

REVIEW ARTICLE



A REVIEW OF PHYTO-CHEMICAL CONSTITUENT AND PHARMACOLOGICAL ACTIVITY OF *THUJA SPECIES*

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Received- 11/October/2020

Revised- 01/November/2020

Accepted- 15/November/2020

Published- 31/December/2020

ABSTRACT

Traditional healthcare systems play an important role in our healthcare system. The villagers use this plant mainly for the treatment of various diseases. Thuja belongs to the family of cupressaceae. This is commonly used in Ayurvedic medicine. There are five species in the thuja genus, three local to eastern Asia and two local to North America. Phylogenomic investigations resolved two sister sets, *T. standishii*- *T. koraiensis* and *T. occidentalis*- *T. sutchuenensis*, with *T. plicata* sister to *T. occidentalis*-*T. sutchuenensis*. This alternative system of medication is increasing expanding fame overall *Thuja species* are generally used as an antiviral, antibacterial, anti-cancer, anti-diabetic, anti-HIV, anti-fungal etc. Antiviral action and immunopharmacological action of *Thuja*, as stimulatory effects on cytokine and antibody production and also activate macrophages cells, have been tested in various *in-vivo* and *in-vitro* study. Thuja species have different chemical substances like thujone, isothujone, fenchone, sabinens and α -pinen. This review article provides comprehensive information on various useful and traditional medicinal properties of chemical composition and pharmacological activity of plants and their components.

KEYWORDS: Thuja, Antiviral, Antibacterial, Anti-cancer, Anti-diabetic

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INTRODUCTION

Ayurveda, an old Indian treatment, is perceived as one of the most significant frameworks of option and integral medication. Like other herbal systems, most medications are based on local herbs. In the recent years, the interest for therapeutic plants has expanded in a lot. Aside from this; western countries are preferred it and conducting various researches on plant based medicines [1].

The *Thuja* grows from 10 to 200 feet in height and is an evergreen tree with a reddish brown crust. Usually the leaves are 1-10 mm long, and the needles are scaly, like in the first year. Most

places are grown as ornamental plants. The leaves are organized on the branches in four rows, substituting decoupage two by two. The flowers are monotonous (a few flowers are male or female, yet are found in both genders on a similar plant) and are pollinated by the wind. Male and female flowers usually grow from separate branches or twigs [2].

Thuja are small, distal and tapered. The cones of the males are round, red or yellowish, while the females are very small, green or purple. It is a large humid place with dense greenery and a habit of growing shrubs [3].

Taxonomical Classification

Domain: Eukaryota
 Kingdom: Plantae
 Subkingdom: Viridiaeplantae
 Phylum: Pinophyta
 Subphylum: Euphyllophytina
 Infraphylum: Radiatopses
 Class: Pinopsida
 Order: Pinales
 Family: Cupressaceae
 Tribe: Spiraeae
 Genus: Thuja

The five species of Thuja are-

- Thuja koraiensis- Korean Thuja
- Thuja occidentalis- Eastern Arborvitae, Northern White cedar
- Thuja plicata- Western Red cedar
- Thuja standishii- Japanese Thuja
- Thuja sutchuenensis- Sichuan Thuja

Thuja koraiensis

The tree of life is the common name for one of the coniferous or evergreen shrubs of the genus *Thuja*, belonging to the evergreen family. Thuja leaves are plentiful in nutrient C and were utilized by Native Americans and early European specialists to treat scurvy. The leaves are utilized to treat rheumatism. Curiosities are often referred to as the herb commonly used to treat human papillomavirus (HPV), genitalia, or warts. Height up to 3-10 m. The leaves form a flat sprayer with large leaves 2 to 4 mm (up to 15 mm if the shoots are very strong), dark green on top and dark white waxy stripes on the bottom. Cones are oval, yellow-green, ripe, reddish-brown, 7-11 mm long, 4-5 mm wide (up to 6-9 mm), with 8 to 12 overlapping scales [4].

Thuja occidentalis

The most common name of *Thuja occidentalis* are Northern white-cedar, thuiercedre, cedre-thuya occidental, eastern whitecedar, American or eastern arborvitae. The Northern White Cedar is a monoecious conifer achieving a height of 15-38 m, having a tendency to be hindered or prostrate in cruel, cold conditions. Sporadically the trunk is partitioned into a few auxiliary stems, frequently imitating from fallen trunks. The skin is reddish brown or

gray, 6-9 mm thick, fibrous and matted. Eggplant leaves are 1.5-3.5 mm long, and both surfaces are pointed in yellow-green. Pollen flowers 1-2 red, ellipsoidal, 9-14 mm long and brown [3].



Figure 1: Plant of *Thuja koraiensis*



Figure 2: Plant of *Thuja occidentalis*

Thuja plicata

Thuja plicata, is a species of Thuja normally called western red cedar or Pacific red cedar, giant arborvitae or western arborvitae, giant cedar, or shingle wood. It's anything but a genuine cedar of the class Cedrus. *Thuja plicata* is among the most expansive trees in the Pacific Northwest. It is related with Douglas-fir and western hemlock in many place where it develops. It is achieve at the height scope of ocean level to a limit of 2,290 m (7,510 ft) above ocean level at Crater Lake in Oregon.

Notwithstanding developing in rich woodlands and mountainsides, western red cedar is likewise a riparian tree, developing in many forested marshes and stream banks in its range. The tree is conceal open minded and ready to recreate under thick shade. It has been familiar with other gentle zones, including western Europe, Australia (at any rate as far north as Sydney), New Zealand, the eastern United States (in any occasion as far north as

Central New York),[citation needed] and higher ascents of Hawaii. *Thuja plicata* is a tremendous to immense tree, going up to 65 to 70 m (213 to 230 ft) tall and 3 to 7 m (9.8 to 23.0 ft) in trunk expansiveness. Trees developing in the open may have a crown that arrives at the ground, though trees thickly dispersed together will display a crown just at the top, where light can arrive at the leaves [5].



Figure 3: Plant of *Thuja plicata*

Thuja sutchuenensis

Thuja sutchuenensis, the Sichuan thuja, is a species of *Thuja*, an evergreen coniferous tree in the cypress family Cupressaceae. It is local to China, where it is an at-risk close by endemic in Chengkou County, on the southern grade of the Daba Mountains.



Figure 4: Plant of *Thuja sutchuenensis*

It is a little or medium-sized tree, showing up at possibly 20 m tall, anyway no trees of this size are starting at now known. The foliage structures in level sprinkles with scale-like leaves 1.5–4 mm long, green above, and with tight white stomatal gatherings underneath. The cones are oval, green developing natural shaded, 5–8 mm long and 3–4.2 mm wide (opening to 7 mm wide), with 8–10 covering scales [6].

Thuja standishii

Thuja standishii (Japanese thuja; nezuko, kurobe) is a species of *Thuja*. It is nearby to southern Japan, where it occurs on the islands of Honshū and Shikoku. It is a medium-sized tree, showing up at 20–35 m tall and with a trunk up to 1 m estimation. The foliage structures in level showers with scale-like leaves 2–4 mm long, matte green above, and with tight white stomatal gatherings underneath. The cones are oval, yellow-green maturing red-hearty hued, 6–12 mm long and 4–5 mm wide (opening to 8 mm wide), with 6–10 covering scales. It is a significant lumber tree in Japan, developed in ranger service manors for its solid, waterproof, alluringly scented wood. There is some proof that concentrates of *T standishii* have biological action. It is having a compound called standishinal which has demonstrated generally intense impacts on the enzyme aromatase. It goes about as an inhibitor, along these lines diminishing the production of Estradiol in the human body. This compound shown even powerful inhibition of Aromatase [7].



Figure 5: Plant of *Thuja standishii*

Phytochemistry

The new plant of *Thuja* (identified with the dry substance) contains 0.6% basic oil, 2.07% diminishing sugar, 4.9% water-dissolvable polysaccharides, 2.11% water-solvent minerals, 1.67% free corrosive and 1.31% tannic operators. The basic oil of the new leaves (identified with the monoterpene division) contains 65% thujone, 8% isothujone, 8% fenchone, 2% α -pinen and 5% sabinen (**Figure 6, 7, 8, 9 and 10**) as the fundamental monoterpenes. Different monoterpenes, in particular carvotanacetone, origanol, origanes, myrcen and camphen, have been portrayed Recently, further bioactive constituents have been found. High sub-atomic weight glycoproteins/polysaccharides are exceptionally pertinent for the

movement of the plant [1]. The most noteworthy substance of fundamental oil was found in removes acquired by refining, while permeation with sanitized water diminished the thujone content in the concentrate to the least level. Using purged water as a dissolvable, a normal of 0.6mg of thujone was extricated from 1g of medication

during permeation. In contrast, when 30% (v/v) ethanol was utilized, 2.8mg of thujone was extricated from 1g of *Thuja occidentalis* spice, and >2.5-fold higher measures of thujone (7.9mg) were accomplished with high ethanol concentration (90% v/v) [3].

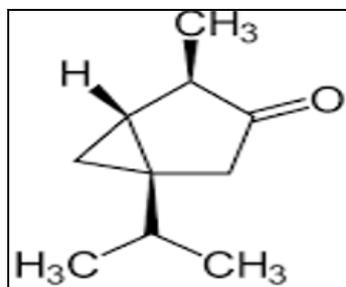


Figure 6: Thujone

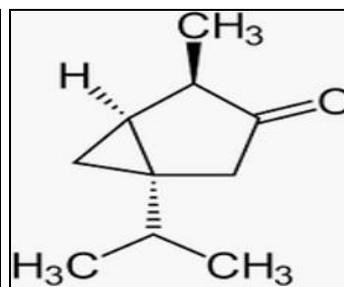


Figure 7: Isothujone

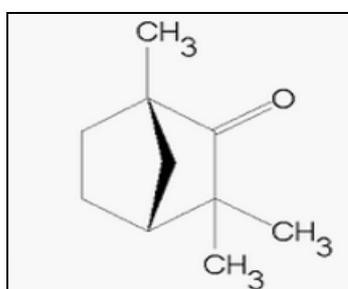


Figure 8: Fenchone

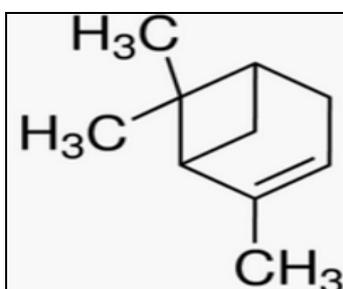
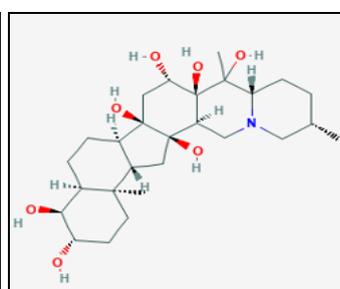
Figure 9: α -Pinene

Figure 10: Sabine

The Five new components including two stilbenes to be specific thujasutchins A and B, two phenolic mixes assigned thujasutchins C and D, as well as one sesquiterpene thujasutchin E (Figure 11), were detached from the 95% ethanolic remove from the trunks and foundations of *Thuja sutchuenensis*. Their structures were assessed by methods for widely spectroscopic examination including UV, IR, HRESIMS, ^1H and ^{13}C NMR (Cozy, HSQC, HMBC). What's more, mixes 1, 3–5 were surveyed for in vitro cytotoxic exercises against SF-268, MCF-7, HepG-2, and A549 tumor cell lines [6].

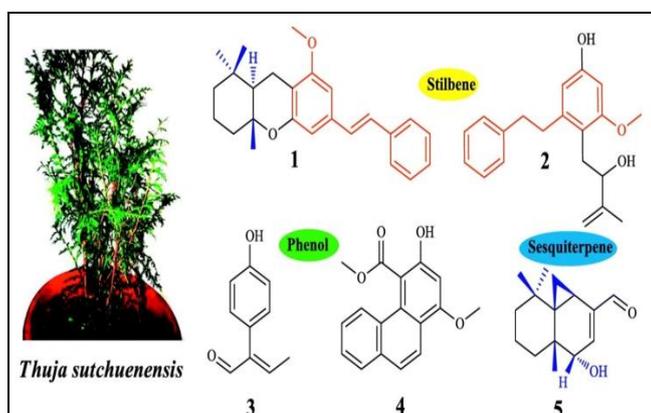


Figure 11: Structure of thujasutchins A (1), B (2), C (3), D (4) and E (5)

Table 1: Constituents of the dried herbal substance *Thuja occidentalis herba*

Group	Constituents
Essential oil (1.4–4% of drug)	Borneol
	Camphene
	Fenchone
	Limonene
	Myricene
	α -Terpine
	Terpinolene
	Thujone (0.76–2.4% of essential oil, 85% α -thujone, 15% β -thujone)
	Thujylalcohol
	Thujone
Coumarins	<i>p</i> -Coumaric acid
	Umbelliferone
Flavonoids	(+/-)-Catechine
	(-)-Gallocatechine
	Kaempferol
	Kaempferol-3- <i>O</i> - α -rhamnoside
	Mearnsitrin
Other	Myricetine
	Myricitrin
	Procyanidin B-3
	Prodelphinidin
	Quercetin
	Quercitrin
	Tannic acid (~1.3% of drug)
	<i>Thuja</i> polysaccharides and proteins (~4% of drug)

The constituents of the dried natural substance *Thuja occidentalis* spice are recorded in **Table 1**. As per Hänsel et al., the medication contains 1.4–4% basic oil, 60% of which is thujone, which relates to 2.4% thujone in the entire medication. Thujone happens in nature as a combination of α - and β -isomers. As per the European Agency for the Evaluation of Medicinal Products (EMA), the substance of thujone in dried twigs was resolved as 7.6mg/g, comprising of 85% α -thujone and 15% β -thujone. The balance blend comprises of 33% α -thujone and 67% β -thujone [3].

Pharmacological Activities

Anti-Microbial activity

The antimicrobial movement of the *T. koraiensis* separate by paper circle scattering look at against the test living beings. The concentrate stifled Gram-positive minuscule creatures *S. aureus* and *B. subtilis*, with breadths across of restriction zone 17 and 13 mm, Gram-negative microorganisms *E. coli* and *S. typhimurium*, with measurements of prevention zone 15 and 12 mm. Particularly, the antimicrobial effect of concentrate at the *B. subtilis* strain was higher than in the control. The MIC esteems went from 0.6 to 12.5% of the concentrate. The concentrate displayed the most elevated action against *B. subtilis*, with MIC of 0.6%. The outcomes demonstrated that *T. koraiensis* remove has antimicrobial action both at gram-positive and gram-negative microscopic organisms.

At different investigations, the development of gram-positive microorganisms was restrained successfully than gram-negative microscopic organisms in an examination utilizing quercetin and naringenin which are single mixes in a phenolic compound, while it had comparable examination results for the *T. koraiensis* remove single compound. Yet, likewise, the consequences of the *T. koraiensis* remove had a superior antimicrobial impact at gram-positive microorganisms in this investigation which may contain phenolic compound in the *T. koraiensis* separate. Further examination was finished breaking down *T. koraiensis* antimicrobial viable single compound using superior fluid chromatography (HPLC) profiling [4].

Leaf oil (CLO), separated from the Westernred cedar, *Thuja plicata*, was utilized as asafeand satisfactory wide range antimicrobial specialist, with a view to its likely applications in structures,

including the all eviation of debilitated structure disorder. Different Gram-positive and Gram-negative human microbes, and two parasitic life forms, all known to be normal atm. circle wellsprings of possible sicknesses, were shown and tried quantitatively, and every one of them were discovered to be defenseless to CLO fluid and vapor [8].

Anti-Viral activity

The antiviral activity of 1% *T. koraiensis* separate against BVD infection. The result exhibited that the MNCC of *T. koraiensis* separate on MDBK cells was 0.031% and the MNTD of concentrate was 0.0195% on BVD infection replication in MDBK cells. Especially, the concentrate at low fixations had a solid antiviral impact at BVD infection; BVD infection is a RNA infection. *T. koraiensis* separate had antiviral impact at RNA infection. *T. koraiensis* separate, which hostile to infection influences, will show up at DNA infection and ought to be more trial test in the future. In rundown, *T. koraiensis* separate would be advised to antiviral impact. Also, we had first recognized that Korean Arbor vitae (*Thuja koraiensis*) remove has sway about antiviral [4].

Anti-Bacterial Activity

The alcoholic concentrate of twigs of *Thuja occidentalis* was set up for Antibacterial activity against both gram negative and gram positive life forms i.e., *Pseudomonas aeruginosa*, *Yersinia aldovae*, *Citrobacter*, *Shigella flexneri*, *E. coli* and *Staphylococcus aureus*, *Vernonia anthelmintica*, *Dryopteris chrysocoma* and *Trachyspermum ammi* were tried In vitro for their antibacterial and antifungal exercises. Antibacterial assessment performed against six microscopic organisms viz., *Escherichia coli*, *Citrobacter*, *Shigella flexenari*, *Yersinia aldovae*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* indicated that had powerful movement against all microorganisms. The antifungal activity of these concentrates was performed against six growths, viz., *S. cereviciae*, *Aspergillus parasiticus*, *Trichophyton rubrum*, *Macrophomina*, *Fusarium solani* and *Candida albicans*. The concentrates showed critical results against different parasitic strains [9].

Anti- Cancer

Thujone rich segment of *Thuja occidentalis* showed noteworthy enemy of malignant growth possibilities confirmations from *in-vitro* examinations on A375 cells. Unrefined ethanolic

concentrate of *Thuja occidentalis* was used as homeopathic mother color (TOΦ) to treat various diseases, particularly moles and tumors, and besides used in various different frameworks of conventional medication. Hostile to proliferative and apoptosis-initiating properties of TOΦ and the thujone-rich portion (TRF) separated from it have been evaluated for their conceivable enemy of disease possibilities in the threatening melanoma cell line A375.

On starting preliminary by S-diphenyltetrazolium bromide measure, both TOΦ and TRF demonstrated greatest cytotoxic effect on A375 cell line while the other three chief parts disengaged by chromatography had irrelevant or no such effect, as a result of which just TRF was moreover depicted and presented to certain different analyzes for deciding its exact enemy of proliferative and apoptotic possibilities. TRF was accounted for to have an atomic equation of C₁₀H₁₆O with a sub-atomic load of 152.

Introduction of TRF of *Thuja occidentalis* to A375 cells in vitro demonstrated more cytotoxic, antiproliferative and apoptotic impacts as contrasted and TOΦ, anyway had immaterial advancement inhibitory reactions when introduced to typical cells (fringe blood mononuclear cell). Additionally, both TOΦ and TRF similarly caused a critical lessening in cell reasonability, actuated between nucleosomal DNA fracture, mitochondrial transmembrane likely breakdown, improve in ROS age, and arrival of cytochrome c and caspase-3 enactment, which are all firmly identified with the enlistment of apoptosis in A375 cells.

Thusly, TRF showed up and composed all the counter malignancy reactions of TOΦ and could be the primary bio-dynamic portion. The usage of TOΦ in customary meds against tumors has, subsequently, an intelligent basis.[10]

Anti-HIV Activity

Thuja polysaccharides (TPS) repressed human immunodeficiency infection (HIV)- subordinate cell passing at a last convergence of 625 µg/ml. At this fixation, TPSg was shown to be totally non-harmful for MT-4 cells, which had not been tainted with HIV-1. TPS were seemed to hinder HIV-1-explicit antigen articulation on newly contaminated MT-2 cells in a portion subordinate manner [10].

Antibody Production

The retentate division conveyed a focus subordinate increment in the amount of immune response creating lymphocytes in the hemolytic plaque examine in vitro. The amount of against SRBC-(sheep red platelet)- IgM-delivering plasma cells rose, as did all Ig-emitting plasma cells, as enlisted by the 'opposite' method utilizing protein A-marked SRBCs. Hatching with lipopolysaccharide (LPS) as certain control likewise prompted a fixation subordinate addition in the amount of plaque-framing cells [10].

Antispasmodic Activity

Antispasmodic action of *Thuja occidentalis* twigs was evaluated by Noorjahn and mansoor Ahemad and found to have noteworthy effect on detached tissues [10].

Antioxidants Activity

Lipid peroxidation action was finished to survey the cell reinforcement potential on took care of rodents. The cancer prevention agent movement of ethanol part was upgraded in a focus subordinate way. Around 100, 150, 200, 250 and 300 µg EFTO (ethanol portion of concentrate of ethereal piece of *Thuja occidentalis*) quelled the FeSO₄ initiated lipid peroxidation in a portion subordinate way and exhibited IC₅₀ esteem 195.60µg/ml. The results acquired in this examination show that EFTO can be a likely wellspring of regular cancer prevention agent and exercises identified with this. The drunkard and fluid concentrate of *Thuja occidentalis* twigs set up for calming and cancer prevention agents activity [10].

Anti-Diabetic Activity

The investigation was to determine the anti-diabetic action of ethanolic fraction of *Thuja occidentalis* (EFTO) and to probe into its mechanism of action. Fasting blood sugar, blood glutathione levels and serum biochemical determination in alloxan induced diabetes were studied. EFTO released a significant anti diabetic action at dose level of 200 mg/kg. EFTO also having significant about increase in blood glutathione level due to its antioxidant activity.[10]

Hepatoprotective Activity

The hepatoprotective possible effect of ethanolic part of *Thuja occidentalis* has been against CCl₄ impelled liver harm in rodents. A

portion of EFTO 400 mg/kg p.o. exhibited basic affirmation from liver harm in intense and ongoing CCl₄ actuated liver harm model. Histopathological appraisal was finished after the treatment to assess hepato assurance. The division was found to have extraordinary hepatoprotective property in ethanolic remove, Hepatoprotective activity was evaluated ^[10].

Insecticidal Activity

Insecticidal movement of two known bug sprays (deltamethrin and imidacloprid), thujone and fundamental oil of rosemary against the hatchlings and grown-ups of sycamore ribbon bug (*Corythucha ciliata*) was assessed. The investigation was coordinated in an exploration office, under room conditions. We tried the activity of each item in three unique focuses. The most appealing insecticidal movement had deltamethrin, which caused directly around 100 % mortality of both formative periods of the vermin at all three fixations.

Succeeding items were imidacloprid, which caused 89.6 % larval mortality at suggested focus, and basic oil of rosemary, which caused 81.7 % grown-up mortality at 1 % fixation. Hatchlings of sycamore trim bug were altogether more defenseless to tried items than grown-ups. Fundamentally the most reduced mortality was resolved one day after treatment (41.7 %), while the most elevated mortality was expressed three days after treatment (71.3 %).

For future decline of the harm brought about by the examined bug on plane trees, we suggest the utilization of thujone and fundamental oil of rosemary, which had all the earmarks of being earth more adequate substances. In our assessment the two operators demonstrated a center fulfilling activity in controlling hatchlings and grown-ups, however they have additionally clear anti-agents movement, which prompts their great suitability in the open. Thujone goes about as repellent specialists to bugs affirmed high mortality of the western corn rootworm hatchlings in light of intense harming with thujone ^[10].

Radioprotective Activity

The effect of *Thuja occidentalis* against hurt provoked by gamma radiation was thought of. Whole body introduction of Swiss pale skinned person mice to gamma-beams (6 Gy) diminished the all-out white platelet check to 1900

cells/mm³ on the third day, which was raised to 2050 cells/mm³ by the organization of alcoholic concentrate of *Thuja occidentalis* (5 mg/portion/ creature, intraperitoneally). Six creatures from each gathering were killed following 2, 7, and 11 days of light to perceive the bone marrow cellularity and radiation-initiated harmfulness. The quantity of bone marrow cells and alpha-esterase positive cells in control creatures following 11 days was diminished to 12.2 x 10⁶ cells/femur and 693.5/4000 cells, individually.

In *Thuja occidentalis* - treated creatures, bone marrow cellularity was upgraded to 16.9 x 10⁶ cells/femur and alpha-esterase positive cells were 940/4000 cells, an almost typical level. Alcoholic concentrate of *Thuja occidentalis* diminished the raised degrees of GPT and soluble phosphatase in liver and serum after illumination. The lipid peroxidation levels were likewise lit in the lighted creatures treated with the *Thuja* remove. Defensive effect against radiation actuated harmfulness in mice evaluated ^[10].

Anti-Atherosclerosis Activity

To survey the hypolipidaemic activity of an (EFTO) ethanol division of concentrate of aerial part of *Thuja occidentalis* Linn. (Cupressaceae) in hypolipidaemic action EFTO at the portion of 200 mg and 400mg/kg body weight altogether diminished serum cholesterol (77 and 92%), LDL (53 and 84%), fatty oils (27 and 46%). The upgrade in HDL to add up to cholesterol proportion and lessening in atherogenic list in EFTO treated gatherings firmly bolsters hostile to atherosclerotic property of *Thuja occidentalis* ^[10].

Neuropharmacological Activity

Watery concentrate of airborne part was investigated for evaluation of neuropharmacological activity by using raised in addition to labyrinth test, open field test in which they were noted ambulation, raising self-prepping, movement in focus, rota pole test and tail suspension test ^[10].

Sedative Activity

The methanolic leaf concentrate of *Thuja occidentalis* was surveyed for conceivable opiate activities in mice. Narcotic activity was surveyed by utilizing gap cross, open field, thiopental sodium-prompted resting time and raised in addition to labyrinth (EPM) tests at 200mg/kg and 400 mg/kg. The concentrate lessened the

locomotor development of mice in gap cross, open field and EPM test and exhibited the surprising results when contrasted with the norm at both referenced portions. Also, the extract significantly limited beginning of rest and amplified the term of dozing time when taken with thiopental sodium and measurably it was noteworthy ($p < 0.05$)^[11].

Anti-Fungal Activity

The basic oils from leaves, twigs and stems of enormous trees and bush like trees of *Thuja sutchuenensis* were extricated by hydro-distillation and supercritical liquid extraction, and broke down by GC and GC-MS. The fundamental oil synthesis contrasted essentially among the three organs, just as between huge trees and bush like trees. Moreover, predictable with the eastern Asia-North American disjunct dispersion of the sort, numerous distinctions in the fundamental oil creation between *T. sutchuenensis* and other *Thuja* species were evident. The fundamental oils showed a particular degree of antifungal activity against six strains of human pathogenic fungi^[12].

CONCLUSION

Our pharmacy industry consistently search new lead atoms having better therapeutic activity and less adverse effect, in previous years lead compounds from natural origin had increasing greater prevalence because of less adverse effects and better therapeutic activity. Specially in antimicrobial area because of suddenly developing resistance to synthetic compounds. Present review indicates that different extracts shows good pharmacological action.

Its immunopharmacological potential has been shows in various *in-vivo* and *in-vitro* test perform on test models showing its immunostimulating and antiviral action. It can be concluded that extraction of *Thuja* having various compound which is safe and effective herbal medicinal product for treatment many kinds of disease.

Thuja species has broad scope to separate many phytochemical compounds and estimate their pharmacological results to get better therapeutic action.

ACKNOWLEDGEMENT

The authors are grateful to Prof. Rajat Yadav and Dr. Nita Yadav, Department of Pharmacy, SRMS CET (Pharmacy), Bareilly, U.P. for their support during review work.

CONFLICT OF INTEREST

None

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How to cite this article:

Gupta M, Sharma K, Solanki D and Yadav R. "A review of phytochemical constituent and pharmacological activity of *Thuja species*". *International Journal of Recent Research in Pharmacy (IJRRP)*, 2020; 1(1A), pp. 180-189.