

PHCOG REV.: Plant Review

Terminalia chebula: An update

R.R. Chattopadhyay, S.K. Bhattacharyya

Agricultural and Ecological Research Unit

Indian Statistical Institute

203, Barrackpore Trunk Road

Kolkata – 7800 108, India

E-mail IDs : rabi@isical.ac.in ; rabi_chattopadhyay@yahoo.com Fax : +(91)(33)2577-3049

Abstract

Terminalia chebula Retz. (Combretaceae) is called the “King of Medicines” in the Tibet and is always listed first in the Ayurvedic materia medica because of its extraordinary powers of healing with a wide spectrum of biological activity. The fruit of *Terminalia chebula* Retz. is being used for the treatment of different types of diseases and disorders since antiquity. During the last five decades, apart from the chemistry of *Terminalia chebula* compounds, considerable progress has been achieved regarding the biological activity and medicinal applications of *Terminalia chebula*. It is now considered as a valuable source of unique natural products for development of medicines against various diseases and also for the development of industrial products. This review gives a bird’s eye view mainly on the biological and pharmacological activities of *Terminalia chebula* extracts and some of its isolated compounds, clinical studies, plausible medicinal applications along with their safety evaluation.

Key words : *Terminalia chebula* ; Phytoconstituents ; Biological and Pharmacological activities ; Clinical studies; Medicinal uses ; Safety evaluation

INTRODUCTION

Medicinal plants are part and parcel of human society to combat diseases, from the dawn of civilization. Herbal medicines are in great demand in the developed as well as developing countries for primary healthcare because of their wide biological and medicinal activities, higher safety margins and lesser costs. *Terminalia chebula* is a plant species belonging to the genus *Terminalia*, family *Combretaceae*. It is a flowering evergreen tree called in English the black myrobalan. It is also known as *Haritaki* (Sanskrit and Bengali), *Harad* (Hindi), *Karkchettu* (Telugu), *Kadukkaya* (Tamil), *Harada* (Marathi & Gujrati). It is native to Indian subcontinent and the adjacent areas such as Pakistan, Nepal and the South-West of China stretching as far south as Kerala or even Sri Lanka where it is called *Aralu*. The fruit of the tree has been used as traditional medicine for household remedy against various human ailments, since antiquity (1-8). *Terminalia chebula* has been extensively used in Ayurveda, Unani and Homoeopathic medicine and has become a cynosure of modern medicine. The Sanskrit name ‘*Haritaki*’ is rich with meaning, referring to the yellowish dye (*harita*) that contains, as well as indicating that it grows in the abode of the god Siva (Hari, i.e. the Himalayas), and that it cures (*harayet*) all diseases (6). Its other commonly used Sanskrit name, *Abhaya*, refers to the ‘fearlessness’ it provides in the face of the disease. According to Indian mythology, this plant originated from the drops of *ambrosia* (Amrita) which fell on the earth when Indra was drinking it (9).

Species identity

Taxonomy

Current Name : *Terminalia chebula*

Authority : Retz.

Family : *Combretaceae*

Synonym(s)

Terminalia parviflora Thwaites

Terminalia tomentella kurz

Terminalia zeylanica van Heurck & Muell, Arg.

Common Names

(Cambodia) : *Sa mao tchet*

(Filipino) : *Chebolic myrobalan*

(French) : *myrobalan noir*

(Malay) : *manja puteri (unripe fruit)*

(Thai) : *samo thai (central)*

(Vietnamese) : *chieu lieu xanh*

Ecology and Distribution

History of cultivation

Terminalia chebula has been introduced to Singapore, where it failed, but it was planted successfully in the botanical garden in Bogor, Java. It was also introduced to Peninsular Malaysia.

Natural Habitat

Terminalia chebula occurs scattered in teak forest, mixed deciduous forest, extending into forests of comparatively dry types.

Biophysical limits

Altitude : up to 1500 (-2000) m,

Soil type : The species is found on a variety of soils, clayey as well as shady.

Botanic Description

Terminalia chebula is a medium to large deciduous tree attaining a height of up to 30 m, with widely spreading branches and a broad roundish crown. The leaves are elliptic

Sl.No	Species Name	Feature	Use	Place of origin
1.	<i>Vijaya</i>	Oval	All the diseases	Vindhya
2.	<i>Rohini</i>	Circular	In wounds and ulcers	Pakisthanka
3.	<i>Putana</i>	Little, Very hard	As a dressing	Sindha
4.	<i>Amrita</i>	Thick outer layer	For purification purpose	Champa Bhagalpur
5.	<i>Abhaya</i>	Having 5 lines	For eye disorders	Champa Bhagalpur
6.	<i>Jivanti</i>	Golden colour	For all diseases	Saurastra Gujrat
7.	<i>Chetaki (white)</i>	Having 3 lines	For purgation	Saurastra Gujrat
8.	<i>Chetaki (Black)</i>	Having 3 lines	For purgation	Himachal

oblong, with an acute tip, cordate at the base, margins entire, glabrous above with a yellowish pubescence below. The flowers are monoecious, dull white to yellow, with a strong unpleasant odour, borne in terminal spikes or short panicles. The fruits are glabrous, ellipsoid to ovoid drupes, yellow to orange brown in colour, containing a single angle stone. *Terminalia chebula* is found throughout deciduous forests of the Indian subcontinent, on dry slopes up to 900 meters in elevation.

Parts used : fruit

Dravyguna : Fresh fruit

Rasa : kasaya, tikta, amla, katu, madhura

Vipaka : madhura

Virya : usna

Karma : dipanapacana, bedhanam (curna), grahi (kvatha, tincture), krmighna, Mutravirecana, jvaraghna, svasahara, kasahara, kusthaghna, sothahara, Medhya, vedanasthapana, sandhaniya, cakusya, hrdaya, rasayanam, tridosaghna

Prabha: named for the god Siva (*Hari*), who brings 'fearlessness' (*abhaya*) in the face of death and disease, and because it purifies the mind of attachment. (10,11).

Species in Ayurveda:

Bhava Prakasha, the author of famous *Ayurvedic Materia Medica* described the seven species of *Terminalia chebula*. This classification is based on the location, qualities and actions of the plant (9,12,13). Generally speaking the *Vijaya* variety is preferred, which is traditionally grown in the Vindhya mountain range of central India, and has a roundish as opposed to a more angular shape (9). For practical purposes, the fruit of *Terminalia chebula* is of three types - actually these are the different stages of maturity of fruits (14,15).

- (a) Small myrobalan - the unripe fruit
- (b) Yellow myrobalan - After the development of seed, the adult stage of the fruit
- (c) Large Myrobalan - The fully matured fruit

Chemical constituents:

Terminalia chebula is rich in tannin. The chief constituents of tannin are chebulic acid, chebulagic acid, corilagin and gallic acid (16-19). Tannin of *Terminalia chebula* are of pyrogallol (hydrolyzable) type. A group of researchers found 14 components of hydrolyzable tannins (gallic acid, chebulic acid, punicalagin, chebulanin, corilagin, neochebulinic acid, ellagic acid, chebulegic acid, chebulinic acid, 1,2,3,4,6-penta-O-galloyl-β-D-glucose, 1,6-di-O-galloyl-D-glucose, casuarinin, 3,4,6-tri-O-galloyl-D-glucose, terchebulin) from

Terminalia chebula fruits (20). One source lists *Terminalia chebula* as having 32% tannin content (21). The tannin content of *Terminalia chebula* varies with geographical variation (22). Besides, fructose, amino acids, succinic acid, betasitosterol, resin and purgative principle of anthroquinone and sennoside nature is also present (19,23). Flavonol glycosides, triterpenoids, coumarin conjugated with gallic acids called chebulin as well as other phenolic compounds were also isolated (24-27).

Biological and Pharmacological activities of *Terminalia chebula*

Antibacterial activity

Terminalia chebula exhibited antibacterial activity against a number of bacterial species (28). One group of researchers found that it is effective in inhibiting the urease activity of *Helicobacter pylori* (*H. pylori*), an ubiquitous bacterium implicated in the development of gastritis, ulcers and stomach cancers (29). Antibacterial activity of *Terminalia chebula* against both Gram positive and Gram negative human pathogenic bacteria has also been reported (30). Gallic acid and its ethyl ester isolated from ethanolic extract of *Terminalia chebula* showed antimicrobial activity against methicillin-resistant *Staphylococcus aureus* (31). Diffusate of *Terminalia chebula* showed an inhibitory effect against strain XC-100 of the bacterium *Xanthomonas Campestris* pv. *citri* indicating its usefulness for the management of citrus canker disease (32). It has also growth inhibitory action against *Salmonella typhi* (33) and intestinal bacteria (34).

Antifungal activity

An aqueous extract of *Terminalia chebula* exhibits antifungal activity against a number of dermatophytes and yeasts (35,36). It is effective against the pathogenic yeast *Candida albicans* and dermatophytes *Epidermophyton*, *Floccosum*, *Microsporum gypseum* and *Trichophyton rubrum* (37). Its inhibitory effect on three dermatophytes (*Trichophyton* spp.) and three yeasts (*Candida* spp.) has also been documented (38).

Antiviral activity

Terminalia chebula fruits afforded four immunodeficiency virus type 1 (HIV-1) integrase inhibitors, gallic acid (1) and three galloyl glucoses (2-4). Their galloyl moiety plays a major role for inhibition against the 3'-processing of HIV-1 integrase of the compounds (39). *Terminalia chebula* has also retroviral reverse transcriptase inhibitory activity (40). It protects epithelial cells against influenza A virus, supporting its traditional use for aiding in recovery from acute respiratory infections (41). It also showed a significant

inhibitory activity on the effects of immunodeficiency virus-1-transcriptase (42). *Terminalia chebula* has demonstrated therapeutic activity against *Herpes Simplex Virus* (HSV) both *in vitro* and *in vivo* tests (43). These finding prompted a team of Japanese researchers to investigate *Terminalia chebulas's* effect on human cytomegalovirus (CMV). They found that *Terminalia chebula* was effective in inhibiting the replication of human cytomegalovirus *in vitro* and in an AIDS model with immunosuppressed mice and concluded that it may be beneficial for the prevention of CMV diseases and immunocompromised patients (44). It is also helpful in sexually transmitted diseases and AIDS (45).

Antimutagenic/anticarcinogenic activity

Antimutagenic activity of hydrolyzable tannins from *Terminalia chebula* in *Salmonella typhimurium* has been documented (46). A group of researchers have reported the inhibitory action on cancer cell growth by the phenolics of *Terminalia chebula* Retz fruit and found that chebulinic acid, tannic acid and ellagic acid were the most growth inhibitory phenolics of *Terminalia chebula* (47). Besides, acetone extract of bark and fruit powder of *Terminalia chebula* harbors constituents with promising antimutagenic/anticarcinogenic activity (48).

Antioxidant activity

Six extracts and four compounds of *Terminalia chebula* fruit exhibited antioxidant activity at different magnitudes of potency (49). Its fruit exerts antioxidant and radioprotective activity in rats (50). Protective effects of an aqueous extract of *Terminalia chebula* fruit on the tert-butyl hydroperoxide (t-BHP)-induced oxidative injury observed in cultured rat primary hepatocytes and rat liver have also been documented (51,52). It has stronger antioxidant activity than alpha-tocopherol; HPLC analysis with diode array detection indicated the presence of hydroxybenzoic acid derivatives, hydroxycinnamic acid derivatives, flavonol aglycones and their glycosides, as main phenolic compounds (53).

Adaptogenic and antianaphylactic activities

Terminalia chebula fruit was one of the six Ayurvedic herbs administered to animals to test their adaptogenic potential. All six traditional rasayana plants were able to aid the animals against a variety of different stressors working in different ways (54). Besides, animal studies show that when extract of *Terminalia chebula* was administered following induction of anaphylactic shock, the serum histamine levels were reduced, indicating its strong antianaphylactic action (55).

Hypolipidemic / Hypocholesterolemic activity

Hypolipidemic activity of *Terminalia chebula* extract against experimentally induced atherosclerosis have been documented (56). It also possessed hypocholesterolemic activity against cholesterol-induced hypercholesterolemia and atherosclerosis in rabbits (57).

Gastrointestinal motility improving and anti-ulcerogenic activity

Although its traditional use as laxative is well established, *Terminalia chebula* fruit has been shown to increase gastric emptying time (58). This action appeared to be balanced with a protective effect on the gastrointestinal mucosa, with

the improvement in the secretory status of Brunner's gland involved in the protection against duodenal ulcer (59).

Hepatoprotective activity

Terminalia chebula extract was found to prevent the hepatotoxicity caused by the administration of rifampicin (RIF), isoniazid (INH) and pyrazinamide (PZA) (combination) in sub-chronic model (12 weeks) (60).

Cardioprotective activity

Terminalia chebula extract pretreatment was found to ameliorate the effect of isoproterenol on lipid peroxide formation and retained the activities of the diagnostic marker enzymes in isoproterenol induced myocardial damage in rats (61). Its pericarp has also been reported to have cardioprotective activity in isolated frog heart model (62).

Cytoprotective activity

Gallic acid (GA) and chebulic acid (CA) were isolated from the extract of the herbal medicine Kashi (myrobalan, the fruit of *Terminalia chebula*) as active principal that blocked the cytotoxic T-lymphocyte (CTL)-mediated cytotoxicity. Granule exocytosis in response to anti-CD3 stimulation was also blocked by GA and CA at the equivalent concentrations (63). The ethanolic extract of *Terminalia chebula* fruit exhibited a notable cytoprotective effect on the HEK-N/F cells. In addition its extract exhibited significant cytoprotective effect against UVB-induced oxidative damage. These observations were attributed to the inhibitory effect of the *Terminalia chebula* extract on the age dependent shortening of the telomere length as shown by the Southern Blots of the terminal restriction fragments (TRFs) of DNA extracted from sub-culture passages (64). It exhibited the development of duodenal ulcers and appeared to exert a cytoprotective effect on the gastric mucosa *in vivo* (65). Cytoprotective effect on oxidative stress and inhibitory effect on cellular aging of its fruits have also been documented (66).

Radioprotective activity

The administration of *Terminalia chebula* extract prior to whole body irradiation of mice resulted in a reduction of peroxidation of membrane lipids in the mice liver as well as a decrease in radiation induced damage to DNA. It also protected the human lymphocytes from undergoing the gamma radiation-induced damage to DNA exposed *in vitro* (67).

Antidiabetic and retinoprotective activity

Terminalia chebula fruit exhibited dose dependent reduction in blood glucose of streptozotocin induced diabetic rats both in short term and long term study and also had retinoprotective activity (68-70).

Antispasmodic activity

One of the numerous studies of *Terminalia chebula* demonstrated its 'anti-vata' or 'anti-spasmodic' properties by the reduction of abnormal blood pressure as well as intestinal spasms. This confirm its traditional usefulness for spastic colon and other intestinal disorders (71).

Wound healing activity

Topical administration of an alcoholic extract of *Terminalia chebula* leaves on the healing of rat dermal wounds showed that *Terminalia chebula* treated wounds healed faster as

indicated by improved rates of contraction and decreased period of epithelialization (72).

Purgative property

Purgative action of an oil fraction from *Terminalia chebula* has been documented (73).

Immunomodulatory activity

Aqueous extract of *Terminalia chebula* produced an increase in humoral antibody (HA) titer and delayed type hypersensitivity (DTH) in mice (74).

Antiamoebic activity

A combination of *Terminalialia chebula* and four other botanicals (*Boerhavia diffusa*, *Berberis aristata*, *Tinospora cordifolia*, and *Zingiber officinale*) had a maximum cure rate of 73% in experimental amoebic liver abscess in hamsters (75) and 89% in experimental caecal amoebiasis in rats showing its antiamoebic activity against *Entamoeba histolytica* (76).

Chemopreventive activity

Terminalia chebula showed chemopreventive effect on nickel chloride -induced renal oxidative stress, toxicity and cell proliferation response in male Wistar rats (77).

Clinical studies :

(a) Oral rinsing with an extract of *Terminalia chebula* was found to significantly reduce both total bacterial counts and streptococcal counts in saliva samples. The protective effect lasted for up to 3 hours after rinsing, demonstrating a potential role for *Terminalia chebula* in the prevention of dental caries (78).

(b) A short term clinical trials have been carried out on patients with simple constipation. *Terminalia chebula* increases the stools and has got property of evacuating the bowel completely (79).

(c) Besides, some Ayurvedic drugs, consisting of *Terminalia chebula* as one of the constituents have been subjected to clinical trials regarding their effects on constipation, mental and physical disability, allergic rhinitis and mental stress. In all the cases *Terminalia chebula* containing drugs showed good effects without showing any adverse effects in the treated groups when compared to their normal control patients (80-83).

Indications

Constipation, diarrhoea, ulcers, gastroenteritis, asthma, cough, dyspnea, dyspepsia, hemorrhoids, candidiasis, parasites, malabsorption syndrome, hepatomegaly, ascotes, vesicular and renal calculi, urinary discharges, tumors, skin diseases, leprosy, intermittent fever, rheumatism, arthritis, gout, neuropathy, paralysis, memory loss, epilepsy, depression, leucorrhoea, diabetes, cardiovascular diseases, anorexia, wounds (1-9).

Contraindications

Pregnancy, dehydration, emaciation (14). *Terminalia chebula* is contraindicated in weak digestion, fatigue due to excessive sexual activity, with alcohol drink and in hunger, thirst and heat stroke (84).

Plausible Medicinal applications of *Terminalia chebula*

Its paste with water is found to be anti-inflammatory, analgesic and having purifying and healing capacity for wounds. These are used for astringent purpose in hemorrhoids as well (1,8). Its decoction is used as gargle in

oral ulcers, sore throat. Its powder is a good astringent dentrifice in loose gums, bleeding and ulceration in gums. It is good to increase the appetite, as digestive aid, liver stimulant, as stomachic, as gastrointestinal prokinetic agent and mild laxative (1,5,7). The powder of *Terminalia chebula* fruit has been used in chronic diarrhoea, sprue with good results. It should be used as hot infusion in these disorders. It is indicated in protected diarrhoea with haematochezia and prolaps of rectum. The chebulic acid from *Terminalia chebula* fruit has shown antispasmodic action like that of Papaverina. Being a mild laxative, it is a mild herbal colon cleanse (7,8). It is a good nerveine. It is used in various weakness, nervous irritability. It promotes the receiving power of five senses (6). It is good for chronic cough, coryza, sore throat and asthma. It is helpful in renal calculi, dysurea and retention of urine (2,6). It is useful in skin disorders with discharges like allergies, urticaria and other erythematous disorders (4). It is given as adjuvant herb in chronic fever. It saves the person from the vitiating effects of bodily humors. Thus it is considered as an alternative and adaptogen (3,5). It reduces the ill effects of the fat rich, creamy and oily food. *Terminalia chebula* is the definite aid for persons who habituating overeat. Further it can supplement to cholesterol normalizing drugs (5).

Safety Evaluation

(a) Most of the toxicological studies report that toxic effects due to the use of herbal medicine are associated with hepatotoxicity. Other toxic effects of the kidney, nervous system, blood and cardiovascular system, as well as mutagenicity and carcinogenicity have also been published in medical journals. Therefore, numerous advance biological experimental techniques have been used as standard safety test prior to the efficacy study. From the literature it has been noted that *Terminalia chebula* exhibited significant hepatoprotective (60), cardioprotective (61,62), antimutagenic/anticarcinogenic (46-48), cytoprotective (63-66), radioprotective (67), antioxidant (49-53), and adaptogenic (54,55) effects indicating that it is a safe substance to be used as a drug ordinarily.

(b) Non-cytotoxic effect

The active crude alcoholic extract of *Terminalia chebula* was assayed for cellular toxicity to fresh sheep erythrocytes and found to have no cellular toxicity (28). Besides, it does not exert any cytotoxic effect in *Allium* model (85). These findings demonstrated its non-cytotoxic effect.

(c) Non-genotoxic effect

Terminalia chebula by itself had no genotoxic effect both in VITOTOX test and Ames assay (86).

(d) A group of researchers however reported that feeding trials in rats with *Terminalia chebula* produced hepatic lesions that included central vein abnormalities and marked renal lesions (87). Given the long history of usage and popularity of *Terminalia chebula*, this single study cannot be reliably extrapolated to human usage.

CONCLUSION

Terminalia chebula is highly regarded as an universal panacea in the Ayurvedic medicine. It is one of the most versatile plants having a wide spectrum of medicinal activities. This versatile medicinal plant is the unique source of various types of compounds having diverse chemical structure. Very little work has been done on the plausible medicinal applications of these compounds and hence extensive investigation is needed to exploit their therapeutic utility to combat diseases. A drug development programme should be undertaken to develop modern drugs with the compounds isolated from *Terminalia chebula*. Although crude extracts from fruit part of *Terminalia chebula* have medicinal applications from time immemorial, modern drugs can be developed after extensive investigation of its bioactivity, mechanism of action, pharmacotherapeutics, toxicity and after proper standardization and clinical trials. As the global scenario is now changing towards the use of nontoxic plant products having traditional medicinal use, development of modern drugs from *Terminalia chebula* should be emphasized for the control of various diseases.

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