

Review

Review on cancer and anticancerous properties of some medicinal plants

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Cancer is a dreadful disease and any practical solution in combating this disease is of paramount importance to public health. Therefore, besides the rationalized allopathic drugs, it is worth evaluating the folk medicine-a plant based therapy which is not a systematized study. Keeping the fact, an attempt has been made to review the work being carried out all over the world about the cancer, its causes and plants as anticancerous agents. 11 different plant sources have been listed in the present review along with the phytoconstituents present in these plants.

Key words: Cancer, anticancer properties, medicinal plants, review.

INTRODUCTION

Cancer

Cancer is a dreadful disease and any practical solution in combating this disease is of paramount importance to public health. Therefore, besides the rationalized allopathic drugs, it is worth evaluating the folk medicine-a plant based therapy which is not a systematized study. An alternative solution to allopathic medicine embodied with severe side effects, is the use of folk medicine plant preparations to arrest the insidious nature of the disease. Many herbs have been evaluated in clinical studies and are currently being investigated phytochemically to understand their anti-tumour actions against various cancers. Thus, cancer patients who already got crippled with this disease, who are further burdened by drug-induced toxic side effects, have now turned to seek help

from the complementary and alternative medicine hoping for a better cure (Rao, 2008). Cancer is a class of diseases characterized by out-of-control cell growth. There are over 100 different types of cancer, and each is classified by the type of cell that is initially affected.

Cancer harms the body when damaged cells divide uncontrollably to form lumps or masses of tissue called tumors (except in the case of leukemia where cancer prohibits normal blood function by abnormal cell division in the blood stream). Tumors can grow and interfere with the digestive, nervous, and circulatory systems and they can release hormones that alter body function. Tumors that stay in one spot and demonstrate limited growth are generally considered to be benign. More dangerous, or malignant, tumors form when two things occur.

A cancerous cell manages to move throughout the body using the blood or lymph systems, destroying healthy tissue in a process called invasion that cell manages to divide and grow, making new blood vessels to feed itself in a process called angiogenesis.

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When a tumor successfully spreads to other parts of the body and grows, invading and destroying other healthy tissues, it is said to have metastasized. This process itself is called metastasis, and the result is a serious condition that is very difficult to treat. Cancer is ultimately the result of cells that uncontrollably grow and do not die. Normal cells in the body follow an orderly path of growth, division, and death. Programmed cell death is called apoptosis, and when this process breaks down, cancer begins to form. Unlike regular cells, cancer cells do not experience programmatic death and instead continue to grow and divide. This leads to a mass of abnormal cells that grows out of control.

Signal transduction pathways in cancer cells

Cancer originates in the genetic material of the tumor cell. Alterations that occur in the genetic material deregulate the cellular functions and lead to uncontrolled proliferation and alterations in the cell morphology. To find effective therapeutic interventions for cancer we need to understand the events that take place during cell transformation (Tsatsanis, 2000). The first step will be the identification of the genes that are altered in the tumor cell. Such genes are defined as oncogenes, and are usually either over expressed or mutated in a way that they cannot be regulated as they used to leading to the oncogenic phenotype. A second category are the onco-suppressor genes, genes that normally function as brakes in the cell cycle or repair damaged DNA and when their function is lost the cell loses control of its division rate or acquires mutations that lead to faster proliferation (Fearon, 1997; Hanahan and Weinberg, 2000). Following the identification of these genes we need to elucidate the role of the proteins encoded by these genes in the cellular environment. In other words we need to understand the function of these proteins in the normal cell and in the tumor cell. By understanding the mechanism through which these proteins induce the tumor we can interfere with therapeutic agents that will be able either to specifically inhibit the function of these genes and therefore eliminate these cells or perturb their proliferation and lead them to extinction (Denhardt, 1996). Oncogenic proteins participate in signal transduction pathways that play central role in the transmission of a signal from the extracellular environment, through the cell membrane, into the cytoplasm and to the nucleus where transcription is initiated to generate proteins that will eventually contribute to the oncogenic phenotype. The function of these proteins is vital for cell and tissue homeostasis and they control processes such as cell division, differentiation and apoptosis. All these molecules are potential targets for anti cancer drug design since inhibition or activation of their function will lead to elimination of the tumor cells.

Growth factors and transmembrane receptors

Growth factors normally play a role in controlling the proliferation and metabolic activation of certain cells. They act by binding on specific receptors of the cell membrane, which, in turn, transmit the signal into the cytoplasm. They are frequently found over expressed in a variety of tumors. The result is that the respective receptors are stimulated at a higher rate and, therefore, the signal that is transmitted is constant. Often tumors are found to secrete growth factors such as epidermal growth factor (EGF), colony stimulating growth factor 1 (CSF1), insulin growth factor I (IGF-I) and platelet-derived growth factor (PDGF) (Kolibaba and Druker, 1997). These factors bind to their receptors and initiate growth and proliferative signals. This mechanism establishes an autocrine loop that leads to tumor growth.

Cytoplasmic molecules

The signal initiated by the growth factors at the cell surface is then transmitted into the cytoplasm and transduced by a cascade of events that includes phosphorylation, farnesylation, ubiquitination and other changes that alter molecules in order to promote or inhibit their activity or interaction with other molecules. Kinases and phosphatases play an important role in the transduction of oncogenic signals. The MAPKinase and the PI3Kinase cascades play a central role during cell activation and proliferation. Several oncogenes are known to act on these pathways and several molecules that participate on these cascades when deregulated they become oncogenic. Ras, a well- studied family of oncogenes, structurally altered in about 25% of all human tumors, functions on activating the Mitogen-activated protein kinase (MAPK) cascade (Spandidos and Anderson, 1990; Kinzler and Vogelstein, 1996; Zachos and Spandidos, 1997). Raf1, a serine threonine kinase that is activated by Ras, is also activated in some myeloid leukemias (Okuda et al., 1994; Schmidt et al., 1994). Serine threonine kinases are another important group of oncogenes. This family of oncogenes includes the Akt family (Akt1, Akt2, Akt3). Akt2 was activated in pancreatic adenocarcinomas, small cell lung cancer, and ovarian cancers (Cheng et al., 1992; Bellacosa et al., 1995; Ruggeri et al., 1998). Akt3 has also been found activated in estrogen receptor deficient breast cancers and androgen independent prostate cancers (Nakatani et al., 1999). The Tpl-2/Cot oncogene is activated in breast (Sourvinos et al., 1999), thyroid and colon tumors (Ohara et al., 1995).

Apoptosis

Apoptosis, a physiological process for killing cells, is

critical for the normal development and function of multicellular organisms. Abnormalities in cell death control can contribute to a variety of diseases, including cancer, autoimmunity, and degenerative disorders (Strasser, 2000). Signaling for apoptosis occurs through multiple independent pathways which include the caspase cascade and the stress-activated protein kinase pathways. The caspase cascade is activated by two distinct routes: one from cell surface and the other from mitochondria. Activation of the route from cell surface requires the cellular components that include membrane receptors, adaptor proteins such as TNFR-associated death domain (TRADD) and Fas-associated death domain (FADD), and caspase-8, while activation of the other from mitochondria requires Apaf-1, caspase-9, and cytosolic cytochrome c, that are initiated either from triggering events within the cell or from outside the cell, for instance, by ligation of death receptors. All apoptosis signaling pathways converge on a common machinery of cell destruction that is activated by a family of cysteine proteases (caspases) that cleave proteins at aspartate residues. Dismantling and removal of doomed cells is accomplished by proteolysis of vital cellular constituents, DNA degradation, and phagocytosis by neighboring cells (Cho, 2002).

Two signaling pathways to activate the caspase cascade

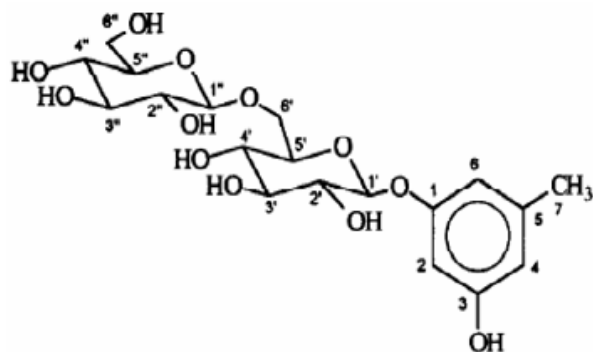
The most-studied and best-understood signaling pathway in apoptosis is the caspase cascade. One route to activate the caspase cascade is the activation that is initiated from the cell surface by apoptotic stimuli (Kaufmann and Hengartner, 2001). For instance, TNF and Fas-L have been shown to induce the caspase cascade by binding and activating their membrane receptors, TNF receptor-1 (TNFR1), and Fas, respectively. These receptors belong to the TNF receptor (TNFR) family in which other related receptors, such as TNFR, Fas/Apo-1/CD95, DR3, DR4, the p75 nerve growth factor receptor, and CD40, are also included (Ashkenazi and Dixit, 1999). Many of the TNFR family members contain the death domain in the cytoplasmic side. Binding of TNF or Fas-L to its specific receptor is shown to induce the formation of the homotrimeric complex of ligand-bound receptors. This structural change appears to enhance the interaction between the death domains of the receptors and the cytoplasmic death domain-containing proteins. For example, TNFR1 associates with the protein TRADD through the death domain-death domain interaction in the cytoplasmic side. Similarly, Fas associates with the protein FADD through the death domain-death domain interaction. FADD has another important domain, the death effector domain (DED). Fas-bound FADD can physically associate with caspase-8, which also contains DED, through the

DED-DED interaction. The interaction of caspase-8, an initiator caspase, with FADD results in the activation of caspase-8, thereby leading to the activation of the downstream caspases, including caspase-3. Besides the FADD-caspase-8 activation, Fas can also interact with Daxx (Yang et al., 1997). The activated Daxx, in turn, associates with and activates the apoptosis signal-regulating kinase 1 (ASK1) that functions as a MAPKKK in the c-Jun N-terminal kinase/stress-activated protein kinase (JNK/SAPK) and p38 MAPK signaling pathways. Thus, Fas induces the JNK and p38 MAPK signaling pathways through Daxx (Chang et al., 1998). The persistent activation of the JNK and p38 MAPK signaling pathways is thought to cause apoptotic cell death. In the TNF signaling, TNFR1-bound TRADD interacts with FADD, which subsequently activates caspase-8 in a manner that is similar to the Fas-FADD-caspase-8 signaling (Baker and Reddy, 1998). The TNFR1-TRADD complex can also interact with TRAF2 (TNFR-associated factor 2), and the resulting TNFR1-TRADD-TRAF2 complex can induce the activation of the NF- κ B signaling, as well as the JNK/SAPK signaling.

Mitochondria are another site for apoptotic stimuli to initiate intracellular signaling that mediates caspase activation. Xiaodong Wang and his colleagues first showed that a protein complex that is obtained from the S-100 cytosolic fractions of HeLa cells could activate caspase-3 *in vitro*. The protein complex was composed of three distinct polypeptides, which were named Apaf-1, Apaf-2, and Apaf-3, respectively (Liu et al., 1996; Li et al., 1997; Zou et al., 1997). Apaf-1 is a novel protein and it turned out to be a mammalian counterpart of ced-4 in *C. elegans*. Apaf-2 was identified to be cytochrome c. These findings first suggested that mitochondria play a central role in the mechanism of apoptosis, and that cytochrome c is released from the intermembrane space of the mitochondria into the cytoplasm in response to apoptotic stimuli. Apaf-3 was identified to be caspase-9, and this observation suggests that caspase-9 functions as an initiator caspase that activates the downstream effector caspases, such as caspase-3.

The stress-activated protein kinase signaling pathway

MAPK signaling pathways mediate intracellular signaling, which is initiated by a variety of extracellular stimuli. This leads to diverse cellular activities, which include cell proliferation, differentiation, and apoptosis (Chang and Karin, 2001). The MAPK signaling pathways include three components: MAP kinase kinase kinases (MAP3Ks), MAP kinase kinases (MAP2Ks), and MAPKs. An activated MAP3K phosphorylates and stimulates MAP2K, which in turn stimulates MAPK through phosphorylation. The mammalian MAPK family includes three subgroups: extracellular signal-regulated kinases



Anacardoside (1)

Figure 1. Anacardoside.

(ERKs), c-Jun N-terminal kinases/stress-activated protein kinases (JNKs/SAPKs), and p38 MAPK. The ERK signaling pathway is often involved in the signal transduction in cell proliferation and differentiation. The JNK/SAPK signaling pathway can be stimulated by a variety of stresses. These include genotoxic stress, heat shock, osmotic shock, and metabolic stress, as well as proinflammatory cytokines, such as TNF and interleukin 1-beta. This signaling pathway may be involved in diverse cellular activities that include cell growth, differentiation, and cell death. The persistent activation of the JNK/SAPK pathway often mediates intracellular signaling that leads to cell death. The p38 MAPK signaling pathway is also stimulated by cellular stress and proinflammatory cytokines in a way that is similar to the JNK/SAPK signaling pathway. Cellular components in the JNK/SAPK signaling pathway include JNK/SAPK, its MAP2Ks such as SEK1/MKK4/JNKK1 and MKK7/JNKK2, and MAP3Ks (such as MEKK1, ASK1, and TAK1) (Davis, 2000). JNK/SAPK phosphorylates many substrate proteins, which includes transcription factors, such as c-Jun, ATF2, Elk1, DPC4, p53, and NFAT4.

Anticancerous properties of plants

Natural products of folk medicine have been used for centuries in every culture throughout the world. Scientists and medical professionals have shown increased interest in this field as they recognized the true health benefits of these remedies. While searching for food, the ancient found that some foods had specific properties of relieving or eliminating certain diseases and maintaining good health. It was the beginning of herbal medicine.

For thousands of years, cultures around the world have used herbs and plants to treat illness and maintain health. Many drugs prescribed today in modern medicinal system are derived from plants. Herbs and plants are valuable not only for their active ingredients but also for

their minerals, vitamins, volatile oils, glycosides, alkaloids, acids, alcohols, esters etc., Complementary and alternative medicine (CAM) can be defined as any treatment used in conjugation (complementary) or in place of (alternative) standard medical treatment. In alternative medicine, medicinal plant preparations have found widespread use particularly in the case of diseases not amenable to treatment by modern method (Majumdar, 2008).

Plants are the reservoirs of a large number of imperative organic compounds and they have long been used as the sources of medicines. Dependence on plants is prevalent in developing countries where the traditional herbal medicine plays a major role in health care and in the treatment of many infectious diseases. The rural population of a country is more disposed to traditional ways of treatment because of its easy availability and cheaper cost. Herbal therapies although, still an unwritten science is well established in some cultures and tradition and have become a way of treatment in almost 80% of the people in rural areas, especially those in Asia, Latin America and Africa. In this present review article an attempt has been made to compile the information on anticancer properties of five commonly available medicinal plants. The details of which have been mentioned below along with their uses and active principles.

Semecarpus anacardium Linn.

S. anacardium (SA) Linn (Family: Anacardiaceae) is distributed in sub-Himalayan region, tropical and central parts of India. The nut is commonly known as 'marking nut' and in the vernacular as 'Ballataka' or 'Bhilwa'. It has high priority and applicability in indigenous system of medicine emecarpus (chopra, 1982; Khare, 1982).

Active principles

Nut shell contain the biflavonoids: Biflavones A, C, A1, A2, tetrahydrorobustaflavone, B (tetrahydromentoflavone) (Gil, 1995), jeediflavone, (Nardkarni, 1976) semecarpufflavone and gullufflavone (Gedam, 1974). Oil from nuts, bhilavinol, contains a mixture of phenolic compounds mainly of 1, 2- dihydroxy-3 (pentadecadienyl-8, 11) benzene and 1, 2- dihydroxy-3 (pentadecadienyl-8', 11') - benzene (Rao, 1973) (Figure 1).

Anti-cancer activity

In traditional medicine, the nut is highly valued for the treatment of tumours and malignant growth. Studies have been also done in proving the anticancer and hepatoprotective activity of *S. anacardium* nut milk

extract against aflatoxin B1 (AFB1) induced hepatocarcinoma in rats and establishing its protective role on deranged cell membrane in AFB1 induced hepatocarcinoma. The biochemical basis of anticarcinogenic potency of *S. anacardium* nut was studied using hepatocellular carcinoma as cancer model in rats. Extensive analysis to study its effect against biochemical abnormalities during cancer shows that the drug modulates the abnormalities of all biochemical pathways including carbohydrate, lipid, cytochrome P-450 mediated microsomal drug metabolism, cancer markers and membrane proteins during cancer progression (Smith, 1995). Recent studies carried out on an Ayurveda marking nut preparation have also shown promising results in the treatment of cancers of the oesophagus, urinary bladder, liver and leukemia (Smith, 1995; Chakraborty, 2004). The dramatic reduction in alpha-fetoprotein level, a specific marker of hepatocellular carcinoma (Chakraborty, 2004; Arathi, 2003) and the histopathological studies had confirmed anticancer efficacy of the drug (Phatak, 1983).

***Trigonella foenum - graecum* Linn.**

T. foenum – graecum Linn. belonging to the family (Fabaceae) commonly known as Fenugreek is a aromatic, 30 - 60 cm tall, annual herb, cultivated throughout the country. 1, 2 a nearly smooth erect annual. Stipulets not toothed. Leaflets 2 - 2.5 cm long, oblanceolate-oblong, toothed. Flowers 1 - 2, axillary, sessile. Calyx-teeth linear. Corolla much exserted. Pod 5 - 7.5 cm long, with a long persistent beak, often falcate, 10 - 29 seeded, without transverse reticulations.

Active principles

The endosperm of the seed is rich in galactomannan; young seeds mainly contain carbohydrates and sugar. Mature seeds content amino acid, fatty acid, vitamins, and saponins. The seeds of fenugreek contain a large quantity of folic acid (84 mg/100 g). It also contents disogenin, gitogenin, neogitogenin, homorientin saponaretin, neogigogenin, and trigogenin (Rastogi and Mehrotra, 1990). The main chemical constituents of *T. foenum – graecum* are fibers, flavonoids, polysaccharides, saponins, flavonoids and polysaccharides fixed oils and some identified alkaloids viz., trigonelline and cholin.

Cyclophosphamide (CP) is a commonly used anti-cancer drug which causes toxicity by its reactive metabolites such as acrolein and phosphoramidate mustard. In the study modulation of toxicity caused by concomitant exposure to CP and L-buthionine-SR-sulfoximine (BSO) by fenugreek (*T. foenum-graecum* L.) Extract was evaluated by measuring lipid peroxidation

(LPO) and anti-oxidants in urinary bladder in mice. Fenugreek, a common dietary and medicinal herb, showed protective effect not only on LPO but also on the enzymatic anti-oxidants. CP-treated animals exhibited a significant decrease in the activities of glutathione S-transferase (GST), glutathione reductase (GR), glutathione peroxidase (GP) and catalase (CAT) when compared to the controls. Level of reduced glutathione (GSH) was also reduced with an increase in LPO in CP-treated animals. BSO treatment depicted an additive toxic effect in CP-treated animals. Pre-treatment of herbal extract restored activities of all the enzymes and thus showed an overall protective effect on additive effect of CP and BSO. Restoration of GSH by extract treatment may play an important role in reversing CP-induced apoptosis and free radical mediated LPO in urinary bladder (Bhatia, 2005).

Anticancer activity

Cancer is the second leading cause of death worldwide. Conventional therapies cause serious side effects and, at best, merely extend the patient's lifespan by a few years. Cancer control may therefore benefit from the potential that resides in alternative therapies. There is thus an increasing demand to utilize alternative concepts or approaches to the prevention of cancer. It showed potential protective effect of Fenugreek seeds against 7, 12-dimethylbenz (a) anthracene (DMBA)-induced breast cancer in rats at 200 mg/kg b.wt. Fenugreek seeds extract significantly inhibited the DMBA-induced mammary hyperplasia and decreased its incidence. Epidemiological studies also implicate apoptosis as a mechanism that might mediate the Fenugreek's antibreast cancer protective effects.

Apoptosis is a type of cell death, and agents with the ability to induce apoptosis in tumors have the potential to be used for antitumor therapy. Flavonoids produce several biological effects, and the apoptosis inducing activities of flavonoids have been identified in several previous studies. (Chen, 2003) Flavonoids and catechins were first shown to be apoptotic in human carcinoma cells. (Ahmad, 2000) Similar observation has since been extended to lung tumor cell lines (Yang, 1998) colon cancer cells, breast cancer cells, prostate cancer cells (Paschka, 1998) stomach cancer cells (Okabe, 1999) brain tumor cells, head and neck squamous carcinoma (Masuda, 2001) and cervical cancer cells (Ahn, 2003) quercetin, rutin, and other food flavonoids have been shown to inhibit carcinogenesis in animal models. They all induce apoptosis in tumor cells (Katdare, 2002; Upadhyay, 2001; Choj, 2001; Iwashita, 2000). It appears that these flavonoids can also differentially induce apoptosis in cancer cells, but not in their normal counterparts. The ultrastructure of mammary acini from protected rats showed dying cells with large numbers of

cytoplasmic vacuoles; some of these vacuoles appear autophagic. Recently, alternative cell death processes have been recognized in epithelial cells, including autophagy and para-apoptosis (Bursch, 2000 Leist, 2001 and Sperandio, 2000). These pathways can be activated in parallel with apoptosis, and significant crosstalk between apoptotic and alternative death pathways may exist (Lee, 2001). Thus, herbal induced autophagic or "type II" cell death may also contribute to the cell death and hence inhibiting the DMBA-induced tumor progression. The present study establishes that *T. foenum-graecum* has appreciable anti-cancer activity. flavonoids seem to be most likely candidates eliciting anti-tumorigenic effect.

***Withania somnifera* Dunal**

W. somnifera Dunal (ashwagandha, WS) is widely used in Ayurvedic medicine, the traditional medical system of India. *W. somnifera*, also known as Ashwagandha, Indian ginseng, Winter cherry, Ajagandha, Kanaje Hindi, Amukkuram in Malayalam and Samm Al Ferakh, is a plant in the *Solanaceae* or nightshade family. It grows as a stout shrub that reaches a height of 170 cm (5.6 ft). Like the tomato which belongs to the same family, it bears yellow flowers and yellow-orange to red berry type fruit, though its fruit is berry like in size and shape. Ashwagandha grows prolifically in India, Nepal Pakistan Shri lanka and Bangladesh. It is commercially cultivated in Madhya pardesh (a state in India).

Ashwagandha is reported to have anti-carcinogenic effects in animal and cell cultures by decreasing the expression of nuclear factor-kappaB, suppressing intercellular tumor necrosis factor, and potentiating apoptotic signalling in cancerous cell lines.

Active principles

The chemistry of *W. somnifera* has been extensively studied and over 35 chemical constituents have been identified, extracted, and isolated (Rastogi, 1998). The biologically active chemical constituents are alkaloids (isopelletierine, anaferine), steroidal lactones (withanolides, withaferins), saponins containing an additional acyl group (sitoindoside VII and VIII), and withanolides with a glucose at carbon 27 (sitoindoside IX and X). *W. somnifera* is also rich in iron.

Anticancer activity

To investigate its use in treating various forms of cancer, the antitumor and radio sensitizing effects of *W. somnifera* have been studied. In one study, *W. somnifera* was evaluated for its anti-tumor effect in

urethane-induced lung adenomas in adult male albino mice (Singh, 1986). Simultaneous administration of *W. somnifera* (ethanol extract of whole plant, 200 mg/kg daily orally for seven months) and urethane (125 mg/kg without food biweekly for seven months) reduced tumor incidence significantly (tumor incidence: untreated control, 0/25; urethane treated, 19/19; *W. somnifera* treated, 0/26, and *W. somnifera* plus urethane treated, 6/24, $p < 0.05$). The histological appearance of the lungs of animals protected by *W. somnifera* was similar to those observed in the lungs of control animals. No pathological evidence of any neoplastic change was observed in the brain, stomach, kidneys, heart, spleen, or testes of any treated or control animals. In addition to providing protection from carcinogenic effects, *W. somnifera* treatment also reversed the adverse effects of urethane on total leukocyte count, lymphocyte count, body weight, and mortality.

The growth inhibitory effect of *W. somnifera* was also observed in Sarcoma 180 (S-180), a transplantable mouse tumor. (Devi, 1995) Ethanol extract of *W. somnifera* root (400 mg/kg and up, daily for 15 days) after intradermal inoculation of 5×10^5 cells of S-180 in BALB/c mice produced complete regression of tumor after the initial growth. A 55% complete regression was obtained at 1000 mg/kg; however, it was a lethal dose in some cases. *W. somnifera* was also found to act as a radio and heat sensitizer in mouse S-180 and in Ehrlich ascites carcinoma (Devi, 1992, 1996, 1995).

Anti-tumor and radiosensitizing effects of withaferin (a steroidal lactone of WS) were also seen in mouse Ehrlich ascites carcinoma *in vivo* (Sharad, 1996). Withaferin A from *W. somnifera* gave a radio sensitizer ratio of 1:5 for *in vitro* cell killing of V79 Chinese hamster cell at a non-toxic concentration of about 2 mM/L. (Devi, 1992, 1996, 1995).

***Morinda citrifolia* Linn.**

M. citrifolia, commonly known as great morinda, Indian mulberry, nunaakai (Tamil Nadu, India), dog dumpling (Barbados), mengkudu (Malaysia), beach mulberry, cheese fruit or noni (from Hawaiian) is a tree in the coffee family, Rubiaceae. *M. citrifolia* is native from Southeast Asia to Australia and is now distributed throughout the tropics. In south India indicated that 12 different species or varieties of Morinda are distributed throughout TamilNadu and Kerala

M. citrifolia grows in shady forests as well as on open rocky or sandy shores. It reaches maturity in about 18 months and then yields between 4 - 8 kg (8.8 - 18 lb) of fruit every month throughout the year. It is tolerant of saline soils, drought conditions, and secondary soils. It is therefore found in a wide variety of habitats: volcanic terrains, lava-strewn coasts, and clearings or limestone outcrops. It can grow up to 9 m

(30 ft) tall, and has large, simple, dark green, shiny and deeply veined leaves.

The plant bears flowers and fruits all year round. The fruit is a multiple fruit that has a pungent odor when ripening, and is hence also known as *cheese fruit* or even *vomit fruit*. It is oval in shape and reaches 4 -7 cm (1.6 - 2.8 in) size. At first green, the fruit turns yellow then almost white as it ripens. It contains many seeds. It is sometimes called starvation fruit. Despite its strong smell and bitter taste, the fruit is nevertheless eaten as a famine food and, in some Pacific islands, even a staple food, either raw or cooked. Southeast Asians and Australian.

Active principle

A number of major compounds have been identified in the *M. citrifolia* plant such as scopoletin, octoanoic acid, potassium, vitamin C, terpenoids, alkaloids, anthraquinones (such as nordamnacanthal, morindone, rubiadin, and rubiadin- 1-methyl ether, anthraquinone glycoside), β -sitosterol, carotene, vitamin A, flavones glycosides linoleic acid, alizarin, amino acids, acubin, L-asperuloside, caproic acid, caprylic acid, ursolic acid, rutin and a putative proxeronine. (Levand and Larson, 1979; Farine et al., 1996; Peerzada et al., 1990; Budhavari et al., 1989; Moorthy and Reddy, 1970; Daulatabad et al., 1989; Balakrishnan et al., 1961; Legal et al., 1994; Singh and Tiwari, 1976; Simonsen, 1920; Heinicke, 1985).

The dominant substances in the fruit are fatty acids, while the roots and bark contain anthraquinone. The seed of *M. citrifolia* contains 16.1% Oil. The main fatty acid components of the oil were linoleic (55%), Oleic (20.5%), Palmitic (12.8%), Ricinoleic (6.8%) and Stearic (4.9%) (Daulatabad et al., 1989; Seidemann, 2002). A research group led by Chi-Tang Ho at Rutgers University in the USA is searching for new novel compounds in the *M. citrifolia* Noni plant. They have successfully identified several new flavonol glycosides, and iridoid glycoside from the Noni leaves, trisaccharide fatty acid ester, rutin and an asperulosidic acid from the fruit. Two novel glycosides and a new unusual iridoid named citrifoliniside have been shown to have inhibiting effect on AP-1 Trans activation and cell transformation in the mouse epidermal JB6 cell lines (Wang et al., 1999; Sang et al., 2001; Liu et al., 2001; Wang et al., 2000). Further, 23 different phytochemicals were found in Noni besides, 5 vitamins and 3 minerals (Duke, 1992).

Anticancer activities

The anticancer activity from alcohol-precipitate of noni fruit juice (Noni-ppt) on lung cancer in c57 B1/6 mice has been presented in the 83 annual meeting of

American Association for Cancer Research. The noni-ppt significantly increased the life of mice up to 75% with implanted Lewis lung carcinoma as compared with the control mice (Hirazumi et al., 1994). It was concluded that the noni-ppt seems to suppress tumor growth directly by stimulating the immune system (Hirazumi et al., 1996). Improved survival time and curative effects occurred when noni-ppt was combined with sub optimal doses of the standard chemotherapeutic agents such as adriamycin (Adria), cisplatin (CDDP), 5-fluorouracil (5-FU) and vincristine (VCR), suggesting important clinical application of noni-ppt as a supplemental agent in cancer treatment (Hirazumi and Furusawa, 1999). These results indicated that the noni-ppt might enhance the therapeutic effect of anticancer drugs. Therefore, it may be a benefit to cancer patients by enabling them to use lower doses of anticancer drugs to achieve the same or even better results. Wang et al. (2002) demonstrated that the cytotoxic effect of Tahitian noni (Mathivanan et al., 2005) Current scenario of noni research 7Juice (TNJ) on cultured leukemia cell line at various concentrations.

They also observed the synergistic effects of TNJ with known anticancer drugs. At a sub-optimal dose, both prednisolone and TNJ could induce apoptosis. When the dose of prednisolone was fixed, the dose of TNJ increased. Therefore TNJ is able to enhance the efficacy of anticancer drugs such as prednisolone. When a single dose of taxol induced a lower percentage of apoptosis in leukemia cells, TNJ enhanced the rate of apoptosis. Hiramatsu et al. (1993) reported the effects of over 500 extracts from tropical plants on the K-Ras-NRK cells. Damnacanth, isolated from noni roots is an inhibitor of Ras function. The Ras oncogene is believed to be associated with the signal transduction in several human cancers such as lung, colon, pancreas, and leukemia. Two glycosides extracted from noni-ppt were effective in inhibiting cell transformation induced by TPA or EGF in the mouse epidermal JB6 cell line. The inhibition was found to be associated with the inhibitory effects of these compounds on AP1 activity. The compounds also blocked the phosphorylation of c-Jun, a substrate of JNKs, suggesting that JNKs are the critical target for the compounds in mediating AP1 activity and cell information (Liu et al., 2001).

Curcuma longa (turmeric)

C. longa (Turmeric) Linn. syn.: *Curcuma domestica*, *Curcuma aromatica* is a perennial from the Zingiberaceae family that is widely cultivated in the tropical regions of Asia, most extensively in India, and Latin America. Other names for turmeric include Indian saffron, turmeric root and yellow root. Turmeric has a warm, bitter taste and should not be confused with Javanese turmeric root. The applicable part of turmeric is the root, which is rich in potassium and iron. Chemical analysis of turmeric yields

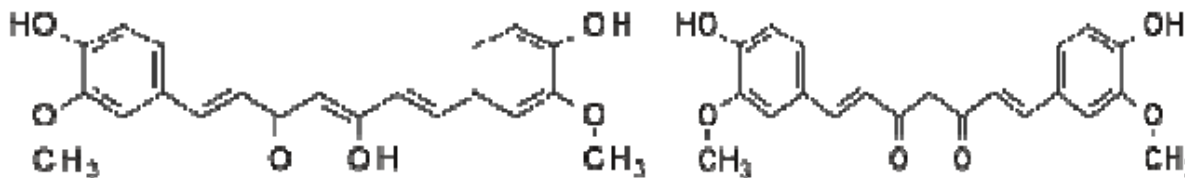


Figure 2. Curcumin enol form.

essential oils and fatty oils (Figure 2).

Active principle

Turmeric contains up to 5% essential oils and up to 5% curcumin, a polyphenol. It is the active substance of turmeric and it is also known as C.I. 75300, or natural yellow 3. The systematic chemical name is (1*E*, 6*E*)-1, 7-bis (4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5-dione.

It can exist at least in two tautomeric forms, keto and enol. The keto form is preferred in solid phase and the enol form in solution. Curcumin is a pH indicator. In acidic solutions (pH <7.4) it turns yellow whereas in basic (pH > 8.6) solutions it turns bright red.

An isolate from turmeric oil has been reported to have antimutagenic activity (Guddadarangavvanahally, 2002). Turmeric also contains curcuminoids: altatone, bisdemethoxycurcumin, dimethoxycurcumin, diaryl heptanoids, and tumerone (Phan, 2001). Synthetic tumerone (turmerone) may act as an anticarcinogen. Curcumin, a polyphenol compound, is responsible for the yellow color of turmeric and is thought to be the most active pharmacological agent. Natural curcumin, isolated from *Curcuma longa*, contains curcumin I (diferuloyl methane as the major constituent), as well as curcumin II (6%) and III (0.3%) (Phann, 2001). Turmeric may be standardized to contain approximately 95% curcuminoids per dose. The dried root of turmeric reportedly contains 4 - 8% curcumin, of which curcumin I is the most abundant, but may not be the most biologically active (Ruby, 1995). Curcumin is insoluble in water and ether, but is soluble in ethanol, dimethylsulfoxide, and other organic solvents (Aggarwal, 2003).

Anticancer activity

Curcumin has been shown to promote apoptosis in certain cancer cell lines, (Kuttan, 1985; Ramachandran, 2002; Goel, 2001; Villasenor, 2002; Bielak-Zmijewska, 2000) and to inhibit telomerase activity, an important factor in tumorigenesis (Kuttan, 1985; Ramachandran, 2002). One possible mechanism for the induction of tumor cell death is through the generation of reactive

oxygen intermediates (Khar, 1999). Although, curcumin is the acknowledged active principal in turmeric, the oleoresin of turmeric (after extraction of curcumin) also was found to have antimutagenic properties, thought to be mediated through its antioxidant action (Guddadarangavvanahally, 2002). The anti-inflammatory properties of curcumin are thought to be due in part to suppression of prostaglandin synthesis (Goel, 2001).

Prostaglandin synthesis from arachidonic acid is catalyzed by two isoenzymes: COX-1 and COX-2, both found in colon tumors of rodents and humans. Goel et al found that curcumin significantly inhibited expression of COX-2 in human colon cancer cells and in COX-2 non-expressing cell lines, without altering the expression of COX-1. This is an important benefit of curcumins since chronic use of nonsteroidal anti-inflammatory drugs (NSAIDs) and non-specific inhibition of COX-1 lead to undesirable gastrointestinal and renal side effects. Curcumin also inhibits the growth of *Helicobacter pylori*, (Mahady, 2002; Somasundaram, 2002) a group 1 carcinogen, as a possible explaining mechanism for its role in prevention of gastric and colon cancers in rodents. The most significant, recent article hypothesized that curcumin's inhibition of the generation of reactive oxygen species (ROS) might interfere with the efficacy of chemotherapeutic drugs that induce apoptosis through the generation of ROS and the JNK pathway (Somasundaram, 2002). Studies in tissue culture showed that curcumin did inhibit the induction of apoptosis by several agents (camptothecin, mechlorethamine, and doxorubicin). This effect was dose and time-dependent, but occurred after even brief three-hour exposures. In their *in vivo* model of human breast cancer, curcumin supplementation significantly inhibited cyclophosphamide-induced tumor regression and decreased activation of JNK and apoptosis.

Moringa oleifera

M. oleifera is the most widely cultivated species of a monogeneric family, the Moringaceae, which is native to the sub-Himalayan tracts of India, Pakistan, Bangladesh and Afghanistan. This rapidly-growing tree (also known as the horseradish tree, drumstick tree, benzolive tree, kelor, marango, mlonge, moonga, mulangay, nébéday,

saijhan, sajna or Ben oil tree), was utilized by the ancient Romans, Greeks and Egyptians; it is now widely cultivated and has become naturalized in many locations in the tropics.

It is a perennial softwood tree with timber of low quality, but which for centuries has been advocated for traditional medicinal and industrial uses. It is already an important crop in India, Ethiopia, the Philippines and the Sudan, and is being grown in West, East and South Africa, tropical Asia, Latin America, the Caribbean, Florida and the Pacific Islands.

Active component

This plant family is rich in compounds containing the simple sugar, rhamnose, and it is rich in a fairly unique group of compounds called glucosinolates and isothiocyanates (Bennett et al., 2003; Fahey et al., 2001). For example, specific components of *Moringa* preparations that have been reported to have hypotensive, anticancer, and antibacterial activity include 4-(4'-O-acetyl- α -L-rhamnopyranosyloxy)benzyl isothiocyanate (Bennett et al., 2003), 4-(α -L-rhamnopyranosyloxy)benzyl isothiocyanate (Fahey et al., 2001), niazimicin (Hatwell, 1967-1971), pterygospermin (Fahey et al., 2004), benzyl isothiocyanate (Juevara et al., 1999), and 4-(α -L-rhamnopyranosyloxy) benzyl glucosinolate (Murakami et al., 1998). While these compounds are relatively unique to the *Moringa* family, it is also rich in a number of vitamins and minerals as well as other more commonly recognized phytochemicals such as the carotenoids (including β -carotene or pro-vitamin A).

Anticancer activity

Since *Moringa* species have long been recognized by folk medicine practitioners as having value in tumor therapy (Hatwell, 1967-1971). Recently, the compounds from *Moringa* were shown to be potent inhibitors of phorbol ester (TPA)-induced Epstein-Barr virus early antigen activation in lymphoblastoid (Burkitt's lymphoma) cells (Juevara et al., 1999; Murakami et al., 1998). In one of these studies, it also inhibited tumor promotion in a mouse two-stage DMBA-TPA tumor model. In an even more recent study, Bharali and colleagues have examined skin tumor prevention following ingestion of drumstick (*Moringa* seedpod) extracts (Bharali et al., 2003). In this mouse model, which included appropriate positive and negative controls has shown a dramatic reduction in skin papillomas. Thus, traditional practice has long suggested that cancer prevention and therapy may be achievable with native plants. Modern practitioners have used crude extracts and isolated bioactive compounds.

Artemisinin annua

A. annua, also known as Sweet Wormwood, Sweet Annie, Sweet Sagewort or Annual Wormwood is a common type of wormwood that is native to temperate Asia, but naturalized throughout the world. It has fern-like leaves, bright yellow flowers, and a camphor-like scent.

Its height averages about 2 m tall, and the plant has a single stem, alternating branches, and alternating leaves which range 2.5 - 5 cm in length. It is cross-pollinated by wind or insects. It is a diploid plant with chromosome number, $2n=18$.

Active component

The presence of alkaloids, glycosides, flavonoids, reducing compounds and polyphenols with flavonoids and polyphenols present in excess and much excess respectively.

Anticancer activity

Artemisinins show promising anti-cancer activities when tested *in vitro* and *in vivo* (Lai and Singh, 1995; Moore et al., 1995; Efferth et al., 2001). Artemisinins contain an endoperoxide group that is essential for their anticancer activities. Like hydrogen peroxide, H_2O_2 , artemisinin reacts with ferrous iron, Fe^{2+} , to generate radical species. The short-lived artemisinin-generated radical species have been linked to its anti-cancer activities. The anti-cancer activity of artemisinin derivatives can significantly increase when iron complexes are added in the cell culture medium (Efferth et al., 2004; Lai and Singh, 1995). A covalent conjugate of artemisinin and transferrin (ART-Tf), an iron transport protein in human, is actively taken up by cancer cells through the transferrin receptor (TfR)-mediated endocytosis pathway, and shows significantly higher anti-cancer activity than unconjugated artemisinin (Singh and Lai, 2001; Lai et al., 2005; Nakase et al., 2009). Like ART-Tf, artemisinin-peptide conjugates that are designed to target TfR also showed highly potent and selective anti-cancer activities (Oh et al., 2009). These studies show the importance of iron metabolism in determining the effectiveness of artemisinin derivatives in killing cancer cells. Artemisinin derivatives induce programmed cell death of cancer cells by activating the intrinsic or the cytochrome C-mediated pathway for apoptosis, although, the initial protein targets of artemisinin derivatives for apoptosis in human cancer cells have not yet been identified (Nakase et al., 2009). Although, the generation of free radicals originating from the reaction of artemisinin with molecular iron is mentioned as one of the main mechanism for its anticancer activity, there are other mechanisms, crucial

for cancer proliferation and survival that are affected by artemisinins.

Taxus brevifolia

T. brevifolia (Pacific Yew or Western Yew) is a conifer native to the Pacific Northwest of North America. It ranges from Southern most Alaska south to central California, mostly in the Pacific Coast Ranges, but with an isolated disjunct population in southeast British Columbia, most notably occurring on Zuckergibb Island near Castlegar and South to central Idaho. It is a small to medium-sized ever green tree growing 10 - 15 m tall and with a trunk up to 50 cm diameter, rarely more. In some instances, trees with heights in excess of 20 m occur in parks and other protected areas, quite often in gullies. The tree is extremely slow growing, and has a habit of rotting from the inside, creating hollow forms. This makes it difficult and impossible to make accurate rings counts to determine a specimen's true age. Often damaged by succession of the forest, it usually ends up in a squat, multiple leader form.

It has thin scaly brown bark, covering a thin layer of off-white sap wood with a darker heartwood that varies in color from brown to a magenta/purplish hue. The leaves are lanceolate, flat, dark green, 1 - 3 cm long and 2 - 3 mm broad, arranged spirally on the stem, but with the leaf bases twisted to align the leaves in two flat rows either side of the stem except on erect leading shoots where the spiral arrangement is more obvious.

Active component

The discovery and isolation of paclitaxel from the bark of the Pacific yew, *T. brevifolia* Nutt. and its introduction in cancer chemotherapy has attracted scientists to investigate the constituents of other *Taxus* species worldwide. Therefore, genus *Taxus* has been one of the most intensely studied genus in all plant genera. So far, the isolation of a large number of taxoids as well as lignans, flavonoids, steroids and sugar derivatives has been reported from different parts of various *Taxus* species. Phytochemical investigation on the chloroform-soluble portion of the ethanol extract of the heartwood of *Taxus baccata* growing in Turkey by successive chromatographic methods resulted in the isolation of six taxoids and five lignans; namely lariciresinol, taxiresinol, 3'-demethylisolariciresinol-9'-hydroxyisopropylether, isolariciresinol and 3-demethylisolariciresinol (Pujol et al., 2007).

Anticancer activity

No bioactive compound discovered over the last 30 years has attracted more public attention than paclitaxel (Pujol et al., 2007). Paclitaxel is a complex taxane diterpene

isolated from the bark of *T. brevifolia* (Kovacs et al., 2007). The cytotoxic activity of the bark extract was first reported in 1963, utilizing KB cytotoxicity assay. Subsequently, Paclitaxel's *in vivo* activity against mouse leukemia was discovered in 1966 (Kingston, 2007), and its structure was described in 1971 (Wani et al., 1971). Microtubule-targeting drugs inhibit the metaphase anaphase transition through suppressing spindle microtubule dynamics, which block mitosis and induce apoptosis (Jordan and Wilson, 2004). Microtubule stabilizing agents (MSA) is a class of these drugs that includes taxanes (paclitaxel and docetaxel), epothilones A and B, discodermolide, eleutherobin (Jordan and Wilson, 2004), and monastrol (Jiang et al., 2006; Cochran et al., 2005). These agents stabilize microtubules by binding to polymeric tubulin, thus preventing disassembly (McGrogan et al., 1985; Zhou and Giannakakou, 2005). Paclitaxel causes polymerization and stabilization of microtubules in tumor cells, thereby inhibiting cell replication through disruption of normal mitotic spindle formation (Amos and Lowe, 1999).

Therefore, cells treated with paclitaxel are unable to proceed normally through the cell cycle and arrest in G2/M phase (Mullan et al., 2001). This halt of the cell cycle at mitosis has been considered the cause of paclitaxel-induced cytotoxicity (Pineiro et al., 2007). Paclitaxel triggers apoptosis by caspase-dependent and independent pathways (Piñero et al., 2007) that regulate the expression of apoptosis-related proteins such as Bim, Bcl-2, Bad, Bcl-XL, p21WAF-1/CIP-1, tumor necrosis factor- α (TNF- α) receptor 1 (TNFR1), and the TRAIL receptors DR4 and DR5 (Pineiro et al., 2007; Sunter et al., 2003; Von et al., 2003; Tudor et al., 2000; Salah-Eldin et al., 2003; Ding et al., 1990). Recently, it has been suggested that paclitaxel changes the translational machinery that occurs during apoptosis. Paclitaxel inhibits the translational machinery by increasing elongation factor eEF2 phosphorylation. In addition to its ability to trigger various signal transduction pathways, including JNK, p38MAPK, and ERK, paclitaxel has also been reported to promote the activation of JNK/SAPK through Ras and ASK1 pathways (Li et al., 1998). JNK phosphorylates and inactivates Bcl-2 at the G2M phase of the cell cycle as demonstrated by the inhibition of paclitaxel-induced phosphorylation of Bcl-2 using dominant negative mutants of JNK and ASK1 (Stewart and Fang, 2005). Following paclitaxel treatment, when mitotic arrest and mitotic slippage occur, surviving is down regulated (Zaffaroni, 2002) and Aurora B is inactivated (Fujie, 2005), enabling apoptosis to occur in G1. Over expression of survivin has been shown to be associated with increased resistance to paclitaxel-induced cell death (Zaffaroni, 2002). On the other hand, inhibition of surviving by mitotic inhibitors such as oxaliplatin, increases paclitaxel-induced apoptosis and cell death in colonic carcinoma cells (Fujie, 2005).

Paclitaxel and cisplatin are widely used anticancer agents for treatment of non-small cell lung cancer (Pontes et al., 2009). Paclitaxel treatment induces the expression of IL-8 in ovarian and in non-small lung cancer cell lines (Gradishar et al., 2009; Toppmeyer et al., 2002) as well as in patients (Chi et al., 2005; Izquierdo, 2005). In addition, Paclitaxel up regulates IL-6 in cell lines and patients (Pusztai, 2005). NF- κ B-dependent transcription of COX-2 is up regulated in the presence of Paclitaxel (Plosker and Keam, 2006). A recent study has documented increased levels of COX-2 in specimens taken from patients undergoing Paclitaxel treatment for non-small cell lung carcinoma, demonstrating the relevance of the clinical effect (Slamon et al., 1989).

A combination therapy of phase II clinical trials with taxane and celecoxib, a COX-2 inhibitor, has yielded mixed results, making further investigation necessary (Modi et al., 2005). Paclitaxel completed many clinical trials from 1982 - 2003 (Kingston, 2007; Wiernik et al., 1987; McGuire et al., 1989; Holmes et al., 1991; Gueritte-Voegelein et al., 1986; Piccart and Cardoso, 2003; Ozols, 2003; Davies et al., 2003). In the phase III MDACC trial (Buzdar et al., 2002), a slight increase in disease-free survival (DFS) and over all survival (OS) was observed in FAC followed by paclitaxel (paclitaxel) (P) (FAC-P) arms compared to FAC alone. The first large prospective trial to examine the addition of paclitaxel to an anthracycline-based regime in node-positive women was undertaken by the CALGB 9344 trial (Henderson et al., 2003). The addition of paclitaxel significantly improved DFS 70 vs. 65% and OS 80 vs. 77%.

In the NSABP B28 trial (Mamounas et al., 2003), the addition of paclitaxel to adjuvant anthracycline therapy improved the 5-year DFS regardless of tumor grade, histological type, patient's age, or number of positive lymph nodes, although there was no improvement in 5-year OS. In the Cancer and Leukemia Group B 9741 trial, doxorubicin (A), cyclophosphamide (C), and paclitaxel (P) administration was compared in sequential versus concurrent regimes in the setting of either conventional administration three times weekly or dose-dense administration twice weekly. Moreover, 2005 women with node-positive metastatic breast cancer were randomly assigned to one of the four treatment arms illustrated (Citron et al., 2003; Xiong et al., 2005); significant improvements were seen in DFS, OS, relapse risk, and mortality risk with dose-dense scheduling. In addition to other micellar formulations in preclinical developments, the paclitaxel based nanoparticulates (NK105) have recently been advanced into clinical trials (Bromberg, 2008; Lee et al., 2007).

***Lawsonia inermis* Linn.**

Genus *Lawsonia* bears one species, *L. inermis* (Henna, Mhendi, Shudi, Madurang, Mendi, Manghati, Madayantika and Goranti) till date, having different synonyms as alba

and spinosa belonging to family Lythraceae. It is a biennial dicotyledonous herbaceous shrub. A native of North Africa and South-West Asia, the plant is now widely cultivated through out the tropics as an ornamental and dye plant. A much branched glabrous shrub or small tree (2 to 6 m in height). Leaves are small, opposite in arrangement along the branches, sub-sessile, about 1.5 to 5 cm long, 0.5 to 2 cm wide, greenish brown to dull green, elliptic to broadly lanceolate with entire margin, petiole short and glabrous and acute or obtuse apex with tapering base.

Active component

The principal colouring matter of henna is lawsone, 2-hydroxy-1:4 naphthaquinone ($C_{10}H_6O_3$, m.p.190° decomp). Besides lawsone other constituents present are gallic acid, glucose, mannitol, fats, resin (2%), mucilage and traces of an alkaloid. Leaves yield hennatannic acid and an olive oil green resin, soluble in ether and alcohol.

Flowers yield an essential oil (0.01 - 0.02%) with brown or dark brown colour, strong fragrance and consist mainly of α - and β -ionones; a nitrogenous compound and resin. Seeds contain proteins (5.0%), carbohydrates (33.62%), fibers (33.5%), fatty oils (10- 11%) composed of behenic acid, arachidic acid, stearic acid, palmitic acid, oleic acid and linoleic acid. The unsaponified matter contains waxes and colouring matter.

Anticancer activity

Isoplumbagin exhibited up to a 1000 fold range of differential sensitivity, which represents distinct fingerprint of cellular responsiveness. At concentration of 10.5-10.8 M, the compound typically produced LC50 – level responses against a majority of the melanoma and colon cancer cell lines as well as against several of the non-small cell lungs, colon, CNS, and renal cell lines. Isoplumbagin showed an interesting profile of cytotoxic activity (Linh et al., 2000). Chloroform extract of leaves of *L. inermis* displayed the cytotoxic effects against liver (HepG2) and Human breast (MCF-7) with IC50 values of 0.3 and 24.85 μ g/ml by microculture tetrazolium salt assay (MTT) (Lee et al., 2000). CAT assay, a zone of inhibition test of bacterial growth and colony-forming efficiency test of transformant *Escherichia coli* strains that express mammalian catalase gene derived from normal catalase mice (Cs a) and catalase-deficient mutant mice (Cs b), Ames mutagenicity assay and H₂O₂ generation assay are carried out. Lawsone generated H₂O₂ slightly in phosphate buffer system and was not mutagenic in Ames assay using TA98, TA100 and TA102, both in the absence and presence of metabolic activation. Lawsone exposure inhibited the growth of both Cs a and Cs b strains in a dose-dependent manner. Oxidative stress probably arises when naphthoquinone part in lawsone

reduced to a semiquinone by enzymatic systems (Ohsugi et al., 1999).

Rhodiola rosea

R. rosea ("golden root" or "Arctic root") is widely distributed at high altitudes in Arctic and mountainous regions throughout Europe and Asia. It is a popular plant in traditional medical systems in Eastern Europe and Asia, with a reputation for stimulating the nervous system, decreasing depression, enhancing work performance, eliminating fatigue, and preventing high altitude sickness.

In addition to *R. rosea*, over 200 different species of *Rhodiola* have been identified and at least 20 are used in traditional medical systems in Asia, including *Rhodiola alterna*, *Rhodiola brevipetiolata*, *Rhodiola crenulata*, *Rhodiola kirilowii*, *Rhodiola quadrifida*, *Rhodiola sachalinensis*, and *Rhodiola sacra*.

Active component

Twenty-eight compounds have been isolated from the roots and above-ground parts of *R. rosea*, including 12 novel compounds. The roots contain a range of biologically active substances including organic acids, flavonoids, tannins, and phenolic glycosides. The stimulating and adaptogenic properties of *R. rosea* were originally attributed to two compounds isolated from its roots, identified as p-tyrosol and the phenolic glycoside rhodioloside. Rhodioloside was later determined to be structurally similar to the known glycoside salidroside found in several other plant species. Salidroside, rhodioloside, and occasionally rhodosin are used to describe this compound and are considered to be synonyms. Additional glycoside compounds isolated from the root include rhodioniside, rhodiolin, rosin, rosavin, rosarin, and rosiridin. These glycoside compounds are also thought to be critical for the plant's observed adaptogenic properties. A range of antioxidant compounds have been identified in *R. rosea* and related species, including p-tyrosol, organic acids (gallic acid, caffeic acid, and chlorogenic acid), and flavonoids (catechins and proanthocyanidins).

Significant free-radical scavenging activity has been demonstrated for alcohol and water extracts of *Rhodiola* spp. and is attributed to the variety of antioxidant compounds. p-Tyrosol has been shown to be readily and dose-dependently absorbed after an oral dose, and appears to produce a significant antioxidant and modest 5-lipoxygenase inhibitory activity *in vivo*. Salidroside (rhodioloside), the additional salidroside-like glycoside compounds (rhodiolin, rosin, rosavin, rosarin, and rosiridin), and p-tyrosol are thought to be the most critical plant constituents needed for therapeutic activity (Visioli

et al., 2000; Bonanome et al., 2000).

Anticancer activity

Administration of *R. rosea* appears to have potential as an anticancer agent, and might be useful in conjunction with some pharmaceutical antitumor agents. In rats with transplanted solid Ehrlich adenocarcinoma and metastasizing rat Pliss lymphosarcoma, supplementation with *R. rosea* extract inhibited the growth of both tumor types, decreased metastasis to the liver, and extended survival times (Udintsev et al., 1991). Administration of *R. rosea* extract also directly suppressed the growth of and the extent of metastasis from transplanted Lewis lung carcinomas (Udintsev et al., 1991). When *R. rosea* extract was combined with the antitumor agent cyclophosphamide in these same tumor models, the antitumor and antimetastatic efficacy of drug treatment was enhanced. The authors have commented that, "complete abrogation of the haematotoxicity of cyclophosphamide" was observed (Udintsev et al., 1991). The chemotherapeutic drug Adriamycin is known to induce pronounced liver dysfunction, generally reflected by an increase in transaminase levels. In animal experiments, adding *R. rosea* extract to a protocol with Adriamycin resulted in an improved inhibition of tumor dissemination (as compared to that found with Adriamycin alone), and the combined protocol prevented liver toxicity (Udintsev et al., 1992).

Catharanthus roseus

C. roseus (Madagascar periwinkle) is a species of catharanthus native and endemic to Madagascar. Synonyms include *Vinca rosea* (the basionym), *Ammocallis rosea*, and *Lochnera rosea*; other English names occasionally used include Cape Periwinkle, Rose Periwinkle, Rosy Periwinkle, and "Old-maid". In the wild, it is an evergreen shrub or herbaceous plant growing to 1 m tall. The leaves are oval to oblong, 2.5 - 9 cm long and 1 - 3.5 cm broad, glossy green, hairless, with a pale midrib and a short petiole 1 - 1.8 cm long; they are arranged in opposite pairs. The flowers are white to dark pink with a darker red centre, with a basal tube 2.5 - 3 cm long and a corolla 2 - 5 cm diameter with five petal-like lobes. The fruit is a pair of follicle 2 - 4 cm long and 3 mm broad.

Active component

Contains more than 70 alkaloids mostly of the indole type and vinblastine and vincristine are alkaloids found in periwinkle. They are all administered intravenously in their sulphate form. These solutions are fatal if they are

Table 1. Some important medicinal plants used against cancer and their plant parts.

S. No.	Botanical name of plant with family name	Parts used and their main active components
1	<i>Agave americana</i> Agavaceae	Leaf contains steroidal saponin, alkaloid, coumarin, isoflavonoid, hecogenin and vitamins (A, B, C).
2	<i>Agropyron repens</i> Poaceae	Rhizome contains essential oil, polysaccharide and mucilage.
3	<i>Agrimonia pilosa</i> Rosaceae	Herb contains agrimonolide, flavonoid, triterpene, tannin and coumarin.
4	<i>Ailanthus altissima</i> Simaroubaceae	Bark contains triterpene, tannin, saponin and quercetin-3-glucoside.
5	<i>Akebia quinata</i> Lardizabalaceae	Fruit contains flavonoid and saponin.
6	<i>Alpinia galanga</i> Zinziberaceae	Rhizome contains kaempferide and flavone.
7	<i>Aristolochia contorta</i> Aristolochiaceae	Root and fruit contain lysicamine and oxaaporphine.
8	<i>Aster tataricus</i> Asteraceae	Whole plant and root contain triterpene, monoterpene and epifriedelanol.
9	<i>Broyonia dioica</i>	Root contains cucurbitacin and glycoside.
10	<i>Cannabis sativa</i> Cannabinaceae	Leaf contains stereo isomers of cannabitol.
11	<i>Chelidonium majus</i> var. <i>asiaticum</i> Papaveraceae	Herb contains alkaloids (sanguinarine, chelerythrine, berberine).
12	<i>Chimaphila umbellata</i> Ericaceae	Whole plant contains ericolin, arbutin, urson and tannin
13	<i>Coix lachryma jobi</i> Poaceae	Seed contains trans-ferulyl stigmaterol.
14	<i>Dryopteris crassirhizoma</i> Polypodiaceae	Rhizome contains filicinic and filicic acids, aspidinol and aspidin.
15	<i>Echinops setifer</i> Asteraceae	Whole plant contains echinopsine.
16	<i>Erythronium americanum</i> Liliaceae	Whole plant contains alpha-methylenebutyrolactone.
17	<i>Euonymus alatus</i> Celastraceae	Whole plant contains triterpene, euolatin, steroid and sesquiterpene alkaloid.
18	<i>Eupatorium cannabinum</i> Asteraceae	Whole plant contains sesquiterpene, lactone, pyrrolizidine alkaloid and flavonoid.
19	<i>Fragaria vesca</i> Rosaceae	Leaf and fruit contain flavonoid, tannin, borneol and ellagic acid.
20	<i>Fritillaria thunbergii</i> Liliaceae	Whole plant contains alkaloid and peimine.
21	<i>Galium aparine</i> Rubiaceae	Cleaver contains iridoid, polyphenolic acid, tannin, anthraquinone and flavonoid.
22	<i>Hydrastis canadensis</i> Ranunculaceae	Whole plant contains isoquinoline alkaloids (hydrastine, berberine, berberastine, candaline), resin and lactone.
23	<i>Hypoxis argentea</i> Hypoxidaceae	Corm
24	<i>Juncus effuses</i> Juncaceae	Whole plant contains tridecanone, effusol, juncanol, phenylpropanoid and a-tocopherol.
25	<i>Knowltonia capensis</i> Ranunculaceae	Leaf
26	<i>Lantana camara</i> Verbenaceae	Whole plant contains alkaloids (camerine, isocamerine, micranine, lantanine, lantadene).
27	<i>Larrea tridentate</i> Zygophyllaceae	Whole plant contains resin.
28	<i>Lonicera japonica</i> Caprifoliaceae	Whole plant, stem and flower contain tannins, saponins and carotenoids.
29	<i>Merwillia plumbea</i> Hyacinthaceae	Bulb
30	<i>Nidus vespae</i>	Whole plant
31	<i>Olea europae</i> Oleaceae	Leaf and oil contain oleic acid and polyphenol.
32	<i>Oldenlandia diffusa</i> Rubiaceae	Whole plant
33	<i>Panax quinquefolium</i> Araliaceae	Root contains ginsenoside, sesquiterpene, limonene and vitamins (B1, B2, B12).
34	<i>Patrinia heterophylla</i> Vlerianaceae	Whole plant
35	<i>Patrinia scabiosaefolia</i> Vlerianaceae	Whole plant
36	<i>Phaleria macrocarpa</i>	Fruit contains gallic acid

Table 1. Contd.

37	<i>Polygonum cuspidatum</i>	Polygonaceae	Whole plant
38	<i>Polygonatum multiflorum</i>	Liliaceae	Whole plant contains saponin, flavonoid and vitamin A
39	<i>Potentilla chinensis</i>	Rolsaaceae	Whole plant contains gallic acid and tannin.
40	<i>Pteris multifida</i>		Whole plant
41	<i>Pygeum africanum</i>	Boraginaceae	Bark contains phytosterol, triterpene and tannin.
42	<i>Pyrus malus</i>	Rosaceae	Bark and fruit contain quercetin, catechin, flavonoid, coumaric and gallic acids, phloridzin and procyanidin.
43	<i>Rhus chinensis</i>	Anacardiaceae	Leaf contains tannin, apigenin and glycoside; seed contains bruceosides (A, B), brucein D and fatty oil.
44	<i>Rosmarinus officinalis</i>	Lamiaceae	Whole plant contains volatile oil, borneal, carnosol, ursolic acid, diterpene, rosmarinic acid, flavonoid and tannin.
45	<i>Rubia akane</i>	Rubiaceae	Whole plant contains anthraquinone and triterpene.
46	<i>Rubus idaeus</i>	Rosaceae	Leaf contains flavonoid and tannin; fruit contains vitamins (A, B, C) and ellagic acid.
47	<i>Scilla natalensis</i>	Hyacinthaceae	Bulb
48	<i>Scrophularia nodosa</i>	Scrophulariaceae	Aerial part contains iridoid, flavonoid and phenolic acid.
49	<i>Scutellaria barbata</i>	Lamiaceae	Whole plant
50	<i>Smilax chinensis</i>	Liliaceae	Rhizome contains tannin, saponins and flavonoid
51	<i>Smilax glabra</i>	Liliaceae	Rhizome
52	<i>Solanum aculeastrum</i>	Solanaceae	Root bark, leaf and fruit.
53	<i>Solanum lyrati</i>	Solanaceae	Whole plant
54	<i>Sophora flavescens</i>	Fabaceae	Root
55	<i>Sophora subprostrata</i>	Fabaceae	Root
56	<i>Tabebuia</i> spp.	Bignoniaceae	Bark contains quinine, bioflavonoid and co-enzyme Q.
57	<i>Taraxacum mongolicum</i>	Asteraceae	Whole plant
58	<i>Thuja occidentalis</i>	Cupressaceae	Whole plant contains flavonoid, tannin, volatile oil and mucilage.
59	<i>Thymus vulgaris</i>	Lamiaceae	Whole plant contains volatile oil, flavonoid and tannin.
60	<i>Trifolium pratense</i>	Fabaceae	Flower contains glucosides (trifolin, trifolitin, trifoliantol), flavonoid and phenolic acid.
61	<i>Tulbaghia violacea</i>	Alliaceae	Bulb
62	<i>Vitex rotundifolia</i>	Verbenaceae	Whole plant contains camphene, pinene and diterpene.

(Ref. Madhuri and Pandey, 2009).

administered any other way and can cause a lot of tissue irritation if they leak out of the vein. Although, these compounds are very similar in structure and have the same basic action, they have distinctly different effects on the body.

Anticancer activity

Catharanthus is in the Apocynaceae family, well known for being rich in alkaloids. A U.S. government screening program incidentally discovered that *Catharanthus* extracts were antineoplastic *in vitro*, leading ultimately to the licensing of the alkaloids vinblastine and vincristine, as well as some synthetic analogs today, as highly toxic chemotherapy drugs. The absolute levels of vinblastine and vincristine are considered far too low to explain the activity of crude extracts of *Catharanthus*. Various studies show the presence of other antineoplastic alkaloids in the plant (El-Sayed and Cordell, 1981; El-Sayed, 1983). This

supports the hypothesis in botanical medicine that herbs work due to a synergy among many different components and it does not matter than two particular alkaloids are only present in tiny amounts. Crude extracts of *Catharanthus* made using 50 and 100% methanol had significant anticancer activity against numerous cell types *in vitro* (at <15 mcg/ml) (Ueda et al., 2002). Greatest activity was seen against multidrug resistant tumor types, suggesting there were compounds in *Catharanthus* that were synergistic or additive with antineoplastic elements by inhibiting resistance to them. Crude decoction (of 200 mg and 1 g herb/ml water) *Catharanthus* showed a moderate anti-angiogenesis affect *in vitro* (Wang et al., 2004) (Table 1).

CONCLUSION

Since the dawn of human civilization medicinal plants have been considered to be the best source of curing

various dreaded disease and cancer is one among those diseases. There are lots of medicinal plants available in nature which has the anticancerous properties and majority of them are still to be exploited. So, considering the facts it is strongly recommended that there is an urge for these plants to be discovered so that the cancer could be totally eradicated.

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