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UNTAPPED POTENTIAL OF THE INDIGENOUS ANTICANCER BIODIVERSITY IN THE INDO-HIMALAYAN HOTSPOT

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ABSTRACT: Cancer is the one of the leading cause of death worldwide. Even though many treatments exists in treating and controlling the progression of the deadly disease cancer, yet important inadequacy for development remain. Several undesired side effects occur when cancer is treated using chemotherapy. Therapies of Mother Earth, that utilizes bioactive products derived from a plant in treating cancer, may lessen the side effects. North-East India is recognized as a rich ethnomedicinal asset. It contributes to the abundant reservoir of plant diversity and is recognized as one of the 'biodiversity hotspots' of the world reinforcing around 50% of the country's biodiversity. There has been an increasing frequency of occurrence of cancer in developing countries like India, Nepal, and Pakistan which has serious implications on the morbidity and mortality in millions of people. Most of the Himalayan plants that have been reported are biologically active against different cancer types. The present statistics of cancer chemotherapy is bleak which is why there is an urgent need to develop and discover potent and novel agents for treating cancer. Over the years traditional herbal knowledge and scientific investigations of the unique biodiversity pool have contributed many potent and novel anticancer agents. About 50% of the modern drugs used clinically are explored from natural origin. Seventy-three anticancer medicinal plants have so far been documented that belongs to 62 genera and 39 families of which 51 plants were documented as from India followed by 22 plants which were reported from neighboring regions of Bhutan, Tibet, and Nepal. Majority of the prepare ethnomedicinal recipes constituted of roots (30% plants) and leaves (32% plants) in the decoction form. Thirty plants had reported with anticancer related pharmacological and phytochemical activities. From these plants, 32 were subjected to *in-vitro* studies on cellular models and 19 for *in-vivo* studies. Ethyl acetate and ethanolic extracts of plants were found showing excellent cytotoxic activities against stomach, blood cancer, and breast cell lines. 15 active secondary metabolites from the studied plants were reported active against different cancer cell lines including glycosides, terpenoids, alkynes, lignans, and phenolic compounds. Vigorous pharmacological investigation and detailed studies on the remarkable sub-Himalayan species is necessary to produce new anticancer drug leads for the development of novel drugs with lesser toxicity. However, this review will emphasize on numerous chemical compounds derived from Indo-Himalayan plants which in recent years have shown promising anticancer action and also their potential mechanism of action will be outlined.

INTRODUCTION: 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 (WHO definition).

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When the cancer cells continuously proliferate, it results in the development of tumor tissues that spreads to other organs by circulatory system proceeding to metastasis.

Tumours are of two types such as malignant tumors in which abnormal cells divide uncontrollably and destroy the body tissue and ultimately results in cancer and benign tumors are cells that are non-cancerous, non-invasive and lacks the ability to metastasize [1]. Metastasis is a multiple step process whereby tumour cells escape from their primary site and intrude other near and far locations in the

body. As per the statistics of the American Cancer Society (ACS), after cardiovascular diseases, infectious and parasitic diseases, cancer is the second most lethal disease, resulting in deaths more than AIDS, tuberculosis, and malaria combined (American Cancer Society Report, 2012). In Australia alone, an estimated 1,14,000 new cancer cases were spotted in 2010 with approximately 43,000 deaths from cancer (Australian Institute of Health and Welfare and Australasian Association of Cancer Registries, 2011) [2].

History of Cancer: The word cancer came from Greek words karkinos by a physician Hippocrates (460-370 B.C), that describes carcinoma tumors but he was not the first to discover the disease. The earliest world record case of breast cancer is from ancient Egypt in 1500 BC, and it was recorded that no treatment was available for this except palliative treatment [3]. In today's world, we are much aware of the human body; wherein early Greek physicians were not so blessed with this information. Hippocrates trusted in the fact that the body constituted of four fluids: phlegm, yellow bile, black bile, and blood. According to Hippocrates when there is an excess of black bile in any part of the body, it results in cancer [4].

Causes of Cancer: When multiple abnormal cells in a specific part of the body begin to grow cancer develops. Some cancerous cells move to other parts of the body *via* blood circulation or lymph vessels (metastasis), whereby they begin to grow [5]. Cancer cells grow and develop from normal cells because of damage of DNA. Smoking and use of tobacco also contribute in the development of cancers of larynx, lungs, esophagus, stomach, pancreas, and kidney as it constitutes a large number of carcinogens that includes nitroamines and polycyclic aromatic hydrocarbons that is responsible for 20% of deaths out of cancer worldwide.

All tumors are not cancerous; some are benign tumors (non-cancerous). Benign tumors do not develop and are not threatening to life. Different types of cancer cells can behave differently. Other cancer-causing agents are ionizing radiations, viral and bacterial infections, hormonal changes, immune system dysfunction and also non-mutagenic carcinogens as because they accelerate excessive growth of cell [6].

Molecular Biology of Cancer: The process that involves the gradual conversion of normal cells to the malignant cell may be the result of endogenous processes like intrinsic chemical instability of certain DNA bases, errors in replication of DNA or from attack by free radicals generated at the time of metabolism. Damage of DNA may also be the outcome of interactions with exogenous agents such as ionizing radiation, UV radiation, and chemical carcinogens. Cells have therefore evolved as a means to repair such damages, but because of various reasons error occurs and bring about permanent changes in the genome. Some inactivating mutations occur in genes that are responsible for maintaining the integrity of the genome and paving the way for acquisition of additional mutations [7].

The new targets which can recognize early and late events in the carcinogenic process offers opportunities for treatment as well as prevention of this deadly disease. Conventional agents must be used at dosages which are effective and safe to the patient. Newer therapies at the molecular level should, therefore, allow the physician to treat cancer without harming the patient and to achieve this it is necessary that genotyped tumors are phenotyped using standard pathological procedures, and this can be achieved by high throughput screening tests that can measure the presence of specific mutations in thousands of individual genes and pattern expression [8].

The most common methods for treatment of cancer include surgery, chemotherapy, radiation therapy, immunotherapy, hormone therapy, and gene therapy [9]. Medicinal plants are in high demand because studies on naturally occurring compounds are known to possess cytotoxicity effects as they display potential to destroy cancer cells also several species of medicinal plants have been investigated and selected for the preparation of cancer medicines [10]. National Cancer Institute has approximately screened 35,000 plant species for their potential anticancer activities. Important anti-cancer agents need to be explored more from a natural source, and more research is to be carried

out to design and develop newer drugs to treat this deadly disease [11].

Pathogenesis: Metastasis is a major cause of death from cancer and can be located in different organs and different parts within the same organ. They significantly affect the response of tumor cells to therapy and drugs that are to be delivered to tumor lesions to destroy cells without any undesirable side effects [12].

Importance of Plant Source as Anti-Cancer Agent: Increased cost and side effects of the medication have made researches focus onto herbal medicines. Therefore in this review, an effort has been made to provide information about the medicinal plants that possess anticancer activity. Plants have been used for a long time in treating cancer. Herbal medicine has become a topic of importance both in world health and international trade. Despite the long history of herbal anticancer treatment, the knowledge, as well as the experience of these herbalists, have not been documented scientifically [13]. The sub-Himalayan region is recognized as a rich ethnomedicinal asset. It forms a part of both the Himalayan as well as Indo-Burma biodiversity hotspots of the world. It has the richest reservoir of plant diversity in Pakistan, Nepal, Bhutan, China, Afghanistan and mainly India [14].

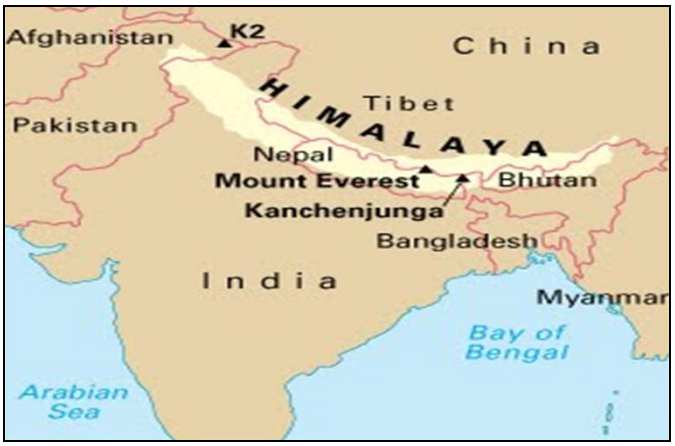


FIG. 1: BIODIVERSITY HOTSPOT IN INDO-HIMALAYAN REGION

Supporting around 50% of the country's biodiversity North East is one of the 'biodiversity hotspots' of the world. The earliest record of medicinal plant use in the Himalayan region is found in the Rigveda (4500 BC and 1600 BC). After Rigveda, Ayurveda (the foundation of the science of life and the art of healing of Hindu culture) describes the medicinal importance of 1200 plants. The Charak or Charaka Samhita (900 BC) and Susruta Samhita (500 BC) has enumerated the art of surgery, therapeutics, and medicines in detail based on Atharvaveda [13, 14]. However, according to the knowledge of the author, regarding the pharmacological aspects, very few investigations have been carried out. Here, in this review article, we tried to summarize the pharmacological aspects of medicinal plants in major sub-Himalayan region[15].

Medicinal Plants of Sub Himalayas based on their Anti-Cancer Activity: [16-39]

1. Botanical Name: *Acorus calamus*

Family: Acoraceae

English: Sweet flag

Hindi: Vekhand

Chemical Constituents: Flavanoids, quinine, saponins, sugars, tannins, triterpenes, gums, lectins, mucilage, phenols.

Anti-Cancer Activity: The plant is mainly also used for the treatment of colic and chronic dyspepsia. They are also used for the treatment of mental ailments like epilepsy, schizophrenia, and memory disorders, chronic diarrhea and dysentery, bronchial catarrh, intermittent fevers, tympanitis, colic, asthma, glandular and abdominal tumor, lung cancer, breast cancer, and liver cancer.

2. Botanical Name: *Aegle marmelos*

Family: Rutaceae

English: Indian bael

Hindi: Bael

Chemical Constituents: Alkaloids, glycosides, phenolic compounds and coumarins.

Anti-Cancer Activity: The plant extract shows inhibitory effect *in-vitro* proliferation of human tumor cell lines such as leukemic K562, T lymphoid Jurkat, B lymphoid and breast cancer MCF7.

3. Botanical Name: *Aloe barbadensis*

Family: Liliaceae

English: Aloe vera

Hindi: Ghrit kumara

Chemical Constituents: Aloin, acemannan, vitamine, dimethyl sulfoxide

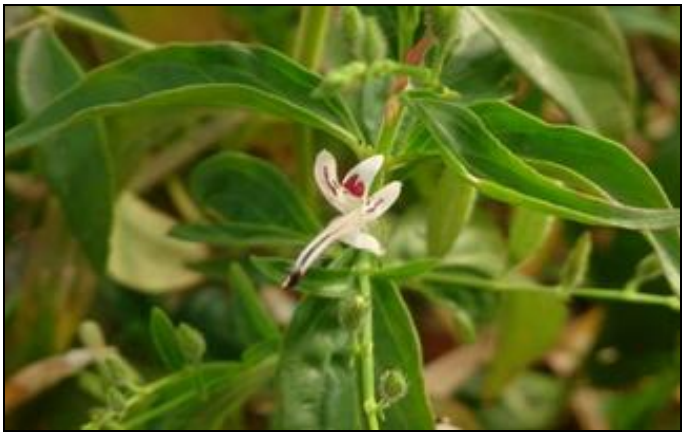
Anti-Cancer Activity: Barbolin, eloe-amodin, and aloesin show significant inhibitory effects on Ehrlich ascites carcinoma cell.

4. Botanical Name: *Andrographalis paniculata*

Family: Acanthaceae

English: Green chiretta

Hindi: Kirayat



Chemical Constituents: Diterpenoids, flavanoids, polyphenols.

Anti-Cancer Activity: Andrographaloside is the main active constituent and shows inhibition property on different tumor cells representing the various type of cancers.

5. Botanical Name: *Asparagus racemosus*

Family: Asparagaceae

English: Shatavari

Hindi: Shatavari

Chemical Constituents: Steroidal saponins, isoflavones, asparagine, racemosol, poly-saccharide, mucilage, vitamins, folic acid.

Anti-Cancer Activity: *Asparagus* contains a protein called histone that is responsible for controlling cell growth.MTT assay using MCF-7 (human breast cancer), HT-29 (human colon

adenocarcinoma), and A-498 (human kidney carcinoma) cell lines were used to evaluate the cytotoxicity (*in-vitro*) of shatavarin IV and other shatavarins rich fraction. The *in-vivo* anticancer activity of shatavarins (containing shatavarin IV) was evaluated against Ehrlich ascites carcinoma (EAC) tumor-bearing mice.

6. Botanical Name: *Betula utilis*

Family: Betulaceae

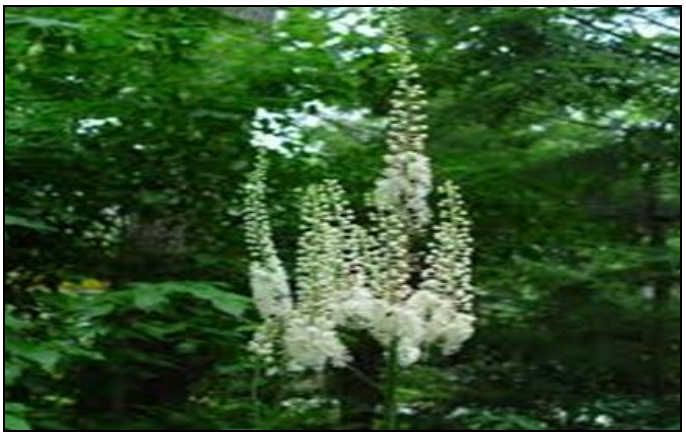
English: Himalayan birch

Hindi: Bhoj patra

Chemical Constituents: Betulin, lupenol, lupenone, sitosterol, methyl betulate, oleanolic acid, acetyloleanolic acid, betulinic acid, and karachic acid

Anti-Cancer Activity: Betulin is the active and potent compound having anticancer activity and suppress the growth of malignant melanoma and cancer of liver and lung.

7. Botanical Name: *Actaea racemosa*



Family: Ranunculaceae

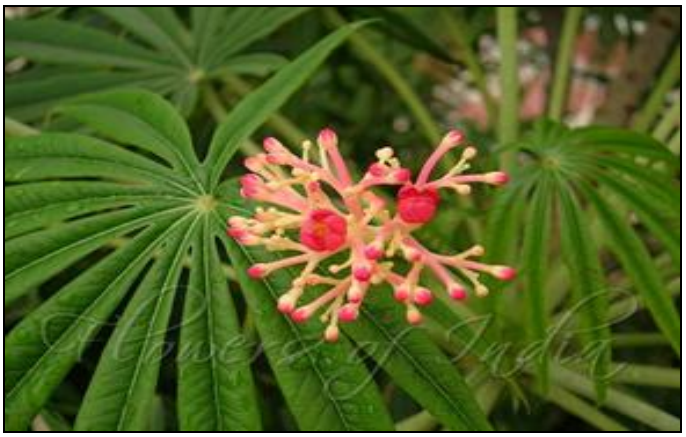
English: Snakeroot

Hindi: Adel

Chemical Constituents: Triterpenoids, cinnamic acid derivates, and cimicifugoside.

Anti-Cancer Activity: The major bioactive compound of this plant is actein and is responsible for inhibiting the human HepG2 liver cancer cells growth by lowering the cholesterol and free fatty acid levels in the liver.

8. Botanical Name: *Ardisia crenata*



Family: Myrsinaceae

English: Spiceberry, red berries, coralberry, and coral bush.

Hindi: Muhurat

Chemical Constituents: The major bioactive constituents are alkenylphenol, cyclic depso-peptide, triterpenoid saponins, and flavonoids.

Anti-Cancer Activity: The presence of ardisiacrispin which is a mixture of 2 triterpenoid saponins, *i.e*. ardisiacrispin A and B ardisiacrispin is responsible for showing the anticancer activity of the plant. It controls the proliferation of uncontrolled liver cancer cell line (Bel-7402) by microtubule disruption and induction of proapoptotic activities.

9. Botanical Name: *Bacopa monnieri*

Family: Scrophulariaceae

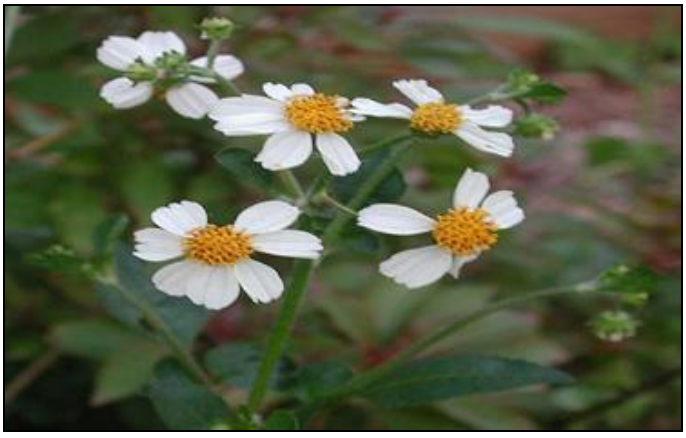
English: Brahmi

Hindi: Brahmi

Chemical Constituents: The bioactive compounds tetracyclic triterpenoid saponins, bacosides A and B, herpestine, brahmine, flavonoids, stigmasterol. Stigmasterol is known to possess anticancer activity by inducing apoptosis mediated by the activation of protein phosphatase 2A by ceramide

Anti-Cancer Activity: Antitumor activity of stigmasterol isolated from *Bacopa monnieri* on ehrlich ascites carcinoma in Swiss albino mice and found that stigmasterol enhanced the life span of tumor-bearing mice by decreasing the tumor volume and viable cell count.

10. Botanical Name: *Bidens Pilosa*



Family: Asteraceae

English: Cobblers pegs

Hindi: Kumur

Chemical Constituents: It contains polyacetylenes, flavonoids, phenylpropanoids terpenoids, and other compounds.

Anti-Cancer Activity: The plant extracts of *Bidens pilosa* in solvent systems of methanol, hexane, and chloroform were tested on various cancer cell lines were found to be effective in the treatment of cancer cell lines

11. Botanical Name: *Catharanthus roseus*

Family: Apocynaceae

English: Rosy periwinkle

Hindi: Sadabahar

Chemical constituents: Vinblastin and vincristine alkaloids.

Anti-Cancer Activity: Vincristine is mainly responsible for arresting mitosis and used for the treatment of acute leukemia in children. Vinblastin, another important anti-cancer compound is also utilized for the treatment of neuroblastoma, carcinoma of the lung, choriocarcinoma, lymphosarcoma, breast and other organs.

12. Botanical Name: *Centella asiatica*

Family: Apiaceae

English: Pennywort

Hindi: Brahmamanduki

Chemical Constituents: It contains numerous compounds such as asiaticoside, pectic acid, hydrocotyline, sterol, flavonoid, vallerine, ascorbic acid, and kunosides. Other constituents include centellose, centelloside, and madecassoside.

Anti-Cancer Activity: *C. asiatica* extract shows anticancer activity by inducing apoptosis in MCF-7 cells which are indicated by nuclear condensation, induction of DNA breaks identified by TUNEL reactivity increased annexin staining and loss of mitochondrial membrane potential.

The plant inhibits lipid peroxidation in various organs like lungs, spleen, kidney, liver, heart, and brain. It shows potential activity towards cancer inhibition.

13. Botanical Name: *Cedrus deodara*

Family: Pinaceae

English: Himalayan cedar

Hindi: Deodar

Chemical Constituents: It contains taxifolin, cedrinoside, cedrin, cedeodarin, and deodarin. Stem extract of *C. deodara* which contains lignin composition

Anti-Cancer Activity: Cytotoxicity to the human cancer cell lines and also induces tumor regression in murine models.

14. Botanical Name: *Citron*

Family: Rutaceae

English: Citrus

Hindi: Saitras

Chemical Constituents: Citrus peels are a rich source of phytoconstituents such as phenols, polysaccharides, limonoids, and flavonoids. The main components of the acidic polysaccharides (CA) are rhamnose (Rha), arabinose (Ara), galactose (Gal), glucose (Glu), mannose (Man) and galacturonic acid (GalA).

Anti-Cancer Activity: It enhances the immune response against cancer cells by increasing the levels of tumor-infiltrating CD8+ T lymphocytes. It inhibits the expression of anti-apoptotic protein BclxL and Mcl-1. The results conclude that acidic polysaccharides from citrus peels could be used as an adjuvant in treating hepatocellular carcinoma. Citrus peels are an abundant source of polyhydroxyl flavonoids (PHFs) such as hesperidin, neohesperidin, and naringin; and polymethoxyflavones (PMFs), most of these components act as potent antitumor compounds. PMFs are reported to significantly inhibit metastasis by restricting cell adhesion and its invasion. It enhances cytolysis by increasing the expression of NK cells. The cell cycle is arrested in the G1 phase by inhibiting cyclin-dependent kinases (Cdk) and enhancing Cdk inhibitor proteins. The efficacy of citrus peels against skin cancer has been studied in a two-stage skin carcinogenesis mode.

15. Botanical Name: *Cynodon dactylon*

Family: Poaceae

English: Dogs tooth grass

Hindi: Dood ghass

Chemical Constituents: Cyclophosphamide.

Anti-Cancer Activity: 96.2% of cancer inhibition was observed. The concentration of petroleum ether extract of *Cynodon dactylon* at 10 mg/ml showed inhibition percent about the cytotoxicity of 93.5% that was comparable to the positive control.

16. Botanical Name: *Languas galangal*

Family: Zingiberaceae

English: Blue ginger

Hindi: Neele dark

Chemical Constituents: 1'-Acetoxychavicol acetate.

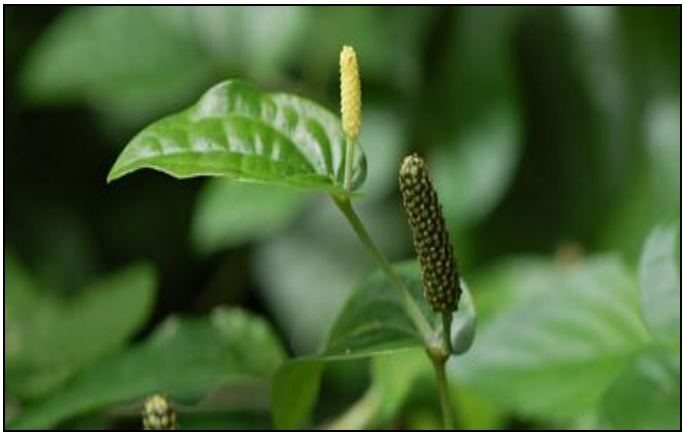
Anti-Cancer Activity: By modulating the activity of transcription factor, NF-kappa B which regulates metastasis and cellular proliferation, ACA mediated its antitumor activity.

17. Botanical Name: *Piper longum*

Family: Piperaceae

English: Long pepper

Hindi: Pipli



Chemical Constituents: -

Anti-Cancer Activity: The extract of *Piper longum* showed inhibitory effects on Human lung cancer (HCC-827cell line) cell lines and viable cell count decrease was recorded as compared to the control value.

18. Botanical Name: *Picrorhiza kurroa*

Family: Plantaginaceae

English: Indian gentian

Hindi: Kutki

Chemical Constituents: Picroside I and II. It contains a bitter glycoside which is known as kutkin. Its rhizome extract is rich in apocynin, caffeic esters, and cucurbitacins aglycone compounds.

Anti-Cancer Activity: It is used for treating hepatic carcinoma.

19. Botanical Name: *Plumbago zeylanica*

Family: Plumbaginaceae

English: White leadwort,

Hindi: Chitrak

Chemical Constituents: The active constituents of the plant include plumbagin, coumarins, saponaretin, steroids, is affine in, isoorientin, glucosides, and psoralen, plumbagin, naphthoquinone.

Anti-Cancer Activity: By controlling the hormone refractory invasive prostate cancer it possesses anti-tumor activity. Inhibitory action of plumbagin against molecular targets (STAT-3, AKT, and PI-3K) results in an invasion of prostate cancer and inhibition of growth. It also shows the induction of apoptosis in cancerous cells and also inhibits their growth.

20. Botanical Name: *Punica granatum*

Family: Lythraceae

English: Pomegranate

Hindi: Anar

Chemical Constituents: The active phytoconstituents in pomegranate includes ellagitannins (ETs), phenolic compounds and ellagic acid (EA).

Anti-Cancer Activity: Urolithins inhibit cancer cells proliferation, interfere with cell cycle and induce apoptosis. Colorectal cancer patients were orally administered ellagitannin containing pomegranate extract in a randomized clinical trial.

21. Botanical Name: *Tinospora cordifolia*

Family: Menispermaceae

English: Heartleaf moonseed plant

Hindi: Giloya

Chemical Constituents: Alkaloids which includes choline, isocolumbin, tinosporin, columbin, magnoflorimne, tetrahydropalmatine, and palmatin.

Anti-Cancer Activity: In mice transplanted with ehrlich ascites carcinoma, *T. cordifolia* showed anti-cancer activity

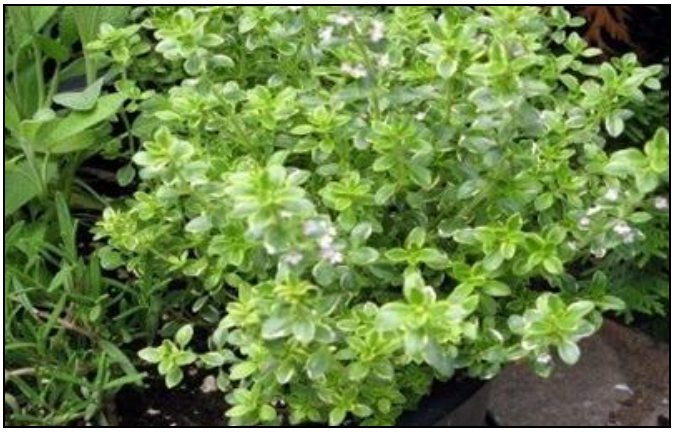
22. Botanical Name: *Thymus vulgaris*

Family: Lamiaceae

English: Garden thyme.

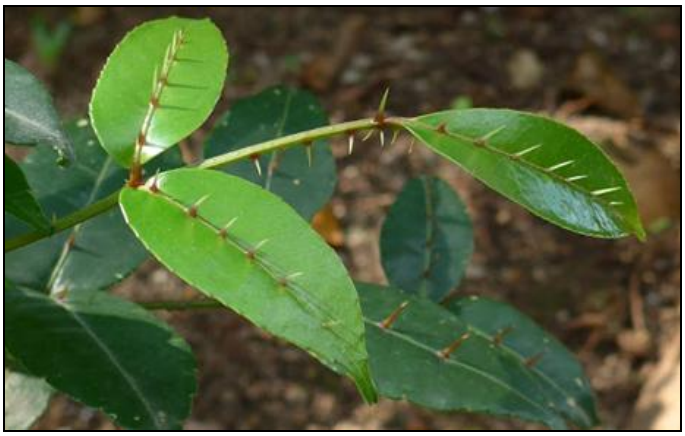
Hindi: Udyaan ajavaayan ke phool

Chemical Constituents: 20–54% thymol, oil of thyme, additional compounds such as p-cymene, myrcene, borneol, and linalool.



Anti-Cancer Activity: The active constituent accelerates cancerous cell death by regulating N-glycan biosynthesis, interferon signaling and extra-cellular signal-regulated kinase 5 (ERK5) signaling.

23. Botanical Name: *Zanthoxylum nitidum*



Family: Rutaceae

English: Shiny-leaf prickly-ash

Hindi: Tejamool

Chemical Constituents: It contains alkaloids, carbohydrates, flavonoids, and amino acids. Its root contains dihydropyridines, oxinitidine, nitidinechlorideskimmianine, α-allocryptopine, and 6-methoxy-5,6-dihydro chelerythrine.

Anti-Cancer Activity: Nitidine possesses the anti-cancer activity, and against LLC (DNA intercalator which is generally classified as topoisomerases I and II inhibitor) which leads to the cancer cells apoptosis it shows cytotoxic activity.

24. Botanical Name: *Cleome viscose*

Family: Cleomaceae

English: Asian spider flower

Hindi: Bagra

Chemical Constituents: fatty acids, methyl esters, stearic acid (7.2-10.2%), oleic acid (16.9-27.1%), palmitic acid (10.2-13.4%) and linoleic acid (47.0-61.1%), palmitoleic acid, arachidic acid, eicosa-(11Z)-enoic acid, linolenic acid, octadec-(11E)-enoicacidheneicosanoic acid, behenic acid, hexacosanoic acid, lignoceric acid, pentacosanoic acid, 12-oxo-stearic acid and alkanes, tetracosane, pentacosane, hexacosane, heptacosane, octacosane, nonacosane, triocontane, dotriacontane and hentriacontane were also identified as small and minor constituents in some of these oils.

Traditional Use: antitumor activity against Ehrlich ascites carcinoma (EAC)-bearing Swiss albino mice.

Anti-Cancer Activity: It has antitumor activity against ehrlich ascites carcinoma.

25. Botanical Name: *Curcumin domestica*

Family: Zingiberaceae

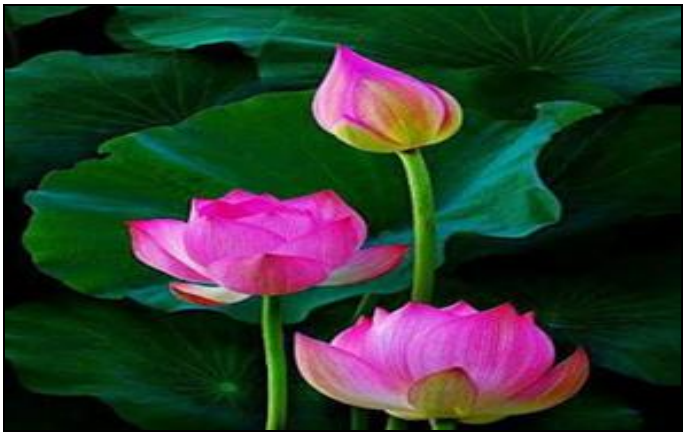
English: Domestic turmeric

Hindi: Haldi

Chemical Constituents: 0.36% and 0.53% of oils (w/v), 95.2% of the oil, of which the major ones were α-turmerone (12.9%), β-turmerone (12.0%) ar-turmerone (31.7%)and (Z) β-ocimene (5.5%). The oils includesterpinolene (8.8%), 1,8-cinceole (7.3%),α-phellantrene (9.1%), undecanol (7.1) and p-cymene (5.5%).

Anti-Cancer Activity: Curcumin is an effective anticancer agent and can be used as alternative cancer therapy or complementary therapy. It provides action against chemo damage of healthy cells and also makes some chemotherapy drugs work in a better way.

26. Botanical Name: *Nelumbo nucifera*



Family: Plantae

English: Lotus

Hindi: Kamal

Chemical Constituents: Beta-sitosterol, 1-undecanol, 1-eicosanol, 10-octacosanol, daucosterol, rhamnetin-3-O-beta-D-glucopyranoside, 6'-hydroxy -4, 4'-dimethoxychalcone, 3, 7, 8-trimethoxy-1-hydroxy- xanthone, chrysoeriol- 7- O- beta- D-glucoside, quercetin-3-O-beta-D-glucopyranoside, hyperoside, quercetin- 3- O- alpha- L- rhamno-pyranosyl, quercetin-3-O-rutinoside, astragalin, isorhamnetin-3-O-alpha- L-rhamnopyranosyl-(1--> 6)-[alpha- D- lyxopyranosyl- (1 -->2) -beta-D-glucopyranoside], isorhamnetin- 3- O- alpha- D-lyxopyranosyl-(1 --> 2) -beta-D-glucopyranoside, isorhamnetin-3-O-beta-D-glucopyranoside stigmast- 7- en- 3- O- beta- D- glucopyranoside, isorhamnetin-3-O-alpha- L-rhamnopyranosyl-(1 --> 6)-beta-D-glucopyranoside, quercetin, kaempferol, dehydronuciferine, roemerine, stigmast-7-en-3beta-ol , and benzene-1,2-diol.

Anti-Cancer Activity: It is used for the treatment of human colon carcinoma HCT-116 cells.

27. Botanical Name: *Ocimum tanuiflorum*

Family: Plantae

English: Holy basil

Hindi: Tulsi

Chemical Constituents: The phytochemical constituents of tulsi are eugenol, carvacrol, linalool, β-caryophyllene (about 8%), oleanolic acid, ursolic acid, rosmarinic acid. Essential oil consists mostly of β-elemene (~11.0%), β-caryophyllene (~8%), eugenol (~70%) and germacrene (~2%) and terpenes.

Anti-Cancer Activity: *Ocimum sanctum* Linn. (Labiatae) is active against human fibrosarcoma cells (HFS cells). When treated with ethanolic extract of *Ocimum sanctum*. It induces cytotoxicity at 50 µg/ml concentration and above. Biochemically the HFS cells treated with extract shows decreased intracellular glutathione and increased lipid peroxidation products. To mice bearing sarcoma-180 solid tumors, administration of aqueous and ethanolic extracts of *Ocimum sanctum* results in a significant reduction in the volume of tumor and an increase in lifespan. Thus it indicates that *Ocimum sanctum* extracts possess anticancer activity.

28. Botanical Name: *Rubia manjith*

Family: Rubiaceae

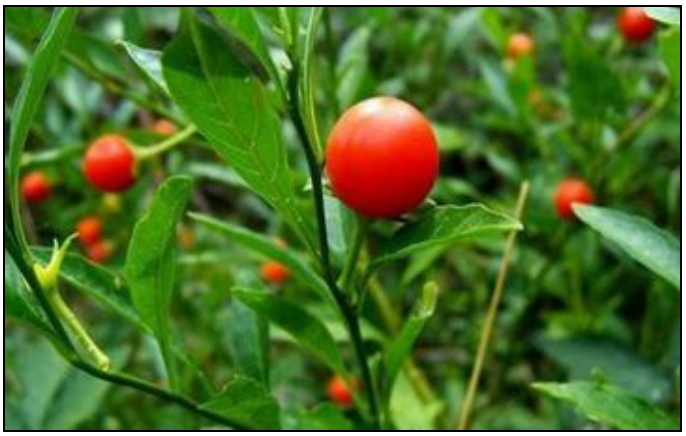
English: Indian madder

Hindi: Manjith

Chemical Constituents: The active constituents in the oil include tridecanal (16.7%), pentadecanal (20.2%) and globulol (7.8%).

Anti-Cancer Activity: The extract of this plant shows anticancer activity against leukemic cells, ascites carcinoma, large intestinal and lung carcinoma, melanoma, *etc*.

29. Botanical Name: *Withania somnifera*



Family: Solanaceae

English: Indian cherry

Hindi: Ashwagandha

Chemical Constituents: Alkaloids like cuseo-hygrine, anahygrine, isopelletierine, anaferine, *etc*., steroidal lactones like withaferins, withanolides and saponins. Anti-stress agents in Ashwagandha are Sitoindosides and acylsterylglucosides.

Traditional Use: It can fight cancer by reducing tumor size and inhibiting the growth of cancer cells.

30. Botanical Name: *Cassia fistula*

Family: Caesalpinaceae

English: Golden rain tree

Hindi: Amultas

Chemical Constituents: Carbohydrates, linoleic acid, stearic acid, oxalic acid, tannins, oxyanthra-quinones, anthraquinones derivatives, rhein glycosides fistulic acids,sennosidesAB,flavanoid-3-ol-derivatives.

Traditional Use: On ehrlich ascites carcinoma (EAC), methanolic extract of *Cassia fistula* seed is effective, and the extract shows decreased tumor volume and viable tumor cell count in the EAC tumor host.

CONCLUSION: An abnormal malignant growth of body tissue or cell is known as cancer. The cancerous growth of cell is called malignant tumor or malignancy, and noncancerous cell growth is called a benign tumor. Cancer metastasis consists of a series of steps, each of which is rate limiting. Plants filled with chemoprotective activities are undergoing a clinical trial. A novel process of cancer therapy is the inhibition of angiogenesis. With different associated philosophies and traditional origins, there are many traditional systems of medicine around the world such as Tibetan traditional medicine remains restricted in

their country of origin; while others such as Chinese and Ayurvedic traditional medicines are used increasingly in various regions of the world. Although, few types of research have been carried out, the vast majority of medicinal plant species of the Himalayan region are still far behind of pharmacological researches to prove their therapeutic potential scientifically. Based on indigenous and ethnic knowledge, a medicinal plant of Sub- Himalayan regions has diverse therapeutic potency. Therefore, concise and continues research with advanced instruments is necessary to explore their pharmacological property which may act as a milestone to decrease the resistance and adverse effect problem of modern allopathic medicine. Herbal anti-cancer agents have enormously contributed to the development of newer drugs.

This review hence emphasizes on sub-Himalayan medicinal plants and their secondary metabolites that have anti-cancer activity. So it can be concluded that medicinal plants and its derivatives derived from the herbal source are potent against different cancer types and such treatment may be proposed to the rural and poor people such that they treat cancer effectively with minimal expense.

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