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Chemical and Pharmacological Aspects of *Toona* (Meliaceae)

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ABSTRACT

The genus *Toona* belongs to family Meliaceae is a group of traditionally important medicinal plants. *Toona* is commonly known as toon, the leaves, barks and roots of toon is commonly used as herbal medicine and also as timber. Extensive research works have been carried out on chemical constituents and biological activities of the genus *Toona*. In this review, we summarize previous and current information regarding chemical constituents and biological activities of the genus *Toona* and provide new insights for future study in this discipline. This study shows that *Toona* species posses several biological activities mainly due to the presence of coumarins, flavonoids, phytosterol, phenols, tenins, alkaloids, triterpenes and anthraquinons.

Key words: *Toona*, *Cedrela*, meliaceae, chemical constituents, biological activities

INTRODUCTION

In 1840, *Toona* was originally described by Endlicher as a section of *Cedrela*. Later Roemer in 1846 recognized that it could be separated by a number of sound morphological characters, raising *Toona* to generic rank. Thus, the old world species of *Cedrela* were transferred to *Toona* (Roemer, 1846). The genus *Toona* (Meliaceae) consists of upland trees that are widely distributed at the higher altitude eastwards from India, Nepal, China, Burma, Thailand, Malaysia, Java to Europe (Edmonds and Staniforth, 1998). About 15 species are found in tropical Asia and Africa, while only 4 species are found in India among them 2 species *T. serreta* and *T. hexandra* are found in north west Himalaya. The leaves of *Toona sinensis* (A. Juss.) Roem are used as vegetable in Tiwan. Its leaves and stems are also used as a carminative and to treat enteritis, dysentery and itch in oriental medicine. *Toona* species are mainly timber yielding plants and well known for their medicinal properties. These are deciduous trees upto 30 m high. *Toona serrata* (Royal) M. Roem. is commonly used in the treatment of ulcers and asthma (Gaur, 1999). Phytochemical screening of *Toona* has been done for retinoid, vitamins, coumaric acid, kaempferol, methyl gallate, quercetin, afzelin, quercitrin, isoquercitrin, rutin, cedrellin and phytol derivatives (Park *et al*., 1994, 1996; Luo *et al*., 2000). The antiangiogenic and antidiabetic activities of rutin and vitamin C were studied using *in vivo* as well as *in vitro* models (Guruvayoorappan and Kuttan, 2007; Alsaif, 2009). The purpose of this review is to collect all the possible information regarding the chemical constituents and biological effects of the genus *Toona*, thus will help to the researchers and scientists to take action for future study in this discipline. However, the literature survey revealed that no work has been done on the quantification of bioactives and mineral elements of *Toona* species by RP-HPLC, HPTLC and ICP-MS, respectively, In the field of natural products analysis, HPLC has gained acceptance as an analytical technique, especially for separation of complex mixtures of secondary constituents.

CHEMICAL CONSTITUENTS

Traditionally, chemical constituents of *Toona* are extracted into ethanol or methanol, after which the solvent was removed by vacuum distillation. The bioactives were separated by column chromatography on silica gel using different ratio of n-hexane: EtOAC, $CHCl_3$: MeOH and EtOAC:MeOH (Hsieha *et al.*, 2006; Zhao *et al.*, 2009) with increasing polarity as a mobile phase (Fig. 1). High performance liquid chromatography is the most important method of choice for the

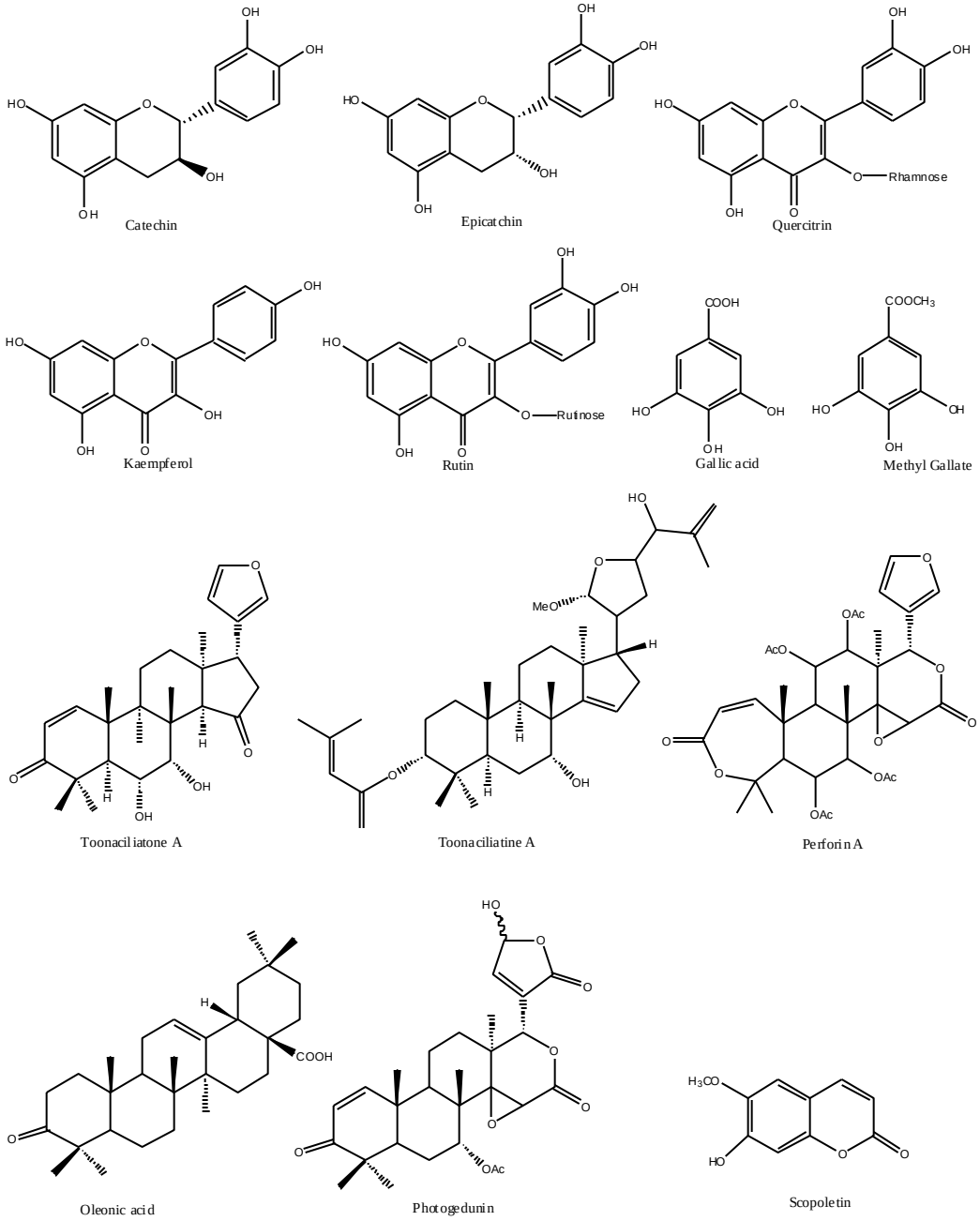

Fig. 1: Structure of isolated compounds from Toona

Table 1: Distribution, chemical constituents, biological activities and traditional uses of Toona species

Plant species	Common name	Distribution	Chemical constituents	Biological activities	Traditional uses
Toona hexandra syn *T. ciliata*, *Cedrela toona*	Toon, suren or Indian mahogany	India, Indonesia and Australia (up to 1000 m)	Coumarin glycosides, flavinoids, phytosterol, phenols and tenins, triperpenoids, Limonoids, Ca, P, Mn, Zn, Ni, Fe, K and Mg	Cytotoxicity, anti-ulcer and antibacterial, antimicrobial activity	Dye, Construction purposes, furniture and other articles
T. serrata syn, *Cedrela serrata*, *C. toona*	Daul	West Himalaya (India)		leishmanicidal activity	Timber, fooder, in the treatment of ulcers and asthma
Toona calantas	-	Indonesia, the Philippines, and Thailand			
Toona sinensis	Chinese mahogany, Chinese Toon, or Red Toon	China, Nepal, India, Myanmar, Thailand, Malaysia, Indonesia	Flavonoids, alkaloids, terpenes and anthra-quinones	Hypoglycemic, antioxidant, heliosis, vomitting, dysentery, detoxification, antiinflammation, antifatigue, antiproliferative, antitumorigenic, anti-inflammatory, anti-cancer and analgesic effects	Construction purposes, furniture and other articles
Toona sureni syn, *Toona febrifuga*	-	Nepal, India, Bhutan, Burma, Bangladesh, Indochina, southern China, Thailand, Indonesia, Philippines, Australia up to 1700-2100 m	Tetranortriterpenoids, methyl gallate,	Antibiotic, antioxidant activity, antiplasmodial activity	Furniture, interior finishing, decorative paneling, crafts, mnsical instruments, cigar boxes, veneers, boxes and for construction and also nsed in diarrhea

separation of bioactives of *Toona*. Both normal phase and reverse phase columns have been used. However, RP-HPLC with C_{18} columns and gradient elution (MeOH:H_2O) seems to be the most preferred method (Zhao *et al*., 2009). Distribution, chemical constituents, biological activities and traditional uses of *Toona* species are shown in Table 1.

A number of compounds including retinoid, vitamins B and C, coumaric acid, kaempferol, methyl gallate, quercetin, afzelin, quercitrin, isoquercitrin, rutin, cedrellin and phytol derivatives have been isolated from this plant (Park *et al*., 1994, 1996; Luo *et al*., 2000). Kaempferol, catechin, epicatechin and Polyphenol Contents also isolated and identified from *Torreya grandis*, *Swietenia macrophylla* and *Indigofera* Species (Saeed *et al*., 2007; Falah *et al*., 2008; Bakasso *et al*., 2008). Methanolic extract of *Toona ciliata* showed carbohydrate, coumarin glycoside, flavinoids, phytosterol, phenols and tenins (Gautam *et al*., 2010). Phytochemical investigations showed that the leaves of *T. sinensis* were rich in flavonoids, alkaloids, terpenes and anthraquinones (Chen *et al*., 2000; Persnol *et al*., 2001). Polyphenols including methyl gallate, gallic acid, kaempferol, quercitin, quercitrin, rutin, kaempferol-glucoside, catechin, epicatechin, stearic acid, palmitic acid, sitosterol, stigmasterol, sitosteryl-glucoside and stigmasteryl glucoside have been determined in *Toona sinensis* by Micellar Electrokinetic capillary Chromatography (MEKC) method, using UV detection (Hsieh *et al*., 2006). Phytochemical work on the *Toona* species has led to the isolation of triterpenes and phenolic compounds (Paula *et al*., 1997; Mulholland and Taylor, 1992; Benencia *et al*., 1999; Veitch *et al*., 1999; Segura *et al*., 1994; Hsieh *et al*., 2004). 3-Acetoxy-17-furan-3-yl-1-hydroxy-1,4,4,10,13-pentamethyl-12-oxo-tetradecahydro-16,20-dioxa-cyclopropa

[14,15] cyclopenta [alpha] phenanthrene-7-carboxylic acid methyl ester, beta-sitosterol, stigmasterol , palmitinic acid, 3-(3-Propyl-[1,1',3',1"]-tercyclohexan-3"-yl)-propan-1-ol were isolated from petrol and chloroform extracts of *Toona ciliata* (Li *et al*., 2009).

Shao-Hong (2010) were studied the inhibitive effects of ethanol extract of *Toona ciliata* leaves on protein non-enzymatic glycation end products formation. The essential oils (sesquiterpenes) of *T. ciliata* have been analyzed by GC-MS. The oils from the leaves (0.05%, v/w) and stems (0.05%, V/W) of *T. ciliata* contained 36 and 31 components (Maia Beatriz *et al*., 2000). Liao *et al*. (2007) isolated norlimonoids and limonoids from the leaves and stems of *T. ciliata*. 12-Deacetoxytoonacilin and 6α-acetoxy-14α,15α-epoxyazadirone have been isolated from the seeds of *T. ciliata* (Neto *et al*., 1995). Mu *et al*. (2007) determined volatile compounds in *T. sinensis* by MAE-HS-SPME followed by GC-MS. Tirucallane-type triterpenoids, pimaradiene-type diterpenoid and limonoids were isolated from the leaves and twigs of *T. ciliata*. Toonaciliatone, methyl-3α-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) were isolated from the leaves of *T. ciliata* (Ning *et al*., 2010). 12-α-Hydroxystigmast-4-en-3-one was isolated from the petroleum ether extract of *T. ciliata* together with two steroids and three C-methyl coumarins (Chowdhury *et al*., 2003a). Cedrelone, a tetranortriterpenoid, isolated from *T. ciliata* on photolysis by UV light yielded a true 14 beta, 15beta, 22beta, 23beta-diepoxy-6-hydroxy-1,5, 20(22)-meliatriene-2,7,21-trione (Gopalakrishnan *et al*., 2000). Lignans, flavonoids and cholestane were isolated from *T. microcarpa* (Fang *et al*., 2010). 21-Hydroxycedrelonelide, 23-hydroxycedrelonelide, limonoids, cedrelone, 23-hydroxytoonacilide, sitosterol, α-amyrin and α-amyrin acylated with fatty acids, coumarins, siderin, scopoletin and isofraxidin were also isolated (Vilela, 1994). Cedrellin, 2,6,10,15-phytatetraene-14-ol, 7α-obacunyl acetate, 6-acetoxyobacunol acetate, 7α-acetoxydihydronomilin, 2,6,10-phytatriene-1,14,15-triol and phytol were isolated from leaves of *Cedrela sinensis* (Luo *et al*., 2000). The eight mineral elements (Ca, P, Mn, Zn, Ni, Fe, K and Mg) have been detected in *Cedrela toona* by AAS (Vermani *et al*., 2010). Tetranortriterpenoids have been isolated from *Toona sureni* (Kraus and Kypke, 1979). Methyl gallate, exhibited potent antioxidant activity has been isolated from the leaves of *Toona sureni* (Ekaprasada *et al*., 2009). Five triterpenes (Cedrelone, Piscidinol A, Niloticin, Bourjotinolone A, 3-Episapelin A) were isolated from EtOAc extract of the leaves of *Toona sureni*, some of them showed significant antiplasmodial activity (Cuong *et al*., 2007).

BIOLOGICAL ACTIVITIES

Bark, oil, seed, flower and leaf of *Toona* have been used in traditional Chinese medicine. The leaves of *T. sinensis* were used medicinally for the treatment of heliosis, vomitting, dysentery, detoxification and antiinflammation (Wang *et al*., 2007). Chang *et al*. (2002) reported that *T. sinensis* possess antiproliferative effect and also promote the apoptosis of human lung cancer cell. Liao *et al*. (2006) showed that the scavenging activities of leaves, roots and barks of *T. sinensis* extract were over 80% at a concentration of 0.625 mg mL^{-1}. Antifatigue activity of water extract of *T. sinensis* have been determined by Feng *et al*. (2009). *T. sinensis* is used for the treatments of enteritis, dysentery and itch in oriental medicine (Edmonds and Staniforth, 1998; Oiano-Neto *et al*., 1998). The leaf extract of *T. sinensis* was found to have an evident effect against Severe Acute Respiratory Syndrome (Chen *et al*., 2008). Glucosidase inhibitory constituents were isolated from the stems of *T. sinensis* (Zhao *et al*., 2009). Toonaciliatin showed moderate antifungal activity

against *Trichophyton rubrum* with an MIC of 12.5 μg mL^{-1} (Chen *et al.*, 2009). The crude extracts and a major isolate, siderin, obtained from the petroleum ether extract of *T. ciliata* were found to exhibit significant cytotoxicity (Chowdhury *et al.*, 2003). Hypoglycemic effects of *T. sinensis* have also been reported. Flavonoid of *T. sinensis* decreased the blood glucose levels of alloxan induced diabetic mice (Zhang *et al.*, 2008). 12-alpha-hydroxystigmast-4-en-3-one was found cytotoxic in a brine shrimp lethality bioassay with LC 50 of 9.9 μg mL^{-1} and it also showed significant antitumor activity (Chowdhury *et al.*, 2003b).

The extract of *T. ciliata* along with siderin, a major coumarin from *T. ciliata*, exhibited significant *in vitro* antibacterial activity (Chowdhury *et al.*, 2003a). The extract of *T. sinensis* and gallic acid was found to possess effective antioxidant activity against various oxidative systems *in vitro* (Hseu *et al.*, 2008). Extract of *T. sinensis* exhibited antiproliferative and antitumorigenic activities (Yang *et al.*, 2010). The ethanol extract of *T. ciliata* Roemer (heart wood) showed anti-ulcer activity against aspirin plus pylorous ligation induced gastric ulcer (antisecretory), HCl-ethanol induced ulcer (cytoprotective) and water immersion stress induced ulcer in rats. The researchers reported that *T. ciliata* extract at a dose of 300 mg kg^{-1} p.o. markedly decrease the incidence of ulcers in all these three models. The plant extract also showed gastro protective activity (Malairajan *et al.*, 2007). *T. sinensis* have been investigated for its potent anti-inflammatory and analgesic effects (Chang *et al.*, 2002). Gallic acid was identified as the major anti-cancer compound in *T. sinensis* leaf extracts. It is cytotoxic to DU145 prostate cancer cells (Chen *et al.*, 2009). Antioxidant activity of the methanol and water extracts of Chinese toon (*Toona sinensis*) has been evaluated using DPPH radical scavenging and lipid peroxidation assays (Cheng *et al.*, 2009). Feng *et al.* (2009) have evaluated the antifatigue activity of water extracts of *T. sinensis* Roemor leaf. Such type of work have been published by the group previously (Negi *et al.*, 2009, 2010a-c; Bhandari *et al.*, 2010).

CONCLUSION

High Performance Liquid Charomatography (HPLC), Capillary Electrophoresis (CE), Micellar Electrokinetic Capillary Chromatography (MEKC) and column charomatography are to be able to provide a rapid separation and high resolution of the principal polyphenols of *Toona*. *Toona* species possess several biological activities such as antifatigue, antifungal, cytotoxicity, hypoglycemic, antidiabetic, antibacterial, antioxidant, anti-ulcer, gastro protective, anti-inflammatory, analgesic, anti-cancer and antiproliferative, mainly due to the presence of coumarins, flavinoids, phytosterol, phenols, tenins, alkaloids, triterpenes, steroid and anthraquinons. Isolation, separation, characterization and quantification of bioactives from some species of *Toona* are in progress.

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