Review Article

REVIEW ON: HERBS AS ANTICANCER AGENTS

*,1Prema R, 2Sathish Sekar D, 3Chandra Sekhar K B

*,1Santhiram College of Pharmacy, Nandyal, Andhra Pradesh, India – 518 501.
2Padmavathi College of Pharmacy & Research Institute, Dharmapuri, TamilNadu, India - 635 205.
3Dept. of Chemistry, Jawaharlal Nehru Technological University Anantapur, Anantapur, India – 515 002.

Abstract

This article has been made to review some medicinal plants used for the anticancer activity. The plant sources of India Are likely to provide effective anticancer agents. Herbs have a vital role in the prevention and treatment of cancer. Examples are provided in this review of promising bioactive compounds obtained from various plants with medicinal and other uses. The phytochemical exploration of these herbs has contributed to some extent in this race for the discovery of new anticancer drugs. In recent years owing to the fear of side effects people prefer more and more use of natural plant products for cancer. This review also helps to summarize the diverse methodologies and ways to evaluate the potential natural compounds having anticancer activity. Although drug discovery from medicinal plants continues to provide an important source of new drug leads, numerous challenges are encountered including the procurement of plant materials and their selection.

Keywords: Medicinal plants, Anticancer agents, Bioactive compounds.

Introduction

The principles underlying herbal medicines are relatively simple, although they are quite distinct from conventional medicine and herbal medicine.[1] Often overlooked distinction exists between herbal medicine (the practice) and the plant based remedies used in the practice of herbal medicine.[2]India is a rich source of medicinal plants and a number of plant extracts are used against diseases in various systems of medicine such as ayurveda, unani and siddha. Only a few of them have been scientifically explored. Plant derived natural products such as flavanoids, terpenes, and alkaloids.[3-5] and soon has received considerable attention in recent years, due to their diverse pharmacological properties including cytotoxic and cancer chemo preventive effects.[6] Plants have a long history of use in the treatment of cancer. Hartwell, in his review of plants used against cancer. Extensive research at Sandoz laboratories in Switzerland in the 1960s and 1970s led to the development of etoposide and teniposide as clinically effective agents which are used in the treatment of lymphomas, bronchial and testicular cancer. Of 2069 anticancer trials recorded by the NCI as being in progress as of July 2004, over 150 are drug combinations including etoposide against a range of cancers.[7]

*** *Author for Correspondence:***

Prema R,
Santhiram College of Pharmacy,
Nandyal, Andhra Pradesh,
India – 518 501.
Email: premajeny@gmail.com

Cancer is the abnormal growth of cells in our body that can lead to death. Cancer cells usually invade and destroy normal cells. More and more cancer research works have been done and yet we do not understand exactly what cancer is? [8] Cancer is the second leading cause of death in America. The major cause of cancer is smoking, dietary imbalances, hormones and chronic infections leading to chronic inflammation.[9] Every year millions of people are diagnosed with cancer leading to death, according to the American cancer society.[10]

Cancer and Its Types

Breast cancer is the most common form cancer in worldwide.[8,11] Amongst south African women, breast cancer is likely to develop in one out of every 31 women in the country .breast cancer in India is the second most common cancer in women after the cancer of uterine cervix. The BRCA2 gene is implicated in approximately30-45%familial breast cancer. The absence of any significant BRCA2 mutation in the level expression of the gene indicates that the BRCA2 gene may not be playing an important role in the sporadic breast as well as familial breast carcinogenesis in Indian women.[12] Human papilloma virus is sexually transmitted and casually related to cervical cancer. Almost of all cervical cancer and high grade cancer precursor caused by specific high risk types of human papilloma virus. [13] Cervical cancer caused by human papilloma virus is the second most common cancer in the world accounting for 280,000deaths and 510,000 new cases each year. It is the commonest cancer in Indian women.[14] And with 126,000 new cases and 760,000 deaths annually. Several high risk human papilloma virus types are known to cause the disease but Indian data is mostly limited to study of a few genotypes.[15] Multidrug resistance in cancer is sometimes associated with overproduction of growth factors like fibroblast growth factor that provide survival signals to neoplastic cells to

overcome the detrimental effects of chemotherapeutic drugs.[16] There is a scant data on the incidence, pattern and genotype of familial cancers or multiple primary neoplasms from India.[17] One hundred and forty six cases of childhood Hodgkin's lymphoma which is caused by Epstein Barr virus was detected immune histo chemically in 91% of childhood in northern india, more often in younger age and lower socio economic status.[18] Non-Hodgkins lymphoma is the 7th most common type of cancer seen in india. Diffuse large Bcell lymphomas represents a clinically and histological diverse group of neoplasms.[19] Cancer of the oral cavity is a disease of acquired occupational, nutritional and environmental insults chronic exposure of the oral cavity to a variety of mutagens/carcinogens present in the betel quid cigarette smoking and alcohol consumption results in the development of clinically a distinct premalignant lesion which got a 5-10%chances of progress towards malignancy in future. Oncogenic alteration has been marked as one of the main causative factors for carcinogenesis.[20]

Oral squamous cell carcinoma is the common malignancy in males and the third most common in females in india. And it is a major cause of cancer morbidity and mortality worldwide. Alterations in the expression of retinoic acid receptors occur early in oral carcinogenesis. Deregulated expression of retinoic acid receptors and cell cycle regulators can serve as a potential predictive marker in the multistep process of development and progression of oral cancer.[21] Also COX-2 may serve as a potential diagnostic marker and target for developing molecular therapeutics for intervention in oral tumourogenesis.[22] Esophageal squamous cell carcinoma has been reported to show geographical variation in its incidence even with area of ethnic homogencity.[23] Apoptosis is highly regulated process defect in apoptic pathway leads to human disease from neurodegenerative disorder to malignancy. A significant pathway of cell death in squamous cell carcinoma of oro-pharynx is by apoptosis. [24] Malignant disorders are no longer considered as a killer disease owing to continuous refinement of cytogenetic and molecular technologies. Chronic myeloid leukemia is the most known established example with the presence of Philadelphia chromosome in 95% cases.[25]

The chemo preventive and chemotherapeutic activities of retinoids may be attributed to their ability to modulate growth, differentiation and apoptosis of epithelial cells, suppress (or) reverse epithelial carcinogenesis. Retinoic acid receptors alterations in their expression may lead to tumourogenesis. [26] Nature as a plant source of useful drugs has been recognized since ancient times. Boerhaavia diffusa is a plant of the family Nictaginaceae, this plant has hepatoprotective, lymphoproliferative and immunomodulatory effects and this plant is further exploredforits cytotoxic components.[27] Transitional cell carcinoma is the commonest cancer of the bladder and constitutes about 80-90%mof urothelial tumours with recurrence rate of 30-90%. Adjuvant chemotherapy and immunotherapy has been used recently as a prophylactic measure to reduce the frequency of recurrences. [28]

Anticancer Activity

Some medicinal plants which are used in the treatment of various types of cancer is Listed in the Table 01. And few medicinal plants have been presented above possess good immunomodulatory and antioxidant properties leading to anticancer activities.[39]

Conclusion

Medicinal plants have contributed a rich health to human beings. Plant extracts and their bioactive compounds present in them which are responsible for anticancer activity have to be screened for their valuable information. This review had given some of the plants possessing anticancer activity for various types of cancer. This review can help others to explore herbs to further extent and its use in various other disease and toxicity studies along with clinical trials.

References

1. An introductory overview seminars in oncology nursing, vol 21, No 3(August) 2005; 102-105.
2. Weiss R. What is herbal medicine? Meuss A, trans.Herbal medicine (6thed). Beaconsfield, UK; Beaconsfield Publishers, 1988.
3. Osawa T, Kawakishi S, Namiki M.In: Kuroda Y, Shankel DM, Waters MD, Antimutagenesisand anticarcinogenesis mechanism II. Newyork: plenum; 1990.p.139-153.
4. Di Carlo G, Mascolo N, Izzo AA, CapassaoF. Flavanoids: old and new aspects of a class of natural therapeutic drugs life sci.1999:65: 337-353.
5. Keith MW, Sally AL, Michael WS, Thomas JG, Garry MM. Taxus Spp. Needles contain amounts of tax oil comparable to the stem bark of taxus brevifolia: analysis and isolation Nat prod.1990; 53:1249-1255.
6. Roja G, Heble MR. The quinoline alkaloid Camptothecin and 9-methoxy camptothecin from tissue cultures and mature trees of Nathapodytes foetida. Phytochemistry.1994; 36:65-66.
7. C.M.Cragg and D.J.Newman. Plants as a source of anticancer agents, National cancer institute, Maryland, USA.
8. Estrogen & Cancer Website,2006; www.womenshealth. com, www.amazon.com.
9. Ames, B.N., Gold, L.S. and Willett, W.C., The causes and prevention of cancer.proc. Natt. Acad.Sci. USA, 1995, 92, 5258-5265.
10. American cancer society, A biotechnology company dedicated to cancer treatment, viewed on 25 January 2006, www. Cancervax.com/info/index.htm.
11. Koduru, S., Grierson, D.s. and Afolayan, A.J., Ethno botanical information of medicinal plants used for treatment of cancer in the Eastern Cape Province, South Africa.Curr.sci., 2007, 92,906-908.
12. Neema Goel, Neeraj jain, Suresh Hedau. Mutation and Expression Analysis of BRCA2 Gene in Breast cancer patients from india. Institute of cytology and preventive oncology (ICMR).1-7, Noida.

Name of the Medicinal Plant	Family	Origin	Chemical Constituents	Type of Cancer
Akebia quinata[29-34]	Lardizabalaceae	Japan, China and Korea.	Limonene, eugenol,octanol and p-cymene, monoterpenoids,saturated short chain aldyhyde, hexanoic acid, palmitic acid, and hexanol	Sarcoma-180 Sarcoma- 37
Taraxacum mongolicum[29-35]	Asteraceae	China, New Zealand, Turkey.	Sesquiterpene lactones, phenyl propanoids, triterpenoid saponins, polysaccharides.	Ascites cancer Sarcoma-180 Lung cancer cells
Vitex rotundifolia[36]	Lamiaceae	India east to Hawaii and from Korea south to Australia	Essential oils: l-d pinene, alpha-pinene, camphene, terpineol acetylester, diterpene alcohol. Alkaloid: vitricine. Monoterpene glucoside:. Flavonols: vitexicarpin (castisin), camphene, casticin, vitamin A. Iridoid glycosides: agnoside, aucbin. Flavonoids: casticin, isovitexin, orientin.	Lung tumour
Sophora flavescens	Fabaceae	China and korea Guangxi, Guizhou, and Yunnan Provinces of China	Alkaloids, Oxymatrine, sophoridine, oxysophocarpine, and sophocarpine	Sarcoma-180
Sophora subprostrata [29-35]	Leguminaceae		matrine and oxymatrine	Leukemia and cervical cancer-14 cells
Scutellaria barbata[29-35]	Lamiaceae	Chinaand Europe	alkaloids, flavones, steroids, and polysaccharides	Sarcoma-180 Ehrlichs ascites carcinoma
Smilax chinensis	liliaceae	Eastern Asia. North America north of Mexico	Sucrose, glucose, maltose, and fructose, stearic and palmitic acids. Glutamic acid and potassium, amino acids and minerals Diosgenin, steroidal sapogenin, parillin (also sarsaparillin or smilacin), sarsapic acid, sarsapogenin and sarsaponin.	Sarcoma-180 Ascites sarcoma
Smilax glabra[29-35]	Smilacaceae			
Solanum lyrati[29-34]	Solanaceae	Hong Kong	Aristolochic acid I (AA-I)	Sarcoma-180, Sarcoma-37 Ehrlichs ascites carcinoma Stomach cancer
Agrimonia pilosa[29-34]	Rosaceae.	china	Triterpenoid; 19α-hydroxyursolic acid.	Sarcoma-180 Intestinal cancer
Ailanthus altissima[29-35]	Simaroubaceae	China and Taiwan	Aliphatic acids and their esters, fatty hydrocarbons and steroids e.g.E-oleic acid, (Z,Z)-octadeca-9,12-dienoic acid	Sarcoma-180 Sarcoma-37 Leukemia-16
Pyrus malus[37]	Rosaceae	Europe and western Asia	$C_{21–29}$ secondary alcohols; *n*-nonacosan-10-ol; $C_{21–29}$ ketones; *n*-nonacosan-10-one	Lung, colon, breast and intestinal cancer.
Pteris multifida[29-34]	Pteridaceae	North America	Sesquiterpenoid, 3β-caffeoxyl-1β,8α-dihydroxyeudesm-4(15)-ene (1), together with two known compounds including ludongnin V (2) and isoneorautenol (3),	Sarcoma-180 Sarcoma-37 Yoshidas sarcoma
Fritillaria thunbergii[35]	Liliaceae	China and india	Steroidal alkaloids, as well as diterpenoids	Throat, chest, neck and breast.
Phaleria macrocarpa	Thymelaeaceae	Papua Nugini(east of Papua)	Kaempferol, myricetin, naringin, and rutin, naringin and quercetin	Esophageal cancer
Nidas vespae[29-34]	Vespidae	China and east asia	Polysaccharide	Gastric and liver cancer
Aegle marmelos[38]	*Rutaceae*	India	Mono-terpene hydrocarbons, sesquiterpene, Limonene, Z)-β-ocimene, and one phenolic compound.	Cancer

Table 01
List of some Plants with Anti-cancer Activity

13. Jayanti Maria-pramanik, Shilpa C. Kerkar., Human papilloma virus infection in women with different clinical manifestations. G.S.Medical College and KEM Hospital, Parel, Mumbai.
14. *Lalit Dar, Neerja Bhatla, Shobha Broor,* Detection and Genotyping of Human Papilloma Virus in Cervical Swab Samples by Reverse Line Blot Assay, Johns Hopkins University,Baltimore,USA.
15. *Neerja Bhatla, Lalit Dar, A. Raj Kumar Patro,*Detection and Genotyping of Human Papillomavirus in Invasive Cervical Cancers by the Reverse Line Blot Assay, All India Institute of Medical Sciences, New Delhi.
16. *Ananda Mookerjeea, P. Duttaa, S. Majumdera, R.N. Baralb, S.K.Choudhuri,* Regulation of Multidrug Resistant Cancer with A Novel Metal ComplexDepartment of Environmental Carcinogenesis and Toxicology, Chittaranjan National Cancer Institute, Calcutta.
17. *Sunita Shankar, Rajiv Sarin, Neena Bhatnagar,* Inherited Predisposition and Environmental Exposure in the Causation of Familial or Multiple Primary Cancer, Cancer Genetics Unit, Mumbai.
18. *Veronique Dinand, Laxman S. Arya, Ramesh Dawar* Hodgkin's Lymphoma in North Indian Children: Prevalence and Significance of Epstein-Barr Virus, Latent Membrane Protein-1 Detection in Hodgkin's and Reed Sternberg Cells, All India Institute of Medical Sciences, New Delhi.
19. *Sasikala P.S., Nirmala Nancy K., Mahji U., Shirley S and Rajkumar T.* a Marker for Germinal Center Transit B Cell Non-Hodgkin's Lymphomas, Cancer Institute (WIA), India.
20. Prishla Varghese, Prabha Balaram, BC.Das. Ras p21and itsExpressional variations in the development of oral squamous cell carcinoma, Regional cancer centrer, Trivandrum, Kerala, India.
21. *Chhavi Sharma, Jatinder Kaur, Nitin Chakravarti,* . Retinoic Acid Receptors and Their Relationship with Cell Cycle Regulators in Oral Carcinogenesis, All India Institute of Medical Sciences, New Delhi, India.
22. *Meenakshi Sawhney1, Nidhi Rohatgil, Siddhartha Datta Gupta,* Deregulated Expression of Cylcooxygenase-2 in Oral Carcinogenesis, Institute of Rotary Cancer Hospital; All India Institute of Medical Sciences, New Delhi, India.
23. *Mohammad M. Mir, Nazir A. Dar, Sailesh Gochhait,* p53 Mutation Profile in Squamous Cell Carcinomas of the Esophagus in Kashmir (India) - A High Incidence Area, Sher-I- Kashmir Institute of Medical Sciences, Soura, Srinagar.
24. *Rakhi Srivastava, Daman Saluja and Madhu Chopra,* Isolation and Screening of Anticancer Metabolites from *Boerhaavia diffusa,* Dr. Br. B. R. Ambedkar Center for Biomedical research, University of Delhi.
25. *Bani B. Ganguly and M.B. Agarwal,* Conventional Cytogenetic and FISH Studies in Diagnosis of Hematological Malignancies, MGM Centre for Genetic Research and Diagnosis, MGM's New Bombay Hospital, Navi Mumbai, India.
26. *Anupam Kumar, Jatinder Kaur, Tushar Kant Chattopadhyay,* Differential Expression of Retinoic Acid Receptors in Normal and Malignant Esophageal Tissues, All India Institute of Medical Sciences, Ansari Nagar,New Delhi, India.
27. *Rakhi Srivastava, Daman Saluja and Madhu Chopra,* Isolation and Screening of Anticancer Metabolites from *Boerhaavia diffusa,* University of Delhi,India.
28. *Abhilasha Agarwal, Saurabh Verma, Usha Burra,* Flow Cytometric Analysis of TH1 and TH2 Cytokines in PBMCs as a Parameter of Immunological Dysfunctionin Patients of Superficial Transitional Cell Carcinoma of Bladder, Institute of Pathology, Safdarjung Hospital Campus, New Delhi.
29. Mingji, Pan, *Cancer Treatment with Fu Zheng Pei Ben Principal*, Fujjan Science and Technology Publishing House, Fuzhou, 1992.
30. Minyi, Chang, *Anticancer Medicinal Herbs*, Human Science and Technology Publishing House, Changsha, 1992.
31. Dewu, Han and Ruiling, Xu, Progress in the research on blood activation and hemostasis removal. *Abstr. Chin. Med.*, 1988, 2, 466–483.
32. Kun, Jia, *Prevention and Treatment of Carcinoma in TraditionalChinese Medicine*, The Commercial Press, Hong Kong, 1985.
33. Hong-Yen, Hsu, *Treating Cancer with Chinese Herbs*, Oriental Healing Arts Institute, Long Beach, CA, 1990.
34. Boik, J., *Cancer and Natural Medicine*, Oregon Medical Press,Princeton, MN, 1995.
35. Prajapati, N. D., Purohit, S. S., Sharma, A. K. and Kumar, T., *A Hand Book of Medicinal Plants*, Agrobios (India), 1st ed. 2003.
36. Hecht, S. S., Kenney, P. M., Wang, M., Trushin, N., Agrawal, S.,Rao, A. V. and Upadhyaya, P., Evaluation of butylated hydroxyanisole,myoinositol, curcumin, esculetin, resveratrol, and lycopeneas inhibitors of benzo(a)pyrene plus 4- (mthylnitrosamino)-1 -(3-pyridyl)-1-butanone induced lung tumorigenesis in A/J mice. *Cancer Lett.*, 1990, 137, 123–130.
37. Eberhsrdt, M. V., Lee, C. Y. and Lui, R. H., Antioxidant activity of fresh apples. *Nature*, 2000, 405, 903–904.
38. Praboth Chanda Sharma, Vivek Bhatia, Nitin Bangal, Areview on Bael tree, Natural product radiance, 2007, 6, 171-178.
39. S.Madhuri and Govind Pandey, Some anticancer medicinal plants of foreign Origin, current science, vol. 96, no. 6, 25, 2009, 145-148.