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Cancer in Perspective of *Dooshivisha* (Latent Poisoning) w.s.r. to Possible Role of *Dooshivishari Agada* in Treating Cancer

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ABSTRACT

With modernisation & urbanisation every individual is frequently exposed to many toxic substances like polycyclic hydrocarbons, nitrosamine, pyrogenic compound & many other which are now known to be potent mutagens & carcinogens. These carcinogens enter in the body through air, water, radiation, drugs, cosmetics & different food product resulting in manifestation of sever disease such as cancer. After studying the etiological factor of cancer in view of Ayurveda as well as modern medicine, it is seen that most of the etiological factor & pathology of cancer can be correlated to *Dooshivisha* which is latent stage of poison explained under the one of disciple of Ayurveda. *Dooshivishari Agad* is one of the formulation mentioned for the management of *Dooshivisha*. After reviewing the experimental study of herbs in *Dooshivishari Agad* it is found that all these herbs are useful in anticancer therapy so formulation may be much more effect due to the synergistic action. Integrated approach of modern medicine with Ayurvedic principle is the time need. Application of management of *Dooshivisha* in this context may be the new horizon for cancer patient. So this review is taken to study cancer & its management in context of Dooshivisha.

KEYWORDS

Cancer, Carcinogen, Dooshivisha, Ayurveda, Dooshivishari Agad



INTRODUCTION

Cancer is the one word which is very scary for every human beings. Every year about 8,00,000 new cancer patients get registered with the national cancer registry program in India¹. Cancer is the second leading cause of death next to cardivovascular diseases². The world's population is expected to be 7.5 billion by 2020 and approximations predict that about 15.0 million new cancer cases will be diagnosed, with deaths of about 12.0 million cancer patients³. Cancer is one of the leading causes of death in India, with about 2.5 million cancer patients, one million new cases are added every year and with a chance five times rising up to 2025⁴. Though heredity plays its role in causing cancer but that include only 5% of cancer cases, non -heredity factors such as life style, food, level of physical activity, personal hygiene, environmental pollution are the major causing factors⁵.

Cancer is a disease in which normal cells damaged and do not undergo are programmed cell death as fast as they divide via mitosis .Today due to modernisation & urbanisation each & every individual is frequently exposed to many substances which are toxic mostly carcinogenic. Polycyclic hydrocarbons, nitrosamine, pyrogenic compound & many other which are now known to be potent

mutagens & carcinogens. These carcinogens enter in the body through air, water, radiation, drugs, cosmetics & different food product. These increase the cancer by altering cellular risk of metabolism or damaging DNA directly in cells, which interferes with biological processes, and induces the uncontrolled, malignant division, ultimately leading to the formation of tumors. Usually, severe DNA damage leads to programmed cell death, but if the programmed cell death pathway is damaged, then the cell cannot prevent itself from becoming a cancer cell⁶. **Carcinogens⁷** (Table 1):

A carcinogen is any substance that promotes the formation of cancer. This may be due to the ability to damage the genome or to the disruption of cellular metabolic processes.Two types of carcinogenic mechanisms have been identified. One is genotoxic that alter genes through interaction with DNA and other is epigenetics. Genotoxic are of three types:

Direct primary or carcinogens: Chemicals that act without any bioactivation; for example, ethylene bis(chloromethyl) ether. dibromide, and dimethyl sulfate.

• **Procarcinogens**: Chemicals that require biotransformation to activate them to a carcinogen; for example, vinyl chloride and 2-naphthylamine. • **Inorganic carcinogen**: Some of these are preliminarily categorized as genotoxic due to potential for DNA damage. Other compounds in the group may operate through epigenetic mechanisms.

• Epigenetic: These are carcinogens that do not act directly with genetic material. Several types are possible:Cocarcinogen: Increases the overall response of a carcinogen when they are administered together; for example, sulfur dioxide, ethanol, and catechol.

• **Promoter**: Increases response of a carcinogen when applied after the carcinogen but will not induce cancer by itself; for example, phenol and dithranol.

• **Solid-state**: Works by unknown mechanism, but physical form vital to effect; for example, asbestos and metal foils.

Table 1 Common carcinogen involving occupation⁹

• **Hormone**: Usually is not genotoxic, but alters endocrine balance; often acts as promoter (e.g. DES and estrogens).

• **Immunosuppressor**: Mainly stimulates virally induced, transplanted, or metastatic neoplasms by weakening host's immune system (e.g., antilymphocytic serum, used in organ transplants).

Genotoxic carcinogens are sometimes effective after a single exposure, can act in a cumulative manner, or act with other genotoxic carcinogens which affect the same organs. Some epigenetic carcinogens, however, only cause cancers when concentrations are high and exposure long. The implication is that while there may be a "safe" threshold level of exposure for some carcinogens,others may have "zero" threshold; that is, one molecule of the chemical can induce a cancer⁸.

Carcinogen	Associated cancer sites or	Occupational uses or sources	
	types		
Arsenic & its compound	Lung ,Skin	Smelting byproduct Component of:	
	,Haemangiosarcoma		
		• Alloys	
		• Electrical and semiconductor devices	
		• Medications (e.g. melarsoprol)	
		Herbicides	
		Fungicides	
		Animal dips	
		• Drinking water from contaminated	
		aquifers.	
Asbestos	Lung, Gastrointestinal tract	Not in widespread use, but found in:	
		Constructions	
		Constructions	
		• Rooming papers	
		• Floor tiles	
		• Fire-resistant textiles	
		Replacement friction linings for	
		automobiles still may contain asbestos	

Dangana	Louisamia Hadalina	
Benzene	Leukenna, Hougkins	• Light fuel oil
	Тутрпота	• Former use as solvent and fumigant
		• Printing
		• Lithography
		• Paint
		• Rubber
		• Dry cleaning
		Adhesives
		• Coatings
		• Detergents
Beryllium & its compound	Lung	<u> </u>
v 1	C	Missile fuel
		• Lightweight alloys
		Aerospace applications
		Nuclear reactors
Cadmium & its compound	Prostate	
Cadmium & its compound	Tiostate	• Vellow nigments
		Dhosphore
		Filosphors Solders
		• Solders
		• Batteries
		Metal paintings and coatings
Hexavalent	Lung	• Paints
chromiumcompound		• Pigments
		Preservatives
IC engine exhaust gas	Lung, Bladder	Exhaust gas from engine
Ethylene oxide	Leukemia	 Ripening agents for fruits& nuts
		Rocket propellant
		• Fumigant for foodstuffs and textiles
		• Sterilant for hospital equipment
Nickle	Nose,Lung	Nickel plating
	-	• Ferrous alloys
		• Ceramics
		Batteries
		• Stainless-steel welding byproduct
Radon & its decay product	Lung	Uranium decay
5 1	e	• Ouarries and mines
		Cellars and poorly ventilated places
Vinyl chloride	Haemangiosarcoma liver	Befrigerant
v myr emorrae	Theomangiosarcoma, nyor	Production for polywinyl chloride
		Adhesive for plastics
		Addesive for plastics
Involuntony, or alive	Lung	Former use in pressurized containers
(Dessive smoking	Lung	
(rassive smoking)	Dono Livor	Nuclear fuel processing
Kadium, Plutonium	Done,Liver	Nuclear fuel processing
		kaulum diai manufacturing.

There are some other carcinogenetic agent which include Gasoline (contains aromatics) Alkylating antineoplastic agents (e.g. mechlorethamine) other alkylating agents (e.g. dimethyl sulfate), Ultraviolet radiation from the sun and UV lamps,Alcohol (causing head and neck cancers),Other ionizing radiation (X-rays, gamma rays, etc.) These carcinogenetic agents cause four main types of cancer, lung cancer, breast cancer, colon cancer & stomach cancer.

Concept of *Dooshivisha* :

Agadtantra is a specialised branch of which deals with Ayurveda the management of toxicity. This specialised branch has given the novel concept of Dooshivisha which is a transformable state of Visha (Toxins) which can be attained by any type of poison, if it is not eliminated from the body completely. Ancient seers describe that it is part of poison originating from inanimate or animate or artificial source which retained in the body after partial expulsion or which are provisionally undergone detoxification, by the antidrug but not completely poisonous eliminated from body .Due to low potency and also due to enveloping (awarana) action by kapha, it does not cause sudden death. It is retained in the body for a long period without producing any grave or fatal symptoms. It slowly vitiates the dosha & then vitiates rasa-raktadi dhatu (tissue). Same pathology is seen in cancer. After long term exposure to carcinogenic substances, Rasaraktadi Dhatu (tissue) get vitiated which causes the mutation of cells¹⁰.

Management of cancer in terms of *Dooshivisha*:

Radiotherapy & chemotherapy are the line of treatment for cancer in conventional medicine which is very effective but on other side it produces harmful toxic effects. So to minimise the toxic effect of this therapy & for the improvement of quality of life in cancer patient, integrated approach of modern medicine with Ayurvedic principle is the time need. Exposure & deposition of carcinogenic substance is lead to cancer which ultimately the type of chronic toxicity. So removal of toxin from body may be effective for the treatment of cancer.Liver, skin, kidney, and lung are the major detoxification centers of the body and in a cancer patient this toxin clearance mechanism get compromised. In Agdtantra in the context of *Dooshivisha* antitoxic treatment modalities is prescribed that includes Vaman (emesis) which eliminate the toxin deposited in the body and after Vamana Dooshivishari agada, which is one of the formulations mentioned for the management of the Dooshivisha, is to be administered .

Pharmacokinetics of *Vamana*: Poison are mainly fat soluble in nature, by the oleation therapy which is carried out before *Vamana* ,these toxic substances dissolve into oil & the toxin which are firstly present in cytoplasm of cell now become membrane bound. After oleation, *swedana* (fomentation) is carried out due to which cell permeability changes leading to excretion of fat soluble protein bound toxin into circulation. Due to emetic agents CTZ (emetic center- chemoreceptor trigger zone)centre get activated with the stimulation of vagus nerve. Vasodilatation of portal vein, superior & inferior mesenteric vein, microvasculature of vellus increased the secretion in gut. By this mechanism the toxin which excretes into circulation is expelled into lumen of gut¹¹.

Sr no.	Drug name	Botanical name	Pharmacological action in terms
			of cancer
1	Pimpali	Piper longum	Immunomodulatory ¹²
			Hepatoprotective
			Anti-cancer activity ¹³
			Anti-oxidative, anti-apoptotic, and
			restorative ability against cell
			proliferative mutagenic response ¹⁴
2	Dhyamaka	Cymbopogon martini	Antioxidant ¹⁵
3	Jatamansi	Nardostachys jatamansi	Hepatoprotective Activity ¹⁶
			Antioxidant Activity ¹⁷
			Antiestrogenic activity ¹⁸
4	Ela	Elattaria Cardamum	Anticancer Activity ¹⁹
			Antioxident Activity ²⁰
5	Lodhra	Symplocos racemosa	Anticancer activity ²¹⁻²²
			Antioxidant Activity ²³
			Hepato-protective activity ²⁴
6	Katunatam/shyonak	Oroxylum indicum	Hepato-protective activity ²⁵
			Anticancer activity ²⁶⁻³⁰
			Immuno-stimulating activity ³¹
			Gastro-protective ³²
7	Tagar	Valeriana wallichii	Radio-protective activity ³³
			Anti-oxident ³⁴
			Cytotoxic activity ³⁵
8	Kuth	Saussurea lappa.	Anti-cancer activity ³⁶⁻³⁹
			Immuno-modulatory activity ⁴⁰
			Hepato-protective ⁴¹
			Angiogenesis activity ⁴²
9	Mulethi	Glycyrrhiza glabra	Antioxidant ⁴³
		Linn.	Hepato-protective ⁴⁴⁻⁴⁵
			Anticancer Activity ⁴⁶⁻⁴⁷
			Immunomodulator ⁴⁸
10	Chandan	Pterocarpus santalinus	Hepatoprotective ⁴⁹
		Linn. f.	Antioxident ⁵⁰
			Anticancer Activity ⁵¹⁻⁵³
11	Suvarchika	Potassium nitrate	
12	Gairik	Red ochre	

Table 2 Pharmacological activity of ingredients of Dooshivishari Agad

DISCUSSION

Cancer is not simply localized lumps and bumps that we have been programmed to accept through the years. Cancer can partly be viewed as a degenerative process with symptoms representative of underlying systemic dysfunction. There are many causative factors, including emotional stress, diet, drugs and chemicals, infections, genetic mutation and environmental pollutants. Out of this various factors various chemicals slowly get deposited in the body and act as carcinogenic.

Dooshivisha is a remaining portion of specific poison after the completion of treatment or cumulative nature of poison that get deposited in body and damage the cell. After reviewing the causative factor of cancer it is found that all get categorized under the heading of Dooshivisha that is artificial poison. This poison cumulatively deposited in particular (Dhatu) tissue then that tissue is more prone to produce cancer. Weakened *dhatus* and *dhatu agnis* were highlighted important Ayurvedic as concepts in the pathophysiology of cancer. The Vaidyas suggested that when the dhatus are weakened, that patients are vulnerable to disease and that in particular a weakened dhatu agni (Harmones & enzymes) predisposes them to cancer in that dhatu. This concept is unique to Ayurveda. However, a parallel exist in biomedicine, in which particular tissues (e.g., sites in the aerodigestive tract after tobacco exposure) are vulnerable to cancer⁵⁴.

The conventional treatment of surgery, radiation and chemotherapy has been the cornerstone of cancer treatment over the past 50 years. Today, the clinical success of these treatments has reached a ceiling but along with their toxic effect. In chemotherapy along with destroying neoplastic cell, it also damages healthy tissue, body fails to eliminate the excess drugs which leads to accumulation of these chemical as in the body & cause health problems of long period. These chemicals are in-excretable & indigestible. Due to these therapy there is anorexia, nausea, fatigue, malaise and drowsiness as acute symptoms. After someday there is ulceration of mouth & GI tract ,diarrhea, hair loss etc. occurs . All these symptoms resembles with the symptoms of *Dooshivisha*. So while treating the cancer patient along with this therapy if integrated approach of *Dooshivisha* is applied then it may be fruitful.

Dooshivsha is managed by detoxification of body with Vaman along with administration of Dooshivishari Agada. For cancer management the formulation needed is having property which strengthen the immune system ,prevent the of cancerous cell, create a spread environment that is unfavorable for cancer growth that means high oxygen level, detoxifying the body fighting free radicles that cause mutational changes. After reviewing pharmacological activity of Dooshivishari Agad it is found that it fulfills all the criteria which are needed for the management of cancer. Herbs of Dooshivishari Agada has individually proved this activity. So synergistic effect of

this formulation will be much more effective in cancer patient.

CONCLUSION

Management of cancer & its prevention can be done effectively if Ayurvedic approach of *Dooshivisha* is applied for the cancer management. Properties and individual actions of ingredients of *Dooshivishari Agada* represent its possible utility in management of cancer, however experimental study has to be carried out to establish them on scientific ground.

REFERENCES

1. Dr. Sangita P. Ingole, Dr. Aruna U. Kakde, Priti B. Bonde, A Review on Statistics of Cancer in India, Journal of Environmental Science, Volume 10, Issue 7 Ver. I (July 2016), PP 107-116

2.<u>https://www.ncbi.nlm.nih.gov/pubmed/1</u> 7237035 accessed Apr052018

3.https://pdfs.semanticscholar.org/2129/3a 0c4f983f9e2ba5920acf5edbb96efbb019.

4.https://www.researchgate.net/publication /305404936_A_Review_on_Statistics_of_ Cancer_in_India [accessed Apr 05 2018]. www.iosrjournals.org

5.Munjal Y,API textbook of medicineVol 2, Association of physician of India, nineth edi 2012,pp 1561.

6.https://en.wikipedia.org/wiki/Carcinogen

 Munjal Y,API textbook of medicineVol
 Association of physician of India, nineth edi 2012,pp1568

8. Created 12/02 UNL Environmental Health and Safety • (402) 472-4925 • http://ehs.unl.edu

9. <u>https://en.wikipedia.org/wiki/Cancer</u> [accessed Apr 05 2018].

10.Sushrut , Sushrut Samhita edited by Murthy K.S .Shastri , Choukhamba Sanskrit Sasnthana Varanasi, Kalpsthana 2/33 , Reprint2007, pp.42.

11. Mangal G, Sharma O, Sharma R, Pharmacokinetics of Vamana & Virechana

Karma, Vol. IV No.1 Jan-Mar 2010 : Journal of Ayurveda

12. Mananvalan G.and Sing J.chemical & some pharmacological studies on leaves ofP.longum,Indian J.pharma.science1979;41-190

13. Pradee CR and Kuttan G, Effect of piperine on the inhibition of lung metastasis induced B16F-10 melanoma cells in mice, J Clin Exp Meta, 19(8),2002, 703-708.

14. Pathak N and Khandelwal S, Modulation of cadmium induced alterations in murine thymocytes by piperine: Oxidative stress, apoptosis, phenotyping and blastogenesis,Biochem Pharmacol, 72(4), 2006,486-497.

15. Lawrence K. Reena Lawrence R.2*,DharmendraP. , Antioxidant activity of Palmarosa essential oil (Cymbopogon martini) grown in north Indian plains, Asian Pacific Journal of Tropical Biomedicine (2012)S888-S891

16. Ali S, Ansari KA, Jafri MA, Kabeer H, Diwakar G. N.jatamansi protects against liver damage by induced bythioacetamide in rats. J Ethonopharmacol 2007; 72:359-363.

17. Rahman H, Shaikh HA, Madhavi P. Areview pharmacognostics &pharmacological property of N. jatamansiDC. Elixir pharmacy 39:5017-5020.

18. Aggarwal SS, Sharma RC, Arora B. Antiestrogenic activity of jatamansone

semicarbazon. Indian J Exper Biol 1973; 11:583.

19. Sengupta A, Ghosh S, Bhattacharjee S. Dietary cardamom inhibits the formation of azoxymethane-induced aberrant crypt foci in mice and reduces COX-2 and iNOS expression in the colon. Asian Pac J Cancer Prev 2005;6(2):118-122.

20. Nair S, Nagar R, Gupta R. Antioxidant phenolics and flavonoids in common Indian foods. J Assoc Physicians India 1998;46(8):708-710. 11229280

21. Raval P. Bhuvan, Patel D. Jignesh , Patel A. Bhavik, Ganure L. Ashok, Potent in vitro anticancer activity of Symplocos racemosa bark , ROM. J. BIOL. – PLANT BIOL., Vol 54, No 2, P. 135–140, BUCHAREST, 2009.

22. Vijayabaskaran M. ,Yuvraja K.R. , Saravanakumar M., Abhenaya K. Evaluation of In vitro Cytotoxic Activity of Ethanolic Extract of Symplocos racemosa Roxb. . International Journal of Pharmaceutical and Clinical Research 2010; 2(1): 28-30.

23. Christudas Sunil, Savarimuthu Ignacimuthu; In vitro and in vivo antioxidant activity of symplocos cochinchinensis S. moore leaves containing phenolic compounds Food and chemical toxicology 49(2011)1604-1609.

24. Wakchaure D., D. Jain, A.K. Singhai and R. Somani, 2010. Hepatoprotective

activity of symplocos racemosa bark on carbon tetrachloride-induced hepatic damage in rats; J. Ayurveda Intregative Med., 2:137-143.

25. Tenpe CR, Aman Upaganlawar, Sushil Burle, Yeole YG. In vitro antioxidant and preliminary hepatoprotective activity of Oroxylum indicum vent leaf extracts. Pharmacologyonline. 2009; 1: 35–43.

 Narisa K, Jenny MW, Heather MAC.
 Cytotoxic Effect of Four Thai Edible Plants on Mammalian Cell Proliferation. Thai Pharmaceutical and Health Science Journal.
 2006; 1(3): 189–95.

27. Roy MK, Nakahara K, Na TV, Trakoontivakorn G, Takenaka M, Isobe Set 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. Pharmazie. 2007; 62(2): 149–53.

28. Nakahara K, Onishi KM, Ono H, Yoshida M, Trakoontivakorn G. Antimutagenic activity against trp-P-1 of the edible Thai Plant: Oroxylum indicum Vent. Biosci Biotechnol Biochem. 2001; 65(10): 2358–60.

29. Tepsuwan A, Furihata C, Rojanapo W, Matsuhima T. Genotoxicity and cell proliferative acitivity of a nitrosated Oroxylum indicum Vent fractioin in the pyloric mucosa of rat stomact. Mutat Res. 1992; 281(1): 55–61. 30. Lotufo LVC, Khan MTH, Ather A, Wilke DV, Jimenez PC, Pessoa Cet al. Studies of the anticancer potential of plants used in Bangladeshi folk medicine. Journal of Ethnopharmacology. 99: 21–30 (2005).

31. Zaveri M, Gohil P, Jain S. Immunostimulant Activity of n-Butanol Fraction of Root Bark of Oroxylum indicum Vent. Journal of Immunotoxicology. 2006; 1; 3(2): 83–99.

32. Zaveri M, Jain S. Gastroprotective effects of root bark of Oroxylum indicum vent. Journal of Natural Remedies. 2007; 7(2): 269–77.

33. Katoch O, Kaushik S, Sadashiv M,
Kumar Y, Paban K. Agrawala, Mishra K.
Radioprotective property of an aqueous extract from Valerian wallichii. Journal of Pharmacy and Bioallied Sciences, 2012: 4;
(4).

34. Kalim M D, Bhattacharya D, Banerjee A, Chattopadhyay S. Oxidative DNA damage preventive activity and antioxidant potential of plants used in Unani system of medicine. BMC Complementary and alternative medicine, 2010; 10: 77.

35. Thusoo S, Gupta S, Sudan R, Kour J,
Bhagat M. Antioxidant activity of essential
oil and extracts of Valeriana jatamansi
roots. Biomed Research International 2014.
36. Lim HS, Jin SE, Kim OS, Shin HK,
Jeong SJ. Alantolactone from Saussurea
lappa exerts anti-inflammatory effects by

inhibiting chemokine production and STAT1 phosphorylation in TNF- α and IFN- γ -induced in HaCaT cells. Phytotherapy Research 2015; 29:1088-1096

37. Youn K, Sung G, Sang M, Yee J, Jeakyung J, Wooyoung K et al. Saussurea lappa Clarke-derived costunolide prevents TNF□-induced breast cancer cell migration and invasion by inhibiting NF-□B activity. Evidence-based Complementary and Alternative Medicine, 2013. ArticleID 936257: 10.

38. Seung H, Seong G, Chan Y, Chong H. Cytotoxic effects of ethanol extracts of Saussurea lappa mediated by mitochondrial apoptotic pathway. Korean Journal of Oriental Medicine. 2004; 25(4):79-89.

39.Ko SG, Kim HP, Jin DH, Bae HS, Kim SH, Park CH et al. Saussurea lappa induces G2-growth arrest and apoptosis in AGS gastric cancer cells. Cancer Letters 2005; (220):11-19.

40. Pandey R. Saussurea lappa extract modulates cell mediated and humoral immune response in mice. Der Pharmacia Lettre. 2012; 4(6):1868-1873.

41. Yaeesh S, Jamal Q, Shah A, Gilani A. Antihepatotoxic activity of Saussurea lappa extract on D-galactosamine and lipopolysaccharide-induced hepatitis in mice Phytotherapy research. 2010; 24(2):233-234. 42. Thara M, Zuhra K. Comprehensive invitro pharmacological activities of different extracts of Saussurea lappa. European Journal of Experimental Biology. 2012; 2(2):417-420.

43. Biondi DM, Rocco C, Ruberto G. New Dihydrostilbene derivatives from the leaves of Glycycrrhiza glabra and evaluation of their anti-oxidant activity. J <at Prod. 2003;
66: 477-480.

44. Jeong HG, You HJ, Park SJ, Moon AR. Hepatoprotective effects of 18β – glycyrrhetinic acids on carbon tetrachloride-induced liver injury, inhibition of cytochrome P450 2E1 expression. Pharmacol Res. 2002, 46: 221-227.

45. Chan HT, Chan C, Ho JW. Inhibition of Glycyrrhizic acid on alfatoxin B1-induced cytotoxicity of hepatoma cells. Toxicology. 2003; 188: 211-217.

46. Watanabe M, Hayakawa S, Isemura M, Kumazawa S, Nakayama T, Mori C, Kawakami. Identification of licocoumarone as an apoptosis -inducing component in licorice. Biol Pharm Bull. 2002; 25: 1388-1390.

47. Hsiang CY, Lai IL, Chao DC, Ho TY.
Differential regulation of activator protein1 activity by glycyrrhizin. Life Sci. 2002;
70: 1643-1656

48. Wagner H and Jurcic K. Immunological studies of Revitonil: a phytopharmaceutical containing Echinacea purpurea and Glycyrrhiza glabra root extract. Phytomedicine. 2002; 9 (5): 390– 397.

49. Hegde K, Deepak TK, Kabitha KK, Hepatoprotective Potential of Hydroalcoholic Extract of Santalum album Linn. Leaves. International Journal of Pharmaceutical Sciences and Drug Research 2014, 6(3), 224-228.

50. Scartezzini P, Speroni E, Review on some plants of Indian traditional medicine with antioxidant activity. J. Ethnopharmacol., 2000; 71: 23-43.

51. Zhang X, Dwivedi C, Skin cancer chemoprevention by □-santalol. Frontiers in Bioscience (Schol Ed.), 2011; 3: 777-787.

52. Santha S, Dwivedi C, Anticancer Effects of Sandalwood (Santalum album). International Journal of Cancer Research and Treatment, 2015; 35 (6): 3137-3145.

53. Dwivedi C, Guan X, Harmsen WL, Voss AL, Goetz-Parten DE, Koopman EM, Johnson KM, Valluri HB, Matthees DP, Chemopreventive effects of □-santalol on skin tumour development in CD-1 and SENCAR mice. Cancer Epidemiology Biomarkers and Prevention, 2003; 12: 151-156.

54. Braakhuis BJ, Tabor MP, Kummer JA, Leemans CR, Brakenhoff RH. A genetic explanation of Slaughter's concept of field cancerization: evidence and clinical implications. Cancer Res 2003;63:1727–1730.