REVIEW ARTICLE

# A review on phytochemical, ethnobotanical, pharmacological, and antimicrobial importance of *Cedrus deodara* (Roxb. Ex D. Don) G. Don

**Dwaipayan Sinha**

*Department of Botany, Government General Degree College, Paschim Medinipur, West Bengal, India*

**Abstract**

*Cedrus deodara* (Roxb. Ex D. Don) G. Don is a conifer that grows in the Himalayan regions of India, Pakistan, and Nepal. The plant is an evergreen tree belonging to the family Pinaceae and forms extensive forest along the Himalayan Mountain. The plant is traditionally used by people for thatching, sheltering, furniture making, fuelwood, and medicinal purposes. The plant is rich in flavonoids and terpenoids such as deodarin, cedrusone A, myricetin, 2R, 3R-dihydromyricetin, quercetin, 2R, 3R-dihydroquercetin, α-pinene, β-pinene, myrcene, limonene-α, β-caryophyllene, β-copaene, α-himachalene, β-humulene, γ-muurolene, β-himachalene, Germacrene D, α-muurolene, δ-cadinene, and γ-amorphene. Research has been carried out to explore the pharmacological and antimicrobial activities of various parts of the plants with promising outcome. Extensive literature survey was made and the information in relation to *C. deodara* was pooled from scientific research papers through electronic search tools available in the internet. This review paper is an attempt to highlight the ethnobotanical, pharmacological, and antimicrobial importance of *C. deodara* along with its wide array of chemical constituent. The plant can be a potent and cheap source of raw materials, leading to drug development for the benefit of the population of India and adjoining countries.

**Key words:** Antimicrobial activity, Cedar, *Cedrus deodara,* pharmacological activity, α-pinene

## INTRODUCTION

The Himalayan region is one of the most important biodiversity hotspots and comprises the highest topographical region of the world including most of the major peaks. The Himalayan biodiversity region arches over 3000 km from northern Pakistan, Northwestern India, Nepal, Sikkim, Bhutan, and Northeastern states of India covering around 750,000 km$^2$.[1] The region is formed due to collision of Indian plate with the Eurasian plate around 40–50 million years ago resulting in the rise of the Himalayan mountains along with Tibetan plateau.[2] It is also assumed that there is phase wise collision between Eurasian and Indian plates during the formation of the Himalayas with a soft collision during the Eocene and a hard collision during the Miocene. This phase wise evolution of the Himalayas provided a golden and unique opportunity to the flora and fauna arriving from various directions of rapidly reorienting landscape to colonize the new region and gradually diversifying themselves in the new ecosystem.[3]

The far-flung geographical stretch and rapid sudden increase in altitude from the alluvial plains of Indus, Sutlej, Ganga, Yamuna, and Brahmaputra resulted in variations in climatic condition of the Himalayas and resulted in species richness of the location. The highest species richness is observed in the biodiversity hotspot of the eastern Himalayas gradually declines toward the west and northwest. The Himalayan regions boast of 10,503 plant species from 240 families and 2322 genera.[4]

Gymnosperms form an important entity of plant biodiversity in the Himalayas. A total of 146 species and eight varieties of 46 genera belonging to 12 families are present in the Indian subcontinent, of which majority grows in the

**Address for correspondence:**
Dwaipayan Sinha, Department of Botany, Government General Degree College, Paschim Medinipur, West Bengal, India. Phone: +91-9007709999.
E-mail: dwaipayansinha@hotmail.com

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Himalayas.[5] The Himalayan cedar or *Cedrus deodara* is one such gymnosperm belonging to the family Pinaceae that grows in abundance in the Himalayan region. The plant is native to large stretch of the Himalayan region starting from Western Himalayas in east Afghanistan, north and northwest Pakistan, North and Central India, southwestern Tibet, and Western Nepal.[6] The plant generally grows at an altitudinal range of 1800 m–2600 m above sea level and a longitude of 69°E–83°E.[7] The total area of *C. deodara* forest in India is estimated to be around 203,263 hectare.[8] The plant finds extensive use among the local people of the region. This paper aims to highlight the traditional use of the plant in the Himalayan region and along with its pharmacological and antimicrobial importance.

## Classification

Kingdom: Plantae
Phylum: Tracheophyta
Division: Pinophyta
Class: Pinopsida
Order: Pinales
Family: Pinaceae
Genus: *Cedrus*
Species: *Deodara*[9]

## Vernacular Names[10]

- Sanskrit: Bhadradaru, Surabhuruha, Amaradaru, Devakastha, Daru, Suradaru, Amarataru
- Assamese: Shajar Tuljeen
- Bengali: Devdaroo
- English: Deodar, Himalayan Cedar
- Gujarati: Devdar, Teliyo Devdar
- Hindi: Devdar, Devdaroo
- Kannada: Deevdar
- Malayalam: Devtaram
- Marathi: Devdar, Telya Dedaroo
- Punjabi: Diyar, Dewdar
- Tamil: Devdaroo
- Telugu: Devdari Chettu, Devdaree
- Urdu: Deodar.

## Description of the Plant

*C. deodara* is a large evergreen tree attaining a height of 65 m and >4 m in girth. The stem is branched and branches arise in an irregular fashion from the stem in slightly ascending or descending fashion [Figure 1a]. The stem is covered by grayish-brown to dark brown barks with vertical or diagonal cracks divided into oblong scales. The leaves are solitary, acicular, and stiff with pointed apex, 25–37 cm long, silvery or silver-blue in color. They are arranged spirally on normal shoots and in pseudowhorls on short arrested shoots. Male flowers solitary, erect, catkin-like, pale green to purplish, oblong, ovoid, 2.5–4.6 cm in length, and 1–1.5 cm in diameter. At maturity, they attain a height of 5–7.5 cm and become yellowish due to the presence of pollen [Figure 1b]. The female flowers are solitary and erect borne at the end of arrested branchlets. At the time of pollination, the female flowers are oblong, ovoid, 1.2–2 cm in length and 0.6 cm in diameter, and pale glaucous green in color. At maturity, the female cones are 7.5–12 cm long and 5–8.7 cm in diameter with numerous fan-shaped scale or megasporophyll arranged in spiral fashion on a persistent woody central axis [Figure 1c]. At maturity, the cones are reddish-brown. Each scale bears a pair of winged seeds which are 2.5–3.7 cm long and 2–2.5 cm broad.[11]

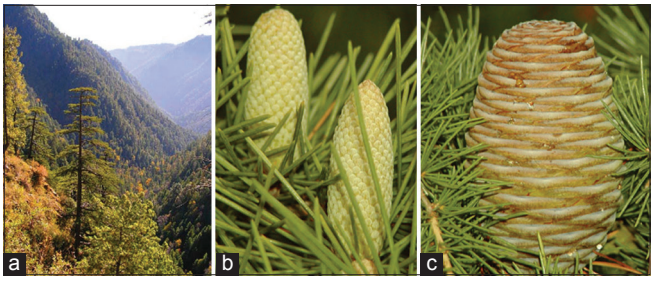


**Figure 1:** *Cedrus deodara* (a) tree in natural habitat, (b) male cones, (c) female cone[12]

## Chemical Constituents

### *Constituents of stem bark*

#### *Flavonoids*

Dihydroflavonol called deodarin was isolated from stem bark of *C. deodara* and from further study of its reaction and spectra, the chemical name 3', 4', 5, 6- tetrahydroxy-8-methyl-dihydroflavonol was assigned to the compound.[13]

### *Constituents of wood and wood oil*

#### *Terpenoids*

An important constituent of wood is sesquiterpene himachalol and possessed spasmolytic activity.[14] Another sesquiterpene by the name Centradol was identified in the wood of the plant and its structure was elucidated as 2β, 7β-dihydroxyhimachal-3-ene through spectroscopic methods.[15] Consequently, the chemical nature and structure of isocentradol were also elucidated.[16] In addition, himachalol and another sesquiterpene, namely β-himachalene, were also isolated from wood oil by chromatographic techniques and both the compounds showed insecticidal principles.[17] The *in vitro* antioxidant activities of the chloroform extract of wood was also investigated and the structures of its constituent compounds were elucidated. Five sesquiterpenes, namely atlantone, himaphenolone, atlantolone, deodardione, and atlantone-2, 3-diol, were identified. It was observed that there was a dose dependent reducing power and strong total antioxidant capacities of himaphenolone and atlantone-2, 3-diol. Deodarone and atlantolone also exhibited antioxidant potentials.[18] Other sesquiterpenoids found in the heartwood of the plant include allohimachalol, himadrol, dewarol dewardiol, dewarenol, and its 4'-glucoside isopermic

**Table 1:** Details of the compounds isolated and identified from various parts of *Cedrus deodara*

| S. No. | Plant parts | Nature of the compound isolated | Name of the compound | Reference |
|---|---|---|---|---|
| 1. | Stem bark | Dihydroflavonol | Deodarin (3', 4', 5, 6-tetrahydroxy-8-methyl-dihydroflavonol) | [13] |
| 2. | Wood | Sesquiterpene | Himachalol | [14] |
| 3. | Wood | Sesquiterpene | Centradol (2β, 7β-dihydroxyhimachal-3-ene) | [15] |
| 4. | Wood | Sesquiterpene | Isocentradol (4β, 7β-dihydroxyhimachal-2-one) | [16] |
| 5. | Wood oil | Sesquiterpene | Himachalol, β-Himachalene, α- Himachalene, Allohimachalol, (+)-longborenol. | [17,19] |
| 6. | Wood | Sesquiterpenes | Atlantone, himaphenolone, atlantolone, deodardione and atlantone-2, 3-diol | [18] |
| 7. | Heartwood | Sesquiterpenoids | Allohimachalol, himadrol, dewarol dewardiol, dewarenol. | [19] |
| 8. | Wood | Dihydroflavonols | Cedeodarin (6-methyltaxifolin), dihydromyricetin, cedrin (6-methyldihydromyrecetin), cedrinoside | [20] |
| 9. | Needle essential oil | Terpenes | α-Pinene, β-pinene, β-myrcene, limonene, α-bisabolol | [21] |
| 10. | Needle essential oil | Terpenoids | α-Pinene, β-pinene, myrcene, limonene-α β-caryophyllene, β-copaene, α-himachalene, β-humulene, γ-muurolene, β-himachalene, germacrene D, α-muurolene, δ-cadinene, γ-amorphene | [22] |
| 11. | Needles | Flavonoid glycosides | Myrecetin-3-O-(6"-O-E-p-coumaroyl)-α-D-glucopyranoside, 3',5'-Di-O-methylmyricetin-3-O-(6"-O-acetyl)-α-D-glucopyranoside, | [23] |
| 12. | Needle | Flavonoids | Cedrusone A, myricetin, 2R, 3R-dihydromyricetin, quercetin, 2R, 3R-dihydroquercetin. | [24] |
| 13. | Needle essential oil | Terpenoids | α-Pinene, α-myrcene dl-limonene, trans-caryophyllene, α-humulene, linalyl propionate, dodecanoic acid, caryophyllene oxide, 1-dodecanol | [25] |
| 14. | Petroleum ether extract of needle | Miscellaneous | α-pinene, 4-allyloxy-2-methyl penta-en-2-ol, 2,2-dimethylpentanal, butyl acetate, 2-methyl-5-phenyl-5-pentanonenitrile, benzoic acid, ethyl ester of dodecanoic acid, caryophyllene oxide, butyl ester of 5-oxohexanethioic acid | [25] |
| 15. | Needles | Polysaccharides | Individual units of glucose, arabinose, mannose, and xylose. | [26] |

form while sesquiterpenoids, namely α- and β-himachalenes, himachalol, allohimachalol, and (+)-longborenol, are present in wood oil of the plant.[19]

### *Flavonoids*

Four dihydroflavonols, namely cedeodarin (6-methyltaxifolin), dihydromyricetin, cedrin (6-methyldihydromyrecetin), and cedrinoside from the wood, were also isolated and identified.[20]

## *Needle and needle essential oil*

### *Terpenoids*

The components identified in the needle essential oil of the plant species can be grouped into compounds containing monoterpene hydrocarbons (44.5–88.1%), oxygenated monoterpenes (0.1–22.8%), and sesquiterpenes hydrocarbons (3.8–17.6%). α-Pinene was the major constituent found in the essential oil of *C. deodara*. The other constituents were β-pinene (5.2–10.3%), β-myrcene (5.3–7.4%), limonene (6.6–16.0%) and α-bisabolol (3.5–6.6%),[21] benzaldehyde (19.4%), β-caryophyllene (10.9%), myrcene (10.7%), and germacrene D (9.35%).[22]

### *Flavonoids*

Among flavonoids, myrecetin-3-O-(6"-O-E-p-coumaroyl)-α-D-glucopyranoside, 3',5'-Di-O-methylmyricetin-3-O-(6"-O-acetyl)-α-D-glucopyranoside, myricetin,[23,24] cedrin and 2R, 3R-dihydromyrecetin,[23,24] cedrusone A, quercetin, and 2R, 3R-dihydroquercetin were isolated and identified from the needles of the plant through gel chromatography followed by nuclear magnetic resonance (NMR) analysis.[24]

## *Miscellaneous compounds*

Among other compounds dodecanoic acid (12.9%) followed by linalyl propionate (10.9%) were important representatives

of needle essential oil while butyl acetate (33.9%) and 4-allyloxy-2-methyl penta-en-2-ol (6.2%) formed the major constituent of the petroleum ether extract.[25] Polysaccharides were also isolated from the needles and antioxidant properties of the same were investigated. Chromatographic and mass spectrometric analysis of the compound isolated from needles of the plant turned out to be an acidic heteropolysaccharide composed of glucose, arabinose, mannose, and xylose in a molar ratio of 45.84:1:2.35:1.73 and a molecular weight of $1.53 \times 10^4$ Daltons. The backbone of the molecule was composed of glucose, mannose, and xylose having 1→4 linkages. In addition to it, the compound exhibited remarkable free radical scavenging activity and inhibited oxidative DNA injury.[26] All the compounds isolated from various plant parts of *C. deodara* discussed in this paper are tabulated in Table 1 while the molecular structures of some compounds are illustrated in Figure 2.

### *Ethnobotanical uses*

*C. deodara* finds extensive use among local people of the Himalayan region. The plant is extensively used for thatching and sheltering purpose,[28] construction of house, temples, furniture, and bridges.[29] In some region, the plant is also used as timber wood, torchwood, and fuelwood.[30] The plant is also extensively used for medicinal purpose by the local people inhabiting in the Himalayan region. The plant is used for the treatment of fever, diabetes, intestinal parasite, and sinusitis.[31] The resin of the plant possesses anthelmintic properties and is used for the treatment of rheumatism,

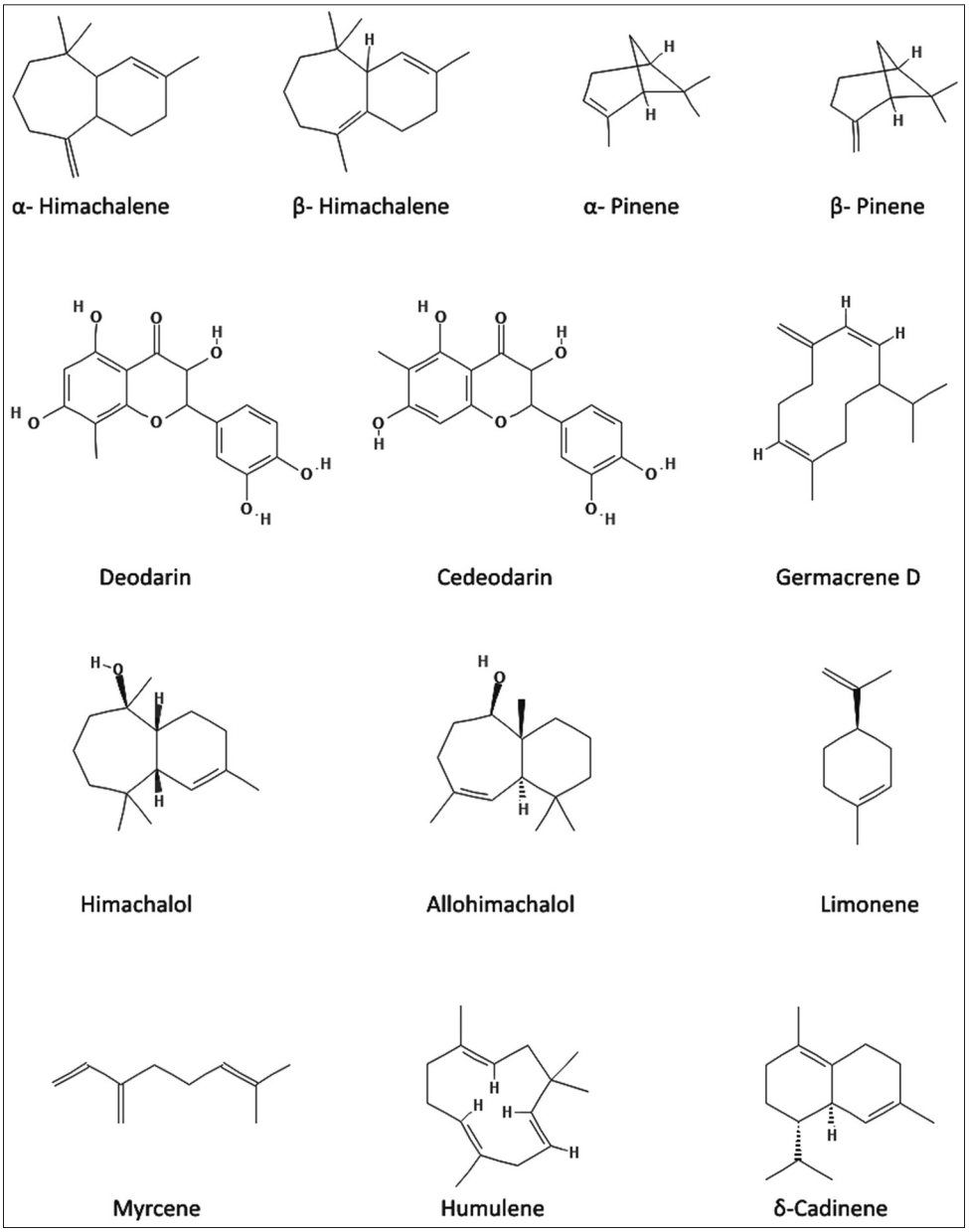


**Figure 2:** Molecular structures of selected chemical compounds isolated from *Cedrus deodara*[27]

ulcers, boils, bone fracture, cracks in sole of feet, leprosy, skin diseases, snakebites, sprains, swellings, ulcers, and urine problems.[32] The wood oil is used for the treatment of arthritis, joints pain, cracks, body ache,[33] skin rashes, external ulcers, and itching,[34] while bark oil is used to cure itching, dermatitis, and relief from stomach worms.[35] The wood has carminative, diuretic, and diaphoretic properties and is used for the treatment of fever, flatulence, heart palpitation, paralysis, pulmonary trouble, and urinary diseases.[36] The extract of leaf is used in massage to get relief from body pain.[37]

## Pharmacological Activity

### *Antiapoptotic activity*

AP9-cd, a standardized mixture of lignans consisting of (-)-wikstromal (75–79%), (-)-matairesinol (9–13%), and dibenzylbutyrolactol (7–11%), obtained from wood powder waste of *C. deodara* was reported to play a role in induction of apoptosis and nitric oxide generation in human leukemia Molt-4 cells and HL-60 cells. The mixture inhibited proliferation of Molt-4 cell, increased sub-G0 cell fraction with no mitotic block, produced apoptotic bodies, and induced the formation of DNA ladder. Generation of nitric oxide, appearance of peroxides, decrease of mitochondria membrane potential, and increase in caspases-3, caspases-8, and caspases-9 activity were also brought about by AP9-cd in Molt-4 and HL-60 cells. The results from the study indicated the initiation of apoptotic pathway, leading to destroy of leukemia cell.[38]

### *Anticancer activity*

A "CD lignan mixture," composed of (-)-wikstromal (75–79%), (-)-matairesinol (9–13%), and benzylbutyrolactol (7–11%), obtained from stem wood of *C. deodara* exhibited anticancer activity *in vitro* cytotoxic studies showed significant dose-dependent effects of the mixture against breast, cervix, neuroblastoma, colon, liver, and prostate cell lines at concentrations of 10, 30, and 100 µg/mL, respectively, with $IC_{50}$ values varying from 16.4 ng/mL to 116.03 µg/mL in various cell lines. The $IC_{50}$ values of CD lignan mixture exhibited a synergistic effect in comparison to its individual constituents. The CD lignan mixture also activated caspases in K562 cells and produced a distinct DNA ladder in HL-60, K562, and MOLT-4 cells. The content of hypodiploid cells (sub-$G_1$ phase) was increased by administration of CD lignan in comparison to control which suggested cytotoxic potential of Cd lignan against human cancer cell lines and induction of tumor regression.[39]

AP9-cd exhibited anticancer activity against Molt-4, HL-60, PC-3, and A-549 cell lines. It was found that AP9-cd significantly reduced the viability of Molt-4 cells in a time and dose-dependent manner with disruption of mitochondrial cristae at 30 µg/mL concentration. This was accompanied by chromatin condensation, vacuolization, and formation of micronuclei. Moreover, surface ultrastructural studies of four different tumor cell lines, namely Molt-4, HL-60, PC-3, and A-549, treated with AP9-cd showed loss of surface projections, condensation, and formation of apoptotic bodies. In addition, it was reported that Drosophila, carrying human adenomatous polyposis coli gene enhanced eye phenotypes when treated with AP9-cd can inhibit Wnt/Wg pathway, an important in the etiology of a number of human cancers. All these results suggested the anticancer potential of AP9-cd.[40]

### *Antiproliferative activity*

The wood essential oil from three species of *Cedrus,* namely *Cedrus atlantica, Cedrus libani,* and *C. deodara* subdued the proliferation of K562 cell line with $IC_{50}$ values 23.38 ± 1.7 µg/mL, 59.37 ± 2.67 µg/mL, and 37.09 ± 1.47 µg/mL, respectively. In addition, the wood essential oil of *C. libani, C. deodara,* and *C. atlantica* induced erythroid differentiation of 15 ± 2% at 5 µg/mL, 20 ± 2% at 25 µg/mL, and 12 ± 1.8% at 10 µg/mL concentrations, respectively. The results suggest that wood essential oil of the three species of *Cedrus* is potent source of active principles required for the production of anticancer drugs.[41]

Flavonoids extracted and purified from needles of *C. deodara* were tested for antitumor activity. It was observed that the total flavonoid content of the needle of *C. deodara* reached up to 54.28% in which quantities of major ingredients, namely myricetin, quercetin, kaempferol, and isorhamnetin were 1.89, 2.01, 2.94, and 1.22 mg/g, respectively. The MTT assay revealed that the extract inhibited the growth of HepG2 cells in a dose-dependent manner having $IC_{50}$ value of 114.12 µg/mL. In addition, the proliferation of human cervical carcinoma HeLa, gastric cancer MKN28 cells, glioma SHG-44 cells, and lung carcinoma A549 than HepG2 cells was also arrested by the extract of the plant. The extract increased the population of HepG2 cells in G0/G1 stage of cell cycle as well as the percentage of apoptotic HepG2 cells.[42]

### *Antihyperlipidemic activity*

Ethanolic and acetone extracts of *C. deodara* showed antihyperlipidemic activity in monosodium glutamate-induced obesity in neonatal rats. It was observed that monosodium glutamate-induced obese rats showed an increase in body weight along with decrease in body temperature. Rats treated with 200 mg/kg of ethanol extract and acetone extract exhibited a 6.54% and 6.73% decrease in body weight when compared with monosodium glutamate control along with significant reduction in weights of heart, liver, spleen, and kidney. Treatment of rats with 100 mg/kg ethanol extract and 200 mg/kg, respectively, resulted in significant increase of locomotor activity as compared to control group. It was also observed that the rats treated with monosodium glutamate showed significantly high serum glucose, total cholesterol, triglyceride, low-density lipoprotein (LDL), and very LDL (VLDL) levels along with a decrease in high-density lipoprotein (HDL) levels as compared to vehicle control group. Treatment with ethanolic and acetone extract resulted in decrease in serum glucose, total cholesterol, triglyceride,

LDL, and VLDL along with an increase in HDL level, suggesting an antihyperlipidemic and antiobesity potential of *C. deodara* extracts.[43]

The hypolipidemic and antidiabetic activity of hydroalcoholic extract of *C. deodara* and *Embelia ribes* was determined in alloxan-induced diabetic rats. The reports indicated that treatment with hydroalcoholic extracts at a dose of 250 mg/kg and 500 mg/kg resulted in significant increase in serum insulin levels along with decrease in blood sugar, total cholesterol, and serum triglycerides. In addition to it, HDL cholesterol also significantly increases on treatment with extracts. Histopathological observation of pancreas of diabetic rats treated with the extracts exhibited regeneration of β-cells, thereby establishing the hypolipidemic effect.[44]

## Antidiabetic Potential and α-amylase Inhibitory Activity

### *Antihyperglycemic activity*

The antihyperglycemic activity of the ethanolic extract of the stem wood of *C. deodara* was studied on Sprague Dawley rats. It was observed that streptozotocin-induced diabetic rats treated with *C. deodara* extract exhibited a lowering of blood sugar level as compared to control from the 1st to 7th h of the study as compared to controls suggesting its antihyperglycemic activity.[45]

The antihyperglycemic activity of the ethanolic extract of the wood of *C. deodara* in alloxan-induced diabetic rats was investigated. A significant reduction in blood sugar level of diabetic rats when treated with glibenclamide and *C. deodara* extract (50 mg/kg and 100 mg/kg) after 5, 10, and 14 days of study was reported. In addition, *C. deodara* extract showed better effect when compared to standard antidiabetic drug glibenclamide.[46]

### *Antidiabetic activity*

The ethanolic extract of the stem bark of *C. deodara* at doses of 250 mg/kg and 500 mg/kg exhibited antidiabetic property in streptozotocin-induced diabetic mice. It was observed that blood glucose levels of diabetic mice were reduced which were related to the number of days of treatment with the extracts, the highest reduction being on the 21st day. The dose of 500 mg/kg proved to be the most significant in lowering of blood glucose level in diabetic mice when compared to standard. Treatment of mice with extract resulted in improvement of body weight in comparison to the diabetic control. The biochemical parameters such as serum glutamic pyruvic transaminase, serum glutamic oxaloacetic transaminase, cholesterol, and triglyceride were also reduced on treatment with the bark extract.[47]

It has also been reported that aqueous extract of *C. deodara* possesses antidiabetic activity. The results suggested that treatment of rats with alloxan resulted in significant increase in blood glucose levels as compared to non-diabetic rats. Treatment with heartwood aqueous extract of *C. deodara* resulted in a dose-dependent decrease in blood glucose level and this effect was detectable within 5 days of treatment as compared to standard antidiabetic drug glibenclamide which was administered for 21 days of study period. In addition, it was also observed that treatment of rats with aqueous wood extract over a study period of 21 days resulted in a dose-dependent decrease in TBARS along with restoration of superoxide dismutase (SOD), catalase, glutathione (GSH), and glutathione S-transferase to normal levels.[48]

### *α-amylase inhibitory activity*

The essential oil extracted from the cones of *C. deodara* was reported to have α-amylase inhibitory activity. It was observed that the essential oil exhibited a concentration-dependent inhibition in activity of α-amylase with a maximum inhibition rate of 88.03% at 600 µg/mL concentration. The $IC_{50}$ value of essential oil was 119.67 ± 0.72 µg/mL indicating its potential as α-amylase inhibitor. The chemical composition of essential oil of the extract was analyzed by gas chromatography–mass spectrometry (MS). A total of 28 compounds representing 97.80% of the extract were characterized and identified, of which cyclofenchene (31.82%), β-pinene (29.69%), D-limonene (12.46%), α-terpineol (11.19%), and β-myrcene (3.30%) formed the important constituent. Finally, *in silico* analysis for screening of α-amylase inhibitors in the essential oil resulted in identification of three compounds having low binding energies with α-amylase, namely Bornyl acetate, germacrene-D, and longipinene. Among these, the binding energy of longipinene was the lowest having a value of 5.93 kcal/mol. *In vitro* studies revealed that longipinene exhibited better α-amylase inhibitory activity than positive control acarbose.[49]

## Antimicrobial Activity

### *Antibacterial activity*

The antibacterial activity of *C. deodara* against foodborne bacteria was investigated. It was observed that the water extracts of needle of the plant inhibited five bacteria, namely *Escherichia coli*, *Proteus vulgaris*, *Staphylococcus aureus*, *Bacillus subtilis*, and *Bacillus cereus* with the diameter of inhibition zones ranging from 16.5 mm to 26.5 mm as compared to positive control whose range of 22.5–27.3 mm. The extract showed high inhibitory activity in case of *S. aureus*, *B. subtilis,* and *B. cereus* having inhibition zones of 26.5 mm, 21.2 mm, and 21.5 mm, respectively, suggesting that Gram-positive bacteria are more sensitive to the extract, the most susceptible being *S. aureus*. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of the water extract against tested microorganisms ranged from 0.78 mg/mL to 12.5 mg/mL and 1.56 mg/mL to 25 mg/mL, respectively. Transmission electron microscopy of

*S. aureus* treated with *C. deodara* extract exhibited lysis with broken cell wall, cell membrane, and release of cytoplasm. Chromatographic analysis followed by time-of-flight MS and NMR analysis revealed that the main antibacterial compound in the extract is shikimic acid.[50]

The antibacterial activity of shikimic acid (SA) obtained from water extracts of needles *C. deodara* was worked on *S. aureus*. It was observed from the study that incubation with SA resulted in a dose-dependent increase $K^+$ and nucleotide release from the bacteria with a maximum efflux after 10 min of treatment indicating its possible effect on membrane permeability. There was a dose-dependent increase in hyperpolarization of bacterial cell membrane on treatment with SA as evident by decrease in fluorescent activity of DiBAC4(3) probe, suggesting a change in membrane potential. Further, flow cytometric analysis revealed that the population of cells with intact membranes was 53.6% as compared to 93.19% for untreated samples when treated with ×1 MIC of SA for 3 h. In addition to it, 46.4% of the cells exhibited membrane damage when treated with ×1 MIC of SA as compared to 6.81% in untreated samples, suggesting that SA exhibited antibacterial action by targeting cytoplasmic membrane.[51]

The antibacterial activity and membrane disruptive potential of 3-p-trans-coumaroyl-2-hydroxyquinic acid (CHQA) isolated from *C. deodara* were investigated against *S. aureus*. It was reported that there was a dose-dependent decrease in fluorescent intensity of $DiBAC_4(3)$ with *S. aureus* cells treated with CHQA with minimum of −117.66 ± 1.77 as compared to untreated cells which was −3.95 ± 0.26 revealing a significant hyperpolarization of cytoplasmic membrane. In addition, flow cytometric analysis of cells using fluorescent probes SYTO 9 and propidium iodide (PI) after 3 h incubation with ×2 MIC of CHQA revealed that the percentage of cells with intact membrane decreased from 90.5% to 48.7% as compared to negative control, suggesting a loss of membrane integrity of *S. aureus*. There was a dose-dependent decrease in fluorescence polarization index of *S. aureus* cells treated with the compound as compared to the control which exhibited maximum fluorescence with fluorescent probe 1, 6-diphenyl, 1, 3, 5-hexatriene (DPH), suggesting an increase in membrane fluidity. It was also observed that the treatment of *S. aureus* with CHQA resulted in changes in conformation of membrane protein as evident by changes in fluorescence peak to red region accompanied by fluorescence emission to larger wavelength region. Transmission electron microscopy of the cells of *S. aureus* treated with CHQA revealed lysis of membrane and leakage of intracellular contents along with small amount of granular agglutinations. All these results suggested the antibacterial property of the compound through membrane disruption activity.[52] The diagrammatic representation of the antibacterial activity of CHQA is represented in Figure 3.

Inhibition of the growth of *S. aureus* by 2R, 3R-dihydromyrecetin (DMY), a compound isolated from needles of *C. deodara,* was also reported. It was observed that the MIC of DMY and epigallactocatechin gallate (EGCG) was 0.125 mg/mL (0.39 mM) and 0.125 mg/mL (0.27 mM), while MBC of DMY and EGCG was 0.25 mg/mL (0.78 mM) and 0.5 mg/mL (1.09 mM), respectively, suggesting that bactericidal potential of DMY was comparable with that of EGCG. The time courses of the growth of *S. aureus* indicated that the growth of the bacteria was completely inhibited after 24 h of incubation with DMY at IX MIC and ×2 MIC. It was also reported from their studies that the treatment of *S. aureus* with DMY resulted in increase in release of nucleotides in dose-dependent manner, suggesting leakage of cytoplasmic contents from the cells. Flow cytometric analysis revealed that the live cell percentage decreased from 90.5% to 59.2% after 3 h of incubation of the cells with DMY at ×1 MIC concentration and 40.8% of DMY treated cells were stained with PI demonstrating membrane damage during 3 h incubation period. Treatment of DMY resulted in significant

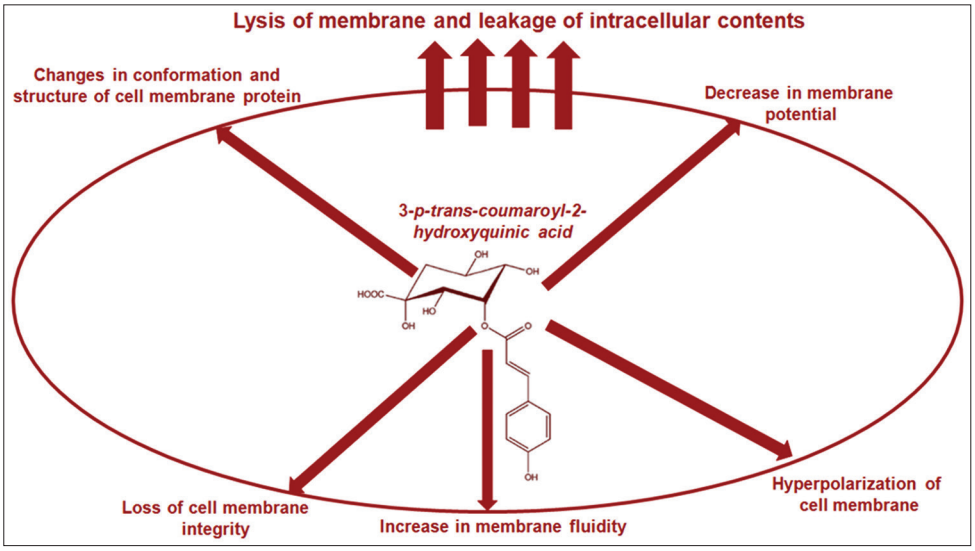


**Figure 3:** Schematic representation of the action of 3-p-trans-coumaroyl-2-hydroxyquinic acid on bacterial cell membrane

hyperpolarization of membrane potential of bacterial cells as evident from lower intensity of the fluorescence of DiBAC4(3) at higher concentrations of DMY indicating disruption of membrane by the treatment of the compound. There was also a reduction in membrane fluidity in cells treated with DMY as evident from a dose-dependent increase in fluorescence polarization of hydrophobic probe DPH. The findings also indicated that DMY influenced the structure of the cell membrane through interaction with membrane proteins, thereby altering the fluidity. Transmission electron microscopy of *S. aureus* cells treated with DMY revealed abnormalities including disappearance of cell wall, distortion of plasma membrane, and leakage of intracellular substances. All these results proved bactericidal properties of DMY extracted from *C. deodara*.[53]

### *Antifungal activity*

Two new sesquiterpenes, namely (E)-(2S, 3S, 6R)-atlantone-2, 3-diol and (E)-(2S, 3S, 6S)-atlantone-2, 3, 6-triol, along with two known sesquiterpenes, namely atlantone and (E)-α-atlantone, isolated from *C. deodara* were reported to have antifungal activity. It was observed that n-hexane extract, chloroform extract, atlantone, and (E)-α-atlantone exhibited inhibition against *Aspergillus flavus, Aspergillus niger*, *Aspergillus ochraceus, Aspergillus parasiticus,* and *Aspergillus sydowii*. In addition to it, weak antifungal activity was exhibited by (E)-(2S,3S,6R)-atlantone-2,3-diol against *A. parasiticus* and *A. sydowii,* while (E)-(2S,3S,6S)-atlantone-2,3,6-triol and both the extracts inhibited *Trichophyton rubrum*.[54]

### *Larvicidal activity*

The essential oil of *C. deodara* exhibited larvicidal activity against diamondback moth, *Plutella xylostella*. It was reported that essential oil obtained from hydrodistillation of wood chips of the plant and its fractions showed larvicidal activity against second instars of diamondback moth *P. xylostella* among which pentane fraction of essential oil was most effective having a $LC_{50}$ value of 287 µg/mL. It was also reported that fractions enriched with himachalenes were more toxic than that of allantone enriched fractions. The above findings indicated that himachalenes and allantone probably contributed for the larvicidal activity.[55]

### *Anthelmintic activity*

The leaf extract of *C. deodara* was reported to have anthelmintic activity**.** It was observed that petroleum ether, chloroform, ethyl acetate, and methanol extracts of the leaf showed better activity against adult *Pheretima posthuma* among which petroleum ether took least time to cause paralysis and death of the worms followed by methanol, ethyl acetate, and chloroform, respectively.[56]

### *Antisecretory and antiulcer activity*

The antisecretory and antiulcer activity of *C. deodara* was investigated on winster rats. It was reported that the volatile oil obtained from the wood of *C. deodara* exhibited significant antisecretory activity as evident by decrease in gastric fluid volume, total acidity, free acidity, and increase in pH of gastric fluid in pylorus-ligated rats. In addition to it, the number of ulcers, ulcer score, and ulcer index was also significantly reduced in the pylorus-ligated rats and ethanol-treated rats pre-treated with *C. deodara*. Histopathological reports of the stomach samples of rats exhibited protection of mucosal layer from ulceration and inflammation.[57]

The protective effect of the chloroform extract of *C. deodara* on experimentally induced gastric ulcers in rat was also illustrated. It was reported that chloroform extract of the plant had a protective effect on gastric mucosa in rats having ethanol-induced or pyrolic ligation-induced gastric ulcers. The extract also reduced the gastric content, total acidity, free acidity, and also increased the pH of the gastric content in rats having pyrolic ligation. In addition, the gastric hemorrhage was markedly reduced and tissue integrity was maintained on treatment with extract.[58]

### *Anticonvulsant activity*

3, 4-bis (3,4-dimethoxyphenyl) furan-2,5-dione (BDFD), a compound isolated from heartwood of *C. deodara,* was reported to have anticonvulsant activity. The results from their study indicate that there was a dose-dependent protective action of BDFD against pentylenetetrazole (PTZ)-, pilocarpine-, and 6-Hz-induced convulsions in albino rats. In addition, therapeutic effects on motor coordination by BDFD were exhibited <100 mg/kg dose in PTZ-, 6-Hz-, and pilocarpine-induced seizures. It was also observed that BDFD treatment resulted in increase of Gamma-aminobutyric acid in the brain of experimental rats. All these results are indicative of anticonvulsant property of BDFD.[59]

## Neuroprotective Activity

Cedrin, a compound isolated from *C. deodara,* is reported to possess neuroprotective effect. It was observed that cedrin improved the viability of PC12 cells injured by treatment with $A\beta_{1-42}$ in a concentration-dependent manner. Treatment of PC12 cells with $A\beta_{1-42}$ resulted in increase in intracellular reactive oxygen species and malondialdehyde (MDA) and decrease in SOD activity. This condition was reversed by pre-treatment of cells with cedrin, indicating its protective nature against $A\beta_{1-42}$-induced oxidative stress. Cedrin also improved mitochondrial membrane potential, mitochondrial permeability transition pore opening in PC12 cells which was initially despaired by $A\beta_{1-42}$. Finally, cedrin inhibited the elevated caspase-3 activity and suppressed Bax expression induced by $A\beta_{1-42}$ and upregulated the Bcl-2 activity which was downregulated by Aβ1-42 all of which indicated neuroprotective effect of cedrin through the improvement of mitochondrial dysfunction and inhibition of apoptosis.[60]

### Cognitive Enhancement

Cognitive enhancement with application of *C. deodara* was observed using aged mice as experimental system. It was observed that the treatment of aged mice with chloroform extract of the plant resulted in a significant decrease in escape latency in both reference and working memory training over a period of 7 days in comparison to the control. It was also observed that in probe trial on the 8$^{th}$ day, the mice treated with plant extract crossed the target area more frequently and spent more time in target quadrant. The extract also resulted in a significant decrease in MDA along with an increase in the level of GSH in both the frontal cortex and hippocampus. The findings suggested that *C. deodara* had a memory-enhancing potential possibly due to its antioxidant potential.[61]

### Antidepressant Activity

The antidepressant activity of BDFD isolated from heartwood of *C. deodara* was studied using albino mice model. The findings indicated that treatment with BDFD results in a significant decrease in immobility time of the mice when subject to forced swim test. In addition to it, BDFD treatment resulted in increased serotonin and noradrenaline levels in the brains which indicated its positive antidepressant action.[62]

### Antiurolithiatic Activity

The petroleum ether extract of the heartwood of *C. deodara* was reported to possess antiurolithiatic activity in rats. The diuretic activity of the petroleum ether extract of *C. deodara* was observed as evident from increased elimination of sodium and chlorides. Pre-treatment of rats with extract prevented the reduction in urine output and decrease in urine pH which was initially induced by sodium oxalate, a urolithiasis generating compound. Urine samples of the rats treated with extract showed the presence of fewer crystals as compared to sodium oxalate administered group where the presence of crystals was maximum. Moreover, treatment with sodium oxalate resulted in reduced elimination of urea, creatinine, uric acid, sodium, potassium, and chloride levels in urine and corresponding elevation in the serum levels indicating improper kidney function as compared to normal rat. This condition was reversed by treatment with extracts. There was also a reduction in lipid peroxide level and calcium oxalate crystals in the kidney of rats treated with extract. The histopathological examination of the kidney of rats also showed protective action of the extract.[63]

### Anti-inflammatory Activity

Anti-inflammatory activity of the essential oil of the wood of *C. deodara* was studied on rats. The results from the study indicated that essential oil extracted from the wood of the plant exhibited significant anti-inflammatory action against carrageenan-induced inflammation at a dose of 50 mg/kg and 100 mg/kg, respectively. In addition, the essential oil also inhibited adjuvant-induced arthritis as evident by suppression of increase in paw thickness of rats. The analgesic activity of the essential oil was also revealed.[64]

## CONCLUSION

The association of plants with human beings is being known through ages. Down the civilization humans have used plants for their daily livelihood and their unending desire to explore has led to the discovery of a wide array of plants with immense value. Some of them are domesticated for food while others are being exploited for medicinal uses while some are used for infrastructural purposes. The earliest mention of the use of medicinal plants for treatment is mentioned in Rig Veda in the time period of 4500–1600 BC.[65] The World Health Organization (WHO) has enlisted 21,000 plants used for medicinal purpose, of which 2500 are Indian species and 150 of them have attained immense commercial importance and popularity. Thus, Indian is also known as the "botanical garden of the world."[66] At present, 80% of the human population of the world is dependent on plants for their health care.[67] The natural remedies for diseases with plants as the backbone have minimum side effects and low cost. Thus, it is used by large proportions of people of the developing countries such as Bangladesh (90%), Myanmar (85%), India (80%), Nepal (75%), Sri Lanka (65%), and Indonesia (60%). It has been estimated by the WHO that the demand for ethnomedicinal plants is 14 billion USD per year, and in India, the plant-related trade is estimated to be around 1 billion USD per year.[68] In the Indian subcontinent, the gymnosperms are largely used by the local people of the mountainous region though it's by-products are commercialized and used elsewhere. This paper highlights the value of one such gymnosperm, namely *C. deodara,* in human society. The plant is extensively used as a timber, thatching, and shelter purpose by the local people of India, Pakistan, and parts of Nepal. The plant also finds its name and usage in Ayurveda for the cure of various diseases, thus hinting long history of its medicinal use. The medicinal importance of plants has been very well elaborated by various groups of researchers. However, most of the explorations are based on animal system or *in vitro* models. Further, the study on the efficacy of the compounds isolated from various plant parts needs to be done and tested on humans through clinical trials. The antimicrobial property of the plant can be further elaborated further in the development of drugs for the cure of bacterial-borne diseases. Thus, in a country like India with an illustrious history of the traditional system of medicine, *C. deodara* can be further exploited for the development of drugs. As the plant is plenty in the Indian Himalayas and adjoining region, it can be a very cost-effective source of raw materials for the development of drugs. Thus, bioprospection of *C. deodara* seems to be of extreme relevance for the treatment of various diseases in and around the Indian subcontinent.

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