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PHARMACOLOGICAL ACTIVITIES OF *CEDRUS DEODARA*: AN OVERVIEW

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ABSTRACT

Doctrines of Ayurveda have momentous value even in the life of present day human life. These principles are based on the extraordinary observations and experimentations at various levels. Hence one cannot easily deny the observations put forward by the philosophers. According to one of its great preceptors Charaka- the dictum of Ayurveda is to maintain health of healthy people and to alleviate disorders in the diseased persons. The references of medicinal uses of herbs are recorded in Rgveda and Atharvaveda. Nighantus, the well-known compilations- are the very rich sources of herbal drug data ranging from identification,collection to therapeutics uses of the drugs. Since previous two decades there has been an increasing status emphasized on screening of herbs for in order to reduce the risk related to diseases. *Cedrus deodara*, the common cedar is an important plant belonging to the family Conifereae. *C. deodara* has been proven to have great pharmacological potential with a great utility and usage as folklore medicine, Heart wood is the most important part used medicinally. This review summarized the plant characteristics with their pharmacological activities.

Keywords: Pharmacological activities, *Cedrus deodara*..

INTRODUCTION

Nature always stands as a golden mark to exemplify the outstanding phenomenon of symbiosis. The plants are indispensible to man for his life. Nature has provided a complete store-house of remedies to cure all ailments of mankind. Major part of our world population utilized plant medicines either in part or entirely. Growing numbers of health care consumers are turning to plant medicines for many reasons- low cost and seeking natural alternatives with fewer side effects are commonly cited.

Traditional use of medicines is recognized as a way to learn about potential future medicines. Plant derived medicines that have been developed as a result of traditional knowledge being handed down from one generation to the next. Various industries are now searching into sources of alternative, more natural and environmental friendly antimicrobials, antibiotics, diabetics, antioxidants and crop protection agents. Medicinal plants have provided a good source of a wide variety of compounds, such as phenolic compounds, nitrogen compounds, vitamins, terpenoids and some other secondary

metabolites, which are rich in valuable bioactivities, e.g., antioxidant, anti-inflammatory, antitumor, anti-mutagenic, anti-carcinogenic, antibacterial and antiviral activities. Medicinal plants have become the main object of chemists, biochemist, and pharmaceutics. Their research plays an important role for discovering and developing new drugs that hopefully have more effectiveness and no side actions like most modern drugs. These plants are also having some non-medicinal uses such as flavors, foods, ornamentals, spices and fumigants [1, 2].

The World health Organisation (WHO) concluded that 4 billion people, 80 percent of the world population, presently use herbal drugs for some aspect of primary health care. Many pharmaceutical companies are currently doing extensive evaluation of plant material collected from the rain forest and other places rich with the potential medicinal value. Number of plants derived pharmaceutical medicine are used in modern medicine in way correlated directly with their traditional uses as plant medicine of native cultures. These herbal medicines are used from the time of indigenous people's traditional medicine and a common element in an Ayurvedic, homeopathic, naturopathic traditional oriental and Native American Indian medicine[3, 4, 5, 6].The different systems of medicine practiced in India, Ayurveda, Siddha, Unani, Amchi and local health traditions, utilize a large number of plants for the treatment of human diseases. Different authors have been described, identified these medicinal plants[7, 8, 9, 10]. A number of medicinal plants are used as rejuvenators as well as for treating various disease conditions. They may be tonics, anti-malarial, antipyretics, aphrodisiacs, expectorants, hepato- protectives, anti-rheumatics, diuretics etc. An upward trend has been observed in the research on herbals. Export- Import Bank reports suggest that the global trade of plant-derived and plant originated products is around US $60 billion As we know that India, with its mega-biodiversity and knowledge-rich ancient traditional systems of medicine viz. Ayurveda, Siddha, Unani and local health traditions, provides a strong base for the utilization of a large number of plants in general healthcare and alleviation of common ailments of the people. In the present era, allopathic medication is showing severe side effects, it is important to look always a new herbal remedy for treating diseases. Based on the reported data, we are trying to give a review on pharmacological activities for the public interest to implement in daily life . So in this review, the literature tells us about the

Cedrus deodara belonging to the family Conifereae. *Cedrus deodara* commonly known as Devdaar, Diar, Diyar (Hindi) Deodar, Himalaya cedar (English). It is an evergreen conifer tree reaching unto 85 m in height with almost rough black, furrowed bark and spreading branches, shoots dimorphic, leaves 2-5,-5-8 cm needle like Triquetrous, sharp, pointed, flowers usually monoecious, but some trees or branches habitually Bear flowers of one sex [11]. All parts are bitter, hot, slightly pungent, oleaginous in nature.,*Cedrus* is basically tropical and subtropical worldwide distribution; the genus is comprised of trees which are sometimes cultivated either for their usefulness to traditional medicine.

PHARMACOLOGICAL ACTIVITIES OF *CEDRUS DEODARA*

Antimicrobial

Anti-bacterial activity:

Chopra AK *et al.* (2004) Leaf and cone part of plant (*C. deodara)* were extracted with chloroform, methanol and acetone. Chloroform and acetone extracts of cones showed 13 and 14 mm zones of inhibition, respectively, whereas acetone and methanol extracts of leaf exhibited 12 and 14 mm, respectively, in broth dilution assay using ampicillin (10g/disc) as positive control exhibiting 14 mm or more zones of inhibition. The chemical composition of *C. deodara* and volatile oils obtained from the leaves by steam distillation was analysed using gas chromatograph and mass spectroscopy analysis (GC-MS). To evaluate in vitro antimicrobial activity, all volatile oils were tested against Gram-positive and Gram-negative bacteria. Volatile oil and α- and β-pinene shows good anti bacterial activity. Extract and oil obtained from the root, stem, and leaf of plant were tested against *E. coli.* Both the oil and extract shows significant inhibition of the test organism [12].

Patel RB (2010) Ethanolic extract from the wood part of plant was evaluated against three gram positive(*Staphylococcus aureus, Enterococcus faecalis, Bacillus cereus*) and three gram negative *(Klebsiella pneumonia, Pseudomonas aeruginosa, Escherichia coli)* micro organism *and C. deodara* found to have a good antibacterial action [13].

Anti-fungal activity:

Yadav RS *et al.* (2006) The fungicidal activity is persisted for longer period in essential oils of the plant [14].

Essien EP and Essien JP (2000) The anti-fungal effects of the essential oil of *Cedrus deodara* Roxb. , as well as some of its active components, against storage moulds of Capsicum annuum L. have been previously investigated [15].

Praveen R *et al.* (2010) The antifungal activity of root oil and compounds isolated from the oil were evaluated against *Candida albicans* and *Aspergillus fumigatus. Cedrus deodara* oil at the concentration of 150 µg/disc showed zone of inhibition against *A. fumigatus* but at the same concentration did not show any antifungal activity against *C. albicans.*Trans-atlantone and allo-himachalol, isolated from the oil also have not shown any antifungal activity, while himachalol at the concentration of 150 µg/disc showed zone of inhibition against *A. Fumigates* [16].

Pawar VC and Thaker VS (2005) The anti-*Fusarium oxysporum* f. sp cicer (*FOC*) and anti-*Alternaria porri* (*A. porri*) effects of C. *deodara* shows potent anti fungal activity against both the fungal strains [17].

Insecticidal activity:

Singh D and Aggarwal SK (1988) Previously, from screening program of natural products for insecticidal properties, it was already found that Himalayan cedarwood oil show cidal property against adult Indian mosquitoes, *Anopheles slephensis*, at low conc. (KD50 0.4452% in acetone). Plant is enriched with qualities like pleasant odor, low cost, abundant availability of raw material and high potency against mosquitoes. These results make us to investigate further the insecticidal principle of Himalayan cedarwood oil. Chromatographic fractions of Himalayan Cedarwood oil were bioassayed against the Pulse beetle (*Callosobruchus analis F.*) and housefly (*Mucus domestica L.*). Almost all fractions showed insecticidal activity against both the test species [18].

Mollusicidal activity:

Singh A and Singh DK (2001) Mixtures of three plants were used against *Lymnea acuminate.* Fruit powder of *Embelia ribes* in combination with *Azadirachta indica* and *Cedrus deodara* oil with synergists MGK-264, piperonyl butoxide (PB) in binary and tertiary combinations. Combination of these three was more toxic with respect to the single treatment of the plant-dervied molluscides. The order of toxicity of various tertiary combinations against *Lymnaea acuminata* was *Lawsonia inermis* seed + *Cedrus deodara* + *Embelia ribes* > *Lawsonia inermis* seed + *Azadirachta indica* + *Embelia ribes* >

Lawsonia inermis seed + *Polianthes tuberosa* + *Embelia ribes* > *Lawsonia inermis* seed + *Allium sativum* + *Embelia ribes.* Combination in the ratio of (1:1:1) of *Lawsonia inermis* seed powder with *Cedrus deodora* oil and *Embelia ribes* fruit powder against *Lymnaea acuminate* revealed maximum inhibition against *Lymnea acuminate* [19].

Anti-tubercular activity:

Gautam R *et al.* (2007) Chloroform and acetone extract obtained from the leaf and cone part of plant shows good anti-tubercular activity caused by mycobacterium tuberculosis in tuberculosis gland. Cone showed 13 and 14mm zone of inhibition and leaf exhibited 12 and 14mm of inhibition respectively. Methodology applied was broth dilution method and ampicillin was taken as positive control, which exhibit 14mm of zone inhibition [20].

Central nervous system

Anxiolytic and anticonvulsant activity:

Emamghareishi M. *et al.* (2005) Currently the most widely prescribed medication for anxiety disorders are Benzodiazepines but because of unwanted side effects, development of new pharmacological agents from plants sources is well justified [21]. For this reason anticonvulsant and anxiolytic activity of the plant was evaluate. The heart wood extracts of *Cedrus deodara* (ALCD) was studied for anxiolytic and anticonvulsant activity by three experimental models namely Elevated plus maze test, Light dark model, locomotor activity by actophotometer and anticonvulsant activity was studied by using Pentylene tetrazole induced convulsions and Maximal electro shock induced convulsions and pretreatment with ALCD followed by estimation of GABA in rat brain tissues was performed to study the effect of ALCD on GABA levels of brain.

Hogg SA (1996), Rodgers RJ and Johnson NJT (1998), Pellow S and File SE (1986) The elevated plus maze is currently one of the most widely used models of animal anxiety [22,23,24]. The animals being exposed to the new environment tend to avoid open entries and prefer to stay in closed arm due to fear. The ALCD at 50, 100 and 200mg/kg doses has significantly increased the time spent and number of entries in to the open arm indicating the test drugs could reduce the fear and anxiety in the mice. In Light dark model, ALCD (50, 100, 200mg/kg) has increased the time spent and number of entries in to the light compartment. Anxiolytics should reduce the natural aversion to light, the essential feature of this model is that anxiolytic drugs increase the number of crossings

and/or the time spent in the light compartment. Khosla P and Pandhi P *et al.* (2001) These results suggests that, extract administration could reduce the aversion fear and produce anxiolytic activity.

Vogel HG and Vogel WH (2000), Viswanatha GL *et.al* (2009) In pentylene tetrazole induced convulsions model [25] the ALCD (100, 200 mg/kg) has significantly increased the onset of clonus, onset of tonus and percentage protection when compare to control group and in MES induced convulsions model [26]. ALCD (100, 200 mg/kg) has significantly decreased the duration of tonic extensor and increased the percentage protection when compare to the control group. GABA appears to play an important role in the pathogenesis of several neuropsychiatric disorders. Many of the traditional agents used to treat psychiatric disorders are known to act, at least in part, by enhancing GABA activity, while some of the newer agents may exert their therapeutic effects exclusively via GABAergic actions. So the result shows that seven days treatment with ALCD (30 mg/kg, 100mg/kg p.o.) and further GABA estimation in brain showed significant enhancement of GABA levels in cerebellum and whole brain other than cerebellum compared to control group [27].

Neuroleptic activity:

Agarwal PK and Rastogi RP (1981) Traditionally the heartwood of *C. deodara* plant was used to enhance cerebral function, balance the mind, body connection, nervous system and strengthen the brain. It was reported to possess CNS depressant and neuroleptic activity [28].

Metabolic Disorder

Anti-diabetic activity:

Pandey S *et al.* (2009) Powdered woods of *C. deodora* defatted with petroleum ether and extracted from ethanol. Further ethanol extract was subjected for physiochemical screening. From phytochemical screening *Cedrus deodora* woods gave positive result for thr presence of glycosides, tannins, fixed oils, flavanoids, and triterpenoids. Preformulation studies were carried out for the investigation of physicochemical character of a drug substances alone and when combined with excipients. The overall objective of preformulation testing was to generate information useful in developing stable and bio available dosage form. In preformulation studies, the formula was designed

(PF1, PF2, PF3) with different concentration of excipients. In PF1 (with lactose) and PF2 (with starch) granules were not found. Formulation PF3 (with microcrystalline cellulose) shown formation of granules and granules were further evaluated for physical character and in vitro studies. The in vitro drug release studies of formulation PF3 showed 80.56 ± 1.06% of drug release.

The *C. deodara* wood extract were, then made into capsule with various pharmaceutical excipients and then evaluated. The formulation F3 (per capsule: crude extract 190 mg, micro crystalline cellulose 159 mg, dicalcium phosphate 71.4 mg, methylparabe sodium 6.6 mg, propyl paraben sodium 5 mg, magnesium stearate 11 mg, talc 7 mg) was selected as best formulation compare to the other formulations. The capsule prepared from the wood extract of the plant, above mentioned formula was subjected to *in vivo* studies, such as, acute toxicity and antidiabetic which revealed that the study had a vital role in the management of diabetes [29].

Antioxidant activity:

Halliwell B and Gutteridge JMC (1989) The brain and nervous system are rich in lipid and iron, both known to be important in generating free radical species, so these two part of our body are highly susceptible to free radical damage than other tissue. *C. deodara* was also reported to have good antioxidant property [30]. Two processes were involved to identify the antioxidant components of *Cedrus deodara.* Fractionation and purification was done of dried heartwood powder of *C. deodara*, first defatted with petroleum ether and then extracted with chloroform. The chloroform extract showed strong antioxidant activity on 1, 1-diphenyl-2-picrylhydrazyl (DPPH) free radical. This fraction was then forwarded to separation and purification using silica gel column chromatography. Three compounds with potent antioxidant activity were isolated in significant yields and identified by spectroscopic methods (1H NMR, 13C NMR, IR, and MS). They were identified as (-)-matairesinol, (-)-nortrachelogenin, and a dibenzylbutyrolactollignan (4, 4', 9-trihydroxy-3, 3'-dimethoxy-9, 9'-epoxylignan).

Kidney and Gastro Intestinal Disorder

Diuretic and Anti- Urolithiatic activity:

C.Ramesh *et al.* (2010) Petroleum ether extract (PECD) of the heart wood of *C. deodara* was tested for its diuretic and anti- urolithiatic activity. Sodium oxalate (70mg/kg, i.p) for

10 days was experimentally used to induce urolithiasis. In sodium oxalate treated rats, crystal was observed in urine under light microscope and elevation of serum parameters indicated the development of nephrolithiasis in the control group. Administration of PECD for 10 days along with inducing agent i.e, sodium oxalate prevented elevated serum biochemical levels due to the elimination of these in urine. Histology study shows that PECD treatement had protected against sodium oxalate induced nephrolithiasis. So from the above study, it was concluded that the plant has great potential to inhibit stone formation [31].

Antispasmodic activity:

Kar K. *et al.* (1975) Himachalol is one of the major constituent of wood of plant, which is having antispasmodic activity. The pharmacological studies of himachalol on various isolated smooth muscles (rat uterus, guinea pig seminal vesicle, and guinea pig ileum and rabbit jejunum) and against different agonists (acetylcholine, histamine, serotonin, nicotine, and barium chloride) indicated spasmolytic activity similar to that of papaverine. It has potent antagonist activity against barium chloride-induced spasm of guinea pig ileum than papaverine but less effective in case of rabbit jejunum and had no relaxing effect alone. In the conscious immobilized cat, intragastric administration of himachalol or papaverine (100 mg/kg) produced same rate of inhibition of carbachol-induced spasm of the intestine, lasting about 2 hr, but himachalol had much faster onset of action than papaverine. Effectiveness of papaverine in antagonizing epinephrine-induced contraction of the guinea pig seminal vesicle was less than himachalol but himachalol was devoid of spasmolytic effect on the bronchial musculature of guinea pig. Intravenous injection of himachalol (3–10 mg/kg) in the cat produced a dose-dependent fall in blood pressure and an increased femoral blood flow [32].

Anti-secretory and anti-ulcer activities:

Kumar A. *et al.* (2011) The volatile oil extracted by steam distillation of *C. deodara* wood was examined for its gastric anti-secretory and antiulcer effect in the pylorus-ligated rat model and ethanol induced gastric lesions in rats. It was reported that volatile oil showed significant anti-secretory activity as evidenced by decreased gastric fluid volume, total acidity, free acidity and increase in the pH of the gastric fluid in pylorus-ligated rats and this study revealed that pretreatment with *Cedrus deodara* significantly

reduced the number of ulcer, ulcer score and ulcer index in pylorus-ligated and ethanol treated rats [33].

Bone and Joint Disorder

Anti-inflammatory and anti-arthritic activity:

Winter CA. *et al.* (1962) Aqueous extract of air dried stem bark of the plant was screened for ifs anti-inflammatory and anti-arthritic activity. In carrageenan induced inflammation utilizing the technique of Winter *et al* 1962 [34]. The animals were injected with 0.05ml of 1% suspension of carrageenin, in the hind paw and then the result of *C. deodara* was compared with standard drug, betamethasone and phenylbutazone. *C. deodara* was found to be less effective than standard. Anti-infammatory activity was further evaluated using granuloma pouch and cotton pellet method.

Standard used were the same and result obtained reveals that Betamethasone shows marked decrease in the volume of exudates as compared to control (40%). On the other hand *C. deodara* and phenylbutazone significantly decrease the volume exudates 20% and 30%. But the anti-inflammatory activity of *Cedrus deodara* did not show significant inhibition of Tuberculin rxn. The volatile oil of the wood of the plant (50 and 100 mg/kg, p.o.) produced a significant inhibition of compound 48/80 and nystatin-induced rat paw edema.

The anti-inflammatory activity of *C. deodara* was further studied on formaldehyde induced arthritis by the method of Selye (1949) [35] and on adjuvant arthritis by the technique of Newbould (1963) [36].

Rathor RS and Goyal HR (1973) Formaldehyde induced arthritis was produced in animals by injecting 0.1 ml of 2% formaldehyde (V/V) into the hind paw under the planter aponeurosis. Similarly, adjuvant arthritis was induced in animals by injecting 0.05 ml of Freund's adjuvant containing a suspension of heat killed tubercle bacilli (human D.T. strain) in liquid paraffin (5 mg/ml).both the standard drug and *C. deodara* shows antiarthritic activity**.** Incidence of gastric ulcer was maximum with betamethasone and minimum with *C. Deodara* [37].

Wound healing property:

Dikshit A and Dixit SN (1982) its oil has been reported to possess anti-inflammatory and anti-microbial activities. The plant has also shown wound healing properties and is particularly useful in infective wounds [38].

Pharmacological Activity on Cells

Immunomodulatory activity:

Shinde VA *et al.* (1999) Volatile oil of *cedrus deodara* at a dose 50 and 100mg/kg significantly inhibit neutrophil adhesion to nylon fibers and also inhibit type III hypersensitivity reaction i.e., arthus reaction induced by methylated bovine serum albumin and it also inhibit the sheep erythrocytes and oxazolone induced delayed type hypersensitive reaction [39].

Cytotoxic activity:

Singh SK *et al.* (2007) "CD lignin mixture" isolated from the stem wood of *Cedrus deodara* consisted of (-)-wikstromal (75 - 79 %), (-)-matairesinol (9 - 13 %) and benzylbutyrolactol (7 - 11 %). This mixture was evaluated for its in vitro anticancer activity. The in vivo anticancer activity of CD lignan mixture was studied using Ehrlich ascites carcinoma and colon carcinoma (CA-51) models in mice. Also effect was studied on annexin V binding, intracellular caspases and DNA fragmentation to gain insight into the mode of action. This lignin mixture showed significant dose-dependent effects against several cancer cell lines such as cervix, colon, liver, prostate and neuroblastoma at 10, 30 and 100 mg/mL [40].

Anti – malarial activity:

Makhaik M *et al.* (2005) Essential oil from *C. deodara* was evaluated for bioactivity against the adults of *Culex quinuefasciatus* and *Aedes aegypti.* Wood chips of plant were used to obtain essential oil. Clevenger's type apparatus was used to obtain essential oil from crushed wood chips of the plant. Adults of *A. aegypti* were insensitive towards the oil of *C. deodara* under the conc. range and 1hr of exposure whereas against *C. quinuefasciatus,* reported LC50 was 2.48% respectively, indicating low effictivity. Plant shows moderate activity against these two mosquitos [41].

Mast cell stabilizing and lipoxygenase inhibitory activity:

Kale RN *et al.* (2010) Volatile oil of *C. deodara,* administered orally at the doses of 50, 100 and 200 mg/kg body weight. It significantly inhibited the pedal edema induced in rat

by 48/80 compound. It also inhibits the enzyme lipooxygenase, key factor to cause edema at a conc. of 200 micrograms/ml. Thus, *C. deodara* wood oil is act as a potent inhibitor of inflammation by showing the property of mast cell stabilizing activity and the inhibition of leukotriene synthesis. Further himachalol which is isolated from the wood part of the plant is also used in asthma, having the property of mast cell stabilization [42].

Anti-allergic activity:

Singh A.P *et al.* (2005) Phytochemical investigation shows that presence of some medicinal important constituents in the plants are responsible for the treatment various disease. Likewise, himachalol is one of the major constituent which is reported to have potent anti-allergic property [43].

DISCUSSION AND CONCLUSION

Herbal medicine has become a popular form of health care, even though several differences exist between herbal and conventional pharmacological treatments. Several specific herbal extracts have been demonstrated to be efficacious for specific conditions. Even though public do the carry risk of taking allopathic medicine instead of herbal treatments. It is seen from the literature that *C. deodara* possesses have many qualities, including anti-inflammatory, antitumor, and immunomodulatory properties, as well as exerting an influence on the nervous system, cytotoxic effect, neuroleptic effect, antioxidant property. Further, clinical studies can be conducted, as well as studies in multiple animal-based models using a variety of suitable biochemical markers to understand its mechanism of action. It is also important for isolation and much more effective when given in combination with other herbs.

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