Taxus baccata L.
(Taxaceae)

(**Syns.**: *T. adpressa* Carrière; *T. aurea* K. Koch)

Abstract

A small to medium-sized evergreen tree, native to southwest Asia, northern Iran, Europe, and northwest Africa. Yew was known to the Greeks and Romans as a poisonous plant. Modern research has shown that the leaves and seeds are poisonous, but not the red pulp surrounding the seeds. Leaves have been recommended in epilepsy and other spasmodic conditions. In India, Sanskrit writers described it as carminative, stomachic, expectorant, tonic and astringent; and useful in phthisis, asthma, bronchitis and vesical catarrh. Powdered leaves are used with the juice of *Adhatoda vasica* and honey in cough, asthma and hemoptysis. Yew played an important role in the mythology of ancient Germans and Medieval Europeans; they knew about its poisonous nature and made their arrows poisonous with its juice for hunting, and used the leaves for homicide and suicide. In Central Italy it was once used during pregnancy, for parturition, nursing and abortion. In *Unani* medicine, leaves are described as cardiotonic, nervine and brain tonic, carminative and stomachic, and used to treat cardiac debility, palpitation, nervous diseases and gastric debility. Paclitaxel and docetaxel were the first representatives of a new class of antitumor compounds, called taxoids, clinically active against breast, ovarian and lung cancers. Paclitaxel, a diterpene with exceptional anticancer activity, occurs as a very minor component in several species of Taxus, and is mainly found in the bark but has been reported from roots, wood, branches, leaves/needles, twigs and seedlings; leaves show the maximum amount. Four taxoids and five lignans were isolated from the heartwood, and all lignans except one exhibit significant antiulcerogenic activity. Ethanol extract of dried powdered bark exhibited potent anti-inflammatory activity, and alcohol leaf extract significantly protected against histamine and ACh aerosol-induced bronchospasm in guinea pigs, and significantly decreased total and differential leukocyte count in sensitized guinea pigs. Methanol leaf and stem extracts significantly decreased total leukocyte count, lymphocytes and cholesterol level of mice and rats treated for up to 30-days.

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Keywords
Eibe · English yew · Ifreteau · Manduparni · Talisfar · Talispatra · Tasso · Teixo · Yaygın porsuk · Zarnab

Vernaculars: **Urd.**: Zarnab; **Hin.**: Barambhi, Talispatra, Thuneer, Thuno, Zarnab, Zirnubbirmi; **San.**: Barahmi, Manduparni, Sthauneyaka, Talispatra; **Ben.**: Barambhi, Bhirmie, Birmi, Burmie, Sugandh, Talispatra, Thuneer, Zarnab; **Ara.**: Zarnab; **Dut.**: Gewone taxus, Taxus; **Eng.**: English yew, European yew, Himalayan yew; **Fre.**: If, If à baies, If commun, If d'Europe, Ifreteau; **Ger.**: Beereneibe, Eibe, Gemeine eibe, Ifenbaum; **Ita.**: Libo, Tasso, Tasso comune; **Per.**: Talisfar; **Por.**: Teixo; **Spa.**: Taxo, Tejo, Tejo común, Tejón; **Tur.**: Yaygın porsuk.

Description: A small to medium-sized evergreen tree, native to southwest Asia, northern Iran, Europe, and northwest Africa, that grows to a height of 10–20 m with a large trunk up to 2 m in diameter. Leaves are dark green, flat, 1–4 cm long and 2–3 mm wide, arranged spirally on stem, with the leaf bases twisted to align leaves in two flat rows on either side of the stem. The drug consists of the small branches of the tree with their linear-lanceolate, rigid, veinless leaves cut up into short length (2.5–5 cm). Male flowers are found upon some of the sprigs and resemble those of the common yew.[XL] Taxonomically yews should be considered as a single species because significant intraspecific differences were found between varieties of *T. baccata*, but no sufficiently distinctive interspecific differences of taxonomic value are obvious between the species [10] (Figs. 1, 2 and 3).

Fig. 1 *Taxus baccata*, 1600 Years Old Yew at Normandy, Roi.dagobert, WikimediaCommons; ShareAlike 3.0 Unported CC BY-SA 3.0, https://commons.wikimedia.org/wiki/File:If_Estry.jpg; https://creativecommons.org/licenses/by-sa/3.0/deed.en

Fig. 2 *Taxus baccata*, Irish Yew, Leaves and Arils, Sannse, WikimediaCommons; ShareAlike 3.0 Unported CC BY-SA 3.0, https://commons.wikimedia.org/wiki/File:English_Yew_close_250.jpg; https://creativecommons.org/licenses/by-sa/3.0/deed.en

Fig. 3 *Taxus baccata*, Shoots with Mature and Immature Cones, Didier Descouens, Wikimedia-Commons; ShareAlike 4.0 International CC BY-SA 4.0, https://commons.wikimedia.org/wiki/File:Taxus_baccata_MHNT.jpg; https://creativecommons.org/licenses/by-sa/4.0/deed.en

Actions and Uses: Yew was known to the Greeks and Romans as a poisonous plant. Modern research has shown that the leaves and seeds are poisonous, but not the red pulp surrounding the seeds. Leaves have been recommended in doses of 60–300 mg in epilepsy and other spasmodic conditions. In India, Sanskrit writers described it as carminative, stomachic, expectorant, tonic and astringent; and useful in phthisis, asthma, bronchitis and vesical catarrh. Powdered leaves are used with the juice of *Adhatoda vasica* and honey in cough, asthma and hemoptysis. A confection called *Talisadya* or *Talisadi churna* is prepared with *Talispatra* (*Abies Webbiana*), black pepper, long pepper, ginger, bamboo-manna, cardamoms, cinnamon, and sugar, and is used for the above-mentioned conditions. Avicenna speaks of it as an Indian bark and described the properties as those by Sanskrit writers; he stated that Galen considered it to be possessed of hot and cold properties in equal proportions, but that other say it is hot and dry.[XL] Yew played an important role in the mythology of ancient Germans and Medieval Europeans; they knew about its poisonous nature and made their arrows poisonous with its juice for hunting, and used the leaves for homicide and suicide [47]. In central Italy it was once used during pregnancy, for parturition, nursing and abortion [27]. In *Unani* medicine, leaves (temperament, hot 2° and dry 2°) are described as cardiotonic, nervine and brain tonic, carminative and stomachic, and used to treat cardiac debility, palpitation, nervous diseases and gastric debility.[LXXVII] Khory and Katrak[LXXXI] mentioned its uses in asthma, hemoptysis, epilepsy and other spasmodic affections due to its antispasmodic property, whereas Nadkarni,[CV] quoting Chopra, described it as carminative, expectorant, stomachic and tonic. It is a very poisonous plant due to its taxine content, a mixture of toxic alkaloids.

Phytoconstituents: Paclitaxel (Taxol®) and docetaxel (Taxotere®) were the first representatives of a new class of antitumor compounds, called taxoids, clinically active against breast, ovarian and lung cancers. Taxoids are highly complex diterpenoids of natural origin [32]. Paclitaxel, a diterpene with exceptional anticancer activity, occurs as a very minor component in several species of Taxus, and is mainly found in the bark but has been reported from roots, wood, branches, leaves/needles, twigs and seedlings; leaves show the maximum amount [46]. To obtain 1 kg of paclitaxel requires about 1,000 kg of bark, and several thousand trees must be cut to get this quantity of bark. Average annual paclitaxel contents of shoots with dark green needles from Irish Yew (*Taxus baccata* var. *fastigiata*) were estimated as 0.0075% [21], and in the bark of trees growing in a homogenous environment in central Himalaya, average paclitaxel concentration was 0.0558 ± 0.008% (of dry wt.), and was about 64% higher for male compared to female trees, and maximum paclitaxel contents were found in the bark samples collected from trees of >110 years age [35].

Four taxoids: taxusin, baccatin VI, baccatin III and 1β-hydroxybaccatin I, and five lignans: lariciresinol, 3′-demethylisolariciresinol-9′-hydroxyisopropylether, isolariciresinol, taxiresinol, and 3-demethylisolariciresinol were isolated from the heartwood [31], and all lignans except 3′-demethylisolariciresinol-9′-hydroxyisopropylether exhibit significant antiulcerogenic activity [25]. Guo et al. [24] isolated 4 α,7

β-diacetoxy-2 α,9 α-dibenzoxy-5 β,20-epoxy-10 β, 13 α, 15-trihydroxy-11 (15 → 1)-abeo-tax-11-ene, taxol, cephalomannine, baccatin III, and taxol C, from stem bark of *T. Baccata*. Five other taxoids, among which two were new derivatives, a taxine B derivative and a xyloside of taxol D were also isolated from stem bark [23]. Biflavones, bilobetin and 4‴-O-methylamentoflavone [29], taxoids, taxine A, B and C [33], teixidol [41], *p*-coumaric acid ester [11], flavonoids: 3-O-rutinosides quercetin, myricetin and kaempferol [30] have been reported from the needles. Essential oil of the twigs and needles of *T. baccata* from Serbia showed the presence of 91 compounds, mainly aliphatic alcohols, terpenes, aliphatic hydrocarbons, and aliphatic aldehydes [42]. Needles from a series of wild yews from Sardinia, despite common geographical origin, showed variations in taxoid profile, and several samples being completely devoid of taxines might explain that most of these plants are actively grazed by goats without toxicity [3].

Pharmacology: Ethanol extract of dried powdered bark exhibited potent anti-inflammatory activity [12], and alcohol leaf extract significantly protected against histamine and ACh aerosol-induced bronchospasm in guinea pigs, and significantly decreased total and differential leukocyte count in sensitized guinea pigs [37]. Methanol leaf and stem extracts significantly decreased total leukocyte count, lymphocytes and cholesterol level of mice and rats treated for up to 30-days [40]. Methanol extract of needles significantly inhibited growth of *S. aureus* [1], the ethanol extract of heartwood was active against Gram-negative bacteria and fungi [13], while the biflavone, 10-deacetylbaccatin III selectively inhibited growth of *L. donovani* intracellular amastigotes within murine macrophages, and the growth of promastigotes at higher concentrations [19].

Taxine has calcium channel blocking effect that is about 13X more selective for heart than for blood vessels and 51X more selective than for the intestine [43]. Paclitaxel, a diterpene, isolated from needles showed highly significant antitumor activity against human tumors implanted as xenografts in athymic mice [28, 38]. Docetaxel is prepared from a noncytotoxic precursor [6, 17], it promotes assembly of microtubules and inhibits their depolymerization [17, 18], and is FDA approved for the treatment of a number of localized and advanced cancers, such as locally advanced or metastatic breast cancer, head and neck cancer, gastric cancer, hormone-refractory prostate cancer [5, 50] and nonsmall cell lung cancer [20].

Mechanism of Action: Paclitaxel and docetaxel bind to microtubules, and stabilize them preventing depolymerization, and cell division.

Human A/Es, Allergy and Toxicity: Taxines, an alkaloidal mixture of taxine A and taxine B, are the active poisonous constituents, and their derivatives have been implicated in animal and human poisonings [49]. Fatal and nonfatal human poisoning due to consumption of leaves decoction for deliberate self-harm have regularly been reported from around the world for over fifty years [2, 4, 7, 8, 15, 16, 22, 26, 36, 44, 48]. Typical clinical signs of poisoning include dizziness (onset 1 h after ingestion), nausea, diffuse abdominal pain, unconsciousness, weak breathing, tachycardia, brief ventricular flutter/fibrillation followed by slow pulse, and finally

death by respiratory arrest and diastolic cardiac standstill [39]. Patients who survive are reported to have long-standing excessive diuresis and hypokalemia [14]. Even breast cancer patient treated with docetaxel reportedly develop allergy and poisoning due to hypersensitivity [9]. Main substance in harvested yew leaves, stomach content and cardiac blood of poisoning victim was identified as 3,5-dimethoxyphenol (3,5-DMP) and was suggested as a marker for yew poisoning [34]. Arens et al. [2] reported serum and gastric concentrations of 3,5-DMP of 86.9 ng/mL, and taxine B of 80.9 ug/mL, after perimortem of a victim of yew poisoning. Toxicity with paclitaxel therapy is associated with neutropenia, peripheral neuropathy, and, rarely, cardiotoxicity; whereas docetaxel toxicity produces myelosuppression and a cumulative dose fluid retention syndrome [45].

Animal Toxicity: Moderate doses of leaves given to animals produced rapid breathing and palpitation of the heart, followed by recovery, while larger doses produced similar effects, followed by death from syncope. Very large doses appear to produce death by syncope without pain or spasm.[XL]

Commentary: This plant is now recognized only for the taxanes or toxoids, and there are no reports of RCTs on any of its traditional medicines uses.

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