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Terminalia bellerica Roxb: an important medicinal plant: A review

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Abstract
Terminalia bellerica Roxb. Is from family combretaceae. It is one of the most commonly used plants in Indian traditional systems of medicine. T. *bellerica* is used for treatment of various diseases such as conjunctivitis, asthma, migraine, baldness, constipation and weak eyesight. It contains different phytoconstituents such as glycosides, flavonoids, tannins, phenolic compound, amino acids and saponins which are responsible for different pharmacological activities as antioxidant, antimicrobial, antidiarrhoeal, anticancer, antidiabetic, antihypertensive and hepatoprotective.

Keywords: *Terminalia bellerica*, chemical compounds, plants, bioactivities

Introduction
Herbal medicines are used as a health care tool in different countries. All the developing countries are fully dependant on herbal remedies. The use of herbal medicine is increasing due to its safety, efficacy and therapeutic potential as compared to synthetic pharmaceutical products. However, the potential of higher plants as a source of herbal medicine is unexplored. Terminalia, comprising about 250 species in the world mostly as medium or large trees, is the second largest genus in the family Combretaceae. The name "Terminalia" is derived from Latin word "terminus", which means the leaves are located at the tip of the branch. The bark of Terminalia plants usually has cracks and branches tucked into layers. Most of the Terminalia plants' leaves are large, leathery with solitary or clustered small green white fowers. Their fruits are yellow, dark red or black; drupe, usually angular or winged. Some fruits are edible, highly nutritious and have medicinal values [1]. Terminalia species are widely distributed in the southern Asia, Himalayas, Madagascar, Australia, and the tropical and subtropical regions of Africa. Terminalia plants in southern Asia have been intensively studied phytochemically due to their wide usage in Asian (India, Tibetan, and Chinese) tra-ditional medicine systems [1].
Terminalia bellerica commonly known as bibhitaki belongs to the family Combretaceae. *Terminalia bellerica* Roxb. 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 [2]. Chemically, the presence of β-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 [3]. 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 [4]. This review was mainly sites the information on highlight the phytochemical profile and bioactivities of *Terminalia bellerica* plant.

Phytochemicals
Plant body
Beta sitosterol, tannins, gaelic, ethyl and ellagic acid, Gallo-tannic acid, Coloring matter, resins and a greenish yellow oil, Tannins, ellagic acid, ethyl gallate, galloyl glucose and chebulinic acid, phyllemblin, β-sitosterol, mannitol, glucose, fructose and rhamnose, Glucoside (bellericanin), Gallo-tannic acid, Ellagic acid, gallic acid, lignans (termilignan and thannilignan), 7-hydroxy 3'4' (methylenedioxy) flavone and Anolignan B. Tannins, ellagic acid, ethyl gallate, galloyl glucose and chebulagic acid, phyllemblin, β-sitosterol, mannitol, glucose, fructose and rhamnose [5-9].

Leaves
Proteins, steroids and terpenoids. Three hydrolysable tannins; gallic acid, ellagic acid and methyl gallate; one flavone; luteolin; two flavonol aglycones; quercetin and kaempferol; and four flavonol glycosides; rutin,, quercetin-3-O-a-L-rhamnopyranoside, quercetin3-O-ß-Dglucopyranoside and kaempferol 3-O-ß-D-glucopyranoside. Saponins, Tannins, Amino acids, Proteins, Alkaloids, Carbohydrates and Flavonoids. 4-hydroxy-(2-methylbutanol) benzoic acid. Pyridine-3-carboxamide, 4-dimethylamino-N, 2, 4-difluorophenyl-β-sitosterol, 1, 5-diphenyl-3 pentanone, 9-Octadecenoic acid [10-14].

Seeds
Cardenolide, cannogenol 3-O-D-galactopyranosyl 14-O-L-rhamnopyranoside and phospholipids. It contained 12.28 % oil on dry basis; Moisture, ash and crude fibre contents of the seed kernel were found to be 8. 43, 2.54, and 8.78 % respectively. Free fatty acids as oleic acid and cholesterol content myristic acid, palmitic acid, 45.67 % oleic acid and 14.93 % stearic acid [15].

Fruit
Tain termilignan, thannilignan, 7-hydroxy-3',4'-(methylenedioxy) flavones, anolignan B 5, gallic acid, ellagic acid, ß-sitosterol. Two new lignans named termilignan and thannilignan, together with 7-hydroxy-3‘,4‘-(methylenedioxy) flavan and anolignan B Flavonoids, sterols and tannins 2, 3, 7, 8 -Tetrao xy-chro meno (5,4,3-cde) chro mene-5,10-dione,. Alkaloid, anthraquinone glycoside, saponins, flavonoids, polysaccharides, Steroid, Tannin Arjungenin, belleric acid, bellericoside, cannogenol 3-O-dgalactopyranosyl-(1g4)-O-l-rhamnopyranoside
sitosterol, ethyl gallate, chebulagic acid, galloyl glucose, mannitol, glucose, galactose, fructose and rhamnose. Gallic acid, ellagic acid and chebulagic acid, Gallo-tannic acid and glycoside bellericanin. Alkaloid, phenol, tannins and flavonoids. Glycosides, flavonoids, tannins, phenols, saponin, carbohydrates and proteins [16-19].

Stem bark
Arjungenin and its glycosides, belleric acid and bellerica sides. Hydrolysable tannins; gallic acid and ellagic acid in the water-soluble extract [20].

Biological activities
Anti-oxidant potential
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 [21].

Hepatoprotective Effect
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 [22].

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 rabbit jejunum, 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 diarrhea 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 [23].

Antihypertensive potential
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 ccurred at similar concentration in the endothelium-denuded tissues. Hence, it can be used for hypertension as it lowers BP through Ca2+ antagonist [24].

Anti-helminthic effect
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 proved significant paralysis and also caused death of worms at higher concentration as compared to Levamisole, reference standard. Hence, it was confirmed that *Terminalia bellerica* fruit has anti-helminthic activity [25].

Analgesic and antipyretic effects
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 has significant analgesic and antipyretic activities [26].

Anti-diabetic activity

A study was carried out to isolate compound from the fruit rind of *Terminalia bellerica* has 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 [27].

Anti-diarrhoeal effect

A study 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 [28].

Anti-salmonella potential

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 proved 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 [29].

Anti-microbial effect

A study was conducted to demonstrate the antimicrobial activity of methanol extract of T. bellerica against respiratory pathogens i.e., Staphylococcus aureus and Klebsiella pneumonia. Preliminary anti-microbial analysis 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 proved T. bellerica has antimicrobial activity against respiratory pathogens and hence can be used for treatment of diseases caused by pathogens [30].

Anti-Alzheimer's effect

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 acetyl cholinesterase inhibitory properties. All extract showed inhibition of enzyme activity in a dose dependent manner. Phytoconstituents as gallic acid, ellagic acid and phenolic acids present in fruit of all three plants inhibited acetyl cholinesterase. Being, acetyl cholinesterase inhibitor, it could be used for symptomatic treatment of Alzheimer's diseases [31].

Anti-cancer potential

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, fibro sarcoma, 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 [32].

Conclusion

Terminalia bellerica has been extensively used as traditional medicine. It has different phytoconstituents such as tannins, flavonoids, steroids, lignin, glycosides, terpenoid, saponins, cardenolides, flavanol glycosides and fatty acids. It has different 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.

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