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NATURAL PRODUCTS USED IN TRADITIONAL MANAGEMENT OF CANCER

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ABSTRACT: Cancer is the second leading cause of global death. Rapid progress in the phytochemical study of plants reveals their anticancer effects as a result plants are becoming an alternative to the current processes used. Common treatments such as radiotherapy and chemotherapy can cause various side effects including several adverse effects on healthy cells. Therefore, alternative and effective medications are required to combat this effect. Using plant-derived products over synthetic medicines has increased the importance of medicinal plants in the field of healthcare. Many plant-derived products can potentially treat cancer by inhibiting cancer activating enzymes, stimulating DNA repair mechanisms, inducing antioxidant action, and promoting protective enzyme production. In the present review, an effort has been made to provide concise information about the medicinal plants and phytoconstituents that have shown potent activity against various forms of cancer.

INTRODUCTION: Plants have been used as therapeutic agents that have helped humanity for thousands of years in traditional medical systems¹. A wide range of phytoconstituents found in medicinal plants is used in the development of drugs². Based on research dating back thousands of years, plants have the ability to treat various ailments³. To treat illness and advance a patient's health, the Plant extract is used as an herbal medicine⁴. One of the worst diseases, cancer, is brought on by uncontrollable cell proliferation⁵. Cancer is still regarded as the second most terrible cause of mortality globally^{6,7}. Cancer is the term used to describe the abnormal proliferation of cells and tissue that results when normal cells lose their regulatory mechanisms and halt apoptosis⁸.

Around one in five cancer deaths worldwide are caused by tobacco⁹. Obesity, nutrition, and physical inactivity are linked to 30-35 percent of cancer deaths¹⁰. Aflatoxin B1 causes liver cancer, eating betel nuts while chewing them promotes mouth cancer, and some specific foods are linked to certain types of cancers¹¹. Through their ability to promote cell proliferation, certain hormones are also significant contributors to the growth of cancer¹². The development of cancerous cells is significantly influenced by insulin-like growth factors and the proteins that bind to them¹³. Chemotherapy is most 2 of the 21 effective ways to treat cancer however, there are a number of negative side effects^{14,15}.

Alternative treatment approaches with no or few side effects are needed for the prevention and treatment of cancer due to the varied negative effects of radiotherapy and chemotherapy¹⁶. Recently, scientists from all over the world have concentrated their efforts on finding novel medications derived from unadulteratedly therapeutic plants and other natural sources¹⁷.

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Many natural substances that are Pharmacologically very powerful against the growth of cancer cells have been discovered recently. According to reports, eating a diet high in phytochemicals can lower the risk of developing cancer¹⁸. The many types of cancer have already been treated with a variety of herbs. In addition to containing a variety of bioactive substances, medicinal plants also exhibit a wide spectrum of biological activity, including anti-tumor. The anticancer characteristics of a number of therapeutic plants are employed to identify a potential molecule that can thwart the growth of cancer¹⁹. In the 1960s, when taxol, vinblastine, camptothecin, and vincristine were being researched as potential cancer medicines derived from therapeutic plants, podophyllotoxin was also identified²⁰. The potential involvement of medicinal herbs in the prevention of cancer cell proliferation has been demonstrated by *Annona muricata*, *Berberis aristata*, *Catharanthus roseus*, *Linum usitatissimum*, *Podophyllum hexandrum*, *Rubia cordifolia* etc. Consequently, this review offers a summary of several natural products, plants and the main bioactive substances they contain in traditional management of cancer.

***Amorphophallus campanulatus* (Hindi Name: Suran):** Elephant foot yam, also known as *Amorphophallus campanulatus*, is a perennial herb of the family Araceae. India is a country where this plant is grown. The corms have astringent, acrid, thermogenic, liver- tonic, reviving, and tonic properties. They are helpful in the treatment of tumors hemorrhoids, and inflammations²¹. The rhizome from it is used to make food. A rhizome is said to have antibacterial, antifungal, and cytotoxic properties²². It is used as an irritant externally to treat acute rheumatism²³. The *A. campanulatus* tuber has also been used traditionally to treat piles, tumors in the abdomen, and liver problems. Additionally, it has been noted that the corm exhibits cytotoxic, hepatoprotective, antioxidant, antibacterial, and antifungal properties²⁴.

***Artemisia vulgaris* (Hindi Name: Davana):** Tall perennial shrub *Artemisia vulgaris* L. is also known as "Fleabane" and grown throughout India, from steep sections of the Northern Himalayas to warm climate regions of South America. The plant contains fernenol, stigmasterol, B-sitosterol, alpha

amyrin, and its acetate, as well as crystalline pentacyclic alcohol²⁵. In Asian cooking, the plant is utilized as a culinary herb in the form of a vegetable or in soup in addition to its therapeutic benefits including its anti-inflammatory, anti-cancer, anti-oxidant and hypolipidemic capabilities²⁶. *Artemisia vulgaris* aqueous extract has been shown to have an anticancer effect against human breast carcinoma T47D cells, human prostate cancer PC-3 cells, human colon cancer RKO cells, Caucasian hepatocyte carcinoma (Hepa-2), human Caucasian larynx carcinoma (Hep-2) and human cancer cell lines, MCF7, A549, and HeLa²². In addition, APME (*Artemisia princeps* methanol extracts) induced P53 expression of HepG2 cells in a dose-dependent manner and played a role in the down-regulation of Bcl-2 and upregulation of Bax in both HepG2 and Hep3B cells²⁷. The proliferation of HL-60 cells was suppressed by oil extracted from buds (AVO-b) and leaves (AVO-l) has been reported. Extracted oil, interestingly, did not cause apoptosis in noncancerous cells, but it did in a number of cancer cell lines²⁸.

***Artemisia absinthium* L (Hindi Name: Afsantin):** Kashmir is home to the Asteraceae family species known as Artemisia, a pungent and bitter shrub²⁹. Research on breast cancer cells MCF-7 and three cancer cells HeLa, HT-29, and MCF7 have been reported. Many cancer cells, including MCF-7, are inhibited by quercetin, while many cancer cells, including MB-435, SKMEL-5, Du-145, MCF-7, and DLD, are inhibited by isorhamnetin. Additionally, one of the most significant artemisinin, artesunate, has anticancer effects on K569 (leukemia cancer). According to additional studies, the presence of the plant's alpha-, beta-, limonene-, and myrcene compounds may serve as inhibitors of the development of melanoma, hepatic, and breast cancer in humans. HT-29 cells (colon cancer) are inhibited by the alpha-pinene, beta-pinene and limonene present in methanol and ethanol extracts of this plant³⁰. AR methanolic extract showed cytotoxic activity on the human colon (DLD-1), endometrium (ECC-1) cancer cells and embryonic kidney (HEK-293) cells³¹. *A. absinthium* leaf extract and *C. paradisi* peel extract had cytotoxic effects on the Huh-7 cancer cell line. Plants are cytotoxic to malignant cell lines because they contain antioxidants that stop the proliferation of cancerous cells³².

Allium sativum L (Hindi Name: Lahsun): *Allium sativum* commonly known as "Garlic" and its organosulfur compounds reduce the risk of cancer in the breast, larynx, colon, skin, womb, gullet, bladder, and lung. Allicin, a significant phytoconstituent of *Allium sativum*, has been shown to have anticancer properties against breast and prostate cancer. This substance has anticancer properties and causes the planned death of cells. Human cancer cells are inhibited from proliferating by allicin. Another substance that inhibits leukemia cell growth and induces programmed cell death is ajoene³⁰. It has been reported that allicin-containing garlic juice has been used to prevent the spread of cancer in mice. Additionally, synthetic allicin inhibits the growth of cancer cells³³. Another study showed that *Allium sativum* bioactive extract caused a significant cytotoxicity effect on MCF-7 and MDA-MB-231 cell lines. Bioactive compounds are responsible for the plant's overall antitumoral and antimotility effects on MDA-MB-231 and MCF-7 human breast cancer cells³⁴. The strongest radical-scavenging activity was demonstrated by the two main components of aged garlic, S-allylcysteine, and S-allylmercapto-L-cysteine. Additionally, S-allylcysteine, can slow the development of chemically induced and transplantable tumors³⁵. Garlic extracts have been shown to promote ROS (Reactive Oxygen Species) dependent cell death in cancer cell lines, including human colon adenocarcinoma (Ht29), human leukemia (U937) and human colon cancer cell line (Colo 205), and mouse chronic myelocytic leukemia (32Dp210)³⁶.

Andrographis paniculate (Hindi Name: Kalamegh): It is a member of the Acanthaceae family and is frequently referred to as "Kalmegh" and "King of Bitters" in English. It can be found all over Sri Lanka and India³⁷. It is one of the classic herbs used in alternative medical practices and used to treat a variety of ailments and diseases, including cancer³⁸. Andrographolide, a diterpene that is white, crystalline in nature is the primary constituent of this plant. It exhibits a cytotoxic effect on colon cancer cells, P388 lymphocytic cells, and MCF-7 breast cancer cells (HCT-116). In the mouse myeloid leukemia M1 cell line, andrographolide promotes the growth and division of human peripheral blood lymphocytes while inhibiting the growth of the colon cancer cell line

(HT 29)³⁷. *In-vitro* proliferation of different tumor cell lines, representing various types of cancers inhibited when treated with Andrographolide has been reported³⁹. *A. paniculata* leaves extracts reported good anticancer properties against neuroblastoma (IMR-32) and human colon (HT-29) cancer cell line⁴⁰. The methanolic extract of leaves also has significant cytotoxic action against culture cells of human epidermoid carcinoma of the nasopharynx (KB) and lymphocytic leukemia (P388). According to recent studies, andrographolide treatment significantly increased the death of several cancer cells in people by increasing the production of the TNF- α (Tumor Necrotic Factor- α) generating ligand⁴¹. Through the activation of the p-38 MAPK signaling pathway, andrographolide can prevent cell migration in CCA (cholangiocarcinoma), cell line (HuCCA-1, K KU-100, K KU-M213, RMCCA-1), and cell line (K KU-100, K KU-M213)⁴².

Azadirachta indica (Hindi Name: Neem): It is a member of the Meliaceae family and is also referred to as "Neem" or "Indian liliac." Leukoderma, ulcers, tumors, and hemorrhoids can all be treated with the bark of this plant⁴³. Neem mostly contains limonoids including azadirachtin and nimbolide, which target various cell signaling pathways to cause tumor cells to undergo apoptosis. Neem extracts increase the effectiveness of several chemotherapeutic medications and make cancer cells more susceptible to immunotherapy and radiotherapy⁴⁴. By inducing apoptosis, *Azadirachta indica* ethanol extract kills prostate cancer cells³⁷. Neem leaf extracts, leaf glycoproteins and liminoids have been reported for their anticancer properties in OSCC (Oral Squamous Cell Carcinoma)⁴⁵.

Apis mellifera (Hindi Name: Sahad Mudhumakhi): The honey bee, from which honey is made, is known by its scientific name, *Apis mellifera*. In the Indian medical system, honey is used to burns, ulcerations, and skin wounds to speed recovery. According to studies, a protein from the *Apis mellifera* plant promotes the proliferation of rat hepatocytes grown in primary culture and inhibits apoptosis.

Additionally, it has demonstrated cytotoxicity in HL-60 cells and regular human lymphocytes. A

significant decrease in wound cancer tumors were observed in the groups of mice that were treated with surgical wounds coated with honey pre and postoperatively⁴⁶. Melittin (MEL) and phospholipase A2 (PLA2), the two main biopeptides of *Apis mellifera* are thought to be the biomolecules responsible for the anticancer activity. The *A. mellifera* venom had a strong cytotoxic effect, and MEL or PLA2 by themselves had a less potent effect. Surprisingly, the cytotoxic effect of MEL and PLA2 was significantly enhanced when they were combined, indicating a synergistic activity on HCT116 cells⁴⁷. A resinous compound gathered from many plant sources known as propolis has a variety of therapeutic benefits, including anti-cancer actions. Study on HNSCC (Head and Neck Squamous Carcinoma) cell lines reported that EAEP (Ethyl Acetate Extract of Propolis) showed cytotoxic action and promoted apoptosis by inhibiting MMP-2 and MMP-9 activity in HNSCC cell lines, and has anti-invasion potential⁴⁸.

***Bidens pilosa* (Hindi Name: Kumur):** Folk medicine made from *Bidens Pilosa*, Family: Asteraceae, contains polyacetylenes, flavonoids, terpenoids, phenylpropanoids, and other chemicals. A putative marker molecule, phenyl-1,3,5-heptatriyne, was identified. In the erythrocyte osmotic fragility assay, this marker molecule revealed the toxicity profile of healthy red blood cells together with other extracts. The anticancer activity of *Bidens pilosa* hexane extracts was shown to have the greatest activity⁴⁹. *In-vitro* testing on Hela cells revealed that the extract from the complete *Bidens pilosa* plant was significantly more cytotoxic than the methanolic extract⁴⁶. Different extracts of *B. pilosa* leaf exhibited potential *in-vitro* anticancer activity⁵⁰.

***Curcuma longa* (Hindi Name: Haldi):** A member of the Zingiberaceae family, turmeric is a plant with the scientific name *Curcuma longa*. Typically, this perennial plant needs a moist, wet habitat. Turmeric is primarily found in hot regions of Asia, including southern China, India, Pakistan, and Indonesia. The rhizome, or underground stem, is called turmeric. According to research on the cytotoxic effects of turmeric on liver cancer cells (Hep-2), the cytotoxicity caused by curcumin, a key component of turmeric, is the treatment of

primary ovarian cancer. Curcumin has been demonstrated to have anticancer properties against malignancies such as leukemia, lymphoma, digestive, urinary, reproductive, breast, uterine, ovary, lung, melanoma, colon, and brain tumors. One study showed that curcumin promotes apoptosis and inhibits the proliferation of cancer³⁰. Curcumin has drawn a lot of interest as an antioxidant, anti-inflammatory and anticancer agent over the past 20 years⁵¹. Another study showed that the turmeric extract inhibited the cell growth in Chinese Hamster Ovary (CHO) cells and was cytotoxic to lymphocytes and Dalton's lymphoma cells⁵². It is reported that curcumin has anti-inflammatory, antiplatelet, antioxidant, hepatoprotective and antitumor activities, particularly against cancers of the liver, skin, pancreas, prostate, ovary, lung and head and neck⁵³.

***Ferulaassa-foetida* (Hindi Name: Hing):** Iran is home to the *Ferulaassa foetida* plant. The perennial plant, Asafoetida has sturdy, thick, and fibrous stems, a resin-producing portion of this plant that is also used to make gum. Asafoetida ethanol extract has been shown to be cytotoxic to liver cancer cells (category HepG2). Additionally, chewing gum made from this plant greatly lowers the risk of developing colon cancer. It has demonstrated a mildly cytotoxic effect on cells, including ovarian carcinoma (CH1), and lung cancer (A549) and melanoma (SK-MEL-28)³⁰. Another study reported that the seed oil of the plant has a strong anticancer effect against AGS (Adenocarcinoma gastric) cell line⁵⁴. Asafoetida and its essential oil and ferulic acid have an inhibitory effect on the growth of breast cancer cell line⁵⁵.

***Glycyrrhiza glabra* (Hindi Name: Mulethi):** The wild plant, *Glycyrrhiza glabra* belonging to the family Glycyrrhiza is found in southern Europe, North Africa, and temperate Asia. Its stems and roots are medicinal. The root extract causes morphological abnormalities and lowers the viability of the mammary cell line 4T1. The primary component of root extract, glycyrrhizin, is a triterpene glycoside that functions as an anti-proliferative agent against tumor cells, particularly breast cancer cell lines (MCF- 7) and HEP-2, and does so by inducing apoptosis. Inducing apoptosis in HT-29 cells, *Glycyrrhiza glabra* root extract is

effective in the treatment of colon cancer³⁰. One study showed an ethanol extract of *Glycyrrhiza glabra* has induced apoptosis in HT-29 (Colorectal cancer cell line) cells and confirmed its anticancer property⁵⁶. Licorice is one of the most commonly used herbal drugs in Traditional Chinese Medicine for the treatment of liver diseases⁵⁷ and its ethanolic extract has been proven effective in treating malignancies like breast, colon and liver⁵⁸.

Lagenaria siceraria Standley (Hindi Name: Kadavilauki): A kind of Cucurbit with yellow skin that is less palatable is the bottle gourd scientifically known as *Lagenaria siceraria* belongs to the Cucurbitaceae family. This plant significantly inhibits human lung cancer cell line A549. Additionally proven is the methanol extract's antitumor action on this plant's aerial parts. Another study established the effects of a water-soluble polysaccharide extracted from this plant on cancer of human breast cell lines (MCF7). The fruit of this plant contains cucurbitacin, beta-carotene, vitamin B group, saponins, and vitamin C. Cucurbitacin is a 4-ring terpene with cytotoxic properties³⁰. Due to its cytotoxicity and antioxidant characteristics, *L. siceraria* may have strong anticancer⁵⁹ and hydroalcoholic extract of *Lagenaria siceraria* caused a significant decrease in proliferation of breast cancer cells and reported anti-tumor activity⁶⁰. n-Butanolextract from fruits powder plant shows promising anticancer activity⁶¹. *Lagenaria* contains cucurbitacin, lagenin and mineral substances which have been utilized as an anti-oxidant, cardiogenic, liver tonic, anti-inflammatory, diuretic, antitumor, anti-HIV, and antiproliferative agent⁶².

Medicago sativa L (Hindi Name: Lusan ghas): The scientific name for alfalfa is *Medicago sativa* L. This plant is typically found throughout most of the world and has been used in traditional medicine to treat a variety of diseases. The plant's phytoestrogens and potent estrogenic action are helpful in treating malignancies that are hormone-dependent. This plant alkaloid is thought to have significant therapeutic properties, including anticancer effects³⁰. Alfalfa seed contains L-canavanine, a potentially toxic antimetabolite of L-arginine that exhibits demonstrable anti-cancer efficacy against a variety of animal-bearing carcinomas and cancer cell lines⁶³. Three terpene derivatives and five flavonoids were discovered

after the fractionation of toluene extract (To-1), the most potent extract found in leaf crude extract. The mouse leukemia P388 cell line and its doxorubicin-resistant counterpart (P388/DOX) cells demonstrated cytotoxic effects of compounds, including (-)-medicarpin, (-)-melilotocarpan E, millepurpan, tricin and Chrysoeriol⁶⁴.

Mentha pulegium (Hindi Name: Vilayati Pudina): The Labiaceae family includes this plant with the common name European pennyroyal and the scientific name *Mentha pulegium*. Leukemia cells reportedly experienced cytotoxicity from the plant before flowering. Pennyroyal contains organic components such as polygon, mentone, piperitone, limonene, isomenthone, and octan-3-ol; in some research, the flavonoids' ability to suppress the growth of cancer cells by inducing apoptosis is mentioned³⁰. The total ethanolic extract of the aerial parts of *Mentha pulegium* L. reported anticancer activity on two cell lines including Human lung carcinoma cells (A549) and human breast cancer (MCF7)⁶⁵.

Nigella sativa L. (Hindi Name: Kalajira): *Nigella sativa*, sometimes known as "black caraway," "black cumin," or "black seed," is a member of the Ranunculaceae family. It is well distributed in Central Asia. Thymoquinone, a secondary metabolite of this plant, has cytotoxic properties because it causes tumor cells to die by inhibiting the signaling pathways for NF-KB, Akt activation, and extracellular signal-regulated kinase, as well as tumor angiogenesis⁶⁶. The crude oil and thymoquinone (TQ) extracted from its seeds and oil are effective against many diseases like cancer, cardiovascular complications, diabetes, asthma, kidney disease *etc*⁶⁷. One more study reported that the seed essential oil and ethyl acetate extracts were more cytotoxic against the P815 cell line than the butanol seed extract. Interestingly, the administration of the essential oil into the tumor site inhibited the incidence of liver metastasis development and improved mouse survival⁶⁸.

Oroxylum indicum (Hindi Name: Sonapatha): The bark of the medicinal plant *O. indicum*, also known as the Indian trumpet tree, has the ability to heal a variety of ailments, including biliousness, fevers, intestinal worms, leucoderma, inflammation, diarrhea, dysentery, and diaphoresis.

Previous studies on the cytotoxicity of *O. indicum* methanol and aqueous extracts in MDA-MB-435S and Hep3B cell lines have been reported. Additionally, it was claimed that *O. indicum* bark extracts have anti-proliferative effects on human breast cancer cells. With regards to estrogen receptor-negative breast cancer, the stem bark extract of *O. indicum* showed significant cytotoxicity, the capacity to induce apoptosis, and specific anti-metastatic potentials. Effective anticancer activity can be found in baicalein, a naturally occurring flavonoid component derived from *O. indicum*⁶⁹. The methanol extract of *Oroxylum indicum* has an anti-proliferative activity and proapoptotic potential for HPV-positive cervical cancer cells⁷⁰. The primary phenolic compounds found in this species, including baicalein, oroxylin A and chrysin, have demonstrated medicinal potential in a number of fields, including anticancer, anti-inflammatory, and antiviral⁷¹. One study was done to determine how four flavonoids furin inhibitory flavonoid compounds baicalein, chrysin, oroxylin A, and its glycoside derived from OI affected CT-26 cell proliferation and migration (anti-tumorigenic activity). Baicalein had the strongest inhibitory effect on migration and proliferation in the examined tumor cell line, according to the data⁷².

***Phyllanthus emblica* (Hindi Name: Amlika):** *Phyllanthus emblica* belongs to family Euphorbiaceae and is known to exhibit various pharmacological properties. One study showed that *Phyllanthus emblica* aqueous extract has antimetastatic potential due to reducing cell proliferation, migration, invasion, and adhesion in both doses- and time-dependent manners and its cytotoxic to human fibrosarcoma cells (HT1080)⁷³. Strong anticancer activities are seen in the fruit extract of the *Phyllanthus emblica* tree, sometimes known as Indian Gooseberries⁷⁴. *P. emblica* manifests its anticancer activities by inhibiting AP-1 and targets the transcription of viral oncogenes responsible for the onset and progression of cervical cancer, suggesting the potential benefit of this compound in the treatment of cervical cancers caused by HPV⁷⁵. The fruit of *Phyllanthus emblica* is rich in vitamin C, flavonoids like quercetin and rutin, and polyphenols like tannins, gallic acid and ellagic acid. According to research reports, amla is expected to have strong neuroprotective,

cardioprotective, gastroprotective, nephroprotective and chemoprotective properties⁷⁶.

***Panax ginseng* (Hindi Name: Indian Ginseng):** Ginsenoside Rp1 from *P. ginseng* (Araliaceae) inhibited insulin-like growth factor 1 receptor and thereby prevented human breast cancer cells from multiplying as well as disrupted the anchorage of cells colonies. Additionally, this bioactive substance caused cell cycle arrest and inhibited cell proliferation by inducing apoptosis. Additionally, it has been shown that *P. ginseng*'s roots and rhizomes prevent the growth of the MCF-7 breast cancer cell line⁷⁷. The main bioactive component of ginseng is ginsenosides, which have gathered attention in the treatment of fatal diseases such as cancer⁷⁸. Another study reported that *in vitro* and *in vivo* animal studies have enhanced the antitumor effect when ginseng is used in combination with some anticancer drugs⁷⁹. Several pre-clinical and clinical studies have reported the anticancer potential of *Panax ginseng*, a widely used traditional Chinese medicine⁸⁰.

***Rheum officinale* (Hindi Name: Atis):** In traditional Chinese and Tiberan medicine, the roots of *Rheum officinale* (Chinese rhubarb) have been employed. It is mostly spread to Europe, Russia, and India. According to the literature, it was utilized to treat the tumor in cases of hepatocarcinoma. *R. officinale* inhibits the proliferation of human lung adenocarcinoma A549 and breast cancer MCF-7 cells. Gemcitabine and emodin, an anthraquinone derivative from *R. officinale*, is used to effectively reduce the formation of tumors in mice that had pancreatic tumor cells implanted into them. This treatment pattern increases apoptosis and destruction in mitochondria. Additionally, it decreased the phosphorylated-Akt (p-Akt) level, NF- κ B activation, and Bcl-2/Bax ratio enhanced caspase-9 and -3 activations, and Cytochrome C (Cyt C) release occurred in combination therapy²². This was claimed that the water extract of Da Huang exerts potential anticancer activity through growth inhibition and apoptosis on MCF-7 and A549 cell lines⁸¹. Genus *Rheum* is medicinally important as it has hepatoprotective, spasmolytic, anticholesterolaemic, antitumor, antiseptic, antifungal, antimicrobial, anti-Parkinson's, anti-proliferative, immuno-enhancing, antiviral and

antioxidant properties⁸². Chrysophanol, emodin, aloe-emodin, fission and rhein are the primary aglycones of rhubarb anthraquinones. Emodin was discovered to suppress cell growth, trigger apoptosis and stop metastases. The cytotoxic effect of emodin and aloe-emodin against oral squamous cell carcinoma and salivary gland cancer is very high. Rhein prevents malignant cells from absorbing glucose and causes them to die. As opposed to aglycons, anthraquinone glycosides have a modest cytotoxic effect⁸³.

***Swertia chirayta* (Hindi Name: Chirayata):**

Swertia chirayita (Gentianaceae) is found and grows well in the temperate climate of the Himalayas and in the hills of Meghalaya. It has diverse therapeutic values and is extensively used as crude medicine. The plant is bitter, equally refrigerant, and thermogenic⁸⁴. According to reports, *Swertia chirata* whole plant aqueous extract inhibited the growth of T47D cells, which are human breast cancer cells. Another study found that *S. chirata* suppressed the growth of human prostate cancer PC-3 cells and colon cancer RKO cells²². *S. chirata* effects on apoptosis and cell proliferation in mice skin exposed to DMBA (Dimethyl benz(a) anthracene) were also investigated. The Amarogentin-rich crude and purified extracts both markedly reduced cell growth and triggered apoptosis. The finding points to *Swertia chirata* potential as a chemopreventive⁸⁵. It showed that both the leaves and the stem's methanol extracts had anticancer activity on the HCT 116 cell lines with the leaves extract having stronger anticancer activity than the stem. Higher amounts of the stem were found to have anticancer action, however, Calu 6 cell line remained unaffected⁸⁶.

Phytochemicals are thought to be abundant in herbal plants. Swertiamarin, Amarogentin, Swechirin, Mangiferin, Sweroside, Gentianine, Amaroswerin, Oleanolic acid, Swertanoone, and Ursolic acid are the principal chemical components⁸⁷. The plant *Swertia chirata* is a useful botanical plant. It helps treat a number of illnesses, including bronchial asthma, liver disorders, fever, anemia, diarrhea and stomach disorders. Numerous biological actions, including those that are antibacterial, antioxidant, anticancer, hepatoprotective, anthelmintic, anti-glycemic,

antihepatotoxic, and hypotensive, are also demonstrated by it⁸⁸. The primary bioactive components of *Swertia* are xanthenes; nevertheless, this species also contains active flavonoids, iridoid glycosides, and triterpenoids as secondary metabolites. The biological activity of these secondary metabolites, such as hepatoprotective, antihepatotoxic, antimicrobial, anti-inflammatory, anticarcinogenic, antileprosy, hypoglycemic, antimalarial, antioxidant, anticholinergic, CNS depressing and mutagenicity, had significant effects⁸⁹.

***Taraxacum officinale* (Hindi Name: Dudhal):** In Indian, Arabian, and Native American traditional medicine, plants of the genus *Taraxacum*, also known as dandelions, have a history of use to cure a range of ailments, including cancer. According to one study, dandelion flower (DFE) and root (DRE) aqueous extracts had no influence on the proliferation of each cell line, while the crude extract of the dandelion leaf (DLE) reduced the growth of MCF-7/AZ breast cancer cells. Additionally, it was discovered that DRE prevented the invasion of collagen type I by MCF-7/AZ breast cancer cells while DLE prevented the invasion of LNCaP prostate cancer cells⁹⁰. The ethyl acetate, butanol, methanol and cold-water extracts of the plant had significantly higher radical scavenging (%) and total phenolic contents. The ethyl acetate extract was potentially very toxic against human mouth epidermal carcinoma (KB) than all other extracts. *Taraxacum officinale* induces cytotoxicity through an increased amount of TNF- α (tumor necrosis factor- α) and IL-1 α (interleukin-1- α) secretion in Hep G2 cells⁹¹.

Taraxacum inhibited invasion and migration as well as caused apoptosis and loss of mitochondrial integrity in neuroblastoma cell lines. Extracts of *taraxacum* and mistletoe showed synergistic effects. This study suggests that *taraxacum* may be used as an adjuvant in pediatric oncology⁹². The potential for dandelion extracts to treat breast tumors is great. Dandelion extracts have a significant potential for use as anti-cancer drugs, and their effectiveness in methanol extract (combined with dandelion extract) was superior to that of ethanol extract⁹³.

In the study, the antiproliferative activity of methanolic extracts of dandelion root (MEDr) on cell viability of HepG2, MCF7, HCT116, and normal Hs27 was investigated and observed that MEDr drastically decreased the growth of the HepG2 cell line, while the effect on MCF7 and HCT116 cell lines was less pronounced and no effect has been observed in Hs27 cell lines⁹⁴.

***Urtica dioica* L (Hindi Name: Kandari):** Nettle is a green, herbaceous perennial with branching legs (scientific name: *Urtica dioica*). Prostate cancer cells have shown a cell growth inhibitory impact from plant aqueous and ethanol extracts (LNCaP and as hPCs). The anticancer properties of this herb against esophageal cancer have also been mentioned in a report. Plant chemicals that include the antioxidant phenol may play a significant role in cancer prevention. Nettle root extract has been found in a study to have an antiproliferative effect on human prostate cancer cells³⁰. The review has reported the cytotoxic, anti-tumor and anti-metastatic effects of *U. dioica* plant on several human cancers⁹⁵. UD inhibited cell proliferation in the Non-small cell lung cancer cells, while no toxic effects were observed in normal lung cells⁹⁶. The cytotoxic activity of UD aqueous extract in LNCaP cells (prostate cancer) is mediated through oxidative stress and apoptosis. These findings could hold positive implications for the potential use of UD extract in prostate cancer therapy⁹⁷. The human breast cancer cell line (MCF-7) and fibroblasts isolated from foreskin tissue were both markedly inhibited by *U. dioica*. The acute myeloid leukaemia (AML) U937 cell line's cell proliferation was dramatically reduced by the aqueous extract of *U. dioica* leaves. Hep2c, RD, and L2OB cells were also shown to be significantly less likely to proliferate in response to the subcritical water extract of *U. dioica*. 5a, 6b-dihydroxy-daucosterol, a bioactive component from *U. laetevirens*, demonstrated anticancer efficacy against MH7A cells by preventing proliferation and causing apoptosis⁹⁸.

***Vinca rosea* (Hindi Name: Sadabahar):** It is an important medicinal plant of significant concern and is a member of the genus *Vinca* and oleander. Human skin cancer cell line A431 was prevented from proliferating by a methanolic extract of the plant. Studying the effects of this plant's alkaloids

on breast, prostate, and cervix cancer cells (MCF-7, PC3- 1C, and HeLa) revealed that these alkaloids' tubular protein links changed their structure by preventing the division of cancerous cells; these substances' antioxidant properties will stop the progression of cancer cells³⁰.

A new clinically confirmed antitumor compound, Vincaloblastine (C₄₆H₅₅O₉N₄), (VLB) as the sulfate has been reported. The greatest activity was seen against the P-1534 acute lymphocytic leukemia in DBA/~ mice. Two other alkaloids, vindoline (C₂₅H₃₂O₂) and catharanthine (C₂₁H₂₄O₂N₂), also obtained from *Vinca rosea*, were devoid of antitumor activity singly or in equimolar concentrations, but have been postulated as the biogenetic precursors of VLB and leurosine. Initial *in-vitro* research found that some substances could reverse the growth-inhibitory effects of VLB on human monocytic leukemia cells. Coenzyme A, aspartic acid, tryptophan, a-ketoglutaric acid, ornithine, citrulline, arginine, and glutamic acid were among these substances⁹⁹. Vinblastine, vinorelbine, vincristine and vindesine are the four main vinca alkaloids with therapeutic effects. A brand-new synthetic vinca alkaloid called vinflunine has received European Union approval for the treatment of second-line urothelial transitional cell cancer. The second-most popular class of cancer medicines is vinca alkaloids¹⁰⁰. Catharoseumine, 14', 15'-didehydro-cyclovinblastine, 17-deacetoxy-cyclovinblastine, and 17-deacetoxyvinamidine are recently isolated indole alkaloids from this plant that efficiently suppressed human cancer cell lines *in-vitro*¹⁰¹. To improve the therapeutic activity against cancer treatment, some semi-synthetic substances that are comparable to vincristine and vinblastine have been created. A significant amount of *in-vitro* cytotoxic activity was demonstrated by anhydrovinblastine, a direct precursor of vinblastine, against human non-small cell lung cancer C4 and human cervical carcinoma, human leukemic cells, and human carcinoma A431 cells¹⁰².

***Withania somnifera* Dunal (Hindi Name: Aśgandh):** The Indian traditional medical system of Ayurvedic medicine makes extensive use of *W. somnifera* Dunal (also known as Ashwagandha, WS). In Bangladesh, India, Nepal, Pakistan and Sri Lanka, Ashwagandha grows in large quantities.

It is grown for profit in Madhya Pradesh (a state in India). Sarcoma 180 (S-180), a transplantable mouse tumor, also demonstrated the growth inhibitory action of *W. somnifera*, and it was reported that Ethanol extract of *W. somnifera* root showed (after intradermal injection of S-180 cell in BALB/c mice) total regression of tumor after the first growth. Additionally, it was discovered that *W. somnifera* acts as a radio and heat sensitizer in Ehrlich ascites cancer and mouse S-180. Withaferin, a steroidal lactone of WS, had anti-tumor and radio sensitizing actions on mouse *Ehrlich ascites carcinoma in-vivo*. The radio sensitizer ratio of 1:5 provided by withaferin A from *W. somnifera* allowed for the *in-vitro* eradication of the V79 Chinese hamster cell carcinoma¹⁰³. Withaferin, a steroidal lactone of WS, also had anti-tumor and radio sensitizing actions on mouse Ehrlich ascites carcinoma *in-vivo*. One study tests the *in vitro* cytotoxicity of a 50% ethanol extract of the root, stem, and leaves of *Withania somnifera* against four different types of human tissues and five cancer cell lines. A-549 (lung), IMR-32, PC-3, DU-145 (prostrate), HCT-15 (colon), and (neuroblastoma). *Withania somnifera* leaf extracts in 50% ethanol demonstrated the highest level of cytotoxicity on the cell lines when compared to the extracts of the root, stem, and leaves¹⁰⁴. According to this research, *W. somnifera* has significant potential as a cancer treatment¹⁰⁵. A key role in apoptosis induction is played by withaferin-A (WA) and withanolides, which are reported to be their most promising anticancer substances¹⁰⁶.

***Zanthoxylum nitidum*:** It is found in Australia and Southeast Asian nations and is a member of the Rutaceae family. Flavonoids, alkaloids, carbohydrates, and amino acids are present. Nitidine chloride, dihydronitidines, oxinitidine, skimmianine, -allocryptopine, and 6-methoxy-5,6-dihydrochelerythrine are all found in the root of the plant. It is used to cure cholera, diarrhoea, rheumatism, coughing, vomiting and stomachaches. Nitidine has anti-cancer properties and cytotoxic activity against the LLC (DNA intercalator), which is typically categorized as an inhibitor of topoisomerases I and II and causes the apoptosis of cancer cells¹⁰⁷. The stems and twigs of *Z. nitidum* were used to isolate three novel alkaloids: zanthocadinanine C (1), 7-methoxy-8-

demethoxynitidine (2) and zanthonitidine I (3). Compound 2 shown considerable cytotoxic effect against all tested human cancer cell lines, according to an evaluation of Compounds 1-3's cytotoxic activity against the human cancer cell lines KB, MCF-7, LNCaP, HepG-2, and LU-1¹⁰⁸. The isolated nitidine and liriodenine from the chloroform and petroleum ether extracts of the roots and leaves of *Z. nitidum* (*Zanthoxylum nitidum*) are promising potential anti-leukemia drug candidates (exhibited good inhibitory activities in the leukemia cell line HEL)¹⁰⁹.

***Zingiber officinale* (Hindi Name: Adrak):** *Zingiber officinale* is a member of the Zingiberaceae family. Ginger or ginger is an edible medicinal plant. It is cultivated throughout India, and run wild in some places in the Western ghats¹¹⁰. The aqueous extract of *Zingiber officinale* is effective on breast cancer cells (MCF-7 line and MDA-MB-231) and morphological changes observed in cancer cells that were extracted under array indicate that the cell death induction program has been destroyed³⁰. The methanolic extract of *Zingiber officinale* rhizome (ZOME) inhibited the proliferation and colony formation in human cervical cancer HeLa cells and breast cancer MDA-MB-231 cells. Additionally, it is suggested that *Z. officinale* has promising anticancer and antioxidant properties¹¹¹.

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