UNIQUE JOURNAL OF PHARMACEUTICAL AND BIOLOGICAL SCIENCES
Review Article

A REVIEW OF THE PHARMACOLOGICAL PROPERTIES OF *TRICHOSANTHES CUCUMERINA* LINN OF SRI LANKAN ORIGIN

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ABSTRACT

Trichosanthes cucumerina Linn. (Family: Cucurbitaceae) is one of the medicinal plants that is often used in Sri Lankan traditional systems of medicine for the preparation of formulations to treat a variety of disease conditions. The aerial parts of *T. cucumerina* are used along with other plant materials for the treatment of indigestion, bilious fevers, boils, sores, skin eruptions such as eczema, dermatitis, psoriasis, inflammation, ulcers and diabetes. Present review summarizes pharmacological and toxicological investigations carried out on *T. cucumerina* of Sri Lankan origin.

Keywords: *Trichosanthes cucumerina*, Cucurbitaceae, Standardization, Bio-activities, Toxicity

INTRODUCTION

Trichosanthes cucumerina Linn. (Fig. 1) is an annual, dioecious climber belonging to the family Cucurbitaceae. It is widely distributed in Asian countries including Sri Lanka, India, Malay Penisula, Thailand and Philippine. The whole plant including roots, leaves, fruits, seeds have medicinal properties. The root is used as a cure for bronchitis, headache and boils. Externally, the leaf juice is rubbed over the liver to relieve liver congestion. Both the root and fruit are considered to be cathartic. The fruit is used as an anthelmintic in French Guiana. The seeds are used for stomach disorders in Malabar Coast and are also considered antifebrile and anthelmintic. The aerial parts of *T. cucumerina* are used along with other plant materials for indigestion, bilious fevers, boils, sores, skin eruptions such as urticaria, eczema, dermatitis, psoriasis diabetes and ulcers[1,2]. A thorough scientific investigation of the pharmacological and toxicological effects of *T. cucumerina*, is important not only to scientifically validate its traditional uses, but also discover any (a) hitherto undiscovered bioactivities that could be exploited and (b) adverse effects it may produce. Further, such a study would help in the isolation of new bioactive compounds that could be developed in the future into novel plant based drug preparations. The following is a brief overview of pharmacological and toxicological investigations carried out on *T. cucumerina* of Sri Lankan origin.

Fig.1. ***Trichosanthes cucumerina*** **Linn. aerial parts**

Antiinflammatory activity: In Sri Lanka, the aerial parts of *T. cucumerina* are used along with other plant materials for inflammatory conditions despite the lack of scientific investigation for such activity in this plant[2]. Carrageenan – induced paw oedema model is widely used for determining the acute phase of inflammation[3,4]. Investigations carried out by Arawwawala and co-workers[5,6], using the above model of inflammation have shown that hot water extract (HWE), cold ethanolic extract (CEE) and fractions (MEF: methanol fraction and AQF: aqueous fraction) of *T. cucumerina* HWE have a marked ability to counter acute inflammation induced by

carrageenan. Apart from the lowest dose of the HWE (375 mg/kg), other tested doses (500, 750, 1000 mg/kg) of HWE and CEE (750 mg/kg) produced a significant ($p \leq 0.05$) inhibition of the inflammation, most pronounced at 5 h after the injection of carrageenan. The antiinflammatory effects induced by 750 mg/kg of HWE and CEE, were comparable to that of the reference drug, indomethacin at 4 and 5 h. Among the tested fractions of HWE, the methanol fraction (MEF) and aqueous fraction (AQF) at a dose of 75 mg/kg significantly inhibited carrageenan-induced hind paw oedema. The antiinflammatory effect induced by MEF, was comparable to that of the reference drug, indomethacin and as well as to the 750 mg/kg of HWE and CEE at 4 and 5 h. In a previous study using carrageenan-induced mouse hind paw oedema model, Kolte and co-workers[7] have also reported the presence of antiinflammatory components in hot aqueous extract of *T. cucumerina* root tubers. Inhibition of histamine and nitric oxide (NO) production and membrane stabilization activities were shown to be probable mechanisms by which *T. cucumerina* mediates its antiinflammatory actions. These findings help to rationalize the traditional use of *T. cucumerina* as an antiinflammatory agent.

Antidiabetic activity: Diabetes mellitus is a chronic metabolic disorder affecting approximately 4% population worldwide and is expected to increase by 5.4 % in 2025. *T. cucumerina* is one of the major ingredients in several polyherbal preparations that are prescribed in Sri Lanka for the control of Diabetes Mellitus[2,8]. Investigations carried out by Arawwawala and co-workers[5,9] using both normoglycemic and streptozotocin (STZ) – induced diabetic rats (Type 1 and Type 2) as experimental models demonstrates that the HWE and CEE of aerial parts of *T. cucumerina* grown in Sri Lanka can significantly ($p \leq 0.05$) reduce serum glucose levels in normoglycemic rats. In STZ-induced Type 1 and Type 2 diabetic rats, no immediate hypoglycemic effect was observed with administration of HWE. However, with continuous administration, there was a gradual reduction in serum glucose levels. At the end of 28 days, in both normoglycemic and STZ-induced diabetic rats (Type 1), there was a significant ($p \leq 0.05$) increase in the levels of liver glycogen and adipose tissue triglyceride levels, in comparison to the respective controls that did not receive HWE. The capability of the HWE to enhance the insulin secretion may be the reason for this. Results of Arawwawala and co-workers[5] with Type 1 diabetic rats are in accordance with findings reported by Kirana and Srinivasan[11], who administered aqueous extract of whole plant of *T. cucumerina* grown in India to STZ- induced Type 2 diabetic mice. Similar to results of Arawwawala and co-workers[5], there was a significant ($p \leq 0.05$) reduction in blood glucose level and significant ($p \leq 0.05$) increase in the levels of liver glycogen and adipose tissue triglyceride levels in STZ-induced Type 2 diabetic mice that received aqueous extract of *T. cucumerina* of Indian origin[11]. Kar and co-workers[12] also reported that administration of ethanolic extract of seeds of *T. cucumerina* grown in India can exert a significant ($p \leq 0.05$) reduction in blood glucose levels in alloxan induced Type 1 diabetes rats. It is interesting to find that in the investigation by Arawwawala and co-workers[10], the HWE of *T. cucumerina* not only lowered serum triglycerides, total cholesterol and LDL levels but also enhanced the cardio protective lipid HDL, in STZ – induced (Type 1 and Type 2) diabetic rats after 28 days treatment. However, HWE failed to inhibit intestinal glucose uptake. Therefore, *T. cucumerina* exerts significant ($p \leq 0.05$) antidiabetic activity, possibly through multiple effects involving pancreatic and extra pancreatic mechanisms rather than inhibition of intestinal glucose uptake. *T. cucumerina* may therefore not only be useful for the control of Diabetes mellitus, but also for management of hyperlipidemia associated with this condition.

Gastroprotection: A polyherbal preparation used in Sri Lanka as a remedy for gastric ulcers is Patoladi decoction[2]. It contains *T. cucumerina* aerial parts and four other plant ingredients: *Terminalia chebula* Retz, *Terminalia belerica* Rox *Phyllanthus emblica* Linn and *Azadirachta indica* A. Juss. Contribution of each component in Patoladi to the alleviation of gastric ulcers has not been evaluated. Recent studies by Arawwawala and co-workers[5,13] have demonstrated that aerial parts of *T. cucumerina* (growing in Sri Lanka) alone has the potential to exert significant ($p \leq 0.05$) gastroprotective activity. Significant ($p \leq 0.05$) inhibition of the formation of gastric ulcers (in terms of length and number) induced by absolute ethanol or indomethacin in rats by HWE (375, 500 and 750 mg/kg) and CEE (750 mg/kg) provides evidence to support the presence of components in *T. cucumerina* that can exert significant ($p \leq 0.05$) gastroprotection. The gastroprotective activity of a 750 mg/kg dose of HWE or CEE was comparable to that mediated by the reference drugs cimetidine and sucralfate. Findings also indicate that increasing the protective mucus layer, decreasing the acidity of the gastric juice and antihistamine activity are probable mechanisms by which *T. cucumerina* mediates its gastroprotective actions.

Antioxidant activity: During the past three decades there has been an increasing interest in finding naturally occurring antioxidants from plant materials to replace synthetic antioxidants consumed as foods or medicines[14]. Investigations have been carried out by Arawwawala and co-workers[15] to evaluate the antioxidant potential of *T. cucumerina* aerial parts, by use of *in vitro* [(a) 2,2-diphenyl- 1- picrylhydrazyl ($DPPH^{\cdot}$) scavenging assay (b) thiobarbituric acid reactive substances (TBARS) assay and (c) β – carotene – linoleic acid assay] methods and *in vivo* studies using a rat model.

The overall results of investigations carried out by Arawwawala and co-workers[15], demonstrate that both HWE and CEE of *T. cucumerina* can exert significant antioxidant activity as evident from their ability to (a) scavenge free radicals such as $DPPH^{\cdot}$ and linoleic *in vitro* (b) enhance activities of the antioxidant enzymes such as superoxide dismutase (SOD) and Glutathione peroxidase (GP_X) *in vivo* and (c) inhibit lipid peroxidation *in vitro* and *in vivo*.

Antimicrobial activity: *Staphylococcus aureus, Streptococcus pyogenes, Escherichia coli, Pseudomonas aeroginosa, Streptococcus pneumoniae* and *Klebsiella pneumoniae* are some important bacterial strains causing wound infections. A wide range of antibiotics (e.g. erythromycin, tetracyclines, trimethoprim, sulfonamides,

gentamicin, etc) are being used at present for treating wound infections[16,17]. Bacterial resistance to antibiotics is a major therapeutic problem and the rate at which new antibiotics are being produced is slowing[18]. The presence of bacteria within a wound cause infections and delay the healing. Investigations carried out by Arawwawala and coworkers[19], using (a) colony count and (b) disc diffusion techniques has demonstrated that aerial parts of *T. cucumerina* of Sri Lankan origin can inhibit the growth of some selected bacterial strains such as *Staphylococcus aureus* (NCTC 25923), *Streptococcus pyogenes* (NCTC 20258), *Escherichia coli* (NCTC 25922) and *Pseudomonas aeroginosa* (NCTC 20620) that are known to cause wound infections. Results also show that the CEE can exert consistently better antibacterial activity than the HWE. It was noted that gram negative (-) bacteria such as *E. coli* and *P. aeroginosa* appear to be less susceptible to the effects of the HWE or CEE than the gram positive (+) bacteria *S. aureus* and *S. pyogenes*.

Toxicity: Herbal medicines are regarded by the public and some health care providers to be gentle and safe, but there is no scientific basis for this belief. The active ingredients of plant extracts are chemicals that are similar to those in purified medications, and they have the same potential to cause serious adverse effects. The usefulness of any drug depends not only on its therapeutic efficacy but also on its lack of toxicity or adverse side effects. Investigations of acute and chronic unacceptable side effects of *T. cucumerina* aerial parts are therefore important.

Using mice as the experimental model, Arawwawala and co-workers[20] have recently demonstrated that extracts (HWE or CEE) of *T. cucumerina* aerial parts do not produce any serious toxic effects or mortality even at a doses up to 30 g/kg. Oral treatment with HWE or CEE for 14 days or 42 days failed to bring about any overt signs of toxicity (salivation, diarrhoea, lacrymation, tremors, ataxia, yellowing of hair, loss of hair, postural abnormalities or behavioral changes), stress (fur erection or exophthalmia), aversive behaviors (biting paw and penis, intense grooming behavior, scratching behavior, licking at tail or vocalization) and mortality. HWE and CEE treated mice showed normal food and water intake. The consistency of faeces and color of urine of the HWE and CEE treated mice were similar to that of respective control groups.

The extracts also did not produce any signs of hepatotoxicity or renotoxicity (as judged by histopathological observations, liver and kidney function assessments) or unacceptable effects on fertility of males or females (as evident from the effects of the HWE and CEE on early aborfacient activity and implantation in female rats and spermicidal activity *in vitro*).

CONCLUSION

In recent years, ethnomedicinal studies received much attention as this brings to light the numerous little known and unknown medicinal virtues especially of plant origin which needs evaluation on modern scientific lines such as pharmacognostical, pharmacological investigations and clinical trials. *T. cucumerina* exerts strong antiinflammatory, antidiabetic and gastroprotective effects, validating the claims in traditional medicinal systems of Sri Lanka. In addition, hitherto unreported bioactivities such as antioxidant and antimicrobial activities were also discovered. However, it is imperative that more clinical and pharmacological studies should be conducted to investigate the unexploited potential of this plant and if possible identify active components responsible for mediating its pharmacological activities.

ACKNOWLEDGEMENT

The authors express their gratitude to National Science Foundation for the Research Grant (NSF/SCH/2005/13).

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Source of support: Nil, Conflict of interest: None Declared