

## The Pharmacognostic Standardization, Phytochemistry and Phytopharmacological Potential of *Toona ciliata* M- An Overview

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### Original Research Article

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**Abstract:** *Toona ciliata* is a plant belongs to a family Meliaceae group of the traditionally important medicinal plant. It is also known as red cedar. The genus *Toona* (Meliaceae) family consists of the highland trees that are broadly distributed at the higher altitude of India, Nepal, China, Burma, Thailand, Australia. *Toona ciliata* has been accepted as a source of medicine to treat different disease and ailments including chronic dysentery, blood complaints ulcer, leprosy, fever, headache, cancer, diarrhea and ringworm. Extensive research works have been conducted out on the chemical constituent, biological and pharmacological activities of the *Toona ciliata*. The pharmacognosy study shows that those leaves are the compound type, 30-50 cm length, shape: lanceolate, apex: acute and having the entire margin. Stomata present in the leaf are the anomocytic type of stomata. These pharmacological activities mainly due to the presence of coumarin, flavanoids, phytosterol, phenol, tannins, triterpenes and anthraquinones.

**Keywords:** *Toona ciliata*, pharmacognostic standardization, phytochemistry and phytopharmacological potential.

### INTRODUCTION

The use of whole herbs and extractives has remained the main approach of folk medicine practitioners in the treatment of infirmities and debilitating diseases. They usually claimed that such whole herbs and extractives are efficacious against several ailments and diseases without recourse to scientific proofs. Increased cases of opportunistic diseases emanating from side effects associated with synthetic drugs continue to necessitate incremental efforts in searching for effective biological substitutes with little or no side effects.

Therefore, efforts are being directed towards elucidating potential sources such as ethnomedicinal plants [2]. New, robust and less cumbersome extraction techniques assisted by recent developments in biotechnology have enhanced investigation of natural compounds faster with more precision than before leading to isolation of bioactive compounds with intense health benefits [2].

*Toona ciliata* (T. ciliata), also commonly known as the red cedar, toon or toona, tuni, Burma cedar, Indian cedar or Indian mahogany, is a forest tree in the mahogany. It grows widely in the regions of southern Asia and Australia. (1, 2). The genus *Toona* (Meliaceae) family consists of the highland trees that are widely distributed at the higher altitude of India,

Nepal, China, Burma, Thailand, Malaysia, and Java to Europe. About 15 species of the toona are found in tropical Asia and Africa, among them, four species are distributed in India, and four species are found in China. Two species of *Toona* namely, *Toona serrata* and *Toona hexandra*, are found in North West Himalaya [3].

### METHODS

The information about the plant *Toona ciliata* L. was gathered using SciFinder, and it was then searched for its phytopharmacological and the phytochemistry. Data was collected from journals accessible in databases such as ScienceDirect, Medline, PubMed etc.

**Table-1: Taxonomic classification of *Toona ciliata* [4,5]**

Taxonomichierarchy	<i>Toona ciliata</i> M.
Domain	Eukaryota
Kingdom	Plantae
Phylum	Spermatophyta
Sub-phylum	Angiospermae
Class	Dicotyledonae
Order	Rutales
Family	Meliaceae
Genus	<i>Toona</i>
Species	<i>Toona ciliata</i>

## RESULTS

### Pharmacognostical features

The plant is found in Sub Himalayan region of India, Assam and through-out hilly regions of central and southern India. The plant of *Toona ciliata* is tall, grow rapidly, large deciduous tree, typically reaching a

height of around 20–30 m tall [6] and with the stem diameters above buttresses of 3 m, but reach up to 40 m high. The crown is spreading and rounded in outline. The pharmacognostic profile of Toonaciliate is shown in Table [7-9].

**Table-1: The pharmacognostic profile of *Toona ciliata***

Evaluated characteristics	<i>Toona ciliata</i>
Leaf	
Shape	Paripinnate
Size	300–600 mm long
Leaflet shape	Lanceolate
Leaflet size	45–160 mm long
Leaflet number	9-17
Margin	Entire
Apex	Accuminate
Flower	
Shape	large, pendent, densely-branched panicles
Sepals	1-mm-long
Petals	white, each 5–6 mm long
Margin	Entire
Aromatic	sweetly
Fruit	
Shape	dry, oblong capsules with five valves
Size	20–30 × 8–12 mm
Colour	Light brown

### Phytochemistry

Cedrelone, a tetra nortriterpenoid compound, isolated from *Toona ciliata* [10]. Compounds such as 12 Deacetoxytoonacilin and 6 $\alpha$ -acetoxy-14 $\alpha$ ,15 $\alpha$ -epoxyazadirone were isolated from the seeds [11], 12- $\alpha$ -Hydroxystigmat-4-en-3-one was isolated from the petroleum ether extract of *Toona ciliata* with two steroids and three C-methyl coumarins [12], norlimonoids and limonoids from the leaves and stems of plant [13], three new norlimonoids (1–3), two new tirucallane-type triterpenoids (4 and 5), and a new pimaradiene-type diterpenoid (6), along with two known limonoids and eight known tirucallane-type triterpenoids, from the leaves and twigs [14], toonaciliatone a constituent, methyl-3 $\alpha$ -acetoxy-1-oxomelic-14(15)-enate, perforin A and cholest-14-ene-3,7,24,25-tetrol-21,23-epoxy-21-methoxy-4,4,8-trimethyl-3-(3-methyl-2 butenoate) from the leaves [15]

and protolimonoids and norlimonoids from the stem and bark of *Toona ciliata* plant [16]. The barks were also found to contain tetranortriterpenoids including toonacilin.

Phytochemical studies reported the presence of cedrelone, quercetin,  $\beta$ -sitosterol, gallic acid, protocatechuic acid, p-hydroxy benzoic acid, chlorogenic acid, caffeic acid, vanillic acid, syringic acid, sesquiterpene, cycloartenol stigmasterol, campesterol, apotirucallene, tirucallene, catechin, proanthocyanidin, leucoanthocyanidin, Toonacilin, 6-acetoxy Toonacilin, Toonacilid, geranylgeranyl,  $\delta$ -cadinene, calamenene, siderin, deoxy-cedrelone, 1,2-dihydrocedrelone, steroids and C-methyl coumarins, 12 $\alpha$ -hydroxystigmat-4-en-3-one ( new bioactive steroid from *Toona ciliata*) [17].

Isolation of the constituents of *Toona ciliata* revealed the presence of 12 limonoids (Toona yunnanins A-L) and 11 known compounds, (a) cedrelone, (b) epoxyazadiradione, (c) Toonafolin, (d) Toonaciliatin E, (e) Toonaciliatin H, (f) dysobinin, (g)

12-deacetoxy-toonacilin, (h) 17-hydroxyazadiradione, (i) dihydroniloticin, (j) dehydroodoratol and (k) 21- $\alpha$ -methylmelianodiol [18].

#### Description and activities of plant

**Table-2: Description and activities of plant *Toona ciliata***

Common name	Botanical name	Phytochemicals	Pharmacological activities
Toon, Toona, Tun, Tuni, Red cedar, Australian cedar, Indian Mahagony,	<i>Toona ciliata</i> Family- Meliaceae (Mahagony)	1. Coumarin 2. Phenolics & Polyphenols 3. Terpenes & Terpenoids 4. Steroids 5. Flavonoids 6. Limonoids & nor-limonoids 7. Polyynes 8. Tannins	1. Anti-oxidant 2. Anti-diabetic 3. Anti-inflammatory 4. Anti-fungal 5. Anti-microbial 6. Anti-inflammatory 7. Anti-ulcer 8. Cytotoxic

#### Different pharmacologically active constituents of *Toona Ciliata*

##### Coumarin

Coumarins are the secondary metabolites widely spread in nature, is found in green plants, fungi, bacteria, in some animal species [19], fruits, green tea and other food and spices. Coumarin is a naturally occurring compound belonging to the large class of phenolic substances which are present an aromatic ring fused to a condensed 6-member lactone ring [20].

Coumarins are derivatives of cinnamic acid with a benzo- $\alpha$ -pyrone skeleton that are widely distributed in plant kingdom [21]. More than 1300 coumarins have been isolated and reported from natural sources. There are four main subtypes of coumarins: the simple coumarin, furanocoumarins, pyranocoumarins and the pyrone-substituted coumarins. Coumarin and its derivatives are principle oral anticoagulants [22]. Coumarin containing plants are tested for their antimicrobial and phototoxic activities. Coumarins have a variety of bioactivities including anticoagulant, estrogenic, dermal photosensitizing, anti-microbial, vasodilator, molluscicidal, antihelmintic, sedative and hypnotic, analgesic and hypothermic activity [23].

Three known coumarins, siderin, scopoletin and isofraxidin were isolated from *Toona ciliata*. Siderin, was isolated from the *Toona ciliata* [24] and the effect of isolate on photosynthesis was tested. Sederin was reported to inhibit both ATP synthesis and electron flow [25].

##### Phenolic

Phenolic compounds are pervasive components of fruits, vegetables, and grains. The term phenolic is used for a distinct class of compounds including low molecular weight flavonoids, phenolic esters and acids, as well as high molecular weight

polyphenols known as tannins [20]. Polyphenol or phenolic are those compounds which contain phenol ring in their chemical structure. Anthocyanins that give the purple colour to grapes are phenolic compounds. Tannins that give astringency to tea are also phenolics. Polyphenols are the most abundant anti-oxidant in the human diet. The phenolic compounds are divided into the phenolic acids, flavonoids, lignans and stilbenes [19].

##### Tannins

Tannins are the astringent, bitter plant polyphenols that either bind and precipitate or shrink proteins. The term is widely used for any large polyphenolic compound containing sufficient hydroxyls (OH) and other suitable groups (such as carboxyls) to form strong complexes with proteins and other macromolecules. Tannins may be used medicinally in antidiarrheal, haemostatic, and antihemorrhoidal compounds. They have also been reported to anti-viral, antibacterial, and antiparasitic effects [26]. Tannins also possess other biological activities. Ellagic acid a constituent was reported to accelerate blood clotting and used to control hemorrhage in both animals and humans. Agrimoniin also shows the beneficial effect to improve immune response [27]. These constituents were then evaluated to estimate the anti-oxidant activity [28]. The tannins present in *Toona ciliata* are ellagic acid, gallic acid, protocatechic acid, chlorogenic acid, caffeic acid, vanillic acid, syringic acid and catechin.

##### Flavonoids

Flavonoids are found in plants from the aromatic amino acids phenylalanine, tyrosine, and malonate [29]. Flavonoids are structurally derived from benzo- $\gamma$ -pyrone displaying a diphenylpropane basic structure, which possesses two aromatic rings (A & B rings) along with an oxygen-containing heterocyclic ring (C ring) 20.

Flavonoids are divided into eight different groups-

Flavanols or catechin 2.flavandiols  
3.dihydroflavanols 4.flavanones 5.flavones  
6.isoflavones 7.flavonols 8.anthocyanidins

(Flavonoids are formed several biological effects such as anti-hepatotoxic, anti-inflammatory and anti-ulcer activity. They also inhibit enzymes such as aldose reductase, cyclooxygenase, Ca ATPase, xanthine oxidase, phosphodiesterase and lipoxygenase [30]. Quercetin, a bioflavonoid found in apples, berries, onions, tea and *Brassica* vegetables, have a wide range of biological activities. Like many other polyphenols, quercetin is also reported to possess free radical scavenging, iron chelating, and anti-inflammatory properties [31].

Several studies reported the anti-oxidant action of flavonoids. The mechanism of anti-oxidant action can include- suppression of ROS, scavenging reactive oxygen species and up-regulating or protecting anti-oxidant defenses [29].

### Steroids

The petroleum ether extract of *Toona ciliata* plant was investigated, and a new hydroxyl steroidal ketone was isolated. The isolated steroid was named as- 12 $\alpha$ -hydroxystigmast-4-en-3-one [32].

The *Toona ciliata* was studied and reported to contain five pregnane steroids<sup>33</sup>-

- Toonasterone A
- Toonasterone B
- (Z)-Aglawone
- (Z)-Toonasterone C
- E)- Toonasterone C.

Plant steroid plays a role in the development of human body. These steroids can be used medicinally as cardiogenic, growth promoter, anti-tumour, anti-tussive antifungal, hepatoprotective, anti-microbial, etc. The examples of these steroids are- bufadienolides, cardiolides, sapogenin/ steroid saponins cucurbitacins, steroidal alkaloids, with asteroid/withanolides[34].

### Terpenes & terpenoids

The terpenes are large and the diverse class of organic compounds, produced by a variety of plants. Terpenes are often strong smelling and thus may have had a protective function. Steroids are derivatives of the triterpene squalene<sup>35</sup>. When the terpenes are modified chemically (such as by oxidation or rearrangement of the carbon skeleton), the resulting compounds are generally called as terpenoids.

Terpenes and terpenoids are the constituents of essential oils of many types of plants and flowers.

Vitamin A is an example of terpene. The fragrance of rose and lavender is due to the monoterpenes. Terpenoids present in the *Toona ciliata* were evaluated for the cytotoxic & anti-inflammatory activity in human cancer cell lines [36]. The plant of *Toona ciliata* (Meliaceae) is a rich source of structurally intriguing limonoids with diverse bioactivities. The chemical constituents of the leaves of *Toona ciliata* have been investigated and to give limonoids and triterpenoids[37].

### Diterpenoids

A new pimaariene-type diterpenoid was isolated from the leaves and twigs of *Toona ciliata* and identified as- Toonaciliatin Mb [38].

### Triterpenoids-

The Terpenoid was obtained as a colourless oil & its molecular formula was determined as C<sub>36</sub>H<sub>56</sub>O<sub>6</sub>. For Eg.- *Toonaciliatone A* and *Toonaciliatine A38*. Two new tircallane-type triterpenoids were identified as- *Toonaciliatin K & L*.

### Tetra-nor-tri-terpenoids

The *Toona ciliata* was reported to contain two Novel B-seco-Tetranortriterpenoids and was reported to the exhibit anti-feeding activity. The B-seco-Tetranortriterpenoids are Toonacillin and 6-AcetoxyToonacilin [39].

The tetranortriterpenoid B-lactone was isolated from the Ether extract of leaves of *Toona ciliata*. The isolated terpenoid compound was known as Toona folin. Toona folin is the first tetranortriterpenoid B-lactone found in Meliaceae family [40].

### Penta-nor-tri-terpenoids

The methanolic extract of *Toona ciliata* was reported to contain two pentanortriterpenoids, 5 $\alpha$ , 6 $\beta$ , 8 $\alpha$ -trihydroxy-28-norisoToonafolin and 5 $\alpha$ , 6 $\beta$ , 8 $\alpha$ , 12 $\alpha$ -tetrahydroxy-28-norisoToonafolin [41].

### Limonoids

Isolation of the constituents of *Toona ciliata* revealed the presence of 12 limonoids (Toona yunnanins A-L) and 11 known compounds, (a) cedrelone, (b) epoxyazadiradione<sup>41,42</sup>, (c) Toonafolin, (d) Toonaciliatin E, (e) Toonaciliatin H, (f) dysobinin, (g) 12-deacetoxy-toonacilin, (h) 17-hydroxyazadiradione, (i) dihydroniloticin, (j) dehydroodoratol and (k) 21- $\alpha$ -methylmelianodiol.

Two novel limonoids were isolated from the dichloromethane extract from the seeds of *Toona ciliata* plant, 12-deacetoxyToonacilin and 6 $\alpha$ - acetoxy- 14 $\beta$ , 15 $\beta$ - epoxyazadirone. An investigation of *Toona ciliata* has led to the identification of two novel meliacin butenolides, 21-hydroxycedrelonide and 23-hydroxycedrelonide. Two known limonoids, cedrelone and 23-hydroxytoonacilide. Three known

coumarins, siderin scopoletin and isofraxidin were isolated. An unusual 9, 11-*seco* limonoid was isolated from the bark of *Toona ciliata* and named as toonasecone[43].

#### **Norlimonoids**

The *Toona ciliata* extract was isolated, and two new norlimonoids was identified as-5 $\alpha$ ,6 $\beta$ ,8 $\alpha$ -trihydroxy-28-nor-iso-toonafolin and 5 $\alpha$ ,6 $\beta$ ,8 $\alpha$ ,12 $\alpha$ -tetra-hydroxy-28-nor-iso-toonafolin [44].

#### **Polyynes**

*Toona ciliata* was evaluated to contain series of the bioactive compounds especially limonoids. Three new polyynes, (1)- (9S,10E,16R)-octadec-10-ene-12,14- diyne-1,9,16-triol, (2)- (9S,10E,16R)-9,16-dihydroxyoctadec-10-ene-12,14-diyne-1-yl acetate, and (3)- (3R,8E,10S)-heptadec-8-ene-4,6-diyne-3,10-diol were isolated from the leaves of *Toona ciliata* plant [45].

#### **Pharmacological Activities**

##### **Antidiabetic activity**

*Toona ciliata* leaves extract has a beneficial effect on decreasing blood glucose levels and also decrease hyperlipidemia which is produced due to diabetes. STZ was dissolved in citrate buffer (pH 4.5) to induce diabetes [46]. The previous studies reported that flavonoids are responsible for the hypoglycemic action of a plant extract [47-50]. The antidiabetic action of extract of *Toona ciliata* might be due to the flavonoids presents in it which was indicated in the preliminary phytochemical screening.

##### **Anti-ulcer activity**

In aspirin plus pylorus ligation induced gastric ulcer the ethanolic extract showed the significant reduction in gastric volume, free acidity, total acidity and ulcer score. In terms percentage ulcer inhibition the ethanol extract of *Toona ciliata* showed 100% activity as compared to control. HCL-ethanol-induced gastric damage in mice possibly through leukotrienes production and also the involvement of 5-lipoxygenase in the formation of ulcer lesion. So the protective effect of the extract *Toona ciliata* against the gastric 5-lipoxygenase or Leukotriene pathway. The anti-ulcer activity of *Toona ciliata* heartwood in this experimental model may be due to the terpenoids and steroids [51].

##### **Anti-oxidant activity**

The *Toona ciliata* leaf was extracted, and chemical constituents were isolated. It was concluded that aqueous and acetone extract of *Toona ciliata* shows anti-oxidant activity. Tannins and flavonoids present in plants can be the chemical to prevent oxidation. The tannins and flavonoids present in *Eucalyptus rostrata* possess the antioxidant activity [28].

Anti-inflammatory activity the ethanolic leaf extract of *Toona ciliata* confers the antioxidant and anti-inflammatory activity. The plant shows the presence of phenolic compounds which can be the responsible for both anti-oxidant and anti-inflammatory activity. *Toona ciliata* was evaluated for cytotoxic 34, and anti-inflammatory activity of triterpenoids presents in it. The new isolates were evaluated for their cytotoxicities using six human cancer cell lines and also for their inhibitory effects on lipopolysaccharide- induced nitric oxide production in cells [45].

##### **Antimicrobial activity**

The methanolic extract of *Toona ciliata* exhibited maximum inhibition against the test human and phytopathogens. The antimicrobial and fungicidal activity of the plant extract was also evaluated and reported [52-54]. The extract of *Toona ciliata* (stem bark) along with siderin, a significant coumarin from *Toona ciliata*, exhibited significant in vitro antibacterial activity. The extract also demonstrated mild anti-fungal effect 55.

##### **Antifungal activity**

Cedrelone is the neither natural tetra nor triterpenoids from *Toona ciliata* which exhibit the antifungal activity. Cedrelone from *Toona ciliata* were tested for antifungal activity. Cedrelone from the *Toona ciliata* was most active among the all in reducing rust pustule emergence [56]. All parts of *Toona ciliata* (stem, leaf and fruit) exhibits a significant reduction in the growth of the fungus [57].

#### **CONCLUSION**

Many of the medicinal plants in India are common and growing like weeds in wild conditions. It is capable of producing various pharmacological effects due to various bioactive constituents. The previous studies suggested some pharmacological activities of different extracts of plant *Toona ciliata*. The events include- Antidiabetic activity, Anti-ulcer activity, Anti-oxidant activity, Anti-inflammatory activity, Antimicrobial activity, Antifungal activity. Phenolic content present in *Toona ciliata* shows the anti-oxidant and anti-inflammatory activity, therefore, it can be useful in the treatment of stress and free radical balancing. The extract of *Toona ciliata* was reported to contain bioactive chemical moieties which include-coumarin, tannins, terpenoids, flavonoids, phenolics and polyphenols, steroids, polyynes etc. which can be used to treat diseases like stress, depression, Alzheimer's disease, Huntington's disease. Previous studies reported the anti-diabetic, anti-fungal, anti-microbial, anti-inflammatory, anti-ulcer and anti-oxidant activities which were possibly due to the bioactive constituent presents in it.

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