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Traditionally used Medicinal Plants as Alternative Source for Future Anticancer Drugs

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Abstract:
Cancer remains the second most deadly disease in the world with increasing incidence and mortality rate. The number of drug for its treatment is increasing and needs more new drugs due to development of resistivity. Several plants were described in Ayurveda for its treatment which have not only therapeutic value, but they also enhanced the quality of life. Several research have been done on these plants to treat cancer and some plant products have been marketed as anticancer drugs like Taxol, Vinblastine, Vincristine, etc. Many research works describe that the anticancer activity of medicinal plants is due to the presence of antioxidants in them. Actually, the medicinal plants are easily available, cheaper and possess no toxicity, as compared to the modern drugs. Thus, the various combinations of the active components of these plants after isolation and identification can be made and have to be further assessed for their synergistic effects. The progressing rate of cancer indicates an urgent need to search new potent and effective drugs from plant source. This article describes the medicinal plants used for cancer treatment in Ayurveda as source of future drugs.

Keywords: *Antioxidants, future drugs, anticancer, medicinal plant and Ayurveda*

1. Introduction

Cancer is a leading cause of death globally which is characterized by rapid and uncontrolled division of abnormal cells that may lead to form a growth or tumor or invade other parts of body. It will be also projected that the burden of cancer will increase to 23.6 million new cases per year by 2030 [i]. Chemotherapy continues to be the most common pharmacological approach for the treatment of cancer. Most chemotherapeutic drugs for cancer treatment are molecules isolated or derived from plants which account of 60% approximately currently used drugs for cancer treatment [ii]. Natural products have continued to receive an increasing attention for their potential as novel cancer preventive and therapeutic agents. These include *vinca alkaloids, Taxus diterpenes, Camptotheca alkaloids* and *Podophyllum lignans, etc* [iii]. But due to the high cost, non-specific, less effective, high toxicity, adverse side effects and development of chemoresistance, there is an urgent need to discover new anticancer agents with improved therapeutic profiles, more effective, affordable. This article highlights some important medicinal plants which are described in Ayurveda as alternative source for future anticancer drug development.

2. Ayurvedic Concept of Cancer

Ayurvedic literature defines three body regulatory systems, namely, *Vata* (the nervous system), *Pitta* (the venous system) and *Kapha* (the arterial system) which mutually regulate the body to perform the normal function. The failure of coordination among them causes illness in the body like cancer. It describes cancer as *Granthi* (minor neoplasm) and *Arbuda* (major neoplasm). In benign neoplasm one or two of these three body regulatory systems are beyond the control but this condition is not too harmful as the body is still struggling to regulate these systems. Malignant tumor is very harmful due to the failure of all these three major body regulatory systems lose mutual coordination which results the tissue damage, resulting a deadly condition [iv].

3. Etiology

According to *Sushruta*, the main reason of major neoplasm is the pathogens that affect all body parts. The pathogenic injuries to the sixth layer of the skin in muscular tissues and blood vessels caused by lifestyle errors, unhealthy foods, poor hygiene and bad habits which results in the derangement of *doshas*, which leads tumorigenesis in the body. It is described that excess of water or fat in the corpus of the tumor and the *doshas* in a particular place are the main cause of non-suppurative and non-infectious abnormal growths. Cancer in person differs from other person according to the exposure to *pathogens* and genetic structures which make different response in different person for the same drug [v].

4. Principles of Ayurvedic Treatment

Mistreatment with nature's law upsets the living systems and causes disease like cancer. The Ayurvedic system of medicine is based on well established fundamental principles of nature and thoroughly study of human physiology carefully. This is the first system to emphasize health as the perfect state of physical, social, psychological and spiritual element of a human being. Finding the cause of an illness is the main objective of ayurvedic therapy. Ayurveda is able to diagnose an illness at initial stages of body imbalance and their therapeutic approach maintains a balance by supplying deficient substances as well as reducing the excessive ones [vi].

5. Development of Anticancer Drugs

The development of new anticancer agents to combat this deadly disease is of paramount importance. Most of chemotherapeutic agents used in modern medicine are either plant derived or semi-synthetic compounds which are used to arrest the insidious character of the disease using the basic concept of Ayurveda. Vinblastine, Vincristine, Paclitaxel, Doxorubicin, Camptothecin, Podophyllotoxin, Mitomycin C, Etoposide, Teniposide, Combretastatins, etc are well known anticancer drugs used for the treatment of different types of cancer which are research output and developed by National Center for Complementary and Alternative Medicine (NCCAM), Bethesda, USA [v]. But these anticancer drugs have severe side effects and several drawbacks like Doxorubicin is known to have severe cardiotoxicity whereas Mitomycin C is known to have pulmonary side effects. Many plants have been evaluated in scientific studies using the concept of Ayurveda for their potential tumouricidal actions against different cancers. The resulting damage in cancer patients due to the toxicity of synthetic drugs during treatment turnes to seek help from Ayurvedic medicine hoping for a better cure. Ayurvedic therapy was found to be able to cure the diseases better, which were previously not amenable to treatment by modern medical practices [vi]. Ayurveda is Indian traditional medicine system which has long history of treatment that fascinate practitioners and researchers for its applications in cancer treatment and research on a systematically proven research background.

6. Potential Benefits of Ayurveda during Cancer Cachexia

Cancer cachexia is a common medical problem that affects the quality of life and survival rate of cancer patients. The tumor induced immune responses and metabolic changes which lead signs like chronic nausea, anorexia and change in body weight. Relief from cancer cachexia is particularly valuable among various potential benefits of Ayurvedic medicine. Ayurvedic plants used in cancer therapy result not only in better healing but also reduce the side effects and cancer related complications. It also avoids the need for supplemental therapy to manage cancer cachexia. Each plant product contains multiple active constituents that produce therapeutic benefits, operate synergistically and lowering the risks on adverse effects [v].

7. Anticancer Plants Claimed in Ayurvedic Texts

Ayurvedic Texts describe a lot of plants with anticancerous properties and herbal decoctions consisting of multiple herbs each having remarkable potential for a cancer treatment. These formulations are reported to work on multiple biochemical pathways and are competent to control several organ systems simultaneously. The herbal decoction is beneficial because it can nourish the body as a whole by supporting different organ systems. Many of the plants mentioned below have scientifically proven anticancer properties and are used for the treatment of various cancers [v].

7.1. Amorphophallus Campanulatus

The methanolic extract of *Amorphophallus campanulatus* tuber has significant role in antiproliferative activity, induction of apoptosis and chemopreventive effect on colon carcinoma [vii-viii].

7.2. Calotropis Procera

Calotropis procera protein isolated from root bark has antitumor activities which inhibit the proliferation and induced apoptosis in breast cancer cells by suppression of nuclear factor kappaB (NF-kB) activation [ix]. Its ethyl acetate and acetone extracts exhibited higher cytotoxic potential against tumor cells [x].

7.3. Cassia Angustifolia

Anthraquinones glycosides isolated from *Cassia angustifolia* have shown antimutagenicity, antiproliferative and apoptotic properties in colon carcinoma [xi].

7.4. Citrullus Colocynthis

Citrullus colocynthis, commonly known as bitter cucumber which belongs to the family of cucurbitaceae, has anticancer property and destroy cell through apoptosis by cellular DNA fragmentation in Hepatocarcinoma, Hep G2 cell line [xii].

7.5. Commiphora Mukul

z-Guggulsterone and gugulipid isolated from *Commiphora mukul* has induced apoptosis through targeting beta-Catenin signaling in human breast cancer, MCF-7 and MDA-MB-231 cell line [xiii]. These compounds have also significant role in prevention of head and neck squamous cell carcinoma by induced apoptosis through epidermal growth factor receptor (EGFR)-signal transducer and activator of transcription (STAT)-3 signaling pathway [xiv-xv].

7.6. Juniperus Communis

7-hydroxysandaracopimaric acid and Deoxypodophyllotoxin isolated from *Juniperas taxifolia* leaves have showed potent differentiation inducing activity, antiproliferative effect and apoptosis inducing activity on human promyelocytic leukemia HL-60 cells [xvi]. Sabiperones, diterpenoids isolated from this plant has showed potential role of antiproliferative effect and apoptosis inducing activity in five human cancer cells, human promyelocytic leukemia (HL-60), human lung adenocarcinoma (A549), human breast adenocarcinoma (MCF7), human hepatocellular carcinoma (HepG2), and human colorectal adenocarcinoma (HCT116) cell lines [xvii].

7.7. Luffa Echinata

The methanolic extract of *Luffa echinata* has anticancer property via inducing the apoptosis by triggering the mitochondrial apoptosis pathway in colon cancer cells (HT-29). It also inhibited the cellular proliferation of HT-29 cells via G2/M phase arrest of the cell cycle [xviii].

7.8. Mallotus Philippinensis

It is commonly known as Rohini and a very common perennial shrub, found northern India. Rottlerin is a polyphenolic molecule isolated from *Mallotus* plant has highest cytotoxic effect against 14 human cancer cell lines [xix].

7.9. Moringa Oleifera

The phenolic compounds present in 70% hydroalcoholic extract of *Moringa oleifera* leaf have exhibited anticancer activity against human cervical carcinoma, HeLa cell line [xx]. The essential oil isolated from its seed has potent cytotoxic activities against five cancer cells, human cervical carcinoma (HeLa), human hepatocarcinoma (HepG2), human breast carcinoma (MCF-7), Caucasian colon adenocarcinoma CACO-2) and mouse fibroblast (L929) cell lines [xxi].

7.10. Nigella Sativa

Nigella sativa is well known as black cumin and used in Indian kitchen. The methanolic extract of *Nigella sativa* seeds induced apoptosis in breast cancer cells, MCF- 7 through p53 and caspases signaling [xxii].

7.11. Plumbago Zeylanica

Plumbagin, a naphthoquinone isolated from *Plumbago zeylanica* has showed anticancer and antiproliferative activities through targeting CRM1 (chromosome maintenance region 1) against HeLa, MCF-7 and A172 cell lines as well as in animal tumor models **[**xxiii].

7.12. Semecarpus Anacardium

Semecarpus anacardium is well known as Ballataka in ayurveda and its nut extract has showed anticancer activity on human breast cancer cell line (T47D) by decreasing Bcl-2 and increasing Bax, cytochrome c, caspases and PARP cleavage and finally by DNA fragmentation [xxiv] and Hepatocellular carcinoma [xxv]**.** Urushiols isolated from *Semecarpus showed* antitumor activity against breast cancer cells, MCF-7 and MDA-MB-231 cell lines **[**xxvi**].**

7.13. Tecomella Undulataa

The bark extract of *Tecomella undulata* has antiproliferative activity against different cancer cell lines K562, COLO-205, MDA-MB231 and HepG2 along with normal cells HEK 293 through apoptosis [xxvii].

7.14. Tephrosia Purpurea

It is well known as *sharpunkha* in ayurveda. Its benzene fraction of leaf extract has anticancer activity against MCF-7 cell line [xxviii].

8. Conclusion

The clinical efficiency and level of toxicity of several anticancer agents are unknown and uncertain. Research on majority of ayurvedic drugs is in the pre-clinical phase or is not being actively pursued. Future research on this topic would help to identify safe and effective anticancer drugs and will further elucidate their mechanism of action. Ayurvedic researchers and practitioners in medical sciences can help to improve this medicine by increasing their involvement and role in the treatment. This review explained the possibility of development of future anticancer drugs from the plants described in Ayurvedic texts.

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9.1. Conflict of Interest
The authors declare that there is no conflict of interest.

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