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Medicinal Plants Used as Anticancer Agents: A Review

Ashutosh Gopal,[1] Ashutosh Kumar[2]

[1]Research Scholar, Faculty of Pharmacy, Sunrise University, Alwar, Rajasthan

[2]Professor, Faculty of Pharmacy, Sunrise University, Alwar, Rajasthan

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Correspondence: Ashutosh Gopal

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Abstract

Common medicinal plants in India with anticancer characteristics are detailed in this review. A plethora of synthetic medicines with anticancer properties are already accessible for use; however, their adverse effects and medication interactions have severely limited their use. Herbal medicines are increasingly becoming recognized as significant sources of powerful anticancer drugs due to their broad therapeutic efficacy and reduced side effects. The antioxidant and anticancer effects of many medicinal plants are due to their secondary metabolites, which include alkaloids, flavonoids, phenolics, tannins, and so on. We have included a synopsis of recent findings from studies on many commonly used medicinal herbs with anticancer effects in this paper.

Introduction

Herbal remedies are an integral aspect of all conventional medical systems. Because they are cheap, readily available, and easy to acquire, plants have been utilized as medicine from the beginning of time. Most of the medications that are used today are derived from natural ingredients. In spite of the progress made in rational drug design and synthetic chemistry, medicinal molecules and building blocks for synthetic analogues are still derived from natural sources. Numerous upcoming pharmaceutical advancements will draw inspiration from the vast pool of unproven natural compounds, thanks to the growing fascination with this resource.[1]

Cancer in humans often begins in a cell and continues to grow and spread over a period of years. Cancer chemoprevention is an excellent strategy for halting the disease's progression in its early stages. The goal of cancer chemoprevention is to stop, slow, or stop the development of carcinogenic substances to invasive cancer by using either manufactured or naturally occurring chemicals. [2] Additionally, the World Health Organization has called for research into the discovery and characterization of novel herbal remedies derived from well-known plants, as well as the creation of new, more effective therapeutic agents, particularly in regions where there is a dearth of contemporary, safe medications for the treatment of long-term health conditions. [3]

Despite improvements in cancer detection, prevention, and treatment, millions of individuals throughout the globe are still impacted by this terrible disease, which has a major influence on the human health care system. Nearly half of all cancer diagnoses and over half of all cancer deaths occur in Asia, according to GLOBOCAN 2018. According to estimates, the share of cancer fatalities in Asia and Africa is 7.3% and 57.3% respectively, whereas the incidence rates are 5.8% and 48.4%, respectively. [4]

The wealth of medicinal properties of plants was well known to ancient times. As a potential anticancer promoter, a chemical is sought after for its strong antioxidant and anti-inflammatory properties. [5]

Nature has blessed us with an abundance of plant life, and many different kinds of plants grow wild in various regions of the nation. The majority of our understanding of medicinal plants comes from our ancestors, and the practice of using plants to treat a variety of illnesses is not limited to medical professionals but also includes many homes. A global trend toward using more natural, plant-based goods, especially therapeutic ones, is on the rise. Also, this

is a good time to think about underappreciated medicinal herbs. [6]

The title of "Botanical Garden of the World" is well-deserved; India is really the world's leading producer of medicinal plants. Nearly half of the world's medical plant species are found in India, out of 8,000 total. Traditional medicinal practices using plants have attracted a lot of attention from researchers in recent years. Despite the widespread use of plants by traditional healers, there is no evidence that many of these herbs really have anticancer properties. Recent reviews of the literature on medicinal plants with anticancer properties have shown substantial favorable data, driving up the demand for these plants as cancer treatments.

Common medicinal plants possessing anticancer property

Aloe vera

Common names for the perennial succulent Aloe vera include "the silent healer" and "the healing plant." It is a member of the Liliaceae family. The arid climates of the Americas, Europe, Asia, and Africa are ideal for its growth. Rajasthan, Andhra Pradesh, Gujarat, Maharashtra, and Tamil Nadu are among of the Indian states where it grows. Some of the 75 active ingredients found in aloe vera include sugars, lignin, saponins, amino acids, salicylic acids, enzymes, minerals, and anthraquinone glycosides. [7-11] Radiation and chemotherapy harm healthy immune cells necessary for healing; aloe vera juice helps the body cure itself from cancer and these damages. With its antineoplastic characteristics, the anthraquinone glycoside emodin may halt the proliferation of cancer cells. [12] Few studies have adequately assessed Aloe's potential carcinogenicity. One possible risk factor for colorectal cancer is the long-term use of laxatives containing anthranoid. [13] Researchers looked examined the efficacy of melatonin and aloe vera tincture as a routine treatment for solid tumors that have spread. [14]

Allium sativum:

Allium sativum is a member of the Alliaceae family and is indigenous to the area between the Mediterranean and China. It comprises ajoene, allicin, alliin, allixin, γ-glutamyl-S-2-propenyl cysteine, diallyl disulfide, methyl allyl disulfide, S-allyl-cysteine, and 1,2-vinyldiithin. Allicin has anticancer efficacy in mice having L5178Y lymphoma. The methanolic extract of A. sativum (MEAS) has anticancer activity against MCF7, A549, DU145, and bladder carcinoma cells. [15,16]

Annona muricata

Annona muricata is a member of the Annonaceae family and is usually referred to as Graviola. It comprises acetogenins, β-sitosterol, stigmasterol, phenolic compounds, alkaloids, annoionoside, annoionol A, B, C, lycopene, lutein, among others. It is found in the tropical areas of Central and South America, Western Africa, and Southeast Asia. Acetogenins is the primary component present in the leaves, seeds, bark, and fruit of this plant. Acetogenins obstruct adenosine triphosphate synthesis, hence inhibiting the efflux pump responsible for expelling anticancer agents from the cell. [17] Acetogenins are recognized as hazardous to several cancer cell lines, including pancreatic cancer, breast cancer, colonic adenocarcinoma, liver cancer, and lymphoma. [18]

Azadirachta indica

Azadirachta indica is a member of the Meliaceae family and is native to India and the Indian subcontinent. It comprises nimbin, nimbinine, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol, amino acids, and nimbiol, among others. It has been used for the treatment of cutaneous cancer, oral cancer, breast cancer, prostate cancer, and stomach cancer. [19] The ethanolic extract of Azadirachta indica induces apoptosis, resulting in the killing of prostate cancer cells. It operates in a dose-dependent way and enhances DNA fragmentation. [20]

Catharanthus roseus

Catharanthus roseus is a significant medicinal plant that belongs to the Apocynaceae family. It is well recognized as Madagascar periwinkle. It comprises vinblastine, vincristine, vindesine, vindoline, tabersonine, among others. Catharanthus is indigenous to Madagascar but is now farmed in Tanzania, Kenya, Kisi, and several other nations. [21] This plant is used for the management of cancer, diabetes, fever, and hypertension. [22] Vinblastine and vincristine are often used in the treatment of leukemia and lymphoma. [23]

Curcuma longa

Curcuma longa is referred to as Haldi in Hindi, harida in Sanskrit, and turmeric in English. It is a member of the Zingiberaceae family. This plant is indigenous to Southern Asia and serves as a coloring agent in Bangladeshi and Indian cuisines, among other applications. It comprises curcumin, curcuminoids, essential oil, turmerone, monoterpenes, diarylpentanoids, diterpenes, sesquiterpenes, triterpenoids, sterols, and alkaloids, among others. Curcumin is the active component of this plant, a polyphenol extracted from its rhizome, used for both cancer prevention and therapy. Curcumin has a protective effect by suppressing the proliferation of certain angiogenesis-related and tumor-associated genes. [24] Curcumin has

antiproliferative properties by downregulating many gene expressions, including activator protein 1, NF-kappa B, cyclooxygenase 2, epidermal growth factor receptor 1, nitric oxide synthase, and tumor necrosis factor. [25]

Emblica officinalis

Emblica officinalis is a significant medicinal plant from the Euphorbiaceae family. It comprises ellagic acid, gallic acid, quercetin, kaempferol, phyllemblin, flavonoids, glycosides, and proanthocyanidins. Emblica officinalis is esteemed for its distinctive tannins and flavonoids, which exhibit potent antioxidant and anticancer characteristics. Ellagic acid is a potent antioxidant that may suppress genetic alterations. Ellagic acid also rectifies chromosomal anomalies. Quercetin, extracted from Emblica officinalis, has hepatoprotective properties. Emblica officinalis impedes the proliferation and dissemination of several malignancies, including those of the breast, uterus, pancreas, stomach, liver, and malignant ascites. Emblica officinalis is a superior rejuvenating and antioxidant plant. It is very nutritious and a significant source of Vitamin C, minerals, and amino acids. Emblica officinalis offers protection against several cancers, notably liver cancer, and mitigates the adverse effects of chemotherapy and radiation. [26]

Glycine max

Glycine max is a member of the Fabaceae family and is indigenous to East Asia. Commonly referred to as soybean, it is abundant in selenium, zinc, vitamins, isoflavones, amino acids, phytosterols, and saponins. A research indicated that soybean agglutinin suppresses tumor development in rats. Isoflavones induce cell differentiation, transforming cancer cells into normal cells. [27]

Podophyllum hexandrum

Podophyllum hexeandrum is a member of the Berberidaceae family and is indigenous to the Himalayan area (Uttarkashi) in India. Commonly referred to as May apple, it comprises podophyllotoxin, kaempferol, quercetin, asiragalin, essential oil, and podophyllin. Podophyllotoxin has been used in the treatment of testicular and lung malignancies, as well as certain leukemias. Podophyllotoxin is mostly located in the roots and is used for the treatment of tumors, ulcers, wounds, constipation, and TB. Controlled clinical experiments have shown that podophyllotoxin produces a colchicine-like effect by halting mitosis in metaphase, leading to the death of epithelial cells. The antimitotic actions of podophyllotoxin stem from its capacity to impede microtubule assembly. Podophyllotoxin seems to bind to cellular proteins, facilitating the integration of amino acids into proteins, inhibiting purine synthesis, and obstructing purine incorporation into RNA. [28]

Ocimum sanctum

Ocimum sanctum, generally referred to as Tulsi or Holy Basil, is a member of the Lamiaceae family. The foliage of Ocimum sanctum has 0.7% volatile oil, which consists of about 71% eugenol and 20% methyl eugenol. The oil furthermore has carvacrol and the sesquiterpene hydrocarbon caryophyllene. The extract of fresh leaves and stem of Ocimum sanctum produced many phenolic compounds (antioxidants) including cirsilineol, cirsimaritin, isothymusin, apigenin, and rosameric acid, along with significant amounts of eugenol. Two flavonoids, namely orientin and vicenin, have been extracted from the aqueous leaf extract of OS. Ursolic acid, apigenin, luteolin, apigenin-7-O-glucuronide, luteolin-7-O-glucuronide, orientin, and molludistin have been extracted from the leaf extract. Ocimum sanctum comprises many sesquiterpenes and monoterpenes, including bornyl acetate, elemene, neral, pinenes, camphene, campesterol, cholesterol, stigmasterol, and sitosterol. Eugenol, orientin, and vicenin suppress the development and dissemination of several malignancies, including breast cancer, liver cancer, and sarcomas, notably fibrosarcoma, by obstructing the flow of oxygen and nutrition to cancer cells, ultimately leading to their demise via starvation. Ursolic acid extracted from Ocimum sanctum has immune-boosting and tissue-protective properties. Polysaccharides extracted from Ocimum sanctum have antioxidant and radioprotective characteristics. Ocimum sanctum offers protection against several malignancies, especially breast cancer, and mitigates the adverse effects of chemotherapy and radiation. [29]

Oroxylum indicum

Oroxylum indicum is a member of the Bigoniaceae family and is indigenous to the Indian subcontinent. It comprises baicalein, chrysin, oroxylin, scutellarein, pinostrobin, and stigmast-7-en-3-ol. Numerous studies have shown the anticancer efficacy of this plant across numerous models. The 95% ethanol extract of this plant exhibited cytotoxic effects on Hep2 cell lines at a concentration of 0.05%. [30]. Baicalein had an anticancer impact on human cancer cell lines, inhibiting the growth of HL-60 cell lines by up to 50% at concentrations of 25-30 μM. [31] The aqueous and methanolic extracts of Oroxylum indicum shown cytotoxicity in certain examined cell lines, and both extracts had a modest capacity for DNA protection against oxidative stress. [32]

Punica granatum

Punica granatum, a deciduous shrub that produces fruit, is generally referred to as pomegranate and belongs to the Lythraceae family. It originated in Iran and has been grown since antiquity throughout the Mediterranean area and northern India. It is a substantial source of phenolic compounds, ellagitannins (ETs), and ellagic acid (EA), which are biologically transformed into urolithins by the gut bacteria. Urolithins are present at elevated levels in colorectal cancer patients, and they impede cancer cell growth and disrupt the cell cycle. [27]. A research demonstrated that compounds produced from pomegranate ellagitannins shown anti-proliferative and anti-aromatase properties in breast cancer cells. [28]

Solanum nigrum

Solanum nigrum, popularly referred to as Black Nightshade, is a member of the Solanaceae family. Flavonoids (e.g., quercetin) and alkaloids (such as solasodine, solanine, and solamargine) are the primary phytoconstituents of the whole Solanum nigrum plant or its fruit, which have been shown to have activity against different tumors. Solamargine and solasonine impede the proliferation and dissemination of several malignancies, including breast, liver, lung, and cystic tumors, choriocarcinoma or chorioadenoma, and leukemia. Solanine and solamergine have potent anticancer effects on mouse tumors. Steroidal glycosides (spirostane, furostane, spirosolane, and pregnane) extracted from Solanum nigrum impede the proliferation and dissemination of colon cancer and pheochromocytoma. Glycoproteins derived from Solanum nigrum have antiproliferative and apoptotic properties against colon and breast malignancies. The polysaccharides of this plant have a substantial inhibitory impact on the proliferation of cervical cancer. S. nigrum impedes the proliferation and dissemination of liver cancer via two separate anticancer mechanisms: apoptosis (programmed cell death) and autophagy (autophagocytosis). Elevated dosages of Solanum nigrum precipitate apoptotic cell death, but diminished amounts result in autophagic cell death of neoplastic cells. Lunasin, extracted from S. nigrum, is a peptide that prevents cancer. S. nigrum and S. lyrati impede the proliferation and dissemination of gastric carcinoma, sarcomas, malignant ascites, and leukemia. The extract of Solanum nigrum leaves has an inhibiting impact on S 180, V 14, and Ec tumor models. [33]

Withania somnifera

Withania somnifera is referred to as ashwagandha in Hindi and Sanskrit, and as winter cherry in English. It is a member of the Solanaceae family and comprises withanolides, withaferins, anferine, isopellertierine, and sitoindoside. This plant mostly thrives in India (notably Madhya Pradesh), Pakistan, Bangladesh, Sri Lanka, and some regions of Northern Africa. Owing to its therapeutic characteristics, leaves and roots have been used in the Indian traditional medicine system and are sold internationally. Twenty-one withanolides extracted from Withania somnifera have structural and functional similarities to ginsenosides, the active compounds of Panax ginseng. Withanolides (including Withaferin A, Sitoindoside IX, Physagulin D, Withanoside IV, and Viscosalactone B) impede the development and dissemination of different malignancies, including breast, lung, colon, and central nervous system tumors, owing to their antiproliferative and antiangiogenic characteristics. Withaferin-A, the principal withanolide, inhibits the development and metastasis of several malignancies, including those of the breast, cervix, colon, prostate, nasopharynx, larynx, malignant ascites, and sarcomas, by causing apoptosis. Withaferin A is efficacious in both androgen-responsive and androgen-refractory prostate tumors.

Sitoindosides VII-X and Withaferin A possess potent antioxidant, antistress, immunomodulatory, anti-inflammatory, and anti-aging activities. Withanolide D suppresses metastatic colony growth in the lungs caused by malignant melanoma. Ashwagandhanolide, a novel dimeric withanolide extracted from Withania somnifera, impedes the proliferation and dissemination of breast, stomach, colon, lung, and central nervous system malignancies. Withania somnifera has immunoenhancing, haemopoietic, and neuroprotective attributes, while mitigating the adverse effects of radiation and chemotherapy. [21]

Table 1: Major groups of anticancer compounds derived from plant:

Sl No:	Plant source	Phytoconstituent	Properties
1	*Aloe vera*, Liliaceae	Aloe emodin	**Induction of apoptosis**
2	*Allium sativum*, Liliaceae	Organo sulfur compounds	**Induce apoptosis**
3	*Annona muricata,* Annonaceae	Acetogenins	**Inhibits mitochondrial complex I, involved in oxidative phosphorylation and ATP synthesis.**
4	*Azadirachta indica*, Meliaceae	Triterpenoids- Nimbine, Nimbinine, Nimbidic acid	**Inhibit proliferation, induce apoptosis, reduce cellular oxidative stress**
5	*Catharanthus roseus*, Apocynaceae	Vincristine , Vinblastine	**Arrest cancer cell proliferation by binding to tubulin in mitotic spindle.**
6	*Curcuma longa*, Zingiberaceae	Curcumin	**Induce apoptosis, inhibit proliferation**
7	*Embilica officinalis*, Euphorbiaceae	Ellagic acid	**Induce apoptosis**
8	*Glycine max*, Fabaceae	Genistein	**Arrest cell growth and proliferatin**
9	*Podophyllum hexandrum,* Berberidaceae	Podophyllotoxin	**Inhibit mitogen induced lymphocytic proliferation and immunoglobulin synthesis.**
10	*Ocimum sanctum,* Lamiaceae	Eugenol, orientin, vicenin	**Blocks the supply of oxygen and nutrients to cancer cells and kill them by starving.**
11	*Oroxylum indicum,* Bigoniaceae	Baicalein	**Inhibits the proliferation of cancer cells.**
12	*Punica granatum,* Lythraceae	Ellagitannins, Ellagic acid	**Inhibits the proliferation of cancer cells by gets converted to urolithins.**
13	*Solanum nigrum*, Solanaceae	Solamargine, solasonine	**Kills the cancer cells by apoptosis and autophagy.**
14	*Withania somnifera,* Solanaceae	Withanolides	**Inhibits proliferation and induce apoptosis.**
15	***Zingiber officinale*, Zingiberaceae**	**Gingeroles**	**Induce apoptosis and autophagy.**

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