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Evaluation of Hypoglycemic Potential of *Trichosanthes dioica* Roxb. for its Possible Therapeutic Use

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Abstract:

Diabetes is a common life style disease that affects a large population but is hard to cure because of its complex metabolic regulation. There is a great variety of drugs that are used to treat hyperglycemia resulting from diabetes but a permanent cure is still elusive because patients have to take hypoglycemic drugs for their whole life. The popularity of herbal solutions for such conditions is unmatched because natural cures are not accompanied with usual side effects. *Trichosanthes dioica* is a common vegetable and is recommended as a candidate drug for treating diabetes. This study was planned to test the validity of such claims in rat models. In this study hexane extracts at a dose of 250 mg/kg b.w. were used to assess their hypoglycemic effect in fasted, fed and glucose-loaded models in *Charles Foster* strain albino rats. Blood sugar level was determined from samples collected from the tail vein at different intervals of time (0, 1, 3, and 4 hours). On the basis of the results obtained, the hexane extract of *Trichosanthes dioica* was found to be significantly effective as a hypoglycaemic agent.

Keywords: Herbal drugs, Diabetes, hypoglycemia, hexane extract, *Trichosanthes dioica*, Insulin

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Introduction:

The growing prevalence of diabetes is a cause of concern across the globe and a cure for its variants is desperately sought by medical practitioners. Diabetes is labeled as the epidemic of the century (Kharroubi & Darwish, 2015). Out of the major types of diabetes, the type 1 diabetes (IDDM, or insulin dependent diabetes mellitus) is less prevalent than type 2 diabetes (NIDDM, or non-insulin dependent diabetes mellitus). What is particularly interesting is that the patterns of incidence of these two types of diabetes are quite different. While type 1 diabetes which involves defective secretion from β-cells of pancreatic islets of Langerhans is an early onset condition, the type 2 diabetes is usually a late-onset disease. The much higher prevalence of type 2 diabetes (80-90 %) than that of type 1 diabetes (5-10 %) makes it a bigger challenge for the medical community the world over (Haddad & Haddad, 2018). The etiology of type 1 diabetes is simpler because it only involves lack of insulin secretion. However, things are much more complex in type 2 diabetes because of the involvement of insulin resistance which may have multiple causes. To further complicate the matters, the disease may have both genetic and environmental origins (Ali, 2013). The sedentary life style, stress and wrong dietary habits are leading cause to growing numbers of diabetics every year. Diabetic complications caused by persistently high blood sugar impact a number of organs, primarily the eyes, kidneys, blood vessels and nerves (Sudha P, 2011).

Prognosis of type 2 diabetes involves the use of several classes of synthetic drugs having multiple mechanisms of action which relieve the symptoms of the disease but have to be taken permanently. Herbal medicines for diabetes are becoming quite popular due to being comparatively safer. Besides, most of the drugs being used in the management of this disease may have many side effects and a search for new class of compounds is essential to overcome diabetic problems (Noor, 2008). Medicinal plants have been used as a source of treatment for at least 4,000 years and are a rich source of pharmaceuticals, binders, flavouring compounds, food additives, lubricants and colorants (Wadkar, 2008).

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Traditionally, a number of plants have been used in various herbal preparations in the management of diabetes and only few of them have been scientifically proven (Jiao, 2009).

The leaves of *Trichosanthes dioica* are used as febrifuge, tonic, and in subacute cases of enlargement of spleen and liver (Nadkarni, 1982). In Charaka Samhita, fruits and leaves are recommended to be used for treating jaundice and alcoholism. Leaves are used traditionally in edema and alopecia (Khare, 2004). It is also used as cardiotonic, antipyretic, diuretic, and laxative. *Trichosanthes*, a genus of family Cucurbitaceae, is an annual or perennial herb distributed in tropical Asia and Australia region. *Trichosanthes dioica* is cultivated throughout the plain of Northern India, extending to Assam and East-Bengal (Kirtikar, 2001). According to previous research and literature it is found that the herbs which are having bitter principles like *Trichosanthes dioica* (parval), are potentially useful medicinal plants for developing a new anti-diabetic drug with less side effects (Chopra, 2002). The aqueous extract of *Trichosanthes dioica* has in fact been shown to be antidiabetic in a previous study (Adiga et al., 2019). Therefore, the hexane extract of *Trichosanthes dioica* was selected for the study of its hypoglycaemic activity in this research work. Further, in the light of a study (Rai, 2013), parwal was found to be antihyperlipidemic as well as antihyperglycemic. Since hyperglycemia is usually associated with hyperlipidemia, *Trichosanthes* can have the added advantage in diabetics.

Materials and Methods:

Plant material: The plants used in the study were collected from the field and authenticated by experts. The plant of *Trichosanthes dioica* was washed thoroughly and subjected to shade dried. Around 500gm of coarsely powdered plant sample was subjected to successive extraction using hexane by continuous hot percolation process in Soxhlet apparatus. The extract was concentrated by using the rotatory evaporator at 40°C and evaporated to dryness in a water bath under controlled conditions. This dried extract was kept in air tight containers for further analysis.

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Experimental Animals: The male rats of *Charles Foster* strain were procured from CDRI Lucknow and were kept in laboratory under standard conditions, temperature 25-26°C, and relative humidity 60-70% and 12/12 hour light/dark cycle. These animals were housed in polypropylene cages with free access to pellet laboratory diet and water *ad libitum*. The animals were acclimatized to laboratory environment one week prior to the study as per OECD guidelines (Oecd, 2008). The animals meant for study were divided into 3 groups i.e, fasted, fed and glucose loaded and were treated according to the CPCSEA guidelines. An average rat weighed 150-200 gm.

The plant extract was suspended in 2% gum acacia. The suspension was orally fed to rat through a narrow rubber tube attached to a hypodermic syringe at a dose of 250 mg/kg body weight. The blood glucose lowering effect of the extract was examined following four different experimental models while the control group was given only 2% gum acacia suspension to increase the sensitivity of the experimental procedure.

The blood sugar lowering efficacy of the extract was examined in three different experimental models as follows:

1: Fasted model: Blood was collected from the tail vein (0 hr) of the overnight fasted rats (18 hrs) the extract of plant *Tricosanthes dioica* was fed to these animals with the dose of 250 mg/kg b.w. Again the blood samples were collected at 1, 3 & 4 hrs. after feeding. Blood sugar was estimated by Nelsons method (Nelson, 1944).

2: Fed model: Excess pellets were kept in the rat cage on the previous evening so that some pellets were left over in the next morning. The experiments were carried out in these fully fed animals in the same way as in fasted model and blood glucose lowering efficacy of plant extract was checked at different interval of time.

3: Glucose-loaded model: This group's animals were fasted for 18 hours before blood was drawn (at 0 hour) to determine blood glucose levels. The animals were then fed the plant extract at the dose of 250 mg/kg body weight. After half an hour, a glucose solution (1.5 gm/kg b.w.) was given orally and blood samples were again collected at 1/2, 1 and 3 hour's

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intervals to assess the concentration of glucose in the blood by using the Nelson-Somogyi method.

Statistical Analysis of Data: Statistical analysis was performed using GraphPad Prism software (version 6.04). The data were expressed as mean ± standard error of the mean (SEM). Statistical analysis was carried out using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test with multiple comparisons to determine the source of significant difference between the groups.

Results:

Effect of crude extract on blood glucose: The crude extract of *Trichosanthes dioica* had a significant hypoglycemic impact in treated group animals as compared to the control group as shown in the table I and II.

Table- I: Effect of Hexane extract of *Trichosanthes dioica (Roxb)* whole plant at a single dose of 250 mg/kg b.w., on the blood sugar level of fatsed, fed male albino rats model.

Group		Blood Sugar Level mg/100ml (Mean ± S.E.) at time (hours)			
		0hr	**1hr**	**3hr**	**4hr**
Fasted	Control	60.48 ± 1.51	61.35 ± 1.00	58.86 ±1.11	57.66 ± 1.18
	Experimental	60.84±1.50	58.06 ± 1.02	52.23±1.8	53.48±0.89
Fed	Control	90.44 ± 1.51	88.48 ± 1.41	84.79± 1.42	83.08± 2.14
	Experimental	93.77± 1.52	84.53±0.91	74.31±1.45	71.31±1.87

Significance between the control and experimental group: * P<0.01

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Table- II: Effect of Hexane extract of *Trichosanthes dioica (Roxb)* at a single dose of 250 mg/kg b.w., on glucose tolerance (1.5 g/kg b.w. orally) of albino rats.

Group		Blood Sugar Level mg/100ml (Mean ± S.E.) at time (hours)			
		0hr	**1/2hr**	**1hr**	**3hr**
Glucose loaded	Control	71 ± 1.8	116 ± 3.2	112 ± 3.1	82 ± 4.1
	Experimental	72 ± 1.2	102± 1.9*	106± 2.8	77± 3.2

Significance between the control and experimental group: * P< 0.01

The results presented here suggest a high sugar-lowering efficacy of *Tricosanthes dioica* in all the models studied. This is quite an encouraging result for people suffering from diabetes. The abundance of parwal makes it easily accessible to everyone looking for a cure in food materials. Besides, it can be exploited therapeutically to produce a herbal medicine based on *Trichosanthes dioica* to treat type II diabetes. It can also be used as a supplement for other blood sugar lowering along with other hypoglycemic drugs.

Conclusion:

The anti-diabetic potential of the hexane crude extract of *Trichosanthes dioica* was investigated in this study by using normoglycemic rats. In the light of the results (Table I and II), treatment of all 3 groups rats with the hexane extract of *Trichosanthes dioica* with dosage of 250 mg/kg body weight significantly decreased the blood glucose level. This could be due to the restoration of a delayed insulin response, restriction of glucose absorption in the intestine, or an increase in glucose utilization. Degranulation in β-cells suggested that the rate of extract-induced insulin release was greater than the rate at which β-cells replenished their insulin storage and resulted in a reduction in blood glucose. Apart

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from old traditional texts, such as Charak Samhita mentioned the protective role of *Trichosanthes* on important body organs such as liver, spleen, heart, etc., many of which are now scientifically proven. In this context, other researchers have also reported that *Syzygium cimini* (Soumya, 2011), *Securigera securida* (Suryavanshi, 2019), *Allium cepa* and *Ocimum sanctum* (Bajpai, 2008) have significant anti-diabetic and glucose tolerance effects in experimentally induced diabetic rats. The authors perceive that *Trichosanthes* may play a significant role in developing formulations for diabetes treatment as it is having almost all the properties of pharmaceutical care (Kumar, 2012). In developing countries like ours one must fully explore this important medicinal plant which might provide us some important leads in near future. If found effective in human trials it can turn out to be of dual advantage as a food as well as a medicine. Further studies along these lines are highly recommended from a therapeutic point of view.

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