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(REVIEW ARTICLE)

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Phytochemical and pharmacological facets of *Terminalia tomentosa* wight and Arn: An updated review

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Abstract

Terminalia tomentosa Roxb. (ex Dc) Wight & Arn, a medicinal plant, belonging to the family Combretaceae, is known to possess copious phytochemical profile. It contains various bioactive constituents such as flavonoids, polyphenols, tannins, steroids, triterpenoids and saponin. The goal of this review is to inspect various aspects like ethnomedical, phytochemical, experimental and clinical studies that reveals the clinical significance of *Terminalia tomentosa*. This review sheds lights on the relevance of extensive research on the plant in order to reveal the prolonged effect with emphasis on the exact mechanism of action of bioactive element.

Keywords: Hepatoprotective; Antiepileptic; *Terminalia tomentosa;* Triterpenoids

1. Introduction

Medicinal plants are the plants which exert beneficial therapeutic effects on animals [1]. Humankind relies on plants as the source of energy. Plants have been used as an indispensable source of drug and remedies in case of ailments and health disorders since human civilization [2]. These are the major component of Indian traditional system of medicine – Ayurveda [3]. Natural drug molecules were recorded in Ayurveda around 5000 years ago [4]. Plants are observed to be less toxic, free from side effects & economical [5]. Natural plant-based medicine is believed to be healthier than synthetic drugs and that made the last decade to "go natural". In India, traditional healers use 2500 plant species and around 70,000 plant species have been used for medicinal purposes [6]. Around the planet, there is a 7-15% growing rate in the use of medicinal plants each year [2]. According to World Health Organization reports, around 4 billion people use herbal medicines [7]. The evaluation of new phytoconstituents has obtained boundless area for research and development because of the unmatched chemical diversity. For millennia, for both modern and traditional medicine, medicinal plants have been an essential part. There has been an extraordinary burst in the search for new and powerful antioxidants and antimicrobials derived from plants because of the adverse effects of synthetic drugs and multiple drug resistance [8]. Phytoconstituents from these medicinal plants serves as lead compounds in drug design and discovery [9].

The secondary metabolites synthesized by plants naturally, such as alkaloids, glycosides, flavonoids, tannins and volatile oils and contain vitamins and minerals, possess medicinal properties [10]. Flavonoids are the most common bioactive compounds that possesses great amount of pharmacological and biochemical effects like, anti-allergic, anti-platelet, antioxidative and anti-inflammatory. They act as health promoting and reduces the risk of many disorders [11]. Polyphenols act as antioxidants; scavenge free radicals, the substances that aid the growth of tumor cells [12].

During ATP production in the mitochondria, free radicals are released by incomplete reduction of oxygen. They are mainly reactive oxygen species and reactive nitrogen species. They generate oxidative stress at higher concentrations and that causes cellular damage and reversible/irreversible tissue injury. This oxidative stress leads to the development

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of inflammatory and degenerative diseases such as arthritis, liver cirrhosis, cancer, atherosclerosis, diabetes, cardiovascular, auto-immune and neurodegenerative diseases [13,14,15]. They also involved in the control of gene expression, receptor activation, signal transduction and maintenance of homeostasis during cellular respiration [16].

Antioxidants, by the removal of free radical intermediates, causes termination of chain reaction. Therefore, plant derived antioxidants contributed an essential role in human health [17]. Leaves, bark, root, berries, seeds and flowers of plant has been used for therapeutic purposes. Many studies have been documented the synthesis and accumulation of secondary metabolites by plants which possess medicinal properties [10]. The secondary metabolites present in plants are classified into, flavonoids, lignans, tannins, stilbenes and phenolic acids [18]. The best-known antioxidants are tocopherols, vitamin C, flavonoids and other phenolic compounds. They scavenge free radicals such as peroxide, hydroperoxide of lipid, hydroxyl and thus prevent degenerative diseases [19].

The genus *Terminalia* comprises of 200 species [20]. Plants of *Terminalia* has been used traditionally to treat inflammation, skin rashes, diarrhea, different bacterial infections and even cancer [21]. Many plants were reported for their biological potential as antioxidant, anti-inflammatory, antidiabetic and cardioprotective. [22,23]

The selected plant, *Terminalia tomentosa* (Synonyms: *Terminalia elliptica* Willd, *Terminalia alata* Heyne ex Roth, *Terminalia crenulata* Roth, *Terminalia coriacea* (Roxb.) Wight & Arn, *Terminalia ovata* Rottler ex C.B. Clarke, *Terminalia macrocarpa* Steud. ex Kurz) [24,25]is widely used in traditional medicine and is one of the paramount medicinal species from this genus. It is a giant tree found in deciduous forests & extensively dispersed in South East Asian countries [22]. It can be identified by its sissred & cracked bark and for this reason the plant is commonly called 'crocodile bark tree' [24,26]. This plant has multitudinous medicinal properties. The spectrum includes antioxidant, antidiarrheal, antifungal, antihyperglycemic and antileucorrheal. [24,27]

2. Plant profile

2.1. Taxonomy

- Kingdom: Plantae – plants
- Subkingdom: Tracheobionta – Vascular plants
- Super division: Spermatophyta - Seed plants
- Division: Magnoliophyte - Flowering plants
- Class: Magnoliopsida dicotyledons
- Subclass: Rosidae
- Order: Myrtales
- Family: Combretaceae
- Genus: *Terminalia*
- Species: *Terminalia tomentosa*

2.2. Common names

- Indian Laurel
- Black Murdah
- Crocodile Bark Tree

Figure 1 *Terminalia tomentosa* Plant

2.3. Microscopical features of stem

Stem pieces are cylindrical with swollen nodes; internodes are cylindrical, 6-11cm in length, 2-4 cm in diameter, finely-longitudinally striated, pale brownish-externally, pale yellowish-internally, no odour with bitter taste [28].

2.4. Macroscopical features of stem

Stem TS shows approximately circular outline, 0.1 mm outer thickness dark brown young cork layer which transforms to rhytidome in older pieces, parenchymatous cortex of 0.2 mm in thickness with continual stone cell layers and after that brown content cells, very narrow pericyclic zone of 0.1mm thickness with transverse fibers, wider phloem traversed with lignified fibers associated with idioblast containing calcium oxalate crystals. Xylem is composed of bunch of 2 to 3 vessels with parenchyma, many fibers with pitted medullary rays, lignified pith, pitted, parenchymatous, encircled with groups of peri medullary phloem [28].

2.5. Diagnostic characters of the stem are,[28]

- Stratified cork
- Groups of lignified stone cells
- Cluster crystals of calcium oxalate
- Uniseriate medullary rays
- Lignified pitted parenchymatous pith

Table 1 Synonyms of *Terminalia tomentosa* in Indian languages [24,25]

Names	Language
Asan	Bengali
Sadad	Gujarati
Saj	Hindi
Karimatti	Kannada
Shardul	Marathi
Sahaju	Oriya
Raktarjun	Sanskrit
Marutamaram	Tamil
Nalla maddi	Telugu
Karimaruthu	Malayalam

3. Habit and habitat

Terminalia tomentosa is a medium to large sized tree, around 20 – 35m high & 1m in diameter. The bark is found to be15 – 20mm thick, surface grey to black and is rough with transverse cracks & vertical fissures. The leaves are hard & simple, on the lower and upper side of the midribs found to be hairy, coriaceous, elliptic, oblong, opposite to subopposite, and rather acute at apex. Flowers are dull yellow, with terminal panicle spikes, without petals & are bisexual. Fruit is large glabrous or hairy, ovoid, 3cm long with 5 wings containing one seed [24,28]. '*Terminalia*'- the generic name is from the word 'terminalis'(Latin) or 'terminus' (ending) that indicates the pattern of the leaves being crowded at the end of the shoots [29]. The plant is native to South – East Asia – India, Myanmar, Bangladesh, Cambodia, Laos, Thailand, Vietnam. It is found common in Sal forests at elevators of 1000m in mixed deciduous forest and in dry dipterocarp forest [24,26].

3.1. Traditional uses

- Bark is effective in haemorrhages, bronchitis, cardiopathy, dysentery, cough, leucorrhoea and burning sensation. It is also used in GI disorders and anti-inflammatory purposes. [24,25]
- Bark is useful in verminosis, gonorrhoea, liver & white leprosy and blood diseases.
- Bark powder is helpful in vertigo and piles.
- Bark decoction is used for the treatment of rheumatism, diabetes, fever and urinary diseases.
- Bark, gum and leaves are used in fever and ear ache.
- Leaf powder is effective in fast healing of cuts and wounds, to promote sexual health &to treat liver problems.
- Dried leaves are expectorant.
- Tender leaves are effective in migraine.
- Dried roots and latex are effective as an antidote for snake poisoning.
- The plant is used in Bone fractures & as an anti-fungal.
- It is helpful in erysipelas, leukoderma, skin diseases and polyuria
- It is beneficial for skins and hairs
- The plant is also a styptic, cardiotonic, astringent, antiseptic and bactericidal. [30]

3.2. Medicinal importance

Terminalia tomentosa plant extracts have been widely explored experimentally and clinically for its diverse pharmacological effects and numerous therapeutic uses. Relevant literatures revealed the plant has plenteous beneficial pharmacological activities, like, antifungal, anti-hyperglycemic, anti-diarrheal, antioxidant, anti-inflammatory, antidiabetic, anti-ulcer, antimicrobial, anti-leucorrheal, and hepatoprotective. [24,25,26,27]

3.3. Phytoconstituents [22,24,25,27,30]

Table 2 Phytoconstituents of *Terminalia tomentosa*

S. No.	Phytoconstituents	Plant parts
1.	Tannins: Arjunic acid, Arjunolic acid, Arjunetin, Ellagic acid, Gallic acid.	Bark [25]
2.	Triterpenoids:Oleanolic acid, Botulinic acid.	Bark and roots [23,25]
3.	Steroid: β-sitosterol.	Bark [23,25]
4.	Flavonoids: Apigenin, Kaempferol, Luteolin, Myricetin, Quercetin, Rutin.	Leaves [31]
5.	Polyphenolic compounds:Barringtogenol and tomentosic acid,Dimethyl ellagic acid,Dimethyl flavellagic acid, 5-aminovaleric acid, Thymin, Quercetin and qynurenic acid, 4-methoxy cinnamic acid, Epigallocatechin, Indole-3-aldehyde,Resveratrol, Chlorogenic acid.	Bark [22,26,27]

Phytochemical investigation of the plant extracts showed the presence of different types of phytoconstituents, which include, carbohydrates, alkaloids, cardiac glycosides, anthocyanins, flavonoids (apigenin, kaempferol, luteolin, myrcetin, quercetin, rutin), α & β amyrin, lupeol, mudarine, resins, a nontoxic proteolytic enzyme calotropin, a powerful bacteriolytic enzyme calactin, phytosterols, tannins, triterpenoids, saponins, proteins, fixed oils and fats [22,24,25].Some of the phytoconstituents isolated are tannins like arjunetin, arjunic acid, gallic acid arjunolic acid, ellagic acid, and triterpenoids like betulinic acid, oleanolic acid and steroid like β – sitosterol. In addition to that some new constituents

like di-n-octyl phthalate, arjunahomosesquiterpenol, dibutyl phthalate, di-isobutyl phthalate, terpene glycoside, flavone and chalcone glycoside. The presence of these biologically active compounds is responsible for the therapeutic value of *Terminalia tomentosa.* [30]

4. Pharmacological potential

4.1. Antioxidant activity

Sharma *et al* screened the aqueous and ethanolic extracts of *Terminalia tomentosa* bark to evaluate in-vitro antioxidant and reactive oxygen species scavenging ability. They have selected DPPH, ABTS, nitric oxide, orthophenenthroline, di-isobutyl phthalate, hydrogen peroxide and superoxide methods for the evaluation. Study reported antioxidant activity in comparison with standard drug ascorbic acid.[32]

4.2. Anti-inflammatory activity

Reddy J.S *et al* conducted a study to establish the anti-inflammatory activity of ethanolic and aqueous bark extracts of *Terminalia tomentosa*. They have selected 3 invitro methods to detect activity, i.e., a) protein denaturation inhibition (bovine serum albumin) b) egg albumin inhibition & c) HRBC membrane stabilization. Both extracts showed significant protein denaturation inhibition in bovine serum albumin denaturation and egg albumin assay when compared with standard drug Diclofenac sodium. HRBC membrane stabilization results showed the extracts possesses membrane stabilization properties.[33]

Mohammed Safwan Ali Khan, Hidayat Ur Rahman *et al* investigated anti-inflammatory activity of methanolic leaf extracts of *Terminalia Coriacea* in Wistar albino rats. Researchers have selected both (acute and chronic) models for the study. Carrageenan induced paw oedema & cotton pellet induced granuloma were the selected acute and chronic models respectively. The standard drug used was Aspirin. Extracts showed marked decrease in the dry & wet weights of granulomatous tissue and paw oedema. Thus, the results of the study revealed the antitransudative, antiedematogenic & antiproliferative properties of *Terminalia Coriacea*.[31]

4.3. Antiarthritic activity.

Srinivasa Reddy Jitta, Prasanthi Daram *et al* undertaken a study to explore antiarthritic and anti-inflammatory activities of aqueous and alcoholic bark extracts of *Terminalia tomentosa* in Wistar rats. They have selected Carrageenan induced air pouch inflammation models to estimate anti-inflammatory activity and complete Freuds Adjuvant induced arthritis to estimate antiarthritic potential. The study was successful in proving the pronounced effects of the plant bark on arthritis and inflammation.[34]

4.4. Hepatoprotective activity

Jitendra *et al* carried out the hepatoprotective activity of methanol leaf extract of *Terminalia coriacea.* They estimated the biomarker levels like, alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), direct & total bilirubin and cholesterol to determine the degree of protection. They have also carried out the histopathology study and compared the results with standard drug Silymarin. Results clearly mentioned the significant hepatoprotective activity of *Terminalia coriacea* leaves.[35]

4.5. Antidiabetic activity

Richard Lobo *et al* evaluated in-vitro antidiabetic activity of aqueous and ethanolic stem bark extracts of *Terminalia tomentosa*. Glycosylation of hemoglobin and α amylase inhibition were studied and were found to be dose dependent manner. Result obtained confirmed the plant bark possesses antidiabetic activity.[36]

Sreelakshmi *et al* examined the antidiabetic and hepatoprotective activities of *Terminalia tomentosa* methanolic bark extracts in Albino rats. Alloxan induced diabetic model & OGTT were used to estimate antidiabetic activity. Biomedical parameters were analyzed to evaluate hepatoprotective activity. Treatment with the extract and the standard drug Glibenclamide showed significant decrease in the FBG levels in dose dependent manner. Lipid profile and liver enzymes were also corrected. Information obtained showed restoration of metabolic changes in the tested animals by the plant extract.[37]

Sravanthi Alladi *et al* investigated the hypoglycemic activity of aqueous and alcoholic leaf extracts of *Terminalia tomentosa* in normal, alloxan & dexamethasone induced diabetic rats. The extracts were found to decrease the blood sugar levels with remarkable improvement in body weight & glucose tolerance in tested male Albino rats. Repeated

administration of extracts in Dexamethasone induced insulin resistant diabetic rats showed inhibition in the increase in blood glucose level & the glucose tolerance was also shown to be improved.[38]

4.6. Antimicrobial activity

Jain Vineet C *et al* carried out a study to examine the antimicrobial and antioxidant activities of alcoholic and aqueous bark extracts of *Terminalia Crenulata* Roth. Both Gram-positive and Gram-negative organisms were selected for the test. To determine the tested sample's sensitivity, agar cup plate method was used, and to find out the minimum inhibitory concentration well micro dilution method was selected. Antioxidant activity was detected by DPPH and nitric oxide radical inhibitory activity. The data obtained showed antimicrobial activity of extracts against all tested organisms. Alcohol extract exhibited direct antimicrobial activity against the tested organisms. The results of DPPH method & nitric oxide scavenging inhibition showed that the bark of *Terminalia Crenulata* possesses potential free radical scavenging activity.[39]

Sarla Saklani *et al* investigated the antibacterial and antioxidant characteristics of aqueous and alcohol extracts of bark, stem, leaves and fruit of *Terminalia alata* Heyne ex Roth. Extracts were tested against *Staphylococcus aureus, Klebsiella pneumoniae,* & *Streptococcus pneumonia.* Results showed inhibitory activity. In the evaluation of antioxidant activity by DPPH scavenging method, extracts showed DPPH radical scavenging activity in dose dependent manner as compared to gallic acid.[40]

V. Asha Krishna *et al* performed a study on antibacterial property of stem bark & leaf extracts of *Terminalia tomentosa*. Pathogenic bacteria selected to detect the antibacterial potential of stem bark & leaf extracts (methanol, ethanol & aqueous), were *Klebsiella pneumoniae, Staphylococcus aureus* & *E. coli.* Highest zone of inhibition was exhibited by ethanolic fraction (stem bark extract against *Staphylococcus aureus* & leaf extract against *E. coli*). [26,41]

4.7. Immunomodulatory and wound healing activity

Rutika Mahendara Khamare *et al* screened the wound healing and bilirubin lowering activity of aqueous bark extracts of *Terminalia tomentosa.* The selected animals were Wistar rats. Rats were treated with phenyl hydrazine & paracetamol to induce hyperbilirubinemia. Silymarin was the standard drug selected. Incision and excision models were used to assess wound healing property by measuring percentage wound contractions, tensile breaking strength & epithelization days. In both hyperbilirubinemic models, the results exhibited a remarkable decrease in serum total bilirubin. The incision wound model results showed significant elevation in breaking strength of sutured skin and the results of excision study showed a remarkable increase in percentage of wound healing, increase in wound contraction and a decrease in epithelization period.[30]

4.8. Anti-obesity activity

Ramavat Ravindar Naik *et al* demonstrated anti-obesity effect of ethanolic bark extract of *Terminalia tomentosa* in diet induced obese rats. The extracts were administered orally to high fat diet induced obese rats. Several parameters like plasma glucose, bone mineral concentration & density, changes in body weight & composition, adiponectin, leptin, liver enzymes, tissue and circulatory lipid profiles, lipid metabolic enzymes, mRNA expressions of fatty acid synthase, leptin and tumor necrosis factor alpha, peroxisome proliferator activated receptor gamma were assessed in the presence and absence of extracts in experimental animals. Results showed reduced body weight & alterations in the pathophysiological conditions in obese rats. This study demonstrated the extracts could attenuate obesity related biochemical, physiological & molecular alterations in diet induced obese rats by balancing adipokines and lipid metabolizing enzymes.[22]

4.9. Antiepileptic activity

Shaikh Gouse Pasha *et al* performed a work to investigate the antioxidant and anti-epileptic activities of methanolic leaf extract of *Terminalia tomentosa*. Pentylene tetrazole induced convulsions and maximum electro shock induced convulsions were used to assess the anti-epileptic activity in rats. Standard phenytoin & diazepam were the drugs used in MES & PTZ induced models respectively. Duration of convulsion, latency, status of animal and percentage protection were the parameters recorded during test session of initial 30 minutes and up to 24 hours. The extract exhibited significant anti-epileptic activity. DPPH assay method (with varying concentrations of methanolic leaf extract of *Terminalia tomentosa*) was used to determine the antioxidant activity with ascorbic acid as the standard using spectrophotometer. The results obtained confirmed the antioxidant activity. The results of the study suggests that, *Terminalia tomentosa* crude methanol extract contains bioactive compounds which are responsible for the anti-epileptic end antioxidant properties. Thus, the study lends pharmacological credence to the folkloric ethnomedical uses of *Terminalia tomentosa* for the treatment of convulsions and as an antioxidant.[42]

Table 3 Beneficial medicinal properties of *Terminalia tomentosa*

Pharmacological activity	**Plant parts**	**Extracts**
Anti-oxidant	Bark	Aqueous and ethanolic [32]
Anti-inflammatory	Bark	Aqueous and ethanolic [33]
	Leaf	Methanolic [31]
Hepatoprotective	Leaf	Methanolic [35]
Antidiabetic	Bark	Aqueous and ethanolic [36]
	Bark	Methanolic [37]
	Leaf	Aqueous and alcoholic [38]
Antimicrobial	Bark	Aqueous and alcoholic [39]
	Bark, stem, leaves and fruits	Aqueous and alcoholic [40]
	Stem, bark and leaves	Methanolic, ethanolic & Aqueous [26,41]
Immunomodulatory and wound healing	Bark	Aqueous [30]
Anti-obesity	Bark	Ethanolic [22]
Antiepileptic activity	Leaves	Methanolic [42]
Antiarthritic	Bark	Alcoholic and aqueous [34]

Table 4 Screening for phytochemicals in stem of *Terminalia tomentosa* [28]

Constituents	**Chloroform**	**Ethyl acetate**	**Alcohol**
Alkaloid	-	-	-
Quinone	+	+	+
Coumarin	+	+	+
Flavone	+	+	+
Steroid	+	+	+
Phenol	+	+	+
Tannin	-	+	+
Glycoside	+	+	+
Terpenoid	+	+	+

'+' and '-' signify the presence or absence of the constituents designated.

Table 5 Phytochemical screening of *Terminalia tomentosa* bark [26]

Constituents	Chloroform	Ethyl acetate	Alcohol	Aqueous
Alkaloids	++	++	++	++
Flavonoids	-	-	++	++
Phenols	-	-	++	++
Steroids	-	-	++	+
Saponins	-	-	-	++
Tannins	-	-	++	++
Anthocyanidins	-	-	++	++
Lignins	-	-	++	++
Indole	-	--	-	-
Glycosides	-	-	-	-

High = ++; Moderate = +; Absent = -

Table 6 Phytochemical screening of *Terminalia tomentosa* leaves [23]

Constituents	Chloroform	Ethyl acetate	Methanol	Aqueous
Alkaloids	-	-	-	-
Glycosides	-	-	+	-
Flavonoids	-	-	+	+
Saponins	-	-	+	-
Phenolics	-	-	+	-
Proteins and Amino acids	-	-	-	-
Carbohydrate	-	-	+	-
Diterpenes	-	-	-	-
Tannin	-	+	+	+

'+' and '-' signify the presence or absence of the constituents designated.

Table 7 Screening for phytochemicals in fruits of *Terminalia tomentosa* [40]

Constituent	Hydroalcoholic
Alkaloids	-
Carbohydrate	+
Saponins	+
Phenolic compounds	+
Tannins	+
Flavonoids	+
Terpenoids	+
Proteins	-

'+' and '-' signify the presence or absence of the constituents designated.

5. Conclusion

The existing literature verification of *Terminalia tomentosa* divulged that every part of this plant is therapeutically significant with remarkable number of phytochemical and pharmacological properties and contain medicinally dominant chemicals such as alkaloids, cardiac glycosides, anthocyanins, flavonoids, phytosterols, tannins, triterpenoids & saponins. These biomedical compounds present are assumed to be in charge of the pharmacological activities like anti-oxidant, anti-inflammatory, hepatoprotective, antidiabetic, antimicrobial, antiepileptic, wound healing. However, extensive research progress on molecular and clinical level are necessary to appreciate primary mechanism of action, drug interactions, drug administration & toxicological studies in order to demonstrate it as a standard drug and so that the plant can be used significantly for the treatment and prevention of ailments.

Significance statement

This review efforts to give the literature aspects such as pharmacognosy, phytochemistry and pharmacological studies on *Terminalia tomentosa*. This can be beneficial for the students and researchers to acquire information in a comprehensive form.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors assure that there is no conflict of interest with the publication of the manuscript.

Author's contribution

- Lavanya KP: First author, Research Scholar
- Dr. Abhinandan Kumar Danodia: Research Guide
- Dr. Ajith Babu TK: Research Co-Guide

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