

An overview of taxus

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ABSTRACT

Plants synthesize certain Phytoconstituents for their protection, which, because they are not of primary need, are known as secondary metabolites. Plant cell factories constitute an alternative source of high added value phytochemical. These secondary metabolites of plants have often been found to have medicinal uses for human beings. One such gymnosperm having secondary metabolites of medicinal potential for humans is *Taxus wallichiana* (Himalayan yew). This plant has been investigated for its essential oil, diterpenoids, lignans, steroids, sterols and biflavonoids. Traditionally, it is used to treat disorders of the digestive, respiratory, nervous and skeletal systems. Although pharmacologically underexplored, it has been used for antiepileptic, anti-inflammatory, anticancer, antipyretic, analgesic, immunomodulatory and antimicrobial activities. The present review compiles traditional uses, phytochemical constituents (specifically the secondary metabolites) pharmacological activities and the toxicity of *T. wallichiana*. This review is focused on recent advances in the production of taxol and related taxanes in *Taxus baccata*. After a short overview of taxol production at an industrial level, the review focuses on taxol biosynthesis in plant cells and the attempts to produce taxol in *T. baccata* cell cultures, giving particular emphasis to the optimization steps that have improved production, and including the most recently developed new tools and Taxines are the active, poisonous constituents in yew plants (*Taxus spp.*) and have been implicated in animal and human poisonings.

Keywords: *Taxus wallichiana*; plants, medicinal; diterpenes; lignans; biflavonoids; pharmacological effect; Taxol; Secondary compounds.

INTRODUCTION

Taxus is a genus of morphologically similar looking yew, distributed in the Northern Hemisphere. The taxonomy of these yews is not well defined, and although taxonomists had previously divided the genus *Taxus* into one species with seven subspecies, it has recently been proposed that the genus should be separated into 24 species with 55 varieties; neither approach has gained universal acceptance. Probably due to this reason, geographic location is also often used for the identification and naming of different populations.

For example, European yew grows in Europe, Canadian yew is distributed within North America and Himalayan yew is the species found in Asia. In the Indian subcontinent, Himalayan yew is widely distributed in the temperate Himalayan region and in the hills of the northern, north eastern and eastern states (*i.e.*, Jammu & Kashmir, Himachal Pradesh, Uttaranchal, Sikkim, Arunachal Pradesh, Assam Meghalaya, Nagaland and Manipur) at an altitude range of 1 800–3 300 m. Morphologically, it is a dioecious evergreen tree reaching nearly 6 m in height with reddish brown bark, distichously

arranged leaves, with flowers arising from the axils of the leaves, 6–14 stamens and solitary female strobili. As mentioned above some ethnobotanical works use the classification suggested by Pilger (1903), where all species of *Taxus* have been classified as subspecies of *Taxus baccata* L. The toxicity of *Taxus baccata* has been known since antiquity and extracts of yew leaves have been used for homicides as well as suicides. Intoxication by parts of the yew plant (the seeds, the bark, the leaves) are well described in the literature but suicidal cases of yew ingestion are rarely known. *Taxus baccata* contains a complex mixture of compounds, including phenolic constituents (e.g. 3,5-dimethoxyphenol), nonalkaloidal diterpenoids (e.g. 10-deactetyl baccatin III), alkaloidal diterpenoids (e.g. paclitaxel, taxine B) or flavonoids (e.g. myricetin) and bioflavonoids (e.g. bilobetin). The temperate zones of the northern hemisphere. It is a small to medium-sized evergreen tree that historically has been used for weapon-making and medicine, and is poisonous except for the fruit. The genus *Taxus* belongs to the Class Pinopsida, the Order Taxales and the Family Taxaceae.



Figure 1:

As the plant species are highly similar, they are often easier to separate geographically than morphologically. Typically, eight species are recognized: *T. baccata* (European or English yew), *T. brevifolia* (Pacific yew or Western yew), *T. canadensis* (Canadian yew), *T. chinensis* (Chinese yew), *T. cuspidata* (Japanese yew), *T. floridana* (Florida yew), *T. globosa* (Mexican yew) and *T. wallichiana* (Himalayan yew). There are also two recognized hybrids: *Taxus × media* = *T. baccata* × *T. cuspidata* and *Taxus × hunne welliana* = *T. cuspidata* × *T. canadensis*. The genus *Taxus* has generated considerable interest due to its content of diterpene alkaloids, particularly taxol and by the registered trade name Taxol BMS [Bristol-Myers Squibb]). The anticancer properties of taxol were discovered in *T. brevifolia* extracts in 1971, while in 1979 Horwitz, working with *T. baccata*, found that the cellular target of taxol was tubulin. In their search for “spindle

poisons” the Potier group in France found that the main taxane in *T. baccata* (European *Taxus*) needles was 10-deacetyl**baccatin III** (0.1% yield in the extracts). After studying the semi-synthesis of taxol from this metabolic intermediate, which has the same action mechanism as taxol. Additionally, lignans, flavonoids, steroids and sugar derivatives have been synthesized in different parts of various *Taxus* species. Recent studies on *Taxus* extracts from needles found about 50 lignans, including neolignans, and a few terpenolignans. Specifically in *T. baccata*, five lignans have been found **lariciresinol**, **taxiresinol**, **3-demethylisolariciresinol-9-hydroxy isopropyl ether**, **isolariciresinol** and **3-demethylisolariciresinol**. In vitro studies have shown that **lariciresinol** and **isolariciresinol** have a powerful inhibitory effect on tumor necrosis factor- α (TNF- α) and **taxiresinol** is reported to be highly protective against gastric lesions.

Anti-Cancer Plant: *Taxus Chinensis*

Taxus Chinensis 红豆杉 is a species of yew. It is commonly called the Chinese yew, though this term also refers to *Taxus Celebica* or *Taxus Sumatrana*.



Figure 2:



Figure 3:

SYNONYMS: yew, talispatra, Himalayan yew.

BIOLOGICAL SOURCE: This consists of dried leaves, bark and roots of various species of *taxus*. The four important species with parts used are as under.

1. *Taxus baccata* mainly leaves.

2. *Taxus brevifolia* mainly stem bark.

3. *Taxus Canadensis* leaves and roots.

4. *Taxus cuspidate* leaves.

GEOGRAPHICAL SOURCE:

it is very slow growing evergreen gymnospermous tree. Found in India, Canada and America. It is reported in temperate Himalayan region of India up to an altitude of 2000-3500 meters.

CHEMICAL CONSTITUENTS:

The main constituent taxol is present in all parts of the plant especially in leaves, roots and bark of the plant.

Taxanes are the most important group of chemical constituents and up to now 4 different taxane compounds have been found, all of which are diterpenoid structures. Among them three most important members are

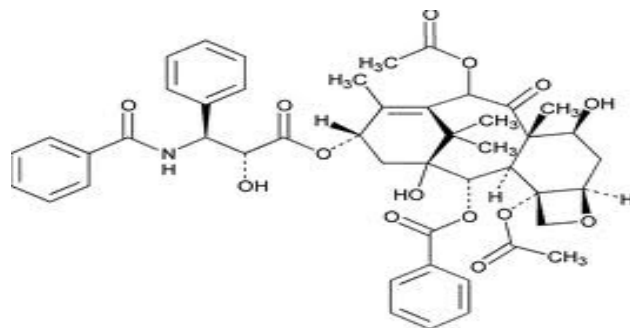


Figure 4: cephlo mannine

A derivative of taxol, called taxotere, has been reported to have better bio-availability and pharmacological properties and has been claimed as a promising anticancer agent.

Description:

Dioecious shrubs or small trees to 15(-25) m tall and 50(-140) cm dbh. Bole straight to contorted, fluted; crown open-conical. Bark scaly, outer scales purplish to purplish brown, inner ones reddish to reddish purple, scales varying widely in size (2-50 mm wide). Branches ascendent to drooping. First-year shoots green, entirely covered by decurrent leaf bases; older twigs red-brown, resembling bark by the third year. Foliage buds inconspicuous, arising terminally or at the adaxial base of a leaf. Leaves green, linear, acute, mucronate, 8-35 mm long, 1-3 mm wide, pliable, often falcate, with a narrow median ridge on the upper surface and stomata in two yellow-green (not glaucous) bands of 5-8 lines on the lower surface, whorled but appearing 2-ranked, with a short (c. 1 mm) petiole and a 5-8 mm long decurrent leaf base; cuticular papillae are present along stomata bands and epidermal cells as viewed in cross section of leaf are mostly taller than wide. Pollen cones solitary or clustered, adaxial on year-old shoots, buds globose, green, ca. 1.5 mm diameter. Seed ovoid, 2-4-angled, 5-6.5 mm, maturing late summer-fall, enclosed in a red aril ca. 10 mm diameter. Wood hard and heavy, about 640 kg/m³ (Hils 1993, Peattie 1950, and my pers. obs.).

taxol, cephalomannine and 10-deacetyl baccatin. In all species, with little variations, taxol occurs from 0.007% to 0.01%. It is mainly obtained from stem bark of *T. brevifolia*. But the method of isolation is tedious and like vinca, yields are also less. It needs at least 60 years old 3-4 trees to get 1 gm of taxol. Yields of 50-150 mg of taxol are obtained from 1 kg dried yew bark. About 10 kg bark is available from an average tree. The most potent compounds include taxol (containing a rare oxetane ring and amide side chain), cephalomannine (0.031%), baccatin-III (0.084%), and 10-deacetyl baccatin III.

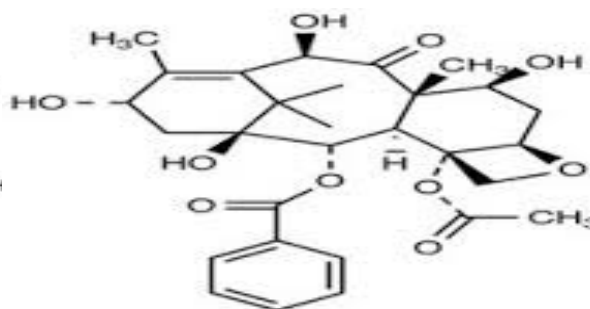


Figure 5: 10-deacetyl baccatin III

APPLICATION OF TAXUS:

1. Traditional use and medicinal importance-

For centuries, the stem bark of Himalayan yew has been used to make tea by the *Bhotiya* tribal community in the Garhwal region of Himalayas and to cure colds, coughs, hypertension and cancer in the buffer zone villages of Nanda Devi Biosphere Reserve. Himalayan yew was in such demand that the use in the buffer zone of the Nanda Devi Biosphere Reserve was about 1.7 (± 0.3) kg dry weight per family per year. Poor families relied on the bark of this species for preparing tea for their own consumption throughout the year, whereas wealthy families also distributed bark to their relatives living elsewhere. This also suggests that Himalayan yew is a separate species. The yews of Hindu Kush-Himalaya and adjacent regions have been divided into two species, on the basis of morphological, molecular and climatic data. *T. contorta* is found in the Western Himalaya, distributed from Afghanistan to central Nepal, and *T. wallichiana* in the Eastern Himalaya, distributed from central Nepal to Yunnan Province in China. The habitat in which *T. contorta* is found includes the Himalayan region that receives low summer rainfall and high winter rainfall, whereas, *T. wallichiana* habitat is characterized by high summer and low winter rainfall. Other authors have named the Western Himalayan yew as *T. fuana* Nan Li & R.R. Mill, which is an evergreen non-resinous gymnosperm, endemic to the Western Himalaya region.

of Pakistan, North India, and Southwest Xizang, China and Nepal. Indeed, using modern techniques to verify the taxonomy of this genus is an area that deserves further attention.

2. Phytoconstituents:

3.1 Essential oils:

T. wallichiana leaves are rich in essential oils. Terpenes and alcohol, aldehyde, organic acid, acid esters, alkanes and alkenes are the main constituents that give it its characteristic flavor and fragrance.

3.2 Diterpenes:

Diterpenes have been the most important phytochemicals of genus *Taxus*. These taxane diterpenoids are biosynthesized from pyruvate and glyceraldehyde-3-phosphate to form isopentenyl diphosphate and dimethylallyl diphosphate, through the 2-C-methyl-D-erythritol phosphate pathway. The isopentenyl diphosphate and dimethylallyl diphosphate act as substrate for geranylgeranyl diphosphate synthase to form geranylgeranyl diphosphate which through extensive oxidative modification leads to the formation of taxol. After the isolation of taxol, every species of the *Taxus* genus was screened for cytotoxic diterpenes.

3.3 Biflavonoids:

The biflavonoids are secondary metabolites that are formed through phenol-oxidative coupling of

flavones, flavonols, dihydroflavonols, flavanones, isoflavones, aurones, auronols or chalcones. For the majority of families belonging to Gymnospermae, including the families Taxaceae and Ginkgoaceae, biflavonoids have provided chemotaxonomic markers. A number of bioflavonoids

have already been reported from genus *Taxus*.

3.4 Phytosterols and phytoecdysteroids:

The biosynthesis of sterols in plants not only regulates fluidity and permeability of membranes to maintain various functions of membranes, but also modulates the activities of membrane-associated proteins including enzymes, receptors and signal transduction components. The sterols reported from *T. wallichiana* belonging to the 4-desmethylsterol type, β -sitosterol and daucosterol (β -glucosylated form of β -sitosterol; Figure 4), have been obtained from the ethanolic extract of bark. β -Sitosterol has shown antiviral, anti-inflammatory, antifebrile and uterotrophic effects, whereas daucosterol has been investigated for its cytotoxic effect [59]. The other steroids present in Himalayan yew are phytoecdysteroids. These phytoecdysteroids are C27, C28 or C29 compounds possessing a 14 α -hydroxy-7-en-6-one chromophore and A/B-cisring fusion [60]. Plants synthesise ecdysteroids as a defence mechanism. Two phytoecdysteroids isolated from the *T. wallichiana* are ponasterone and ecdysone.

Table 1: Essential oil composition of *Taxus wallichiana* Zucc. leaves.

Essential oil	Chemical constituents
Alkane	<i>n</i> -Eicosane, docosane, <i>n</i> -pentacosane
Alkene	Santolina triene
Alcohol	1-Hepten-3-ol, (E)-2-hexenol, <i>n</i> -hexenol, <i>n</i> -heptan-2-ol, <i>n</i> -heptanol, (E)-2-octen-1-ol, (Z)-2-octen-1-ol, 1-octanol, (E)-verbenol, (E)-2-nonenol, myrtenol, geraniol, eugenol, globulol.
Aldehyde	<i>n</i> -Heptanal, benzaldehyde, <i>n</i> -octanal, (E)-2-octenal, <i>n</i> -nonanal, (E)-2-nonenal, dodecanal, <i>n</i> -nonanal, anisaldehyde.
Ketones	(Z)-3-Hexenone.
Organic acid	Hexanoic acid, benzoic acid.
Organic acid esters	(Z)-3-Hexenyl formate, (Z)-3-hexenyl acetate, (E)-2-hexenyl acetate, methyl benzoate, (E)-3-heptenyl acetate, octyl formate, benzyl acetate, methyl salicylate, <i>n</i> -octyl acetate, isopropyl-n-octanoate, sabinyl acetate, (E)-2-hexenyl- <i>n</i> -hexanoate, anisyl acetate, (Z)-3-hexenyl benzoate, geranyl tiglate, <i>n</i> -amyl anisoate, geranyl- <i>n</i> -heptanoate, (Z)-3-hexenyl benzoate, geranyl tiglate, <i>n</i> -amyl anisoate, geranyl- <i>n</i> -heptanoate, geranyl benzoate.
Monoterpenes /monoterpene Hydrates	α -Pinene, β -pinene, camphor, β caryophyllene, (Z)- β -ocimene, (Z)-sabinene hydrate, pinene hydrate.
Sesquiterpene	β -Caryophyllene, (E)- α -bergamotene, α -humulene, (E)- β -farnesene, caryophyllene oxide, (E,E)fernesol.

Taxus Health Benefits:

Due to its past usage, it is termed as obnoxious fruit. Later it was revealed that it has several nutritional properties which can cure several health problems. Earlier it was used as a cough medicine and later in landscaping and horticulture. It is also used in..-

- Aiding abortion
- Cold rheumatic fever
- Arthritis
- Menstrual stimulation

If you are new to Durian fruits then the very first sight of this fruit could remind you of a porcupine! Credit goes to the spikes present on this henna-green skinned fruit. The flesh, in contrast, is rich, juicy, and succulent. The flesh emits a very strong smell, which could ideally dissuade a first-time eater from trying it. Despite possessing a very strong odor, it is known to have a fantastic effect on the taste buds. Unique in taste, this fruit is packed with assorted nutrients and hence, offers benefits that surely are noteworthy.

A single durian weighs nearly 602 grams and is a good source of energy. 100 grams of this fruit renders about 147 Kcal of energy, which is about 7% of the Recommended Dietary Allowance (RDA).

Used in Medical treatment of:

- Breast cancer
- Ovarian cancer
- Lung cancer
- Snake bites
- Blood clots
- Rabies
- Wound related diseases

With its specific health benefits, it is highly advisable for women with hormone imbalance to consume the fruit, which relieves and allow them to lead normal healthy life.

Medicinal Properties of Taxusbaccata:

Taxusbaccata is derived from more than four hundred yew cultivators. Paclitaxel is removed from the bark of Taxus and is now an FDA approved component for medicinal treatments. Many cancer training and treatment institutes such as U.S National Cancer Institute have recommended it as the most advanced and effective in cancer therapy. With visible success in treating breast and ovarian cancer, its properties have been widely accepted and are being used in medicines.

Nutritional Benefits of Taxus:

Apart from the nutritional value of this fruit, it is also important to note the dosage of this one, which was potentially considered poisonous at a time. Until then it was not tested but is completely tested and approved for personal use now. These days' pharmaceutical companies

are endorsing its inclusion in their formulas. You need to decide on the dosage according to your requirement with a health specialist before consuming it randomly. One of the most important ingredients in Taxus is Taxol. It is used as an anti-cancer drug in various cancer treatments. The drug is obtained from a type of photochemical comprised in Taxus. It is a very nutritious element which assists in ailments related to the ovaries, pancreas, bladder and prostate. The taxane photo-chemicals are very helpful belonging to the Terpene family.

- Taxus is preferred more for its nutrition values along with other components in the medicinal field.
- Its dosage is strictly prescribed and is not a normal fruit that can be made available for consumption.
- Detailed research and prescriptions must follow before its use in your diet.
- Its wide range of disease curing capabilities is making it more prominent in modern medicines.
- The mere use of it defines a serious purpose on health grounds which call for expert advice.

The microtubules are responsible for the formation of mitotic spindle necessary for cell division. taxol bring out the polymerization to microtubules in absence of MAP and GTP. Due to this, microtubule formation is much enhanced which causes detrimental effects on dividing cells which leads to blockade of cell cycle. Eventually, multiple abnormal esters are formed from microtubules and get distributed in cytoplasm. taxol has been approved by USFDA for treatment of refractory ovarian cancer. it has also a promising role against non-small cell lung carcinoma, gastric and cervical cancers and also carcinomas of head, neck, prostate and colon.

Conclusion:

Himalayan yew is a gymnosperm that has widespread traditional use. During the early and late 1990's there was intense focus on the cytotoxic chemical constituents from this plant, and there was little interest in experimental validation of its traditional uses. During the last decade traditional uses have received increased scrutiny in suitable *in vitro* and *in vivo* animal models. Although recent studies have contributed to confusion in the taxonomy of the genus, the species in western and eastern Himalaya have been argued to show morphological diversification due to environmental and climatic effects. This re-enforces the need of further experimentation beyond ethanopharmacological screening, focusing on the chemotaxonomical difference between these species. Identifying distinctions in morphological characters may be a useful tool for proper identification of these two species, and may be further useful for ethano

pharmacological and phytochemical studies. Furthermore, the widespread traditional uses of Himalayan yew suggest a difference in toxicity between Himalayan and European yew, emphasizing the need for further investigation. In the present review, chemical, pharmacological and toxicological studies of Himalayan yew have been discussed, in addition to a review of its traditional uses and taxonomic ambiguities, suggesting several avenues for further study.

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