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A pharmacognostic, phytochemical and pharmacological review of *Terminalia bellerica*

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Abstract
Terminalia bellerica (T. bellerica) is a tree belonging to the family Combretaceae. In Ayurvedic system of medicine, it is used as "health – harmonizer" in combination with *Terminalia chebula* and *Emblica officnalis.* It is a large deciduous tree found all over in Asia, mostly native to Sri Lanka. Traditionally, *T. bellerica* is used for treatment of various diseases such as conjunctivitis, asthma, migraine, baldness, constipation and weak eyesight. It contains various phytoconstituents such as glycosides, flavonoids, tannins, phenolic compound, amino acids and saponins which are responsible for various pharmacological activities like anti-diabetic, anti-microbial, anti-salmonella, anti-biofilm, anticancer, hepatoprotective, anti-pyretic and anti-diarrheal. This review article provides comprehensive information on pharmacognostic, phytochemical and pharmacological properties of *T. bellerica,* as a source for further research studies.

Keywords: *Terminalia bellerica,* Ayurveda system of medicine, phytoconstituents, pharmacological activity

Introduction
Nature serves as primary source for the cure of ailments [1]. It is estimated that, in many developing countries, two third of the population is dependent on medicinal plants to meet primary healthcare needs [2]. The use of herbal medicine is increasing due to its safety, efficacy and therapeutic potential as compared to synthetic pharmaceutical products [3]. However, the potential of higher plants as a source of herbal medicine is unexplored [1]. Therefore, there is a need for thorough literature search on some species to update the current state of knowledge and one such plant is *Terminalia bellerica.*

Terminalia bellerica commonly known as bibhitaki belongs to the family Combretaceae. It is called vibheetaki in Sanskrit which means "fearless", the fruit that takes away the fear of disease. In Indian history, it is said that, *T. bellerica* is inhabited by demons and those who sat under its shade were vulnerable to an attack by the same. Due to its medicinal properties tree has Sanskrit synonym of Anila-ghnaka, or "wind-killing". The generic name 'Terminalia' is derived from Latin word, 'terminus' or 'terminalis' (ending), which means habit of the leaves being crowded or borne on the tips of shoots. It is a compound of *rasayana* preparation, made up of three myrobalan fruits, known as Triphala, which is important in Indian as well as Tibetan traditional medicines [4].

Scientific classification [4]

Kingdom	:	Plantae
Division	:	Magnoliophyta
Class	:	Mangoliopsida
Order	:	Myrtales
Family	:	Combretaceae
Genus	:	Terminalia
Species	:	*Terminalia bellerica*

Synonyms [5]
Bahera, Baheda, Bibhitaki, Belleric Myrobalan, Bedda Nut Tree, Beach- Almond, Aksha, Karshaphala, Kalidruma, Bhutavasa, Kaliyugalaya.

Vernacular names [5]
English: Belleric myrobalan, Hindi: Bahera, Baheda, haira, Bulla, Assam: Bhomora, Bhomra, Bhaira, Bauri, Hullach, Bengali: Bayada, Bahura, Gujarati: Bahedan, Bero, Behasa, Kannada: Tara kai, Santikayi, Yahela, Kashmiri: Babelo, balali, Malayalam: Tannikka, Thanni, Marathi: Baheda, Bhirda, Oriya: Bahada, Bhara, Punjabi: Bahera, Balela, Tamil: Thanrikkai, Kaattu-elupoe, Telugu: Thanikkaya, Tandra, Bahadrha, Urdu: Bahera.

Distribution and habitat [6]
It grows wild at an elevation of upto 2000m in wide variety of ecologies. It is native to Sri Lanka, India, Bangladesh, Bhutan, Thailand, China, Indonesia, Pakistan, Malaysia, Nepal, Cambodia and Vietnam. In India, it is commonly found in Madhya Pradesh, Uttar Pradesh, Punjab and Maharashtra.

Ecology: It is mostly found in monsoon forests, mixed deciduous forests or dry deciduous dipterocarp forests, associated with teak [7].

Biology: It flowers in the month of October-November and fruits in November-December. The tree sheds leaves in November with young ones appearing together with flowers [7].

Biophysical limits [7]
Altitude: 0-2000m
Mean annual rainfall: 900-3000 mm
Mean annual temperature: 22-28°C
Soil type: It grows well loamy fertile soil with good drainage.

Plant description [8]
It is large deciduous tree with the height of 50m and diameter of 30m with a rounded crown. It is branchless upto 20m. It is perennial and requires cold climate.

Bark: The outer bark is bluish or ashy-grey whereas inner-bark is yellow in colour. The bark contains number of longitudinal cracks.

Leaves: Young leaves are copper red in colour which turn into parrot green and later they become dark green. Leaves are large, alternate, glabrous, with the dimension of 4-24cm x 2-11cm, mostly clustered at the twig ends. Leaf tip is narrowly pointed. Base of the leaf is rounded to cunate, rufous-serious which turn to glabrescent, having 6-9 pairs of secondary veins. Secondary and tertiary venation are prominent on both the surfaces generally clustered towards the ends of branchlets. Petiole is 2.5-9cm long, flat above, with pair of sessile glands just above the middle, sometimes indistinct. Lamina is broad elliptical or broad obovate with the dimension of 8-20 x 4-14 cm. Apex is rounded to abruptly short acuminate. Margin is entire.

Flowers: They are greenish white in colour usually appear along with new leaves having an offensive odour or strong honey like smell. Flowers are simple, solitary and sessile. Inflorescence is axillary spikes generally 3-15cm long. Upper flowers of the spike are male. Lower flowers are bisexual. Calyx tube is sericeous or tomentulose.

Fruit: It is light yellow in colour. It is drupe, globose or ovoid, densely velutinous or sericeous, 2-4 x 1.8-2.2 cm. It is slightly 5 ridged, 3cm across. It is one seeded and covered with minute pale pubescence.

Fig 1: Whole plant of *T. bellerica*

Fig 2: Leaves of *T. bellerica*

Fig 3: Flowers of *T. bellerica*

Fig 4: Fruits of *T. bellerica*

Microscopy [3]

The various microscopical details that can be observed are hairs, stone cells, fibres, starch grains, xylem and calcium oxalate crystals. The details of which are as follows:

Table 1: Microscopic characters of powder of *T. bellerica*

Colour	Yellowish brown
Hairs	Length - 168 µm -91 µm Breadth - 14 - 7 µm
Stone cells	Single stone cells Length - 378-42 µm Breadth - 70-28 µm Group of stone cells Length – 462 µm-112 µm Breadth - 308-70 µm.
Fibres	Length - 630 µm - 105 µm Breadth - 1.16 µm
Starch grains	Simple starch grains Spherical with diameter ranging from 35 µm-14 µm Oval with the length of 31.5 - 28 µm and breadth of 28 – 21µm. Compound starch grains Diameter - 85.9 µm to 112 µm
Xylem	Spiral vessels with an average diameter of 17.5 µm to 70 µm Pitted vessels with an average diameter of 27.13 µm to 92.16 µm Pitted trachieds
Calcium oxalate crystals	Needle shape crystals

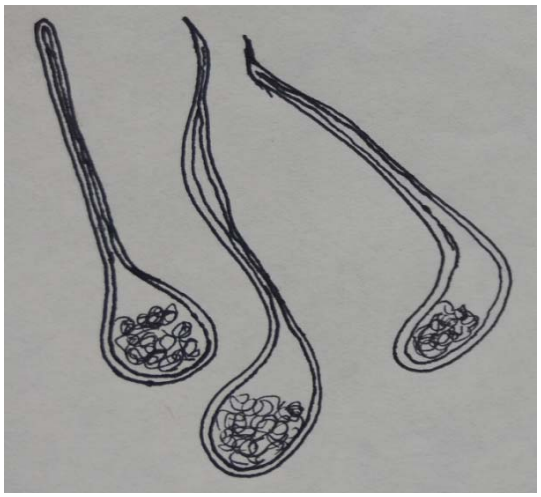

Fig 5: Hair present in powder of *T. bellerica*

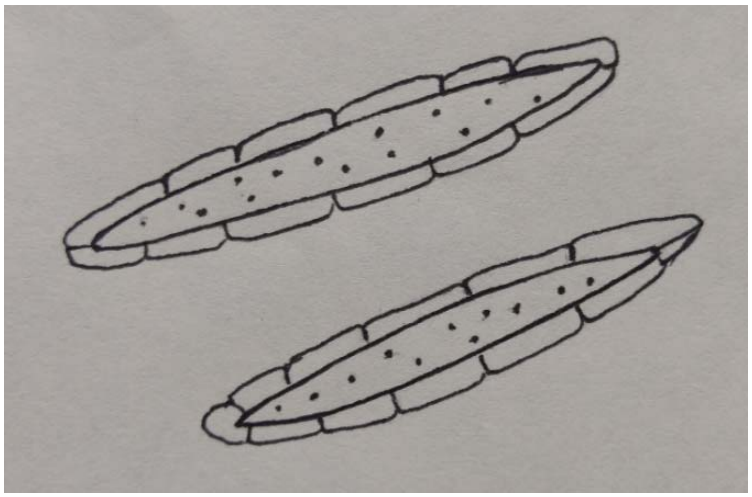

Fig 6: Stone cells present in powder of *T. bellerica*

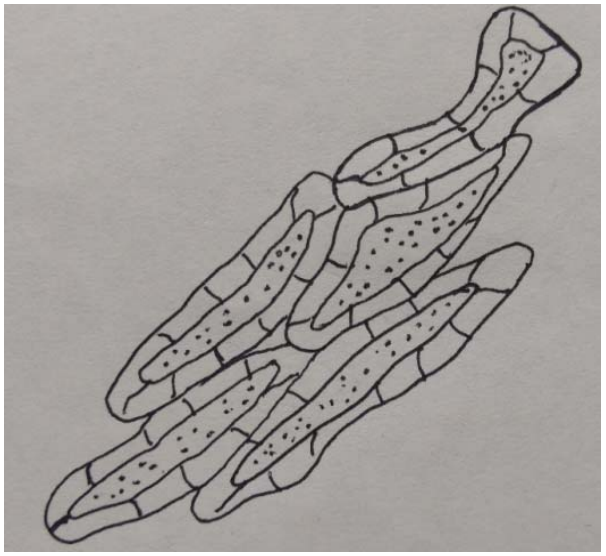

Fig 7: Group of stone cells present in powder of *T. bellerica*

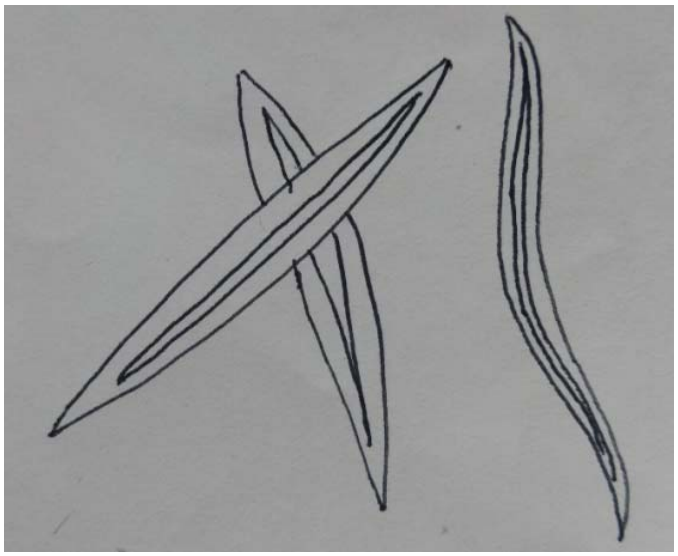

Fig 8: Fibers present in powder of *T. bellerica*

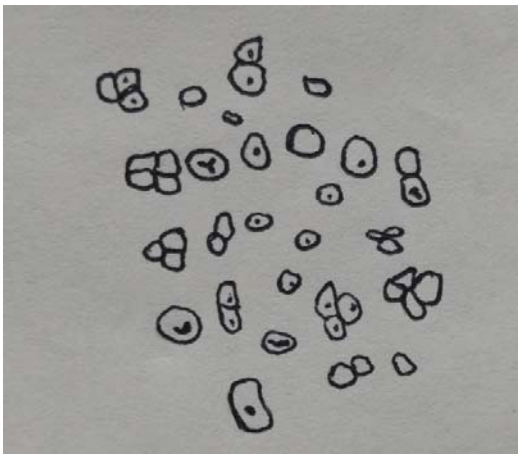

Fig 9: Starch grains present in powder of *T. bellerica*

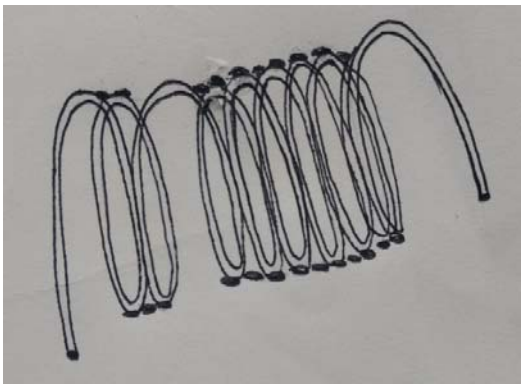

Fig 10: Spiral xylem vessels present in powder of *T. bellerica*

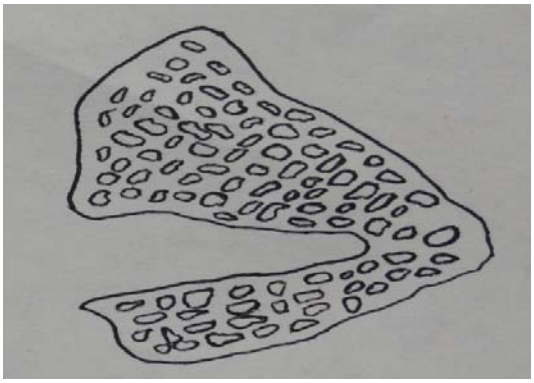

Fig 11: Pitted xylem vessels present in powder of *T. bellerica*

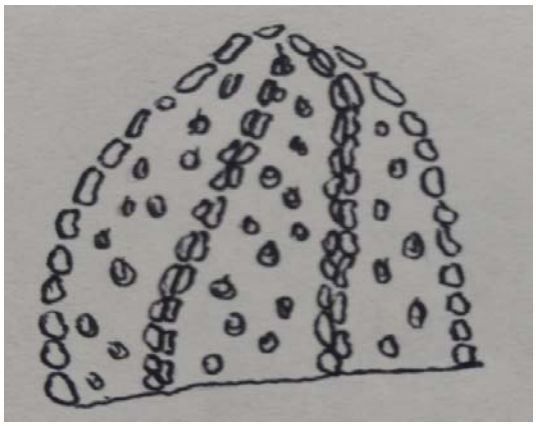

Fig 12: Pitted trachieds vessels present in powder of *T. bellerica*

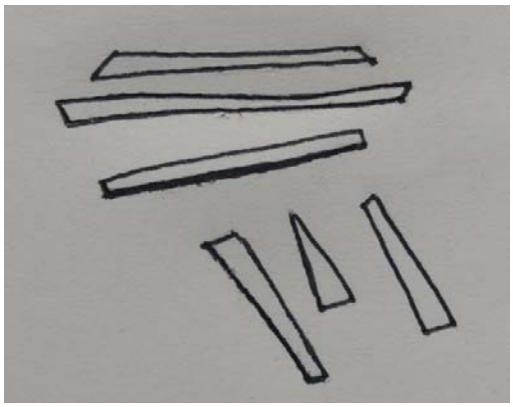

Fig 13: Needle shaped calcium oxalate crystals present in powder of *T. bellerica*

Photochemistry

The different phytoconstituents which have been isolated and reported so far have been represented below

Table 2: Phytochemicals present in *T. bellerica*

Compounds	Chemical constituents
Flavone	7-hydroxy 3', 4'(methylenedioxy)flavone [9], luteoline [10]
Steroids	β- sitosterol [11]
Lignans	Termilignan [9], thannilignin [9], anolignan B [9]
Tannins	Gallic acid [10], ellagic acid [10], methyl gallate [10], ethyl gallate (Phenyllemblin) [11], chebulagininc acid [11], chebulagic acid [12], hexahydroxydiphenic acid ester [12]
Glycosides	Fructose, sucrose, galactose, D-glucose, mannose, rhamnose [11]
Terpenoid	Belleric acid [12], chebulagic acid [11], arjungenin [12]
Saponin	Bellericoside and bellericanin [12]
Cardenolide	Cannogenol 3-O-β-galactopyranosyl-(1→4)-O-α-L-rhamopyranoside [13]
Flavonol aglycones	Quercetineand kampferol [10]
Flavonol glycosides	Quercetin-3-O-[6''-α-L-rhamnopyranosyl]-(1→6)-β-D-glucopyranoside (rutin), quercetin-3-O-α-L-rhamnopyranoside, quercetin-3-O-β-D-glucopyranoside and kaempferol-3-O-β-D-glucopyranoside [10]
Fatty acids present in oil	Palmitic acid, linoleic acid, stearic acid, myristic acid and oleic acid [14]
Glycerides of fatty acids	Palmitooleolinolein, stearo-oleolinolein, palmitodiolein, stearodiolein, dioleolinolein and triolein [15]

Ayurvedic properties [8]

- Rasa (taste) – Kashaya (astringent)
- Guna (qualities) – Rooksha (dry), Laghu (light to digest)
- Vipaka (taste conversion after digestion) – Madhura (sweet)
- Veerya (potency) – Ushna (hot)
- Effect on Tridosha – Balances Kapha and Pitta
- Bhedanam – Eases motion, has laxative action
- Kasanashanam – relives cough, cold
- Netrahitam – good for eyes
- Keshya – improves hair quality and promotes hair growth
- Kruminashanana – relives worm infestation
- Vaisvaryanashana – relives hoarseness of voice
- It detoxifies blood, lymph, muscle and fatty tissue of the body
- The seed kernel of vibhitaki is useful in

- Trut – excessive thirst
- Chardi – vomiting

Pharmacological activity

Table 3: Medicinal properties of *T. bellerica*

Part of plant	Activities reported
Whole plant	Antibiofilm [16], Anticancer [17], Anti-inflammatory [18], Antimutagenic [19], β-lactamase inhibitor [20]
Fruit	Analgesic [21], Antidepressant [22], Antidiabetic [23], Anti diarrhoeal [24], Antifertility [25], Antiandrogenic [25], Antifungal [26], Anti-helminthic [27], Antihypertensive [28], Antimicrobial [29], Anti-HIV-1 [30], Antioxidant [31], Antipyretic [21], Anti-salmonella [32], Antisecretory [33], Anti-spasmodic and bronchodialatory [34], Antithrombotic and thrombolytic [35], Anti-ulcer [36], Hepatoprotective [37], Wound healing [38], Anti-Alzheimer's [39], Anti-atherogenic [40], Anti-plasmodial [41], Cough, spleen, gastrointestinal disorders, clear bowels, flatulence, dysentery [42]
Bark	Immunomodulatory [43]

The various reasons reported for the presence of the above mentioned phytoconstitutents and their pharmacological activities are as follows**:**

- **Antispasmodic and bronchodilatory activity:** *In-vivo* and *in-vitro* studies were conducted to determine the mechanism of action for the medicinal use of *T. bellerica* fruit in hyperactive gastrointestinal and respiratory disorders. It showed combination of anticholinergic and Ca++ antagonist effects. In rabbitjejunum, it causes relaxation of spontaneous contractions. It inhibited carbacol and K+ induced contraction as well as it showed right shift in Ca++concentration response curves. In guinea-pig ileum, it produced rightward parallel shift of acetylcholine-curve followed by non-parallel shift with the suppression of maximum response at higher doses. In rodents, it showed protective effect against castor-oil induced diarrhoea and carbacol-mediated bronchoconstriction. In guinea pig trachea, it exhibited relaxation of contractions induced by CCh, right shift in CCh curves and inhibition of K+ contractions. Both chloroform, ethyl acetate and aqueous fraction exhibited anticholinergic effect whereas only aqueous fraction showed calcium channel blocking effect [34].
- **Anti-fungal activity:** An investigation was conducted to determine the anti-fungal activity of ethanolic extract of *Terminalia bellerica* fruit against five clinical and five environmental isolates of *Cryptococcus neoformans.* Anticryptococal activity was evaluated by disc diffusion method. It was found that clinical isolates were more susceptible as compared to environmental isolates. Hence, ethanol extract of *T. bellerica* fruit exhibited antifungal activity with the potential to inhibit drug resistant fungal strains [26].
- **Anti-salmonella activity:** A study was carried out to determine anti-salmonella activity of different extracts i.e., petroleum ether, chloroform, acetone, alcohol and water extracts of *T. bellerica*. Alcoholic and water extract of *T. bellerica* showed significant anti-salmonella activity. Results suggested that aqueous extract exhibited bactericidal activity at higher concentration and bacteriostatic activity at low concentration. *T. bellerica* extract did not show any *in-vitro* cellular toxicity. Mice on pre-treatment with aqueous extract of *T. bellerica* showed 100% survival when challenged with lethal doses of *S. typhimurium* [32].
- **Anti-microbial activity:** A study was conducted to demonstrate the antimicrobial activity of methanol extract of *T. bellerica* against respiratory pathogens i.e., *Staphylococcusaureus* and *Kledsiella pneumonia.* Preliminary anti-microbialanalysis showed that it inhibits coagulase activity of *S. aureus* whereas it causes biochemical alternation in both the strains. In *Klebsiella pneumonia* it causes major alternation in the capsular morphology after 24hr and 48hr of treatment respectively. The results indicate that *T. bellerica* possessantimicrobial activity against respiratory pathogens and hence can be used for treatment of diseases caused by pathogens [29].
- **Anti-oxidant activity:** Free radical scavenging activity and antioxidant potential of acetone extract of *T. bellerica* fruit was determined by *in-vitro* assays. Acetone extract was subjected to partitioning with ethyl acetate and water. Ethyl acetate fraction was found to be more effective as compared to crude acetone extracts in all anti-oxidant assays i.e., DPPH, β-carotene bleaching inhibition and reducing power whereas for chelating ability on Fe+2 ion, crude acetone extract showed higher activity. It was concluded that polyphenolic rich fractions were more effective than the crude extract [31].
- **Anti-biofilm activity:** Ethanol extract of *T. bellerica* plant was checked for its activity against the oral plaque forming bacteria *Streptococcus* mutants. It showed strong activity against *Streptococcus* mutans causing inhibition of biofilm formation. Hence, the study indicated that *T. bellerica* can be used as antibiofilm agent [16].
- **Anti-ulcer activity:** Anti-ulcer activity of ethanolic extract of*T. bellerica* fruit was determined in wistar rats by pylorus ligation and ethanol induced ulcer models. Ethanol extract showed inhibition of the gastric lesion induced by pylorus ligation induced ulcer and ethanol induced gastric ulcer along with reduction in free acidity and ulcer index as compared to control. Hence, it exhibits potential anti-ulcer activity [36].
- **Anti-Alzheimer's activity:** A comparative study was carried out using methanol extract of Triphala and its three major ingredients i.e., fruits of *Terminalia chebula, Terminalia bellerica* and *Emblica officinalis* for their acetylcholinestrase inhibitory properties. All extract showed inhibition of enzyme activity in a dose dependent manner. Phytoconstituents like gallic acid, ellagic acid and phenolic acids present in fruit of all three plants inhibited acetylcholinestrase. Being, acetylcholinestrase inhibitor, it could be used for symptomatic treatment of Alzheimer's diseases [39].
- **Antihypertensive activity:** A study was carried out to determine the mechanism of blood-pressure lowering effect of crude extract of *Terminalia bellerica.* In rats under anaesthesia, it induced a dose dependent fall in arterial BP where as in isolated guinea pig atria; it inhibited the force and rate of arterial contraction. In rabbit thoracic aorta, it causes relaxation of phenylephrine and K+ induced contractions as well as suppression of PE peaks in Ca2+ free medium. The vasodilator effect was endothelium-independent and it

occurred at similar concentration in the endothelium-denuded tissues. Hence, it can be used for hypertension as it lowers BP through Ca2+ antagonist [28].

- **Anti-atherogenic activity:** Anti-atherogenic effect of *T. bellerica* was studied by investigating the effect of hot water extract of *T. bellerica* fruit on low-density lipoprotein oxidation and inflammation on macrophages. It showed DPPH radical scavenging activity and 15-lipoxygenase inhibitory activity along with significant *in-vitro* inhibition of free-radical induced LDL oxidation as compared to solvent control. On treatment with *T. bellerica* extract showed significant decrease in m-RNA expression of tumour necrosis factor-alpha (TNF-α), interleukin-1 βeta and lectin-like oxidised LDL receptor-1 (LOX-1) and reduction in matrix metalloproteinase (MMP)-9 secretion and intracellular reactive oxygen species (ROS) production in THP-1 macrophages. The results indicate that *T. bellerica* extract had *in-vitro* inhibitory effects on LDL oxidation and macrophage inflammatory response. Hence, it can be used *in-vivo* to inhibit atherosclerosis plaque progression [40].
- **Immunomodulatory effect:** Methanolic extract of *Terminalia bellerica* fruit showed stimulation of morphage phagocytosis through the production of superoxide and acid phosphatase. It also showed activation in lymphocyte proliferation assay with phytohemagglutinin, concanavalin A, lipopolysaccharide and pokeweed nitrogen. However, at lower concentrations, it showed suppressant activity with concanavalin A and pokeweed nitrogen. The results indicated that T-lymphocyte proliferation effect of extract occurred through the same mechanism exhibited by phytohemagglutinin, concanavalin A whereas B-lymphocyte proliferation effect occurred through T-cell independent and T-cell dependent mechanisms, similar as lipopolysaccharide and pokeweed mitogen. Hence, the mouse immune system, specifically *in-vitro* cellular and humoral immune response was affected by methanol extract of *Terminalia bellerica* making it useful for the treatment of human immune mediated diseases [42].
- **Wound healing activity:** A study was conducted to evaluate the wound healing activity of ethanol extract of *Terminalia bellerica* fruit used in the form of ointment on excision and incision wound model. It exhibited greater wound healing contracting ability as compared to standard [38].
- **Antifertility activity:** Benzene and ethanol extracts of *Terminalia bellerica* bark were administered orally for 50days to adult male rats. Biochemical estimation was done after dissecting and weighing epididymis and vas deferens. A decrease in the weight of accessory reproductive ducts was observed after treatment with *Terminalia bellerica* extract. It also showed an increase in total cholesterol content whereas a significant decreased in epididymal sperm count was observed. The results indicated the non-availability of androgens in rats treated with *Terminalia bellerica*bark [25].
- **Anti-diarrhoeal activity:** An investigation was carried out to determine the anti-diarrhoeal effect of aqueous and ethanolic extract of *Terminalia bellerica* fruit in castor oil induced diarrhoea, PGE2 induced enter pooling and gastrointestinal motility test. The percentage protection in castor oil induced diarrhoea was found to be 73.37 and 63.58 by aqueous and ethanol extract respectively. Both the extracts showed significant anti-enter pooling effect in PGE2 induced enter pooling as in gastrointestinal motility test, percentage protection of aqueous and ethanolic extract was found to be 67.20 and 68.27 respectively. The results indicate that extracts exhibit prominent anti-secretory effect as compared to reduction in gastrointestinal motility. Presence of tannins, flavonoids and alkaloid could be responsible for anti-diarrhoeal effect, either by stimulating the reabsorption or anti-secretory effect in the intestinal lumen as well as significantly enhancing intestinal transit time and intestinal motility decreased [24].
- **Anti-cancer activity:** A comparative study was performed to determine *in-vitro* anti-cancer and antioxidant effects as well as total phenolic contents of five different extracts of *Terminalia bellerica* leaves i.e., methanol, aqueous methanol, ethyl acetate, chloroform and pet ether. A moderate correlation was observed between the total phenolic content of all the extracts whereas the anti-oxidant activity and the total phenol content increased with increase in polarity. Pet ether extract showed most potent anti-cancer activities followed by chloroform against all cell lines namely ovarian carcinoma, liver carcinoma, breast carcinoma, HeLa contaminant, cervical carcinoma, breast carcinoma, cervical carcinoma, CNS-human glioblastoma, non-small lung cancer, colon adenocarcinoma, fibrosarcoma, leukemia and melanoma. Other extracts showed potent anticancer activity against leukemia and melanoma. According to results, petroleum ether extract exhibited the highest anti-cancer activity which would be used for further purification to isolate compound(s) responsible for the activities [17].
- **Anti-plasmodial activity**: Antiplasmodial activity and cytotoxicity of water extract of *Phyllanthus emblica* Linn, *Terminalia bellerica* Retz and *Terminalia bellerica* (Gaertn) Roxb was evaluated by *in-vitro* and *in-vivo* studies. *In-vitro* anti-plasmodial studies were done by assessing the ability of all plant extracts to inhibit the uptake of [3H] hypoxanthine-resistant strain and *in-vivo* anti-plasmodial activity was evaluated by the standard 4-day suppressive test in P*lasmodium berghei*infected mice. Cytotoxic studies were carried out on Vero cell line. All plant extracts showed antimalarial activity. *Terminalia bellerica* showed highest *in-vitro* antiplasmodial activity followed by *Phyllanthis emblica* Linn and *Terminalia chebula* Retz. All plants showed cytotoxic activity with the selectivity index ranging from 11 to 17. At 250mg/kg/day, all plant extracts showed *in-vivo* antiplasmodial activity with good suppression activity in standard 4-day suppressive test on *P. berghei*infected mice [41].
- **Anti-diabetic activity:** A study was carried out to isolate compound from the fruit rind of *Terminalia bellerica* possessing anti-diabetic activity. Gallic acid was isolated from *Terminalia bellerica* by bioassay-guided fractionation. Isolated and synthetic gallic acid was administered to Streptozotocin (STZ) – induced diabetic male wistar rats at different doses for 28 days. A significant dose-dependent reduction in plasma glucose level was observed. Gallic acid treated rats showed regeneration of β-islets cells as compared to untreated diabetic rats in histopathological examination. Oral administration of gallic acid showed decreased serum total cholesterol, triglyceride, LDL-cholesterol, urea, uric acid, creatinine along with marked increase in plasma

insulin, C-peptide and glucose tolerance level. It also restored total protein, albumin and body weight of diabetic rats. Hence gallic acid isolated from *Terminalia bellerica* could be used as anti-diabetic agent [23].

- **Hepatoprotective activity:** Ethyl acetate extract of *T. bellerica* aerial parts was administered to BALB/CN mice, once a day for two consecutive days followed by carbon tetrachloride intoxication. It significantly ameliorated hepatic necrosis along with decreased expression of oxidative stress biomarkers, 4-hyrdroxynonenal (4-HNE) and 3-nitrotyrosine (3-NT) and restored P450 2E1 (CYP2E1) expression. It also showed reduction in nuclear factor-kappa B (NF-κB), cyclooxygenase-2 (COX-2) and tumour necrosis factor alpha (TNF-α) overexpression in injured livers, indicating amelioration of inflammatory response. There was significant suppression of hepatic fibrosis which was confirmed by transforming growth factor-beta 1 (TGF-β1) and alpha smooth muscle actin (α-SMA) expression. Hence, results indicate that *T. bellerica*possess hepatoprotective activity [37].
- **Anti-helminthic activity:** A study was conducted to evaluate the anti-helminthic potential of ethanolic and aqueous extract of *Terminalia bellerica* fruit pulp at various concentrations using *Phesentia posthuma* as test worms. Various bioassay methods were used, such as determination of time of paralysis and time of death of the worms. The results indicate that both the extracts showed significant paralysis and also caused death of worms at higher concentration as compared to Levimasole, reference standard. Hence, it was confirmed that *Terminalia bellerica* fruit possess anti-helminthic activity and further studies can be carried out to isolate active principle(s) responsible for this activity [27].
- **Anti-depressant activity:** An investigation was carried out to study the anti-depressant activity of aqueous and ethanolic extracts of *Terminalia bellerica* fruits in Swiss young male albino mice using forced swim test (FST) and tail suspension test (TST). Both the extracts were administered orally for 10 successive days. Ethanol extract and aqueous extract showed significant reduction in dose dependent manner in the mobility time of mice in FST as well as TST whereas there was no significant effect was observed on locomotor activity of mice. Activities of both the extract were found to be similar as imipramine and fluoxetine. Both the extracts showed reversed reserpine-induced extension of immobility period of mice in FST and TST. The aqueous and ethanolic extract induced antidepressant like effect in TST was significantly alternated by prazosin, sulpride and p-chlorophenylalanine. Hence, both the extracts exhibited significant anti-depressant-like effect in mice by interaction with adrenergic, dopaminergic and serotonergic systems [22].
- **Analgesic and antipyretic activity:** A study was done to investigate the analgesic and antipyretic activities of ethanolic and aqueous extract of *Terminalia bellerica* fruits in acetic acid induced writhing, Eddy's hot plate method and brener's yeast induced fever models in mice and rats. It was observed that both the extract showed a significant decrease in the number of writhes in acetic acid induced writhing and increase in licking time to heat stimuli in hot plate method. There was a significant inhibition of elevated body temperature by both extracts as compared to the corresponding control group. Hence, results indicate that the ethanolic and aqueous extract possessed significant analgesic and antipyretic activities [21].
- **Acute and subacute toxicities:** Acute and subacute toxicities of ethanol extract of *T. bellerica*were studied and it was found, a single oral dose of ethanol extract did not produce signs of toxicity, behavioural changes, mortality and differences on gross appearance of internal organs. In sub acute toxicity, all rats were administered with a repeated oral dose of ethanol extract for 14 days whereas the satellite group also administered with ethanol extract for same period but kept for further 14 days to check the delayed effects or reversibility of toxic effects. The results indicated that the ethanol extract did not show any change in general behaviours, mortality, weight gain, haematological or clinical blood chemistry parameters as well as gross and histological examination showed normal appearance of the internal organs as compared to control group [44].
- **Cytogenetical effect:** A study was conducted to demonstrate cytogenetical effects of mother tincture of *Terminalia bellerica*fruit at different concentrations on the root meristem of *Viciafoba*to determine the clastogeneic potential. Various clastogenic abnormalities were observed such as reduction in mitotic index, inhibition of cell division, stickiness of chromosomes, chromatin bridge, fragments of chromosomes and lagging chromosomes. The mother tincture of *Terminalia bellerica*acts as stathmokinetic agent, since its effects were prominent on the spindle. Hence, this study reveals that injudicious use of mother tincture of *Terminalia bellerica*may lead to genetic deformities in bio-organisms which are safe with no potential side effects [45].

Contraindications [46]

- It should be avoided during pregnancy as it is unsafe during pregnancy and breast feeding.
- It has blood sugar lowering activity, hence, diabetes medications needs to be adjusted for diabetic patient.
- Due to its blood sugar lowering activity, it may interfere with blood sugar control surgery, hence it should not be taken at least 2 weeks before surgery.

Conclusion

Terminalia bellerica has been extensively used as traditional medicine. It is a large deciduous tree, mostly native to Sri Lanka. Pharmacognostic evaluation of fruit powder showed presence of hairs, single and group of stone cells, fibres, simple and compound starch grains, spiral and pitted vessels, pitted tracheids and needle shaped calcium oxalate crystals. Phytochemical studies revealed the presence of various phytoconstituents such as tannins, flavonoids, steroids, lignin, glycosides, terpenoid, saponins, cardenolides, flavanol glycosides and fatty acids. It possess various pharmacological activities such as antispasmodic and bronchodilatory, anti-fungal, anti-salmonella, anti-microbial, anti-oxidant, anti-biofilm, anti-ulcer, anti-Alzheimer's, antihypertensive, anti-athrogenic, immunomodulatory effect, wound healing, antifertility, anti-diarrhoeal, anti-cancer, anti-plasmodial, anti-diabetic, hepatoprotective, anthelmintic, anti-depressant, analgesic and antipyretic activity. It does not possess any acute and subacute toxicities. It is contraindicated during pregnancy and diabetic patients. This review has provided a complete insight into the pharmacognostic, phytochemical and pharmacological activity of *Terminalia bellerica.*

However, there is a need for further study on phytochemistry and mechanism of action of pure compounds to fully understand the phytochemical profile and pharmacological effect of this plant.

References

1. Oke JM, Hamburger MO. Screening of some Nigerian medicinal plants for antioxidant activity using 2, 2, diphenyl-picryl-hydrazyl radical. Afr. J. Biomed. Res. 2002; 5:1-2.
2. Farnsworth NR, Soejarto DD. Global importance of medicinal plants. The conservation of medicinal plants. 1991; 26:25-51.
3. Abraham A, Mathew L, Samuel S. Pharmacognostic studies of the fruits of *Terminalia bellirica* (Gaertn.) Roxb. J Pharmacogn Phytochem. 2014; 3(2):45-52.
4. https://www.mdidea.com/products/proper/proper06001.html
5. Kadian R, Parle M, Yadav M. Therapeutic potential and phytopharmacology of *Terminalia bellerica*. WJPPS. 2014; 3(10):804-19.
6. https://www.planetayurveda.com/library/bibhitaki-terminalia-bellerica
7. http://www.worldagroforestry.org/treedb/AFTPDFS/Terminalia_bellirica.PDF
8. https://www.easyayurveda.com/2013/01/13/bibhitaki-baheda-terminalia-bellerica-uses-ayurveda-details/
9. Valsaraj R, Pushpangadan P, Smitt UW, Adsersen A, Christensen SB, Sittie Nyman A *et al*. New anti-HIV-1, antimalarial, and antifungal compounds from *Terminalia bellerica*. J. Nat. Prod. 1997; 60(7):739-42.
10. Ayoob FA, Awad HM, El-Kousy SM, Rashed KN, Al-Sayed NH. Phytochemical and biological investigations of *Terminalia bellerica* Roxb. leaves. J Pharm Res. 2014; 8(4):500-10.
11. Indian Herbal Pharmacopoeia. Revised New Edition. Published by Indian Drug Manufacturer's Association, Mumbai. 2002, 429-38.
12. The Herbs, Habitat, Morphology and Pharmacognosy of Medicinal Plants. First Edition 2008, Published by Smt. PremLata Gupta. 2008, 434-35.
13. Yadava RN, Rathore K. A new cardenolide from the seeds of *Terminalia bellerica*. Fitoterapia. 2001; 72(3):310-2.
14. Molla MT, Alam MT, Islam MA. Physico-chemical and nutritional studies of *Terminalia belerica* Roxb. seed oil and seed kernel. J. Biosci. 2007; 15:117-26.
15. Bawa Karatar Singh, Abhay Kumar. Chemical Examination of the Fruits of *Terminalia bellerica* Roxb, Part II. The Component Glycerides of the Fatty acids. 1946, 379-83.
16. Yadav S. Antibiofilm Formation Activity of *Terminalia bellerica* Plant Extract Against Clinical Isolates of Streptococcus mutans and Streptococcus sobrinus Implication in Oral Hygiene. IJPBA. 2012; 3(4):816-21.
17. Hanem Awad M, Fathalla Ayoob A, Mohamed Abdalla M. Evaluation of Total Phenol, Anticancer and Antioxidant Properties by Different Extracts of *Terminalia Belerica* Roxb. Leaves: An *In Vitro* Analysis. RJPBCS. 2015; 6(3):360-67.
18. Saraphanchotiwitthaya A, Sripalakit P, Ingkaninan K. Effects of *Terminalia bellerica* Roxb. Methanolic extract on mouse immune response *in vitro*. Maejo Int. J. of Sci. and Tech, 2008; 2(2):400-7.
19. Kaur S, Arora S, Kaur S, Kumar S. Bioassay-guided isolation of anti mutagenic factors from fruits of *Terminalia bellerica*. J Environ Pathol Toxicol Oncol. 2003; 22(1):69-76.
20. Shaikh S, Lochan R, Kaul P, Tandon GD. Beta lactamase Inhibitors from Indigenous Herbs and Spices. Res. J. of Pharmaceutical, Biological and Chemical Sci, 2014; 5(2):275-85.
21. Sharma US, Sharma UK, Singh A. Screening of *Terminalia bellirica* fruits extracts for its analgesic and antipyretic activities. Jordan j. boil. sci. 2010; 3(3):121-4.
22. Dhingra D, Valecha R. Evaluation of antidepressant-like activity of aqueous and ethanolic extracts of *Terminalia bellirica*Roxb. fruits in mice. Indian J Exp Biol. 2007; 45(7):610-6.
23. Latha RC, Daisy P. Insulin-secretagogue, antihyperlipidemic and other protective effects of gallic acid isolated from *Terminalia bellerica*Roxb. instreptozotocin-induced diabetic rats. Chemico-biological interactions. 2011; 15;189(1):112-8.
24. Kumar B, Divakar K, Tiwari P, Salhan M, Goli D. Evaluation of anti-diarrhoeal effect of aqueous and ethanolic extracts of fruit pulp of *Terminalia belerica* in rats. Int. J. Drug Dev. & Res. 2010; 2(4):769-79.
25. Sharangouda JP, Satishagouda S, Vishwanatha T, Saraswati B. Effect of *Terminalia bellirica* barks extracts on activities of accessory reproductive ducts in male rats. 2010; 1(2):015.
26. Valli S, Shankar GS. *Terminalia bellerica*-A promising challenge to cryptococcosis. Int. J. of Pharmaceutical Res. and Bio-Science. 2013; 2(5):154-69.
27. Kumar B, Kalyani D, Hawal LM, Singh S. *In vitro* anthelmintic activity of ethanolic and aqueous fruit extract of *Terminalia belerica*. J Pharm Res. 2010; 3(5):1061-2.
28. Khan AU, Gilani AH. Pharmacodynamic Evaluation of *Terminalia belerica* for its Anti Hypertensive Effect. J.of Food and Drug Analysis, 2008; 16:6-14.
29. Sabnis S. Antimicrobial efficacy of *Terminalia bellerica* against virulence factors of respiratory pathogens. Int. J Curr. Microbiol & Appl Sci. 2014; 3:215-21.
30. Valsaraj R, Pushpangadan P, Smitt UW, Adsersen A, Christensen SB, Sittie A *et al*. New anti-HIV-1, antimalarial, and antifungal compounds from *Terminalia bellerica*. J. Nat. Prod. 1997; 60(7):739-42.
31. Guleria S, Tiku AK, Rana S. Antioxidant activity of acetone extract/fractions of *Terminalia bellerica* Roxb. fruit. Indian J Biochem Biophys. 2010; 47:110-6.
32. Madani A, Jain S. Anti-Salmonella activity of *Terminalia belerica*: *In vitro* and *in vivo* studies. Indian J Exp Biol. 2008; 46(12):817-21.
33. Khan AU, Gilani HA. Anti-Secretory & Analgesic Activities of *Terminalia belerica*. African J. of Biotech, 2010; 9(18):2717-19.
34. Gilani AH, Khan AU, Ali T, Ajmal S. Mechanisms underlying the antispasmodic and bronchodilatory properties of *Terminalia bellerica* fruit. J Ethnopharmacol. 2008; 116(3):528-38.
35. Ansari AV, Siddiqui HH, Singh PS. Antithrombotic and Thrombolytic activity of *Terminalia belerica* fruit extracts. Res. J. of Pharmaceutical, Biological and Chemical Sci, 2012; 3(2):471-78.
36. Choudhary GP. Anti-ulcer activity of the ethanolic extract of *Terminalia belerica* Roxb. Int. j. pharm. Chem. Boil. sci. 2012; 1(4):1293-7.
37. Rashed K, Potočnjak I, Giacometti J, Škoda M,

Domitrović R. *Terminalia bellerica* aerial parts ethyl acetate extract exhibits antioxidant, anti-inflammatory and antifibrotic activity in carbon tetrachloride-intoxicated mice. J Funct Foods. 2014; 8:319-30.
38. Choudhary GP. Wound healing activity of the ethanol extract of *Terminalia bellirica* Roxb. fruits. NPR. 2008; 7(1):19-21.
39. Nag G, De BR. Acetylcholinesterase inhibitory activity of *Terminalia chebula*, *Terminalia bellerica* and *Emblica officinalis* and some phenolic compounds. Int J Pharm Pharm Sci. 2011; 3(3):121-4.
40. Tanaka M, Kishimoto Y, Saita E, Suzuki-Sugihara N, Kamiya T, Taguchi C *et al*. *Terminalia bellirica* Extract Inhibits Low-Density Lipoprotein Oxidation and Macrophage Inflammatory Response *in Vitro*. Antioxidants. 2016; 5(2):20.
41. Pinmai K, Hiriote W, Soonthornchareonnon N, Jongsakul K, Sireeratawong S, Tor-Udom S. *In vitro* and *in vivo* antiplasmodial activity and cytotoxicity of water extracts of *Phyllanthusemblica*, *Terminalia chebula*, and *Terminalia bellerica*. J Med Assoc Thai. 2011; 23;93(12):120.
42. Das PR, Tabibul Islam Md, SaleHin Bin Mahmud ASM, Kabir MH, Ehasanul Hasan Md *et al*. An ethnomedicinal survey conducted among the folk medicinal practitioners of three villages in Kurigram district, Bangladesh. Am.-Eurasian J. Sustain. Agric, 2012; 6(2):85-96.
43. Saraphanchotiwitthaya A, Sripalakit P, Ingkaninan K. Effects of *Terminalia bellerica* Roxb. methanolic extract on mouse immune response *in vitro*.
44. Thanabhorn S, Jaijoy K, Thamaree S, Ingkaninan K. Acute and subacute toxicities of the ethanol extract from the fruits of *Terminalia belerica* (Gaertn) Roxb. J Pharm Sci. 2006; 33(1-4):23-30.
45. Asthana M, Kumar A, Sharma S. Cytogenetical Effects of *Terminalia bellerica*, Roxb. on Root Meristem of Viciafaba. Adv. Biores. 2011; 2(1):174-77.
46. www.m.webmd.com/vitamins/ai/ingredientmono-811/terminalia