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Medicinal Plants and Herbal Compounds: Cancer Prevention and Treatment

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Abstract

Objective: The global burden of cancer is increasing due to aging, population growth, poor nutrition, inadequate exercise, as well as high-risk behaviors such as smoking and alcohol consumption. According to the World Health Organization, in 2008, the ASR (Age Standardized Rate) of cancers of both sexes (according to the global reference population) in Iran is 107.7 per 100,000 population, and its five most common cancers are stomach, breast, colorectum, Bladder, and leukemia. According to global ASR statistics, the most common cancers in both sexes are 181.6 and five cancers are lung, breast, colorectal, stomach, and prostate. With the increase in life expectancy and the increase in the aging index in the population of Iran, it is expected that the incidence of various cancers will increase in the coming years and a lot of humans and financial capitals will be wasted. On the other hand, with the advancement of technology in bioinformatics and molecular techniques, a lot of information has been obtained that will help in the early detection of cancer. Meanwhile, despite much research on cancer and its treatment, this disease is still one of the biggest health problems in human societies.

Material and Methods: This research has been prepared in the form of a library, also articles reported in authoritative sources such as Springer, Elsevier, PubMed, Nature, etc. in 2021.

Results: Alfalfa extract and *Aloe vera* L. have been used to treat breast cancer and prevent dermatitis. *Nigella sativa* and boron have been used in the treatment of prostate, breast, cervical and lung cancers. Wild pistachio has been shown to affect colon cancer cell line. Artichokes improve the liver, bile, lower cholesterol and blood lipids. The leaves of the Hedera plant (*Hedera pasuchovii* G.Woronow) have been shown to affect breast cancer cell line (MCF-7) and uterus (Hela) as well as blood lymphocytes. Bakhtiari savory has been effective on Hela cancer cell line.

Conclusion: Considering that chemical drugs used in the treatment of cancer, in addition to creating drug resistance the study of medicinal plants and factors of natural origins, such as compounds derived from medicinal plants used in the treatment of cancer is one of the most important objectives of the present study.

Introduction

Inflammation refers to the uncontrolled growth of tissue that results from an imbalance between cell division and the phenomenon of apoptosis due to complex factors. In cancer cells, there are no cell cycle controls and they do not respond naturally to the body's control mechanisms. The proteins involved in the signaling pathways that affect the cell cycle are altered, and cell cycle disruption is observed, with cells behaving differently and requiring different therapies. It is a combination of genetic events and environmental and lifestyle factors and is one of the leading causes of death worldwide. It is the third leading cause of death in Iran after cardiovascular disease and accidents [1].

Lung cancer is the third most common cancer after prostate and breast cancers and is the most common cause of cancer death worldwide, with 1.59 million deaths reported in

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2012. Among women, cervical cancer and breast cancer are the most common and malignant cancers in women [2].

According to official statistics, the incidence of cancer in Iranian men and women is 134 and 128 per 100,000 population, respectively, while the global average incidence of cancer in men and women is 205 and 165, respectively. Therefore, the incidence of cancer in Iran is lower than the global average. The most common cancers in Iranian men are skin, stomach, prostate, bladder and colon, and the most common cancers in Iranian women include breast, skin, colon, and stomach cancers, respectively [3].

Cancer is one of the three leading causes of death in women in the world so that It is diagnosed in every woman, one in three (11.38%) cancer in all areas, one in eight (56.12%) breast cancer, one in 17 (69.5%) lung cancer, one case out of every 18 patients (55.5%) colorectal cancer, one case out of every 37 patients (69.2%) uterine cancer, one case out of every 58 patients (1/1) 72%) Ovarian cancer, one in every 128 (0.78%) cases of cervical cancer [4].

Many of these cancers can be prevented by adopting a healthy lifestyle. Many, if diagnosed early, are easier to treat and patients are much more likely to recover. Today (2019), the number of people dying from cancer is down from three decades ago. Half of the people being treated for cancer today will be five years old, and more than 40% of them will still be alive after 10 years. The average 10-year survival rate for cancer has doubled in the last 30 years. The most important reason for improving patient survival in addition to effective treatments is to increase public awareness and improve early detection methods for cancer [3].

So far, more than 200 different types of cancer have been identified, most of which have no definitive cure, but to prevent their growth and progression, surgery, radiotherapy, chemotherapy, hormone therapy, gene therapy are used [5]. Despite much research on cancer and its treatment, it is still one of the biggest health problems in human societies.

Due to the fact that chemical drugs used in the treatment of cancer, in addition to drug resistance, also have side effects, the study of factors of natural origin, such as compounds derived from plants that have less harmful effects, is one of the most important goals. Research in the field of cancer treatment [6, 7]. On the other hand, with technological advances in bioinformatics and molecular techniques, a lot of information has been obtained that will help in the early detection of cancer [7].

In studying the drugs used to treat cancer, scientists are always looking for more effective drugs with less toxicity on healthy cells. Today, the use of medicinal plants (native plants) in the treatment of cancer is extremely important. Despite the beneficial effects of anticancer drugs, several mechanisms have been reported for their side effects of cardiac and hepatotoxicity, including the production of free radicals, mitochondrial damage, and cytotoxicity [8].

The reason for the growing concern about the side effects of chemical drugs and the ineffectiveness of some of them in long-term use, the use of natural compounds has received more attention as an alternative or adjunct to treatment [9]. Therefore, efforts to find more effective drugs with fewer side effects for cancers using native species are of interest. Even in some treatments, knowing the relationship between estrogen and breast cancer can provide a good perspective. In addition, phytoestrogens (isoflavones, omstans and Lignans) are natural compounds found in plants and are used in the treatment of many cancers [10]. There are many different treatments for cancer. Apart from the common methods, today natural products and derivatives of medicinal plants can play an important role in the treatment of cancer.

Due to the cytotoxic effects of *Taverniera cuneifolia* on human cancer cell lines, it can be studied in the line of anti-cancer plants. Field pumpkin (*Cucurbita pepo*) is used to treat prostate swelling, urinary tract irritation and increase the body's resistance to pathogens. Nettle extract has a growth inhibitory effect on cervical cancer cells. Carrots are known as anti-cancer herbs with their anti-proliferative effect on cervical and breast cancer cells. Medicinal plants effective in preventing various types of cancer include green tea, squash, asparagus and turmeric, which are considered to be nutritious [11].

The study of factors of natural origin, such as compounds derived from plants that have less harmful effects, is one of the most important goals of research in the field of cancer treatment. For this purpose, extensive studies have been conducted on various plants and they have been studied and evaluated for their cytotoxic and anti-cancer effects. Therefore, in the present study, some medicinal plants and their derivatives in the treatment of cancers were investigated.

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This research has been prepared in the form of a library as well as articles reported in authoritative sources such as Springer, Elsevier, PubMed, Nature, etc. in 2021. We tried to use more articles that were published in the period 2000 to 2021, with an emphasis on 2015 to 2021. Some words that were Searched, are like these: herbs, alfalfa, *Aloe vera* L. *Nigella sativa*, Boron, Hedra, Savory, Breast cancer, Dermatitis, Breast cancer, Cervix, Lung cancer, Colon cancer, Liver, Cholesterol and hyperlipidemia, Blood lymphocytes, etc.

Material and methods

In this research was used some keywords, like: Savory, Breast cancer, Alfalfa, Pistachio, Boron, Eugene, Thymoquinone, Medicinal plants, Cancer, prevention and treatment, Fennel flower, *Aloe vera* , Artichoke, Hedera plant, *Satureja hortensis* L., Figs, Lemongrass, and Herbal compounds used to treat cancer. These keywords were search in some website and publisher like: PubMed, Elsevier, Scopus, WOS, Science direct, CRC, Springer, Google scholar and etc. from 2010 to 2022

Phenolic substances of medicinal plants

Today, more than 60% of the anti-cancer compounds used to treat cancer patients come from plant, marine and microorganism sources. Secondary metabolites in plants have several biological effects including anti-inflammatory, anti-cancer, analgesic and cardiovascular effects [12, 13].

In fact, the phenolic compounds of the extract increase the inhibition of cancer cells due to their abundant antioxidant properties [14]. Phenolic compounds in medicinal plants play an important role in the prevention and treatment of cancer. Phenolic compounds include phenolic acids, flavonoids, tannins, curcuminoids, coumarins, lignans, quinones, etc., and have properties such as antioxidants, anticoagulant, anti-inflammatory effects [15-17]. These isolated derivatives of medicinal plants have been studied in various cancer cell lines, including strawberries and raspberries, which have been studied in breast, colon, and prostate cancer cell lines, and various concentrations of these phenolic compounds have been shown to inhibit cell growth [18, 19].

Results

Alfalfa

Alfalfa (*Medicago Sativa* L.) seeds rich in cannabinoids (L-Canavanine, a non-protein amino acid that is a potentially toxic anti-metabolite of L-arginine that has demonstrative anti-neoplastic activity against a number of cancers and cancer cells), containing 1.4 to 1.8% of dry weight matter. The cannabinoid content of alfalfa seeds has been reported to be comparable to the levels present in the seeds of genus *Canavalia* members, which are abundant sources of this anti-metabolite [20].

Alfalfa ethanolic extract is rich in antioxidant compounds. Phenolic and carotenoid contents were reported to be 32.63±1.17 mg/gDWt and 33.41±2.22 mg/gFW, respectively [21].

Alfalfa extract can be useful in improving the cancer disease with its effect on estradiol levels and lipid profiles in mice with breast cancer [10].

Different concentrations of alfalfa ethanolic extract significantly reduced cell growth compared to the control group and had the highest antioxidant activity and cytotoxicity against MCF7 cell line. The most prominent growth inhibition was recorded at 83.74% at a concentration of 400 µg/ml. In addition, different concentrations of alfalfa have been effective in inhibiting DPPH radicals. The highest inhibitory effect (53.4%) was obtained at concentrations of 3.4 mg of the extract [21].

The effects of cytotoxicity of alfalfa leaf extracts were investigated on the leukemia cell line of P388 mice and their doxorubicin-resistant counterpart (P388/DOX). It was concluded that inhibition of cell growth induced by alfalfa leaf extract is mediated through induction of apoptosis. DNA fragmentation analysis showed that the execution of programmed cell death was achieved by activation of caspase-3 and led to PARP. Toluene extract (To-1), the most active extract obtained from crude alfalfa extract, led to the identification of 3 terpene derivatives and 5 flavonoids. Among them, (-) - medcarpine, (-) - mililotocarpane E, milpurpan, trisine and chrysolirol have been shown to have cytotoxic effects on P388 as well as P388/DOX cells. It has been reported that alfalfa leaf extract may have acceptable potential in chemotherapy and cancer prevention [22].

Boron

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Boron-rich diets significantly reduce the risk of cancers including prostate, breast, cervical and lung cancers. The mechanisms by which boron may affect cancer are still unknown, but evidence suggests that boron appears to have antioxidant and anti-inflammatory properties. Other suggested mechanisms for boron activity in cancer cells include inhibition of protease cell activity, dehydrogenase, mRNA editing, and cell division, and induction of apoptosis. Boron-based compounds show promising effects for the chemotherapy of a variety of cancers.

Fennel flower

One of the medicinal plants that plays an important role in respiratory diseases and cancers is *Nigella sativa*, the active ingredient of which is thymoquinone. Research has shown that herbs, including *Nigella Sativa*, play an important role in the prevention and treatment of cancer by modulating cellular signaling pathways [9,24,25]. Although possible mechanisms have been proposed, the results of studies on the association are inconsistent between *Nigella sativa* supplementation and VEGF levels, Inhibition of growth and angiogenesis of prostate cancer cells is *in vivo* and *in vivo* [26, 27], while it is related that the expression of VEGF-A gene in cells treated with *Nigella sativa* extract compared to Control cells did not change significantly [27].

Due to the effect of NNK on inflammation and subsequent lung cancer and malignancies [28] on the one hand and the multiple role of VEGF in inflammatory processes and tumor progression [29], The use of active ingredients of medicinal plants in the form of nanocapsules in the first stage can control the drug delivery system. Then the concentration of the drug in the blood plasma is maintained for a long time, without reaching the undesirable and ineffective areas. It is also possible to provide drugs that are more effective in a shorter period of time or in lower doses [30].

The effect of a period of consumption of *Nigella sativa* nanocapsules on histopathological structure and endothelial growth factor levels of lung tissue of rats exposed to tobacco-derived nitrogen amine ketone and concluded that consumption of *Nigella sativa* nanocapsules by reducing VEGF levels can reduce pulmonary inflammation Cigarette smoke. NNK exposure has also been shown to significantly increase vascular endothelial growth factor and increase levels of inflammation. However, due to the anti-inflammatory role of *Nigella sativa* nanocapsule supplementation, it is to a large extent effective in preventing the harmful conditions of NNK in the lungs of rats and can be considered as a treatment strategy. It seems that with the change in the number of days and the dose of *Nigella sativa* nanocapsules and NNK, other pathological changes in lung tissue occur, so further research is recommended in this regard [2].

Pistachio

The results of analysis of *Pistacia lentiscus* L essential oil by GC-MC showed the presence of Sesquiterpene at a rate of 4% and no monoterpene alcohol was observed in it [12]. In other studies on *Pistacia khinjuk* Stocks and *Pistacia chinensis* Bunge, 16% and 8% of monoterpene alcohol have been reported, respectively [12]. The main constituents of *Pistacia Khinjuk* essential oils are pinene, β-pinene, myrcene, beta-caryophyllene, germacrene B and spathulenol, which are responsible for antioxidant and antifungal activity [31].

The results obtained from the analysis of *Pistacia Khinjuk* fruit essential oil showed that its main components include phellandrene, α-pinene and Limonene-Δ, the amounts of which were reported to be 52.33%, 15.27% and 4.08%, respectively [32,33]. On the other hand, antioxidant and antimicrobial activity for *Pistacia Khinjuk* leaves was reported due to the presence of their phenolic compounds [31, ,k.hj 34].

Pistachio and its skin are rich sources of phenolic, antioxidant and anti-inflammatory compounds such as gallotannins, gallic acid, myricetin and quercetin and are in the top 50 rich sources of phenolic compounds. These compounds are more in the skin of pistachios than in *pistachio kernels*. Different species of pistachios as well as different components of pistachio trees and fruits show antioxidant properties. Including pistachio leaves and fruits has shown antioxidant properties [35].

The effect of methanolic extract of wild pistachio on colon cancer cell line was concluded and it was concluded that wild pistachio contains significant amounts of polyphenolic compounds, flavonoids and anthocyanins. Due to the presence of bioactive compounds, methanolic extract of wild pistachio has significant cytotoxic effects. It has been shown to be against human HT29 colon cancer cells [36]. Also, the effect of coriander skin (wild pistachio) on T47D breast

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cancer cell line has been investigated and its anti-cancer properties have been confirmed [37]. The effect of hexane, ethyl acetate, methanol and aqueous extract of pistachio on clone and breast cancer was investigated by MTT method and the results showed that the reduction of cell viability of these cancers was achieved [38]. Coriander-derived compounds induce apoptosis in human intestinal cancer cells [39].

The cytotoxic effects of pistachio leaf extract (*Pistacia khinjuk*) on Hela cancer cell line have been investigated and has been confirmed the role of flavonoids in relation to anticancer effects. The anticancer effects of polyphenol compounds are associated with mechanisms such as inducing programmed cell death, inhibiting cell growth, inhibiting protein kinase activity, and preventing cell invasion [40].

Toxicity effect of pistachio skin hydroalcoholic extract and its liposomal form on liver cancer cell line (HepG2) was concluded and it is related that hydroalcoholic extract of pistachio skin reduces the survival of HepG2 cells and the cell viability decreases with increasing time and increasing concentration [41].

The cytotoxic effect of ethanolic extract of wild pistachio leaf (*Pistacia Khinjuk*) was conduacted on two cancer cell lines Hela and MCF-7 and it is related that the ethanolic extract of wild pistachio leaf significantly decreased the growth of Hela and MCF-7 cells, in different concentrations Compared to the control group after 72 hours. The highest percentage of growth inhibition at a concentration of 0.156 mg/mL was 81.33% and 76.76%. IC50 values of 2.41 and 2.40 mg/mL were calculated for Hela and MCF-7 cells, respectively [1].

Artichoke

The artichoke plant belongs to the chicory family and is also known in Persian as Ardeh Shahi. Artichoke plant supports the liver, antimicrobial, lowers cholesterol and blood lipids, stimulates the expression of nitric oxide synthetase gene and improves endothelial cells in atherosclerosis. Artichoke leaves contain phenolic, flavonoid and acidic compounds. Caffeic acid and esters of caffeic acid, chlorogenic and pseudochlorogenic acid that improves liver damage and insulin resistance by autophagy suppression mechanism by inactivating the JNK pathway in the NAFLD mouse model Neochlorogenic acid, cinnaric acid and major caffeic acid. They are considered to have liver-improving, biliary, cholesterol-lowering and lipid-lowering effects [42].

Hedera plant

The effects of cytotoxicity of *Hedera pasuchovii* G.Woronow leaf extract was conducted on breast cancer cell line MCF-7 and uterine Hela as well as on peripheral blood lymphocytes. It was concluded that methanolic extract of *Hedera pasuchovii* G.Woronow leaf inhibits cell growth and induces apoptosis in Hela and Mcf-7 cancer cells. This extract has also reduced the genetic toxicity of cisplatin at high doses [43].

Methanolic extract of Hedera leaves significantly reduced the growth of cancer cells compared to the control group at doses of 500 and 1000 mg/ml. At a concentration of 1000 mg, the rate of primary apoptosis was 40.71% and secondary apoptosis was 27.17%. In MCF-7 cell and in Hela cell, the rate of primary apoptosis was 33.57% and secondary apoptosis was 14.68%. In terms of genetic toxicity, extract-treated cells had a significant reduction of micronuclei by approximately 68% and 91% in cells at doses of 5000 M and 1000 Mμ, respectively, compared to cisplanin [43].

Aloe vera

The *Aloe vera* (*Barbadensis Miller Aloe vera*) plant has compounds with antioxidant properties. *Aloe vera* has several properties: anti-cancer, antioxidant, anti-inflammatory, immune and liver protection, stomach ulcer healing and anti-diabetic. *Aloe vera* is an industrial product. a wide range of commercial products are available in the market based on *Aloe vera* [8].

The fleshy leaves of Aloe vera contain a gel that contains all the properties of the plant. Aloe vera gel is used as a source for the production of healthy foods, especially drinks with health effects. 99% of the gel of *Aloe vera* is water. The rest of the gel ingredients are various chemical compounds including glucomannan, water-soluble polysaccharides, prostaglandin precursors, vitamins A, C, E, lignin, saponin, plant sterols. It includes amino acids, anthocyanins, flavonoids, etc. Sky from the carbohydrates in *Aloe vera* has anti-tumor properties. Mannan, one of the compounds in aloe, has a great effect in preventing the activity of cancer cells [8].

Effect of *Aloe vera* (L.) Burm.f. wan investigated on the prevention of dermatitis in women with breast cancer undergoing radiotherapy and it is concluded that topical use

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of *Aloe vera* gel has been effective in preventing and delaying the onset of dermatitis due to radiation therapy [44].

In a study, different concentrations of *Aloe vera* gel were investigated compared to doxorubicin and cisplatin (as a positive control) and they concluded that The IC50 level of doxorubicin on HT-29 cell line was 5.528 µmol/mL. The IC50 level of cisplatin in this cell line was 54.53 µmol/mL. The IC50 level of doxorubicin on HGF cell line was 3.178 µmol/mL. The IC50 level of cisplatin in this cell line was 85.53 µmol/mL. *Aloe vera* gel was significantly different from the positive control group in Concentrations of 500 and 1000 µg/mL in HT29 cell line and concentrations of 250, 500, 1000 000 g/mL in HGF cell line [8].

Aloe vera gel (100 and 200 mg/kg) orally for 10 days provides significant protection against DOX-induced cardiotoxicity by significantly reducing serum LDH, serum CPK, cardiac lipid peroxides, tissue catalase and SOD. Tissue is associated with increased GSH levels in blood and tissue. *Aloe vera* gel has been reported to provide a dose-dependent protection against DOX-induced cardiovascular disease [45].

The apoptotic effects of aloe-emodin on MCF-7 cell slaves were investigated and it was concluded that by increasing the concentration of aloe-emodin in a dose- and time-dependent manner, the viability of the cells decreased. The highest effect of *Aloe vera* was related to the concentration of 100 µmol at 72 hours after cell treatment. Apoptosis was induced and Fas expression was dose-dependent. Concentration of 100 µmol of aloe-amodine showed the highest percentage of apoptosis and the highest expression of Fas activity in MCF-7 cells [46].

Satureja hortensis L.

Savory is a plant of the mint family and in Iran there are 12 species of annual and perennial grasses, 8 of which are specific to Iran. Savory is used in the treatment of muscle aches, cramps, nausea, infectious diseases and diarrhea, and is also a digestive, diuretic, expectorant, analgesic, anti-cancer, stimulant and stomach tonic [46-48]. Aqueous extract of safflower reduces the growth of *Aspergillus flavus* and also inhibits the production of toxins. MIC of aqueous extract and savory essential oil were obtained at concentrations of 0.031 and 1% mg/ml, respectively [49].

The cytotoxic effect of *Satureja bachtiarica Bunge* hydroalcoholic extract on Hela cancer cell line has been investigated and it has been concluded that *Satureja bachtiarica Bunge* hydroalcoholic extract has a dose and time dependent anti-cancer effect on Hela cancer cells, so that the highest percentage of cell death has been observed by increasing the extract concentration and incubation 72 Hours. The plant extract did not show significant cytotoxicity on normal fibroblast cell lines. Therefore, it has been suggested that it seems that with more research in the future, its compounds can be used in the treatment of cancer [50].

Figs

The cytotoxic effects of different extracts and latex of *Ficus carica* L. on HeLa cell line were investigated and the results showed that the latex and various extracts (ethanol, ethyl acetate and dichloromethane of leaves and fruit) of *Ficus carica* L. can cause Hela Cells to survive at concentrations of at least 2 µg/mL in a dose-dependent manner. Approximate IC50 values of ethanolic extract, ethyl acetate and dichloromethane of leaves and fruits were 10, 19, 12 µg/mL and 12, 12, 11.5 µg/mL, respectively. The IC50 for latex was about 17 micrograms per milliliter [51].

Lemongrass

Lemongrass (*Melissa officinalis* L.) is belongs to the mint family and has antibacterial, anti-depressant, anti-inflammatory, anti-cancer and anti-viral medicinal properties. Most of the medicinal effects of this plant are attributed to its active ingredient, rosmarinic acid [52].

Phytochemical evaluation of cytotoxic, antioxidant and antibacterial toxicity of Lemongrass (*Melissa officinalis* L) essential oil in Marivan region was investigated and they concluded that the extraction efficiency of Lemongrass essential oil was 18.1% and its main components were geranium (39.30%) and geranium (19.26%). Based on the results of beta-carotene decolorization test, inhibition of oxidation of linoleic acid by lemongrass essential oil and butyl hydroxytoluene standard, 48.72% and 48.96%, respectively. LC50 content of lemongrass essential oil and vincristine sulfate were obtained 76.62 and 75.10 µg/mL, respectively, based on the results of saline shrimp lethality test [53].

Plants of the *Caesalpinia gilliesii* family

The *Caesalpinia gilliesii* plant is a shrub of the bean genus that is somewhat drought tolerant but sensitive to cold, so that in cold regions it dries out and begins to grow in the spring of next year. The root of this plant is used to treat fever, wounds and cough. Some also believe that eating its root in early pregnancy can cause miscarriage. However, it should be

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noted that the seeds and pods of green seeds of this plant are toxic, irritating and cause severe vomiting and other abdominal symptoms [54].

Different species of *Caesalpinia gilliesii* plants have been studied for phytochemical composition and biological effects. The results showed that different parts of plants, including leaves, seeds, stems, roots and pods of fruit, contain diterpene compounds. Among these species, the effects of cytotoxicity on different categories of cancer cells have been investigated and some of them have significant cytotoxic effects [54].

Herbal compounds used to treat cancer

The first herbal medicine, the anti-leukemic alkaloids vincristine and vinblastine are derived from the medicinal plant Periwinkle. Taxel is prepared from the medicinal plant (which has a wide spread in the forests of northern Iran), which is a valuable option in the treatment of common cancers. Silymarin in marijuana has strong anticancer effects on a variety of tumor cells such as the prostate, clone and bladder. The furanocoumarin in oral angelica may be useful in developing new drugs to treat a variety of cancers, such as breast cancer. Cynigrin in mustard produces isothiocyanate under the influence of the enzyme myrosinase, which has been shown to prevent cancer in studies in mice [11, 55].

Taxel is a plant-based anticancer drug that is widely used to treat a variety of cancers. On the other hand, the presence of DBAT gene and production of taxel anticancer drug in endophytic fungi isolated from native Iranian yew (Taxus baccata) in vitro and concluded that a total of 60 isolates of endophytic fungi isolated from native Iranian yew and presence The DBAT gene has been confirmed in 22 isolates. The results of thin layer chromatography have proven the production of taxel in the culture medium of some isolates. It has been suggested that endophytic fungi producing yew taxel can be a suitable alternative source for taxel supply [56].

Delivery to the target tissue

Cancer is the second deadliest disease in the world, which in recent years, especially with the increase in the use of chemicals and other mutagens and on the other hand, the increase in life expectancy due to medical advances and thus its prevalence in various communities, has become one It has become the biggest challenge of medical science in the world. Due to the special conditions of this disease and the fact that the drugs used to control this disease have serious and many side effects on the proliferative tissues of the body such as immune cells and also that rapid proliferation with many mutations in tumor tissues causes drug resistance. Targeting drugs to cancer tissues and cells is the most important challenge in fighting this disease [41,57].

Many drugs are used to treat different cancers depending on the type and stage of the disease. In many cases, the use of a very effective drug is impossible or very difficult due to characteristics such as hydrophobicity or instability in the body, and these disadvantages make the drug effective in treating the disease. It strongly affects. In order to solve these problems, many drug delivery systems have been proposed by various research groups for this purpose, and some of them have reached the commercial stage or are in the clinical trial stages [41, 58, 59].

Use of nanotechnology to treat and diagnose cancers

Today, the use of nanotechnology to treat and diagnose a variety of diseases, including cancer, has received much attention. Nanotechnology focuses on new and alternative methods of transporting and delivering drugs and increasing their effectiveness in the treatment of cancer. Drug delivery is one of the most important fields of research in the world and includes various sectors such as regulating the physicochemical properties of effective factors in drugs, targeted delivery of drugs to the target organ, kinetic control of drug release and designing appropriate drug formulations [41, 58].

One of the most active areas of research for drug delivery systems today is the ability to encapsulate and release drugs in response to an acidic environment. Due to the fact that the pH in the areas of tumor tissue has more acidity than blood and other tissues, so using pH-sensitive nanocarriers, the drug can be delivered to cancer cells in a targeted manner. Porous nanoparticles are good candidates for pH-sensitive drug delivery systems. Drug delivery under nanoparticle conditions must be biocompatible. Metal-organic framework nanoparticles have been considered in drug delivery today due to their large size pores, high specific surface area, selective adsorption of small molecules [41, 57, 59].

Conclusion

Since the study of different methods of cancer treatment is one of the most important goals of medical research in the present age, so to find appropriate and effective treatments,

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extensive efforts have been made, including the study of the effects of cytotoxicity. Materials derived from plants in vitro using the MTT assay method.

Although MTT assay is a widely used method in various laboratories and research centers, but it also has its drawbacks, including the fact that this method is based on the activity of mitochondria of living cells and using the results of this diagnostic test. The reduction in cell number cannot be judged with absolute certainty, because if a substance causes a change in the number of mitochondria in a cell, its effect will be interpreted by this test as similar to a change in the number of cells. On the other hand, for clinical use of plant compounds, more and more accurate tests are needed. On the other hand, for clinical use of herbal compounds, more and more accurate tests are needed. Therefore, it is recommended to study *in vivo*, isolation and purification of active compounds in the extract, determine the structure of the active component of the extract, determine the biochemical mechanism of anti-cancer activity and study the anti-cancer effects of the extract of this plant.

To prevent and reduce the risk of cancer, it is necessary to maintain a ratio of physical activity and regular exercise, maintaining a normal weight, breastfeeding and not consuming postmenopausal hormones in women, avoiding high-fat and fried foods, salty and ready-to-eat foods. And canned food, increase the consumption of fruits, vegetables and grains and fish meat, early diagnosis including self-examination, examination by a doctor and mammography, radiography and ultrasound should be done with the necessary care.

Conflict of interest

None of the authors have any conflict of interest to declare.

Consent for publications

All authors approved the final manuscript for publication.

Availability of data and material

Data are available on request from the authors.

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Ethics approval and consent to participate

No human or animals were used in the present research.

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