

**A COMPREHENSIVE REVIEW ON NATURAL SOURCES AGAINST  
CANCER****Kishore Mendam\*, V. Mangesh, S.Vamshi, S. Jithender Kumar Naik**

Toxicology Lab, Department of Zoology, Osmania University, Telangana, India.

Article Received on  
16 Oct 2015,Revised on 07 Nov 2015,  
Accepted on 29 Nov 2015**\*Correspondence for  
Author****Kishore Mendam**Toxicology Lab,  
Department of Zoology,  
Osmania University,  
Telangana, India.**ABSTRACT**

This article review on some medicinal plants used for the prevention and treatment of cancer among population. Many of the environmental pollutants, drugs, chemicals, residues of pesticides and toxins present in food are common carcinogenic agents of cancer in human population. Herbs are play a vital role in prevention and treatment of several diseases. Medicinal plants and their products cure various diseases including cancer without causing toxicity. Hence there is a need to find natural anti-carcinogenic agents having the anti-cancer potential to prevent cancer. Plants have a long history of use in the treatment of cancer. A number of scientific investigations have highlighted the importance and contribution of many plant families are

used as medicinal plants. Medicinal plants play a vital role for the development of new drugs. The herbal medicines (or) natural drugs are plant derived material or preparations, which contain either raw or processed ingredients from one or more plants. These compounds have been used as natural drugs, either in their original or Semi-Synthetic form. This review summarizes some important pharmacological and preliminary studies on anti cancer potential medicinal plants, source , products and their physiological activities or pharmacological activities, which can be investigated further to achieve lead molecules in the search of modern herbal drugs to treat several diseases. The continued search for natural medicines is necessary for finding additional sources of active components that are suitable for clinical application.

**KEYWORDS:** medicinal plants, Cancer, natural drugs.

## INTRODUCTION

Complementary and Alternative Medicine (CAM) is a group of diverse healthy care and medicinal practices and products that are not generally considered to be part of conventional medicine and that is not integrated in to the dominant health care system. Sometime other names used it describe this health care practices include “non conventional medicine”, “natural medicine” and “holistic medicine “. [1] There are several modalities of CAM such as chiropractics and herbal medicine etc. [2] Herbal medication is the most popular form of traditional medicine (TM) .The provision of effective and safe traditional medicine and /or complementary and alternative medicine therapies could become a critical tool to increase access to health care. Botanical Scientists are identified around 3, 50,000 plant species. In these only 20-30% are investigated for their therapeutic effect ,and 5-10% of them are used in different diseases as traditional medicines. [1] According to the appointed world committee of medicinal plants ,378 plants are investigated as authentic medicinal plants,245 medicinal plants have official monographs available in well known pharmacopeias and WHO guidelines. [3]

Several plants used in native folk medicine around the world have been a good source of therapeutic agents. More than half of the commercially available drugs are plant derived or mimics of plant derived substances. [4&5] Plants have chemical define mechanisms that synthesize a variety of compounds and secondary metabolites that can be used to perform important biological functions and to defend against attack from predators. Many of these plant derived substance or phytochemicals have useful effects, but some can have adverse of lethal effects on humans. [6] (Humans have used plants as diet and natural medicines since ancient times. Natural medicine safer than synthetic drugs. [7] Several medicinal plants have may pharmacological activities like anti inflammatory activity anti diabetic activity, antifilarial activity, analgesic activity, anti microbial activity and many more. [8]

Natural medicines have been used as anti cancer agents. [7] Research on medicinal plants and their derivatives has show that they are very important source of effective anti tumor agents. More than half of the drugs use in cancer treatment is derived from medicinal plants as natural soruces. [9] Complementary and alternative medicine (CAM) has played a important role in cancer treatment. In 1999, the National Institutes of Health (NIH) created the National center for complementary and Alternative Medicine (NCCAM) in recognition of this growing field. [10]

An alternative medicine is used instead of conventional medicine and alternative therapy is using a special diet to treat in place of undergoing chemo therapy, surgery or radiation that has been recommended by a conventional doctor. Cancer is the abnormal growth of cells in our body that can cause to death cancer cells are usually invade and destroy normal cell.<sup>[11]</sup>

The group of substances or chemicals or factors cause cancer in human and animals are collectively referred to as carcinogens. Carcinogens are involved in carcinogenesis, mutagenesis and genotoxicity. Carcinogens are the physical, chemical and biological agents that can cause cancer. The physical agents like ultraviolet (UV) and X-rays cause the deletion of nucleotides. The physical agents produce lesions in DNA including DNA base damage, dimerisation of DNA bases and breakage of DNA strand. Chemical agents like Asbestos, Benzene and Vinyl Chloride etc., and Biological agents as Epstein-Bar – virus (EBV), Human papilloma virus (HPV) etc., cause cancer. Many extrinsic and intrinsic factors induce the process of carcinogenesis.<sup>[12]</sup> Carcinogenesis is a multistage process by which a normal cell is transformed into a cancerous cell. Transformation involves initiation, typically from DNA damaging agents; promotion, during which cell proliferation is increased and progression, involving additional genetic alterations.<sup>[13]</sup> Carcinogenic includes three steps initiation, promotion and progression.<sup>[12]</sup>

**Initiation:** It is an irreversible process and begins when the cells in normal tissues are exposed to a carcinogen. It leads to genomic DNA damage that remains un-repaired and cause to mutation.

**Promotion:** It is expansion of the damaged cells to form an actively proliferating multi cellular pre-malignant tumor cells.

**Progression:** It is an irreversible process and tumor cells grow and invade into the surrounding normal tissue or organs.

There are four cancer causing genes are Oncogenes, tumor suppressor genes, Suicide genes and DNA-repair genes also cause cancer.<sup>[14]</sup> Anti carcinogenic agents can prevent the transformation of a Pro-carcinogenic substance into carcinogenic substance or (and) inactivate the carcinogen or (and) prevent the reaction between genomic DNA and mutagen. In another way anti carcinogens may induce, repress or inactivate indirectly or directly the enzymes of the DNA repair.<sup>[15]</sup>

**Causes of cancer**<sup>[14]</sup>

- 1) Environmental and occupational exposure as ionizing, UV radiation, exposure to chemicals including Benzene, Asbestos and vinyl chloride.
- 2) Medication such as alkylating agents and immunosuppressant's.
- 3) Viruses such as Epstein – Virus ,Human papilloma virus ,Hepatitis-B-virus
- 4) Genetic factors such as inherited mutations, cancer causing genes, defective tumor suppressor genes.
- 5) Life style factors like high-fat, low fiber diets, tobacco, ethanol etc.

**Method:** Medicinal herbs are selected through the study of their literature from the online journal and publications. The collected literature of the medicinal plants related to the plant family, source or part are used , uses or physiological activities or pharmacological activities and plant derivative compounds are put in tabular form for the analyzation.<sup>[16]</sup>

**Table-1: Some Medicinal Plants Have Anti Cancer Potential**

S.No	Plant Name	Family	Component	Parts used	Pharmacological activity/uses
1	<i>Cynara Cardunculus</i>	Compositae	$\alpha$ & $\beta$ amyryn , taraxasterol and $\Psi$ – taraxasterol	Flowers	Suppressed tumor promotion <sup>[17]</sup>
2	<i>Vitis vinifera L.</i>	Vitaceae	Resveratrol, por anthocynidins	Grape skin ,seeds	Inhibit tumor promotion , anti oxidant <sup>[18,19,20]</sup>
3	<i>Rosemarinus officinalis L.</i>	Labiatae	Ursolic acid carnosol	Oil	Suppressed tumor promotion , analgesic, treat headaches, and epilepsy <sup>[21]</sup>
4	<i>Perilla frutescens</i>	Labiatae	Luteolin, Rosmarinic acid and Caffeic acid	Seeds	Inhibit colon carcinogenesis <sup>[22,23]</sup>
5	<i>Chrysantthemum</i>	Compositae	Triterpenoids, heliantriol C.	Flowers	Inhibit tumor promotion , used in hypertention , angina, coronary artery disease and liver related disorders <sup>[24,25]</sup>
6	<i>Citrus unshiu</i>	Rutaceae	$\beta$ - cryptoxanthin, hesperidin	Peel , juice	Inhibit colon carcinogenesis, used for gastric secretion promotion, sedative effect and inhibition of airway constraction <sup>[26,27]</sup>
7	<i>Brassica oleracea L.</i>	Cruciferae	Vit-c , glutaminie and indole -3- carbinol	Flowers	Inhibit tumor promotion , anti inflammatory <sup>[28]</sup>

8	<i>Beta vulgaris L.</i>	Chenopodiaceae	Betaine, vit-c	Various parts	Inhibit tumor promotion anti oxidant activity <sup>[29,30]</sup>
9	<i>Achyranthes aspera L.</i>	Amaranthaceae	Saponins, Flavonoids and Phenolic compounds	Leaves	Suppresses carcinogenesis, use in treatment of malarial fever, dysentery, asthma and diabetes <sup>[31]</sup>
10	<i>Carthamus tinctorius L.</i>	Compositae	Phytosterols, stigmasterol	Seeds	Inhibit tumor promotion <sup>[32]</sup>
11	<i>Zingiber officinale</i>	Zingiberaceae	Zingerone, shogaols and gingerol	Rhizomes	Inhibit tumor promotion <sup>[33]</sup>
12	<i>Camellia Sinensis L.</i>	Theaceae	Epigallocatechin gallate(EGCG)	Leaves	Inhibit tumor promotion <sup>[34]</sup>
13	<i>Withania Somnifera</i>	Solanaceae	Polyphenols, alkaloids-isopelletierine, steroidal lactones	Bark, gel	Reduce tumor growth, anti-inflammatory, anti tumor, anti oxidant, anti stress activity <sup>[35,36]</sup>
14	<i>Pfaffia paniculata</i>	Amaranthaceae	Saponins	Roots	Inhibitory action on the growth melanoma, cytotoxic activity <sup>[37]</sup>
15	<i>Oroxylum indicum</i>	Bignoniaceae	Baicalin, chrysin, biacalein	Bark	Inhibit proliferation of cancer cells, induce apoptosis, used in treatment of gastric ulcer, tonsil pain, scabies and moth cancer <sup>[38,39]</sup>
16	<i>Calotropis procera</i>	Asclepiadaceae	Cordenolide	Root bark	Inhibit cancer cells, used in treatment of leprosy, ulcers, piles, and tumors <sup>[40,41]</sup>
17	<i>Baerahaavia diffusa</i>	Nyctaginaceae	Rotenoids-boeravinones G&H	Various parts	Used in the treatment of cancer, jaundice, dyspepsia, and inflammation <sup>[42]</sup>

TABLE -2: OTHER MEDICINAL PLANTS WITH ANTI CANCER ACTIVITY

S.No	Plant Name	Family	Parts used
1	<i>Andrographis paniculata</i>	Acanthaceae	Areal Parts <sup>[43]</sup>
2	<i>Azadirachta Indica</i>	Meliaceae	Leaves <sup>[44,45]</sup>
3	<i>Calycopteris floriabunda</i>	Combretaceae	Leaves <sup>[46]</sup>
4	<i>Curcuma longa</i>	Zingiberaceae	Rhizomes <sup>[47,48]</sup>
5	<i>Morinda citryfolia L.</i>	Rubiaceae	Roots and Fruit <sup>[49,50]</sup>
6	<i>Mangifera Indica</i>	Anacardiaceae	Fruits, Bark and Leaves <sup>[51]</sup>
7	<i>Polylthia Longifolia</i>	Annonaceae	Leaves <sup>[52]</sup>
8	<i>Tephrosia Purpurea</i>	Fabaceae	Roots <sup>[53]</sup>
9	<i>Nerium oleander</i>	Apocynaceae	Leaves and Flowers <sup>[54]</sup>
10	<i>Codiaeum variegatum</i>	Euphorbiaceae	Leaves <sup>[55]</sup>

**TABLE-3: MARINE DERIVED POTENTIAL ANTI CANCER AGENTS**

S.No	Organism	Compound	Mechanism of action
1	<i>Ascidian</i>	Aplidine	Induction apoptosis with concomitant G <sub>1</sub> arrest and G <sub>2</sub> blockage <sup>[56]</sup>
2	<i>Mollusc</i>	Dolastatin 10	Binds to amino-terminal peptide of $\beta$ – tubulin containing cysteine <sup>[57-59]</sup>
3	<i>Bryozoans</i>	Bryostatin-1	Potential of ara-C induced apoptosis by PKC-dependent release of TNF- $\alpha$ <sup>[60-63]</sup>
4	<i>Ascidian</i>	Ecteinascidin-743	Telomere dysfunction increases susceptibility to ET-743 <sup>[64,65]</sup>

## DISCUSSION AND CONCLUSION

The selected medicinal plants and marine sources in this review have several pharmacological activities like anti cancer activity, anti oxidant activity, anti filariasis activity, anti inflammatory activity, anti diabetic activity and many more. Several medicinal herbs and their derived substance have been a prime source for the treatment of cancer and many other diseases, many of which are consumed daily with the diet. These medicinal plants possess good immunomodulatory and anti oxidant properties leading to anti cancer activity. The anti oxidant medicinal herbs and their products prevent from the cancer and other diseases by protecting cells from damage. The observation of the tabular form shows that there are several families in the plant kingdom and almost all families have one or more pharmacological activities. This review may helpful to the researches for easy analyzation of medicinal plants and their family, plant derived substances and their pharmacological activities or uses.

## ACKNOWLEDGEMENT

I greatly acknowledge one of authors S.Jithender Kumar Naik, Toxicology lab, Department of Zoology, Osmania University, Telangana, India, for the support and encouragement throughout the study.

## REFERENCES

1. Sunitha A.Choudary , Krupa V.Gadhvi,Ankit B.Choudary . Comprehensive review on world herb trade and most utilized medicinal plant. International journal of applied biology and pharmcentical Technology., 2010; Volume: I: Issue-2: 510-517.
2. NIH, simile C, hardy AM(2002) Utilization of Complementary and alternative medicine by United States adults: results from the 1999 national health interview survey. Med care., 1999; 40: 353-358

3. National Institutes of Health, National center for Complementary and alternative medicines. U.S. Department of Health and Human Services, D347, Updated February 2007; page: 1-5.
4. Pezzuto, J.M Plant-derived anti cancer agents. *Bio chem..pharmacol.*, 1997; 53: 121-133.
5. Geissman, T.A New substance of plant origin. *Alnnu.Rev.pharmacol.*, 1964; 4: 305-316.
6. Hsieh YJ, Leu YL, Chang CJ. The anti-cancer activity of *Kalanchoe tubiflora* .*OA Alternative Medicine.*, 2013 Aug 01; 1(2): 18.
7. Medicinal and Edible Plants as cancer preventive Agents by Ken (Yasukwa), school of pharmacy, Nihon University, Japan.
8. Venkat Raji Reddy.G., Vijay Kumar.R and Krishna Reddy.M. A short review of medicinal plants with their families . *World journal of pharmacy and pharmaceutical.*
9. Newman DJ, Cragg GM. Natural products as sources of new drugs over the 30 years from 1981 to 2010 *J Nat Prod.*, 2012 Mar 23; 75(3): 311-35.
10. Parikh R, Jaganathan N (2014) A short Review: Complementary and Alternative Medicine (CAM) in lung Cancer. *J Anc Dis prev Rem* 2:115. Doi:10.4172/2329-8731.1000115.
11. Prushine Thakore. *IJPRD*, 2011; (2(11): January-2012(129-136).
12. Sanjib Bhattacharya .Anticarcinic property of medicinal plants. *Medicinal plants as anti-oxidant agents: Understanding their mechanism of Action and Therapeutic Efficacy*, 2012:83-96. ISBN: 978-81-308-0509-2.
13. Rajandeep Kaur, Karun Kapoor, Harpreet Kaur. Plants as a source anti-cancer agents. *J.Nat.Prod.Plant Resour.*, 2011; 1(1): 119-124.
14. M.Dhanamani, S.Lakshmi Devi, S.kannan. *Hygeia.J.D.Med.*, 2011; 3(1): 1-10
15. Ferguson, L.R, *Mutat. Res.*, 1994; 307: 395-410.
16. Venkat Raji Reddy.G., Vijay Kumar.R and Krishna Reddy.M. A short review of medicinal plants with their families . *World journal of pharmacy and pharmaceutical.*
17. Yasukawa, K.(2010). Cancer chemopreventive agents: natural pentacyclic Triterpenoids, In: *pentacyclic Triterpenes as Promising agents in cancer*, J.A.R/Sa; vadpr.(ed) pp.127 - 167, Nova publilsher ISBN 978-1-70876 -973-t, New York, U.S.A.
18. Alam, A.; Khan N.; Sharma, S.; Saleem, M. & Sultana, S.(2002). Chemopreventive effect of *Vitis vinifera* extract on 23-O-tetradecanoyl-13-phorbol acetate-induced cutaneous oxidative stress and tumor promotion in murine skin, *pharmacological Research*, Vol.57, No. 6, pp.557-564, ISSN 1043-6618.

19. Bomser, J.A.; Singletary, K.W.; Walling, M.A.&Smith, M.A.L.(1999).Inhibition of TPA-induced tumor promotion in CD-1 mouse epidermis by a polyphenolic fraction from grape seed, *cancer letters*, 1999; 135: No.2, pp.=.151-157,ISSN 0304-3835
20. J.; Wang,J.;Chen, Y.&Agarwal, R. (1999). Anti-tumor –promoting activity of a polyphenolic fraction isolated from grape seed in the mouse skin two-stage initiation-promotion protocol and identification of procyanidin B5-3'-gallate as the most effective antioxidant constituent, *carcinogenesis*, 1999; 20,No.9,pp.1737-1745,ISSN 0143-3334.
21. Huang, M.-T.; Ho,C.[T.; Wang, Z.Y.; Ferraro, T.; Lou, Y.[R.; Stauber, K.;Ma, W.; Georgergenesis by rosemary and its constituents carnosol and ursolic acid, *cancer Research*,Vol.54No.3,pp.701-708, ISSN 0008-5472.
22. Narisawa, T.; Takahashi, M.; Kotanagi, H.; Kusaka, H.; Yamazaki, Y.; Koyama, H.;Fukaura, Y.; Nishizawa, Y.; Kotsugai, M.;Isoda, Y.; Hirano,J. & Tanida, N. (1991). Inhibitory effect of dietary Perilla oil rich in the n-3 polyunsaturated fatty acid  $\alpha$  – linolenic acid on colon carcinogenesis in rats, *Japanese Journal of Cancer Research*, Vol.82, No. 10,pp.1089-1096,ISSN 0910-5050
23. Narisawa, T.; Fukaura, Y.;Yazawa, L.; Ishikawa, C.; Isoada, Y.;Nishizawa, Y. (1994). Colon cancer prevention with a small amount of dietary perilla oil high in alpha =; omega; emoc acid in an animal model,,*cancer*, Vol.73, NO. 8, pp. 2069-2075,ISSN 0008-543X
24. Yasukawa, K.; Akihisa, T.;Oinuma H.; Kasahara, Y.;Kimura Y.; Yamanouchi, S; Kumaki,K.; Tamura, T. &Takido, M.(1996d).inhibitory effect of di-and trihydroxy triterpenes from the Compositae flowers on 12-O-tetradecanoylphorbol-13-acetate induced inflammation in mice, *Biological & Pharmaceutical Bulletin*, Vol.19, No.10,pp.1329-1331,ISSN 0918-6158
25. Yasukawa, K.;Akihisa, T.;Kasahara, Y.;Ukiya, M.;Kumaki,K.;Tamura T.;Yamanouchi, S.&Takido, M.(1998b).Inhibitory effect of helianthriol C, the component of the flower of edible Chrysanthemum, on tumor promotion by 12-O-tetradecanoylphorbol-13-acetate in two-stage carcinogenesis in mouse skin, *Phytomedicine*, Vol.5.No.3, pp.215-218,ISSN 0944-7113
26. Narisawa, T., Oshima, S.; Inakuma, T.; Yano, M. &Nishino, H. (1999). Chemoprevention by the oxygenated carotenoid beta- cryptoxanthin of NB-methylnitrosourea[induced colon carcinogenesis in F344 rats, *Japanese Journal of Cancer Research*, Vol. 90, No. 10, pp. 1061-1065, ISSN 0910 -5050.

27. Tanaka, H.; Makita, H.; Kawabata, K.; Mori, H.; kakumoto, M.; Satoh, K.;Hara, A.; Sumida. T.; Tanaka, T. & Ogawa, H. (1997b). Chemoprevention of azaoxymethan – induced rat hesperidin, *Carcinogenesis*, Vol. 18, NO. 5, pp.957-965, ISSN 0910-5050.
28. Srinivastava , B.& Shukla ,Y.(1998).Antitumour promoting effect of mouse skin carcinogenesis, *cancer letters*,Vol.134,No.1, pp.91-95, ISSN 0304-3835
29. Kadadia ,G.J.;Tokuda, H.;KOnoshima, T.&Nishino, H. (1996). Chemoprevention of lung and skin cancer by Beta vulgaris (beet) root extract, *Cancer Letters*, Vol.100, No.11-2, pp.211-214, ISSN 0304-3835.
30. Kapadia, G.J Azuine , Ma. A.;Sridhar, R.;Okuda, Y.; Tsuruta,A.;Ichiishi,E.; Mukainake t.; Takasaki,M.;Nishino,H.&Tokuda,H.(2003). Chemoprevention of DMBA –induced UV-B promoted, NOR-1-induced TPA promoted skin carcinogenesis, and DEN-induced ,Phenobarbital promoted liver tumors in mice by extract of beetraoot, *pharmacological Research*, vol.47,No.2,pp.141-148,ISSN 1043-6618.
31. Chakraborty, A.; Brantner A.; Mukainaka, T.; BNobukuni, Y.; Kuchide, M.; konoshima, T.;Tokuda, H. &Nishino, H. (2002).Cancer chemopreventive activity of *Achyranthes aspera* leaves on Estein –Barr virus activation and two –stage mouse skin carcinogenesis, *Cancer Letters*, vol.177,No.1,pp.1-5,ISSN 0304-3835.
32. Kasahar , Y.; Kumaki, K.; Katagiri, S.; Yasukawa,K.; Uamanouschi, S.; Takido, M.;Akihisa, T.; Tamura, T.(1994).Carthami Flos extract and its component , Stigmasterol, inhibit tumor promotion in mouse skin two –stage carcinogenesis, *Phytotherapy Research*, vol.8, No.6, PP. 327-331, ISSN 0951-418X
33. Katiya, S.K.; Agarwal, R.&Mukhtar, H. (1996). Inhibition of tumor promotion in SENCAR mouse skin by extract of *Zingiber officinale* rhizome, *Cancer Research*, Vol.56, No.5, pp.1023-1030, ISSN 0008-5472.
34. Yoshizawa, S.; Horiuchi, T.; Fuijiki, H.; Yoshida. T; Okuda, T.&Sugimura, T. (1987).Antitumor promoting activaiity of (-) – epigallocatechin gallate, the main constituent of Tannin in green tea, *Phytotherapy Research* , Vol.1, NO.1,pp.44-47,ISSN 0951-418X.
35. Mishra LC,Singh BB, Dagenais S. Scientific Basis for the Therapeutic use of *withania somnifera* (Ashwagandha): A Review. *Alternative Medicine Review*2000; 5(4):334-336.
36. Davis L, Kuttan G. Effect of *withania somnifera* on catl activity *journal of Experimental and clinical cancer Research.*, 2002; 21(1): 115-118.
37. Takemoto T, Nishimoto N, Nakai S, Takagi N, Hayshi S, Odashima S, et al. Pfaffic acid, a novel nortrierpene from *pfaffia paniculata* Kuntze. *Tetrahedran Lett.*, 1983; 24: 1057-60

38. Roy Mk, Nakahara K, Na thalang V, Trakoontivakom G, Takenaka M, isobe S, et al. Baicalein, a flavanoid extracted from methanolic extract of *Oroxylum indicum* inhibits proliferation of a cancer cell line in vitro via induction of apoptosis. *Die pharmazie-An international J of Pharmceusc.*, 2007; 62(2): 149-153
39. Mao AA. *Oroxylum indicum* vent-a potential anticancer medicinal plant. *Indian Journal of Traditional Konowledge.*, 2002; 1(1): 17-21.
40. Kumar VL, Arya S. Medicinal uses and pharmacological properties of *Calotropis procera*. In: Govil Jn, editor. *Recent Progress in Medicinal Plants*. 11<sup>th</sup> vol Texas: Studium Press., 2006; 373-388.
41. Choeden T, Mathan G, Arya S, Kumar VL, Kumar V. Anticancer and cytotoxic properties of the latex of *calotropis procera* in a transgenic mouse model of hepatocellular carcinoma. *World Journal of Gastroenterology.*, 2006; 12(16): 2517-2522.
42. Manu KS, Kuttan G. Effect of punarnavine, an alkaloid from *Boerhaavia diffusa*, on cell-mediated immune responses and TIMP-1 in B17F-10 metastatic melanoma-bearing mice. *Immunopharmacology and immunotoxixology.*, 2007; 29(3-4): 569-586.
43. Geethanjali M, Rao YK, Fangs S, et al., Cytotoxic constituents from *Andrographis paniculata* induce cell cycle arrest in jurkat cells. *Phytother Res.*, 2008; 22: 1336-1341.
44. Gangar SC, Koul A. *Azadirachta Indica* modulates carcinogen biotransformation and reduced glutathione at peri-initiation phase of benzo(a) pyrene induced murine forestomach tumorigenesis. *Phytother Res.*, 2008; 22: 1229-1238.
45. Kumar S, Suresh PK, Vijayababu MR, et al., Anticancer effects of ethanolic neem leaf extract on prostate cancer cell line. *J Ethanopharmacol.*, 2006; 105: 246-250.
46. Ali H, Chowdhary AKA, Rahman AKM, et al., Induction Pachypodol a flavonol from the leaf of *calycopteris floribunda*, inhibits the growth of CaCo-2 colon cancer cell line in vitro. *Phytother Res.*, 2008; 22: 1684-1687.
47. Lee YK, Lee WS, Hwang JT, et al., Curcumin exert anti-differentiation effect through AMPK  $\alpha$  -PPAR-  $\gamma$  in 3T3-L1 adipocytes and antiproliferatory effect through AMPK  $\alpha$  -COX - 2 in cancer cells. *J Agric Food Chem.*, 2009; 57: 305-310.
48. Hsu Y, Weng H, Lin S, et al., Curcuminoids- Cellular uptake by human primary colon cancer cells as quantitative by a sensitive HPLC assay and its relation with the inhibition of proliferation and apoptosis. *J. Agric Food Chem.*, 2007; 55: 8213- 8222.
49. Kamiya K, Hamabe W, Tokuyama S, et al., Inhibitory effect of anthraquinones isolated from the *Morinda citrifolia* root on animal A, B and Y families of DNA polymerases and human cancer cell proliferation. *Food Chem.*, 2009; 188: 725-730.

50. Anekepankul T, Goto M, Sasaki M, et al., Extraction of anti cancer damnacanthol from roots of *Morinda citrifolia* by subcritical water. *Sep Purif Technol.*, 2007; 55: 343-349.
51. Rajendran P, Ekambaram G, Sakthisekaran D. effect of mangiferin on benzo(a) pyrene induced lung carcinogenesis in experimental Swiss albino mice. *Nat Prod Res.*, 2008; 22: 672-680.
52. Verma M, Singh SK, Bhushan S, et al., In vitro cytotoxic potential of *polyalthia longifolia* on human cancer cell line and induction of apoptosis through mitochondrial dependent path way in HL-60 cells. *Chemico – Biol Interact.*, 2008; 171: 45-56.
53. Kavitha K, Manoharan S. Anticarcinogenic and antilipidperoxydative effects of *Tephrosia purpurea* L. in 7, 12- dimethylbenz(a)anthracene (DMBA) induced hamster buccal pouch carcinoma. *Indian J Pharmacol.*, 2006; 38: 185-189.
54. Calderon- Montano JM, Burgos –Moron E, Orta ML, Mateos S, Lopez- Lazaro M. A hydroalcoholic extract from the leaves of *Nerium oleander* inhibits glycolysis and induces selective killing of lung cancer cells. *Planta Med.*, 2013; 79(12): 1017-1023.
55. Hassan EM, Hassan RA, Sakib JY, Mahamed SM, El-Toumy SA. Chemical constituents and cytotoxic activity of *Codiaeum variegatum* CV *petra*. *Journal Applied Sciences Research*, 9(8): 2013.
56. Geldof AA, Mastbergen SC, Henrar REC, et al. Cytotoxicity and neurocytotoxicity of new marine anticancer agents evaluated using invitro assays. *Cancer chemotherapy Pharmacol.*, 1999; 44: 312-318.
57. Poncet J. The dolastatins, a family of promising antineoplastic agent. *Curr Pharm Des.*, 1999; 5: 139-162.
58. Bai R, Pettit GR, Hamel E. Dolastatin 10, a powerful cytostatic peptide derived from a marine animal. Inhibition of tubulin polymerization mediated through the vinca alkaloid binding domain. *Bilchem Pharmacol.*, 1990; 39: 1941-1949.
59. Pathak S, Multani AS, Ozen M, et al. Dolastatin 10 induces polyploidy, telomeric associations and apoptosis in a murine melanoma cell line. *Oncol Res.*, 1998; 5: 373-376.
60. Pettit GR. The bryostatins. *Fortschr Chem Org Naturst.*, 1991; 57: 153-195.
61. Pagliaro L, Daliani D, Amato R, et al. Phase II trial of bryostatin 1 for patients with metastatic renal cell carcinoma. *Cancer.*, 2000; 89: 615-618.
62. Varterasian ML, Mohammad RM, Shurafa Ms, et al. Phase-II trial of bryostatin 1 in patients with relapsed low-grade non-Hodgkin's lymphoma and chronic lymphocytic leukemia. *Clin Cancer Res.*, 2000; 6: 825-828.

63. Zonder JA, Shields AF, Zalupski M, et al. A Phase-II trial of bryostatin 1 in the treatment of metastatic colorectal cancer. *Clin Cancer Res.*, 2001; 7: 38-42.
64. Demetri G, Garcia – Carbonero R, Harmon D, et al. Ecteinascidin-743 (ET-743) induces objective responses and disease control in patients with advanced non-osseous sarcomas: results from Phase II trials. *Ann Oncol.*, 2000; 11(Suppl 4): 126.
65. Erba E, Bergamaschi D, Bassano L, et al. Ecteinascidin-743 (ET-743), a natural marine compound, with a unique mechanism of action. *Eur J Cancer.*, 2001; 37: 97-105.