Available online on www.ijppr.com
International Journal of Pharmacognosy and Phytochemical Research 2023; 15(1); 1-9

eISSN: 0975-4873, pISSN: 2961-6069

Review Article

A Review on Anti-Cancer Potential of Herbal Drugs

Rohit R. Bhosale[1]*, Dhanashri D. Chavan[2], Vandana M. Thorat[2], Amol S. Shete[3]

[1]*Department of Pharmaceutics, Krishna Foundation's Jaywant Institute of Pharmacy, Wathar Tal. Karad- 415539, Maharashtra, India*
[2]*Department of Pharmacology, Krishna Vishwa Vidyapeeth (KVV) Deemed to be University, Karad- 415539, Maharashtra, India*
[3]*Department of Pharmaceutics, Krishna Institute of Pharmacy, Krishna Vishwa Vidyapeeth (KVV) Deemed to be University, Karad- 415539, Maharashtra, India.*

Received: 30th January 23; Revised: 18th February 23; Accepted: 25th February 23; Available Online: 25th March 23

ABSTRACT
Cancer is a multistep process and characterized by irregular proliferation of cells. Usually, these cells invade and destroy the normal cells, thus creating an imbalance in the body. Cancer is caused due to various factors like tobacco consumption, exposure of body to chemicals, dietary factors and environmental factors. Conventional medication for the treatment of cancer has several impacts on healthy cells. There is also a problematic issue of an increase in tumour resistance to the current therapeutic agents. Due to this, there is a great need to fight this disease with more effective medication. The present piece of writing provides information regarding different medicinal plants possessing anti-cancer activity.
Keywords: Medicinal plants, Cancer, Phytocompounds, Anticancer activity.

INTRODUCTION

Cancer is an abnormal growth of cells in our bodies that can lead to death. It destroys the normal cells and creates and imbalance in the body. It is one of the most severe health problems in both developing and developed countries. It is very difficult to find the specific cause for cancer. However, tobacco use, alcohol consumption, environmental pollutant, infectious agents, custom habits and lifestyles are some commonly known reasons responsible for this disease. Environmental factor that contributes to the cancer deaths includes tobacco, obesity, radiation, infection, heredity, stress, environmental pollutants and lack of physical activity (lifestyle, economic and behavioural factors). Smoking causes 90% of lung cancer[1]. It also causes kidney, stomach, pancreas, larynx, and bladder cancer[2]. Tobacco is responsible for about one in five cancer death cases globally[2]. Physical inactivity, obesity and diet are related to 30-35% of cancer deaths[3]. Physical inactivity is believed to contribute to the cancer risk. More than half of the effect from diet is due to the over nutrition. Some specific foods are related to the specific type of cancers like high salt diet causes gastric cancer, aflatoxin B1 causes liver cancer and chewing betel nut causes oral cancer[4].

Exposure to ionizing and non-ionizing ultraviolet radiation causes cancer (up to 10%). Source of ionizing radiations includes radon gas and medical imaging; this radiation is not particularly a strong mutagen. When radiation combines with other cancer-causing agents then it is more potent like radon with the tobacco smoke[5]. Prolonged ultraviolet ray exposure from sun light leads to skin cancer. Hereditary also causes cancer in some cases, less than 0.3% population carries genetic mutations that cause cancer. Examples of cancer due to hereditary include inherited mutation in BRCA1 and BRCA2 genes, hereditary non-polyposis colorectal cancer. Some hormones also play an important role in the cancer development by promoting the cell proliferation[6]. Insulin like growth factors and their binding proteins play an important role in proliferation of cancerous cell[7].

**Author for Correspondence: bhosalerohit707@gmail.com*

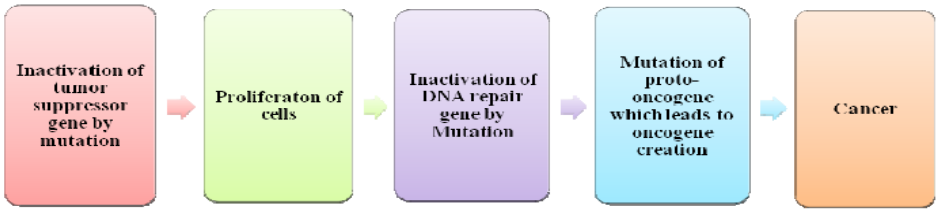

Figure 1: Development of cancer

'Staging' is a very important parameter in determining the severity of cancer. Depending on the stage of cancer, patients can be recommended drugs accordingly. There are four stages of cancer, each showing different properties and symptoms. These are tabulated as under: STAGE 1 This is the primary stage of cancer with no visible symptoms. The tumour is not fully grown. A routine medical examination can help detect the presence of first stage cancer. If cancer is detected in this stage, it would be easier to cure it. STAGE 2 The tumour in this case is easily visible through scans. There are a few visible symptoms. STAGE 3 The benign tumour is fully grown with detectable symptoms. STAGE 4 This is the terminal stage cancer and no cure is possible in this stage. There is metastasis (spread) of tumour to distant parts of body. There are visible symptoms of cachexia (sudden significant weight loss), patches on skin in case of skin cancer.

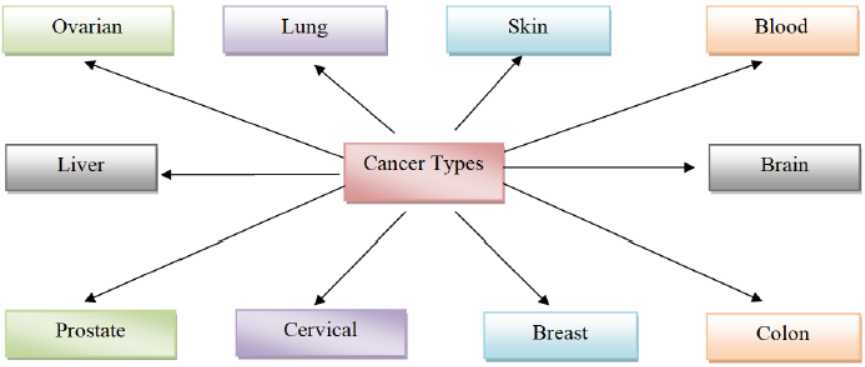

Figure 2. Types of cancer

The important preventive methods for most of the cancers include dietary changes, stopping the use of tobacco products, treating inflammatory diseases effectively, and taking nutritional supplements that aid immune functions. Current treatment for the cancer includes radiotherapy, chemotherapy and chemically derived drugs. Most commonly used cancer chemotherapy includes anti-metabolites, alkylating agents, platinum analogs and anti-tumor antibiotics. However, chemotherapy and radiotherapy put patients under lots of strain and further causes health damage. Thus, discovery of new anticancer agents from nature, especially plants is currently under investigation. Plants have always been a basis for the traditional medicine systems and they have provided continuous remedies to the mankind for thousands of years. Therapeutic potential of plants is based on the findings of thousands of years of use. First written records on hundreds of medicinal plants including opium and myrrh are listed on the clay tables[8]. Herbal medicines have been used for the centuries to treat various diseases. Herbal medicine uses plant extracts to treat the disease and promote the health of the patient. Aim of the herbal medicine is to restore the ability of body to protect, regulate and heal. Several modern drugs are made from the medicinal plants. Herbal products are taken in form of powder, paste, pills, liquid or raw material (extract). Use of certain herbal products tends to produce side effects and toxicities. In most cases, problem arises due to the inappropriate use of the herbal products, mislabelling of plant materials, botanical misidentification, etc. This can be toxic when used for inappropriate indications or used in large amount or prepared inappropriately[9]. Knowledge of the medicinal plants for the preparation of various drugs has been of great significance. Medicinal plants are considered as a rich source of wide variety of ingredients which can be used for the development of drug. Anticancer properties of several medicinal plants are used to find a lead compound that can block the development of cancer. Medicinal plant has various secondary metabolites such as terpenoids, flavanoids, alkaloid and steroids that have different pharmacological properties[10]. Medicinal plants such as *Allium sativum, Annona muricata, Berberies aristata, Catharanthus roseus, Linum usitatissimum,*

Podophyllum hexeandrum, Rubia cordifolia, Withania somnifera, etc., show potential role in the inhibition of cancer cell proliferation. Therefore, this chapter provides an overview of various medicinal plants and their major bioactive compounds utilized for treatment of cancer.

ANTICANCER ACTIVITY OF MEDICINAL PLANTS

1. Allium sativum

Allium sativum belongs to the *Alliaceae* family and native to the region between Mediterranean and China. It contains ajoene, allicin, alliin, allixin, γ-glutamyl-S-2-propenyl cysteine, diallyl disulfide, methyl allyl disulfide, S-allyl-cysteine and 1,2-vinyldiithin. Allicin shows antitumor activity in L5178Y lymphoma bearing mice. Methanolic extract of A. sativum (MEAS) shows anticancer activity against MCF7, A549 & DU145 and cell carcinoma of the bladder[11,12].

2. Annona muricata

Annona muricata belongs to the *Annonaceae* family and commonly known as Graviola. It contains acetogenins, β-sitosterol, stigmasterol, phenols, alkaloids, annoionoside, annoionol A, B, C, lycopene, lutein etc. It is distributed in the tropical regions of Central and South America, Western Africa and Southeast Asia. Acetogenins is the main compound and found in the leaves, seeds, bark and fruit of this plant. Acetogenis block the adenosine triphosphate production which inhibits the pump that removes cancer drug from the cell[13]. Acetogenins is identified to be toxic for various cancer cell lines such as pancreatic cancer, breast cancer, colonic adenocarcinoma, liver cancer and lymphoma[14].

3. Astragalus membranaceus

Astragalus membranaceus belongs to the *Fabaceae* family and is commonly known as Mongolian milkvetch. It contains astragloside, astraglan, calycosin, soyasapogenoside, quercein, kaempferol, etc. This plant is typically found in parts of China. It is used by the Chinese doctors to treat advanced cases of the liver cancer. A study reported that administration of this plant along with conventional treatment has shown higher survival rate of patients with advanced stage liver cancer as compared to the patients who were given conventional treatment. Astragalus membranaceus protects liver from toxic effects of chemotherapy[15]. Swainsonine which is an important compound of this plant is known to prevent metastases[16].

4. Azadirachta indica

Azadirachta indica belongs to the *Meliaceae* family and found in India and Indian subcontinent. It contains nimbin, nimbanene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol and amino acid, nimbiol, etc. It has been used for the treatment of skin cancer, buccal cancer, mammary cancer, prostate cancer and gastric cancer[17]. Ethanolic extract of Azadirachta indica causes prostate cancer cell death by apoptosis induction. It acts in a dose dependent manner and increase the fragmentation of DNA[18].

5. Berberis aristate

Berberis aristata belongs to the *Berberidaceae* family and commonly found in temperate and sub-tropical regions of Asia, Europe, and America. It is commonly known as Daruhaldi and roots of this plant contain berberine, berbamine, oxyxanthine, jatrorhizine, epiberberine[19]. Methanolic extract of B. aristata showed potential anticancer activity against the human colon cancer cell line and inhibits HT29 cells in a concentration dependent manner[20]. It also significantly inhibits the carcinogenesis induced by 20-methylcholantherene in a dose dependent manner[21].

6. Camellia sinensis

Camellia sinensis belongs to the *Theaceae* family and is commonly known as green tea. It contains caffeine, theobromine, gallic acid, catechin, ampelopsin, epicatechin, etc. This plant is native to East Asia, the Indian Subcontinent and Southeast Asia but in today's time it is cultivated also in tropical and subtropical regions in the world. It contains polyphenolics possess anti-cancer and anti-mutagenic activity. Some evidence suggested that this plant has a protective effect against the colon and stomach cancer[22]. A study reported that green tea extract significantly inhibited the liver and leukemia tumor cells from DNA synthesis[16]. It also inhibits the cancer growth by eliminating the free radicals from the body.

7. Cannabis sativa

Cannabis sativa belongs to the *Cannabinaceae* family and native to the South Africa. It contains cannabinoids, cannabinol, anandamide, pinene, myrcene, etc. Cannabinoids shows potential inhibition towards cancer based on the experiments performed both in cultured cells and in animal models of cancer[23]. Cannabinoids present an interesting therapeutic potential such as antiemetics, analgesics, appetite stimulants in debilitating diseases, treatment of multiple sclerosis, spinal Tourette's syndrome, cord injuries, glaucoma and epilepsy[24]. Antineoplastic and proapoptotic properties of cannabinoids show emphasis effects of N-acylethanolamines[25]. Cannabinoids induces cancer cell death by apoptosis and inhibits proliferation of cancer cell[26].

8. Catharanthus roseus

Catharanthus roseus is an important medicinal plant and belongs to the *Apocynaceae* family. It is commonly known as Madagascar periwinkle. It contains actineoplastidemeric, vinblastin, vincrestine, vindesine, vindeline, tabersonine etc. Catharanthus is native to Madagascar but now-a-days it is being cultivated in Tanzania, Kenya, Kisi and many other

countries. This plant is used for the treatment of cancer, diabetes, fever and hypertension[27]. It contains many bioactive compounds which include vinblastine, vincristine, ajmalicine and serpentine. Vinblastine and vincristin are commonly used for the treatment of leukemia and lymphoma[28].

9. Curcuma longa

Curcuma longa is commonly known as haldi in Hindi, harida in Sanskrit and turmeric in English. It is belonging to the *Zingiberaceae* family. This plant is native to Southern Asia and is also used as a coloring agent in Bangladeshi cuisine, Indian cuisine and also for many other purposes.

It contains curcumin, curcuminoids, essential oil, turmerone, monoterpenes, diarylpentanoids, diterpenes, sesquiterpenes, triterpenoids, sterols, alkaloid, etc. Curcumin is the active ingredient of this plant, which is a polyphenol derived from plant rhizome and this plant is used for both cancer prevention and treatment. Curcumin shows protective effect by inhibiting the growth of several angiogenesis associates and tumor associated genes[29]. Curcumin possesses anti-proliferative property by down regulating the numerous gene expressions which includes activator protein 1, NF-kappa B, cycloxygenase 2, epidermal growth receptor 1, nitric oxidase synthase and tumor necrosis factor[30].

10. Glycine max

Glycine max belongs to the *Fabaceae* family and native to East Asia. It is commonly known as Soya bean and rich in selenium, zinc, vitamins, isoflavones, amino acids, phytosterols and saponons. A study reported that soybean agglutinin inhibits the tumor growth in rats[31]. Isoflavones converts cancer cells to the normal by inducing cell differentiation. Genistein induce apoptosis in the cancer cells[16].

11. Linum usitatissimum

Linum usitatissimum belongs to the *Linaceae* family and is rich in lignans. This short-lived perennial plant found in the western and southern Europe and western Asia. These plant lignans are converted to mammalian lignans (enterodiol and enterolactone) by bacterial fermentation in the colon[32] and they can then act as estrogens. Mammalian lignans appear to be anti-carcinogenic, lignan metabolites bear a structural similarity to estrogens and can bind to estrogen receptors and inhibit the growth of estrogen-stimulated breast cancer[33]. Root extract of *Linum usitatissimum* induce significant amount inhibition of cell vitality and proliferation without performing the strong cytotoxicity in the human breast cell line MCF7[34].

12. Podophyllum hexeandrum

Podophyllum hexeandrum belongs to the *Podophyllaceae* and found in Himalayan region. It is commonly known as Mayapple and contains podophyllotoxin, kaempferol, quercetin, asiragalin, essential oil, podophyllin. Podophyllotoxin has been used for the treatment of testicular and lung cancer as well as in certain leukemias[35]. Podophyllotoxin majorly found in the roots of this plant and used for the treatment of cancers, ulcers, wounds, constipation and tuberculosis[35].

13. Oroxylum indicum

Oroxylum indicum belongs to the *Bignoniaceae* family and is native to the Indian subcontinent. It contains baicalein, chrysin, oroxylin, scutellarein, pinostrobin, stigmast-7-en-3-ol. Several studies have shown the anticancer potential of this plant in various models. Ethanol extract (95%) of this plant showed cytotoxic effects against the Hep2 cell lines at 0.05% concentration[36].

Baicalein showed the antitumor effect on the human cancer cell lines and inhibits proliferation of HL-60 cell lines up to 50% at 25-30 µM concentration[37].

Aqueous and methanolic extract of Oroxylum indicum showed cytotxicity in selected tested cell lines and both the extracts exhibited moderate level of DNA protection against the oxidative stress[38].

14. Punica granatum

Punica granatum belongs to the *Lythraceae* family and fruit bearing deciduous shrub which is commonly known as pomegranate. It is originated in Iran and has been cultivated since ancient times throughout the Mediterranenan region and northern India. It is rich source of phenolic compounds, ellagitannins (ETs) and ellagic acid (EA) that metabolically convert to urolithins by the gut microbiota. Urolithins are found in high concentrations in colorectal cancer patients and urolithins inhibit proliferation of cancer cells and interfere with cell cycle and induce apoptosis[39]. In a study, potential of pomegranate ellagitannins-derived compounds exhibited anti-proliferative and anti-aromatase activities in breast cancer cells[40].

15. Rubia cordifolia

Rubia cordifolia belongs to the *Rubiaceae* family and is commonly known as Indian madder. It contains cordifoliol, cordifodiol, anthraquinone, alizarin, etc. Mollugin showed anticancer activity against the lymphoid leukemia in mice and also inhibited the passive cutaneous anaphylaxis in rats[41]. Quinones and hexapeptides found in this plant showed the potential antitumor activity by 80S ribosome binding and this resulted in the inhibition of peptidyl tRNA and aminoacyl-tRNA binding which is required for the protein synthesis[42].

16. Silybum marianum

Silybum marianum belongs to the *Asteraceae* family and native to Southern Europe to Asia. It contains silymarin, silydianin, silychristin, silibinin, tyramine, histamine, essential oil, gamma linoleic acid, mucilage, etc. Silymarinis is the main compound

of this plant which showed anticancer property against UV radiation induced skin cancer in mice and reduces the tumor multiplicity up to 78%[43]. Silymarins down regulates the gene product which is associated in the tumor cells proliferation, angiogensis, invasion and metastasis[44]. Silibinin also showed beneficial role in the human breast cancer[45].

17. Taraxacum officinale

Taraxacum officinale belongs to the *Asteraceae* family and is commonly known as Dandelions. It is a perennial plant and found in the temperate regions of the world such as Western, Central and Southern Europe, Northwest Africa, Northern Iran and Southwest Asia. It contains glycosides, terpenoids, carotenoids, choline, potassium salts, vitamin A, lecithin, etc. Taraxacum officinale decreased cell viability and increased the production of tumor necrosis factor α and interlukine-1α[46]. Leaves, root and flowers extracts of this plant was investigated against progression of tumor, among all the extracts leaf extract showed inhibition of breast cancer cell growth[47].

18. Vernonia amygdalina

Vernonia amygdalina belongs to the *Compositae* family and grows in tropical Africa. The bitterness in the plant extract is due factors such as glycoside, saponins, alkaloids and tannins. Vernonia amygdalina reverses the tumor in 106 MCF-7 breast cancer cells and also increased the basal apoptotic but decreased the angiogenic activity in mice[48]. Vernonia amygdalina shows anticancer activity in the human breast cancer cell lines (MCF-7 and MDA-MB-231) and inhibits the proliferation of cell lines in a dose and time dependent manner[49].

19. Vismia laurentii

Vismia laurentii belongs to the *Guttiferae* family and is found in the tropical and sub-tropical regions of world. It contains anthraquinones, xanthones and prenylated anthrones. It is used for the treatment of wounds and skin diseases. Xanthone V1 has shown anticancer potential against numerous cancer cell lines. It induces apoptosis and caspase-3 activity in CCRF-CEM cell line[50]. Fruits and seeds of this plant contain xanthones, naphtoquinones and anthraquinones which are thought to be responsible for the anticancer activity of this plant[51].

20. Withania somnifera

Withania somnifera is commonly known as ashwagandha in Hindi and Sanskrit, winter cherry in English. It belongs to the *Solanaceae* family and contains withanolides, withaferins, anferine, isopellertierine and sitoindosise. Due to its medicinal properties, leaves and roots have been used in the Indian traditional system of medicine and marketed globally. Extract of Withania somnifera modulates various biological responses[52]. It has been used in various preparations for its anti-stress, antiperoxidative, anti-ageing, anti-inflammatory, antioxidant, anti-tumor, cardiotonic, and immunomodulatory properties. Withanolide A and withaferin A is the main constitute of this plant. Withaferin A which is mostly present in the leaves produces rapid apoptosis in the cancer cells. Cell signaling pathways by this plant formulation largely depends up on the high content of withferin A present in it[53].

OTHER MEDICINAL PLANTS WITH ANTI-CANCER ACTIVITY

Plant derived anticancer agents are effective inhibitors of cancer cells lines. Due to which there is a high demand of these plants for the production of therapeutically important compounds. There are several other medicinal plants all over the world, which are being used traditionally for cancer prevention and treatment. Some phytochemicals that are important active constituents of plants, including catechins, ursolic acid, silymarin, hecogenin glycyrrhizin, berberine, campothecin, gallic acid and various types of flavonoids, have shown promise in future cancer management. Some of the other medicinal plants that possess anticancer activity are discussed in the Table 1.

Table 1: List of other medicinal plants with anticancer activity.

Plants	Family	Anti-cancer agents	References
Aegle marmelos	Rutaceae	Lupeol	54
Ailanthus altissima	Simaraubaceae	Ailantenol	55
Andrographis paniculata	Acanthaceae	Andrographolide	56
Apium graveolens	Umbelliferae	Apigenin	57
Aloe ferox	Liliaceae	Aloe-emodin, emodin	58,59
Alpinia galanga	Zingiberaceae	Pinocembrin	54
Ananas comosus	Bromeliaceae	Ananas bromelain	60
Aphanamixis polystachya	Meliaceae	Amooranin	54
Astragalus membranaceus	Papilionaceae	Swainsonine	61
Berberis vulgaris	Berberidaceae	Berberine	54
Betula utilis	Betulaceae	Betulin	62
Bleckeria vitensis	Apocynaceae	Ellipticine	63

Brucea antidysenterica	Simaraubaceae	Bruceantin	63
Campotheca acuminate	Nyssaceae	Campothecin	63
Chlorella pyrenoidosa	Oocystaceae	Lysine	64
Cephalotaxus harringtonia	Cephalotaxaceae	Homoharringtonine	63
Chelidonium jajus	Papaveraceae	Sanguinarine	65
Colchicum luteum	Liliaceae	Colchicines	66
Croton lechleri	Euphorbiaceae	Taspine	67
Diphylleia grayi	Berberidaceae	Diphyllin	63
Dysoxylum binectariferum	Meliaceae	Rohitukine	63
Echinops setifer	Asteraceae	Echinopsine	68
Euphorbia semiperfoliata	Euphorbiaceae	Jatrophane	67
Fagopyrum esculentum	Polygonaceae	Rutin	66
Indigofera tinctoria	Leguminosae	Indirubins	63
Ginkgo biloba	Ginkoaceae	Ginkgolide	69
Glycyrrhiza glabra	Leguminosae	Glycyrrhizin	70
Gossypium barbadense	Malvaceae	Gossypol	71,72
Larrea tridentate	Zygophyllaceae	Terameprocol	73
Lentinus edodes	Agaricaceae	Lentinan	74
Lonicera japonica	Caprifoliaceae	Luteolin	75
Mappia foetida	Icacinaceae	Camptothecin	76
Paris polyphilla	Trilliaceae	Polyphyllin	77
Podophyllum hexandrum	Berberidaceae	Podophyllin	78
Plumbago zeylanica	Plumbaginaceae	Plumbagin	79
Scrophularia nodosa	Scrophulariaceae	Iridoid	80

CONCLUSION

Every year, cancer takes the life of millions of people. Various therapies are available for the cancer treatment, but they have several limitations such as kidney damage, gastro-intestinal disorder, etc., due to which an alternative solution to this problem is required. Plant derived compounds possessing anti-cancerous activities have received huge amount of scientific attention. They play vital role in the cancer prevention and treatment. Pharmaceutical research has been done in countries like Germany, USA, Japan, France and China to improve the quality of herbal medicine for the cancer treatment. Plants are the major source of secondary metabolites and an important source of pharmaceutical drugs. Herbal drug treatment is an ideal choice as it is comparatively cheaper and may be highly recommended to the poor and rural people for the effective treatment of cancer. Anticancer agents discovered from medicinal plants have played an important role in cancer treatment. It is documented that the medicinal herbs have rich anticancer potential due to their immunemodulatory and antioxidant properties, and on the forefront whenever we talk about anticancer remedies, they are a significant source of synthetic and/or herbal origin. Bioactive compounds significantly influenced the cancer research on various aspects. Secondary metabolites from medicinal plants inhibits the DNA damage, arrest the cell cycle, inhibits the tumor cell angiogenesis and induce apoptosis thus prevents the cancer. Researchers must pay attention to the scientific rigor of studies of herbal drugs in the future to improve the status. Only few medicinal plants have been explored for their biological activity from 1000 species, so further investigations of plants in cancer treatment show a promising activity and it must be taken into consideration.

REFERENCES

1. Biesalski HK, Bueno de Mesquita B, Chesson A, Chytil F, Grimble R, Hermus RJ, Köhrle J, Lotan R, Norpoth K, Pastorino U, Thurnham D. European Consensus Statement on Lung Cancer: risk factors and prevention. Lung Cancer Panel. Cancer J Clinic. 1998; 48(3): 167- 176.
2. Kuper H, Boffetta P, Adami HO. Tobacco use and cancer causation: association by tumour type. J Int Med. 2002; 252(3): 206-224.
3. Kuper H, Adami HO, Boffetta P. Tobacco use, cancer causation and public health impact. J Int Med. 2002; 251(6): 455-466.
4. Kushi LH, Byers T, Doyle C, Bandera EV, McCullough M, McTiernan A, Gansler T, Andrews KS, Thun MJ. American Cancer Society Guidelines on Nutrition and Physical Activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. Cancer J Clinic. 2006; 56(5): 254-281.
5. Park S, Bae J, Nam BH, Yoo KY. Aetiology of cancer in Asia. Asian Pac J Cancer Prev. 2008; 9(3): 371-380.
6. Goubran HA, Kotb RR, Stakiw J, Emara ME, Burnouf T. Regulation of tumor growth and

metastasis: the role of tumor microenvironment. Cancer Growth Metastasis. 2014; 7: 9-18.
7. Henderson BE, Bernstein L, Ross RK. Chapter 13: Hormones and the Etiology of Cancer. In: Bast RC, Kufe DW, Pollock RE, et al. Holland-Frei Cancer Medicine (5th ed.). Hamilton, Ontario: B.C. Decker. 2000.
8. Rowlands M-A, Gunnell D, Harris R, Vatten LJ, Holly JMP, Martin RM. Circulating insulin-like growth factor peptides and prostate cancer risk: a systematic review and metaanalysis. Int J Cancer. 2009; 124(10): 2416-2429.
9. Phua DH, Zosel A, Heard K. Dietary supplements and herbal medicine toxicities - when to anticipate them and how to manage them. Int J Emerg Med. 2009; 2(2): 69-76.
10. Sumner J. The natural history of medicinal plants. Timber Press. 2000.
11. Abdullaev FI. Plant derived agents against cancer. In: Gupta SK, editor. Pharmacology and therapeutics in the new millennium. Narosa publishing house: New Delhi, India 2001: 345-354.
12. Karmakar S, Choudhury SR, Banik NL, Swapan RK. Molecular mechanisms of anti-cancer action of garlic compounds in neuroblastoma. Anticancer Agents Med Chem. 2011; 11(4): 398-407.
13. Thomson M, Ali M. Garlic (Allium sativum): a review of its potential use as an anti-cancer agent. Curr Cancer Drug Targets. 2003; 3(1): 67-81.
14. Muriel J. M., Herbs or natural products that decrease cancer growth. Oncol Nursing Forum. 2004; 31(4): E75.
15. Prakash Om, Amit Kumar, Pawan Kumar, Ajeet. Anticancer potential of plants and natural products: a review. Am J Pharmacol Sci. 2013; 1: 104-115.
16. Wang J, Ito H, Shimura K. Enhancing effect of antitumor polysaccharide from Astralagus or Radix hedysarum onC3 cleavage production of macrophages in mice. Department of Pharmacology, Mie University School of Medicine, Japan. Mem Inst Oswaldo Cruz. 1991; 86(2): 159-164.
17. Sakarkar DM, Deshmukh VN. Ethnopharmacological review of traditional medicinal plants for anticancer activity. Int J Pharm Tech Res. 2011; 3: 298-308.
18. Pandey G, Madhuri S. Some medicinal plants as natural anticancer agents. Pharmacognosy Rev. 2009; 3: 259-263.
19. Kumar S, Suresh PK, Vijaybabu MR, Arunkumar A, Arunakaran J. Anticancer effects of ethanolic neem leaf extract on prostate cancer cell line (PC-3). J Ethnopharmacol. 2006; 105(12): 246-250.
20. Saied S, Batool S, Naz S. Phytochemical studies of Berberis aristata. J Basic Appl Sci. 2007; 3(1): 1-4.
21. Das S, Basu SP. Cytotoxic activity of methanolic extract of Berberis aristata DC on colon cancer. Global J Pharmacol. 2009; 3(3): 137-140.
22. Sharma K, Bairwa R, Chauhan N, Shrivastava B, Saini NK. Berberis aristata: a review. Int J Res Ayurveda Pharm. 2011; 2(2): 383-388.
23. Dreosti IE. Bioactive ingredients: antioxidants and polyphenols in tea. Nutr Rev. 1996; 54: S51-58.
24. Guzman M. Cannabinoids potential anticancer agents. Nature Rev Cancer. 2003; 3: 745- 755.
25. Ben Amar M. Cannabinoids in medicine: a review of their therapeutic potential. J Ethnopharmacol. 2006; 105: 1-25.
26. Pushkarev VM, Kovzun OI, Tronko MD. Antineoplastic and apoptotic effects of cannabinoids. N-acylethanolamines. J Cancer Res Exp Oncol. 2008; 30(1): 6-21.
27. Velasco G, Sánchez C, Guzmán M. Towards the use of cannabinoids as antitumour agents. Nature Rev Cancer. 2012; 12(6): 436-444.
28. Don G. Catharanthus roseus. In: Ross IA, ed. Medicinal plants of the world: chemical constituents, traditional and modern uses. Vol 1. Totowa, New Jersey, USA: Humana Press; 2003: 175-196.
29. Van Der Heijden R, Jacobs DI, Snoeijer W, Hallard D, Verpoorte R. The Catharanthus alkaloids: pharmacognosy and biotechnology. Curr Med Chem. 2004; 11(5): 607-628.
30. Pratheeshkumar P, Sreekala C, Zhang Z, et al. Cancer prevention with promising natural products: mechanisms of action and molecular targets. Anti-Cancer Agents Med Chem. 2012; 12(10): 1159-1184.
31. Liener IE. Implications of antinutritional components in soybean foods. Crit Rev Food Sci Nutr. 1994; 34: 31-67.
32. Thompson LU, Robb P, Serraino M, Cheung F. Mammalian lignan production from various foods. Nutr Cancer. 1991; 16: 43-52.
33. Serraino M, Thompson LU. The effect of flaxseed supplementation on the initiation and promotional stages of mammary tumorigenesis. Nutr Cancer. 1992; 17: 153-948.
34. Szewczyk M, Abarzua S, Schlichting A, Nebe B, Piechulla B, Briese V, Richter DU. Effects of extracts from Linum usitatissimum on cell vitality, proliferation and cytotoxicity in human breast cancer cell lines. J Med Plants Res. 2014; 8(5): 237-245.
35. Imbert TF. Discovery of podophyllotoxins.

Biochimie. 1998; 80: 207-222.
36. Sharma RK, Sharma S, Sharma SS. Seed germination behaviour of some medicinal plants of Lahaul and Spiti cold desert (Himachal Pradesh): implications for conservation and cultivation. Curr Sci. 2006; 90(8): 1113-1118.
37. Narisa K, Jenny MW, Heather MAC. Cytotoxic effect of four Thai edible plants on mammalian cell proliferation. Thai Pharmac Health Sci J. 2006; 1(3): 189.
38. Roy MK, Nakahara K, Na TV, Trakoontivakorn G, Takenaka M, Isobe S, et al. Baicalein, a flavonoid extracted from a methanolic extract of Oroxylum indicum inhibits proliferation of a cancer cell line in vitro via induction of apoptosis. J Archiv Pharmazie. 2007; 62(2): 149.
39. Kumar R.A., Rajkumar V., Guha G., Mathe L. Therapeutic potentials of Oroxylum indicum bark extracts. Chinese J Nat Med. 2010; 8(2): 121.
40. Adams LS, Zhang Y, Seeram, NP, Heber D, Chen S. Pomegranate ellagitannin-derived compounds exhibit antiproliferative and antiaromatase activity in breast cancer cells in vitro. Cancer Prev Res. 2010; 3: 108-113.
41. Devi PM, Siril EA. Traditional and modern use of Indian madder (Rubia cordifolia L.): an overview. Int J Pharmac Sci Rev Res. 2014; 25(1): 154-164.
42. Gupta PP, Srimal RC, Verma N, Tandon JS. Biological activity of Rubia cordifolia and isolation of an active principle. Pharmac Biol. 1999; 37(1): 46.
43. Itokawa H, Wang X, Lee KH. Homoharringtonine and related compounds, in anticancer agents from natural products. Cragg GM, Kingston DGI, Newman DJ, eds. Brunner-Routledge Psychology Press, Taylor & Francis Group, Boca Raton, Chapter 4, 2005: 47.
44. Agarwal R, Agarwal C, Ichikawa H, Singh RP, Agarwal BB. Anticancer potential of silymarin: from bench to bed side. Anticancer Res. 2006; 26(6B): 4457.
45. Kim S, Choi JH, Lim HI, Lee SK, Kim WW, Kim JS, et al. Silibinin prevents TPA-induced MMP-9 expression and VEGF secretion by inactivation of the Raf/MEK/ERK pathway in MCF-7 human breast cancer cells, Phytomed. 2009; 16(6-7): 573.
46. Li YL, Gan GP, Zhang HZ, Wu HZ, Li CL, Huang YP, Liu YW, Liu JW. A flavonoid glycoside isolated from Smilax china L. rhizome in vitro anticancer effects on human cancer cell lines. J Ethnopharmacol. 2007; 113(1): 115.
47. Hyun NK, Seung HH, Bong KS, Cheorl HK, Young HY, Hyung MK. Taraxacum officinale induces cytotoxicity through TNF-α and IL-1α secretion in Hep G2 cells. Life Sci. 2004; 74(9): 1149.
48. Sigstedt SC. Evaluation of aqueous extracts of Taraxacum officinale on growth and invasion of breast and prostate cancer cells. Int J Oncol. 2008; 32(5): 1085.
49. Lecia JG, Jetaime R, Ernest B I. Vernonia amygdalina: anticancer activity, authentication, and adultration detection. Int J Environ Res Public Health. 2008; 5(5): 342.
50. Wong FC, Woo CC, Hsu A, Tan BKH. The anti-cancer activities of vernonia amygdalina extract in human breast cancer cell lines are mediated through caspase-dependent and p53-independent pathways. PLoS One. 2013; 24: 8.
51. Kuete V, Wabo HK, Eyong KO, Feussi, MT, WienchB, Krusche B, et al. Anticancer activities of six selected natural compounds of some cameroonian medicinal plants. PLoS ONE. 2011; 6: 8.
52. Winters M. Ancient medicine, modern use: Withania somnifera and its potential role in integrative oncology. Altern Med Rev. 2006; 11(4): 269-277.
53. Alam S, Katiyar D, Goel R, Vats A, Mittal A. Role of herbals in cancer management. J Phytopharmacol. 2013; 2(6): 46-51.
54. Govind P. Some important anticancer herbs: a review, International Research Journal of Pharmacy, 2011, 2(7), 45-52
55. Chang M. Anticancer medicinal herbs. Human Science and Technology, Publishing House, Changsha, 1992.
56. Kumar RA, Sridevi K, Kumar NV, Nanduri S, Rajagopal S. Anticancer and immunostimulatory compounds from Andrographis paniculata. J Ethnopharmacol. 2004; 92(2-3): 291-295.
57. Sultana S, Ahmed S. Inhibitory effect of celery seeds extract on chemically induced hepatocarcinogenesis: modulation of cell proliferation, metabolism and altered hepatic foci development. Cancer Lett. 2005; 221: 11-20.
58. The effect of aloe-emodin on the proliferation of a new merkel carcinoma cell line. Am J Dermatopathol. 2002; 24(1): 17-22.
59. Pecere T, Gazzola MV, Micignat C. Aloe-emodin is a new type of anticancer agent with selective activity against neuro-ectodermal tumors. Cancer Res. 2000; 60: 2800-2804.
60. The wealth of India ‘a dictionary of Indian raw materials and industrial products. Vol. i (ab), 1985, p. 79.
61. The wealth of India ‘a dictionary of Indian raw materials and industrial products. Vol. i (ab), 1985, p. 109.

62. The wealth of India 'a dictionary of Indian raw materials and industrial products. Vol. i (ab), 1985, p. 185.
63. Cragg GM, Newman DJ. Plants as a source of anti-cancer agents. J Ethnopharmacol. 2005; 100(1-2): 72-79.
64. Kantrajian HM, Talpaz M, Smith TL, Cortes J, Giles FJ. Homoharringtonine and low-dose cytarabine in the management of late chronic-phase chronic myelogenous leukemia. J Clin Oncol. 2000; 18: 3513-3521.
65. Senchina DS, Shah, Nisarg B, Busch MG. Effects of berberine, chelerythrine, and sanguinarine on proliferation in four human immortalized cell lines. J Iowa Acad Sci. 2012; 119: 1-4, 22-27.
66. Bruneton J. Pharmacognosy, phytochemisty medicinal plants. Lavoisier publisher, France, 1993, pp. 771-777.
67. Chavan SS, Damale MG, Shamkuwar PB, Pawar D. Traditional medicinal plants for anticancer activity. Int J Curr Pharmac Res. 2013; 5: 4.
68. Cavallito CJ, Haskell TH. Alpha-methylene butyrolactone from Erythronium americanum. J Am Chem Soc. 1946; 68(11): 2332-2334.
69. Tyler V. Herbs of choice. The therapeutic use of phytomedicinals. New York: Haworth press, 1994, pp. 32-33.
70. Ambasta SP, ed. The useful plants of India. 4th edn, National Institution Sci. Communication, Delhi, 2000, p. 239.
71. Ambasta SP, ed. The useful plants of India. 4th edn, National Institution Sci. Communication, Delhi, 2000, p. 243.
72. Brown PN, Roman MC. Determination of hydrastine and berberine in goldenseal raw materials, extracts, and dietary supplements by high-performance liquid chromatography with UV: collaborative study. J Aoac Int. 2008; 91(4): 694-701.
73. Prajapati ND, Purohit S, Sharma AK, Kumar T. Handbook of medicinal plants. Agrobios (India), 1st edn, 2003.
74. Ladanyi A, Timar J, Lapis K. Effect of lentinan on macrophage cytotoxicity against metastatic tumor cells. Cancer Immunol Immunother. 1993; 36: 123-126.
75. Mingji P. Cancer treatment with fu zheng pei ben principal. Fujjan Science and Technology publishing house, Fuzhou, 1992.
76. Desai AG, Qazi GN, Ganju RK, El-Tamer M, Singh J, Saxena AK, Bhat HK. Medicinal plants and cancer chemoprevention. Curr Drug Metab. 2008; 9(7): 581-591.
77. Henry SH, Bowers JC. Aflatoxin, hepatitis and worldwide liver cancer risks. Adv Exp Med Biol. 2002; 504: 229-233.
78. Nagar N, Jat RK, Saharan R, Verma S, Sharma D, Bansal K. Podophyllotoxin and their glycosidic derivatives. Pharmacophore. 2011; 2(2): 124-134.
79. Hazra B, Sarkar R, Bhattacharyya S, Ghosh PK, Chel G, Dinda B. Synthesis of plumbagin derivatives and their inhibitory activities against Ehrlich ascites carcinoma in vivo and Leishmania donovani promastigotes in vitro. Phytother Res. 2002; 16: 133-137.
80. Ardeshiry LA, Rezaie-Tavirani M, Mortazavi SA, Barzegar M, Moghadamnia SH, Rezaee MB. Study of anti-cancer property of Scrophularia striata extract on the human astrocytoma cell line (1321). Iran J Pharmac Res. 2010; 9(4): 403-410.