

ड्रग्स एण्ड फार्मास्यूटिकल्स
करेंट आर एण्ड डी हाईलाइट्स

Drugs and Pharmaceuticals
Current R&D Highlights

Incorporating Patent Information

Vol. 29

No. 2

April-June, 2006

(Cancer)



BTIS Centre for Bioinformatics (DBT)
Central Drug Research Institute, Lucknow



Cancer Treatment with Traditional Herbal Medicines

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In the year 2000, approximately 10 million new cases of cancer were diagnosed, and there were 6 million cancer related deaths, globally. Taken together, 22 million people were living with cancer that had been diagnosed within the previous 5 years [1]. The World Cancer Report, issued by International Agency for Research on Cancer tells, us that cancer rates are set to increase at an alarming rate globally [2]. Cancer rates could increase by 50 % to 15 million new cases in the year 2020. This will be mainly due to steadily aging populations in both developed and developing world and also due to current trends in tobacco usage and the growing adoption of unhealthy lifestyles. The report also reveals that cancer has emerged as a major public health problem in developing countries.

Great advances have been made in the treatment of some cancer / tumors and new advances in surgery, radiotherapy, and chemotherapy have lead to an increase in cure rates. But the price of conventional care is often out of reach for majority of cancer patients living in the developing world [3]. Moreover, in the post trade-related intellectual property right (TRIPS) era, many drugs have become extremely expensive. TRIPS now propagates monopoly, allowing multinationals to fix exorbitant prices for patented medicines. Product patents reduce accessibility and affordability of drugs that generic drugs have not allowed to happen so far. Gleevec (patented by Novartis) is used for treating Chronic Myeloid Leukaemia (CML) a life threatening cancer. Novartis used court injunction to force the withdrawal of generic or "copycat" versions of

Gleevec priced between Rs. 9000 - 12000 per month. Now CML patients have to purchase the drug from Novartis at Rs. 1.2 lakhs a month or go without treatment.

Patients confronting the diagnosis of advanced (Stage 4) cancer face the statistical reality that conventional chemotherapy can affect a cure for only a tiny minority of all such cases. More often, the reasonable impulse of these patients is to venture into various alternative options like herbal medicines [4]. The use of plants for healing purposes predates human history and forms the origin of much modern medicine. Many conventional drugs originated from plant sources: a century ago, most of the few effective drugs were plant based. Examples include aspirin (willow bark), digoxin (from foxglove), quinine (from cinchona bark), and morphine (from the opium poppy). More than 3000 species of herbs used in treating cancer since 2838 BC are known to biomedicine, yet popular lay literature persists in perpetrating the myth that medicine has ignored the potential.

Plant Derived Anti-cancer Drugs

Plant-derived compounds have a great significance to cancer therapy. Many herbs were the starting point of important chemotherapeutic drugs. It was, for instance, only upon the addition of the *Vinca* alkaloid vincristine or oncovin (isolated from *Catharanthus roseus*) to mechlorethamine, prednisone, and procarbazine (the MOPP regimen) that the first cures in a human cancer (Hodgkin's disease) was achieved. The combination of the epipodophylotoxin etoposide

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(derived from the mandrake plant *Podophyllum peltatum* and the wild chervil *P. emodi*), bleomycin, and cisplatin is currently a highly active and curative regimen in testicular cancer. Etoposide is furthermore one of the most active agents against small cell lung carcinoma [5]. The more recent development of the structurally and mechanistically novel taxanes (extracted from the bark of the *Taxus brevifolia*, *T. canadensis*, or *T. baccata*) and the camptothecins (derived from the bark and wood of the *Camptotheca acuminata*) in the 1990s represented a landmark in cancer research because of their significant anti-solid tumor efficacy. Paclitaxel is in many countries approved for the treatment of ovarian and breast carcinoma and also has important activity against non-small cell lung cancer.

Popular Herb-based Cancer Therapies

Some forms of popular herbal cancer remedies can be found in most areas of the world. Although many herbal remedies are claimed to have anticancer effects, only a few have gained substantial popularity as alternative cancer therapies. Essiac is one of the most popular herbal cancer alternatives in North America. It was popularized by a Canadian nurse, Rene Caisse (Essiac is Caisse spelled backwards) but was developed initially by a Native Canadian healer who reported that it had cured her breast cancer. Essiac comprises of four herbs burdock root (*Arctium lappa*), Indian rhubarb (*Rheum palmatum*), Sheep sorrel (*Rumex acetosella*), and the inner bark of slippery elm (*Ulmus fulvaor* U. *rubra*). Researchers at the NCI and at Memorial Sloan-Kettering Cancer Centre have found that it has no anticancer effect. For 40 years Rene Caisse gave Essiac to several hundreds of cancer patients. She reportedly administered one of the herbs by injection and others as tea and modified the formula several times on the basis of her experience. During 1959 - 1978 Cassie worked in partnership with a prominent American physician, Dr. Charles Brusch, to modify the recipe and promote its use. As a result of their clinical and laboratory work, they added 4 herbs to the original recipe - water cress, blessed thistle, red clover and

kelp - which they believed potentised its action and improved its taste. More importantly, the new mixture did not require injection and could therefore be used at home. The Department of National Health and Welfare placed restriction on the promotion of Essiac for use in the treatment of cancer in 1982. The formula is now manufactured as Eassiac by Essiac Products in New Brunswick and is available in the Health Canada's emergency drug release program on compassionate grounds. Another Canadian product-Flor-Essence believed to be the 8-herb recipe is manufactured in British Columbia and is widely available in health food stores. The proponent and manufacturers of Flor-Essence are careful not to make claims that it is useful as cancer therapy; they promote it as a health enhancement herbal tea. Most people trying Essiac today use it in addition to conventional treatment or as a component of care for terminal disease [6].

Mistletoe, a parasite plant that grows on the top of trees holds a great interest as a popular cancer remedy in Europe where it has been used as flock treatment for centuries. Mistletoe is available in many mainstream European Cancer clinics. The Mistletoe extract has been shown to kill cancer cells *in vitro* and to stimulate immune system cells both *in vitro* and *in vivo* and is classified as a type of biological response modifier. Several components of Mistletoe, namely alkaloids, viscotoxins, and lectins may be responsible for these effects. The commercially available products of Mistletoe are marketed under the brand names Iscador, Eurixor, Helixor, Isorel, Vysorel, and ABNOB Aviscum. Despite its fairly widespread use, few clinical trials have been conducted and documented anticancer effects of Mistletoe in humans are sparse.

PC-SPES is one of the most studied herbal therapies in prostate cancer. A combination of eight herbal compounds: *Ganoderma lucidum*, *Scutellaria baicalensis*, *Rhodosia rubescens*, *Isatis indigotica*, *Dendranthema morifolium*, *Serenoa repens*, *Panax pseudoginseng*, and *Glycyrrhiza uralensis*. PS-SPES appeared to have estrogenic activity. Early anecdotes of PS-SPES suggested

that this therapy was effective in reducing PSA level in men with prostate cancer who have not been treated with hormonal therapy. There have been many clinical and laboratory-based studies of PC-SPES, but no randomized studies [7]. St. John's wort is widely available as over-the-counter herbal product that has gained popularity as a treatment for mild to moderate depression, which can be common among cancer patients. A few studies have reported that green tea and its extracts reduce the metastatic potential of cancer in some animal systems. These findings, together with the evidence that green tea extract suppresses chromosomal abnormalities induced by carcinogens, have generated some interest because they play a role in delaying the cumulative genetic damage necessary for a cell to evolve from normalcy to one with aggressive metastatic capabilities. Pau d'arco tea is said to be an old Inca remedy for many illness including cancer. It is made from the bark of an indigenous South American evergreen tree, and its active ingredient, lapachol, has shown to have anticancer activity.

Chinese Anti-cancer Herbs

Recent evidence suggests that many traditional Chinese medical therapies can be effective for the supportive care of cancer patients [8]. Roots of ginseng were found to have antitumor activity, inhibit platelets aggregation and inhibit chemotherapy induced immunosuppression. Glycyrrhizic acid has antitumor activity, and anti-inflammatory activity by increasing serum cortisol and also has increased natural killer (NK) cell activity against cancer cells. Roots of *Astragali membranaceus* and *Angelicae sinensis* are powerful stimulator of the immune system, have antitumor activity and inhibit platelet aggregation. Rhizome of *Atractylodis macrocephala* has antitumor activity and is an antithrombotic and fibrinolytic agent. In China, Fu Zheng herbs have been reported to increase survival when combined with radiotherapy for patients with nasopharyngeal cancer, and when combined with chemotherapy for patient with stomach and liver cancer. Fu Zheng herbs, including roots of ginseng, *Ganoderma*, *Astragali membranaceus*, *Angelicae sinensis*,

Cordyceps sinensis and *Fructus lycii*, have been shown to enhance the body's defense mechanisms. Clinical studies, have found that the NK and OKT4 (immune-enhance lymphocyte) cell count were increased with the use of Fu Zheng herbs. The Chinese herbal medicine extracts OLEN, SPES were found cytotoxic to both drug-resistant and drug-sensitive lung cancer cells, show some tumor cell specificity compared to their effect on normal cells, and are proapoptotic as measured by DNA breaks and gene - expression. The reaction of the tumor cells to these extracts was found similar to their reaction to conventional chemotherapeutic drugs.

Indian Herbal Cancer Therapies

India is home to a variety of traditional healing practices. Some are indigenous while a few are from other parts of the world. In course of time, they developed, flourished and became established traditional Systems of Medicine for example Ayurveda, Siddha and Unani. All these traditional systems heavily depend on the use of various herbs for treatment. Over half of the population in our country utilizes alternative and traditional systems of medicine [9]. Cancer treatment with herbal medicines is very common in our country and Ayurveda is the most popular option cancer patients opt for. Ayurveda is a fusion of religious, philosophical, anthropological, medical and psychological concepts. It involves a holistic approach to heal and incorporates our entire life, body, mind and spirit. It describes a theory of humoral balance within the body. Ayurveda considers the physiology of the human body in three Humors (*Vata*, *Pitta* and *Kapha*) and the human mind in another set of three Humors (*Satwa-Rajo-Tama*). Equilibrium of these humors denotes positive health and an imbalance causes illness. It also lays emphasis on the promotion of health through various approaches such as diet, life-style, exercise, personal hygiene and practicing the concept of *Rasayana* or rejuvenation in daily life. According to Ayurvedic scripts, *Rasayana* is generally used to rejuvenate the general health of the body or aims at achieving the body's maximum potential. *Rasayana* medicines (medicinal

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rejuvenation) utilize a group of individual herbs or medicinal drug preparations that are customarily complex mixtures based mostly on herbal products.

Laboratory and clinical studies conducted with various Rasayana : i.) Brahma Rasayana; ii.) Narasimha Rasayana; iii.) Amruthaprasham; and iv.) Ashwaganda Rasayana or Ashwagandhadi Lehya indicates that Rasayanas are effective myeloprotective agents in cancer patients undergoing chemotherapy and /or radiotherapy. Rasayanas were also found to protect tissue from cytotoxic injury associated with reduced serum and liver lipid peroxides, alkaline phosphatase, and glutamate pyruvate transaminase in cyclophosphamide – and radiation-treated animals [10]. The herbs that are used in various Rasayanas are mentioned below:

Brahma Rasayana: *Embelica officinalis*, *Terminalia chebula*, *Urarira picta*, *Desmodium gangeticum*, *Gmelina arborea*, *Solanum nigrum*, *Tribulus terrestris*, *Aegle marmelos*, *Premna tomentosa*, *Stereospermum suaveolens*, *Oroxylum indicum*, *Sida rhombifolia*, *Boerhaavia diffusa*, *Ricinus communis*, *Vigna vexilata*, *Phaseolus adenanthus*, *Asparagus racemosus*, *Holostemma annulare*, *Leptadenia reticulata*, *Desmostachya bipinnata*, *Saccharum officinarum*, *Oryza malampuzhensis*, *Cinnamomum iners*, *Elettaria cardamomum*, *Cyperus rotundus*, *Curcuma longa*, *Piper longum*, *Aquilaria agallocha*, *Santalum album*, *Centella asiatica*, *Mesua ferrea*, *Clitoria ternata*, *Acorus calamus*, *Scirpus crossus*, *Glycyrrhiza glabra* and *Embelia ribes*.

Amruthaprasham: *Withania somnifera*, *Pueraria tuberosa*, *Hemidesmus indicus*, *Cuminum cuminum*, *Aloe barbedensis*, *Vitis vinifera*, *Elettaria cardamomum*, *Zingiber officinale*, *Piper nigrum* and *Piper longum*.

Narasimha Rasayana: *Acacia catechu*, *Plumbago zeylanica*, *Xylia dolabriformis*, *Pterocarpus marsupium*, *Embelia ribes*, *Semicarpus anacardium*, *Eclipta alba*, *Terminalia chebula*, *Embelica officinalis* and *Terminalia bellerica*.

Ashwaganda Rasayana: *Holstemna annulare*,

Vigna vexilata, *Phaseolus adenanthus*, *Glycyrrhiza glabra*, *Zingiber officinale*, *Asparagus racemosus*, *Boerhaavia diffusa*, *Sida retusa*, *Clerodendrum serratum*, *Macuna pruriens*, *Hedychium spicatum*, *Phyllanthus amarus*, *Piper longum*, *Vitis vinifera*, *Embelica officinalis*, *Pueraria tuberosa*, *Saccharum officinalum*, *Piper nigrum*, *Cinnamomum zeylanica*, *Elettaria cardamomum*, *Garcinia Morella* and *Mesua ferrea*.

Many poly-herbal based therapies have become popular as Cancer Complementary and Alternative Therapies (CCAT) in India. Hundreds of cancer patients try these alternatives every year. Over the years the popularity of these CCAT is also increasing. One of the reasons behind this popularity could also be the effectiveness of these therapies. Some prominent among these are Maharishi Amrit Kalash, HUMA, Sarvapisti, CARCTOL etc.

MAHARISHI AMRIT KALASH (MAK)

MAK is produced by the 'Maharishi Ayurveda Products'. This poly-herbal preparation contains many important Ayurvedic herbs. MAK is processed in the extract of *Aegle marmelos*, *Oroxylum indicum*, *Gmelina arborea*, *Stereospermum suaveolens*, *Clerodendron phlomidis*, *Desmodium gangeticum*, *Urarira picta*, *Solanum indicum*, *Solanum xanthocarpum*, *Tribulus terrestris*, *Pedaliium murex*, *Phaseolus trilobus*, *Teramnus labialis*, *Ricinus communis*, *Sida cordifolia*, *Saccharum spontaneum*, *Eragrostis cynosuroides*, *Asparagus racemosus*, *Boerhaavia diffusa*, *Leptadenia reticulata*, *Saccharum officinarum*, *Gymnema aurantiacum*, *Ipomoea digitata*, *Pueraria tuberosa*.

MAK- 4 (Paste) contains: *Phyllanthus emblica*, *Terminalia chebula*, *Santalum album*, *Mesua ferrea*, *Convolvulus pluricaulis*, *Cinnamomum zeylanicum*, *Elettaria cardamomum*, *Centella asiatica*, *Curcuma longa*, *Piper longum*, *Glycyrrhiza glabra*, *Embelia ribes*, *Cyperus rotundus*, *Cyperus scariosus*.

MAK-5 (Tablet) contains: *Withania somnifera*, *Glycyrrhiza glabra*, *Ipomoea digitata*, *Asparagus adscendens*, *Embelica officinalis*,

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Tinospora cordifolia, *Asparagus racemosus*, *Vitex trifolia*, *Convolvulus pluricaulis*, *Argyreia speciosa*, *Curculigo orchoides*, *Capparis aphylla*, *Acacia arabica*.

Clinical studies of MAK, conducted in AIIMS, New Delhi and KGMU, Lucknow showed that MAK administered patients had high incidence of complete remission of the cancer / tumor as opposed to patients receiving only chemotherapy. Patients who took MAK had a drastic reduction of side effects like loss of appetite, weight loss and nausea, while there was a lowering of the incidence of fever, pain and ulceration of the mouth.

HUMA

The alternative poly-herbal cancer therapy HUMA was advocated by a Lucknow based Ayurvedacharya Dr. S M Atiq in the mid 80's. The herbal preparation HUMA contains various important Ayurvedic herbs viz. *Azadirachta indica*, *Acacia catechu*, *Asparagus racemosus*, *Curcuma longa*, *Calotropis procera*, *Catharanthus roseus*, *Embelica officinalis*, *Ocimum sanctum*, *Plumbago zeylanica*, *Semecarpus anacardium*, *Tinospora cordifolia*, *Tiliacora racemosa*, *Withania somnifera*, etc. This herbal preparation was tested in Central Drug Research Institute, Lucknow and was found to be non-toxic in animals. After publication of news reports of few long-term cancer survivors with HUMA therapy, hundreds of cancer patient all over the country now try this therapy every year. This therapy was effective in treatment of many advanced stage cancer patients without any adverse side effects. Over the years this therapy has become very popular among patients because it is cost effective, free from serious adverse side effects, orally administered, and has shown to be effective in improving quality of life in some terminal cancer patients. Objective evidence about the effectiveness of this alternative therapy in regression of oral cancer was recently reported [11].

SARVAPISTI

A dietary regimen known as Sarvapisti developed by the scientist of D S Research Centre,

Varanasi is a very popular alternative therapy among cancer patients. Sarvapasti was evolved in 1983 by using over hundreds of medicinal herbs and plants. A book published from the center recently, "Cancer is Curable Now," provided documentary evidence of more than 100 patients where marked remission of the cancer / tumor was observed along with substantial increase in the disease free survival.

CARCTOL

Carctol was devised by Dr Nand Lal Tiwari from Rajasthan, who has been giving it to patients for the last 25 years. Carctol comprises of the seeds, roots and leaves of eight Ayurvedic herbs. *Blepharis edulis*, *Piper Cubeba* Linn, *Smilax china* Linn, *Ammani vesicatoria*, *Hemidesmus indicus*, *Lepidium sativum* Linn, *Rheum emodi* Wall, *Tribulus terrestris*. Studies have shown that Carctol is excellent when used during radiotherapy and chemotherapy, as it prevents patients from becoming neutropenic (i.e. there is no compromise of white cells). This would give your body more of a "fighting chance". The oncology unit of Strong brook Hospital, New York reports Carctol as a positive factor in the health of a two-year-old with cancer. She had no negatives during chemotherapy and even put on weight.

Conclusion

Despite the fact that there is some positive research data from experimental and preclinical studies, and the anecdotal clinical experience of many practitioners, patients, and cancer survivors the potential of herbal cancer therapies is largely untapped and large scale clinical trials are generally unavailable. The reasons for this are multifactorial, and include historical, political, and cultural factors – and almost invariably a misunderstanding of the core principles of herbal medicine itself. In India, where majority of the cancer patients cannot be offered modern curative treatment at the time of diagnosis, herbal therapies can hold a great promise in cancer treatment and palliative care

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References:

1. Schwartzmann G et al. Anticancer drug discovery and development throughout the world. *J Clin Oncol* 2002; 20: 47s -59s.
2. Stewart BM, Kleinues P (Eds.). World cancer report 2003. IARC Press, Lyon.
3. Pal S K. Use of alternative cancer medicines in India. *Lancet Oncol* 2002; 3: 394 - 395.
4. Treasure J. Herbal medicine and cancer: An introductory overview. *Semin Oncol Nurs* 2005; 21: 177 -183.
5. Mans D R A, Da Rocha A B, Schwartzmann G. Anti-cancer drug discovery and development in Brazil: targeted plant collection as a rational strategy to acquire candidate anti-cancer compounds. *Oncologist* 2000; 5: 185 -198.
6. Pal S K. Complementary and alternative medicine: An overview. *Curr Sci* 2002; 82: 518 - 524
7. Shukla Y, Pal S K. Complementary and alternative cancer therapies: past, present and the future scenario. *Asian Pac J Cancer Prev* 2004; 5: 3 - 14.
8. Sagar S M, Wong R. Chinese medicine and supportive cancer care: a model for an evidence-based, integrative approach. *Evidence-Based Integrative Med* 2003; 1: 11-25.
9. Pandha H S, Kirby R S. PC-SPES: phytotherapy for prostate cancer. *Lancet* 2002; 359: 2213 - 2214.
10. Vayalil P, Kuttan G, Kuttan R. Protective effects of *Rasayanus* on cyclophosphamide and radiation-induced damage. *J Alter Compl Med* 2002; 8: 787 - 796.
11. Pal S K, Fatima S H, Mehrotra R. Oral cancer treatment with an alternative poly-herbal therapy 'HUMA' in two patients with advanced disease. *Elements* 2006; 4: 12 - 16.

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