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Phytoconstituents and Therapeutic potential of *Thuja occidentalis*

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ABSTRACT

The traditional system of medicine plays a significant role in our health care system for the treatment of mankind. *Thuja occidentalis* is commonly used herb in Ayurvedic medicine. *Thuja occidentalis* (Northern white cedar) belongs to the family Cupressacae. The plant is highly used by rural people in curing various disorders. *Thuja occidentalis* has an effective natural origin that has a tremendous future for research as the novelty and applicability of *Thuja occidentalis* are still hidden. Such things can be overcome through modern scientific research. The present article describes various traditional and medicinal utility of the chemical composition and pharmacological activity of the plant and its constituents.

Keywords: *Thuja occidentalis*; traditional uses; phytochemistry; pharmacological activities.

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INTRODUCTION

Thuja occidentalis belonging to family Cupressacae is a well known medicinal plant. *Thuja occidentalis*, commonly known as American Arbor vitae or white cedar, is indigenous to eastern North America and is grown in Europe as an ornamental tree [1]. The plant was first identified as a remedy by native Indians in Canada during a 16th century expedition and was found to prove effective in the treatment of weakness from scurvy [2]. In folk medicine, *Thuja occidentalis* has been used to treat bronchial catarrh, enuresis, cystitis, psoriasis, uterine carcinomas, amenorrhea and rheumatism [3, 4]. In combination with other immunomodulating plants, such as Echinacea purpurea, Echinacea pallida and Baptisia tinctoria, this medicinal plant is also used as evidence-based phytotherapy for acute and chronic infections of the upper respiratory tract [5] and as an adjuvant to antibiotics in severe bacterial infections such as bronchitis, angina and pharyngitis. Several reviews and monographs describe the botany, constituents and some pharmacological properties, and the use of this herbal substance in the treatment of the common cold [6].This review is to give comprehensive information on the chemical constituents and medicinal importance of *Thuja occidentalis*.

Taxonomical classification:

- Domain : Eukaryota
- Kingdom : Plantae
- Subkingdom : Viridaeplantae
- Phylum : Pinophyta
- Subphylum : Euphyllophytina
- Infraphylum : Radiatopses
- Class : Pinopsida
- Order : Pinales
- Family: Cupressaceae
- Tribe: Spiraeeae
- Genus: Thuja
- Specific epithet: Occidentalis
- Botanical name: *Thuja occidentalis*

Morphology

Leaves: evergreen, scale-like, on main shoots, ¼" long with long points. Lateral shoots are flattened, 1/8 inch long with short points. Leaves - opposite; scale-like, closely overlapping, successive pairs at right angles; upper and lower leaves flat, with a protruding resin gland, lateral leaves folded, clasping the flat leaves.

Stem: Twigs are green and scale-like, turning brown, occurring in flattened foliar sprays.

Bark: Fibrous, red-brown to gray where weathered. Diamond-shaped patterns are usually apparent.

Flowers: Monoecious; solitary, females green with 4 to 6 scales; males are green tipped with brown and globose. Flowers- monoecious, the male and female flowers of eastern white-cedar are usually borne on separate twigs or branchlets; they are tiny, terminal, cone-like bodies. Male flowers are yellowish and arise from branchlets near the base of the shoot; female flowers are pinkish and appear at the tips of short terminal branchlets.

Fruits: A monoecious conifer with a narrow, almost columnar crown.

Ethanopharmacology

Cedar trees in general have a long history of use for furniture and buildings as well as in various herbal remedies and aromatherapy preparations. The fragrant wood was also used by Americans as well as the ancient Egyptians, Greeks, and Romans as an ingredient in incense blends.

In Western herbal medicine, cedar leaf oil was used as an emmenagogue, abortifacient, vermifuge, diuretic, and digestive aid. It was applied externally to relieve the pains of arthritis and rheumatism, to treat external fungal infections of the skin (ringworm and thrush), and to remove anal or genital warts. Native Americans used cedar leaf preparations to relieve headache and to prevent scurvy. Cedar leaves and twigs are in fact rich in vitamin C, and it was their effectiveness in preventing or treating scurvy that led to the tree's being called arbor vitae or tree of life. In addition, recent research has shown that extracts prepared from either *Thuja occidentalis* or Thuja plicata do in fact have antiviral, anti-inflammatory, and antibacterial properties. A group of German researchers reported in 2002 that an extract prepared from cedar leaf, alcohol, and water inhibits the reproduction of influenza virus type A, while a team of researchers in Japan found that an extract of Western red cedar was effective in treating eczema. Lastly, another group of Japanese researchers reported in 2003 that several compounds isolated from the stem bark of Japanese cedar appear to have significant antitumor activity [7].

In traditional Chinese medicine, the leaves and stems of Thuja orientalis are used to treat nervous disorders, insomnia, and heart palpitations, as well as to stop hemorrhages and bring down fevers. Traditional Chinese physicians also make a preparation of fresh cedar leaves steeped for seven days in a 60% alcohol solution to promote hair growth. The mixture is rubbed on the bald spots three times daily.

The homeopathic preparation known as Thuja is made from the leaves of *Thuja occidentalis*, and is given to treat soft or bleeding rats on the genitals or anus. The most widely used homeopathic materia medica [8], or reference book, also recommends Thuja for headaches that feel like a nail is being driven into the head; vertigo brought on by standing up; emotional depression and restlessness; pain or itching in the scalp; painful swallowing or a feeling of obstruction in the throat; intense thirst at night or early in the morning; stomach cramps that are worse in the evening; difficulty in breathing combined with a violent thirst for

cold water; frequent need to urinate, with frothy or cloudy urine; insomnia or restless sleep; or fever and chills that grow worse toward evening.

In aromatherapy, cedar leaf oil is classified as a base note, which means that it has a long-lasting scent when added to a perfume or incense blend. It is considered to have a sedative or calming effect, and is recommended for treating anxiety states a as well as asthma, bronchitis, and head colds. Some aromatherapists also recommend cedar leaf oil for treating acne and dandruff.

Cedar leaf oil is still used in some mainstream over-the-counter (OTC) preparations to relieve congestion in the upper respiratory tract. The best-known of these cold remedies is Vicks VapoRub™, which can be applied directly to the chest and covered with a hot towel, or added to a vaporizer to produce fragrant steam. Cedar leaf oil is also added to pest repellant sprays and paints to protect against mites, moths, and rodents.

Thuja's main action is due to its stimulating and alterative volatile oil. In bronchial catarrh Thuja combines expectoration with a systemic stimulation beneficial if there is also heart weakness. Thuja should be avoided where the cough is due to over stimulation, an in dry irritable coughs. *Thuja occidentalis* has a specific reflex action on the uterus and may help in delayed menstruation, but because of this action is should be avoided in pregnancy. Where ordinary incontinence occurs due to loss of muscle tone, *Thuja occidentalis* may be used. Also used in the treatment of psoriasis and rheumatism. Externally it may be used to treat warts. A marked anti-fungal effect is found if used externally for ringworm and thrush.

Thuja or Cedarwood (*Thuja occidentalis*) is a versatile and useful plant and has been used successfully for the treatment of psoriasis, rheumatism, and for warts. Also known as the Tree of Life or Arborvitae, it is useful as a counter-irritant in the relief of muscular aches and pains, including those of rheumatism. It can be applied externally in a salve for warts and other skin problems.

Phytochemistry

The fresh plant (related to the dry substance) contains 0.6% essential oil, 2.07% reducing sugar, 4.9% water-soluble polysaccharides, 2.11% water-soluble minerals [9], 1.67% free acid and 1.31% tannic agents The essential oil of the fresh leaves (related to the monoterpene fraction) contains 65% thujone, 8% isothujone, 8% fenchone, 5% sabines and 2% α-pinen as the main monoterpenes [10]. Other monoterpenes, namely carvotanacetone, origanol, origanes, myrcen and camphen, have been described [11-12]. Recently, further bioactive constituents have been found. High molecular weight glycoproteins/polysaccharides are highly relevant for the activity of the plant [13].

According to Hansel et al [14] the constituents of the dried herbal substance contains 1.4–4% essential oil, 60% of which is thujone, which corresponds to 2.4% thujone in the whole drug. Thujone occurs in nature as a mixture of α- and β-isomers [15, 16]. According to the

European Agency for the Evaluation of Medicinal Products (EMEA) [17], the content of thujone in dried twigs was determined as 7.6 mg/g, consisting of 85% α-thujone and 15% β-thujone .The equilibrium mixture consists of 33% α-thujone and 67% β-thujone [18].

A critical factor for *Thuja occidentalis* use as a medicinal herb is its content of essential oil. Indeed, the content of thujone seems to be significantly affected by different extraction procedures. The highest content of essential oil was found in extracts obtained by distillation, whilst percolation with purified water reduced the thujone content in the extract to the lowest level [19] Using purified water as a solvent, an average of 0.6 mg of thujone was extracted from 1 g of drug during percolation. In contrast, when 30% (v/v) ethanol was used, 2.8 mg of thujone was extracted from 1 g of *Thuja occidentalis* herba, and >2.5-fold higher amounts of thujone (7.9 mg) were attained with high ethanol concentration (90% v/v) [20]. From the result of 12 batches, the mean value for the thujone content was 1.16 mg/g of herbal substance and the maximum value was 2.95 mg/g, corresponding to 0.30%. Using a special extraction procedure with 30% (v/v) ethanol, the content of thujone in the extract can be reduced to one-third of the amount obtained by extraction with ethanol.

PHARMACOLOGICAL ACTIVITIES

ANTIBACTERIAL ACTIVITY

The alcoholic extract of twigs of *Thuja occidentalis* was established for Antibacterial activity against both gram negative and gram positive organisms i.e., Pseudomonas aeruginosa, Yersinia aldovae, Citrobacter, Shigella flexneri, E. coli and Staphylococcus aureu, Vernonia anthelmintica, Dryopteris chrysocoma and Trachyspermum ammi were tested In vitro for their antibacterial and antifungal activities. Antibacterial study performed against six bacteria viz., Escherichia coli, Citrobacter, Shigella flexenari, Yersinia aldovae, Staphylococcus aureus and Pseudomonas aeruginosa indicated that had potent activity against all microorganisms. The antifungal activity of these extracts was performed against six fungi, viz., Saccharomyces cereviciae, Aspergillus parasiticus, Trichophyton rubrum, Macrophomina, Fusarium solani and Candida albicans. The extracts showed significant results against different fungal strains [21].

ANTI- CANCER

Thujone rich fraction of *Thuja occidentalis* demonstrated major anti- cancer potentials evidences from in vitro studies on A375 cells [22]. Crude ethanolic extract of *Thuja occidentalis* was used as homeopathic mother tincture (TOΦ) to treat various ailments, particularly moles and tumors, and also used in various other systems of traditional medicine. Anti-proliferative and apoptosis-inducing properties of TOΦ and the thujone-rich fraction (TRF) separated from it have been evaluated for their possible anti-cancer potentials in the malignant melanoma cell line A375. On initial trial by S-diphenyltetrazolium bromide assay, both TOΦ and TRF showed maximum cytotoxic effect on A375 cell line while the other three principal fractions separated by chromatography had negligible or no such effect, because of which only TRF was further characterized and subjected to certain other assays for determining its precise anti-proliferative

and apoptotic potentials. TRF was reported to have a molecular formula of C10H16O with a molecular weight of 152. Exposure of TRF of *Thuja occidentalis* to A375 cells in vitro showed more cytotoxic, antiproliferative and apoptotic effects as compared with TOΦ, but had minimal growth inhibitory responses when exposed to normal cells (peripheral blood mononuclear cell). Furthermore, both TOΦ and TRF also caused a significant decrease in cell viability, induced inter-nucleosomal DNA fragmentation, mitochondrial transmembrane potential collapse, increase in ROS generation, and release of cytochrome c and caspase-3 activation, all of which are closely related to the induction of apoptosis in A375 cells. Thus, TRF showed and matched all the anti-cancer responses of TOΦ and could be the main bio-active fraction. The use of TOΦ in traditional medicines against tumors has, therefore, a scientific basis.

ANTI-HIV ACTIVITY

Thuja polysaccharides (TPS) inhibited human immunonodeficiency virus (HIV)-dependent cell death at a final concentration of 625 µg/ml. At this concentration, TPSg was shown to be completely non-toxic for MT-4 cells, which had not been infected with HIV-1. TPS were shown to inhibit HIV-1-specific antigen expression on freshly infected MT-2 cells in a dose-dependent manner [23].

ANTIBODY PRODUCTION

The retentate fraction produced a concentration-dependent increase in the number of antibody-producing lymphocytes in the hemolytic plaque assay in vitro. The number of anti-SRBC-(sheep red blood cell)-IgM-producing plasma cells rose, as did all Ig-secreting plasma cells, as registered by the 'reverse' technique using protein A-labeled SRBCs. Incubation with lipopolysaccharide (LPS) as positive control also led to a concentration-dependent increase in the number of plaque-forming cells [24].

Antispasmodic Activity

Antispasmodic activity of *Thuja occidentalis* twigs was evaluated by Noorjahn and mansoor Ahemad and found to have significant effect on isolated tissues [25].

ANTIOXIDANTS ACTIVITY

Lipid peroxidation activity was carried out to evaluate the antioxidant potential on fed rats. The antioxidant activity of ethanol fraction was increased in a concentration dependent manner. About 100, 150, 200, 250 & 300 µg EFTO (ethanol fraction of extract of aerial part of *Thuja occidentalis*) inhibited the FeSO4 induced lipid peroxidation in a dose dependent manner and showed IC50 value 195.60µg/ml. The results obtained in this study indicate that EFTO can be a potential source of natural antioxidant and activities related to this. The alcoholic and aqueous extract of *Thuja occidentalis* twigs established for anti-inflammatory and antioxidants activity by Dubey and Batra [26].

Anti Diabetic Activity

The study was to evaluate the anti diabetic activity of ethanolic fraction of *Thuja occidentalis* (EFTO) and to probe into its mechanism of action. Fasting blood sugar, blood glutathione levels and serum biochemical analysis in alloxan induced diabetes were investigated. EFTO produced a significant anti diabetic activity at dose level of 200 mg/kg. EFTO also showed significant increase in blood glutathione level due to its anti oxidant activity by Dubey and Batra [26].

Hepatoprotective Activity

The hepatoprotective potential effect of ethanolic fraction of *Thuja occidentalis* has been assessed against CCL4 induced liver damage in rats. A dose of EFTO 400 mg/kg p.o. exhibited significant protection from liver damage in acute and chronic CCL4 induced liver damage model. Histopathological examination was carried out after the treatment to evaluate hepato protection. The fraction was found to possess good hepatoprotective property in ethanolic extract, Hepatoprotective activity was estimated by Dubey and Batra [28].

INSECTICIDAL ACTIVITY

Insecticidal activity of two known insecticides (deltamethrin and imidacloprid), thujone and essential oil of rosemary against the larvae and adults of sycamore lace bug (Corythucha ciliata) was evaluated. The experiment was conducted in a laboratory, under room conditions. We tested the activity of each product in three different concentrations. The most desirable insecticidal activity had deltamethrin, which caused almost 100 % mortality of both developmental stages of the pest at all three concentrations. Succeeding products were imidacloprid, which caused 89.6 % larval mortality at recommended concentration, and essential oil of rosemary, which caused 81.7 % adult mortality at 1 % concentration. Larvae of sycamore lace bug were significantly more susceptible to tested products than adults. Significantly the lowest mortality was determined one day after treatment (41.7 %), while the highest mortality was stated three days after treatment (71.3 %). For future reduction of the damage caused by the studied pest on plane trees, we recommend the application of thujone and essential oil of rosemary, which appeared to be environmentally more acceptable substances. In our study both agents showed a middle satisfying activity in controlling larvae and adults, but they have also obvious repellent activity, which leads to their better efficacy in the open. Thujone acts as repellent agents to insects confirmed high mortality of the western corn rootworm larvae due to acute poisoning with thujone [29].

RADIOPROTECTIVE ACTIVITY

The effect of *Thuja occidentalis* against damage induced by gamma radiation was studied. Whole-body exposure of Swiss albino mice to gamma-rays (6 Gy) reduced the total white blood cell count to 1900 cells/mm(3) on the third day, which was elevated to 2050 cells/mm(3) by the administration of alcoholic extract of *Thuja occidentalis* (5 mg/dose/animal, intraperitoneally). Six animals from each group were killed after 2, 7, and 11 days of irradiation

to detect the bone marrow cellularity and radiation-induced toxicity. The number of bone marrow cells and alpha-esterase positive cells in control animals after 11 days was reduced to 12.2 x 10(6) cells/femur and 693.5/4000 cells, respectively. In *Thuja occidentalis* -treated animals, bone marrow cellularity was increased to 16.9 x 10(6) cells/femur and alpha-esterase positive cells were 940/4000 cells, a nearly normal level. Alcoholic extract of *Thuja occidentalis* reduced the elevated levels of GPT and alkaline phosphatase in liver and serum after irradiation. The lipid peroxidation levels were also lowered in the irradiated animals treated with the Thuja extract. Protective effect against radiation induced toxicity in mice estimated by Sunila et al [30].

ANTI ATHEROSCELOROSIS ACTIVITY

To evaluate the hypolipidaemic activity of an (EFTO) ethanol fraction of extract of aerial part of *Thuja occidentalis* Linn. (Cupressaceae) in hypolipidaemic activity EFTO at the dose of 200 mg and 400mg/kg body weight significantly reduced serum cholesterol (77 and 92%), LDL (53 and 84%), triglycerides (27 and 46%). The increase in HDL to total cholesterol ratio and reduction in atherogenic index in EFTO treated groups strongly supports anti-atherosclerotic property of *Thuja occidentalis* [31].

NEUROPHARMACOLOGICAL ACTIVITY

Aqueous extract of aerial part was investigated for evaluation of neuropharmacological activity by using elevated plus- maze test, open field test in which they were noted ambulation, rearing self grooming, activity in center, rota rod test and tail suspension test by Dey et al [32].

CONCLUSION

Despite the access to a large ethnobotanic florilegium in libraries and databases, the yield in numbers of herbs are the natural drugs used to regain the alterations made in the normal physiological system by foreign organisms or by any malfunctioning of the body.

The present review reveals that the plant *Thuja occidentalis* is found to have therapeutic uses in treating various ailments. A detailed research work in the characterization and standardization is strongly required for this potential plant in developing its various formulations, which can ultimetly be beneficial for humans as well as animals. Further studies are warranted to explore much depth about this plant known by the name “The tree of life”.

REFERENCES

[1] Chang LC, Song LL, Park EJ. J Nat Pro 2000; 63(9):1235–1238.
[2] British Herbal Pharmacopoeia. Thuja, British HerbalMedicine Association, West Yorks, UK 1983.
[3] Shimada K. Okajimas Folia Anatomica Japonica 1956; 28:207–227.
[4] Baran D. “Arbor vitae, a guarantee of health,” Revista Medico-Chirurgicala a Societatii de Medici si Naturalisti din Lasi 1991; 95(3-4): 347–349.

[5] Reitz HD, Hergarten H. Notabene Medici 1990; 20:304–6, 362–6.
[6] Bodinet C, Mentel R, Wegner U. Planta Medica 2002; 68: 896–900.
[7] Iwamoto M, Minami T, Tokuda H. Planta Medica 2003; 69–72.
[8] Cummings MPH, Stephen MD, and Ullman D. Everybody's Guide to Homeopathic Medicines, revised ed. NY: G. P. Putnam's Sons, 1991.
[9] Harnischfeger G, Stolze H. Bewahrte Pflanzendrogen in Western Medicine. Notamed Verlag, Bad Homburg/Melsungen. 1983; 250–915.
[10] Witte l, Berlin J, Wray V, Schubert W, Kohl W, Hofle G, Hammer J. Planta Med 1983; 49:216–21.
[11] Berlin J, Witte L, Schubert W, Wray V. Phytochem 1984; 23:1277–9.
[12] Hänsel R, Keller R, Rimpler H, Schneider G. Hagers Handbuch der Pharmazeutischen Praxis: Drogen P -Z (Thuja) 5th edn. Berlin: Springer Verlag; 1994; 955–66.
[13] Kawai S, Hasegawa T, Gotoh M, Ohashi H. Phytochemistry 1994; 37:1699–702.
[14] Neth R, Drize N, Gohla S, Offergeld R, Reski R, Schruhm S. Z Allgemeinmed 1995;71:522–30.
[15] Sondermann W, Schweers W. Tetrahedron Lett 1962; 7:259–60.
[16] Traud J, Musche H. Z Anal Chem 1983; 315:221–6.
[17] EMEA–The European Agency for the Evaluation of Medicinal Products. Committee for veterinary Medicinal Products—*Thuja occidentalis*. 1999. Summary Report.
[18] NIH. Executive Summary–Thujone Information, www.erowid.org. 7 June 2001.
[19] Tegtmeier M, Harnischfeger G. Pharmazie 1994; 49:56–8.
[20] Tegtmeier M, Harnischfeger G. Eur J Pharm Biopharm 1994; 40:337–40.
[21] Jahan N, Ahmad M, Mehjabeen M, Zia-ul-haq S, Alam M, Qureshi M. Pak J Bot 2010; 42(6):4281-4284.
[22] Biswas R, Mandal SK, Dutta S, Bhattacharyya SS, Boujedaini N, Anisur RKB. Evidences fromIn Vitro Studies on A375 Cells Evidence-Based Complementary and Alternative Medicine 2011; Article ID 568148, 16.
[23] Gohla SH, Zeman RA, Gartner S. AIDS Res Hum Retroviruses 1990; 6:131.
[24] Bodinet C, Freudenstein J. Planta Med 1999; 65:695–699.
[25] Jahant N, Mehjabeen M, Ahmed M, Shah NM, Chishti AK, Hamid S, Rehman AB. Inti Chem Phan 11 Med J 2004; 1(2):135-140.
[26] Dubey SK, Batra A. Asian J Pharm Clin Res 2009; 2:73–76.
[27] Dubey SK, Batra A. Asian J Res in Chem 2008; 1:32–35.
[28] Alfaro RI, Pierce HD, Borden JH, Oehlschlager AC. J Chem Ecol 1981; 7:39-48.
[29] Hwang YS, Wu KH, Kumamoto J, Axelrod H, Mulla MS. J Chem Ecol 1985; 11:1297–1306.
[30] Sunila ES and Kuttan G. Integr Cancer Ther 2005; 4(4):322–328.
[31] Dubey SK and Batra A. J Pharm Res 2009; 2:651–654.
[32] Deb L, Dey A, Agrawal S, Jain A. Inter Res J Pharm 2011; 2(3):143-148.