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Cultivation & Isolation of T. brevifolia

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Abstract
This review work focus on the study of the cultivation, extraction, isolation and medicinal uses of T. brevifolia. T. brevifolia consist of the various chemical consituents such as Taxane alkaloids, diterpenoids (taxane skeleton), lignans, biflavonoids, steroids, sugar derivatives, etc. The T. brevifolia has created considerable interest due to the presence of taxol. The taxol is one most selling drug in the market which is obtained from T. brevifolia. Taxol is act as a anticancer drug which is approved in 1994 by FDA in the treatment of ovarian, lungs, breast and Kaposi's sarcoma. It works by the inhibits mitosis of cancer cell and microtubule stabilizing compound.
Keyword: - *Taxol, Cultivation, Extraction, isolation, Medicinal use*

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I. Introduction

A small evergreen conifer(occasionally appearing as a shrub), the Pacific yew grows to 10 – 15 m(33 – 49 ft.) altitudinous and with a box up to 50 centimeters(20 in) periphery, infrequently more. In some cases, trees with heights in excess of 20 m(66 ft.) do in premises and other defended areas, relatively frequently in gullies. The tree is extremely slow growing, and has a habit of rotting from the inside, creating concave forms. This makes it delicate and occasionally insolvable to make accurate ring counts to determine a instance's true age. frequently damaged by race of the timber, it generally ends up in a thickset, multiple- leader form, suitable to grow new sprouts from guillotined wholes. [4] In its shrub form, occasionally called" yew encounter", it can reproduce vegetatively via layering.[7]

It has thin, scaled dinghy, red also purplish- brown, covering a thin subcaste of out-white tire wood with a darker heartwood that varies in color from brown to a purplish tinge to deep red, or indeed bright orange when lately cut. The leaves are lanceolate, flat, dark green, 1 – 3 cm(3⁄8 – 13⁄16 in) long and 2 – 3 millimetres(3⁄32 – 1⁄8 in) broad, arranged spirally on the stem, but with the splint bases twisted to align the leaves in two flat rows either side of the stem except on erect leading shoots where the helical arrangement is more egregious.7 The wood is hard, heavy, and resistant to decay. Although not of great interest to the timber products assiduity, it has numerous special uses.[8]

Kingdom:	Plantae
***Clade*:**	Tracheophytes
***Clade*:**	Gymnosperms
Division:	Pinophyta
Class:	Pinopsida

Order:	Cupressales
Family:	Taxaceae
Genus:	*Taxus*
Species:	*T. brevifolia*

Table.1-Plant Profile

Geographical source

It grows in varying types of surroundings; still, in drier surroundings it's substantially limited to sluice-side territories, whereas in wettest surroundings it'll grow up onto pitches and ridge tops, 10 at least as high in altitude as,400 meters(,600 ft.) above ocean position.9 Pacific yew is shade tolerant, but can also grow in sun.11 The tree's shade forbearance allows it to form an understory, which means that it can grow along aqueducts furnishing shade to maintain water temperature.[12]

Climate

Pacific yew is found over a wide range of moisture and temperature conditions. In dry, sub humid areas with an average annual precipitation as low as 470 mm (19 in), it is confined to streamside areas and the lower third of north-facing slopes. Some large specimens can be found in such environments; for example, the largest known yew tree in Idaho-848 cm (33.4 in) d.b.h. and 8.5 m (28 ft.) tall-is at the bottom of Hell's Canyon in an area that receives about 500 mm (20 in) of precipitation annually . On the Queen Charlotte Islands, Pacific yew is confined to the borders of inlets (44). Throughout much of its range within humid and super humid forests (precipitation of 1400 to 4000 mm 155 to 157 in), it can be found on all slopes, benches, and ridge tops. For example, a large yew tree in Oxbow County Park near Troutdale, Oregon (precipitation about 1450 mm 157 in]), is on the highest point in the park, a 210-m (690-ft) ridge overlooking the Sandy River 168 m (550 ft.) below (3). Pacific yew is found from sea level in coastal areas to 2440 m (8,000 ft.) in the Sierra Nevada. Length of growing season ranges from 60 to 300 days, with annual minimum temperatures from -15" to 12 " C (5" to 10" F).[15.16,18]

Soils

Pacific yew grows best on deep, moist or rich, rocky or gravelly soils. In dry interior forests, the species develops best along mountain streams, and in shady canyons, ravines, and coves. Within the moist maritime climate of the Pacific Northwest, it grows most abundantly in drier, warmer environments. A partial list of soils on which Pacific yew grows includes those in the orders Ultisols, Alfisols, and Inceptisols.[13]

Cvlization

Nearly 190 ornamental cultivars of yew have been recognized[20]. Although yew has a long history in European folklore—from the Iron Age [21]—its horticultural value is evident from topiary work at Elvaston Castle as exemplified here from [22]. Many cultivated forms compare closely with specimens of wild plants. These include the English yew, Irish yew, and many European varieties of *T. baccata*. There may be a parallel history of yew cultivation in Asia that has yet to be documented. Noted that many yews in Japan were cultivated, while in other cases he was uncertain whether the plants he saw were wild or cultivated. Yews in Japan were reportedly introduced into Europe by Robert Fortune in 1860 at the Cheswick Nursery, and into the United States in 1862 at Parsons Nursery by George Hall [23].Soon after the Hall introduction, Parsons Nursery obtained seed and several clones of 'Nana', 'Dense' and 'Aurescens' from sources in[24]. Subsequently, numerous cultivars have been developed, the best collection of which is maintained at the Secrets Arboretum in Wooster, Ohio [25]

Chemical constituents:

The chemical constituents of different Taxus species have been studied for over a hundred years. Taxane alkaloids, diterpenoids with taxane skeleton, lignans, biflavonoids, steroids, sugar derivatives and diterpenes possessing tropone skeleton are commonly found to occur in this genus.

Taxol

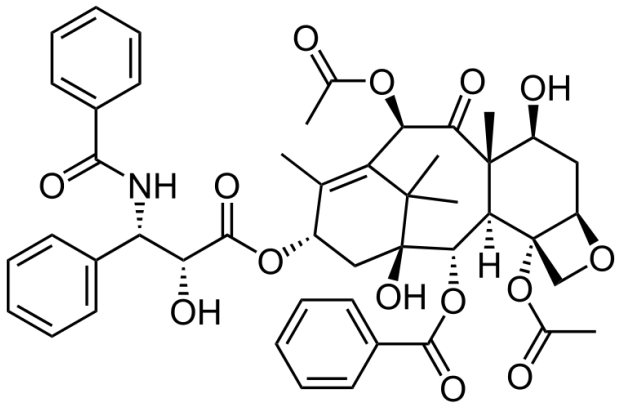


Fig. Structure of Taxol[27]

Molecular formula: C47H51NO14
Molecular Weight : 853.9
Appearance : white to off-white crystalline powder
Chemical name : 5β, 20–Epoxy-1, 2α, 4, 7β, 10β, 13α–hexahydroxy tax-11-en-9-one 4, 10 - diacetate 2-benzoate13esterwith (2R,3S)-N-benzoyl-3-phenylisoserine .
Melting point : 216-217 ºC
Solubility : Insoluble in water

Taxol is a plant alkaloid which can shows the anti-cancer. Chemical name of Taxol (trade name) is paclitaxel.It is a natural product with anti-tumor activity. Paclitaxel is obtained from various species of Taxus such as Taxus wallichiana, Taxus baccata, Taxus brevifolia.[26]

Part of Taxus and their Uses

Leaf:-Taxus leaves is used for cough, bronchitis, and asthma.
Fruit:-Taxus fruit is used as sedatives and antispasmodic.
Bark:-Taxus bark sused as anti- tumor agent and to cure cancer particularly of breast and uterus

Traditional use of Taxus

It has been used by the native populations for treating common cold, cough, fever, and pain. Its uses are described in Ayurveda and Unani medicine. It received attention recently as its leaves and bark were found to be the prime source of taxol, a potent anticancer drug Was sometimes used in Native American[(14)] (Algonquin) smoking mixtures called kinnikinnick Wood was used by Native American ribes to make how's Needles of Taxus with uva- ursi plant said to produce "too strong of an effect

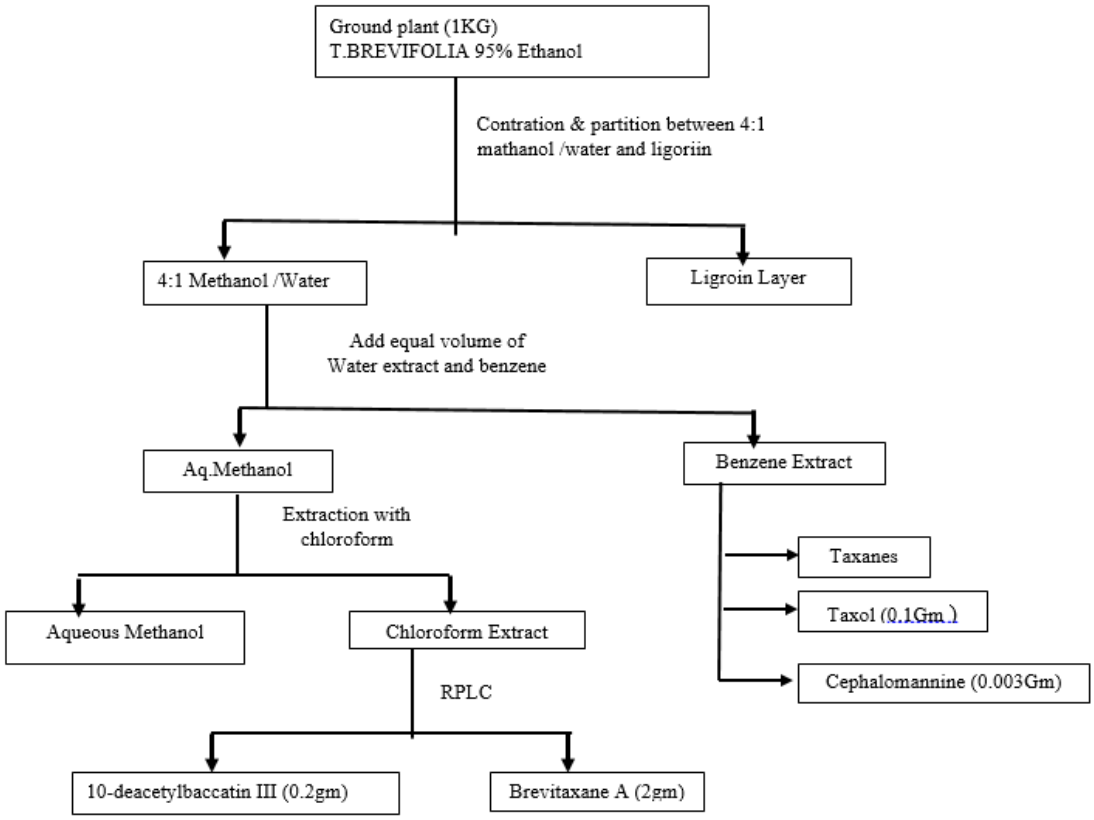
Modern uses of Taxus

Taxol the most well-known natural-source cancer drug in the United States, is derived from the bark of the Pacific yew tree (Taxus brevifolia). Taxol is microtubule stabilizing drug that is approved by the Food and Drug Administration. Chemotherapy medication used to treat a number of types of cancer. This includes ovarian cancer, esophageal cancer, breast cancer, lung cancer, Kaposi's sarcoma, cervical cancer, and pancreatic cancer. It is administered by intravenous injection.[14]

Special Uses

The wood of Pacific yew has been used for archery bows, canoe paddles, tool handles, gunstocks, boat decking, furniture, musical instruments, carved figurines, and miscellaneous novelty items.[18]

EXTRACTION OF TAXOL



Material to be extracted can be either fresh or dried. Preferably, the bark or the needles are used. In this extraction process, the material is first air dried at room temperature and ground to a suitable particle size ranges from 0.001 to 10 mm.Ground material then extracted with a polar solvent such as an alcohol, ethanol (95%), menthol. The extraction normally continues to 24 hours at ambient temperature. Solvent material is concentrated at 5-10% of its original volume at reduced pressure. After equilibration, the organic-phase is separated and the aqueous phase is extracted with organic solvent. The combined organic phase is concentrated at reduced pressure to dryness.[4, 5, 6]

Isolation

The discovery of paclitaxel (taxol) as a potent anticancer drug, initially isolated from Taxus brevifolia, has spurred several groups all over the world to conduct research work on other Taxus species,to isolate potentially more effective paclitaxel derivatives or as starting materials for semisynthesis. So far more than 550 taxanes have been identified, and new taxanes continue to be isolated fromthe needles, bark, stem, and roots of Taxus species.[18]

Separation Procedures.[1]

1) Extraction with alcohol and concentration.
2) Partition between water and dichloromethane.
3) "Filtration chromatography."
4) Silica column chromatography.
5) Alumina chromatography.
6) Medium pressure silica column chromatography.
7) Preparative HPLC.

For the other analogues, two or three other chromatographic columns, followed by preperative HPLC, were used. Other schemes for the large-scale production of taxol from T. brevifolia bark have also been developed. One such method used by Polysciences, It includes the followiing steps, [6]

i) The dried ground bark was extracted with methanol or ethanol and the combined extract concentrated to remove most of the alcohol.
ii) The concentrate was then extracted with dichloromethane and the solvent extract concentrated to a powder.
iii) This powder was stirred with a mixture of acetone and ligroin (1:1) and filtered to remove the insoluble matter.

iv) The filtrate which contained taxol was concentrated, dissolved in 30% acetone in ligroin, and applied to a column of Florisil.
v) The taxol fraction from the column was purified by crystallization twice.
vi) The crystalline taxol was further subjected to chromatography on a silica column. In this step, the closely related analogue, cephalomannine, was separated from taxol.
vii) The purified taxol. Obtained from the column was crystallized twice.
viii) Unseparated mixtures and mother liquors were recycled through the silica column to obtain additional amounts of pure taxol.

II. Conclusion

The antitumor properties of taxol is based on the ability to bind and to stabilize microtubules. Taxol is distributed among all parts of the tree of Taxus sp. and the yield of taxol is from 0.004% to 0.1% on dry weight basis. Economically buildup agriculture sector in cultivation of T. brevifolia. It is on the World Health Organization's List of Essential Medicines.

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