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Review Article

Pharmacological potential of *Trichosanthes dioica:* Current prospects

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ABSTRACT

Trichosanthes dioica Roxb. (family: Cucurbitaceae), is widely grown throughout India. The herb has been used for overcoming problems like constipation, fever, skin infection, wounds and also improves appetite and digestion from time immemorial . Juice of leaves of T. dioica are used as tonic, febrifuge, in oedema, alopecia and in subacute cases of enlargement of liver. The present review describes the morphological and pharmacological aspects of T. dioica and summarizes the most interesting findings obtained in the preclinical and clinical research related to the plant.

Keywords: *Trichosanthes dioica*, preclinical and clinical studies, safety and efficacy, current prospects.

INTRODUCTION

The Indian subcontinent represents one of the richest diverse genetic resources. Of the estimated 250,000 species of flowering plants at global level, about 3000 are regarded as food source; out of which only 200 species have been domesticated. Global diversity in vegetable crops is estimated to be about 400 species of which about 80 species of major and minor vegetables are reported to have originated in India[1]. Plants have been a valuable source of new molecules and considered as an alternative strategy in search for new drugs. Pointed gourd (cucurbitaceae) is a dioecious perennial herbaceous vegetable. The crop is of Indo- Malayan origin and distribution and is extensively grown in eastern India[2] and to a lesser extent in other parts of South Asia.[3] *Trichosanthes dioica* Roxb. (family: Cucurbitaceae), commonly known as "Sespadula" in English and "Parwal" in Hindi, is widely grown throughout India.[2] Fruits of this plant are used as vegetable in Indian traditional food system since ancient times. Besides fruits, other parts of the plant, such as the leaves and tender shoots, have also been used in the traditional system of medicine.[4-6] Some specific medicinal properties have been identified, viz., hypocholesterolemic, hypoglyceridimic, and hypophospholipemic[4,7]. Most recently, its seeds and leaves have also been found as antidiabetic agents[8,9]. It also serves as a rich source of vitamin C[4]. *Trichosanthes*, a genus of family Cucurbitaceae is an annual or perennial herb distributed in tropical Asia, Polynesia, & Australia. Over 20 species are recorded in India of which two namely *T. anguina & T. dioica* are cultivated as vegetable. Other important species found in the world are *T. palmata, T. cordata, T nervifolia, T. cucumerina, T. wallichiana, T. cuspida, T.incisa, T. laciniosa, T. kirilowii,* etc[10].

Description of Plant

Pointed gourd (*T.dioica*) is one of the most nutritive cucurbit vegetables holds a coveted position in the Indian market during summer and rainy season. It is a perennial crop highly accepted due to its availability for eight months in a year (February–September). Being very rich in protein and vitamins A and C, it has certain medicinal properties and many reports are available regarding its role in circulatory system especially in lowering blood sugar and serum triglycerides.[12,22] The fruits are easily digestible and diuretic in nature[11]. It is also known to have antiulcerous effects[13].

Morphology

The plant is a perennial, dioecious, and grows as a vine (Fig. 1) *T.dioica* . Vines are pencil thick in size with dark green cordate, ovate, oblong, not lobed, rigid leaves. Roots are tuberous with long tap root system. Flowers are tubular white. Stigma remains viable for approximately 14 hours and 40–70% of flowers set fruit. Based on shape, size and striation, fruits can be grouped into 4 categories4:[14](1) Long, dark green with white

stripes, 10–13 cm long (2) Thick, dark green with very pale green stripes, 10–16 cm long (3) Roundish, dark green with white stripe, 5–8 cm long (4) Tapering, green and striped, 5–8 cm long[6]. [Figure- 1]

Cultivation

T.dioica is usually propagated through vine cuttings and root suckers. Seeds are not used in planting because of poor germination and inability to determine the sex of plants before flowering. As a result, crop established from seed may contain 50% nonfruiting male plants. Both pre-rooted and fresh vine cuttings are used for propagation. Vine cuttings made in the fall of previous year and rooted during winter. Fresh vines used for field planting should have 8–10 nodes per cutting. The distance between plants is kept between 1.5–2.0 m × 1.5–2.0 m. A female: male ratio of 9:1 is optimum for ensuring maximum fruit set[15].

Chemical Constituents

Earlier chemical study reveals that in addition to a number of tetra and pentacyclic triterpenes, the toxic bitter principles cucurbitacins (a group of often highly oxygenated tetracyclic compounds with a unique carbon skeleton and almost a carbonyl group in ring C) may be considered as a taxonomic character of Cucurbitaceae.[figure-2], [figure-3], [figure-4], [figure-5]

T.dioica is rich in vitamins and contains 9.0 mg Mg, 2.6 mg Na, 83.0 mg K, 1.1 mg Cu, and 17.0 mg S per 100 g edible part.[6] The various chemical constituents present in *T. dioica* are vitamin A, vitamin C, tannins, saponins.[16] Two main phytosterols present in *T. dioica* are namely, 24α-ethylcholest-7-enol & 24β-ethylcholest-7-enol.[17] Also seeds of *T. dioica* contain lectin, a carbohydrate (specifically galactose) binding protein which is homologous to Type-II ribosome inhibitory proteins (Type-II RIP).[18]

Preclinical Studies

Antidiabetic activity

Earlier studies showed that glycemic attributes of an aqueous extract of *T. dioica* leaves in normal as well as various diabetic models. The variable doses of 250, 500, and 750 mg kg- 1 body weight of the extract were administered orally to normal and streptozotocin (STZ) induced sub and mild diabetic rats in order to define its glycemic potential. This evidence clearly indicates that the aqueous extract of *T. dioica* leaves has good hypoglycemic potential along with a high antidiabetic profile.[19] It had been showed that in rats with streptozotocin induced severe diabetes mellitus, aqueous extract of *T. dioica* fruits dose of 1000mg/kg body weight daily once for 28 days reduced the levels of fasting blood glucose, postprandial glucose, asparate amino transferase, alanine amino transferase, alkaline phosphatase, creatinine, urine sugar and urine protein where as total protein and body weight was increased. No toxic effect was observed during LD50. This study suggests that further detailed toxicity studies and mechanism of action of *T. dioica* would be useful for undertaking human trials[20]. It was also reported that pointed gourd possesses the medicinal property of lowering blood sugar level in rats[21].

Blood Sugar, Serum Lipids, Lipoproteins and Faecal Sterols

Effect of oral administration of 2 ml per day of suspension (in water) of alcoholic extract of whole fruit of *T.dioica* (2%) (= 100 g fresh wt. = 7 g dry wt. = 1/15 g of alcoholic extract) with the help of catheter along with basal diet for four weeks have been studied in the normal albino rabbits. It was observed that this extract lowered the blood sugar, total cholesterol, low density lipoprotein cholesterol and triglyceride levels, and increased the high density lipoprotein cholesterol, phospholipid and faecal sterol levels. Such effects are manifested from the very first week of feeding and are statistically significant[22].

Cholesterol-Lowering Activity

This study was to examine the effects of single and repeated oral administration of the aqueous fruit extract of *T.dioica* at a dose of 50 ml/kg b.w in normal and streptozotocin-induced diabetic rats. The aqueous fruit extracts of *T.dioica* (50 ml/kg) were administered orally for 15 days, to normal and diabetic rats. The effect of the fruit extracts on cholesterol and triglycerides, were studied. The body weights of the rats were observed. The effect of the fruit extract was compared with vanadate, a reference drug. In normal rats, the aqueous fruit extract of *T.dioica* induced significant decrease of plasma cholesterol and triglyceride concentrations 6hrs after a single oral administration, and also in 2 weeks after repeated oral administrations. *T.dioica* treatment caused significant decrease of plasma cholesterol levels after a single administration, and after repeated oral administrations. Significant increase of triglyceride levels was observed 6hrs after a single oral administration of the *T.dioica* aqueous fruit extract. One week after repeated oral administration of aqueous extract of *T.dioica*, the plasma triglyceride levels were significantly decreased. The decreasing trend continued even after 2 weeks. On the other hand, repeated oral administration of *T.dioica* aqueous fruit extract, caused significant decrease of body weight after 2 weeks of treatment in both normal and diabetic rats. The study indicated that the aqueous fruit extract of *T.dioica* exhibits cholesterol and body weight-lowering activities in both normal and hyperglycemic rats[23].

Hepatoprotective activity

The study was carried out to assess the potential of *T.dioica* as a hepatoprotective agent in ferrous sulphate (FeSO4) intoxicated rats. Liver damage was induced in Wistar rats by administering ferrous sulphate (30 mg/kg, p.o) on 10th day. Ethanolic and Aqueous extracts of TD at different doses (100, 200 and 400 mg/kg) and silymarin (100 mg/kg) were administered orally for 10 days. *T.dioica* at dose of 200mg/kg showed decrease in the levels of AST, ALT, TB, ALP and increase in TP. The groups treated with 400 mg/kg aqueous and ethanolic extract showed significant reduction in AST, ALT, ALP, TB and increase in TP level. The pretreatment with *T.dioica* extracts showed profound histopathological protection to liver cells as evident from histopathological studies. Hence it can be concluded that *T.dioica* has significant hepatoprotective activity.[24]

Burns And Wound Healing

The methanolic extract of the *T.dioica* was selected for assessment of healing potential in the form of simple ointment using full thickness burn wound model in rats. The effect produced by the extract ointment showed significant healing when compared with the control and standard groups. All parameters such as wound contraction, epithelialization period, hydroxyproline content, and histopathological studies were observed significant in comparison to control group.[25]

Clinical Studies

T. dioica is known to have antiulcerous effect in polyherbal preparation. Two formulations have been clinically investigated as given below:

1) It was found that Patoladi kasaya a polyherbal formulation, consisted of 11 herbs viz., *T.dioica, Haritaki, Bibhitaka, Amalaki, Kutaki, Cirayata, Amrta, Pittapapada, Sunthi, & Bhrngaraja* exhibited complete improvement in 50% cases & partial improvement in 40% cases with peptic ulcer (10 patients case study)[26].

2) In one clinical study on 33 patients of duodenal ulcer involves evaluation of formulation of Patoladi kasaya which consisted of the herb and another herbs namely *Sunthi, Amrta,*. The formulation in dose of 40ml/kg in two divided doses was effective in relieving patients off their symptoms/complications of duodenal ulcer. It normalized both hyper & hypoacidity of these patients.[26]

3) It was also studied that the efficacy of single herb *T.dioica* in 20 patients with duodenal ulcer. Efficacy of the herb in duodenal ulcer was found 45% excellent response out of 20 cases.[26]

Side Effects and Toxicity

The LD_{50} of Aqueous extract of *T. dioica* in rats was found above 15g/kg by intraperitoneal route respectively.[18] The extract/fractions of *T. dioica* were safe up to a dose of 2000 mg kg^{-1} (p.o.) bodyweight. Behavior of the animals was closely observed for the first 3 h then at an interval of every 4h during the next 48 h. All extract/fractions did not cause mortality in mice and rats during 48 h observation but little behavioral changes, locomotor ataxia, diarrhea and weight loss were observed[27]. Hence these extracts was considered to be safe and non-toxic for screening.

Herbal Drug Interaction

Despite, efficacy of the plant was confirmed in many studies reported in the past the herb-herb interactions or herb-drug interaction is not very well studied, till date the research on this area is the current need of the hour. Since the plant have proven antioxidant activity therefore direct correlation between antioxidant capacity and reducing power of plant extract has been reported[28]. Thus the mechanism of possible inhibitory action of the herb is similar to NSAID's like Indomethacin. So it can be postulated that the extract may show possible synergistic effect and in similar way the drug may antagonize the same[27].

Current Findings

Very recently, a study was reported on antidiarrhoeal activity of *T.dioica*[29]. The inhibition of characteristic diarrhoeal droppings was recorded in magnesium sulphate-induced diarrhea as well as castor oil induced diarrhea. The extracts at dose of 200 mg/kg and 400 mg/kg were found to reduce the total number of faeces significantly.It was postulated that effect was due to their action on the secretion/absorption process in the biological system. Ricinoleic acid, the active constituents of castor oil has been reported to reduce active Na+ and K+ absorption and decrease Na+, K+ ATPase activity in the small intestine and colon.[30] The antidiarrhoeal activity was evident from the reduction of total number of wet faeces in the test groups. Magnesium sulphate has been reported to induce diarrhoea by increasing the volume of intestinal content through prevention of reabsorption of water.[31] It has also been demonstrated that it promotes the liberation of cholecystokinin from the duodenal mucosa, which increases the secretion and motility of small intestine and thereby prevents the reabsorption of sodium chloride and water.[32,33] The ethyl acetate, methanol and water extracts were also found to alleviate the diarrhoeic condition. Besides, antidiarrhoeal activity of flavonoids has already been ascribed to their ability to inhibit intestinal motility and hydro-electrolytic secretion, which are known to be altered in this intestinal condition.[34] In addition, flavonoids will be responsible for the inhibitory effects exerted upon several enzymes including those involved in the arachidonic acid metabolism.[35] It is possible that the flavanoids

present in the herb along with different phytoconstituents are responsible for its antisecretory and antioxidant properties which may contribute to the observed antidiarrhoeal effect.

One latest study reported hepatoprotective effect of the herb in paracetamol induced hepatotoxicity[36].As the herb is rich in protein and vitamin A, vitamin C, carotene, tannins and saponins it possess antioxidant activity responsible for above mentioned beneficial effect.[37,38]Beta carotene and other carotenes have antioxidant properties in vitro and in vivo models.[40] The levels of vitamin C and E were significantly depleted in paracetamol intoxication which was said to be due to excessive utilization of quenching the enormous free radicals produced during paracetamol intoxication.

Numerous studies on the herb shows that *T. dioica* is potential herb with wide range of therapeutic actions. It would be fruitful to investigate further, the specific active constituents in the plant responsible for its therapeutic actions. Also, along with its varied pharmacological actions, it is imperative to study the herb-drug and herb-herb interaction with *T. dioica*, for it may exist and have the serious consequences.

Fig. 1: Trichosanthes dioica

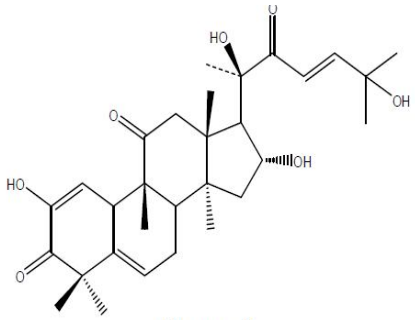

Figure 2

Cucurbitacin- j (Molecular formula- $C_{30}H_{42}O_7$)

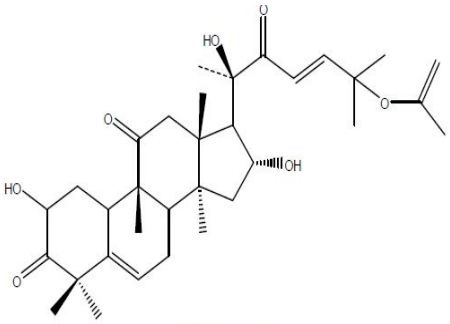

Figure 3

Cucurbitacin-B (Molecular formula- $C_{32}H_{46}O_8$)

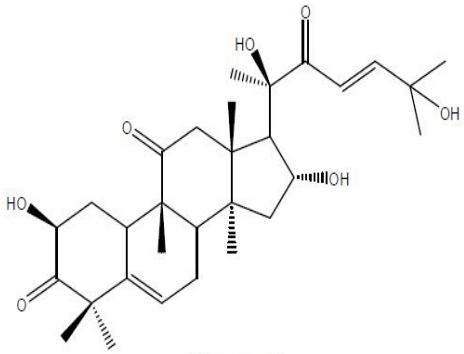

Figure 4
Cucurbitacin-D (Molecular formula- *($C_{30}H_{44}O_7$)*

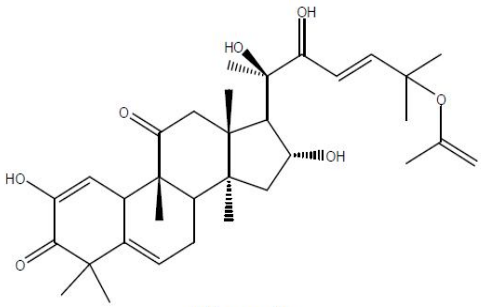

Figure 5
Cucurbitacin- E *(Molecular formula-* ***$C_{32}H_{44}O_8$)***

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