International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 1905-1912 www.ijprajournal.com ISSN: 2249-7781

Herbalmedicines: Boon to Cancer Therapy

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Submitted: 05-02-2023 Accepted: 20-02-2023

ABSTRACT:
All over world cancer is one of the most life-threatening diseases which normally affect the human being. It is characterised by the uncontrollable and unwanted growth of body cells. There is a requirement of new preventing methods for this disease. Conventional therapies have various adverse effects on other healthy cells, Due to that, an alternative therapy and effective medication are required for cancer cure. There are various benefits of using plant derive product as compare to other synthetic medicine. This increase the importance of medicinal plants in the field of healthcare. Many plants derive product has sufficiently effective in treatment of cancer by stimulate DNA repair mechanism, inhibiting cancer activating enzymes, promote protective enzymes production and induce antioxidant action. In this review, an effort has been done to provide information about the various compounds present in the medicinal plants that have shown potent activity against various forms of cancer.

I. INTRODUCTION:

Cancer is one of the major causes of death in theworld, and it is the second leading cause of death after cardiovascular diseases.[1] Cancer starts with the distortion of a natural cell caused by genetic mutations in Deoxyribose nucleic acid. This abnormal cell reformation in an abnormal way by asexual reproduction, that is, it ignores signals correlated to regulation of cell's growth around it and obtains appropriation characteristics and causes changes in surrounded tissues.[2]Cancer is an major health problem in developing and developed countries. Every year, an average 182 per 100000 persons suffer from cancer in worldwide, and 102 die by cancer. According to the World Health Organization (WHO), 14 million people suffer from cancer and 8 million die by cancer in worldwide. The prevalence rate of cancer in Iran is 7/134 per 100000 people. Based on this statistics, 85000 people suffer from cancer in Iran every year, and 55000 people die by cancer.[3]Death caused by cancers is increasing throughout the world, and it is predicted that more than 13.1 million people deaths will occur due to cancer worldwide by 2030.[4]

Nowadays, numerous methods are used in the treatment of cancer such as chemotherapy, but in this method, because of nonselective nature of medicines, a high percentage of healthy cells will be lost with cancer cells. The most important problem in the cancer treatment is destroying tumour cells in the presence of natural cells, without damaging natural cells. In order to over come this disadvantage of anticancer medicines, we use natural resources like plants, screening raw extracts of plants is necessary and testing cytotoxic compounds.[5]

Different developments are reported in common treatments of cancer by findingmedicinal herbs and secondary compounds of natural products. It is believed that anticancer effects of plants improve by suppressing cancer's stimulating enzymes, stimulating production of antitumor enzymes in cell, repairing DNA, inducing antioxidant effects and increasing body immunity.[6]Cancer is an painful disease and fighting against this disease is very important for a public health. Regarding the fast growth in the phytochemical study of herbal products, plants are transforming to popular anticancer sources. In cancer, initially tumors will be treated by chemical supplement therapies or surgery. But cancers in the metastasis stage will resist against care.[7]But in chemotherapy, due to nonselectivity used of medicines, a high percentage of healthy cells will be destroyed with cancer cells. Nowadays, more than 60% of anticancer drugs that are useful for cancer patients are obtained from herbal, microorganism sources and marine.

ANTICANCERACTIVITY OF MEDICINAL PLANTS:

Medicinal plants have numbers of advantages as compared to other marketed chemical products, because the plant derived compounds are more tolerated and non-toxic to the

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normal human body cells. Already available conventional therapies for the treatment of cancer are radiotherapy and chemotherapy and they have possesses various side effects like cardiac, neurological, renal and pulmonary toxicity, which seriously affects the health of the person which administered. Therefore, an alternativemethod is required to develop that include less toxic and more potent anticancer drug as compare to the drugs available in the marketfor the treatment of cancer.

1] Boswellia Serrata:

Boswelliaserrata is belongs to Bursersceae family and found in India, Middle East and North Africa. It is commonly known as olibanum Frankincense. It contains various compounds like terpenoids, sugars and oils.The major component of this plant is Boswellic acid [8]. Gummy exudates of this plant are associated with the therapeutic effect which includes anti-septic, anti-arthriticc, stimulant and astringent effects. Acetyl-11-keto-β-boswellic acid which is an active compound of the this plant shows potential activity to inhibit tumor angiogenesis through the vascular endothelial growth factor signaling.

In another study, alcoholic extract of olibanum caused disorder in the biosynthesis of RNA and DNA and proteins inhibit the tumor growth and induce apoptosis in cancerous cells in mice. In a research on leukemic cells HL60, it was indicate that frankincense reduces viability of the cells.[9,10]Monoterpene, diterpene, triterpene and boswellic acid are the main ingredients of frankincense resin, which can start the apoptosis in cancerous cells.[11] In fact, frankincense extract, by increasing production of reactive oxygen species and by activating caspases, causes apoptosis and severe damage to cells.[12]

Figure No-1

2] Curcuma Longa:

Turmeric is a plant whichscientifically named as Curcuma longa from the family Zingiberaceae. This plant usually requires rainy and humid environment to grownup till puberty. The main habitat of turmeric is hot areas of Asia named India, Indonesia, Pakistan, and southern China, and it is native of South America and Africa. Turmeric has an underground stem called rhizome. There are some aerial shoots having length of 1.0 to 1.5 meters from these rhizomes. Edible part of the turmeric is dried rhizomes.[13]

The study of cytotoxic characteristics of turmeric on liver cancer cells (Hep-2) indicates that the cytotoxicity mediated by curcumin in a dose dependent manner which leads to the cell death of cancer cells through mitochondrial pathway.[14]The results of studying the effects of turmeric extract on telomerase activity in breast cancer showed anti-proliferative and inhibitory effects of telomerase.[15]In another study, it was found that turmeric imposes its cytotoxic effects on lung cancer causing cells by the inhibition of telomerase activity in a dose dependent manner.[16]Curcumin, is an important constitution of turmeric which plays a supportive role in the treatment and prevention of primary ovarian cancer, and multiple clinical studies have proven its effectiveness.[17]The anticancer potential of curcumin have been shownagainstleukemia, breast cancer, lymphoma, digestive, lung, ovary, urinary, reproductive, uterus, melanoma, colon cancers, and brain tumours.Free radicals and toxic products of oxidative stress play a significant role in the development of many other diseases, including cancer, and curcumin has antioxidant effects that reduce or inhibit damage, that caused by free radicals.[18]

One study showed that treatment of human blood lymphocytes with curcumin significantly reduces genetic damage caused by radioactive iodine-131.[19] Another study showed that curcumin inhibits proliferation of cancer cells and induces apoptosis. Apoptosis occurs due to the release of cytochrome and its effect on P53 protein as well as the effect on intracellular signals is responsible for stopping cell growth.90 In fact, the mechanisms by which curcumin inhibits tumor formation are combination of properties including antioxidant,anti-angiogenic, anti-inflammatory, anti-metastatic, inhibition of cell cycle, and proapoptotic, which induce inhibitory effects on the cancer through regulating genes and molecules involved in this paths.[20]

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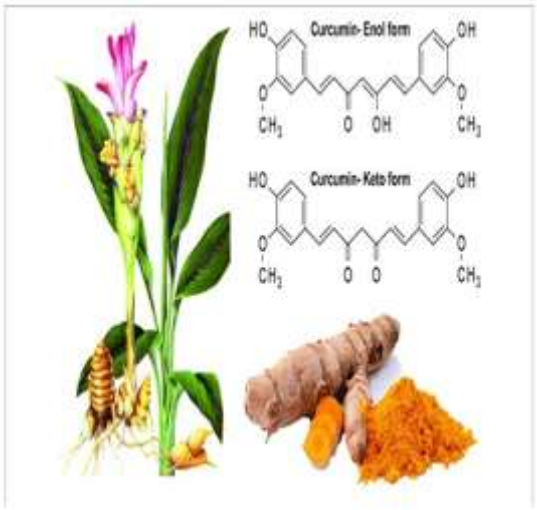

Figure No-2

3]Artemisia absinthium L:

Artemisia is a plant from Asteraceae family. Artemisia has 200 to 400 species that have bitter flowers and clustered. One species, Artemisia absinthium L, is grown in Asian moderate areas, vast are as of America and north of Africa. The size of this plant is usually 80 to 120 cm. Flowers of this plant are yellow in colour.[21]A research on breast cancer cells MCF-7 has been reported.Similar results related to the anticancer characteristics of this plant on 3 cancer causing cells MCF7, HT-29 and HeLa have been reported. In a study about the effect of Artemisinin plant on breast cancer cells, it was determined that plethoric reaction in cancer cells involves inhibiting cell's growth, preventing angiogenesis,apoptosis, preventing cell migration, and decreasing responses of core receptors.[22] Quercetin, alphapinin, isorhamnetin, limonene, kamfrolinalol and myrecene are the other chemical compounds present in this plant.

Quercetin prevent growth of number of cancer causing cells such as MCF-7 and isorhamnetinretards the growth of many cancer causing cells in body tissues such as Du-145, MB-435, MCF-7 and SKMEL-5.[23] Also, artesunate is one of the major important artemisinin compound that has angiogenic effect, and in addition to anticancer effects on K569 (leukemia cancer), it inhibits the production of angiogenic factor i.e. VEGF. According toanother research, alpha-pinene,limonene, beta-pinene and myercin available in this plant are capable factors for inhibiting the growth of human breast cancer causing cells and melanoma and hepatic cells. Alpha-pinene, beta pinene, and limonene available in methanol and ethanol extracts of this plant are inhibitory factor of HT-29 cells (colon cells of cancer).[24]

Figure No-3

4] Saffron (Crocus sativus L):

Saffron Crocus sativus L fromthe family ofIridaceae. This plant found inIran.Saffron is a perpetual plant, which has near about 10 to 30 cm in length, from the bulbs of this plant, with narrow leaves exits. This plant having 1 to 3 purple flowers. The used part of this plant is stigma, called as saffron.[25]Various in vitro studies on this plant shows that it has anticancer effect; for example, Escribano et al, in this a study the effect of extractedsaffron on human cancer cells, found that the materials separated from saffron such as, picrocrocin, crocetin,crocin and safranal induced apoptosis in cancer cells.[26]

In another newer study, the effect of extract saffron and other major plant constituent know as quercetin has an anti cancer effect on colorectal cancer cells was studied and the results showed the toxic effects of this plant on these cells.[27] Another study also showed the antiangiogenic effects of this plant on breast cancer cells (MCF-7) and extract of this plant inhibits angiogenesis in these cancer causing cells.[28]In fact, the saffron extract, gives anticancer effect by inhibiting the DNA synthesis in cancer cells.However, in the consumption of high doses of this plant extracts, there is some evidence of it's toxicity to human normal body cell, Sowe take the precaution in consumption of high dose of saffron.[29]

Another research has studied effect of cellular toxicity and apoptogenic properties of

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saffron extract on the cancer cells and concluded that saffron can plays very important role in cell death of HeLa and HepG2 cells. In future Saffron can be used as a chemotherapeutic agent to treat cancer in the human.[30]

Figure No-4

5]WithaniaSomnifera:

WithaniaSomnifera is commonly known asashwagandha in Hindi and Sanskrit and winter cherry in English. It belongs to the family Solanaceae and it's subtropical shrub found in Mediterranean, India and Africa. It contains withanolides, withaferins, isopellertierine, anferine and sitoindosise. Due to its medicinal properties, roots and leaves have been used in the Indian traditional system of medicine and marketed globally. Extract of Withaniasomniferagivesnumbers of biological and therapeuticresponses.[31]It has been used in various preparations for its anti-stress, anti-inflammatory, anti-ageing, cardiotonic, anti-peroxidative, anti-oxidant, anti-tumor, and immunomodulatoryproperties.[40]Withanolide A and withaferin A is the major constitute of this plant. Withaferin A which is mostly present in the leaves produce the rapid cell deathof cancer causing cells.[32] Cell signaling pathways by this plant formulation largely depends on the high content of withferin A present in it.[32] Formulation of Withaniasomnifera showed induction in cell cytotoxicity in various human cancer causing cell.Withaniasomnifera formulation also up regulates the population of T-cell in mice (bearing tumor) with increased expression of IFN-gamma and IL-2 levels.[33]

Figure No-5

Withaniasomnifera has also been demonstrated to have higher bioavailability as in case of Withanolide A, when Withaniasomnifera root extract was administered to Albino Swiss female mice orally.[34]The half life of withanolides was evaluated in the same study where t1/2 of Withaniasomnifera A was shown to be approximately 60 minutes whereas Withanolide A had a half life of 45 minutes.[34] Given this rapid half-life, it may be worth considering twice daily or three times daily of Withaniasomnifera in dosing regimens. While withanolides as a whole possess several properties that could potentially be utilized against a varieties of diseases, the majority of the research work that has been conducted on withanolides involves Withania A. This in part, is due to the notion that Withania A is the most potent withanolide ever identified, thus from the Ashwagandha plant, Withania A was the first withanolides to ever be isolated.[35,36]The pathways for the biotransformation and metabolism of the withanolides of Withaniasomnifera are poorly understood. In vitro microbial transformation of Withania A to 14 alpha-hydroxywithaferin A has been shown [37]. Given the structure of Withanaia A, it is likely that it undergoes hydrolysis (by epoxide hydrolase) and other reduction/oxidation reactions followed by conjugation to glutathione, sulfates or glucuronides. However, experimental evidence to support this claim is limited and is therefore an area that require to be considered especially when studying the pharmacokinetics of withanol

6]Camellia sinensis :

The plant of tea that is obtained from the petals and buds of fresh herb. In the process of producing this tea, small oxidation process occurs.

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Tea is a natural source of caffeine, thianin, theophylline and antioxidants. The study on rats, founds that the green tea could inhibit 5-alfardoctase enzymes. This enzyme converts testosterone to dihydrotestosterone, which is a prostate carcinogenic agent. Accordingly, it has been found that green tea can have a preventing effect on prostate cancer.[38] In this regard, the antitumor effect of green tea on prostate cancer has been shown.[39] Green tea constitutes polyphenols includesepigallocatechin, epigallocatechin-2, epigallocatechin-3 and epicatechin which shows anticancer effects.[40] Cytotoxic effects of green tea on breast cancer cells has exhibited.[41]

In a research conducted by Colleagues and Wang at China, they concluded that the drinking habit of green tea, including regular drinking, greater amount of intake, reduced the risk of gastric cancer.[42]

Figure No-6

7]PhyllanthusAmarus:

PhyllanthusAmaru belongs to the family Euphorbiaceae and known as jaramla in Hindi, stone breaker in English and bhumyamalaki Sanskrit. It is found in the Asia and especially warmer parts of India. Whole plant(shoots, leaves and roots)has medicinal uses.Phyllanthusamarus contains tannins, flavanoids and lignans and used in the liver, kidney, stomach, spleen and genitourinary system problems. The extract of Phyllanthusamarus administration orally to reduce tumor size and increase life span in mice bearing Erlich ascites carcinoma and Dalton's lymphoma [43]. Anticancer activity of this plant are due to the ability to inhibit cell cycle, it interferes with DNA repair and inhibition of metabolic activation of carcinogenic compounds [43]. Extract of Phyllanthusamarus also showed antiangiogenic effects in mice by interfering with the vascular endothelial cells migration [44].

Figure No-7

8]. Plumbagozeylanica:

Plumbagozeylanica belongs to the familyPlumbaginaceae and commonly known as white leadwort, Ceylon leadwort and chitrak. It is found in theSri Lanka andwarmer part of India Several studies provides evidence of presence of various phytocompounds in this plant which includes plumbagin, plumbagin acid, saponaretin, coumarins, isoaffinetin, isoorientin, glucosides, steroids and psoralen [45]. This plant shows therapeutic activity against skin diseases, rheumatic pain, scabies and wounds.[46] Plumbagin is a napthoquinone derivative which is isolated from the roots of this plant and it possess anticancer activity by controlling the hormone refractory invasive prostate cancer. Inhibitory effect of plumbagin against various molecular targets (AKT, STAT-3and PI-3K) results in the growth retardation and invasion of prostate cancer. Plumbaginresponsible for cell death induction in cancer cells and also prevent growth of these cells.

Figure No-8

Several therapeutic procedures are unit accessible for the treatment of cancer, and in most

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cases, undesirable side effects (GIT disorders, kidney damage, and other complications) are associated with them. These compounds include phenol compounds, alkaloids and monoterpenes. In addition to these, indicators like vinblastine, vincristine, boswellicacid,Taxol and umbelliprenin and compounds such as quercetin, catechin, cucurbitacin, kaempferol, thymol, carvacrol, 1 and 1,8-cineole, myrecene,α-pinene and β-sitosterol have anticancer effects. These compounds have antioxidant properties, and inhibition of damage to DNA, cell cycle arrest, induction of apoptosis, inhibition of angiogenesis in tumor cells, and its anticancer effects are new and more effective.

Conflicts of interest

The authors confirm that this article content has no conflict of interest**.**

Aknowledgement

Declared none.

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