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A REVIEW ON PLANTS HAVING ANTI-CANCER ACTIVITY

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Abstract
Cancer is one of the leading causes of death and globally the numbers of cases of cancer are increasing gradually. It is a major health problem in both developed and developing countries. After cardiovascular disease it is the second leading cause of death. There are several medicines available in the market to treat the various types of cancer but no drug is found to be fully effective and safe. Plants have been used for treating diseases since time immemorial. Plants and plant derived products have proved to be effective and safe in the treatment and management of cancers. These days, most of the research works on anticancer drugs focus on plants and plants derived natural products. Many natural products and their analogues have been identified as potent anti-cancer agents and the anti-cancer property of various plants is being identified. Here an attempt is being made through this review to highlight the natural products and their analogues established as anti-cancer agents and the new plant species identified with anti-cancer properties either in vivo or in vitro.

Keywords : Cancer cells, Medicinal plants, Mutations, Tumours, Active constituents, Traditional.

Introduction
In 2012, the estimates of the International Agency for Research on Cancer (IARC) showed that cancer is one of the leading causes of morbidity and mortality, with approximately 14.1 million new cancer cases and 8.2 million cancer deaths worldwide. By 2030, the global burden is expected to grow to 21.7 million new cancer cases and 13 million cancer deaths. Approximately 70% of deaths from cancer occur in low and middle income countries and such could be avoided with early detection, treatment and prevention (Global cancer statistics 2012). Over the years, various plant products have been used for the treatment of cancer. Currently medicinal plants have become the paramount source of drug

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discovery in research for treating diverse form of diseases including Cancer. There is a broad scope to derive the potent anticancer agents from medicinal plants, which need thorough research (Kayande & Patel 2016). According to WHO "Cancer is a generic term that involves in disruption of normal cell division and apoptosis and is characterized by the growth of abnormal cells beyond their usual boundaries and that can intrude on the adjoining body parts and spread to other organs". Cancer begins with mutations in DNA, which instructs the cells how to grow and divide. Normal cells have the ability to repair most of the mutations in their DNA, but the mutation which is not repaired and causing the cells to grow becomes cancerous .The continuous proliferation of cancer cells develops into tumour tissues which spreads to other organs via circulatory system resulting in metastatis. There are two types of tumours such as (a) Malignant tumours, in which abnormal cells divide uncontrollably and destroys the body tissue and ultimately results in cancer and (b) Benign tumours are the cells that are non-cancerous, non-invasive and lacks the ability to metastasize. Metastasis is a multiple step process whereby tumour cells escape from their primary site and intrude to the other parts of the body. According to the statistics from the American Cancer Society (ACS 2012), cancer is the second most lethal disease after cardiovascular , infectious and parasitic diseases, causing more deaths than AIDS, tuberculosis, and malaria (American Cancer Society Report 2012; Ferlay *et al*, 2007). In Australia alone, an estimated 1, 14,000 new cases of cancer were diagnosed in 2010 with approximately 43,000 cancer deaths (Australian Institute of Health and Welfare and Australasian Association of Cancer Registries 2011; Chaffer *et al,* 2011; Sudhakar 2017). From the earliest times plants, herbs have been prized for their pain-relieving and healing abilities and we still largely depend on the curative properties of plants in novel drug discovery fields. According to World Health Organization, 80 % of the people living in rural areas depend on medicinal plants, herbs as primary healthcare system. The synthetic anticancer remedies are beyond the reach of common man because of cost factor. Medicines from plant source have a vital role in the prevention and treatment of cancer and medicinal herbs are commonly available and comparatively economical. Scientists all over the world are concentrating on the herbal medicines to boost immune cells of the body against cancer. By understanding the complex synergistic interaction of various anticancer constituents of plants, formulations can be designed to attack the cancerous cells without harming normal cells of the body. (Ames *et al,* 1991; Brunetton 1993). India has a rich

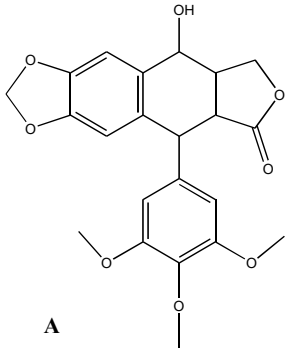
culture of medicinal herbs and spices, which includes about more than 2000 species and has a vast geographical area with high potential abilities for Ayurvedic, Unani, Siddha traditional medicines but
only very few have been studied chemically and pharmacologically for their potential medicinal value. In conclusion, this article provides the knowledge about anticancer medicinal plants of Indian and Foreign origin, which are used by people all over the world. Also it is of significance to exploit novel anticancer drugs from medicinal plants. However, the mechanism of the anticancer role has not yet been fully elucidated of many plants. Further research is needed to explore the molecular mechanism of herbal drugs (Shital *et al,* 2013). In this review medicinal plants showing higher activity towards the cancer cell line by inhibiting their progression are reported. This will benefit the researchers to carry out their research in the field of drug development against cancer.

Method

Literature survey was carried out on the basis of which various plants having anticancer properties were selected for this review. Plants which are traditionally used, scientifically proved and reported for having anticancer properties are considered, which are alphabetically arranged according to their scientific names. However, those plants were not included, where there was limitation in accessibility and/or detail information was not available.

Results

Various plants with their scientific names, common names, family, origin, parts used and active constituents are listed in Table 1 and structure of some plant derived anticancer agents (Prakash *et al*, 2013; PubChem open chemistry database), are given in Fig 1.



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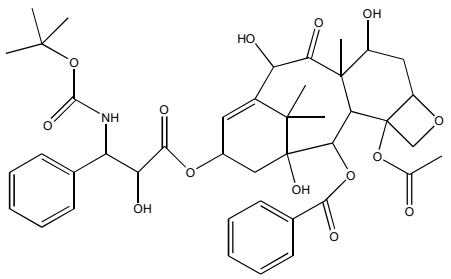

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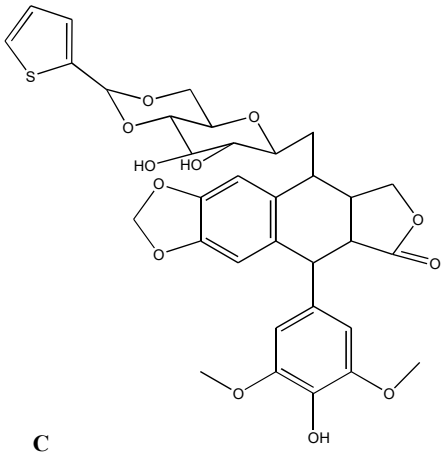

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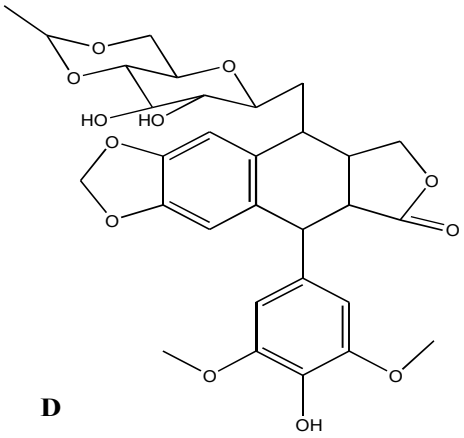

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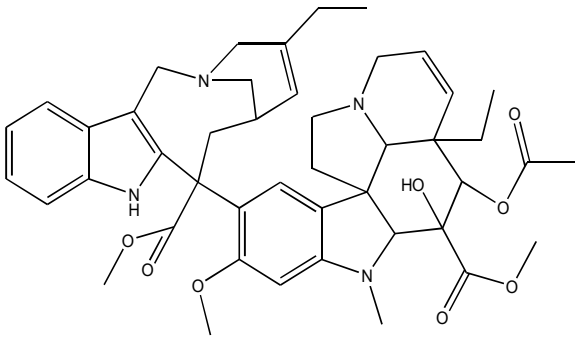

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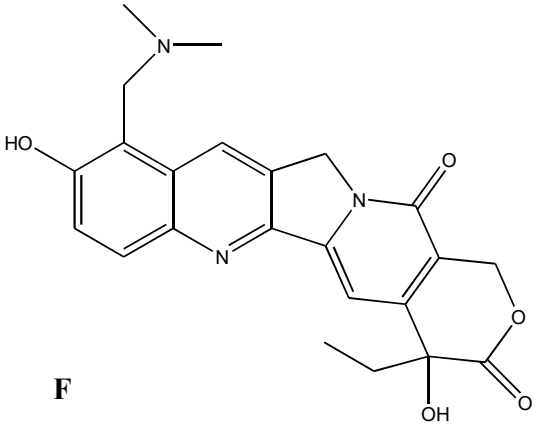

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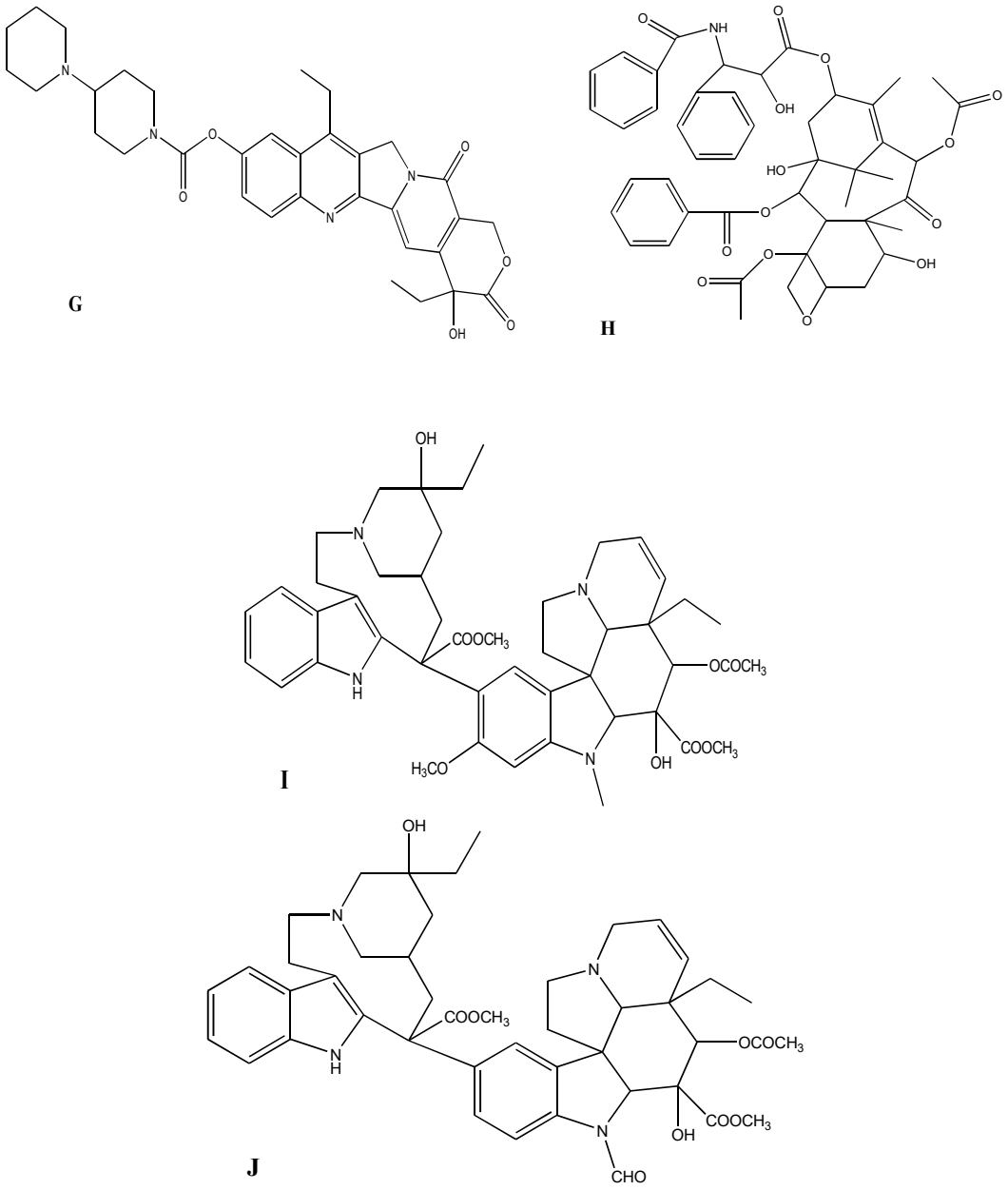

Fig 1: Structures of some plant-derived anti-cancer agents in clinical use or under clinical trial, where, A= Podophyllotoxin, B= Docetaxel, C= Teniposide, D= Etoposide, E= Vinorelbine, F= Topotecan, G= Irinotecan, H= Taxel, I= Vinblastine, J= Vincristine.

Table 1: List of plants and plant parts used traditionally in the treatment of cancer.

Botanical name of plant	**Common name (English)**	**Family**	**Origin/ native place**	**Parts Used**	**Active Constituents**	**Reference(s)**
Actinidia chinensis	Hardy kiwi	Actinidiaceae	China	Fruit	Polysaccharide known as "ACPS-R"	Zhou *et al* 2011; The wealth of India 1985
Agapanthus africanus	Lily of The nile	Amaryllidaceae	South Africa	Rhizome, Leaves	Isoliquiritigenin	Srinivas & Afolayan, 2007
Aglaila sylvestre	Lapak	Meliaceae	Thailand, New Guinea	Seeds, fruit	Silvesterol	Chang 1992
Ailanthus Altissima	Chouchun	Simaraubaceae	China	Bark, root, Glandulosa	Ailnthone,	Chang 1992
Allium cepa	Onion	Alliaceae	India	Bulb	Allicin alliin, diallyldisulphide , quarcetin, flavonoids, vit.C and E.	Govind 2011

Allium sativum	Garlic	Liliaceae	India	Bulb	Alliin ,allicin (SAC), diallyldisulphide alliin, alliinase.	Lau *et al* 1990; Belman 1983; Milnar 1996; Thomson & Ali 2003
Aloe ferox, Aloe barbadenis	Indian aloe	Liliaceae	India	Leaves	Aloe-emodin, emodin, aloin ,Acemannan.	Wasserman *et al* 2002; Pecere *et al* 2000
Alpinia galanga	Galangal	Zingiberaceae	Japan	Roots Rhizomes	Acetoxy Chavicol Acetate, pinocembrin, galangin	Govind 2011
Ananas comosus	Pineapple	Bromeliaceae	Central & South America	Fruit	Ananas bromelain	The wealth of India 1985
Andrographis paniculata	Kalmegh	Acanthaceae	India	Dried Leaves	Andrographolide	Hossain *et al* 2014; Akbar 2011; Prakash *et al* 2013
Angelica sinensis	Female ginseng	Umbelliferae	China, Korea, Japan	Roots	Angelica Polysaccharide fraction of known as “AR-4”	The wealth of India 1985
Aphanamixis polystachya	Rohituka tree	Meliaceae	India, Pakistan	Seeds,bark, Leaves	Amooranin	Govind 2011

Apium graveolens	Celery	Apiaceae	America	Stalks, Leaves	Apigenin	Sultana & Ahmed 2005
Arctium lappa	Burdock	Asteraceae	England, Europe,North en asia	Root, Seeds	Arctigenin, arctiin, daucosterol	Wang *et al* 1991; Lin *et al* 1996; Morita 1985; Wang & Yang 1993
Astragalus membrane-aceus	Mongolioan milkvetch	Fabaceae	China	Roots	Swainsonine	The wealth of India 1985
Bauhinia variegate	Orchid tree	Fabaceae	Nepal, India, Burma,Sri Lanka	Root	Lupeol, β-sitosterol, kaempferol, ombuin	Govind 2011
Betula Alba	Birch	Betulaceae	Canada and the Northern part of the United States	Leaf	Betulinic acid	Pandey & Sharma 2006; Gupta & Tandon 2004
Butea monosperma	Palash	Fabaceae	India	Bark	Butin,isobutin, coreoopsin,butrin, palasitrin,	Bandara *et al* 1989; Sumitra *et al* 2005; Wagner *et al* 1986; Wright *et al* 1981

					,miroestrol	
Cajanus cajan	Arhar dal	Fabaceae	Africa, Asia, Latin America	Leaves	Cajanine,cajanolactone ,vitexine,prunetin,cajanol, pinostrobin	Ahsan & Islam 2009; Yuan-gang Zu *et al* 2010; YujieFu *et al* 2006
Calotropis gigantean	Madar	Apocynaceae	Thailand ,Malaysia ,India	Whole plant	Calotropnapthalene, calotropises fuiterpinol	Roja & Rao 2000
Camellia sinensis	Green tea	Theaceae	Southeast Asia	Leaves ,buds	Epigallocatechin gallate	Dreosti 1996; Kim *et al* 1994; Lea *et al* 1993; Prakash *et al* 2013
Camptotheca Acuminata	Xi shu, happy tree,camptotheca	Nyssaceae	China, Tibbet	Bark,stem	Camptothecia, topotecan, cpt-11, 9-aminocamptothecin	Cragg & Newman 2005
Cannabis Sativa	Marijuana, Bhang, Ganja,& Hashish	Cannabaceae	Central Asia, Europe and the Americas	Leaves	Delta-9-Tetrahydrocannabinol, myrcene,linalool	Izquierdo & Guzman 2000; Manuel 2003; Prakash *et al* 2013
Cassia	Tarwar	Caesalpinaceae	India	Root,bark,	Avaraol,	Umadevi *et al*

auriculata				Leaves	avaraoside	2013
Cassia senna	Senna	Caesalpinaceae	India, South China	Leaves	Sennosides A,B,C,D,rhein aloe-emodin, barbaloin.	Umadevi *et al* 2013
Catharanthus roseus	Vinca	Apocynaceae	Madagascar	Whole plant	Vinorelbine, vindesine, vincristine ,vinblastin.	Cragg & Newman 2005; Bruneton 1993; Prakash *et al* 2013
Citrus medica	Lemon	Rutaceae	Asia,India,Pakistan	Root	Citric acid, methyl ferulic acid,betulinic acid, nicotinamide	Umadevi *et al* 2013
Cleistanthus collinus	Karra	Euphorbiaceae	India	Leaves	Cleistanthin, collinusin	Shital *et al* 2013
Colchicum Autumnale	Naked Ladies,Colchicum,	Liliaceae	Europe, Northern Africa	Leaves, flowers	Colchicine	Madhuri & Pandey 2009; Desai 2008; Mohammad 2006
Colchicum luteum	Suranjan	Liliaceae	Pakistan , India	leaves	Colchicines, demecolcine	Bruneton 1993; Shital *et al* 2013

Combretum caffrum	Cape bush willow	Combretaceae	S.Africa	Bark	Combrestatins	Mohammad 2006
Croton lechleri	Sabgre de grado	Euphorbiaceae	South America	Bark Resin, Leaves	Taspine	Hartwell & Lloydia 1969; Shital *et al* 2013
Curcuma longa	Turmeric	Zingibaracae	Asia	Rhizome	Curcumin, curcuminoid, bisdemethoxy-curcumin	Bhide & Nagabhushan 1992; Chan & Fong 1994
Daucus Carota	Carrot	Apiaceae	Europe, Asia, Australia	Root	Carotene	Umadevi *et al* 2013
Dysoxylum binectariferum	Rosewoods	Meliaceae	India	Barks	Rohitukine	Cragg & Newman, 2005
Emblica officinalis	Gooseberry	Euphorbi-aceae	India	Bulb	Ellagic acid, gallic acid, quercetin, emblicannins A and B	Govind 2011
Erythroxylum pervillei	Pervillei	Erythroxyl-aceae	Madagascar	Stem, bark	Pervilleine,	Shital *et al* 2013

Euphorbia semiper-foliata	Spurge	Euphorbiaceae	Europe	Flower, latex	Jatrophane	Cragg & Newman, 2005
Fagopyrum esculentum	Buckwheat	Polygonaceae	India	Hull, Seeds	Amygdalin, rutin	Bruneton 1993
Fragaria vesca linn	Wild straw-berry	Rosaceae	Northern Hemi-sphere	Fruit	Borneol,ellagic acid	Govind 2011
Fritillaria thunbergii	Zhe bei mu	Liliaceae	China, Japan	Whole plant	Zhebeinone	Shital *et al* 2013
Ginkgo biloba	Ginkgo	Ginkoaceae	China	Leaves	Ginkgolide-B, A, C and J.	Bruneton 1993; Umadevi *et al* 2013; Kleijnen & Knipschild 1992
Glycine max	Soybean	Leguminosae	India	Oil,Seeds ,flower	Genistein & daidzein	Tyler 1994; Umadevi *et al* 2013
Glycyrrhiza glabra	Liquorice	Leguminosae	India	Roots	Glycyrrhizin	Umadevi *et al* 2013; Ambasta 2000

Gossypium barbadense	staple cotton	Gunneraceae	Egypt	Seeds	Gossypol	Ambasta 2000
Jatropha curcas	Danti	Euphorbiaceae	Mexico,central America	Leaves Seeds, oils	Jatropholone A/B, caniojane,taraxerol.	Roja & Rao 2000; Bruneton 1993
Mimosa Pudica	Mint	Mimosaceae	Bangladesh,vietnam,India	Whole plant	Mimosine, n,n dimethyltryptamine	Umadevi *et al* 2013
Morinda citrifolia	Indian mulberry	Rubiaceae	Asia, Australia	Fruit	6α-hydroxyadoxoside, 6β,7β-epoxy-8-epi-splendoside.	Govind 2011
Nicotiana tabacum	Tobacco	Solanaceae	Worldwide	Leaves	Nicotelline,nicotianine, nicotine,anatabine,myosmine,cotinine	Umadevi *et al* 2013
Ochrosia elliptica	Ochrosia	Apocynacae	North-eastern Australia.	Trunk bark	Elliptinine, ellipticine, methoxy ellipticine, elliptine.	Chang 1992
Ocimum sanctum linn	Holy basil	Lamiaceae	India	Leaves	Eugenol, orientin and vicenin	Prakash *et al* 2013
Panax ginseng	Ginseng	Araliaceae	China, Korea, Bhutan	Root	Ginsenosides, panaxosides	Yun & Choi 1995; Attele *et al* 1999; Cragg *et al* 1993

Polygonatum multiflorum	Solomon's seal	Liliaceae	Asia, Europe, North America	Whole plant	Saponin, flavonoid and vitamin A	Madhuri & Pandey 2009; Desai 2008; Prakash *et al* 2013
Potentilla chinensis	Silver weed	Rosaceae	China, Japan, Korea	Whole plant	Gallic acid and tannin	Prakash *et al* 2013
Podophyllum peltatum	May apple	Berberidacae	U.S., Canada	Dried rhizome	Podophyllotoxin, α/β peltatin	Umadevi *et al* 2013
Semecarpus anacardium	Bhilwa	Anacardi-aceae	India, Himalayas	Fruit	Anacardoside,semecarpetin,galluflavanone, nallaflavanol	Umadevi *et al* 2013
Smilax chinensis	China root	Liliaceae	China, Japan	Rhizomes	Tannin, saponins and flavonoid	Kaur *et al* 2011
Solanum nigrum	Black nightshade/ makoi	Solanaceae	South Africa, Australia	Leaves,stem,flowers, whole plant	Solamargine and solasonine, spirostane, furostane,	Shital *et al* 2013
Taxus	Yew	Taxaceae	Africa,	Shoots	Docetaxel, taxol	Kim *et al* 1994

Baccata			Iran			
Terminalia arjuna	Arjuna bark	Combertacae	India, Sri Lanka, Africa	Bark	Arjunic acid, arjunolic acid, arjungenin, arjunglycosides, arjunone,arjunolone,luteolin, gallic acid, ellagic acid	Pandey & Sharma 2006
Tinospora cordifolia	Giloy	Menisperm-aceae	India, Myanmar	Stem, Roots , Leaves.	Arabinogalactan, syringine, columbin,cordiol, cordioside, tinosporal, cordifoliosides (A & B)	Kayande & Patel 2013
Thuja occidentalis	American arborvitae	Cupressaceae	Northeastern USA, Europe	Whole plant	Flavonoid, tannin, volatile oil and mucilage	Cragg *et al 1993;* Prakash *et al* 2013
Thymus vulgaris	Garden thyme	Lamiaceae	South Europe	Whole plant	Volatile oil, flavonoid and tannin	Prakash *et al* 2013
Trifolium pratense	Red clover	Fabaceae	Asia, Europe, Africa, Australia	Flower	Glucosides (trifolin, trifolitin, trifolianol), flavonoid	Kaur *et al* 2011
Tylophora	Indian	Asclepiad-	*India*	Leaf ,root	Sigmasterol,coutchone,	Romero *et al* 2005;

indica	ipecac	aceae			kaempferol,α &β7amyrins	Umadevi *et al* 2013
Vaccinium stamineum	Deerberry	Ericaceae	North America, Mexico	Fruit	Resveratrol, pterostilbene, piceatannol	Kayande & Patel 2013; Chang 1992
Vitex trifolia	Nichinda	*Verbanaceae*	East Africa	Leaf,fruit	Casticin,trimethylquercetagetin	Romero *et al* 2005; Yu *et al* 2004
Zingiber officinalis	Ginger	*Zingibaracae*	India, southeast asia	Rhizome	Gingerol, shogaol, zingerone	Kokate *et al* 2006; Nadkarni 1908; Katiyar *et al* 1961

Discussion

There are numbers of plants worldwide which are having the anti carcinogenic properties, and many of them are yet to be discovered. In this review such 70 plants having anticancer properties were selected among which Liliaceae family was found to have highest numbers of plants with Indole ring system as common moiety in most of their isolated compounds. Literatures have already reported that Indole moiety is a tubulin inhibitor. With its anti proliferative property it inhibits cancerous cell lines. There are several reports on the use of north eastern traditional plants of India for the treatment of cancer (Dolui *et al,* 2004; Sharma *et al,* 2001; Jamir *et al,* 1999). Traditionally almost all parts of the plants are used to treat various types of cancers. Here, among these listed 70 plants almost all the parts such as root, leaves, seed, oils, bark, flowers etc are found to have anticancer properties. The literature evidences quoted in various Ayurvedic texts and recent pharmacological studies on medicinal plants, inferred that medicinal plants represent a good source of pharmacologically active agents treating various type of malignancies. Also, since many herbs play chemo protective action, a combination of Ayurvedic medicine and conventional therapy could also be recommended to inhibit the growth of cancer cells and to reduce the side effects of radiation and chemotherapy (Kayande and Patel, 2013).

Conclusion

There are many traditional systems of medicine in the world, each with different associated philosophies and cultural origins. Some of these, such as Tibetan traditional medicine remain relatively localised in their country of origin, while others such as Ayurvedic and Chinese traditional medicines are increasingly used in many different areas of the world. Ayurveda is the most widely practised of the Indian traditional medicine systems, but there are others such as Siddha and Unani which are also used in the Indian subcontinent. Cancer is a major public health burden in both developed and developing countries. It is an abnormal malignant growth of body tissue or cell. A cancerous growth is called a malignant tumour or malignancy. A noncancerous growth is called benign tumour. The process of cancer metastasis is consisting of series of sequential interrelated steps, each of which is rate limiting. Some of the plants loaded with chemo protective activities are undergoing clinical trial. Inhibition of angiogenesis is a novel process of cancer therapy. The selected plants may be used in anti-angiogenic therapy and thus in cancer management. Medicinal plants maintain the health and vitality of individual and also cure various diseases including cancer without

causing toxicity. Natural products discovered from medicinal plants have played an important role in treatment of cancer. This review highlighted the plants reported to have anticancer activity and it has been found that most of them are form Liliaceae family. Indole was found as common moiety in most of the potent isolated anticancer compounds like vincristine, vinblastin, vinoralbine, etc., and it is already reported that Indole ring bearing compounds have tubulin polymerization inhibition ability with antiproliferative activities against tumor cell lines THP1 and MCF7.

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