DEVELOPMENT OF AN AYURVEDIC PHARMACEUTICAL PREPARATION FROM *Tragia involucrata* Linn. (*WEL KAHAMBILIYA*) AND EVALUATION OF ITS EFFICACY AND SAFETY ON HYPERGLYCAEMIC SUBJECTS

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Abstract

Tragia involucrata Linn. (Family: Euphorbiaceae, S. *Wel Kahambiliya*) is a highly used medicinal plant in both Sri Lankan traditional medicine as well as in Ayurveda medicine. This plant is used for diseases such as diabetes mellitus, wounds, asthma, dysuria and epilepsy. Although there have been previous studies performed on this plant, the safety and efficacy of the whole plant decoction of *T. involucrata* towards diabetes mellitus has not been scientifically validated. The aims of the present study were to, standardize and authenticate the plant material; scientifically investigate whether *T. involucrata* possesses hypoglycaemic, anti-diabetic, anti-dyslipidaemic, diuretic properties in rats as claimed by traditional practitioners; evaluate the toxic effects (sub-acute and sub-chronic toxicity) of the decoction in rats, and investigate the anti-diabetic activity in patients with type II diabetes mellitus.

The plant material was standardized by developing its TLC fingerprint and determination of physico-chemical parameters such as total ash, water soluble ash, and acid insoluble ash. Ten extracts of the plant were prepared using solvents having different polarities and screened for the presence for common chemical compounds such as alkaloids, coumarins, saponins, tannins, flavonoids, glycosides, and other phenolic compounds. The polar solvents yielded a higher percentage of extract compared to non-polar solvents. Hence, hot water extract showed the highest yield. Total flavonoid and total phenol content were quantified. There was a considerable amount of both. The presence of these potent antioxidants in the plant might be the reason for its health benefits.

The hot water extract of *T. involucrata* (TWE) at the therapeutic dose of 550 mg/kg significantly ($p<0.05$) reduced the serum glucose concentration and glucose tolerance effect when challenged with a glucose load, in high fat diet (HFD) fed streptozotocin-induced diabetic rats. The effect was compared with metformin which was the reference drug. Other doses of TWE such as 875 and 1100 mg/kg, also significantly ($p<0.05$) reduced the serum glucose concentration, but the therapeutic dose was more effective in reducing serum glucose concentration than the other two doses. The extract also improved the HDL-C concentration and lowered the triglyceride concentration. The same tests were carried out on normoglycaemic rats in which the extract failed to reduce the serum glucose concentration and the glucose tolerance effect. Hence, the present investigation showed that although TWE did not increase the secretion of insulin from pancreatic cells, the extract did enhance the insulin mediated uptake of serum glucose into extra pancreatic tissues such as the liver and adipose tissue, and positively influenced the lipid metabolism. Therefore, the study demonstrates that the TWE shows insulin mimicking action in order to exert the antidiabetic effect, but the extract did not show hypoglycaemic effect.

Studies were also carried out to evaluate the efficacy towards the most common complications of type II diabetes mellitus, hypertension and dyslipidaemia. Therefore, the diuretic action and the anti-dyslipidaemic action of TWE were evaluated.

The results revealed that the extract exerted a significant dose-dependent diuretic activity and natriuretic and kaleuretic activities in urine excretion. The urine excretion was

gradually increased with the increased dose which were 550, 1100, 1650, and 2200 mg/kg. The dose 1650 mg/kg showed the maximum activity and the same response was observed in 2200 mg/kg. Furosemide was used as the reference drug.

The study also revealed the presence of anti-dyslipidaemic activity of TWE on HFD fed rats. The study showed that on day 14 and 28 there was a significant decrease ($p<0.05$) in TC and TG concentrations in the test rat group and reference (atorvastatin) rat group compared to the negative control rat group.

Results of TWE sub-acute toxicity study (5000 mg/kg dose) and the TWE sub-chronic toxicity study (550 mg/kg dose) showed that the oral administration of the extract did not produce any toxic effects in terms of hepatotoxicity; renotoxicity; heamotoxicity; gross morphology and weights of organs; stress and aversive behaviors nor death.

The randomized, open label clinical trial evaluating the efficacy of TWE in patients with type II diabetes mellitus showed that the fasting serum glucose concentration of the test group on day eight and day 15 compared to day 0 have significantly ($p<0.05$) decreased. The extract also did not cause changes to the liver and renal functions.

In conclusion, the results of this study evidenced the presence of bioactivities such as anti-diabetic, anti-dyslipidaemic and diuretic activities, but no toxic side effects at the doses tested. Further the clinical trial agrees with the antidiabetic activity on patients with type II diabetes mellitus.

KEY WORDS

Tragia involucrata; biological activities; toxicity; clinical trial