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## Ethno and Modern Pharmacological Profile of Baheda (*Terminalia bellerica*): A Review

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**Abstract** *Terminalia bellerica* is an important traditional Indian medicinal plant used in various ailments and rituals. The use of different parts of this plant like leaves and fruits as a medicament for treatment of various conditions is well documented in literature. *Terminalia bellerica* Roxb. (Combretaceae) is one of the ingredients of ayurvedic purgative medicament of 'Triphala' available in the Indian market for the treatment of dyspepsia, diarrhea, dysentery, inflammation of the small intestine biliousness, flatulence, liver disease and leprosy. It is the rich source of the presence of  $\beta$ -sitosterol, gallic acid, ellagic acid, galactose, ethyl gallate, chebulagic acid, mannitol, glucose, galactose, fructose and rhamnose in plant fruit extracts. The present review clarified the main active ingredients and pharmacological effects of *Terminalia bellerica* as a promising plant as a result of effectiveness and safety.

**Keywords** *Terminalia bellerica*, Gallic acid, Ethnopharmacology, Traditional use.

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### Introduction

Plants have been an important source of medicine with qualities for thousands of years. Plants are used medicinally in different countries, and they are the source of many potent and powerful drugs. Mainly on traditional remedies such as herbs for their history, they have been used popular folks medicine [1]. *Triphala* is regarded as an important rasayana in ayurvedic medicine. *Triphala* powder consists of three plant fruits (*Terminalia chebula*, *Terminalia bellerica* and *Phyllanthus embelica* ratio for *Triphala* is 1:1:1) [2]. *Terminalia bellerica* Roxb. (Combretaceae) is one of the ingredients of ayurvedic purgative medicament of 'Triphala' available in the Indian market for the treatment of dyspepsia, diarrhea, and dysentery, inflammation of the small intestine biliousness, flatulence, liver disease and leprosy [3]. Chemically, the presence of  $\beta$ -sitosterol, gallic acid, ellagic acid, galactose, ethyl gallate, chebulagic acid, mannitol, glucose, galactose, fructose and rhamnose in the fruit of *Terminalia bellerica* have also been reported [4]. Active principle such as gallic acid (3, 4, 5-trihydroxybenzoic acid) has also been identified. It shows marked bile stimulating activity and has strong antioxidant properties [5]. This review was mainly sites the information on highlight the modern and traditional therapeutically pharmacological profile of *Terminalia bellerica* plant belonging to family Combretaceae, which may serve as a source for further studies.

### Plant Profile [6-7]

**Botanical Name:** *Terminalia bellerica*

**Family:** *Combretaceae*

**Vernacular Names:** *Vibhitaki, Bibhitaka, Aksha, Kalidruma, Baheraa, Baleela, Thandri*

**Part used:** Fruit

**Dose:** Powder 3-6 g



**Botany:** *Terminalia bellerica* is a large deciduous tree with a buttressed trunk, thick brownish-grey bark with shallow longitudinal fissures, attaining a height of 20 and 30 m. The leaves are crowded around the ends of the branches, alternately arranged, margins entire, elliptic-obovate, rounded tip or sub acute, midrib prominent, pubescent when young and become glabrous with maturity. The flowers are pale greenish-yellow with an offensive odour, borne in axillary spikes longer than the petioles but shorter than the leaves. The fruits are ovoid drupes grey in colour, obscurely five-angled when dry, containing a kernel within. *Terminalia bellerica* is found growing wild throughout the Indian subcontinent, Sri Lanka and SE Asia, up to 1200 m in elevation, in a wide variety of ecologies [8-9].

**Chemical Constituents:** Fruits contains several triterpenoids, including belleric acid,  $\beta$ -sitosterol, and the saponin glycosides bellericoside and bellericanin. Other constituents include polyphenols (gallic acid, ellagic acid, phyllembin, ethyl galate, and chebulagic acid), lignans (termilignan, thannilignan, hydroxy-3',4'-[methylenedioxy] flavan, anolignan B), and a fixed yellow oil [10-11]. The fruit contains all the components of *Terminalia chebula*, except corilagin and chebulic acid. Fleshy fruit pulp contains 21.4 % tannin [12].

**Traditional Uses:** In Ayurveda it is used as bitter, acrid, astringent, laxative, germicidal and antipyretic and is applied in a diverse range of conditions including cough, tuberculosis, eye diseases, dyspepsia, diarrhea, and dysentery, inflammation of the small intestine, biliousness, flatulence, liver disease and leprosy. It is also said to cleanse the blood and the voice and to promote hair growth. Fruits are laxative, astringent, anthelmintic and antipyretic useful in hepatitis, bronchitis, asthma, dyspepsia, piles, diarrhoea, coughs, hoarseness of voice, eye diseases and scorpion-sting; used as a hair tonic. Decoction of the green fruit is used for cough. Pulp of the fruit is useful in dysenteric-diarrhoea, dropsy, piles and leprosy. Half ripe fruit is used as purgative. Kernel of the fruit is narcotic. Fruits are used in menstrual disorder in Khagrachari. Seed oil is used in rheumatism. Gum of the bark is demulcent and purgative. The triterpenoid present in the fruits possess significant antimicrobial activity. Kernel oil has purgative action and its prolonged use was well tolerated in mice [13].

## Pharmacological Profile

### Anti-Diabetic Effects

The various studies have been attempted to explore the antidiabetic effect of fruit extract. Sabu and kuttan (2009) have reported administration of 75% methanolic extract of fruits of *Terminalia bellerica* Roxb. suspended in water was studied in alloxan induced hyperglycemia and antioxidant defense mechanism in rats. The study results suggested that *Terminalia bellerica* fruit extract possessed anti-diabetic and antioxidant activity and these activities may be interrelated [14]. Kasabri *et al* (2010) have reported the efficacy and mode of action of *Terminalia bellerica* used traditionally for the treatment of diabetes in India. *Terminalia bellerica* aqueous extract stimulated basal insulin output and potentiated glucose-stimulated insulin secretion concentration-dependently in the clonal pancreatic b-cell line, BRIN-BD11 ( $P < 0.001$ ). Furthermore, the extract did not increase insulin secretion in depolarised cells and did not further augment insulin secretion triggered by tolbutamide or glibenclamide. *Terminalia bellerica* extract also displayed insulin-mimetic activity and enhanced insulin-stimulated glucose uptake in 3T3-L1 adipocytes by 300% [15].

Another investigators try to study of antidiabetic effect of *Terminalia bellerica* extract besides confirming hypoglycemic activities of the experimental herbal samples; help identify more potent indigenous hypoglycemic herbs (in crude ethanolic extract) from the comparative study of the reported experimental results [16]. Rathor *et al* (2016) have reported an Ayurvedic polyherbal extract (PHE) comprising six herbs one of which *Terminalia chebula* and *Terminalia bellerica* is mentioned as an effective anti-hyperglycemic agent in 'Charaka Samhita', the classical text of Ayurveda. Investigators referred to previous, antidiabetic drug metformin was found to elicit antiaging effects and PHE was also found to exhibit antidiabetic effects in humans. Investigators reported that PHE treated worms having oxidative stress resistance in both wild type and stress hypersensitive *mev-1* mutant along with up regulation of stress response genes *sod-3* and *gst-4*. They have been suggested PHE significantly improves the oxidative stress and life span in *C. elegans* [17]. Makihara *et al* (2016) have reported the effects of a hot water extract of *Terminalia bellerica* fruit (TB) on obesity and insulin resistance in spontaneously obese type-2 diabetic



mice. The study findings indicate that gallic acid mediates the therapeutic effects of TB on metabolic disorders by regulating adipocyte differentiation [18]. Rosemary *et al* (2011) have reported the antidiabetic compound from the fruit rind of *Terminalia bellerica* and assess its chemico-biological interaction in experimental diabetic rat models. Investigation have prove that gallic acid present in fruit rind of *Terminalia bellerica* is the active principle responsible for the regeneration of  $\beta$ -cells and normalizing all the biochemical parameters related to the patho-biochemistry of diabetes mellitus and hence it could be used as a potent antidiabetic agent [19].

Yang *et al* (2013) have reported the effects of the constituents of *Terminalia bellerica* and *Terminalia chebula* fruit extracts on PPAR $\alpha$  and PPAR $\gamma$  signaling/expression, cellular glucose uptake and adipogenesis. PPAR $\alpha$  and PPAR $\gamma$  signaling and expression (luciferase assay and western blot) and the insulin-stimulated uptake of 2-NBDG were determined in HepG2 cells. Investigators were reported that out of the 20 compounds, two ellagitannins, chebulagic acid (1) and corilagin (2), and three gallotannins, 2,3,6-tri-O-galloyl- $\beta$ -D-glucose (3), 1,2,3,6-tetra-O-galloyl- $\beta$ -D-glucose (4), and 1,2,3,4,6-penta-O-galloyl- $\beta$ -D-glucose (5), showed the enhancement of PPAR $\alpha$  and/or PPAR $\gamma$  signaling [20].

### Antioxidant Activity

Fruit of this plant rich source of gallic acid and other polyphenols, so they have possessed good antioxidant activities. Several studies were confirming antioxidant effects of plant. Guleria *et al* (2010) have reported *Terminalia bellerica* Roxb. have antioxidant properties. The study reported to the free radical scavenging activity and antioxidant potential of acetone extract of fruit was investigated using *in vitro* assays, including scavenging ability against DPPH,  $\beta$ -carotene bleaching inhibition, reducing power and chelating ability on  $\text{Fe}^{2+}$  ions. Fraction rich in polyphenolic content were more effective than the crude extract [21]. Pfundstein *et al* (2010) have reported methanol extracts of the fruits of *Terminalia bellerica* antioxidant capacities and the major isolated substances were determined using the 1, 1-diphenyl-2-picrylhydrazyl radical (DPPH), oxygen radical absorbance capacity (ORAC) and ferric reducing ability of plasma (FRAP) *in vitro* assays and indicated that chebulic ellagitannins have high activity which may correlate with high potential as cancer chemo preventive agents [22]. Vani *et al* (1997) have reported the *in vitro* antioxidant potential of *Triphala* and its constituents was tested with the following systems radical scavenging activity measured by DPPH reduction, and superoxide radical and peroxy radical scavenging properties measured by riboflavin/light/NET reduction and linoleic acid peroxidation, respectively. The extracts also prevented lipid peroxidation induced by  $\text{Fe}^{3+}$ /ADP/Ascorbate system in rat liver mitochondria. The major phenolic compounds such as gallic acid (main phytoconstituents of *Terminalia bellerica* plant) of the alcohol extracts were confirmed as tannins, responsible to its antioxidant effects [23]. Naik *et al* (2005) have evaluated that the aqueous extract of fruits of *Emblia officinalis* (T1), *Terminalia chebula* (T2) and *Terminalia bellerica* (T3) and mixture of *Triphala* for their *in vitro* antioxidant activity. Gamma radiation induced strand break formation in plasmid DNA (pBR322) was effectively inhibited by *Triphala* and its constituents in the concentration range 25–200  $\mu\text{g}/\text{mL}$  with a percentage inhibition of T3 (8%–58%). These studies revealed that all three constituents of *Triphala* are active and they exhibit slightly different activities under different conditions. Further, authors suggested that the mixture of *Triphala*, is expected to be more efficient due to the combined activity of the individual components [24].

High antioxidant levels have also been shown to act as a preventative against the development of degenerative diseases such as cancer, neural degeneration, diabetes and obesity [25-26].

### Antimicrobial Effects

Elizabeth (2005) has reported the antimicrobial activity of crude and methanol extract of *Terminalia bellerica* fruits was tested by disc diffusion method, against 9 human microbial pathogens. Crude aqueous extract of dry fruit at 4 mg concentration showed zone of inhibition ranging from 15.5-28.0 mm. *S. aureus* was found to be highly susceptible forming highest zone of inhibition, suggesting that *Terminalia bellerica* was strongly inhibitory towards this organism. Investigator reported the MIC of crude and methanol extracts determined by both dilution technique which ranged from 300 to >2400  $\mu\text{g}/\text{ml}$  and 250 to >2000  $\mu\text{g}/\text{ml}$  respectively, indicating that *Terminalia bellerica* was highly effective against *S. aureus* with lower MIC values [27]. Another study claim the ethnopharmacology



profile to the antimicrobial activity of plant, they have active against *Salmonella typhi* and *Salmonella typhimurium*. *In vitro* cellular toxicity also performed by them. The aqueous extract of plant fruit showed significant anti-salmonella activity [28]. Other investigation authors reported that the ethanolic extract of a plant was tested for its antimicrobial activity against the oral plaque forming bacteria *Streptococcus mutans*. It was found to significantly inhibit biofilm formation. The extract also prevents the formation of biofilm by the bacteria [29]. The herbal extract of *Baheda* showing good  $\beta$ -lactamase inhibitor activity *In vivo* and *In vitro* against *Staphylococcus aureus* as the test organism [30].

### Wound Healing Activity

Choudhary (2008) has reported the wound healing activity of ethanol extract of *Terminalia bellerica* Roxb. fruit was evaluated on excision and incision wound model, in albino rats, in the form of an ointment with 2 and 4% two concentrations of fruit extract in simple ointment base. Both concentrations of the ethanol extract showed significant response in both the wound types tested when compared with the control group [31]. Gupta *et al* (2011) have reported the herbal drug combination one of which *Terminalia bellerica*, effective for wound healing activity, on excision wound of albino rats. Wound healing activity of the herbal combination was evaluated by formulating the drug in ointment dosage form and then compared with a marketed formulation (Soframycin cream) as reference drug. The herbal drug combination has been observed to promote healing of wounds in animals [32].

Another ethnopharmacological effects have been shown *Terminalia belliricia* extracts have proper efficacy on wound healing. Herbal paste preparation showed significant ( $P < 0.05$ ) improvement on maturation, wound contraction and epithelialization [33].

### Hepatoprotective Activity

Jadon *et al* (2007) have reported the protective effect of *Terminalia bellerica* fruit and its active principle, gallic acid at different doses against carbon tetrachloride intoxication. Treatments with *Terminalia bellerica* extract (200, 400 and 800 mg/kg, p.o.) and gallic acid (50, 100 and 200 mg/kg, p.o.) showed dose-dependent recovery in all these biochemical parameters but the effect was more pronounced with gallic acid. Conclusion of this study gallic acid has more effective as compared to plant fruit extract [34]. Anand *et al* (1997) have reported Compound I isolated from fraction TB5 of *Terminalia bellerica* and finally identified as 3,4,5-trihydroxy benzoic acid (gallic acid) was evaluated for its hepatoprotective activity against carbon tetrachloride ( $\text{CCl}_4$ )-induced physiological and biochemical alterations in the liver. Investigators reported the Compound I led to significant reversal of majority of the altered parameters. Study results confirm the presence of hepatoprotective activity in Compound I [35]. Other ethno study has been revealed that hepatoprotective effect of drug in hepatic cancer cell lines. *Terminalia belliricia* extracts have also demonstrated growth inhibitory effects towards human A549 lung cancer cell lines and HepG2 hepatocarcinoma cell lines without the presence of the other plant components present in *Triphala* [36].

### Antiulcer and Antidiarrhoeal Activity

Pandey *et al* (2017) have reported comparing the antidiarrhoeal effect of grilled fruits (GF) with dried fruits (DF). The 50% ethanolic extracts of GF and DF were successively fractionated the antioxidant and bacterial inhibition activity were studied using DPPH free radical scavenging, anti-lipid peroxidation and broth dilution method respectively. In this study plant extract protective in castor oil induced diarrhoea. *In vivo* antidiarrhoeal activity DF and GF (100 mg/kg oral) inhibited diarrhoea by 41.87% and 71.72% respectively. Grilling significantly altered the levels of metabolites in *T. bellerica* fruits which could be responsible for its increased therapeutic potential [37]. The mature, dried fruit of *Bibhitaka* is effective in the treatment of dysentery and intestinal parasites but should be taken along with purgatives such as *Markandika* to counteract its constipating effects the sun-dried unripe fruit, however, is gently aperient and can be used on its own [38]. *Terminalia belliricia* extracts have antidiarrhoeal activity using castor oil induced diarrhea, PGE2 induced entero pooling and gastrointestinal motility test was performed in this study. Aqueous and ethanolic extract showing antidiarrhoeal effect on 334 mg/kg dose [39].



*Terminalia belliricia* extract have antiulcer activity in pylorus ligation and ethanol induced ulcer model in wistar rats. The orally dose 250 and 500 mg/kg of extract produced significantly inhibition of the ulcer in both animal models [40].

#### **Antiplatelet and Antithrombotic Activity**

Ansari *et al* (2016) have reported the ethanolic extract of fruit and its isolated compound (Tb-01) were intended to estimate antiplatelet and anti-oxidant activities. The ethanolic extract was submitted to Si-gel CC and compound was isolated. Present study revealed that antiplatelet activity was carried out by using platelet rich plasma (PRP) prepared by centrifugation of rabbit whole blood (containing 0.9% sodium citrate as anticoagulant) and antioxidant activity using 1, 1-diphenyl-2-picrylhydrazyl (DPPH), reducing power and nitric oxide anion scavenging activity models. Further investigators have been reported Tb-01 was found as amorphous brownish powder; yield 0.64% (w/w); mp 105-110 °C, R<sub>f</sub> value at 0.42 in methanol : chloroform (20:80) solvent system, UV absorption maxima at 243 nm and molecular peak [M + H]<sup>+</sup> at 394.15 m/z. They were observed that ethanolic extract and Tb-01 at different concentrations showed significant antiplatelet and anti-oxidant activity [41]. The fruit extract of *Terminalia belliricia* have showing antithrombotic activity. An *In vitro* model was used to check the clot lysis and antithrombotic effect of fruits along with Streptokinase as a positive control. For thrombolytic activity, at concentration 1.00 mg/dl the clot dissolution time is minimum i.e. 58 and 66 min for aqueous and alcoholic extracts respectively [42].

#### **Anticancer Activity**

The Ayurvedic medicine *Triphala* in which *Terminalia belliricia* is the main constituents, has cytotoxic effects against various cancer cell lines, thymic lymphoma cells, human breast cancer cell lines, human prostate cancer cell lines and human pancreatic cancer cell lines [43]. Acetone extract of *Terminalia belliricia* have exhibited antimutagenic potency using Salmonella/microsome assay. Extract having variable inhibitory activity of 65.6% and 69.7% with 4-O-nitrophenylenediamine (NPD) and sodium azide respectively (as direct –acting mutagens) [44].

#### **Cardioprotective and Antihyperlipidemic Activity**

Shailla *et al* (1995) have reported hypercholesterolemia and atherosclerosis were induced experimentally in rabbits by cholesterol feeding. The effect of an indigenous drug, *Terminalia belliricia*, was evaluated in these hypercholesterolemia rabbits. *Terminalia belliricia* reduced the levels of lipids in hypercholesterolemia animals. There was also a significant decrease in liver lipids and heart lipids (P <0.05) in the drug-treated animals [45]. Kannan *et al* (2012) have reported the effect of *Terminalia bellerica* fruit extracts on diabetic related atherosclerosis. Investigators have used different extracts such as Hexane (HETB), Chloroform (CETB), Ethanol (EETB), Aqueous (AETB) at the dose of 200mg/kg were administered to high fat diet associated with alloxan induced diabetic hyperlipidemic rats. Aqueous extract of *Terminalia bellerica* fruit extracts, have more significant activity on reducing the Total cholesterol, LDL, VLDL levels and significantly increase in HDL Levels [46]. *Terminalia belliricia* extracts have posse's antihypertensive activity. This is carried out using an isolated guinea-pig atria, inhibition of force and rate of atrial contraction noted. Also they have relaxed rabbit thoracic aorta after the induction of contraction which was induced by phenylephrine [47].

#### **Other Ethnopharmacological Activity**

The *Terminalia belliricia* extract affected T cell proliferation mainly through the same mechanism as PHA. The extract affected cellular mediated immunity (CMI) rather than humoral mediated immunity (HMI) [48]. The *Cakradatta* states that the fruit pulp mixed with *gharta* is covered with cow dung and heated in a fire, and held in the mouth to control coughing. For severe cough and asthma the *curna* of the dried fruit may be taken with honey. Mixed with *saindhava*, *Pippali* and buttermilk, *Bibhitaka* is taken in hoarseness [49-50]. Gilani *et al* (2008) have reported the medicinal use of *Terminalia bellerica* in hyperactive gastrointestinal and respiratory disorders. Crude extract of *Terminalia bellerica* fruit (Tb.Cr) was studied in *in vitro* and *in vivo*. Tb.Cr caused relaxation of



spontaneous contractions in isolated rabbit jejunum at 0.1–3.0 mg/mL. These study results indicate that *Terminalia bellerica* fruit possess a combination of anticholinergic and Ca<sup>2+</sup> antagonist effects, which explain its folkloric use in the colic, diarrhea and asthma [51].

Sireeratawong *et al* (2013) have reported acute and chronic toxicities of the water extract from the dried fruits of *Terminalia bellerica* (Gaertn.) Roxb. For the study of acute toxicity, a single oral administration of the water extract at a dose of 5,000 mg/kg body weight (10 female, 10 male) was performed and the results showed no signs of toxicity such as general behavior changes, morbidity, mortality, changes on gross appearance or histopathological changes of the internal organs of rats. The study of chronic toxicity was determined by oral feeding both female and male rats (10 female, 10 male) daily with the test substance at the dose of 300, 600 and 1,200 mg/kg body weight continuously for 270 days. Study was suggested that, the water extract from the dried fruits of *Terminalia bellerica* did not cause acute or chronic toxicities in either female or male rats [52].

A decoction of the dried fruit may be taken internally and externally as eyewash in the treatment of ophthalmological disorders indicates that the fresh fruit pulp is used as a collyrium in the treatment of non-traumatic corneal ulcer [53]. The oil from the seeds is trichogenous, and can be used topically for leucoderma and skin diseases [54]. The kernel is typically removed before *Bibhitaka* is used, and specifically stated to be *madakari* (narcotic), used topically as an analgesic in the treatment of inflammation and pain, and internally in vomiting, bronchitis and colic [55]. The antipyretic activity of ethanolic and aqueous extracts of *Terminalia belliricia* fruits (200 mg/kg, p.o.) was reported in brewer's yeast-induced fever models in mice and rats. Both extracts showed a significant inhibition of elevated temperature when compared to corresponding control [56]. The fruit of *Terminalia bellirica* is a celebrated constituent of *Triphala*, along with *Haritaki* and *Amalaki*, stated specifically to be a *rasayana* for *kapha*, useful for reducing excess *medas* [57]. In ancient India *Bibhitaka* fruits were used as a form of dice [58]. *Bibhitaka* fruits containing phenolics interact directly with receptors or enzymes involved in signal transduction [59]. *Bibhitaka* fruits studied antiprotozoal, antimalarial and antitrypanosomiasis (sleeping sickness) bioactivities [60].

### **Current Medical Research Study of *Bibhitaka* fruits**

**Human trials:** Anti-asthmatic, antispasmodic, expectorant, antitussive [61].

**In vitro study:** Anti-HIV-1, antimalarial, antifungal [62], antimutagenic [63], antibacterial [64-65].

**Indications:** Dyspepsia, flatulence, haemorrhoids, constipation (unripe fruit), chronic diarrhoea and dysentery (dry fruit), hepatosplenomegaly, intestinal parasites, cholelithiasis, fever, sore throat, pharyngitis, laryngitis, cough, catarrh, bronchitis, asthma, skin diseases, oedema, ophthalmia, alopecia and premature greying, headache.

**Contraindications:** *Vatakopa* [66].

**Toxicity:** No data found

### **Conclusion**

Medicinal plants have been identified and used through human history. *Terminalia bellerica* Roxb. (Combretaceae) is one of the ingredients of ayurvedic purgative medicament of '*Triphala*' available in the Indian market [3]. Chemically, the fruit of *Terminalia bellerica* have rich source of gallic acid, ellagic acid and other polyphenols [4]. These compounds are believed to be responsible for the pharmacological activities of plant extract. The present review clarified the main active ingredients and pharmacological effects of *Terminalia bellerica* as a promising plant as a result of effectiveness and safety. Further studies should be carried out this plant to discover the unrevealed part of it which may serve for the welfare of mankind.

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