Review

Tectona grandis L.f: A comprehensive review on its patents, chemical constituents, and biological activities

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Abstract

Tectona grandis L.f is a timber plant that is commonly referred to as teak. Its wide use as a medicine in the various indigenous systems makes it a plant of importance. A wide gamut of phytoconstituents like alkaloids, phenolic glycosides, steroids, etc. has been reported. A renewed interest in this plant has resulted in scientific investigations by various researchers towards the isolation and identification of active constituents along with scientific proof of its biological activities. The different parts of the plant have been scientifically evaluated for their antioxidant, antipyretic, analgesic, hypoglycemic, wound healing, cytotoxic, and many more biological activities. Documentation of this scientific knowledge is of importance to have consolidated precise information encompassing the various aspects of this plant, which could provide a base for future studies. This review is a compilation of the salient reports on these investigations concerning phytochemistry, the methods used to identify and quantify the constituents, the evaluation methods of the biological activity, toxicological studies, allergies and the patent/patent applications. This will further help researchers to find an area of the gap for future studies.

Keywords: Tectona grandis L.f Phytochemical profile Biological activities Patents

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1. Introduction

Plants are indispensable sources of medicine. Research on products obtained from nature is usually aimed to determine the medicinal values by exploring the available scientific knowledge and traditional uses. The phytochemicals isolated from these plants can be used as templates for further optimization of the lead molecules. It has been reported that in developing countries, 25% of the drugs are based on plants and their derivatives (Ramesh et al., 2013; Nahida et al., 2012). Several plants have been investigated for their phytochemical and pharmacological activities by various groups of researchers. One such plant of interest is *Tectona grandis* L.f (TG). It belongs to the family Verbenaceae. It is commonly referred to as teak. It is a large deciduous tree and may reach a height of 30–40 m with fluting and buttresses found at the base of older trees. The color of the bark is light grayish-brown. The leaves are large, shiny, opposite, and elliptic. The lower surface of the leaf is gray and covered with glandulous hairs. The flowers are small, white in color, and bisexual, appearing as large panicles. The fruit is a green, hairy, woody, irregularly rounded drupe (Nilesh et al., 2017). The tree can be found in several regions of south Asian countries and its parts such as root, bark, flowers, wood and oil are reported to be an important source of medical properties. The various parts of the plant have been used traditionally and ethnopharmacologically for the treatment of common cold, headache, in wound healing, bronchitis scabies, as a laxative, diuretic, antidiabetic, anti-inflammatory, antioxidant, lipid disorders, constipation, and diuretic (Kruger and Schulz, 2007). These pharmacological activities were found to be augmented when combined with other extracts. The unique combinations of such natural ingredients have been filed for patents. This review intended to compile the phytoconstituents identified along with the part and the solvent used for the extract and methods utilized for quantifying these compounds, listing the biological activities along with the methods applied, the extracts used, a brief account of toxicological evaluation, allergic manifestations and also the list of important information regarding patents/patent applications that have been filed concerning this plant.

1.1. Search strategy, inclusion and exclusion criteria

The search engines used for retrieving published data include databases that are universally recognized, specially Scopus, PubMed, Science Direct, Web of Science and Google Scholar. The
various search terms used as key words were Tectona grandis L.f, phytochemical, biological activities, toxicology, allergy, phytoconstituents, HPLC, UV, IR, GC–MS. The related articles were identified and screened for the title and abstract. Data extracted included the title, author(s), journal and year of publication. Related articles were retrieved in full text and validated for including them in the review. This study focused on all the major aspects of the plant under consideration. Papers that reported the pharmacology, phytoconstituents, allergy, toxicological were included in this study. Dissertations were also included. The studies included in this review were in English language. Inappropriate articles were excluded for the following reasons i.e. unrelated topic, insufficient data, duplication and unavailability of the abstract or full-text. The qualification of each paper was assessed by reading the full-text. There was no limitation in the search period. In the systematic review, articles were included from the available databases from 1986 to 2021.

2. Phytochemical profile of Tectona grandis

Several instrumental methods are available for identifying and quantifying the phytoconstituents in plants. The literature review describes the use of classical techniques such as high-performance liquid chromatography (HPLC), high-performance thin-layer chromatography (HPTLC), gas chromatography-mass spectrometry [GC–MS], and various other methods in the field of medicinal and aromatic plants (Kruger and Schulz, 2007). Researchers have reported a wide gamut of phytoconstituents. The preliminary investigation of the different parts of the plant, such as bark, wood, leaves, flowers, fruits, etc. has revealed the presence of flavonoids, phenolics, alkaloids, and certain glycosides (Nayeem and Karvekar, 2011a). Several methods have been reported for quantifying the secondary metabolites found in the various parts of TG following the ICH guidelines.

The chemical structures of the different constituents of TG are provided in earlier publications (Neha and Sangeetha, 2013; Vyas et al., 2019; Goswami et al., 2009). The chemical structures of some important constituents of TG are provided below.

Some phytoconstituent, along with their techniques of identification/quantification, are listed in the following Table 1.

3. Biological activities of Tectona grandis L.f (non-patent literature)

The plant has been used by traditional healers from time immemorial. Some of the mentioned traditional used in the literature are laxative, sedative, in treatment of piles, dysentery, leukoderma, anti-inflammatory, in bronchitis, urinary and liver related troubles, as hair promoter and useful in scabies (Deepali et al., 2010a; Kruger and Schulz, 2007; Nayeem and Karvekar, 2011a, 2011b). Review reports several in vitro and in vivo biological activities of the plant of interest (Singh et al., 1996; Ramesh and Mahalakshmi, 2014). Extracts isolated from different parts of the plant is used either alone or in combination with other extracts for various diseased conditions. Some of the active constituents
identified for the therapeutic activities include; 5-hydroxy-1,4-naphthalenedione (antibacterial), 4-hydroxy lapachol (cytotoxic), naphthaquinone (anti-ulcerogenic), benzene-1-carboxylic acid-2-hexadecanate (antiviral), lapachol (anti-tumor), 4-naphthaquinone (anti-plasmodic) (Vyas et al., 2019; Goswami et al., 2021). Some of the pharmacological activities reported are compiled in Table 2.

### 4. Toxicological studies

Acute toxicity studies are designed so as to determine the dose that will produce death or serious toxicological manifestations when the dose is given once or over a few administrations. These studies are significant in determining the margin of safety of a drug. Several reports are available for the toxicological screening of the different parts of TG. Review reveals that various parts were evaluated for their toxicity in a dose ranging from 1000 mg/kg to 5000 mg/kg body weight. The solvents used for the preparation of the extracts were water, methanol and ethanol. The extract of the different parts of TG. Review reveals that various parts were evaluated for their toxicity in a dose ranging from 1000 mg/kg to 5000 mg/kg. However the maximum dose used in most of the studies was found to show no signs of toxicity even at a dose of 5000 mg/kg. The following table depicts some of the toxicological studies conducted on the plant along with the part, solvent and animal used.

### 5. Teak allergy

Plants are one of the major causes of contact dermatitis (Verma et al., 2001). Dust from tropical hardwoods such as teak can cause
Teak is a fairly potent sensitizer it contains primary irritants and both irritant contact dermatitis and allergic contact dermatitis. It has been confirmed by various studies (Rao and Balachandran, 2010; Estlander et al., 2001). The main allergens that have been identified are polyphenols, naphthoquinones, their dimers, lapachol and are polyphenols, naphthoquinones, their dimers, lapachol and

| S. No. | Part (Solvent) | Activity | Animal/Microorganism/Other | Method of evaluation | Ref. |
|--------|----------------|----------|---------------------------|---------------------|------|
| 1      | Leaf (Hydroalcoholic extract) | Wound healing | Sprague Dawley rat | Burn wound, Excision wound, incision wound, dead space wound | Nayeem and Karvekar, 2011a, 2011b |
| 2      | Bark, fruit (Methanol, Ethanol) | Anti-bacterial | Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumonia, Escherichia aerogenes | Disc diffusion, Broth micro-dilution method | Neamatallah et al., 2005; Lanka and Parimala, 2017; Ramath and Shabary, 2020 |
| 3      | Bark (Ethyl acetate, Petroleum, Ethanol, Water) | Anti-asthmatic | Swiss albino mice | Clonidine induced catelepsy, haloperidol-induced catelepsy, milk induced leucocytosis, in vivo animal models like mast cell degranulation and capillary permeability | Goswami et al., 2010a; Goswami et al., 2010b |
| 4      | Heartwood, Stem bark, leaves (Petroleum ether, Methanol) | Anti-tumor | Artemia salina | Brine shrimp assay | Pathak et al., 1988; Ghareeb et al., 2014 |
| 5      | Heartwood, Sawdust (Dichloromethane) | Antifungal | Aspergillus niger, Phanerochaete chrysosporium Pheritima posthumaas | Disc diffusion | Florence et al., 2012; Sumthong et al., 2006; Bhat et al., 2010 |
| 6      | Leaves, Fruits (Ethanol) | Anthelmintic | Time of paralysis and time of death | Gururaj et al., 2011; Akshay et al., 2019 |
| 7      | Bark (Petroleum ether, Chloroform, Ethanol, Water) | Anticonvulsant | Male Wistar rats | Maximal electroshock induced seizures and pentyletenetetazole induced seizures | Azzah et al., 2017 |
| 8      | Seeds (Methanol) | Hepatoprotective | Rats | CCl4 and Ranitidine induced hepatotoxicity model | Rawal and Patil, 2017; Jangame et al., 2017; Jangme et al., 2017 |
| 9      | Fruit (Chloroform, Acetone, Methanol, Water) | Anti-urelothelial | Calcium oxalate crystals | In vitro dissolution calcium oxalate crystals | Dudulkar et al., 2016 |
| 10     | Leaves, Flowers (Petroleum ether, Chloroform, Ethanol, n-Butanol, Ethanol, Water) | Antidiabetic | Rats | Alloxan-induced diabetes | Pradeep et al., 2012; Ramachandran and Rajasekaran, 2014; Shukla et al., 2010 |
| 11     | Stem, Flowers (Methanol) | Analgesic and anti-inflammatory | Albino rats, mice | Radiant heat method, Writhing test Carragenenan of rat paw, Acetic acid, Hot plate | Giri and Varma, 2015; Ramachandran et al., 2011; Nayeem and Karvekar, 2010a, Nayeem and Karvekar, 2010b | Nayeem and Karvekar, 2012 |
| 12     | Roots (Methanol, Water) | Antitussive | Rats | Cough model induced by sulfur dioxide gas | Kaushik et al., 2011 |
| 13     | Plant (Ethanol) | Gastroprotective | Rats | Cold restraint and pyloric ligation induced gastric ulcer models | Singh et al., 2010 |
| 14     | Roots (Not mentioned) | Anti-ulcerogenic | Rats and guinea pigs | Experimentally induced ulcers | Goel et al., 1987 |
| 15     | Stem bark (Ethanol) | Antioxidant | In vitro studies | DPPH, FRAP, H2O2 scavenging assay | Ghaisas et al., 2008; Sahay and Sharma, 2015 |
| 16     | Plant (Aqueous) | Diuretic | Wistar rats | Hydrochlorothiazide induced | Kore et al., 2011 |
| 17     | Roots (Methanol) | Hypoglycemic | Albino rats | Alloxan induced, Dexamethasone induced | Mahesh et al., 2009; Pooja et al., 2011 |
| 18     | Leaves (Ethanol) | Anti-hemolytic anemia. | Rats | Induced by intraperitoneal injection of phenylhydrazine | Diallo et al., 2008 |
| 19     | Root, heartwood (Petroleum ether) | Cytotoxic activity. | Artemis | Brine shrimps’ assay | Rafullah and Suleiman, 1999 |
| 20     | Seeds (Petroleum ether) | Hair growth activity | Albino mice | Shaved demed skin of albino mice | Deepali et al., 2010b |
| 21     | Leaves (Methanol) | Antiplasmoidal | P. falciiparam | In vitro | Osman and Hadiani, 2018 |
| 22     | Leaves (Ethanol) | Anti-hypertensive | Wistar rats | Renal artery occluded hypertensive rats | Ajayi et al., 2011 |
| 23     | Leaves (Methanol) | Antifungal | Arthrinium phaeospermum, Aspergillus fumigatus, Aspergillus flavus | Well diffusion method, Agar slant double dilution tubes method | Astiti and Suprapti, 2012; Kouassi et al., 2014 |
| 24     | Stem extract (Not mentioned) | Uterine relaxant activity. | Female albino Wistar rats | Estradiol benzoate injected uterus | Deepali et al., 2010a |
| 25     | Leaves | Hepato protective | Mice | CCI4 induced liver injury | Somayya et al., 2021 |
| 26     | Seeds | Antipyretic activity. | Adult Wistar rats | Yeast induced antipyretic model | Jhansi and Lakshmi, 2021 |
Table 3
Toxicity studies of TG.

| No. | Part | Solvent | Animal used | Lethal dose (DL50) | Reference |
|-----|------|---------|-------------|--------------------|-----------|
| 1   | Leaves | Aqueous | Wistar albino rats | No signs of toxicity, even at a dose of 5000 mg/kg in a single administration. | Kamsu et al., 2021 |
| 2   | Leaves | Ethanol | Wistar rat | No physiological changes or toxicity, even at a dose of 5000 mg/kg | Hanidin et al., 2019 |
| 3   | Seed | Methanol | Albino mice | No mortality up to 1000 mg/kg | Dokuparthi et al., 2017 |
| 4   | Stem bark | Ethanol and water | Wistar rats | No toxicity up to 2000 mg/kg | Asil, 2011 |
| 5   | Seeds | Methanol, petroleum ether | Male albino rats | No toxicity up to 2000 mg/kg | Jangme et al., 2017 |
| 6   | Root | Methanol | Albino rats | No toxicity up to 3000 mg/kg | Pooja et al., 2011 |
| 7   | Seed | Methanol | Mice | No mortality up to 1000 mg/kg | Jhansi and Lakshmi, 2019 |
| 8   | Leaves | Methanol | Male Wistar rats | No mortality up to 2000 mg/kg | Nayeem and Karvekar, 2012 |
| 9   | Leaves | Methanol | Sprague Dawley strain | No mortality up to 2000 mg/kg | Kushwah et al., 2018 |

Table 4
Patent Literature of TG.

| S. No. | Patent / Patent Application Number (Publication Date) | Assignee/Name of the First inventor | Short Description | Ref. |
|--------|----------------------------------------------------|------------------------------------|------------------|-----|
| 1      | CN108938948A (December 7, 2018)                    | Wang Dengsheng                     | It discloses an incense coil containing a specified amount of teak wood, cypress seed, hehuangpi, lavender, lemongrass, Lingzhi, lounge, starch, and CM-cellulose for tranquilizing the nerves and aiding in sleep | Dengsheng, 2018 |
| 2      | CN106822380A (June 13, 2017)                       | Jinan Haoyu Qingtian Medical Technology Co., Ltd. (China) (JHQMTCL) | It discloses a pharmaceutical composition comprising TG, Trigonella rutherica, Pedicularis longiflora, maritimitin, and Lindera obtusiloba for the prevention and treatment of optic atrophy | Jinan Medical Technology Company, 2017a |
| 3      | CN106728432A (May 31, 2017)                        | JHQMTCL                            | It discloses a pharmaceutical composition comprising TG, Plagiozia distinctissima, jujube, B, Lysimachia heterogeneus, and Centaurium pulchellum for treating/preventing pneumonia | Jinan Medical Technology Company, 2017b |
| 4      | CN106728431A (May 31, 2017)                        | JHQMTCL                            | A pharmaceutical composition for the treatment of synovitis of the knee comprising TG, Petrospermum minor, aceroline, and neroelaid as crude drugs | Jinan Medical Technology Company, 2017c |
| 5      | CN106728433A (May 31, 2017)                        | JHQMTCL                            | A pharmaceutical composition for the prevention and treatment of insomnia comprising TG, Doryogteris concolor, Lonicera caerulea, saikosaponin C and Sinn suave as crude drugs | Jinan Medical Technology Company, 2017d |
| 6      | CN10668346A (May 17, 2017)                         | JHQMTCL                            | A pharmaceutical composition for the prevention and treatment of thyroid diseases comprising TG, Parthenocissus himalayana, Dalbergia hancei, caparapine, and xilopine as a crude drug | Jinan Medical Technology Company, 2017e |
| 7      | CN106683137A (May 17, 2017)                        | JHQMTCL                            | A pharmaceutical composition for the treatment of optic atrophy comprising TG, trifloruhizin, and Lindera obtusiloba as a crude drug | Jinan Medical Technology Company, 2017f |
| 8      | CN106683263A (May 17, 2017)                        | JHQMTCL                            | A pharmaceutical composition for the treatment of otitis media comprising TG, Myriophyllum spicatum, asiatic acid, Euonymus myrianthus, and Ulva conglobata as a crude drug | Jinan Medical Technology Company, 2017g |
| 9      | CN106540004A (March 29, 2017)                       | JHQMTCL                            | A pharmaceutical composition for the treatment of diabetic retinopathy comprising TG, rose apple, esculentoside B, Parthenocissus himalayana, and globe amaranth as bulk drugs | Jinan Medical Technology Company, 2017h |
| 10     | CN106138463A (November 23, 2016)                   | JHQMTCL                            | A pharmaceutical composition for treating advanced bladder cancer comprising TG, Limnaea, β-amyrin acetate, mesembrine, and dryocorsisin | Jinan Medical Technology Company, 2016a |
| 11     | CN106138462A (November 23, 2016)                   | JHQMTCL                            | A pharmaceutical composition for treating advanced colon cancer comprising TG, Diplazium donianum, and Notobasymnymus japonicum | Jinan Medical Technology Company, 2016b |
| 12     | CN106074957A (November 9, 2016)                    | Yantai Ruizhi Biomedical Technology Co., Ltd. (China) | The invention relates to a traditional Chinese medicine composition for treating liver and stomach disfunction by esophageal hiatus hernia comprising TG, Tetrapanax papyrius, Mangifera indica, Citrus meja, Citrus ilicifolia, Aamuam tosko, Lithocarpus polytachys, Pyropilum adammantium, Kadsura coccine, Microsorum dilatatum, Scirpus triqueter, Croenadodium lilae, Requus multif, Rosa bracteae, coriander fruits, Actinidia arguta, and Glycyrrhiza sp. Roots | Yantai Biomedical Technology company, 2016 |
| 13     | IN3267/CHE/2014A (February 12, 2016)               | Rajarajan Swaminathan              | A method for preparing a lyophilized extract from TG for treating the Asian and East Central South African genotype of Chikungunya virus. | Rajarajan et al., 2016 |
| 14     | CN103356878B (November 25, 2015)                   | Cheng Yueyin                       | A traditional Chinese medicine powder for treating pediatric eczema comprising TG, Arangeltia leuvenia, penny, celasalins leaves, Aspergillus brachyphyllus, pine bark, Corea lanceolata, Vaccinium fragile, Cudrania tricuspidata, and talc | Yueyin, 2015 |
| 15     | WO2006075336A1 (July 20, 2006)                     | Katkar Rama Dhondiba              | Herbal composition for treatment of blood and heart/skin related diseases comprising TG, Muraya Paniculata, Latane camara, Terminalia, Todalia asiatica, and Chawat | Dhondiba, 2006 |

(continued on next page)
deoxylapachol. The presence of these constituents explains the allergenic properties of this plant species. Lapachol is less potent than deoxylapachol as sensitizer (Christensen, 2018; Carrieri et al., 2014). The most common reactions are eye, skin, and respiratory irritation and nausea.

6. Patent literature of *Tectona grandis* Lf

The patents for plants were filed in diversified areas taking into consideration the cultivation, harvesting, drying, extraction, standardization, formulation methods, the devices used, etc (Pennyroyal et al., 2011). The patent literature of TG was collected by performing the Keyword search (*Tectona grandis* and teak wood) in the Espacenet Patent Search database (https://worldwide.espacenet.com/patent/search). The claims of the obtained patents/patent applications were reviewed. The patents/patent applications mentioning the name of TG or teak wood along with pharmaceutical use were segregated. Authors independently analyzed the language, content and description mentioned in the patents. The important data from the selected patent applications are mentioned in Table 3.

It is evident from the data of Table 4 that TG is present as an ingredient in many pharmaceutical compositions, which are claimed to have different therapeutic uses. These uses include treatment/prevention of optic atrophy, pneumonia, synovitis, insomnia, thyroid diseases, otitis media, diabetic retinopathy, bladder cancer, colon cancer, esophageal hiatus hernia, Chikungunya, insomnia, thyroid diseases, otitis media, diabetic retinopathy, bladder cancer, colon cancer, esophageal hiatus hernia, Chikungunya, insomnia, thyroid diseases, otitis media, diabetic retinopathy, bladder cancer, colon cancer, esophageal hiatus hernia, Chikungunya, insomnia, thyroid diseases, otitis media, diabetic retinopathy, bladder cancer, colon cancer, esophageal hiatus hernia.

| S. No. | Patent / Patent Application Number (Publication Date) | Assignee/Name of the First Inventor | Short Description | Ref. |
|--------|------------------------------------------------------|------------------------------------|------------------|-----|
| 16     | JP2013224318A (October 31, 2013)                      | Kawabata Aya                      | It claims an active oxygen scavenger comprising the extracts of TG, *Anacampsis pyrethrum*, *Anacampsis pyrethrum*, *Oclacarpus longifolius*, and *Aganosma marginata*. | Aya and Misao, 2010 |
| 17     | JP2010018545A (January 28, 2010)                      | Kawabata Aya                      | A reactive oxygen scavenger comprising extracts of TG, *Parkia speciosa*, *Anachomus pyrethrum*, *Ochrocarpus longifolius*, *Wrightia tomentosa*, *Dispyros rhodolocarpus*, and *Burmannia Griff*. | Aya and Misao, 2010 |
| 18     | JP2006176445A (July 6, 2006)                          | Ikeda Naosuke                     | It relates to a composition comprising about 10 herbal drugs including TG that is effective for health promotion and nutrition. | Naosuke, 2006 |
| 19     | JP2006166803A (June 29, 2006)                         | Nobashi Kenzou                    | A shelf life-improving composition comprising an organic acid and an acetone extract of TG. | Kenzou, 2006 |

7. Conclusion

Herbs are widely used for the treatment of various diseases. This review highlights the importance of phytochemistry, biological activity, and the patents of *Tectona grandis*. The result of the phytochemical study shows that it contains compounds with diverse structures. The different parts of the plant possess various activities like antioxidants, wound healing, analgesic, anti-inflammatory, anti-platelet, etc. However, it has come to the notice that very few patents have been filed concerning this plant, thereby paving the way for more studies and applications of patents in the future.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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