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REVIEW ARTICLE

A REVIEW UPDATED ON ETHNOPHARMACOLOGICAL PROFILE OF *KIRGANELIA RETICULATA* POIR (BAILL). : AN IMPORTANT HERBAL PLANT

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ABSTRACT

Kirganelia reticulata (Poir.) Baill. is known for its importance in various traditional medicines around the world. In present review covers a literature survey across from 1971 to 2014 until now. The some information collected from published literature on species of *Kirganelia reticulata* (Poir.) Baill. (=Syn. *Phyllanthus reticulatus* Poir.).The extract and the compounds isolated from *Kirganelia reticulata* show a wide spectrum of biological activities including antidiabetic, antibacterial, antioxidant, hepatoprotective, antiplasmodial, anticiceptive, analgesic and anti-inflammatory properties.

Keywords: *Kirganelia reticulata* (Poir) Baill, Ethnopharmacological properties.

INTRODUCTION

Herbal drugs play an important role in the healthcare programs. Ancient literature incorporates a remarkable broad definition of medicinal plants and considers all parts of the plant to be potential source of medicinal substances. The main hindrance in the acceptance of herbal medicines is the lack of documentation and quality control. So it becomes extremely important to make an effort towards standardization of the plant material to be used as medicine[1]. India is a varietal emporium of the medicinal and aromatic plants (MAPs) and we have well-established local healthcare tradition still relevant in indigenous healthcare system. As per World Health Organisation (WHO) estimates, almost 80% of the population of developing countries relies on traditional medicines, mostly plant drugs, for their primary health care needs. In developed countries, the use of Indian traditional medicines is quite prevalent and also, modern pharmacopoeia still contains at least 25% drugs derived from plants. The use of medicinal plants in the Indian subcontinent can be traced back to the Vedic period. The texts mentioning the uses of different medicinal plants are the Rigveda (written between 4500 and 1600 BC), the Atharveda (2000–1000 BC), the Charaka Samhita (~900 BC) and the Sushruta Samhita (~600 BC); these texts are written in Sanskrit[2].

Kirganelia reticulata (Poir) Baill. is belonging to the family Euphorbiaceae, popularly known as "potato plant or potato bush" and are variously named in different parts of the world. Synonymously, it is also named as *Phyllanthus reticulatus* Poir. and commonly used in Indian Ayurvedic system of medicine in various ailments related to liver, kidney, genitourinary system and stomach. It has properties of *Rasa (Kashaya, Tikta, Madhura, Guna (Lakhu)* and *Veerya (Seeta)*. The Ayurvedic literature has shown its wide utilization as in Vata, Pitta, diabetes, burning sensation, burns, skin diseases, obesity and urinary retention, skin eruption. The use of this drug is now gaining momentum because of its novel antiviral activity against Hepatitis B virus and for several other biological activities such as hypotensive effects viral infections; hepatotoxicity causing liver diseases and jaundice[3]. Some plant images are given in **Figure No. 1**.

ETHNOPHARMACOLOGICAL PROPERTIES

In ethnopharmacological activity survey on worldwide generally seen that different country gives different activity such as In Tanzania, the parts of leaves extract with water and methanol gives various activity[4,5]. And also root extract and entire plant extracts gives antifungal and in vitro Hypotensive activity[5,6,7]. In Thailand, dried roots of *K. reticulata* against many bacterial species gives no irritant or tumor-promoting activity found (Hecker, personal communcitation)[8]. In Indonesia: West Sumatra. Leaves give negative test for alkaloids[9]. Generally known to contain terpenoids betulinic acid and friedelin[10]. In India, Uttar Pradesh: Lucknow, extracts of the above ground part of the plants give hypotensive activity *in vivo* of dog and also give antispasmodic activity[11]. These are described as following:

Antidiabetic activity, Anti- hyperglycaemic and hypoglycaemic activities

The plant *K. reticulata* is claimed to have antidiabetic activity in tribal area. To validate the tribal claim, the petroleum ether and ethanolic extracts of leaves of the *K. reticulata* were orally tested at 500 and 1000 mg/kg for hypoglycaemic effect in alloxan induces diabetic mice. It shows antidiabetic activity at the dose of 1000mg/kg. The phytochemical screening of the residues revealed the presence of terpenoids glycosides, protein, carbohydrates and absence of alkaloids and steroids[12,13,14].

(A) **(B)**

(C) **(D)**

Figure 1 (A): Showing plant, (B): Showing cutting of root part, (C): Showing collection of root part & (D): Showing authentication of plant.

Antibacterial activities

The *in vitro* antibacterial activities of leaf extract (Methanol and Ethanol) from 10 genus species. Which are medicinally important, were investigated by agar-well diffusion method against four food borne human pathogens (*Staphylococcus aurous*, *Salmonella typhi*, *Vibrio cholera* and *Pseudomonas aeruginosa*). Leaf extracts contained high level of phenols and exhibit differential antibacterial activity against all four tested human pathogenic bacteria. The phenolic constituents of the tested extracts are closely associated with antibacterial activity. Highest antibacterial activity is exhibited by *K. reticulata* and can be used as a promising source of antibacterial drug[15]**;** methanol, chloroform and hexane extracts from leaves of *K. reticulata*, used in Indian Ayurvedic Medicine for the treatment of several ailments of microbial and non-microbial origin were evaluated for potential antibacterial activity against methicillin isolated from clinical specimen was studied. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) resistant *Staphylococcus aureus* (MRSA). Antibacterial activity and biofilm production of crude extracts against MRSA (ATCC 25923) values of the methanol, chloroform and hexane extracts were in the range of 12.5 to 50.0 mg/ml and 25.0 to 100.0 mg/ml, respectively. Amongst the evaluated extracts, the methanolic extract showed the strongest antibacterial effect as well as biofilm inhibition. Micro plate screening used for detection of biofilm formation by *Staphylococci* is a quantitative model to study its adherence level and has been a sensitive method[16]**;** and the in vitro antibacterial activity

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of crude methanolic, chloroform and hexane extracts of the leaves of *K. reticulata* were investigated. Susceptibility of some Gram-negative organisms (*Escherichia coli*, *Pseudomonas aeruginosa* and *Salmonella typhi)* and Gram-positive organism (*Staphylococcus aureus*) were tested. Agar well diffusion and broth dilution methods were used to determine the minimum antibacterial activity against all the tested microorganisms. The extracts exhibited antibacterial activities with zones of inhibition ranging from 9.07-30.10 mm, 8.17-24.57 mm and 5.60-14.67 mm for methanol, chloroform and hexane extracts respectively. Screening of crude extracts showed notable minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) at concentrations of 100 to 6.25 $mgml^{-1}$. The organisms were more sensitive to the methanolic extract of the leaves, where as extracts from other solvents like chloroform and hexane showed moderate to weak activity respectively. Similar results have been showed in MIC and MBC[17].

Antioxidants activities and Free radical scavenging

Antioxidant activity of entire plant of *K. reticulata* by performing different in *vitro* antioxidant assays, including 2,2-Diphenyl-1- Picrylhydrazyl (DPPH) radical scavenging, beta-carotene bleaching, superoxide anion radical scavenging, reducing power and metal chelating assay at different concentrations (100, 200 and 400µg/ml). The entire plant powder of *K. reticulata* shows good antioxidant activity of about 90.0% when compared with standard butylated Hydroxy Toluene (BHT) (85%) at a concentration of 400µg/ml. Results obtained reveal that methanolic extracts of entire plant of *K. reticulata* tapossess higher antioxidant activity when compared when compared with ethanolic extract. Thus, this study suggests that *K. reticulata* plant can be used as a potent source of nature antioxidants[18]; Free radicals are implicated for many diseases including Diabetes mellitus, arthritis, cancer, ageing. etc. In treatment of these diseases, antioxidant therapy has gained utmost importance. *K. reticulata* popularly important medicinal plant. Keeping in view of the cited activity, it is contemplated to screen the plant for *in vitro* antioxidant activity using different models *viz.* DPPH radical scavenging, ABTS radical scavenging, iron chelating activity and lipid peroxidation assay, nitric oxide scavenging assay, alkaline DMSO assay, total antioxidant capacity and non- enzymatic haemoglobin glycosylation assay . The results were analyzed statistically by regression method. Its antioxidant activity was estimated by IC50 value and the values are 20.36 µg/ml (DPPH radical scavenging), 42.59 µg/ml (ABTS radical scavenging), 32 µg/ml (Iron chelating activity) and 41.91 µg/ml (lipid peroxidation), 122.8 µg/ml (nitric oxide scavenging) and 2.57 µg/ml (alkaline DMSO). In total antioxidant capacity assay, 1 mg of extract is equivalent to 51 µg of ascorbic acid. It showed 66.64% inhibition of haemoglobin glycosylation. In all the testing, a significant correlation existed between concentrations of the extract and percentage inhibition of free radicals, metal chelation or inhibition of lipid peroxidation. The antioxidant property may be related to the polyphenols and flavonoids present in the extract. These results clearly indicate that *K. reticulata* is effective against free radical mediated diseases[19]; antioxidant properties of the medicinal plant *K. reticulata.* The different solvent extracts of *K. reticulata* leaves were screened for their *in vitro* phytochemical and antioxidant activity. Leaves were extracted with solvents of different polarities like aqueous, ethanol, methanol, chloroform, acetone and hexane. The distributions of the main active principles such as alkaloid, flavonoids, phenols, steroids tannins etc. present in the plant were analyzed. It was also focused to determine the total phenolic and flavonoid content present in the extracts. Extracts showed promising results for total antioxidant capacity and reductive capability when compared with standard drug. The ethanol extract was found to possess excellent phytochemical and antioxidant activities. The antioxidant property may be attributed to the presence of flavonoids and phenolics present in the drug. The ability of the crude extracts of *K. reticulata* towards reduction, presence of phenol, flavonoid and antioxidant is an indication of its broad spectrum potential which may be employed in the management of various diseases[20]. Many plants possess antioxidant ingredients that provided efficacy by additive or synergistic activities. Antioxidant activity of the methanol crude extract of entire plant of *K. reticulata* was assessed using DPPH, superoxide anion and metal chelating assays at different concentrations. The potent extract of *K. reticulata* was tested for *in vivo* efficacy. The methanol extract exhibited potent antioxidant activity compared to known antioxidant. *In vivo* studies on potent extract of *K. reticulata* demonstrated dose dependent reduction in hepatic malondialdehyde (330.70, 279.40 and383.79µMmg^{-1} protein) with simultaneous improvement in hepatic glutathione (7.03, 18.16 and 6.88µgmg-1 protein) and catalase levels (678.10, 787.00 and 522.00µgmg^{-1} protein) respectively for 50, 100$mgkg^{-1}$ dose and control) compared to control group. Due to its natural origin and potent free radical scavenging ability *K. reticulata* could be used as a potential preventive intervention for free radical mediated diseases[21].

Antiplasmodial activity

Antiplasmodial of *K. reticulata* medicinal plants were extracted and tested for in vitro antiplasmodial activity against chloroquine-sensitive (K67) and chloroquine-resistant (ENT36) strains of *Plasmodium falciparum*. Out of 16 extracts, 12 were active against ENT36 strain while seven were active against K67 strain, that is, IC50 < or = 50 micrograms/ml. The most active extracts on both strains were those of leaves of *K. reticulata* with IC50 < or = 10 micrograms/ml. The stem barks of *Terminalia spinosa* Engl. (Combretaceae) and the stems of *Dissotis brazzae* Cogn. (Melastomataceae) had IC50 < or = 10 micrograms/ml for strains K67 and ENT36, respectively. A phytochemical analysis of these plants revealed the presence of different classes of primary and secondary metabolites[22].

Antinociceptive activity

K. reticulata is used in folk medicinal practices of Bangladesh as an antinociceptive (reducing sensitivity to painful stimuli). The study was to investigate the

antinociceptive activity of methanolic leaf extract of *K. reticulata* in Swiss albino mice. A model of acetic acid-induced gastric pain in mice was utilized to determine the antinociceptive effects. In writhing assays induced by acetic acid, the methanolic leaf extract showed significant inhibition compared to control. The maximum writhing inhibition (39.1%) was found at a dose of 200 mg extract/kg body weight which, however, was lesser than that of the antinociceptive drug, aspirin (50.4%), when used at a dose of 200 mg/kg body weight. Maximum tolerance (35.0%) was showed at 400 mg extract/kg body weight, compared to that of the standard drug, glibenclamide at 10 mg/kg body weight (57.8%). The methanol extract of *K. reticulata* leaves had beneficial effects as a pain reliever which validates the use of the plant in Bangladesh folk medicinal practices as a treatment for pain[14].

Analgesic activity

The petroleum ether, ethyl acetate, and methanol extracts of *K. reticulata* were chosen for pharmacological screening. In the acetic acid-induced writhing test, the ethyl acetate extract in doses of 150 and 300 mg/kg showed 51.23 and 65.12% inhibition of writhing, respectively. A significant elongation of tail-flick time was evident both in the ethyl acetate and the methanol extracts (42.38 and 60.49%) only at the 300 mg/kg dose level. The extracts of *K. reticulata* possess significant shows analgesic properties[23].

Antiviral activity

K. reticulata is a reputed medicinal plant used in Bangladesh and India for the treatment of gastric complaints including colic, constipation etc. The study was to evaluate the antiviral activity of this plant against hepatitis B virus (HBV) using HBsAg positive serum sample from hepatitis B virus infected patients. Two semi-purified organic fractions designated as PR1 and PR2 of the fat free ethanolic extract were tested at both lower and higher concentrations (20 mg/ml and 40 mg/ml respectively) for their anti hepatitis B virus surface antigen (anti-HBsAg) activity using an *in vitro* system by Reverse Passive Haemagglutination (R-PHA) method. SERRODIA-Anti-HBsAg- Diagnostic kit was used for detection of Anti-HBsAg antibody. Both fractions showed anti-HBsAg activity. But it was found the fractions have little inhibitory action on HBsAg at lower concentration whereas at the higher concentration they have prominent inhibitory action on the antigen. To the best of our knowledge this is the first report of the antiviral activity of *K. reticulata* against HBV. The Anti-HBsAg activity observed by the fractions may be due to the binding of the agents with the antibody binding sites present on HBsAg. Thus the fractions might be the potential sources of the active principles responsible for antiviral activity[24].

Anti-inflammatory activities

The present study pharmacognostic evaluation and anti-inflammatory activity of *K. reticulata* fruit. The hydroalcoholic extract of ripe fruits and petroleum ether, ethyl acetate, and methanolic extracts of aerial parts was also screened for anti-inflammatory activity by carrageenan induced left hind paw oedema in rat at doses of 200 mg/kg and 400 mg/kg, orally[23,25]. In recently have worked on root part of this plant showed well potential effect of anti-inflammatory activities by Soni *et al*[26].

Insectisidal activity

Chemical constituents as well as insecticidal activity of the crude methanol extract from the leaves of *K. reticulata.* were investigated. (5*R**,6*R**)-4, Dimethoxycarbonyl-5-[2′,3′,4′-trihydroxy-6′-(methoxycarbonyl) phenyl]-5,6-dihydro-2*H* pyran-2-one along with 3,4,3′-tri-*O*-methylellagic acid, and methyl gallate were isolated from the dichloromethane extract. Determination of their structures was based on spectroscopic analysis. Compound 1 possessed a very weak insecticidal activity against *Spodoptera frugiperda* (Sf9) with an IC50 value of 27.27 μg/mL[27].

Hepatoprotective activities

Two partially purified organic fractions designated by PR1 and PR2 of the fat free ethanol (95%) extract of aerial parts of *K. reticulata* were tested for the hepatoprotective activity in rats against CCl4-induced liver damage. The rats receiving the fractions showed promising hepatoprotective activity as evident from significant changes of pentobarbital-induced sleeping time, changes in serum levels of sGPT, sGOT, sALP and bilirubin and also from histopathological changes as compared to CCl4-intoxicated rats[28]. In other hand the ethanolic (95%) roots extract of this plant have also reported hepatoprotective activity by paracetamol induced hepatotoxicity in wistar rat. Wistar rats of either sex were divided into six groups with six in each group. Group 1-Normal control: The animals were maintained under normal control, which were given 0.5% Tween 80 used as vehicle. Group 2-Induction of hepatotoxicity: The animals received paracetamol (2gm/kg, *p.o.*) every 72 h for 7 days. Group 3: The animals were treated with Silymarin (100 mg/kg, *p.o*) which served as standard. Groups 4 to 6: Animals received ethanolic root extract of *K. reticulata* (EEKR) at (100, 200 & 300 mg/kg, *p.o.*) everyday for 7 days. Groups 3 to 6 were intoxicated with paracetamol (2gm/kg, *p.o.*) 1 h before the administration of extract or Silymarin for 7 days. Histopathological findings, different hepatic biochemical parameters viz. Serum glutamic-oxaloacetic transaminase (sGOT), serum glutamic pyruvic transaminase (sGPT), serum alkaline Phosphatase (sALP), Total bilirubin, Total albumin & blood urea were evaluated to investigate the hepatoprotective activity. Paracetamol induced a significant rise in sGOT, sGPT, sALP, Total bilirubin, Total albumin, & blood urea estimation. Administration of 300 mg/kg, *p.o.* ethanolic root extract of *K. reticulata* less effectively reduced these pathological damages caused by paracetamol intoxication. The ethanolic root extract of *K. reticulata* also promoted the body weight in Wistar rats. Histopathological changes of the liver were compared with the normal control. The ethanolic roots extract at dose of 300mg/kg, *p.o.* of *K. reticulata* have significant effect on hepatoprotective activity against paracetamol induced hepatotoxicity in Wistar rats[29].

CONCLUSION

The goal of ethnopharmacological studies on medicinal plants should not be restricted to find new prototype pure compounds as drugs. Active extracts, fractions or mixture of fractions/extracts may prove very effective drugs. Plant drugs (combinations or individual drug) for liver diseases should possess sufficient efficacy to cure severe liver diseases caused by toxic chemicals, viruses (Hepatitis B, Hepatitis C, etc.), excess alcohol intake, etc. A single drug cannot be effective against all types of severe liver diseases. Effective formulations have to be developed using indigenous medicinal plants, with proper pharmacological experiments and clinical trials. The manufacture of plant products should be governed by standards of safety and efficacy.

From the above review on *Kirganelia reticulata*, we can conclude how important the medicinal effect plant. There is coexistence between some of traditional usages of this plant like applying on inflammation, Liver protective etc and experimentally observed effect of the extracts as mentioned above but various biological studies available on components of this plant.

CONFLICT OF INTEREST: We declare that we have no conflict of interest.

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