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Review Article

Medicinal plants as therapeutic agents for cancer treatment

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Abstract
Medicinal plants are potent natural sources of drugs to treat different human inflammations since ancient time. Many of anticancer lead bioactive molecules such as vinca alkaloid, vinblastine, vincristine, camptothecin, and taxanes have been characterized from different medicinal plants and are used as therapeutic agents in worldwide. Technical strategies based on the natural yield of drug innovation, ethnomedicines and traditional pharmacology is reemerging to caring good base as striking discovery train. The current declined in the number of new molecular entities from the medicinal industry, unique anticancer agents are being required from traditional medicines. According to recently published data, this article reports a detailed review of ethnomedicinally important anticancerous medicinal plants. It will provide a new way to explore the therapeutic value of plants and characterization of biologically active compounds from them that may lead towards developing anticancer drugs and proper treatment of cancer.
Keywords: Cancer, Anticancer, Medicinal plants, Pharmacological effects of herbs.

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INTRODUCTION

Medicinal plants are a category of the plants that includes specific chemical compounds in their body and are useful for multifold directions. These are also variable in their habits like herbs, shrubs, trees, climber and creepers *etc.* (Patel, 2014). Natural medicinal plants provide an opportunity for a new medicinal an approach for new medicinal products. Traditional and alternative medicines are reemerging as novel scientifically practical options (Patwardhan and Mashelkar, 2009). Approximately 35,000 to 70,000 plant species have been used for medicinal purposes in the world. Out of them, 6,500 species are used in Asia alone as home remedies against different diseases (Amiri *et al.,* 2014).

Medicinal plants variety, distribution, and native uses were recorded by Sharma and Samant (2014). Important medicinal plants of tehsil, Joginder Nagar district Mandi H.P., India was carried out by Kumar (2014). Indigenous knowledge of medicinal plants among tribals was focused by Geetha (2010) whereas plant biodiversity of Akola and Washim (Bhadange, 2011) district of M.H. for medicinal use was examined by Bhadange (2011). Exploration of ethnomedicinal values of imperative plants with shrubs was analyzed by Majeed *et al.* (2011). Phytochemical study of some famous plants belonging to Pakistan's areas such as Dir, Kohistan valley, Khyber Pukhtunkhwa by Hazrat *et al.* (2011). Yashwant (2014) studied on endangered medicinal plant *Caesalpinia bonduc,* germination, and growth Status (Linn.) Roxb. Commercially Important Medicinal Plants of South Africa reviewed by Street and Prinsloo (2012). Bhat *et al.* (2013) focused on Need and importance of conservation of *Tinospora cordifolia* a threatened medicinal plant. Diversity, Ethnomedicinaluses Conservation of the medicinal plants studied by Adhikari (2010).

Current literature survey on "medicinal plant diversity and importance" provided the enormous beneficial health care aspects that increased the demand for medicinal plants in both developing and developed countries. According to the survey, more than 50000 species are used for therapeutic purposes; among them, 13 percent are flowering plants

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(Schippmann *et al.,* 2002). Approximately 45000 plant species has been used in India and among them several thousand have been possessed medicinal properties. Current literature suggests that 80% drug components are natural products or natural compounds inspired (Harvey, 2008). However, 60% of anticancerous and 75% of anti-infective medicines accepted from 1981-2002 could be declared as herbal products (Gupta *et al*., 2005). From literature survey, it should be concluded that biologically active compounds of plants are used as a major source for treatment of many diseases.

Compounds of plants that normally used in traditional medicines present better tolerance and safety as compared to other chemical entities used (Patwardhan *et al*., 2004). Traditional medicine based bioprospecting offer supreme structural variety as potent for new leads (Koehn and Carter, 2005). Natural phytochemical constituents derived from medicinal herbs have played important role in organization of numerous human clinical aspects, such as cancer (Mehta *et al*., 2010; Desai *et al*., 2008; Guilford and Pezzuto, 2008).

Trade species over-exploitation, a collection of medicinal plants in a destructive way, susceptibility due to evolutionary pressure are major threats to thesurvival of medicinal plants. To achieve feasible yield of medicinal plants and other non-timber forest products (food i.e. wild edibles, fuel, lumber, agricultural tools, fiber and various other purposes), there must be a need of advanced approach which include socio-biological, ecological, socio-cultural and economic aspects of the species (Ghimire *et al*., 2004).

Plant extracts evaluation as prophylactic agents

Now a day, most research has been established to estimate the effect of medicinal plant extracts against cancer-causing agents. Altogether, the synergetic effects of the concoction of plant metabolites and numerous level of interference present higher effectiveness throughout chemoprevention regimens (Guilford and Pezzuto, 2008). The inhibition of tumor promotion process by natural bioactive compounds vary from the prevention of gene-damaging effects, elevated anti-inflammatory and antioxidants activities, proteases inhibition, cell proliferation and defense between intracellular connections to change signal transduction pathways and apoptosis (Soobrattee *et al*., 2006).

The clarification of effectiveness of plants could direct the establishment of an alternative and complementary technique against cancer. However, research on medicinal plants has recently been responsible for explosive advances in drug discovery, separation techniques, extract preparation methods, physicochemical measurements and new concepts. Numerous naturally occurring compounds from plants are being used as anticancerous agents and are currently undergoing medical development (Kim *et al*., 2015) as shown in table 1. *Artemisia* is a large and diverse genus have been used as food additives as well as antimalarial and antihepatotoxic (Bora and Sharma, 2011; Gilani *et al*., 2005), antiinflammatory (Abad *et al*., 2012), antimicrobial and antiviral agents (Aniya *et al*., 2000; Kordali *et al*., 2005a; Kordali *et al*., 2005b). Many plants like *Petasites japonicas* (Kim *et al*., 2015), *Amorphophallus campanulatus* (Ansil *et al*., 2012), *Curcuma aromatic* (Li *et al*., 2014), *Panax ginseng, Salvia miltiorrhiza* (Wang *et al*., 2012), *Tripterygium wilfordii* (Chen *et al*., 2012), *Astragalus* (Chen *et al*., 2011) and many other plants used as an anticancerous agents with minimum toxicity. *Dracocephalum kotschyi* has a selective effect on liver cancer cell mitochondria to activate apoptosis signaling (Talari *et al*., 2014).

Graptopetalum paraguayense may represent a therapeutic option for treating hepatic inflammation and fibrosis (Su *et al*., 2013). The root of *Cynanchum auriculatum* have number of biologically active compounds, C-21 steroidal glycosides, are of significant attention because of their bioactivities, with prevention and therapy of chronic hepatitis (Yin *et al*., 2007), hepatic fibrosis (Lv *et al*., 2009) and liver cancer (Wang *et al*., 2007; Bi *et al*., 2008). *Silybum marianum* is used against hepatoprotective and tumorigenic effects *in vitro* and *in vivo* conditions by suppressing oxidative stress and proliferation (Manuscript, 2013). *Nigella sativa* (NS) has been shown several pharmacological activities, including antioxidant, inhibit inflammation, chemotherapeutic and anti-tumor activities (Padhye *et al*., 2008), as well as hepatoprotective activity (Salama *et al*., 2006).

Most glycoproteins originating from *Zanthoxylum piperitum* DC (ZPDC) have immunerelated factors that work as anti-inflammatory, anti-apoptosis and anticancerous, and it is unspecified that ZPDC glycoprotein has potential against hepatocarcinogenesis in an animal model (Oh *et al*., 2009; Lee and Lim,

2007). From Simaroubaceae plants, *Bruceajavanica*is extracted. It has low toxicity but high anti-cancer effectiveness (Chen *et al*., 2013; Gao *et al*., 2011). *Nigella sativa* seeds, oils, and extracts have been used against cancer. Current scientific research to investigate anticancer activity of *N. sativa*is a comparatively modern affair (Permalatha *et al*., 1997).*Cassia fistula* and *Picrorhiza scrophulariflora* are used as anticancerous on HCC patients (Rafiq *et al*., 2015). *Petasites japonicus* (PJ) is also known as anti-inflammatory and antiallergenic (Lee *et al*., 2011; Lee *et al*., 2013). The methanolic extract of *Petasites japonicus* roots may alter molecular signaling pathways and inhibit HCC cells proliferation (Kim *et al*., 2015). It is reported that the *Amorphophallus campanulatus* have antioxidant and hepatoprotective activity (Ansil *et al*., 2012). *Curcuma aromatica*, with multiple ingredients, has been indicated as anti-inflammatory, anti-oxidant and anticancer properties (Quiles *et al*., 2002).

TYPICAL MEDICINAL PLANTS AND THEIR USES AS ANTICANCER AGENTS

Amorphophallus campanulatus

Common name: Elephant foot yam

*Amorphophallus campanulatus,*a perennial herb belongs to *Araceae* family, and usually called as elephant foot yam. *A. campanulatus,* a tuber crop of South East Asian in origin mostly cultivated all over the plains ofIndia and their rhizome used as a food product (Das *et al*., 2009). Its rhizome is extensively used in many Ayurvedic medicines and also against liver infections, bronchial infections, abdominal pain,asthma, dysentery, spleen enlargement, elephantiasis diseases due to vitiated blood and sore swellings. The important constituents of the rhizome are lupeol, sitosterol, stigmasterol, galactose, palmitic acid, betulinic acid, glucose, rhamnose and xylose (Khare, 2007). It is reported that rhizome possesses an antibacterial, antifungal and cytotoxic activities (Khan *et al*., 2007).

Artemisia vulgaris

Common name: Mugwort

Globally *Artemisia vulagaris* L. occurs in the climatic region and is reported to occur from the high mountainous regions of the Northern Himalayas to warm temperature regions of South America. In traditional ethnomedicine, leaves extract of *A. vulgaris*is used as antiparasitic, anti-inflammatory, antibacterial and also stimulant various disorders such as hepatosis (Duke *et al.*, 2002).

Anticancer activity of *Artemisia vulgaris* aqueous extract against human breast carcinoma T47D cells, human prostate cancer PC-3 cells, and colon cancer RKO cells for 24, 48 and 72h treatment has been reported (Nawab *et al*., 2011). *Artemisia* species also showed good cytotoxicity against three human cancer cell lines, MCF7, A549 and HeLa (Sura *et al*., 2011). Emami *et al*. (2009) established study for the toxicity investigation of Artemisia sp. against human Caucasian hepatocyte carcinoma (HepG-2) and human Caucasian larynx carcinoma (Hep-2). *In vitro,* quantitative MTT assay and cytotoxic effects against two human tumor cell lines HepG2 and Hep2 were established (Emami *et al*., 2009).

Astragalus hamosus

Common names: Milkvetch, locoweed, goat's thorn

Separation of new flavonol glycoside 7-O-methyl-kaempferol-D-galactopyranoside and known flavonols hyperoside isoquercitin and astragalin take place through phytochemical examination of the leaves of *A. hamosus* (Krasteva *et al*., 2007). In plants commonly occurring secondary metabolites are Flavonoids. The commonest groups of flavonoids are polyphonic compounds which are used by humans as dietary components. Polyphonic compounds work against allergic conditions, inflammation, microbial infections and cancerous activities (Yamamoto and Gaynor, 2001; Cushnie and Lamb, 2005). A flavonoid, rhamnocitrin 40-b-D-galactopyranoside (RGP) separated from *A. hamosus* L. leaves, possessed hepatoprotective activity (Saleem *et al*., 2013).

Bergenia ciliata

Common Name: Winter begonia

Bergenia ciliata belongs to family *Saxifragaceae* has various medicinal properties. These properties included antibacterial, antioxidant, anti-inflammatory, anti-diabetics and antiviral activities (Kumar *et al.*, 2002; Rajbhandari *et al.*, 2009; Ruby *et al.*, 2012). Potential drugs that used against tumors for chemoprevention or chemotherapy are derived from *Bergenia ciliate* rhizome, methanolic and aqueous extract (Chauhan *et al*., 2012). *B. ciliata*have potential to work against neoplastic activities due to which it act as defensive medicine (Bhandari *et al*., 2008). It is reported

that rhizome of *B*. *ciliata* work against urolithiasis infections, inflammations, oxidative processes and bacterial infections (Sinha *et al*., 2001).

Bryonia laciniosa

Common name: Bryony, Snakeweed, Shivlingi

It is native to Europe, Mediterranean region and Central Asia (Kirtikar and Basu, 1987). As a folk medicine, the plant is used in the treatment of gastrointestinal disorders, respiratory infections, and metabolic diseases, as well as in hepatic infections (Gabrielian and Gevorgovich, 1997; Acharya and Shivlingi, 2007). Alpana *et al*. (2011) have tested *in vitro*cy to toxicity of *B. laciniosa* leaves the water, methanol, and chloroform extract on human Breast adenocarcinoma (Mcf-7), Human squamous cell carcinoma; cervix (SiHa) cell lines and one non-cancer normal cell line Vero (monkey kidney cell line). The results showed that aqueous extract possesses property to work against cancer cells and are able to kill all cancer cells without leaving residual population (Alpana *et al*., 2011).

Table I: Anticancerous medicinal plants

Botanical name of plants	Plants common name	Family name	Active components of main parts used	Origin of medicinal plant	Medicinal importance	References
Amorphophallus campanulatus	Elephant foot Yam	*Araceae*	Rhizome	South East Asianorigin and plains ofIndia	Having antioxidant and hepatoprotective activity	Ansil *et al*., 2012
Artemisia vulgaris	Mugwort	*Compositae*	Aerial parts	The Himalayas to warm temperature regions of South America	Mostly used against liver disorders	Gillani *et al*., 2011; Nawab*et al*., 2005
Astragalus hamosus	Milkvetch	*Fabaceae*	Aerial parts	Syrian Pasture	Having hepatoprotective and antioxidant activity	Saleem *et al*., 2013; Burdina*et al*., 2013
Bergenia ciliate	Winter begonia	*Saxifragaceae*	Rhizome	Nepalese origin	Antioxidant. anti-bacterial and anti-tussive properties	Rajkumar *et al*., 2010; Chauhan *et al*., 2012
Bryonia laciniosa	Bryony, Shivlingi, Snakeweed	*Cucurbitaceae*	Leaves	Europe, Mediterranean region, and Central Asia	Used in treatment of gastrointestinal, respiratory, rheumatic, metabolic disorders and liver's infectious diseases	Acharya, 2007
Nigella sativa	Kalaunji, Black cumin	*Ranunculaceae*	Seeds	Widely grown in India and Pakistan	It has great medicinal value as a carminative, stimulant, analgesic, anti-inflammatory and diuretic.	Ayman and Elkady, 2012

Botanical name of plants	Plants common name	Family name	Active components of main parts used	Origin of medicinal plant	Medicinal importance	References
Oroxylum indicum	Indian trumpet tree	*Bignoniaceae*	Leaves	Indian deciduous forests	used for curing gastric ulcer, anti-cancerous, anti-inflammatory, anti-metastatic potentials and anti-microbial	Mao, 2002; Naveen *et al*., 2012
Petasites japonicas	Japanese butterbur	*Asteraceae*	Roots	Korea, China, Japan origin	anticancer	Kim *et al*., 2015
Rheum officinale	Chinse rhubarb	*Polygonaceae*	Whole plant	India, Russia, Europe	anti-tumor activity with hepatocarcinoma	Cao *et al*., 2005
Swertia chirayta	Chirata, Kirata-tikta	*Gentianaceae*	Whole plant	The Himalayas and in hills of Meghalaya	It possesses anti-helminthic, hypoglycemic, febrifuge, anti-malarial, anti-diarrheal and antipyretic properties	Nawab *et al*., 2011

Nigella sativa

Common name: Kalaunji, Black cumin

The Prophet Muhammad (Sallalaho Alaihi Wasallam) said:*"Black Cumin is the cure of all the diseases except Saam and "Saam is death"* (Narrated by Abu Huraira, Bukhari, Muslim, Ibn Maja, Musnad Ahmad). *Nigella sativa* (NS), the common name is black seed or black cumin 'Al-Habba Al-Sauda' (in Arabic), is a seed of a capsulated plant that belongs to the *Ranunculaceae* family. *Nigella sativa* have a potential to work as a flavor and food additive, as well as a defensive and medicinal agents for numerous disorders (Sayed, 1980). *N. sativa*seed contains 36–38% fixed oils, alkaloids, proteins, saponin and 0.4–2.5% unsaturated fatty acids as an essential oil (Houghton *et al*., 1995). The chief active components are thymoquinone (TQ; 27.8–57.0%), q-cymene (7.1–15.5%), carvacrol (5.8–11.6%), tanethole (0.25–2.3%), 4-terpineol (2.0–6.6%) and longifoline (1.0–8.0%) (Burits and Bucar, 2000). TQ readily dimerizes to form dithymoquinone (DTQ), which is believed to be nigellone (Omar *et al*., 1999; Salem, 2005) and is a chief bioactive ingredient of the volatile oil of NS seeds. It has been shown to exert several pharmacological activities, including antioxidant, antiinflammation, chemotherapeutic and antitumor (Padhye *et al*., 2008), as well as hepatoprotective activity (Salama *et al*., 2006).

Petasites japonicus

Common name: Japanese butterbur

Petasites japonicus cultivated in eastern Asia, it is also known as Butterbur and is used by a human as a vegetable and traditional drug. *Petasites japonicus* possess potential to work as anti-inflammatory and antiallergenic (Lee *et al*., 2011; Lee *et al*., 2013). It was investigated that rate of apoptosis and growth of Hep3B HCC cells is controlled by PJE methanol extract *in vitro* and *in vivo* conditions. In concentration dependent approach methanolic extract of *Petasites japonicus* was used to reduce the cell capability. The growth of Hep3B HCC cells through inhibiting the Akt/mTOR and Wnt signaling pathways is inhibited by methanol extract of *Petasites japonicus* and suggested as an anticancerous on Hep3B HCC cells (Kim *et al*., 2015).

Oroxylum indicum

Common name: Indian trumpet tree

Oroxylum indicum are commonly colonized in Indian deciduous forests and moist areas. The roots possess sweet, astringent, bitter, acrid, refrigerant, expectorant, carminative, anti-inflammatory properties and used against microbial activities. Methanolic extract of *O. indicum* fruit repressed explosion of HL-60 cell line.

The induction of apoptosis in HL-60 cell line is caused by an active compound known as flavonoids baicalein (Roy *et al*., 2007). Nasopharyngeal cancer treatment is taking place through the use of boiling a mixture of *O. indicum* slab. Another beneficial aspect is used against gastric ulcer. The paste of the bark is used for the treatment of mouth cancer, tonsil soreness, scabies and other infections (Mao, 2002). Both *in vitro* and *in vivo O. Indicum* methanolic crude extract was successfully used to cure Dalton's lymphoma disease (Brahma *et al*., 2011). Formulation organized by the diverse quantity of stem bark extract of *O. indicum* with *Tecomella undulate, Buahinia variegate* and leaves of *Indigo feratinctoria* (SJT ONC-1) showed significant cytotoxicity against human breast adenocarcinoma (MCF-7) and human colon adenocarcinoma (Caco-2) cell lines as compared to control (Savjiyani *et al*., 2012). Therefore, effective cytotoxicity and distinctive apoptosis inducing abilities present in the non-ionic extract of *O. indicum* and also have antimetastatic potential (Naveen *et al*., 2012).

Rheum officinale

Common name: Chinse rhubarb

The roots of *Rheum officinale*have been used in traditional Chinese and Tiberan medicine. Mostly it is extended to India, Russia, and Europe. The literature reported that it was used against the tumor in case of hepatocarcinoma (Cao *et al*., 2005). In human breast cancer, MCF-7 and human lungs adenocarcinoma A549 cells proliferation is repressed by *R. officinale in vitro*, confirmed through cell feasibility and colony formation assays. In both A549 and MCf-7 cell lines, aqueous extract treatment showed in inter-nucleosomal DNA damage, whereas the inter-nucleosomal DNA from untreated cancer cells remained undamaged (Li *et al*., 2009). Tumor growth in mice induced with pancreatic tumor cells is efficiently suppressed via treatment of gemcitabine combined with emodin, an anthraquinone derivatives from *R. officinale*. This treatment pattern increases apoptosis and destruction in mitochondria. Additionally, it decreased the phosphorylated-Akt (p-Akt) level, NF-κBactivation, and Bcl-2/Baxratio enhanced caspase-9 and -3 activations, Cytochrome C (CytC) release occurred in combination therapy (Wei *et al*., 2011).

Swertia chirayta

Common name: Chirata, Kirata-tikta

Swertia chirayta set up in the temperate Himalayas and in hills of Meghalaya. It has diverse therapeutic values and is extensively used a crude medicine. It possesses anti-helminthic, hypoglycemic, febrifuge, anti-malarial, anti-diarrheal and antipyretic properties. Aqueous extract of *Swertia chirayta* (whole plant) exhibited 5-24% inhibition in human breast cancer cell T47D cells at 1.0 to10% concentration for 24 h. Human colon cancer RKO cell inhibited to 8-28%, moreover, prostate cancer PC-3 cells exposed to *S. chirayta*exhibited 2-28% inhibition at similar doses for the 24 h dosage (Nawab *et al*., 2011).

Conclusion and Future prospects of Medicinal Plants

The paper reviewed the anticancerous, antioxidant, antimalarial, antihepatotoxic, anti-inflammatory,antimicrobial, antiviral and anti-chronic hepatitis effects of the medicinal plantsagents with minimum toxicity. All the results are taken together, this comprehensive review can open a new door for their utilization in medical applications as a result of effectiveness and safety**.**

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