NATURALISTA CAMPANO
ISSN: 1827-7160
Volume 28 Issue 1, 2024

Comparison Based on Pharmacognostical and Pharmacological Profile of Thuja Orientalis Linn. And Thuja Occidentalis Linn.: A Review

Esha Vatsa[1*], Mehak Aggarwal[2], Nidhi Chaudhary[3], Shipra Gautam[4], Neeru[5], Nitin Kumar[6]

[*1,3]School of Pharmaceutical Sciences, Himgiri Zee University, Dehradun, Uttarakhand, India.
[2,4,5]Department of Pharmacy, Himachal Institute of Pharmacy, Paonta Sahib, Himachal Pradesh, India.
[6]Department of Pharmacy, HIMT Group of Institutions, Greater Noida, Uttar Pradesh, India.

Email: [1*]eshavatsa.2010@gmail.com

Abstract: Background: Thuja is an ornamental tree. It is a very vast genus that belongs to the Gymnosperms group of plants. The leaves, bark and fruits of genus Thuja have been used as a folk medicine for the treatment of uterine carcinomas, cystitis, respiratory tract infections, bacterial skin infections, osteoarthritis and several nerve disorders. It can also be used as an abortifacient and contraceptive. These claims can be validated through previously done studies over the Thuja species. This review based of exhaustive evidence, vital considerations of botanical expression, traditional uses, physicochemical parameters, phytochemical study and relevant pharmacological activity studies justifies the comparison between two very potent species of the genus Thuja.
Method: A virtual search of technical databases such as Google Scholar (4), Science Direct (6), Web of Science (5), PubMed (10), and Research Gate (8) was done to collect the data. Information was also acquired from research articles, review articles, relevant books and theses to organize all the scientific literature presented to deliver a portion of inclusive evidence on the comparison of these Thuja species.
Results: Several pharmacological findings discovered broad spectrum of animal activities like anti-inflammatory, analgesic and antioxidant properties. Both species of Thuja like T. occidentalis and T. orientalis screening parameters phytochemically leads to the detection of flavonoids, terpenoids, tannins, phenols, alkaloids, saponins, coumarins, steroids and cardiac glycosides in diverse areas of these species of the plant. The therapeutic components isolated from T. occidentalis and T. orientalis are (viz., ursolic acid, β-sitosterol, quercetin, dalspinin, rutin, tannic acid, kaempferol and epigallocatechin). Among these compounds few of them also revealed varied therapeutic activities including antineoplastic, hepatorenal protective, anti-oxidant, cardio-protective, anti- inflammatory, neuroprotective, immune- regulatory and anti-diabetic vindicating some of the traditional uses of this plant. The majority of the studies carried out on T. occidentalis and T. orientalis engrossed on their anti-microbial and anti-inflammatory activities specifically.
Conclusion: In this study, comparative analysis has been quoted between both the species of Thuja and medicinal potential of both the species was discussed which anticipates in making up-to-date substantiation for exploring the scientific and therapeutic potentials of the aforementioned species for the future study purpose and acts as a very potent analytical tool for researchers who want to work on these species in future.

Keywords: Herbal Remedies, Pharmacology, Phytochemically Potent, Thuja Occidentalis, Thuja Orientalis, Therapeutically Active, Traditional Use.

1. Introduction

Thuja, the general name for the trees of the genus Thuja, is a coniferous tree in Cupressaceae (cypress) family. These are the evergreen trees. They are also called 'Arborvitae' (1). The word arborvitae originated from the Latin Language which means 'tree of life'. The word Thuja is given by the Swedish botanist Linnaeus, is from a Greek word 'Thuo', which means 'to sacrifice'. Thuja is a type of conifer which generally comprises division Coniferae within Plant Kingdom (Plantae) (2). They are gymnosperms i.e., they are cone-bearing seed plants (not covered by the ovary) and also, they are woody. Some features of Thuja genus are (3):

- They grow up to 3-60m and have reddish-brown woody bark.
- Their leaves have flattened fan shaped grouping arrangement.
- Their branches are flattened in one plane.
- Their juvenile leaves are awl-like and mature leaves are scale-like.
- Their leaves are always in opposite direction.
- They may have raised a gland on their leaves back.
- The trees in this genus are also known as Tree of Life.

Thuja orientalis commonly known as 'Morpankhi' is an ornamental tree that has been widely distributed in cool and moist places (4) (Fig.1). It is primarily grown in gardens in temperate and semi-temperate climates where it is wet, well-drained soil, and receives full light. Rhodoxanthin, Amentoflavone, Hinokiflavone, Quercetin, Myricetin, Carotene, Xanthophylls, and Ascorbic acid are chemical elements of T. orientalis leaf, α-Thujone and β-Thujone, two diastereomeric forms of Thujone, are also found in leaves. Due to its small weight, plant wood is used in guitar soundboards. Bronchial catarrh, enuresis, cystitis, uterine cancer, amenorrhea, psoriasis, and rheumatism are all treated with it. It's also used to treat skin conditions and blood disorders (5,6). It is useful in the treatment of warty excrescences, spongy tumors, and kidney, brain, and gastrointestinal problems. Thujone is present in the oil of Thuja has lethal properties and therefore is studied for its GABA receptor antagonism (7, 8 and 9). Batra & Dubey reported the antioxidant &hepato-protective activity of T. orientalis (10) and T. orientalis was tested for its anti-proliferative and apoptosis-inducing activities by Biswas(11).
T. occidentalis, popularly known as White Cedar or American Arbor Vitae, is a Cupressaceae family medicinal plant (12) (Fig.2). It's a flowering plant native to Eastern North America. It is primarily stunted in cold and severe settings. Its bark is reddish or greyish-brown and fibrous. Wild T. occidentalis species are threatened in many areas where the deer population is high. Thujone, Isothujone, Fenchone, Sabines, and α-pinene are among the chemical components and essential oils found in its leaves (13).
It has many benefits and is used as a medicinal plant. It is used as an astringent, antifungal, antioxidant, anti-inflammatory, hepatoprotective, antibacterial and stimulant also (14,15 and 16).

2. Research Methodology

A literature survey of this review was obtained by investigating several electronic scientific books databases including Google Scholar (4), Science Direct (6), Web of Science (5), PubMed (10), and Research Gate (8). The relevant information was gathered from public domain open-source articles. The keywords such as "Thuja orientalis", "Thuja occidentalis", "therapeutically active", "phytochemically potent", "herbal remedies", "traditional uses", and "Pharmacology" were used to search the information. Various articles from the above-mentioned databases were studied exhaustively and during the reviewing process several articles were discarded too based on insufficient data available among the articles about the species of Thuja which is required for the creation of this manuscript and the numerals mentioned after the name of every database justifies the number of articles included from that particular database in the present manuscript. English-language publications only were allowed in the literature collections.

3. Results and Discussion

3.1. Taxonomy and geographic distribution of T. orientalis and T. occidentalis

T. orientalis: It is endemic to northwest China and has spread throughout Asia, including east Korea and Japan, south to northern India, and west to north Iran. It is a small, slow-growing tree with a trunk diameter of 0.5 m and a height of 15-20 m (7).
T. occidentalis: Northern White Cedar is native of NE Illinois and categorized as threatened in Kew's Plants of World Online database. The plant is more abundant in the state's boreal regions. Wooded wetlands, seepages,

and springs are common ecosystems in Illinois. It can also be found in wooded wetlands and along rocky cliffs outside of the state. Due to development, this tree has been uprooted in certain Illinois sites. An overabundance of deer in the state also poses a hazard. Northern white cedar is a popular landscape tree in backyards, parks, and cemeteries across the state. These cultivated trees, on the other hand, have rarely, if ever, escaped into natural areas (10).

Taxonomy to both species of Thuja is mentioned in **Table 1**.

Table 1: Taxonomical Classification of Thuja orientalis and Thuja occidentalis

	T. orientalis	**T. occidentalis**
Kingdom	Plantae	Plantae
Division	Coniferophyta	Pinophyta
Class	Pinopsida	Pinopsida
Order	Pinales	Pinales
Family	Cupressaceae	Cupresseaceae
Genus	Thuja	Thuja
Species	orientalis	occidentalis

3.2. Pharmacognostic features of T. orientalis and T. occidentalis

3.2.1. Macroscopic features: T. orientalis: In the case of T. orientalis after 3-4 seasons, the light green or yellowish green leaves turn brown. It's leaves are persistent and scale-like, in opposite pairs and decussate (17) (Fig.1). Its flowers are monoecious and have no ornamental importance. The fruits of T. orientalis are fleshy and glaucous during development. They are brown-colored, woody, and horn-like cones. The bark is greyish-brown and frayed (4).

T. occidentalis: Leaves of T. occidentalis are evergreen, broadly granulated with long points. Its leaves are generally paired at right angles, opposite and overlapping with a prominent resin gland along with folded side leaves. Shoots are long with short plump points. Flowers are monoecious, cone, and small in size. Female flowers are pink and male flowers are globular yellow. Females emerge at the tips of the short branches while males arise from small branches near the base of the buds. The fruit is brown colored, oval in shape, dry and hard shell (10) (Fig.2).

The comparison of the macroscopic features of T. orientalis and T. occidentalis are mentioned in **Table 2**.

Table 2: Comparison of Macroscopy of Thuja orientalis and Thuja occidentalis

Thuja orientalis		**Thuja occidentalis**
Leaves	Leaves are generally light green or yellow-green and become brown after 3-4 seasons. Its leaves are persistent and are scale-like, in opposite-decussate pairs.	The leaves are scale-liked with long points and are evergreen. Its shoots are long with short points and flattered. Its leaves are generally paired at right angles, opposite and overlapping with projecting resin gland and lateral leaves are folded.
Flower	Its flowers are monoecious and are not ornamentally important	Its flower is monoecious. The females are pinkish and the males are spherical and yellowish. Its flowers are cone-like and tiny. Females appear at the tips of short terminal branchlets while males arise from branchlets near the base of shoots.
Fruit	The fruits of Thuja orientalis are fleshy and glaucous when developing. They are woody and horn-like cones of brown colour when matured	Fruit is generally brown coloured and oval-shaped. It also has a covering that is dry and hard.
Bark	Its bark is of grey-brown colour and shredding	The bark grows in an upright position with no thorns present on it. Its twig is thin and generally of green or brown colour (13).


Fig.1: Whole plant of Thuja orientalis Fig. 2: Whole plant of Thuja occidentalis

3.2.2. Microscopic features

T. orientalis: Bark of T. orientalis has cork cells and cortex also present in the inner cork cells. Corks are polygonal cells that are thick-walled and flat. Below the cork, phellogen and phelloderm are present. There are large, isolated oil cells in the cortex area and the medullary rays are prominent with parenchymal (thick-walled) cells (18) (Fig.3). Leaves contain single-layered epidermis with a thick striated cuticle followed by thick-walled hypodermis. Stomata can be found in the epidermal layer, which is xerophytic. The endodermis is made up of a single layer of barrel-shaped cells. Individual bi-collateral bundles were also detected in transfusion cells, which contained parenchymal cells, resin cells, and tracheids (19) (Fig.4).

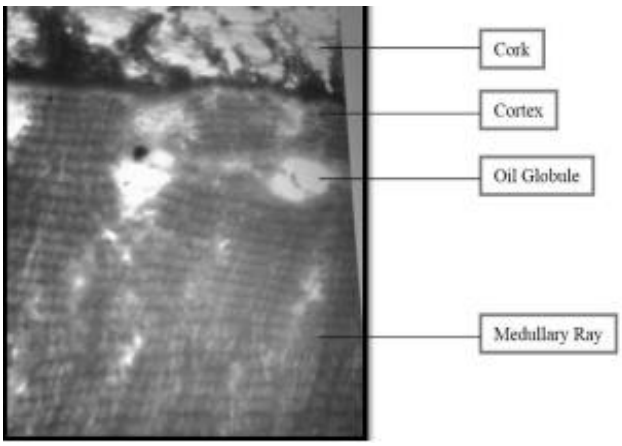
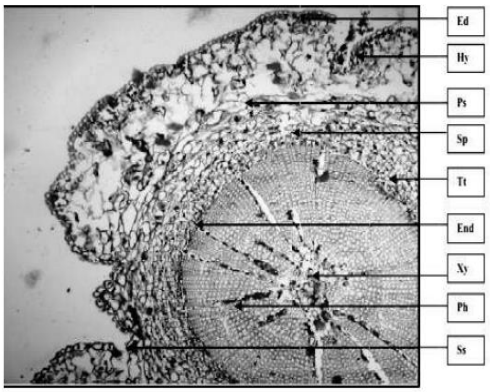


Fig.3: Microscopy of bark of Thuja orientalis



Ed:Epidermis, Hy:Hypodermis, Ps:Palisade cells, Sp:Spongy Parenchyma, Tt:Transfusion tissue, End:Endodermis, Xy:Xylem, Ph:Phloem, Ss:Sunken stomata

Fig.4: Microscopy of leaves of Thuja orientalis

T. occidentalis: Bark of T. occidentalis contains 6-7 layers of cork cells embedded with brown content. The cortex consist of two-layered, thin-walled cells of hypodermis and sclerenchyma. The phloem consists of phloem parenchyma and phloem fibers (alternate layers) (Fig.5). Leaves consists of a single layer of the epidermis, a resin duct, mesophyll (thin-walled) cells, endoderm around the stele, and xylem around the phloem. Leaves are isobilateral and largely elliptical (13) (Fig.6).

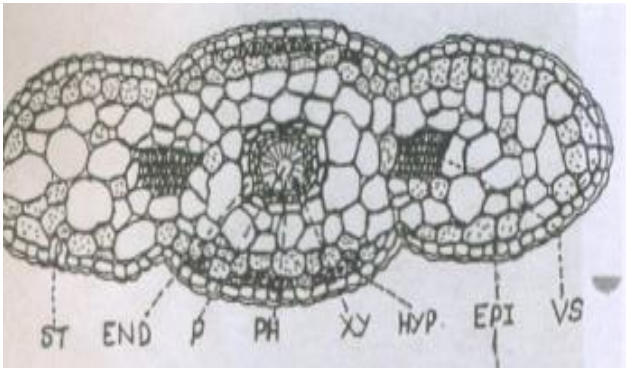


Fig.5: Microscopy of bark of Thuja occidentalis

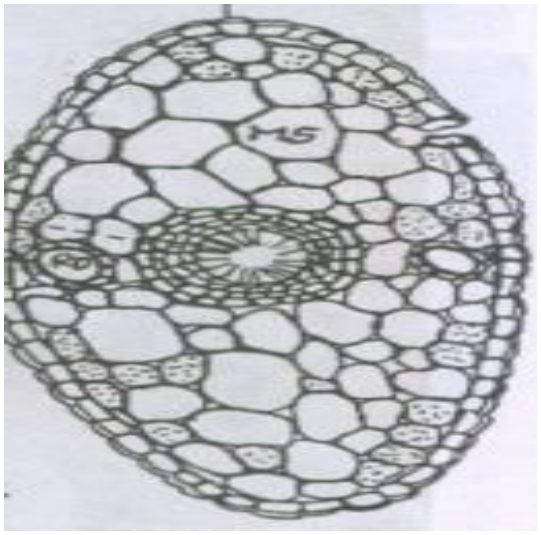


Fig.6: Microscopy of leaves of Thuja occidentalis

Comparison of microscopic features of T. orientalis and T. occidentalis are mentioned in **Table 3**.

Table 3: A Comparison of Microscopy of Thuja orientalis and Thuja occidentalis

	Thuja orientalis	**Thuja occidentalis**
Bark	Cork cells are present and cortex is also present in inner cork cells. Cork is the polygonal cells that are thick walled and flat. Below cork, phellogen and phelloderm is present. Big and isolated oil cells are present in the cortex region and medullary rays are prominent multiseriate with parenchymatous cells (thick-walled).	Cork cells are present in 6-7 layers with brown contents. Thin-walled cortex with two layered hypodermis and sclerenchymatous is also present. Phloem consists of phloem parenchyma and phloem fibers (alternate layers).
Leaves	Single layered epidermis with a thick, striated cuticle and thick-walled hypodermis beneath the epidermis layer is present. Stomata is present in epidermis layer which is xerophytic in nature and barrel-shaped cells of single	The single layered epidermis is present. Its leaves are isobilateral and broadly elliptical. Consists of parenchyma containing one resin duct, mesophyll cells (thin-walled), endodermis around the stele, and xylem around the phloem.

	continuous layer are endodermis. Parenchymatous cells, resin, and tracheid cells are the compositions of transfusion tissue where the single bi-collateral bundles were also present.	

3.3. Ethnomedicinal use in traditional medicine

T. orientalis: T. orientalis is a common herb in Chinese herbal medicine, and is one of the 50 basic herbs. Antibacterial, antipyretic, antitussive, astringent, diuretic, emmenagogue, emollient, expectorant, febrifuge, hemostatic, refrigerant, and stomachic properties are all found in the leaves. Plants can also help with hair growth (4 and 20). Cough, bleeding, heavy menstruation, bronchitis, asthma, skin infections, mumps, bacterial dysentery, arthritic pain, and premature balding are all treated with them internally. As needed, fresh and dried leaves can be picked. Pregnant women should not be given this treatment. The seed is tasty, calming, and relaxing (20). Internally, it is used to treat palpitations, sleeplessness, neurological problems, and constipation in the elderly. Burns and scalds can be treated with the root bark (21). Cough, cold, dysentery, rheumatism, and parasitic skin illnesses are all treated using the plant's stem.

T. occidentalis: T. occidentalis has been used to treat liver illness, bullous bronchitis, psoriasis, enuresis, amenorrhea, cystitis, uterine cancer, diarrhea, and rheumatism in traditional medicine (22, 23, 24, 25 and 42). Fungal infections, cancer, and intestinal worms have all been treated with essential oil extracted from the leaves (11). Warts, papillomata, and warts caused by the human papillomavirus have all been treated using T. occidentalis tincture (HPV) (25 and 26). This plant's essential oil has been utilized in folk medicine since ancient times. Hepatoprotection, bronchial catarrh, rheumatism, psoriasis, and even uterine carcinomas have all been treated with T. occidentalis containing thujone. The mother tincture is also used in homeopathy to treat a variety of ailments. Thuja is one of the principal medicines in homeopathy for psychotic conditions, such as snake bites, smallpox, and vaccination-induced toxicity (27). Thuja concoctions containing thujone have long been employed by traditional American Indian healers. Constipation and headaches can be relieved by a tea made from the inner bark of non-woody twigs.

3.4. Comparison of Physico-Chemical profile of T. orientalis and T. occidentalis

Ash value: The ash values provide a useful indication of the purity of raw drugs and provide information on possible contamination with inorganic materials such as silica and metallic salts. Water-soluble ash is a good indicator for both previous extractions of water-soluble salts in the material or indication of incorrect preparation. The total ash content in T. orientalis was found to be 18.21% w/w whereas 6.92% w/w in T. occidentalis. The water-soluble ash value of T. orientalis was found to be 4.36% w/w whereas of T. occidentalis it was 3.65% w/w.

Loss on drying: Water and volatiles of any kind that can be removed under specified conditions cause weight loss, which is reported as a percentage w/w**.** Loss on drying was found to be 8.79% w/w in T. orientalis and 6.92% w/w in T. occidentalis.

Volatile oil: Essential oils are volatile components found in plants' different sections. It's made up of terpenes, sesquiterpenes, and their oxygenated derivatives, as well as certain aromatic chemicals, all of which are volatile at room temperature and have an oily look. T. orientalis contain 1.0% w/w volatile oil and T. occidentalis contain 0.87% w/w volatile oil.

The physicochemical profile comparison of T. orientalis and T. occidentalis are mentioned in **Table 4**.

Table 4: Comparison of Physico-Chemical profile of Thuja orientalis and Thuja occidentalis

S. No.	**Evaluation Parameter**	**Thuja orientalis**	**Thuja occidentalis**
1.	Total Ash Value	18.21% w/w	6.92% w/w
2.	Water Soluble Ash Value	4.36% w/w	3.65% w/w
3.	Loss on Drying	8.79% w/w	6.92% w/w
4.	Volatile oil	1.00% w/w	0.87% w/w

3.5. Comparison of Phytochemical profile of T. orientalis and T. occidentalis

Carbohydrates, alkaloids, glycosides, phenolic compounds, tannins, saponins, flavonoids, fixed oil, and fat were

found in powdered T. orientalis and T. occidentalis, according to preliminary phytochemical analysis (18, and 28) **Table 5**. The secondary plant metabolites contained in medicinal plants are thought to be responsible for the observed therapeutic benefits. These metabolites may contribute to the folklore usage of T. orientalis and T. occidentalis as medicines.

Table 5: Comparison of Phytochemical Profiles

S. No.	**Chemical Constituents**	**Test**	**Thuja orientalis**	**Thuja occidentalis**
1.	Carbohydrates	Fehling's test Molisch's test	Positive Positive	Positive Positive
2.	Alkaloids	Dragendorff's test Mayer's test Wagner's test Hager's test	Positive Positive Positive Positive	Negative Positive Positive Positive
3.	Glycosides	Molisch test Keller-killani test With conc. H_2SO_4	Positive Positive Negative	Positive Positive Positive
4.	Phenolic compounds and Tannins	With 5% ferrous sulphate and sodium potassium tartarate Lead acetate test, ferric chloride test	Positive Positive	Positive Negative
5.	Saponins	Foam test Lieberman-Burchard reaction (For steroidal saponins)	Positive Positive	Positive Positive
6.	Flavonoids	5% NaOH test Lead acetate test H_2SO_4 zinc test	Positive Positive Negative	Positive Positive Positive
7.	Fixed oils and fat test	Spot test	Positive	Positive

3.6. Pharmacological studies of extracts of T. orientalis and T. occidentalis
The main components of the essential oils are mono and sesquiterpene, including carbohydrates, phenols, alcohols, ethers, aldehydes and ketones that are responsible for the biological activity of aromatic and medicinal plants (29 and 30).

T. orientalis: T. orientalis is used internally in the treatment of cough, bleeding, excessive menstruation, bronchitis, asthma, skin infections, mumps, bacterial dysentery, and arthritic pain. The leaves of the plant are antipyretic, astringent, diuretic, emmenagogue, emollient, expectorant, refreshing and stomachic. The plant is reported to improve hair growth (4). It is used internally in the treatment of palpitations, insomnia, nervous disorders and constipation in old people. The bark is used in the treatment of burns and scalds. Cough, cold, dysentery, rheumatism, and parasitic skin illnesses are all treated using the plant's stem. When compared to psychotropic cannabinoids, thujone was a mild acyl-CoA inhibitor: Lys phosphatidylcholine acyltransferase activity in mouse brain synaptosomes (21 and 45).

3.6.1. Anti-bacterial: Plants and their essential oils have antibacterial properties that could be therapeutic. T. orientalis has high levels of three compounds (alpha, beta, and gamma Thujaplicin), which act as chelators for Solmonella typhimurium at low concentrations (31)**.** T. orientalis inhibited the growth of Solmonella mutans serotypes c and d with a MIC of less than or equal to 2.0-7.8 mg/ml (32). Thuja orientalis leaves were pulverized, and two solvent systems—(E 1) ethyl acetate: chloroform: ethanol (40:30:30) and (E 2) methanol: distilled water—were used in the soxhlet extractor to extract the materials (70:30). The crude E 1 and the E 2 extract and its fractions were screened for phytochemical components, antioxidant activity, and antibacterial activity in this work. By using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) test, antioxidant activity was measured. According to the findings, E 2 extract, which is 70% methanolic, had the maximum antioxidant effect (85.25% inhibition) at a concentration of 100 g/ml, while E 1 and E 2 crude extracts both had significant (P 0.05) inhibitory action against both gram-positive and gram-negative organisms. Additionally, all of the

chosen bacteria were resistant to the fractions' antimicrobial effects (28).

3.6.2. Anti-fungal: In a direct bioautography study, the essential oil extracted from lipophilic leaves extract of T. orientalis demonstrated antifungal efficacy against Alternaria alternate and Currularia lunata. Rf = 0.80 was shown to be the best bioactive component for antifungal activity. It has created inhibitory zones with diameters of 30 and 22 mm against A. alternative and C. lunata, respectively. Six strains of human pathogenic fungi were tested, and the essential oils showed some antifungal action (17).

3.6.3. Anti-viral activity: GC/MS analysis was used to evaluate the chemical composition of the essential oil of T. orientalis scent. Essential oils were tested in vitro for inhibitory efficacy against the coronaviruses that cause SARS and herpes simplex virus type 1 (HSV-1) by visualizing the pathogenic effect of cells following infection with the viruses. T. orientalis allopathic extracts have been shown in numerous investigations to be effective antiviral agents against plant and animal viruses (4).

3.6.4. Anti-inflammatory activity: The suppression and advancement of cardiovascular disease, including atherosclerosis, is influenced by vascular inflammation. In human umbilical vein endothelial cells, the anti-inflammatory activity of an aqueous extract of T. orientalis (ATO) and its probable mechanisms was investigated (HUVEC). The pre-incubation with ATO suppressed tumor necrosis factor and also prevented the adhesion of U937 monocytes to TNF-stimulated HUVECs, implying that it may limit monocyte adherence to the endothelium. TNF-induced generation of reactive intracellular oxygen species was also dramatically reduced by ATO (ROS). Overall, ATO inhibits intracellular ROS production, NF-kB activation, and cell adhesion molecule in HUVECs, which is at least in part owing to a TNF-induced decrease in endothelium adhesion to monocytes (11).
T. occidentalis: T. occidentalis is used to treat diarrhea, uterine carcinomas, bronchitis, amenorrhea, cystitis, psoriasis, enuresis, and rheumatism when taken internally (22,23,24 and 25). Different types of fungal diseases, intestinal worms, and cancer are treated with the separated volatile oil (11). T. occidentalis essential oil has been utilized in folk medicine since ancient times. T. occidentalis contains the active phytoconstituent thujone, which has traditionally been used to treat bronchial catarrh, rheumatism, hepatoprotection, psoriasis, and uterine carcinomas. Thujone has several pharmacological effects (43 and 44).

3.6.5. Anti-bacterial: T. occidentalis constitutes two important constituents i.e., α-thujone and β-thujone, which revealed protective effects against Gram-negative bacteria like Pseudomonas aruginos and Klebsiella pneumonia and a mild protective effect against Staphylococcus aureus, Escherichia coli and Candida albicans (33). Essential oil extracted from the leaves and cones of T. occidentalis was found to have antibacterial activity against gram-negative bacteria such as E. coli, Salmonella typhimurium, Aeromonas hydrophila, and Pseudomonas aeruginosa in a recent study. Listeria monocytogenes, Staphylococcus aureus, and Bacillus cereus are Gram-positive bacteria.

3.6.6. Anti-fungal: T. occidentalis possess antifungal properties against Saccharomyces cerevisiae, Aspergillus niger, Aspergillus flavus, Aspergillus parasitious, Macrophomina, Trichophyton rubrum and Fusarium solani (34). Aspergillus flavus and Aspergillus niger are fungi. Candida albicans is a type of yeast (35).

3.6.7. Anti-viral activity: T. occidentalis consists of several polysaccharides which revealed antiviral and immune stimulating potential. It also has the capability for inhibition of HIV-1 and influenza viruses. Later, the anti-viral property of fractions of higher molecular weight polysaccharides was found very active against HIV-1(36).

3.6.8. Anti-inflammatory activity: T. occidentalis comprises of several polysaccharides which have been shown potent for the reduction of mice-induced inflammation. They also ensure the capability for the prevention of metastasis by waning the inflammatory cytokines, like IL-6, IL-1β, TNF-α and granulocyte-macrophage colony-stimulating factor (GM-CSF). Furthermore, these polysaccharides aid in the stimulation of cell-mediated antibody-dependent cytotoxicity (ADCC), natural killer (NK) cells, and complement-mediated cytotoxicity (ACC), as well as the activity of anti-tumor agents such as TIMP and IL-2 (37). The purpose of another study was to determine whether the polysaccharide fraction and aqueous extract of T. occidentalis L. have any anti-inflammatory effects on mice. Their analyses of the effects of aqueous extract and polysaccharide fraction (3, 10, and 30 mg/kg, i.p.) on paw edema caused by carrageenan, dextran sulfate, compound 48/80, serotonin, bradykinin, histamine, and prostaglandin E2 revealed a significant (p 0.05) reduction. Additionally, it reduced

myeloperoxidase activity, tumor necrosis factor, and interleukin-6 levels, vascular permeability, nitrite concentration, and malondialdehyde concentration while maintaining the GSH levels in the peritoneal exudate. It also prevented neutrophil recruitment (38).

3.7. Toxicity Study

Toxicity studies are very essential for the genus and its associated species, their prepared herbal extracts and their isolated compounds in a very precise way before their solicitations are subjected to clinical trials. There is also a very strong insight that herbal medications consist of very lower risk value. However, the evidence available in very recent years, concerning the adverse effects of herbal medicinal products imposed thorough studies on the toxicity profile. Genus Thuja is quite safe when taken orally with a specified amount of food, but there isn't enough research to tell if it's safe when taken in typical therapeutic doses. If a person consumes too much Thuja, they may have nausea, biliousness, painful diarrhoea, asthmatic problem, convulsions, and even death. Genus Thuja also constitutes Thujone as an active constituent which can cause lowering of blood pressure, seizures, asthma, and death. During pregnancy and for breast-feeding mother it is very unsafe to take Thuja by the oral route as Thuja might cause a miscarriage.

Pharmacological studies are mentioned in **Table 6** of T. orientalis and T. occidentalis.

Table 6: Pharmacological studies on Thuja orientalis and Thuja occidentalis.

Biological activity	**In Vitro studies**	**In Vivo studies (Animal Model)**	**Reference**
Thuja orientalis			
Anti-bacterial	Inhibit the growth of serotypes c and d of Salmonella mutants	--	Jain, et al., 2017
Anti-fungal	Inhibit Candida albicans	--	Singh, et al., 2002
Anti-viral	Inhibit HIV-1	--	Gohla, et al., 1992
Anti-inflammatory	--	Carrageenan-induced inflammatory model on albino rats	Panthong, et al., 1986
Thuja occidentalis			
Anti-bacterial	Decrease in gram-negative/positive bacteria	--	Bellili., et al., 2018
Anti-fungal	Inhibitory activity against the fungi causing keratitis	--	Asha, et al., 2016
Anti-viral	Inhibition of HIV-1	--	Gohla, et al., 1992
Anti-inflammatory	--	TNBS-induced colitis mouse model	Stan, et al., 2019 and Caruntu, rt al., 2020

3.8. Critical assessments of the papers reviewed

The data, research, and review papers that were included in this study have already been assessed, and they were especially commended for identifying gaps during research. The occurrence of shortcomings, several probable drawbacks, and issues are enlisted for researchers who want to conduct further studies on the above-mentioned plant species.

(i) The pharmacological activities conducted on the above-mentioned plant species are too preliminary with the availability of insufficient data for a researcher e.g., in the case of antifungal and anti-microbial activity of T. occidentalis, there is no significant data available to draw any noteworthy conclusion. As a result, there is a requirement for supplementary deeper studies to confirm the reported activity.

(ii) Most of the research data quoted in this review article denote the pharmacological activities of both the above-mentioned species.

(iii) Also, there is insufficient data available for the concerned in vivo studies of various pharmacological activities mentioned in this article.

(iv) There are just a few articles on these plant species that contain the details of the ethical permission, including the registration number from the IEC (Institutional Ethics Committee) that approved the experimental design.

(v) Furthermore, certain activities are known that were carried out more superficially and were limited to the identification of a few cell lines without distinguishing the mode of action.

(vi) Some activities have not mentioned phytochemical screening of the extracts used, which will only give a general sense of the extracts utilized in the study, as well as the repeatability of the particular pharmacological activity using standard extracts. This may also result in a lack of data for the investigation of the major active ingredients responsible for specific biological activity.

3.9. Concluding remarks and future perspectives

In the present review, we reviewed various properties of the genus Thuja and compared various pharmacognostic, physico-chemical, phytochemical properties and pharmacological activity studies of T. orientalis and T. occidentalis. Based on the comparison of several of the aforementioned parameters, it is reasonable to conclude that thujone is the most active constituent in both species of the genus Thuja, and that the isolated essential oil from the leaves of the plant has the dynamic potential which is solely responsible for the majority of pharmacological activities. A critical analysis of the literature revealed that these plants contain different chemical constituents which are responsible for various therapeutic activities. Antipyretic, antibacterial, antioxidant, anthelminthic, anti-inflammatory, analgesic, hair growth promoter, anti-microbial, and anti-cancer activities are all present in these plants. These have been used to treat skin ailments such as warts and corn since ancient times. However, some of the claims based on the traditional use of these plant species still require pharmacological validation too. These may include the use of T. orientalis and T. occidentalis for the further study of the antihypertensive, anti-hyperlipidemic and study of the purgative potential of the plant species. Furthermore, the study can be conducted on the aforementioned component for the understanding of their general mechanism of action for acknowledged ethnomedicinal purposes and associated pharmacological activities, by clinical research or human trials.

Traditional uses, phytochemistry, physicochemical parameters, and pharmacological aspects of T. orientalis and T. occidentalis have all been thoroughly reviewed in this study, which has also provided all-inclusive evidence on these plant species, as well as some guidelines for future research on these plant species. However, various flaws and pitfalls have been recognized; these plant species also offer a lot of promising predictions for innovative drug development, and the aforementioned concerns are taken seriously.

4. Acknowledgement

Department of Pharmacy, Banasthali University, Banasthali, Tonk, Rajasthan; Department of Pharmacy, Himachal Institute of Pharmacy, Paonta Sahib, Himachal Pradesh and Faculty of Pharmaceutical Sciences, The ICFAI University, Baddi, Solan, Himachal Pradesh, INDIA supported this work.

Conflict of Interest

No conflict of interest is associated with this review work.

Funding Sources

There are no Funding sources.

5. References

1. Farzon A. Pinacear. drawings, and descriptions of the genera Alies; Cedrus,Pseudolarix, Ketelecria, Nothotsuga, and Tsuga. Cathaya, Pseudotsuga, Larix, and Picea. Regnum Vegetahile. 1990; 11: 1-330.
2. Hart J.A. A Cladistic Analysis of Conifers: Preliminary Results, J Arnold Arbor. 1987; 68:269-307.
3. LePage B. A new species of Thuja (Cupressaceae) from the Late Cretaceous of Alaska: Implications of being evergreen in a polar environment. American Journal of Botany. 2003; 90:167-174.
4. Yeung H.M. Handbook of Chinese herbs and formulas. Institute of Chinese Medicine. Los Angeles, C.A. 1985.
5. Hassanzadeh M. K, Rahimizadeh M. Fazly Bazzaz B.S, Emami S.A, Asili J. Chemical and antimicrobial studies of Platycladus orientalis essential oils. Pharm. Biol. 2001; 5: 388- 390.
6. Kumar P.V, Chauhan S.N, Padh H, Rajani M. Search for antibacterial and antifungal agents from selected Indian medicinal plants. J. Ethnopharmacol. 2006; 107:182-188.
7. Yan-hua L, Zhi-yong L, Zheng-tao W, Dong-zhi W. Quality evaluation of Platycladus orientalis (L.) Franco through simultaneous determination of four bioactive flavonoids by high-performance liquid chromatography. J. Pharm. Biomed. Anal. 2006; 4:1186-1190.

8. Kuo Y.H, Chen W.C. 15-Hydroxypinusolidic acid, a new diterpene from the pericarp of Platycladus orientalis Franco, Heterocycles.1990; 31:1705-1709.
9. Koo K.A, Sung S.H, Kim Y.C. A new neuroprotective derivative from the leaves of Biota orientalis. Chem. Pharm. Bull. 2002; 50:834-836.
10. Dubey S.K, Batra A. Antioxidant activities of Thujaoccidentalis Linn. Asian J. Pharm. Clin. Res. 2009; 2:73-76.
11. Biswas R, Mandal S, Dutta S, Bhattacharya S, Boujedaini N, Khuda-Bukhsh A.R. Thujone-rich fraction of Thuja occidentalis demonstrates major anti-cancer potentials; Evidances from in-vitro studies on A375 cells. Evid. Based Complement. Alten. Med. 2011; 1:1-16.
12. Keita S.M, Vincet C, Schmidt J, Arnason J.T. Insecticidal Effects of Thuja occidentalis essential oil on Callosobruchus maculates. Canadian J Plant Sci. 2000; 4:173- 177.
13. Dhiman A, Bhan M, Lal R, Dhiman B,Singla C. An Appraisal of Pharmacognosy, Phytochemistry and Bioactivity of Thujaoccidentalis Linn. (Cupressaceae). Journal of Pharmaceutical and Scientific Innovation. 2012; 1: 1-5.
14. Gupta G, Srivastava A.K, Gupta N. Mycoses: An Update over Clinical Cure with Homeopathic Drugs. Homeopathic J. 1997; 7:67-96.
15. Jahan N, Ahmad M, Mehjabeen Zial-ul-haq M, Alam S.M, Qureshi M. Antimicrobial Screening of Some Medicinal Plants of Pakistan. Pak J Bot. 2010; 42:73-79.
16. Lokesh D, Amitabha D, Aggarwal S, Jain A. Neuropharmacological Exploration of Thujaoccidentalis Linn. Inter Res J Pharm. 2011; 2:143-148.
17. Ohmoto T, Yamaguchi M. Constituents of Pollen. XV. Constituents of Biota orientalis. Chem. Pharm. Bull. 2002; 36:807-811.
18. Kshirsagar S, Malode S, Aher A.N. Pharmacognostical Standardization of Bark of Thuja orientalis Linn. Journal of Pharmacognosy and Phytochemistry. 2017; 6:740-743.
19. Singh S, Thukral S.K. Pharmacognostical Standardization of Leaves of Thuja orientalis (Linn.) Franco. Scholars Research Library. 2014; 6:15-19.
20. Bown D. Encyclopacdia of Herbs and their Uses. Dorling Kindersley. London. 1995.
21. Duke J.A, Ayensu E.S. Medicinal plants of China. Reference Publ., Inc. Algonac. Michigan. 1985; 705: 20-24.
22. Naser B, Bodinet C, Tegtmeier M, Lindequist U. Thuja occidentalis (Arborvitae): A Review of its pharmacological, pharmaceutical and clinical properties. Evid. BasedComplement. Alternated. 2005; 2:69-78.
23. Akkol E.K, Ilhan M, Demirel M.A, Keles H, Tumen I, Suntar I. Thuja occidentalis L. and its active compound, a-thujone: Promising effects in the treatment of polycystic ovary syndrome without inducing osteoporosis. J. Ethnopharmacol. 2015; 168:25-30.
24. Brijesh K, Ruchi R, Sanjita D. Phytoconstituents and therapeutic potential of Thuja occidentalis. Res. J. Pharm. Biol. Chem. Sci. 2012; 3:354-362.
25. Shimada K. Contribution to anatomy of the central nervous system of the Japanese. Okajimas Folia Anat. Jpn. 1956; 28:207-2227.
26. Alves L.D.S, Figueredo C.B.M, Silva C.R, Marques G.S, Ferreira P.A, Soares M.F, Silva R, Rolim-Neto PJ. Thuja occidentalis L. (Cupressaceae): Review of botanical, phytochemical, pharmacological and toxicological aspects. Int. J. Pharm. Sci. Res. 2014; 5:1163-1177.
27. Nash E.B. Expanded Works of Nash Hardcover. B Jain Publishers Put Lid., Noida. India. 2002.
28. Jasuja N.D, Sharma S, Saxena R, Chaoudhary J. Antibacterial, Antioxidant and Phytochemical Investigation of Thuja orientalis leaves. Journal of Medicinal Plant Research. 2013; 7:1886-1893.
29. Perry N.B, Anderson R.E, Brennan N.J, Douglas M.H, Heaney AJ, McGimpsey J.A, SmallfieldB.M.Essential oils from dalmatian sage (Salvia officinalis L.) Variations among individuals. plants parts. seasons. and sites. J. Agric. Food Chem. 1999; 47(5):2048-2054.
30. Sokovic M, Glamoclija J, Marin P.D, Brkic D, Van Griensven L. Antibacterial effects of the essential oils of commonly consumed medicinal herbs using an in vitro model. Molecules. 2010; 15:7532-7546.
31. Akers H.A, Abrego V.A, Garland E. Thuja plicins from Thuja plicata as iron transport agents for Salmonella typhimurium. J. Bacteriol. 1980; 141(1):164-168.
32. Chen C.P, Lin C.C, Namba T. Screening of Taiwanese crude drugs for antimicrobial activity against Streptococcus mutans. J. Ethnopharmacol. 1989; 27:285-295.
33. Jirovetz L, Buchbauer G, Denkova Z, Slavchev A, Stoyanova A, Schmidt E. Chemical composition, anti- microbial activities and odor descriptions of various Salvia sp. And Thuja sp. Essentialoils. ErnahrungNutr. 2006; 30: 152-159.
34. Digrak M, Bagci E, Alma M.H. Antibiotic action of seed lipids from five tree species grown in Turkey.

Pharm. Biol., 2002; 40: 425 428.
35. Bellili S, Aouadhi C, Dhifi W, Ghazghazi H, Jlassi C, Sadaka C, Beyrouthy M, Maaroufi A, Cherif A, Mnif W. The influence of organs on biochemical properties of Tunisian Thuja occidentalis essential oils. 2018; 10: 649.
36. Gohla S.H, Zeman R.A, Bogel M, Jurkiewicz E, Schrum S, Haubeck H.D, SchmitzH, Hunsmann G, Neth R.D. Modification of the in vitro replication of the Human immunodeficiency Virus HIV-1 by TPSg. a Polysaccaride Fraction Isolated from the Cupressaceae Thuja occidentalis L. (Arborvitae), Haematol. Blood Transfus. 1992; 35: 140-149.
37. Sunila E.S, Hamsa T.P, Kuttan G. Effect of Thuja occidentalis and its polysaccharide on cell-mediated immune responses and cytokinesvels of metastatic tumor-bearing animals. Pharm. Biol. 2011; 49: 1065-1073.
38. Silva I.S, Nicolau L.A.D, Sousa F.B.M, Araujo S, Oliveira A.P, Araujo T.S.L, Souza L.K.M, Martins C.S, Aquino P.E.A, Carvalho L.L, Silva R.O, Neto P.J, Medeiros J.V.M, Evaluation of anti-inflammatory potential of aqueous extract and polysaccharide fraction of Thuja occidentalis Linn. in mice. Int. J. Bio. Macro. 2017; 105(1): 1105-1116.
39. Shah W.A, Qadir M. Chemical composition, antioxidant and antibacterial activity of Thuja orientalis essential oil. World J Pharm. Sci. 2014; 2(1): 1-136.
40. Sah S.N, Regmi S, Tamang M.K. Antibacterial effects of Thuja leaves extract. Int. J. App. Sci. Biotech. 2017; 5(2): 256.
41. Caruntu S, Ciceu A, Olah N.K, Don I, Harmenean A, Cotoraci C. Thuja occientalis L. (Cupressaceae): Ethnobotany, Phytochemistry and Biological Activity. Molecules. 2020: 25(22):5416.
42. Loonat A, Chandran R, Pellow J, Abrahamse H. Photodynamic effects of Thuja occidentalis on lung cancer cells. Front. Pharmacol. 2022.
43. Bhargava S, Singh T.G, Mannan A, Singh S, Gupta S. Pharmacological evaluation of Thuja occidentalis for the attenuation of nephropathy in streptozotocin-induced diabetes in rats. Obesity medicine. 2022: 31;100391.
44. Pal A, Das S, Basu S, Kundu R. Apoptotic and autophagic death union by Thuja occidentalis homeopathic drug in cervical cancer cells with thujone as the bioactive principle. Journal of Integrative medicine. 2022: 20(5);463-472.
45. Jung J, Chun Y, Jang Y.P, Oh M.S, Kim J.H, Kim J. An alcoholic extract of Thuja orientalis L. leaves inhibit autophagy by specially targeting pro-autophagy PIK3C3/VPS34 complex. Scientific reports. 2021: 11.