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Anticancer Potential of Medicinal Plants: A Comprehensive Review

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Abstract: Cancer poses a significant global health challenge, affecting both developed and developing nations and ranking second only to cardiovascular disease as a leading cause of death. It results from abnormal cell growth and can often be fatal. Due to the high mortality rates and severe side effects associated with conventional treatments like chemotherapy and radiation therapy, many cancer patients turn to alternative and complementary therapies. Medicinal plants have been used therapeutically since ancient times, and more than half of modern pharmaceuticals are derived from natural sources, underscoring their medicinal potential. These plants contain a variety of biologically active compounds, such as alkaloids, flavonoids, phenolics, carotenoids, and other secondary metabolites. These compounds demonstrate anticancer properties and may help prevent cancer initiation, progression, and promotion. Utilizing medicinal plants in healthcare offers advantages over synthetic medicines, given their natural origins and associated benefits. This review highlights the importance of exploring the anticancer properties of medicinal plants and their phytochemical constituents to advance the development of new and improved cancer therapies. Such research is crucial in addressing the global impact of cancer. In summary, this review emphasizes the critical role of medicinal plants as a valuable resource in combating cancer and underscores the necessity for ongoing research and development in this field.

Keywords: Antioxidants, Cancer, Medicinal Plants, Phytochemical compounds

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Introduction

Cancer is characterized by the abnormal growth and invasion of cells in the body, potentially leading to fatal outcomes as these cells disrupt and destroy normal tissues. It often stems from bodily

imbalances, which, when corrected, may aid in its treatment. Despite the billions invested in cancer research, its exact nature remains incompletely understood. Each year, millions of people worldwide receive cancer diagnoses, resulting in significant mortality rates (Bray *et al.*, 2018). According to the American Cancer Society, cancer-related deaths account for 2–3% of global annual deaths, totalling approximately 3.5 million fatalities annually. The primary cause of death is lung cancer, followed by cancers of the breast, colorectal region, stomach, and liver. Some common characteristics of cancers include evasion of apoptosis (Snellenberg *et al.*, 2014), angio-genesis, uncontrolled replication (Mar *et al.*, 2015), growth signal production (Courtnay *et al.*, 2015), insensitivity to anti-growth signals, and metastasis. These features enable cancer cells to sustain continuous growth, long-term survival, and the ability to invade normal cells. If these activities are not inhibited, cancer cells will continue to proliferate, overwhelm, and ultimately kill the patient (Shonia *et al.*, 2019). In 2020, cancer claimed the lives of 10 million people, and over 19 million individuals were affected by the disease. Normally, cells in the body proliferate in a regulated manner, essential for the proper functioning of bodily systems. However, cancer arises when cells grow uncontrollably or abnormally, and this growth is not confined to a specific organ but can spread to other tissues. Typically, cells can detect and repair DNA damage (Henderson *et al.*, 2000). When normal cells are damaged beyond repair, they undergo a process called apoptosis, or programmed cell death. A tumor refers to an abnormal mass of cells. Benign tumors develop locally and do not spread, whereas malignant tumors grow rapidly and invade nearby tissues through a process known as metastasis (Goubran *et al.*, 2014). Malignant tumors can spread to other parts of the body via the bloodstream or lymphatic system, affecting organs such as the lungs, liver, brain, bones, and others. While some metastatic cancers can be cured, many remain incurable. There are over 100 types of cancer, with the most common being skin cancer, breast cancer, lung cancer, liver cancer, colon cancer, lymphoma, stomach cancer, prostate cancer, and cervical cancer.

Several chemo-preventive agents are available for treating cancer, their use is limited due to associated toxicities. Consequently, there is a growing focus on alternative treatments and therapies to combat cancer. The important preventive methods for most of the cancers include dietary changes, stopping the use of tobacco products, treating inflammatory diseases effectively, and taking nutritional supplements that aid immune functions. Current treatment for the cancer includes radiotherapy, chemotherapy and chemically derived drugs. Most commonly used cancer chemotherapy includes anti-metabolites, alkylating agents, platinum analogs and anti-tumor antibiotics.

Medicinal plants have played a crucial role in treating human diseases since ancient times. Approximately 80-85% of the global population relies on traditional medicines for their primary healthcare needs, often utilizing plant extracts or bioactive compounds extensively (Cragg and Newman, 2005). These plants are renowned for their immunomodulatory, antioxidant, and anticancer properties. They stimulate both non-specific and specific immunity, enhancing the body's resistance to infections by restoring physiological balance and conditioning tissues. Many medicinal plants are currently being investigated for their anticancer potential, with the goal of identifying key compounds that can inhibit cancer progression (Pandey and Madhuri, 2009). Secondary metabolites found in these plants, such as flavonoids, alkaloids, terpenoids, and steroids, exhibit diverse pharmacological effects. Several therapeutic plants show promise in restraining the proliferation of cancer cells. Therefore, this review provides an overview of various medicinal plants and their primary bioactive components utilized in cancer treatment (Madhusudan and Middleton, 2005)

The data was collected via Science Direct, Web of Science, PubMed, Clarivate Analytical, Google

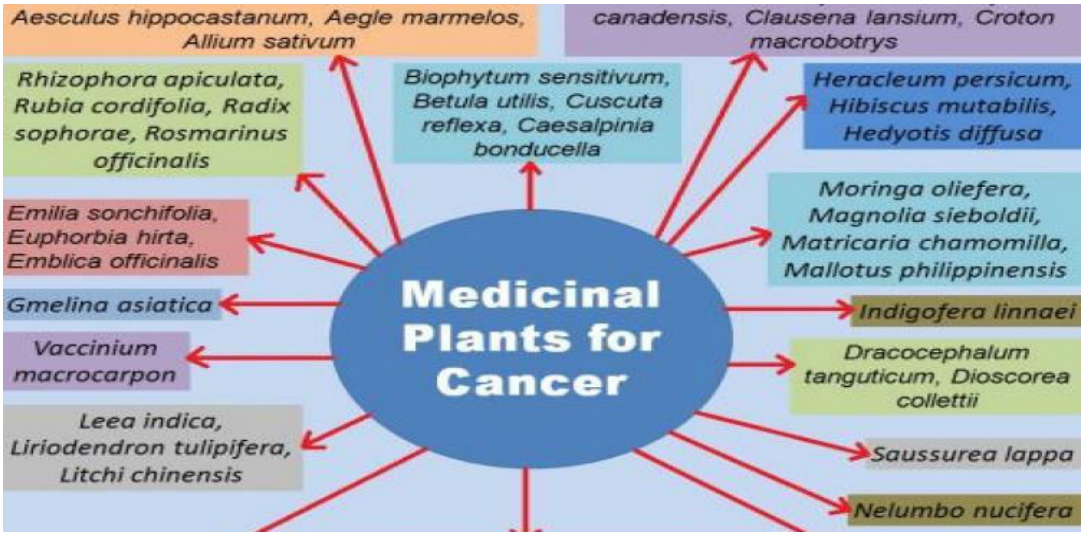

Fig. 1: Medicinal plants used for treatment of cancer.

Scholar, Core Collection, Scopus, MDPI, and Scientific Electronic Library Online (SciELO). The used search terms were: anticancer potential of medicinal plants, anticancer activity, anticancer methods, pharmacological activity.

Medicinal plants having anticancer activity

Anticancer drugs derived from plants are effective inhibitors of cancer cell lines, making these plants highly sought after for their ability to produce medically significant compounds. Numerous medicinal plants have been used for cancer prevention and treatment (Fig. 1) in traditional cultures worldwide. Compounds such as curcumin, allicin, vincristine, vinblastine, silymarin, hecogenin, glycyrrhizin, berberine, camptothecin, gallic acid, and various other bioactive constituents, which are the key active ingredients in these plants, have shown considerable promise for future cancer treatments (Fabricant and Farnsworth, 2001).

Anticancer medicinal Plants (Table 1)

Allium sativum:

Allium sativum, commonly known as garlic, belongs to the Alliaceae family and is native to the region between the Mediterranean and China. It contains various bioactive compounds, including ajoene, allicin, alliin, allixin, γ-glutamyl-S-2-propenyl cysteine, diallyl disulfide, methyl allyl disulfide, S-allyl-cysteine, and 1,2-vinyldiithin. Notably, allicin has demonstrated antitumor activity in mice bearing L5178Y lymphoma. The methanolic extract of *Allium sativum* (MEAS) exhibits anticancer effects against MCF7 (breast cancer), A549 (lung cancer), DU145 (prostate cancer), and bladder carcinoma cells (Karmakar *et al.*, 2011).

Aloe vera:

Aloe vera (Ghrit kumara), belonging to the Asphodelaceae family, exhibits a wide range of pharmaceutical activities (Pooja, 2017). The leaves of *A. vera* contain various secondary metabolites such as doxorubicin, butyl p-tolyl sulphide, lupeol, isobarbaloin, 6-methyl-4-chromanone, barbaloin, lectin, emodin, aloe-emodin, aloesin, acemannan, anthrone-C-glycosides, sitosterol, alexin-B, campesterol, and butylated hydroxyanisole. Isolated compounds from *A. vera* leaves were tested against ovarian cancer (OVCAR-3), human colon cancer (HCT-116 and IGROV-1), and breast cancer (MCF-7) cell lines using the MTT assay to evaluate their *in vitro* cytotoxic activity (Karpagam *et al.*, 2019).

Azadirachta indica:

Azadirachta indica, also known as neem, belongs

to the Meliaceae family and is found in India and the Indian subcontinent. It contains various bioactive compounds, including nimbin, nimbanene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol, and amino acid nimbiol (Savarkar and Deshmukh, 2011). Neem has been used for the treatment of skin cancer, buccal cancer, mammary cancer, prostate cancer, and gastric cancer. The ethanolic extract of *Azadirachta indica* induces apoptosis in prostate cancer cells, causing cell death in a dose-dependent manner and increasing DNA fragmentation (Pandey and Madhuri, 2009).

Boswellia serrata:

Boswellia serrata, also known as guggul, is a member of the Burseraceae family. It is commonly used to treat inflammatory conditions such as viral infections, fungal diseases, asthma, and more (Sudhanshu *et al.*, 2020). Studies have demonstrated that the oleo gum resin extract of *Boswellia serrata* exhibits significant anticancer effects on various human cancer cell lines, including those associated with laryngeal carcinoma, bladder carcinoma, and myelogenous leukaemia (Nand *et al.*, 2019).

Catharanthus roseus:

Catharanthus roseus, commonly known as Madagascar periwinkle, is a valuable medicinal plant belonging to the Apocynaceae family. Originally native to Madagascar, it is now widely cultivated in countries like Tanzania, Kenya, and Kisi. This plant is rich in bioactive compounds, including vinblastine, vincristine, ajmalicine, and serpentine (Velasco *et al.*, 2012). Vinblastine and vincristine, in particular, are used in the treatment of cancer, diabetes, fever, and hypertension. They are also commonly prescribed for cases of leukemia and lymphoma (Don, 2003).

Centella asiatica

Centella asiatica, belonging to the Apiaceae family, is a traditional medicinal plant of India and China (Bisht *et al.*, 2011). The ethyl acetate, aqueous, acetone, and methanol extracts of *C. asiatica* leaves contain alkaloids that have been assessed for their cytotoxic effects on the human lung epithelial carcinoma (A-549) cell line using a colorimetric MTT assay. *C. asiatica* leaf extracts demonstrated significant cytotoxic activity. After 48 hours of incubation, the ethyl acetate extract of *C. asiatica* leaves exhibited the highest cytotoxic activity, with an IC50 of 82 µg/mL (Iwan *et al.*, 2016).

Curcuma longa:

Curcuma longa, commonly known as haldi in Hindi, harida in Sanskrit, and turmeric in English, belongs to the Zingiberaceae family. Native to Southern Asia, this plant is used not only as a coloring agent in Bangladeshi and Indian cuisine but also for various other purposes. It contains a variety of compounds including curcumin, curcuminoids, essential oil, turmerone, monoterpenes, diterpenes, sesquiterpenes, triterpenoids, sterols, and alkaloids. Curcumin, the active ingredient in turmeric, is a polyphenol derived from the plant's rhizome and is used for both cancer prevention and treatment. Curcumin exhibits a protective effect by inhibiting the growth of several angiogenesis-associated and tumor-associated genes (Van Der Heijden *et al.*, 2004). It also possesses anti-proliferative properties by downregulating the expression of numerous genes, including activator protein 1, NF-kappa B, cyclooxygenase 2, epidermal growth factor receptor 1, nitric oxide synthase, and tumor necrosis factor (Pratheeshkumar *et al.*, 2012).

Linum usitatissimum:

Linum usitatissimum, a member of the Linaceae family, is abundant in lignans. This plant, a short-lived perennial, thrives in areas of western and southern Europe as well as western Asia. The plant lignans are transformed into mammalian lignans (enterodiol and enterolactone) through bacterial fermentation in the colon. These mammalian lignans display anti-carcinogenic properties as they resemble estrogens and can bind to estrogen receptors, thereby impeding the growth of estrogen-stimulated breast cancer. Research has shown that root extract of *Linum usitatissimum* can effectively inhibit cell

Table 1: Medicinal plants and anticancer compounds

S. No.	Plant Name	Family	Anticancer compounds	References
1	*Aegle marmelos*	Rutaceae	Lupeol	Govind (2011)
2	*Beberis aristata*	Berberidaceae	Berberine, *β*-sitosterol, palmatine, aromoline, berbamine, jatorrhizine, quercetin, columbamine, caffeic acid, chlorogenic acid and rutin	Saranya *et al.* (2019); Ibrahim *et al.* (2016)
3	*Cleome viscosa*	Cleomaceae	aspartic acid, ursolic acid, chrysosplenetin,	Anuj *et al.* (2018); Subhash *et al.* (2021)
4	*Curcuma longa*	Zingiberaceae	Curcumin, glucuronide, demethoxycurcumin and bisdemethoxycurcumin	Ahmad *et al.* (2015)
5	*Diphylleiagrayi*	Berberidaceae	Diphyllin	Cragg *et al.* (2005)
6	*Dioscorea bulbifera*	Dioscoreaceae	Diosgenin	Hilda *et al.* (2019)
7	*Glycyrrhizaglabra*	Leguminosae	Glycyrrhizin	Jung *et al.* (2001)
8	*Glycyrrhiza glabra*	Leguminosae	Glycyrrhizin	Ambasta (2000)
9	*Nelumbo nucifera*	Nelumbonaceae	Liensinine, isoliensinine, roemerine, neferine and procyanidins.	Xin *et al.* (2017)
10	*Indigofera tinctoria*	Leguminosae	Indirubins	Cragg and Newman (2005)
11	*Phyllanthus amarus*	Euphorbiaceae	Quercetin, phyltetralin, phyllanthin, lignans niranthin	Saranya *et al.* (2019)
12	*Podophyllum emodii*	Berberidaceae	Epipodophyllotoxin	Henry *et al.* (2002)
13	*Rubia cordifolia*	Rubiaceae	Rubidianin, rubiadin, purpurin,	Govind (2011)
14	*Taxus brevifolia*	Taxaceae	Taxanes,taxolcepholomannine	Prota *et al.* (2013)
15	*Ziziphus nummularia*	Rhamnaceae	Betulin, betulinic acid, oleic acid, squalene, tetratetracontane,	Joelle *et al.* (2021)

proliferation and vitality in the MCF7 human breast cell line without inducing significant cytotoxicity (Szewczyk *et al.*, 2014).

Rubia cordifolia:

Rubia cordifolia also known as Indian madder, from the Rubiaceae family, contains various compounds like cordifoliol, cordifodiol, anthraquinone, and alizarin. A component called mollugin in this plant has shown promising anticancer effects against lymphoid leukemia in mice and has demonstrated the inhibition of passive cutaneous anaphylaxis in rats (Devi and Siril, 2014). Furthermore, quinones and hexa-

peptides found in Indian madder have displayed potential antitumor properties by binding to the 80S ribosome, which disrupts the protein synthesis process crucial for tumor growth (Gupta *et al.*, 1999).

Tinospora cordifolia:

Tinospora cordifolia, also known as Giloe or Guduchi and part of the Menispermaceae family, can be found in various regions including China, Japan, India, Europe, and East Asia (Singh *et al.*, 2019). The extract derived from T. cordifolia is utilized in the treatment of brain, intestine, breast, head, vaginal, prostate, and neck cancers. Studies have shown that the methanolic, aqueous, and ethanolic extracts of *T. cordifolia* stems have the ability to induce programmed cell death and inhibit apoptosis. The cytotoxic effects of DMSO and ethanolic extracts from *T. cordifolia* stems were tested against murine monocyte/ macrophages (J-774-A-1), human melanoma (A-375), and human breast cancer (MCF-7) cell lines using the MTT assay and TBE method (Ani *et al.*, 2008).

Withania somnifera:

Withania somnifera is commonly known as ashwagandha in Hindi and Sanskrit, and winter cherry in English. It belongs to the Solanaceae family and contains withanolides, withaferins, anferine, isopellertierine and sitoindosise. This plant grows majorly in India (especially Madhya Pradesh), Pakistan, Bangladesh, Sri Lanka and parts of Northern Africa. Due to its medicinal properties, leaves and roots have been used in the Indian traditional system of medicine and marketed globally. Extract of *Withania somnifera* modulates various biological responses (Winters *et al.*, 2006). It has been used in various preparations for its anti-stress, anti-peroxidative, anti-ageing, anti-inflammatory, anti-oxidant, anti-tumor, cardiotonic, and immunomodulatory properties.Withanolide A and withaferin A is the main constitute of this plant. Withaferin A which is mostly present in the leaves produces rapid apoptosis in the cancer cells. Cell signaling pathways by this plant formulation largely depends up on the high content of withferin A present in it (Alam *et al.*, 2013).

Conclusion

All of the fundamental medicines are found in plants. Plant bioactive compounds have been shown to suppress cancer. The current study aims to compile a list of plants containing active phytochemicals with anti-cancer potential, as well as data supporting their use in cancer therapy, animal models, and their pharmacological properties. The chosen plants with anticancer properties showed essential role in battling oral, breast, colon, lung, stomach, cervical, hepatic, and blood cancer malignancies. The secondary metabolites present in the plant extracts inhibited cancer cells by causing DNA damage and activating apoptosis-inducing enzymes *in vitro*. Also, *in vivo* studies of these plants and their phytochemical actions revealed significant outcomes in cancer suppression in animal models.

Conflict of Interest

The authors declare no conflicts of interest.

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