Pharmacological Activities of *Bridelia retusa*: A Review

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ABSTRACT

*Bridelia retusa* is commonly known as Asana in Marathi. It has long been used in Indian folk medicine to treat broad spectrum of diseases, such as liver diseases, for removal of urinary concretion, inflammatory diseases etc. Phytochemical studies on *Bridelia retusa* disclosed major chemical constituents including steroids, triterpenoids, tannins and flavonoids. A research report on *Bridelia retusa* reveals for its analgesic activity, anti-inflammatory activity, hepatoprotective activity, antimicrobial activity, immunomodulatory activity and hypoglycemic effect. Hence in this article, we discuss the biochemical constituents, traditional uses and therapeutic potentials of *Bridelia retusa*.

KEY WORDS: *Bridelia retusa*, polyphenols, analgesic, hepatoprotective.

INTRODUCTION:

Herbal medicine is still the mainstay of about 75-80% of World population, mainly in the developing countries for primary health care because of better cultural acceptability, better compatibility with human body and lesser side effects. The chemical constituents present in them are a part of the physiological function of living flora and hence they are believed to have better compatibility with human body. Ancient literature also mentions herbal medicine for age related diseases namely memory loss, osteoporosis, diabetic wounds, immune and liver disorder etc. for which no modern medicine or only palliative therapy is available.  

*Man has been using herbs and plant products for combating diseases since times immemorial. The Indian subcontinent is enriched by a variety of flora - both aromatic and medicinal plants. This extensive flora has been greatly utilized as a source of many drugs in the Indian traditional system of medicine. In India, the earliest mention of the use of medicinal plants is to be found in Rigveda which was written between 4500-1600 BC.*

*Bridelia retusa* is a small or moderate sized deciduous tree up to 7 m in height, armed with long conical thorns when young and having dark brown bark. Exfoliation is irregular flakes, lanceolate or ovate – lanceolate leaves, flowers present in long axillary or terminal spikes and greenish yellow fruits.

It is frequently found in the forests around Gorakhpur and in the Western Ghat of South Maharashtra.

Plant is pungent, bitter, and useful in vata, lumbago and hemiplegia. The bark is good for removal of urinary concretion. The bark is used as liniment with gingelly oil in rheumatism. Stem bark powder is mixed with water given during fever. It is also used in jaundice with combination with other plants.

A) Chemical Composition/Key Active Constituents: Antifungal activity guided fractionation of solvent extracts of the stem bark of *Bridelia retusa* of the family Euphorbiaceae against *Cladosporium cladosporioides*, furnished new bisabolane sesquiterpenes, (E)-4-(1,5-dimethyl-3-oxo-1-hexenyl)benzoic acid, (E)-4-(1,5-dimethyl-3-oxo-1,4-hexadienyl) benzoic acid, (R)-4-(1,5-dimethyl-3-oxo-4-hexenyl)benzoic acid and (-)-isochaminic acid, together with the known (R)-4-(1,5-dimethyl-3-oxohexyl)benzoic acid (ar-todomatuic acid), 5-allyl-1,2,3-trimethoxybenzene (elemicin), (+)-sesamin and 4-isopropylbenzoic acid (cumic acid). All these compounds showed fungicidal activity on TLC bioautography method at very low concentrations except elemicin.

B) Pharmacological review:

1. Antinociceptive, anti-inflammatory and antioxidant activities: Antinociceptive and anti-inflammatory potentials of methanolic extract of *Bridelia retusa* fruit (BRME) against different animal models.
was evaluated in rodents. Antinociceptive effects of BRME were assessed in mice using the acetic acid-induced writhing and formalin test. Anti-inflammatory effects of BRME in three different doses, namely, 100, 200, and 400 mg/kg, were evaluated by utilizing different animal models representing various changes associated with inflammation, namely, carrageenan-induced paw oedema, histamine and serotonin-induced paw oedema, arachidonic acid-induced paw oedema, formalin-induced paw oedema, TPA-induced ear oedema, acetic acid-induced writhings vascular permeability, total WBC count in paw fluid, and myeloperoxidase assay. The BRME did not exhibit any signs of toxicity up to a dose of 2000 mg/kg. The extract showed statistical significant inhibition of induced nociception and inflammation in dose dependent manner. The higher dose of extract significantly inhibited pain and inflammation against control (P < 0.001). The present study scientifically demonstrated the antinociceptive and anti-inflammatory potential of fruit of B. retusa methanolic extract. These effects may be attributed to the presence of polyphenolic phytoconstituents in the extract. Chitosan the flavonoid isolated from the ethanol extract of leaves of Bridelia retusa. Phytochemical screening was carried out according to standard procedures from the leaves of Bridelia retusa. The isolated flavonoid was characterized by spectral studies and screened for anti-inflammatory and analgesic activity in experimental animal models. The anti-inflammatory activity was determined by formalin induced paw edema and carrageenan induced paw-edema method, and the analgesic activity was determined by tail flick method and hot plate latency method by using external standard indomethacin and Chitosan isolated from ethanol extract of Bridelia retusa. Chitosan significantly (P<0.05) showed the anti-inflammatory and analgesic activity in experimental animals. Therefore the present study justifies that the isolated flavonoid exhibits significant analgesic and anti-inflammatory activity at a dose of 250 mg/kg.9

Aqueous and alcohol extract of bark of Bridelia retusa exhibited dose dependant significant activity against carrageenan induced rat paw edema in the dose of 50 and 100 mg/kg, p.o.10 Petroleum ether, chloroform, methanol and aqueous extracts of the stem bark of Bridelia retusa -shawii. (Euphorbiaceae) were evaluated by using carrageenan induced rat paw edema and cotton pellet granuloma method in rat. The anti oxidant activity of all the extracts was determined by using Nitric oxide scavenging assay. It was observed that, all the extracts significantly inhibited the carrageenan induced rat paw edema at the dose of 200 mg/kg b.w. orally, when compared with control and standard drug Ibuprofen. Extracts also suppressed the granulomatous tissue formation of chronic inflammation, when compared with standard drug Diclofenac sodium. The stem bark of B. airy – shawii extracts showed significant free radical scavenging activity against nitric oxide (NO*) induced release of free radicals.11

2. Antimicrobial activity: Antimicrobial activity of 10 plant extracts and their 34 fractions was evaluated against three sexually transmitted/reproductive tract pathogens - Neisseria gonorrhoeae, Haemophilus sudreyci and Candida albicans. The plant parts were selected; the extracts/fractions were prepared and screened by disc diffusion method. The minimum inhibitory and minimum cidal concentrations were determined. The qualitative phytochemical analysis of selected extracts/fractions showing activity was performed. Out of the extracts/fractions tested, three inhibited C. albicans, ten inhibited N. gonorrhoeae and five inhibited H. ducreyi growth. Study demonstrated that Terminalia paniculata Roth. extracts/fractions inhibited growth of all three organisms. The ethyl acetate fraction of Syzygium cumini Linn and Bridelia retusa (L.) Spreng. Extracts was found to inhibit N. gonorrhoeae at lowest concentrations.12 Screening methanolic leaf extracts of 21 timber-yielding plants for antibacterial activity against nine species of uropathogenic bacteria isolated from clinical samples of a hospital (Enterococcus faecalis, Staphylococcus aureus, Acinetobacter baumannii, Citrobacter freundii, Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, and Pseudomonas aeruginosa) by the Kirby-Bauer’s disc diffusion method. Two Gram-positive isolates, E. faecalis and S. aureus, were resistant to 14 of the 18 antibiotics used. Gram-negative isolates A. baumannii, C. freundii, E. aerogenes, E. coli, K. pneumoniae, P. mirabilis, and P. aeruginosa were resistant to 10, 12, 9, 11, 11, 10, and 11 antibiotics, respectively, of the 14 antibiotics used. Methanolic leaf extracts of Anogeissus acuminata had the maximum zone of inhibition size-29 mm against S. aureus and 28 mm against E. faecalis and P. aeruginosa. Cassia tora had 29 mm as the zone of inhibition size for E. faecalis, E. aerogenes, and P. aeruginosa. Based on the minimum inhibitory concentration and minimum bactericidal concentration values, the most effective 10 plants against uropathogens could be arranged in decreasing order as follows: C. tora > A. acuminata > Schleichera oleosa > Pterocarpus santalinus > Eugenia jambolana > Bridelia retusa > Minusops elengi > Stereospermum kunthianum > Tectona grandis > Anthocephalus cadamba. The following eight plants had moderate control capacity: Artocarpus heterophyllus, Azadirachta indica, Dalbergia latifolia, Eucalyptus citriodora, Gmelina arborea, Pongamia pinnata, Pterocarpus marsupium, and Shorea robusta. E. coli, followed by A. baumannii, C. freundii, E. aerogenes, P. mirabilis, and P. aeruginosa were controlled by higher amounts/levels of leaf extracts.13 The in vitro antimicrobial activity of the crude methanolic and ethanolic leaf extract of Bridelia retusa (L.) Spreng was studied against four gram negative and two gram positive bacteria. The results showed that both the extracts showed antimicrobial activity. Maximum zone of inhibition was observed in the methanolic extract against Escherichia coli which was 29.5 ± 0.50 mm. However,
ethanolic extract showed least activity against Staphylococcus aureus. The basis of this plant extract in the traditional treatment of diarrhea in human is highlighted.\textsuperscript{14} Bark extract of \textit{B. retusa} was studied against 4 bacterial species viz. Staphylococcus aureus, Klebsiella pneumonia, Pseudomonas aeroginosa and Proteus vulgaris and 2 fungal species \\textit{Candida albicans} and Aspergillus niger. Acetone extract showed MIC values ranging from 25, 42.5 to 85 mg/ml against the tested strains.\textsuperscript{15}

3. Protective role on kidney and liver after \textit{CCl4} intoxication: Protective role of bark extracts of \textit{Bridelia retusa} S. was studied on the liver and kidney after \textit{CCl4} intoxication. The bark of \textit{Bridelia retusa} S. was powdered and subjected to sequential extraction based on polarity using solvents such as petroleum ether, chloroform, ethanol and distilled water. The extract was filtered, concentrated, dried and stored in refrigerator until further use. Oral suspensions containing 25 and 50 mg/kg body weight of ethanolic and aqueous extracts were administered for 5 days to carbon tetrachloride treated female mice. The protective role of ethanolic and aqueous stem bark extracts of \textit{Bridelia retusa} S. were investigated on histological profiles of liver and kidney. The effect of 50 mg of ethanolic extract was visible by reduced \textit{CCl4} induced toxicity on the histology of liver and kidney which were restored to that of normal better than aqueous extract wherein steatosis and dilation of central vein caused by \textit{CCl4} was reduced and normalized hepatocytes. Hence, the present study indicates that both the extracts possessed amelioration of histological changes in the liver and kidney of \textit{CCl4} intoxicated mice though ethanolic extract showed better recovery in dose dependent manner.\textsuperscript{16}

Oral suspensions containing 25 and 50 mg/kg body weight of ethanolic and aqueous extracts of bark of \textit{Bridelia retusa} S. were administered for 5 days to carbon tetrachloride treated female mice. The protective role of ethanolic and aqueous stem bark extracts of \textit{Bridelia retusa} S. were investigated on histological profiles of liver and kidney. The effect of 50 mg of ethanolic extract was visible by reduced \textit{CCl4} induced toxicity on the histology of liver and kidney which were restored to that of normal better than aqueous extract. It was observed that both the extracts possessed amelioration of histological changes in the liver and kidney of \textit{CCl4} intoxicated mice though ethanolic extract showed better recovery in dose dependent manner.\textsuperscript{17}

4. Immunomodulatory activity: Immunomodulatory effect of \textit{Bridelia retusa} was studied in experimental rats. \textit{Bridelia retusa} was administered orally at a dose of 200 mg/kg to healthy rats divided into three groups consisting of six animals each. The assessment of immunomodulatory activity was carried out by testing the humoral (antibody titre) and cellular (foot pad swelling) immune responses to allergic challenge by sheep RBCs and by neutrophil adhesion test. On oral administration of the extract a significant increase neutrophil adhesion in and delayed type hypersensitivity response whereas the humoral response to sheep RBCs was unaffected. Thus \textit{Bridelia retusa} significantly potentiated the cellular immunity by facilitating the foot pad thickness responses to the sheep RBCs in sensitized rats. With a dose of 200 mg/kg the delayed type hypersensitivity response, the responses were statistically significant when they were compared with the control. The study stated that \textit{Bridelia retusa} shows a significant stimulation of the cell mediated immunity and no effect on the humoral immunity.\textsuperscript{18}

5. Total phenolic content and antioxidant activity: Effect of influence of solvents (possessing different dielectric constant values) and geographical location on the Total Phenolic Content (TPC) and antioxidant activity of extracts of \textit{Bridelia retusa} bark was studied. The bark was collected from two different geographical locations of India [Maharashtra (MAH) and Andhra Pradesh (AP)]. The highest extractive values were found to be as 20.70 ± 0.56 %/w/w and 18.43 ± 0.97 %/w/w in case of methanolic extracts of \textit{Bridelia retusa} bark collected from MAH and AP regions respectively while the total polyphenolic contents in the methanolic extract of \textit{Bridelia retusa} bark were 32.52 ± 0.24 mg/100 gm and 28.04±0.67 mg/100gm in MAH and AP regions respectively. The methanolic extract of the species from MAH exhibited the highest radical scavenging activity while that from AP showed less scavenging activity. The extracts showed a positive correlation between the polyphenol contents and solvent’s dielectric constant (R=0.728, P<0.05). This suggests that dielectric constant value significantly influences the choice of solvent for extraction as well as the total phenolic contents and subsequently the antioxidant activity of the plant extract.\textsuperscript{19}

6. Hypoglycemic effect: \textit{Bridelia retusa} bark was screened for hypoglycemic effect on alloxan induced rats. Albino rats were divided into groups received different treatments consisting of control, methanolic, pet-ether and n-butanol extracts (200 and 400 mg/kg) and standard drug Glibenclamide (5 mg/kg, p.o.) blood glucose level was estimated using GOD/POD method. Results showed that \textit{Bridelia retusa} extracts does not affected blood glucose in normal rats but in alloxan induced diabetic rats n-butanol extract showed significant fall of blood glucose level. Phytochemical analysis showed presence of steroids, triterpenoids, tannins and flavonoids as major constituents.\textsuperscript{20}

CONCLUSION: Now a days, research on Indian traditional medicinal plants has gained a new recommence. Although, the other systems of medicine are effective they come with a number of undesired effects that often
lead to serious complications. Being natural, herbal medicine alleviates all these problems. *Bridelia retusa* bark has been used traditionally in Indian medicine for the treatment of broad spectrum of disorders. The present study scientifically demonstrated the antinociceptive and anti-inflammatory potential of fruit of *B. retusa* methanolic extract. These effects may be attributed to the presence of polyphenolic phytoconstituents in the extract. While studying the antimicrobial potentials of bark extract of *B. retusa* it shows significant activity against various pathogens. The extract was investigated for nephroprotective and hepatoprotective activity. The present study indicates that both the extracts possessed amelioration of histological changes in the liver and kidney of CCl₄ intoxicated mice though ethanolic extract showed better recovery in dose dependent manner. While studying the immunomodulatory activity it is observed that *Bridelia retusa* significantly potentiated the cellular immunity by facilitating the foot pad thickness responses to the sheep RBCs in sensitized rats. The total polyphenolic contents in the methanolic extract of *Bridelia retusa* bark were 32.52 ± 0.24 mg/100 gm which was responsible for significant antioxidant activity. During study of hypoglycemic activity results showed that *Bridelia retusa* extracts does not affected blood glucose in normal rats but in alloxan induced diabetic rats n-butanol extract showed significant fall of blood glucose level. All the above mentioned activities may be attributed due to presence of steroids, triterpenoids, tannins and flavonoids as a major phytoconstituents.

REFERENCES


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