December 30, 2018

PharmacologyOnLine

Archives • 2018 • vol.3 • 37-48

A PHARMACOLOGICAL REVIEW ON THE TWO TRADITIONAL PLANTS USED IN BANGLADESH FOR JAUNDICE

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Abstract

Since the inception of the universe, nature has been enriched with abundant resources are being given away for the betterment of humanity. Nature has the plethora of biologically active compounds those are potential to prevent ailments. By virtue of natural favor, Bangladesh has been a domain with plenty of natural plants possessing great therapeutic significance. Over time myriad medicinal plants have been identified and used in Bangladesh to treat various types of diseases. Hepatic diseases are progressively increasing in Bangladesh and it has been a challenge to achieve expected compounds that elicit effective potential against these complications. Various traditional plants have been used in treating hepatic diseases and jaundice since ancient period. The current review has focused largely on the manifold aspects of pharmacological actions of *Asparagus racemosus* and *Terminalia chebula*, two indigenous traditional plants used in Bangladesh for the treatment of jaundice. Alongside it has also demonstrated the current traditional formulation of these plants used for the treatment of jaundice.

Keywords: *Asparagus racemosus, Terminalia chebula, jaundice, pharmacological activities, Bangladesh.*

Introduction

Nature is considered as eternal sources for various medicinal agents and drug development. There are about 250000 species of plants in the universe among them 6% have been found to be biologically active and 15% have undergone phytochemical testing [1]. It is estimated that about 80% out of more than 4000 million people of the world depend on the traditional medicines to meet the demand for primary health care needs [2]. Whereas 70-80% people of developing Asian countries rely on the traditional medicine despite the availability of allopathic medicines in many areas of the community [3]. The utilization of plant-based medicines is known as ethnomedicine. The aim of ethnopharmacology is to facilitate the discovery of the bioactive compounds from natural sources [4]. Plants remain an excellent source of new drugs, and new chemical entities. Medicinal plants serve for the development of both natural products and their derivatives. For example anti-malarial drug arteetheris derived from artemisinin which is isolated from the traditional plant, Artemisia annua L. (Asteraceae). There are few more derivatives of artemisinin under clinical trials in Europe to be used as anti-malarial drugs [5]. Evidence shows that there was an involvement of the use of various traditional medicines in the early health care systems of developing countries [3]. The rapid increase of the knowledge regarding the optimistic effects of the plant-derived compounds accelerates using these agents to cure diseases [6].

Jaundice is not a disease but it is a sign that may result from conditions like viral hepatitis, gallstones, hemolytic anemia, pancreatic cancer, parasite infection of the liver, autoimmune hepatitis, or use of certain drugs etc. In recent days jaundice is very common in Bangladesh because of the rapid increase in the various hepatic diseases [6, 7]. There is no effective treatment for jaundice and hepatitis to be covered by current allopathic and homeopathic treatment procedure [6].

In this review article, the authors have tried to put together information of two exclusively used plants with their activity against jaundice along with other investigated pharmacological effects.

Methods

Asparagus racemosus and *Terminalia chebula* were selected from searching literature, and then their inclusion was confirmed in the Ethnobotanical Database of Bangladesh (EDB), which ensures their indigenous identity in Bangladesh. Most of the information required to prepare the manuscript were collected by the comprehensive searching of literature. Google scholar was the preliminary tool for searching and identifying appropriate published works. Then these articles were accumulated from various reputed electronic sites like Elsevier, ScienceDirect, Springer, PubMed, PMC, Wiley Online Library, Hindawi, and Taylor & Francis etc.

Traditional uses for the treatment of jaundice

Exploration of literature claimed that different parts of the plants are used for the treatment of jaundice and these parts of the plants include roots and fruits. In most of the cases, root of *A. racemosus* are taken as juice and fruits of *T. Chebula* are taken orally [8-11].The common forms of use of these two selected plants are given in the table 1.

Table 1: Mode of use of reviewed plants in jaundice

Pharmacological activities

4.1. Pharmacological activities of *A. racemosus*

4.1.1. Antitussive effect

Study reported that methanol roots extract of *A. racemosus* (AR) given at the dose of 200 and 400 mg/kg, orally showed the antitussive effects on SO_2 induced cough in mice model. The dose 200 and 400 mg/kg showed 40% and 58.5% cough inhibition respectively those were comparable to that of 10 and 20 mg/kg of codeine phosphate that resulted in 36% and 55.4% inhibition respectively when used as standard [12].

4.1.2. Antiulcer activity

Crude extract of *A. racemosus* was administered at the dose of 100 mg/kg body weight, treatment improved condition of indomethacin plus pyloric ligation (PL)-induced gastric ulcer in rat models. The gastric ulcer reduction was also comparable to the standard antiulcer drug Ranitidine given at the dose of 30 mg/kg/day [13]. Methanol extract of *A.*

racemosus dose-dependently protected gastric ulcers when administered to test animals at the dose of 25–100 mg/kg twice daily for 5 days [14].

4.1.3. Adaptogenic activity

Standardized methanol extract of *A. racemosus* (AR) was applied at various doses (50, 100, and 200 mg/kg, BW orally) to test animals for assessing physiological modulation of the stress pathways. Methanol extract of AR (MAR) decreased the plasma corticosterone and norepinephrine levels in a dose-dependent manner. Tissue level of monoamines (serotonin, dopamine, and norepinephrine) was increased in hypothalamus by MAR. The dose 100 mg/kg was found to show its ceiling effect at which it produced its maximum effect [15].

4.1.4. Anticancer activity

The anticancer activity of the extract of *A. racemosus* was evaluated using HT-29 (human colon adenocarcinoma), MCF-7 (human breast cancer), and A-498 (human kidney cancer) cell lines. Oral administration of the test material at the doses of 250 and 500 mg/kg body weight caused significant reduction in tumor volume, packed cell volume, percent increase in body weight, viable tumor cell count, and increase in non-viable cell count compared to control group [16].

4.1.5. Antidepressant activity

Study reported that methanol extract of *A. racemosus* (MAR) showed antidepressant activity when administered at the dose of 100, 200 and 400 mg/kg daily for 7 to test animals. The study results showed that MAR decreased immobility in forced swim test and increased avoidance response in learned helplessness test that could be interpreted as antidepressant activity [17].

4.1.6. Antihypercholesterolemic activity

Study conducted on male albino rats suggested that the root powder of *A. racemosus* when provided with diet to hypercholesteremic rats showed reduction in both plasma and hepatic lipid profiles. Treatment also increased excretion of cholesterol in feces together with increased hepatic HMG-CoA reductase activity and bile acid content [18].

4.1.7. Antiosteoporotic activity

A. racemosus revealed significant ($P<0.05$) impact on various processes of bone viz. ossification, mineralization, and suppression of ovariectomized rats. Treatment of ovariectomized rats with root extracts of *A. racemosus* caused reduction in serum alkaline phosphatase and serum calcium accompanied by inhibition of excessive loss of calcium in urine. In addition, extracts of *A. racemosus* improved hardness of 4th lumbar vertebra, length of femoral bone and its weight [19].

4.1.8. Antioxidant activity

Crude and purified aqueous fraction of *A. racemosus* were investigated to assay its antioxidant activity against membrane damage of hepatic mitochondria of rats caused by the free radical generation during exposure to γ-radiation. Lyophilized polysaccharides (stated as P3) was found to be effective even at the concentration of 10 µg/ml. Both the P3 fraction and the crude extract resulted in significant inhibition of protein oxidation and lipid peroxidation. The antioxidant effect of P3 fraction was more effective against lipid peroxidation, while the crude extract was measured more effective in inhibiting protein oxidation [20]. Methanol root extracts obtained from the *A. racemosus* significantly increased superoxide dismutase, ascorbic acid and catalase, whereas it decreased lipid peroxidase product in animal models [21].

4.1.9. Enzyme inhibitory activity

In a study, methanol root extract of *A. racemosus* was administered at a dose of 50,100 and 200 mg/kg orally, treatment significantly shortened the immobility periods in a dose dependent manner that can be measured by both tail suspension test and forced swim test. It was suggested that this might result from the reduction of Monoamine oxidase-A (MAO-A) and Monoamine oxidase-B (MAO-B) in brain after the administration of methanol extract of *A. racemosus* [22]. Another study reported that liposomal formulations of *A. racemosus* root extract (AR1-6) showed in vitro tyrosinase inhibitory activity [23].

4.1.10. Hepatoprotective effect

Ethanol extract obtained from the roots of *A. racemosus* was co-administered orally with isoniazid at the dose of 50 mg/kg BW which showed hepatoprotective effects through free radical scavenging. Reduction of free radical generation resulted from the inhibition of hepatic enzyme (CYP2E1) activity and removal of free radical occurs due to induction of antioxidant enzymes and improvement of non-enzymatic thiol antioxidant glutathione [24]. Study conducted on Wistar rats revealed that pretreatment with the aqueous extract obtained from the roots of *A. racemosus* showed potential to prevent hepatocarcinogenesis caused by Diethylnitrosamine [25].

4.1.11. Hypoglycemic activity

Ethanol extract of *A. racemosus* was administered to type 2 diabetic rats twice daily for 28 days. It significantly reduced the serum glucose levels and increased the level of serum insulin by 30% when compared with control. Moreover, the extract significantly decreased postprandial glucose level after ingestion [26].

4.1.12. Immunomodulatory activity

One study reported that a unique polyhydroxylated steroidal sapogenin acid isolated from the roots of *A. racemosus* could booster the immune system of experimental animals with cyclosporine-A induced immune suppression [27]. A study postulated that treatment on experimental animal with (100 mg/kg b.w. p.o.) aqueous roots extract of *A. racemosus* revealed considerable increase in CD4/CD8+ and CD3+ counts that indicated activation of T cell. Animals model showed significant increase in Th1 (IL-2, IFN-g) and Th2 (IL-4) cytokines which suggested its mixed Th1/Th2 adjuvant potential [28].

4.1.13. Neuroprotective effects

This study was performed using five groups of adult female Wistar rats where three ovariectomized (OVX) groups received ethanol root extract of *A. racemosus* at the dose of 100 mg/kg BW, 1000 mg/kg BW and 17α-ethynylestradiol (EE) at the dose of 0.1 mg/kg BW during experimental period. The rat groups treated with ethanol root extract and 17α-ethynylestradiol manifested significantly upper recognition index than that of OVX group. It is suggested that the root extracts and EE reduced the neuronal loss in the brain and thereby improved cognitive function of ovariectomized rats [29]. Methanol root extract of *A. racemosus* was used against kainic acid (KA) induced hippocampal and striatal neuronal damage in female Swiss albino mice. Administration of kainic acid (KA) caused an increase in protein carbonyl content and lipid peroxidation and decrease in glutathione peroxidase (GPx) activity and reduced glutathione (GSH) content. The mice model treated with *A. racemosus* root extract displayed an improvement in GPx activity and GSH content but reduction in protein carbonyl and membranal lipid peroxidation [30].

4.1.14. Prokinetic activity

Study showed that *A. racemosus* (Shatavari) and metoclopramide significantly reduced gastric emptying halftime (GE t1/2). The basal GE t1/2 in volunteers was 159.9 +/- 45.9 min which was reduced to 101 +/- 40.8 min by Shatavari ($P<0.001$) and to 85.3 +/- 21.9 by metoclopramide ($P<0.001$). Both of the agent did not differ significantly in their effects [31].

4.1.15. Teratogenic activity

When methanol extract of *A. racemosus* given at the dose of 100 mg/kg for 60 days to test animals showed teratological changes including increased resorption of fetuses, gross malformations including swelling in legs and intrauterine growth retardation with reduced placental size [32].

4.1.16. Miscellaneous effects

Searching of various literatures revealed that various forms of extracts of *A. racemosus* showed distinctive pharmacological activities. Methanol extract of *A. racemosus* root showed antiuremic activity and antiamnesic activity, ethanol extract of roots showed antiurolithiatic activity, ethanol and aqueous extracts of *A. racemosus* root showed antidiarrheal activity, aqueous solution of the crude alcoholic extract of the roots exhibited antiprotozoal activity, alcohol extract of the roots of *A. racemosus* produced positive ionotropic and chronotropic effect, leaf extracts of *A. racemosus* were responsible for its antimicrobial effects, hydro-alcoholic extracts of roots of *A. racemosus* showed

meaningful aphrodisiac activity, aqueous roots extract of *A. racemosus* exhibited immunoadjuvant and antidiuretic activity, study conducted using incision and excision model revealed wound healing activity of *A. racemosus*, root extract of *A. racemosus* has been prescribed to augment the secretion of milk of lactating mother, lyophilized extracts of *A. racemosus* were found to be beneficial to improve fertility, alcoholic extract of rhizome of *A. racemosus* exhibited oesterogenic effects, ethanol leaf extract of *A. racemosus* showed anti-inflammatory effect, asparagamine A of *A. racemosus* showed anti-abortifacient effect [33-47].

5.2. Pharmacological activities of *Terminalia chebula*

5.2.1. Adaptogenic activities

The ethanol extracts of *T. chebula* showed anti-stress activity by preventing stress-induced increased levels of various biochemicals like triglycerides, cholesterol, blood urea nitrogen (BUN), glucose plasma corticosterone. Treatment also reduced blood cell count (RBC and WBC) and prevented alteration of weights of organs like liver, spleen, testis, and adrenal glands etc. [48].

5.2.2. Antibacterial activity

Various extracts of *T. chebula* showed varying degree of antibacterial potential against specific bacterial strain i.e. ethanol extract was superior against E. coli and hot aqueous extract showed superiority against S. aureus. Whereas cold aqueous extract exhibited the least antibacterial activity against all the tested strains [49]. Study reported that ethanol fruit extract of *T. chebula* was highly effective against Salmonella typhi SSFP 4S, Staphylococcus epidermidis MTCC 3615, Staphylococcus aureus ATCC 25923, Bacillus subtilis MTCC 441 and Pseudomonas aeruginosa ATCC 27853 [50].

5.2.3. Anticlastogenic activity

The anticlastogenic activity of *T. chebula* extract has been reported against micronuclei formation and chromosomal aberration induced by cyclophosphamide in mice bone marrow cells. It dose dependently and significantly ($P<0.05$) inhibited micronuclei formation and chromosomal aberration when compared with the standard cyclophosphamide group [51].

5.2.4. Antidiabetic activities

Ethyl Acetate-Soluble portion of ethanol extract of *T. chebula* fruit (EETC) improved streptozotocin induced diabetic mellitus in rats. High dose (500 mg/kg BW) of extract (HEETC) decreased the blood glucose and serum lipid levels, treatment also reduced serum and thoracic aorta concentrations of malondialdehyde in diabetic rats [52]. It was revealed that the oral administration of ethanol extract of the fruits at the dose of 200 mg/kg BW for 30 days significantly reduced levels of blood glucose and glycosylated hemoglobin in streptozotocin induced diabetic rats [53].

5.2.5. Anti-inflammatory activity

In vivo anti-inflammatory activity of *T. chebula* fruit was evaluated at different doses ranged from 50 to 500 mg/kg, p.o. against carrageenan-induced inflammation in rats. Study revealed that standardized extract at the dose of 250 mg/kg, p.o. caused 69.96% reduction in carrageenin-induced paw edema in rats [54].

5.2.6. Antioxidant activity

The polyphenolic extract of *T. chebula* fruits has been demonstrated to have antioxidant activity. It was authenticated by determining DPPH radical concentration (IC50 14 µg/mL), the reducing power, total antioxidant capacity, nitric oxide radical concentration (IC5030.51 µg/mL) and hydrogen peroxide scavenging activity (IC50265.53 µg/mL) under in vitro conditions [55].Study showed that aqueous extract of fruit of *T. chebula* (TCE) significantly reversed the t-BHP-induced cell cytotoxicity and lactate dehydrogenase leakage in rat models. TCE also exhibited in vitro ferric-reducing antioxidant activity and 2,2-diphenyl-1-picryhydrazyl free radical-scavenging activities [56].

5.2.7. Anti-platelet activity

T. chebula fruit extract showed dose dependent inhibition of arachidonic acid induced human platelet aggregation. More than 30% inhibition was observed at 5 mg/ml dose while maximum inhibition of 95% was obtained at the dose of 10 mg/ml (IC50: 6.74 mg/ml) [57].

5.2.8. Antiulcer activity

Study demonstrated that pretreatment with hydroalcoholic extract of *Terminalia chebula* fruit at the doses of 200 and 500 mg/kg caused significant reduction in lesion index, total affected area and percentage of lesion in comparison with control group ($P < 0.05$ and $P < 0.01$) in the aspirin, ethanol and cold restraint stress-induced ulcer in rat models [58].

5.2.9. Enzyme inhibitory activity

Acetylcholinesterase inhibitors are employed for the symptomatic treatment of Alzheimer's disease. Methanol extracts of *T. chebula* of ayurvedic herbal drug 'Triphala' showed acetylcholinesterase inhibitory activity. Gallic acid and ellagic acid, and the phenolic acids present in the fruits inhibited the enzyme acetylcholinesterase [60]. Another study reported to isolate 1,2,3,4,6-penta-O-galloyl-β-D-glucose, a compound from *T. chebula* showed significant acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitiory activities with IC50 values of 29.9±0.3 µM and 27.6±0.2 µM, respectively [61].

5.2.10. Hepatoprotective effects

T. chebula water extract (TCW) ameliorated tert-butylhydroperoxide-(t-BHP-) induced acute liver injury in C57/BL6 mice model. Tert-butylhydroperoxide-(t-BHP-) dramatically elevated the serum AST, ALT, and LDH level, while animals pretreated with TCW showed significant reduction of these biomarkers [62].

5.2.11. Hypocholesterolemic activity

Study reported Haritaki that is *Terminalia chebula*, when administered to atherogenic diet induced hyperlipidemic rat models, treatment caused reduction in total cholesterol, triglycerides, total protein and elevation of high density lipoprotein cholesterol. It was also suggested that Haritaki at concentrations of 1.05 and 2.10 mg/kg BW worked as an excellent lipid-lowering agent [63].

5.2.12. Immunosuppressive activity

Study reported that gallic acid (GA) and chebulagic acid (CA) extracted from the fruits of the *T. chebula* revealed immunosuppressive activity. They blocked the cytotoxic T lymphocyte mediated (CTL) mediated cytotoxicity. GA and CA were found to inhibit the activity of CD8+ CTL clone at IC50 values of 30 µM and 50 µM, respectively [64].

5.2.13. Neuroprotective effect

In vitro neuroprotective effect of various extracts (water, methanol, and 95% ethanol) of the *T. chebula* was evaluated by the inhibition of H_2O_2-induced rat pheochromocytoma cell (PC12) death. Application of H_2O_2 induced a dose-dependent loss in viability of PC12 cells. Among the three extracts water extract showed the greatest neuroprotective activity [65].

5.2.14. Miscellaneous effects

Oil fraction from *T. Chebula* possessed purgative activity, polyhedral formulation of *T. chebula* exhibited antiallergic activity, combination of *T. chebula* with other botanicals showed antiprotozoal activity, acetone extract of *T. chebula* showed antimutagenic activity, ethyl acetate, methanol and acetone extracts of *T. chebula* revealed anthelmintic activity, *T. chebula* extract showed prokinetic activity, methanol extract of *T. chebula* fruit showed anticancer activity, ethyl acetate and ether extract of fruits of *T. chebula* were found to be active against pathogenic fungal strains, ripe *T. chebula* fruits expressed Immunomodulatory activities, alcohol extract of *T. chebula* manifested cardioprotective effect, aqueous extract of *T. chebula* showed renoprotective, antiurolithiatic, anticaries and radioprotective activity,various organic and aqueous extracts of *T. chebula* ashowed wound healing activities, compounds of *T. chebula* showed activity against hepatitis C virus, water soluble fraction of *T. chebula* exhibited antianaphylactic effect, acetone extract of *T. chebula* fruits possessed antiarthritic activity, ethanol extract of *T. chebula* showed anticonvulsant activity [66-81].

Discussion

Literature review revealed that both of the plants are used for the treatment of jaundice as folk medicine in Bangladesh. Besides this review also manifested many distinctive pharmacological activities of these plants. It is important to rationale and prioritize the promising pharmacological effects with a view to fitting contemporary treatment need.

This review is likely to provide new glimpse to the researcher of relevant fields to find out any lead candidate or its derivatives for the effective treatment of Jaundice or any other ailments which are postulated by the pharmacological activities of these medicinal plants.

Acknowledgments

Authors are thankful to the Department of Pharmacy, University of Development Alternative for giving technical support.

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Table 1. Mode of use of reviewed plants in jaundice

Sl. No	Scientific name	Local name	Parts used	Mode of use
1.	*Asparagus racemosus*	Satamuli	Root	Juice made from the tuberous roots
2.	*Terminalia chebula*	Horitoki	Fruit	Fruits are taken orally