Abstract

Trichosanthes cucumerina Linn. (Family: Cucurbitaceae; S. Dummela) 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. However, validity of most of these claims has not been scientifically investigated so far. The toxic effects of *T. cucumerina* are also not known. The aims of the present study were to (a) standardize hot water (HWE) and cold ethanolic (CEE) extracts of *T. cucumerina* aerial parts, (b) scientifically investigate whether *T. cucumerina* possesses anti-inflammatory, antidiabetic and gastroprotective properties as claimed by traditional physicians, (c) discover hitherto unreported pharmacological activities (e.g. antioxidant and antibacterial activities), (d) evaluate toxic potential (acute and chronic toxicity) of the plant extracts and (e) identify the active fractions responsible for the best two bioactivities demonstrated in the present study by *T. cucumerina*.

Both extracts (HWE and CEE) were standardized by developing their TLC and HPLC fingerprints and determination of physico – chemical parameters such as total ash, water soluble ash and acid insoluble ash. Both HWE and CEE contain common chemical compounds such as alkaloids, coumarins saponins, tannins, flavonoids and other phenolic compounds. However, chemical differences between the HWE and CEE were reflected in the TLC and HPLC fingerprints of these extracts. The greater solubility of non polar components in ethanol extract may account for the differences in the TLC and HPLC

fingerprints of the HWE and the CEE observed during this investigation. Results revealed that both HWE and CEE of *T. cucumerina* aerial can exert significant ($P \leq 0.05$) anti-inflammatory, antidiabetic, gastroprotective and antioxidant activities in rats. In addition, the HWE and CEE have also been shown to contain chemical constituents that can exert antioxidant and antimicrobial activities.

Anti-inflammatory effect was dose – dependent for acute inflammation. Both HWE and CEE at a dose of 750 mg/kg significantly inhibited the paw oedema induced by carrageenan (HWE by 73 % and CEE by 74 %) and their effects were comparable to that produced by the reference drug, indomethacin at 5 h. Inhibition of NO production, antihistamine and membrane stabilization activities demonstrated by the plant extracts are probably some of the mechanisms by which their anti-inflammatory actions are mediated.

Both HWE and CEE significantly ($P \leq 0.05$) reduced the blood glucose levels in normoglycemic (HWE by 35 % and CEE by 30 % at 4 h) and (STZ) – induced (Type 1 and Type 2) diabetic rats (Type 1: HWE by 64 % and Type 2: HWE by 31 % at end of 28 days) and effects were comparable to that of reference drugs tolbutamide (reduction of 40 % at 4 h) in normoglycemic rats and glibenclamide (reduction of 66 % in Type 1 and 39 % in Type 2 at end of 28 days) respectively. The present investigation has shown that *T. cucumerina* extracts can enhance (a) the secretion of insulin from pancreatic cells, and (b) insulin-mediated uptake of blood glucose into extra pancreatic tissues such as the liver and adipose tissue. Therefore, these are mechanisms that may be used by *T. cucumerina* extracts to exert anidiabetic effects.

T. cucumerina extracts also provided dose dependent and significant ($P \leq 0.05$) protection against, gastric damage induced by ethanol (750 mg/kg of HWE: reduced gastric lesion length by 92% and number of gastric lesions by 88%) or indomethacin (750 mg/kg of CEE: reduced lesion length by 88% and number of gastric lesions by 84%). Inhibition of acidity (both total and free), enhancement of mucus content and antihistamine activities have been demonstrated to be possible mechanisms or by which the *T. cucumerina* extracts mediate gastroprotection. The gastroprotective effect of a 750 mg/kg dose of HWE or CEE was superior to that exhibited by doses of cimetidine and sucralfate the (reference drugs) that corresponded to the normal human therapeutic dosages.

Results of the present investigation has also revealed that both HWE and CEE of *T. cucumerina* can exert significant ($P \leq 0.05$) antioxidant activity. This is evident from their ability to (a) scavenge free radicals such as DPPH· (EC_{50}: 39.2 ± 0.2 μg/mL and 15.7 ± 0.6 μg/mL for HWE and CEE respectively) and linoleic *in vitro* (AA%: 76.9 ± 0.9 and 81.2 ± 1.8 for HWE and CEE respectively) (b) enhance activities of antioxidant enzymes such as SOD (HWE increased SOD: by 21.3 % while CEE increased SOD: by 24.1 %) and GP_X (HWE increased GPX by 20.4% while CEE increased GPX by 22.54 %) *in vivo* and (c) inhibit lipid peroxidation *in vitro* (% AI: 26.5 ± 0.2 and 32.4 ± 0.8 for HWE and CEE respectively) and *in vivo* (inhibition of lipid peroxidation by 48.6% and 65.2% for HWE and CEE respectively). *T. cucumerina* has also been shown to exert significant ($P \leq 0.05$) antibacterial activity against gram (+) ve bacterial strains such as

S. aureus, *S. pyogenes* and gram (-) ve bacterial strains such as *E. coli* and *P. aeroginosa*. Administration of the HWE or CEE to mice did not result in acute or chronic toxic effects as evident from their effects on (a) liver function (b) kidney function and hematological parameters such as RBC, WBC, differential WBC, % PCV and Hb concentration. Further, the HWE and CEE did not appear to mediate any unacceptable effects on the fertility of males or females as evident from their effects on (a) early abortifacient activity and implantation in female rats, and (b) spermicidal activity *in vitro*.

Among the tested fractions of HWE, the MEF (methanol fraction) and the AQF (aqueous fraction) showed maximum anti-inflammatory and antidiabetic activities respectively. In conclusion, the results of this study have helped to (a) rationalized the ethnopharmacological uses of *T. cucumerina*, (b) discover some hitherto unreported bioactivities of the plant such as antioxidant and antibacterial activities (c) identify the active fraction/s of HWE responsible for its anti-inflammatory and antidiabetic activities and (d) demonstrate that extracts of *T. cucumerina* at the doses tested do not produce any serious toxic side effects.