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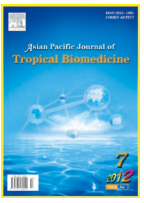

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Biological activities and medicinal properties of Gokhru (*Pedalium murex* L.)

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ABSTRACT

Bada Gokhru (*Pedalium murex L.*) is perhaps the most useful traditional medicinal plant in India. Each part of the neem tree has some medicinal property and is thus commercially exploitable. During the last five decades, apart from the chemistry of the *Pedalium murex* compounds, considerable progress has been achieved regarding the biological activity and medicinal applications of this plant. It is now considered as a valuable source of unique natural products for development of medicines against various diseases and also for the development of industrial products. This review gives a bird's eye view mainly on the biological activities of some of this compounds isolated, pharmacological actions of the extracts, clinical studies and plausible medicinal applications of gokharu along with their safety evaluation.

1. Introduction

Pedalium murex (*P. murex*) Linn (Family: Pedaliaceae) is annual herb, which grows abundantly on the sea costs in South India, Srilanka, Ceylon, Mexico and tropical Africa. In and around Visakhapatnam the plant is very prolific after summer rains. The plant has medicinal attributes. Dinatoin glycoside and diosmetin glucuronides are isolated from the leaves of *P. murex*[1]. An infusion from leaves and stems was reported to be used in the treatment of gonorrhea and dysurea. In the past several flavonoids have been isolated from the leaves and flowers. Recently, two new compounds are isolated from the fruits (Heptatriacontan-4-one,tetratriacontanyl octacosanoate[2]. A decoction of the fruits was mentioned to be effective as demulcent, diuretic, antispasmodic and aphrodisiac. The decoction of root is used as antibiliary. These studies revealed that *P. murex* is a source of medicinally active compounds and have various pharmacological effects, hence, the plant encourage finding its new therapeutic uses. This plant can be explored as biopesticidal plant in the near future and potent fertility enhancing drug[3]. 2′,4′,5′-trihydroxy 5,7-dimethoxy flavones and triacotanyl dotriacontanoate were isolated from the fruits. It is also used in the treatment of urinogenital disorders[4].

It has been traditionally used for the treatment of puerperal diseases, digestive tonics, ulcers, fevers, wounds, other ailments and general debility. The present investigation was intented to evaluate the preliminary phytochemical characters of this plant. Phytochemical studies facilitate new discovery for the synthesis of more potent drugs.

India is a varietal emporium of medicinal plants and is one of the richest countries in the world in terms of genetic resources of medicinal plants. It exhibits a wide range in topography and climate, which has a bearing on its vegetation and floristic composition. Moreover, the agro-climatic conditions are conductive for introducing and domesticating new exotic plant varieties.

Since time immemorial, the traditional medicinal practices have been known for the treatment of various ailments in India. A vast knowledge about the use of plants against different illnesses may be expected to have accumulated in areas where the use of plants is still a great importance. The medicinal value of a plant lies in some of its chemical substances (phytochemicals) that produce a definite physiological action on the human body. The most important

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bioactive compounds of plants are alkaloids, flavonoids, tannins and phenolic compounds.

Rural communities, in particular Warangal district tribes, depend on plant resources mainly for herbal medicines, food, forage, construction of dwellings, making household implements, sleeping mats, and for fire and shade. The use of medicinal plants as traditional medicines is well known in rural areas of many developing countries. In developing countries, low-income people such as farmers, people of small isolated villages and native communities use many native plants for the treatment of common diseases. An extensive survey and interaction with local ethanopharmacologists, herbal drug sellers and rural native healers revealed that the native plants *P. murex* plant parts are routinely and widely used for the treatment of various ailments of humans and live-stock.

Naturally, it tempted us to verify the traditional wisdom of local community in using these plants as herbal drugs. Though, they have wide range of applications we focused on their antimicrobial properties. In fact, there are not many scientific studies that confirm the biological properties of this plant. As the phytochemical research based on the ethanopharmacological information is generally considered an effective approach for logical conclusions.

P. murex has many other names, such as Telugu-Yenugu palleru, Sanskr-Brihat gokshur, Hindi-Bada goshur, English-Large caltrops.

The taxonomical classification are as follows:
Kingdom: Plantae, Plant
Phylum/Division: Magnoliophyta,
Class: Magnoliopsida (Dicotyledonae),
Subclass: Lamiidae,
Order: Caryophyllales,
Family: Pedaliaceae,
Genus: Pedalium,
Species: *P. murex* L.

2. Botanical plant description

It is a creeper that is about 2 to 3 feet long having branches spread all over, leaves are in pairs of 5 to 8 and is of irregular shape. Flowers are small and yellow colored. Fruits are round and possess 5 to 12 compartments and each compartment contains a seed. The seeds contain aromatic oil. Roots are 4 to 5 inch long, brown in color and bear a sweet aroma. The plant flowers in early winters followed by fruiting. *P. murex* L. is a succulent herb found near sea coast of south India and some tropical areas of India. It appears during the month of July - September. It grows luxuriously in fertile soils and crop land as a weed at temperatures of 25-30 degrees.

3. Chemical constituents

Fruit: Alkaloids 3.5%-5%, stable oil, aromatic oil, resins, glycosides, carbohydrates, saponins and triterpenoids.

Stem: Saponins, herman, phytosterols, tannins and carbohydrates.

Root: Reducing sugars, phenolic compounds, saponins, xanthoproteins, alkaloids, triterpenoids and flavonoids.

Leaves: Flavonoids, alkaloids, steroids, resins, saponins and proteins.

4. Phytochemical studies

Preliminary chemical examination of *P. murex* revealed presence of naturally occurring different chemical constituents. Whole plant is reported to contain medicinally important. Mainly fruits contain alkaloids (3.5%-5%), stable oil, aromatic oil, resins, carbohydrates, saponins, glycosides, and Triterpenoids and also two important flavonoids like 2′, 4′, 5′-trihydroxy-5, 7-dimethoxy flavones[1] and triacontanyl dotriacontanoate. The study on leaves reports some important flavonoids like dinatin and 7-glucoronide, diosmetin and its 7-glucoronide, pedaltin and pedalin. Alkaloids, steroids, resins, saponins and proteins ae also reported. The root contained novel phenolic compounds[5] like phenol,2-(5,6-dimethyl pyrazinyl) methyl. Saponins, phytosterols, tannins and carbohydrates were reported from stem. Quercetiin, dinatin, querimctrin and an unidentified di glycoside of quercetin were reported from the flower.

5. Pharmacological studies

5.1. Insecticidal and anti-feedent effect activity

Impact of ethanol extract of *P. murex* root (0.1%, 0.2%, 0.4% and 0.8%) were screened for its anti-feedent and insecticidal activities against third, fourth and fifth instar larvae of *Spodoptera litura* (*S. litura*) (Fab.) by leaf-dip method. The larval mortality more than 50 percent at higher concentration (0.8%) was observed in the ethanol root extract. Stage dependant LC_{50} value was observed for *S. litura* (0.100%, 0.118% and 0.258% for third, fourth and fifth nymphal instars). *P. murex* reduced the food consumption index, growth rate, approximate digestibility, efficiency of conversion of ingested food, efficiency of conversion of digested food of *S. litura* indicating the anti-feedent activity of this plant. *P. murex* impact was stronger than the neem based biopesticidal of neem gold. Hence this plant can be explored as biopesticidal plant in the near future[5].

5.2. Anti-hyperlipidemic activity

The anti hyperlipidemic potential of the ethanolic extract from the fruits of *P. murex* at doses of 200 and 400 mg/kg, *p.o.* in high fat diet fed rats. Biochemical parameters *viz.*, serum total cholesterol (TC), High density lipoproteins (HDL), Low density lipoproteins (LDL), very low density lipoproteins (VLDL) and triglycerides (TG) levels were measured and

compared with animals concurrently treated with reference standards gemfibrozil and atorvastatin. The ethanolic extract showed a significant decrease in triglycerides ($P<0.01$), LDL ($P<0.001$), VLDL ($P<0.01$), cholesterol ($P<0.001$) and significant increase in HDL ($P<0.05$) levels at tested doses[6].

5.3. Anti-nephrolithiatic activity

P. murex (Linn), (Pedaliaceae), a plant which is useful in urinary diseases conditions is distributed in the coastal areas of south India. The aim of the work was to study the anti nephrolithiatic activity of various extracts of *P. murex*. Petroleum ether, chloroform, ethanol and aqueous extracts of the plant were prepared and evaluated for anti nephrolithiasis activity. Albino rats were treated with the prepared extracts. Thus it may be concluded that *P. murex* possesses significant anti nephrolithiatic activity[7].

5.4. Nephroprotective activity

The ethanolic extract of dried fruits of *P. murex* was evaluated for nephroprotective activity in cisplatin induced renal damage in rats. Nephrotoxicity was induced in Wistar rats by intraperitoneal administration of cisplatin 5 mg/kg. Effect of concurrent administration of *P. murex* ethanolic extract at a dose of 250 mg/kg given by oral route was determined using serum creatinine and blood urea and change in body weight as indicators of kidney damage. Cystone was used as standard drug. The extract significantly decreased the cisplatin induced nephrotoxicity. Remarkable changes were observed in body weight, serum creatinine and urea levels. It was observed that the ethanolic extract significantly protected the kidneys from injury. Current study results show that the ethanolic extract of dried fruits of *P. murex* is an excellent nephroprotective as compared to cystone[8].

Life style and dietary changes are most prominent causes of peptic ulcer and related acid peptic disease untreated peptic ulcer are capable of inducing upper gastro intestinal bleeding[9]. The high degree of efficacy and safety with herbal medicines make them more acceptable compared to other. Therapeutic intervention[10] determined the anti ulcer activity of *P. murex* was propelled by the presence of its active constituents and to corroborate its traditional claim.

5.5. Antiulcer activity

Peptic ulcer is manifested largely due to an alteration in lifestyle and diet. The antiulcer efficacy of the aqueous extract of leaves of *P. murex* on ethanol induced gastric lesions was investigated in our studies. This has been substantiated by ascertaining the content of total acid, acid volume, total protein, ulcer index and glutathione. Ulceration was induced in 36 hours fasted rats by the administration of 80% ethanol (1 mL/kg) orally. The reference standard (famotidine, 3 mg/kg) and aqueous extract of leaves of *P. murex* in doses of 50, 100, 200 mg/kg was given to different groups, one hour before the administration of ethanol. Marked gastric mucosal lesions were observed with ethanol. A perceptible elevation in ulcer index, total acidity, acid volume, total protein and diminution of glutathione was observed. Pretreatment with aqueous extract of leaves of *P. murex* particularly at a dose of 200 mg/kg in a single schedule and 100 mg/kg for 15 and 30 days treatment annihilated these alterations and elevated the level of glutathione. Therefore the aqueous extract of leaves of *P. murex* could be regarded as a favorable anti-ulcerogen which could be attributed to its content of flavonoids and mucilage[11].

5.6. Anti-inflammatory activity

The various parts of *Abutilon indicum* and *P. murex* such as root, leaves and seeds are documented to possess various medicinal properties. Animal studies were performed using carrageenan induced paw edema principle in albino wistar rats. Both the plants possessed anti-inflammatory activity. Out of the two plants *P. murex* had shown more anti-inflammatory activity, when compared with *Abutilon indium* species. plethysmometer (UGO Basil, Italy). The edema component of inflammation was quantified by measuring the increase in paw volume (mL) at before carrageenan injection and at 1, 2, 3, 4, 5 and 24 h after carrageenan injection with respect to the pre-injection value for each animal[12].

5.7. Antioxidant activity (CCl_4)

In this study on antioxidant activity of methanol extract of fruits of *P. murex* (MEC) was investigated using carbon tetrachloride (CCl_4)-intoxicated rat liver as the experimental model. The hepatotoxic rats were administered with MEC for 90 days (daily, orally at the dose of 70 mg per kg bodyweight). Lipid peroxidation in CCl_4-intoxicated rats was evidenced by a marked incrementin the levels of thiobarbituric acid reactive substances and diene conjugates, andalso a distinct diminution in glutathione content in the liver. In CCl_4 + MEC-treated ratsthese biochemical parameters attained an almost normal level. The decreased activity ofantioxidant enzymes, such as superoxide dismutase, catalase, glutathioneperoxidase and glutathione reductase in CCl_4-intoxicatedrats, and its retrievaltowards near normalcy in CCl_4 + MEC-administered rats revealed the efficacy of MEC incombating oxidative stress due to hepatic damage. Elevated level of glutathione transferase observed in hepatotoxic rats too showed signs of returning towards normalcy in MEC coadministeredanimals, thus corroborating the antioxidant efficacy of MEC. The findings provide a rationale for further studies on isolation of active principles and its pharmacological evaluation[13].

The ethyl acetate (EA) fraction was found to have high levels of phenolic content [(298.72±2.09) mg GAE/g]. This fraction exhibited higher total antioxidant capacity, higher percentage of DPPH radical scavenging activity [(135.11±

2.95) μg/mL], nitric oxide [(200.57±4.51) μg/mL], hydrogen peroxide [(217.91±6.12) μg/mL], deoxyribose [(250.01±4.68) μg/mL] and higher reducing power. Correlation coefficient (r^2-0.914) was found to be significant between total phenolic content and total antioxidant activity. The results indicate that the EA fractions are rich in phenolic anti oxidants with potent free radical scavenging activity implying their importance to human health[14].

In Indian system of medicine *P. murex* (Bada Gokharu) is an important medicinal plant and it has been used traditionally in various disorders and as a health tonic. To understand the mechanisms of pharmacological actions, the *in vitro* antioxidant activity of aqueous extract of *P. murex* was investigated for DPPH scavenging activity and superoxide scavenging activity. Percentage inhibition of free radicals was measured. The antioxidant property may be related to the phenolic acids and micronutrients present in the extract. Results clearly indicate that *P. murex* is effective free radical scavenger[15].

5.8. Antibacterial activity

Methanolic extract of leaf and fruit was used against 12 different pathogenic microorganisms for their antibacterial activity. The maximum antibacterial activity was noted against gram positive bacteria than gram negative bacteria. Positive control (streptomycin) showed antibacterial activity and there was no inhibition with negative control[16].

The petroleum ether, chloroform, acetone and methanolic extract of *P. murex* root was subjected to preliminary phytochemical compounds and antibacterial activity of certain human pathogenic organisms. The extract indicated the presence of flavonoids, glycosides, steroids, phenols, alkaloids and tannins. More antibacterial activity was observed in methanolic extract against gram positive bacteria *Streptococcus progeny* and *Enterococcus faccalis* than the gram negative bacteria[17].

5.9. Protective effect of prostane in experimental prostatic hyperplasia in rats

P. murex is a one of the component in prostane, a polyherbal formulation, and was evaluated for its efficacy on 5α-reductase inhibition, α-adrenergic antagonistic activity and testosterone-induced prostatic hyperplasia by 5α-reductase inhibition, which was evaluated using rat prostate homogenate as an enzyme source. Adrenergic antagonistic activity was evaluated using isolated rat vas deferens. Experimental prostatic hyperplasia was induced in rats by giving testosterone 3 mg/kg *s.c.* for 21 days. The prostane dose-dependently inhibited 5α-reductase activity and exhibited α-adrenergic antagonistic activity. The treatment with prostane at 250, 500 and 750 mg/kg body weight, *p.o.* for 21 days significantly reduced the prostatic weight, the epithelial height and the stromal proliferation in experimental prostatic hypertrophy[18].

5.10. Hepatoprotective activity

The role of oxidative stress and reactive oxygen species (ROS) generation has been proved in the pathogenesis of liver damage. ROS initiate auto oxidation of cellular membrane lipids, can lead to cellular necrosis. Thus they are well known to be cytotoxic and have been implicated in the etiology of hepatotoxicity. They possibly represent the hepatotoxic principle of alcohol and various drugs. In this present study, we have assessed acute oral toxicity of aqueous-alcoholic extract of fruits of *P. murex* on female Swiss albino mice by AOT 425 guideline. Hepatoprotective activity of aqueous-alcoholic extract of fruits of *P. murex* (200, 400 mg/kg) was carried out using alcohol (40% ethanol) and isoniazide induced liver damage in wistar albino female rats. In same models, we have measured free radical scavenger enzymes (SOD, catalase) level. Aqueous and alcoholic extract of fruits of *P. murex* did not show any mortality up to 5 000 mg/kg. Significant hepatoprotective activity at 400 mg/kg dose of aqueous-alcoholic extract was observed in alcohol and isoniazide induced liver damage. All the elevated liver biochemical parameters (SGPT, SGOT, TB, TG and TC) in alcohol and isoniazide intoxicated rats decreased significantly near to normal level by aqueous-alcoholic extract of fruits of *P. murex*. Photomicrograph of liver sections also has shown hepatoprotective activity. SOD and glutathione level was significantly increased and lipid peroxidation was significantly reduced with 400 mg/kg dose of aqueous-alcoholic extract of fruits of *P. murex*. Flavonoids and tannins present in aqueous alcoholic extract may be responsible for hepatoprotective action by scavenging free radicals[19-22].

5. 11. Aphrodisiac activity and curative effects

Chronic ethanol exposure may result in testicular damage and infertility in males. Petroleum ether extract of *P. murex* (PEPM) is evaluated in this study for its ability to increase aphrodisiac activity and to cure ethanol induced germ cell damage and infertility in male rat models. Doses of 200 and 400 mg/kg of PEPM showed a significant increase ($P < 0.01$, $P < 0.001$) in mating and mounting behavior. The effect on fertility factors such as total body weight, percentage of pregnancy, litter size were also significantly increased ($P < 0.01$) in comparison with the ethanol-treated group. Significant increases in sperm motility and count were observed in PEPM treated groups in a dose-dependent manner ($P < 0.01$; $P < 0.001$) as compared with the ethanol-treated group. Similarly, reductions in the percentage of abnormal sperm were noted in animals treated with PEPM 400 mg/kg. The effects of PEPM on total protein, total cholesterol and testosterone were satisfactory, the levels being increased significantly for protein ($P < 0.05$), cholesterol ($P < 0.01$) and testosterone ($P < 0.05$) by 400 mg/kg PEPM. Microtome sections of the testes of animals treated with 400 mg/kg PEPM exhibited restoration and recovery of germinal cells and the luminal spermatozoa and were

comparable with the control group animals. These effects of PEPM make this natural herb ideal as an aphrodisiac and a potent fertility enhancing drug[23].

6. Other attributes

Natural plant drugs and excipients have gained importance over synthetic materials because they are nontoxic, less expensive and freely available. The purpose of this study is to search for a cheap and effective natural excipient that can be used as an effective alternative for the formulation of pharmaceutical suspensions. The suspending properties of *Malva sylvestris* and *P. murex* mucilage were evaluated comparatively with *Acacia* at concentrations of 0.5%, 1.0%, 1.5%, and 2% w/v in calcium carbonate suspension. Characterization tests were carried out on purified *Malva sylvestris* and *P. murex* mucilage. Sedimentation profile, redispersibility, rheology, particle size analysis were employed as an evaluation parameters. The values obtained were used as basis for comparison of the suspending agents studied. The results suggested that, *Malva sylvestris* and *P. murex* mucilage could be used as a suspending agent. They have low rate of sedimentation, high viscosity, slightly basic pH and are easily redispersible[24].

P. murex is a valuable source of medicinally useful compounds that have been used traditionally for various ailments. Leaf and fruit extracts of this plant showed good source for the bioactive compounds in various studies of researchers. Thus plant studied here can be a potential source for useful drugs, if it is involved in further research.

Conflict of interest statement

We declare that we have no conflict of interest.

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