

# Phytochemical and Biological Effects of *Terminalia Chebula* Retz: A Short Review

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## ABSTRACT

*Terminalia chebula* Retz. commonly known as 'Harar' belongs to the family Combretaceae. It is found in deciduous forests throughout the greater part of India, China, Myanmar, Sri Lanka, Vietnam, Bangladesh, etc. In India, it is distributed throughout the greater part except in arid zones. *T. chebula* (Family: Combretaceae) is a medicinal plant with a wide spectrum of medicinal properties and is reported to contain various biochemicals such as hydrolysable tannins, phenolic compounds, and flavonoids, so it may prove to be a good therapeutic alternative. The fruits are common constituent of 'Triphala', capable of imparting youthful vitality and receptivity of mind and sense and are extensively used for clinical research, tanning and furniture purposes and also contain 1.73% nitrogen and 2.75% Calcium. The demand for its fruit has increased tremendously, because of its medicinal value.

**Keywords:** *Terminalia Chebula*; Chemical Compounds; Plants; Bioactivities

## Introduction

Plants have been an important source in cancer drug discovery. The medicinal values of plants lie in their phytochemicals, which makes specific physiological actions on the human body. Phytochemicals are compounds found in plants that are utilized as food and medicine to top reserve against illness and to ensure human health.

One particular herbal remedy is *Terminalia chebula* Retz. (Combretaceae) because of its numerous and different types of phytoconstituents such as polyphenols, terpenes, anthocyanins, flavonoids, alkaloids, and glycosides. In traditional medicine, the fruits of the *T. chebula*, which hold various chemically active compounds responsible for its medicinal properties, have been used in Unani, Ayurveda, and homeopathic medicine since antiquity to treat geriatric diseases and improve memory and brain function (Saleem, et al. 2007, Ali, et al. [1]). *Terminalia chebula* Retzius (Family: Combretaceae), as a shade and ornamental tree with 250 species, is a medicinal plant that grows in the Middle East and tropical regions such as India, China, and Thailand. It can grow to be 25 meters tall and has a variable appearance and spreading branches. The color of the bark is dark brown

and is usually cracked. Leaves are thin, elliptic-oblong, cordiform at the base, elliptical, and 7-12 cm long and 4-6.5 cm in width and have a leathery form with entire margins. The upper surface of the leaves is glabrous opposite of the surface beneath. The lower surface is fultile with a white to yellowish color and unsightly odor. Flowers have 5-7 cm long spikes, simple or branched, about 4mm across.

The ovary is inferior with 10 stamens. Fruits are yellow to orange-brown when ripe and 2.5-5 cm long and unruled with an ovate-drupe shape. It is also commonly used to treat numerous diseases such as cancer, cardiovascular diseases, paralysis, leprosy, ulcers, gout, arthritis, epilepsy, cough, fever, diarrhea, gastroenteritis, skin disorders, urinary tract infection, and wound infections (Rathinamoorthy, et al. [2,3]). Recent studies show that *T. chebula* is effective in the treatment of diabetes (Rao, et al. [4]), bacterial and fungal infections (Aneja, et al. [5,6]), immunodeficiency diseases (Ahe, et al. [7,8]), hyperlipidemia (Maruthappan, et al. [9]), liver diseases (Srigopalram, et al. [10]), stomach ulcer (Sharma, et al. [11]), and wounds (Singh, et al. [12]). This review gives previous phytochemical studies and biological activities of *Terminalia chebula*.

## Phytochemicals

In *Terminalia chebula*, the main phytoconstituents in it are hydrolysable tannins (which may vary from 32 phytoconstituents present in *Terminalia chebula* steroids, amino acids, fructose, resins, fixed oils, anthraquinone, carbohydrates, glucose, sorbitol etc. the plant fairly rich in hydrolysable tannins. Researchers found that *Terminalia chebula* components of hydrolysable tannins like gallic acid, chebulic acid, punicalagin, chebulanin, corilagin, neochebulinic, ellagic acid, chebulagic acid, 1,2,3,4,6,1,6-di-o-galloyl-D-glucose and Terchebulin (Kumar, et al. [13,14]). The main phytoconstituents in it are hydrolysable tannins (which may vary from 32-34%) other *Terminalia chebula* compounds are flavanoids, steroids, amino acids, fructose, resins, fixed oils, carbohydrates, glucose, sorbitol etc. the plant is fairly rich in hydrolysable tannins. *Terminalia chebula* contain 14 components of hydrolysable tannins like gallic acid, chebulic, corilagin, neochebulinic, ellagic acid, chebulagic acid, 1,2,3,4,6-penta-orgalloyl- $\beta$ -D-glucose, glucose and Terchebulin (Kumar, et al. [13]). Phytochemicals as anthraquinone ethadiolic acid, sennoside, 4,2,4-chebylyl-d-glycopyranose terpenes and terpinols have also been reported. The tannin content varies with geological variations. Some other minor chemical constituents were polyphenols such as corilagin, galloyl glucose, punicalagin, terflavinA, maslimic acid. Fructose, amino acid, succinic acid, betasitosterol, resin and purgative principle of anthraquinone are also present (Quanbin, et al. [15]).

12 fatty acids were isolated from *Terminalia chebula* has palmitic, linoleic acid and oleic acid were main constituents. Triterpenoid glycosides such as chebulosides 1 and 2, arjunenin glucoside, 2 $\alpha$ -hydroxymicromiric acid and 2 $\alpha$ -acid also have been reported. The leaves were found to contain polyphenols such as punicalin, punicalagin, terflavins B, C and D (Patel, et al. [16,17]). The plant is also is also found to contain phloroglucinol and pyragallo, along with phenolic acids such as ferulic, p-coumeric, caffeic and vanillic acids. Recent studies show that *Terminalia chebula* contains more phenolics than other plants (Mahajan, et al. [18]).

## Biological Activities

**Anti-Bacterial Effect:** Reported antibacterial property of *Terminalia chebula* indicated activity against different gram positive and gram negative bacteria as salmonella typhi, staphylococcus epidermidis, staphylococcus aureus, bacillus subtilis and pseudomonas aeruginosa suggesting that it is a broad spectrum antibacterial remedy. Gallic acid and ethyl ester, these two antibacterial compounds have been isolated from ethyl extract of fruits of *Terminalia chebula*, these two acts against helicobacter pylori. Ether and alcohol extract of *Terminalia chebula* were tested against helicobacter pylori. The aqueous extract of the plant, at a concentration of 1.2-5mg/ml, inhibited urease activity oh helicobacter pylori. Ethanediolic acid present in *Terminalia chebula* indicated strong inhibitory effect against clostridium perfringens and it showed moderate inhibitory activity against

*Eischerechia coli*. In both the cases there is no adverse effects on the growth of these four tested lactic acid producing bacteria. Ellagic acid exerted a potent inhibitory effect against clostridium perfringens and E.coli, but little or no inhibition was observed for behenic acid;  $\beta$ -caryophyllene, eugenol, isoquercetin, oleic acid,  $\alpha$  phellendone,  $\beta$ -sitosterol, stearic acid,  $\alpha$  terpinene, terpinolene or triacontanoic acid. *Terminalia chebula* fruit extract had strong antibacterial activity against intestinal bacteria, clostridium perfringens and E.coli. Overall studies prove that ethanol extract is effective against salmonella typhi, staphylococcus aureus, bacillus subtilis. Ether, alcoholic and aqueous extract has potent activity against helicobacter pylori (Kannan, et al. [19]).

**Anti-Fungal Effect:** Aqueous extract of *Terminalia chebula* showed antifungal activity against a number of dermatophyte and yeasts. The alcoholic ethyle acetate extract shows the effect against Aspergillus niger, aspergillus flavus, alternate. 70% of methanol ethylacetate, hexane, chloroform extract shows activity against fusarium oxysporum, phytophthora capsici, fusarium solani etc (Dutta, et al. [6]; Mehmood, et al. 1999).

**Immunomodulatory Effect:** Aqueous extract of *Terminalia chebula* showed an increase in humoral antibody, titre and delayed type of hypersensitivity in mice. Alcoholic extract of *Terminalia chebula* shows immunomodulatory activity in male wistar rats. *Terminalia chebula* stimulated cell mediate immune response in experimental amoebic liver abscess in golden hamsters. *Terminalia chebula* found to be effective against the progression of advanced glycation end products induced endothelial dysfunction (Sohni, 1996).

**Antioxidant Effect:** Prominent antioxidant property is reported in *Terminalia chebula*. The activity is reported in the leaves, bark and fruit of *Terminalia chebula*. Analysis of the fruit of *Terminalia chebula* extract shows that it contains phenolic compound which are good scavengers of free radicals. It also exhibit anti lipid peroxidation, antiperoxide radical formation and free radical scavenging activity. It is found that the methanolic extract has the greatest triterpenoid content and exhibited good antioxidant activity in HRP-luminal-H<sub>2</sub>O<sub>2</sub> assay, on the other hand aqueous extract has the greatest phenolic and tannin content and showed good antioxidant activity in both copper sulphate phen-VC-H<sub>2</sub>O<sub>2</sub> and luminal H<sub>2</sub>O<sub>2</sub> assays. *Terminalia chebula* when used in a polyherbal formulation (Alter-7/NR-AZ) inhibited free radical induced hemolysis and also significantly inhibited NO release from lipopolysaccharide stimulated murine macrophages. Acetone extract shows stronger antioxidant activity than alpha tocopherol. An aglycone isolated from the fruit of *Terminalia chebula*, significantly inhibited ferrous shulphate /cyst-induced microsomal lipid peroxidation and protect both H<sub>2</sub>O<sub>2</sub> induced hemolysis and auto RBC hemolysis in dose dependent manner. The results demonstrated that triethylchebulate was a strong antioxidant and free radical scavengers, which might contribute to the antioxidant property (Cheng, et al. [20,21]).

**Anti-Mutagenic and Anti-Carcinogenic Effects:** The 70% methanolic extract of fruit of *Terminalia chebula* was studied on the growth of several malignant cell lines including a human (MCF-7) and mouse (S11S) breast cancer cell line, a human osteosarcoma cell line (HOS-1), a human prostate cancer cell line (PC-3) and non-tumorigenic immortalized human prostate cell line (PNT1A) using array for proliferation (3H-thymidine incorporation and counter counting, cell viability (ATP determination and cell death flow cytometry and horchst DNA staining). The chloroform extract, acetone, and aqueous extract of *Terminalia chebula* indicated activity against salmonella typhimurium. All the extracts studied in several cell lines shows a decreased cell viability, inhibited cell proliferation and induced cell death in dose dependent manner. Chebulagic acid showed potent dual inhibition against COX and 5-LOX. It also show antiproliferative activity against HCT-15, COLO-205, MDA-MD-231 DU-145 and K562 cell lines. In another study acetone extract of bark and fruit powder of *Terminalia chebula* showed anticarcinogenic activity (Reddy, et al. [22,23]).

**Anti-Amoebic and Anti-Protozoal Effects:** *Terminalia chebula* showed antiamoebic activity against entamoeba histolytica in experimental caecal amoebiasis *in vivo*. The extract of *Terminalia chebula* seeds showed anti plasmodial activity against plasmodium falciparum (Sohni, et al. [24,25]).

**Anti-Arthritic Effect:** *Terminalia chebula* could be used as a disease modifying agent in treatment of rheumatoid arthritis. Studies show that acetone extract of fruit of *Terminalia chebula* have better effect on controlling CFA induced arthritis showing the definite effect in reducing the inflammatory components. Aqueous extract of dried fruit of *Terminalia chebula* showed anti-inflammatory by inhibiting inducible NO synthesis. Chebulagic acid isolated from the ethanolic extract of *Terminalia chebula* fruit significantly suppressed the onset and progression of collagen induced arthritis in mice. The hydrochloric extract of *Terminalia chebula* indicated a significant inhibition of joint swelling as compared to control in both formaldehyde induced and CFA induced arthritis. Polyherbal formulation of *Terminalia chebula* (Alter-7) exhibited anti-inflammatory effect against arthritis in rats (Nair, et al. [26]).

**Anti-Diabetic Activity:** 75% methanolic extract of *Terminalia chebula* lowered the blood sugar level in normal and alloxan induced diabetic rats significantly within 4 hours when administered orally. Dose dependent reduction in blood glucose of streptozotocin induced diabetic rats both in short term and long term study is reported in ethanolic extract of *Terminalia chebula* seeds (200mg/kg body weight). The chloroform extract of *Terminalia chebula* seeds (100, 200 and 300mg/kg body weight) indicated dose dependent reduction in blood glucose of diabetic rats in both short term and long term. The aqueous extract of *Terminalia chebula* (200mg/kg body weight for 2 months) reduced the elevated blood glucose and increase in glycosylated hemoglobin. The same dose also showed a marked improvement in con-

trolling the elevated blood lipids as well as decrease in serum insulin levels. The *in vitro* studies with pancreatic islets showed that the insulin release was nearly 2 times more than that in the untreated diabetic animals (Rao, et al. [4,27]).

**Wound Healing Effect:** An alcoholic extract of the leaves of *Terminalia chebula* caused much faster healing of rat dermal wounds which when applied topically. Studies revealed increase in total protein DNA and collagen content in the granulation tissues of treated wounds. Hydroalcoholic extract of *terminalia chebula* showed effective wound healing property in alloxan induced diabetic rats. 90% of the ethanolic extract of *Terminalia chebula* indicated wound healing property in wistar albino rats. The levels of hexosamine and uronic acid also increased upto day 8 post wounding. Tannins extracted from immature fruits of *terminalia chebula* inhibited staphylococcus aureus, klebsiella and pneumonia *in vitro* and promoted cutaneous wound healing in rats due to a powerful antibacterial and angiogenic activity of the extract. The wound healing activity of ethanolic extract of fruits *Terminalia chebula* in the form of an ointment with 2 concentrations (5% and 10% w/w ointment of bark extract in simple ointment base) showed significant response in excision and incision models in albino rats compared to controls (Sugun, 2006) (Singh, et al. [12]).

**Anti-Viral Effect:** A study proved that *Terminalia chebula* fruits contain 4 human HIV type I integrase inhibitors such as gallic acid and 3 galloyl glucose. The aqueous extract of *Terminalia chebula* exhibited the most prominent anti HBV activity by decreasing the level of extracellular HBV virion DNA at concentration ranging from 64-128µg. The extracts of fruit of *Terminalia chebula* showed inhibitory effect on human immunodeficiency virus reverse transcriptase. Acetone extract of *Terminalia chebula* indicated antiviral activity against swine influenza A virus and aqueous extract of *Terminalia chebula* showed antiviral extract against hepatitis B virus (Mekaway, et al. [28]) (Yuhan, et al. 1996).

**Anti-Convulsant Effect:** The ethanolic extract of *Terminalia chebula* significantly reduced the duration of seizures induced by maximal electro shock. Ethanolic extract conferred protection on the mice. Ethanolic extracts possess anticonvulsant activity since it reduces the duration of seizures produced by maximal electro shock and delayed the latency of seizures produced by pentylentetrazole and picrotoxin (Hogade, et al. [29]).

**Cytoprotective Effect:** The ethanolic extract showed a significant cytoprotective effect against UV-B induced oxidative damage. The observation were attributed to the inhibitory effect of the *Terminalia chebula* on the age dependent shortening of the telomere length as shown by southern blots of the terminal restriction fragments of DNA extracted from subculture passages. The gallic acid and chebulagic acid isolated from fruit extract of *Terminalia chebula*, blocked cytotoxic lymphocyte-mediated cytotoxicity (Na, et al. [30]).

**Anti-Anaphylactic Effect:** The extract of *Terminalia chebula* was administered into the animals followed by induction of anaphylactic shock, the serum histamine levels were reduced, indicating its strong antianaphylactic action. Aqueous extract of *Terminalia chebula* showed a significant increased effect on TNF $\alpha$  production from rat peritoneal mast cells representing its strong anti-anaphylactic action (Shin, et al. [31]).

**Cardioprotective Effect:** 95% of ethanol extract of *Terminalia chebula* (500mg/kg body weight) was investigated in isoproterenol induced myocardial damage in rats. Pretreatment with *terminalia chebula* extract has cardioprotective effect due to lysosomal membrane stabilization prevents the myocardial necrosis and inhibits alterations in the heart's mitochondrial structure and functions in the experimental rats. Its pericarp has also been reported to have cardioprotective activity in isolated frog heart model (Suchalatha, et al. [32]).

**Hypolipidemic and Hypocholesterolemic Effects:** Extract of *Terminalia chebula* indicated hypolipidaemic activity against experimentally induced atherosclerosis. Extract also showed hypocholesterolemic activity against cholesterol induced hypercholesterolemic and atherosclerosis in rabbit. Triphala (*Terminalia chebula*, *Terminalia bellerica*, *Embelica officianalis*) formulation is found to have hypolipidemic effect on the experimentally induced hypercholesteremic rats (Thakur, et al. [33,34]).

**Hepatoprotective Effect:** The 95% ethanolic extract of *Terminalia chebula* fruit show strong hepatoprotective activity. It also shows similar property against anti-tubercular drug rifampin, isoniazid and pyrazinamide induced toxicity due to its prominent antioxidative and membrane stabilizing activity. Aqueous extract of fruit of *Terminalia chebula* tert-butyl hydroperoxide induced oxidative injury was observed in cultured rat primary hepatocytes and rat liver has also been documented (Tasduq, et al. [35]).

**Gastroenteric Effect:** The methanolic extract of *Terminalia chebula* show significant reduction in gastric volume, free acidity and ulcer index in pylorus ligation and ethanol induced ulcer model in wistar rats. *Terminalia chebula* increase the percent of gastric emptying in the Charles foster rats. Intra-gastric administration of the crude drug to rat, at a dose of 1.5g/l for 15 days, decreases the number of gastric ulceration induced by pentagastrin and carbacol (Sharma, et al. [11]).

**Anti-Plasmodial Effect:** Aqueous extract of *Terminalia chebula* proved antiplasmodial activity, *in vitro* in MDR strain of plasmodium falciparum and *in vitro* studies of *Terminalia chebula* acetone extract of seed of the plant show anti-plasmodial activity in a study (Pinmai, et al. [36]).

**Anti-Caries Effect:** Sucrose induced adherence and glucan induced aggregation of streptococcus mutant's growth were inhibit-

ed strongly by the aqueous extract of *Terminalia chebula*. The 10% solution of the extract used in mouth rinsing show inhibition of the salivary bacterial count and glycolysis of salivary bacteria for up to 90 minutes post rinsing (Aneja, et al. [5]).

**Nephroprotective Effect:** The extract of fruit of *Terminalia chebula* helps to alleviate the cadmium induced nephrotoxicity. Its decoction showed significant reduction in hyper lipidemia in increased fat died induced hyperlipidemic rats (Anju, et al. [37]).

**Anti-Spermatogenic Effect:** The 50% ethanolic extract of bark of *Terminalia chebula* indicated histological alterations in seminiferous tubules in testes of mice at dose of 300 mg/kg for 28 days. The extract of fruit of *Terminalia chebula* given at dose of 100 mg/kg show significant decrease in motility count, and in morphological abnormalities in spermatozoa (Srivastava, et al. 2010) [38-44].

## Conclusion

*Terminalia chebula* had number of phytochemical constituents which are found to be associated with the plant extract that include mainly chebulic acid, gallic acid, ellagic acid, tannins acid, amino acid, flavanoids, like luteolin, rutins and quercetin etc. All these compounds are found to be responsible for many of pharmacological activities. It is an important herbal drug as it is used for treating many diseases including diseases such as cancer. Many pharmacological investigation have been carried out based on its chemical constituents.

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