Turkish Journal of Botany

Volume 38 | Number 6 Article 1

1-1-2014

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TÜBİTAK

Turkish Journal of Botany

http://journals.tubitak.gov.tr/botany/

Review Article

Turk J Bot
(2014) 38: 1027-1035

doi:10.3906/bot-1405-93

Phytochemical importance of medicinal plants as potential sources of anticancer agents

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Received: 30.05.2014 • **Accepted:** 16.10.2014 • **Published Online:** 17.11.2014 • **Printed:** 28.11.2014

Abstract: The diverse and magnificent plant kingdom of the world is widely known for its medicinal importance. The potential medicinal properties of plant species have contributed significantly in the development of various herbal therapies for a number of diseases across the globe. The benefits of herbal medicine over allopathic medicine have helped medicinal plants to regain their importance in the field of health and medicine. Cancer is one of the major health problems that have widely affected the world's population. There is a great need to combat this disease with better and more effective medication as compared to existing therapies. A vast number of medicinal plants are known to have biochemical constituents with anticancer properties. The chemical metabolites of natural origin that possess anticancer properties can serve as potential lead compounds in drug designing. This association of medicinal plants and cancer needs further research and experimentation in order to develop and design anticancer drugs. The present review is an effort to compile information on some of the geographically diverse and important medicinal plants that possess anticancer activity.

Key words: Biochemical constituent, anticancer properties, medicinal plants, drug designing, antiinflammatory, antiviral, antitumor, antimalarial, analgesic

1. Introduction

Medicinal plants are considered a repository of numerous types of bioactive compounds possessing varied therapeutic properties. The therapeutic potential of plants has been well explored over a very long time period. The vast array of therapeutic effects associated with medicinal plants includes antiinflammatory, antiviral, antitumor, antimalarial, and analgesic. Cancer is one of the major obstacles to human health around the world. Among all epidemic diseases, cancer holds the first place as a death-causing disease. The main reason behind the growing number of cancer cases is the changing lifestyle of the population across the globe. Keeping in view the statistical data, the most prevalent cancer among females is breast cancer, accounting for about 23% of total cancer cases; in males, the most prevalent is lung cancer, which accounts for 17% of total cancer cases (Jemal et al., 2011). Poor survival rate of cancer patients in developing countries is attributed to the lack of timely diagnosis and limited treatment facilities. There is a great need to address this epidemic disease with more effective therapeutic and preventive strategies, which could be possible with the use of natural compounds.

Recently the scientific world has experienced an upsurge of interest in the therapeutic potential of medicinal plants as a source of promising anticancer agents. However, the application of plant-based compounds for the treatment of cancer can be traced back to 1950s. Some of the very first anticancer agents derived from plants are vinca alkaloids, vinblastine, vincristine, and cytotoxic podophyllotoxins. Statistical data suggest that 16 plant-derived anticancer drugs have been subjected to clinical trials thus far (Belayachi et al., 2013). Landmarks of these clinical trials are flavopiridol, isolated from the Indian tree *Dysoxylum binectariferum*, and meisoindigo, isolated from the Chinese plant *Indigofera tinctoria*, which have been documented to have less toxicity than conventional chemotherapeutic anticancer drugs (Saklani and Kutty, 2008). These discoveries have propelled the scientific interest of various research groups in the discovery of new anticancer agents from all-natural product sources, inclusive of plant secondary metabolites. The emerging importance of natural anticancer agents demands more research and experimentation in order to develop successful natural therapeutic options for this disease. This review focuses on the phytochemical aspect of some of the potential anticancer medicinal plants with data gathered from the scientific literature of the PubMed database. Thus, the present review aims to assemble information on some of the medicinal plants that possess anticancer properties and thus great potential for cancer treatment.

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2. Medicinal plants as the best choice for cancer treatment

The chemical components of medicinal plants mainly possess antioxidant properties that contribute to their anticancer potential. Flavones, isoflavones, flavonoids, anthocyanins, coumarins, lignans, catechins, and isocatechins are the major classes of bioactive constituents responsible for the antioxidant action (Nema et al., 2013). The great potential of plant-based compounds for the treatment and prevention of cancer is attributed to their safety, low cost, and oral bioavailability. However, a few plant-based compounds induce some side effects. These side effects can be overcome by dose-dependent administration and usage, and do not in any case make them unsuitable for phytochemical research. The already available expensive conventional therapies for cancer like chemotherapy and radiotherapy have a number of side effects such as myelosuppression and neurological, cardiac, pulmonary, and renal toxicity, which pose serious harm to the quality of life (Alonso-Castro et al., 2011). Therefore, there is a need to develop treatment options that include more potent and less toxic anticancer drugs as compared to existing drugs. The market statistics mark the availability of approximately 60% plant-based anticancer drugs (Gordaliza, 2007). Medicinal plants constitute a common alternative to cancer treatment in many countries of the world (Gerson-Cwilich et al., 2006; Tascilar et al., 2006). Cytotoxic screening of a number of plants has been done to correlate their anticancer activity and further expand their scope for drug development (Akter et al., 2014). Owing to potential benefits of plant-based drugs for cancer treatment, their use is increasingly growing from 10% to 40% across the globe; specifically, on the Asian continent, it has reached 50% (Cassileth and Deng, 2004; Molassiotis et al., 2006). Anticancer benefits associated with natural plant derivatives demand extensive scientific screening and clinical experimentations for the development of improved drugs.

3. Medicinal plants with anticancer properties

3.1. *Actaea racemosa* L.

Actaea racemosa belongs to the family Ranunculaceae and has its origin in eastern North America. Its common names are 'black cohosh' and 'black snakeroot'. The main characteristic chemical compounds present in this plant are cycloartenol-type triterpenoids, cimicifugoside, and cinnamic acid derivatives. The plant is well known for its use in conditions such as chronic ovaritis and amenorrhea (Mahady et al., 2002). An active metabolite of this plant, actein has been shown to inhibit the proliferation of human breast cancer cells and human liver cancer cells (HepG2) and thus possess antitumor activity. Actein alters the expression of cholesterol and fatty acid biosynthetic genes, p53 pathway genes, CCND1, and ID3. Actein-induced inhibition of growth of human HepG2 liver cancer cells is because of the reduced free fatty acid and cholesterol levels in the liver (Einbonda et al., 2009).

3.2. *Allium sativum* L.

Allium sativum is commonly known as garlic and belongs to the family Liliaceae/Alliaceae. It contains sulfur compounds, numerous enzymes, 17 amino acids, and minerals like selenium. Garlic contains much bioavailable selenium, which is an antioxidant and could be chemopreventive (Ip and Lisk, 1996). It is used in the treatment of earaches, deafness, leprosy, severe diarrhea, fever, and stomachaches. One of its chief therapeutic effects is to treat cardiovascular diseases by lowering blood pressure as well as cholesterol. It also acts as an antimicrobial and chemopreventive agent. S-Allylmercaptocysteine is the most important antitumor constituent of aged garlic extract. The antiproliferative effect of thioallyl compounds has been studied in a number of cell lines and the results have shown sensitivity of these compounds to breast and prostate cell lines (Sigounas et al., 1997).

3.3. *Andrographis paniculata* Wall. ex Nees

Andrographis paniculata is a herbaceous plant that belongs to the family Acanthaceae. It is extensively grown on the Asian continent. It is commonly known by the names 'king of bitters' and 'creat'. Four lactones, chuanxinlian A (deoxyandrographolide), B (andrographolide), C (neoandrographolide), and D (4-deoxy-11,12-didehydroandrographolide), constitute its important secondary metabolites. The plant possesses antibacterial, antifungal, antiviral, choleretic, hypoglycemic, hypocholesterolemic, and adaptogenic effects (Bhatnagar et al., 1961). Its blood-purifying property makes it a choice for the treatment of a number of disease conditions such as boils, skin eruptions, chronic undetermined fevers, and scabies. The plant also contains an anticancer agent called andrographolide, which is an antiinflammatory diterpenoid lactone that inhibits interleukin-6 (IL-6) expression, suppresses IL-6-mediated signals, and induces cell apoptosis by the activation of apoptosis-related proteins/mitogen-activated protein kinases, and thus plays an important role as a cytotoxic agent in the case of liver cancer (Ji et al., 2007).

3.4. *Ardisia crenata* Roxb.

Ardisia crenata is a member of the family Myrsinaceae, which is mostly found in the warm climates of tropical and subtropical regions. This plant is also known by the names 'coral bush', 'coralberry', 'hen's eyes', 'spiceberry', and 'red berries'. Numerous chemical constituents that have been extracted and characterized from this plant include cyclic depsipeptide, peptide, alkenylphenol, and triterpenoid saponins (Horgen et al., 1997). It has been

widely used as traditional medicine to cure diseases such as pulmonary tuberculosis, hepatitis, chronic bronchitis, and irregular menstruation. Its cytotoxic effect is attributed to ardisiacrispin, which is a mixture of 2 triterpenoid saponins, ardisiacrispins A and B. Experimental studies have shown that the mixture of triterpenoid saponins inhibits the uncontrolled proliferation of the Bel-7402 liver cancer cell line by inducing proapoptotic and microtubule disruptive activities (Li et al., 2008). Microtubules play an important role in mitosis, and so targeting them yields antiproliferative effects in cancer cells.

3.5. *Boswellia serrata* Roxb.

Boswellia serrata belongs to the family Burseraceae and is extensively found in India, North Africa, and the Middle East. Its common names include 'Indian olibanum tree', 'olibanum', 'luban', and 'gond'. It contains an array of chemical constituents like oils, terpenoids, sugars, and volatile oils. B-Boswellic acid is the major constituent among 4 pentacyclic triterpene acids of this plant (Krieglstein et. al., 2001). The plant's gummy exudates are associated with therapeutic effects, including astringent, antiarthritic, expectorant, stimulant, and antiseptic effects. Acetyl-11-keto-β-boswellic acid (AKBA), an active component from this medicinal plant, has the ability to strongly inhibit tumor angiogenesis induced through vascular endothelial growth factor (VEGF) signaling. It also inhibits multiple steps of VEGF-induced cell proliferation, migration, invasion, and tube formation. Studies have shown that AKBA suppressed tumor growth in human prostate tumor xenograft mice treated daily with a dose of 10 mg/kg after solid tumors reached ~100 mm^3 (n = 5). Thus, the compound AKBA is antitumorous in nature (Pang et al., 2009).

3.6. *Catharanthus roseus* (L.) G.Don

Catharanthus roseus belongs to the family Apocynaceae and is commonly known as Madagascar periwinkle. It is originally native to the island of Madagascar. Alkaloids, its main chemical constituents, are employed in the treatment of circulatory diseases, and specifically in the relief of obstruction of normal cerebral blood flow. The plant also possesses medicinal activities like astringent, diuretic, and antidiabetic effects and can serve as a cold remedy to ease lung congestion and inflammation. Two pharmacologically active alkaloids, vinblastine and vincristine, are well known for their significant curative effects against human neoplasms. Vinblastine sulfate (sold as Velban) is also employed in therapy for lymphosarcoma, choriocarcinoma, neuroblastoma, and carcinoma of the breasts, lungs and other organs in acute and chronic leukemia. Vincristine sulfate (sold as Oncovin) is known to arrest mitosis and is thus used as a treatment for acute leukemia in children and lymphocytic leukemia. Vincristine sulfate is also used as therapy for Hodgkin disease, Wilkins tumor, neuroblastoma, and reticulum cell sarcoma (Noble, 1990).

3.7. *Centella asiatica* L.

Centella asiatica is a small herbaceous perennial plant and a member of the family Apiaceae. Its common names are 'Asiatic pennywort' and 'gotu kola'. The plant is native to India, China, Indonesia, Australia, the South Pacific, Madagascar, and South and Central Africa. Phytochemical studies have shown the presence of glycoside asiaticoside and asiatic and madecassic acid. Its medicinal importance in chronic diseases has already been mentioned in the Ayurvedic system of medicine, where it is known as a 'brain tonic' for various mental disorders. It is being employed for the treatment of heatstroke, diarrhea, ulcerations, eczema, and traumatic diseases. The presence of asiatic acid, a pentacyclic triterpene, in this plant has added to its medicinal importance as an anticancer agent. The cytotoxic effect of asiatic acid has been investigated and it has been shown to decrease the viability of HepG2 cells in the case of liver cancer. The decrease in cell viability is due to increased expression of a tumor-suppressor p53 gene mediated by increased levels of intracellular calcium (Lee et al., 2002).

3.8. *Curcuma longa* L.

Curcuma longa belongs to the family Zingiberaceae and is widely grown in Asiatic countries, mainly in India and China. It is commonly known as turmeric. Biliary disorders, anorexia, coryza, cough, diabetic wounds, hepatic disorder, rheumatism, and sinusitis are some of the conditions for which the plant has shown its medicinal properties (Ammon et al., 1992). An array of pharmacological activities of this plant includes antiinflammatory, antihuman immunodeficiency virus, antibacterial, and antioxidant effects and nematicidal activities. Its major chemical constituent is curcumin and it exhibits numerous biological actions. The curcumin compound also exhibits antitumor potential via suppression of the various events involved in multiple steps of carcinogenesis such as transcription factor, NF-κB, AP-1, and STAT-3 and the ability to repress proinflammatory pathways of COX-2 and iNOS (Plengsuriyakarn et al., 2012).

3.9. *Fagara zanthoxyloides* L.

Fagara zanthoxyloides belongs to the family Rutaceae, widely distributed in Uganda and other African countries. It is commonly known by the name 'candlewood'. Root-bark extract is used in treating elephantiasis, toothache, sexual impotence, gonorrhea, malaria, dysmenorrhea, and abdominal pain. The benzophenanthridine alkaloid fagaronine exhibits antitumor activity against P388 and L1210 murine leukemic cell lines in vivo. Fagaronine inhibits the DNA replication of rapidly growing cancer cells by inhibiting DNA and RNA polymerase activities

and protein synthesis. Fagaronine leads to the disruption of replication in rapidly growing cancer, thus affecting their growth. Reverse transcriptases are also inhibited by fagaronine (Fleury et al., 2000).

3.10. *Glycyrrhiza glabra* L.

Glycyrrhiza glabra is commonly known by the name 'sweetwood' and belongs to family Fabaceae. The Mediterranean and certain areas of Asia are its habitat. It contains an active chemical complex composed of triterpene saponins, flavonoids, polysaccharides, pectins, simple sugars, amino acids, mineral salts, and various other substances (Obolentseva et al., 1999). Important secondary metabolites glabridin and hispaglabridins A and B are associated with significant antioxidant activity, and estrogen-like activity is contributed by glabridin and glabrene. It has been used against the human immunodeficiency virus (Hattori et al., 1989), cytomegalovirus, and herpes simplex virus. The antitumor activity of the plant is attributed to the metabolite isoliquiritigenin (2′,4′,4-trihydroxychalcone), which has shown potential chemopreventive activity through various mechanisms like induction of phase II enzymes such as quinone reductase 1, increased expression of glutathione peroxidase 5, and downregulation of several cytochrome P450 genes (Cuendet et al., 2010).

3.11. *Indigofera tinctoria* L.

Indigofera tinctoria belongs to the family Papilionaceae and is found in most countries of Africa, Australia, and Asia. It is commonly known as indigo. Phytochemical screening has shown that the plant contains flavonoids, terpenoids, alkaloids, and glycosides as its chemical constituents (Verma and Suresh, 2002). Medicinal benefits of the plant include treatment of chronic bronchitis, asthma, ulcers, skin diseases, gastropathy, and epilepsy; it also contributes to growth of hair and acts as an antidepressant. The contribution of this plant towards potential antitumor activity is because of its metabolite indirubin, which has the ability to inhibit Lewis lung carcinoma (LLC) in mice. Indirubin is also a potent inhibitor of cyclin-dependent kinases. Indirubin-3′-monoxime inhibits the proliferation of a large range of cells, mainly through arresting the cells in the G2/M phase of the cell cycle. The inhibition of DNA polymerase I activity and subsequently DNA synthesis contributes to antitumor activity. Experimental studies in several cell lines, in cell-free assay, and in rats with Walker 256 sarcoma have shown that indirubin significantly inhibits DNA synthesis (Hoessel et al., 1999).

3.12. *Mangifera indica* L.

Mangifera indica belongs to the family Anacardiaceae and is commonly known as mango. *M. indica* has its origins in India and Myanmar and it is the most cultivated *Mangifera* species. It has applications as a medication for gastrointestinal disorders, bilious disorders, blood disorders, scurvy, and vitamin A deficiencies (night blindness). Fresh mango leaves have also been used for the treatment of diabetes (Shah et al., 2010). In addition to the above medicinal importance, a recent study reported the presence of a triterpene called lupeol in mango fruit that possesses cytotoxic effect against skin cancer, as it has been shown to induce apoptosis in human epidermoid carcinoma A431 cells. Apoptosis is induced in a dose-dependent manner in association with the caspase-dependent mitochondrial cell death pathway. It also inhibits the Akt/PKB signaling pathway by inhibition of Bad (Ser136) phosphorylation. Thus, lupeol is anticancerous in its ability to inhibit several molecular targets involved in cancer (Prasad et al., 2009).

3.13. *Morinda citrifolia* L.

Morinda citrifolia is commercially known by the name 'noni' and it is a member of family Rubiaceae. It is native from Southeast Asia (Indonesia) to Australia. The major secondary metabolites of this plant are lignans, oligo- and polysaccharides, iridoids, fatty acids, scopoletin, flavonoids, catechin, β-sitosterol, damnacanthal, and alkaloids (Wang et al., 2002). Its pharmacological benefits include use in treatment for malaria, jaundice, hypertension, boils, carbuncles, stomach ulcers, stomachache, fractures, diabetes, loss of appetite, urinary tract ailments, abdominal swelling, hernias, and human vitamin A deficiency, as well as use as a general febrifuge and for analgesic effect. Two unique glycosides, 6-O-(β-D-glucopyranosyl)-1-O-octanoyl-β-D-glucopyranose and asperulosidic acid, have been isolated from the noni fruit's juice and were found to be highly efficient in inhibiting TPA- or EGF-promoted cell transformation as well as related AP-1 activity in the mouse epidermal JB6 cell line (Liu et al., 2001). Increased AP-1 activity is associated with malignant transformation and cancer-promoting agents. Thus, the ability to inhibit AP-1 activity marks the importance of these glycosides as antitumor agents.

3.14. *Newbouldia laevis* Seem.

Newbouldia laevis is commonly known as the African Border tree and belongs to the family Bignoniaceae. It is used as a therapy against many diseases. Its potential applications are as a remedy for epilepsy and convulsions in children, in treatment of rheumatism, and as a febrifuge. Its extracts have also been shown to exhibit antimicrobial activity (Kuete et al., 2007) and antimalarial properties (Eyong et al., 2006). The cytotoxic effect of the plant is attributed to its compound 2-acetylfuro-1,4-naphthoquinone, which induces apoptosis, even without caspase 3/7 activation. In pancreatic cancer cell lines, it is known to inhibit the formation of blood capillaries (Kuete et al., 2011).

3.15. *Nigella sativa* L.

Nigella sativa is commonly called 'black caraway', 'black cumin', or 'black seed' and belongs to the family Ranunculaceae. It is well distributed in Central Asia. Phytochemical studies have reported the presence of a number of chemical constituents like nigellicine, nigellidine, nigellimine-N-oxide, thymoquinone, dithymoquinone, thymohydroquinone, nigellone, thymol, arvacrol, oxy-coumarin, 6-methoxycoumarin and 7-hydroxycoumarin, α-hedrin, and steryl glucoside, as well as rich amounts of flavinoids, tannins, essential fatty acids, essential amino acids, ascorbic acid, iron, and calcium. Its medicinal values include analgesic, antiinflammatory, antihistaminic, antiallergic, antioxidant, anticancer, immune stimulation, antiasthmatic, antihypertensive, hypoglycemic, antibacterial, antifungal, antiviral, and antiparasitic effects (Ali and Bluden, 2003). Thymoquinone, a secondary metabolite of this plant, has cytotoxic effects as it induces apoptosis in tumor cells by suppressing NF-κB, Akt activation, and extracellular signal-regulated kinase signaling pathways; it also inhibits tumor angiogenesis (Plengsuriyakarn et al., 2012).

3.16. *Panax ginseng* C.A.Mey.

Panax ginseng is a prevalent perennial herb that belongs to the family Araliaceae and is commonly known as ginseng. It is widely found in China, Korea, Japan, Russia, and the United States. The active chemical components include a diverse group of steroidal saponins that are known as ginsenosides (Attele, 1999). It exhibits a multitude of pharmacological effects including immunomodulatory and antiinflammatory, and it helps in improvement of physical stamina, stimulation of the appetite, and enhancing of learning, memory, and behavior (Sun, 2004). It is also well known for its adaptogenic effects that help to improve resistance to stress. Its polyphenol compounds and saponins contribute to its antitumor potential. The cytotoxic nature of ginsenosides is clearly shown by their potential to induce cell death (such as apoptosis and necrosis), and by their association with antiproliferation, antiinvasion, and antiangiogenesis properties. Thus, ginseng is anticancerous in nature (Yue et al., 2007).

3.17. *Plumbago zeylanica* L.

Plumbago zeylanica is a member of the family Plumbaginaceae and originated from Southeast Asia. Its common names are 'white leadwort', 'Ceylon leadwort', 'plumbago', and 'chitrak'. Chemical screening studies have shown the presence of a number of secondary metabolites: plumbagin, coumarins seselin and suberosin, 2,2-dimethyl-5-hydroxy-6-acetylchromene, plumbagin acid, β-sitosteryl-glucoside, bakuchiol, 12-hydroxyisobakuchiol, saponaretin, isoorientin, isoaffinetin, and psoralen. Its wide-ranging medicinal applications include its use in treatment of fever and malaria, diarrhea, piles, dyspepsia, skin diseases (leprotic lesions) (Gupta et al., 1993), gastrointestinal complaints (Giday et al., 2006), ulcers, and scabies. Plumbagin, a quinoid isolated from the plant's root, has been shown to possess antitumor activity by potential effects in the control of hormone-refractory invasive prostate cancer (PCa). The inhibitory effects of plumbagin against a number of molecular targets like protein kinase C epsilon (a PCa proliferative marker), STAT-3, AKT, and PI-3K result in the inhibition of growth and invasion of PCa. Plumbagin, in addition to inhibiting growth of cancer cells, also induces apoptosis in cancer cells (Aziz et al., 2008).

3.18. *Rhinacanthus nasutus* (L.) Kurz

Rhinacanthus nasutus belongs to the family Acanthaceae and is widely distributed in parts of subcontinental India and in Southeast Asia and China (Rao et al., 2010). The plant is commonly known by the name 'snake jasmine'. Naphthoquinone, rhinacanthins (A–D, G–Q), rhinacanthone, and lignan groups are the major phytochemical compounds of this plant (Thirumurugan et al., 2000). Pharmacological benefits attributed to its active constituents include treatment of eczema, pulmonary tuberculosis, herpes, hepatitis, diabetes, hypertension, and various skin diseases. Studies have suggested that rhinacanthins M, N, and Q and related naphthoquinone esters as well as synthetic compounds, 1,2-naphthoquinones and 1,4-naphthoquinones, are antitumorous as they selectively inhibit the growth of KB, HeLa, and HepG2 human cancer cells and normal Vero cells. The partial arrest of cells at the G2/M phase in rhinacanthin N treatment has been observed experimentally, which helped to prevent further damage and gave cells the time to repair the defect or undergo apoptosis (Siripong et al., 2006).

3.19. *Scutellaria baicalensis* Georgi

Scutellaria baicalensis belongs to the family Lamiaceae. It is native to eastern Asia and has major applications in traditional Chinese medicine. Its common names are 'Chinese skullcap', 'baikal', 'scute', and 'scutellaria'. Root extracts of this plant contain almost 70 flavonoids, anthocyanidins, chalcones, flavanonols, flavonols, flavanones, and flavones. The pharmacological effects of this plant include antidiabetic, antiinflammatory, antioxidative, hepatoprotective, antiviral, antianxiety, antitumor, and antihypertensive effects (Bhandari et al., 2010). Its antitumor activity is attributed to baicalein, wogonin, wogonoside, and skullcapflavone II (neobaicalein). All these metabolites at micromolar concentrations have shown inhibitory effects against the proliferation of human tumor cell lines LXFL and 529L (large-cell lung carcinomas). Baicalein inhibits 12-lipoxygenase activity and contributes to anticancer potential against a number of other cancers, also. The inhibition of 12-lipoxygenase

activity acts as interference in the signaling mechanism needed for tumor growth (Zhou et al., 2008).

3.20. *Solanum incanum* L.

The geographical habitat of *Solanum incanum*, a member of the family Solanaceae (nightshade plants), is the temperate and tropical regions of the world. The plant is commonly known by the names 'bitter apple' and 'thorn apple'. The main chemical constituents of the plant are steroid glycosides, which are known to possess defensive role against pathogens and predators of the plant. Solanin and solasonine are steroid alkaloids, which have applications against cutaneous mycotic infections and other infectious conditions (Al-Fatimi et al., 2007). Another metabolite, solamargine, is known to have cytotoxic activity towards normal skin fibroblasts by its ability to induce cell apoptosis. The cytotoxic effects of solamargine have been experimentally studied in 4 human lung cancer cell lines. The molecular effects of this metabolite that clearly validate its potential as an anticancer agent for tumor necrosis factors and Bcl-2-related resistance of human lung cancer cells include the release of cytochrome c, downregulation of antiapoptotic Bcl-2 and Bcl-xL, increase of caspase-3 activity (important for apoptosis), and DNA fragmentation (Liu et al., 2004).

3.21. *Vismia laurentii* De Wild.

Vismia laurentii belongs to the family Guttiferae and is widely distributed in the tropical and subtropical regions of the world. There is no English common name for this plant. Chemical studies have reported the presence of xanthones, anthraquinones, and prenylated anthrones in this plant. Recently, in a systematic search for new bioactive lead structures, 1 new xanthone, laurentixanthone C, and 3 known compounds identified as vismiaquinone, bisvismiaquinone, and dammaradienol were isolated from *V. laurentii* (Hussain et al., 2012). It is used as a remedy for the treatment of skin diseases (such as dermatitis, leprosy, scabies, and eczema) and wounds. Experimental studies suggesting the anticancer potential of xanthone V1 have already been done in a number of cancer cell lines. The effects of xanthone V1 on the cell cycle distribution, apoptosis induction, and caspase-3/7 activity have been investigated in the CCRF-CEM cell line and show evidence for its anticancer potential as a cytotoxic agent. Xanthone V1 leads to activation of caspase-3/7 enzymes, which play important roles as apoptosis inducers (Kuete et al., 2011).

3.22. *Withania somnifera* (L.) Dunal

Withania somnifera is a minor, timbered shrub in the family Solanaceae that is commonly known as ashwaganda. It is found in Africa, the Mediterranean, and India. The major biochemical constituents are steroidal alkaloids and steroidal lactones, and as a class of constituents, they are called withanolides. Therapeutic values associated with this plant are adaptogen, aphrodisiac, antiinflammatory, deobstruent, antibiotic, diuretic, narcotic, sedative, abortifacient, immune system-stimulating, astringent, and antioxidant effects (Singh et al., 2010). The antitumor property of the plant is well defined by the fact that withaferin A, a chemical constituent of this medicinal plant, inhibits growth of MDA-MB-231 and MCF-7 human breast cancer cells and MDA-MB-231 xenografts in vivo, in association with apoptosis induction mediated by reactive oxygen species production due to the inhibition of mitochondrial respiration (Hahm et al., 2011).

3.23. *Xanthium strumarium* L.

The genus *Xanthium* is a member of the family Asteraceae, comprising 25 species of American origin (Oudhia, 2001). *X. strumarium* is commonly known as 'cocklebur' or 'burweed'. In India it is well known for its use as a remedy in hemicrania diseases (Kamboj and Saluja, 2010). Its health-promoting benefits include antitumor, antibacterial, antifungal, antiinflammatory, antinociceptive, antitussive, hypoglycemic, antimitotic, antitrypanosomal, antimalarial, diuretic, antioxidant, analgesic, repellent, and insecticidal activities. Its metabolite, 8-epi-xanthatin, and its epoxide show strong evidence of being antitumorous as they significantly inhibit the proliferation of cultured human tumor cell lines. 8-epi-Xanthatin acts by farnesyltransferase inhibitory effect and also inhibits microtubule-interfering agents. These inhibitions contribute to the anticancer activity of 8-epi-xanthatin (Kim et al., 2003).

3.24. *Zanthoxylum nitidum* (Roxb.)

Zanthoxylum nitidum belongs to the family Rutaceae and is widely distributed in Southeast Asian countries and Australia (Hu et al., 2007). It is commonly known by the name 'prickly ash'. The presence of true alkaloids, carbohydrates, flavonoids, and amino acids has been revealed by phytochemical studies (Bhattacharya and Zaman, 2009). Nitidine chloride, oxynitidine, dihydronitidine, 6-methoxy-5,6-dihydrochelerythrine, α-allocryptopine, and skimmianine are the main alkaloids isolated from its roots. The medical application of the plant includes the cure of toothache, stomachache, fever, rheumatism, paresis, boils, cough, colic, vomiting, diarrhea, and cholera. The anticancer potential of the plant is attributed to the chemical constituent nitidine, known for its ability to exhibit cytotoxic activity against LLC. It is a DNA intercalator that is generally classified as an inhibitor of topoisomerases I and II. The inhibition of these enzymes leads to subsequent apoptosis in cancer cells (Fang et al., 1993).

4. Discussion

Medicinal plants have contributed richly to the health of human beings. The vast potential of plant-based medicines in the treatment of numerous diseases has

always contributed to the value of the plant community as a major area of research and development. Chemotherapy is an important option in modern cancer treatment, and plant-derived chemotherapeutic agents have contributed greatly to the progress of oncology/chemotherapy development and to clinical practice. The need to cure cancer and find better ways to combat this disease has raised the need to find anticancer compounds in the plant kingdom. Plant extracts and the bioactive compounds present in them, which are responsible for anticancer activity, have to be screened for valuable information. Innovations in multidisciplinary investigative methods offer great promise for plant-derived drug discovery and development. This review includes medicinal plants with chemical constituents that possess anticancer properties. Most of the plant compounds described in this review are antitumorous, as explained by in vitro studies. Some of their metabolites are cytotoxic in nature, with the ability to induce apoptosis in cancer cells; this includes *Andrographis paniculata*, *Centella asiatica*, *Newbouldia laevis*, *Nigella sativa*, *Panax ginseng*, *Plumbago zeylanica*, *Solanum incanum*, and *Vismia laurentii*. According to the International Union for the Conservation of Nature's Red List of Threatened Species (www.iucnredlist.org.), the most comprehensive inventory for the conservation status of biological species, most of the above-mentioned plants have not yet been evaluated for their conservation status, except for *C. asiatica* and *M. indica*, whose status is "Least Concern" and "Data Deficient", respectively. In addition, the medicinal plants mentioned here are not confined to a particular geographical region; rather, they are diversely present across various regions of the world. In vitro studies have revealed the anticancer potential of the metabolites discussed in this review, so they hold scope for further experimentations. The plant metabolites mentioned in this review possess varying mechanisms of action that contribute to their anticancer nature. Some metabolites work by selectively killing the rapidly dividing cancer cells, while others target molecular factors (mostly proteins) that are abnormally expressed in cancer cells. The cytotoxicity of cancer cells is induced by impairing the cell cycle (mitosis) at certain stages and also by promoting molecular factors responsible for apoptosis (increase of caspase-3/7, down regulation of Bcl-2, etc.). The antitumor effect of certain metabolites is observed in their ability to inhibit abnormally expressed growth factors (mostly protein tyrosine kinase) and thus inhibit the growth of cancer cells. The anticancer metabolites mentioned in this review can be further researched based on prior toxicological investigations to develop them as anticancer drugs. In the process of drug development, they can be subjected to clinical trials to account for their safety and effectiveness. Therefore, in the present review, an effort has been made to compile information about some of the plants possessing anticancer activity for various types of cancer. This review can help others to explore herbs to further extend and promote the use of medicinal plants as potential tools to treat cancer.

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