

A Review on Medicinal Plants against Cancer

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Abstract

Cancer is one of the life-threatening diseases which creates major problem in both the developing and developed countries. Demand for new methods to prevent this disease is growing increasingly. Plants have always been a basis for the traditional medicine systems and they have provided continuous remedies to the mankind for thousands of years. Medicinal plants are considered as a repository of various bioactive compounds and used for long time due to its therapeutic properties. Plant derived product has benefits over synthetic medicine which increased the utilization of medicinal plants in the healthcare sector as several plants' derived compounds show potential role against cancer treatment. Plant based anticancer agents includes vincristine, taxol, vinblastin, stigmaterol, camptothecin, resveratrol, etc., are in clinical use all over the world. In the present review, an effort has been made to provide the information about the role of various medicinal plants against cancer.

Keywords: Cancer; Anticancer agent; Medicinal plants; Bioactive compounds; Cytotoxicity

naturally occurring compounds known to possess cytotoxicity effects, as they display potential to destroy cancer cells. Due to these advantages of medicinal plants they are in high demand and several species of medicinal plants have been investigated and selected for the preparation of cancer medicines. Recently, there has been an increased scientific interest in the study of materials from plant source as an anticancer compound. Several studies have found the role of medicinal plants in prevention and treatment of cancer [2]. National Cancer Institute has approximately screened 35,000 plant species for their potential anticancer activities and they have found that among them about 3,000 plant species have shown reproducible anticancer activity [3]. Emergence of important anti-cancer agents from natural source requires more research in order to develop more drugs to treat this disease. Medicinal plants contain wide ranges of secondary metabolites which include flavonoids, flavones, anthocyanins, lignans, coumarins, isocatechins and catechins [4]. These bioactive compounds are mainly responsible for the antioxidant prosperity of medicinal plants. The increasing side effects and expensive medication has tilted the focus of researches on herbal medicines. Therefore in this review an effort has been made to provide information about the medicinal plants that possesses anticancer activity.

Introduction

Cancer is one of the deadly diseases which are characterized by the irregular cell proliferation. The most common reason behind the cancer is lifestyle changes and therefore an urgent need to find a better treatment for the disease is required. According to World Health Organization [1], more than 14 million people diagnosed with cancer and 8 million died in 2012 (www.who.int). High mortality and incidence make it an important public health and economic issue which requires an effective prevention. Medicinal plants have various advantages over chemical products, because plant derived compounds are more tolerant and non-toxic to the normal human cells. Already available conventional therapies for the treatment of cancer are radiotherapy and chemotherapy which have various side effects like neurological, cardiac, renal and pulmonary toxicity, seriously affecting the health of the person. Therefore, an alternative method is required to develop that include less toxic and more potent anticancer drug as compare to the drugs available in the market. Several studies [2] have been made on

Anticancer Activity of Medicinal Plants

Actaea racemosa

Belonging to the family Ranunculaceae is commonly known as black cohosh and black snakeroot. It contains cycloartenol type triterpenoids, cinnamic acid derivatives and cimicifugoside. This plant is also well known for its role in amenorrhea and ovaritis [5]. The main compound of this plant is actein and it shows inhibition of human HepG2 liver cancer cells growth by reducing the cholesterol and free fatty acid levels in liver [6].

Ardisia crenata

It belongs to the Myrsinaceae family and commonly known as coral bush, spice berry, red berries and coralberry. It is commonly found in warm climate of tropical and sub-tropical regions. It contains cyclic depsopeptide, triterpenoid saponins and alkenylphenol [7]. Anticancer activity of this plant is due to the presence of ardisiacrispin, which is a mixture of two triterpenoid saponins i.e. ardisiacrispin A and B. One study

showed that the ardisiacrispin inhibits proliferation of uncontrolled liver cancer cell line (Bel-7402) by microtubule disruption and induction of proapoptotic activities [8].

Bacopa Monnieri

It belongs to the Scrophulariaceae family and found throughout the plains in India. It is reported to contain tetracyclic triterpenoid saponins, bacosides A and B, herpestine, brahmine, flavonoids, stigmasterol [9]. Stigmasterol is known to possess anticancer activity by inducing apoptosis mediated by the activation of protein phosphatase 2A by ceramide. Study conducted by Ghosh [10] evaluated the antitumor activity of stigmasterol isolated from *Bacopa Monnieri* on Ehrlich Ascites Carcinoma in swiss albino mice and found that stigmasterol enhanced the life span of tumor bearing mice by decreasing the tumor volume and viable cell count.

Bidens Pilosa

It belongs to the Asteraceae family and native to the America. It contains polyacetylenes, flavonoids, phenylpropanoids terpenoids, and others compounds. Phenyl-1, 3, 5-heptatriyn possesses toxicity profile on normal blood cells in erythrocyte osmotic fragility experiments along with other extracts [11]. Hexane, methanol and chloroform extracts of *Bidens pilosa* and their fractions were tested on various cancer cell lines. Results showed the antitumor activity of extracts among which hexane extract showed maximum activity [12].

Catharanthus roseus

It belongs to the Apocynaceae family and commonly known as rosyperiwinkle or Madagascar periwinkle. Its main compound is alkaloids, and used for the circulatory diseases treatment and provide relief to the normal cerebral blood flow obstruction. Vinblastin and vincristine are the two well-known compounds which significantly effects against the human neoplasm. Vincristin sulfate arrest mitosis and utilized for the treatment of acute leukemia in children and vinblastin sulfate is utilized for the treatment of choriocarcinoma, lymphosarcoma, neuroblastoma and carcinoma of lung, breast and other organs [13].

Centella asiatica

It belongs to the Apiaceae family and commonly known as brahmamanduki in Hindi, mandukaparni in Sanskrit and pennywort in English. It is commonly found in India, Australia, Pacific Islands, New Guinea, Iran and Malaysia. It contains numerous compounds such as asiaticoside, pectic acid, hydrocotyline, sterol, flavonoid, vallerine, ascorbic acid and thankunosides [14]. Partially purified fraction of *Centella asiatica* suppressed mouse lung fibroblast cell proliferation and oral administration slowed the solid development and ascites tumours [15]. Pre-treatment with this plant increase the survival time of irradiated animals and show protection against radiation induces damage in liver [16]. This plant shows inhibition in lipid peroxidation in various organs like lungs, liver, heart, brain,

spleen and kidney and shows potential towards the cancer inhibition [3].

Cedrus deodara

It is belongs to the Pinaceae family and found in the Western Himalaya, northern Pakistan, north central India, eastern Afghanistan, western Nepal and south-western Tibet. It is known as deodar in Hindi and devdar in Sanskrit. It contains taxifolin, cedrin, cedrin, cedodarin and deodarin. Stem wood extract of *C. deodara* which contains lignin composition exhibits cytotoxicity to the human cancer cell lines [17] and also induce tumor regression in murine models [18]. Bark of this plant shows potential in the rheumatoid arthritis inflammation, fever, cancer, dysentery, diarrhea and ulcer [3].

Citrus

Citrus fruits belong to the family, Rutaceae found all over the world and top the world fruit market. There are four important species in citrus fruit with a wide variety of hybrid species as well. Several reports show citrus as a potent anti-tumor agent. Citrus peels are a rich source of phytochemicals such as phenols, limonoids, flavonoids and polysaccharides. Zhao et al. [19] extracted and purified an acidic polysaccharide from the peels of *Citrus aurantifolia*. The main components of the acidic polysaccharides (CA) are rhamnose (Rha), arabinose (Ara), galactose (Gal), glucose (Glu), mannose (Man) and galacturonic acid (GalA). The antitumor activity of CAs was evaluated in mice transplanted H22 hepatoma cells. CA restricted the tumor cell cycle in S phase and stimulated the expression of proapoptotic factor caspase 3. CA enhances immune response against cancer cells by increasing the levels of tumor infiltrating CD8+ T lymphocytes. It inhibits the expression of anti-apoptotic protein BclxL and Mcl-1. The results conclude that acidic polysaccharides from citrus peels could be used as an adjuvant in treating hepatocellular carcinoma [19]. Park et al. [20] characterized a pectic polysaccharide, rhamnogalacturonan II (CPE-II) from peels of *Citrus unshiu*. Citrus peels are an abundant source of polyhydroxyl flavonoids (PHFs) such as hesperidin, neohesperidin and naringin; and polymethoxyflavones (PMFs), most of these components act as potent antitumor compounds. PMFs are reported to significantly inhibit metastasis by restricting cell adhesion and its invasion [20]. It enhances cytolysis by increasing the expression of NK cells. Cell cycle is arrested in G1 phase by inhibiting cyclin-dependent kinases (Cdk) and enhancing Cdk inhibitor proteins. The efficacy of citrus peels against skin cancer has been studied in a two stage skin carcinogenesis model [20].

Cynodon dactylon

It belongs to the Poaceae family and possesses several medicinal activities which include anti-helminthic, anti-diuretic, hepatoprotective, anti-inflammatory activity, prostatitis, dysentery, etc. The nontoxic dose of the petroleum ether of *Cynodon dactylon* on normal vero cell line showed the cell viability of 97% at a concentration of 0.007 mg/ml which decreased with increase in concentration. Extract showed a potential cytotoxic activity against Hep-2 laryngeal cancer cell

line. Cyclophosphamide served as pcontrol and 96.2% cancer inhibition was observed. The concentration of petroleum ether extract of *Cynodon dactylon* at 10 mg/ml showed inhibition percent with regard to cytotoxicity of 93.5% that was comparable to the positive control [21].

Languas galangal

It belongs to the Zingiberaceae family and commonly known as the blue ginger or Thai ginger is a common culinary herb used in Thai cuisines. 1'-Acetoxychavicol acetate (ACA) extract from *Languas galanga* and *Alpinia galangal* is a potent anti-tumor agent. It has been documented to suppress chemical and virus induced tumor initiation and proliferation. A study reported that ACA mediated its antitumor activity by modulating the activity of transcription factor, NF-kappa B which regulates metastasis and cellular proliferation [22].

Piper longum

It belongs to the Peparaceae family and used as a spice. It contains longumine and used for the treatment of cough, chronic bronchitis, and cough. *Piper longum* extract showed inhibitory effects on the growth of Human lung cancer (HCC-827 cell line) and recorded in term of viable cell count decrease as compared to the control value and inhibition is dose dependent [23]. It is also used as an antidote in scorpion sting and snake biting [24].

Picrorhiza kurroa

It belongs to the Plantaginaceae and found in the Himalayan region and Nepal. It contains a bitter glycoside which is known as kutkin. It is used for the treatment of digestive problems, liver damage, asthma, vitiligo and wound healing (Kumar and Ramesh, 2014). Rhizome extract of *Picrorhiza kurroa* is rich in caffeic esters, apiocynin and *cucurbitacines aglycone* compounds and they possess cytotoxic effects on mammalian cell lines [25].

Plumbago zeylanica

It belongs to the Plumbaginaceae family and commonly known as white leadwort, chitrak and Ceylon leadwort. It is found in the warmer part of India and Sri Lanka. Several studies reveal the presence of various phytochemicals in this plant which includes plumbagin, plumbagin acid, coumarins, saponaretin, isoaffinetin, isoorientin, steroids, glucosides and psoralen. This plant shows therapeutic activity against skin diseases, rheumatic pain, wounds and scabies [26]. Plumbagin is a naphthoquinone which is isolated from the roots of this plant and it possess anti-tumor activity by controlling the hormone refractory invasive prostate cancer. Inhibitory effect of plumbagin against various molecular targets (STAT-3, AKT and PI-3K) results in the growth inhibition and invasion of prostate cancer. Plumbagin shows apoptosis induction in cancer cells and also inhibits growth of these cells [27,28].

Punica granatum

It belongs to the Lythraceae family and commonly known as Pomegranate. Pomegranate is a rich source of phenolic compounds, Ellagitannins (ETs) and ellagic acid (EA) that metabolically convert to urolithins by the gut microbiota. Urolithins are found in high concentrations in colorectal cancer (CRC) patients. This has diverted researches towards the anticancer activity of pomegranate. Urolithins inhibit proliferation of cancer cells and interfere with cell cycle and induce apoptosis. In a randomized clinical trial by Syed et al. [29] colorectal cancer patients were orally administered ellagitannin-containing pomegranate extract.

Tinospora cordifolia

It belongs to Menispermaceae family and commonly found in Sri Lanka, India, Myanmar and China. Stem and roots contain important alkaloids. It is known as 'giloya' in Hindi, 'guduchi' in Sanskrit and heartleaf moonseed plant in English. Root of this plant contains various alkaloids which includes tinosporin, choline, isocolumbin, columbin, tetrahydroplamatin, magnoflorimne and palmatin [30,21]. *Tinospora cordifolia* stem is generally used for the treatment of fever, dyspepsia, jaundice, skin and urinary disease [31]. *In vitro* study shows *Tinospora cordifolia* able to kill HeLa cells; this shows the potential of this plant as an anticancer agent. *Tinospora cordifolia* extract shows dose dependent cell death as compared to the controls [32]. Dichloromethane extract of *T. cordifolia* showed anticancer activity in mice transplanted with Ehrlich ascites carcinoma [33].

Thymus vulgaris

It belongs to the Lamiaceae family and commonly known as the German thyme or Garden thyme. Sertel et al. (2011) studied the cytotoxic activity of thyme against head and neck squamous cell carcinoma. The essential oils in Thyme induced cancer cell death by regulating interferon signaling, N-glycan biosynthesis and extracellular signal-regulated kinase 5 (ERK5) signaling [34].

Zanthoxylum nitidum

It belongs to the Rutaceae family and found in the Australia and Southeast Asian countries. It contains flavonoids, alkaloids, carbohydrates and amino acids [35]. It root contains nitidine chloride, dihydronitidines, oxinitidine, skimmianine, α -allocryptopine and 6-methoxy-5,6-dihydrochelerythrine. It is used for the treatment of stomachache, toothache, rheumatism, cough, vomiting, cholera and diarrhea. Nitidine possesses the anti-cancer activity and shows cytotoxic activity against the LLC (DNA intercalator which is generally classified as topoisomerases I and II inhibitor) and which leads to the cancer cells apoptosis [36,37].

Conclusions

Cancer is one of major problem in both developing and developed countries. Chemotherapy and radiation therapy causes various side effects therefore there is requirement of an alternative medicine to treat cancer. Medicinal plant contains

various secondary metabolites which show their potential activity against various diseases. Anti-cancer agents derived from the plant source have largely contributed to the development of new drugs. This review provides the information about medicinal plants with their secondary metabolites that show anti-cancer activity. So it can be concluded that herbal medicinal plants and its derivatives are active against different type of cancers. Herbal drug treatment may be recommended to the rural and poor people to treat effectively the cancers as it is cheaper. Screening of medicinal plants for anticancer activity provides a huge space for development of strong anticancer agents.

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