A review on phyto-pharmacological potentials of *Juniperus recurva*

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**ABSTRACT**

*Juniperus recurva* is a small tree or spreading shrub distributed from Afghanistan eastward through the Himalayas to southwest China. It is predominant in woodlands of the wetter areas of Himalayas (altitude of 1800 m to 3900 m), with moist and well-drained soils. It holds great potential as a medicinal plant. It has been traditionally used as anti-rheumatic, antiseptic, antispasmodic, antitoxic, aphrodisiac, astringent, carminative, rubificant and stomachic. However, very few authentic pharmacological studies on medicinal benefits of this plant have been conducted thus far. In a first of its kind, we review this plant for its chemical constituents, pharmacological activity and medicinal benefits. Keeping in view its success record as a traditional medicine to cure different ailments, it would be of interest to look for various bioactive natural products that might have therapeutic potential.

**KEY WORDS:** *Juniperus recurva*, Distribution; Pharmacological Activity.

**INTRODUCTION**

*Juniperus* L. (family Cupressaceae), a genus of evergreen aromatic shrubs or trees is distributed in temperate and cold regions of northern Hemisphere [1]. Depending on taxonomic viewpoint, between 50 and 67 species of *Juniperus* are widely distributed throughout the northern Hemisphere, from the Arctic, south to tropical Africa in the old world, and to the mountains of central America, Pakistan, India and China [2–6]. Leaves remain green for several years and even after drying may remain on the shoots for indefinite period [2–6]. Flowers are unisexual [2–6]. In some species flowers of both the sexes occur on the same plant [2–6]. All the species can be propagated through seeds; seeds retain viability for several years when stored in cool dry place [2–6]. Junipers like open positions and chalky or limestone soils [2–6]. Common *Juniperus* species of Himalayan range include: *J. communis*, *J. indica*, *J. recurva* and *J. squamata* [2, 7]. *Juniperus recurva* is commonly known as the ‘Drooping Juniper’ [2].

**METHODS**

Authors carried out electronic searches in PubMed, Embase, Medline Google Scholar, Scopus and Cochrane Library. Authors screened the titles and abstracts independently to identify potential eligible articles. Then full-text articles were retrieved if necessary. Authors used controlled vocabulary and text words to construct a highly sensitive search strategy during the entire process of literature survey. No limits were imposed in terms of author or type of publication.

**OCCURRENCE AND MORPHOLOGY**

*J. recurva* grows from Pakistan to south west China and is particularly common in Nepal and Kashmir [2–6]. It can be found as a large shrub in hilly region of Nepal. It can also be tree having height of 6-20 m and a trunk up to 2 m diameter and a broadly conical to rounded or irregular crown. In Nepal it is widely spread in east side of Himalaya region. In Kashmir it is found in Khilanmarg and on the route from Sonamarg to Amarnath cave at an altitude of 3000-4000 m. It mainly grows at altitude of 3000-4000 m. Two varieties of *J. recurva* have been named: *J. recurva* var. *recurva* found throughout the Himalayan range and *J. recurva* var. *coxi* mainly confined to the eastern Himalaya on high rainfall sites [2, 8]. However, a report has listed *J. recurva* var. *squamata* and *J. recurva* var. *coxi* as the two species of Himalayas [9].

*J. recurva* is monoecious or rarely dioecious. Trunk bark is generally light grayish brown or brown, crown conical or broadly pyramidal. Branches are ascending in apical part of plant and spreading toward base. Leaves are needle-like, 5-10 mm long, arranged in six ranks in alternating whorls of three. Seed cones are berry-like, globose to ovoid, 5-10 mm long and 4-7 mm diameter, glossy blue-black, and contain one seed; they are mature in about 18 months. The male cones are 3-4 mm long, and shed their pollen in early spring [2].
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SCIENTIFIC CLASSIFICATION
(1) Kingdom: Plantae
(2) Division: Pinophyta
(3) Class: Pinopsida
(4) Order: Pinales
(5) Family: Cupressaceae
(6) Genus: Juniperus
(7) Species: Juniperus recurva

THREATS
In the IUCN (International Union for Conservation of Nature) Red List of Threatened species Juniperus recurva var. coxii has been put in the category of Near Threatened [10]. Having previously been listed as Vulnerable, it was considered that there is insufficient evidence to assume an overall reduction greater than 30%. In certain areas, e.g. Yunnan, deforestation has been cause of reduction in area of occupancy, but elsewhere the forest is still intact. It seems more appropriate to list this taxon as Near Threatened [10]. In its native countries J. recurva is used for timber as well as ornamental trees in gardens of monasteries and temples. The wood and foliage are burned for incense in Buddhist temples [8]. In Myanmar (Burma) the wood of large trees is used to make coffins. The drooping form J. recurva var. coxii is a highly ornamental tree much valued and often planted in regions of Europe with a mild, moist climate [8].

CHEMICAL CONSTITUENTS
Analysis of the composition of the leaf oils of J. recurva from India (Sikkim, Nepal) and its comparison to the composition of J. recurva var. squamata from western India has been reported [6]. The major components of J. recurva oil were α-pinene, sabinene, 6,3-carene, limonene, terpinen-4-ol, γ-cadinene, δ-cadiene, elemol, cubenol, epι-α-cadinol, epi-α-muurolol, α-cadinol and 4-epi-abietal [6]. Study on essential oils of leaves and twigs of Juniperus recurva var. squamata by gas liquid chromatography (GLC), mass spectrometry (MS), and nuclear magnetic resonance (NMR) spectroscopy has also been performed [11]. Main constituents were monoterpen hydrocarbons (68%); in addition, about 12% of sesquiterpene hydrocarbons, 9% of oxygenated sesquiterpenes, and 5% of oxygenated monoterpenes were identified. 4β-Hydroxygermacra-1,5-diene, β-oplopenone, oplopanone, 8-acetoxy elemol, and manool were found as trace components (Figure 1) [11].

Recently a study was conducted on the phytochemical screening for the presence of different phytochemicals like alkaloids, tannins, reducing sugar, coumarin, glycosides, quinones, steroids, terpenoids and saponin in the different plant parts of J. recurva [12]. Leaf and seed fractions demonstrated differences in the presence of various phytochemicals. Leaf fractions showed only the presence of coumarins and quinones with the absence of other mentioned phytochemicals. Seed fractions showed the presence of tannins, coumarin, glycosides, saponin, alkaloids, steroids and terpenoids [12]. In a preliminary phytochemical screening of methanolic extract of six species of Juniperus including J. recurva, the presence of alkaloids, tannins, flavonoids, terpenoids and steroids was reported [13]. The contents of phenolic compounds were highest in J. communis and the total flavonoid contents were highest in J. indica. For J. recurva total phenolic content in (equiv L⁻¹) was 2.10 ± 0.13 and total flavonoid content (equiv L⁻¹) was 0.890 ± 0.17 [13]. Amentoflavone was also isolated from aerial parts of different Juniperus species including J. recurva and authenticated by high performance liquid chromatography (HPLC) and physicochemical parameters [13].

Production of podophyllotoxin by an endophytic fungus Fusarium oxysporum isolated from the medicinal plant J. recurva has been reported [14]. Further confirmation and quantification of podophyllotoxin was performed by HPLC, liquid chromatography-mass spectrometry (LC-MS), and LC-MS/MS [14]. Podophyllotoxin is a well-known naturally occurring aryltetralin lignan that occurs in few plant species that is used as a precursor for the chemical synthesis of the anticancer drugs like etoposide, teniposide and etopophose phosphate. The availability of this lignan is becoming increasingly limited because of the scarce occurrence of its natural sources and also because synthetic approaches for its production are still commercially unacceptable [14].

PHARMACOLOGICAL ACTIVITIES AND MEDICINAL USES
Essential oils and their components are widely used in medicine as constituents of different medical products, in the food industry as flavouring additives and also in cosmetics as fragrances and pharmaceutical industries [15, 16]. Essential oils are valuable natural products used as raw materials in many fields, including perfumes, cosmetics,
Juniperus recurva possess various medicinal properties. Among these, the essential oil of Juniperus recurva has been found to possess antimicrobial activity against Bacillus subtilis, Erwinia chrysanthemi, Escherichia coli, and other bacteria. The oil has also been used in the management of bronchitis as an expectorant and as an antiseptic. Berries of Juniperus recurva are recommended in cough, infantile tuberculosis, and diabetes, whereas, ash of the bark is used for certain skin diseases. Essential oils of Juniperus recurva have also been reported to have insecticidal activity against adult lace bugs.

**Insecticidal Activity**

Many insecticidal principles have been reported in the heartwood of Juniperus recurva including thujopsene and 8-cedren-13-ol. Additional 12 sesquiterpenes were also detected in the neutral fraction of ether extracts. The active components from the heartwood of Juniperus recurva were monitored for the insecticidal activity against mosquito female adults (Culex pipiens pallens) with topical application test. Essential oils of two Tibetan Junipers, J. saltuaria and J. squamata var. fargesii have also been reported to have insecticidal activity against adult lace bugs.

**Xanthine Oxidase Inhibitory Activity**

Xanthine oxidase inhibitory activity of Juniperus recurva has been recently assessed. The inhibitory effect of polyphenolic rich fractions of Juniperus recurva was determined to find out the natural inhibitors of xanthine oxidase. Xanthine oxidase is a cytoplasmic enzyme, converting hypoxanthine to xanthine and generating superoxides and uric acid. Gout attacks can be treated with the use of xanthine oxidase inhibitors. Allopurinol is generally used in the management of gout and conditions associated with hyper-uricemia but its adverse effect leads to GIT distress, hypersensitivity reactions and hepatitis. It was reported that the methanol fraction of Juniperus recurva has more inhibition against xanthine oxidase activity in the samples treated with different concentrations of hypoxanthine on second, third, fourth and fifth weeks as compared to other plant extracts.

**Antimicrobial Activity**

Antimicrobial assay with the leaf and seed plant extracts of Juniperus recurva by agar plate diffusion method has been reported. Five antibiotics were used as standard drugs. Six different bacteria Bacillus cereus, Bacillus thuringiensis, Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis and Proteus mirabilis were used for the assay. The antimicrobial activity was assayed by measuring the diameter Zone of Inhibition in millimetres (ZOI) of different extracts on the agar disc plate. Both the Juniperus recurva leaf and seed extract fractions showed the concentration dependence antimicrobial activity towards the bacteria used with the highest ZOI being 17 mm for the Juniperus recurva leaves at 200 mg/ml. Various other species of Juniperus have also been reported to have antimicrobial activity. Sensitivity of five pathogenic multi drug resistant bacteria (Bacillus subtilis, Erwinia chrysanthemi, Escherichia coli, Agrobacterium tumefaciens and Xanthomonas phaseoli) was tested against the crude leaf organic extracts (methanol, ethanol, chloroform and hexane) and aqueous extracts of a Kumaon Himalayan gymnospermous plant J. communis, employing disc diffusion method. All the extracts of J. communis were found effective by showing a mark zone of inhibition except aqueous extract. Antimicrobial activity of Juniper essential oil has also been reported in many other studies.

**Antioxidant Activity**

Furthermore, antioxidant (2,2-diphenyl-1-picrylhydrazyl; DPPH) assay of different plant parts of Juniperus recurva has also been investigated. The results demonstrate that the selected plant extract fractions of Juniperus recurva possess significant antioxidant activities. Antioxidants compounds scavenge free radicals such as peroxide, hydroperoxide or lipid peroxyl and thus inhibit the oxidative mechanisms that lead to degenerative diseases. The protective effect of methanolic extracts from different species of Juniperus in different concentration has been reported against hydrogen peroxide induced oxidative damage in human erythrocytes and leucocytes. Human blood cells are the key fighters against various oxidative stress diseases and remain the primary target for natural products and plants. These cells are continuously exposed to radicals and are unable to replace damaged components, especially polyunsaturated fatty acids chains from peroxidation. The measurements of different antioxidant parameters like superoxide dismutase, glutathion peroxidase, lipid peroxidase, catalase and glutathione levels were performed under each set of extracts including Juniperus recurva. Isolated fractions from all the six Juniperus species were reported as potential source of natural antioxidants for treatment and prevention of diseases in which oxidative stress takes place. Antioxidant potential has also been reported for essential oils of Juniper berries of different species of Juniperus.

**Cytotoxic Activity**

In-vitro cytotoxicity assay with the leaf and seed plant extracts of Juniperus recurva demonstrated its anticancer properties against MCF7 (Breast Cancer) cell lines. The cytotoxic effect or the inhibitory effect of these extracts was compared with standard (Doxorubicin). The inhibition was reported to be concentration dependent. It was suggested that isolated pure compounds with bioassay guided extraction, could possibly get the higher inhibitory
effect against MCF7 cells from the plant *J. recurva*. Essential oils of few other species of *Juniperus* have also been reported to have cytotoxic activity [35–37].

**Other Uses**

Various parts of *J. recurva* are tradition used as anti-rheumatic, anti-septic, anti-spasmodic, astringent, carminative, depurative, stimulant, stomachic, tonic, and in aroma industry. One of the most ancient rituals of the Himalayan region is the burning of *J. recurva* on mountain tops to purify and sanctify the area. *J. recurva* has also been reported to be useful in the treatment of various ailments including fever, headache, cough, cold and kidney problems. High F$_{IC}$ (informat consensus factor) value was obtained for these ailments, indicating that the *J. recurva* traditionally used to treat these ailments is worth searching for bioactive compounds [38]. Summary of its pharmacological activities and traditional uses is given in Figure 2.

**CONCLUSION**

In this review paper various traditional and medicinal aspects of *J. recurva* have been discussed. There is a shortage of research reports on *J. recurva*. It remains one of least studied species of *Juniperus*. Further evaluation needs to be carried out on *J. recurva* in order to establish and confirm its medicinal uses and development of formulations containing this plant for their practical clinical applications, which can be used for the welfare of mankind.

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**CONFLICT OF INTERESTS**

The authors declare that there is no conflict of interests regarding the publication of this paper.

**REFERENCES**