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VARIOUS HERBAL PLANTS ARE USED AS ANTICANCER AGENTS

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ABSTRACT: Cancer is the world's second-largest cause of death. Although substantial progress has been made in treating and controlling cancer progression, there are still significant flaws and space for improvement. During chemotherapy, several unfavourable side effects might arise. Natural-derived substances are attracting scientific and academic attention since they are thought to have fewer hazardous side effects than conventional treatments like chemotherapy. Natural secondary metabolites produced by plants are being studied for their anticancer properties, which could lead to the creation of novel therapeutic medications. The demand for naturally produced chemicals from medicinal plants and their features that make them possible anticancer treatments are discussed in this review.

INTRODUCTION: Cancer is responsible for one out of every six fatalities worldwide, with 70 percent of cancer deaths occurring in low- and middle-income nations [1]. Cancer has been a constant battle worldwide and there has been a lot of progress in terms of cures and preventative medications. The condition is characterized by the inability to control or stop cells in the human body from increasing indefinitely. As a result, malignant cells create tumors that can spread [2]. Chemotherapy, radiation, and chemically generated medications are among the current treatments. Chemotherapy, for example, can put patients under a lot of stress and wreak havoc on their health. As a result, there is an emphasis on employing alternative cancer treatments and therapies [3].

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This could be attributed to behavioral and dietary concerns such as inactivity, smoking, alcohol consumption and a diet lacking in fruits and vegetables. An aging population and exposure to certain chemicals, metals, and infectious agents contribute to the high incidence rate [4]. Plants have played an important part in treating a variety of ailments, including cancer. The sheer variety and amount of medicinal plants found worldwide are mind-boggling. Around 70,000 plant species, ranging from lichens to towering trees, have been employed for medical reasons at one point or another.

Healing herbs were revered by ancient tribes, as evidenced by finds from the excavation of a 60,000-year-old burial site in Iraq. Eight different medicinal plants were discovered; their presence in the tomb suggests that they had supernatural significance and medical benefit [5]. Plant-derived drugs have played an important role in cancer treatment. In his articles, Hartwell listed approximately 3000 organisms that have anticancer effects [6]. Herbal medicines have long been and

continue to be utilized as the primary source of medical care in impoverished countries. The natural antibacterial qualities of plants have long been employed in medicine. As a result, research has focused on the features and applications of terrestrial plant extracts in developing possible nanomaterial-based therapies for diseases such as cancer [7]. Several plant species are already being utilized to treat or prevent cancer. Multiple studies have identified plant species with anticancer characteristics, emphasizing those utilized in herbal medicine in developing nations [2, 8-12]. Compounds that are found in plants and are required for plant survival and "housekeeping" of the organism are being studied for their capacity to stop malignant cells from growing and initiating apoptosis. This article aims to provide an overview of present plant-derived chemicals with anticancer therapeutic capabilities, as well as their progress in the area.

Various Plants used in the Cancer Treatment:

***Andrographis paniculata* (Nilavembu):** It belongs to the Acanthaceae family and is known as kalmegha in Hindi and king of bitters in English. Medicinally, the roots and leaves of this plant are used; the extract includes flavonoids, stigma sterols, and diterpenes [13]. The and rographolide, a diterpene that is colourless, crystalline in nature, and bitter in taste, is the main compound of this plant. The leaves have the highest concentration of and rographolide (approximately 2.25 percent), while the seeds have a very low concentration. *Andrographis paniculata* stimulates the immune system in mice, activating both antigen-specific and non-specific T cells [14]. Andrographolide shows cytotoxic effects against various cancer cells [15].

***Allium sativum L* (Poondu):** The plant *Allium sativum* belongs to the Amaryllidaceae family [16]. Other studies discuss the function of the most effective Allium sativum compound, Allicin, and its antitumor properties against breast and prostate cancer are demonstrated. This substance causes cells to die in a regulated manner and has anticancer properties [17, 18]. As *Allium sativum* is crushed and cracked, Allicin 1 transforms into Allicin 2 due to the action of an enzyme. Allicin inhibits the growth of malignant human cells. Ajoene is another compound that inhibits leukaemia cell proliferation and causes cell death [19, 20]. Ajoene is a result of the rearrangement of allicin, which is a major component of raw garlic. Human primary fibroblasts, a permanent, nontumorigenic cell line derived from baby hamster kidney cells and a tumorigenic lymphoid cell line derived from a Burkitt lymphoma were used to assess its cytotoxic impact. The cytotoxic activity ranged from 2 to 50 g/ml [21].

Ammi majus: *Ammi majus* is a white flower that belongs to the Apiaceae family [22]. The effect of this plant's ethanol extract on HeLa and MCF7 cells was investigated, and the results revealed that this plant's extract is toxic to these cells [23] Comorian compounds (as part of phenol compounds) are major compounds in this plant and they are responsible for the majority of the plant's biological activities. The cell toxicity of coumarin compounds on cell lineages has been studied, and apoptosis induction by these compounds has been reported. The most important coumarin compound in this plant with anticancer properties is psoralens [24].

Ammi visnaga: *Ammi visnaga* L is a Mediterranean perennial plant with a garmineous appearance. This species has three parts: alegrian, furanochromones, and flavonoids [25]. This odorant plant is of Apiaceae family, and its antibacterial, antifungal and therapeutic effects in vitiligo have been published [26]. The killing activity of different extracts of the above-ground part of this plant on T47D cancer cells has been studied [27]. Also, this plant's inhibitory and dose-dependent effect on 2 human cell lineages, pelvic rhabdo-myosarcoma and L20B of mice, have been proven [28]. Khellol, visnadine, cimitugin, and β-sitosterol are the most important compounds of this plant. Flavonoids like quercetin and kaempferol are isolated from the aqueous extract of this plant, and these compounds can justify the anticancer effects of this plant [29].

Artemisia absinthium L: Artemisia is a plant in the Asteraceae family. Research on breast cancer cells MCF-7 has been reported [30]. Compounds found in this plant include quercetin, isorhamnetin, kamfrolinalol, alphapinin, limonene, and myrcene. Isorhamnetin inhibits the growth of many cancer cells, and quercetin inhibits the growth of many cancer cells, including MCF-7 [31]. Artesunate is also one of the most effective artemisinin with an angiogenic function, inhibiting the synthesis of the angiogenic factor VEGF in addition to its

anticancer effects on K569 (leukaemia cancer) [32]. In other studies, alpha-pinene, beta-pinene, limonene, and myercin found in methanol and ethanol extracts of this plant (colon cancer) [33] have been shown to inhibit the growth of HT-29 cells human breast cancer, as well as hepatic and melanoma cancers.

Astragalus cytosus: *Astragalus cytosus* is a perennial Leguminoseae plant. In a clinical trial involving 24 patients with lung cancer, 21 of them showed a positive response to this plant's extract [34]. Flavonoids found in other species of this plant have been shown to induce apoptosis in carcinoma cells *in-vitro* [35].

Astrodaucus orientalis: This plant belongs to the umbellate family and is a biennial. This plant's root and above-ground parts have antiproliferative properties in breast cancer cells (T47D) [36]. α-Pinene, α-thujene, α-copaene, fenchyl-acetate, anisole, myrecene and sabinene are the most important compounds in this plant [37]. The key mechanism of the plant's anticancer effects is cell cycle inhibition and activation of apoptosis [38].

Avicennia marina: Avicennia marina is a mangrove plant genus. Its leaf extract contains flavonoid compounds that have anticancer properties in human breast cancer BT-20 cells. In another study, the anticancer effect of naphthoquinone on laryngeal cancer cells was demonstrated by extracting it from the plant's leaf [39]. The extract has a cytotoxic effect on breast cancer cells (row 231MDA-MB) [40].

Aegle marmelos: Lupeol, an anticancer compound isolated from Aegle marmelos, is effective against breast cancer, malignant lymphoma, malignant melanoma, malignant ascites, and leukaemia.

Aegle marmelos have high antioxidant activity and can help with chemotherapy and radiotherapy side effects [41].

Agave americana: The ethanolic extract of *A. americana* leaves has a cytotoxic and antitumor activity. The leaf contains steroidal saponin, alkaloid, coumarin, isoflavonoid, hecogenin and Vitamins (A, B, C). Therefore, this plant has the potential to be utilized for the development of novel anticancer drug leads [42].

Achillea wilhelmsii: The Achillea vine, *Achillea wilhelmsii*, belongs to the Asteraceae family. Methanol extracts and the essence of this plant's leaves have cytotoxic effects on colon cancer cells (HT-29), with the essence having a higher cytotoxic impact [43]. Other research has shown the effects of methanol extracts of plant leaves against cell lineage of stomach cancer and breast cancer have been shown in other research [44]. Methanol extract of the plant contains phenol compounds, especially flavonoids, which inhibit cancer cell reproduction by inducing apoptosis [45]. 1,8-cineole and -piene, which are found in the leaves of this plant, induces apoptosis in human melanoma cells. Monoterpene essence is one of the essential monoterpene essences [46].

Alpinia galangal: Acetoxy-chavicol-acetate (ACA), a compound derived from *Alpinia galanga*, has anticancer properties in the breast, lung, stomach, colon, prostate, multiple yeloma, and leukaemia. Pinocembrin, a compound derived from Alpinia galanga, prevents colon cancer growth and spread by halting cell proliferation and inducing apoptosis. Galangin, a flavonoid derived from the *Alpinia galanga* plant, has anticancer, antioxidant, antimutagenic and anti-inflammatory effects. Galangin helps to prevent cancers of the breast and prostate [47].

Amoora rohituka: By arresting the G2/M step of the cell cycle and inducing apoptosis, Amooranin (a triterpene acid) isolated from *Amoora rohituka* inhibits the growth and spread of breast and cervical cancers. Both chemotherapy-sensitive and chemotherapy-resistant cancers react well to amooranin and its derivatives. Amooraninhas the ability to overcome (reverse) multidrug resistance in breast cancer, colon cancer and leukaemia [48].

Annona muricata: *Annona muricata* is the scientific name for Graviola. Acetogenins are an essential class of medicinal components found in graviola. Acetogenins were discovered in the graviola plant's berries, seeds, leaves, and bark. According to preliminary studies, acetogenins prevent the development of adenosine triphosphate, which inhibits the pump that extracts cancer drugs from the cell, making chemotherapy more effective. Furthermore, research suggests that acetogenin may have chemotherapeutic potential,

especially in treating cancers resistant to multiple drugs [49]. Graviola can cause Parkinson's-like symptoms when taken orally. Various cell lines include lung solid human-breast cancer, tumour carcinoma, pancreatic carcinoma, prostatic adenocarcinoma, colonic adenocarcinoma, human lymphoma, liver cancer and multiple-drug resistant human-breast adenocarcinoma, have been confirmed to be toxic for particular acetogenins [50].

Apis mellifera: The scientific name for the honey bee, *Apis mellifera*, is *Apis mellifera* Honey is used in Indian medicine to speed up the healing of skin wounds, ulcers, and burns. A protein from the honeybee *Apis mellifera* has been shown to promote proliferation and suppress apoptosis in primary-cultured rat hepatocytes [51]. It has also shown cytotoxicity in normal human lymphocytes and HL-60 cells.

Ananas comosus: Bromelain is a mixture of proteases and other enzymes found in *Ananas comosus*. Bromelain boosts the body's anticancer defence system by increasing the cytotoxic activity of monocytes and macrophages, which slows cancer development. It's a drug that's used to treat leukaemia [52].

Angelica sinensis: The herb *Angelica sinensis* is used by Chinese doctors to cure cervical cancer. *Angelica sinensis'* polysaccharide component, called "AR-4," has immuno-stimulating effects, including initiating interferon production, boosting immune cell proliferation, and improving antitumor efficacy [53].

Annona species: Acetogenins, present in Annona bacteria, have potent anti-leukemic and anti-sarcoma properties. Acetogenins have been found to be effective in the treatment of nasopharyngeal cancer [54].

Arctium lappa: The anticancer substances identified in Arctium lappa inhibit oncogene mutations. It has been used to treat malignant melanoma, lymphoma, and malignancies of the pancreas, breast, ovary, oesophagus, gut, bile duct, and bone. According to a review, it reduces tumour growth, lowers pain, and increases survival time [55].

Astragalus membranaceus: Patients with advanced liver cancer are prescribed *Astragalus membranous* by Chinese doctors. Swainsonine, a product of Astragalus membranous, has been found to stop cancer cells from spreading. According to a study, patients with advanced-stage liver cancer who got Astragalus membranous coupled with standard treatment had a greater survival rate than those who had standard treatment alone. *Astragalus membranous* protects the liver from the adverse effects of chemotherapy. *Astragalus membranous* and Panax ginseng are sometimes mixed. Natural killer cells are regulated by the combination of ginseng and astragalus (GAC). According to studies, GAC also protects the body against the negative effects of chemotherapy and enhances immune cell function. GAC has been identified to regulate the stress hormone cortisol [56].

Boswellia serrata: It is a member of the Burseraceae family. It's also known as *Indian olibanum* or olibanum. It contains terpenoids, oils, and sugars, among other things. This plant's main ingredient is boswellic acid [57]. Anti-arthritic, astringent, stimulant, and anti-septic characteristics are among the medicinal effects of this plant's gummy exudates. Acetyl-11-keto-boswellic acid, the active ingredient in this plant, has been demonstrated to suppress tumour angiogenesis via inhibiting vascular endothelial growth factor signalling. Treatment with acetyl-11-keto-boswellic acid (dose-10mg/kg) reduced tumour development in xenograft mice with human prostate tumours [58]. This shows the antitumor activity of this plant.

Bauhinia variegate: Cancers of the breast, lung, liver, oral cavity, larynx, and malignant ascites are all prevented by *Bauhinia variegata's* cyanidin glucoside, malvidin glucoside, peonidin glucoside, and kaempferol galactoside. Hepatoprotective effects are also found in Bauhinia variegate [59].

Berberis vulgaris: *Berberis vulgaris* root contains berberine, berbamine, chelidonic acid, citric acid, columbamine, hydrastine, isotetrandrine, jacaranone, magnoflorine, oxycanthine and palmatine. Berberine (an isoquinoline alkaloid) has anticancer, anti-inflammatory and immune-boosting properties. Berberine causes apoptosis by halting the G1 phase of the cancer cell cycle. In the cases of prostate cancer, liver cancer, and leukaemia, berberine has potent anticancer properties. Berberine interferes with P-glycoprotein

in chemotherapy-resistant tumours. Berberine also helps chemotherapy drugs work better on intracranial tumours by allowing them to pass through the blood-brain barrier. *Berberis vulgaris* generates three phenolic chemicals in its root bark: tyra. Cannabisin-G and lyoniresinol are both powerful antioxidants. Cannabisin-G protects against breast cancer. *Berberis vulgaris* also helps to prevent stomach and mouth cancers from developing [60].

Betula alba: The common name for this tree is birch. The birch tree, also known as *Betula alba*, serves a variety of purposes. In medicine, it's used as a diuretic, anti-inflammatory, and pain reliever. Dr. Brij Saxena of Weill Cornell Medical College discovered that the effects of Betulinic Acid kill malignant cells, and that it is very effective in the treatment of prostate cancer patients. This medication has no negative side effects in the majority of patients. However, more research is being done to establish if the substance is safe for HIV patients [61].

Betula utilis: *Betula utilis* contains betulin, which is readily converted to betulinic acid. According to studies, betulinic acid helps prevent malignancies of the liver and lungs and malignant melanoma [62].

Bidens pilosa: *Bidens pilosa*, a traditional medicine, contains polyacetylenes, flavonoids, terpenoids, phenylpropanoids and other chemicals. After a thorough investigation on several extracts of *Bidens pilosa* and additional fractionation, the putative marker chemical phenyl-1,3,5-heptatriyne was isolated and characterized. This marker molecule with hexane, chloroform, and methanol extracts of *Bidens pilosa* and their fractions were tested on several cancer cell lines. Extracts were shown to have anticancer action, with hexane extract demonstrating the most noteworthy effect [63].

Bolbostemma paniculatum: After extracting and fractionating a triterpenoid saponin from the Chinese herb *Bolbostemma paniculatum*, Tubeimoside-V was identified and characterized (Cucurbitaceae), it was discovered to kill glioblastoma cells through apoptosis, demonstrating that it plays an important function in antitumor chemotherapy. Tubeimosides like tubeimodes-I, tubeimoside-II and tubeimoside-II demonstrated promising cytotoxic effect, which could be associated to DNA synthesis inhibition and phenotypic reversal in tumour cells [64].

Boesenbergia pandurata: It is a perennial herb that belongs to the Zingiberaceae family. *Boesenbergin*, *cardamonin*, pinostrobin, pinocembrin, panduratin A, and 4-hydroxypanduratin A are the active compounds in B. pandurata. Antioxidant, antibacterial, antifungal, anti-inflammatory, antitumor, and anti-tuberculosis properties are all present in these compounds. Panduratin A, a cyclohexenylchalcone derivative found in B. pandurata, has been shown to inhibit the growth of HT-29 colon cancer cells and induce apoptosis [65].

Capparis spinosa: It is a Capparaceae family member. Caper contains anticancer chemicals such as flavonol glycoside, rutin, and 5-caffeoyl-quinic acid, as well as various volatile and non-volatile substances. A protein analogus to imidazole glycerol phosphate synthase purified from fresh Caper seeds inhibited the proliferation of hepatoma HepG2 cells, colon cancer HT29 cells, and breast cancer cells. MCF-7 cells are a cancer cell type [66]. Essential oils and aqueous infusions obtained from Caper have been found to decrease HT-29 cell proliferation and nuclear factor-kB (NF-kB) function in a dose-dependent manner. Caper essential oil and aqueous infusion stopped cells in the G2/M phase of the cell cycle. Spinosa extract caused apoptosis in SGC-7901 cells by permeabilization of mitochondria and activation of Caspase [67].

Centella asiatica: It belongs to the Apiaceae family. Among the substances are asiaticoside, pectic acid, hydrocotyline, sterol, flavonoid, vallerine, ascorbic acid, and thankunosides [68]. Oral injection of a partly filtered fraction of *Centella asiatica* inhibited the proliferation of mouse lung fibroblast cells and slowed the progression of solid tumours and ascites tumours [69]. Pre-treating irradiated animals with this plant extend their survival period and protect them from radiation-induced liver damage [70]. This plant inhibits lipid peroxidation in a variety of organs, including the lungs, liver, heart, brain, spleen and kidney, and has the potential to suppress cancer.

Curcuma longa: It belongs to the Zingiberaceae family. The active element in this plant is curcumin, a polyphenol extracted from plant rhizome that is utilized for both cancer prevention and treatment. In multiple studies, curcumin has been demonstrated to trigger apoptosis, reduce proliferation, and interfere with cell cycle progression [71]. Curcumin has also been demonstrated to prevent colon and stomach cancer in animals [72]. Curcumin inhibits the growth of specific angiogenesis and tumor-associated genes, which protects against tumour formation [73]. Curcumin has anticancer properties by reducing tumour cell proliferation. Curcumin suppresses cell proliferation by decreasing the expression of a number of genes, including activator protein 1, NF-kappa B, cycloxygenase 2, epidermal growth receptor 1, nitric oxidase synthase and tumour necrosis factor [74].

Citrullus colocynthis: *Citrullus colocynthis* is a member of the Citrullus genus and the Cucurbitales order [75]. This plant's extract (Hep2) was found to be toxic to laryngeal cancer cells in sample [76].

Chemical constituents of this herb, such as cucurbitales, have been used as anticancer medicine in cancers such as liver (HepG2) and breast (MCF7) cancers, according to reports; quercetin and -sitosterol as antitumor agents have also been studied in several studies. These compounds work by stopping the cell cycle (at G2/M) and inducing apoptosis, which has anticancer properties [77-78].

Crocus sativus L **(Saffron):** Crocus sativus L is a member of the Iridaceae family [79]. In a study on the impact of saffron extract on human cancer cells, Escribano *et al.* found that materials separated from saffron, such as crocin, crocetin, picrocrocin, and safranal, induced apoptosis in cancer cells [80].

Another research looked at the effects of saffron extract and another major plant substance called quercetin on colorectal cancer cells. The findings revealed that this plant is toxic to these cells [81].

Cannabis sativa: *In-vitro* tests of marijuana (Cannabis sativa) components show that they can inhibit human breast cancer cells and eliminate tumours. It was discovered that giving marijuana to animals with malignant brain tumors dramatically improved their survival rate. Cannabinoids are the active ingredients in Cannabis sativa. Cannabinoids and their derivatives have anti-nausea, anti-vomiting, and anti-pain properties in cancer patients and stimulate appetite. By modulating main cell-signaling pathways, these compounds have also demonstrated anti-tumour activity in cell culture and animal models [82].

Chlorella pyrenoidosa: Lysine, found in Chlorella pyrenoids, is a powerful detoxifying agent. Chlorella pyrenoids also have a high albumin content, which helps to neutralize free radicals. Chlorella pyrenoids is a cancer-fighting algae [83].

Colchicum luteum: Tropolone groups of alkaloid colchicines are found in *Colchicum luteum* and C. autumnale. Colchicine has antimitotic properties and is used in cancer therapy to disperse tumours and treat a variety of neoplastic diseases [84].

Daphne mezereum: Daphne mezereum is a herb that has long been used as a folk remedy for cancer-like symptoms. In mice with lymphocytic leukaemia, a hydro alcohol extract of Daphne mezereum showed potent antileukemic activity. Mezerein was isolated and characterized as a potent antileukemic compound after further fractionation experiments on the extract [85].

Echinacea angustifolia: Arabinogalactan, found in *Echinacea angustifolia*, protects the body from cancer by activating macrophages. *Echinacea angustifolia* is used to treat metastatic oesophageal and colon cancer [86].

Fagopyrum esculentum: *Fagopyrum esculentum* includes amygdalin, which Chinese doctors have utilized to cure various tumours for over 3,500 years. The anticancer action of Amygdalin, which is produced from *Fagopyrum esculentum*, has been validated by Ernest Krebs, a well-known researcher. Amygdalin is a nitriloside (naturally occurring cyanide-containing chemical) made up of two molecules: benzaldehyde and cyanide. In the body, an enzyme called beta-glucosidase splits these two molecules apart in the liver to generate glucuronic acid. Another enzyme called glucuronidase, which is found in larger amounts in malignant cells, breaks down glucuronic acid to generate cyanide, which destroys the cancerous cells.

It's worth noting that malignant cells lack an enzyme called rhodanese (sulphur transferase), which is abundant in healthy cells. Rhodanase protects normal human cells from cyanide poisoning by turning free cyanide into a comparatively innocuous chemical called thiocyanate [87].

Glycyrrhiza glabra: Extract contents of *Glycyrrhiza glabra* root lead to morphological changes in the mammary cell line 4T1 and reduce their viability [88]. Its root extract induces BCL2 phosphorylation and like Taxol, inhibits the cell cycle at the G2/M phases in tumor cell lines [89] Glycyrrhizin, is a triterpene glycoside that is the main compound in root extract and acts as an anti-proliferative agent against tumor cells, especially breast cancer cell line (MCF-7) and HEP-2 and plays its role by inducing apoptosis [90, 91].

Ginkgo biloba: *Ginkgo biloba's* Ginkgetin and Ginkgolides (A and B) suppress the growth and spread of invasive estrogen-receptor negative breast cancer, glioblastoma multiforme, hepatocellular carcinoma and malignancies of the ovary, colon, prostate and liver by causing apoptosis. The antioxidant effect of Ginkgo biloba extract is widely recognised. Chemotherapy and radiotherapy side effects are also reduced by ginkgo biloba [92].

Gossypium hirsutum: *Gossypium hirsutum* or *Gossypium herbaceum*, often known as Gossypol or cottonseed oil, is a male contraceptive that is also used to treat metastatic endometrial or ovarian cancer, as well as HIV. Gossypol has anticancer activities in several cytosolic and mitochondrial enzyme systems essential for tumour cell proliferation, including melanoma, endometrial, colon, lung, prostate, breast, brain, and adrenocortical cancers, according to certain *in-vivo* and *in-vitro* investigations [93]. However, no typical dose is yet suggested for cancer treatment, and self-medication with gossypol is not safe because of its potential toxicity [94].

Gyrophora esculenta: *Gyrophora esculenta* is a mushroom that slows cancer growth by boosting the activity of natural killer cells. It was discovered in a study that it prevents carcinogenesis and metastasis [95].

Heracleum persicum: Methanol and petroleum ether extracts from the root and fruits of *Heracleum persicum* (Apiaceae) displayed antitiumor action and inhibited Agrobacterium tumefaciens caused crown gall tumours on potato discs. *H. persicum* essential oils also had anticancer activity, with an IC_{50} value of 2.24 mg/mL [96].

Indigofera tinctoria: This research aimed to assess the antibacterial, antioxidant, and cytotoxic properties of the leaf extract Indigofera tinctoria. On a lung cancer cell line, the cytotoxic activity of leaf extract was determined. GC-MS analysis was used to identify the compounds in the extract. Bioactive substances such as flavonoids, saponins, tannins, steroidal terpenes, phenols, and anthraquinone were discovered in the extract tested for photochemical analysis [97].

Lentinus edodes: The anticancer efficacy of lentinan, a -glucan found in shiitake mushrooms, has been demonstrated; it proved effective against lung carcinoma [98]. Natural killer cells and macrophages, which attack tumour cells are stimulated by lentinan, which increases their production and activity [99]. Shiitake extracts may also have hypolipidemic and antithrombotic properties, according to preliminary research [100]. Several anticancer chemicals have been found by screening studies on Polyporaceae fungi, including a range of terpenoids and steroids, polysaccharides, and an organic germanium compound [101].

Linum usitatissimum: Flaxseed (*Linum usitatissimum*) includes a lot of lignans. Bacterial fermentation in the colon converts these plant lignans to mammalian lignans (enterolactone and enterodiol) [102]. They then can behave like oestrogens. Lignans from mammals appear to be anticarcinogenic; lignan metabolites have a structural similarity to oestrogens and can bind to oestrogen receptors, inhibiting estrogen-stimulated breast cancer growth [103]. In women with breast cancer, urinary lignan excretion is reduced, whereas flaxseed powder consumption increases urinary lignan concentrations several-fold [104].

***Lagenaria siceraria* Standl:** Bottle gourd is a Cucurbits species with yellow skin that is less palatable. The effect of the plant extract on the human lung cancer cell line A549 has been studied,

and the extract has been proven to significantly inhibit the cell line [105]. The antitumor activity of a methanol extract of this plant's aerial parts has been proven [106]. Another study proved the effectiveness of a water-soluble polysaccharide extracted from this plant on cancer of human breast cell lines (MCF7) [107].

Lepidium sativum: In Iranian traditional medicine, watercress is referred to as Jrjizbastany and Rashad. The bladder cell line (ECV-304) is cytotoxic by a methanol extract of cress seeds [108]. In addition, Aslani *et al.* demonstrated the cytotoxic effect of aerial parts of the plant on K562 leukaemia blood lines in a study of aerial components of the plant [109]. The effects of aqueous extract of seed on breast cancer cells (MCF-7) via activation of apoptosis were demonstrated in another investigation [110]. Antioxidants such as vitamins E, C, B, A, isothionate, and omega-3 fatty acids such as alpha-linolenic acid and glucosinolates are abundant in this plant, and these chemicals can exert anticancer effects by acting as antioxidants and inhibiting plant cell growth [111].

Matricaria chamomilla: The anticancer capabilities of chamomile (*Matricaria chamomilla*, Asteraceae) flower extracts against diverse human cancer cell lines cause moderate growth inhibitory responses in normal cells a considerable decrease in cell viability in several human cancer cell lines. The primary ingredient of chamomile, apigenin 7-O-glucoside, was established by chamomile extract [112].

Mentha species: Phenolic antioxidants found in Mentha species such as *Mentha piperita*, *Mentha longifolia*, and Mentha aquatica help to prevent cancer recurrence. The essential oils of had OH-radical scavenging activity, which reduced OH-radical production by 24% in the Fenton reaction [113]. Monoterpene ketones were the most effective scavenging components in *Mentha piperita* oil. By exerting direct effects on active metabolites, spearmint tea inhibits carcinogen activation [114, 115].

Morinda citrifolia: Damnacanthol, NB10, and NB11, all derived from *Morinda citrifolia*, have potent anticancer properties against a variety of malignancies, including lung cancer and sarcomas. *Morinda citrifolia* is a powerful antioxidant, hepatoprotective, and immune-boosting plant [116].

***Medicago sativa* L:** Alfalfa is a plant with the scientific name *Medicago sativa* L that grows in most parts of the world and has been used in traditional medicine to cure conditions like liver problems [117]. The plant's phytoestrogens and significant estrogenic activity make it effective for treating hormone-dependent tumours. Alfalfa is high in practically all vitamins, flavonoids, digestive enzymes, coumarin, an alkaloid amino acid, and trepans, and it can help prevent breast cancer and enhance breast milk production. Triconlin, a plant alkaloid molecule that acts as a hormone in the plant, is found in alfalfa. This plant alkaloid is thought to have major therapeutic qualities, such as anticancer capabilities [118, 119].

Mentha pulegium: The Labiaceae family includes this plant with the scientific name *Mentha pulegium.* Before flowering, Aslani and colleagues conducted study on the plant's cytotoxicity effect on leukaemia cells. Pennyroyal polygon contains natural chemicals such as mentone, piperitone, limonene, isomenthone and Octaan-3-ol [120]. Pennyroyal has been linked to the inhibitory effect of flavonoids on cancer cell proliferation via apoptosis induction in several studies [121].

Nervelia fordii: In China, the medicine Nerveliafordii is utilised as a folk treatment. Mice models were used to test the anticancer activities of petroleum ether and ethyl acetate extracts of Nerviliafordii. Both extracts have showed significant anticancer effects in S-180 and H-22 mouse models, as well as extending the lives of cancer-bearing animals. This study implies that Nerviliafordii could be used as a cancer-fighting agent, but more research is needed to isolate the active ingredient(s) in the medicine [122].

Ochrosia elliptica: Ellipticine and 9-methoxy ellipticine are pyridocarbazole (monomeric indole) alkaloids derived from the *Ochrosia elliptica* plant, which has anticancer properties. Breast and kidney cancers are treated with elipticine and its derivatives. Lipophilic ellipticine derivatives work via DNA binding [123].

***Occimum basilicum* (Basil):** Basil is well-known for its therapeutic properties. This common herb has been proven to offer the chemoprotective potential for colon cancer and anti-inflammatory,

blood pressure-lowering, and nervous system-stimulating qualities. Basil was discovered to substantially impact the reduction of colon cancers in experimental mice in a study. However, no human clinical trials have been carried out to support this claim [124].

Oldenlandia diffusa: In *Oldenlandia diffusa*, you'll find oldenlandosides, stigmasterol, ursolic acid, oleanolic acid, betasitosterol, p-coumaric acid, and flavonoid glycosides. Ursolic acid inhibits cancers of the lung, ovary, uterus, stomach, liver, colon, rectum, brain, malignant melanoma, malignant ascites, lymphosarcoma, and leukaemia. Ursolic acid has a cytotoxic impact and triggers apoptosis, which causes cancer cells to die [125].

Origanum vulgare: Oregano has the highest antioxidant content of all the dried herbs. Oregano contains rosmarinic acid, which has high antioxidant properties. Oregano supplementation of 40 mg per kg of body weight had a modulatory effect on tissue lipid peroxidation in colon cancer-bearing experimental animals, according to an Indian study. The dosage for humans has yet to be determined, however, how much oregano you need to flavour your dish depends on the amount of oregano you use [126].

Picrorrhiza kurroa: *Picrorrhiza kurroa* (Kutki) has been found to inhibit the establishment of liver cancer in those who have been exposed to chemicals. Kutki is made up of picrosides I, II, and III and kutkoside, which are active herbal ingredients.

Picrorrhiza kurroa has been proven to lower levels of free radical-producing enzymes lipid peroxidases and hydroperoxides and aid in the recovery of a potent antioxidant in the liver essential to avoid oxidative damage [127].

Podophyllum hexandrum: Podophyllotoxin and podophyllin (lignans) extracted from *Podophyllum hexandrum* (Himalayan May Apple) suppress the growth and spread of cancers such as breast, ovary, lung, liver, urinary bladder, testis, brain, neuroblastoma, Hodgkin's disease, non-lymphoma, Hodgkin's and leukaemia. Podophyllotoxin is the most potent anticancer chemical found in nature. *Podophyllum hexandrum* has radioprotective and haemopoietic characteristics as well [128].

Prunella vulgaris: Isolated from *Prunella vulgaris*, ursolic acid, and oleanolic acid suppress the growth and spread of cancers of the breast, cervix, lung, oral cavity, oesophagus, stomach, colon, thyroid, malignant lymphoma, intracranial tumours and leukaemia. *Prunella vulgaris* has long been used in China to heal mouth and throat sores. *Prunella vulgaris* has immune-boosting, hepatoprotective, antioxidant, anti-HIV and anti-Herpes effects, among other things. On the bone marrow, *Prunella vulgaris* exerts a normoblastic impact [129].

Psoralea corylifolia: *Psoralea corylifolia* contains avachinin, corylfolinin, and psoralen, which have strong anticancer action against lung cancer, liver cancer, osteosarcoma, fibrosarcoma, malignant ascites, and leukaemia. Psoralen boosts the body's immunity by boosting the activity of natural killer cells. Psoralidin, a compound derived from the *Psoralea corylifolia* plant, suppresses the growth and spread of stomach and prostate cancers by blocking the G2/M phase of the cell cycle. In both androgen-responsive and androgen-refractory prostate tumours, psoralidin promotes apoptosis. *Psoralea corylifolia* is also high in antioxidants, immunostimulants, and hepatoprotective compounds [130].

***Pegaum harmala* L:** The perennial Zyqophyllaceae family includes this herbaceous perennial plant. The viability of epithelial cervical cancer cells and colon carcinoma cells was likewise lowered by its extract [131]. The principal constituents of this plant are alkaloids, which have anticancer properties. The antioxidant properties of these alkaloids against human breast cancer cells were discovered in another investigation utilising chemical analysis [132].

Polygonum aviculare: Polygonum is a genus of Caryophyllales Polygonaceae plants. The effect of the extract on the prevention of proliferation of cancer cells HeLa has been shown to be reasonable in several investigations [133, 134]. The effects on cell proliferation and production of apoptotic genes in breast cancer cells (MCF7) revealed that extracts of the plant can cause cytotoxicity in breast cancer cells by inducing apoptosis [135, 136]. The most important components of this plant are tannins, flavonoids, and alkaloids [137]. However, research of anticancer effects revealed that, despite the

presence of phenol chemicals, the plant's effects are thought to be the primary reason [138, 139].

Rhinacanthus nasutus: It is a member of the Acanthaceae family and can be found in India, China, and Southeast Asia's subcontinental regions. Snake jasmine is the popular name for it. Rhinacathins (A-D, G-Q), naphthoquinone, lignin groups and rhinacanthone are all present [140].

This plant may be used to treat pulmonary tuberculosis, eczema, diabetes, and herpes. Rhinacanthins M, N and Q have been shown to suppress the proliferation of human cancer cells (HeLa, HepG2 and KB) as well as normal Vero cells in studies. Rhinacanthins N inhibits further cell damage and repairs cell abnormalities by partially arresting M phase cells [141].

Rubia cordifolia: *Rubidianin, rubiadin*, RA-7, RA-700, and RC-18, all derived from *Rubia cordifolia*, have been shown to suppress the growth and spread of malignancies of the breast, ovary, cervix, colon, lung, malignant ascites, malignant lymphoma, malignant melanoma sarcoma, and leukaemia. Rubiadin also has hepatoprotective properties [142].

***Rosa damascenes* Mill:** Rose has been cultivated for centuries in various climates. It belongs to the Rosaceae family, and the active element is tannin, which is found in the plant's flowers and leaves.

This essential oil has been shown to be harmful to lung cancer cell lines (A549) and breast cancer cell lines (MCF7). Cervical cancer cells are killed by an ethanol extract of the plant cell (HeLa) Rosa Damascenes essential oil has two distinct effects on stomach cancer cells: the soluble phase promotes cell viability, whilst the vapour phase reduces cell survival. Flow cytometry also revealed that apoptosis is an important process that occurs in conjunction with cell death [143].

Rhizophora apiculata: The entire plant extract of *Rhizophora apiculata* (Rhizophoraceae) was discovered to protect mice from cyclophosphamide (CTX)-induced leukopenia. The *R. apiculata* extract-treated animals had considerably higher leukocyte counts (10425 163 mm3) than the control group (7855 282 mm3). Furthermore, in treated mice, *R. apiculata* extract prevented organ weight loss and raised organ weight [144].

Salvia miltiorrhiza: Tanshinone-I, isolated from the traditional herb Salvia miltiorrhiza, was studied for its effect on intercellular adhesion molecule expression. The study discovered that tanshinone-I had an anticancer effect on breast cancer cells, implying that tanshinone-I could be used as a treatment for breast cancer [145]. Tanshinone II-A, a compound isolated from Salvia miltiorrhiza, caused apoptosis and was connected to proteolytic cleavage of a key component in the apoptotic cell death pathway [146].

Saussurea lappa: *Saussurea lappa* sesquiterpenes and costunolidedehy drocostus lactone prevent breast cancer growth and spread. Cynaropicrin, a compound derived from *Saussurea lappa*, has potent anticancer properties against malignant lymphoma and leukaemia. Isolated from *Saussurea lappa*, costunolide suppresses the growth and spread of intestinal cancer.

In leukemic cells, mokkolactone extracted from *Saussurea lappa* promotes apoptosis. Anticancer activity of shikokiols extracted from *Saussurea lappa* against malignancies of the ovary, lung, colon and central nervous system. *Saussurea lappa* suppresses cancer cell proliferation and spread by halting cell division in the G2 phase and triggering apoptosis [147].

Silybum marianum: It is a member of the Asteraceae family. Milk thistle is a Mediterranean plant that has spread throughout Europe [148]. On the 4T1 cell line, silymarin promotes cell cycle arrest and apoptosis, according to a study [149].

Scutellaria baicalensis: It is located in eastern Asia and belongs to the Lamiaceae family. Chalcones, anthocyanidins, flavanones, flavonols, flavanonols, and flavones are all found in it.

The presence of wogonosid, wogonin, baicalein, and skull cap flavone II gives it anti-tumour properties. These substances (at micro molar concentrations) suppress the proliferation of human tumour cell lines 529L and LXFL. Baicalein inhibits 12-lipoxygenase activity and contributes to anticancer efficacy against a variety of different malignancies [150]. Anti-inflammatory, anti-diabetic, antitumor, hepatoprotective, anti-anxiety, and anti-hypertensive properties are also present [151].

***Taverniera spartea* D:** *Taverniera spartea* D, also known as silver spartea, is a plant that thrives on Iran's southern coast, including Bandar Abbas, Minab, and Baluchistan. Methanol extracts of the plant, particularly chloroform fractions, were hazardous to human prostate cell lines (MCF-7 and BT474) and breast cancer cell lines (MCF-7 and BT474) (PC-3 and DU-145) [152]. The anticancer effects of the plant have been reported.

***Taxus baccata* L:** *Taxus baccata* L is a gymnosperm from the Taxaceae family. This is one of the first plants on which a considerable study on the effects of cancer prevention has been conducted. Taxol is a natural component of the plant that possesses anticancer properties [153, 154]. The acetone-dichloromethane extracts of the plants have been proven to be cytotoxic to cancer cells k562, HeLa, and MDA-MB-468 in study [155].

Thymbra spicata: The Zufaee thyme plant belongs to the Labiaceae family. Biological action is due to the presence of thymol and carvacrol. The effect of hydro-alcoholic plants on lung cancer cells (SK-Mes-1) has been demonstrated [156]. The most important plant phenol components with antioxidant characteristics are thyme, thymol, and carvacrol, which protect DNA from oxidative damage and so help to prevent cancer [157].

Thymus vulgaris: Garden thyme is the English name for *Thymus vulgaris* L and belongs to the Lamiaceae family. Thyme extract prevents the growth of aberrant and precancerous lesions and treats prostate cancer in rats, according to a study [158]. In addition, it inhibits the growth of squamous cell carcinoma of the head and neck (in laboratory circumstances) [159]. Flavonoids are among the chemicals found in this plant. The most important plant phenol chemicals that are useful in the treatment of breast cancer and colorectal cancer are thymol and carvacrol. The effect of growth inhibition in human breast and colorectal cancer was demonstrated in another study [160].

Tinospora cordifolia: It is found in Sri Lanka, India, Myanmar, and China and belongs to the Menispermaceae family. Alkaloids are abundant in the stem and roots. In English as heartleaf moonseed plant. Tinosporin, choline, isocolumbin, columbin, tetrahydroplamatine, magnoflorimne, and palmatin are among the alkaloids found in the root of this plant [161]. *Tinospora cordifolia* has been shown to kill HeLa cells in *in-vitro* research, indicating its potential as an anticancer drug. In comparison to the controls, *Tinospora cordifolia* extract causes dose-dependent cell death [162]. In mice transplanted with Ehrlich ascites carcinoma, a dichloromethane extract of *T. cordifolia* showed antitumor efficacy [163].

Taxus species: Taxanes, such as paclitaxel (Taxol) and docetaxel, are found in *Taxus brevifolia*, Taxus yunnanensis, *Taxus baccata* and *Taxus wallichiana* (Taxotere). Taxanes have a distinct mechanism of action on malignant cells than podophyllin and vinca alkaloids. By cross-linking the microtubules, taxanes stop malignant cells from multiplying. Leukemia and malignancies of the breast, ovary, colon, and lung are treated with taxanes [164].

Terminalia chebula: *Terminalia chebula* is a source of hydrolysable tannis and it has been shown to have antimutagenic effect in Salmonella typhi [165]. Chebulinic acid, tannic acid and ellagic acid are cancer growth inhibitors discovered in *Terminalia chebula* fruits [166]. *Terminalia chebula* fruits powder and bark acetone extract have been shown to have antimutagenic and anticarcinogenic properties [167].

Viola tricolor: *Viola tricolour* is a violet plant with a scientific name. This plant's aqueous extract has a strong inhibitory effect on cervical cancer proliferation, and the active chemical responsible for this action is ethyl acetate [168]. This plant includes a lot of chemicals that can cause potent cells to die [169]. Flavonoids have been shown in studies to have anticancer properties [170].

Vitis vinifera: It is a member of the Vitaceae family and is frequently referred to as grape vine. Grape extracts have been shown to kill PC-3, A-549 and MCF-7 cancer cells. In human breast cancer, cell lines MCF-7 and MDA-MB-23), colon (HT29), renal (786-0 and Caki-1), thyroid (K1), hepatocellular carcinoma cell lines, oral squamous cell carcinoma and normal human fibroblasts, extracts obtained from grape seeds and stems displayed anticancer activity [171]. Resveratrol, a chemo-prevention substance found in grape skin, causes autophagy and functions as an anticancer

agent. Methanolic extracts from Greek raisins were found to reduce stomach cancer cell proliferation, and mRNA levels of ICAM-1 in TNF-alpha activated cells and induce cell apoptosis and suppress inflammation in a clinical investigation [172].

***Viscum album*:** *Viscum album* contains lectins (such as viscumin), polypeptides (viscotoxins), and phenolic compounds (such as digallic acid) that inhibit the growth and spread of cancers of the breast, cervix, ovary, lung, stomach, colon, rectum, kidney, urinary bladder, testis, malignant melanoma, sarcomas, fibrosarcoma, malignant ascites, lung metastasis and lectins extracted from Viscum album have anticancer and immune-stimulating properties. Viscumin, which is responsible for the majority of Viscum album's biological actions, operates by bringing immune system effector cells and cancer cells together. Lectin-II activates caspase cascades in cancer cells, causing them to die [173].

Xanthium strumarium: Burweed or cocklebur is a plant that belongs to the Asteraceae family. This North American plant identifies anti-bacterial, anti-fungal, antitumor, anti-tussive, anti-inflammatory, anti-mitotic, anti-malarial, antioxidant, analgesic, and insecticidal properties.

It contains xanthinin, xanthumin, xanthostrumarin, xanthatin, phytosterols, xanthanolides, isoxanthonol, xanthanol and xanthinosin, as well as phytosterols, phytosterols, xanthanolides, isoxanthonol, xanthanol and xanthanol. The inhibition of tumour cell proliferation demonstrates the antitumor effect of 8-epi-xanthatin and its epoxide.

8-epi-xanthatin is a farnesyl transferase inhibitor that also inhibits microtubule interfering compounds, demonstrating its anticancer potential [174].

Ziziphus nummularia: It belongs to the Rhamnaceae family. Betulinic acid and betulin (found in the stem and bark) are the main ingredients in this plant with antitumor properties [175]. Betulinic acid is cytotoxic to a variety of tumour cell lines and promotes apoptosis by inhibiting topoisomerase I, generating reactive oxygen species, inhibiting angiogenesis and modulating pro-growth transcriptional activators [176].

Zingiber officinale: The Zingiberaceae family includes *Zingiber officinale*. The aqueous extract of *Zingiber officinale* is effective against breast cancer cells (MCF-7 and MDA-MB-231), and morphological changes in cancer cells extracted under array suggest that the cell death induction program has been eliminated [177].

CONCLUSION: Cancer is becoming a high-profile disease in both the industrialized and developing worlds. Drugs derived from chemicals have been produced, and various cancer treatments are available. Current techniques, such as chemotherapy, have limits because of their toxic effects on non-targeted tissues, exacerbating human health issues. As a result, there is a demand for alternative cancer treatments based on naturally produced anticancer chemicals, with plants as the preferred source. Plant-derived medications have been produced due to favorable research findings and are now being tested in clinical studies.

Drugs derived from vinca alkaloids were among the first to be used, and they are currently being tested in clinical Phase III studies with Paclitaxel and other anticancer drugs. These substances can be found in abundance in nature and are relatively non-toxic to healthy human cells. In addition, novel technologies like as nanoparticles are being developed for application in the administration of anticancer drugs and therapies. Their research could be used to modulate drug release over time and aid in the development of tissue-specific medicines, decreasing the severity of treatment side effects. Plant-derived medication demand increases, putting pressure on high-value medicinal plants and jeopardizing their biodiversity.

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