



## Review Article

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### PHYTOPHARMACOLOGICAL SIGNIFICANCE OF *TERMINALIA CATAPPA* L.: AN UPDATED REVIEW

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Received on: 07/01/16 Revised on: 17/02/16 Accepted on: 29/02/16

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DOI: 10.7897/2277-4343.07272

#### ABSTRACT

*Terminalia catappa* L., a large spreading tree belonging to the family Combretaceae, is distributed throughout the tropics in coastal environments. Different parts of this tree have been used in folklore medicine and research studies also exhibited various medicinal properties such as antibacterial, anti-fungal, anti-inflammatory, antioxidant, anti-tumour, anti-HIV, hepato-protective and anti-diabetic of this plant. This review work focused on phytopharmacological significance of *T. catappa* L. besides its traditional medicinal uses and major chemical constituents reported on this tree. Pharmacological activities reported in the review provide scientific evidences for the numerous traditional uses and folklore claims of this plant.

**Key words:** *Terminalia catappa* L., Ethnomedicinal uses, Pharmacological activity.

#### INTRODUCTION

Combretaceae is one of the largest families of flowering plants including trees, shrubs, and lianas comprising about 20 genera and 600 species. *Terminalia* is a genus of large trees belonging to the family Combretaceae, comprising around 200 species distributed in tropical regions of the world. This genus gets its name from Latin word *Terminus*, referring to the fact that the leaves appear at the very tips of the shoots. Trees of this genus are known as a good source of secondary metabolites such as cyclic triterpenes and their derivatives, flavonoids, tannins, and other aromatics.

Tropical almond botanically equated as *Terminalia catappa* L. is a tall deciduous and erect tree reaching 25-40 m, trunk 1-1.5m in diameter. Younger trees display a characteristic pagoda form, with a single bole and monopodial horizontal branching in regular false whorls of 4-5 branches. Along each lateral, new

branches are formed in a characteristic, bifurcating pattern. The tiered crown becomes flatter with widespread branches in older specimens. The trunk is usually straight and reasonably cylindrical, but in exposed coastal situations it may be crooked and/or leaning. Buttresses, when present, are up to 3 m (10 ft) in height, variable, straight to curved, thick to thin, sometimes branching. Large trees may develop big, occasionally branching buttresses and often have twisted, leaning trunks (Figure 1).

It is commonly called as Indian almond, Bengal almond, Country almond, False kamani, Indian almond, Malabar almond, Sea almond and Tropical almond. Synonyms for *catappa* L. are *Terminalia mauritiana* Blanco, *Terminalia moluccana* Lamk and *Terminalia procera* Roxb.<sup>1</sup> Regional names of this species include Jangli badam (Hindi), Jangli badam (Marathi), Nattuvadamai (Tamil), Ketapag (Malayalam), Tapasataruvu (Telugu), Kadubadami (Kannada), Desiyobadamo (Oriya), Badamalili (Gujarati), Kshudrabija and Desabadama (Sanskrit).



Figure 1: Morphology and growth habit of *Terminalia catappa* L.

It is called in different names in different languages and various countries around the world like English (Beach almond; Country almond; Indian almond; Malabar almond; Sea almond; Tropical almond), Spanish (Almendra; Almendro), French (Amandier de la Martinique; Amandier des Indes; Badamier; Myrobolan), Portuguese (Amendoeira; Amendoeira da Índia), Andaman & Nicobar (White Bombay; White bombway), Australia (Kotamba), Cambodia (Barang; Châmbak barang; Kapang; Pareang prang), Colombia (Kotamba), Cuba (Almendro de la India), Fiji (Tavali; Ttivi), Germany (Etangen baum; Indischer Mandelbaum; Katappenbaum), Hawaii (False kamani; haole; Kamani-haole), Indonesia (Ketapang), Java (Katapang), Malaysia (Jelawai ketapang; Ketapang), Myanmar (Badan), Netherlands (Amandel boom; Wilde amandel), Peru (Castana), Philippines (Dalinsi; Kalumpit; Logo; Talisai), Solomon Islands (Saori) and Sri Lanka (Kottamba).

#### **Distribution**

Tropical almond has a vast natural distribution in near-coastal areas of the Indian Ocean, through tropical Asia, and into the Pacific Ocean. The extent to which its range has been increased through movement and dispersal by humans is difficult to determine. It extends from the Seychelles through India, the Andaman and adjacent islands, and throughout Southeast Asia (Myanmar, Thailand, the Malay Peninsula, Vietnam, the Philippines, and Indonesia) to Papua New Guinea and northern Australia as far south as the Tropic of Capricorn. The species is found throughout the South Pacific region, including the Solomon Islands, Vanuatu, and Fiji. It is present on nearly all the high archipelagos of Polynesia and Micronesia but may be an aboriginal introduction to the eastern parts of its current range (including all of eastern Polynesia). Tropical almond has been introduced, and frequently naturalized, in many tropical parts of the world including Brazil, the Caribbean, and East Africa. It is naturalized in Florida and Puerto Rico. In Hawai'i, the species was introduced very early, probably before 1800, and is now naturalized at low altitudes, mainly near beach shores.<sup>2</sup>

#### **Habitat**

A conspicuous semi-deciduous tree of coastal areas found throughout the warm tropics. It grows best in moist tropical climate. The tree is well adapted to sandy and rocky coasts and flourishes on limestone. The species loses its leaves twice a year in most areas, with a brilliant red and yellow display of leaf colour before doing so. Leaf loss helps it tolerate 1 or 2 annual dry seasons when it occurs. Although Indian almond does grow when planted on uplands, the natural habitat of the species is in areas just inland from ocean beaches, near river mouths, and on coastal plains. These areas are typically flat, but they may have dunes or rocky bluffs.

#### **Biophysical limits**

Altitude: 0-800 m, mean annual temperature: 15-35<sup>0</sup> C, Mean annual rainfall: 750-3000 mm Soil type: Olitic limestone. The species grows in greatest concentration on sands and loamy sands. Also found on silts, loam, and clays. Soil pH is usually neutral to moderately alkaline and rich in bases. However, it will also grow in strongly acid soils. Good drainage is required on clay soils.<sup>3</sup>

#### **BOTANICAL DESCRIPTION**

##### **Flowers**

The flowers are small (4–6 mm across), white or cream-colored, five-lobed, arranged on long (8–25 cm auxiliary spikes, with a mildly unpleasant smell. Within a spike the majority of the

flowers are male, with only a few bisexual flowers positioned toward the base. Flowering occurs up to 3 times a year. The ratio of male to hermaphroditic (female) florets is 16:1. Various insects (Coleoptera, Diptera, Hemiptera, Hymenoptera and Lepidoptera) pollinate the flowers. Plants usually commence flowering and fruiting from a young age of 2–3 years of out planting, but this varies with site and genotype. On highly fertile sites mature fruits have been collected from 18 month old plants. Trees may re-leaf and flower very soon (within 6 weeks) after being completely defoliated by cyclonic winds.

##### **Leaves**

Leaves are single, alternate obovate with short petioles, spirally clustered at the branch tips, 15-36 cm long, 8-24 cm wide, dark green above, pale beneath, leathery and glossy. Before dropping, leaves turn bright scarlet, dark red, dark purplish red or yellow. During winter, especially after a sudden rain, leaves are shed all at once and are quickly replaced with lustrous, silky, purplish new foliage. In Asia, there is a foliage change twice a year.

##### **Fruit**

Typically, one to five fruits develop on the basal part of the flower spike. The fruit is a sessile, laterally compressed, and ovoid to ovate, smooth-skinned drupe. During maturation, it changes color from green through yellow to bright red or dark purplish-red at full maturity. Fruit size varies considerably. The kernel consists of two delicate and intricately entwined cotyledons enclosed in an inconspicuous cream-colored, rarely red, testa. Fruits are produced when tree is three years old and are edible in nature. Fruits vary greatly in shape, size and colour.

##### **Seeds**

Each fruit contain a cream coloured seed, which encloses the kernel (Nut). The rind of the fruit is a light, pithy, or corky tissue that enables the fruit to float and be dispersed by sea currents. Trees are also found away from coasts due to fruits being carried inland and dropped by frugivorous birds and bats, and as a result of deliberate planting by humans.

##### **Nuts**

The kernel can be eaten raw or roasted and has an almond like taste. Sun-dried kernels yield 34-54% of bland, yellow, semi-drying oil that is edible but becomes turbid on standing. The oil is mainly used in cooking.

##### **Bark**

The bark is gray to dark gray-brown and shallowly fissured. Continuous vertical fissuring and discontinuous horizontal cracks produce a grid appearance; the somewhat flaky bark peels off in curved or straight scales along these lines.

##### **Wood**

The tree provides a red, good-quality, elastic, cross-grained timber that seasons well and works easily. Density of the wood is 450-720 kg/m<sup>3</sup> at 12% mc. It is strong and pliable and is used for the construction of buildings, boats, bridges, floors, boxes, crates, planks, carts, wheelbarrows, barrels and water troughs. The trunk is a source of gum and black dye; it is used in leather preparation and as a base for ink.

##### **Rooting habit**

The trees usually have a spreading, fibrous, near-surface lateral root system, although the species is normally deep rooted in sand.<sup>4</sup> Shallow lateral root systems can develop in response to high water tables, making such trees susceptible to wind throw.<sup>5</sup>

**Folklore claims**

*Terminalia catappa* is a provider of natural medicines. In South-East Asia the leaves, fruit and bark are used for treating dysentery. Young leaves are used in South America to treat colic. Parts of the tree, such as the leaves and fruit, are astringent. The leaves, crushed with *Dacrydium elatum* and rhizomes of *Cyperus rotundus*, are combined to treat dysentery. The red leaves act as a vermifuge. Leaves may be rubbed on breasts to cure pain or, when heated, may be applied to numb parts of the body. Leaves bark and fruit are used to treat yaws. The bark and root are useful for bilious fever, diarrhoea, thrush, and as a remedy for sores and abscesses. It is recommended as a

mild laxative and a galactagogue for women, but too frequent use causes diarrhoea.

**Phytochemistry**

The phytochemicals of this plant include tannins (punicalagin, punicalin, terflavins A and B, tergalagin, tercatatin, chebulagic acid, geranin, granatin B, corilagin), flavanoids (isovitexin, vitexin, isoorientin, rutin) and triterpenoids (ursolic acid, 2a, 3a, 23-trihydroxyurs-12-en-28-oic acid).<sup>6</sup> Hydrolysable ellagitannins and other tannin related compounds have been isolated from the leaves and the bark of *T. catappa*.

**Table 1: Medicinal uses of *Terminalia catappa* reported from various countries**

Country	Parts used	Medicinal use	Reference
China	Leaves	Sudorific	Anonymous <sup>11</sup>
India	Leaves, bark, fruits	Dressing of rheumatic joints, Dermatitis, Antipyretic	Untwal and Kondawar <sup>12</sup>
	Fruits	Leprosy and Headache	Kirthikar and Basu <sup>13</sup>
	Fallen leaves	Liver diseases	Morton <sup>14</sup>
	Leaves	Scabies and leprosy	Kirthikar and Basu <sup>13</sup>
	Bark	Diuretic and cardio-tonic	Parrotta <sup>15</sup>
Indonesia	Leaves, bark and fruits	Dressing of rheumatic joints, Dermatitis,	Kasahara and Hemmi <sup>16</sup>
Malaysia	Leaves, bark and fruits	Dermatitis, antipyretic	Lin <sup>17</sup>
Mexico	Fruit and bark	Asthma	Annegowda et al. <sup>18</sup>
	Green leaves	Stop bleeding during tooth extraction	Untwal and Kondawar <sup>12</sup>
Nigeria	Leaves	Tonsillitis	Aimola et al. <sup>19</sup>
Pakistan	Leaves	Scabies and leprosy	Annegowda et al. <sup>18</sup>
Philippines	Green leaves	For internal parasites, eye problems, and rheumatism	Asiah et al. <sup>20</sup>
	Fallen leaves	Liver diseases	Fan et al. <sup>21</sup>
	Leaves, bark and fruits	Dermatitis, antipyretic	
Samoa	Fruit and bark	Cough	Lin et al. <sup>22</sup>
Sri Lanka	Different parts	Diarrhoea, gonorrhoea	Ratnasooriya and Dharmasiri <sup>23</sup>
	Kernel	Aphrodisiac, antibacterial	
Taiwan	Kernel	Aphrodisiac, antibacterial	Christian and Ukhu <sup>24</sup>
	Fallen leaves	Liver diseases	Wee <sup>25</sup>

**Table 2: Chemical constituents of *Terminalia catappa* L.**

Parts	Chemical constituents	Reference
Bark	(+)-Catechin, (-)-epicatechin, 3,3',4-tri-o-methyl-ellagic-acid, 3,3'-di-o-methyl-ellagic-acid, arjunolic-acid, arjunolic-acid-28-o-β-d-glucoside, β-sitosterol, betulinic-acid, daucosterol, ellagic-acid, leucocyanidin, oleanolic-acid, oxalic-acid, tannin	Duke <sup>26</sup>
	2,3-(S)-HHDP-D-glucose, punicalagin, corilagin, tercatatin, casuarinin, castalagin, grandinin, castalin, 3-methoxy-4-hydroxyphenol-1-O-b-D-(6-é-O-galloyl)-glucoside, 3,5-dimethoxy-4-hydroxyphenol-1-O-b-D-(6-é-O-galloyl)-glucoside, (-)-epicatechin-3-O-gallate, (-)-epigallocatechin-3-O-gallate, procyanidin B-1, 3-é-O-galloyl procyanidin B-2, acutissimin A, and eugenigrandin A	Lin and Hsu <sup>27</sup>
	Ursolic acid and 2, 3â, 23-trihydroxyurs-12-en-28-oic acid, isolated from the chloroform fraction	Fan et al. <sup>21</sup>
Leaves	1-degalloyl-eugenin, 2, 3-(4, 4', 5, 5', 6, 6'-hexahydroxy-diphenyl)-glucose, chebulagic-acid, corilagin, gentisic-acid, geraniin, granatin-b, kaempferol, punicalagin, punicalin, quercetin, tercatatin, terflavin-a, terflavin-b, tergalagin	Duke <sup>26</sup>
	Reddish brown leaves contain flavonoid apigenin 6-c-(2-galloyl)-L-D-glycoside, apigenin 8-c-(2-galloyl)-L-D-glycoside, isovitexin, vitexin, isoorientin, rutin and tannin; gallic acid, ellagic acid, punicalagin, punicalin	Chen et al. <sup>28</sup> ; Yun-Lian et al. <sup>29</sup>
	The aqueous extract from red fallen leaves contain six phenolic compounds such as p-hydroxybenzoic acid, 4-hydroxyphenylpropionic acid, m-coumaric acid, 3,4-dihydroxybenzoic acid, p-coumaric acid and gallic acid	Chyau et al. <sup>30</sup>
Seeds	Arachidic-acid, ascorbic-acid, carbohydrates, beta-carotene, fat, fibre, iron, kilocalories, Linoleic-acid, myristic-acid, niacin, oleic-acid, palmitic-acid, palmitoleic-acid, phosphorus, potassium, protein, riboflavin, stearic-acid and thiamine	Duke <sup>26</sup>
Fruits	Corilagin, brevifolin-carboxylic-acid, beta-carotene, cyanidin-3-glucoside, ellagic-acid, gallic-acid, glucose, pentosans, tannin	Duke <sup>26</sup>
Nuts	Phosphorus, carbohydrates, crude fat, magnesium, calcium, iron, zinc, sodium, manganese, vitamins A and C	Christian and Ukhu <sup>24</sup>

## PHARMACOLOGICAL ACTIVITIES

### Antibacterial activity

The antibacterial effects of the petroleum ether, chloroform and methanol extracts of the dried roots of *T. catappa* were determined by the cup plate agar diffusion method. The petroleum ether extract was devoid of antimicrobial activity. Both the chloroform and methanol extracts showed good antimicrobial activity against Gram positive and Gram negative microorganisms. Compared to the other extracts, the chloroform extract showed prominent antimicrobial activity against *S. aureus* and *E. coli*. The methanol extract exhibited potent activity against *E. coli*.<sup>7</sup>

Shahina et al.<sup>8</sup> had reported the antibacterial activity of *T. catappa* leaves and fruits against species of *Corynebacteria*, *Staphylococci*, *Enterococci*, *Escherichia*, *Salmonella* and *Shigella*. Opara et al.<sup>9</sup> had reported antibacterial activity of aqueous and ethanolic extracts of *T. catappa* leaves against *S. typhi*, *E. coli*, *S. aureus* and *P. aeruginosa*. Anti bacterial activities of aqueous and ethanolic extracts of leaves and bark of *T. catappa* was carried out.<sup>10</sup>

Anti bacterial activity of aqueous ethyl acetate and hexane extracts of *T. catappa* bark was carried out against some pathogenic bacteria. Among the three extracts, aqueous extract exhibited potent antibacterial activity against all the selected bacterial pathogens even at minimum concentration. The activity of the extracts was compared with a standard antibiotic Ciprofloxacin. The extracts exhibited growth inhibitory activity in a dose-dependent manner.<sup>31</sup> Aqueous, ethyl acetate and hexane extracts of *T. catappa* wood were evaluated against some pathogenic bacteria.<sup>32</sup> It was found that aqueous extract exhibited potent antibacterial activity against all the selected bacterial pathogens even at minimum concentration. The activity of the extracts was compared with a standard antibiotic Chloramphenicol.

### Antifungal activity

The methylene chloride and methanol extracts of *T. catappa* showed antifungal activity against *Pythium ultimum*, *Rhizoctonia solani*, *Sclerotium rolfsii*, *Aspergillus fumigatus* and *Phytophthora parasitica*. The methanol extract showed marked antifungal activity against *Pythium ultimum* and *Phytophthora parasitica*.<sup>33</sup> Parimalagandhi et al.<sup>34</sup> had reported antifungal activity of the aqueous, ethyl acetate and hexane extracts of *T. catappa* wood and bark against some fungal species. Among the three extracts, hexane extract exhibited potent antifungal activity against all the selected fungal species. The activity is compared with a standard antibiotic Clotrimazole. The extracts exhibited growth inhibitory activity in a dose-dependent manner.

### Anthelmintic activity

Crude extract of *T. catappa* leaves was evaluated for anthelmintic activity against *Trichostrongylus colubriformis*, *Cooperia curticei* and *Haemonchus contortus* and it was suggested that *T. catappa* leaves could serve as a potential anthelmintic agent.<sup>35</sup>

### Antidiabetic activity

The antidiabetic effect of the petroleum ether, methanol, and aqueous extracts of the fresh, unripe, green fruits of *T. catappa* were determined in alloxan-induced diabetic rats. Extracts produced a dose-dependent fall in blood sugar levels by 25–62% with the maximum effect seen after 15 days of treatment. Methanol and aqueous extracts of *T. catappa* fruits elicited significant anti-hyperglycemic activity, improved the lipid profile and produced regeneration of the pancreas of diabetic animals which were previously necrosed by alloxan, comparable

to the effect of standard antidiabetic drug, glibenclamide.<sup>36</sup>

The aqueous and cold extracts of the fresh tender leaves of *T. catappa* showed antidiabetic effect in alloxan-induced diabetic rats. Three weeks of daily treatment with the aqueous extract (43 g/kg per day p.o.) or with the cold extract (46 mg/kg per day p.o.) elicited a dose-dependent drop in blood sugar levels by 25–62% with the maximum effect attained after 15 days and remaining at the same level in the third week. The extracts also reversed alloxan-induced decreases in the body weights of rats beginning from the 7<sup>th</sup> day of treatment. Histologically, both extracts produced regeneration of the  $\beta$ -cells of the pancreas which were previously necrosed by alloxan. The regeneration was comparable to that produced by glibenclamide.<sup>6</sup> Ethanol (70%) extract of *T. catappa* leaves (300 mg/kg/day) exhibited significant antihyperglycemic activity in glucose loaded rats and in alloxan induced diabetic rats with significant improvement in body weight, protein, albumin, haemoglobin level and reduction in blood glucose and urea.<sup>37</sup> Methanolic extract of *T. catappa* leaf extract exhibited dosage-dependent increase in inhibitory effect on  $\alpha$ -glucosidase enzyme (up to 73.2%) and  $\alpha$ -amylase enzyme (up to 54.04%).<sup>38</sup>

### Antioxidant activity

The concurrent pretreatment of the Chinese hamster ovary-K1 (CHO-K1) cells with the aqueous extract of *T. catappa* leaf considerably suppressed mitomycin C-induced micronuclei. It also inhibited lipid peroxidation (LPO) and hydrogen peroxide formation induced by TPA in human mononuclear leukocytes in a dose-dependent manner.<sup>39</sup> Two extracts from *Terminalia catappa* showed remarkably potent activity in all assay systems. The HPLC analysis of the extracts indicated the presence of ellagic acid. The isolated ellagic acid showed strong antioxidant activity in the assay systems used.<sup>40</sup> Lin et al.<sup>22</sup> evaluated the antioxidant activity of tannin components, Punicalin and Punicalagin present in *T. catappa* leaves. Ko et al.<sup>41</sup> isolated squalene from the leaves and seeds of *T. catappa* by gas chromatography-mass spectrometry and high-performance liquid chromatography spiking analyses in supercritical carbon dioxide (CO<sub>2</sub>). The leaf extracts of *T. catappa* show strong 2,2-Diphenyl-1-picrylhydrazyl (DPPH) scavenging and antioxidative activities. Conversely, the seed extracts only exhibited strong inhibition of conjugated diene hydroperoxide formation and very low DPPH scavenging activity. Annegowda et al.<sup>18</sup> found that *T. catappa* leaves extract obtained with 40 min of sonication possessed significant polyphenolic contents when compared with 20 min and 60 min of sonication and control. The antioxidant assays also show that 40 min of the sonicated extract indicate significant vitamin C equivalent values than other different intervals of sonication and control. The polyphenolic content may be responsible for this activity. Chanda et al.<sup>42</sup> had performed free radical scavenging activities of acetone and methanol extracts of *T. catappa* leaves. The maximum scavenging activity was found in the methanolic extract which was comparable to standard ascorbic acid.

### Antitumor activity

Aqueous extract of *T. catappa* leaves (25-00  $\mu$ g/mL) and its major tannin component, punicalagin (1.0  $\mu$ g/mL) significantly protected CHO-K1 cells against bleomycin-induced hprt gene mutation frequency when the cells were pre treated with the extract or with punicalagin for 24 hours prior to exposure to bleomycin (2.25 mU/mL) for another 24 hours.<sup>28</sup> The supercritical CO<sub>2</sub> extract of *T. catappa* leaves (0-500  $\mu$ g/mL) elicited dose-dependent growth inhibition of both human hepatoma (Huh 7) and normal liver (Chang liver) cells but cytotoxicity of the extracts to the hepatoma cells was greater than to normal liver cells.<sup>43</sup>

The hot water extract of *T. catappa* showed potent short-term chemopreventive action on biomarkers of colon carcinogenesis. It also significantly reduced cell proliferation activity of colonic mucosal epithelium as the proliferating cell nuclear antigen index was lower than that of the control. The protection afforded by *T. catappa* against colon carcinogenesis was postulated to be related to its antioxidant activity.<sup>44</sup>

*T. catappa* water extract suppressed the growth of H-ras-transformed NIH3T3 cells in a concentration-dependent manner. Punicalagin also inhibited the growth of H-ras-transformed NIH3T3 cells in a concentration-dependent manner. IC<sub>50</sub> values for the water extract and punicalagin on H-ras-transformed NIH3T3 cells were 45 and 17 µg/mL, respectively.<sup>45</sup> The ability of the water extract of *T. catappa* to prevent metastasis was investigated *in vitro*, using A549 cell line, a highly metastatic human lung cancer cells, and *in vivo*, using Lewis lung carcinoma (LLC)-bearing mice, an established animal model for metastasis. The levels of the specific endogenous inhibitors of proteolytic enzymes, TIMP-2 and PAI-1, were gradually decreased by the water extract (10-100 µg/mL) in both A549 and LLC cancer cells. *In vivo*, the water extracts decreased lung metastases of LLC-bearing C57BL/6 mice by 68% compared to controls. These results indicate that the water extract of *T. catappa* is a potentially important agent for the prevention of lung cancer metastasis.<sup>46</sup>

Methanolic extract of *T. catappa* leaves produced a concentration dependent cytotoxic effect in EAC cells.<sup>47</sup> Antitumor activity of flavonoid fraction of *T. catappa* leaves against EAC cells in mice was evaluated<sup>48</sup>. Cytotoxicity of the aqueous extract of bark was evaluated against Ehrlich Ascites Carcinoma cell line using Tryphan blue dye exclusion method and MTT assay. The results clearly depicted that the extract has potent antitumor activity<sup>49</sup>.

#### Antiviral activity

The punicalin and punicalagin inhibited HIV replication in infected H9 lymphocytes with little cytotoxicity, and inhibited purified HIV reverse transcriptase with ID<sub>50</sub> values of 8 and 5 µM, respectively.<sup>39</sup> The chebulagic acid and punicalin blocked the binding of recombinant HIV coat protein gp120 (rgp120) to its normal cellular receptor, CD4.<sup>39</sup> The fruit of *T. catappa* contains ellagic-acid which has anti-HIV activity.<sup>36</sup>

#### Anti-inflammatory activity

The ethanolic extract of *T. catappa* leaves showed anti-inflammatory activity in acute and chronic mouse models of 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced ear edema. The activity was attributed to ursolic and 2a,3b,23-trihydroxyurs-12-en-28-oic acids which were isolated from the chloroform fraction. In the acute model, the chloroform fraction (1 mg/ear) exhibited significant anti-inflammatory activity which was comparable to that of indomethacin (0.3 mg/ear). The ethyl acetate fraction showed mild antiedema effect, while the crude ethanol extract showed little or no anti-inflammatory effect. Both ursolic acid and 2a,3b,23-trihydroxyurs-12-en-28-oic acid produced over 50% reductions in edema in the acute model. In the chronic ear edema model, the crude ethanolic leaf extract (1 mg/ear) and the chloroform fraction reduced ear edema by 32.0 and 66.0%, respectively, while ursolic and 2a,3b,23-trihydroxyurs-12-en-28-oic acids (each at a dose of 0.3 mg/ear) reduced ear edema by 96.9 and 94.8%, respectively. The chloroform fraction and the two isolated compounds produced a concomitant decrease in neutrophil infiltration as detected by reductions in myeloperoxidase activities by 59.0%, 92.6% and 90.9%, respectively. In contrast, the crude ethanolic leaf extracts reduced myeloperoxidase activity by 17.6%.<sup>21</sup>

*In vitro* antioxidant and anti-inflammatory activities of bark, wood and fruits of *T. catappa* were studied. *In vitro* antioxidant studies were performed using DPPH assay and lipid peroxidation assay. *In vitro* anti-inflammatory studies were performed using protease inhibition activity, membrane stabilization and protein denaturation inhibition assays. Aqueous extract of bark has shown maximum antioxidant and anti-inflammatory activities when compared to that of wood and fruits. The results of the study clearly revealed the dose-dependent activities of all the parts selected.<sup>50</sup> Sivaranjani *et al.*<sup>51</sup> had reported the anti-inflammatory and antioxidant potentials of aqueous extract of *T. catappa* fruits *in vitro*.

#### Analgesic activity

The analgesic, anti-hyperalgesic and anti-inflammatory activities of the extracted juice from the tender leaves of *T. catappa* were investigated in rats. Results suggest that antinociception by the extract was mediated supraspinally as the hot plate test largely measures supra spinally organised responses while tail flick test predominantly measures spinal reflexes. The extract (10 mL/kg) also produced significant analgesia in female rats which was not affected by the estrous cycle. Antinociception by the extract was neither antagonised by naloxone nor by metochlopramide. The onset of the analgesic action was slow (3 hours) and of short duration (reversible by 5 hours). Thus for use as an analgesic, it is only recommended for mild to moderate pain. The extract did not induce sedation. Neither anti-inflammatory nor antihyperalgesic activities were exhibited by the extract in the carrageenan-induced paw edema model. Pain in the early phase of the formalin pain test was significantly reduced by the extract but no reduction was seen in the late phase.<sup>52</sup>

#### Antiparasitic activity

Dried leaves of Indian almond were ground and dissolved in water. A variety of concentrations of this solution were used to determine resulting activities against tilapia pathogens. The results indicated that *Trichodina*, fish ectoparasites, were eradicated at 800 ppm.<sup>53</sup>

#### Hepatoprotective activity

Hepatoprotective effect of *T. catappa* chloroform extract against CCl<sub>4</sub>-induced liver injury in mice and its effects on IL-6 gene overexpression were determined.<sup>54</sup> Protective effect of the chloroform fraction of the ethanol extract of *T. catappa* leaves (TCCE) was evaluated in CCl<sub>4</sub>-induced hepatotoxicity in mice.<sup>55</sup> The extract of *T. catappa* leaves protected mice against D-GalN-induced liver injury. The extract was able to completely block the increase in serum ALT activity caused by D-GalN, denoting hepatoprotection as the ALT enzyme is an index for cell membrane damage. *In vitro* study on *T. catappa* leaf extract (0.1, 0.5 and 1.0 mg/mL) protected against D-GalN-induced cytotoxicity in primary cultured hepatocytes from fetal mice in a dose-dependent manner. 2a, 3b, 23-Trihydroxyursane-12-en-28-oic acid (50, 150 and 500 µmol/L) isolated from *T. catappa* leaf, showed dose-dependent inhibition of Ca<sup>2+</sup>-induced mitochondrial swelling and dose-dependent scavenging of superoxide radicals.<sup>56</sup>

CCl<sub>4</sub>-induced over-transcription of IL-6 gene was markedly suppressed by chloroform fraction of the ethanol extract of *T. catappa* leaves (10 or 30 mg/kg, intra gastric administration) which also blocked the expression of IL-6 protein especially in the area surrounding the terminal hepatic vein.<sup>57</sup> CCl<sub>4</sub> caused massive fatty change, gross necrosis, and broad infiltration of lymphocytes and Kupffer cells around the central vein and loss of cellular boundary in the liver. Pre treatment with the chloroform extract of *T. catappa* leaves effectively prevented

CCl<sub>4</sub>-induced disruption of liver mitochondrial membrane potential, intra mitochondrial Ca<sup>2+</sup> overload and CCl<sub>4</sub>-induced suppression of mitochondrial Ca<sup>2+</sup>-ATPase activity.<sup>58</sup>

#### Hypocholesterolemic activity

*T. catappa* (500 mg/kg) markedly reversed the altered lipid levels to normal range in tumor bearing mice.<sup>59</sup> *T. catappa* fruit extract and fallen dry leaf decoction have also been reported to have hypocholesterolemic effects on rats.<sup>60</sup>

#### Immunomodulatory activity

Immunomodulatory activity of flavonoid fraction of *T. catappa* leaves was investigated in Swiss albino mice. The flavonoid fraction was administered by intra-peritoneal at a dose of ED50 to healthy albino mice. Intra-peritoneal administered Tc<sub>ff</sub> showed a significant increase in neutrophil adhesion and phagocytic index.<sup>48</sup>

#### Wound healing activity

Wound healing activity of *T. catappa* bark was evaluated on excision wound model in rats. A circular wound of 2 cm in diameter was made on the depilated dorsal thoracic region of the rats under ether anesthesia in aseptic conditions. The ointment was applied for 18 days and percent wound closure observed along with the parameters viz. Epithelization, granuloma weight and scar formation. Animals were observed on 3<sup>rd</sup>, 6<sup>th</sup>, 9<sup>th</sup>, 12<sup>th</sup>, 15<sup>th</sup> and 18<sup>th</sup> post-wounding day. Wound healing activity was compared with that of control and Betadine ointment as standard drug. Animals treated with *T. catappa* ointment exhibited 97% reduction in wound area as compared to the control animals (81%). Ointment treated wounds were found to induce epithelisation faster compared to the control.<sup>61</sup> *T. catappa* was reported to exhibit wound healing effect similar to various herbs.<sup>62</sup> Other medicinal properties of *T. catappa* such as anti-aging, anticancer, aphrodisiac was also reported.<sup>63-65</sup>

#### CONCLUSION

The present literature review delineated above on the phytopharmacological value of *Terminalia catappa*. It is observed that this ancient tree is economically, medicinally and environmentally important, beside various parts of this tree are enriched with bioactive molecules. Wide spectrum of biological activities is reported from various parts of this plant. Hence, such collection of information regarding the medicinal effects and pharmacological activities of this plant will be useful to the research community, who are looking for the development of natural, safe and plant-based source of medicine for various human diseases. Further in-depth studies can contribute in developing scientifically validated herbal medicine from this potential plant source.

#### ACKNOWLEDGMENTS

Authors extend a deep sense of gratitude to Hon'ble Vice Chancellor, SASTRA University, Thirumalaisamudhrum, Thanjavur, Tamilnadu for providing necessary infrastructure and one of the Authors (PV) is thankful to the Management, S.T.E.T. Women's College, Mannargudi for their constant support and encouragement.

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**Cite this article as:**

P. Venkatalakshmi, V. Vadivel, P. Brindha. Phytopharmacological significance of *Terminalia catappa* L.: An updated review. Int. J. Res. Ayurveda Pharm. Mar - Apr 2016;7(Suppl 2):130-137 <http://dx.doi.org/10.7897/2277-4343.07272>

Source of support: Nil, Conflict of interest: None Declared

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