

# Therapeutic Plants of Ayurveda; A Review on Anticancer

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## ABSTRACT

Cancer is actually a group of many related diseases that all have to do with cells. Cells are the very small units that make up all living things, including the human body. There are billions of cells in each person's body. Cancer happens when cells that are not normal grow and spread very fast. Normal body cells grow and divide and know to stop growing. Over time, they also die. Unlike these normal cells, cancer cells just continue to grow and divide out of control and don't die when they're supposed to. A number of synthetic anticancer drugs are available in practice, however their effectiveness does not hold true with the entire range of population suffering from this disorder. Moreover the side effects and the drug interactions are major restrictions in its clinical utility. On the other hand, herbal medicines are now attracting attention as potential sources of anticancer agents are widely used across the globe due to their wide applicability and therapeutic efficacy coupled with least side effects, which in turn has accelerated the scientific research regarding the anticancer activity. In this overview we have summarized the current research advancements on plants belongs to different families like Apocyanaceae, Taxaceae, Beriberidaceae, Solanaceae, Cupressaceae etc. having anticancer activities along with their other activities.

**Key words:** Cancer, Anticancer herbal medicines.

## INTRODUCTION

An attempt has been made to review some medicinal plants used for the prevention and treatment of cancer in India and foreign countries. Place of these plants have been collected from the literature. The extracts or decoctions of these are generally used. The medicinal plants contain several phytochemicals such as vitamins (A, C, E, K), carotenoids, Terpenoids, flavonoids, polyphenols, alkaloids, tannins, Saponins, enzymes, minerals, etc. These phytochemicals possess antioxidant activities, which prevent or can be used in the treatment of many diseases, including cancer. Herbal drugs are also known to have good Immunomodulatory properties. These act by stimulating both non-specific and specific immunity. Over the past decade, herbal medicines have been accepted universally, and they have an impact on both world health and international trade. Hence, medicinal plants continue to play an important role in the healthcare system of a large number of the world's population. Traditional medicine is widely used in India. Even in USA, use of plants and

phytomedicines has increased dramatically in the last two decades. A National Centre for Complementary and Alternative Medicine has been established in USA. The herbal products have been classified under 'dietary supplements' and are included with vitamins, minerals, amino acids and 'other products intended to supplement the diet'. Use of plants as a medicinal remedy is an integral part of the South African cultural life. It is estimated that 27 million South Africans use herbal medicines from more than 1020 plant species. In fact, there are several medicinal plants all over the World, including India, which are being used traditionally For the prevention and treatment of cancer.

### ***Alstonia scholaris***

*Alstonia scholaris*, commonly known as saphthaparna, has been used for centuries in Ayurvedic medicine for treatment of various disorders. The objective of this study was to investigate the possible chemopreventive and anti-oxidative properties of this medicinal plant on two-stage process of skin carcinogenesis induced by a single application of 7, 12-dimethyabenz(a)anthracene (100 lg/100 ll acetone), and two weeks later, promoted by repeated application of croton oil (1% in acetone/thrice a week) till the end of the experiment (16 weeks) in Swiss albino mice. The tumor incidence, tumor yield, tumor burden and cumulative number

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**Table 1: Medicinal plants with anticancer activity and their beneficial properties**

Plant name	Ayurvedic/common name	Anticancer and other beneficial effect in traditional medicine	Reference
<i>Alstonia scholaris</i>	Sapthaparna	Chemopreventive and anti-oxidative	1
<i>Piper nigrum</i>	Pipper	Carminative, Stimulant, Anticancer, Stomachic	2
<i>Withania somnifera</i>	Ashwagandha	Anticancer, Sedative and Hypnotic, Gout, Hypertension	3
<i>Cymbopogon flexuosus</i>	Lemon grass oil	Anticancer	4
<i>Saussurea lappa</i>	Costus root	Anticancer, Bronchial asthma	5
<i>Andrographis paniculata</i>	Kalmegh	Anticancer, Hepatoprotective	6
<i>Tanacetum gracile</i>	Feverfew	Anticancer, Antipyretic	7
<i>Abrus agglutinifolius</i>	Abrin	Antitumor	8
<i>Curcuma longa</i>	Turmeric	Antioxidant, Antiinflammatory, Antiviral, Antibacterial, Anticancer	9
<i>Saussurea costus</i>	Kuth	Anticancer, Ulcer, Inflammatory diseases, Asthma	10
<i>Crocus sativus</i>	Saffron	Antitumor agent, Antispasmodic	11
<i>Ficus benghalensis</i>	Banyan tree	Malignant disease, Anti-inflammatory	12
<i>Calotropis procera</i>	Giant Swallow Wort	Antibacterial, Anthelmint, Anti-diarrhoeal, Ascaricidal, Schizonticidal	13
<i>Cassia auriculata</i>	Senna	Anticancer, Cathartic	14
<i>Punica granatum</i>	Anar	Anticancer, Anti-inflammatory	15
<i>Carica papaya</i>	Papain	Anticancer, Anti-inflammatory	16
<i>Capsicum annum</i>	Chillies	Anticancer, Stomachic, Carminative, Counter irritant	17
<i>Vernonia amygdalina</i>	Bitterleaf	Anticancer	18
<i>Vitis vinifera</i>	Grape	Anticancer, Hepatoprotective, Anemia	19
<i>Ziziphus jujube</i>	Jujube	Anticancer, Antianxiolytic, Antifungal, Antispastic, Cardiotonic, Antifertility	20
<i>Passiflora incarnate</i>	Passion flower	Anticancer, Antianxiety, Insomnia, Cough, Sexual dysfunction, Convulsion	21
<i>Emblica officinalis</i>	Amla	Anticancer, Hepatoprotective, Antioxidant, Antitumour	22
<i>Poncirus trifoliata</i>	Tang-ja-na-moo	Anticancer, Antioxidant	23
<i>Hedychium spicatum</i>	Kapur Kachari	Anticancer, Stomachic, Stimulant, Tonic,	24
<i>Cynodon dactylon</i>	Grass	Anticancer, Antioxidant	25
<i>Tabernaemontana divaricata</i>	Chameli	Anticancer	26
<i>Nigella sativa</i>	Kalonji	Anticancer, Immunomodulator	27
<i>Gingiber officinalis</i>	Ginger	Anticancer, Antioxidant, Anti-inflammatory	28
<i>Berberis vulgaris</i>	Barberry	Anticancer, Antidiabetic, Heart failure	29
<i>Sauromatum venosum</i>	Voodoo lily	Anticancer	30
<i>Eulophia compestris</i>	Salam	Antitumors	31
<i>Ipomoea bahiensis</i>	Krishnabija	Sarcoma cancer	32
<i>Mangifera indica</i>	Mango	Anticancer, Antibacterial, Antioxidant	33
<i>Podophyllum emodi</i>	Himalayan May-apple	Anticancer, Purgative, Bitter tonic	34
<i>Polyalthia longifolia</i>	Asoka	Anticancer	35
<i>Tinospora cordifolia</i>	Guduchi	Anticancer, Gout, Skin disease, Hepatoprotective	36
<i>Bauhinia variegata</i>	Kachnar	Antitumour	37
<i>Thea sinensis</i>	Tea	Anticancer, Diuretics, CNS stimulant	38
<i>Phyllanthus amarus</i>	Bhumyaamalaki	Anticancer	39
<i>Bidens pilosa</i>	Black jack	Anticancer, Antitumour	40
<i>Solanum nigrum</i>	Makoi	Anticancer, Antiviral, Anti-inflammatory	41
<i>Vinca rosea</i>	Periwinkle	Anticancer	42
<i>Eurycoma longifolia</i>	Pasak bumi	Anticancer	43
<i>Coptidis rhizoma</i>	Huanglian	Antineoplastic	44
<i>Ximenia americana</i>	Wild lime	Antineoplastic	45
<i>Eruca sativa</i>	Diplotaxis	Anticancer	46
<i>Podophyllum hexandrum</i>	Himalayan May-apple	Anticancer, Bitter tonic, Purgative	47
<i>Taxus bacata</i>	European yew	Anticancer	48
<i>Cedrus deodara</i>	Dvedar	Anticancer	49
<i>Podophyllum hexandrum</i>	Hymalayan mayapple	Anticancer	50
<i>Scutellaria baicalensis</i>	Baikal skullcap	Anticancer	51
<i>Silybum marianum</i>	Marian Thistle	Anticancer, Hepatoprotective	52
<i>Panax ginseng</i>	Panax	Anticancer, Immunomodulator,	53
<i>Cynara cardunculus</i>	Hathichuk	Anticancer	54
<i>Radix sophorae</i>	Flavescent sophora root	Anticancer	55
<i>Sophora flavescens</i>	Yellow sophora	Antitumour	56
<i>Allium sativum</i>	Garlic	Anticancer, Carminative, Expectorant, Stimulant, Disinfectant, Antihypertensive	57
<i>Solanum lycopersicum</i>	Tomato	Anticancer	58

Plant name	Ayurvedic/common name	Anticancer and other beneficial effect in traditional medicine	Reference
<i>Leucaena leucocephala</i>	White leadtree	Anticancer	59
<i>Annonia reticulata</i>	Vanya Kahu	Antiproliferative	60
<i>Chlorophytum borivilianum</i>	Safed musli	Antiproliferative	61
<i>Rhodola imbricata</i>	Rose root	Antioxidant, Anticancer	62
<i>Ipomoea batatas</i>	Shakarkand	Cancerchemoprotective	63
<i>Hygrophila spinosa</i>	Gokulakanta	Anticancer	64

of papillomas were found to be higher in the carcinogen treated control (without ASE treatment) as compared to experimental animals (ASE treated).<sup>[1]</sup>

### Pipper nigrum

The first stereoselective total synthesis of new natural amide alkaloids 1-3 have been achieved from commercially available starting materials. Wittig olefination, Sharpless asymmetric dihydroxylation, epoxidation, a trans regioselective opening of 2,3-epoxy alcohol, Horner-Wadsworth-Emmons (HWE) olefination and amide coupling are the key steps. The amide alkaloids 1-3 are evaluated for their anticancer activity against colon (HT-29), breast (MCF-7) and lung (A-549) human cancer cell lines for the first time.<sup>[2]</sup>

### Withania somnifera

Ashwagandha is an Ayurvedic shrub that forms a common ingredient of health supplements, tonics, and Indian home remedies designed to promote health and quality of life. Though sustained through experience and history, there are only a limited laboratory studies and experimental evidence to its effects. In our efforts to characterize Ashwagandha activities and their molecular mechanisms, we initially prepared leaf extract of Ashwagandha (i-Extract) that showed tumor-inhibitory activity. In the present study, we demonstrate that a major component of i-Extract and withanone (i-Factor) protected the normal human fibroblasts against the toxicity caused by withaferin A. We report here the isolation, structure elucidation, and biological properties of this compound, which showed good anti-inflammatory and anticancer activities.<sup>[3]</sup>

### Cymbopogon flexuosus

The essential oil from a lemon grass variety of *Cymbopogon flexuosus* was studied for its *in vitro* cytotoxicity against twelve human cancer cell lines. The *in vivo* anticancer activity of the oil was also studied using both solid and ascitic Ehrlich and Sarcoma-180 tumor models in mice. In addition, the morphological changes in tumor cells were studied to ascertain the mechanism of cell death.<sup>[4]</sup>

### Saussurea lappa

The dried roots of *Saussurea lappa*, called costus roots, are used in the traditional system of medicine for the treatment of cancer. In our investigation for the anticancer constituents

from the hexane extract of this plant, a new sesquiterpene was isolated along with the known compounds costunolide, beta-cyclocostunolide, dihydro costunolide and dehydro costuslactone.<sup>[5]</sup>

### Andrographis paniculata

Herbal medicines are now attracting attention as potential sources of anticancer agents. *Andrographis paniculata* is a traditionally used anticancer herb in Indian and Chinese herbal medicine. Phytochemical investigation of the ethanol extract of the aerial parts of this herb resulted in the isolation of 14 compounds including flavonoids and labdane diterpenoids. This is the first isolation of compounds from a natural source, and the aerial parts of *A. paniculata* are a rich source for the molecule andrographolide (9, 1.375%, w/w).<sup>[6]</sup>

### Tanacetum gracile

The essential oil of *Tanacetum gracile* (Accession no. AT-01 termed AT-01 in the manuscript), a cold desert alpine highly aromatic herb, has 40 constituents including lavendulol (21.5%), lavendulol acetate (1.7%), alpha-pinene (11.2%), 1,8-cineole (15.2%), CIS-beta-ocimene (6.9%), borneol (6.1%), limonene (5.1%) and chamazulene (3.7%). AT-01 was evaluated for its anticancer activity. It inhibited HL-60 cell proliferation with an IC (50) of 27 microg/mL.<sup>[7]</sup>

### Abrus agglutinin

In our previous study, *Abrus agglutinin* showed antitumor activity both native and heat-denatured condition in mouse model. The purpose of this study is to explore the presence of anticancer peptide in agglutinin, and to elucidate the mechanism of its activity *in vitro*. A tryptic digested *Abrus agglutinin* peptide fractions obtained from 10-kDa molecular weight cut off membrane permeate (10 kMPP), was found to have selective antiproliferative activity (1-10 microg/ml) on several tumor cell lines *in vitro* without having any cytotoxic effect on normal cell lines with dose of 100 microg/ml.<sup>[8]</sup>

### Curcuma longa

Turmeric, derived from the plant *Curcuma longa*, is a gold-colored spice commonly used in the Indian subcontinent, not only for health care but also for the preservation of food and as a yellow dye for textiles. Since the time of Ayurveda (1900 Bc) numerous therapeutic activities have

been assigned to turmeric for a wide variety of diseases and conditions, including those of the skin, pulmonary, and gastrointestinal systems, aches, pains, wounds, sprains, and liver disorders.<sup>[9]</sup>

### Saussurea costus

*Saussurea costus* (Falc.) Lipschitz, *Saussurea lappa* C.B. Clarke is a well known and important medicinal plant widely used in several indigenous systems of medicine for the treatment of various ailments, viz. asthma, inflammatory diseases, ulcer and stomach problems. Sesquiterpene lactones have been reported as the major phytoconstituents of this species.<sup>[10]</sup>

### Crocus sativus

The primary goal of this study was to propose saffron as a sustainable substitute crop with high added value in some Moroccan agricultural areas with low and erratic rainfalls, for their socio-economical development.<sup>[11]</sup>

### Ficus benghalensis

This review explores medieval, ancient and modern sources for ethnopharmacological uses of *Ficus* species, specifically for employment against malignant disease and inflammation. The close connection between inflammatory/infectious and cancerous diseases is apparent both from the medieval/ancient merging of these concepts and the modern pharmacological recognition of the initiating and promoting importance of inflammation for cancer growth. Also considered are chemical groups and compounds underlying the anticancer and anti-inflammatory actions, the relationship of fig wasps and fig botany, extraction and storage of fig latex, and traditional methods of preparing fig medicaments including fig lye, fig wine and medicinal poultices.<sup>[12]</sup>

### Calotropis procera

Despite significant progress in oncology therapeutics in the last decades, the urge to discover and to develop new, alternative or synergistic anti-cancer agents still remains. For centuries it has been known that the coarse shrub *Calotropis procera* is a very promising source of ascaricidal, schizonticidal, anti-bacterial, anthelmintic, insecticidal, anti-inflammatory, anti-diarrhoeal, larvicidal and cytotoxic chemicals. Different compounds like norditerpenic esters, organic carbonates, the cysteine protease procerain, alkaloids, flavonoids, sterols as well as numerous types of cardenolides have provided this plant for centuries with scientist's interest inducing activities.<sup>[13]</sup>

### Cassia auriculata

The *in vitro* anti-cancer effect of *Cassia auriculata* leaf extract (CALE) was evaluated in human breast adenocarcinoma MCF-7 and human larynx carcinoma Hep-2 cell lines. CALE preferentially inhibited the growth of both the cell lines in

a dose-dependent manner with IC<sub>50</sub> values of 400 and 500 µg for MCF-7 and Hep-2 cells, respectively. The results showed the anti-cancer action is due to nuclear fragmentation and condensation, associated with the appearance of A<sub>0</sub> peak in cell cycle analysis that is indicative of apoptosis.<sup>[14]</sup>

### Punica granatum

The last 7 years have seen over seven times as many publications indexed by Medline dealing with pomegranate and *Punica granatum* than in all the years preceding them. The use of juice, peel and oil have also been shown to possess anticancer activities, including interference with tumor cell proliferation, cell cycle, invasion and angiogenesis. The phytochemistry and pharmacological actions of all *Punica granatum* components suggest a wide range of clinical applications for the treatment and prevention of cancer, as well as other diseases where chronic inflammation is believed to play an essential etiologic role.<sup>[15]</sup>

### Carica papaya

Aim of the study various parts of *Carica papaya* Linn. CP have been traditionally used as ethnomedicine for a number of disorders, including cancer. There have been anecdotes of patients with advanced cancers achieving remission following consumption of tea extract made from CP leaves. However, the precise cellular mechanism of action of CP tea extracts remains unclear.<sup>[16]</sup>

### Capsicum annum

We have demonstrated a synergy between a decaffeinated green tea concentrate and a vanilloid-containing *Capsicum* preparation obtained commercially. At a ratio of 25 parts green tea concentrate to 1 part *Capsicum* preparation, the resultant product exhibited efficacy in the killing of cancer cells in culture 100-times that of green tea on a weight basis. The activity of the protein target was inhibited by the tea catechins and the *Capsicum vanilloids*. As with growth, the tea and *Capsicum* preparations evaluated were synergistic in their inhibition of the target enzymatic activity.<sup>[17]</sup>

### Vernonia amygdalina

Evidence suggests that most chemotherapeutic agents are less effective as treatment in patients with estrogen receptor-negative (ER-) breast carcinomas compared to those with estrogen receptor-positive (ER+) breast carcinomas. Moreover, African American Women (AAW) is disproportionately diagnosed with ER- breast cancer compared to their white counterparts. Novel therapies effective against ER- breast carcinomas are urgently needed to ameliorate the health disparity. Previous reports show that low concentrations (microgram/ml) of water-soluble leaf extracts of a Nigerian edible plant, *V. amygdalina* (VA), potently retards the proliferative activities of ER+ human breast cancerous cells (MCF-7) *in vitro* in a concentration-dependent fashion.<sup>[18]</sup>

### Vitis vinifera

Grapes and grape extracts were compared for inhibition of a growth-related and cancer-specific form of cell surface NADH oxidase with protein disulfide-thiol interchange activity designated tNOX from human cervical carcinoma (HeLa) cells and growth of HeLa and mouse mammary 4T1 cells in culture and transplanted tumors in mice. Grapes and grape extracts of several varieties had activity. The grape extracts interacted, often synergistically, with decaffeinated green tea extracts both in the inhibition of tNOX activity and in the inhibition of cancer cell growth.<sup>[19]</sup>

### Ziziphus jujuba

Herbs have always been the natural form of medicine in India. Medicinal plants have curative properties due to presence of various complex chemical substances of different composition which contain secondary metabolites such as alkaloids, flavonoids, terpenoids, saponin and phenolic compounds distributed in different parts of the plants. *Ziziphus jujuba* Mill, a member of the family Rhamnaceae, commonly known as Bor, is used traditionally as tonic and aphrodisiac and sometimes as Hypnotic-sedative and Anxiolytic, anticancer (Melanoma cells), Antifungal, Antibacterial, Antiulcer, Anti-inflammatory, Cognitive, Antispastic, Antifertility/contraception, Hypotensive and Antinephritic, Cardiotoxic, Antioxidant, Immunostimulant, and Wound healing properties.<sup>[20]</sup>

### Passiflora incarnata

In our country, more than 2000 medicinal plants have been recognized. *Passiflora incarnata* (Passifloraceae; passion flower Family) is an important medicinal plant of tropical and subtropical India. Its medicinal usage has been reported in the traditional systems of medicine such as Ayurveda, Siddha and Unani. *P. incarnata* has been described as a passion flower and has been used extensively for treatment of some diseases like as anxiety, insomnia, convulsion, sexual dysfunction, cough and cancer. The present article including the detailed exploration of phyto-pharmacological properties of *P. incarnata* is an attempt to provide a direction for further research.<sup>[21]</sup>

### Emblia officinalis

Aqueous extract of *Emblia officinalis* (E.O) was found to be cytotoxic to L 929 cells in culture in a dose dependent manner. Concentration needed for 50% inhibition was found to be 16.5 µg/ml. E.O and chyavanaprash (a non-toxic herbal preparation containing 50% E.O) extracts were found to reduce ascites and solid tumours in mice induced by DLA cells. Animals treated with 1.25 g/kg b.wt. of E.O extract increased life span of tumour bearing animals (20%) while animals treated with 2.5 g/kg b.wt. of chyavanaprash produced 60.9% increased in the life span. Both E.O and chyavanaprash significantly reduced the solid tumours.<sup>[22]</sup>

### Poncirus trifoliata

Recently several plant derived natural compounds have been screened for their anticancer activity in order to identify putative compounds with novel structures or mechanism of action. In the present study, fruits of *Poncirus trifoliata* were extracted with acetone and loaded onto silica gel column chromatography. The column was eluted with different solvents to obtain two bioactive compounds. The purity of compounds was analyzed by HPLC and their structures were identified by <sup>1</sup>H and <sup>13</sup>C NMR experiments as β-sitosterol and 2-hydroxy-1,2,3-propanetricarboxylic acid 2-methyl ester (HPCME). β-Sitosterol, HPCME, and trolox were tested for their antioxidant capacity by oxygen radical absorbance capacity (ORAC) measurement. Growth inhibition assay suggested the potential use of bioactive compounds as cancer chemopreventive and therapeutic agents. This is the first report on HPCME isolation and identification from Rutaceae family and β-sitosterol from *P. trifoliata*.<sup>[23]</sup>

### Hedychium spicatum

Phytochemical investigation of CHCl<sub>3</sub> extract of the rhizomes of *Hedychium spicatum* led to the isolation of two new labdane-type diterpenes, compounds **1** and **2** along with five known compounds (**3-7**). Their structures were established on the basis of NMR (1D and 2D) and mass spectroscopic analysis. In addition, all the isolates were tested for their cytotoxicity against the Colo-205 (Colo-cancer), A-431 (skin cancer), MCF-7 (breast cancer), A-549 (lung cancer) and Chinese hamster ovary cells (CHO). Two new compounds **1** and **2** were shown good cytotoxic activity.<sup>[24]</sup>

### Cynodon dactylon

The present study was aimed at evaluating the chemopreventive property of *Cynodon dactylon*. The antioxidant, antiproliferative and apoptotic potentials of the plant were investigated by 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay, nitric oxide radical scavenging activity (NO<sup>-</sup>) and MTT assay on four cancer cell lines (COLO 320 DM, MCH-7, AGS, A549) and a normal cell line (VERO). *In vivo* chemopreventive property of the plant extract was studied in DMH-induced colon carcinogenesis. The methanolic extract of *C. dactylon* was found to be antiproliferative and antioxidative at lower concentrations and induced apoptotic cell death in COLO 320 DM cells. The present investigation revealed the anticancer potential of methanolic extract of *C. dactylon* in COLO 320 DM cells and experimentally induced colon carcinogenesis in rats.<sup>[25]</sup>

### Tabernaemontana divaricata

In the present investigation, the cytotoxic, hydroxyl radical scavenging and topoisomerase inhibition activities of *Tabernaemontana divaricata* (Apocynaceae) were evaluated.

The extracts from leaves of the plant were prepared with different solvents viz. chloroform, methanol, ethyl acetate and hexane. In, *in vitro* cytotoxicity assay, with cell lines viz HCT-15 (Colon), HT-29 (Colon), 502713 (Colon), MCF-7 (Breast), PC-3 (Prostate), it was observed that the ethyl acetate extract was effective against only one colon cell line (502713) at the lowest dose i.e. 10 µg/ml, whereas the chloroform extract was effective against all the three colon cancer cell lines, at 30 µg/ml. In order to evaluate the mechanism of cytotoxicity of these extracts, they were assessed for their ability to scavenge hydroxyl radicals in plasmid nicking assay with pBR322.<sup>[26]</sup>

### **Nigella sativa**

Aim of the study *Nigella sativa*, also known as blackseed, has long been used in traditional medicine for treating various conditions related to the respiratory and gastrointestinal systems as well as different types of cancers. In this study, the potential immunomodulatory effects of *Nigella sativa* are investigated in light of splenocyte proliferation, macrophage function, and NK anti-tumor activity using BLAB/c and C57/BL6 primary cells.<sup>[27]</sup>

### **Zingiber officinalis**

Ginger, the rhizome of *Zingiber officinalis*, one of the most widely used species of the ginger family, is a common condiment for various foods and beverages. Ginger has a long history of medicinal use dating back 2500 years. Ginger has been traditionally used from time immemorial for varied human ailments in different parts of the globe, to aid digestion and treat stomach upset, diarrhoea, and nausea. Some pungent constituents present in ginger and other zingiberaceous plants have potent antioxidant and anti-inflammatory activities, and some of them exhibit cancer preventive activity in experimental carcinogenesis. The anticancer properties of ginger are attributed to the presence of certain pungent vallinoids, viz. [6]-gingerol and [6]-paradol, as well as some other constituents like shogaols, zingerone etc.<sup>[28]</sup>

### **Berberis vulgaris**

Berberine, an isoquinoline plant alkaloid, is widely distributed in plant used in the traditional Chinese medicine. It displays a wide range of biological activities and the mechanism of action. Our previous studies of the anticancer activity of berberine against the cancer cell lines HeLa and L1210 were extended to the human tumour U937 cell line and the murine melanoma B16 cell line growing *in vitro*. Berberine acted cytotoxically on both tumour cell lines. The melanoma B16 cells were much more sensitive to berberine treatment than the U937 cells. The value of  $IC_{100}$  was below 100 µg/ml for the U937 cells and below 1 µg/ml for the B16 cells. As for both cell lines under the long-term influence the values of  $IC_{50}$  were found to be less than 4 µg/ml. No effect

of berberine on the cell cycle profile of the U937 and B16 cells was detected.<sup>[29]</sup>

### **Sauromatum venosum**

A new lectin with the potent mitogenic and *in vitro* anti-proliferative activity was isolated from the tubers of a wild monocotyledonous plant *Sauromatum venosum* (Schott), from the family Araceae. The apparent native molecular mass of *S. venosum* lectin (SVL), as determined by gel filtration chromatography, was 54 kDa. In HPLC, size exclusion and cation exchange chromatography, SVL gave a single peak and also a single band of 13.5 kDa in SDS-PAGE, pH 8.3, under reducing and non-reducing conditions, indicating that the lectin is composed of four identical subunits. The amino acid composition showed that lectin contained a high amount of aspartic acid and glycine but totally devoid of cysteine. However, trace amounts of methionine was present. The lectin showed a potent mitogenic response towards BALB/c splenocytes and human lymphocytes. This lectin is endowed with proliferation of T cells as revealed by IL-2 bioassay but showed no production of immunoglobulins thus indicating the non-stimulation of B cells. SVL significantly inhibited the proliferation of murine cancer cell-lines. Thus the anti-proliferative ability of SVL may be helpful in identification of new lectin probes that can lead to better understanding in the detection and study of certain types of cancer.<sup>[30]</sup>

### **Eulophianuda nuda**

Ethnopharmacological relevance *Eulophia nuda* L. (Orchidaceae) is a medicinally important terrestrial orchid used for the treatment of tumours and various health problems by the local healers throughout the Western Ghats region in Maharashtra (India).<sup>[31]</sup>

### **Ipomoea bahiensis**

Four new antimicrobial glycosides have been isolated from *Ipomoea bahiensis*. Spectroscopic properties and basic and acidic hydrolysis characterized them as derivatives of 11-hydroxy hexadecanoic and 11-hydroxy tetradecanoic acid, glycosidically linked in the 11-position to a trisaccharide unit composed of glucose, rhamnose and fucose which is esterified by tiglic and 3-hydroxy-2-methylbutyric acid. One of these compounds revealed significant activity against Sarcoma 180 in mice.<sup>[32]</sup>

### **Mangifera indica**

The antioxidant and antiproliferative properties of flesh and peel of mango (*Mangifera indica* L.) were investigated. The cytoprotective effect of mango flesh and peel extracts on oxidative damage induced by  $H_2O_2$  in a human hepatoma cell line, HepG2, were determined, and the underlying mechanism was examined by a single-cell electrophoresis assay (comet assay). Treatment of HepG2 cell with mango peel extract prior to oxidative stress was found to inhibit

DNA damage. Thus, mango peel, a major by-product obtained during the processing of mango product, exhibited good antioxidant activity and may serve as a potential source of phenolics with anticancer activity.<sup>[33]</sup>

### **Podophyllum emodi**

This review deals with the historical discovery of particularly important lignan derivatives used in cancer chemotherapy. From isolation of the naturally occurring podophyllotoxin, an inhibitor of microtubule assembly, to hemisynthesis of the clinically important anticancer drugs etoposide and teniposide, it will be demonstrated how the activities and the ability of this class of compounds to inhibit topoisomerase II were discovered by different research teams. By virtue of these discoveries, new hemisynthetic derivatives, with different mechanisms of action, are bringing improvements in the ability to treat cancer.<sup>[34]</sup>

### **Polyalthia longifolia**

*Polyalthia longifolia* is a lofty evergreen tree found in India and Sri Lanka. We are reporting first time the anticancer potential of *P. longifolia* leaves extract (A001) and its chloroform fraction (F002). Both inhibited cell proliferation of various human cancer cell lines in which colon cancer cells SW-620 showed maximum inhibition with IC<sub>50</sub> value 6.1 µg/ml. Furthermore, F002 induce apoptosis in human leukemia HL-60 cells as measured by several biological end points. F002 induce apoptotic bodies formation, DNA ladder, enhanced annexin-V-FITC binding of the cells, increased sub-G<sub>0</sub> DNA fraction, loss of mitochondrial membrane potential, release of cytochrome c, activation of caspase-9, caspase-3, and cleavage of poly ADP ribose polymerase (PARP) in HL-60 cells. All the above parameters revealed that F002-induced apoptosis through the mitochondrial-dependent pathway in HL-60 cells.<sup>[35]</sup>

### **Tinospra cordifolia**

Exposure of HeLa cells to 0, 5, 10, 25, 50 and 100 µg/ml of guduchi extracts (methanol, aqueous and methylene chloride) resulted in a dose-dependent but significant increase in cell killing, when compared to non-drug-treated controls. The effects of methanol and aqueous extracts were almost identical. However, methylene chloride extract enhanced the cell killing effect by 2.8- and 6.8-fold when compared either to methanol or aqueous extract at 50 and 100 µg/ml, respectively. Our results demonstrate that guduchi killed the cells very effectively *in vitro* and deserves attention as an antineoplastic agent.<sup>[36]</sup>

### **Bauhinia variegata**

The antitumour activity of the ethanol extract of *Bauhinia variegata* (EBV) has been evaluated against Dalton's ascitic lymphoma (DAL) in Swiss albino mice. A significant enhancement of mean survival time of EBV-treated tumour

bearing mice was found with respect to control group. EBV treatment was found to enhance peritoneal cell counts. After 14 days of inoculation, EBV is able to reverse the changes in the haematological parameters, protein and PCV consequent to tumour inoculation.<sup>[37]</sup>

### **Thea sinensis**

We investigated the anticancer effects of green and black tea polyphenols alone and in combination with bovine milk lactoferrin (bLF) on human tongue squamous carcinoma (CAL-27) and normal human gingival fibroblast (HGF) cells. Both green (Polyphenon-E;P-E) and black tea polyphenols (Polyphenon-B;P-B) preferentially inhibit the growth of CAL-27 cells in a dose-dependent manner. Based on the IC<sub>50</sub> values, P-E was found to be more effective than P-B and the combination of P-E and bLF (1:2 ratio) exhibited synergistic inhibition of CAL-27 cells.<sup>[38]</sup>

### **Phyllanthus amarus**

This study deals with establishment of hairy root cultures of *Phyllanthus amarus* using *Agrobacterium rhizogenes* and cytotoxic effects of methanolic extract of hairy roots on human adenocarcinoma cell line, MCF-7. The hairy root extract displayed a linear concentration- and time-dependent cytotoxicity. Further, increased concentration of the root extract showed an increase in the percent apoptotic cells from 26% to 36% as determined by annexin V-FITC and propidium iodide.<sup>[39]</sup>

### **Bidens pilosa**

Aim of the study *Bidens pilosa* (L.) (Asteraceae) is a medicinal plant traditionally used in Brazil for treating conditions that can be related to cancer. Therefore the present study was carried out to evaluate the antitumor activity of extracts obtained from the aerial parts of this plant species.<sup>[40]</sup>

***Solanum nigrum*:** Plants are used worldwide for the treatment of diseases, and novel drugs continue to be developed through research from plants. It possesses antiviral, anti-inflammatory, and analgesic effects. Also, *Solanum nigrum* has been used as a diuretic and an antipyretic agent and it has also been used to cure inflammation, edema, mastitis and hepatic cancer. In this investigation, cytotoxicity of specific concentrations of hydro-alcoholic extracts of *C. pepo* and *S. nigrum* was studied on normal [Chinese hamster ovarian cells (CHO) and rat fibroblast] and cancer (HepG2 and CT26) cell lines.<sup>[41]</sup>

### **Vinca rosea**

The novel third-generation bifluorinated semisynthetic vinca alkaloid, vinflunine, is a microtubule inhibitor that shows superior antitumor activity and a favorable safety profile compared with other vinca alkaloids. The main antineoplastic effects of vinflunine arise from its interaction with tubulin,

the major component of microtubules in mitotic spindles. Vinflunine is known to have low affinity for tubulin, high intracellular accumulation, and important effects on microtubule dynamics. It has been shown to have activity against transitional cell carcinoma of the urothelial tract.<sup>[42]</sup>

### **Eurycoma longifolia**

Twenty-four quassinoids isolated from *Eurycoma longifolia* Jack were investigated for their cytotoxicity against a panel of four different cancer cell lines, which includes three murine cell lines [colon 26-L5 carcinoma (colon 26-L5), B16-BL6 melanoma (B16-BL6), Lewis lung carcinoma (LLC)] and a human lung A549 adenocarcinoma (A549) cell line. Among the tested compounds, eurycomalactone (9) displayed the most potent activity against all the tested cell lines; colon 26-L5 (IC<sub>50</sub> = 0.70 microM), B16-BL6 (IC<sub>50</sub> = 0.59 microM), LLC (IC<sub>50</sub> = 0.78 microM), and A549 (IC<sub>50</sub> = 0.73 microM). These activities were comparable to clinically used anticancer agent doxorubicin (colon 26-L5, IC<sub>50</sub> = 0.76 microM; B16-BL6, IC<sub>50</sub> = 0.86 microM; LLC, IC<sub>50</sub> = 0.80 microM; A549, IC<sub>50</sub> = 0.66 microM).<sup>[43]</sup>

### **Coptidis rhizoma**

Coptidis Rhizoma (*Huanglian*) and its major component, berberine, have drawn extensive attention toward their antineoplastic effects in the recent years. The antineoplastic effects are related to the Chinese Medicine (CM) properties of Huanglian in treating diseases by removing *damp-heat* and purging *fire* and counteracting toxicity.<sup>[44]</sup>

### **Ximenia americana**

The antineoplastic activity of a plant powder used in African traditional medicine for treating cancer was investigated by analyzing the activity of various extracts *in vitro*. The most active, aqueous extract was subsequently subjected to a detailed investigation in a panel of 17 tumor cell lines, showing an average IC<sub>50</sub> of 49 mg raw powder/ml medium. The sensitivity of the cell lines varied by two orders of magnitude, from 1.7 mg/ml in MCF7 breast cancer cells to 170 mg/ml in AR230 chronic-myeloid leukemia cells.<sup>[45]</sup>

### **Eruca sativa**

Eruucin (ER) is a dietary isothiocyanate present in cruciferous vegetables, such as rocket salads (*Eruca sativa* Mill., *Diplotaxis* sp.), that has been recently considered a promising cancer chemopreventive phytochemical. Biological activity of ER was investigated on human lung adenocarcinoma A549 cells, analyzing its effects on molecular pathways involved in apoptosis and cell cycle arrest, such as PARP-1 cleavage, p53 and p21 protein expression.<sup>[46]</sup>

### **Podophyllum hexandrum**

Polymer-linked (podophyllotoxin) conjugates have been designed to improve the therapeutic efficacy of PT. A new

PT-conjugate, 3,6-*endo*-methylene-1,2,3,6-tetrahydrophthalimido-acetamidoglycylglycine podophyllotoxin ester (ETPA-gly-gly-PT), was synthesized by covalently coupling its hydroxyl group onto the phthalimido monomer through a glycine-glycine-glycine spacer. Its homo- and copolymer with acrylic acid (AA) were prepared by photopolymerization using 2,2-dimethoxy-2-phenylacetophenone (DMP) as a photoinitiator. The *in vitro* antitumor activity of these conjugates and polymers were determined and used to evaluate the potential applications in antitumor drugs. The IC<sub>50</sub> values indicated that the synthesized ETPA-gly-gly-PT and its polymers against cancer cells were much better inhibitors than PT.<sup>[47]</sup>

### **Taxus bacata**

The taxanes, paclitaxel and docetaxel are microtubule-stabilizing agents that function primarily by interfering with spindle microtubule dynamics causing cell cycle arrest and apoptosis. However, the mechanisms underlying their action have yet to be fully elucidated. These agents have become widely recognized as active chemotherapeutic agents in the treatment of metastatic breast cancer and early-stage breast cancer with benefits gained in terms of overall survival (OS) and disease-free survival (DFS). overexpression of the drug efflux pump MDR-1/P-gp, altered expression of microtubule-associated proteins (MAPs) including tau, stathmin and MAP4 may help to identify those patients who are most at risk of recurrence and those patients most likely to benefit from taxane treatment.<sup>[48]</sup>

### **Cedrus deodara**

AP9-cd, a standardized lignan composition from *Cedrus deodara* consisting of (-)-wikstromal, (-)-matairesinol, and dibenzyl butyrolactol, showed cytotoxicity in several human cancer cell lines reported earlier. An attempt was made in this study to investigate the mechanism of cell death in human leukemia Molt-4 and HL-60 cells. It inhibited Molt-4 cell proliferation with 48-h IC<sub>50</sub> of ~15 µg/ml, increased sub-G0 cell fraction with no mitotic block, produced apoptotic bodies and induced DNA ladder formation.<sup>[49]</sup>

### **Podophyllum hexandrum**

It has been hypothesized that cancer stem cell is responsible for the refractoriness of glioblastoma therapy. This study is to observe the influence of Etoposide on anti-apoptotic and multidrug resistance-associated protein genes in glioblastoma stem-like cells. U251 glioblastoma cells were cultured and CD133 positive cancer stem-like cells were isolated and identified. After Etoposide intervention glioblastoma stem-like cells showed a stronger resistance to apoptosis and death, and the anti-apoptotic gene livinβ was more related with the high survival rate and MRP1 appeared to be more related with transporting chemotherapeutics out of glioblastoma stem-like cells.<sup>[50]</sup>



### Scutellaria baicalensis

Traditional Chinese medicines have been recently recognized as a new source of anticancer drugs and new chemotherapy adjuvant to enhance the efficacy of chemotherapy and to ameliorate the side effects of cancer chemotherapies however their healing mechanisms are still largely unknown. *Scutellaria baicalensis* is one of the most popular and multi-purpose herb used in China traditionally for treatment of inflammation, hypertension, cardiovascular diseases, and bacterial and viral infections. Accumulating evidence demonstrate that *Scutellaria* also possesses potent anticancer activities. The bioactive components of *Scutellaria* have been confirmed to be flavones. The major constituents of *Scutellaria baicalensis* are Wogonin, Baicalein and Baicalin. These phytochemicals are not only cytostatic but also cytotoxic to various human tumor cell lines *in vitro* and inhibit tumor growth *in vivo*. The antitumor functions of these flavones are largely due to their abilities to scavenge oxidative radicals, to attenuate NF- $\kappa$ B activity, to inhibit several genes important for regulation of the cell cycle, to suppress COX-2 gene expression and to prevent viral infections.<sup>[51]</sup>

### Salybum marianum

Natural compounds play a key role in the cancer prevention and treatment. Among them stilbene-based compounds are widely distributed in nature and show a wide range of biological activities. Certain poly-hydroxylated *cis*-stilbenes and their analogues bind in the colchicin site of tubulin and inhibit cancer cell proliferation. Up-to-now the most promising of these compounds is combretastatin A-4 (*cis*-3,4,4',5-tetramethoxy-3'-hydroxy stilbene) which has been shown to cause mitotic arrest in a variety of cancer cell lines, including multi-drug-resistant ones, and has also demonstrated cancer antiangiogenic properties.<sup>[52]</sup>

### Panax ginseng

Our previous studies demonstrated that KG-135, a quality-controlled red ginseng-specific formulation containing approximately equal amounts of three major ginsenosides (Rk1, Rg3 and Rg5), down-regulated G1 cyclin-dependent kinase in HeLa cells. In the present work, we have found that KG-135 potentiates cytotoxicity of etoposide by modulating apoptotic signaling. Co-treatment of etoposide and KG-135 markedly elevated the expression and phosphorylation at the serine 15 residue of p53 as well as the cellular levels of Bax and p21<sup>Waf1/Cip1</sup>. The increased accumulation and phosphorylation of p53 (Ser15) were attenuated by treatment of cells with wortmannin, a pan-phosphatidylinositol-3 kinase inhibitor.<sup>[53]</sup>

### Cynara cardunculus

Sixteen edible plants from Southern Italy were evaluated for their *in vitro* antiproliferative properties, using the

sulforodamine B (SRB) assay, on four human cancer cell lines: breast cancer MCF-7, prostate cancer LNCaP, amelanotic melanoma C32 and renal adenocarcinoma ACHN. After 48 h of incubation the most antiproliferative plant extract was *Cynara cardunculus* ssp. *cardunculus* on C32 and ACHN cell lines with IC<sub>50</sub> of 21 and 18  $\mu$ g/ml, respectively. *Mentha aquatica* showed a selective antiproliferative activity on breast cancer while significant activity was exerted by *Cichorium intybus* on melanoma. These species contained the highest amount of phenolics.<sup>[54]</sup>

### Radix sophorae

The Chinese herbal medicine *Radix Sophorae* is widely applied as an anti-carcinogenic/anti-metastatic agent against liver cancer. In this study, Leachianone A, isolated from *Radix Sophorae*, possessed a profound cytotoxic activity against human hepatoma cell line HepG2 *in vitro*, with an IC<sub>50</sub> value of 3.4  $\mu$ g/ml post-48-h treatment. Its action mechanism via induction of apoptosis involved both extrinsic and intrinsic pathways. Its anti-tumor effect was further demonstrated *in vivo* by 17-54% reduction of tumor size in HepG2-bearing nude mice, in which no toxicity to the heart and liver tissues was observed. In conclusion, this is the first report describing the isolation of Leachianone A from *Radix Sophorae* and the molecular mechanism of its anti-proliferative effect on HepG2 cells.<sup>[55]</sup>

### Sophora flavescens

The objective of this study was to investigate the anti-tumor activity of a lectin from *Sophora flavescens* and explore its potential apoptotic induction mechanism. Here, an elegant series of biochemical and cell biology methods were carried out in a sequential procedure (e.g., MTT, cell morphologic changes and LDH assays, DNA ladder as well as flow cytometric assay). As a result, we found that this lectin shows a strong cytotoxicity against HeLa cells and induces apoptosis in a time- and dose-dependent manner. Subsequently, according to caspase inhibition and Western blot analysis, we further demonstrated that it is a typical caspase-dependent apoptotic mechanism.<sup>[56]</sup>

### Allium sativum

The reputation of garlic (*Allium sativum*) as an effective remedy for tumours extends back to the Egyptian Codex Ebers of 1550 B.C. Several garlic compounds including allicin and its corresponding sulfide inhibit the proliferation and induce apoptosis of several human non-leukaemia malignant cells including breast, bladder, colorectal, hepatic, prostate cancer, lymphoma and skin tumour cell lines. Ajoene (4,5,9-trithiadodeca-1,6,11-triene-9-oxide) is a garlic-derived compound produced most efficiently from pure allicin and has the advantage of a greater chemical stability than allicin. Ajoene was shown to inhibit proliferation and induce apoptosis of several human leukaemia CD34-negative cells

including HL-60, U937, HEL and OCIM-1. Also, ajoene induces 30% apoptosis in myeloblasts from chronic myeloid leukaemia patient in blast crisis. More significantly, ajoene profoundly enhanced the apoptotic effect of the two chemotherapeutic drugs: cytarabine and fludarabine in human CD34-positive resistant myeloid leukaemia cells through enhancing their bcl-2 inhibitory and caspase-3 activation activities.<sup>[57]</sup>

### Solanum lycopersicum

Epidemiologic studies suggested a protective effect of tomatoes against prostate cancer brought by lycopene, a carotenoid conferring the red colour of tomatoes. However, intervention studies on patients have shown that the preventive effect of tomato was more potent than that of lycopene. The aim of this study was to compare the effects of red tomato, yellow tomato (devoid of lycopene) and lycopene on Connexin43 (Cx43) expression, a protein regulating cell growth, on a prostate cancer cell line expressing the androgen receptor.<sup>[58]</sup>

**Leucaena leucocephala:** This work aimed to prove that simple chemical modification could provide new cancer chemopreventive and/or anticancer properties to the inactive extracted polysaccharide derived from *Leucaena leucocephala*. Unmodified crude extract was neither active as cancer chemopreventive nor as anti-proliferative. In conclusion, chemical modification of *Leucaena* gum induced its cancer chemopreventive and anti-proliferative activities.<sup>[59]</sup>

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