7. Ethnomedicinal plants to fight neoplastic diseases

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Abstract. According to one of the ancient proverbs in India, “there is no plant on earth which has no medicinal property.” More than 90% of the compounds used in modern medicine have their origin from plant sources. A large number of plants have been used by man from ancient times as medicine for curing various ailments. In recent times there is an upsurge of interest and focus on the importance of medicinal plants and traditional health systems in solving the health care problems of the world. This article gives an overview and a brief account of the important ethno-medicinal plants used in treating neoplastic diseases.

Introduction

Cancer is one of the most dreaded diseases of mankind and it is considered as an adversary of modernization and the pattern of socio-economical life dominated by western medicine. Multidisciplinary scientific investigations are making best efforts to combat this disease, but a perfect cure is yet not realized in modern medicine. Recently, a greater emphasis has been given towards the researches on complementary and alternative medicine.
that deals with cancer management. Several studies employing methodologies of modern medicine have been conducted on a multitude of herbs of ethno-botanical importance (Dahanukar et al., 2000; Duke and Ayensu, 1985). Ayurveda, the traditional Indian system of medicine, has been successful from ancient times in using natural drugs, mostly herbal preparations, in preventing or suppressing various tumors using several lines of treatment. Thousands of herbal and traditional compounds are being screened worldwide to validate their use as anticancerous drugs (Diwanay et al., 2004; Liu et al., 1998; Premalatha and Govindarajan, 2005). The science of Ayurveda describes modalities on the curative aspects of cancers that have resemblance with clinical entities of arbuda and granthi mentioned in Sushruta Samhita. An integrated approach is need of the day to manage cancer using the growing body of knowledge gained through scientific developments. The emerging integrative model of cancer treatment recognizes the importance of botanical medicine. The principles underlying herbal medicine are relatively simple, although they are not quite well understood and distinct from modern medicine.

Cancer therapy-a practical dilemma

Any practical solution in combating cancer is of paramount importance. Many herbs have been evaluated in clinical studies and are currently being investigated phytochemically to understand their tumouricidal actions against various cancers. The traditional Indian system of medicine with its evolution through centuries has always fascinated practitioners and researchers on a scientifically proven research background. Herbal medicines have a vital role in the prevention and treatment of cancer. Some herbs protect the body from cancer by enhancing detoxification functions of the body (Bradstreet, 1997). Certain biological response modifiers derived from herbs are known to inhibit growth of cancer by modulating the activity of specific hormones and enzymes. Some herbs reduce toxic side effects of chemotherapy and radiotherapy and are often employed for cancer treatment (Kapoor 1990). Research work at the Sino-Vedic Research Centre, [Sino-Vedic Cancer Clinic, FB-12, Shivaji Enclave, New Delhi-110 027 (India)] aims to develop herbal formulations to boost immune system of the body against cancer, improve quality of life and prolong comfortable lifespan in the patients suffering from advanced stages of cancer.

The recent upsurge of global interest in herbal medicines can be attributed to the spread of the traditional knowledge of the orient along with the realization and deeper understanding of the side effects and the waning effectiveness of some the conventional modern medicines such as antibiotics, which once had near-universal effectiveness against serious infections.
The traditional Indian system of medicines, Ayurveda, uses about 2,000 plant species, while the Chinese Pharmacopoeia lists over 5,700 traditional medicines, most of which are of plant origin. Some of the ethnomedicinally important plants used to fight against cancer in traditional health care are listed below.

1. **Andrographis paniculata**  
*Family: Acanthaceae*  
Since ancient times, *Andrographis paniculata* (*Kalmegh*) is used as a wonder drug in traditional Siddha and Ayurvedic systems of medicine as well as in tribal medicine in India and some other countries for multiple clinical applications. The plant extract exhibits anti-typhoid and anti-fungal activities. This plant is also reported to possess anti-hepatotoxic, anti-malarial and anti-inflammatory properties, besides its general use as an immuno stimulant agent (Trivedi and Rawal, 2001). Andrographolide is the major constituent from the leaves which is a bicyclic diterpenoid lactone. Many *in vitro* studies have been conducted and andrographolide looks promising to be developed as a normal pharmacophore in cancer treatment (Kumar *et al.*, 2004; Kumaran *et al.*, 2003). Andrographolide treatment inhibited the proliferation of different tumor cell lines, representing various types of cancers. The compound exerts direct anticancer activity on cancer cells by cell cycle arrest at G0/G1 phase through induction of cell cycle inhibitory protein p27 and decreased expression of Cyclin dependent Kinase 4 (CDK4) (Rajagopal *et al.*, 2003). Immunostimulatory activity of andrographolide is evidenced by increased proliferation of lymphocytes and production of interleukin 2 (Kumar *et al.*, 2004). Andrographolide also enhanced the Tumor necrosis factor-α production and CD marker expression, resulting in increased cytotoxic activity of lymphocytes against cancer cells, which may contribute for its indirect anticancer activity (Kumar *et al.*, 2004).

2. **Aegle marmelos**  
*Family: Rutaceae*  
*Aegle marmelos* is commonly known as Bael tree in India and considered sacred by Hindus. The extract of the plant is found to contain lupeol, a known tri-terpenoid, as a major bioactive component (Lambertini *et al.*, 2005). It was found to stimulate and increase the expression of Era gene in MDA-MB-231 Era-negative breast cancer cells and also inhibited cell proliferation. Phytoconstituents derived from the fruit of *Aegle marmelos* were found to
have strong anti-cancer activity against thyroid cancer (Lampronti et al., 2003). It is also used in the treatment of primitive neuro ectodermal tumors and malignant ascites, in addition it also possesses anti-viral and anti-inflammatory properties (Jagetia et al., 2005). The medicinal value of the bael fruit is enhanced due to the presence of tannin in its rind. A pyranocoumarin isolated from its seed gave significance protection against pylorus ligation and aspirin induced gastric ulcers in rats. (Dahanukar et al., 2000). Anticancer active principles derived from the herb Aegle marmelos, are used in the treatment of primitive neuro-ectodermal tumours (PNET) and also used in the treatment of various malignant tumours of brain and spinal cord (http://www.cancercliniconline.com/sinovedicanticancerherbs/htm).

3. **Centella asiatica**

**Family: Apiaceae**

*Centella asiatica* is a profusely branched prostrate herb consisting of active principles such as vallarine, asiaticoside, sitosterol, tannin, oxyasiaticoside (Brinkhaus et al., 2000). Asiaticoside stimulates the healing of chronic lesions such as ulcers, surgical wounds, fistula and gynecological and bladder lesions (Maquart and Francois, 1990). It is also used for treatment of psoriasis and found to be effective in destroying cultured cancer cells (Maquart and Francois, 1990). *Centella asiatica* protects from cancer by enhancing immune functions of the body (Punturee et al., 2007). The extract of the whole plant has shown strong anticancer activity (Yu et al., 2006). In Brazil, *Centella asiatica* is used to treat the uterine cancer (Yoshida et al., 2005).

4. **Curcuma longa**

**Family: Zingiberaceae**

*Curcuma longa* extract exhibits antioxidant properties and contains a yellow-orange polyphenol (Srivastava et al., 1995). The strong anti-oxidant and anti-inflammatory characteristics are its most obvious medicinal properties (Mukophadhyay et al., 1982). The major constituents of the extracts are curcumin sulphate and glucuronide. It causes apoptosis in various cancer cell types including skin, colon, fore-stomach, duodenum and ovary (Lee et al., 2002). The plant extract also possess anti-viral, anti-bacterial and anti-fungal activities (Babu et al., 2006). Curcumin, one of the most studied chemopreventive agent, is a natural compound extracted from *Curcuma longa* that allow suppression, retardation and invasion of carcinogenesis. Curcumin is also described as an anti-tumoral, anti-oxidant and anti-inflammatory agent capable of inducing apoptosis.
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in numerous cellular systems (Duvoix et al., 2005). Curcumin can interfere with the cell growth cycle of A549 cell and suppress cell growth (Zhang et al., 2004). It has been shown to inhibit the growth of cancer by preventing production of harmful eicosanoid such as PGE-2 (Srivastava et al., 1995). The anticancer effect of curcumin has been demonstrated in all the steps of cancer development, i.e., initiation, promotion and progression of cancer (Mahady et al., 2002). In addition to inhibition of the genesis of cancer curcumin promotes the regression of cancer (Duvoix et al., 2005). Curcumin suppresses mutagenic effect of various mutagens including cigarette smoke condensates, 7, 12-dimethylbenz (a) anthracene (DMBA) and benzoyprene. Curcumin is found to decrease levels of urinary mutagens (Polasa et al., 1992). It also possesses anti-inflammatory and antioxidant properties (Mukophadhyay et al., 1982). The protective effects of *Curcuma longa* and its derivatives are partially due to direct antioxidant effect (Selvan et al., 1995). Studies have revealed that *Curcuma longa* inhibits production of nitrosamine that enhances natural antioxidant functions of the body (Churchill et al., 2000). *Curcuma longa* increases levels of glutathione and other non-protein sulfhydryls (Biswas et al., 2005). It acts directly on several enzymes. Curcumin is used to treat squamous cell carcinoma of the skin and the ulcerating oral cancer. *Curcuma longa* also prevents malignant transformation of leukoplakia (Cheng et al., 2001).

5. *Heliotropium indicum*

Family: *Boraginaceae*

*Heliotropium indicum*, a widely used indigenous plant in Ayurvedic medicine. The whole plant is used as a medicine. The leaves are useful in fever, urticaria, ulcers, wounds, localized inflammation, gonorrhoea, ringworm, rheumatism and erysipelas (Srinivas et al., 2000 and Reddy et al., 2002). The major constituents of the extract of *Heliotropium indicum* are tannins and alkaloids (Singh et al., 2003). Indicine-N-oxide derived from *Heliotropium indicum* has been found to have an antitumor activity and has been used in clinical trials as a chemotherapeutic agent for leukemia and solid tumors (Rao and Mcbride, 1968). Extracts of *Heliotropium indicum* showed significant activity in several experimental tumor systems (Kugelman et al., 1976).

6. *Aloe vera*

Family: *Aloaceae*

The plant *Aloe vera* has been used in several ayurvedic medicine. *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 metastasis (Lissoni et al., 1998). Lectin from Aloe, when injected directly into tumors activated the immune system to attack the cancer (Akev et al., 2007). Killer T cells, white blood cells that bind to invading cells and destroy them, began to attack tumor cells injected with lectin. Extract of Aloe has been prove to activate macrophages (white blood cells which "swallow" antigens), causing the release of immune-activating (and anticancer) substances such as interferons, interleukins and Tumor necrosis factor. In addition, it was found to promote the growth of normal (non-cancerous) cells and halt the growth of tumors (Choi and Chung, 2003). In addition the extract lowered the level of serum cholesterol, inflammation and arthritis and protected the body from oxidative stress (Saada et al., 2003).

7. Rubia cordifolia

Family: Rubiaceae

Rubia cordifolia (Linn) is a common plant found in southern parts of India and is used in indigenous systems of medicine. The extract of this plant has been reported to possess a significant antioxidant activity as well as immunomodulating properties (Joharapurkar et al., 2003). The major chemical constituents of the extract are rubiadin, ruberythrinic acid, purpurin, alizarin, pseudopurpurin and munjistin etc. (Tripathi et al., 1997). The extract of this plant shows anti-cancer ativity against a spectrum of tumor models such as leukemia, ascitic carcinoma, large intestinal and lung tumors, melanoma etc. (Adwankar and Chitinis, 1982). The extract of this plant has been reported to contain a number of cyclic hexapeptides with potent anti tumor activity (Wakita et al., 2004 and Hideji et al., 1984). The methanol extract of the herb has 80% inhibitory rate against ascitic S180 murine tumor (Kinghorn et al., 1999). In vitro test showed that water extract of the herb has 100% inhibitory rate against human cervical carcinoma JTC-26 cell line (Premalatha and Govindarajan, 2005).

8. Withania somnifera

Family: Solanaceae

The plant Withania somnifera is known in India as Ashwagandha, also called Indian ginseng. Extract of this herb is nontoxic and have been considered as an adaptogen having nonspecific activity to normalize physiological function, working on the Hypothalamic Pituitary Adrenal
Plants to fight neoplastic diseases (HPA) axis and the neuroendocrine system (Thatte et al., 1999). The roots and berries of the plant are used in herbal medicine. In Ayurveda, the fresh roots are sometimes boiled in milk, prior to drying, in order to leach out undesirable constituents (Elsakka et al., 1990). The major chemical constituents are Anaferine alkaloid, Anahygrine, Beta-Sisterol, Chlorogenic acid (in leaf only), Cysteine (in fruit), Iron, Scopoletin, Somniferine, Somniferiene, Tropanol, Withanine, Withananine and Withanolides A-Y (Steroidal lactones) (Elsakka et al., 1990). Among withanolides, which possess immuno-modulatory activity, Withaferin A and Withanolide D found in Withania somnifera was reported to inhibit growth of cancer (Mathur et al., 2006). Studies have revealed that Withania somnifera enhances the therapeutic effect of radiotherapy. The principle constituents of its roots, withanolides have been believed to account for the multiple medicinal applications of ashwagandha (Dhar et al., 2006). These molecules are steroidal lactones with ergostane, which include withanone, withaferin, withanolides, withasomidienone, withanolide C and alkaloids about 0.2%. The extract of this plant inhibited benzo(a)pyrene-induced forestomach papillomagenesis, showing up to 60 and 92% inhibition in tumor incidence and multiplicity, respectively (Wattenberg et al., 1980). Similarly, Withania inhibited 7,12-dimethylbenzanthracene-induced skin papillomagenesis, showing up to 45 and 71% inhibition in tumor incidence and multiplicity (Padmavathi et al., 2005). Thus the root extract has a chemopreventive efficacy against forestomach and skin carcinogenesis.

9. Ocimum sanctum

Family: Lamiaceae

The plant Ocimum sanctum, is called Tulsi in India is considered sacred by the Hindus. It is a tropical, much branched, annual herb. In several ancient systems of medicine including Ayurveda, Greek, Roman, Siddha and Unani, Ocimum has vast number of therapeutic applications such as in cardiopathy, haemopathy, leucoderma, asthma, bronchitis, catarrhal fever, otalgia, hepatopathy, lumbago, hiccups, ophthalmia, gastropathy, genitourinary disorders, ringworm, verminosis, skin diseases, etc. A variety of biologically active compounds have been isolated from the leaves of this plant and these include ursolic acid, apigenin, luteolin, ocimumosides A and B and ocimarin, apigenin, apigenin-7-O-β-D-glucopyranoside, apigenin-7-O-β-D-glucuronic acid, apigenin-7-O-β-D-glucuronic acid 6′-methyl ester, luteolin-7-O-β-D-glucuronic acid 6′-methyl ester, luteolin-7-O-β-D-glucopyranoside, luteolin-5-O-β-D-glucopyranoside, and 4-allyl-1-O-β-D-glucopyronosyl-2-hydroxybenzene, and two known cerebrosides (Gupta et al., 2007). Ocimum sanctum extract was found to be active against multidrug-resistant strains of Staphylococcus
aureus that were also resistant to common beta lactam antibiotics (Barghava and Singh, 1981). Moreover Tulsi juice of fresh leaves has antibacterial, anti-diabetic, antifungal, antitubercular, anti-stress, hypotensive, anti-asthmatic and anti-inflammatory properties (Barghava and Singh, 1981) Anticancer and chemopreventive properties of Ocimum have been reported (Karthikeyan et al., 1999). Topical application of Ocimum extract significantly reduced the cumulative number of papillomas in 7,12-dimethylbenz(a)anthracene-induced skin papillomagenesis in rats (Prashar et al., 1994). A significant 2-fold elevation of reduced glutathione content and increased glutathione S-transferase activity was also observed in the skin of extract treated animals. Rat hepatocytes pretreated with the extract and then with DMBA showed significant reduction in DMBA-DNA adducts (Prashar et al., 1998). Pretreatment with 500 micrograms of the extract caused a 93% reduction in the mean values of DMBA-DNA adducts (Prashar et al., 1998). Similar effects were also noted with DMBA-induced hamster buccal pouch carcinogenesis (Karthikeyan, et al., 1999). The extract have been reported to shown increased activities of cytochrome p450, cytochrome b5, aryl hydrocarbon hydroxylase and glutathione S-transferase, all of which are important in the detoxification of carcinogens and mutagens (Prashar et al., 1994). Beneficial effects of the extract of this plant have also been reported in radiotherapy of human cancer (Ganasoundari et al., 1998).

10. Plumbago zeylanica

**Family: Plumbaginaceae**

The plant species Plumbago zeylanica (known in India as Chitraka), of the Plumbaginaceae family, is distributed as a weed in throughout the tropical and subtropical countries of the world. The family Plumbaginaceae consists of 10 genera and 280 species. The genus Plumbago includes 3 species, namely Plumbago indica L. (P. rosea L.) P. capensis L., and P. zeylanica L., which are distributed in several parts of India. The root of Plumbago zeylanica (Chitraka or Chitramulamu) has numerous therapeutic uses. In Indian system of medicine, Ayurveda the root of the plant is known to be abortifacient and having vesicant property. It is used as an appetizer and is diuretic. It is used for treating diarrhea, dysentery, piles and peptic ulcers. The bioassay-guided fractionation of the dichloromethane extract of aerial parts of Plumbago zeylanica led to the isolation of β-sitosterol, β-sitosteryl-3β-glucopyranoside, β-sitosteryl-3β-glucopyranoside-6′-O-palmitate, lupenone, lupeol acetate, plumbagin and trilinolein (Nguyena et al., 2004). Plumbagin modulates cellular proliferation, carcinogenesis, and radioresistance, all known to be regulated by the activation of the transcription factor NF-κB, suggesting plumbagin might affect the NF-κB activation pathway (Santosh et al., 2006). Thus plumbagin inhibited NF-κB activation induced by TNF, and other carcinogens and
inflammatory stimuli (e.g. phorbol 12-myristate 13-acetate, H₂O₂, cigarette smoke condensate, interleukin-1β, lipopolysaccharide, and okadaic acid). Plumbagin also suppressed the constitutive NF-κB activation in certain tumor cells (Santosh et al., 2006). The suppression of NF-κB activation correlated with sequential inhibition of the tumor necrosis factor (TNF)-induced activation of IκB α kinase, IκB α phosphorylation, IκB α degradation, p65 phosphorylation, p65 nuclear translocation, and the NF-κB-dependent reporter gene expression activated by TNF, TNFR1, TRAF2, NIK, IKK-β, and the p65 subunit of NF-κB (Chen et al., 2007). Plumbagin also suppressed the direct binding of nuclear p65 and recombinant p65 to the DNA, and this binding was reversed by dithiothreitol (Santosh et al., 2006). Plumbagin down-regulated the expression and activity of NF-κB-regulated expressions of anti-apoptotic genes (IAP1, IAP2, Bcl-2, Bcl-xL, cFLIP, Bfl-1/A1, and survivin), proliferative (cyclin D1 and COX-2), and angiogenic (matrix metalloproteinase-9 and vascular endothelial growth factor) gene products (Hsu et al., 2006). This led to potentiation of apoptosis induced by TNF and paclitaxel and inhibited cell invasion (Hsu et al., 2006).

11. Semecarpus anacardium

Family: Anacardiaceae

Semecarpus anacardium is a common tree of dry deciduous forests, easily recognized by large leaves and the red blaze exuding resin which blackens on exposure (Kirthikar and Basu, 1975). It is known as Bhallatak in India. The nuts of S. anacardium showed the presence of biflavonoids, phenolic compounds, bhilawanols, minerals, vitamins and amino acids. In addition to these, anacardic acid, cardol, catechol, anacardol and fixed oil were also found to be present in this plant (Premalatha and Sachdanandam, 1999). The fruits of the plant were reported to possess good anti-inflammatory agent and effective in various types of cancers (Chitinis et al., 1980). The nut extract of S. anacardium was found to reduce the extracellular matrix (ECM) which normally present at an elevated level in the early stage of invasion and was also responsible for the development of vascular bed, endothelial cell proliferation and invasion of tumour cells (Mathivadhani et al., 2007). The nut extract also caused the turnover restoration of the factors associated with matrix and expression of MMP-1, MMP-2, MMP-3, TIMP-1 and TIMP-2 near to normal values (Mathivadhani et al., 2007). The stabilization of the ECM with the decreased activity of proteases might inhibit the epithelial–endothelial interaction and tumour cell migration thus, preventing the adjacent invasion and tumour growth resulting in antineoplastic activity (Mathivadhani et al., 2007). In addition to the anti cancer activity, plant extract of S. anacardium also possess immunomodulatory and anti-inflammatory properties (Ramprasath et al., 2006).
12. Glycyrrhiza glabra

Family: Fabaceae

Glycyrrhiza glabra, otherwise known as Licorice been used in food and medicinal remedies for thousands of years (Naik et al., 2003). The major chemical constituents of the extract of this plant are glycyrrhizin, glabridin, glycyrrhetic acid, gycyrrhetinic acid and glycyrrhizic acid (Yamamura et al., 1992 and Obolentseva et al., 1999). Glycyrrhizin, one of the major component found in licorice has been reported to prove to reduce inflammation (Akamatsu et al., 1991). Glycyrrhizin and other licorice components appear to possess anticarcinogenic properties as well (Jung et al., 2001). The extract of the plant and glycyrrhizic acid possessed radioprotecting property (Shetty et al., 2002 and Gandhi et al., 2004). Although the exact mechanisms are still under investigation, research has demonstrated that they inhibit abnormal cell proliferation, as well as tumor formation and growth in breast (Shiota et al., 1999), liver and skin cancer (Nishino et al., 1984, Liu W et al., 1998). In traditional American herbalism it is used in the anti cancer formula. Licochalcone (LA) is a novel estrogenic flavanoid isolated from PC-SPES composition herb licorice root that was reported to show significant antitumor activity in various malignant human cell lines. LA induced modest level of apoptosis but had more pronounced effect on cell cycle progression, arresting cells in G2/M, accompanied by suppression of Cyclin B1 and cdc2. It also inhibited phosphorylation of Rb, specifically phosphorylation of S780 with no change of phosphorylation status of T821, decreased expression of transcription factor E2F concurrent with reduction of Cyclin D1, down-regulation of CDKs 4 and 6, but increased Cyclin E expression (Fu et al., 2004).

13. Piper longum

Family: Piperaceae

Piper longum sometimes called Indian Long Pepper, is a flowering vine cultivated for its fruit, which is usually dried and used as a spice and seasoning. The major chemical constituents of the dried fruits are piperine, piperalonguminine, sylvatine, guineensine, piperalongumine, filfiline, sitosterol, methyl piperate and a series of piperine-analog retrofractamides (Nakatani et al., 1986). The extract of Piper longum was found to inhibit significantly (50.6%) the number of tumor-directed capillaries induced by injecting B16F-10 melanoma cells. Administration of the methanolic extract of the plant was found to differentially regulate the level of proinflammatory cytokines like IL-1β, IL-6, TNF-α, GM-and CSF which were found to be at
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an elevated levels during the development of cancer (Sunila and Kuttan, 2006). The level of IL-2 and tissue inhibitor of metalloprotease-1 (TIMP-1) was increased significantly when the angiogenesis-induced animals were treated with the extract of *P. longum*. Moreover, *P. longum* was also able to inhibit the VEGF-induced proliferation, cell migration and capillary-like tube formation of primary cultured human endothelial cells (Sunila and Kuttan, 2006).

14. **Tinospora cordifolia**

**Family: Menispermaceae**

*Tinospora cordifolia* (Guduci) is one of the most versatile rejuvenative herbs and is called in Sanskrit by the name *Guduci* meaning the one which protects the body (Singh *et al.*, 2003). It is also called as *amrta* or nectar, as it is extremely useful in strengthening the immune system of the body and keeping the functions of its various organs in harmony (Desai *et al.*, 2002). The extract of the plant contain several bitter principles, glucoside and alkaloids, a glycoside – giloin and a non-glucoside – gilenin, gilosterol, alkakoid tinosporin, tinosporic acid, tinosporol and berberine, tinosporidine and sitosterol isolated from stem, cordifol, heptacosanol and octacosonal and a new furanoid diterpene – tinosporide (Singh *et al.*, 2003). Administration of the polysaccharide fraction from *Tinospora cordifolia* was found to be very effective in reducing the metastatic potential of B16F-10 melanoma cells (Leyon and Kuttan, 2004). Antiangiogenic activity was studied using B16F10 melanoma cell-induced capillary formation in animals (Leyon and Kuttan, 2004). *Tinospora cordifolia* is reported to have immunostimulatory properties (Mathew and Kuttan, 1999). It is considered as general tonic in Ayurveda. The positive effect of *Tinospora cordifolia* on leucocytes suggests its use as an adjuvant in cancer therapy (Leyon and Kuttan, 2004). Activation of macrophage by *Tinospora cordifolia* leads to increased in colony forming units, leading to leucocytosis and improvement in neutrophil function. It was found that the herbal mixture containing this plant was effective in treatment of advanced malignancies. In addition it helped in diseases like raktapitta, anaemia, cardiac debility, diabetes, sexual debility and splenic disorders, due to vitiation of pitta (Singh *et al.*, 2003).

15. **Podophyllum hexandrum**

**Family: Berberidaceae**

The perennial herb *Podophyllum hexandrum* (syn. *Podophyllum emodi*), bearing the common names Himalayan may apple or Indian may apple, is
native to the lower elevations in and surrounding the Himalaya (Polunin and Stainton, 1984). The whole plant, especially the root, is cholagogue, cytostatic and purgative (Uphof, 1959). The plant contains podophyllin, which has an antimiotic effect, it interferes with cell division and can thus prevent the growth of cells (Chattopadhyay et al., 2004). It is, therefore, a possible drug for the treatment of cancer, especially in the treatment of ovarian cancer (Kumar et al., 2003). The roots of this plant also contain several important anti-cancer lignans, including podophyllin and berberine (Duke and Ayensu, 1985). The rhizome of the plant contains a resin, known generally and commercially as Indian Podophyllum Resin, which also can be processed to extract podophyllotoxin, or podophyllin. Podophyllotoxin is the most active cytotoxic natural product from this plant. It has been used as starting material for the synthesis of the anticancer drug etoposide and teniposide. Podophyllotoxin acts as an inhibitor of microtubule assembly (Giri and Narasu, 2000). These drugs have been used to treat lung cancer, testicular cancer, neuroblastoma, hepatoma and other tumors. (Giri and Narasu, 2000).

16. Phyllanthus niruri

Family: Euphorbiaceae

Phyllanthus niruri is a herb commonly known as stonebreaker. (Nishiura et al., 2004). Phyllanthus niruri has a long history in herbal medicine systems worldwide. The active compounds isolated from this plant are phyllanthin, hypophyllanthin, lignansniranthin, nirtetralin, quercetin and phyltetralin (Amir et al., 2003). The whole plant and its aerial parts have been used for many traditional remedies, mostly biliary and urinary (Naik and Juvekar, 2003). Some examples are kidney and gallbladder stones, hepatitis, colds, flu, tuberculosis, and other viral infections (Chopra et al., 1986). It has also been proven effective in liver diseases like jaundice and liver cancer (Chatterjee and Sil, 2006). The extract of the plant has been used for bacterial infections such as cystitis, prostatitis, venereal diseases, and urinary tract infections (Nishiura et al., 2006). It also assisted in reducing anemia symptoms, diabetes and hypertension (Nwanjo, 2007), and showed diuretic, analgesic, stomachic, antispasmodic, febrifugal, and cell protective properties (Unander et al., 1995). The plant extract was found to decrease the amount of hepatitis B virus found in the blood stream (Venkateswaran et al., 1987). The plant extract have been reported to block DNA polymerase, the enzyme needed for the hepatitis B virus to reproduce (Rajeshkumar et al., 2002).
17. *Terminalia arjuna*

**Family: Combretaceae**

The genus *Terminalia* consists of large wooded trees and occurs in almost every part of India. Every part of the plant has useful medicinal properties (Bone K, 1996). *Terminalia arjuna* holds a reputed position in both Ayurvedic and Yunani Systems of Medicine. According to Ayurveda it is alexiteric, styptic, tonic, anthelmintic, and useful in fractures, ulcers, heart diseases, biliousness, urinary discharges, asthma, tumours, leucoderma, anaemia, excessive perspiration etc. The extract of the plant has been used as expectorant, aphrodisiac, tonic and diuretic (Kapoor, 1990). The major chemical constituents are glucoside – arjunetin, flavones – arjunoone, cerasidin, sitosterol, friedlin, methyl oleanolate, gallic, ellagic and arjunic acids-arjnetosides I, arjnetosides II, arjnetosides III and arjnetosides IV. Apart from this, Tannins and triterpenes have been found in the extract and were reported to show antigenotoxic or antimutagenic effects (Scassellati-Sforzolini *et al.*, 1999). It was also found out that the flavone Luteolin isolated from *T. arjuna* has a well established record of inhibiting various cancer cell lines. (Pettit *et al.*, 1996). The chemical Casuarinin isolated from the Bark of *Terminalia arjuna* inhibited breast cancer cell growth (Kuo *et al.*, 2005). Moreover this could induce apoptosis and cell cycle arrest in human breast adenocarcinoma MCF-7 Cells (Kuo *et al.*, 2005).

18. *Alstonia scholaris*

**Family: Apocynaceae**

The plant *Alstonia scholaris* has been used in different system of traditional medicine for the treatment of diseases. The extract of the plant showed pharmacological activities ranging from antimalarial to anticancer properties (Gandhi and Vinayak, 1990). Almost all parts of the plant contained active principles and has been reported to contain various alkaloids, flavanoids and phenolic acid (Jagetia and Baliga, 2006). The major chemical components are Alstonine, Echitamine chloride, Villastonine and three alkaloids Ditamine, Echitamine or Ditaine, and Echitenines. In addition to these compound, several fatty and resinous substances were also present in the extract (Dung *et al.*, 2001). Echitamine chloride showed anticancer activity in S-180, regression of tumor growth and fibro sarcoma (Kamarajan *et al.*, 1991). Villastonine has antiamoebic activity and *in vitro* anticancer activity against human lung cancer cell lines MOR-P (adeno carcinoma) and COR-L23 (larger carcinoma) (Keawpradub *et al.*, 1997). The extract of this
plant also possessed antimutagenic and immuno modulating properties (Lim-Sylianco et al., 1990).

19. Asparagus racemosus

**Family: Liliaceae**

Asparagus racemosus has been used in traditional ayurvedic medicine, which is rich in phytoestrogens, a group of naturally occurring compounds that have a chemical structure very similar to estrogen. These phytoestrogens are estimated 100-500 times less potent in their estrogen effect than human estrogen. These were found to maintain a hormonal balance by acting as anti-estrogen when the body's natural levels of the hormone was high and they acted as human estrogen when levels are low (Bopana and Saxena, 2007). Cancer cells also use estrogen to promote their growth (Herman et al., 1995). Asparagus therapy has been used to treat various forms of cancer and reversal of the disease has been reported in a number of cases (Diwanay et al., 2004). Asparagus contained more glutathione than any other food ever tested by the National Cancer Institute (Demirkol et al., 2004). It also contained high levels of Vitamins A and C, folic acid, iron, potassium and calcium. In addition, extract of Asparagus contained a protein called histone which can be believed to be active in controlling cell growth (Davies et al., 1996).

20. Catharanthus roseus

**Family: Apocynaceae**

Catharanthus roseus (Periwinkle) has been in use from ancient times for the treatment of blood pressure, diabetes mellitus, etc. in Indian system of medicine as well as in folk-lore medicinal practice (Gilman et al., 1985; Bhattacharya, 1988). The extract of this plant has been found to contain alkaloids having anti mitotic and anti microtubule activities. The vinca alkaloids include vinblastine, vincristine, vindesine and vinorelbine. They are dimeric compounds in which indole and dihydro indole nuclei are joined with other complex ring systems (Pearce 1990). They are used in acute leukemia, Hodgkin’s disease, non Hodgkin’s lymphoma, rhabdomyosarcoma, neuroblastoma, Swing’s sarcoma and Wilms tumour (Johnson et al., 1963; Johnson, 1968). Vincristine has been used to treat many solid tumours like breast, colon, cervical and neck and head cancers in combination with other drugs. A new vinca alkaloid derivative, S12363 (vinfosiltine), is 36 and 72 times more cytotoxic *in vitro* than vincristine.
and vinblastine, respectively (Adenis et al., 1995). Vinca alkaloids are involved in disruption of microtubules, inhibition of protein and nucleic acid synthesis, elevation of oxidized glutathione, alteration of lipid metabolism and membrane lipid content, elevation of cAMP and inhibition of calcium- calmodulin regulated cAMP phosphodiesterase (Wilson, 1975; Tucker et al., 1977). Vinblastine and vincristine, interfere with the dynamics of microtubules and have shown significant cell killing activity in a variety of tumor cells through induction of apoptosis (Huang et al., 2004). Vinca alkaloid induced apoptosis via a pathway independent of cell cycle arrest. Vincristine and analogues are still crucial in the treatment of hematological malignancies and few solid tumour like lung and colon tumours.

21. *Taxus brevifolia*

**Family: Taxaceae**

*Taxus brevifolia* (Pacific yew) is a medium sized evergreen conifer. Infusions, decoctions, and poultices of leaves and bark of the tree are used for treating lung problem, stomach ache, wounds and pain (Moerman, 1986). The extract of the plant contains paclitaxel, commonly known by the name taxol, a potent anticancer drug used to treat ovarian, breast, lung cancers and Kaposi’s sarcoma (Luck and Roche 2002; Ghamande et al., 2003; Sunwoo et al., 2001). Its structure was elucidated by Wani and Wall in 1971. The initial biological activity of this compound was related to the microtubule destabilizing properties of vinca-alkaloids. Studies have revealed a unique complimentary effect of its binding to polymerized tubulin, stabilizing it against disassembly and consequently inhibiting mitosis (Schiff et al., 1979, 1980). The remarkable stability of microtubules induced by paclitaxel is damaging to cells because of the perturbation in the dynamics of various microtubule dependent cytoplasmic structures that are required for cellular functions such as mitosis, maintenance of cellular morphology, shape changes, neurite formation, locomotion and secretion (Masurovsky et al., 1983; Thuret-Carahan et al., 1985). Paclitaxel also inhibits cells in G2 and M phase at lower concentrations and inhibits cells in interphase at higher concentrations (Fan, 1999).

**Epilogue**

Man has been dependent on the flora and fauna around him for his food and medicine from time immemorial. Modern medicine and sophisticated therapeutic
strategies, though effective in controlling and management of most of the diseases that plague humanity, do not reach all sections of human populations in all corners of the world due to the problems of affordability and as a consequence, large number of human populations still depend up on plant based traditional alternative systems of medicine to combat debilitating diseases. Several of the modern drugs have their origin from plants. Many compounds isolated from herbal extracts as such or with chemical modifications are used to treat various diseases in modern medicine because of their potent biological activities. Due to the awareness about the side effects and toxicity of the synthetic drugs used in modern medicine, there is an increasing interest in herbal drugs or traditional medicine in recent times, apart from the economic aspects. However rigorous safety and quality evaluation and comparative clinical studies using modern techniques are essential to validate the efficacy of several of the herbal traditional drugs. In case of herbal drugs proper standardization of the methods of production of raw materials, good agricultural practice, collection of plant material, good post harvest handling, good manufacturing practices, etc. have to be followed. Isolation and purification of biologically active components from the bulk extract and their use as in the case of modern medicine may not be practicable in traditional system of medicine as the yield of the ingredients in the extract could be very low or negligible. Also some compounds in the whole extract or preparation may have synergistic activity. Thus the wholesome use of herbal or traditional medicine may be more effective and advisable than the use of individual isolated purified components. To understand the basic mechanisms of the drug action, purified components may be essential. Plant kingdom with its enormous diversity is a store house of large number of compounds with potent therapeutic activities. In treatment of neoplastic diseases, use of herbal extracts are of particular relevance because of their cytotoxic, cytoprotective and chemopreventive activities. Herbal drugs with their long history are the only answer to provide an integrated health care for the suffering populations of humanity, particularly in the developing world, at affordable cost.

References

Plants to fight neoplastic diseases


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