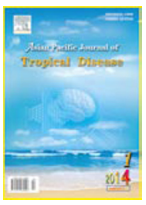
Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Disease

journal homepage: www.elsevier.com/locate/apjtd



Document heading doi: 10.1016/S2222-1808(14)60409-6

Luffa echinata Roxb.-A review on its ethanomedicinal, phytochemical and pharmacological perspective

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PEER REVIEW

Peer reviewer

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Comments

This is a good review in which the authors have compiled up-date information on traditional uses, phytoconstituents present and pharmacological works done on different parts of *L. echinata*. The article shall lead the researchers to unexplored area of the potent herb. I recommend this article to be published.
Details on Page S11

ABSTRACT

Luffa echinata Roxb. (Cucurbitaceae) is a spreading climbing herb of tremendous medicinal importance, distributed throughout Pakistan, India, Bangladesh and Northern Tropical Africa. Traditionally various parts of the plant are being used for the treatment of different ailments such as jaundice, intestinal colic, enlargement of liver and spleen, leprosy, diabetes, bronchitis, nephritis, rheumatism, cirrhosis, dropsy, anthelmintic, stomach ache, snake bite, dog bite, fever, diarrohea and hemorrhoid disorder. The plant also possesses antioxidant, analgesic, anti-inflammatory, antidepressant, anxiolytic, antiepileptic, hepatoprotective, antibacterial, antifungal, antiulcer and anticancer activity. Research has been carried out using different techniques to support most of these claims. This review is an attempt to compile an up-to-date data on its ethanomedicinal, phytochemical and pharmacological perspective.

KEYWORDS

Luffa echinata, Cucurbitaceae, Cucurbitacin, Chrysirol, Hepatoprotective

1. Introduction

Ayurveda is the most ancient traditional system of medicine in India with sound philosophical, experiential and experimental basis, which is used to treat the human disease[1]. Due to increased side effects, high cost of new drugs, lack of curative treatment at root level and development of new disease, people not only in developing countries but also in developed countries rely on herbal medicines[2]. India has 2.4% of world's area with 8% of global biodiversity; more than 1.5 million practitioners are using herbs or herbal formulations based on 25 000 medicinally important plants, for the effective management and treatment of human diseases[3]. Though scientific studies have been carried out by scientists on many Indian botanicals, but still numerous drugs have entered the international market through the exploration of ethanopharmacology and traditional medicine[4].

Luffa echinata (*L. echinata*) belongs to family Cucurbitaceae which includes about 130 different genera and about 800 species of medicinally important plants[5,6]. Few plants from this family posses ribosomal inactivation proteins (such as MAP30, Luffin A and B) and triterpenes with immunomodulator, antiretroviral, anti-HIV activities besides other pharmacological action such as antidiabetic, antihyperlipideamic, anticancer and free

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Article history:
Received 15 Nov 2013
Received in revised form 26 Nov, 2nd revised form 4 Dec, 3rd revised form 12 Dec 2013
Accepted 27 Dec 2013
Available online 28 Jan 2014

radical scavenging[7]. The genus *Luffa* comprises more than eight species, three of which are found in India *viz.* *Luffa acutangula* Roxb., *Luffa aegyptiaca* Mill. and *L. echinata* Roxb[8]. *L. echinata* is a spreading climber herb, with bifid bristly or smooth tendrils and extremely bitter taste, grows widely in Pakistan, India, Bangladesh and Northern Tropical Africa. In India, it is mainly found in Gujarat, Bihar, Rajasthan and Madhya Pradesh. It is known by various names *viz.* English: Bristly Luffa; Sanskrit: Koshataki; and in Hindi: Bindaal, Bidali, Kukurlata, Ghagerbel. Infusion of the fruit is given orally in biliary and intestinal colic while applied to the body in case of putrid fever. Roots of the plant are used for the treatment of bronchitis, piles, jaundice, vaginal discharge, laxative and analgesic. Apart from that, entire herb is used as stomachic, emetic, anthelmintic, dropsy, nephritis, chronic bronchitis and abortifacient[9-11]. Saponins isolated from *L. echinata* fruits are reported to have antihypertensive effect in cat and dogs and diuretic activity in dogs and rats[12]. The hydro alcoholic extract of the plant has been reported to potentiate pentobarbitone induced hypnosis in mice[13] and have hypoglycemic action in rats[14]. The aqueous extract of fruits is beneficial in jaundice as it significantly lower serum bilirubin level in chlorpromazine induced jaundice in rats and human patients[15]. Clinical studies revealed that fruits have significant therapeutic action against viral hepatitis[16] while seeds have anthelmintic activity[17]. Therefore, an attempt has been made to compile the data of *L. echinata* which covers its ethanomedicinal, phytochemical and pharmacological perspective.

2. Ethanomedicinal uses

2.1. Traditional uses

L. echinata is a well known ethanomedicinal plant used in Ayurveda. Its uses in the Indian traditional medicine are well documented. The uses of different parts of *L. echinata* in traditional system of medicine are given in Table 1.

2.2. Alternative and complementary medicinal uses

Among various species of *Luffa*, *L. echinata* is used extensively throughout the world. Its polyherbal formulation containing *Acacia catechu*, *Andrographis peniculata*, *Azadirachta indica*, *Boerhaavia diffusa*, *Curcuma longa*, *Eclipta elba*, *Emblica officinalis*, *Picrorrhiza kurroa* and *Phyllanthus amarus* showed significant ($P<0.05$) prophylactic and curative effect against carbon tetrachloride (CCl_4) and paracetamol induced hepatic damage[27]. *L. echinata* fruits have been incorporated in Hepia-10, a polyherbal hepatoprotective formulation[28].

3. Morphology of *L. echinata*

3.1. Fruits

Fruits are ashy, oblong, ovoid having 2-5 cm length and densely covered with 4-7 mm long bristles. Seeds are ovate, black 4-5 mm long, 3-5 mm broad and 2 mm thick[9,10].

3.2. Stems

Stem pieces are slender, yellowish-brown to blackish-brown in color, longitudinally furrowed, glabrous, measuring 1.5-1.7 cm in length and 5-8 mm diameter[20].

3.3. Flowers

Flowers are white, stalked, about 2.5 cm wide. Male flowers are borne in 5-12 flowered raceme having length up to 15 cm long. Sepal tube is about 5.6 mm long and hairy. Sepals are lance shaped while petals are ovate, 1.0-1.2 cm long, blunt and hairy at the base[29].

Table 1
Ethanomedicinal uses of different parts of *L. echinata*.

Part	Disease/ Uses	Method of administration
Fruits and stems	Biliary and intestinal colic, jaundice, fever enlarged liver or spleen, cirrhosis, ascites	Tincture (1 in 20) or hot/cold infusion (10-20 mins) taken internally or applied externally to the body[10]. Fruits are used as snuff for the treatment of jaundice in Gartwal hills in Uttar Pradesh[18].
Fruits	Diabetes	Fruits are crushed into a fine powder and one teaspoon full of it is given with water twice a day to a diabetic patient[19,20].
	Dropsy and diuretic	Hot infusion (1 in 80) in a dose of 1-2 ounce three times in a day has powerful effect against dropsy. In combination with nitrohydrochloric acid acts as potent diuretic[10].
	Purgative	Decoction of fruits has been used as enema for the elimination of toxins[21,22].
	Anestrus	Fruits has been given to animals along with thick rota (flat bread) twice a day for 7-8 d[23].
	Dog bite	Fine powder of mature fruits with 'Bael' (*Aegle marmelos*) leaves and Betle (*Piper betle*) leaves is given in case of dog bite once a week for three weeks[19]. Mature sponge of fruit is soaked in a glass of water for 5-10 min and squeezed properly. The extract obtained is given to dog bite victim in the morning with empty stomach[24].
Root	Hemorrhoid	Roots powder is given orally daily in the morning[25].
	Leprosy	Root paste fried in mustard oil is applied externally on body surface[26].
Leaves	Blood Purifier	Juice of the fresh leaves[19]
	Rheumatism	Decoction is applied externally to treat rheumatism[26].
	Fever	Decoction of stems and leaves is used in the treatment of fever[26].

3.4. Leaves

Leaves are kidney-shaped, round, shallowly or deeply 5-lobed. Tip is rounded or rarely pointed, bristly on both surfaces, margin is minutely toothed and leaf stalk is stout, bristly, up to 12 cm long[10].

4. Phytochemistry of *L. echinata*

Phytochemical analysis of aerial parts of *L. echinata* revealed the presence of alkaloid, glycoside, carbohydrate, proteins and flavonoids in ethanolic extract; while that of the roots revealed sterols, triterpenes, reducing sugars, glycosides, flavones and tannins[30,31].

A number of compounds such as cucurbitacin-B, eletarin (cucurbitacin-E), eletarin-2-glucoside, Isocucurbitacin B, β-sitosterol glucoside, chrysirol-7-glucoside, chrysirol-7-epiglucoside, echinatol A, echinatol B, echinatin have been isolated from *L. echinata* fruits and their chemical structures have been confirmed using chromatography and nuclear magnetic resonance spectroscopy. Graveobiosides-B on hydrolysis gives apegenin and luteolin[32-34]. Datiscacin (cucurbitin-20-acetate), a bitter principle compound with antitumor property has been isolated along with 2-O-β-D-glucopyranosyl cucurbitacin B, 2-O-β-D-glucopyranosyl cucurbitacin S from *L. echinata* fruits[35].

Two other flavonoids, luteolin-7-glucoside and chrysoeriol-7-glucoside have been isolated from flowers and leaves of *L. echinata*. Chemical structures of these compounds have been confirmed by comparing the R_f values and color characteristics[36].

A potent diuretic saponin, containing gypsogennin as sapogenin and mixture of sugars *i.e.* glucose:xylose:rhamnose (3:2:1) have been isolated from seed of *L. echinata* whose structure has been confirmed by elemental analysis, molecular mass determination and infrared spectroscopy[37]. Seeds also contain cucurbitacin-B, triterpene, fatty acid (25% saturated and 75% unsaturated), saponins containing oleanolic acid as sapogenin[14,29]. Phytoconstitutents present in various parts of plant are given in Table 2 and Figure 1.

5. Pharmacological activities of *L. echinata*

5.1. Antioxidant activity

Free radical scavenging activity of hydro alcoholic (50:50) extract of *L. echinata* fruits has been evaluated using *in vitro* methods *viz.* 1, 1-diphenyl-2-picryl hydrazyl free radical (DPPH), hydroxyl radical and inhibition of lipid peroxidation effect. Extract showed concentration dependent activity and maximum protection was found at 1 000 μg/mL which was 84.05%, 73.07% and 59.83% respectively[12]. In another study, free radical scavenging effect of hydro-methanolic (20:80) extract of fruits has been evaluated using different *in vitro* methods *viz.* DPPH, ORAC and TEAC. IC_{50} value was found to be 188.00±0.87 μg/mL, 253.7 μmol TE/g and 0.34 mmol/g respectively. It is suggested that free radical scavenging activity and inhibition of lipid peroxidation might be due to presence of flavonoids[38].

Free radical scavenging effect of methanolic extract of

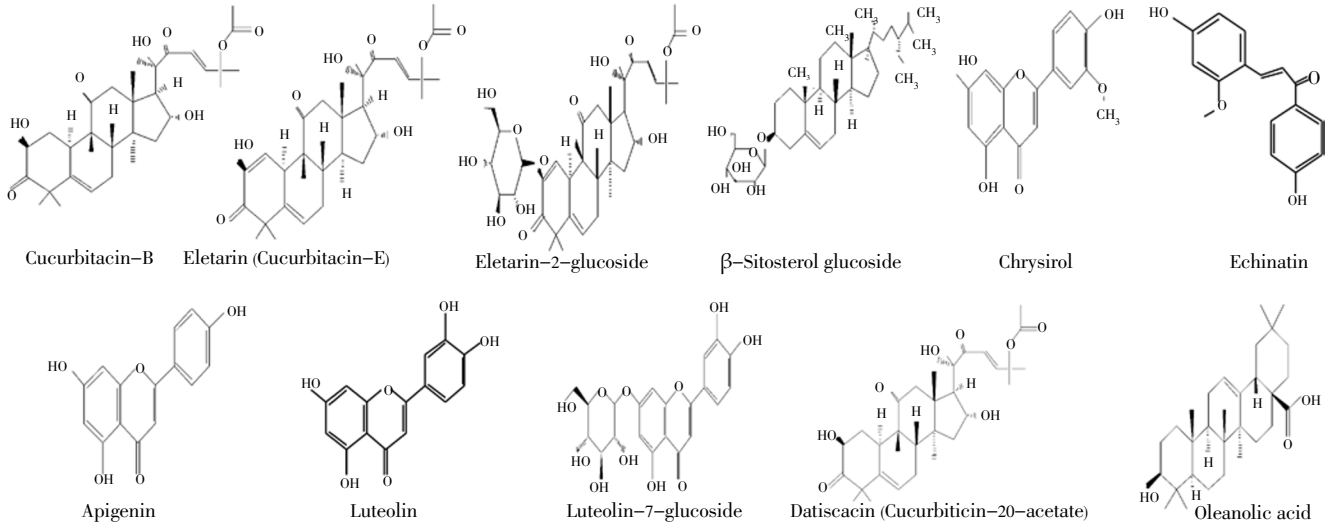

Figure 1. Chemical structures of phytoconstitutents present in various parts of *L. echinata* Roxb.

Table 2
Chemical constituents present in various parts of *L. echinata*.

Parts of plants	Phytoconstitutents
Leaves	Luteolin-7-glucoside, Chrysoeriol-7-glucoside[36]
Fruit	Chrysoeriol, cucurbitacin-B, elaterin (cucurbitacin-E), elaterin-2-glucoside, β - sitosterol glucoside, apigenin, luteolin, echinatol A, ehinatol B, Datiscacin (cucurbitacin-20-acetate), 2-O-β-D-glucopyranosyl cucurbitacin B, 2-O-β-D-glucopyranosyl cucurbitacin S[32-35]
Flowers	Luteolin-7-glucoside, chrysoeriol-7-glucoside[36]
Seeds	Cucurbitacin-B, triterpene, fatty acid, saponin containing oleanolic acid as sapogenin[14,29]

L. echinata seeds has been evaluated by DPPH and H_2O_2 method and maximum protection *i.e.* 89.69% and 69.16% was observed at a concentration of 150 μg/mL, respectively. Results suggested that hydro methanolic extract has significant free radical scavenging activity which might be due to the presence of flavonoids, tannins or other phytoconstitutents[13,39].

5.2. Analgesic and anti-inflammatory activity

Methanolic extract (50, 100, 200 mg/kg, *p.o.*) of *L. echinata* seeds has been evaluated for analgesic and anti-inflammatory activity. Analgesic effect has been evaluated by eddy's hot plate and tail immersion methods using diclofenac sodium (10 mg/kg, *p.o.*) as standard. Treatment with extract showed significant ($P<0.05$) dose dependent increase in basal reaction time *i.e.* licking response (7.47, 7.75 and 8.31 seconds) or tail flicking (10.13, 11.70 and 15.17 seconds) as compared to normal control (3.39 and 3.55 seconds) as well as positive control (9.45 and 17.10 seconds) respectively. Anti-inflammatory effect has been evaluated by using carrageenan (0.1% w/v, 1 mL/kg) and extent of oedema was measured by mercury displacement method using plethysmograph as positive response. Treatment with extract showed significant ($P<0.05$) dose dependent decrease in paw oedema (60.57%) induced by carrageenan as compared to normal control and positive control (70.16%)[13].

5.3. Antidepressant, anxiolytic and antiepileptic activity

Methanolic extract of *L. echianta* (200 mg/kg, *p.o.*) fruits was evaluated for antidepressant, anxiolytic and antiepileptic activities. Antidepressant and anxiolytic effects were evaluated by behavior model *viz.* open field and elevated plus maze using diazepam (2 mg/kg, *p.o.*) as control. Treatment with extract significantly ($P<0.05$) reduced number of square crossed and number of rearing (antidepressant activity) while simultaneously increased the time spent in open arm (anxiolytic activity) as compared to control. Antiepileptic activity was evaluated using maximal electric shock model with phenytoin (25 mg/kg, *p.o.*) as a control. Treatment with the extract significantly ($P<0.05$) reduced extension, stupor and total recovery as compared to control[40].

5.4. Antiulcer activity

Ethanolic extract of defatted aerial parts of *L. echinata* (200 and 400 mg/kg, *p.o.*) showed significant protection ($P<0.001$) against pylorus ligation and diclofenac sodium induced gastric ulcer using ranitidine (20 mg/kg) as standard drug. The protection was found dose dependent in both models[41].

5.5. Antibacterial and antifungal activity

L. echinata fruits extract (dichloromethane:methanol; 1:1 v/v) has been evaluated for antibacterial and antifungal effect against number of microorganism by agar dilution streak method using ciprofloxacin (3 μg/mL) and amphotericin B (3 μg/mL) as positive control. At a dose of 500 μg/mL, extract showed complete inhibition of *Bordetella bronchiseptica*, *Streptococcus faecalis* and partial inhibition of *Staphylococcus aureus* while a dose of 1 000 μg/mL showed complete inhibition of *Micrococcus luteus*, *Staphylococcus aureus* and partial inhibition of *Bacillus subtilis* and *Aspergillus niger*. It did not show any effect on *Bacillus cereus* var. *mycoides*, *Bacillus pumilus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Candida albicans*, *Saccharomyces cerevisiae* and *Aspergillus niger*[42].

5.6. Hepatoprotective activity

Prophylactic and curative effect of ether extract (cucurbitacin and elaterine-2-glycoside, 3 mg/kg, *p.o.*) and alcoholic extract (chrysirol and β-chrysoeriol-7-aploglucoside, 10 mg/kg, *p.o.*) of *L. echinata* have been evaluated against CCl_4 (0.25 mL/100 g, *s.c.*) induced liver damage in rats. Histopathological examination revealed that ether extract has more protective effect than ethanolic extract[43]. *L. echinata* fruits have been successively extracted with petroleum ether, acetone and methanol by cold percolation method and evaluated for protective effect at a dose of 250 mg/kg against CCl_4 (1:1 olive oil, 1 mL/kg, *s.c.*) induced liver damage using silymarin (10 mg/kg, *p.o.*) as positive control. Treatment with extracts significantly decreased serum glutamic oxalacetic transaminase, serum glutamic pyruvate transaminase, alkaline phosphatase, total protein and total albumin induced by CCl_4. All the extracts contain some active principles (triterpenes); responsible for hepatoprotective activity[34,44-46]. Methanolic extract of *L. echianta* fruits (50, 100, 200, 400 and 800 μg/mL) did not show any significant effect on human hepatocellular liver carcinoma cell (HepG2)[47].

In another study, acetone extract (250 mg/kg, *p.o.*) of *L. echinata* root was evaluated for protective effect against CCl_4 (1:1 olive oil, 3 mL/kg, *s.c.*) induced liver damage using silymarin (25 mg/kg, *p.o.*) as standard. Treatment with the extract causes significant ($P<0.05$) decrease in serum enzyme level induced by CCl_4. Histopathological examination of rat liver also supports the protecting effect of root extract. It is suggested that the protecting effect of roots might be due to the existence of flavonoids, tannins, steroids and terpenoids[31].

5.7. Anti cancer effect

Methanolic extract of *L. echinata* fruits (50, 100 and 200 μg/mL) has been evaluated for *in vitro* anti-proliferative effect on human colon cancer cell (HT29). Cell viability was determined at 6, 12, 24, 48 and 72 h using MTT assay. Extract showed dose and time dependent significant ($P<0.05$, IC_{50}: 80.6 μg/mL) inhibition of HT29 cell proliferation. It is suggested that anti-proliferative effect was shown by inducing apoptotic cell death which caused cell arrest in G2/S phase. It also promoted reactive oxygen species generation (65.85%), loss of mitochondrial membrane integrity and increased the ratio of

apoptotic genes (Bcl-2 and Bax)[47].

6. Conclusion

Although herbal medicines have been used for thousands of years in human health care, but the safety of herbs is a myth. Number of people experience negative or adverse effects of these drugs due to various reasons including insufficient procedure for cultivation and collection, lack of quality assurance and control in manufacturing, inadequate practices to study the drug safety, and concomitant administration of the medicine from different systems[48]. Increased use of herbal therapies demands scientifically sound evidence for principles behind therapies and for effectiveness of medicine[49]. Progress in genomics and proteomics has opened a new gateway in therapeutics and drug discovery. This development has also helped in better understanding of human genomes and scientific variation in human beings[3]. Traditional Indian system of medicine can be benefited numerously by selective amalgamation of traditional Indian system of medicine with modern science and modern medicine[50]. Basic research programmes need to develop comprehensive policies regarding legislation, regulation, quality control and safety regulation[51]. Without all these measures, it is impossible to realize the dream to become "a global leader in herbal drug industry" despite having golden mines of well documented and well practiced traditional herbal medicines. *L. echinata* appears to have a broad spectrum of activity on several ailments. Various parts of the plant have been explored for antioxidant, analgesic, anti-inflammatory, antidepressant, anxiolytic, antiepileptic, hepatoprotective, antibacterial, antifungal, antiulcer and anticancer activity. Ethanomedicinal uses and pharmacological studies reported in this review confirm the therapeutic value of *L. echinata*. However, very less information is available regarding the clinical toxicity and phytoanalytical properties of this plant. Several phytochemical studies have been reported but still for better insight of phytochemical analysis, modern tools are required. Availability of information on ethanomedicinal uses, active phytochemicals present and pharmacological perspectives will help to explore it on scientific basis as well as to establish and validate the quality and practice of this herbal medicine in current scenario.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

Authors are thankful to Dr. Sunil Kumar Jain Director, ADINA Institute of Pharmaceutical Sciences, Sagar (M.P.) India, to provide facilities during preparation of this article.

Comments

Background

L. echianta Roxb. is a spreading climbing herb, used traditionally in the treatment of variety of diseases. This plant also posses potent hepatoprotective activity and is also included in marketed hepatoprotective formulation.

Research frontiers

The authors have put the effort and compiled all the updated information available on this plant which shall be useful in identifying and exploring the plant potential more significantly.

Related reports

The article has been prepared on the basis of earlier scientific reports published.

Innovations & breakthroughs

Authors have attempted to compile different traditional uses, phytoconstituents present and pharmacological works reported on distinctive parts. All this information will help researchers to explore its scientific evidence based on modern era.

Applications

It will be significant to know traditional uses and phytoconstituents present in different plant parts to expend unexplored area by scientific evaluation.

Peer review

This is a good review in which the authors have compiled up-date information on traditional uses, phytoconstituents present and pharmacological works done on different parts of *L. echinata*. The article shall lead the researchers to unexplored area of the potent herb. I recommend this article to be published.

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