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Cancer—an ayurvedic perspective

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Abstract

An integrated approach is needed to manage cancer using the growing body of knowledge gained through scientific developments. Thousands of herbal and traditional compounds are being screened worldwide to validate their use as anti-cancerous drugs. The science of Ayurveda is supposed to add a step on to the curative aspects of cancers that have resemblance with clinical entities of *arbuda* and *granthi* mentioned in *Sushrutha samhita*. Hence, an attempt is made in this review to discuss about the pathology and therapeutic management of various cancers described in Ayurveda. Review of literature on anticancer drugs of plant origin revealed identification of newer ayurvedic drugs that are not mentioned in the ancient texts. These new findings add up to ayurvedic science that has been developed through ages. In addition, details of experimental and clinical studies conducted on single and compound ayurvedic preparations for their anticancer efficacy strongly emphasize ayurvedic therapy as a scientifically driven one and not simply unconventional.

Keywords: Cancer; Ayurveda; Treatment; Medicine; Herbal

1. Introduction

Cancer is one of the most dreaded diseases of the 20th century and spreading further with continuance and increasing incidence in 21st century. In the United States, as the leading cause of death, it accounts for 25% of all the deaths in humans presently. It is considered as an adversary of modernization and advanced pattern of socio-cultural life dominated by Western medicine. Multidisciplinary scientific investigations are making best efforts to combat this disease, but the sure-shot, perfect cure is yet to be brought into world medicine.

Recently, a greater emphasis has been given towards the researches on complementary and alternative medicine that deals with cancer management. Several studies have been conducted on herbs under a multitude of ethno botanical grounds. For example, Hartwell [1–9] has collected data on about 3000 plants, those of which possess anticancer properties and subsequently been used as potent anticancer drugs [10]. Ayurveda, a traditional Indian medicine of plant drugs has been successful from very early times in using these natural drugs and preventing or suppressing various tumours using various lines of treatment.

The broad aim of this article is to provide a general outline on descriptions of cancers and their management from an ayurvedic practitioners' perspective underlying its scientific principles involved in treating these conditions with the use of natural products. This article reviews the available literature regarding researches on anti-cancerous ayurvedic herbs and also includes a summary of treatment strategies for various cancers. It is written with an intention to raise awareness and encourage implementation of ayurvedic therapies for combating cancer and suggesting an integrated approach in tumour management and treatment.

1.1. Ayurvedic concept of cancer

Charaka [11] and *Sushruta* [12] samhitas, two well-known Ayurvedic classics, describe cancer as inflammatory or non-inflammatory swelling and mention them as either *Granthi* (minor neoplasm) or *Arbuda* (major neoplasm). Ayurvedic literature defines three body-control systems, viz., the nervous system (*Vata* or air), the venous system (*Pitta* or fire), and the arterial system (*Kapha* or water) which mutually coordinate to perform the normal function of the body. In benign neoplasm (*Vataja*, *Pittaja* or *Kaphaja*) one or two of the three bodily systems are out of control and is not too harmful because the body is still trying to coordinate among these systems. Malignant tumours (*Tridosaja*) are very harmful because all the three major bodily

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systems lose mutual coordination and thus cannot prevent tissue damage, resulting in a deadly morbid condition [12].

1.2. Fundamental classification

Ayurvedic classification of neoplasm depends on various clinical symptoms in relation to *Tridoshas*.

Group I: Diseases that can be named as clear malignancy, which includes *arbuda* and *granthi*, e.g. *mamsarbuda* (melanoma) and *raktarbuda* (leukaemia), *mukharbuda* (oral cancer), etc.

Group II: Diseases that can be considered as cancer, such as incurable ulcers with e.g. *tridosaj gulmas* (abdominal tumours like carcinomas of the stomach and liver or lymphomas).

Group III: Diseases with the possibility of malignancy, e.g. *Visarpa* (erysipelas), *asadhya kamala* (incurable jaundice) and *nadi vrana* (sinusitis) [13,14].

1.3. Etiology

According to *Sushruta*, the fundamental cause of major neoplasm is the pathogens that affect all parts of the body. He called the sixth layer of the skin as '*Rohini*,' (epithelium) and pathogenic injuries to this layer in muscular tissues and blood vessels caused by lifestyle errors, unhealthy foods, poor hygiene and bad habits results in the derangement of doshas, which leads to the manifestation of tumours [12,15]. Excess of water or fat in the corpus of the tumour and the stability and rigid confinement of the *doshas* in a particular place were described as reasons for the non-infectious and non-suppurative nature of these abnormal growths [12,16]. Cancer in each person differs according to the person's exposure to *pathogens* and genetic constitutions which make each of them to react differently to the same diet.

The factors responsible for the vitiation of *doshas* are discussed here [17].

a. *Vata aggravating factors*: excessive intake of bitter, pungent, astringent, dry foods and stressful conditions.
b. *Pitta aggravating factors*: excessive intake of sour, salty, fried foods and excessive anger.
c. *Kapha aggravating factors*: excessive intake of sweet, oily food and sedentary nature.
d. *Rakta aggravating factors*: excessive intake of acid or alkali containing foods. Fried and roasted foods, alcoholic beverages, sour fruits are some examples. Excessive anger or severe emotional upset, sunbathing or working under scorching sun or near fire and hot conditions, etc. are some other causes [11].
e. *Mamsa aggravating factors*: excessive use of exudative foods like meat, fish, yoghurt, milk and cream. Behaviours leading to exudation like sleeping during the day and overeating are some of the causes for pathogens invading the fatty tissues [11].
f. *Medo aggravating factors*: excessive intake of oily foods, sweets, alcohol and lazy attitude [11,12].

1.4. Pathogenesis of tumours

According to Ayurvedic principles, the disease cannot be named on its own because it differs between persons in terms of illness, clinical presentation and also the treatment required [14]. Thus, pathogenesis in Ayurveda is explained on the basis of *Tridoshas*. *Agni* or *Pitta*, which is present in each and every cell, is responsible for digestion and metabolism in human body. The decrease in *agni* is inversely proportional to the related tissue and therefore in *arbuda*, the decreased state of *dhatwagni* (deranged metabolism) will result in excessive tissue growth.

Vata can be correlated with the anabolic phase of growth whereas *kapha* to the catabolic phase. Cancer originates due to a metabolic crisis, i.e. aggravation of *vata* forces and suppression of *kapha* forces, both interacting with one another resulting in proliferation. However, the abnormal cancerous growth at a specific organ (*Ekadesavriddhi*) is managed by compensation from other parts of the body (*Anyasthaniyakshaya*), e.g. body weight loss (cachexia) [17]. *Sushruta* has proposed six stages in the pathogenesis of all diseases but his concept suits more to the pathology of the tumour than pathogenesis itself.

1. *Sanchaya*: early stages of localized neoplastic changes.
2. *Prakopa*: transformation of primary growths into metastatic tumours.
3. *Prasara*: metastasis.
4. *Sthana samsraya*: complete metastasis and secondary growth.
5. *Vyakti*: clinical signs and symptoms are expressed.
6. *Bheda*: the stage where differentiation of growth occurs on the basis of histopathology [17].

2. Cancer therapy—a practical dilemma

Any practical solution in combating this dreadful disease is of paramount importance. An alternative solution to western medicine embodied with severe side effects is the use of medicinal 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 tumouricidal actions against various cancers. Thus, cancer patients who already got crippled with this disease, 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. Ayurvedic therapy was found to be able to cure these chronic diseases better, which were previously not amenable to treatment by western medical practices. This traditional Indian medicine with its evolution through centuries has always fascinated practitioners and researchers for its applications

in cancer treatment on a scientifically proven research background.

2.1. Principles of ayurvedic treatment

Abuse of nature's law upsets the human system and ends up in disease like cancer. It is again the nature, the foremost physician who brings the cure. The Ayurvedic system of medicine was well founded on the basic principles of nature and its elements after a careful and thorough study of human physiology. This is the first system to emphasize health as the perfect state of physical, psychological, social and spiritual component of a human being.

The therapeutic approach of Ayurveda has been divided into four categories as *Prakritisthapani chikitsa* (health maintenance), *Roganashani chikitsa* (disease cure), *Rasayana chikitsa* (restoration of normal function) and *Naishthiki chikitsa* (spiritual approach) [18].

Finding the cause of an illness is the basic goal of ayurvedic therapy. It classifies disease development into six stages that include aggravation, accumulation, overflow, relocation, build-up in a new location, and manifestation into a recognizable disease. Ayurvedic physicians can diagnose an illness at even initial stages of body imbalance and their therapeutic approach maintains a balance by supplying deficient substances as well as reducing the excessive ones. Surgery is considered only for advanced cases.

2.2. Ayurvedic texts about cancer treatment

During the 7th century BC, Atreya and Dhanwantari used herbal medicines for treating the early stages of cancer and surgery in advanced cases. In the 8th century AD, Vagbhata, a Buddhist physician composed two texts: *Astanga Hrdaya* [19] and *Astanga sangraha* [20] where new methods for cancer treatment were introduced. Other Ayurvedic texts of internal medicine, viz., Chakradatta [21] composed by Chakrapani (10th century AD), the *Sarangadhara Samhita* [22] by Sarangadhara (14th century AD), the *Bhavaprakasha Samhita* [23] by Bhavamisra (15th century AD), the Satmya Darpan Samhita by Viswanath (16th century AD), the Vaisajya Ratnabali by Binoda Lala Sen Gupta (18th Century AD), the Rasatarangini by Sadananda Sharma (19th century AD), etc. explain numerous remedies to treat internal and external neoplasms.

2.3. Treatment modalities

Sodhana chikitsa (purification process), which eliminates vitiated *doshas*, have been primarily used for medical management of cancer. When both internal and external medications were given then it is called as *panchakarma chikitsa*. The other type of curative therapy is called *somana chikitsa*, which pacifies *dosha* and gradually relieves the disease. However, this treatment is prescribed only to weaker patients for whom *sodana chikitsa* is contraindicated. In *Rasayana prayoga* (immunotherapy), certain poisonous plants, mercury like metals and animal products were rendered non-toxic and harmless by the use of alchemy and are used as rejuvenating drugs. Other methods of treatment include, *dhatwagni chikitsa* (correction of metabolic defects), *vyadhipratyanika chikitsa* (specific anti-cancerous drugs) and *lakshanika chikitsa* (symptomatic treatment) [24].

When medical treatment practices fail, then the case was left to surgeons. Surgical cancer management in *Ayurveda* include the principles of fomentation by means of external application, cleansing by internal medication, treatment to liquefy the contents of the swelling, opening the tumour surgically for evacuation of its contents, cauterisation to avoid recurrence and post-operative care for healing the wound [15].

Cauterisation with alkalis and acids and other surgical procedures were performed with herbal and mineral medicines. *Arbuda* is excised completely from its deep root seat and cauterisation done to destroy any of the remaining cell particles [24].

2.4. Classical drugs claimed in ayurvedic texts

Traditional line of treatment: Traditional methods employed in treatment of various cancers were given in Table 1. In addition to these traditional methods, various herbal combinations mentioned in Ayurvedic texts are listed in Table 2. The main objective of these tables is to support the physicians and researchers to utilize these traditional methods as well as herbal drugs for an effective cancer treatment.

2.5. Scientific principles of Ayurvedic anticancer drugs

Herbal decoctions consisting of multiple herbs each possessing tremendous potential for a cancer cure are commonly used in Ayurveda. These formulations are reported to work on multiple biochemical pathways and are capable of influencing several organ systems simultaneously. The benefit of an herbal decoction is that it can nourish the body as a whole by supporting various organ systems [25]. Many of the herbs mentioned below have scientifically-proven anti-cancerous properties and are used for the treatment of various cancers.

2.6. Andrographis paniculata

The extract and isolated diterpenes (andrographiside and neoandrographolide) from this plant are proved to be beneficial against tumourigenesis by their anti-lipoperoxidative action and by enhanced carcinogen detoxification action [26–29].

2.7. Annona atemoya/muricata

Bullatacin, an acetogenin isolated from the fruit of *Annona atemoya*, induces apoptosis, preceded by chromatin margination and tumour cells condensation [30]. Several

Table 1
Classical treatment protocols for various tumours in Ayurveda

Type of tumour	Tumour subtypes	Classical treatment procedures
Granthi	*Vatika granthi*	*Helloborus niger*, *Tinospora cordifolia*, *Clerodendron serratum*, *Aegle marmelos*, *Hoya viridiflora*, *Elephantopus scaber*, *Soymida febrifuga* and *Gynandropis pentaphylla*were applied locally [16]
	Paittika granthi	*Terminalia chebula* powder *with* either grape or sugarcane juice were used orally. The paste of *Glycyrrhiza glabra*, *Eugenia jambolana*, *Terminalia arjuna* or *Calamus rotang* were used of external application [16]
	Kapaja granthi	Paste of *Capparis spinosa*, *Capparis sepiaria*, *Agati grandiflora*, *Lagenaria vulgaris*, *Premna herbacea*, *Pongamia glabra*, *Musa sapientum* and *Randia dumetorum* used in local application [16]
Arbuda	Classical procedures	Fomentations, cauterisation, scraping, blood letting, medicated enemata and other surgical procedures [17]
	Traditional treatment	Habitual intake of *Basella rubra* or application of alkali preparation of *Musa paradisiaca*, *Conch shell ash*, *Elaeocarpus tuberculatus*, *Sulphur*, *Potassium carbonate*, *Embelia ribes* and *ginger* were used to cure *arbuda* [16]
	Vataja arbuda	Paste of *Benincasa cerifera*, *Cucumis memordica*, *Cocos nucifera*, and *Eranda beeja*, *Ricinus communis* along with butter or milk were applied [65]
	Pittaja arbuda	Tumours were treated with leaves of *Ficus glomerata*, *Tectona grandis*, and *Elephantopus scaber* repeatedly and then with a honey mixed fine paste of *Aglaja roxburghiana*, *Caesalpinia sappa*, *Symplocos racemosa*, *Terminalia arjuna*, *Xanthium strumarium* was applied [16]
	Kaphaja arbuda	After surgical removal of tumour, a drug that remove doshas from both the ends (vomiting and purgation) were employed. Then for purification, a decoction of *Clitoria ternatea*, *Jasminum grandiflorum* and *Nerium odorum* leaves was used. For the postoperative care, oil cooked with *Premna herbacea*, *Embelia ribes*, *Cissampelos pareira* was applied
	Medoja arbuda	*Curcuma domestica*, *Triticum sativum*, *Symplocos racemosa*, etc. were made into a powder and applied externally by mixing them with honey. Oil from *Pongamia glabra* were used of internal administration [65]

Table 2
List of herbs commonly used in ayurvedic anticancer treatment

No.	Name of the herb	Method and use
1	*Vitis vinifera*	The mixture of *Terminalia chebula*, grape juice and *sugar cane juice* has been used (3). Resveratrol, a natural product derivative from grape juice has been proved to possess cancer chemopreventive activity [66]
2	*Baliospermum montanum*	The paste comprising of *Baliospermum montanum*, *Plumbago zeylanica*, *Euphorbia neriifolia*, *Calotropis procera*, jaggery, *Semecarpus anacardium* applied over the tumours [12]
3	*Madhuca indica*	This paste is prepared from the barks of *Madhuca indica*, *Syzygium cumini*, *arjuna Terminalia arjuna* and *Salix caprea* and prescribed for local application [12]
4	*Pandanus odoratissimum*	A paste of *Pandanus odoratissimum* with sugar was applied externally [12]
5	*Pterospermum acerifolium*	The flowers of *Pterospermum acerifolium* mixed with sugar to be applied locally
6	*Raphanus sativus*	Local application of *Raphanus sativus* powder paste with the radish ash was considered effective against *kaphaja arbuda*
7	*Barleria prionitis*	The *Barleria prionitis* oil prepared with whole plant is indicated for external application during acute stages of cyst in blood vessels [20]
8	*Prosopis cineraria*	This paste made up of *Prosopis cineraria* seeds, *Raphanus sativa*, *Moringa oleifera*, barley and mustard with sour buttermilk was applied locally for disintegrating cysts [20]
9	*Amorphopallus campanulatus*	The mature tuber is first burnt and then mixed with butter and jaggery and applied for tumour destruction [12]
10	*Oxoxylum indicum*	The drug *Oxoxylum indicum* prescribed in treatment of *granthi* [12]
11	*Basella rubra*	The plant and leaves are ground with sour buttermilk with salt for preparing a poultice and indicated for *arbuda* [12]
12	*Flacourtia romantchi*	The paste of *Flacourtia romantchi*, *Cassia fistula*, *Capparis sepiaria*, is recommended for *kaphaja* tumours [12]
13	*Moringa oleifera*	The paste of *Moringa oleifera* seeds, *Solanum xanthocarpum*, *Sinapis dichotoma*, *Holarrhena antidysenterica* and *Nerium odorum* roots prepared with buttermilk is used for *arbuda* tumours [23]
14	*Ficus bengalensis*	Application of mixture of *Ficus bengalensis* and *Saussurea lappa* pacify tumour growth on bone [23]
15	*Curcuma domestica*	The *Curcuma domestica* powder in combination with *Symplocos racemosa*, *Soymida febrifuga*, is mixed with honey and this is used as an external remedy [23]

other annonaceous acetogenins, e.g. muricins A–G, muricatetrocin A and B, longifolicin, corossolin, and corossolone are also showed to be significantly selective in bringing in vitro cytotoxicities to tumour cells [31].

2.8. Phyllanthus niruri/amarus

An aqueous extract of *P. amarus* increases the life span of the tumour bearing rats and normalizes γ-glutamyl transpeptidase activity [32]. It plays a major role in disruption of HBsAg mRNA transcription and post-transcription which could be beneficial against viral carcinogenesis [33].

2.9. Piper longum

Piperine, an active alkaloid extracted from this plant has been used as an ingredient of ayurvedic anticancer formulations because of its anti-oxidative potency in both in vitro and in vivo conditions [34].

2.10. Podophyllum hexandrum linn. (Podophyllin)

It is a powerful anticancer drug against various cancers for e.g. sarcomas, adenocarcinoma and melanoma. Podophyllin and its active principle, podophyllotoxin are known for their cytotoxic effect by virtue of their properties of mitotic inhibition, nuclear fragmentation, impaired spindle formation and they are also found to be karyoplastic. The mechanism of action has been suggested as necrosis and is a direct consequence of its cytotoxic effect on tumour tissues. These derivatives have been analysed in cancer chemotherapeutic studies and the methods of preparation of these compounds are patented [10].

In recent days, chemically modified podophyllotoxins are widely used in cancer therapeutics. VP-16 (etoposide), a podophyllotoxin derivative has been tested against in vitro and in vivo cancer cells and been used against hepatic cancers for more than a decade [35]. It has proved its efficacy in combination with epirubicin in phase II studies [36,37]. By this combination therapy at least 3% of the patients had complete cure and 36% had partial response. P-glycoprotein, a drug efflux pump, seems to be less effective in reducing VP-16 concentration in cancer cell lines and hence this drug proves to be more efficient in these cells [38]. It is also safe even above therapeutic dosage without much toxic effects [39].

2.11. Tinospora cordifolia

The active principles from *T. cordifolia* enhance host immune system by increasing immunoglobulin and blood leukocyte levels and by the stimulation of stem cell proliferation. It has the ability to reduce solid tumour volume by 58.8%, which is comparable to cyclophosphamide, a known chemotherapeutic agent [40–42]. These immunostimulating properties can be used in the prevention of tumour mediated immunosuppression and hence could be a drug choice for various cancers.

2.12. Semecarpus anacardium

In Ayurveda classics, numerous references are available on the anticancer properties of *Semecarpus anacardium* nuts [43]. An extensive review describes the phytochemical and pharmacological properties of *S. anacardium* [44]. The chloroform extract of *S. anacardium* nut possess antitumour action with increased life span against leukaemia, melanoma and glioma [45,46]. The milk extract of *S. anacardium* produces regression of hepatocarcinoma by stimulating host immune system [47] and normalizing tumour markers including alpha-fetoprotein levels [48,49]. This preparation stabilizes the lysozomes, and normalizes glycoprotein and mineral content in the body during cancer progression [50,51]. It also corrects hypoglycaemia [52] and controls abnormal lipid peroxidation [53] by the maintenance of antioxidant defense status [54]. In the microsomes, it acts as a bifunctional inducer of both phase I and II biotransformation enzymes and prevents tumour initiation by preventing carcinogen activation [55,56]. Histologically, on treatment with the *S. anacardium* extract to hepatocarcinoma animals, the liver sections showed almost a normal architecture. The nodules become completely regressed and further cell necrosis was prevented [57]. *Anacartin forte*, another preparation from *S. anacardium* has been used for several decades as an anticancer drug since it is giving health improvement with alleviation or disappearance of troublesome symptoms. It provides clinical benefit with an extension of survival time in various cancers including oesophageal, chronic myeloid leukaemia, urinary bladder and liver cancer [58]. Another Ayurvedic drug containing *S. anacardium*, *Amura rohitaka*, *Glycyrrhiza glabra* and copper powder were reported to inhibit breast tumour development in mice by significantly extending the survival period. This drug was also found to be efficient in clinical trials [13].

Ayurvedic herbs, which are widely used and scientifically proven of their anticancer properties, are presented in Table 3. Smit et al. [59] have also elaborately listed ayurvedic herbal drugs with anticancer activity. Some of these herbs are shown to enhance the therapeutic efficacy and/or reduce the toxicity of anticancer drugs used in chemotherapy. Also few of them possess radiosensitising effect too (see Table 4). Pharmacological details of ayurvedic herbs like therapeutic dosage, side effects, and comments about safety and herb-drug interactions were given in Table 5.

3. Potential benefits of Ayurveda during Cancer cachexia

Cancer cachexia is a common clinical problem that substantially impacts upon the quality of life and survival of

Table 3
Scientific evidence on herbs used in Ayurveda proven to have anticancer property

Name of the herb	Indications	References
Abrus precatorius	Yoshida sarcoma (rats) Fibrosarcoma (mice) Ascites tumour cells	Subbareddy and Sirsi [67]
Albizzia lebbeck	Sarcoma 180 (mice)	Dhar et al. [68]
Allium sativum	Sarcoma (rat)	Hu et al. [69]
Aloe vera	Yoshida AH-130 ascite hepatoma (pleural tumour) human neuroectodermal tumours	Corsi et al. [70], Pecere et al. [71]
Alstonia scholaries	HSI human sarcoma benzo(a)pyrene induced forestomach carcinoma	Dhar et al. [68], Jagetia et al. [72]
Amura rohitaka	Leukaemia	Prasad and Deshpande [73], Rabi and Gupta [74]
Anacardium occidentale	Hepatoma 129	Dhar et al. [68]
Asparagus racemosa	Human epidermoid carcinoma	Dhar et al. [68]
Bacopa monniera	Walker carcinosarcoma 256	Bhakuni et al. [75]
Berberis aristata	Human epidermal carcinoma of the nasopharynx *N*-nitrosodiethylamine induced carcinogenesis	Bhakuni et al. [75], Anis et al. [76]
Boswellia serrata	Human epidermal carcinoma of the nasopharynx Leukaemia and brain tumours	Dhar et al. [68] Hostanska et al. [77]
Calotropis gigantea	Human epidermal carcinoma of the nasopharynx	Bhakuni et al. [75], Dhar et al. [68]
Curcuma longa	Fibrosarcoma Preclinical and clinical trials review	Sriganth and Premalatha [78] Aggarwal et al. [79]
Datura metel	Human epidermal carcinoma of the nasopharynx	Dhar et al. [68]
Erythrina suberosa	SARCOMA 180	Dhar et al. [68]
Euphorbia hirta	Freund virus leukaemia	Dhar et al. [68]
Gynandropis pentaphylla	Hepatoma 129	Dhar et al. [68]
Heliotropium indicum	P-388 lymphocytic leukaemia	Pal et al. [80]
Hygrophila spinosa	Dalton's lymphoma Ehrlich ascites carcinoma and Sarcoma-180	Maiti [81] Mazumdar et al. [82]
Ixora undulata	P-388 lymphocytic leukaemia	Dhawan et al. [83]
Juniperus indica	Human epidermoid carcinoma of the nasopharynx	Dhawan et al. [83]
Luffa cylindrica	Schwartz leukaemia	Bhakuni et al. [84]
Melia azedarach	Walker carcinosarcoma 256	Bhakuni et al. [75]
Moringa oleifera	Human epidermoid lymphocytic leukaemia Skin papillomagenesis	Dhawan et al. [83] Bharali et al. [85]
Nerium indicum	Erlish ascites carcinoma	Pal et al. [80]
Nigella sativa	Lewis lung carcinoma Colon cancer	Dhar et al. [68] Salim and Fukushima [86]
Ocimum sanctum	Skin and liver tumours	Dubey et al. [87]
Paederia foetida	Human epidermoid carcinoma of the nasopharynx	Dhar et al. [68]
Picrorrhiza kurroa	Hepatic cancers	Dhar et al. [68]
Plumbago zeylanica	Hepatoma	Parimala and Sachdanandam [88]
Rubia cordifolia	P-388, L-1210, B-16 melanoma, colon 388, Lewis lung carcinoma, mammary carcinoma	Itokawa et al. [89]
Taxus buccata	Cytotoxic against various tumours	Melado et al. [90]
Vinca rosea	P-1534, carcinoma of the breast, cervix, kidney, lung and ovary	Rastogi and Mehrotra [91]
Withania somnifera	Various tumours	Dhar et al. [68]

cancer patients. The pathophysiology of this syndrome implicates tumour induced metabolic changes and immune responses. Clinical manifestations include anorexia, chronic nausea and change in body image. Among several potential benefits of ayurvedic medicine, relief from cancer cachexia is especially valuable. Ayurvedic herbs used in cancer therapy results not only in total healing, but also reduces the side effects and cancer associated complications. It also avoids the need for supplemental therapy to manage cancer cachexia. Each herbal product contains multiple active principles that may operate synergistically, producing therapeutic benefits and lowering the risks on adverse effects.

The anorexia or weight loss could be effectively managed by *Withania somnifera*, *Sida cordifolia*, *Asparagus*

Table 4
Therapeutic enhancement potential of ayurvedic herbs on cancer chemotherapy/radiation

Name of the herb	Chemotherapy/ayurvedic herb intervention studies
Allium sativum	Water-soluble derivative of garlic, S-allylmercaptocysteine (SAMC), inhibited proliferation and cell cycle progression in two human colon cancer cell lines, SW-480 and HT-29, similar to the effects of sulindac sulfide (SS), a well-known colon cancer chemopreventive agent. Co-administration of SS with SAMC enhanced the growth inhibitory and apoptotic effects of SS, suggesting the usefulness of SAMC alone or in combination with SS or other chemopreventive agents [92]
Aloe vera	In a randomised double-blinded clinical trial, comparing mild soap and aloe vera gel against incidence of radiation therapy induced skin reactions, the median time of five weeks was taken to show any skin changes in the aloe/soap treatment versus three weeks in the soap only treatment. The protective effect of adding aloe to the soap regimen increases during long time radiation exposure [93]. In another clinical trial involving patients with advanced solid tumours, for whom no other standard effective therapy was available, combination of pineal indole melatonin (MLT) plus Aloe vera extracts produced some therapeutic benefits, at least in terms of stabilization of disease and survival when compared to MLT alone treatment [94]
Alstonia scholaris	The *Alstonia scholaris* extract pre-treatment increased the effect of radiation as by enhancement of cell killing in HeLa and KB cells, followed by HL60, MCF7, and HePG2 cells. In in vivo studies, with Ehrlich ascites carcinoma bearing mice the pre-treatment of extract caused increased life span of animals when compared with untreated irradiated group [95]. The combination treatment of *Alstonia scholaris* extract with cyclophosphamide was also found to be most effective against Ehrlich ascites carcinoma as it caused the highest tumour regression and enhanced the mean and average survival time when compared with cyclophosphamide alone treated group [96]
Curcuma longa	When radiation and curcuma were applied together as synergical therapy, curcuma showed a radiation sensitising effect in HeLa, K-562 and IM-9 cell lines [97]. Curcumin, the active constituent from *Curcuma longa* also enhances the anticancer potential of Cisplatin and reduces its nephrotoxicity in fibrosarcoma bearing rats [78]
Heliotropium indicum	In a Phase I study consisting of Solid tumour patients who have undergone prior chemotherapy/ radiation therapy, Indicine N-oxide, an alkaloid from *Heliotropium indicum* have shown some improvement against skin melanoma and ovarian carcinoma [98]
Moringa oleifera	Pre-treatment with the leaf extract of *M. oleifera* exhibits significant radiation protection to the bone marrow chromosomes in mice and this could be useful to overcome side effects of radiation therapy [99]
Nigella sativa	In mice bearing Ehrlich ascites carcinoma, thymoquinone (TQ), the main constituent of the *Nigella sativa* oil, significantly enhanced the therapeutic efficacy of ifosfamide by improving its antitumour effect and reducing its nephrotoxicity. Furthermore, mice treated with ifosfamide in combination with TQ showed less body weight loss and mortality rate compared to IFO single therapy [100]
Ocimum sanctum	Orientin and Vicenin, two water-soluble flavonoids isolated from the leaves of *Ocimum sanctum* have shown significant protection to the human lymphocytes against the clastogenic effect of radiation, radiation lethality and chromosomal aberrations in vivo. This radioprotection associated with their antioxidant activity may have clinical potential in cancer therapy [101]
Taxus buccata	In a Phase II study, the triplet regimen based on taxol (active constituent of *Taxus buccata*), ifosfamide, and carboplatin has proved active, safe, and easy to deliver on an outpatient basis for patients with advanced stage IIIB-IV non-small-cell lung cancer [102]. Another combination of Herceptin with Taxol significantly improves the overall response rate, increases the time to progression and the overall survival in breast cancer patients. These effects are more pronounced in patients characterized with HER/2 +++ over expression [103]. Taxol also exerts a weak radiosensitising effect on breast and cervical carcinoma cells on the basis of an optimal Taxol/radiation scheduling [104]
Withania somnifera	*W. somnifera* when administered for 4 days before paclitaxel treatment and continued for 12 days caused significant reversal of neutropenia of paclitaxel in mice. It can be used as an adjuvant during cancer chemotherapy for the prevention of bone marrow depression associated with anticancer drugs [105]. The active component, withaferin A isolated from the extract showed significant antitumour and radiosensitising effects in experimental tumours in vivo, without any noticeable systemic toxicity [106]. In Ehrlich ascites carcinoma mice, the extract showed dose dependent inhibition on tumour growth and increased the survival rate. Combination of radiation therapy with extract increased tumour cure and tumour-free survival [107]. It also reduces cyclophosphamide induced myelosuppression and leucopoenia can be useful in combination chemotherapy [108,109]

racemosa, *Vitis vinifera*, *Plumbago zeylenica*, *Tinospora cordifolia*, *Zingiber officinale*, *Coptidis rhizoma*, etc. These herbs have been shown to improve appetite, food intake, malnutrition, fatigue and sensation of well-being which could elicit bodyweight gain. These herbs might stimulate the flow of digestive juices, thereby improving digestion and increasing the appetite. *Aegle marmelos*, *Holarrhena antidysenterica*, *Punica granatum*, *Cyperus rotundus*, *Emblica officinalis*, and *Plumbago zeylanica* can be used as anti-diarrhoeals when diarrhoea becomes one of the complications of cancer cachexia. *Terminalia chebula* could be useful against chronic constipation and digestive disorders which are common in cancer patients resulting in loss of appetite. *Eclipta prostrata*, *Emblica officinalis*, *Withania*

Table 5
Pharmacological details of Ayurvedic anticancer herbs [110–114]

Name of the herb	Therapeutic dose	Safety/duration/toxic dose	Side effects/contraindications	Interactions with other herbs/drugs
Abrus precatorius	Leaf decoction: 56–112 ml, root powder: 0.5–1 g	Likely safe	Nausea, stomach cramping, coma, circulatory collapse	None known
Allium sativum	2–5 g per day, solid extract: 0.3–1 g, oil: 0.03–0.12 ml t.i.d.	Likely safe	Excess can cause stomach upset. May increase the risk of hemorrhagic complications	May interact with aspirin
Aloe vera	Extract: 10–20 ml, powder: 0.05–0.2 g	Safe for short term therapy	Long term intake may aggravate ulcers, haemorrhoids	Possibly interact with cardiac glycosides and diuretics
Alstonia scholaris	Liquid extract: 4–8 ml	Insufficient information available	Lethargy, Nasal congestion, allergy	Interact with St. John's wort, general anaesthetics
Amorphopallus campanulatus	0.3–0.6 g	Likely safe	None reported	None known
Anacardium occidentale	No typical dosage	Safe	None reported	None known
Andrographis paniculata	Powder: 1.5–6 g, juice of leaves and stem: 1–4 ml t.i.d., andrographolide: 4–6 mg	Safe	Nausea, anorexia, emesis, Urticaria	Interact with anticoagulant and antihypertensive drugs/herbs
Asparagus racemosa	Powder: 20–30 g	Safe	No adverse effects	None known
Bacopa monniera	5–10 g (0.4–0.5 g 8×) per day	Safe	Rarely cause dermatitis	None known
Berberis aristata	Powder: 1–3 g	May be toxic at higher dosage	May cause lethargy, nose bleeds, nausea, vomiting, diarrhoea	May interfere with Vitamin B assimilation
Boswellia serrata	0.4 g/2–3 times a day, gum resin: 2–3 g, oil: 1–1.5 ml, bark decoction: 56–112 ml	Safe	No adverse effects reported	None known
Calotropis cylindric	0.5–1 g	Likely unsafe	Vomiting, diarrhoea, bradycadia	May interact with cardioactive herbs and horsetail
Curcuma longa	1.5–3.0 g	Safe, non-toxic	Contraindicated in gastric ulcers	No interactions reported
Datura stramonium	0.05–0.1 g	Likely unsafe	Vomiting, hypertension, loss of consciousness. May lead to coma	May interact with anti-cholinergic drugs
Erythrina suberosa	28–32 g	Insufficient information available	Insufficient information available	Insufficient information available
Euphorbia hirta	Powder: 0.12–0.3 g, liquid extract: 0.1–0.3 ml	No information about safety. Tolerable dose: up to 1 g/i.p. in mice	Nausea, vomiting, dermatitis with skin contact	No interactions known to occur
Ficus religiosa	Powdered bark: 1–3 g, liquid extract: 60–120 ml	Likely safe at given dosage	Large amounts can cause catharsis/allergies	None reported
Gynandropis pentaphylla	2 g	Insufficient information available	Insufficient information available	Insufficient information available
Hygrophila spinosa	Seed powder: 2–8 g, liquid extract: 40–50 ml	Insufficient information available	Insufficient information available	Insufficient information available
Ixora crocinea	2–2.5 g	Insufficient information available	Insufficient information available	Insufficient information available
Juniperus communis	2–10 g per day	Limit to maximum of 6 weeks Likely safe for short term	Long term may cause kidney damage	Possibly interact with anti-diuretic drugs
Luffa cylindrica	1.3 –1.9 g	Likely safe	None reported	No interactions known to occur
Melia azedarach	Liquid extract: 15–30 ml	Insufficient information available	Insufficient information available	Insufficient information available
Nerium indicum	0.25–0.4 g	Likely unsafe	Nausea, vomiting, diarrhoea	None known
Nigella sativa	1–3 g	Safe	No adverse effects reported	No interactions known

Table 5 (*Continued*)

Name of the herb	Therapeutic dose	Safety/duration/toxic dose	Side effects/contraindications	Interactions with other herbs/drugs
Ocimum sanctum	1–3 g, leaf infusion: 4–12 ml	Likely safe	May cause constipation at higher dosage for long term	None known
Paederia foetida	2–4 g, infusion: 12–24 ml, liquid extract: 56–112 ml	Non-toxic up to 2 g/kg in rats and mice	Insufficient information available	Insufficient information available
Phyllanthus niruri	Powder: 3–6 g	Safe	None reported	None reported
Picrorrhiza kurroa	0.5–1 g	Low potential for toxicity	Nausea, diarrhoea, skin rash at high doses, contraindications in pregnancy	None known
Piper longum	0.5–1 g	Likely safe	May have contraceptive activity, avoid use during pregnancy and lactation	Piperine may interact with enzymatic drug biotransformation
Plumbago zeylanica	1–2 g	Plumbagin LD_{50} 10 mg/kg in mice, whole plant: 0.5 g/kg/i.p.	None reported	None known
Raphanus sativus	15–23 g, liquid extract: 50–100 ml	Likely safe	Large amounts may cause irritation of GI mucus membrane	No interactions known to occur
Rubia cordifolia	Powder: 1–3 g, liquid extract: 56–112 ml	Generally recognized as safe	No adverse effects reported	None known
Semecarpus anacardium	Oil: 1–2 drops, fruit: 0.5–1.5 g	Likely unsafe	Anacardic acid may be allergenic	No sufficient information available
Taxus buccata	Dosage depends on severity of the disease	Likely unsafe	Vomiting, abdominal pain, dyspnea	No interactions known to occur
Tinospora cordifolia	Powder: 1–3 g, liquid extract: 56–112 ml	Safe	Nausea	Excessive dose might inhibit Vitamin B assimilation
Vinca rosea	Dosage depends on severity of the disease	Likely unsafe	GI upset, hepatotoxicity, nausea, vomiting, may also cause hypoglycemia	No interactions known to occur
Vitis vinifera	0.15–0.3 g	Safe	None reported	None known
Withania somnifera	2–6 g	Likely unsafe	Nausea, dermatitis, abdominal pain, diarrhoea	May potentiate the action of barbiturates and benzodiazepines

somnifera, *Piper longum* can be directed to correct nausea and vomiting [60]. Among the above-mentioned herbs, *Withania somnifera* [61] and *Tinospora cordifolia* [42] are also proven to be powerful immunostimulants, which could increase body resistance power during cancer associated immunosuppression.

Ayurvedic anticancer therapy includes recommendations for lifestyle and use of specific foods and herbs which are very helpful not only in preventing the progression of the disease but also makes the patients feel better and comfortable overcoming the symptoms. *Allium sativum* (garlic) could be helpful to manage pain and ache. *Bacopa monniera* strengthens mental faculties and helps to manage insomnia or sleeplessness due to stress [62]. An herbal combination of *Withania sominifera*, *Asparagus racemosa*, *Hydrocotyle asiatica*, *Nardostachys jatamamsi*, *Elettaria cardamomum*, *Tribulus terrestris*, *Zingiber officinalis* and *Eclipta alba* could also be useful in the treatment of anxiety, tension and insomnia. *Ocimum sanctum* is beneficial against stress and depression during cancer. *Curcuma longa*, *Zingiber officinale*, *Glycyrrhiza glabra*, *Terminalia chebula*, *Ocimum sanctum* and *Adhatoda vasica* are used to control cough and shortness of breathe especially for lung cancer patients [60]. Thus, ayurvedic therapeutic regimen rejuvenates the body tissues, tones up the systems and act as a tonic to the body against cancer cachexia. This kind of orientation toward total healing and health promotion makes ayurvedic treatment approach to cancer therapy promising.

4. Cancer therapy in Ayurveda—learning from the past, examining the present and advancing to the future

Because large population use ayurvedic medicine worldwide, there is an urgent need for additional, carefully conducted, high-quality intensive research to evaluate its efficacy and to develop this discipline to meet ever-new challenges of modern medicine in the field of oncology. The most stringent evaluation should take place with gold standards for clinical research—the randomised controlled clinical trial (RCT). Priority for research funding should be given to clinical investigations in Ayurveda involving well-designed studies with encouraging results especially for diseases like cancer to which conventional medicine

has been shown to be less effective. Attention should be given not only to the evaluation of safety and examination of effectiveness in treatment strategy, but also to the consideration of community practice settings, patient expectations, compliance and cost effectiveness. Standardization and quality production of herbal products may allow us to develop low cost therapies with reduced risk over pharmaceuticals. In any case, studies on anticancer ayurvedic drugs will be popular from the economy point of view because cancer is becoming the major cause of death.

5. Conclusion and future directions

The clinical efficacy and extent of toxicity of numerous anticancer agents are unknown and uncertain. For example, research on majority of ayurvedic drugs is in the pre-clinical phase or is not being actively pursued. Future research on this topic would help to identify safe and effective anticancer drugs and will further the exploration of their mechanism of action. Ayurvedic practitioners and researchers in medical sciences can help to improve this medicine by increasing their involvement and contribution. Case study is the research design, which can form basis for future research directions and can provide valuable contributions to the medical field with minimal cost budgets. Case studies have also been suggested by the NCCAM (National Center for Complementary and Alternative Medicine, Bethesda, USA) as a means to determine whether a complementary anticancer therapy demonstrates potential efficacy against particular cancer and whether clinical development of the therapy should continue [63,64]. It is no longer an option to ignore ayurvedic drugs or treat them as something unconventional from regular medical practices. The challenge put before this medicine is to move forward carefully, using both reasoning and wisdom.

References

[1] Hartwell JL. Plants used against cancer. A survey. Lloydia 1969;32:247–96.
[2] Hartwell JL. Plants used against cancer. A survey. Lloydia 1969;32:153–205.
[3] Hartwell JL. Plants used against cancer. A survey. Lloydia 1969;32:78–107.
[4] Hartwell JL. Plants used against cancer. A survey. Lloydia 1970;33:288–392.
[5] Hartwell JL. Plants used against cancer. A survey. Lloydia 1970;33:97–194.
[6] Hartwell JL. Plants used against cancer. A survey. Lloydia 1971;34:386–425.
[7] Hartwell JL. Plants used against cancer. A survey. Lloydia 1971;34:204–55.
[8] Hartwell JL. Plants used against cancer. A survey. Lloydia 1971;34:310–61.
[9] Hartwell JL. Plants used against cancer. A survey. Lloydia 1971;34:103–50.
[10] Pandey G. Anticancer herbal drugs of India with special reference to Ayurveda. New Delhi: Sri Satguru Publications; 2002:18–121.
[11] Sharma PV. Charaka samhita. Varanasi: Choukhamba Orientalia; 1981.
[12] Bhishagratha KL. Sushruta samhita. Varanasi: Choukhamba Orientalia; 1991.
[13] Prasad GC. Studies on cancer in Ayurveda and its management. JRAS 1987;3:147–67.
[14] Singh RM. An assessment of ayurvedic concept of cancer and a new paradigm of anticancer treatment in Ayurveda. J Altern Complement Med 2002;8:609–14.
[15] Sankaran PS. Swellings. In: Prasad GC, Udupa KN, editors. Susruta's contribution to surgery. Varanasi: Indological Book House; 1976. p. 99–111.
[16] Dash B, Kashyap L. Diagnosis and treatment of Galaganda, Gandamala, Apaci, granthi and arbuda. In: Dash B, Kashyap L, editors. Diagnosis and treatment of diseases in ayurveda. New Delhi: Concept Publishing Company; 1987. p. 437–66.
[17] Sastry JLN. Introduction to oncology, cancer in Ayurveda. Varanasi: Chaukhambha orientalia; 2001. p. 1–24.
[18] Thatte U, Dhahanukar S. Ayurveda, the natural alternative. Sci Today 1991;2001:12–8.
[19] Ram A. Astanga-hrdaya of vagbhata. vol. III. Uttara-sthana. Delhi: Uppal Publishing House; 1999.
[20] Kinjavadekara RS. Astanga sangraha. New Delhi: Uppal Publishing House; 1998.
[21] Sharma PV. Chakradatta: a treatise on principles and practices of Ayurvedic medicine. New Delhi: Vedams Books International; 1998.
[22] Murthy KRS. Sarangadhara samhita. Varanasi: Chaukambha Orientalia; 1987.
[23] Murthy KRS. Bhavaprakasa of bhavamisra. vol. II. Madhya and Uttara Khanda. Varanasi: Krishnadas Academy; 2001.
[24] Sonata S. The efficacy of Ayurveda drugs on Cancer (*Arbuda*). Workshop on cancer souvenir. Chennai: Central Research Institute for Siddha; 1986.
[25] Treadway S. An Ayurvedic herbal approach to a healthy liver. Clin Nutr Insights 1998;6:1–3.
[26] Trivedi N, Rawal UM. Effect of aqueous extract of *Andrographis paniculata* on liver tumour. Indian J Pharmacol 1998;30:318–22.
[27] Trivedi NP, Rawal UM. Hepatoprotective and antioxidant property of *Andrographis paniculata* in BHC induced liver damage in mice. Indian J Exp Biol 2001;39:41–6.
[28] Singh RP, Bannerjee S, Rao AR. Modulatory influence of *Andrographis paniculata* on mouse hepatic and extrahepatic carcinogen metabolising enzymes and antioxidant status. Phytother Res 2001;15:382–90.
[29] Kapil A. Antihepatoxic effects of major diterpenoid constituents of *Andrographis paniculata*. Biochem Pharmacol 1993;46:182–5.
[30] Chih H, Chiu HF, Tang KS, Chang FR, Wu YC. Bullatacin, a potent antitumour annonaceous acetogenin, inhibits proliferation of human hepatocarcinoma cell line 2.2.15 by apoptosis induction. Life Sci 2001;69:1321–31.
[31] Chang FR, Wu YC. Novel cytotoxic annonaceous acetogenins from *Annona muricata*. J Nat Prod. 2001;64:925–31.
[32] Rajeshkumar NV, Kuttan R. *Phyllanthus amarus* extract administration increases the life span of rats with hepatocellular carcinoma. J Ethnopharmacol 2000;73:215–9.
[33] Lee CD, Ott M, Thyagarajan SP, Shafritz DA, Burk RD, Gupta S. *Phyllanthus amarus* down-regulates hepatitis B virus mRNA transcription and replication. Eur J Clin Invest 1996;26:1069–76.
[34] Koul IB, Kapil A. Evaluation of the liver protective potential of piperine. Planta Med 1993;59:413–7.
[35] Cavalli F, Tschopp L, Gerber A, Sonntag RW, Ryssel HJ, Brunner KW. Therapiersultate mit VP 16.213 allein oder kombiniert mit 5-fluorouracil beim leberzell karzinom (hepatoma), Schweiz. Med Wochenschr 1977;107:1960–6.

[36] Pallavacini EB, Porta C, Moroni M, Moroni M, Bertulezzi G, Civelli L, et al. Epirubicin and etoposide combination chemotherapy to treat hepatocellular carcinoma patients: a phase II study. Eur J Cancer 1997;33:1784–8.
[37] Nerenstone SR, Ihde DC, Friedman MA. Clinical trials in primary hepatocellular carcinoma: current status and future directions. Cancer Treat Rev 1988;15:1–31.
[38] Park JG, Lee SH, Hong IG, Kim HS, Lim KH, Choe KJ, et al. MDR1 gene expression its effect on drug resistance to doxorubicin in human hepatocellular carcinoma cell lines. J Natl Cancer Inst 1994;86:700–5.
[39] Aita P, Robieux I, Sorio R, Tumolo S, Corona G, Cannizzaro R, et al. Pharmacokinetics of oral etoposide in patients with hepatocellular carcinoma. Cancer Chemother Pharmacol 1999;43:287–94.
[40] Sohini YR, Bhatt RM. Activity of a crude extract formulation in experimental hepatic amoebiasis and in immunomodulation studies. J Ethnopharmacol 1996;54:119–24.
[41] Kapil A, Sharma S. Immunopotentiating compounds from *Tinospora cordifolia*. J Ethnopharmacol. 1997;58:89–95.
[42] Matthew S, Kuttan G. Immunomodulatory and antitumour activities of *Tinospora cordifolia*. Fitoterapia 1999;70:35–43.
[43] Sharma PV, Chaturvedi C, Bandhopadhyaya NG. A study on dosage and toxicity of Bhallataka (*Semecarpus anacardium* Linn.). J Res Indian Med 1966;I:130.
[44] Premalatha B. *Semecarpus anacardium* Linn. nuts—a boon in alternative medicine. Indian J Exp Biol 2000;38:1177–82.
[45] Cassady JM, Chang CJ, McLaughlin JL. Recent advances in the isolation of structural elucidation of antineoplastic agents of higher plants. In: Beal JL, Reinhard E, editors. Natural products as medicinal agents. Verlag: Hippokrates; 1981. p. 93–105.
[46] Chitinis MP, Bhatia KG, Phatak MK, Kesava Rao KV. Antitumour activity of the extract of *Semecarpus anacardium* L. nuts in experimental tumour models. Indian J Exp Biol 1980;18:6–8.
[47] Premalatha B, Sachdanandam P. Immunomodulatory activity of *Semecarpus anacardium* Linn. Nut milk extract in Aflatoxin B_1 induced hepatocellular carcinoma in rats. Pharm Pharmacol Commun 1998;4:507–10.
[48] Premalatha B, Muthulakshmi V, Sachdanandam P. Anticancer potency of the milk extract of *Semecarpus anacardium* Linn. nuts against aflatoxin B_1 mediated hepatocellular carcinoma bearing Wistar rats with reference to tumour marker enzymes. Phytother Res 1999;13:183–7.
[49] Premalatha B, Sachdanandam P. Effect of *Semecarpus anacardium* nut milk extract on rat serum alpha-fetoprotein level in aflatoxin B_1 mediated hepatocellular carcinoma. Fitoterapia 1999;70:279–83.
[50] Premalatha B, Sachdanandam P. Stabilization of lyzosomal membrane and cell membrane glycoprotein profile by *Semecarpus anacardium* Linn. Nut milk extract in experimental hepatocellular carcinoma. Phytother Res 2000;14:352–5.
[51] Premalatha B, Sachdanandam P. Regulation of mineral status by *Semecarpus anacardium* Linn. nut milk extract in aflatoxin B_1 induced hepatocellular carcinoma. J Clin Biochem Nutr 1998;25:63–70.
[52] Premalatha B, Sujatha V, Sachdanandam P. Modulating effect of *Semecarpus anacardium* Linn. nut extract on glucose metabolising enzymes in aflatoxin B_1 induced experimental hepatocellular carcinoma. Pharmacol Res 1997;36:187–92.
[53] Premalatha B, Muthulakshmi V, Vijayalakshmi T, Sachdanandam P. *Semecarpus anacardium* nut extract induced changes in enzymic antioxidants studied in aflatoxin B_1 caused hepatocellular carcinoma bearing Wistar rats. Int J Pharmacog 1997;35:1–6.
[54] Premalatha B, Sachdanandam P. *Semecarpus anacardium* L nut extract administration induces the in vivo antioxidant defense system in aflatoxin B_1 mediated hepatocellular carcinoma. J Ethnopharmacol 1999;66:131–9.
[55] Premalatha B, Sachdanandam P. Potency of *Semecarpus anacardium* Linn. nut milk extract against aflatoxin B_1 induced hepatocarcinogenesis: reflection on microsomal biotransformation enzymes. Pharmacol Res 2000;42:161–6.
[56] Premalatha B, Sachdanandam P. Modulating role of *Semecarpus anacardium* L. nut milk extract on aflatoxin B_1 biotransformation. Pharmacol Res 2000;41:19–24.
[57] Premalatha B, Sachdanandam P. Effect of *Semecarpus anacardium* nut extract against aflatoxin B_1 induced hepatocellular carcinoma. Fitoterapia 1999;70:484–92.
[58] Vad BG. Study of complete regression in four cases of cancer. The Indian Practitioner 1973;26:253–63.
[59] Smit HF, Woerdenbag HJ, Singh RH, Meulenbeld GJ, Labadie RP, Zwaving JH. Ayurvedic herbal drugs with possible cytostatic activity. J Ethnopharmacol 1995;47:75–84.
[60] Nayak B. *Pharmacological index-Ayurmedline*. Bangalore: Seetharam Prasad; 2002. p. 447–682.
[61] Agarwal R, Diwanay S, Patki P, Patwardhan B. Studies on immunomodulatory activity of *Withania somnifera* (Ashwagandha) extracts in experimental immune inflammation. J Ethnopharmacol 1999;67:27–35.
[62] Bakhru HK. Conquering cancer naturally. Delhi: Chaukhamba Sanskrit Pratishthan; 2000. p. 1–6.
[63] OAM. Office of alternative medicine workshop on the collection of clinical research data relevant to alternative medicine and cancer. Bethesda: Office of Alternative Medicine; 1994.
[64] Boik J. Conducting research on natural agents. In: Boik J, editor. Cancer and natural medicine. Minnesota: Oregon Medical Press; 1996: p. 176–87.
[65] Singhal GD, Singh LM. The management of glandular swellings, cervical lymphadenopathy, tumours and goiters. In: Singhal GD, Singh LM, editors. Operative considerations in ancient Indian surgery based on *Susruta Samhita*, Cikitsa sthana. Varanasi: Singhal Publications; 1982. p. 339–56.
[66] Jang M, Cai L, Udeani GO, Beecher CWW, Fong HHS, Farnsworth NR, et al. Cancer chemopreventive activity of Resveratrol, a natural product derived from Grapes. Science 1997;275:218–20.
[67] Subbareddy VV, Sirsi M. Effect of *Abrus precatorius* Linn. on experimental tumours. Cancer Res 1969;29:1447–51.
[68] Dhar ML, Dhar MM, Dhawan BN, Mehrotra BN, Ray C. Screening of Indian plants for biological activity, Part-I. Indian J Exp Biol 1968;6:232–47.
[69] Hu X, Cao BN, Hu G, He J, Yang DQ, Wan YS. Attenuation of cell migration and induction of cell death by aged garlic extract in rat sarcoma cells. Int J Mol Med 2002;9:641–3.
[70] Corsi MM, Bertelli AA, Gaja G. The therapeutic potential of *Aloe vera* in tumour-bearing rats. Int J Tissue React 1998;20:115–8.
[71] Pecere T, Gazzola MV, Mucignat C, Parolin C, Vecchia FD, Cavaggioni A, et al. Aloe-emodin is a new type of anticancer agent with selective activity against neuroectodermal tumours. Cancer Res 2000;60:2800–4.
[72] Jagetia GC, Baliga MS, Venkatesh P. Effect of *Sapthaparna* (*Alstonia scholaris* Linn) in modulating the benzo(a)pyrene-induced forestomach carcinogenesis in mice. Toxicol Lett 2003;144:183–93.
[73] Prasad GC, Deshpande PJ. Effect of Rohitaka (*Amura rohitaka*) on leukaemia. J Res Indian Med 1968;3:36.
[74] Rabi T, Gupta RC. Antitumour and cytotoxic investigations of *Amura rohitaka*. Int J Pharmacogn 1995;33:359–64.
[75] Bhakuni DS, Dhar ML, Dhar MM, Dhawan BN, Mehrotra BN. Screening of Indian plants of biological activity, Part-II. Indian J Exp Biol 1969;7:250–62.
[76] Anis KV, Rajeshkumar NV, Kuttan R. Inhibition of chemical carcinogenesis by berberine in rats and mice. J Pharm Pharmacol 2001;53:763–8.
[77] Hostanska K, Daum G, Saller R. Cytostatic and apoptosis-inducing activity of boswellic acids toward malignant cell lines in vitro. Anticancer Res 2002;22:2853–62.
[78] Sriganth NPI, Premalatha B. Dietary curcumin with cisplatin administration modulates tumour marker enzymes indices

in experimental fibrosarcoma. Pharmacol Res 1999;39:175–9.
[79] Aggarwal BB, Kumar A, Bharti AC. Anticancer potential of curcumin: preclinical and clinical studies. Anticancer Res 2003;23:363–98.
[80] Pal S, Chakraborti SK, Banerjee A, Mukerji B. Search for anticancer drugs from Indian medicinal plants. Indian J Med Res 1968;56:445–55.
[81] Maiti B. Antineoplastic effects of the root extract of *Hygrophila spinosa*. In: Proceedings of the International Conference on Current Progress in Medicinal and Aromatic Plant Research. Calcutta, India; 1994. p. 135–40.
[82] Mazumdar UK, Gupta M, Maiti S, Mukherjee D. Antitumour activity of *Hygrophila spinosa* on Ehrlich ascites carcinoma and sarcoma-180 induced mice. Indian J Exp Biol 1997;35:473–7.
[83] Dhawan BN, Dubey MP, Mehrotra BN, Rastogi RP, Tandon JS. Screening of Indian plants for biological activity, Part-IX. Indian J Exp Biol 1980;18:594–606.
[84] Bhakuni DS, Dhar ML, Dhar MM, Dhawan BN, Gupta B, Srimal RC. Screening of Indian plants of biological activity, Part-III. Indian J Exp Biol 1971;9:91–102.
[85] Bharali R, Tabassum J, Azad MR. Chemomodulatory effect of *Moringa oleifera* Lam., on hepatic carcinogen metabolising enzymes, antioxidant parameters and skin papillomagenesis in mice. Asian Pac J Cancer Prev 2003;4:131–9.
[86] Salim EI, Fukushima S. Chemopreventive potential of volatile oil from black cumin (*Nigella sativa* L.) seeds against rat colon carcinogenesis) seeds against rat colon carcinogenesis. Nutr Cancer 2003;45:195–202.
[87] Dubey NK. Cytotoxicity of the essential oil of *Cymbogon citrus* and *Ocimum gratissimum*. Indian J Pharm Sci. 1997;59:263–9.
[88] Parimala R, Sachdanandam P. Effect of Plumbagin on some glucose metabolising enzymes studied in rats in experimental hepatoma. Mol Cell Biochem 1993;125:59–63.
[89] Itokawa H, Takeya K, Mori N, Hamanaka T, Sonobe T, Mihara K. Isolation and antitumour activity of cyclic hexapeptides isolated from *Rubia radix*. Chem Pharm Bull 1984;32:284–90.
[90] Mellado W, Magri NF, Kingston DG, Garcia-Arenas R, Orr GA, Horwitz SB. Preparation of biological activity of taxol acetates. Biochem Biophys Res Commun 1984;124:329–36.
[91] Rastogi RP, Merhotra BN, editors. Compendium on Indian medicinal plants. New Delhi: CSIR publications; 1993.
[92] Shirin H, Pinto JT, Kawabata Y, Soh JW, Delohery T, Moss SF, et al. Antiproliferative effects of S-allylmercaptocysteine on colon cancer cells when tested alone or in combination with sulindac sulfide. Cancer Res 2001;61:725–31.
[93] Olsen DL, Bradley C, Johnson M, Macias JL, Love V, Markoe A. The effect of *Aloe vera* gel/mild soap versus mild soap alone in preventing skin reactions in patients undergoing radiation therapy. Oncol Nurs Forum 2001;28:543–7.
[94] Lissoni P, Giani L, Zerbini S, Trabattoni P, Rovelli F. Biotherapy with the pineal immunomodulating hormone melatonin versus melatonin plus aloe vera in untreatable advanced solid neoplasms. Nat Immun 1998;16:27–33.
[95] Jagetia GC, Baliga MS. Treatment with *Alstonia scholaris* enhances radiosensitivity in vitro and in vivo. Cancer Biother Radiopharm 2003;18:917–29.
[96] Jagetia GC, Baliga MS. Modulation of antineoplastic activity of cyclophosphamide by *Alstonia scholaris* in the Ehrlich ascites carcinoma-bearing mice. J Exp Ther Oncol 2003;3:272–82.
[97] Baatout S, Derradji H, Jacquet P, Ooms D, Michaux A, Mergeay M. Effect of curcuma on radiation-induced apoptosis in human cancer cells. Int J Oncol 2004;24:321–9.
[98] Ohnuma T, Sridhar KS, Ratner LH, Holland JF. Phase I study of indicine N-oxide in patients with advanced cancer. Cancer Treat Rep 1982;66:1509–15.
[99] Rao AV, Devi PU, Kamath R. In vivo radioprotective effect of *Moringa oleifera* leaves. Indian J Exp Biol 39:858–63.
[100] Badary OA. Thymoquinone attenuates ifosfamide-induced Fanconi syndrome in rats and enhances its antitumour activity in mice. J Ethnopharmacol 1999;67:135–42.
[101] Vrinda B, Uma Devi P. Radiation protection of human lymphocyte chromosomes in vitro by orientin and vicenin. Mutat Res 2001;498:39–46.
[102] Zaniboni A, Ardizzoni A, De Marinis F, Portalone L, Boni C, Meriggi F, et al. Phase II study of Taxol combined with ifosfamide and carboplatin in the treatment of stage IIIb-IV non-small-cell lung cancer. Am J Clin Oncol 2003;26:84–8.
[103] Lang I. Possibilities and results with Herceptin-Taxol combination in the treatment of breast cancer. Magy Onkol 2002;46:195–6.
[104] Rave-Frank M, Meden H, Jaschke A, Tanzer A, Boghun O, Fietkau R. The effect of paclitaxel on the radiosensitivity of gynecological tumour cells. Strahlenther Onkol 1997;173:281–6.
[105] Gupta YK, Sharma SS, Rai K, Katiyar CK. Reversal of paclitaxel induced neutropenia by *Withania somnifera* in mice. Indian J Physiol Pharmacol 2001;45:253–7.
[106] Devi PU. *Withania somnifera* Dunal (Ashwagandha): potential plant source of a promising drug for cancer chemotherapy and radiosensitisation. Indian J Exp Biol 1996;34:927–32.
[107] Sharada AC, Solomon FE, Devi PU, Udupa N, Srinivasan KK. Antitumour and radiosensitising effects of withaferin A on mouse Ehrlich ascites carcinoma in vivo. Acta Oncol 1996;35:95–100.
[108] Praveenkumar V, Kuttan R, Kuttan G. Chemoprotective action of Rasayanas against cyclophosphamide toxicity. Tumouri 1994;80:306–68.
[109] Davis L, Kuttan G. Suppressive effect of cyclophosphamide-induced toxicity by *Withania somnifera* extract in mice. J Ethnopharmacol 1998;62:209–14.
[110] Williamson EM. Major herbs of Ayurveda. London: Churchill Livingstone; 2002.
[111] Jellin JM, Gregory P, Batz F, Hitchens K. Pharmacist's letter/prescriber's letter natural medicines comprehensive database. 3rd ed. Stockton, California: Therapeutic Research Facility; 2000.
[112] Ross IA. Medicinal parts of the world. New Jersey: Humana Press; 1999.
[113] Forget L, Goldrosen J, Hart JA, Hyun T, Meachen D, Tyler T, et al. Herbal companion. Bethesda: American Society of Health System Pharmacists; 2000.
[114] Kuhn MA. Winston D. Herbal therapy and supplements. Philadelphia: Lippincott; 2000.