International Journal of Botany Studies
www.botanyjournals.com
ISSN: 2455-541X
Received: 28-12-2021, Accepted: 12-01-2022, Published: 28-01-2022
Volume 7, Issue 1, 2022, Page No. 547-556

Thujopsis dolabrata and its potential to undergo biotransformation: A review

Sibange Paul[1], Shiny C Thomas[2*]
[1] Department of Biotechnology, Assam Don Bosco University, Tapesia Campus, Sonapur, Assam, India
[2] Department of Biochemistry, Assam Don Bosco University, Tapesia Campus, Sonapur, Assam, India

Abstract
Thujopsis dolabrata, a monoecious coniferous tree, have its place in the Cupressaceae family. The plant with terrestrial habitat and evergreen leaf sheddability is native to Japan and for environmental stress factors got distributed to wider locations. This current review abridges the detailed information about the properties of the compounds extracted from this plant and the research work carried out on it in order to offer updated information that could be beneficial for the future exploitation of the plant. The review summarizes the bioactivity and the chemical identity of *T. dolabrata* studied by various researchers from 1965 to till date. Due to the availability of this plant in India, other than Japan, makes it convenient to carry out more studies and experiments on the subject. In fact, the lack of any scientific study on the plant reported from India makes it further more significant and opens up the scope for substantial new findings. The review also seeks the possibility of biotransformation of *T. dolabrata*, by a bacterial or a fungal agent, which may alter the chemical constituents present in the plant for enhanced or novel beneficial activities.

Keywords: bioactivity, chemical compounds, coniferous, morphology, propagation

Introduction
Thujopsis dolabrata, a monoecious coniferous tree, belongs to the Cupressaceae family. The plant with terrestrial habitat and evergreen leaf sheddability is native to Japan and for environmental stress factors got distributed to wider locations. This non-flowering type plant bearing no fruits have been in use in the folklore medicine as a remedy for jaundice in Japan. For centuries it has been in use in the traditional architecture of Japan in the form ancient buildings like Konjiki-do, many Buddhist temples and Shinto shrines. The study of the leaf extracts of this plant revealed much about its composition and other beneficial properties. *T. dolabrata* is one of such plants, which although have been known for their ornamental properties for centuries, is also a rich source of oils having properties like anti-pest, anti-fungal, anti-microbial and so on. Compounds such as thujopsene, β -dolabrin, and hinokitiol (β -thujaplicin), hinokitiol-related compounds, γ -thujaplicin and carvacrol extracted from *T. dolabrata* have been reported for strong antifungal, antibacterial, anitipest, insecticidal, anticancer, anti-hepatotoxicity, and phyto-growth inhibitory activities (Morita *et al*. 2001; Morita *et al*. 2003; Morita *et al*. 2004a; Morita *et al*. 2004b ; Inamori *et al*. 2006; Morita *et al*. 2007; Pohlit *et al*. 2011; Kim *et al*. 2013 ; Kim *et al*. 2015). Desoxypodophyllotoxin and β-peltatin, and hinokitiol and thujopsene like compounds are reported to add to the pharmacological value of the plant for offering benefits like being derivatives of compounds used for semi-synthetic anticancer drugs synthesis or as anti-allergens (Nam *et al*. 2011; Suzuki *et al*. 2019). The review summarizes the bioactivity and the chemical identity of the *T. dolabrata* studied by various researchers from 1965 (Shô Itô *et al*. 1965) to till date. Due to the availability of this plant in India, other than Japan, makes it convenient to carry out more studies and experiments on the subject. In fact, the lack of any scientific study on the plant reported from India makes it further more significant and opens up the scope for substantial new findings. The review also seeks the possibility of biotransformation of the chemical composition of *T. dolabrata* for an enhancing effect on its anti-microbial, anti-termite and other such properties or even for the formation of any novel compounds.

Material and Methods
A literature search was conducted using the keywords "*T. dolabrata*," "Geographical distribution of *T. dolabrata*," "Ornamental value of *T. dolabrata*," "Chemical composition of *T. dolabrata*," "biological activities of *T. dolabrata,*" "Antipest property of *T. dolabrata*,'' "Ethno botany of *T. dolabrata*,'' "Insecticidal property of *T. dolabrata*,'' "Phytogrowth inhibitory property of *T. dolabrata*'' and "Biotransformation on *T. dolabrata*'' on electronic databases NCBI, PubMed, Google scholar, science direct, and traditional and Ayurvedic books were thoroughly referred to compile published research works since 1965 till May 2021.The bibliographies of the cited articles were also tracked for complete documentation.

Morphology of *Thujopsis dolabrata*
Thujopsis dolabrata is a monoecious coniferous tree, belonging to the clade Tracheophytes, Pinophyta division, Pinosida class, and Pinales order, a member of the Cupressaceae family. Leaf morphology comprises simple

scales with obovate to obdeltoid facial shape and obtuse facial apex, with Dolabriform lateral shape, and incurved, obtuse or acute lateral apex (Wu *et al*. 2014) (Figure 1E, 1F). The barks are red-brown exfoliating in vertical strips (Figure 1H). It possesses leathery evergreen needled decussate pairs of scale-like leaves (Figure 1J). The thick fleshy leaves are glossy on top with white stomata on the underside. With a woody lifecycle it may spread to up to 15 to 25 ft wide, growing 30 to 50 ft tall (North Carolina Extension Gardener Plant Toolbox).

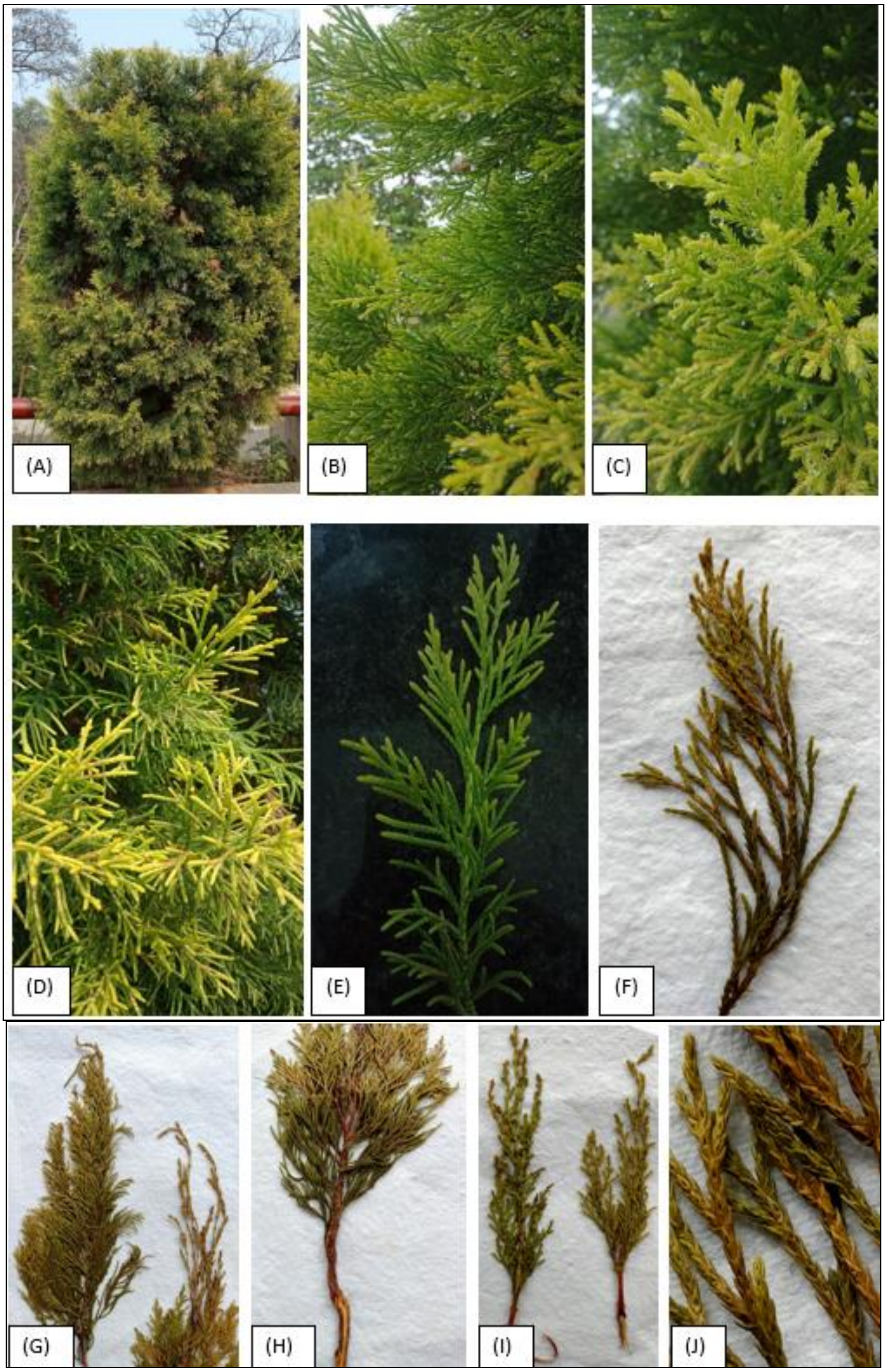


Fig 1: (A); (B); (C). *Thujopsis dolabrata* at a natural habitat at Assam Don Bosco University, Tepesia, Assam; (D). Microsporophylls (fertile modified leaves) on the plant; (E). Morphology of leaves on a fresh twig of *T. dolabrata*; (F). Morphology of leaves on a dry twig of *T. dolabrata*; (G). A thick twig of *T. dolabrata*; (H). Reddish-brown bark of a branch of *T. dolabrata*; (I). Morphology of immature leaves on *T. dolabrata*; (J). Scales of a mature leaf of *T. dolabrata*

The monoecious *T. dolabrata* possesses male cones (pollen) and female cones (seed cones) in on the same plant separately. The cones grow a few centimeters on the branches terminally, in cylindrical shapes. The pollens develop initially from microsporophylls (Leaflike structure on which spores or pollens are enclosed). Each male cone encloses about 12-20 microsporophylls (Figure 1D), the fertile modified leaves. The egg shaped and woody seed cones in contrast on maturity, produce 3-5 seeds (Conifers of UBC).

Growth and Propagation of *T. dolabrata*

Trees of *T. dolabrata* are a plant with slow rate of growth requiring medium maintenance. In the daytime the tree requires direct sunlight for about 6 hours and a partial shade requirement for the rest of the time (North Carolina Extension Gardener Plant Toolbox). This Japan endemic plant could be classified into two broad genuses: *Thujopsis dolabrata* (L.f.) Siebold et Zucc. var. *dolabrata* (southern variety, Td) and *Thujopsis dolabrata* (L.f.) Siebold et Zucc. var. *hondae* Makino (northern variety, Th). SSRs, the simple sequence markers based on EST, the expressed sequence tag aided structure analysis suggests the two identified genetic clusters to be related to these regions of distribution here, (Inanaga *et al*., 2020). Place other than Japan it is cultivated rarely in Poland, mainly in the northern and the western region where they were planted before the World War II (Danielewicz 1987). The survival marked their acclimatization to the Polish climate, (Danielewicz 1987). This drought intolerant plant is also planted in Europe and North America in areas with assured good rainfall or source of irrigation (American conifer society) and is also widely distributed in Korea (Nam *et al*. 2011). In the north-eastern India it is available in parts of Assam with considerable cool climatic conditions (Figure 1), where the plant under close observation for about five years is shown not to bear cones for an awaited maturation. The plant being a gymnosperm conifer in general takes about 15 – 20 years of maturation to bear cones.

The plant grows in a loamy (silt) soil texture with acidic to neutral pH (6-8) requirement. Dry soils are not suitable for their growth and require good drainage. The plant is a non-flowering type bearing no fruits, but tiny thick brown and violet with white wax ovoid seed cones (North Carolina Extension Gardener Plant Toolbox). It is adapted to wind mediated pollen- and seed-dispersal system (Inanaga *et al*. 2020).

Ornamental value

The ornamental value of *T. dolabrata* accounts for its use in the traditional architecture in Japan dates for more than a century. The study of the leaf extracts of this plant revealed much about its composition and other beneficial properties. The plants mite resistance property, apart from others explains its suitability and choice for architectural purposes better. *T. dolabrata* is one of such plants, which although have been known for their ornamental properties for centuries, is a rich source of oils having properties like anti-pest, anti-fungal, anti-microbial and so on (Liu *et al*. 2014).

Chemical Compounds Isolated from *T. dolabrata*

Wood oil extracted from the leaves of the plant were reported to be composed of numerous compounds, among which thujopsene was a major one (Liu *et al*. 2014). Additionally, the wood extracts consisted of other compounds like β -dolabrin, and hinokitiol (β -thujaplicin), hinokitiol-related compounds, reported for strong anti-microbial properties, and **γ** -thujaplicin for strong antifungal activity (Inamori *et al*. 1999). These three compounds were reported for both strong insecticidal properties (Inamori *et al*. 2000), and an anti-fungal action against wood-rotting fungi. Discovery of these beneficial properties revealed the reason for the intact and preserved condition of ancient buildings like Konjiki-do, many Buddhist temples and Shinto shrines in Japan (Inamori *et al*. 2006). In addition, *T. dolabrata* was also reported to be a source of citronellic acid (Sandermann 1962). The chemical compounds reported to be present in this plant *T. dolabrata* are cited in the following Table 1 with each of its bioactivity mentioned respectively.

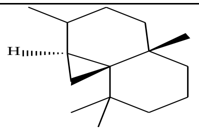
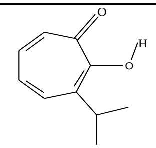
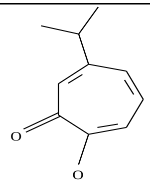
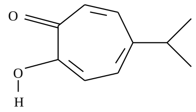
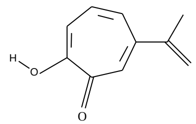
Ethno Botany

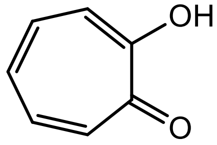
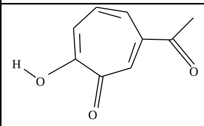
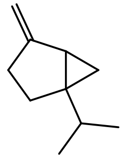
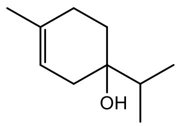
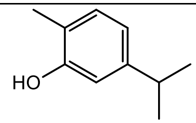
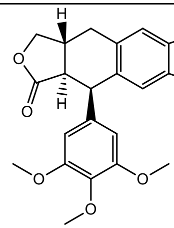
In addition to all these *Thujopsis* leaves have been in use in the folklore medicine as a remedy for jaundice in Japan (Hikino *et al*. 1979). The Makino bark of the *hondae var of T. dolabrata* for its soft, durable, elastic wood has been in use for construction, cabinet work, water pipes, ship building etc, for match cord, for filling (caulking) between boards on boats etc (Acharya Balkrishna *et al*. 2018).

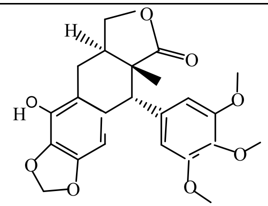
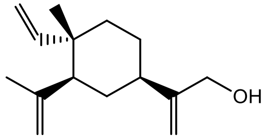
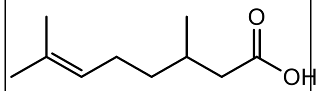
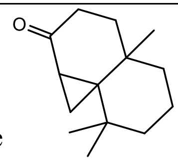
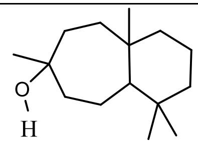
Anti Pest Property

Thujopsene ($C_{15}H_{24}$), classified as a sesquiterpene and a major compound of many other essential oils, has been tested positively for its toxicity against two mite species *Dermatophagoides farinae* and *Tyrophagus putrescentiae* considered as two important allergens. Hence thujopsene containing fumigant sprays has potential to be used as an effective indoor mite control product (Kim *et al*. 2015). Two other hinokitiol compounds, 4-acetyltropolone and α –thujaplicin in addition to previously mentioned three, also showed strong anti-mite property against *Dermatophagoides farinae* (Morita *et al*. 2004b; Inamori *et al*. 2006). In addition, hinokitiol, γ-thujaplicin and β-dolabrin and tropolone were reported to have acaricidal activity on *Tyrophagus putrescentiae* and *Coptotermes formosanus* (Inamori *et al*. 2000; Morita *et al*. 2003).

Table 1: Chemical compounds isolated from *T. dolabrata* with bioactivity

SL No	Name of the compound	IUPAC name	Molecular Formula	Molecular weight	Chemical Structure	Bioactivity	References
1	Thujopsene	(1aS,4aS,8aS)-2,4a,8,8-tetramethyl-1,1a,4,5,6,7-hexahydrocyclopropa[j]naphthalene	$C_{15}H_{24}$	204.35 g/mol	 Thujopsene	Antipest, Anti-allergic activity and Stress-relieving property	Pohlit *et al*. 2011; Kim JR *et al*. 2015 Kim CH *et al*. 2013; Matsuura T *et al*. 2014
2	α-thujaplicin	2-hydroxy-3-propan-2-ylcyclohepta-2,4,6-trien-1-one	$C_{10}H_{12}O_2$	164.2 g/mol	 alpha-thujaplicin	Strong anti-mite property, Antifungal activity against plant pathogenic fungi, Anti-bacterial activity	Morita *et al*. 2004a, Inamori Y *et al*. 2006; Morita *et al*. 2003, Morita *et al*. 2004a, Morita *et al*. 2004b; Morita *et al*. 2001
3	β-thujaplicin	2-hydroxy-6-propan-2-ylcyclohepta-2,4,6-trien-1-one	$C_{10}H_{12}O_2$	164.2g/mol	 Beta-thujaplicin	Antimicrobial properties, Strong insecticidal property and Antifungal	Inamori Y *et al*. 1999; Inamori Y *et al*. 2000; Inamori Y *et al*., 2006
4	γ -thujaplicin	2-hydroxy-5-propan-2-ylcyclohepta-2,4,6-trien-1-one	$C_{10}H_{12}O_2$	164.2g/mol	Beta-dolabrin  gama-thujaplicin	Antifungal, Strong insecticidal, Acaricidal activity, Phytogrowth-inhibitory property, Antifungal against plant pathogenic fungi, Anticancer property	Inamori Y *et al*. 1999; Inamori Y *et al*. 2006); Inamori Y *et al*. 2000); Inamori *et al*. 2000; Morita *et al*. 2003; Sakagami Y *et al*. 2000; Morita *et al*. 2003, Morita *et al*. 2004a, Morita *et al*. 2004b; Miyamoto *et al*. 1998, Matsumura E *et al*. 2001, Morita *et al*. 2004a, Morita *et al*. 2004b
5	β –dolabrin	2-hydroxy-6-(prop-1-en-2-yl) cyclohepta-2,4,6-trien-1-one	$C_{10}H_{10}O_2$	162.18g/mol	 Beta-dolabrin	Antimicrobial, Strong insecticidal, Anti-fungal property, Acaricidal, Antifungal against plant pathogenic fungi, Antibacterial, Phytogrowth-inhibitory property and Anticancer property	Inamori Y *et al*. 1999; Inamori Y *et al*. 2000); Inamori Y *et al*. 2006) Inamori *et al*. 2000, Morita *et al*. 2003; Morita *et al*. 2003, Morita *et al*. 2004a, Morita *et al*. 2004b; Morita *et al*., 2001; Sakagami Y *et al*. 2000; Miyamoto *et al*. 1998, Matsumura E *et al*. 2001, Morita *et al*. 2004a, Morita *et al*. 2004b;

6	Tropolone	2-hydroxycyclohepta-2,4,6-trien-1-one	$C_7H_6O_2$	122.12g/mol	 Tropolone	Acaricidal activity	Inamori *et al*. 2000; Morita *et al*. 2003;
7	4-acetyltropolone	6-acetyl-2-hydroxycyclohepta-2,4,6-trien-1-one	$C_9H_8O_3$	164.16 g/mol	 4-acetyltropolone	Strong anti-mite property, Antifungal activity against plant pathogenic fungi, Antifungal property,	Inamori Y *et al*. 2006, Morita *et al*. 2004b; Morita *et al*. 2003, Morita *et al*. 2004a, Morita *et al*. 2004b; Morita *et al*. 2002;
8	Sabinene	4-methylidene-1-propan-2-ylbicyclo [3.1.0] hexane	$C_{10}H_{16}$	136.23g/mol	 Sabinene	Insecticidal property	Pohlit A M, *et al*. 2011
9	4-terpineol	4-methyl-1-propan-2-ylcyclohex-3-en-1-ol	$C_{10}H_{18}O$	154.25g/mol	 4-terpineol	Insecticidal property	Pohlit A M *et al*. 2011;
10	Carvacrol	2-methyl-5-propan-2-ylphenol	$C_{10}H_{14}O$	150.22 g/mol	 Carvacrol	Insecticidal, Antignawing and, Acaricidal activity	Pohlit A M *et al*. 2011; Ahn YJ *et al*. 1995; Ahn *et al*. 1998;
11	Desoxypodophyllotoxin	(5R,5aR,8aR)-5-(3,4,5-trimethoxyphenyl)-5a,8,8a,9-tetrahydro-5H-[2] benzofuro [5,6-f][1,3]benzodioxol-6-one	$C_{22}H_{22}O_7$	398.4 g/mol	 Desoxypodophyllotoxin	Anti-hepatotoxicity activity	Hikino H *et al*. 1979;

12	β-peltatin		——	——	 beta-peltatin	Podophyllotoxin derivatives	Suzuki, Shiro *et al*. 2019
13	(−)-Elema-1,3,11(13)-trien-12-ol	2-[(1R,3S,4S)-4-ethenyl-4-methyl-3-prop-1-en-2-ylcyclohexyl]prop-2-en-1-ol	$C_{15}H_{24}O$	220.35g/mol	 (-)-Elema-1,3,11(13)-trien-12-ol	Anti-allergic activity	Kim CH *et al*. 2013
14	Citronellic acid	3,7-dimethyloct-6-enoic acid	$C_{10}H_{18}O_2$	170.25g/mol	 Citronellic acid	Not reported any bioactivity	W. Sandermann. 1962
15	mayurone	4a,8,8-trimethyl-1a,5,6,7-tetrahydro-1H-cyclopropa[j]naphthalen-2-one	$C_{14}H_{20}O$	204.31g/mol	Mayurone 	Not reported any bioactivity	Liu, Yiyang *et al*. 2014
16	Widdrol	(7S,9aS)-4,4,7,9a-tetramethyl-1,2,3,6,8,9-hexahydrobenzo [7] annulen-7-ol	$C_{15}H_{26}O$	222.37g/mol	 widdrol	Not reported any bioactivity	Liu, Yiyang *et al*. 2014

Insecticidal Property

The three compounds β-dolabrin, β-thujaplicin, and γ-thujaplicin (hinokitiol-related compounds) were also reported for strong insecticidal properties (Inamori *et al*., 2000). 4-acetyltropolone and α–thujaplicin also showed insecticidal activity (Inamori *et al*., 2006). Hinokitiol was reported to have a toxic activity against the malaria causing *Plasmodium falciparum* with 50% inhibitory concentration (IC50) values which were equivalent or less than 1.0 µg/ml (Fujisaki *et al*. 2012). The compounds (sabinene, carvacrol, thujopsene, 4-terpineol, hinokitiol, thujaplicine) identified from 2.1% of **e**ssential oil extracted from *T. dolabrata* by steam distillation were cited in the patented mosquito repellent inventions (Pohlit *et al*. 2011). Carvacrol was reported as an active compound of T. dolabrata var. hondai sawdust for the acaricidal and insecticidal activity against the arthropod pests, *Sitophilus oryzae*, *Reticulitermes speratus*, *Callosobruchus chinensis*, *Myzus persicae*, *Plutella xylostella*, *Lasioderma serricorne*, *Tetranychus urticae*, and *Blattella germanica*, (Ahn *et al*. 1998). Carvacrol was reported to be the most potent antignawing agent in comparison to thujopsene and β –thujaplicine present in the steam-distillate of *T. dolabrata* (Ahn *et al*. 1995).

Phytogrowth-Inhibitory Property

β-dolabrin and γ-thujaplicin (hinokitiol-related compounds) isolated from *T. dolabrata* were also reported for phytogrowth-inhibitory property by inhibiting seed germination by reducing the chlorophyll content when tested against *Brassica campestris L.* subsp. *rapa Hook f. et Anders*, *Sesamum indicum Linne* and *Echinochloa utilis* Ohwi et Yabuno (Sakagami *et al*. 2000).

Antifungal Activity

Essential oils prepared from waste wood chips made from used sake barrels of Thujopsis dolabrata, as a means of reuse of the waste wood, showed strong anti- fungal activity against the causal agent of the tinea disease *Trichophyton rubrum* and inhibited the DNA polymerase activity in an extract from *T. rubrum* mycelia (Takao *et al*. 2012). Thujopsene, other than the three compounds, β-dolabrin, and hinokitiol (β-thujaplicin), hinokitiol-related compounds, from the wood of *T. dolabrata* have been reported for strong anti-microbial properties, but γ -thujaplicin specifically for strong antifungal activity (Inamori *et al*. 1999). α-Thujaplicin, β-dolabrin, γ-thujaplicin and 4-acetyltropolone components from the heartwood of *Thujopsis dolabrata* var. *hondai* showed strong antifungal activity against seven species of plant pathogenic fungi (Morita *et al*. 2003; Morita *et al*. 2004a; Morita *et al*. 2004b). A strong antifungal activity was also reported on *Daedalea dickinsii* and *Coriolus versicolor* by 4-acetyltropolone, a minor component of *T. dolabrata* (Morita *et al*., 2002).

Antibacterial Activity

Hinokitiol isolated from *T. dolabrata* was also tested for the antibacterial activity against *Escherichia coli* (IFO 3301) and *Staphylococcus aureus* (IFO 12732), which revealed that the compound's mechanism of action is suppression of respiration of the bacteria (Morita *et al*. 2007). With a minimum inhibitory concentration (MIC) of 1.56 mg/ml, alpha- Thujaplicin, a component of *T. dolabrata*, was reported to have an anti-bacterial activity on *Enterococcus faecalis* IFO-12965, stronger than that of hinokitiol related compounds (Morita *et al*., 2001). However, its antibacterial activity on *Staphylococcus epidermis* was lower than that of hinokitiol and beta-dolabrin but stronger than that of the anti-biotic gentamicin, used as the positive control (Morita *et al*. 2001).

Anticancer and Anti-hepatoxicity Property

Alcoholic extracts from *T. dolabrata* had been observed to inhibit HeLa cell division at the metaphase strongly (Akahori *et al*. 1972). γ -thujaplicin and β -dolabrin, the hinokitiol-related compounds were reported for their considerably strong cell growth inhibition activity against human stomach cancer KATO-III cell line at 0.32 microg/ml by 85 and 67%, and against Ehrlich's ascites carcinoma cell line by 91 and 75% (Matsumura *et al*. 2001). Established human tumor cell lines, human stomach cancer cell lines, murine P388 lymphocytic leukemia and other tumors and other diseases were reported to be countered on by the strong cytotoxic effects of hinokitiol and hinokitiol related compounds (Miyamoto *et al*. 1998; Matsumura *et al*. 2001; Morita *et al*. 2004a; Morita *et al*. 2004b). MKN45 cells injected in female nude mice established a gastric cancer, which was reported to be inhibited when treated with Hiba Essential oil. MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay revealed that the essential oil had a time-and concentration-dependent inhibitory activity against the gastric tumor growth (Nagata *et al*. 2016).

Desoxypodophyllotoxin extracted from *T. dolabrata* leaves, tested on CCl_4 (Carbon tetra chloride)-induced liver damage in mice was reported to have an active protective principle against CCl_4 hepatotoxicity (Hikino *et al*., 1979).

Pharmacological Property

Methyl ether in the 70% acetone/water extract of *T. dolabrata* needle was found to contain 1.1% of deoxypodophyllotoxin and 0.56% of β-peltatin. Thus *T. dolabrata* is also a good source of podophyllotoxin derivatives, for podophyllotoxin being a starting material of the semisynthetic anticancer medicine etoposide, teniposide, and etopophos (Suzuki *et al*. 2019). Hinokitiol compounds in the essential oils from *T. dolabrata* were reported as potential anti-allergens against 2, 4-dinitrochlorobenzene (DNCB) induced atopic dermatitis like skin lesions in five-week-old male NC/Nga mice, purchased from Central Lab. Animal, Inc. (Seoul, Republic of Korea), by inhibiting serum IgE and histamine production and degranulation of mast cells induced due IgE (Nam *et al*. 2011). Later, a study revealed the anti-allergic effect of the compounds (−)-Elema-1,3,11(13)-trien-12-ol and Thujopsene against IgE antibody induced RBL-2H3 Cells by exhibiting inhibition of β-Hexosaminidase release, IL-4 Secretion, IL-4 mRNA and Protein Expression (Kim CH *et al*. 2013). Extracted essential oils from *T. dolabrata* were also reported for stress-relieving property. Stress-HEO rats (stressed rats inhaled Hiba wood essential oil after the restraint stress period) showed decreased levels of stress and anxiety-like behavior, and the study suggested inhibition of sympathetic nervous system activity to be causative principle for stress relieve. Although the oil inhalation could not completely recover the stress-HEO rats, but the study advocates thujopsene to be the essential oil component responsible for the stress-relieving property (Matsuura *et al*. 2014).

Biotransformation as new approach for novel compounds

The conversion of a chemical compound from one form to another within a living system is a phenomenon called as biotransformation, which can either occur naturally or can be induced. As a naturally occurring phenomenon, biotransformation is necessary for carrying out the basic metabolic activities or as defence mechanism for survival during stress or threat (ToxTutor). Conversely, a biotransformation, induced by an external agent or organism or organism residing within the system, can be a promising approach for the synthesis of novel chemical compounds having important characteristics, either toxic or non-toxic to the system (Lorenz *et al*. 2019). The process is employed in the production of many valuable synthetic bioactive compounds but by biological systems. Many volatile compounds with properties such as antimicrobial, antifungal, antiviral, somatic fat reducing, antioxidant, blood-pressure regulating, anti-inflammatory and many other such desirable properties are synthesized by employing the process of biotransformation (Pimentel *et al*. 2011). Essential oil extracted from of *Piper aduncum L*., a plant used in traditional Ecuadorian medicine for its antiseptic and antibiotic properties, studied for biotransformation by the endophytic fungi isolated from aerial parts of the plant, reported two transformed terpenoid compounds (Scalvenzi and Laura, 2014). *Seiridium cardinale*, a canker causing fungus was reported to have biotransformed three terpenes secreted by *Cupressus semperviren*, a member of the Cupressaceae family, in defense to the pathogen, and was capable of detoxifying them in its immediate surrounding environment outside its fungal mycelium (Achotegui-Castells *et al*. 2016). Bacteria such as *Lactobacillus* species are other candidates for transformation of essential compounds and production of new, simpler and more bioactive compounds (Muñoz *et al*. 2017).

Thus, both fungi and bacteria are suitable bio transformers used for the production of important bioactive compounds and thereby production of value-added products beneficial for human use.

Plants serving as the rich source of such bioactive and therapeutic compounds become an important subject of study and analysis.

Discussion

Thujopsis dolabrata thus could serve as a versatile subject of study, which although having been known for their ornamental properties for centuries, its rich essential oil content having properties like anti-pest, anti-microbial, anti-cancer, pharmacological and so on (Liu *et al*. 2014), could be subjected to biotransformation by a suitable organism. The transformation could serve as a means of certain beneficial chemical modifications in the important components or even in the entire chemical composition of the plant. Modification or transformation could have significant change in the fragrance of the extract, which could be utilized for the purpose of commercializing. The modified compounds could be a potential drug candidate, given that the plant comprises of a derivative compound used for anti-cancer drug synthesis. Given that the oil has considerably strong anti-cancer activity and as studies propose inhalation of this Hiba oil as a potential novel cancer treatment strategy (Nagata *et al*. 2016), biotransformation could have an enhancing effect on the bioactivity of the oil. Additionally, the transformation process could bring about an enhancing effect in the extract's anti-microbial and anti-termite properties. Furthermore, to these, the process is also promising for the formation of a novel compound, which with further in-silico and in-vitro studies and analyses could reveal its significant chemical properties.

Due to the availability of this plant in India, other than Japan, Poland, America, and Korea, makes it convenient to carry out more studies and experiments on the subject. In fact, the lack of any scientific study on the plant reported from India makes it further more significant and opens up the scope for substantial new findings. The present review summarizes the detailed information about the properties of the compounds extracted from this plant and the research work carried out on it in order to offer updated information that could be beneficial for the proposed work of biotransformation. Thus, it could be a major and a propitious approach towards the possibility of remarkable new findings.

References

1. Acharya Balkrishna, Uday Bhan Prajapati, Anupam Srivastava and Rajesh Mishra. Phytoetymology and ethnobotany of indigenous or introduced gymnosperms in India. International Journal of Unani and Integrative Medicine,2018:2(4):44-51.
2. Achotegui-Castells A, Della Rocca G, Llusià J, Danti R, Barberini S, Bouneb M *et al*. Terpene arms race in the Seiridium cardinale - Cupressus sempervirens pathosystem. Sci Rep,2016:6:18954. doi: 10.1038/srep18954. PMID: 26796122; PMCID: PMC4726198.

3. Ahn YJ, Lee SB, Okubo T, Kim M. Antignawing factor of crude oil derived fromThujopsis dolabrata S. et Z. var.hondai sawdust against mice. J Chem Ecol,1995:21(3):263-71. doi: 10.1007/BF02036716. PMID: 24234059.
4. Ahn, Young-Joon, Lee Seong-Baek, Lee Hoi-Seon, Kim, Gil-Ha. Insecticidal and acaricidal activity of carvacrol and β-thujaplicine derived from Thujopsis dolabrata var. hondai sawdust. Journal of Chemical Ecology,1998:24(1):81-90. https://doi.org/10.1023/A:1022388829078.
5. Akahori A, Yasuda F, Ando M, Hori K, Okanishi T. Cytotoxic agents of Thujopsis dolabrata (L. fil.) Sieb. et Zucc. Chem Pharm Bull (Tokyo),1972:20(6):1150-5. doi: 10.1248/cpb.20.1150. PMID: 5071252.
6. Danielewicz W. *Thujopsis dolabrata* in Poland. Foreign Title: W. Żywotnikowiec japoński (*Thujopsis dolabrata* Sieb. et Zucc.) w Polsce. Journal article: Prace z Zakresu Nauk Leśnych,1987:64:25-32. ref.39 ISBN:8301077077https://www.cabdirect.org/cabdirect/abstract/19930670496
7. Fujisaki R, Kamei K, Yamamura M, Nishiya H, Inouye S, Takahashi M, Abe S. *In vitro* and *in vivo* anti-plasmodial activity of essential oils, including hinokitiol. Southeast Asian J Trop Med Public Health,2012:43(2):270-9. PMID: 23082579.
8. Hikino H, Sugai T, Konno C, Hashimoto I, Terasaki S, Hirono I. Liver-protective principle of Thujopsis dolabrata leaves. Planta Med,1979:36(2):156-63. doi: 10.1055/s-0028-1097256. PMID: 461568.
9. Inamori Y, Shinohara S, Tsujibo H, Okabe T, Morita Y, Sakagami Y *et al*. Antimicrobial activity and metalloprotease inhibition of hinokitiol-related compounds, the constituents of Thujopsis dolabrata S. and Z. hondai MAK. Biol Pharm Bull,1999:22(9):990-3. doi: 10.1248/bpb.22.990. PMID: 10513629.
10. Inamori Y, Sakagami Y, Morita Y, Shibata M, Sugiura M, Kumeda Y *et al*. Antifungal activity of Hinokitiol-related compounds on wood-rotting fungi and their insecticidal activities. Biol Pharm Bull,2000:23(8):995-7. doi: 10.1248/bpb.23.995.
11. Inamori Y, Morita Y, Sakagami Y, Okabe T, Ishida N. The excellence of Aomori Hiba (Hinokiasunaro) in its use as building materials of Buddhist temples and Shinto shrines. Biocontrol Sci,2006:11(2):49-54. doi: 10.4265/bio.11.49.
12. Inanaga M, Hasegawa Y, Mishima K, Takata K. Genetic Diversity and Structure of Japanese Endemic Genus *Thujopsis* (Cupressaceae) Using EST-SSR Markers. Forests,2020:11(9):935. https://doi.org/10.3390/f11090935
13. Kim CH, Lee T, Oh I, Nam KW, Kim KH, Oh KB *et al*. Mast cell stabilizing effect of (-)-Elema-1,3,11(13)-trien-12-ol and thujopsene from Thujopsis dolabrata is mediated by down-regulation of interleukin-4 secretion in antigen-induced RBL-2H3 cells. Biol Pharm Bull,2013:36(3):339-45. doi: 10.1248/bpb.b12-00375.
14. Kim JR, Perumalsamy H, Kwon MJ, Chae SU, Ahn YJ. Toxicity of hiba oil constituents and spray formulations to American house dust mites and copra mites. Pest Manag Sci,2015:71(5):737-43. doi: 10.1002/ps.3843.
15. Liu Y, Liniger M, McFadden RM, Roizen JL, Malette J, Reeves CM *et al*. Formal total syntheses of classic natural product target molecules via palladium-catalyzed enantioselective alkylation. Beilstein J Org Chem,2014:10:2501-12. doi: 10.3762/bjoc.10.261.
16. Lorenz P, Bunse M, Sauer S, Conrad J, Stintzing FC, Kammerer DR. Conversion of Plant Secondary Metabolites upon Fermentation of *Mercurialis perennis* L. Extracts with two Lactobacteria Strains. Fermentation,2019:5(2):42. https://doi.org/10.3390/fermentation5020042
17. Matsumura E, Morita Y, Date T, Tsujibo H, Yasuda M, Okabe T *et al*. Cytotoxicity of the hinokitiol-related compounds, gamma-thujaplicin and beta-dolabrin. Biol Pharm Bull,2001:24(3):299-302. doi: 10.1248/bpb.24.299.
18. Matsuura T, Yamaguchi T, Zaike Y, Yanagihara K, Ichinose M. Reduction of the chronic stress response by inhalation of hiba (Thujopsis dolabrata) essential oil in rats. Biosci Biotechnol Biochem,2014:78(7):1135-9. doi: 10.1080/09168451.2014.918492.
19. Miyamoto D., Kusagaya Y., Endo N., Sometani A., Takeo S., Suzuki T., Arima Y., Nakajima K., Suzuki Y.: Thujaplicin-copper chelates inhibit replication of human influenza viruses. Antiviral Res,1998:39(2):89-100. doi: 10.1016/s0166-3542(98)00034-5. PMID: 9806486.
20. Morita Y, Matsumura E, Tsujibo H, Yasuda M, Sakagami Y, Okabe T *et al* Biological activity of alpha-thujaplicin, the minor component of Thujopsis dolabrata SIEB. et ZUCC. var. hondai MAKINO. Biol Pharm Bull,2001:24(6):607-11. doi: 10.1248/bpb.24.607. PMID: 11411545.
21. Morita Y, Matsumura E, Tsujibo H, Yasuda M, Okabe T, Sakagami Y *et al*. Biological activity of 4-acetyltropolone, the minor component of Thujopsis dolabrata SIeb. et Zucc. hondai Mak. Biol Pharm Bull,2002:25(8):981-5. doi: 10.1248/bpb.25.981. PMID: 12186430.
22. Morita Y, Matsumura E, Okabe T, Shibata M, Sugiura M, Ohe T *et al* Biological activity of tropolone. Biol Pharm Bull,2003:26(10):1487-90. doi: 10.1248/bpb.26.1487. PMID: 14519960.
23. Morita Y, Matsumura E, Okabe T, Fukui T, Shibata M, Sugiura M *et al*. Biological activity of alpha-thujaplicin, the isomer of hinokitiol. Biol Pharm Bull,2004a:27(6):899-902. doi: 10.1248/bpb.27.899. PMID: 15187442.
24. Morita Y, Matsumura E, Okabe T, Fukui T, Ohe T, Ishida N *et al*. Biological activity of beta-dolabrin, gamma-thujaplicin, and 4-acetyltropolone, hinokitiol-related compounds. Biol Pharm Bull,2004b:27(10):1666-9. doi: 10.1248/bpb.27.1666. PMID: 15467216.

25. Morita Y, Sakagami Y, Okabe T, Ohe T, Inamori Y, Ishida N. The mechanism of the bactericidal activity of hinokitiol. Biocontrol Sci,2007:12(3):101-10. doi: 10.4265/bio.12.101. PMID: 17927050.
26. Nagata T, Fujino Y, Toume K, Xiao Long L, Yamaguchi T, Okumura T *et al*. Anti-cancer Effect in Volatile Components of Hiba Essential Oil (Thujopsis dolabrata). Clin Exp Pharmacol,2016:6:214. doi:10.4172/2161-1459.1000214.
27. Nam K-W, Noh J-K, Kim S-K, Lee S-J, Kim K-H, Oh K-B *et al*. Essential Oil of Thujopsis dolobrata Suppresses Atopic Dermatitis-Like Skin Lesions in NC/Nga Mice. Biomolecules and Therapeutics,2011:19(1):102-108.https://doi.org/10.4062/biomolther.2011.19.1.102
28. Pimentel MR, Molina G, Dionísio AP, Maróstica Junior MR, Pastore GM. The use of endophytes to obtain bioactive compounds and their application in biotransformation process. Biotechnol Res Int, 2011:576286.doi: 10.4061/2011/576286. Epub, 2010-2011. 26. PMID: 21350663; PMCID: PMC3042614.
29. Pohlit AM, Lopes NP, Gama RA, Tadei WP, Neto VF. Patent literature on mosquito repellent inventions which contain plant essential oils--a review. Planta Med,2011:77(6):598-617. doi: 10.1055/s-0030-1270723.
30. Muñoz R, B de las Rivas, F López de Felipe, I Reverón, L Santamaría, M Esteban-Torres *et al*. Biotransformation of Phenolics by Lactobacillus plantarum in Fermented Foods, Editor(s): Juana Frias, Cristina Martinez-Villaluenga, Elena Peñas, Fermented Foods in Health and Disease Prevention, Academic Press, 2017, 63-83. ISBN 780128023099,https://doi.org/10.1016/B978-0-12-802309-9.00004-2.
31. Sakagami Y, Inamori Y, Isoyama N, Tsujibo H, Okabe T, Morita Y *et al*. Phytogrowth-Inhibitory activities of beta-dolabrin and gamma-thujaplicin, hinokitiol-related compounds and constituents of Thujopsis dolabrata Sieb. et Zucc. var hondai Makino. Biol Pharm Bull,2000:23(5):645-8. doi: 10.1248/bpb.23.645. PMID: 10823681.
32. Scalvenzi, Laura. New frontiers of essential oils research: biotransformation of the phytocomplex and its pure compounds by endophytic fungi. Acta Hortic,2014:1030:125-132. doi:10.17660/ActaHortic.2014.1030.15
33. Shô Itô, Katsuya Endo, Hinako Honma, Koji Ota. New constituents of *Thujopsis dolabrata*. Tetrahedron Letters,1965:6(42):3777-3781, ISSN 0040-4039. https://doi.org/10.1016/S0040-4039(01)99563 (https://www.sciencedirect.com/science/article/pii/S0040403901995632)
34. Suzuki S, Suzuki H, Tanaka K, Yamamura M, Shibata D, Umezawa T. *De novo* transcriptome analysis of needles of *Thujopsis dolabrata* var. *hondae*. Plant Biotechnol (Tokyo),2019:36(2):113-118. doi: 10.5511/plantbiotechnology.19.0220a. PMID: 31768112; PMCID: PMC6847777.
35. Takao Y, Kuriyama I, Yamada T, Mizoguchi H, Yoshida H, Mizushina Y. Antifungal properties of Japanese cedar essential oil from waste wood chips made from used sake barrels. Mol Med Rep,2012:5(5):1163-8. doi: 10.3892/mmr.2012.821.
36. Sandermann W. Terpenoids: Structure and Distribution**Translated from the German by Dr. Herbert S. Heineman, University of Pittsburgh School of Medicine., Editor(s): Marcel Florkin, Howard S. Mason, Comparative Biochemistry, Academic Press, 1962, 503-590. ISBN 9780123955449, https://doi.org/10.1016/B978-0-12-395544-9.50021-2 (https://www.sciencedirect.com/science/article/pii/B9780123955449500212)
37. Wu JY, Ding ST, Li QJ, Zhao ZR, Sun BN. First occurrence of Platycladus from the upper Miocene of Southwest China and its phytogeographic implications. PLoS One,2014:9(12):e115141. doi: 10.1371/journal.pone.0115141. PMID: 25517767; PMCID: PMC4269418.
38. https://blogs.ubc.ca/conifersubc/?page_id=125
39. https://conifersociety.org/conifers/thujopsis-dolabrata/
40. https://plants.ces.ncsu.edu/plants/thujopsis-dolabrata/http://www.toxmsdt.com/121-introduction-to-biotransformation.html