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ANTICANCER POTENTIAL OF INDIAN MEDICINAL PLANTS–A REVIEW

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ABSTRACT

It is the medicinal plants which are used to combat against various ailments since time immemorial. Next to cardiovascular diseases, it is the cancer which is the leading cause of death. Even though there is a constant demand for new therapies to treat cancer, naturally derived compounds are drawing attention due to their less toxic effects compared to chemotherapy. Still there exists a continuous thirst for medicinal plants and plant-based phytochemicals to provide a safer and more effective chemoprevention. In this review we try to bring the attention of certain Indian medicinal plants which have been reported to treat cancer.

KEY WORDS

Cancer, in vitro screening, phytochemicals, MTT, Sulforhodamine B assay

Introduction

Medicinal plants have been identified and used from time immemorial. Plants contain many chemical compounds for biological functions, including defence against insects, fungi and herbivorous mammals. Over 12,000 active compounds are known to science. These chemicals work on the human body in exactly the same way as pharmaceutical drugs, so herbal medicines can be beneficial and have harmful side effects just like conventional drugs. WHO (World Health Organization) estimated that 80 percent of people worldwide rely on herbal medicines for some aspect of their primary health care needs. According to WHO, around 21,000 plant species have the potential for being used as medicinal plants. Treatment with medicinal plants is considered very safe as there is no or minimal side effects [1]. Certain biological response modifiers derived from herbs are known to inhibit growth of cancer by modulating the activity of specific hormones and enzymes. Some herbs reduce toxic side effects of chemotherapy and radiotherapy. Scientists all over the world are concentrating on the herbal medicines to boost immune cells of the body against cancer. By understanding the complex synergistic interaction of various constituents of anticancer herbs, the herbal formulations can be designed to attack the cancerous cells without harming normal cells of the body [2].

Cancer is a general term applied to a series of malignant diseases that may affect different parts of the body. It is characterised by rapid and uncontrolled growth of abnormal cells forming a tumour which can proliferate throughout the body initiating abnormal growth at other sites [3]. If the process is not stopped it will lead to death of the individual. There are many types of cancer treatment. World Health Organization (WHO) has estimated up to 13.1 million deaths by cancer in 2030[4]. The types of treatment depend on the type of cancer and how advanced it is. The main forms of treatment being radiation, surgery and drugs.

Types of cancers (www.cancerindex.org) [5]

1) Cancers of Blood and Lymphatic Systems: Hodgkin's disease, Leukemias, Lymphomas, Multiple myeloma, Wald Enstrom's disease
2) Skin Cancers: Malignant Melanoma
3) Cancers of Digestive Systems: oesophageal cancer, Stomach cancer, Panceatic Cancer, Liver cancer, Colon and Rectal cancer, Anal cancer
4) Cancers of Urinary system: Kidney cancer, Bladder cancer, Testis cancer, Prostate cancer

5) Cancers in women: Breast cancer, Ovarian cancer, Gynaecological cancer, Choriocarcinoma
6) Miscellaneous cancers: Brain cancer, Bone cancer, Carcinoid cancer, Nasopharyngeal cancer, Retroperitoneal sarcomas, Soft tissue cancer, Thyroid cancer

***In vitro* Screening methods of anticancer activity**

MTT assay [6,7]

The MTT assay is a colorimetric assay for assessing cell metabolic activity. Yellow tetrazolium MTT (3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide) is reduced by metabolically active cells, in part by the action of dehydrogenase enzymes, to generate reducing equivalents such as NADH and NADPH. The yellow tetrazolium, is reduced to purple formazan. The intracellular purple formazan can be solubilized and quantified by spectrophotometrically.

Trypan blue dye exclusion assay [8]

Trypan blue is a vital stain used to selectively colour dead tissues or cells blue. It is a diazo dye. Live cells or tissues with intact cell membranes are not coloured. Since cells membranes are selectively permeable, trypan blue is not absorbed in a viable cell however, it traverses the membrane in a dead cell. Hence, dead cells exhibit a distinctive blue colour under a microscope. Since live cells are excluded from staining, this staining method is also described as a dye exclusion method.

Sulforhodamine B assay [9]

Sulforhodamine B assay is a bright pink amino xanthene dye that binds to basic amino acids in mild acidic conditions and dissociates under basic conditions. It is used for cell density determination, based on the measurement of cellular protein content.

LDH (Lactic dehydrogenase) Assay [10]

Lactate Dehydrogenase (LDH) assay quantifies LDH activity in a variety of biological samples such as serum or plasma, cells, culture medium and fermentation. In this assay LDH reduces NAD to NADH, which then interacts with a specific probe to produce a colour change from yellow to red.

Herbs with anticancer activity

Acacia catechu (Mimosacea): It is indigenous to India, other Asian countries, and East Africa [11]. The heartwood extract contains catechins namely catechin, epicatechin and epigallocatechin. The extract can arrest cell cycle at sub G1 in a dose dependant manner. It mediates apoptosis by increased cleavage of caspase 9, activation of caspase 3 and degradation of PARP. The active constituents increase Bax/Bcl2 ratio which results in the activation of caspase cascade [12].

Ginkgo biloba (Ginkgoaceae): The active constituents are Ginkgolide A, B, C and J. It inhibits development and spread of prostate, colon, ovarian and liver cancer by induction of apoptosis [13]. Kampferol is the constituent responsible for its activity on pancreatic cancers. *Ginkgo biloba* extract is rich in antioxidants that provide protection against oxidative cell damage [14].

Adenium Obesum (Apocynaceae): This plant is native to Africa however it is now cultivated in all parts of the world including India [15-17]. The active constituents of the plant are honghelosides A, honghelin, cardenolides (somalin and 16-acetylstrospeside) and the flavonol 3, 3'- bis (O-methyl) quercetin [18]. It shows cytotoxic activity to colon carcinoma, murine leukemia, breast cancer, cervix cancer and epidermoid carcinoma of the nasopharynx. It is a strong inhibitor of the hedgehog Hh/GLI pathway [19]. The hedgehog pathway is an important therapeutic target in cancer, it causes formation and progression of tumours in humans.

Acorus calamus (Araceae): The plant is found in Europe, North America and Asia. Lectin is the active constituent isolated from the rhizomes [20]. It inhibits production if nitric oxide therefore has antioxidant activity and inhibits interleukin 2 and tumour necrosis factor alpha. It has significant anti-proliferative activity. (http://bsienvis. nic.in /medi. htm#Acoruscalamus)

Podophyllum hexandrum (Berberidaceae): The plant contains lignans mainly podophyllotoxin which is the starting material for the drugs etoposide and teniposide. It is an inhibitor of microtubule assembly, arresting mitosis in metaphase thus stopping cell

division [21]. It is effective in lung cancer, testicular cancer, neuroblastoma and Hodgkin's lymphoma. Podophyllotoxin is also an inhibitor of topoisomerase II. Topoisomerase II relaxes the negative and positive supercoils during cell division [22].

Calotropis gigantean (Asclepiadaceae): The plant is also known as milk weed. The plant thrives in tropical regions and is abundant in India, Bangladesh, Pakistan and Burma [23]. The latex is cytotoxic against hepatocellular carcinoma and cervical cancer. The plant has a number of phytoconstituents but the most active against cancer were found to be desmosterol and gamma sitosterol [24, 25].

Allium sativum- (Liliaceae): The constituents with anti-carcinogenic properties are Diallyltrisulphide, diallyldisulphide and s-allyl cysteine [26]. Rapidly dividing cancer cells have a high concentration of sulphur enzymes. *Allium sativum* reacts with these enzymes and thereby decreases their concentration which leads to inhibition of tumour growth. The extract of *Allium sativum* enhances the activity of natural killer cells and macrophages. It increases the count of suppressor T cells and makes the lymphocytes more cytotoxic to cancerous cells [27]. The extract prevents the adhesion of circulating cancer cells thereby inhibiting metastasis. *Allium sativum* protects DNA from the effects of carcinogens and increases the activity of detoxifying enzymes [28].

Ailanthus excels (Simarubaceae): The tree is indigenous to central and southern India. The potential anticancer agents are glaucarubinone, ailanthum and dehydroglaucarubol 15-isovalerate. They have antitumor and cytotoxic activity. They are mainly active against lymphatic leukaemia [29, 30]. They inhibit protein synthesis of ribosomal peptidyl transferase leading to termination of chain elongation thereby exhibiting anticarcinogenic activity.

Panax ginseng- (Araliaceae). *Panax ginseng* contains several active constituents with the main being ginsenosides which are triterpene saponins. Other constituents that exhibit anticancer properties include essential oils, phytosterols, amino acids, flavonoids and polyacetylenes [31, 32]. Ginseng saponins inhibit invasion and metastasis. Rh2 active has the ability to reverse transform cancerous cells into normal cells [33]. Rg3 inhibits lung metastasis by inhibiting adhesion and invasion of tumour cells and it also has anti-angiogenesis activity [34]. *Panax ginseng* regenerates natural killer cells which were damaged by chemotherapy and radiotherapy, stimulates macrophages and promote production of antibodies. *Panax ginseng* is most active against stomach cancer, oesophagus cancer, pancreas cancer and to a lesser extent breast, bladder, cervical and thyroid cancer.

Glycyrrhiza glabra- (Fabaceae). The liquorice plant contains a glycoside called glycyrrhizin. Glycyrrhizin reduces the activity of enzymes that break down prostaglandin *E. Liquorice* shows anti-infective and anticancer properties. Some chemical constituents derived from liquorice have shown anticancer activity in animal studies and in laboratory cultures of human cancer cells [35]. Additionally, true liquorice may have some ability to improve the functioning of the immune system.

Discussion

Chemotherapeutic agents (drugs) often provide temporary relief of symptoms, prolong life and occasionally cure. Most of the cancer chemo-therapeutic agents that have been synthesized have a lot of side effects. An ideal anticancer drug should be effective on killing cancerous cell or stopping cancer progression without causing damage to normal cells, however such properties in an anticancer drug are difficult if not almost impossible to find. Much effort and resources have been dedicated in finding such a drug or modifying known drugs. Recent studies have shown that tumour inhibiting compounds of plant origin may provide new templates for prototype drugs with the desired characteristics. Therefore, identification and development of natural products used for cancer prevention have attracted a lot of attention globally. Herbal extracts with their proven potential and less side effects in therapeutics have replaced the synthetically derived drugs in modern allopathic medication system. This has led to a shift in anti-cancer research towards this line of study.

Conclusion

Cancer is becoming a high-profile disease in developed and developing worlds. Although many chemically derived drugs have been developed and other cancer treatments pre-exist, current methods such as chemotherapy have their own limitations due to toxic effects on non-targeted tissues further worsening human health problems. Therefore, there is a demand

for alternative treatments with naturally-derived anticancer agents with plants being the desired source. Medicinal plants maintain the health and vitality of individual and also cure various diseases including cancer without causing toxicity. They have found direct medical application as drug entities, but also serving as chemical models or templates for the design, synthesis, and semi synthesis of novel substances. Although there are some new approaches to drug discovery, such as a combination of chemistry and computer-based molecular modelling design, none of them can replace the important role of natural products in drug discovery and development.

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