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Review Article

**A REVIEW ON HERBAL AND MEDICINAL PLANTS:
A NEW DIMENSION FOR THE ANTICANCER
TREATMENT**

Reshma B V*

Assistant Professor, Department of Pharmacology, SKCPRC, Trivandrum, Kerala-
695502, India**Article Received:** August 2019 **Accepted:** September 2019 **Published:** October 2019**Abstract:**

Cancer is one of the leading and most fatal diseases in the present decade, every year millions of people die because of various types of cancers. Many aspects relate to the cause of disease besides heredity, food habits, smoking, nutritional behaviours, radiation etc. The successful cancer therapy till now has been under research, only chemotherapy and radiation treatments are at times successful and much times toxic and lethal. Alternative and less toxic medication is very much in need towards the disease, the use of concepts of herbal medicine with knowledge of Ayurveda could present better drug leads towards the inhibitory treatment of Cancer. Natural products especially plants have been used for the treatment of various diseases promisingly from the decades by knowledge of Ayurveda in our country Nature shows plethora of medicinal plants with anticancer and antioxidant activities which may suppress the disease completely. The search for cancer drugs from natural sources started in late 1960s, lead to discoveries of vincristine, vinblastine, camptothecin and taxol. This review certainly focuses on the herbal medicine from natural products for the discovery of new drug leads towards the cancer treatment. From the study it is concluded that the herbal and medicinal plants are highly useful for the treatment of cancer.

Keywords: Ayurveda, Cancer, Chemotherapy, Herbal medicine, Potent compounds (Secondary metabolites).**Corresponding author:****Reshma B. V,**Assistant Professor SKCPRC,
Thiruvananthapuram, Kerala, India.Email id: reshmabv93@gmail.com,

Contact number: 9526793086

QR code



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INTRODUCTION:

Cancer is the second leading cause of death worldwide. Cancer remains one of the leading causes of morbidity and mortality globally. Although great advancements have been made in the treatment and control of cancer progression, significant deficiencies and room for improvement remain. A number of undesired side effects sometimes occur during chemotherapy. Natural therapies, such as the use of plant-derived products in cancer treatment, may reduce adverse side effects. Currently, a few plant products are being used to treat cancer. However, a myriad of many plant products exist that have shown very promising anti-cancer properties *in vitro*, but have yet to be evaluated in humans[1]. Further study is required to determine the efficacy of these plant products in treating cancers in humans. This review will focus on the various plant-derived chemical compounds that have, in recent years, shown promise as anticancer agents and will outline their potential mechanism of action.

Chemotherapy is routinely used for cancer treatment. Since cancer cells lose many of the regulatory functions present in normal cells, they continue to divide when normal cells do not. This feature makes cancer cells susceptible to chemotherapeutic drugs. Approximately five decades of systemic drug discovery and development have resulted in the establishment of a large collection of useful chemotherapeutic agents. However, chemotherapeutic treatments are not devoid of their own intrinsic problems. Various kinds of toxicities may occur as a result of chemotherapeutic treatments. For example, 5-fluorouracil, a common chemotherapeutic agent, is known to cause myelotoxicity, cardiotoxicity and has even been shown to act as a vasospastic agent in rare but documented cases.[2] Another widely used chemodrug, doxorubicin causes cardiac toxicity, renal toxicity, and myelotoxicity. Similarly, bleomycin a well known chemotherapeutic agent, is known for its pulmonary toxicity. In addition, bleomycin shows cutaneous toxicity. Cyclophosphamide, a drug to treat many malignant conditions, has been shown to have bladder toxicity in the form of hemorrhagic cystitis, immunosuppression, alopecia and at high doses cardiotoxicity. So there are different adverse reactions associated with chemotherapy. So to overcome these shortcomings we can focus on the herbal and medicinal plants.

The toxicity of chemotherapeutic drugs sometimes creates a significant problem in the treatment of cancer using allopathy or established medicine. Various therapies have been propounded for the

treatment of cancer, many of which use plant-derived products. There are four classes of plant-derived anticancer agents in the market today, the vinca alkaloids (vinblastine, vincristine and vindesine), the epipodophyllotoxins (etoposide and teniposide), the taxanes (paclitaxel and docetaxel) and the camptothecin derivatives (camptotecin and irinotecan). Plants still have enormous potential to provide newer drugs and as such are a reservoir of natural chemicals that may provide chemoprotective potential against cancer. Recently, Taneja and Qazi, have suggested a number of compounds from medicinal plants with potential anti-cancer activities

Natural products especially plants have been used for the treatment of various diseases promisingly from the decades by knowledge of Ayurveda in our country. In developing countries herbal medicine is the source of new discoveries for the new drug leads towards various healthcare issues and synthesis of new formulations. Traditional medicine when compared to other sources of drug discoveries had contributed many novel therapeutic compounds for preventive and curative medicine. Secondary metabolites like polyphenols, terpenes and alkaloids have been reported to possess antimutagenic and anticancer properties in many studies.[3] Several researches on cancer drugs and discovery of new lead molecules towards anticancer activity by using medicinal plants was put forward, reason to explain- as medicinal plants are reservoirs of antioxidants and possess no toxicity as compared to the modern drugs; concept of combining Ayurveda with advanced drug discovery may bring some lead compounds towards various human sufferings.

Natural lead molecules towards treatment of Cancer

Cancer is one of the most life threatening diseases and possess many health hazard in both developed and developing countries, characterized by irregular proliferation of cells. Every biological change can be seen when a normal cell progresses to cancerous one. Since many treatments are available for cancer therapy still cancer is the 2nd leading cause of death in the globe, Chemotherapy and modern drugs for treatment of cancer reported more side effects in the patients treated. Every year, millions of people are diagnosed with cancer, leading to death. Cancer kills about 3500 million people annually all over the world; it accounts more than 2-3% of the annual deaths recorded worldwide. Treatment of Cancer is somewhat successful with chemopreventive agents but usage is left against risk because of their toxicity. Smoking, dietary imbalances, hormones and chronic infections leading to chronic inflammation accounts high casuals for cancer

disease. In view of serious side effects of chemotherapy and radiation treatment for cancer, there should be immediate search for alternative and safer methods of treatment. As age old saying always prevention is better than cure, cancers can be preventive by proper dietary habits, saying no to tobacco, treatment of inflammatory diseases effectively, and taking nutritional supplements that aid immune functions. Chemotherapy, presently the only major treatment modality used for the control of advanced stages of malignancies, exhibits severe toxicity on normal tissues. The search for cancer drugs from natural sources started with discovery of Podophyllotoxin in late 1960s, further lead to discoveries of vincristine, vinblastine, camptothecin and taxol.[4] Nature counting more than 1000 species of plant varieties which possess significant anti-cancer properties. Taxol, one of the most outstanding agents, has been found beneficial in treatment of refractory ovarian, breast and other cancers, Podophyllotoxin, synthetic modification of this molecule led to the development of Etoposide, known to be effective for small cell cancers, of the lungs and testes. The discovery of medicinally important herbs and their mechanism of action would provide an alternative and effective treatment towards the cancer prevention. Since decades plethora of drugs have been developed from potent compounds which are isolated from medicinal plants. The process of drug discovery and development includes three main following research approaches

- (1) Bioactivity- based on mechanism of specific action-directed isolation and characterization of active compounds,
- (2) Rational drug design - involves modification and synthesis of analog, and
- (3) Mechanism of action studies.

Traditional medicine and knowledge of Ayurveda help in the discovery of new drug leads with high activity and low toxicity for cancer therapy, initial research focuses on the isolation of bioactive lead compounds, chemical modification and improving other pharmacological profiles. The use of traditional medicine for treatment of various diseases is continued in the Indian sub- continent with greater botanical diversity. Ethno historical accounts shows that medicinal plants have been used as a remedy for various human ailments, the reason of using these plants is that they are reservoirs of potent chemical compounds which acts as a curative medicine with fewer side effects. Over the past decade, healthcare system is all around the herbal medicine and gained global importance, making an impact on both world health and international trade. Due to the low economic rate of the majority of population in developing countries

and high cost of Western medicine, herbal medicine has a long and uninterrupted history of continuous usage by a large proportion of the population in the developing countries. In addition from their cultural and spiritual points herbal medicines are more acceptable in these countries. Cancer would be probably the most important genetic disease to carry out treatment with medicinal plants.

Microtubulin assembly into coiled spiral aggregates induced by self-association of tubulin is under the influence and mode of action of Vincristine. Etoposide is a topoisomerase II inhibitor causes DNA breaks, whereas topoisomerase I is inhibited by the action of Docetaxel. Drugs made of synthetic chemistry and use of technological combinatorial chemistry in the synthesis of new leads, still today drugs derived from natural product make an enormous contribution to drug discovery.[5] Nature is an attractive source of new therapeutic candidate compounds as a tremendous chemical diversity is found in millions of species of plants, several plant-derived compounds are currently successfully employed in cancer treatment.

AYURVEDIC CONCEPT OF CANCER

Cancer described as “*granthi*” and “*arbuda*” in Charaka and Sushruta Samhita by two great Indians and explained the disease conditions reasons responsible behind the cause of cancer. Charaka and Sushruta explained cancer as inflammatory or devoid of inflammation, based on the doshas involved. Three doshas “*Vata, Pitta and Kapha*” in body are responsible for disease and the balanced coordination of these doshas in body, mind and consciousness is the definition of health in Ayurveda. A morbid condition arises in cancer is the state where all three major body humors lose mutual coordination and it is explained.[6] as *Tridoshicarbudas* in Ayurveda. In ayurveda the concept of Neoplasm shows various clinical symptoms. *varous types of cancers were much earlier classified in to three groups in ayurveda. The three groups divided in ayurveda based on their occurrence.*

Group I: malignancies which includes sarcomas, leukaemia, oral cancer, and incurable or malignant ulcers.

Group II: Inflammatory conditions that can be altered to a probable malignancies, such as ulcers and growths under certain influences like radiation, change in dietary habits, stress, smoking etc. Examples of these are growth of lips, incurable thyroid tumour, abdominal tumours like carcinomas of the stomach and

liver or lymphomas.

Group III: Diseases in which there is a possibility of malignancy, such as incurable jaundice, intreatable sinusitis.

PLANTS USED FOR CANCER TREATMENT

The annual deaths across the globe according to American cancer society accounts for more than 3 million cancer deaths, ongoing research is being done throughout the world to seek out effective treatments for cancer, Chemotherapy which includes the high risk dosage of chemical drugs

leading to high toxic cases at times. Medicinal plants relieve and treat cancer by making use of the compounds naturally present with antioxidant, anticancer activities that are known to inhibit or kill carcinogenic cells, Some plants may contain properties that naturally have the ability to prevent the spread or risk of developing various forms of cancer.[7] Some examples of plants that may be used for cancer treatment are discussed with their respective advancements are listed in below

Some examples of secondary metabolites having anticancerous activity

Drug	Medical use	Mechanism of action
Vinblastine	Breast, lymphoma, germ-cell and renal cancer	Inhibits cell proliferation by acts as mitotic block
Vincristine	Leukemia, lymphoma, breast, lung, pediatric solid cancers and others	It inhibits cell proliferation by acts as mitotic block
Taxol	Anticancer agent	Antimitotic agent
Docetaxel	Breast and lung cancer	Prevents mitosis by binding to microtubules
Topotecan	Ovarian, lung and pediatric cancer	Through inhibition of DNA topoisomerase I
Irinotecan	Colorectal and lung cancer	Through inhibition of DNA topoisomerase I

The following are the list of plants which are used for the treatment of cancer

Achillea wilhelmsii

Achillea plant with scientific name *Achillea wilhelmsii* is from Asteraceae order and Compositae genus. *Achillea* has different species but *Achillea wilhelmsii* is more frequent in Iran and grows in different areas. *Achillea wilhelmsii* is a gramineous, perennial, and short plant of 15 to 40 cm.

Methanol extracts and essence of leaves of this plant have cytotoxic effects on colon cancer cells (HT-29) and cytotoxic effects of essence are higher. In other studies, effects of methanol extracts of plant's leaves against cell lineage of colon cancer and cancer of stomach and breast are shown.²³ Methanol extract of plant contains phenol

compounds, especially flavonoids, which suppress reproduction of cancer cells through inducing apoptosis. One of the most important monoterpene compounds of this plant that causes apoptosis in human melanoma cells is 1,8- cineole and α -piene in plants' leaf essence.[8]

***Allium sativum* L**

Allium sativum is a plant from Aparagales order, Amaryllidaceae family, Allianceae subfamily and *Allium* genus. *Allium sativum* is a garmineous and permanent plant, with a stem size of 40 cm. Its underground part is inflated and composed of 5 to 12 parts enclosed in fine and slender membranes in gray-white. Its leaf is thin and filet in dark green, and its flowers are small and pink like an umbrella at end of the stem.[9]

Various research have shown that *Allium sativum* and organosulfuric compounds reduce the risk of cancer in breast, larynx, colon, skin, womb, gullet, bladder, and lung. In other research, we refer to the role of the most important *Allium sativum* compound, that is, Allicin, and the antitumor characteristics of this compound on breast and prostate cancer are proved. This compound induces planned death of cells and has a anticancer role. When *Allium sativum* is crushed and cracked up, Allicin 1, under the effect of an enzyme, changes to Allicin 2. Allicin is a proliferation inhibitor of malignant human cells. Ajoene is another compound that suppresses proliferation of leukemia and will cause planned death of cell.[10]

Ammi majus

A white flower with scientific name *Ammi majus* belongs to Apiaceae family, and it is an annual and dicotyledonous plant with autumn germination. It is a long and thin plant that grows to 100 cm in general conditions, in wet and soft lands, saline grassland, and coastal areas. This plant is cultivated in Europe and Mediterranean area, western Asia, and even in India.[11]

The effect of ethanol's extract of this plant on HeLa and MCF7 was studied and results showed that this plant's extract has toxic effect on these cells. Comorian compounds (as part of phenol compounds) are major compounds of this plant, and main biological activities of this plant are attributed to them. Research has referred to cell toxicity of coumarin compounds on cell lineages, and apoptosis induction by these compounds is studied and confirmed. Psoralens are the most important coumarin compounds of this plant that can play an anticancer role, inhibiting cytochrome p450 activity.[12]

Ammi visnaga

Ammi visnaga L is a garmineous and perennial plant that grows in Mediterranean areas. This species is divided into 3 components: alegrian, furanochromones, and flavonoids.³⁶ It is seen in the north of Iran in Geilan, Roudbar, Manjil and in south of Iran in Bushehr and Shahbazan at a height of 800 meters. Its leaves have more cuttings and its flowers are white and umbellate. This odorant plant is of Apiaceae family, and its antibacterial, antifungal, and therapeutic effects in vitiligo have been published.[13]

The killing activity of different extracts of the above-ground part of this plant on T47D cancer cells has been studied. Also, the inhibitory and dose-dependent effect of this plant on 2 human cell lineages, pelvic rhabdomyosarcoma and L20B of mice, have been proven. 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 plants.[14]

***Artemisia absinthium* L**

Artemisia is a plant in the Asteraceae family. *Artemisia* has 200 to 400 species that have clustered and bitter flowers. One species, *Artemisia absinthium* L, is native of Asian moderate areas, north of Africa, and vast areas of America. The size of this plant is 80 to 120 cm. Flowers of this plant are yellow and clustered.[15]

A research on breast cancer cells MCF-7 has been reported. Similar results related to the anticancer characteristics of this plant on 3 cancer cells HeLa, HT-29, and MCF7 have been reported. In a study about the Artemisinin effect of this plant on breast cancer cells, it was determined that plethoric reaction in cancer cells involves inhibiting cell's growth, apoptosis, preventing angiogenesis, preventing cell migration, and decreasing responses of core receptors. Quercetin, isorhamnetin, kamfrolinalol, alphapinin, limonene, and myrcene are the other compounds of this plant.

Quercetin inhibits growth of many cancer cells such as MCF-7, and isorhamnetin inhibits growth of many cancer cells such as MB-435, SKMEL-5, Du-145, MCF-7, and DLD. Also, artesunate is one of the most important artemisinin that has angiogenic effect, and in addition to anticancer effects on K569 (leukemia cancer), it inhibits the production of angiogenic factor VEGF.⁴⁵ In other research, alpha-pinene, beta-pinene, limonene, and myrcin available in the plant are probable factors of inhibiting the growth of human breast cancer and hepatic and melanoma. Alpha-pinene, beta pinene, and limonene available in methanol and ethanol

extracts of this plant are inhibitory factor of HT-29 cells (colon cancer).[16]*Astragalus cytosus*

Astragalus cytosus is perennial plant from the Leguminosae family and its height reaches to 75 cm. Its reproduction is done by seeds. Its stems are dark purple. Its leaves are composed of leaflets that are placed in 11 to 30 pairs in each leaf's axis. Its flowers are usually amethystine, blue, or white close to the end of flowering branches.

More than 200 species of *Astragalus cytosus* grow in Iran. In a research on HeLa cancer cells, the effect of toxicity of this plant's extract on cancer cell was shown. Also in a clinical study on 24 patients suffering from lung cancer, 21 patients showed positive response to this plant's extract. In vitro studies show that flavonoids in other species of this plant can direct carcinoma cells to apoptosis.[17]

Astrodaucus orientalis

This is biennial plant from the umbellate family. Extract of root and above-ground part of this plant show antiproliferation effects on breast cancer cells (T47D). α -Pinene, α -thujene, α -copaene, fenchyl-acetate, anisole, myrcene, and sabinene are the most important compounds in this plant. Inhibition of cell cycle and also induction of apoptosis is the main mechanism of anticancer effects of the plant.[18]

Avicennia marina

Avicennia marina is species of mangrove plants. Mangrove plants are halophyte plants resistant against sea salt. Mangrove is dominant species in the Mangro ecosystem. This plant is like a bush or shrub with a height of 1 to 10 meters. It has a white shell or gray or yellowish green, and its leaves are oval or sharp. Its flowers have 4 white or yellowish orange petals.

Flavonoid compounds of its leaf extract have anticancer effect on human breast cancer BT-20 cells. In another study, by separating naphthoquinone from leaf of the plant, anticancer effect of this compound on laryngeal cancer cells (kb) was shown. A cytotoxic effect of the extract on breast cancer cells (row 231MDA-MB) is confirmed.[19]

Boswellia serrata

Boswellia serrata is a medical plant from Spindales order and Burseraceae family with names Olibanum or Frankincense. It is obtained from specie *B sacara*, *B frereana*, and *B serrate* in Bosoolia. Hydroalcoholic extract of this plant causes death of cervical cancer cells (HeLa cell) and this effect is dependent on dosage and time.

In another study, alcoholic extract of frankincense resin caused disorder in the biosynthesis of DNA and RNA and proteins inhibit the tumor growth and induce apoptosis in cancerous cells in mice. In a research on leukemic cells HL60, it was shown that frankincense reduces viability of the cells. Monoterpene, diterpene, and triterpene and boswellic acid are the main ingredients of frankincense resin, which can induce apoptosis in cancerous cells. In fact, frankincense extract, by increasing production of reactive oxygen species and by activating caspases, causes apoptosis and severe damage to cells.[20]

Camellia sinensis

This plant is a kind of tea that is obtained from the buds and petals of fresh herb. In the process of producing this tea, little oxidation occurs. Tea is a natural source of caffeine, theophylline, thianin, and antioxidants. In a study on rats, it was found that green tea could inhibit 5- α reductase enzymes. This enzyme converts testosterone to dihydrotestosterone, which is a prostate carcinogenic agent. Accordingly, it has been found that green tea can have an inhibitory effect on prostate cancer. In this regard, the antitumor effect of green tea on prostate cancer has been shown. Green tea contains polyphenols such as epicatechin, epigallocatechin, epigallocatechin, and epigallocatechin-3, which have anticancer effects. Cytotoxic effects of green tea on breast cancer cells has been demonstrated. In a research conducted by Wang and colleagues in China, they concluded that green tea drinking habits, including regular drinking, greater amount of intake, and lower temperature were associated with reduced risk of gastric cancer.[21]

Citrullus colocynthis

Citrullus colocynthis belongs to Cucurbitales order and *Citrullus* genus. Used part of the plant is yellow and a very bitter fruit with the size of an apple. A study showed that the extract of this plant may (Hep2) have toxic effects on larynx cancer cells. According to studies, chemical constituents of this plant such as cucurbitales are used as anticancer medicine in cancers such as liver (HepG2) and breast (MCF7) cancers; quercetin and β -sitosterol as antitumor agents have been studied in many researches. These compounds act by inhibiting cell cycle (cycle stops at G2/M), and the induction of apoptosis can impose anticancer effects.[22]

Saffron (Crocus sativus L)

Saffron *Crocus sativus* L belongs to the Iridaceae family. This plant in Iran is native of Khorasan. Saffron is a perennial plant, with height 10 to 30 cm, from the bulbs of this plant, with narrow leaves

exits. This plant has 1 to 3 purple flowers. The used part of this plant is stigma, known as saffron.[23]

Various studies showed anticancer effect of the saffron extract on cancer cells in vitro; for example, Escribano et al, in a study on the effect of saffron extract on human cancer cells, found that the materials separated from saffron such as crocin, crocetin, picrocrocin, and safranal induced apoptosis in cancer cells.

In another study, the effect of saffron extract and other major plant substance called quercetin on colorectal cancer cells was studied and the results showed the toxic effects of this plant on these cells. Another study also showed the anti-angiogenic effects of this plant on breast cancer cells (MCF-7), and extract of this plant inhibits angiogenesis in these cells.[24]

In fact, the saffron extract, by inhibiting DNA synthesis, can exert its anticancer effects. However, in the consumption of high doses of this herb, the necessary precautions should be taken because according to Rahimifard et al's study on the human cervical cancer cells, larynges cancer cells, and natural human monkey kidney, it was observed that toxicity on natural cell is higher than 2 cancer lines, which indicated precaution in consumption of high dose of saffron.

Another research has studied effect of cellular toxicity and apoptogenic properties of saffron extract on the cancer cells and concluded that saffron can play an important role in cell death of HeLa and HepG2 cells and apoptosis. Saffron can be used as a chemotherapeutic agent to treat cancer in the human in future.[25]

Curcuma longa

Turmeric is a plant with scientific name *Curcuma longa* from the Zingiberaceae family. This perennial plant usually requires humid and rainy environment. The main habitat of turmeric is hot areas of Asia such as India, Pakistan, Indonesia, and southern China, and it is native of Africa and South America. Turmeric has underground stem called rhizome. Several aerial shoots as high as 1 to 1.5 meters exit from these rhizomes. Edible part of turmeric is dried rhizomes.

The study of cytotoxic properties of turmeric on liver cancer cells (Hep-2) showed that the cytotoxicity mediated by curcumin in a dose-dependent manner leads to apoptosis of cancer cells through mitochondrial pathway. The results of studying the effects of its extract on telomerase activity in breast cancer showed anti-proliferative

and inhibitory effects of telomerase.[26]

In another study, it was found that turmeric imposes its cytotoxic effects on lung cancer cells through inhibition of telomerase activity in a dose-dependent manner. Curcumin, as an important ingredient of turmeric, plays a significant role in the prevention and treatment of primary ovarian cancer, and multiple clinical studies have proven its effectiveness.

The anticancer potential of curcumin against cancers, including leukemia, lymphoma, digestive, urinary, reproductive, breast, uterus, ovary, lung, melanoma, colon cancers, and brain tumors have been shown. Free radicals and toxic products of oxidative stress play a significant role in the development of many diseases, including cancer, and curcumin has antioxidant effects that reduce or inhibit damage caused by free radicals.[27]

One study showed that treatment of human blood lymphocytes with curcumin significantly reduces genetic damage caused by radioactive iodine-131. Another study showed that curcumin induces apoptosis and inhibits proliferation of cancer cells. Apoptosis occurs due to release of cytochrome and its effect on P53 protein as well as the effect on intracellular signals is responsible for stopping cell growth. In fact, the mechanisms by which curcumin inhibits tumor formation are combination of properties including antioxidant, anti-inflammatory, anti-angiogenic, anti-metastatic, inhibition of cell cycle, and proapoptotic, which induce inhibitory effects on the cancer through regulating genes and molecules involved in these paths.[28]

Ferula assa-foetida

Ferula assa-foetida plant grows in Iran in different regions of Khorasan, Sistan, and Baluchestan and southern parts of Iran such as Kerman, Dasht-e Murghab, Abade, and Nain. Asafoetida is a perennial plant with strong, thick, and fiber stems. Used part of this plant is a resin, which is used as a gum. Cytotoxic effect of ethanol extract of asafoetida on liver cancer cells has been proved (category HepG2). Also, consuming gum of this plant has significantly reduced the risk of colon cancer. The most important ingredients in coumarin compounds are sulfur-containing compounds, and compounds such as β -sitosterol and oleic acid.[29] In order to justify anticancer effects of ethanol extract of this plant and organosulfuric compounds, different mechanisms are suggested, including inhibition of gene mutation, effect on the activity of enzymes, inhibition of DNA destruction, effect on cell proliferation, and changing the activity of enzyme. However, induction of planned cellular

death is an important mechanism for anticancer effects of this plant. Cytotoxic activity of phytochemical compounds in some species of *Ferula* against cell lines including ovarian carcinoma (CH1), lung cancer (A549), and melanoma (SK-MEL-28) has been studied, and it has been shown that these compounds can have mild killing effect on cells.

Glycyrrhiza glabra

Glycyrrhiza glabra is wild plant from vegetables family, native to southern Europe, North Africa, and temperate regions of Asia. It grows in most parts of Iran, especially in the eastern and northeastern Khatam Marvatsi city and territories as well as Azerbaijan and Eghlid city. Its leaves are compound and consists of 4 to 7 leaf pairs plus an end leaflet that is sticky due to secretion of juice. Flowers are blue and its fruit contains 5 to 6 brown seeds.[30] Its roots and stems have medical use.⁹⁸ Extract contents of the root lead to morphological changes in the mammary cell line 4T1 and reduce their viability.⁹⁹ Its root extract induces BCL2 phosphorylation and, like Taxol, inhibits the cell cycle at the G2/M phases in tumor cell lines.

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. *Glycyrrhiza glabra* root extract induces apoptosis in HT- 29 cells; therefore, it is useful in the treatment of colon cancer.

***Lagenaria siceraria* Standl**

Bottle gourd is a species of Cucurbits that has yellow skin and is less edible. This plant has a very large head and a small head and a narrow waist. The naming of the pumpkin is because of its shape. The effect of the plant extract on human lung cancer cell line A549 has reviews, and it has been shown that the extract could significantly inhibit the cell line.[31]

Antitumor effect of methanol extract of aerial parts of this plant has been demonstrated.¹⁰⁵ In another study, water-soluble polysaccharide isolated from this plant and its effect on carcinoma of human breast cell lines (MCF7) has been proven. In addition, its fruit is a source of vitamin C, beta-carotene, vitamin group B, saponins, and cucurbitacin. Cucurbitacin belongs to 4-ring terpenoids that has cytotoxic activity.

Lepidium sativum

Watercress is an annual plant that is known as Jrijzbastany and Rashad in Iranian ancient medicine. It has light green leaves, small red or

white flowers with gentle fragrance that jointly appear at the end of branch. The fruit is oval with an approximate length of 50 mm and a width of 4 mm. Cytotoxic effects of methanol extract of cress seeds on the bladder cell line (ECV-304) has been reported. Also, Aslani et al have shown, in a study of aerial parts of the plant, the cytotoxic effect on K562 leukemia blood lines. In another study, the effects of aqueous extract of seed on breast cancer cells (MCF-7) through induction of apoptosis have been demonstrated.[32]

This plant is rich in antioxidants such as vitamins E, C, B, A, isotiosinat, and omega-3 fatty acids such as alpha-linolenic acid as well as glucosinolates, and these compounds can impose their anticancer effects through antioxidant properties and inhibit the proliferation of plant cell.

***Medicago sativa* L**

Alfalfa is plant with scientific name *Medicago sativa* L that is usually found in most parts of the world and has been used in traditional medicine for the treatment of various diseases such as hepatic disorders. Phytoestrogens in the plant and strong estrogenic activity of this plant is useful in treating hormone-dependent cancers.

Alfalfa contains large amounts of almost all vitamins, flavonoids, digestive enzymes, coumarin, the alkaloid amino acid, and trepans, and it is also useful for breast cancer and also increases the breast milk. Alfalfa contains triconlin, which is a plant alkaloid compound and has a hormone role in the plant. It is believed that this plant alkaloid has important medicinal properties such as anticancer effects.[33]

Mentha pulegium

This plant with the scientific name *Mentha pulegium* and the English name European pennyroyal belongs to the Labiaceae family. Pennyroyal is a gramineous plant, and its shrubs grow to a height of 60 cm, and grows wild in many fields. This plant has oval leaves and small, regular sharp teeth. Flowers of this plant with leaves and stalks are mostly in the upper shaft and the colors are purple. Aslani and colleagues reported research before flowering the plant's cytotoxicity effect on leukemia cells. There are natural substances that are included in Pennyroyal polygon, mentone, piperitone, limonene, isomenthone, and Octaan-3-ol in some studies the inhibitory effect of flavonoids on proliferation of cancer cells via apoptosis induction refers to Pennyroyal.[34]

Myrtus communis

The scientific name *Myrtus* or Mort is a genus of

Murdian. Genus of evergreen shrubs or trees with 1 or 2 species native to southern Europe and North Africa are *Murdian*. This plant is an evergreen shrub or bush that sometimes reaches a height of 5 meters. Its leaves are about 3 to 5 inches long and have a nice smell. It has petals of white color and blue ball-shaped fruits. In some studies, the plant has been referred for its anticancer effects. The plant also shows cytotoxic activity on cancer cell lines MCF7. Polyphenols, myrtucommulone, semi-myrtucommulone, 1,8-cineole, α -pinene, myrtenyl acetate, limonene, linalool, and α -terpinolene are some of the most important compounds found in this plant. In most studies anticancer properties of this plant are attributed to plant phenolic compounds (especially mitocomolon). Cell cytotoxic effects are on their cell layer.[35]

Nigella sativa

Black seed is of the Ranunculales Ranunculaceae family. This annual flowering plant is native to southwest Asia. This plant grows in abundance in Arak and Isfahan in Iran. A study presented an overview of the antioxidant protective effects on the liver of the anticancer effects of the plant *Nigella*.¹⁰ In this context, evaluation of alcohol on the effects of *Nigella sativa* on kidney cancer cells (ACHN) showed an apoptotic effect on these cells. Its Kvyynvny compounds and dinitro-quinone are like thimoquinone. In a study of colorectal cancer cells, the effects of thimoquinone on inhibiting cancer cell growth, apoptosis, and increased cell morphological changes was shown. It also has been shown to induce programmed cell death, with the anticancer activity being observed in an alcoholic extract of *Nigella sativa*. In a study the effect and mechanism of black beans has been shown in the treatment of breast cancer. In a research conducted by Elkady and colleagues, the effect of *Nigella* and the mechanism in the treatment of colon cancer in humans was demonstrated.[36]

Olea europae

Olive plant with the scientific name *Olea europae* L. contains approximately 35 to 40 species and belongs to the family Oleaceae. Since ancient time hot or lukewarm areas such as the Mediterranean, North Africa, Southeast Asia, north to southern China, Scotland and East Australia have a wide distribution.[37] Olive tree leaves are narrow, dark green, and permanent evergreen. Olive flower clusters have leaves that appear from the side and have 4 petals and 2 flaps and flower cluster.

In a study of the anticancer effects of olive oil, the most important leaf and its compounds (especially

oleic acid) are mentioned. In other anticancer effects, pinoresinol found in olive oil has an effect on colon cancer. The role of phenolic compound oleuropein in olive oil is also important, suggesting that this compound acts directly on the her-2 gene in breast cancer cells and controls. The study also showed that acidic triterpenes found in olive oil can inhibit tumor cell proliferation and induction of apoptosis in some categories. Two of these compounds, maslinic acid and oleanolic acid, showed acceptable antitumor effect on colon cancer model in rats, and these compounds inhibiting tumor growth and angiogenesis are important factors.[38]

***Pegaum harmala* L**

This herbaceous perennial plant is from the perennial family Zygophyllaceae Nitrariaceae. This plant grows in Mediterranean regions such as North Africa, Turkey, Syria, and usually grows in arid lands. It grows to about 30 to 50 cm length, and has a plant-like appearance, with green leaves and regular water-filled narrow divisions. It has large flowers with greenish-white sepal and large petals. Its extract also reduced the viability of epithelial cervical carcinoma cells and carcinoma of the colon.¹³⁶ This plant is made up of mainly alkaloids and these alkaloids have anticancer effects. In another study that was conducted using chemical analysis, the antioxidant activities of these alkaloids against human breast cancer cells were noted.[39]

***Centella asiatica* Linn**

Centella asiatica, known as mandukaparni in Sanskrit, brahmamanduki in Hindi and asiatic pennywort in English, is another plant that has shown potential as an anticancer agent. This plant is commonly found in India, Australia, Pacific Islands, New Guinea, Malaysia, and Iran. The whole plant or its leaves are being traditionally used for their therapeutic properties. Partially purified fractions of *C. asiatica*, dose-dependently inhibited the proliferation of transformed cell lines, including Ehrlich ascites tumor cells and Dalton's lymphoma ascites tumor cells. However, practically no toxic effects were detected in normal human lymphocytes. Partially purified fractions of *C. asiatica* also significantly suppressed the proliferation of mouse lung fibroblast cells in long-term culture. Oral administration of *C. asiatica* extracts slowed the development of solid and ascites tumors and increased the total life span of tumor-bearing mice. The mechanism underlying the antitumor activity of *C. asiatica* is suggested to be a direct inhibition of DNA synthesis.[40]

Physalis alkekengi

It is a perennial herbaceous plant with creeping rhizome stems of potato corners. The effect of

aqueous extract of this plant on U937 cell cytotoxicity was positive. The basic compounds of physalin plants belong to the group of triterpenoids. Anticancer cytotoxic activity of physalins B and M extracted from the plant on cancer cells (especially human cell line HeLa and Hepatum cell lines SMMC-7721 and HL-60) is verified.

Polygonum aviculare

Caryophyllales Polygonaceae plant belongs to the genus *Polygonum*. *Aviculare* plants grow throughout the year and the chronometer stem reaches a length of 50 centimeters. Its leaves are small and sharp, with tiny pink flowers in it. This plant grows in most areas of Asia, Europe, Africa, and America and in most parts of Iran. In some studies, the effect of the extract on the inhibition of proliferation of cancer cells HeLa has been reasonable. The effects on cell proliferation and expression of apoptotic genes in breast cancer cells (MCF7) showed that extracts of the plant through the induction of apoptosis can cause cytotoxicity in cancer cells of breast. Tannins, flavonoids, and alkaloids are the most important components of this plant. However, studies of anticancer effects showed that despite phenol compounds the effects of the plant is considered the main cause.[41]

Rosa damascenes Mill

Rose or rose (scientific name: *Rosa damascenes Mill*) has long been cultivated in different climatic conditions. It is from the family Rosaceae and the flowers and leaves of the plant are its active ingredient is tannin. It is a perennial shrub, close to 5.1 meters in height, and has a cylindrical shaper without grooves.

The toxic effects of this essential oil on lung cancer cell lines (A549) and breast (MCF7) have been reported. The ethanol extract of the plant cell has killing effect on cervical cancer cells (HeLa). *Rosa Damascena* essential oil affects gastric cancer cells in 2 specific ways: the soluble phase increases cell viability, while the vapor phase decreases cell survival. Also, flow cytometry showed that apoptosis is the important mechanism accompanied with cell death.

Silybum marianum

It belongs to the family Astir Asteraceae. Milk thistle is a plant native to the Mediterranean and spread throughout Europe. It grows in vegetative arid land, roadsides, arable land, and similar places such as beaches and mountains. The vehicle and shrubs are for the duration of 1 or 2 years. It appears from 30 to 200 cm and its cone-shaped flower colors are red to purple.

Also a study has shown that silymarin causes cell cycle arrest and apoptosis on the 4T1 cell line.

Taverniera spartea D

Silver spartea plant with the scientific name *Taverniera spartea D* usually grows on the southern coast of Iran including Bandar Abbas, Minab, and Baluchistan. This woody plant, shrubs growing to a height of 50 to 110 cm, is covered with fluff on a bed, with short shoot. The flowers of this plant are purple and pink. This plant is flowering to March.²¹ Methanol extract of the plant, especially chloroform fractions, showed toxic effects on breast cancer cell lines (MCF-7 and BT474) and human prostate cell lines (PC-3 and DU-145).²¹ The anti-cancer effects of the plant have been reported.[42]

Taxus baccata L

Yew tree with the scientific name *Taxus baccata L* is gymnosperms from the family Taxaceae. There are 3 species of yew trees, and *Taxus baccata L* is the only species native to Iran. Yew is an evergreen tree with a very long life and slow growth. This tree has a smooth trunk has a height of up to 30 meters and diameter up to 5 meters. This species is native to Europe, the Caucasus, North Africa, and Iran. Yew in the woods of northern Iran is often Azadshahr from Astara. Yew tree grows at high altitudes in mountain areas, deep dark valleys, steep slope ranging from rocky and semihumid to wet and cold conditions.[43]

This plant is one of the first plants on which extensive research has been done on the effects of cancer prevention. Taxol is one of the natural ingredients of the plant that has anticancer effects. A study has shown that the acetone-dichloromethane extracts of the plants have a cytotoxic effect on cancer cells k562, HeLa, and MDA-MB-468.

Thymbra spicata

Zufae thyme plant is from the family Labiaceae, and the plant grows preferably in dry and sunny areas and on the slopes of dunes. There are various plants that grow to 15 to 40 cm in height and has flowers that are purple. It is because of thymol and carvacrol that there is biological activity. Various parts of the plant essential oil is a good source of antibacterial and antioxidant properties. Hydro-alcoholic plant inhibitory effect on lung cancer cells (SK-Mes-1) has been shown. Thyme, thymol, and carvacrol are the most important plant phenol compounds with antioxidant properties, prevents oxidative damage to DNA, and thus can prevent cancer.[44]

Thymus vulgaris

Thymus vulgaris L has the the English name garden thyme. It belongs to the family Lamiaceae and has a straight stem and is herbaceous or woody and grows to a height of 20 to 30 cm. This plant has branched stems that are covered with white fluff. This plant has aromatic leaves that are usually evergreen and flowers are pale purple to white in color.

In the prostate study on rats it was found that thyme extract inhibits the growth of abnormal and precancerous lesions and treats and also inhibits the growth (in laboratory conditions) of squamous cell carcinoma of the head and neck. This plant has a variety of compounds, including flavonoids.[45] Thymol and carvacrol are the most important plant phenol compounds that are useful in the treatment of breast cancer and colorectal cancer.

***Annona atemoya* Mabb./ *Annona muricata* Linn**

Annona atemoya/muricata is a native of Caribbean, Central and South America. It is also commonly grown in South East Asia especially in eastern part of India. This plant is traditionally known as mamaphal in Hindi and sour-sop of America in English. The parts of the plant that are generally used for medicinal purposes are the root, bark, leaf and fruit.

The fruit of *A. atemoya* contains bullatacin (chemical structure shown below), an acetogenin known to have antitumor properties. Bullatacin induces chromatin margination and tumor cell condensation, followed by apoptosis. *A. atemoya* contains two annonuricins namely A and B, which have shown cytotoxicity in human solid tumor cell lines A-549 lung carcinoma, MCF-7 breast carcinoma, and HT-29 colon adenocarcinoma cell lines. *A. atemoya* contains several other acetogenins that have also been shown to selectively induce cell death in tumor cells *in vitro*.[46] In particular, two annonaceous acetogenins were found to produce cell death in the human hepatoma cell line HepG2 and hepatoma 2.2.15 cells

***Ziziphus nummularia* Wight**

Ziziphus nummularia also known as bhukamtaka sukhsharanphala in Sanskrit, harbor in Hindi and wild jujube in English, is a thorny small bush or a divaricating shrub, with pale-purplish stems and or grey-velvety stipular prickles in pairs. The different parts of the plant that are used for medicinal purposes are root, bark, stem, flowers and seeds. This shrub is generally found in India, Pakistan, Afghanistan, Egypt, Iran, Iraq, and Israel.

Betulin and betulinic acid (chemical structures shown on next page) are present within the bark and stem of *Z. nummularia* and have been shown to have

antitumor activity. Betulinic acid glycosides produce differential cytotoxicity, such that cancer cell lines are more sensitive than normal cells. Similarly, betulinic acid, a naturally occurring pentacyclic triterpenoid, shows selective cytotoxicity against a variety of tumor cell lines.[60] Betulinic acid has been suggested to induce apoptosis by generation of reactive oxygen species, inhibition of topoisomerase I, activation of the mitogen activated protein kinase (MAP kinase) cascade, inhibition of angiogenesis, and modulation of pro-growth transcriptional activators and aminopeptidase-N activity. Furthermore, betulinic acid has been shown to induce apoptosis by a p53- and CD95- independent mechanism. These mechanisms may be responsible for the ability of betulinic acid to effectively kill cancer cells that are resistant to other chemotherapeutic agents.[47]

***Trigonella foenum-graecum* L**

Fenugreek or Shanblid (scientific name: *Trigonella foenum-graecum*) is a plant of the Fabaceae family with height of 10 to 50 cm with single flowers that are bright yellow to brown. This plant is native to Iran and in most parts of Iran, including Azerbaijan, Isfahan, Fars, Khorasan, Semnan, and Damghan and are edible vegetables.[59] In a study of the effects of crude extract of fenugreek, there was selective cytotoxicity against some cell lines such as MCF7, TCP (T-cell lymphoma), FRO (thyroid papillary carcinoma), and brain tumors. It is also protective effect against breast cancer induced by DMBA (7,12-dimethylbenz(a) anthracene) in mice.[48]

In another study, the inhibitory effects of the plant extract on the growth of cancer cells EAC was shown. Flavonoids and alkaloids in the plant, such as ginger, cadence, zinger one, vanillin, and eugenol, have been shown to be involved in anticancer effects. The main mechanism of anticancer activity is apoptosis induction.

***Urtica dioica* L**

Nettle (scientific name: *Urtica dioica*) is a grassy, herbaceous perennial with branched legs. Shoot is straight and square, and leaves of bitter Azkrk are covered. It can be seen in the wile in Iran near Tehran, in Karaj in Alborz slopes, and the hive Shemiranat, and in the northern regions in Mazandaran and Gilan and Drazrbayjan, on the slopes of Sahand, Zanghab, and Lorestan (in the river). Studies have shown cell proliferation inhibitory effect on prostate cancer cells (LNCaP and as hPCPs) by aqueous and ethanol extracts of the plant.[58] Also, a report has referred to the anticancer effects of this plant against esophageal cancer. Plant compounds with antioxidant phenol compounds are those that may have an important

role to prevent cancer. In a study, the anti-proliferative effect on human prostate cancer cells by nettle root extract has been proven.[49]

Phyllanthus amarus

Phyllanthus amarus is found in tropical Asia, especially in warmer parts of India and is known as bhumyamalaki in Sanskrit, jaramla in Hindi and stone breaker in English. The whole plant, leaves, roots and shoots are reportedly used for their medicinal values.[57] *P. amarus* contains various lignans, flavanoids and tannins, and evidence suggests that *P. amarus* extract may exert antitumor effects. Oral administration of *P. amarus* extract significantly increased the life span and reduced tumor size in mice bearing Dalton's lymphoma ascites (DLA) and Erlich ascites carcinoma. The chemoprotective properties of this plant may be related to its ability to inhibit metabolic activation of carcinogenic compounds, induce cell cycle arrest and interfere with DNA repair.[50]

Andrographis paniculata

Andrographis paniculata, commonly known as bhunimba and kalmegha in Sanskrit, kiryat in Hindi and the king of bitters and chiretta in English, is found in India and Sri Lanka. The parts of the plant generally used for medicinal purposes are the roots and the leaves. *A. paniculata* extract contains diterpenes, flavonoids and stigmaterols. The primary medicinal component of *Andrographis* is the diterpene andrographolide (chemical structure shown below). Andrographolide, described as a "diterpene lactone" due to its ring like structure, has a very bitter taste and has a colorless crystalline appearance. *Andrographis* leaves contain the highest concentration of andrographolide (~ 2.25%), while the seeds contain the lowest.[51]

Tinospora cordifolia,

also known as guduchi in Sanskrit, giloya in Hindi and heartleaf moonseed plant in English, under cultivation at experimental fields of IIM, Jammu, India. According to ancient Ayurvedic lexicons, *T. cordifolia* is also referred to as "amrita". The term "amrita" is ascribed to this plant due to its ability to impart youthfulness, vitality and longevity. The stem of *T. cordifolia* is used for general debility, dyspepsia, fever, urinary disease, and jaundice. The extract of its stem is used in treating skin diseases. There are certain curative properties of the root of *T. cordifolia* which allow for its use as antidote in snake bite, in combination with other drugs. *T. cordifolia* is well known in modern medicine for its adaptogenic, immunomodulatory and anti-oxidant activities.[52] *T. cordifolia* is also known to have anti-inflammatory, anti-arthritis, anti-allergic properties. This plant is also useful in treating skin

diseases, vomiting, anemia, piles, chronic fever, and emaciation.

Vinca rosea

Belonging to the genus *Vinca* and oleander it has for a very long time been an important medicinal plant of great concern. In a study on human skin cancer cell line A431, the methanol extract of the plant had a positive effect on reducing the proliferation in this category.[56] Alkaloids such as vincristine, vindoline, vinblastin, vinflunine, and catharanth in the aerial parts are different from vincristine and vinblastine, and among them 2 combinations of plant secondary metabolism are used today as anticancer drug.[170,171] The effects of this plant's alkaloids on cancer cells of breast, prostate, cervix (MCF-7, PC3-1C, HeLa) were studied, indicating that these alkaloids' tubular protein links changed its structure by blocking the division of cancerous cells; these compounds with antioxidant properties will prevent cancer cells from progression.[53]

Viola tricolor

Violet plant with the scientific name *Viola tricolor*. Violets are herbaceous plants, resistant to cold throughout the year and grows to a height of up to 25 cm. Small flowers of this plant with different colors including bright and family purple, white, and yellow flowers that appear in spring and summer and become the fruit capsule. Aqueous extract of this plant has a strong inhibitory effect on proliferation of cervical cancer, and the active ingredient of the plant responsible for this effect is ethyl acetate. This plant contains a number of compounds that have cytotoxic effects of potent cells. Studies have shown that flavonoids can have anticancer effects.[54]

Zingiber officinale

Zingiber officinale is a member of the Zingiberaceae family. Ginger or ginger or Shengir is an edible and medicinal plant. It is grown all over India, especially in hot and humid areas. Ordinary ginger rhizomes of ginger powder is spicy and aromatic spices are used for savory dishes traditionally. This plant has bright green slender stalks that grow from glandular stem. Ginger flowers are yellowish green with purple edges and pale spots. 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 cell death induction program has been destroyed.[55]

CONCLUSION:

Medicinal plants are rich sources of herbal properties contributing in the discovery of new

drugs towards various disorders, diseases including cancer without showing no toxic affects on the individuals treated. Treatment of cancer by use of natural products and traditional medicine by applying the concepts of Ayurveda is attaining a great significance scope of cancer research. In this review author presented the importance of traditional medicine, medicinal plants in cancer treatment, anti cancer properties of natural products in brief. Medicinal plants contain good immunomodulatory and antioxidant properties which leads them to be a anticancer drug. Only few selected plants have been explored for biological activity from around 1000 species and much more, so further investigations into anticancer activity of the plants showing promising activity, must be undertaken. *Vinca rosea* alkaloids, Vinblastine and Vincristine, are one of the most potent anticancer drugs known. Taxol isolated from *Taxus brevifolia* has figured high in the therapeutic segment of cancer. From this review, it can be concluded that cancer is the leading cause of death in developing countries like India. The less expensive herbal drug treatment may highly be recommended to the rural and poor people to treat effectively the cancers of various type is an ideal choice.

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