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A review on phytochemistry and medicinal uses of *Taxus wallichiana* L. (Himalayan Yew)

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Abstract

Himalayan yew (*Taxus wallichiana*), a member of family Taxaceae is an evergreen, medium sized, drought tolerant tree which has been used traditionally to cure epilepsy, respiratory infections, colds, cough, asthma, and liver disorders. Recently, plant received great attention of researchers as its bark and leaf are major sources of anticancer drug (Taxol). Other potent chemical constituents include bioflavonoids, lignans, phytosterols, and phytoecdysteroids. Present review focuses on chemical composition, traditional medicinal, and pharmacological uses of Himalayan yew.

Key words: Taxol, Himalayan Yew, archeological evidence, anticancer activities

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1. Botany

1.1. Introduction

Himalayan Yew (*Taxus wallichiana*) is an ever green tree belonging to family Taxaceae and genus *Taxa*. The genus *Taxa* contains about twenty species. *Taxus baccata*, *Taxus brevifolia*, *Taxus canadensis*, *Taxus cuspidate*, *Taxus floridana* and *Taxus wallichiana* are the prominent species of Taxa. Himalayan Yew is a multipurpose tree having high medicinal and ethnobotanical importance. Plant received great attention in recent years as its bark and leaf are the richest source of Taxol (potent anticancer drug), which is used widely to cure breast and ovarian cancers. Taxol was first reported from *Taxus brevifolia*, since then taxoids have been isolated from several other species including *Taxus wallichiana*. Incautious and extensive collection of plant for medicinal and other purposes are the reasons bringing it under critical rare category, since it is a very slow growing tree, and regeneration is only possible through vegetative propagation [1-2]. *Taxus wallichiana* is known by different names depending where you are in the world. In English, it is called Yew, Common Yew or European Yew. In Hindi and Sanskrit it is called Talispatra. In Irish, it is known as Irish Yew. Its Arabic name is Talisfar, while, it is known as Zarnab in Urdu. In Himalayan region is known as Himalayan yew.

1.2. History

Taxus species have a long history of utilization throughout human history. Various archeological studies suggest that yews were used to make spears, bows, and axe shafts in Neolithic and Roman periods [3]. The oldest spear found in Essex of England, made from the wood of European yew (*Taxus baccata* L.) is a strong evidence of yew wood durability. Yews were considered a symbol of eternal life and were planted in Churchyards because of their long life spans (approximately 41000 years). Furniture and utensils made from yews wood was highly prized by Asian and North American local communities due to its decay resistant properties and durability. Yews also got a lot of importance from various medicinal systems including Ayurveda and Unani (India) or Han pharmacopoeia (China) [4].

1.3. Demography/Location

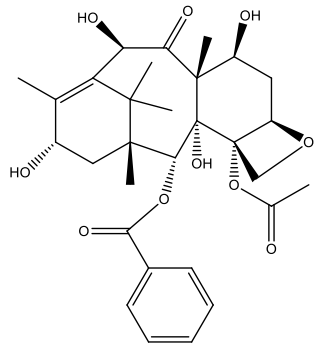
Generally, *Taxus wallichiana* grows in a wide variety of climatic conditions, but flourish best on loamy soil having neutral or acidic pH and appropriate moisture content. Yews grow best in partial shade or open sun and don't tolerate extreme heat or cold. They are widely distributed in North America (Great Lakes and mid-Atlantic areas), Japan, Europe (western, southern, and northern regions), Malaysia, Algeria, Afghanistan, Vietnam, Philippines, North India, Nepal, Tibet, Russia, Bhutan, China, Iran, and Pakistan [2-5].

1.4. Botany, Morphology, Ecology

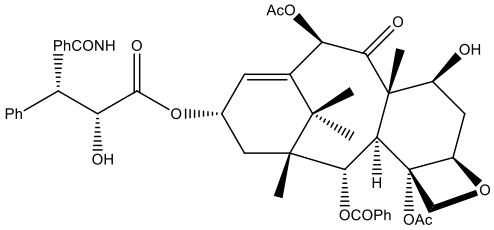
Taxus wallichiana is a medium-sized evergreen tree having 10-20m height and 1.5 to 1.8m girth. Bark is thin, scaly, and reddish brown in color. Branches are arranged irregularly. Branclets are slender and orange brown in color. Leaves are 2 to 4cm long, leathery, linear with re-curved margins, shining above, rusty red or yellow brown below. Flowers are dioecious. Male strobili globose, stalked, sub-sessile, solitary, auxillary, each comprising of 6 to 14 stamens. Female strobili are stalked, auxillary, green in color when young and becomes red or orange at maturity. Seeds are ovoid, hard, with 4.5 to 5.7 mm fleshy cups [1-6]. Plant grows well under partial shade (warm and dry areas), and in full sun (coastal areas). It can grow on all soil types having adequate drainage but prefers humus rich soils. Yews can't tolerate prolonged cold and frosts. They can tolerate drought and are able to survive under temporary flooding, but can't tolerate poor drainage for longer time. Their extensive roots system is capable of penetrating highly compressed soils and makes them able to survive in critical situations like vertical cliff faces and rocky terrain [7].

2. Chemistry

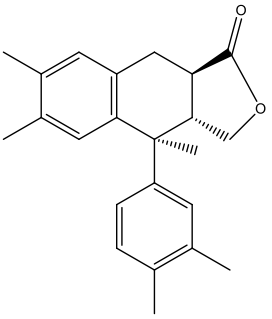
Systematic studies conducted on compounds isolated from different parts (stem, leaf, and bark) of the plant *Taxus wallichiana* revealed the presence of over 3000 taxoids. Among them Taxol (a diterpenoid alkaloid) is the major taxoid which is mainly obtained from bark and varies in concentration from 0.007 to 0.01%, in different *Taxus* species. About 1g taxol can be obtained from 3 to 4 trees of age 60. Approximately, 50 to 150mg of taxol can be obtained from 1kg dried bark and 10kg bark is obtained from an average tree. Taxotere (derivative of taxol) has been claimed as a promising anticancer agent. Other potent taxoids found in *Taxus wallichiana* include baccatin-III (0.084%), cephalo mannine (0.031%), and 10-deacetyl baccatin-III. Another important class of compounds (lignans) is found in heartwood of plant. These include isoliovil, conidendrin, α-conidendrin, hydroxymatairesinol, texiresinol, β-conidendrin, (–)-secoisolariciresinol, isotexiresinol. These lignans have anticancer as well as antiulcer potentials. Major bioflavonoids found in *T. wallichiana* include sciadopitysin and amentoflavone. Phytosterols (daucosterol, 4-desmethylsterol type, and β-sitosterol), and phytoecdysteroids (ponasterone and ecdysone), have also been reported from *T. wallichiana* bark. Structures of some important compounds found in *Taxus wallichiana* are shown in figure 1. Appreciable amount of essential oil is present in the leaves of *T. wallichiana*. Generally GCMS analysis is used to find out the chemical profile of essential oils [8-13]. Major constituents include terpenes, alkanes, alkenes, alcohols, esters, aldehydes, and organic acids which impart characteristic aroma and flavor to the plant [14].



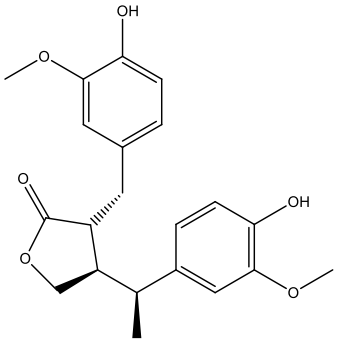
10-deacetyl baccatin-III



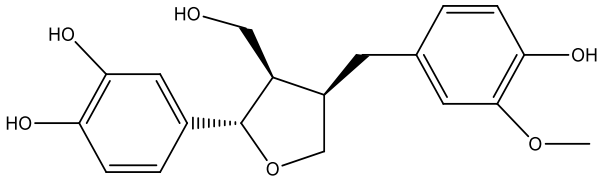
Taxol



α –conidendrin



Hydroxymatairesinol



Texiresinol

Fig. 1. Structures of some important compounds found in *Taxus* Species

3. Post-harvest technology

Conventionally, harvesting time of Himalayan Yew can be variable depending on the component, the plant collected for. Collection of leaves for essential oil can be done early in the morning before the day temperature starts increasing due to strong essential oil activity in morning. Leaves can be stored when wrapped in appropriate packing

in air tight bags. For long term storage leaves should be dried well and drying should avoid any breakage to avoid loss of essential oil and taxanes. Arils turn red when seeds are fully grown. Predator may attack the aril, so should be picked as soon as possible to avoid losses. Seeds are extracted from fruit following the pre-chilling treatments and stored at recommended temperature for further production if required. Warm stratification following chilling should be done wisely as they may affect the development cycle of yew seeds. Preserved seeds can be pre-treated and seeded in spring. Seeds have adequate amount of fat so should be dried to low moister content following the freezer preservation to keep the viability of seeds. Harvesting the fully developed green seed before drying on the plant and then following the sowing has not been proposed to lessen the germination time because factors that slower the germination time develop even early. Pricking out the young seeds into the separate pots once they are grown enough to handle and grow them again in pots in cold frame. Young plants are slow developing and will apparently demand minimum two years of pot cultivation before being grown enough to plant out. Planting out is preferred in either in late spring or in early summer while cuttings the half ripe terminal shoots five to eight centimetre in length in July/August in a shaded frame and root by late September but keep them in the frame over winter and plant out in late spring.

4. Processing

Himalayan Yew like other plants is consumed in a variety of ways and for various purposes. In addition to fresh leaves, other processed forms of Himalayan Yew include dry, freezing, powdered leaves and extracted essential oils. The shelf life of whole shrub or chopped leaves can be extended by freezing with or without additives e.g. salts or other oils.

5. Value addition

T. wallichiana can be combined with other plants for various purposes. But it is traditionally used alone but not always due to poisonous nature of plant. The pulp of aril is sweet and can be used in jams, when toxic seed is removed. Various parts of *T. wallichiana* such as bark and leaves are employed in Unani medicine as an origin of drug Zarnab. The inner bark of the tree is dried, powdered and boiled with a small quantity of common salt and refined butter and taken as a substitute of tea, in the areas of Garhwal hills. The red arils are sweet in taste and can be eaten. Bark of plant is use as herbal tea locally in India. It is used mainly for wood carvery, marquetry and turnery. The wood being colourful (red heartwood, white sapwood) used to apply thin decorative coating on furniture in UK, to make lute bodies, bowls, tankards, combs, tool-handles, shoulder poles, bows in India and various art objects. Presently, it is used primarily as an ornamental plant in gardens and churchyard. The green shoots are managed to ornament houses in Nepal during religious ceremonies.

6. Traditional medicinal uses

T. wallichiana has a wide variety of traditional medicinal uses. It has been utilized to cure of high fever and chronic inflammatory diseases. Its decoctions, juice, and herbal tea are consumed to cure epilepsy, cough, cold, indigestion, and respiratory infections [15-16]. Young shoots are used to make tincture to cure falling pulse, coldness, headache, biliousness, giddiness, and feeble [17]. A decoction made from bark is used in the treatment of muscle and joint pain and rheumatism. However, leaves decoction is used in the treatment of liver disorders. Tree extracts are also used in herbal treatment of hairs. Stem decoction is widely used to cure tuberculosis in many regions of the world [18]. Various part of *T. wallichiana* such as bark and leaves are employed in Unani medicine (Zarnab); a sedative and aphrodisiac drug which is used to cure bronchitis, asthma, snake bite, epilepsy, and scorpion stings [19-20].

7. Pharmacological uses

7.1. Antioxidant Activity

T. wallichiana is reported as a potent antioxidant. Different assay such as lipid per-oxidation assays, total phenolics, DPPH, reducing power and DNA sugar damage were used to evaluate antioxidant activity of different extract of *T. wallichiana*. Maximum percentage inhibition recorded for standard methanolic, ethyl acetate, chloroform and petroleum ether extracts was 72.78%, 72.45%, 68.3% and 94.81% respectively. Another antioxidant assay the microsomal lipid peroxidation system was also employed to determine the antioxidant activity and petroleum ether extract was again observed to be the most potent (97.63%) followed by methanolic extract (97.56%). Above studies promise remarkable antioxidant activities of raw extracts of the *T. wallichiana* [21].

7.2. Anti-inflammatory and analgesic activities

The pain relieving and anti-inflammatory effects of the bark extract of *T. wallichiana* has been studied. Tasumatrol B, 4-deacetylbaccatin III (4DAB), and 1, 13-diacetyl-10-deacetylbaccatin III (10DAD), were reported from the bark of *T. wallichiana*. These substances were evaluated using an acetic acid induced writhing test, carrageenan based paw edema model, and lipoxygenase inhibitory assay *in vitro*. All the substances, particularly tasumatrol B, showed remarkable anti-inflammatory properties in carrageenan based edema model [22], [23]. Taxusabietane A, identified from *Taxus Wallichiana* extract, was examined for *in vitro* and *in vivo* anti-inflammatory properties by applying the lipoxygenase inhibitory assay and carrageenan based edema model. Significant anti-inflammatory action was exhibited by Taxusabietane A [24]. Analgesic action of *T. wallichiana* bark extracts was examined using acetic acid abdominal writhing assay. Remarkable analgesic action was shown by tasumatrol B [22]. Analgesic activities of extracts of *T. wallichiana* were

due to their inhibitory effects of *T. wallichiana* extracts on biosynthesis of metabolites [22].

7.3. Anti-convulsant and antipyretic activities

T. wallichiana extracts possess potential antipyretic and anticonvulsant properties [25]. The plant extract retarded the pentylene tetrazol induced convulsions in model animals. The extract, when provided in measure of 0.1g/kg and 0.2g/kg, inhibited clonus and myoclonus significantly. Antipyretic activity was also examined using yeast induced pyrexia model. Extract at dose level of 0.2g/kg exhibited remarkable inhibitory effect while less significant effect was shown at dose levels of 0.05 and 0.1 g/kg [25-27]. The anticonvulsant and antipyretic activities of *T. wallichiana* support its traditional uses in epilepsy and pyrexia.

7.4. Antibacterial and antifungal activities

Extracts as well as essential oils extracted from aromatic plants have been reported to show potential antifungal and antibacterial activities [11-28]. In a study, antibacterial activities of extracts (methanolic) from leaf, heartwood and bark of *T. wallichiana* were examined against *Salmonella typhi*, *Staphylococcus aureus*, and *Pseudomonas aerugenosa*. Minimum inhibitory concentration values ranged from 0.08 to 200 mg/ml. Antifungal properties were found against three fungal strains (*Fusarium solani*, *Trichophyton longifusus*, and *Microsporum canis*) [15]. *T. wallichiana* bark extract (ethanolic) also exhibited antifungal activity against *Blastoschizomyces capitatus* [29].

7.5. Anticancer activity

Pacitaxel (a diterpenoid alkaloid), is widely used to cure various forms of cancer (lung, breast, blood and liver cancers). A taxoid named as taxawallin I isolated from the methanol extract of *T. wallichiana* bark showed potent cytotoxic activity *in vitro* against various cancer cell lines (A498, MDR 2780AD, NCI-H226, and HepG2) [30]. Anticancer activity of 1-hydroxy-2-deacetoxy-5-decinnamoyltaxinine J (another taxoid) was determined using clonogenic and MTT assays. Significant anticancer action was observed against Colo 320DM, MCF-7, KB PA-1, and WRL-68 cancer cell lines, in a dose dependent manner [31]. Other phytochemicals (lignins) are also reported to have some anticancer potential. Taxiresinol I (lignan) isolated from *T. wallichiana* heartwood showed anticancer activity against ovarian, colon, breast, and liver cells, *in vitro* [32].

8. Toxicity

Recently, it has been reported that all ornamental varieties of genus *Taxus* including *T. baccata*, T. brevifolia, and *Taxus cuspidate* are toxic in nature [33]. The compounds responsible for yews toxicity are diterpenes (basic or alkaloid). These diterpenes namely as “taxines” have not been reported from *Taxus wallichiana*. Therefore, plant has been reported to have little or no toxicity.

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