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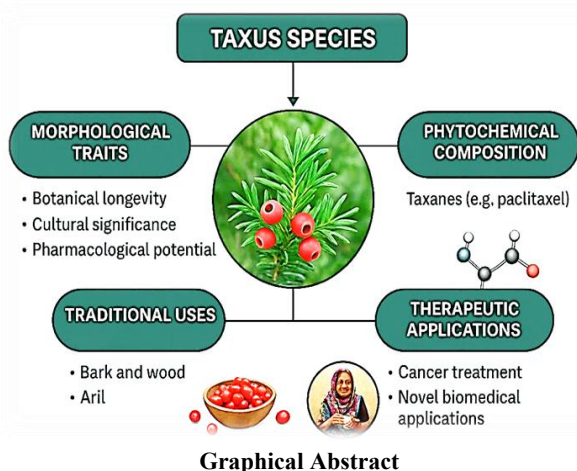
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Taxus wallichiana: A versatile phytomaterial for applications in modern medicine

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ABSTRACT

A distinct group of gymnosperms, the *Taxus* genus is well-known for the medicinal properties, cultural importance, and long history of use of its plants. *Taxus* species are the subject of this review, which delves into their many facets, including their morphology, phytochemical makeup, traditional usage, and medicinal benefits. Taxanes, and paclitaxel in particular, have been game-changers in cancer therapy due to their ability to stabilize microtubules. In addition to the traditional uses of the plant's bark and leaves, this study compiles new findings on the aril, a non-toxic and antioxidant-rich component of the plant, and proposes new uses for it in biomedicine. This paper highlights the significance of *Taxus* in both traditional medicine and modern drug development by combining ethnobotanical knowledge with pharmacological insights. The results highlight the need for further collaborative studies across disciplines and environmentally responsible methods of extracting the medicinal properties of the species without endangering its rich biodiversity.



Keywords: *Taxus* Spp., *Taxus* Aril Yew, Anticancer Properties, Medicinal Uses, Phytochemicals, Green Medicine.

INTRODUCTION

A group of long-lived gymnosperms with a wealth of botanical and medicinal history is the genus *Taxus*, often known as yew. Many ancient civilizations, including the Celts, the Greeks, and the Romans, held *Taxus* trees in high esteem due to their mythical status and the fact that they are among the oldest tree families in Europe [1]. Both physically and spiritually, they represented death, rebirth, and immortality due to their strong wood and physical endurance, which were important in ancient civilizations. The yew tree's distinctive qualities have made it an essential element of many European religious places [2]. Many anticancer drugs, including paclitaxel (Taxol®), docetaxel (Taxotere®), and cabazitaxel (Jevtana®), are derived from taxanes, which are diterpenoid alkaloids. This is why *Taxus* species are botanically noteworthy. Wall and Wani's 1965 discovery of paclitaxel in *Taxus brevifolia* bark was a watershed moment in the history of cancer therapy. The medicinal importance and efficacy of this drug have led to its inclusion on the essential medicines list maintained by the World Health Organization. Taxanes are highly regarded anticancer drugs that, depending on when therapy begins, may put cancer patients into partial or total remission in around 30-50% of instances.

Paclitaxel has been an essential chemotherapeutic tool in the fight against lung, ovarian, and breast malignancies since it was approved by the FDA in the early 1990s [3]. Semisynthetic synthesis from precursors like 10-deacetylbaccatin III produces paclitaxel and other important compounds like docetaxel and cabazitaxel. Just like paclitaxel, docetaxel promotes microtubule stability, which is useful in the treatment of breast and non-small cell lung cancers, among other cancers. [4]. More and more, people are worried about the long-term viability of taxane sources. Legislative protections and the exploration of other sources, such as cell culture systems and synthetic biology approaches, have been prompted by the overharvesting of taxus bark and the slow growth rate of the species. It is possible to synthesize paclitaxel via a chemical conversion of 10-deacetylbaccatin III, a precursor molecule found in taxus needles, which allows for more sustainable and scalable production techniques than natural extraction [5]. Predictions show that the worldwide taxane market will continue to expand from 2020 to 2029 across a range of product types (including nanoparticles and liposomes), formulations (including branded and generic drugs), and cancer indications (including breast, ovarian, and prostate cancer). Reasons for the surge include improvements in formulation technology, an increase in cancer cases worldwide, and easier access inside big North American healthcare systems. Europe, the Americas, and the Asia-Pacific region. Taken as a whole, the dynamics highlight taxanes' strategic relevance in the worldwide cancer pharmaceutical industry [6]. In most cases, you may find paclitaxel concentrations between 0.007 and 0.01% in the bark of taxus species. The average concentration of paclitaxel in the bark of male trees is about 64% greater than that of female trees. Three or four trees that are sixty years old may provide around one gram of paclitaxel, according to the experts. On average, a tree will produce roughly 10 kg of bark, and from that, around 50-150 mg of paclitaxel may be recovered per kilogram of dried bark. With an expected annual demand for the pure chemical nearing 250 kg, paclitaxel is in high demand across the world. One kilogram of pure paclitaxel is needed to treat 500 cancer patients. This needs over 10 metric tons of bark and the destruction of more than 700 mature trees. In order to meet the present therapeutic needs, up to 750,000 trees are cut down each year since it takes between 7,000 to 10,000 kg of bark to make 1 kilogram of pure Taxol. According to the National Cancer Institute (NCI), the concentration of paclitaxel in taxus bark, which is limited in nature, is not high enough to meet the needs of both businesses and researchers. Taxus trees have a slow growth rate, which renders this production strategy economically burdensome and environmentally unsustainable due to the considerable extraction costs and the ecological effects of widespread harvesting [7].

Recent study has brought attention to the pharmacological potential of taxus aril, a fleshy, red, and non-toxic seed attachment, in addition to the well-studied anticancer compounds found in the bark and leaves. Mucilages, antioxidants, carotenoids, and flavonoids abound in the aril. These bioactives have antibacterial, hypoglycemic, hepatoprotective, and anticancer effects, among other health benefits. Based on what we know so far, compounds produced from arils, including rhodoxanthin, may have antioxidant and natural preservation properties, as well as anti-melanoma effects in food and cosmetics [8]. The intricacy and importance of taxus in ancient and modern medicine are highlighted by its dual nature as a toxic and therapeutic agent. Traditional medicine relied on extracts from various parts of the body to treat conditions including fevers, respiratory illnesses, and epilepsy. However, modern scientific study has validated many of these traditional techniques via mechanistic pharmacological studies [9]. This research seeks to provide a comprehensive review of the species taxus by investigating its botanical features, ancestral medicinal uses, modern pharmaceutical uses, phytochemical diversity, and historical and ethnomedicinal significance. The review notes new information on the nutritional and medicinal possibilities of the aril, the only non-toxic portion of the plant, in order to expand future scientific research and understanding of this genus beyond its well-established anticancer benefits.

Botanical Examination of Taxus Species

Taxa belonging to the genus *Certain taxus* plants have been known to survive for up to five thousand years, making them one of the longest-lived gymnosperms. These trees may range in height from 10 to 30 meters, depending on the species and the circumstances in which they grow. They are often of moderate to medium size. Juvenile trees grow at a slow rate of around 30 centimeters per year, and after a century or more, they frequently stop growing vertically. Very slender and supple branches stay green for two years before becoming a reddish-brown. Trunk sizes may range from 2 to 4 meters, and in older specimens they can even exceed 5 meters. The bark is thin, scaly, smooth, and reddish-brown in color. The leaves are arranged in a pectinate or spiral pattern and are persistent, leathery, and have a dark green top surface and a paler underside. Their linear-lanceolate form has a single midvein, acuminate, cuspidate, or mucronate ends, moderately revolute margins, and a length of 1-4 cm and a width of 2-3 mm. They might have short petioles or be sessile. Although germination may take more than 18 months, sexual reproduction in taxus species occurs when seeds mature in October and November. For the purpose of dispersal, animals consume the red, fleshy aril, which is the sole non-toxic portion of the plant, and wraps around some or all of the ovoid seeds (5-8 mm) that are encased in a woody episperm. The yew tree is dioecious, meaning that different trees produce male and female cones. Wind pollination happens between the months of September and April, whereas flowering takes place between the months of March and May. Along branches grow male cones, which are round and pale yellow in color. Inside each cone are 8-14 microsporophylls, each of which contains 4-8 pollen sacs. At the tips of the branches, female cones emerge, and then the leaves take the form of sterile scales [10]. Many taxus species thrive in cold, wet, and shaded environments typical of temperate forests. They thrive on moist, well-drained soils and are often found beneath mixed or coniferous forest canopy. It is common to see *Taxus baccata* on limestone soils and calcareous substrates in Europe, while *T. wallichiana* is more often found in the Himalayas, namely on north-facing slopes with deep, moist soil profiles, in montane and subalpine areas (2000-3300 m). Both *T. cuspidata* and *T. canadensis* thrive in North American and acidic, humus-rich forest floors, while *T. cuspidata* is more common in northeastern Asia. Many species, despite their flexibility, are sensitive to changes in their habitat and the loss of tree cover, which have contributed to the fragmentation and decline of populations in different parts of the world [11]. Because of their extraordinary longevity and shrinking natural habitat, taxus species are formally protected in a number of nations. India forbids their export whereas China provides prime protection. They are under danger due to factors such as slow growth, reduced fertility, dispersed populations, shifting weather patterns, illegal trade, and overharvesting for taxane production. The species is becoming extinct and is now found only in small, isolated groups [12]. The conservation status of various *Taxus* species, along with the major threats they face globally, has been documented according to the IUCN Red List (Table 1) [13].

Conventional applications in ethnomedicine

Due to their various medicinal properties, taxus species, particularly *T. wallichiana* and *Taxus baccata*, have great significance in traditional medicine and folk cures. Ancient civilizations all over the world, from those in the Himalayas to those in Europe's indigenous populations, revered these trees for the therapeutic properties of their bark, leaves, and arils [14]. In most cases, taxus is prescribed to patients suffering from respiratory illnesses. Traditional medicine has long relied on taxus leaves and bark to calm a runny nose, cough, or fever. Its anti-inflammatory properties make it a popular choice among Ayurvedic and Unani practitioners for treating cold symptoms and inflammation [15]. Additionally, medicinal wine with purported curative properties is made from taxus arils, which are particularly popular in the Mediterranean region. Also, compounds derived from taxus have strong anticancer effects, according to studies. This is mostly because they can inhibit cell division by interacting with

biological pathways. The chemotherapy medication paclitaxel has risen to prominence in modern oncology; it is a molecule derived from the bark of the Pacific yew (*Taxus brevifolia*). Traditional medicine has long held the belief that extracts from the plant's leaves and stems may be effective in treating cancer [16]. There is hope that taxus species may help with the treatment of metabolic disorders and diabetes, in addition to respiratory ailments and cancer. Based on anecdotal evidence, taxus's abundance of phytochemicals may make it useful for controlling blood sugar levels [17]. taxus is highly esteemed in many cultures for its ceremonial and defensive amuletry uses. Many Indigenous communities hold the tree in high regard and employ its parts in age-old ceremonies meant to promote well-being, protect members from harm, and unite the group in harmony. It is important to note that taxus species were processed in various ways to reduce the amount of toxic components (taxines) when they were employed in folk medicine. However, due to the plant's innate toxicity, it is strongly cautioned against consuming raw taxus material directly since it is harmful and not recommended in modern practice. To lessen the impact of taxus species, traditional healers came up with practical detoxification methods, particularly in South Asian and Himalayan systems (such as Ayurveda and Unani). Boiling the bark or leaves for lengthy periods of time (often more than two or three hours) was a common method. This was thought to break down thermolabile toxic compounds like taxines A and B, which are vulnerable to heat and oxidation. Simmering taxus bark powder with milk, honey, ghee, or jaggery was believed to bind or neutralize poisons and increase the bioavailability of beneficial compounds in several traditional Himalayan formulas. Some people thought that these carriers, which are rich in sugar or lipid, could bind toxins that are soluble in fat (like ghee) or make the formulation more tolerable (like honey and milk), all while improving its flavor and stability and reducing the amount of toxic substances in the decoction that were free to dissolve. The plant material was fermented or sun-dried for many days in certain formulations, which may have helped break down unstable components via enzymatic or microbiological processes [18].

Phytochemical analysis of Taxus species

There is a lot of variation in the percentage of bioactive chemicals across species, according to the research. Some species have far higher amounts of specific bioactive compounds. Environmental, epigenetic, and genetic factors all play a role in this variety. Over the years, various analytical methods have discovered over three thousand diterpene alkaloids in *Taxus* species' bark and leaves. In addition, there are hundreds of other types of flavonoids, including biflavones, flavonols, dihydro-flavonols, dihydro-flavonol-glycosides, flavanols, chalcones, and flavones [19]. The following other classes of secondary metabolites have been identified: coumarins, phytosterols, phytoecdysteroids, and volatile compounds (including alcohols, alkanes, alkenes, organic acids, and terpenes) [20]. Taxanes, a class of diterpene alkaloids well recognized for their critical role in cancer therapy, are one of several phytochemicals found in abundance in the bark of taxus species. Paclitaxel, cephalomannin, 10-deacetylpacitaxel, 10-deacetylbaccatin III, baccatin III, and 7-xylosyltaxanes are only a few of the useful taxanes found in the bark, according to research. Both in traditional medicine and in the creation of contemporary anticancer medications, paclitaxel has been highly esteemed for its bioactive characteristics. Research has uncovered new substances, such as taxusumatin, a diterpene alkaloid found in *Taxus sumatrana* bark [21]. Not only may different species of taxus have different chemical compositions, but even within the same species, factors like manufacturing methods and geographic location might influence this. The bioactivity and therapeutic properties of taxus leaves are greatly affected by changes in their chemical composition, which is why these changes are so important. There have been findings of diterpene alkaloids in the leaves, including paclitaxel, cephalomannin, and 10-deacetylbaccatin III. Another class of chemicals found in abundance in taxus leaves are flavonoids. Phytochemical investigations place special emphasis on the distribution, biological activity, and structural characteristics of flavonoids. In order to better understand their pharmacological

characteristics and explore their potential applications in future research and development, scientists have looked at the distribution of flavonoids among taxus species and the intricate structures that make them up [22]. Using state-of-the-art analytical methods, such as ultra-performance liquid chromatography coupled with electrospray ionization tandem mass spectrometry (UPLC-ESI-MS/MS), researchers have investigated the metabolic alterations of flavonoids in *Taxus* leaves. The flavonoid concentration of several taxus species varies significantly, according to this study [23]. Additionally, the leaves include other useful compounds such as volatile oils, which include benzene propanenitrile, 1,4-dioxan-2,3-diol, and 3-bromo-3-methyl butyric acid, among others. The identification of these specific volatile compounds, together with their shown antibacterial capabilities, provides crucial information on the potential dermatological uses of these plant extracts. The leaves also include polysaccharides, steroids, and lignins [24]. Alkaloids, flavonoids, lignans, polysaccharides, and steroid derivatives are only a few of the phytochemicals found in taxus seeds. This variety in chemical composition is really remarkable. One of the most significant bioactive compounds with notable pharmacological effects is paclitaxel. In addition, the seeds contain a number of alkaloids, including taxinin A, baccatin III, 2-deacetyltaxinin, taxezopidin G, 2-deacetoxitaxynin J, and 2-deacetoxitaxuspin C. Flavonoids such as naringenin, aromadendrin, galanin, epigallocatechin, and galocatechin have also been found in the seeds [25]. The presence of taxoleic acid, a special Δ^5 -olefinic acid, in taxus seeds indicates their unique fatty acid makeup. Taxus is distinguished from other gymnosperms by its particular makeup [26]. Recent phytochemical investigations have started to reveal the beneficial properties of taxus arils, despite the lack of prior research on these fruits. Lipids, amino acids, vitamins, carbs, carotenoids, flavonoids, phenolic acids, and terpenoids are only some of the many primary and secondary metabolites found in arils. The diverse array of phytochemicals found in arils provides insight into their untapped medicinal, nutraceutical, and dermatological properties, positioning them as a promising asset to the area of medico-pharmaceutical research [27]. The chemical composition of different plant parts of taxus species is thoroughly analyzed in Figure 1, which shows the major classes of primary and secondary metabolites in the genus *Taxus*. The most prevalent compounds in each class are also listed. This visual aid aids in the comprehension of the biochemical diversity among taxus species by illustrating the significance of these metabolites in ecological interactions and their medicinal applications. Though alkaloids and flavonoids are secondary metabolites that have gained interest because to their medicinal properties and important roles in defense mechanisms, carbohydrates, proteins, and lipids are essential for development and growth [28,29].

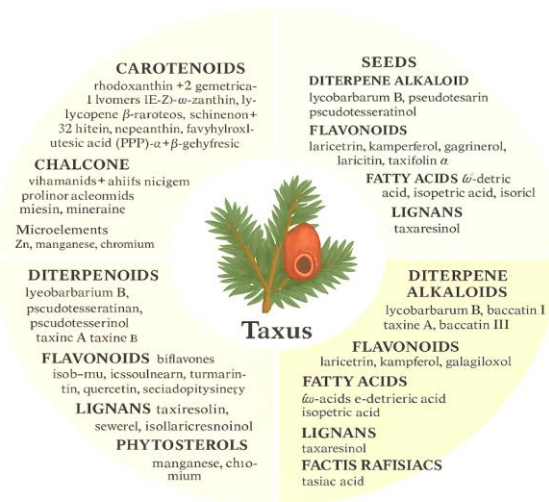


Figure 1: Principal classes of primary and secondary metabolites found within the genus *Taxus* [7]

Therapeutic and pharmacological applications

The chemical composition of different plant parts of taxus species is thoroughly analyzed in Figure 1, which shows the major classes of primary and secondary metabolites in the genus taxus. The most prevalent compounds in each class are also listed. This visual aid aids in the comprehension of the biochemical diversity among taxus species by illustrating the significance of these metabolites in ecological interactions and their medicinal applications. Though alkaloids and flavonoids are secondary metabolites that have gained interest because to their medicinal properties and important roles in defense mechanisms, carbohydrates, proteins, and lipids are essential for development and growth^[30]. A powerful anticancer drug used to treat a range of cancers, including sarcomas, melanomas, and carcinomas, paclitaxel is a crucial component obtained from taxus species. In addition, it is a powerful anti-cancer drug that targets ovarian, lung, and breast tumors. To achieve their anticancer effects, taxanes, most notably paclitaxel and docetaxel, disrupt normal mitotic spindle dynamics by stabilizing microtubules^[31]. This stabilization leads to cell cycle arrest in the M phase, ultimately triggering apoptosis in rapidly dividing cancer cells^[32]. This protein hinders mitosis and other microtubule-dependent processes by affixing to the tubulin β -subunit and preventing its depolymerization. In addition, taxanes have the potential to inhibit the nuclear accumulation of the androgen receptor and other factors critical for tumor development, which is particularly relevant in the case of prostate cancer^[33]. Although docetaxel has a higher affinity and anticancer activity than paclitaxel, both drugs are necessary for cancer therapy. Essential to the medicinal efficacy of taxus species are the large concentrations of taxanes and flavonoids found in their leaves, which make them particularly valuable. Empirical studies have shown that aqueous leaf extracts of taxus species have anticancer properties and are effective in the treatment of pancreatic and lung cancers^[34].

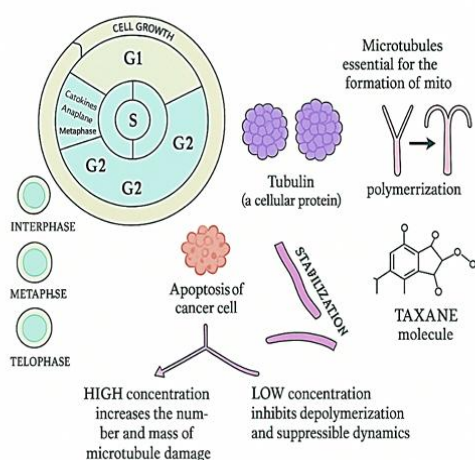


Figure 2: Mechanism of action of Taxanes in cancer cells^[31]

The fact that these water-based extracts significantly inhibited adenosine deaminase (ADA) activity in human cancerous colon and stomach tissues lends credence to their anticancer claims^[35]. The cytotoxic effects of bark, leaves, and young branches from several taxus species were thoroughly tested using a variety of cancer cell lines, such as HELA, T47D, MCF-7/HER2, LS174T, A549, MCF-7, and SMMC-7721. This study lends credence to the long-held belief that some species of taxus possess anticancer properties, since it demonstrates that these plants may significantly kill cancer cells^[36]. Flavonoids found in taxus species, such as sciadopitysin, quercitrin, and ginkgetin, have been shown to have anticancer qualities as well as positive benefits on the treatment of several illnesses, including osteoporosis, diabetic osteopathy, and Alzheimer's disease. High concentrations of bioactive substances, particularly flavonoids essential for providing antioxidant qualities, exist in the leaf of taxus species. The analgesic and anti-inflammatory properties of these bioactive ingredients have supported their historic medical uses. Additionally, research indicates that some species of taxus have

antipyretic and anticonvulsant qualities^[37]. The carotenoid rhodoxanthin is mostly responsible for the antiproliferative and pro-apoptotic actions seen in the aril of Taxus species^[38]. Rhodoxanthin, which was extracted from the aril of *Taxus baccata*, has been linked to the suppression of tumor development and the regulation of antioxidant activity. Additionally, metabolomics and antioxidant activity evaluations have been used to examine a variety of Taxus medium tissues, including the aril, demonstrating its potential for treating renal ailments and decreasing blood glucose levels, among other conditions^[39]. Furthermore, the aril's polymethylated fatty acids (PMI-FAs) have hypolipidemic, immunomodulatory, and antihypertensive qualities. They may help improve cognitive function^[40]. The antibacterial activity of silver nanoparticles synthesized from *T. wallichiana* leaf extract is comparable to that of methanolic, chloroformic, ethyl acetate, and petroleum ether extracts. These nanoparticles are effective against both Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*, *Bacillus cereus*, and *Corynebacterium xerosis*) and Gram-negative (*Staphylococcus aureus*, *Salmonella paratyphi B*, *Salmonella typhimurium*, *Pseudomonas aeruginosa*, *Pantoea agglomerans*, and *Yersinia pestis*) and Gram-negative (*Staphylococcus aureus*, *Salmonella paratyphi B*, *Salmonella typhi*)^[41]. The main cause of this antibacterial effectiveness is the presence of volatile chemicals, which are mostly present in Taxus species leaves and include benzaldehyde, pentenyl-ethyl alcohol, and cis-3-hexen-1-ol^[42]. Taxus species exhibit antifungal action against *Aspergillus brasiliensis* and several species of *Candida*, including *albicans*, *tropicalis*, *parapsilosis*, *krusei*, and *glabrata*, in addition to their antibacterial properties^[43]. Taxus species' antidiabetic qualities have attracted a lot of academic attention, and several species-such as *Taxus chinensis* var. *mairei*, *Taxus cuspidata*, and *T. wallichiana*-have shown remarkable effectiveness in traditional medical practices for the treatment of diabetes. These Taxus species' hypoglycemic effects have been confirmed by both *in vitro* and *in vivo* studies. Mechanisms such as decreased insulin production, increased peripheral tissue glucose absorption, inhibition of enzymes that break down carbohydrates, and imitation of insulin action define these effects^[44]. Empirical research supports the anti-asthmatic impact of traditional medicine. According to research, species of the genus *Taxus* have strong anti-asthmatic qualities that might provide therapeutic benefits for the treatment of asthma. This goal is accomplished by lowering bronchial hyperreactivity and relaxing bronchial smooth muscle^[45].

Biological Effects of Taxus sp.

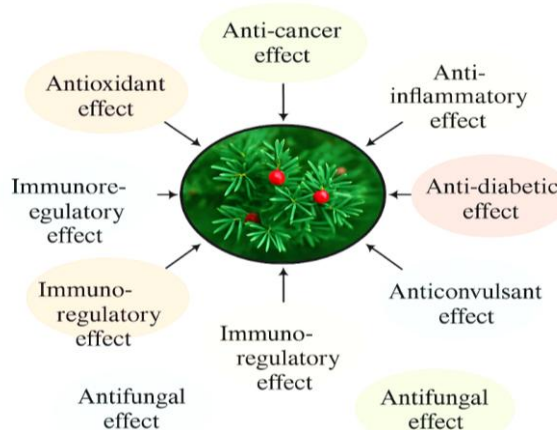


Figure 3: Pharmacological properties associated with Taxus species^[42]

Taxus species are an important source of bioactive substances with various therapeutic uses, including antibacterial, anti-inflammatory, anti-cancer, antioxidant, and antidiabetic effects^[46]. The taxus genus's intricate chemical makeup highlights its use in both conventional and modern medical procedures. Researchers are interested in the nutraceutical potential of taxus species' aril because of its rich chemical makeup, which includes both primary and secondary metabolites. The phytochemical components of the aril have been clarified by recent research, and they contain high levels of volatile

chemicals, carotenoids, polyphenols, and ascorbic acid. These elements support the antioxidant qualities of aril, which helps to reduce oxidative stress [47]. A great source of bioactive chemicals and important nutrients, arils are distinguished by their necessary micro- and macro elements, high-quality protein, amino acids, and low amounts of simple carbs, according to research. This highlights the possible future use of arils as a nutritional component, especially as a low-calorie snack, since researchers have shown that 100 g of arils contains around 106 kcal. Furthermore, 100 g of arils provides the required daily intake of zinc, potassium, chromium, and iron, making them an excellent source of these elements [48]. The red arils (RAs) of *Taxus baccata* were first thoroughly described by Tabaszewska *et al.*, indicating that this little-studied plant portion may be a useful source of nutraceutical chemicals [26]. It was discovered that the arils were very abundant in a number of important nutrients and bioactive compounds, which may be usefully contextualized by contrast with other common food sources. Together, these characteristics imply that taxus arils combine fruit characteristics with nutritional concentrations and useful substances that are usually found in seeds and medicinal plants. The inclusion of uncommon lipid mediators, vital nutrients, and bioactive pigments offers a compelling argument for further research into the aril's potential as a nutraceutical, even if the majority of the information now available is compositional. According to research, aril juice may help prevent and treat Alzheimer's disease by affecting a number of important biological processes linked to neuronal deterioration. These mechanisms include insulin release, oxidative stress, T-cell co-stimulation, amyloid fiber formation, neuronal death, and the inflammatory response [49]. The potential use of taxus arils as a dietary antioxidant source is still being investigated and discussed by scientists. The nutritional and functional profiles of the arils' flavonoids, carotenoids, and other phenolic constituents have not yet been as fully characterized as those of widely recognized antioxidant sources like rosemary (*Rosmarinus officinalis L.*), green tea (*Camellia sinensis Knutze*), or turmeric (*Curcuma longa L.*), despite initial analyses showing their presence [50]. Additionally, the restricted geographic range of taxus species and the comparatively low availability of arils limit their potential as widely used food additives or nutraceuticals. Therefore, even though arils have intriguing antioxidant potential, their use in the food industry needs to be done carefully. This calls for more thorough toxicological evaluations, standardized bioactive content, and comparative

effectiveness studies against well-known botanical antioxidants. The arils are the only part of a taxus plant that is not harmful; all of the other parts, including the leaves, bark, and seeds, contain powerful toxic alkaloids, and there is little difference between therapeutic and toxic dosages of these alkaloids. Their direct usage in formulations is problematic due to their intrinsic toxicity. Therefore, extracts from poisonous portions of the plant should be used very carefully in any prospective dermatological uses. To guarantee safety and adherence to legal requirements, such usage would need thorough pharmaceutical documentation, toxicological profiling, and regulatory clearance. The partial clarification of the variety of important phytochemicals found in taxus species' arils [51] has led scientists to investigate these arils' possible uses in oncologic dermatology. The characteristics of the retro-structured carotenoid rhodoxanthin, which was extracted from the arils of *Taxus baccata*, were shown in research using the murine malignant melanoma model B16F10. Significant tumor growth inhibition and antioxidant activity modulation against mouse malignant melanoma were shown by this drug [52]. Since antioxidants are crucial for shielding the skin Rhodoxanthin's antioxidant action is particularly relevant to dermatology due to its effects on oxidative stress and its ability to prevent premature aging [53]. Additionally, this compound's anticancer capabilities are quite interesting when it comes to treating skin cancer and other malignant skin disorders. The beneficial effects of *Taxus cuspidata* extract on several skin conditions, including inflammation, melanin deposition, oxidative stress, and allergic reactions, were shown by *in vivo* studies conducted on animal skin tissues. Research suggests that the essential oil mainly increases the expression of important antioxidant enzymes, such as glutathione peroxidase 4 (GPX4) and superoxide dismutase (SOD), to provide its antioxidant benefits. In addition, the extract has demonstrated antiallergic properties, which could be useful in treating skin allergies, by reducing histamine release and modifying pro-inflammatory cytokines like interleukin 1-beta (IL-1 β) and tumor necrosis factor-alpha (TNF- α). Furthermore, it has been shown that the extract reduces melanin deposits by inhibiting tyrosinase, an enzyme essential to melanin formation, which results in a depigmenting effect. Together with their well-established anticancer qualities, these recently discovered pharmacological activities of taxus species point to a hopeful growth in therapeutic applications in the dermatological field [54].

Table 1: Status on the IUCN red list and threats to various *Taxus* species worldwide [13]

species	IUCN Status	Geographic Distribution
<i>T. wallichiana</i>	Endangered	Himalayas: Afghanistan, India, Nepal, Bhutan, southern China
<i>Taxus baccata</i>	Least concern	Europe, North Africa, Western Asia
<i>Taxus brevifolia</i>	Near threatened	Pacific Northwest (USA: California to Alaska), British Columbia
<i>Taxus canadensis</i>	Least concern	Eastern Canada, Northeastern USA (Appalachians, Great Lakes region)
<i>Taxus calcicola</i>	Vulnerable	China (Yunnan, Guizhou)
<i>Taxus chinensis</i>	Endangered	Southern China (Yunnan, Guizhou, Sichuan), northern Vietnam
<i>Taxus contorta</i>	Endangered	Western Himalayas (Pakistan, India, Nepal)
<i>Taxus cuspidata</i>	Least concern	Northeast China, Korea, Japan, Russian Far East
<i>Taxus floridana</i>	Critically endangered	Northern Florida (Gadsden and Liberty Counties)
<i>Taxus globosa</i>	Endangered	Mexico and Central America (Sierra Madre Oriental)
<i>Taxus mairei</i>	Vulnerable	Southern and eastern China, Vietnam, Taiwan

PROSPECTIVE AVENUES

With its complex interactions between ethnobotany, pharmacology, and phytochemistry, the genus taxus continues to be a fundamental component of medicinal botany. taxus species have been shown to have a variety of uses via this study. Thanks to its abundance of

bioactive compounds, such as flavonoids and taxanes, the genus is a treasure trove of therapeutic agents, particularly for the treatment of cancer, metabolic diseases, inflammatory illnesses, and neurological disorders. Equally important is the new focus on taxus aril, a previously disregarded plant part that is now receiving more attention because of its anticancer, antibacterial, and antioxidant qualities.

Furthermore, since there are little research and the data that is now available is preliminary, scientific knowledge of the taxus aril is still restricted, despite its significant pharmacological potential. Further research is necessary to confirm these initial results and clarify the mechanisms of action, safety profiles, and therapeutic applications of molecules derived from aril. The ecological cost of paclitaxel extraction emphasizes the urgent need to find sustainable alternatives, even in light of the significant advancements in taxane separation and semi-synthesis. There are promising new avenues for ecologically friendly and scalable taxonomy production thanks to innovations in synthetic biology, plant cell culture, and endophytic fungal-mediated biosynthesis. Additionally, the ethnopharmacological confirmation of traditional applications creates new opportunities for the development of plant-based medicines, especially for the treatment of metabolic, hepatic, and respiratory conditions.

The following avenues should be the focus of future research: investigation of neglected plant components, including arils, to find new bioactives with therapeutic potential. The development of green synthesis techniques for taxanes should include methods such as tissue culture optimization and metabolic engineering in microbial systems. research on combinatorial treatments that make use of the synergy between taxanes and other chemicals derived from plants or contemporary drug delivery systems, particularly nanocarriers. Researchers are applying lesser-known substances, like polymethylated fatty acids and biflavonoids, in immunology, neurology, and cancer through clinical translation. Map species-specific metabolic pathways and comprehend interspecies diversity in phytochemical composition using integrative omics techniques. Future studies could help create novel applications that combine the traditional knowledge of taxus plants with the rigorosity of modern scientific validation by clarifying the complex relationships between the chemical components of these plants and their corresponding biological effects. This dual strategy guarantees that Taxus' promise is supported by empirical data while also paying tribute to the plant's historical relevance in various therapeutic scenarios. The usefulness of taxus in contemporary medicine may be increased if new bioactive chemicals and their modes of action are discovered as a result of such studies.

CONCLUSION

In conclusion, taxus species constitute a bioscientific frontier with a wealth of uncharted medicinal potential in addition to a botanical history with profound cultural roots. To realize their full therapeutic potential while maintaining ecological responsibility and protection, ongoing multidisciplinary research is necessary.

Conflict of interest

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