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Mini review

Anticancer properties of medicinal plants: prospects and challenges in cancer treatment

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Abstract

India has a long history and strong tradition for Ayurveda and other traditional medical system. Medicinal plants play significant role in treating and preventing various diseases. Medicinal plants have been associated with the development of human civilization around the world. These plants are considered as rich sources of phytochemicals which enable to have huge medicinal value. The application of these herbal remedies is not only cost effective than other synthetic drugs but also safe and almost free from numerous side effects. The tribal, farmers and village elders have tremendous knowledge about these medicinal plants. In this century, the pharmacological effects of plants have been considered as a promising future medicine or drug for the management of various diseases, including cancer. Hence, the main aim of the present review is to understand the knowledge of the medicinal plants for the treatment of cancer.

Keywords: Medicinal plants, phytochemicals, herbal medicine, cancer

Introduction

Phytomedicine or herbal medicine is the use of plants for therapeutic and medicinal purpose for improving human health or curing of diseases. Medicinal plants have various secondary metabolites commonly called phytochemicals. These phytochemicals protect plants against infestation by pests or microbial infections. Phytochemicals are highly active components which possess therapeutic applications that are considered as a drug or medicine. Plants used as traditional medicine and are more likely to yield pharmacologically important compounds. The medicinal properties of these plants have been studied in the recent scientific developments throughout the world, due to their antioxidant activities and therapeutic efficacy, economic viability and no side effects. Medicinal plants are mainly serving as potent raw material for drugs which are reasonable and effective health care for people. Plants are rich dietary sources of vitamins, biomolecules and minerals which are very critical for maintaining human health (Martinez et al., 2008).

Many medicinal plants have pharmacological effects due to the presence of various metabolites. These metabolites are organic compounds which can be classified into primary- and secondary-metabolites.

Primary metabolites are organic compounds include starch, glucose, polysaccharide, lipids, proteins and nucleic acids which are very beneficial for development and growth of the human body. Medicinal plants produce secondary metabolites which include flavonoids, alkaloids, saponins, steroids, terpenoids, glycosides, volatile oil, tannins etc. (Maurya et al., 2008). The therapeutic properties of medicinal plants are mainly because of the presence of phytochemicals. These include alkaloids have an antimalarial, antispasmodic, analgesic, diuretic activities; Terpenoids have antihelmintic, antiviral, anticancer, antibacterial, anti-inflammatory properties; Glycosides have antibacterial and antifungal properties; Flavonoids and phenols have an antioxidant, antibacterial and antiallergic properties. Saponins are widely reported to have antiviral, plant defence activity and anti-inflammatory properties (Chopra and Doiphode, 2004).

Medicinal plants as a potential source of novel drugs

Medicinal plant is widely practiced throughout the world. For centuries, people have been used these natural medicines to cure common ailments such as allergy, cold, toothache, stomach upset and this trend is increasing rapidly in recent years. According to the World Health Organization (WHO), 4 billion people use herbal medicines for some aspect of primary healthcare to treat various diseases. Herbal medicine has been recognized by WHO as an important component for primary health care and more than 11% of the 252 reported drugs are derived from medicinal plants (Leslie, 2000)

Diversity of medicinal plants in Himalayan region

In India, about 7500 medicinal plants are known for medicinal properties. This proportion of medicinal plants is the richest proportion of medicinal plants known for their medical properties in any country of the world for the existing flora of that particular country. Ayurveda is the oldest medical system in Indian medicine, has alone reported more than 2000 medicinal plant, followed by Unani and Siddha (Shiva, 1996). Presently, more than 25% of drugs are derived from medicinal plants, and many others are synthetic analogues built on prototype compounds isolated from plant species in modern pharmacopoeia. The North east part of India harbours a good diversity of medicinal plants because of the majestic Himalayan range. About 8000 species of angiosperms, 600 pteridophytes and 44 species of gymnosperms have been reported in the Indian Himalaya (Prajapati et al., 2003). In Indian states, about 1748 plant species were reported in Utharanchal followed by North Bangal (Samant et al., 1998). Many medicinal plant species are endemic to the Himalayan region. Of the medicinal plants, 62 plant species are endemic in this region and 208 plant species are near to endemic (Chatterjee, 1939). More than 200 medicinal plants in Himalayan region are consumed as roasted, raw, fried, boiled, cooked, jams or pickles to treat and cure various diseases (Dhyani and Dhar, 1994). The indigenous communities widely use some medicinal plants as a potential source of fodder, food, timber as well as various other ethnobotanical purposes (Samant et al., 2001).

Herbs with anticancer properties

Cancer disease severely affects the human health. Hence there is a continuous demand for the discovery of novel drugs to prevent and to treat this life-threatening disease (Greenwell and Rahman, 2015). Medicinal plant-derived drugs are highly useful for the treatment of cancer as they are readily available and found in nature. They can be administered orally as part of

patient's dietary intake (Amin et al., 2009). These naturally occurring plants are non-toxic to normal human cells. *Acacia catechu* is indigenous to Asian countries, India and East Africa (Chopra et al., 1996). This plant extract contains epicatechin, catechin and epigallocatechin. The extract can arrest cell cycle at sub G1 cycle in a dose dependant manner. *Ginkgo biloba* (Ginkgoaceae) contains Ginkgolide A, B, C and J. These components inhibit development and spread of colon, prostate, liver cancer by induction of apoptosis (Tyler, 1994). *G. biloba* extract is rich in antioxidant substances that provide protection against oxidative cell damage (Kleijnen and Knipschild, 1992). *Adenium obesum* (Apocynaceae) is now cultivated almost all parts of the world including India and is native to Africa (Dimmit and Hanson, 1991). The active metabolites of this medicinal plant are honghelin, cardenolides, hongheloside A and the flavonol 3, 3'- bis (O-methyl) quercetin (Hoffmann and Cole, 1977). *Acorus calamus* (Araceae) is found in North America, Europe and Asia. The potent secondary metabolites from this plant inhibit production of nitric oxide therefore inhibits interleukin 2 and tumour necrosis factor. *Podophyllum hexandrum* (Berberidaceae) contains potent anticancer molecules arresting mitosis in metaphase thus arresting cell division (Schacter, 1996). *Calotropis gigantea* (Asclepiadaceae) grows in tropical regions and is widely distributed in Burma, Pakistan, India and Bangladesh. This medicinal plant has various phytochemical constituents and highly active against cancer because of the presence of gamma sitosterol and desmosterol (Choedon et al., 2006).

Classification and mechanism of plant based cancer drugs

Plant-derived anticancer drugs can fall under four classes of drugs and have some biological activities. These include, DNA damage preventive drugs, methytransferase inhibitors, mitotic

disruptor, antioxidants and histone deacetylases inhibitors. The compounds such as, isothiocyanates, sulforaphane, pomiferin and isoflavones inhibit the activity of carcinogenic proteins (Amin et al., 2009). Derivatives of vinca alkaloids, vinblastine, vindesine, vinorelbine, vincristine and vinflunine are drugs which inhibit the dynamics of microtubules by binding to β -tubulin. Taxanes such as paclitaxel and docetaxel are microtubule disruptors, cause cell cycle arrest by inhibiting cell cycle phase transitions from metaphase to anaphase and apoptosis. Paclitaxel was one of the first ever cancer drugs to have a huge impact on the treatment of cancer. Vinblastine and vincristine were two of the drugs isolated from the medicinal plants (Khazir et al., 2014). Combinations of drugs derived from *Taxus diterpenes*, vinca alkaloids, Camptotheca alkaloids and *Podophyllum lignans* critically enhance their anticancer properties and improve their efficacy as therapeutic molecules (Khazir et al., 2014). Solowely *et al.* (2014) investigated the effects of anticancer agents from plants on a wide range of cancer cell lines such as, colon, prostate, breast and lung lines.

Many medicinal plants and their phytochemicals isolated from *Catharanthus roseus* and are employed in the treatment of various types of cancer including, leukemia, breast, testes, liver and lung cancer. Many medicinal plants and their phytochemicals significantly inhibit the development and progression of cancer (Aung et al., 2017). The vinca alkaloids specifically bind on a specific site called as tubulin heterodimers and disrupting the important functions of microtubules or by critically arresting metaphase cycle (Maryam et al., 2013). Taxanes represent significant anticancer agents that act by binding to microtubules and play key role in cell division (Xie and Zhou, 2017). Cephalotaxus alkaloids are multipurpose group of phytochemicals that are mainly used against range of cancer including HeLa, SGC-7901 gastric cancer

and A-549 lung cancer. They function by inhibiting the synthesis of protein and targeting the molecular events in initiation of protein synthesis, polyribosome degradation and release of nascent peptide (Heibliga et al., 2014). Colchicine is a natural bioactive compound separated from *Colchicum autumnale* (Colchicaceae) and has been widely studied to treat various diseases such as, cirrhosis and crystal arthritis. It binds irreversibly to tubulin, stabilizes the formation of microtubule, arrests cell cycle at various phases and induces apoptosis. Some of the plants derived cancer drugs are not specific, hence semisynthetic derivatives also tried to treat cancer. The semisynthetic derivatives such as, deacetylcolchicine and colchicinamide have been developed which are less toxic and are used for the treatment of type of cancers including chronic granulocytic leukemia, colorectal, central nervous system, melanoma, and breast cancers (Xie and Zhou, 2017). Colchicine intercalation with DNA in order to avoid proliferation and considered to be topoisomerase II inhibitor (Stiborova et al., 2015). Berberine is a potent anticancer molecule in terms of its clinical trials and efficacy isolated from the rhizome and root of *Tinospora cordifolia*, *Berberis aquifolium*, *Berberis vulgaris* and *Rhizoma coptidis*. It has been widely used to treat variety of cancers namely; prostate, breast and colorectal cancer (Barzegar et al., 2015). Berberine induces apoptosis and cell cycle arrest at G2/M phase in colorectal, breast and liver cancer, inhibit anti-apoptotic proteins and activate pro-apoptotic proteins (Xu et al., 2013). Combretastatins is a class of anti-angiogenic molecule isolated from the medicinal plant, *Combretum caffrum* and specifically suppresses tumour angiogenesis. The various parts of Indian medicinal plant *Terminalia bellerica* fruit, bark and kernel are used in isolation of active combretastatins with potent anticancer properties (Lauritano et al., 2016).

Triterpenoid acids have potent anticancer properties and have shown significant anticancer activity *in vivo* and *in vitro* against pancreatic, leukemia and breast cancer. Other anticancer substances such as, CDDO (2-cyano-3, 12- dioxoolean1, 9-dien-28-oic acid) and its methyl ester are highly active against ovarian cancer (Cragg and Newman, 2005). Betulinic acid is another type of triterpenoid isolated from *Ziziphus rugosa*, *Ziziphus mauritiana*, *Betula* sp. and *Ziziphus oenoplia* showed potent cytotoxic activity against a wide range of cancer (Prakash et al., 2013).

Future prospects of cancer drugs

There are many advantages in herbal medicine. These include, utilizing the traditional herbal medicine knowledge and by discovering the medicinal plants more rapidly, disease targeted approach of “Silver bullets” and synergy between the various components of the selected herbs (Li, 2002). The disadvantage related to phyto medicines is the lack of international standardization in terms of methods for evaluating their composition, safety, consistent manufacturing practices, efficacy, quality and approval processes. In the last decade various drugs were discovered and available for human use. Coordination and collaboration between Federal Drug Administration, World Trade Organization and leading pharmaceutical industry worldwide may helpful to develop novel anti-cancer and other health promoting drugs.

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