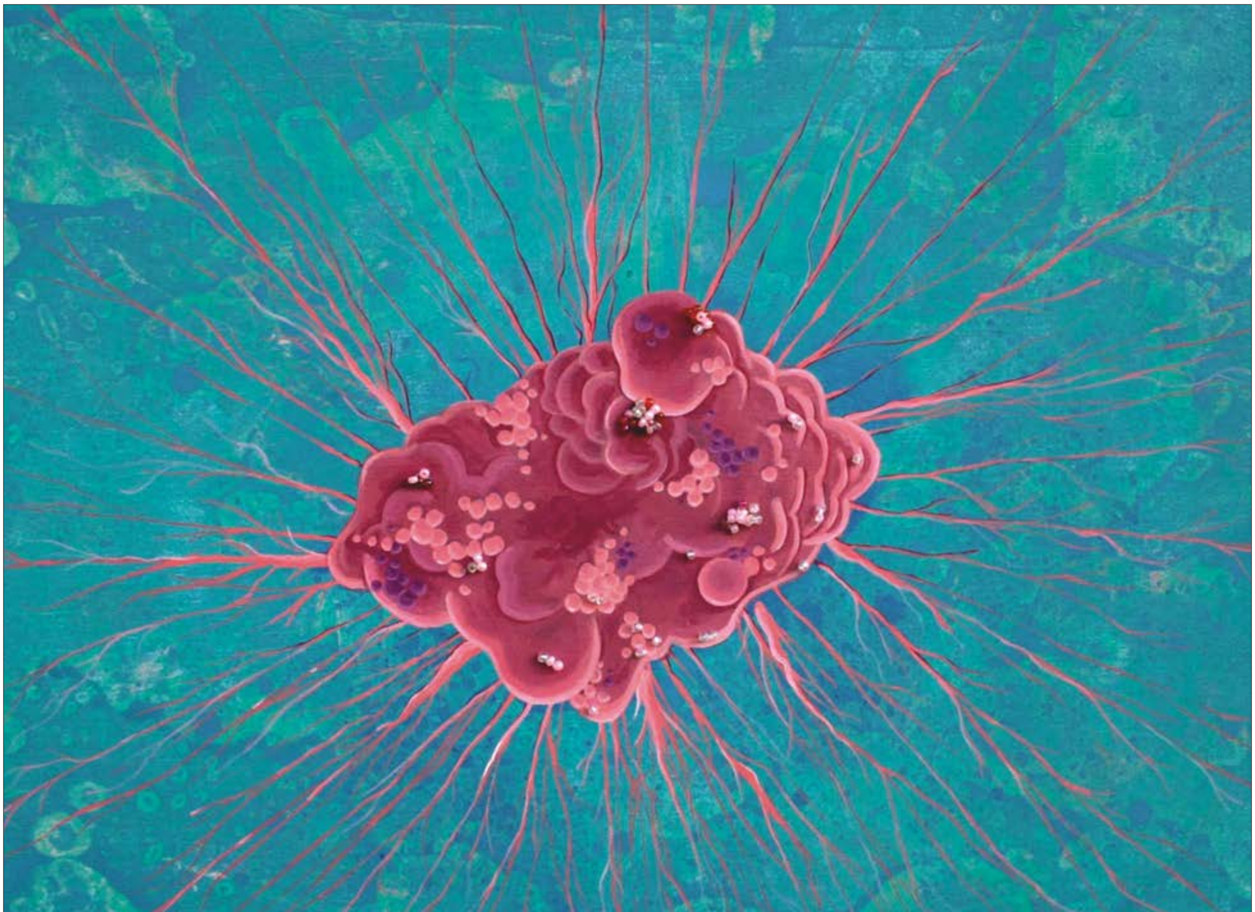

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# A Review: Cancer Research of Natural Products in Asia

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**Abstract:** With the increasing level of the carcinogenic and mutagenic substances in the environment, the research to explore new anticancer compounds has become crucial day after day. Although, many chemical anticancer agents are available, the wide spectrum side effects and emergence of chemotherapy resistant cancer cells among patients have made cancer research and discovery of new anticancer agents from natural products particularly medicinal plants pivotal. This review highlights the cancer research led to new natural anticancer agents discovered by Asian scientists in the period from 2000 to 2008. This review focuses also on the evidence based scientific research that proved the importance of dietary habits particularly the vegetarian diet as a potent factor in reducing the risk of carcinogenesis. Many components isolated from plants have been approved to be potent anticancer agents. The plant-derived polyphenolic compounds are promising nutraceuticals for control of various disorders and cancer. These compounds may be the future developing anticancer drugs with no side effect and low cost for people all around the world. The much lower risk of colon, prostate and breast cancers in Asians, who consume more vegetables, fruits and tea than populations in the western hemisphere, raises the role of flavonoid components as protective factors against carcinogenesis.

**Key words:** Anticancer, antimutagenic, medicinal plants, polyphenols, diet, natural products

## INTRODUCTION

There is currently a large and ever-expanding global population that prefers the use of natural products in treating and preventing medical complications (Gautam *et al*., 2007; Jassim and Naji, 2003). The worldwide upsurge in the use of herbal preparations and active ingredients isolated from medicinal plants have provided the pharmaceutical industry with one of its most important sources of lead compounds, as up to 40% of modern drugs are derived from natural sources, using either the natural substance or a synthesized version. Furthermore, over a 100 new products are in clinical development, particularly as anti-cancer agents and anti-infectives (Gautam *et al*., 2007; Harvey, 2008; Jassim and Naji, 2003).

Epidemiological studies have shown an inverse relationship between vegetarian dietary practices and the incidence of cancer, cardiovascular diseases and mortality (Rajaram and Sabaté, 2000). Similar outcomes were also observed in countries where animal-based foods are included in the diet but the

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in take of plant-based foods was high. This suggests a potential therapeutic role of edible plants in human health (Liu and Li, 2000). Japanese researchers have found that there is a strong relationship between meat consumption and colorectal cancer cases in Japan. They also found that the incidence of colorectal cancer in Asian countries is increasing. The change to a more westernized diet is known to be related to these increases (Lee *et al*., 2008a, b). Recent physiological, pharmacological and biochemical studies appear to support the wisdom of the traditional dietary practices. They proved that phytochemicals from fruits and vegetables have shown to exert varied beneficial biological functions (Harborne and Williams, 2000).

Review of the epidemiological data, including both cohort and case-control studies, of all cancer sites strongly suggests that plant foods also have preventive potential and that consumption of the following groups and types of vegetables and fruits is lower in those who subsequently develop cancer, raw and fresh vegetables (Yun *et al*., 2008), leafy green vegetables (Shao *et al*., 2001), Cruciferae (Morimitsu *et al*., 2000), carrots (Galeone *et al*., 2007), broccoli and cabbage (Hara *et al*., 2003), lettuce and raw and fresh fruit (including tomatoes and citrus fruit) (Do *et al*., 2007a; Huang *et al*., 2004).

Asians have a long history of medicinal use of plants, some of which have proved useful as pharmaceuticals. Besides, traditional Asian diet contains less animal fats and higher plant-based foods as it is compared to western diet. Such a higher consumption of plant foods in Asian countries as a result of their tropical climates, results in a wider choice of edible plants (Runnie *et al*., 2004). The practice of medicine-both in the past and present, of ten involves the prescription of specific foods (almost always plants) or their potent derivatives, to treat a wide spectrum of illnesses (Rigas *et al*., 2008).

A good example of such Asian foods are Indian food ingredients which can be used in preventive strategies aimed at reducing the incidence and mortality of different types of cancers because of their antioxidative (Devasagayam and Sainis, 2002), antimutagenic and anticarcinogenic properties (Arora *et al*., 2003). Such vital ingredients used in Indian cooking include *Curcuma longa* L. (turmeric), *Zingiber officinale* Rosc. (ginger) and *Elettaria cardamomum* (L.) Maton (cardamom) which all belong to Zingiberaceae family, *Syzygium aromaticum* (L.) Merrill and Perry (cloves, Myrtaceae), *Pimpinella anisum* L. (aniseed, Apiaceae), *Brassica nigra* L. (black mustard seeds, Brassicaceae), *Crocus sativus* L. (saffron, Iridaceae) and *Allium sativum* L. (garlic, Liliaceae). Garlic is also an indispensable ingredient of Indian food and the chemopreventive efficacy of garlic and its components on colon carcinogenesis has been shown (Krishnaswamy, 2008; Sengupta *et al*., 2004) . Ayurveda, whose history goes back to 5000 B.C., is one of the ancient health care systems. The plant species mentioned in the ancient texts of these Ayurveda and other Indian systems of medicines may be explored with the modern scientific approaches for the discovery of newer, safer and affordable medicines (Mukherjee and Wahile, 2006; Patwardhan, 2005).

The aim of this study is to give an overview on the progress of anticancer medicinal plant research around the continental Asia, focusing on the most important findings of scientists in this field (Table 1). We have tried to explore the discovered plants' components with proved anticancer activity both *in vivo* and *in vitro*. These herbal components are considered as promising, inexpensive and effective anticancer agents. Finally, the review discusses the importance of the daily diet habits in reducing the risk of cancer development which have been proved by many studies.

**Plant Components as Promising Anticancer Agents**

High number of components isolated from plants and food plants have been recorded by Asian scientists. Recent research has shown that plant-derived polyphenolic compounds are promising nutraceuticals for control of various disorders such as cardiovascular, neurological and neoplastic disease. The richness of the polyphenolic contents of green tea and red wine has made them popular choices for associated anticancer and cardiovascular health benefits (Ullah and Khan, 2008).

Table 1: Summary of the important findings regarding the natural anticancer products from Asian plants against different types of the cancer cells in the period from 2000 to 2008

| Scientific name of the plant | Common name of the plant | Used part(s) | Family name | Type of the tested cancer cells | Reference No. |
|---|---|---|---|---|---|
| *Allium sativum* L. | Garlic | Whole fruit | Liliaceae | Colon cancer cell line | (Krishnaswamy, 2008; Sengupta *et al*., 2004) |
| *Blumea lacera* (Burm. f.) DC. | Malay blumea | Whole plant | Asteraceae | K562, L1210, P3HR1, Raji and U937 leukemia cell lines | (Chiang *et al*., 2004) |
| *Cinnamomum kotoense* Kaneh. and Sas. | Canela | Leaves | Lauraceae | Human non-small lung cancer cell line (A549) | (Chen *et al*., 2008) |
| *Coptis chinensis* Franch. | Chinese goldthread | Root | Ranunculaceae | Hepatoma and leukaemia cancer cell lines | (Lin *et al*., 2004) |
| *Curcuma mangga* Valeton and van Zijp | Mangor ginger | Rhizome | Zingiberaceae | Human prostate cancer cell line (DU-145), non-small lung cancer cell line (NCI-H460) and breast cancer cell line (MCF-7) | (Abas *et al*., 2005, 2006) |
| *Epimedium sagittatum* (Sieb. and Zucc.) Maxim. | Horny goat weed | Whole plant | Podophyllaceae | Leukaemia cancer cell line | (Lin *et al*., 2004) |
| *Erycibe elliptilimba* Merr. and Chun. | No common name | Stem | Convolvulaceae | SKBR3 and MDA-MB435 human breast cancer cell lines | (Kummalue *et al*., 2007) |
| *Garcinia atroviridis* Griff. ex T. Anders | No common name | Root,fruit, leaf stem and trunk bark | Clusiaceae | HeLa cell line (cervical cancer cells) | (Mackeen *et al*., 2000; Permanaa *et al*., 2001) |
| | | Root | | Human breast adenocarcinoma cell line (MCF-7), human prostate cancer cell lines (DU-145) and human lung cancer cells (H-460) | (Permanaa *et al*., 2005) |
| *Garcinia cantleyana* T.C.Whitmore | No common name | Leaves and trunk bark | Clusiaceae | Breast cancer cell line (MDA-MB-231), ovarian cancer cells (CaOV-3), (MCF-7) and HeLa cancer cell-lines | (Shadid *et al*., 2007) |
| *Garcinia penangiana* Pierre | No common name | Leaves | Clusiaceae | (DU-145), (MCF-7) and (NCI-H460) | (Jabit *et al*., 2007) |
| *Hemidesmus indicus* (L.) W. T. Aiton | East Indian-sarsaparilla | Root | Apocynaceae | HepG2 cell line | (Perera and De Silva, 2002) |
| *Ixeris chinensis* Thunb. Nakai | No common name | Whole plant | Asteraceae | K562 cell line | (Chiang *et al*., 2004) |
| *Kadsura interior* A. C. Sm. | Dragon liane | Stem | Schisandraceae | Raji cells | (Chen *et al*., 2002) |
| *Manihot utilissima* Pohl. | Cassava | Shoot | Euphorbiaceae | Breast cancer cell lines | (Rahmat *et al*., 2004) |
| *Nigella sativa* L. | Black-cumin | Seed | Ranunculaceae | HepG2 cell line | (Perera and De Silva, 2002) |
| *Rhinacanthus nasutus* (Linn.) Kurz. | Rhinacanthus nasutus | Root | Acanthaceae | Human cervical carcinoma HeLaS 3 cells | (Siripong *et al*., 2006 a, b) |
| *Rhus succedanea* L. | Poison sumac | Tree sap | Anacardiaceae | Human promyelocytic leukemia cells (HL-60) | (Huang *et al*., 2008; Wu *et al*., 2002) |

Table 1: Countinued

| Scientific name of the plant | Common name of the plant | Used part(s) | Family name | Type of the tested cancer cells | Reference No. |
|---|---|---|---|---|---|
| *Sauropus* and *rogynus* (L.) Merr. | Star gooseberry | Shoot | Euphorbiaceae | Breast cancer cell lines | (Rahmat *et al*., 2004) |
| *Smilax glabra* Roxb. | Chinese smilax | Rhizome | Simlacaceae | HepG2 cell line | (Perera and De Silva, 2002) |
| *Tinospora cordifolia* (Willd.) Hook. f. and Thomson | Gulancha tinospora | Whole plant | Menispermaceae | Skin cancer cells | (Chaudhary *et al*., 2008) |

The flavonoids are polyphenolic compounds found as integral components of the human diet. They are universally present as constituents of flowering plants, particularly of food plants (Miean and Mohamed, 2001). Several plants and spices containing flavonoid derivatives have found application as disease preventive and therapeutic agents in traditional medicine in Asia for thousands of years (Nakatani, 2000). Many studies around the world proved that the selection of a particular food plant, plant tissue or herb for its potential health benefits appears to mirror its flavonoid composition. The ability of flavonoids to scavenge free-radicals and block lipid peroxidation raises the possibility that they may act as protective factors against arcinogenesis (Tseng and Lee, 2006; Zhou *et al*., 2003). An impressive body of information exists on the antitumor action of plant flavonoids. *In vitro* work has concentrated on the direct and indirect actions of flavonoids on tumor cells and has found a variety of anticancer effects such as cell growth (Weng *et al*., 2007), kinase activity inhibition (Yagura *et al*., 2008), apoptosis induction (Lee *et al*., 2005), suppression of the secretion of matrix me talloproteinases and of tumor invasive behavior (Ha *et al*., 2004). Furthermore, some studies have reported the impairment of *in vivo* angiogenesis by dietary flavonoids (Zhou *et al*., 2003). Many of experimental animal studies indicate that certain dietary flavonoids possess antitumor activity. The hydroxylation pattern of the bring of the flavones and flavonols, such as luteolin and quercetin, seems to critically influence their activities, especially the inhibition of protein kinase activity and antiproliferation (Ong *et al*., 2004; Steffan *et al*., 2005). The different mechanisms underlying the potential anticancer action of plant flavonoids await further elucidation. Certain dietary flavonols and flavones targeting cell surface signal transduction enzymes, such as protein tyrosine and focal adhesion kinases and the processes of angiogenesis appear to be promising candidates as anticancer agents (Kandaswami *et al*., 2005). In present opinion further *in vitro* and *in vivo* studies of these bioactive constituents are deemed necessary in order to develop flavonoid-based anticancer strategies. Other data suggest that foods high in phytoestrogens, particularly soy (which contains isoflavones) (Do *et al*., 2007 b; Dos Santos Silva *et al*., 2004; Lu *et al*., 2000; Sakauchi *et al*., 2007; Wu *et al*., 2008) and also phytoestrogens derived from some vegetables and berries as well as grains and seeds (Ozasa *et al*., 2005), or high in precursor compounds that can be metabolized by gut bacteria into active agents, particularly some grains and vegetables with woody stems (which contain precursors to lignans) (Cai *et al*., 2005; Dos Santos Silva *et al*., 2004; Kumar *et al*., 2004; Penalvo *et al*., 2008) are plausibly associated with a lower risk of sex-hormone-related cancers. Phytoestrogens compete with estradiol for estrogen receptors in a way that is generally antiproliferative. The lower incidence of hormone-dependent tumors in Asian population compared to Europeans is believed to be related their rich phytoestrogen diet (Vij and Kumar, 2004; Waldschlager *et al*., 2005). Consumption of diets low in plant foods results in a reduced intake of a wide variety of these substances that can plausibly lower cancer risk. There are many biologically plausible reasons why consumption of plant foods might slow or prevent the appearance of cancer.

These include the presence in plant foods of such potentially anticarcinogenic substances as carotenoids and vitamin C (Huang *et al*., 2007; Kapil *et al*., 2003), vitamin E (Xu *et al*., 2007), selenium (Cai *et al*., 2006; Pourmand *et al*., 2008), dietary fibre and its components (Bolin, 2008; Dos Santos Silva *et al*., 2002), isothiocyanates (Moy *et al*., 2008), indoles (Hecht *et al*., 2004), phenols (Kandaswami *et al*., 2005; Saxena *et al*., 2007), protease inhibitors (Seo *et al*., 2005), allium compounds (Setiawan *et al*., 2005), plant sterols (Iwashima *et al*., 2002) and limonene (Tsuda *et al*., 2004). Most of the data for the observations on the anticarcinogenic potential of all of these compounds have come from animal and *in vitro* studies.

Studies confirmed that in every stage of cancer process, identified phytochemicals are shown to alter the likelihood of carcinogenesis in a way that reduces risk but usually in a favorable direction. Examples of these phytochemicals are: glucosinolates and indoles, thiocyanates and isothiocyanates, phenols, coumarins and glutathione S-transferase (GST) which can induce a multiplicity of phase II (solubilizing and usually inactivating) enzymes. The activity of these compounds depends on the fact that the exposure of human cells to a wide variety of chemoprotective compounds confers resistance against a broad set of carcinogens. For a subset of the chemoprotective compounds, protection is generated by an increase in the abundance of the protective phase II detoxification enzymes (Morimitsu *et al*., 2002; Steffan *et al*., 2005; Win *et al*., 2008; Youn *et al*., 2008).

Other phytochemicals with anticancer activity are ascorbate and phenols which block the formation of carcinogens such as nitrosamines (Mitacek *et al*., 2008; Qiu *et al*., 2005; Takeyama, 2005); flavonoids and carotenoids act as antioxidants, essentially disabling the carcinogenic potential of specific compounds by having cytoprotective effects against ONOO- and HOCl mediated cytotoxicity (Persson *et al*., 2008; Rose *et al*., 2005); lipid-soluble compounds such as carotenoids and sterols may alter membrane structure or integrity and show significant growth inhibition activity against various human cancer cell line (Damu *et al*., 2007; Iwashima *et al*., 2002); carotenoids can suppress DNA synthesis and enhance differentiation (Kawashima *et al*., 2007); some sulphur-containing compounds suppress DNA and protein synthesis. Sulfur is commonly used in Asia as a herbal medicine to treat inflammation and cancer. The potent chemopreventive effects have been demonstrated in various *in vivo* and *in vitro* models for sulfur-containing compounds found in naturally occurring products (Lee *et al*., 2008a).

Turmeric, derived from the plant *Curcuma longa* L. (Zingiberaceae), is a gold-colored spice commonly used in the Indian subcontinent, curcumin, which gives the yellow color to turmeric, was first isolated almost two centuries ago and its structure as diferuloylmethane was determined in 1910 (Jagetia and Aggarwal, 2007). Both turmeric and curcumin were found to increase detoxifying enzymes (Nishinaka *et al*., 2007), prevent DNA damage and improve DNA repair (Krishnaswamy, 2008), decrease mutations and tumor formation (Ragunathan and Panneerselvam, 2007) and exhibit antioxidative potential in animals (Surh and Chun, 2007). Recently, several molecular targets have been identified for therapeutic/preventive effects of turmeric (Itokawa *et al*., 2008; Marcu *et al*., 2006). These effects are mediated through the regulation of various transcription factors (Shishodia *et al*., 2007), growth factors (Lin and Chen, 2008), inflammatory cytokines (Bachmeier *et al*., 2008), protein kinases and other enzymes (Chen *et al*., 2001). Considering the recent scientific bandwagon, multitargeted therapy is better than monotargeted therapy for most diseases, curcumin can be considered an ideal spice for life (Aggarwal *et al*., 2007).

The anticancer activity of many of natural compounds isolated from different Asian plants' extracts has been reported. Studies done by our team in 2005 and 2006 revealed that Zerumin B, demethoxycurcumin, bisdemethoxycurcumin and curcumin which were isolated from rhizomes of *Curcuma mangga* Valeton and van Zijp (Mango ginger one of the Zingiberaceae family member), exhibited cytotoxic activity against a panel of human tumor cell lines. Present study ended with the characterization of two other compounds; namely: diacetyldemethoxycurcumin and triacetyldemethylcurcumin. These both compounds exhibited high antioxidant activity and potent anticancer activity against a human prostate cancer cell line (DU-145), non-small lung cancer cell line (NCI-H460) and breast cancer cells (MCF-7) (Abas *et al*., 2006, 2005). Other recent study on the anticancer effect on human non-small lung cancer cell line (A549) found that the isoobtusilactone A (IOA), a constituent isolated from the leaves of *Cinnamomum kotoense* Kaneh. And Sas. (Canela, Lauraceae) has inhibited the migration and invasion of A549 cells (Chen *et al*., 2008). Further recent study has isolated cytotoxic alkyl hydroquinone compound, a potential anticancer agent and it ascertained that its structure could be a model for anticancer drug design. The same team in 2002 had isolated three structurally similar cytotoxic alkyl hydroquinone compounds from the sap of the lacquer tree *Rhus succedanea* L. (Poison sumac) belonging to the Sumac family (Anacardiaceae), which have a long history of medicinal use in Asia. Their results suggest that Topo II is the cellular drug target. In HL-60 cells, the component promptly inhibited DNA synthesis, induced chromo somal breakage and led to cell death with an EC 50 about one-tenth that of hydroquinone. (Huang *et al*., 2008; Wu *et al*., 2002).

The studies are characterized a prenylated compound (depsidone atrovirisidone) which was isolated from the roots of *Garcinia atroviridis* Griff. ex T. Anders (Asam gelugur, Clusiaceae). This compound showed some cytotoxicity against HeLa cells and this finding was in harmony with previous scientists manifestations that the crude methanol extracts of fruit, leaf stem and trunk bark of this plant provoked antitumor activity reaching to >95% inhibition (Mackeen *et al*., 2000; Permanaa *et al*., 2001). Further cytotoxic activity of this prenylated compound (atrovirisidone B) was investigated by our team. The cytotoxic activity assays found that this prenylated depsidone compound which was also isolated from the roots of *G. atroviridis* has cytotoxic activity against (MCF-7), (DU-145) and human lung (H-460) cancer cells (Permanaa *et al*., 2005).

The studies on different species o f *Garcinia* sp. trying to isolate new compounds or even known compounds with anticancer activity. Two new xanthones, characterized as 4-(1,1-dimethylprop-2-enyl)-1,3,5,8-tetrahydroxyxanthone and penangianaxanthone, with three known xanthones, cudratricusxanthone H, macluraxanthone C and gerontoxanthone C, were isolated from the leaves of *Garcinia penangiana* Pierre. Significant cytotoxicity against (DU-145), (MCF-7) and (NCI-H460) cancer cell lines was demonstrated by those compounds, with IC50 values ranging from 3.5 to 72.8 µM (Jabit *et al*., 2007). More cytotoxic xanthones compounds were isolated from the leaves of *Garcinia urophylla* Scortech.ex King which also revealed cytotoxic activity against variety of cancer cells at laboratory (Khalid *et al*., 2007). Additionally, the phytochemical studies on the leaves and trunk bark of *Garcinia cantleyana* T.C. Whitmore yielded two caged-xanthonoids including cantleyanones B-D and 7-hydroxyforbesione and known compounds deoxygaudichaudione A and macranthol. Those compounds proved their significant cytotoxicity against breast cancer cell line (MDA-MB-231), ovarian cancer cells (CaOV-3), (MCF-7) and HeLa cancer cell-lines with IC (50) values ranging from 0.22 to 17.17 µg $mL^{-1}$ (Shadid *et al*., 2007).

Further studies which aimed at isolating anticancer natural products were continued on many of Asian medicinal plants. A study on one of Asian medicinal plants demonstrated two new lignans, interiotherins C and D, together with the known compounds interiorin, heteroclitin F, neokadsuranin, heteroclitin D, kadsurin, gomisin A, schisandrin C, interiotherin A, angeloylgomisin R, gomisin G, interiotherin B and gomisin C, which were isolated from the stems of *Kadsura interior* A. C. Sm. (dragon liane, Schisandraceae). They were screened as potential antitumor promoters by examining their ability to inhibit Epstein-Barr virus early antigen (EBV-EA) activation (induced by 12-O-tetradecanoylphorbol-13-acetate) in Raji cells. Neokadsuranin and schisandrin C were the most potent compounds. These data suggested that some neolignans might be valuable antitumor promoters or chemopreventors (Chen *et al*., 2002). Moreover, a new flavonoid, dihydroglychalcone-A (2'-hydroxy-4,6'-dimethoxy-3',4'-(2",2" dimethylpyrano) and two known sulphur-containing amides, dambullin and gerambullin were isolated from the leaves extract of *Glycosmis chlorosperma* (Blume) Spreng (Rutaceae). The leaves extract was also found to exhibit cytotoxic activities against human cancer cell lines (Rahmani *et al*., 2004).

The discovery engine is still working to unveil new and potent natural compounds but more *in vivo* and clinical trials are still needed to prove the anticancer activity of these compounds and reduce the chance of their toxicity against human body.

**Anticancer Bioactivity of Some of Asian Plants**

Hepatocellular carcinoma (HCC) is the most common cancer found in Southeast Asia and Southern Africa, but it is rare in Europe and North America (Okuda, 1992). Several risk factors, such as exposure to aflatoxins and infection with hepatitis B (HBV) or C (HCV), are known to be associated with HCC (Tong *et al*., 1979). Traditional Chinese Medicines (TCM) have long been consumed to prevent and treat various kinds of cancers prevalent in Taiwan, mainland China and Japan (Lau *et al*., 1994). *Coptis chinensis* Franch. (Chinese goldthread, Ranunculaceae) and *Epimedium sagittatum* (Sieb. And Zucc.) Maxim. (horny goat weed, Podophyllaceae) are important plant materials used in TCM preparations. Lin *et al*. (2004) revealed the potential of *Coptis chinensis* root extract, berberine and coptisine to treat hepatoma and leukaemia cancers and the *Epimedium sagittatum* extract to treat leukaemia. Although the possible mechanism(s) of the pharmacological actions of these compounds remain unknown, their results suggested that berberine and coptisine, the major constituents of *C. chinensis*, may play an important role in the cytotoxic effect of this plant species against hepatoma and leukaemia cell growth (Lin *et al*., 2004).

The studies are conducted by Kummalue *et al*. (2007), on a Thai traditional medicine, found that a fraction from methanolic stem extract of *Erycibe elliptilimba* Merr. And Chun. (Convolvulaceae), which is widely used in the treatment of various infectious and malignant diseases, has antiproliferative effect on SKBR3 and MDA-MB435 human breast cancer cells. These results indicated that the extract fraction could induce cell cycle arrest in some way (Kummalue *et al*., 2007). In addition, Pudhom *et al*. (2007) isolated four novel furanocembranoids from the stem bark of *Croton oblongifolius* Roxb. (Nagdanti, Euphorbiaceae), which exhibited good cytotoxicity against several human tumor cell lines (Pudhom *et al*., 2007). A similar study on the Thai medicinal plants found that rhinacanthins-C, -N and -Q, three main naphthoquinone esters, which were isolated from the roots of Thai medicinal plant; *Rhinacanthus nasutus* (Linn.) Kurz. (*Rhinacanthus nasutus* root, Acanthaceae), induced apoptosis of human cervical carcinoma HeLaS3 cells. Based on these results, their findings demonstrated that rhinacanthin-N suppresses tumor growth *in vivo* (Siripong *et al*., 2006 a, b).

Moreover, a study on the direct relationship between the diet habit and cancer risk by a Taiwanese group in 2001 revealed that the mung bean aqueous extract showed the best hepatoprotective effect on hepatotoxicity. The pathological changes of liver injury were improved by the treatment with all of the legume extracts belonging to Fabaceae family: *Phaseolus aureus* or *Vigna radiate* (L.) R. Wilczek (mung bean), *Vigna angularis* (Willd.) Ohwi and H. Ohashi (adzuki bean), *Castanospermum australe* A. Cunn and C. Fraser ex Hook (black bean) and *Vigna umbellate* (Thunb.) Ohwi and H. Ohashi (rice bean). When compared to silymarin as a standardized drug, these beans are used as foods and folk medicines in Taiwan. In addition, the extract of mung bean acted as a potential hepatoprotective agent in dietary supply (Wu *et al*., 2001). In view of the vast data available online regarding the bioactive principles from plants against different human cancer cells with proved *in vivo* and *in vitro* studies, it is suggested that dietary prevention coupled with other life-style changes is perhaps the right answer for prevention of cancer and other chronic diseases.

Other commonly used plants by Asian countries people are *Boesenbergia pandurata* (Roxb.) Schltr. (Chinese ginger, Zingiberaceae), *Languas galanga or Alpinia galanga* (L.) Willd. (Siamese ginger, Zingiberaceae) and *Citrus hystrix* DC. (kaffir lime, Rutaceae) which are edible plants that are commonly used as flavors or condiments in various Thai food dishes. They are known to exert strong anti-promoting activity in a test of tumor promoter-induced Epstein-Barr Virus (EBV) activation (Tiwawech *et al*., 2000).

In Asian countries, herbal formulations prepared from a mixture of plants are often used by traditional medical practitioners for the treatment of cancer (Eum *et al*., 2005; Sliva *et al*., 2003). In herbal medicines containing a mixture of plants, the total herb extract often has better effects than an equivalent dose of an individual plant in the mixture or chemical compounds isolated from the plant material (Thabrew *et al*., 2005; Wang *et al*., 2008). One such remedy used by a family of indigenous medical practitioners in Sri Lanka, is a decoction prepared from *Nigella sativa* L. (black-cumin, Ranunculaceae), *Hemidesmus indicus* (L.) W. T. Aiton (East Indian-sarsaparilla, Apocynaceae) and *Smilax glabra* Roxb. (Chinese smilax, Simlacaceae). In Sri Lanka, all three of the plant species in this decoction are used in the preparation of medications for the treatment of boils and other skin conditions. The *in vitro* assay demonstrated that the decoction prepared from a mixture of *N. sativa* seeds, *H. indicus* roots and *S. glabra* rhizome has powerful cytotoxic properties towards human liver cancer cells as assessed by the resulting inhibitory effects. The aqueous extracts of each of the three individual plants used for the preparation of the decoction were shown to be cytotoxic to HepG2 cells (Perera and De Silva, 2002).

In Taiwan, medicinal plants have been historically used as treatment for different kinds of human diseases. Chiang *et al*. (2004) used the hot water extract of Taiwanese traditionally used medicinal plants to evaluate their *in vitro* anti-leukemic properties (including anti-K562, L1210, P3HR1, Raji and U937 leukemia cells). Results showed that *Blumea lacera* (Burm. f.) DC. (Malay Blumea, Asteraceae) exhibited broad anti-leukemic activity at magnitudes ranging from moderate to mild and *Ixeris chinensis* Thunb. Nakai (Asteraceae) is effective at inhibiting the proliferation of K562 cells (Chiang *et al*., 2004). Another study done on the shoot extracts of *Sauropus androgynus* (L.) Merr. (Star gooseberry, Euphorbiaceae) and *Manihot utilissima* Pohl. (Cassava, Euphorbiaceae) suggested that *S. androgynus* shoots and *M. utilissima* shoots have potential as an anticancer agent against breast cancer cell lines (Rahmat *et al*., 2004).

*In vivo* study in India on *Tinospora cordifolia* (Willd.) Hook. f. and Thomson (*Gulancha tinospora*, Menispermaceae) extract, an Indian medicinal plant, was conducted to explore antitumor promoting activity in a two-stage skin carcinogenesis model. The results strongly suggest that the *T. cordifolia* extract has anti-tumor potential in a two-stage skin carcinogenesis mouse model by recording significant reduction in tumor weight, tumor incidence in comparison to control. Furthermore, cumulative number of papillomas, tumor yield, tumor burden and tumor weight showed significant reduction along with significant elevation of phase II detoxifying enzymes and inhibition of lipid peroxidation in liver and skin in the animals administered with such plant extract was concomitant to carcinogen exposure (Chaudhary *et al*., 2008).

## CONCLUSION

Asia is one of the most promising regions for discovering novel biologically-active substances from its flora. More efforts are needed to explore potent anticancer plants from the mother earth and save humans around the world from cancer. Although cancer is a multifactorial disease, researches have shown that a healthy diet rich in vegetables and low in fats is the key to lower the risk of such catastrophic diseases.

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