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Ethnobotany and Herbal Medicine: Some Local Plants with Anticancer Activity

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Abstract
Cancer is the second foremost cause of death worldwide since few year back. There is a steady require for new therapies to treat and prevent this life-threatening disease. The scientific and research interest is drawing its attention towards naturally derived compound as they consider to have less toxic side effects than modern treatment strategies like chemotherapy. The plant kingdom produces naturally happening secondary metabolites which were being investigated for their anticancer activities most important to the design and development of new clinical drugs. The present study revealed the anticancer activities of some most common plants like Cedrus deodara, Catharanthus roseus, Piper longum, Vitex negundo, Curcuma longa, Picrorhiza kurroa, Berberis aristata, Datura stramonium, Cannabis sativa, Ocimum sanctum and Azadirachta indica. The C. roseus be full of vinblastin which is use to cure lung, breast, head and neck cancer; and vincristine employed to treat acute leukemia. The anti-proliferative potential of hydro-alcoholic extract of C. deodara is helpful to cure oral, lung, breast, bladder, colon, cervix, and prostate cancer etc. The cannabinoids present in the Cannabis is used to treat the cancer also. The active intergradient in turmeric is curcumin or diferuloyl methane, which showed the anticancer potential on cancer cell lines.

INTRODUCTION

Globally cancer is one of the leading cause of morbidity and mortality. Amongst the non-communicable diseases, cancer is the second leading cause of death after cardiovascular diseases (WHO, 2005; Hoyert et al., 2006; Lopez et al., 2006; Mathers and Loncar, 2006). Cancer is responsible for one in eight death worldwide *i.e.* more than AIDS (Acquired Immunodeficiency Syndrome), malaria and tuberculosis (TB) together (Sener and Grey, 2005; Kumar et al., 2018; Upadhyay et al., 2019). Over all cancer incidence and mortality are higher in North America, Australia, New Zealand and Western Europe compared to rest of the world (Parkin et al., 2001; Parkin, 2004;). In USA, one of four deaths is attributed to cancer (Jemal et al., 2007). Globally, it is estimated that, the mortality due to cancer increase from 7.1 million in 2002 to 11.5 million in 2030 (Mathers and Loncar, 2006). Traditionally, plants have been utilized for their pain-relieving and healing abilities and today we still

depend on the curative properties of plants. According to World Health Organization, 80% of the people living in rural areas depend on medicinal plants as primary health care system (WHO, 2005). The synthetic anticancer medicines are out of there ach of common man due to cost factor. Herbal medicines have a vital role in the prevention and treatment of cancer and medicinal plants are commonly available and comparatively economical (Kayande, and Patel, 2016; Singh et al., 2018, 2019, 2020). The National Cancer Institute has approximately screened 35,000 plant species have shown reproducible anticancer activities. Most of the effective drugs derived from the higher plants were vinca alkaloids *viz* vinblastin and vincristine are derived from *Catharanthus roseus* are used to treat leukemia, bladder and testicular cancer (Moudi et al., 2013). Paclitaxel (Taxol TM) was originally isolated from *Taxus brevifolia* used in treatment of ovarian and breast cancer which was assumed to bind the tubulin subunit of microtubule and stabilize the microtubule to normal disassembly (Zhu and Chen, 2019) . Isolation of podophyllum and several other compound (known as lignans) from the common apple (*Podophyllum peltatum*) ultimately lead to the development of drugs used to treat testicular and small lung cancer (Pettit et al., 1995; Moraes et al., 2002; Ardalani et al., 2017). Ashwagandha (*Withania somnifera*) also known as winter cherry or Indian ginseng, is a proud of Ayurveda. Many toxicological studies have demonstrated that Ashwagandha, in its reasonable dose, is a nontoxic, safe and edible herb. Extract derived from Ashwagandha root or whole plant, have been shown to possess anticancer activities that operates through diverse yet conversing pathways (Yadav et al., 2010; Rai et al., 2016).

Turmeric (*Curcuma longa*) is a type of herb belonging to ginger family, which is widely grown in southern and south western tropical Asia region. Turmeric has been used in Chinese and Indian pharmacopoeia for thousands of year, it is known for its anti-inflammatory properties used in treating several conditions such as chest pain, urinary tract infection, jaundice and colic (API, 2011; Kocaadam and Sanlier, 2017). Turmeric active intergradient is an extracted compound called curcumin. Studies shows that curcumin helps prevent several form of cancer including breast, lung, stomach, liver, and colon because of its anti-inflammatory and antioxidant properties. It stop the development of interfering with the cellular signaling aspects of the chronic disease (Benzie and Wachtel-Galor, 2011; Willken et al., 2011). Since cancer chemo preventive and chemotherapeutic strategies are usually aimed at preventive or treating a specific type of cancer, first aim of this work is to compile the most relevant cancer related effect of curcumin on several common type of cancer (Vallianou et al., 2015; Tomeh et al., 2019). In addition, this article also provides evidence that suggest that the cancer related activities of curcumin may be linked to its known antioxidant properties. Cancer defines a large group of diseases originating from uncontrolled cell division in any part of the body. About 5% of all cancers are strongly here dietary and the others, arising from the internal and external environmental impact, show increase in incidence with increasing age (Aly, 2012). Already available conventional therapies for the treatment of cancer are radio therapy 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. Nature always stands as a golden mark to exemplify the outstanding phenomena of symbiosis (Verma and Singh, 2008). Nature has provide a complete store-house of remedies to cure all ailments of mankind. Growing number of healthcare consumers are turning to plant medicine for many reason low cost and seeking natural alternatives with fewer side effect.

In this study, we have selected few medicinal plants which showed high potency toward the cancer cell line by inhibiting their progression. These selected medicinal plants showed the anticancer, antioxidant properties and can be used for further treatment of cancer (Bruneton, 1993). The phytoconstituents derived from the *Cedrus deodara, Catharanthus roseus, Piper longum, Vitex negundo, Curcuma longa, Picrorhiza kurroa, Berberis aristata, Datura stramonium, Cannabis sativa, Ocimum sanctum* and *Azadirachta indica* have been chosen in this study.

Figure 1: Plants with anticancer properties. A. *Cedrus deodara*; B. *Catharanthus roseus*; C. *Piper longum*; D. *Vitex negundo*; E. *Curcuma longa*; F. *Picrorhiza kurroa*; G. *Berberis aristata*; H. *Datura stramonium*; I. *Cannabis sativa*; J. *Ocimum sanctum*; K. *Azadirachta indica*.

PLANTS WITH ANTICANCER PROPERTIES (Fig. 1)

A. *Cedrus deodara* Pinaceae

Chemical constituent: *Cedrus deodara* (Roxb.) Loud (normally called as deodar), one out of four species in the genus *Cedrus*, exhibits widely biological activities. The bark of *C. deodara* contains large amount of taxifolin. The deodar also contains lignans and the phenolics ses quiterpene himase colon together with isopimaric acid. The main component of the needle essential oil include limonene (17.01%), anethole (14.57%), euginol (2.14%). The wood contains cedeodarin (6-methyltaxifolin), cedrin 6-methyldihydromyricetin): (Ambasta, 2000; API, 2011; Wei–Cai et al., 2012).

Uses: The inner wood is aromatic and used to make incense. Inner wood is distilled in to essential oil and used as insect repellent on the feet of horses, cattle and camels. It has some potential for control of fungal deterioration of spices during storage. The bark and stem of *C. deodara* are a stringent (Bruneton, 1993).

Anticancer evaluation: The anti-proliferative activity of hydro-alcoholic extract of *C. deodara* was screened against a panel of 14 human cancer cell line representing different tissues including lung, pancreas, colon, cervix, oral, bladder, breast etc. (API, 2011).

B. *Catharanthus roseus* Apocynaceae

Chemical constituent: The tropical plant Madagaskar Periwinkle (*Catharanthus roseus*) (L.) is an important medicinal plant of family Apocynaceae. It is cultivated mainly for its alkaloids, which are having anticancer activities The main constituent of white flower of *C. roseus* were limonene (23.2%), geraniol (7.3%), and citral (7.0%) from the leaf. The pink flower *C. roseus* has its leaf oil consisting mainly of linolenic acid ethylester (43.9%), stearic acid (10.6%). It also contains vinblastin and vincristine (Agrawal et al., 1980; Roja and Rao, 2000).

Uses: Its alkaloid is used for the circulatory disease treatment and provide relief to the normal cerebral blood flow obstuction.

Anticancer evaluation: Vincristine sulfate arrest mitosis and utilized for the treatment of acute leukemia in children. The vinblastin sulfate is utilized for the treatment of choriocarcinoma, lymphosarcoma, carcinoma of lung, breast, and other organs.

C. *Piper longum* Paparaceae

Chemical constituents: The genus *Piper* (Piperaceae) contains approximately 2000 species, of which 10 species have been used in traditional medicines to treat cancer or cancer-like symptoms. *P. longum* (long pepper) is commonly used in traditional medicine and contains the chemical compound piper longumin (Brunetone, 1993).

Uses: The plant has been used in traditional medicine as well as in the Ayurvedic system against various disorders and infections. Unriped, dried fruits are used as an alternative to tonic. Various plant preparation like decoction of young fruits and roots are used for treating chronic bronchitis, cough and cold also used as antidote in snake biting and scorpion sting.

Anticancer evaluation: The anticancer activity of the different extracts of fruits of *P. longum* on human lung epithelial adenocarcinoma cell line has been assessed *in vitro* using 3-(4,5–dimethylthiazol-2yl)-2,5–diphenyl tetrazolium bromide. The potency of plant extracts to inhibit the cancerous growth was recorded in terms of disease in viable cell count as compared to the control value (Sawhney et al., 2011).

D. *Vitex negundo* Lamiaceae

Chemical constituents: *Vitex negundo*, commonly known as the Chinese chaste tree, five-leaved chaste tree, or horseshoe vitex, is a large aromatic shrub with quadrangular, densely whitish, tomentose branchlets. The principal constituent of the leaf juice are casticin, isoorientin, luteolin, p-hydroxybenzoic acid and D-fructose. The main constituent of the oil are sabinene, terpinen-4-ol, linalool. *In vitro* and animal studies have shown that chemicals isolated from the plant have potential anti-inflammatory, antibacterial, antifungal and analgesic activities (Chattergy and Prakash, 1999).

Anticancer evaluation: The antitumour activities of the ethanolic extract of leaves of *V. negundo* has been evaluated against Daltonascitic lymphoma in Swiss albino mice at the dose of 250 and 500mg/kg, body weight. The experimental parameter used tumour cell count, viable tumour cell count, increase in life span to assess antitumour activity (Nandu and Patil, 2015).

E. *Curcuma longa* Zingiberaceae

Chemical constituents: From turmeric, *Curcuma longa* L. (Zingiberaceae), three curcuminoids, curcumin, demethoxy curcumin, and bis-demethoxy curcumin, were found. It contains the ar-turmerone (20.50%), B-sesquiphellandrene (5.20%) and curcumenol (5.11%).

Uses: Curcumin is a substance found in the spice turmeric has long been used in Asian medicine to treat a variety of maladies. Curcumin is thought to have antioxidant properties, which means it may decreases welling and inflammation. Laboratory and animal research suggests that curcumin may prevent cancer, slow the spread of cancer, make chemotherapy more effective and protect healthy cells from damage by radiation therapy.

Anticancer evaluation: The 61 curcumin related compounds were synthesized for their anticancer activity towards cultured prostate cancer Pc-3 cells, pancreas cancer Panc-1 cells and colon cancer HT-29 cells. Inhibitory effects of these compounds on the growth of Pc-3, Panc-1 and HT-29 cells were determined by 9MTT [3-(4,5-Dimethylthiazol-2-yl)-2,5 Diphenyl tetrazolium Bromide] assay. The active compounds were potent stimulators of apoptosis (Wei et al., 2012).

F. *Picrorhiza kurroa* Plantaginaceae

Chemical constituents: *Picrorhiza kurroa* is one of the major incomes generating non-timber forest products found in the Nepalese Himalayas commonly called Kutki or Kutaki. Chemical present in it are kutkin, a bitter glycocide which contains two C-9 iridoid-glycosides-Picrosidel and kutakoside (Jeena et al., 1999).

Uses: The rhizome has a long history of use in Indian Ayurvedic medicine for the treatment of digestive problems. Its appear to be relatively safe based on its long history of traditional.

Anticancer evaluation: Nano-encapsulated extract formulation from rhizome of *P. kurroa* enriched with apocyanin, caffeicester and cucurbitacins a glycone compounds, to produce any cytotoxic effect on mammalian cell line. Madin-Darby Canine Kidney (MDCK) cytotoxicity results support that formulation is less cytotoxic in normal cell lines, as MDCK is a non-cancerous cell line (Hemanth and Kumar, 2014).

G. *Berberis aristata* Berberidaceae

Chemical constituents: *Berberis aristata* DC (Berberidaceae) commonly known as Daruhaldi and Citra, is an important medicinal herb native to Northern Himalaya region. The plant is used traditionally in Indian system of medicine as an antibacterial, antiperiodic, antidiarrheal and anticancer and also used in treatment of ophthalmic infections. The root bark contains berberine, quartenary ammonium salt of isoquinoline alkaloid (Rathi et al., 2013).

Uses: The fruit of the species are eaten by people living in areas where the plant is found often as a desert. The fruit is juicy and contain plenty of sugar and other nutrient that supplemented their diet. The root can also be used for making an alcoholic drug. The stem extract of *Berberis* is used to treat cancer (Serasanambati and Chilakapati, 2015).

Anticancer evaluation: The methanolic extract of stems of *B. aristata*, was used to investigate its anticancer activity in human breast cancer cell line (MCH-7). Different concentration of the methanolic extract were subjected to determine the cytotoxic effect by measuring the cell proliferation activity in MCH-7 breast cancer cell line up to 48hour of incubation. In addition significant increase of apoptosis at 500µg of extract in MCH-7 cells was evidenced by live/ dead assay (Ali et al., 2008; Das et al., 2009).

H. *Datura stramonium* Solanaceae

Chemical constituents: *Datura stramonium* is a widespread annual plant from the Solanaceae family. This plant has contributed various pharmacological actions in the scientific field of Indian systems of medicines like analgesic, anticancer and antiasthmatic activities. It contains n-trans-feruloyl tryptamine, hyoscyamilactol, scopoletin, umckalin, daturaolone, daturadiol, N-trans-ferulicacyl-tyramine, fraxetin and scopolamine (Soni et al., 2012).

Uses: Burning leaf smoke of *Datura* is good to treat asthma bronchitis. *Datura* leaf are used to treat cancer.

Anticancer evaluation: HePG2 (liver cancer cell line) cell culture were procured from National Center for Cell Sciences (NCCS) Pune, India. Stock cell were cultured in Dulbecco's Modified Eagle's Medium (DMEM). Medium was supplemented with 10% inactivated Fetal Bovine Serum (FBS), penicillin and streptomycin, in a humidified atmosphere of 5% CO_2 at 37^0C.

I. *Cannabis sativa* Cannabaceae

Chemical constituents: *Cannabis sativa* L. (Cannabaceae) is one of the earliest known cultivated plants. It include about 120 compounds responsible for its characteristic aroma. Cannabinoids represent the most studied group of compounds, mainly due to their wide range of pharmaceutical effects in humans, including anticancer activities. These are mainly volatile terpenes and sesquiterpenes, alpha-pinene, myrcene, linalool, limonene etc.(Andre et al., 2016).

Uses: Dranabinol (marinol) is a gelatin capsule containing delta-9-tetra hydro cannabinol (THC) that's approved by the US Food and Drug Administration (USFDA) to treat nausea and vomiting caused by cancer chemotherapy as well as weight loss. The Nabilone (cesamet) is a synthetic cannabinoid that acts much like THC. It can be taken by mouth to treat nausea and vomiting caused by chemotherapy when other drugs have not worked.

Anticancer evaluation: Acetaldehyde is an ubiquitous genotoxic compound that has been classified as a possible carcinogen to humans. It can react with DNA to form primarily as chiff base N2-ethyldene-2'-deoxyguanosine adduct.

J. *Ocimum sanctum* Lamiaceae

Chemical constituents: *Ocimum sanctum* Linn (known as Tulsi), a small herb seen throughout India, have been recommended for the treatment of various common diseases. It has also been suggested to possess antifertility, anticancer, antidiabetic, antifungal, antimicrobial, hepatoprotective, cardioprotective, antiemetic, antispasmodic, analgesic, adaptogenic and diaphoretic actions. Tulsi contains phenols, terpenes, aldehydes, apart from volatile oil the plant also has been reported to contains alkaloids, glycoside, saponins and tanins (Cohen, 2014).

Uses: According to research published in the journal 'Nutrition and Cancer', tulsi and its phytochemicals (including euginol, myretenol, luteolin, carnosic acid). In some cases, may help prevent chemical-including lung, liver, oral and skin cancer because they increase antioxidant activity. The phytochemicals help to induce cancer cell growth and stop metastasis-which is spread of cancer from one organ to another. It protect the normal tissue against the destructive effects of radiation.

Anticancer evaluation: Oral squamous cell carcinoma line (KB mouth cell line) were seeded into 96 well plate. After 24hours, the cell were treated with *O. sanctum* extracts concentration and exhibited cytotoxic and antiproliferative activity on KB cell lines (Shivpuje et al., 2015; Sireesha et al., 2019).

K. *Azadirachta indica* Meliaceae

Chemical constituents: Neem (*Azadirachta indica*) is a member of the Meliaceae family and its role as health-promoting effect is attributed because it is rich source of antioxidant. Neem has been used extensively by humankind to treat various ailments before the availability of written records which

recorded the beginning of history. Since prehistoric times, neem has been used by humankind. Neem plant contain azadirachtin and nimbolide, can be obtained through butanol, ethylacetate extract, hexane extract, methanol extract (Alzohairy, 2016).

Uses: Neem seed oil inhibits growth of Hela cervical cancer cells (Priyadarsini et al., 2010). The nimbolide disrupt cell cycle progression and inhibit proliferation of Hela (Elumalai et al., 2012), breast cancer (Harish et al., 2009), choriocarcinoma, lymphoma (Roy et al., 2007), leukemia and melanoma (Manikandan et al., 2009).

Anticancer evaluation: The protective effects of subfractions of the ethylacetate fraction (EAF) and the methanolic fraction (MF) from the crude ethanolic extract (CEE) of *A. indica.* Neem leaves against various free radicals and hydrogen peroxide induce oxidative damage to red blood cells (RBCs) and pBR322 DNA (Manikandan et al., 2009).

CONCLUSIONS

The literature evidence quoted in various Ayurvedic text and recent pharmacological studies on medicinal plants, inferred that medicinal plant represent a good source of pharmacological active agents treating various type of malignancies. Also, since many herb play chemo protective action, a combination of Ayurvedic medicine and conventional therapy could also be recommended to inhibit the growth of cancer cell and to reduce the side effect of radiation of chemotherapy. Our result summarize that the extract from following plant shows anticancer activity by decreasing cell proliferation, increasing intra cellular ROS (Reactive Oxygen Species), alteration in mitochondrial membrane potential and apoptosis in NCI-H460 cell line. The result obtain from our investigation conform the therapeutic potency of plants. Further research is warranted to isolate the phytochemicals that is responsible for cancer cell apoptosis. *C. deodara* posses have many qualities, including anti-inflammatory, antitumor and immunomodulatory properties as well as exerting and an influence on the nervous system, antioxidant properties.

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