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By

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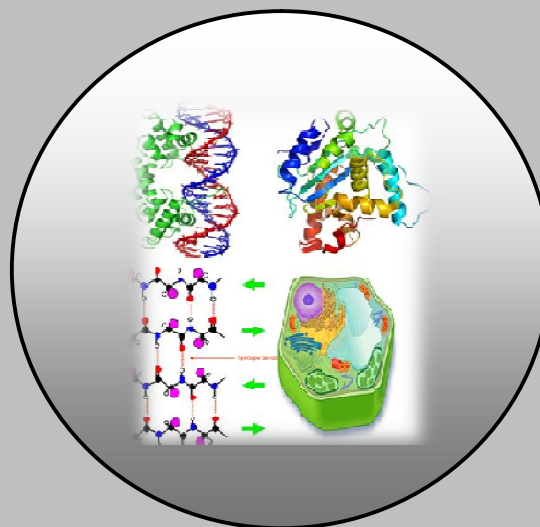
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REVIEW ARTICLE

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Anticancerous Potential of Plant Extracts and Phytochemicals

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ABSTRACT

There is a demand for natural source of pesticides in food, cosmetics & therapeutic industry. Due to their low cost, high stability, compatibility and environment friendly, we found that plants are the good source of natural antimicrobial agents due to the presence of phytochemicals. Plant extracts appears to be one of the better alternatives as they are known to have minimal environmental impact and danger to consumers in contrast to synthetic pesticides. The use of and search for drugs and dietary supplements derived from plants have accelerated in recent years. Ethno-pharmacologists, botanists, microbiologists, and natural products chemists' are combining the Earth for phytochemicals and "leads" which could be developed for treatment of infectious diseases. Many pathogenic microbes have capability to develop resistance against synthetic formulation. Synthetic formulation is very toxic and destroys the soil fertility and ecological balance. Plant based formulation are least toxic and better for environment balance so it can be replace by synthetic formulation. Antimicrobial activity of plants is mainly due to the presence of secondary metabolites. Plants are rich in wide variety of secondary metabolites such as tannins, terpenoids, alkaloids, and flavonoids, which have been found in vitro to have antimicrobial properties. This review attempts to summarize the current status of phytochemicals to protect one against cancer.

Keywords: *Phytochemicals, Anticancerous potential, Plant Extracts, Secondary Metabolites and Infectious diseases.*

INTRODUCTION

Medicinal plants have been used as remedies for human diseases for centuries. The reason for using them as medicine lies in the fact that they contain chemical components of therapeutic value (Nostro et al. 2000). The medicinal value of plants lies in some chemical substances (usually secondary metabolites), that produce a definite physiological action on the human body. The most important of these bioactive compounds of plants are alkaloids, flavanoids, tannins and phenolics (Edeoga et al. 2005).

Phytochemicals are non-nutritive plant chemicals that work with nutrients and dietary fiber to protect one against diseases. There are more than a thousand known phytochemicals. They are not essential nutrients and are not required by the human body for sustaining life. Research suggests that phytochemicals, found in fruits, vegetables and nuts, may help slow the aging process and reduce the risk of many diseases, including cancer, heart disease, stroke, high blood pressure, cataracts, osteoporosis, and urinary tract infections. Foods containing phytochemicals are already part of our daily diet. In fact, most foods contain these chemicals except for some refined foods such as sugar or alcohol. Some foods, such as whole grains, vegetables, beans, fruits, and herbs, contain many phytochemicals. The easiest way to get more phytochemicals is to eat more fruit and vegetables. These biologically active micronutrients exhibit their activity as antioxidants, detoxifying agents or simply by physico-chemical means in the case of dietary fiber. They can have complementary and overlapping mechanisms of action in the body, including antioxidant effects, modulation of detoxification enzymes, stimulation of the immune system, modulation of hormone metabolism, and antibacterial and antiviral effect.

A RAINBOW OF PROTECTION

Cancer is the cause of more than six million deaths each year in the world. In 2001, about 1,268,000 new cancer cases and 553,400 deaths were reported in the United States. For a long time, plants are being used in the treatment of cancer. According to an estimate, 50% of breast cancer and 37% of prostate cancer patients use herbal products. Pigmented plant compounds are important anti-inflammatory and antioxidant substances, and people who eat more of them have a decreased risk of cancer. Plant pigments are mostly polyphenolic, meaning they are multiphenol-containing molecules, and include chlorophyll, carotenoids and bioflavonoids. Green plants contain particularly large amounts of chlorophyll, which are a detoxifier and possibly an anticancer agent. Foods rich in chlorophyll include *chlorella* and other blue-green algae, beet greens, bok choy, collards, dandelion greens, kale, mustard greens and nettles. These greens--among the most nutritious of all plants or plant parts--also contain other diverse nutrients and healthy constituents.

The blue-green algae family has high chlorophyll content and has been credited with immune-enhancing effects including stimulation of phagocytosis and enhanced response to tumors and microbes. *Chlorella* powder, specifically, may reduce side effects of chemotherapy for some patients and may possess direct anticancer activities. Orange, yellow and red-orange foods are rich in carotenoids such as beta-carotene, lutein and lycopene. These constituents are antioxidants and anticancer agents due to several different mechanisms. More than 600 carotenoids occur naturally, but carotenes are the most widely known. Carotenes seem to offer protection against lung, colorectal, breast, uterine and prostate cancers. Carotenes, which destroy oxygen free radicals in lipids, enhance immune response and protect cells against UV radiation. Foods rich in these flavonoids include apricots, carrots, citrus fruits, squash and tomatoes in addition to many green foods. The anthocyanidins are a type of complex flavonoid that produces blue, purple or red colors. Foods rich in these phytochemicals include beets, blackberries, blueberries, cherries, purple and red grapes, and purple cabbage. Anthocyanidins support connective tissue regeneration and are anti-inflammatory; they promote blood flow and reduce cholesterol, in addition to being antioxidants. Anthocyanidins seem to stabilize and protect capillaries from oxidative damage and have been shown to stabilize connective tissue, promote collagen formation, improve microcirculation and help protect blood vessels from oxidative damage. Thus, by eating these antioxidant pigments, some believe cancer risk can be reduced because the antioxidants protect against damage and help repair connective and vascular tissues. Proanthocyanidins are the precursors to anthocyanidins, and are comprised of smaller units including catechins and epicatechins. Catechins are simple flavonoids that are abundant in green tea. Several Japanese studies show that tea consumption is protective against breast and other types of cancer.

PHYTOCHEMICAL DEFENCE

Detoxifying, stimulating and spicy sulfur compounds are present in a variety of colorful foods including broccoli, garlic and pineapple. Sulfur-containing compounds in plants are active, or at least protective, against cancer because many pathogens are deterred by sulfur. Sulfur compounds also chelate mercury out of the body. The crucifer family--which includes broccoli, Brussels sprouts, cabbage, cauliflower, mustard greens, radishes and turnips--has many sulfur-containing compounds as well as indoles, a subclass of phytonutrients that binds chemical carcinogens and activates detoxification enzymes, mostly in the gastrointestinal tract. Indoles and related compounds may promote metabolism of carcinogens as well as improve estrogen balance, which could reduce the risk of estrogen-related cancers such as breast cancer. The lily family includes garlic (*Allium sativum*) and onions (*Allium cepa*), both of which also contain sulfur compounds. Studies have shown the sulfur compounds diallyl disulphide and diallyl trisulfide--two of the active agents in garlic oil--and *S-allyl cysteine*--found in crushed garlic--to inhibit tumor metabolism and enhance immune response.

Allyl sulfides also enhance glutathione S-transferase enzyme systems, which are biochemical pathways involved in the liver's detoxification of carcinogenic substances. Allium species also have immune-enhancing actions that include promotion of lymphocyte synthesis, cytokine release, phagocytosis and natural killer-cell activity.

Several animal studies have shown that garlic and onions prevent cancer and inhibit the progression of existing cancers, especially stomach and gastrointestinal cancers. Garlic appears particularly effective in reducing the risk of N-nitroso-induced cancers. N-nitroso compounds, also known as nitrosamines, are potent carcinogens formed within the intestines as a result of bacterial degradation of nitrates and nitrites, two common food chemicals used in the processing of ham, sausages and other meat products.

All forms of garlic have been shown to have some medicinal activity. Pineapples contain bromelain, a sulfur-rich proteolytic enzyme that has been investigated for antitumor effects. U.S. and French research shows oral bromelain can reduce cancer in animals. Some documented cases show cancerous tumors regressing as a result of bromelain therapy. Bromelain may also have antimetastatic effects. It has been examined in vitro to both oppose leukemia by promoting the normalization of blood cells and to reduce metastasis in lung-cancer cells.

Other protective phytochemicals include the caffeic, ferulic and ellagic acids, which have been shown to degrade carcinogenic substances. Among other things, caffeic acid helps degrade carcinogens, and ferulic acid helps prevent *nitrates* in the digestive tract from being converted into the carcinogenic nitrosamines. Caffeic and ferulic acids are found in green tea. Ellagic acid, which is particularly plentiful in pomegranates, also prevents carcinogen oxidation of cellular membranes. Ellagic acid is also found in blueberries, grapes, raspberries and strawberries.

Limonene is a bioflavonoid substance found in citrus rinds that stimulates both the glutathione transferase and the cytochrome p-450 liver detoxification systems. These enzymatic liver reactions break down carcinogenic substances in the body and help prevent them from damaging cellular DNA. Another bioflavonoid, quercitin, is ubiquitous in higher plants and has been widely studied for its antioxidant and concomitant anticancer actions.

REVIEW OF LITERATURE

Carotenoids are a subclass of terpenes that are present in citrus fruits, cruciferous vegetables, spinach, tomato, yam, egg plant, mint, basil, and cherries. Terpenes are plant foods that act as antioxidants. Alpha carotene inhibits tumor growth. Lycopene is a carotenoid found in dark yellow orange and deep green vegetables and fruits, especially tomatoes. It is the most effective biological singlet-oxygen quencher, two times as powerful as beta-carotene in the destruction of free radicals. Research has shown that lycopene-rich foods reduce the risk of prostate cancer. Carotenoids like lutein and zeaxanthin reduce the risk of lung and breast cancer.

Limonoids are found in citrus fruits like grape fruit and orange juice and act as chemo preventive agents that induce enzymes in the liver's phase I and II enzyme detoxification system. This system detoxifies carcinogens by making them more water soluble for excretion. Grape juice and red wine are good sources of phenols and phenolic compounds. Flavonoids scavenge free radicals and their complexes. By scavenging activated mutagens and carcinogens, flavonoids may also decrease the risk of cancer. Caffeic and ferulic acids present in whole grains have been classified as cancer inhibitors. They act by preventing the formation of carcinogens from precursor compounds and by blocking the reaction of carcinogens with critical cell macromolecules. The potentially anticarcinogenic properties of these phenolic compounds involve the induction of detoxification systems in the cell. Isoflavones are found in beans and legumes, especially soy and its products. The phytochemical in soy foods acts as an antioxidant and carcinogen blocker or tumor suppressor and may exert a protective effect against hormone-related cancers like breast and prostate cancer. Thiols are sulphur containing phytonutrients found in cruciferous vegetables. These organosulphuric compounds regulate the enzymes involved in the detoxification of carcinogens and other foreign compounds. Organo sulphur compounds are also found in the allium or onion family including garlic, shallots, and leeks. Lignans are phytochemicals found in flax seeds, wheat bran, and barley, and they have a protective effect against hormone-sensitive cancers by virtue of their interference with the metabolism of sex hormones. Phytic acid forms chelates with various metals that suppress iron-catalyzing redox reactions that can be pretty damaging to tissues. Colonic bacteria produce oxygen radicals in appreciable amounts, and dietary phytic acid can suppress damage to the intestinal epithelium and neighboring cells. To date, several hundred scientific studies focused on the activity of non-nutritional compounds present in the diet, preventing the occurrence of degenerative diseases, such as cancer. This heterogeneous class of molecules, generally known as phytochemicals includes vitamins (carotenoids) and food polyphenols, such as flavonoids, phytoalexins, phenolic acids, indoles and sulfur rich compounds (Russo 2007; Sporn and Suh 2002 and Surh, 2003). More than 10,000 phytochemicals have been described, and among them more than 6,000 compounds are included in the class of flavonoids (Hairborne 1993). They are widely present in plant derived foods and beverages (fruits, vegetables and beverage such as tea, wine beer and chocolate), and in many dietary supplements or herbal remedies. Due to the variety of their physiological roles in plant tissues in regulating enzymes involved in cell metabolism and in mechanisms of defence against foreign agents (radiations, viruses, parasites), phytochemicals have been associated to pleiotropic effects in animal cells. Phytochemicals attracted scientists' interests since the demonstration that their biological targets in mammalian cells were the same involved in inflammatory processes and oncogenic transformation, such alterations of cell cycle control, apoptosis evasion, angiogenesis and metastases.

In addition, a large number of epidemiological studies suggest that a daily intake of phytochemicals can reduce the incidence of several types of cancers (Russo 2007; Sporn and Suh 2002; Russo et al. 2005 and D'Incalci et al. 2005). However, we and others already underlined the discrepancy between phytochemical concentrations applied in *in vitro* studies. In fact, many phytochemicals, including polyphenols, are rapidly degraded and metabolized in the human body. Moreover, genetic variation in pathways affecting absorption, metabolism, and distribution of these natural substances, could influence exposure at the tissue level, thus modifying disease risk in individuals (Manach et al. 2009 and Ross, 2007). Nevertheless, this wide group of natural molecules represents a promising class as anticancer drugs, since their multiple targets in cancer cells, with limited toxic effect on normal cells. Phytochemicals can prove their therapeutic efficacy in mono-treatments or in association with classical chemotherapeutic drugs. In the latter case, a double positive effect can be expected: i. phytochemicals can synergize with cytotoxic drugs, increasing their efficacy and lowering the toxic side effects on normal cells; ii. Combined treatment can delay resistance onset.

Despite this encouraging preamble and the abundant literature describing the molecular mechanisms triggered by phytochemicals to inhibit cell growth and induce apoptosis in cancer cells, only few of them entered clinical trials. Here, we will focus our attention on a selection of representative molecules, namely isothiocyanate, curcumin, genistein, epigallocatechin gallate, lycopene and resveratrol, largely present in the literature. For each of them, we will summarize their putative mechanism(s) of action from *in vitro* and animal studies, and the current status of their clinical application in view of their realistic adoption as single chemotherapeutic agents or as chemo-sensitizers, in association with canonical and novel anti-cancer drugs.

Cranberry fruit has a diverse phytochemical profile that includes 3 classes of flavonoids (flavonols, anthocyanins, and proanthocyanidins), catechins, hydroxycinnamic and other phenolic acids, and triterpenoids. Several groups of researchers examined activity of whole polyphenolic extracts of the fruit or spray-dried juice. Our group developed a bioassay-guided fractionation approach to identification of antitumorigenic compounds while researching plants used in traditional Peruvian medicine (Neto et al. 2000). Our strategy used a simple NCI tumor growth inhibition assay (Skehan et al. 1990) to screen for activity in several tumor cell lines. Antitumor activities of not only whole cranberry fruit and juice extracts has been examined but also individual compounds and groups of compounds to identify active constituents. Curcumin is a natural phytochemical obtained from dried root and rhizome of Turmeric (*Curcuma Longa*). It has been shown to interfere with multiple cell signaling pathways, including apoptosis (activation of caspases and downregulation of antiapoptotic gene products), proliferation (HER-2, EGFR, and AP-1), angiogenesis (VEGF), and inflammation (NF-kappaB, TNF, IL-6, IL-1, COX-2, and 5-LOX). In the last decade it has been much explored and various synthetic analogues have been prepared and evaluated for various pharmacological activities.

Most of the analogues have shown very good anticancer activity in various models and various cell lines. However, some analogues have also shown antioxidant, anti-HIV, antimutagenic, antiangiogenic, antimalarial, antitubercular, antiandrogenic, COX inhibitory activities (Agrawal and Mishra 2010).

Ficus racemosa extract at a dose of 200 and 400 mg/ kg when given orally a significant decrease in lipid peroxidation, xanthine oxidase, γ glutamyl transpeptidase and hydrogen peroxide (H_2O_2) generation with reduction in renal glutathione content and antioxidant enzymes generated by potassium bromate ($KBrO_3$), a nephrotoxic agent that induces renal carcinoma in rats. There was significant recovery of renal glutathione content and antioxidant enzymes (Veerapur et al 2009). This suggests that *Ficus racemosa* extract is a potent chemopreventive agent and suppresses ($KBrO_3$) mediated nephrotoxicity in rats. Fruit extracts of *Ficus religiosa* exhibited antitumor activity in the potato disc bioassay. None of the tested extracts showed any marked inhibition on the uptake of calcium into rat pituitary cells GH4 C1 (Mousa 1994).

Combretastatins were isolated from the bark of the South African tree *Combretum caffrum* (Combretaceae). Combretastatin is active against colon, lung and leukemia cancers and it is expected that this molecule is the most cytotoxic phytomolecule isolated so far (Itokawa and Wang 2005). Emodin (1, 3, 8-trihydroxy methylantraquinone) is a naturally occurring anthraquinone present in the roots and barks of *Cassia tora* as an active ingredient. At present, its role in combination chemotherapy with standard drugs to reduce toxicity and to enhance efficacy is pursued vigorously. Its additional inhibitory effects on angiogenic and metastasis regulatory processes make emodin a sensible candidate as a specific blocker of tumour associated events. Additionally, because of its quinone structure, emodin may interfere with electron transport process and in altering cellular redox status, which may account for its cytotoxic properties in different systems. This biological property of emodin molecule is offering a broad therapeutic window, which in future may become a member of anticancer (Wu et al. 2001).

Polyphenols particularly are among the diverse phytochemicals that have the potential in the inhibition of carcinogenesis (Liu 2004). Phenolics acids usually significantly minimize the formation of the specific cancer- promoting nitrosamines from the dietary nitrites and nitrates. Glucosinolates from various vegetable sources as broccoli, cabbage, cauliflower, and Brussel sprouts exert a substantial protective support against the colon cancer. Regular consumption of Brussel sprouts by human subjects (up to 300 g.day⁻¹) miraculously causes a very fast (say within a span of 3 weeks) an appreciable enhancement in the glutathione-S- transferase, and a subsequent noticeable reduction in the urinary concentration of a specific purine metabolite that serves as a marker of DNA-degradation in cancer. Isothiocyanates and the indole-3- carbinols do interfere categorically in the metabolism of carcinogens thus causing inhibition of procarcinogen activation, and thereby inducing the 'phase-II' enzymes, namely:

NAD(P)H quinone reductase or glutathione S-transferase, that specifically detoxify the selected electrophilic metabolites which are capable of changing the structure of nucleic acids. Sulforaphane (rich in broccoli) has been proved to be an extremely potent phase-2 enzyme inducer. It predominantly causes specific cell-cycle arrest and also the apoptosis of the neoplasm (cancer) cells. Sulforaphane categorically produces d-D-gluconolactone which has been established to be a significant inhibitor of breast cancer. Indole-3-carbinol (most vital and important indole present in broccoli) specifically inhibits the Human Papilloma Virus (HPV) that may cause uterine cancer. It blocks the estrogen receptors specifically present in the breast cancer cells as well as down regulates CDK6, and up regulates p21 and p27 in prostate cancer cells. It affords G1 cell-cycle arrest and apoptosis of breast and prostate cancer cells significantly and enhances the p 53 expression in cells treated with benzopyrene. It also depresses Akt, NF-kappaB, MAPK, and Bel-2 signaling pathways to a reasonably good extent. Phytosterols block the development of tumors (neoplasms) in colon, breast, and prostate glands. Although the precise and exact mechanisms whereby the said blockade actually takes place are not yet well understood, yet they seem to change drastically the ensuing cell-membrane transfer in the phenomenon of neoplasm growth and thereby reduce the inflammation significantly. A grass obtained from the plant *Cymbopogon citratus* belongs to the family citronella, lemon grass as an herb has been used for centuries for its positive health effects. The fresh grass is used in Indigenous medicine systems around the world. Recently the essential oil has been the subject of scientific studies regarding its effects on cancer cells. Lemon grass appears to be effective as forms of Chemotherapy causing cell death to occur. The research indicates that the oil has a promising anticancer activity and causes loss in tumor cell viability by activating the apoptotic process. The studies indicate that lemon grass essential oil with its low toxicity has the potential of being an inexpensive, alternative treatment in the future (Koganov et al. 1994 and Sieges et al. 1999). Wheat Grass is known as wholesome food and the king of alkaloid foods as it is high in alkalinity that helps to fight off acidic body. It contains chlorophyll which is having similar structure of hemoglobin, known as Green blood. It increases production of hemoglobin that Kills cancer by getting more oxygen. Selenium, superoxide dismutase (SOD) and abscisic acid are other anticancer agents present in this. Since an acidic body is a magnet of chronic diseases, taking wheat grass helps to prevent cancer by balancing the pH and bring it to the desired alkalinity level in our body (Sheela et al. 2010). Sea-Buckthorn acts by enhancing immune system which contains very high amounts of antioxidant called carotenoids. Sea-buckthorn prevents the growth of cancer cells and also preventing free radical oxidation. Seeds are in rich of unsaturated fatty acids which is good for vascular system. Fruits pulp has high vitamin E responsible for the potent anticancer properties. Lingzhi used in Japan, it is a fungus known as Herb of deathlessness, Herb of longevity and Celestial herb. It has been praised for it's promoted vitality and longevity.

Lingzhi (*Gandoerma lucidum*) is a mushroom i.e. rich in beta-D-glucose (using water – alkali extract) that have a antitumor activities which currently used as an adjunctive in treatment of reducing side effects of chemotherapeutic agents. Amalkai is an Ayurvedic plant, known as a mother of Healing system. It contains vitamin C and superoxide dismutase (SOD) and other antioxidants that fight off damaging free radicals to prevent cancer. It is also rich in polyphenols, tannin, Bioflavonoids and amino acids (Krishnaswami and Raghuramuls 1998). Garlic has anticancer compound called dually sulfide. Raw -uncooked garlic i.e. chopped has much more potent anticancer effect than garlic supplements (kken et al. 1999). *Zingiber officinale* belonging to family Zingiberaceae contains pungent ingredients in which gingerol and pardol have shown antitumor promotional and Anti-proliferative effects. *Aloe vera* and other species of aloe contain aloe emodin which activates the macrophages to fight cancer. *Aloe vera* also contains acemannan which enhances the activity of immune cells against cancer. Crude extract of *Viburnum foetens* showed remarkable anticancerous activity against MCF-7 cell line at all concentrations in a dose dependent manner. The average absorbance decreased by increasing the concentration of crude extract. Highest absorbance of 0.2006 was recorded when determining 28.4% inhibition at 10 µg/ml, while at the concentration of 500µg/ml of crude extract, 0.065 absorbance was recorded with 98.5% inhibition (Yamin et al. 2010). Anti-tumour activity of *Cassia fistula* seed extract based on cytological studies reveal that a reduction in the mitotic activity can be the leading mechanism of action against tumorigenesis. Indeed the appearance of membrane blebbing and intracytoplasmic vacuoles in the treated tumour cells suggest that these pathways may account for the reduction in tumour volume (Gupta et al. 2000). Fractions (EtOAc and *n*-BuOH) of different parts of *Conocarpus erectus* L. were investigated *in vitro* towards two kinds of human cancer cell lines; liver carcinoma cell line (HepG2) and breast carcinoma cell line (MCF-7) at the National Cancer Institute in Egypt (El-Sayed et al. 2012). The methanol and fractionated extracts (hexane, ethyl acetate and water) of *Alpinia mutica* (Zingiberaceae) rhizomes were investigated for their cytotoxic effect against six human carcinoma cell lines, namely KB, MCF7, A549, Caski, HCT116, HT29 and non-human fibroblast cell line (MRC 5) using an *in vitro* cytotoxicity assay. The ethyl acetate extract possessed high inhibitory effect against KB, MCF7 and Caski cells (IC₅₀ values of 9.4, 19.7 and 19.8 g/mL, respectively). Flavokawin B (1), 5, 6-dehydrokawain (2), pinostrobin chalcone (3) and alpinetin (4), isolated from the active ethyl acetate extract were also evaluated for their cytotoxic activity. Of these, pinostrobin chalcone (3) and alpinetin (4) were isolated from this plant for the first time. Pinostrobin chalcone (3) displayed very remarkable cytotoxic activity against the tested human cancer cells, such as KB, MCF7 and Caski cells (IC₅₀ values of 6.2, 7.3 and 7.7 g/mL, respectively). This is the first report of the cytotoxic activity of *Alpinia mutica* (Abdul et al. 2011).

The stem of *V. diospyroides* Symington, an endemic medicinal and fragrant dipterocarp of Thailand peninsula, has strong anticancer activity (Seo et al. 1999 and Kinghorn et al. 2011). Apple contains anti cancer substances known as phenols, which neutralize certain carcinogens, disrupt the transformation of precancerous cells into the cancerous ones, and stimulate the body's production of natural cancer fighters. Pectin, a natural fiber present in apple, is known to reduce the risk of colon cancer. Apple is a good heart medicine, lowers the blood cholesterol, lowers blood pressure, stabilizes blood sugar, regulates appetite, kill infectious viruses. Apricot is a cancer inhibitor, especially lung, smoking related cancer. *Asparagus* is commonly referred to as the 'king of vegetables' by the ancient Romans and Greeks, can be used to treat arthritis, tooth ache and infertility. Researchers have found out that it contain the potent antioxidant glutathione, which is helpful in the fight against cancer, cataracts and heart diseases. Barley lowers blood cholesterol, inhibits cancer and improves bowel functions, relieves constipation. Beans power houses of nutrition are also versatile in kitchen. They contain good amounts of protease inhibitors like lignans, phytoestrogens and fiber. All are potent cancer fighters. Studies show that people who make beans a significant part of their diet are less likely to have breast cancer and pancreatic cancer. Isoflavones and flavonoids compounds that are commonly found in various legumes including soybeans are very effective antitumour compounds. One of the most important components in beans is Genistein as it closely resembles human estrogen. For this reason it is very important to include beans, especially soybeans as part of an anticancer diet. Fermented soybeans products such as miso, tempeh and shoyu tamari go through complex chemical processes that are of particular benefit in the prevention and treatment of cancer. Research has shown that soybean products contain five cancer preventive or reversal chemical agents namely (1) protease inhibitors, which hold off activation of the specific oncogenes that cause cancer; (2) phytate, which binds iron in the intestines to prevent it from generating free radicals resulting in cancer; (3) phytosterols, which neutralize the breakdown of cholesterol and reduce the development of colon tumors and skin cancer; (4) saponins, which stop cellular mutations that could inevitably lead to cancer; (5) isoflavones, which are plant estrogens with strong inhibiting effects in hormone related malignancies such as prostate, ovarian, cervical and breast cancers. The frequent consumption of cruciferous vegetables like Broccoli is associated with a decreased risk for cancer. Women must have concern about breast cancer, while men should be more worried about prostate cancer. If one is concerned about either breast cancer or prostate cancer, he or she should realize that eating cruciferous vegetables, such as broccoli and cabbage, is really good for him/her. Eating half of a head of cabbage each day or extremely large amounts of other cruciferous vegetables is what it would take to get the kind of health risk reduction one is looking for and that is neither practical nor palatable (Mohammad et al 2009).

Anona muricata extract had greater anticancer potential; *Anona muricata* was active against the lung cancer cell lines at IC₅₀ value of 7.29 while that of *A. paniculata* was 10.60. This shows that the extract of *A. muricata* and *A. paniculata* were active against the lung cancer cell line. AM and AP contained copious amount of phytoestrogens such as flavonoids which could be responsible for the anticancer activity. Some groups of flavonoids are known for their anti-inflammatory and anti-allergic, anti-thrombotic, vasoprotective and antitumour activities (Anne et al 2007). Anticancer evaluation of *Adiantum venustum* Don. Against Ascites carcinoma in animal model indicated that the ethanolic extract possess significant anti-cancer activity also reduce elevated level of lipid Peroxidation due to higher content of terpenoids and flavanoids. the ethanolic extract of *Adiantum venustum* could have vast therapeutic application against cancer (Pandey and Devmrari 2009). Anti-tumor activity of different concentrations of ethanolic extracts of *Kaempferia galanga*, *Clerodendrum viscosum*, *Jatropha curcus* and *Lens culinaris* was evaluated. Ethanolic extracts demonstrated strong inhibitory effect on the growth of cancer cells in DLA tumor bearing mice. Based on *in vitro* studies like brine shrimp lethality assay, potato disc method and onion root tip inhibition studies, the ethanolic extract of *Kaempferia galanga* was found to possess significantly better anticancer activity (Bagya et al 2011). *Asclepias curassavica* (L.) contains highly potential esterified polyhydroxy pregnane glycoside that shows antitumour and anticancer property (Kingham 2001). Extracts (methanol) of the leaves, stem and rhizome of *Boesenbergia* species possess total phenolics and flavonoid contents, antioxidant as well as anticancer properties. The plants revealed the presence of polyphenols such as quercetin, kaempferol, rutin, naringin, hesperidin, caffeic acid, p- coumaric acid, ferulic acid, sinapic acid, chlorogenic acid, gallic acid, luteolin and diosmin by using High Performance Liquid Chromatographic (HPLC). Cytotoxicity assay of *B. rotunda* showed the most prominent and promising result as anticancer medicinal plant. It showed positive antiproliferative effect against five cancer cell lines: ovarian (CaOV3), breast (MDA-MB-231 and MCF-7), cervical (HeLa) and colon (HT-29) cancer cell lines with 3-(4, 5-dimethylthiazol-2-yl) -2, 5- diphenyltetrazolium bromide (MTT) assay conducted. In addition, the rhizome of *B. pulchella* var *attenuate* and *B. armeniaca* shown positive result in cytotoxicity assay tested against breast cancer (MCF-7). Thus, the *Boesenbergia* species investigated would be a promising anticancer remedy for breast cancer (Ling et al 2010). Garcinol, a polyisoprenylated benzophenone, is extracted from the rind of the fruit of *Garcinia indica*. It's biological activities, specifically its anticancer potential is a result of recent scientific investigations. The anticarcinogenic properties of garcinol appear to be moderated via its antioxidative, anti-inflammatory, antiangiogenic, and proapoptotic activities. In addition, garcinol displays effective epigenetic influence by inhibiting histone acetyltransferases (HAT 300) and by possible posttranscriptional modulation by mi RNA profiles involved in carcinogenesis.

In vitro as well as some *in vivo* studies have shown the potential of this compound against several cancers types including breast, colon, pancreatic, and leukemia. Although this is a promising molecule in terms of its anticancer properties, investigations in relevant animal models, and subsequent human trials are warranted in order to fully appreciate and confirm its chemo preventative and/or therapeutic potential (Saadat and Gupta 2012).

lycopene, the carotenoid in tomatoes that accounts for their red color. Consumption of whole, cooked tomatoes protect against prostate cancer and provide anticancer activity. In a study conducted in 2005, cancer patients ate tomato sauce on pasta for just three weeks before their PSA levels were retested and compared to baseline. Patients experienced a significant reduction in blood levels of PSA, indicating that the cancer progression was slowed or stopped. The researchers also reported that cancer cells were dying at a rapid rate. They believe that other phytochemicals in the tomatoes may be acting synergistically with the lycopene to produce these effects (Stacewicz-Sapuntzakis and Bowen 2005). Methanol extract of *Heritiera fomes* Buch. Ham. leaf and stem powder showed anticancer properties with 40 % inhibition against B16 mouse melanoma (in vitro system) and Ehrlich Ascites Carcinoma (EAC) in Swiss albino mice (in vivo system). The partial characterizations of the methanol extract by TLC, HPLC, ¹H NMR and FTIR spectral analysis revealed phenolic as the lead compounds. Overall results showed that both the leaf and stem extracts of *H. fomes* possess strong anticancer properties along with the presence of most of the phytochemicals (Patra and Thatoi 2013). Grape Seed Extract have excellent anticancer and chemopreventive efficacy against skin, colorectal, prostate, and breast cancers. Apart from this anticancer efficacy of this extract has also been observed against human lung cancer A427, A549, and H1299 cells, human gastric adenocarcinoma CRL-1739 cells, oral squamous cell carcinoma CAL27 and SCC25 cells, Jurkat, U937, and HL-60 (Ye et al 1999; Akhtar et al 2009 and Gao et al 2009). GSE as well as red wine have been shown to significantly reduce the number of metastatic nodules on the surface of lung in Swiss mice inoculated with B16F10 melanoma cells (Martinez et al 2005). *Scutellaria baicalensis* is a widely used Chinese herbal medicine historically used as anti-inflammatory and anticancer therapy that is being tested as a treatment for prostate cancer. Two human prostate cancer cell lines (LNCaP, androgen dependent, and PC-3, androgen independent) were assessed for growth inhibition when exposed to *S. baicalensis*. *S. baicalensis* exerted dose- and time-dependent increased growth inhibition in both cell lines. After treatment with *S. baicalensis*, PGE2 synthesis in both cells was significantly reduced, resulting from direct inhibition of COX-2 activity rather than COX-2 protein suppression. *S. baicalensis* also inhibited prostate-specific antigen production in LNCaP cells. Finally, *S. baicalensis* suppressed expression of cyclin D1 in LNCaP cells, resulting in a G1 phase arrest, while inhibiting cdk1 expression and kinase activity in PC-3 cells,

ultimately leading to a G2/M cell cycle arrest. In animal studies, after a 7-week treatment period with *S. baicalensis*, tumor volume was reduced by 50%, demonstrating that *S. baicalensis* may be a novel anticancer agent for treating prostate cancer (Ye et al 2007). Methanol extract of *Scutellaria orientalis* showed potent anti-leukemic activity against HL-60 cell line (Ozmen et al 2010). The water extract of *Rheum officinale* exhibited significant antiproliferative activity by inducing apoptosis in MCF-7 and A549 cell lines (Li et al 2009). A potent antiproliferative activity was also reported for the hexane extract of *Casearia sylvestris* stem bark against different cancer cell lines (Mesquita et al 2009) and the butanol extract of *Pfuffia paniculata* demonstrated high cytotoxic activity against MCF-7 cell line (Nagamine et al 2009). The aqueous methanol extract of *Ononis hirta* and *Inula viscosa* showed high ability to selectively target MCF-7 cancer cells and induced apoptosis (Talib and Mahasneh 2010a). Genistein, daidzein and isoflavonoids in soybean are thought to play an important role in breast cancer prevention (Singh et al 2002 and Wang et al 2002). Two other examples of natural compounds with anticancer properties are quercetin and apigenin. Quercetin is one of the major flavonoids found in the human diet which exerts a dose-dependent inhibitory effect on cell proliferation with cell cycle arrest in G2/M phase. Quercetin has also been shown to inhibit cell proliferation in colon carcinoma (HCT-116 and HT-29) and mammary adenocarcinoma (MCF-7) cell lines after 24 h of exposure (Ramos 2007 and Ong et al 2007). Apigenin a flavone found in celery has antiproliferative effect with cell cycle arrest in G2/M in MCF-7 cells and induces caspase activities in HL-60 cells (Yin et al 2001 and Wang et al 1999). Bioassay results of the total methanolic extract of *Kigelia pinnata* stem bark showed that the total extract displayed prominent cytotoxic activity in a concentration-dependent manner. The cell lines with most pronounced chemo sensitivity to the extract were the breast cancer derived MCF-7, the murine Lewis lung cancer (cell line) and the acute T-cell leukemia SKW-3, whereby the IC₅₀ values were significantly lower as compared to those obtained in the other cell lines (Denitsa et al 2012). Ethanol Extract of *Impatiens balsamina* was investigated for anticancer and in-vitro cytotoxic activities against transplantable tumors and human cell line. In vitro cytotoxicity was evaluated in Hela and NIH3T3 cells by MTT assay and in-vivo antitumor activity with Dalton's ascites lymphoma (DLA) tumor bearing mice. The extract exhibited strong in vitro cytotoxicity against Hela cell line, it was found to be safe with normal cell. EEIB at the doses 200 and 400 mg/kg significantly increase the life span and decrease in the cancer cell number and body weight ($P < 0.01$) and exert protective effect on the hemopoietic system. The results showed significant antitumor and cytotoxic effects against DLA and human cancer cell line and support the ethno-medical use of *Impatiens balsamina* in cancer therapy. The extract exhibited strong in vitro cytotoxicity against Hela cell line, it was found to be safe with normal cell.

EEIB at the doses 200 and 400 mg/kg significantly increase the life span and decrease in the cancer cell number and body weight ($P < 0.01$) and exert a protective effect on the hemopoietic system. The results showed significant antitumor and cytotoxic effects against DLA and human Cancer Cell line and support the ethno-medical use of *Impatiens balsamina* in cancer therapy (Baskar et al 2012). *In-vivo* study with rodents showed that cyanidin 3-glucoside and a bilberry extract, containing high levels of cyanidin-3-glucoside, reduced the formation of intestinal adenoma by up to 45% in a mouse model of human familial adenomatous polyposis (Cooke et al 2006).

Cyanidin inhibited the mitogen-induced metabolic activity, reduced free intracellular calcium and inhibited growth of the colon carcinoma cells. Neurotensin and epidermal growth factor (EGF) have been associated with colon cancer. Cyanidin was able to inhibit the increase of intracellular calcium induced by neurotensin. The epidermal growth factor acts by binding to receptor on the cell surface and stimulating the intrinsic protein-tyrosine kinase activity, which in turn, initiates a signal transduction cascade. This results in biochemical changes within the cell, such as rise in intracellular calcium levels, increased glycolysis and protein synthesis that ultimately lead to cell proliferation. Cyanidin reduced the metabolic activity and reduced the cell growth (Briviba et al 2001). *Polyalthia longifolia* possess a potential inhibiting activity towards HeLa-B75 [(68.22 \pm 0.71) %] HEP-3B [(39.15 \pm 0.12)%] and PN-15 [(55.21 \pm 0.42)%] cancer cell lines (Rajesh et al 2011). Cinnamaldehyde, piperine, and resveratrol offer significant *in vitro* anti-proliferative effects on cultured human colon cancer cells. While each phytochemical exhibited significant anti-proliferative effects, resveratrol results were most impressive in that lower concentrations administered at regular intervals were significantly effective. These results taken together with everyday dietary availability of concentrations used in this study strongly suggest that regular intake of low doses of these phytochemicals offer preventive effects against colon cancer (Duessel et al 2008). BZL101 is an aqueous extract from the *Scutellaria barbata* plant shown to have anticancer properties in a variety of human cancers. BZL101 induces distinct cell cycle arrests in early and late stage breast and prostate cancer cell lines. Along with an increase in cells with a sub-G1 DNA content, flow cytometry profiles revealed that treatment of the reproductive cancer cell lines with the corresponding optimal doses of BZL101 induced distinct cell cycle arrests (Marconett et al 2010).

The anticancer activity of methanol extracts of leaves of *Sansevieria roxburghiana* was performed on HepG2 cancer cell lines showed a potent cytotoxic activity against HepG2 liver cancer cell line PC- cyclophosphamide served as a positive control and 85% cancer inhibition was observed (Philip et al 2011). Crude extracts of *Petunia punctata*, *Alternanthera sessilis*, and *Amoora chittagonga* showed cytotoxicity to three cancer cell lines with IC50 values ranging between 20.3 - 31.4 μ g/mL, 13.08 - 34.9 μ g/mL, and 42.8 - 49.8 μ g/mL, respectively (George et al 2010).

Anti-tumor potential of the crude extract and isolated compounds from inflorescences of *Piper clausenianum* revealed the presence of phenolic metabolites in the methanol crude extract. Phytochemical procedures lead to the isolation of the major flavonoids, 2',6'-dihydroxy-4-methoxychalcone, 5,7-dihydroxyflavanone and 5-methoxy-7-hydroxyflavanone that were assayed for inhibition or viability stimulation of the human breast cancer cell line MCF-7. The results suggest the 2',6'-dihydroxy-4-methoxychalcone as the biologically active compound in the crude methanol extract of inflorescences from *P. clausenianum*. The crude extract was found as potential natural source of compounds with breast cancer cell inhibition properties (Marques et al 2013). *Allium sativum* contains more than 100 biologically useful secondary metabolites, which include alliin, alliinase, allicin, S-allyl- cysteine (SAC), diallyldisulphide (DADS), diallyltrisulphide (DATS) and methylallyltrisulphide (Charfenberg et al 1990). *Aloe vera* contains aloe-emodin, which activates the macrophages to fight cancer. *Aloe vera* also contains acemannan, which enhances activity of the immune cells against cancer. *Aloe vera* is found to inhibit metastases (Pecere et al 2000). *Aesculus indica* (Linn.) (Sapindaceae) is an ethanobotanically important plant species traditionally used against rheumatism, skin and vein complaints. Cytotoxic potential of *Aesculus indica* crude leaf extract and its fractions was investigated against MCF-7 cell line. Crude extract of *Aesculus indica* was prepared in methanol by maceration technique. Crude extract was fractionated into four organic and one aqueous fraction on polarity basis. MTT assay was used to evaluate the reduction of viability of MCF-7 breast cancer cell line. Cell viability was inhibited by *Aesculus indica* crude extract in a dose dependent manner ranging from 34.2% at 10 µg/ml to 94% at 500µg/ml. Activity was found in an ascending order from hexane showing 29.8% inhibition to aqueous fraction indicating maximum inhibition, 60%. Phytochemical analysis of crude and fractionated extracts revealed presence of flavonoids, saponins, coumarins and tannins upto varying degrees. Methanol and aqueous fraction of methanol extract of *Aesculus indica* can be good source of cytotoxic compounds (Bibi et al 2012).

Morinda citrifolia showed of cancer preventive effective on both clinical practice and laboratory animal models (Wang et al 2001). An alcoholic extract of *Biorhizoma sensitivum* for antitumor activity could inhibit the solid tumor development on mice induced with Dalton's lymphoma ascites (DLA) cells and increase the life span of mice bearing Ehrlich ascites carcinoma (EAC) tumors (Guruvayoorappan and Kuttan 2007). Edible fruits and berries served the source for novel anticancer agents, given that extracts of those foods have demonstrated cytotoxic activity against tumor cell lines (Ferguson et al 2006). Nimbolide, a triterpenoid extract from the flowers of the neem tree was found to have antiproliferative activity against some cancer cell lines (Roy et al 2007). *Semecarpus anacardium* Linn. nut milk extract exerts its anticancer effect through quenching-reactive oxygen species (Arulkumaran et al 2006). The Pomegranate extracts inhibits the growth of breast cancer cells (Jeune et al 2005).

Brassinosteroids, steroid plant hormones are promising leads for potential anticancer drugs (Malikovia et al 2007). The *Careya arborea* bark significantly reduced the solid tumor volume induced by DLA cells (Natesan et al 2007). The methanol extract of *Bauhinia racemosa* stem bark exhibited antitumor effect in EAC bearing mice (Gupta et al 2004). The antitumor activity of the ethanol extract of *Indigofera aspalathoides* was established (Rajkapoor et al 2004).

CONCLUSION

From the present review, it can be concluded that cancer is the leading cause of death in developing countries like India. As there is an enormous increase in the population day by day, the alternative therapy in the market is getting its glimpse. The cheap herbal drug treatment may highly be recommended to the rural and poor people to treat effectively the cancers of various type is an ideal choice. Based on that the siddha medicines are coming up in combination with metals and other essential supplements to improve the immune status of the cancer patients in India. The above survey reveals the role of Indian medicinal plants and the various phytochemicals may be treated effectively for cancer. The available literature finds to be very impressive which may give an indication for the therapeutic usefulness. The isolation, identification of active principles and pharmacological studies of the active phytoconstituents may be considered and studied elaborately to treat effectively for various types of cancer.

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