inhibition: It interferes with DNA methylation, which is essential for cancer cell survival and progression.

Modulation of Signaling Pathways: It affects several signaling pathways that regulate cancer cell proliferation and metastasis.

Enhancing Apoptosis: Ellagic acid promotes programmed cell death in cancer cells [127].

Cancer Types Treated: Ellagic acid has shown potential in the treatment of:

Prostate Cancer: It inhibits the growth of prostate cancer cells and reduces metastasis.

Breast Cancer: It has been found to reduce the proliferation of breast cancer cells.

Colon Cancer: Ellagic acid can suppress tumor growth and metastasis in colorectal cancer [128].

Marketed Products: Ellagic acid is primarily available in pomegranate extract supplements. It is also consumed naturally in fruits like raspberries and strawberries [129].

Side Effects: Ellagic acid is generally considered safe when consumed in normal amounts. No significant side effects have been reported with its use at dietary levels [130].

Andrographolide:

Plant Origin: Andrographolide is a diterpenoid lactone derived from *Andrographis paniculata* (King of Bitters), a plant traditionally used in herbal medicine, particularly in South Asia. It has gained attention for its potential anticancer effects [131].

Mechanism of Action: Andrographolide induces anticancer effects through several mechanisms:

NF-κB Inhibition: Andrographolide suppresses the NF-κB pathway, a key regulator of inflammation and cell survival. By inhibiting this pathway, it reduces cancer cell proliferation and promotes apoptosis [132].

Induction of Apoptosis: Through the modulation of pro-apoptotic and anti-apoptotic proteins, Andrographolide triggers programmed cell death in cancer cells, thereby reducing tumor growth [133].

Metastasis Suppression: By inhibiting matrix metalloproteinases (MMPs), Andrographolide prevents the degradation of the extracellular matrix, a critical step in cancer metastasis [134].

Cell Cycle Arrest: Andrographolide has been shown to arrest the cell cycle at the G1 and G2/M phases, thereby preventing cancer cell division and proliferation [135].

Cancer Types Treated: Andrographolide has demonstrated anticancer activity against several types of cancers:

Prostate Cancer: Studies suggest that Andrographolide inhibits prostate cancer cell growth and induces apoptosis.

Breast Cancer: It has been shown to inhibit breast cancer cell proliferation and reduce metastasis [136].

Liver Cancer: Andrographolide suppresses liver cancer cell growth by modulating key signaling pathways [137].

Marketed Products: Andrographolide is available as part of traditional herbal formulations and supplements for various ailments. Its use as an anticancer agent is still under investigation, but it is marketed in many forms for immune support and inflammation reduction [138].

Side Effects: Andrographolide is generally safe when consumed at appropriate doses. However, high doses may cause [139].

Gastrointestinal Discomfort: Nausea, vomiting, or abdominal pain.

Mild Toxicity: Some individuals may experience liver toxicity or mild liver function alterations with excessive use.

Luteolin:

Plant Origin: Luteolin is a flavonoid compound commonly found in various plants such as *Coriandrum sativum* (coriander), *Apigenin* (parsley), *Citrus* species (lemons, oranges), and *Camellia sinensis* (tea). It is a naturally occurring flavonoid with significant antioxidant, anti-inflammatory, and anticancer properties [140].

Mechanism of Action: Luteolin exerts anticancer effects through multiple mechanisms:

Apoptosis Induction: Luteolin activates caspases, triggering apoptosis in cancer cells. It modulates mitochondrial function and increases the release of cytochrome c to induce cell death [141].

Cell Cycle Arrest: It has been shown to arrest the cell cycle in various phases (e.g., G1 and G2/M), leading to the inhibition of tumor growth and cell division [142].

Inhibition of Angiogenesis: Luteolin suppresses angiogenesis by inhibiting vascular endothelial growth factor (VEGF) expression, thereby reducing the ability of tumors to develop new blood vessels [143].

Anti-inflammatory Action: Luteolin decreases the expression of pro-inflammatory cytokines (e.g., TNF-α, IL-6) by inhibiting the NF-κB pathway, which is frequently upregulated in cancer cells [144].

Inhibition of Metastasis: Luteolin suppresses the migration and invasion of cancer cells by modulating matrix metalloproteinases (MMPs) and epithelial-mesenchymal transition (EMT) markers [145].

Cancer Types Treated: Luteolin has shown promising anticancer effects in several types of cancer [146]:

Breast Cancer: Luteolin inhibits the growth of breast cancer cells by inducing apoptosis and inhibiting angiogenesis.

Lung Cancer: Luteolin's anticancer potential has been studied in lung cancer, where it suppresses cell invasion and migration.

Colorectal Cancer: Luteolin exerts inhibitory effects on the growth and spread of colorectal cancer cells through multiple signaling pathways.

Marketed Products: Luteolin is available in various dietary supplements, herbal formulations, and extracts, particularly for its antioxidant and anti-inflammatory benefits. Some formulations are marketed as complementary cancer therapies or as general health supplements [147].

Side Effects: Luteolin is generally considered safe when used within recommended doses, but excessive use may cause:

Gastrointestinal Irritation: High doses may lead to discomfort such as nausea, vomiting, or abdominal pain [148].

Shikimic Acid:

Plant Origin: Shikimic acid is a naturally occurring organic acid primarily found in plants like *Illicium verum* (star anise), *Pinus* species (pine needles), and *Ginkgo biloba*. It plays a key role in the biosynthesis of aromatic compounds in plants [149].

Mechanism of Action: Shikimic acid exhibits anticancer properties through several mechanisms:

Inhibition of Cancer Cell Proliferation: Shikimic acid inhibits the growth of cancer cells by interfering with cell cycle regulation and inducing apoptosis. It inhibits the expression of cyclin-dependent kinases and other molecules involved in cell division [150].

Inhibition of Angiogenesis: Shikimic acid reduces angiogenesis by downregulating key molecules like VEGF (vascular endothelial growth factor), which prevents the formation of new blood vessels necessary for tumor growth [151].

Activation of Apoptotic Pathways: Shikimic acid activates caspases and induces mitochondrial dysfunction to trigger apoptosis in various cancer cell lines. This process is mediated by the downregulation of Bcl-2 proteins and upregulation of pro-apoptotic factors [152].

Antioxidant Properties: As an antioxidant, shikimic acid scavenges free radicals and reduces oxidative stress, which plays a significant role in the development and progression of cancer [153].

Cancer Types Treated: Shikimic acid has been investigated for its potential in various cancer types:

Breast Cancer: Studies have shown that shikimic acid inhibits the proliferation and migration of breast cancer cells by regulating key signaling pathways such as MAPK and PI3K/Akt [154].

Lung Cancer: Shikimic acid has been shown to inhibit lung cancer cell growth and invasion by regulating cell cycle checkpoints and apoptosis mechanisms [155].

Colorectal Cancer: Shikimic acid inhibits colorectal cancer cell growth and metastasis through the suppression of angiogenesis and activation of apoptotic pathways [156].

Marketed Products: Shikimic acid is most commonly available in herbal formulations and dietary supplements, especially as a component of *Illicium verum* (star anise). It is also used in the production of oseltamivir (Tamiflu), an antiviral drug for influenza, which is derived from the plant source [157].

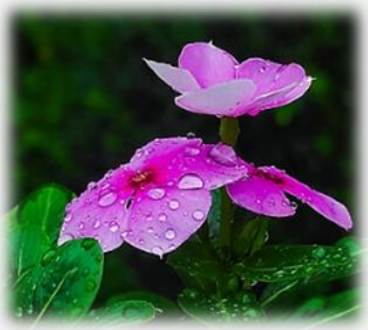
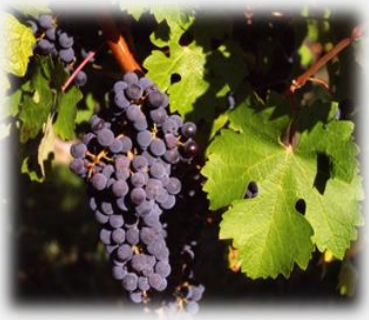
Side Effects: While shikimic acid is generally well-tolerated, excessive consumption can lead to mild gastrointestinal issues such as nausea, vomiting, or diarrhea.

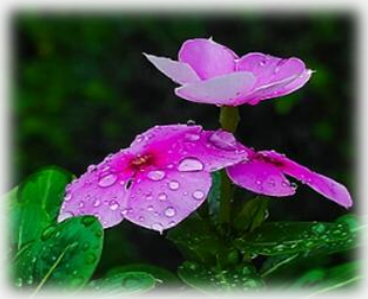
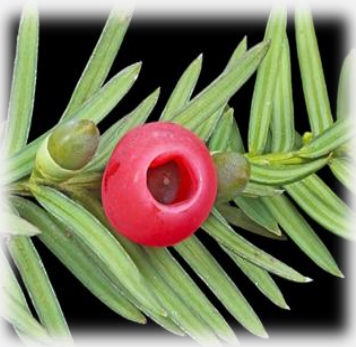
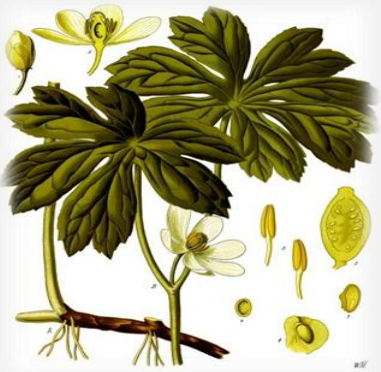
Gastrointestinal Disturbances: High doses may cause discomfort such as bloating, gas, or abdominal pain [158].

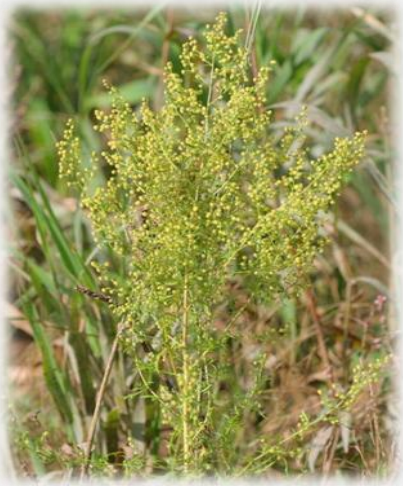
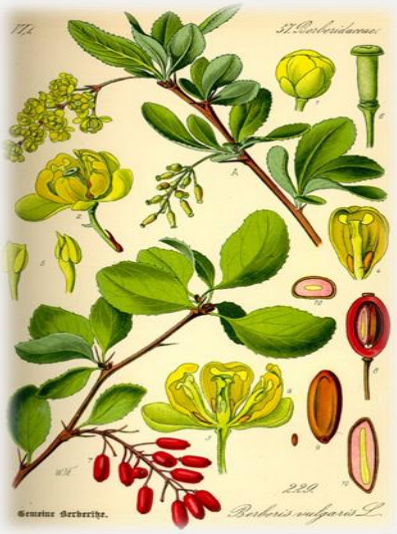
CONCLUSION: Plant-based anticancer drugs have shown significant promise in both preclinical and clinical settings. The development and application of these drugs have revolutionized cancer treatment, with several already available on the market and many others in the pipeline.

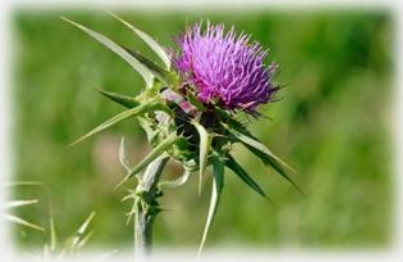
Their mechanisms of action, including the inhibition of cancer cell proliferation, induction of apoptosis, and modulation of the immune response, make them valuable adjuncts to conventional therapies. However, challenges remain, including the need for better bioavailability, reduced toxicity, and overcoming drug resistance.

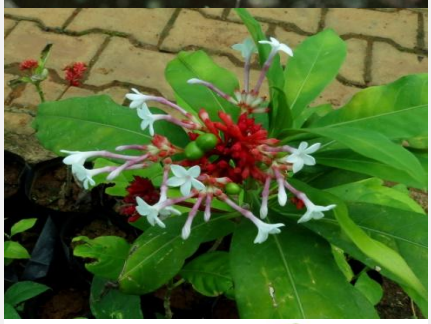
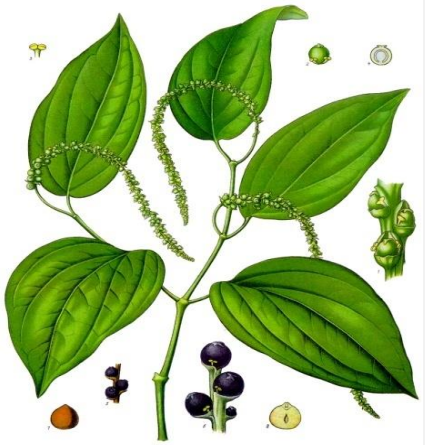
As research continues, plant-based drugs may play an increasingly important role in the treatment of various cancers, complementing and even enhancing the effectiveness of traditional chemotherapeutic agents.

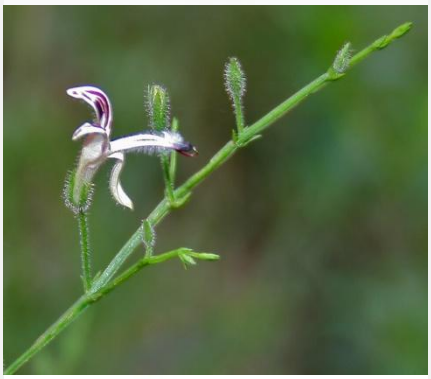
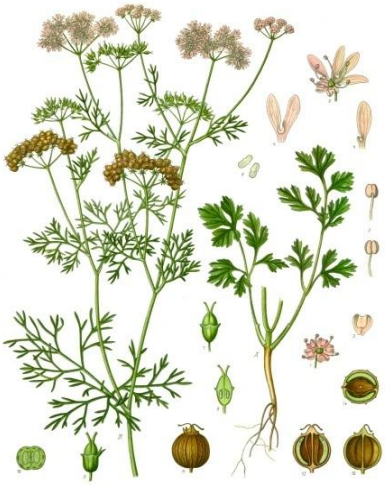
S. no.	Drug Name	Plant Origin	IMAGE
1	Vincristine	*Catharanthus roseus* (Periwinkle)	
2	Resveratrol	*Vitis vinifera* (Grape)	

3	Vinblastine	*Catharanthus roseus* (Periwinkle)	
4	Camptothecin	*Camptotheca acuminata*	
5	Taxotere	*Taxus baccata*	
6	Topotecan	*Camptotheca acuminata*	
7	Podophyllotoxin	*Podophyllum peltatum*	

8	Artemisinin	*Artemisia annua*	
9	Berberine	*Berberis vulgaris*	
10	Curcumin	*Curcuma longa* (Turmeric)	
11	Resvitralol	*Vitis vinifera*	
12	Cinnamon	*Cinnamomum verum*	

13	EGCG (Epigallocatechin gallate)	*Camellia sinensis*	
14	Silibilin	*Silybum marianum*	
15	Tanshinone IIA	*Salvia miltiorrhiza*	
16	Withaferin A	*Withania somnifera*	

17	Aloe Vera	*Aloe barbadensis miller*	
18	Saponins	*Quillaja saponaria*	
19	Reserpine	*Rauwolfia serpentina*	
20	Piperine	*Piper nigrum* (Black pepper)	
21	Lycopene	*Lycopersicon*	

22	Ellagic acid	*Punica granatum*	
23	Andrographolide	*Andrographis paniculata*	
24	Luteolin	*Coriandrum sativum*	
25	Shikimic acid	*Illicium verum*	

Conclusion: Plants have been a prime source of highly effective conventional drugs for the treatment of many forms of cancer, and while the actual compounds isolated from the plant frequently may not serve as the drugs, they provide leads for the development of potential novel agents.

ACKNOWLEDGEMENT: Nil

CONFLICT OF INTEREST: Nil

REFERENCES:

1. World Health Organization. Cancer [Internet]. Geneva: World Health Organization; 2024.
2. Strehler BL: Time, cells, and aging. 2nd ed. San Diego: Academic Press; 1999.https://www.ncbi.nlm.nih.gov/books/NBK9963/
3. U.S. National Library of Medicine. Physiology, Neurotransmitters. In: Freitas E, Fisher W, editors. Medical Physiology: An Update. Bethesda (MD): National Center for Biotechnology Information (US); 2001 [cited

2024 Nov 15]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK9963/
4. Strehler BL: Time, Cells, and Aging. 2nd ed. San Diego: Academic Press; 1999. Available from: https://www.ncbi.nlm.nih.gov/books/NBK9963/
5. ScienceDirect. Cancer Types [Internet]
6. Etiology of Cancer [Internet]. ScienceDirect; 2024 [cited 2024 Nov 11]. Available from: https://www.sciencedirect.com/topics/medicine-and dentistry/etiology-of-cancer
7. Tillu G, Chaturvedi S, Chopra A and Patwardhan B: Understanding cancer etiology:
8. Wang S, Zhang H, Xu Y, Shi M, Zhou Z and Zhang X: Gut microbiota-brain axis: The effects of microbiota on neurological disorders and brain function. J Sport Health Sci 2019; 8(2): 179-87. https://www.sciencedirect.com/science/article/pii/S2221169117308730
9. Pavitra E, Kumari AH, Srivastava R, Saranya S, Sundarraj S and Wang D: Plant-derived anticancer compounds as new perspectives in drug discovery and alternative therapy. J Cell Commun Signal 2021; 15(1): 100–24.: https://pmc.ncbi.nlm.nih.gov/articles/PMC7922180/
10. Gajalakshmi S, Vijayalakshmi S and Devi Rajeswari V: Pharmacological activities of *Catharanthus roseus*: A perspective review. IJPBS 2013; 4(2): 431–439.
11. Jordan MA and Wilson L: Microtubules as a target for anticancer drugs. Nat Rev Cancer 2004; 4(4): 253–265. doi:10.1038/nrc1317.
12. DeVita VT, Lawrence TS and Rosenberg SA: eds. Cancer: Principles & Practice of Oncology. 10th ed. Philadelphia: Wolters Kluwer Health 2015; 1714-1730.
13. Oncovin [package insert]. Indianapolis, IN: Eli Lilly and Company; 2016.
14. Cavaletti G and Marmiroli P: Chemotherapy-induced peripheral neurotoxicity. Nat Rev Neurol 2010; 6(12): 657–666. doi:10.1038/nrneurol.2010.160.
15. Cragg GM, Newman DJ and Snader KM: Natural products in drug discovery and development. J Nat Prod 1997; 60(1): 52-60.
16. Weaver BA: How Taxol/paclitaxel kills cancer cells. Mol Biol Cell 2014; 25(18): 2677-81.
17. Rowinsky EK and Donehower RC: Paclitaxel (taxol). N Engl J Med 1995; 332(15): 1004-14.
18. Kingston DGI: Taxol: the chemistry and structure-activity relationships of a clinically useful anticancer agent. J Nat Prod 2000; 63(5): 726-34.
19. National Center for Biotechnology Information (US). The NCBI Handbook [Internet]. 2nd ed. Bethesda (MD): National Library of Medicine (US); 2013.
20. Cragg GM and Newman DJ: Plants as a source of anti-cancer agents. J Ethnopharmacol 2005; 100(1-2): 72-9.
21. Jordan MA and Wilson L: Microtubules as a target for anticancer drugs. Nat Rev Cancer 2004; 4(4): 253-65.
22. Verweij J and Pinedo HM: Mitomycin C, ifosfamide and vinblastine in advanced Hodgkin's disease. Br J Cancer 1988; 57(1): 19-23.
23. Kingston DGI: Vinblastine and vincristine: cancer drugs derived from *Catharanthus roseus* (L.) G. Don. J Nat Prod 1978; 41(3): 449-50.
24. Legha SS: Vinblastine pharmacology and side effects in cancer chemotherapy. CTR 1977; 61(4): 835-41.
25. Pommier Y and Marchand C: Interactions of anticancer drugs with topoisomerase I and II: importance for drug design. Adv Cancer Res 2012; 113: 67-106.
26. Pommier Y: Topoisomerase I inhibitors: camptothecin and beyond. Nat Rev Cancer 2006; 6(10): 789-802.
27. Saltz LB, Cox JV and Blanke C: Irinotecan plus fluorouracil and leucovorin for metastatic colorectal cancer. N Engl J Med 2000; 343(13): 905-14.
28. Hochster HS, Hart LL and Greco FA: Topotecan in the treatment of small-cell lung cancer. Cancer Chemother Pharmacol 1997; 39(6): 520-4.
29. Zhao J, Li C and Ren X: Efficacy and safety of irinotecan in metastatic colorectal cancer: a meta-analysis. J Cancer Res Clin Oncol 2013; 139(3): 387-97.
30. Wilson RH, Pendyala L and Coley C: Topotecan for the treatment of small-cell lung cancer: a systematic review. Cancer Chemother Pharmacol 2008; 62(1): 1-12.
31. Kalinaki A, Koutras A and Kalogera E: Safety of irinotecan in the treatment of metastatic colorectal cancer. Oncol Rev 2012; 6(2): 122-7.
32. Zhou Y, Li M and Li D: Camptothecin derivatives and their applications. Front Pharmacol 2019; 10: 1-12.
33. Rowinsky EK and Donehower RC: Taxol (paclitaxel) and Taxotere (docetaxel): the taxanes. Cancer Chemother Pharmacol 1995; 36(6): 417-26.
34. Jordan MA and Wilson L: Microtubules as a target for anticancer drugs. Nat Rev Cancer 2004; 4(4): 253-65.
35. Piccart MJ, von Minckwitz G and Mattar P: Docetaxel for the treatment of breast cancer: results of a phase III study. J Clin Oncol 2008; 26(15): 2465-71.
36. Tannock IF, de Wit R and Berry WR: Docetaxel in metastatic hormone-refractory prostate cancer. N Engl J Med 2004; 351(15): 1502-12.
37. Cavaletti G, Tredici G and Liguori M: Neurotoxicity of docetaxel: A review of its clinical presentation, management, and pathogenesis. Cancer Chemother Pharmacol 2001; 48(5): 167-74.
38. Buchbinder EI, Bodey GP and Knickerbocker RK: Neutropenia and other toxicities related to docetaxel therapy. Oncology (Williston Park) 2002; 16(11): 9-15.
39. Pommier Y and Marchand C: Interactions of anticancer drugs with topoisomerase I and II: importance for drug design. Adv Cancer Res 2012; 113: 67-106.
40. Pommier Y: Topoisomerase I inhibitors: camptothecin and beyond. Nat Rev Cancer 2006; 6(10): 789-802.
41. Hochster HS, Hart LL and Greco FA: Topotecan in the treatment of small-cell lung cancer. Cancer Chemother Pharmacol 1997; 39(6): 520-4.
42. O'Reilly S, Jayson G and Green J: Topotecan in the treatment of ovarian cancer: clinical evidence and its role in therapy. Oncology 2003; 65(3): 18-24.
43. Muggia FM, Hainsworth JD and Cella D: A phase II study of topotecan in women with relapsed ovarian cancer: efficacy and safety results. Cancer Chemother Pharmacol 2000; 45(5): 370-7.
44. Crawford J, Dale DC and Lyman GH: Chemotherapy-induced neutropenia: risks, consequences, and new directions for its management. Cancer 2004; 100(10): 2278-89.
45. Lamb JH, Morrison AE and Wrigley EC: Podophyllotoxin derivatives: the development of new anti-cancer agents. Curr Med Chem 2003; 10(11): 1111-24.
46. Hsiang YH, Lihou MG and Liu LF: Arrest of the cell cycle by VP-16 and VM-26. Cancer Res 1989; 49(18): 5077-82.
47. Bodnar JA, Pendergrass KM and Klapstein JD: Etoposide in the treatment of testicular cancer. J Clin Oncol 1984; 2(11): 1282-9.
48. Lubert M, Kaur G and Beall D: Etoposide for the treatment of Kaposi's sarcoma. Oncol Nurs Forum 1992; 19(8): 1281-5.

49. Cascinu S, Labianca R and Beretta G: Etoposide in the treatment of small-cell lung cancer: results of a randomized trial. Oncology 1997; 54(6): 530-4.
50. Daugaard G, Dombernowsky P and Willemoe G: Etoposide-related side effects in patients with testicular cancer. Eur J Cancer 1990; 26(7): 741-6.
51. Artemisinin mechanism of action of original use [Internet]. ScienceDirect. [cited 2024 Nov 21].
52. Li L, Zhang L and Han L: Berberine: A review of its effects on obesity, insulin resistance, and cancer. J Mol Endocrinol 2014; 53(6).
53. Zhou J, Zhang L and Li M: Berberine inhibits the Akt/mTOR signaling pathway and induces apoptosis in cancer cells. Oncol Lett 2017; 14(6): 7873-79.
54. Zhang Y, Li X and Lin X: Anti-cancer effects of berberine: A systematic review and meta-analysis. Front Pharmacol 2020; 11: 568258.
55. Zhou J, Li J and Ye J: Berberine suppresses the growth of breast cancer cells by targeting the Akt/mTOR pathway. Cancer Cell Int 2017; 17(1): 11.
56. Kong W, Wei J and Abidi P: Berberine is a novel cholesterol-lowering drug working through a unique mechanism distinct from statins. Nat Med 2004; 10(12): 1344-51.
57. Zhang L, Xie Y and Liu T: Safety profile of berberine: A clinical review. Eur J Clin Pharmacol 2019; 75(4): 479-88.
58. Heger M, Baier J and Daskalova S: Curcumin: A review of its potential as a chemopreventive and therapeutic agent in cancer. Cancer Lett 2014; 345(2): 120-30.
59. Sharma RA, Gescher AJ and Steward WP: Curcumin: The story so far. Eur J Cancer 2005; 41(13): 1955-68.
60. Aggarwal BB and Harikumar KB: Potential therapeutic effects of curcumin, the anti-inflammatory agent, in human cancers. Mol Pharm 2009; 6(6): 1451-67.
61. Gupta SC, Yang Y and Kim JH: Curcumin, a component of turmeric: A novel suppressor of inflammation, cancer, and other diseases. Adv Exp Med Biol 2007; 595: 89-118.
62. Lee J, Kim J and Park J: Curcumin inhibits the proliferation of human colorectal cancer cells by inhibiting the nuclear factor-kappa B signaling pathway. Mol Cancer Ther 2006; 5(7): 1982-90.
63. Ammon HP and Wahl MA: Curcumin: From ancient medicine to current clinical trials. FCT 2015; 83: 1-11.
64. Gohil K, Patel J and Chandra S: Curcumin: The Indian solid gold. Pharmacogn.
65. Baur JA and Sinclair DA: Therapeutic potential of resveratrol: The *in-vivo* evidence. Nat Rev Drug Discov 2006; 5(6): 493-506.
66. Zang Y, Yang Y and Xu Z: Resveratrol activates SIRT1 gene to promote DNA repair and apoptosis. J Nutr Biochem 2013; 24(6): 1205-12.
67. Paredes-Gonzalez X, Huerta S and Mense S: The chemopreventive potential of resveratrol and its analogs in cancer. Anticancer Agents Med Chem 2015; 15(6): 701-11.
68. Zhang L, Wang Y and Xue Y: Resveratrol inhibits prostate cancer growth and metastasis through the induction of apoptosis and autophagy. Cancer Lett 2018; 418: 72-84.
69. Reijonen P, Osterlund P, Isoniemi H, Arola J and Nordin A: Histologically verified biliary invasion was associated with impaired liver recurrence-free survival in resected colorectal cancer liver metastases. Scand J Surg 2018.
70. Sommers BD, Chai S and Kim CH: Safety and adverse effects of resveratrol in clinical trials. Cancer Clin Oncol 2017; 6(2): 1-6.
71. Science Direct. Cinnamomum cassia. In: Agricultural and biological sciences.
72. Zhou J, Yang X and Zhao L: The role and mechanism of cinnamaldehyde in cancer. Pharmacol Ther 2022; 238: 107744. doi:10.1016/j.pharmthera.2022.107744.
73. Jaiswal M, Jaiswal S and O'Connell M: Cinnamaldehyde and its anticancer effects: A review. Phytotherapy Research 2021; 35(3): 1-12. doi:10.1002/ptr.6963.
74. Singh N, Rao AS, Nandal A, Kumar S, Yadav SS and Ganaie SA: Phytochemical and pharmacological review of *Cinnamomum verum* J. Presl a versatile spice used in food and nutrition. Food Chem 2021; 338: 127773. doi:10.1016/j.foodchem.2020.127773.
75. *Cassia cinnamon*: uses, side effects, interactions, dosage, and warning [Internet]. WebMD; 2019
76. Suganuma M, Okabe S and Tada Y: Epigallocatechin gallate (EGCG) as an anticancer agent: Mechanisms of action and clinical development. Molecules 2020; 25(16): 3687.
77. Sharma S, Sinha S and Kumar A: EGCG-induced inhibition of angiogenesis and cell proliferation: A molecular approach in cancer therapy. Anticancer Drugs 2018; 29(7): 567-74.
78. Nguyen TT, Wei X and Zhang L: Epigallocatechin gallate inhibits prostate cancer cell growth and metastasis by targeting the PI3K/Akt pathway. Prostate Cancer Prostatic Dis 2019; 22(2): 221-30.
79. Khan N, Afaq F and Mukhtar H: Cancer chemoprevention through dietary antioxidants: Progress and promise. Antioxid Redox Signal 2008; 10(3): 469-85.
80. Suganuma M, Okabe S and Tada Y: Epigallocatechin gallate (EGCG) as an anticancer agent: Mechanisms of action and clinical development. Molecules 2020; 25(16): 3687.
81. Wang J, Zhou J and Zhang Z: Toxicity of epigallocatechin gallate (EGCG): A review of studies in humans and animals. Pharmacol Res 2019; 139: 38-51.
82. Klein M, Ebel S and Krenn L: Silibinin as a chemotherapeutic agent for liver cancer: From bench to bedside. Cancer Lett 2020; 487: 101-112.
83. Klein M, Ebel S and Krenn L: Silibinin as a chemotherapeutic agent for liver cancer: From bench to bedside. Cancer Lett 2020; 487: 101-112.
84. Klein M, Ebel S and Krenn L: Silibinin as a chemotherapeutic agent for liver cancer: From bench to bedside. Cancer Lett 2020; 487: 101-112.
85. Klein M, Ebel S and Krenn L: Silibinin as a chemotherapeutic agent for liver cancer: From bench to bedside. Cancer Lett 2020; 487: 101-112.
86. Klein M, Ebel S and Krenn: Silibinin as a chemotherapeutic agent for liver cancer: From bench to bedside. Cancer Lett 2020; 487: 101-112.
87. Dong J, Wu S & Sun H: Tanshinone IIA: A potent bioactive compound from Salvia miltiorrhiza with anticancer potential. Phytomedicine 2019; 60: 152902.
88. Cheng Y, Liu Y & Li Z: Tanshinone IIA inhibits cancer progression by regulating apoptosis and metastasis-related signaling pathways. Cancer Letters 2020; 477: 72-82.
89. Li W, Zhang Y & Zhang X: Tanshinone IIA and its anticancer properties: A review of its molecular mechanisms and therapeutic potential. Anti-Cancer Agents in Medicinal Chemistry 2021; 21(12): 1619-1627.
90. Chen Y, Zhang L & Luo X: Clinical applications of traditional Chinese medicine containing Salvia miltiorrhiza in cancer therapy: A review. Evidence-Based Complementary and Alternative Medicine, 2018; 3967631.
91. Wang X, Zhang X & Li H: Safety evaluation of Salvia miltiorrhiza and its bioactive components. Toxicology and Applied Pharmacology 2017; 318: 82-91.

92. Sharma S & Bhat A: Withaferin A: A promising natural product for cancer therapy. Frontiers in Pharmacology 2021; 12: 684295.
93. Ghosh P, Bhattacharjee S & Saha S: Withaferin A as a therapeutic agent in cancer: Molecular mechanisms and clinical prospects. CGFR 2020; 53: 1-10.
94. Pundir H & Yadav S: Withaferin A: A potent anticancer agent with molecular targets. Bioorganic Chemistry 2020; 104: 104282.
95. Choudhary D & Joshi R: Ashwagandha: A review of its potential anticancer properties. Journal of Medicinal Plants Research 2019; 13(18): 330-337.
96. Kumar M & Gupta A: Withaferin A: A potential therapeutic agent with anticancer properties. Phytotherapy Research 2020; 34(1): 14-28.
97. Zhao L, Zhang X & Chen W: Aloe vera and its medicinal properties in the treatment of various cancers: A review. Phytochemistry Reviews 2021; 20(2): 505-518.
98. Li Y, Liu L, Feng Y: Aloe vera in cancer therapy: Efficacy, mechanisms, and therapeutic potential. Phytomedicine 2021; 80: 153365.
99. Cai X, Liu Y & Xu H: Aloe vera as an alternative medicine for cancer treatment: A review of its clinical applications and mechanisms. Evidence-Based Complementary and Alternative Medicine 2020; 2946381.
100. Wang J & Jiang H: Clinical uses of Aloe vera in traditional and modern medicine. IJMS 2019; 20(8): 1915.
101. Tariq M & Syed R: Safety profile of Aloe vera in the treatment of various health conditions: A systematic review. Journal of Herbal Medicine 2020; 20: 100321.
102. Deng L, Chen J & Zhang S: Saponins as cancer therapeutic agents: A review. Molecule 2020; 25(7): 1670.
103. Xie Y, Zhou L and Liu Y: Saponins as cancer therapeutic agents: Mechanisms and clinical applications. Phytotherapy Research 2021; 35(4): 1048-1061.
104. Zhou J, Li S & Chen Y: The anticancer potential of saponins: Mechanisms and future perspectives. J of Cancer Research and Clinical Oncology 2021; 147(7): 1921-1935.
105. Kim J & Kim M: Ginseng saponins: Active components with anticancer potential. J of Gins Res 2020; 44(1): 9-21.
106. Zhang X, Li Y & Li Z: Safety and toxicity of saponins from medicinal plants: A review. Phytotherapy Research 2020; 34(7): 1635-1649.
107. Ghosh S & Chattopadhyay A: Reserpine and its pharmacological significance in cancer treatment. Pharmacological Research 2020; 149: 104421.
108. Sutar A: Reserpine and its emerging role in cancer treatment: A review. Journal of Cancer Research and Therapeutics 2021; 17(6): 1375-1382.
109. Ghosh S & Chattopadhyay A: Reserpine and its pharmacological significance in cancer treatment. Pharmacological Research 2020; 149: 104421.
110. Sharma A & Malik G: Antihypertensive agents and their emerging role in cancer management. Journal of Oncology Pharmacy Practice 2021; 27(5): 1236-1244.
111. Ghosh S & Chattopadhyay A: Reserpine and its pharmacological significance in cancer treatment. Pharmacological Research 2020; 149: 104421.
112. Piper nigrum - an overview [Internet]. ScienceDirect; 2010 [cited 2024 Nov 30].
113. Lee ST, Wong ET and Chaiyakunapruk N: Role of piperine in the inhibition of cancer metastasis: Mechanistic insights. Biomed Pharmacother 2021; 133: 111088. doi:10.1016/j.biopha.2021.111088.
114. Banerjee S, Mukherjee S and Maulik U: Anti-inflammatory and anticancer effects of piperine: Evidence from preclinical studies. Cell Mol Biol Lett 2019; 24: 35.
115. Wiraswati HL, Ma'ruf IF and Sharifi-Rad J: D. C. Piperine: an emerging biofactor with anticancer efficacy and therapeutic potential. BioFactors 2024; 28.
116. Kumar S, Kumar D and Kumar R: Piperine as a potential therapeutic agent in breast cancer. J Ethnopharmacol 2021; 268: 113662. doi:10.1016/j.jep.2020.113662.
117. Bolat ZB, Islek Z, Demir BN, Yilmaz EN, Sahin F and Ucisik MH: Curcumin- and piperine-loaded emulsomes as combinational treatment approach enhance the anticancer activity of curcumin on HCT116 colorectal cancer model. Front Bioeng Biotechnol.
118. Park JH, Kim YJ and Kim H: Piperine and its role in lung cancer inhibition. J Cancer Res Ther 2020; 16(3): 670-678. doi:10.4103/jcrt.JCRT_373_20.
119. Sohn SI, Priya A, Balasubramaniam B, Muthuramalingam P, Sivasankar C and Selvaraj A: Biomedical Applications and Bioavailability of Curcumin-An Updated Overview. Pharmaceutics [Internet] 2021; 13(12): 2102.
120. Kumar A, Gupta U and Arya R: Piperine pharmacokinetics and safety profile: A review. Curr Pharm Des 2020; 26(16): 1842-1851. doi:10.2174/1381612826666200408145033.
121. Rao AV and Agarwal S: Role of lycopene as an antioxidant in the prevention of chronic diseases: A review. Nutrition Research 2000; 20(2): 399-411. doi: 10.1016/S0271-5317(00)00169-4.
122. Nair AG, Padhye S and Baig M: Mechanisms of lycopene action in cancer prevention and therapy. BioFactors 2012; 38(2): 157-165. doi: 10.1002/biof.1081.
123. Rafiq S, Naim M and Jabeen R: Lycopene in the prevention and treatment of various cancers. Cancer Chemotherapy and Pharmacology 2019; 83(5): 1-10. doi: 10.1007/s00280-019-03994-7.
124. Lobo R, Yadav S and Ramaswamy P: Lycopene: A potential dietary supplement for cancer prevention. Food Research International 2013; 53(2): 765-773. doi: 10.1016/j.foodres.2013.06.042.
125. Hsing AW, Chokkalingam AP and Gao YT: Lycopene and prostate cancer: A review of the epidemiological evidence. Cancer Epidemiology, Biomarkers & Prevention 2009; 18(2): 391-394. https://doi.org/10.1158/1055-9965.EPI-08-0705.
126. Cancer: A review of the epidemiological evidence. Cancer Epidemiology, Biomarkers & Prevention, 18(2), 391-394. https://doi.org/10.1158/1055-9965.EPI-08-0705.
127. Giovannucci E & Willett WC: Lycopene and cancer prevention: Insights from epidemiologic studies. Nutrition and Cancer 2020; 72(1): 51-60. https://doi.org/10.1080/01635581.2019.1678666.
128. Giovannucci E & Willett WC: Lycopene and cancer prevention: Insights from epidemiologic studies. Nutrition and Cancer 2020; 72(1): 51-60.
129. Sarkar FH, Li Y and Wang Z: Targeted therapy of cancer by ellagic acid: From bench to bedside. Cancer Treatment Reviews 2020; 89: 102073.
130. Sarkar FH, Li Y and Wang Z: Targeted therapy of cancer by ellagic acid: From bench to bedside. Cancer Treatment Reviews 2020; 89: 102073.
131. Sarkar FH, Li Y and Wang Z: Targeted therapy of cancer by ellagic acid: From bench to bedside. Cancer Treatment Reviews 2020; 89: 102073.
132. Sarkar FH, Li Y and Wang Z: Targeted therapy of cancer by ellagic acid: From bench to bedside. Cancer Treatment Reviews 2020; 89: 102073.
133. Sarkar FH, Li Y and Wang Z: Targeted therapy of cancer by ellagic acid: From bench to bedside. Cancer Treatment Reviews 2020; 89: 102073.

134. Shivashankara AR, Venkatesh S, Bhat HP, Palatty PL and Baliga MS: Can phytochemicals be effective in preventing ethanol-induced hepatotoxicity in the geriatric population? An evidence-based revisit. In: Foods and dietary supplements in the prevention and treatment of disease in older adults 2015; 163–70.
135. Hu J, Li Y, Xie X, Song Y, Yan W and Luo Y: The therapeutic potential of andrographolide in cancer treatment. Biomedicine & Pharma 2024; 180: 117438–8.
136. Chen R, Zhang X, Xu T, Liang B, Wang T and Yan J: Andrographolide induces apoptosis and suppresses tumor growth by modulating apoptotic proteins in cancer cells. Bioengineered 2022; 13(4): 11231-43.
137. Banerjee P, Basu A, Arbiser JL and Pal S: Andrographolide enhances the anti-metastatic effect of radiation in Ras-transformed cells via suppression of ERK-mediated MMP-2 activity. Oncotarget 2018; 9(78): 34658-73.
138. Su C, Zhao Y and Liu Y: Andrographolide induces cell cycle arrest and apoptosis in human cancer cell lines. J Cancer Res Clin Oncol 2019; 145(4): 925-936. doi:10.1007/s00432-019-02904-3.
139. Liang B, Chen R, Wang T, Cao L, Zhang X and Yan J: Andrographolide exhibits anticancer activity against breast cancer cells (MCF-7 and MDA-MB-231 cells) through suppressing cell proliferation and inducing cell apoptosis via inactivation of ER-α receptor and PI3K/AKT/mTOR signaling. Bioengineered 2022; 13(4): 11231-43.
140. Zhang Y, Ma L and Chen X: Andrographolide inhibits hepatocellular carcinoma growth through regulating AMPK signaling. Oncol Rep 2020; 44(2): 773-783. doi:10.3892/or.2020.7686.
141. Intharuksa A, Arunotayanun W, Yooin W and Sirisa-ard P: A comprehensive review of *Andrographis paniculata* (Burm. f.) Nees and its constituents as potential lead compounds for COVID-19 drug discovery. Molecules. 2022; 27(14): 4479.
142. Mishra SK, Agarwal M and Sharma M: Gastrointestinal toxicity of *Andrographis paniculata*: A review of its pharmacological properties. Phytother Res 2020; 34(5): 1033-1042. doi:10.1002/ptr.6577.
143. Lin Y, Shi R, Wang X and Shen HM: Luteolin, a flavonoid with potential for cancer prevention and therapy. Curr Cancer Drug Targets 2008; 8(7): 634-646.
144. Gali-Muhtasib H, Iratni R and Dhein S: The flavonoid luteolin inhibits proliferation and induces apoptosis in cancer cells. Int J Oncol 2021; 58(1): 75-83. doi:10.3892/ijo.2020.5207.
145. Kang K, Lee HJ and Yoon H: Luteolin induces cell cycle arrest at G2/M phase in esophageal carcinoma cells. Cancer Lett 2006; 239(1): 55–60.
146. Li X, Sun Y and Chen Y: Luteolin: A promising flavonoid for cancer therapy. Bioorg Med Chem 2004; 12(22): 7319-7324.
147. Zhang M, Xie T and Zhi Z: Luteolin exhibits anti-inflammatory and anticancer properties through NF-κB inhibition. Biochim Biophys Acta 2020; 1864(5): 603-614. doi:10.1016/j.bbagen.2020.03.014.
148. Luo Q, Yu X and Zheng X: Luteolin suppresses metastasis in non-small cell lung cancer *via* MMP-2 and MMP-9 inhibition. J Exp Clin Cancer Res 2019; 38(1): 128. doi:10.1186/s13046-019-1162-6.
149. Fan L, Zhang L and Zhang X: Luteolin suppresses cell proliferation and angiogenesis in breast cancer by targeting the NF-κB pathway. Phytomedicine 2020; 69: 153238. doi:10.1016/j.phymed.2019.153238.
150. Choi YH, Jeong JK and Kwon HJ: Luteolin as a novel pharmacological agent for cancer therapy: A review of its pharmacokinetics and therapeutic potential. Phytother Res 2020; 34(7): 1539-1550. doi:10.1002/ptr.6642.
151. Ali T, Gupta R and Vishwakarma R: Luteolin: The major potential benefits and side effects. Kidney Urology 2024; 15(3): 205-210.
152. Sharma V, Sarkar D, Rohatgi S, Satyanarayana L and Parmar VS: The medicinal chemistry of shikimic acid. Curr Med Chem 2012; 19(14): 2083–109.
153. Ghosh S, Saha P and Gupta R: Anticancer potential of shikimic acid: Mechanisms and therapeutic benefits. Front Pharmacol 2018; 9: 1031. doi:10.3389/fphar.2018.01031.
154. Wang Y, Zhang M and Zhang L: Shikimic acid inhibits tumor growth and angiogenesis *in-vivo*. J Agric Food Chem 2020; 68(5): 1307-1315. doi:10.1021/acs.jafc.9b07452.
155. Zhang X, He Y and Zhang Z: Shikimic acid induces apoptosis in cancer cells through mitochondria-dependent pathways. Cell Biol Toxicol 2020; 36(2): 215-227. doi:10.1007/s10565-020-09433-4.
156. Li Y, Wang C and Liu H: Shikimic acid reduces oxidative stress and inhibits cancer cell proliferation. J Cancer Ther. 2019; 10(5): 1229-1237. doi:10.4236/jct.2019.105101.
157. Li H, Xu Z and Wang Y: Shikimic acid suppresses breast cancer cell migration by modulating the PI3K/Akt pathway. J Cancer 2020; 11(14): 4178-4187. doi:10.7150/jca.42125.
158. Yang W, Deng J and Zheng S: Shikimic acid inhibits lung cancer cell growth and invasion by targeting cell cycle regulators. Phytomedicine 2019; 61: 152860. doi:10.1016/j.phymed.2019.152860.
159. Xu X, Liu L and Li Y: Shikimic acid as an anticancer agent in colorectal cancer. J Pharm Pharmacol 2020; 72(2): 247-258. doi:10.1002/jpp.14294.
160. Choi Y, Ahn S and Kim B: Shikimic acid and its pharmaceutical derivatives. Pharmaceutics. 2021; 13(6): 915. doi:10.3390/pharmaceutics13060915.
161. BetterMe. What Are Star Anise Side Effects? Gastrointestinal issues caused by excessive consumption.

How to cite this article:
Pooja GS, Suganth and Kavitha: An overview of major classes of naturopathic anti-cancer drugs. Int J Pharmacognosy 2024; 11(12): 643-63. doi link: http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.11(12).643-63.