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An Evaluation of Antidiabetic Potential ofMethanolic Extractof *Swertia Chirata* in Streptozotocin Induced Diabetic rats.

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ABSTRACT

The present study evaluates the antidiabetic activity of *Swertia chirata* (methanolic extract) on the blood glucose level of streptozotocin induced diabetic rat models. To study the antidiabetic activity of methanolic extract of *Swertia chirata* in streptozotocin induced diabetes in albino rats. To compare the antidiabetic activity of *Swertia chirata* extract with that of standard drug glibenclamide used in the treatment of type 2 diabetes mellitus. In the present study 24 male albino wistar rats divided into 4 groups with 6 animals in each group was taken. One group as control was given normal saline for 21 days daily. Other 3 groups were induced diabetes. Standard and test groups were fed with glibenclamide (0.5mg/kg) and methanolic extract (50mg/kg) daily for 21 days respectively. The results were analysed with ANOVA (Analysis of Variance) and comparison with standard, test and control groups done by post hoc tukeys test. $p<0.001$ was considered highly significant. An analysis of results shows that methanolic extract group (M3) of *Swertia chirata* have significant antidiabetic activity in comparison to respective control groups (M1,M2)but less marked antidiabetic activity when compared to the standard glibenclamide group (M4). Methanolic Extract of *Swertiachirata* at a dose of 50 mg/kg body weight has exhibited antidiabetic activity in streptozotocin induced diabetes in rats but exhibits less marked antidiabetic activity when compared to standard drug glibenclamide.

Keywords: antidiabetic activity, *Swertia chirata*, methanolic extract, glibenclamide.

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INTRODUCTION

Diabetes Mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemias [1]. Depending on the aetiology of the DM, factors contributing to hyperglycaemia include reduced insulin secretion, decreased glucose utilisation, increased glucose production [1].DM is the leading cause of end-stage renal disease, non traumatic lower extremity amputations and adult blindness and predisposes to cardiovascular diseases.

Currently the number of cases of diabetes worldwide is estimated to be around 150 million.

This number is predicted to double by 2025, with the greatest number of cases being expected in China and India [2].India has now been declared by WHO as the 'diabetes capital of the world [3].Despite the availability of many antidiabetic medicines in the market, diabetes and its related complications continue to be major medical problems. The currently used hypoglycaemic drugs in the treatment of diabetes are not completely effective and are associated with adverse effects both in the short and long run.

Several herbs have been tried in various studies to prevent or delay type2 diabetes. Aeglemarmelose, Aloe vera, Artemisia pallens, Coccinia indica, Swertia chirayita and many others have been shown to have antidiabetic activity [4]. The antihyperglycemic effects of these plants are attributed to their ability to increase insulin output from the pancreas or inhibit intestinal absorption of glucose or some other processes.Among the different species of Swertia, Swertia chirata is considered for its medicinal properties as antihelminthic, antipyretic, hypoglycaemic and antifungal properties [5].

Few studies have reported the antidiabetic activity of methanolic extract of *Swertia chirata*. So this study is undertaken to evaluate the antidiabetic activity of methanolic extract of*Swertia chirata*in streptozotocin induced diabetes in rats.

Aims and Objectives

The present study evaluates the antidiabetic activity of *Swertia chirata*on the blood glucose level in streptozotocin induced diabetic rat models.

To study the antidiabetic activity of methanolic extract of *Swertia chirata* in streptozotocin induced diabetes in albino rats.

To compare the antidiabetic activity of *Swertia chirata* extract with thatof standard drug glibenclamide used in the treatment of type 2 diabetes mellitus.

Epidemiology

Diabetes mellitus is pandemic in both developed and developing countries. Worldwide the prevalence of diabetes mellitus is estimated to be 2.8% and is set to rise to 4.4% by 2030 [2].

The greatest relative rise is predicted in developing countries of the Middle Eastern crescent, sub-Saharan Africa and Indian subcontinent.In developed countries as U.S.A , about 5-10 % of all diabetics have type 1 DM. Geographic variations also alter the incidence of Type 1 DM and Type 2 DM.I.Type 1 diabetes (β-cell destruction, usually leading to absolute insulin deficiency).II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretory defect with insulin resistance) [1].

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Swertia chirata

This plant belongs to Gentianaceae family. It is a medicinal plant indigenous to temperate Himalaya. This plant is known by an array of names, for example *chiravata* (Urdu*), Nelabevu* (Kannada), *Shirattakuchi* (Tamil), *Nelavembu* (Telugu).The trade name is *Chiretta [5].* The plant is a native of temperate Himalayas, found at an altitude of 1200-1300 m from Kashmir to Bhutan and in the Khasi hills at 1200-1500 m. It can be grown in sub temperate regions, at altitudes 1500-2100 m. The genus Swertia consists of annual and perennial herbs [5].

The plant can be grown in a variety of soils with sandy loam rich in carbon and humus. Also found in open ground and recently slashed and burnt forests. The plant contains a bitter glycoside chirantin which on hydrolysis yields two bitter principles ophelic acid and chirantin [6]. The ash of *Chirata* yields carbonates and phosphates of calcium, potassium and magnesium [7].Its medicinal properties, anti helminthic, hypoglycaemic [8] and antipyretic, anti-inflammatory, analgesic, anti micro bialare attributed to its active principles amarogentin , swerchirin and swertiamarin. Its secondary metabolites xanthones, seco-iridoid glycoside, triterpenoid alkaloid & hexane fraction also contribute to its medicinal properties [5].

MATERIALS AND METHODS

This Study was conducted at the Department of Pharmacology, Karnataka Institute of Medical Sciences, Hubli, after approval from Institutional Animal Ethics Committee.

Materials

Animals: The animals used in the present experimental work were healthy albino rats of Wistar strain of male sex weighing between 150-250 g .The animals were maintained under standard laboratory conditions with free access to food and water. Each group consisted of randomly selected six animals.

Drugs

Streptozotocin (STZ): After weighing the required quantity of STZ powder, fresh STZ solution was prepared in 0.1M sodium citrate buffer of pH 4.5. STZ was administered at a dose of 50-60 mg/kg by intraperitoneal route [9]. STZ was purchased from Sisco Research Lab, Ahmedabad.

Sodium citrate buffer

Glibenclamide: In this study glibenclamide was taken as the standard drug at a dose of 0.5 mg/kg b.w. by oral route Glibenclamide powder dosage form was purchased from Bangalore (Aventis Pharma).

Test drug (*Swertia Chirata*): - Methanolic extract of *Swertia chirata* at a dose of 50 mg/kg b.w by oral administration was used. *Swertia chirata* extract was procured from Department of Rasayanashastra, Ayurveda Mahavidyalaya; Bengeri, Hubli.

Methods

Inclusion Criteria

- Animals weighing 150-250
- Healthy male rats with normal behaviour & activity

Exclusion Criteria

- Animals weighing <150 g and >250 g.
- Female rats.

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In the present study, diabetes was chemically induced by streptozotocin (STZ) which produced permanent hyperglycaemia in rats. Blood glucose levels were measured by glucometer. A total of 24 animals were used for the study .They were divided into 4 groups of 6 animals each. Out of 24 rats, only 18 rats were induced diabetes

Induction of diabetes

After an 18hrs fasting, diabetes was induced in 36 rats by intra-peritoneal (i.p.) injection of streptozotocin (STZ) dissolved in 0.1 M sodium citrate buffer (pH 4.5) at a dose of 50-60 mg/kg b.w [8].

Animals were observed for first 24 hrs following the injection of STZ for any evidence of allergic reactions, behavioural changes and convulsions. Animals were fed with 5% glucose solution to overcome the STZ induced hypoglycaemia [8]. No untoward reaction was observed in any animal. After 72 hrs of STZ induction, blood glucose levels were recorded. Only those animals whose blood glucose levels were between 200-300 mg/dl with glycosuria were selected for the study and were divided into 4 groups as follows. Animals not given STZ were considered as non-diabetic or normal control group. The animals in other 3 (M2, M3 & M4) groups were observed for evidence of any behavioural changes, hyper or hypoglycaemia and convulsions. All the animals were fed for a period of 21 days.

***Swertia chirata* Methanolic Extract**

Normal control group (M-1): This group of animals received 0.5 ml of carboxy- methyl-cellulose [CMC] daily for 21 days by oral route. Blood glucose levels were recorded before the administration of CMC on day 0 at 9 am, then on 3^{rd}, 7^{th}, 14^{th}& 21^{st} day at 9 a.m after administration of CMC. Diabetic control group (M-2): The blood glucose levels of this group were recorded at 9 am on day 0 before administering CMC. Later the animals were fed with 0.5 ml of CMC daily orally for 21 days. Methanolic extract test group (M-3): The blood glucose levels of this group were recorded at 9 am on day 0 before the administration of the test drug. Then methanolic extract at a dose of 50 mg/kg b.w. was fed to 6 animals orally for 21 days daily. The blood glucose levels were recorded on 3^{rd}, 7^{th}, 14^{th} and 21^{st} day. Glibenclamide standard group (M-4): The blood glucose levels of this group were recorded at 9 am on day 0 before the administration of glibenclamide. Later the animals were fed with glibenclamide at a dose of 0.5 mg/kg b.w. daily orally in the morning for 21 days. Their blood glucose levels were recorded on 3^{rd}, 7^{th}, 14^{th} and 21^{st} day. They were observed carefully for evidence of hypoglycaemia and convulsions.

Statistical analysis: In the present study, Statistical analysis was done using Analysis of Variance (ANOVA). Tukey's test was used for post-hoc comparison test.

RESULTS

Table 1: Mean ± SD values of blood glucose levels in different groups of rats treated with Methanolic Extract of Swertia chirata on Days 0, 3, 7, 14, 21.

GROUPS	day0	day3	day7	day14	day21
M1	79.00±11.87	83.33±7.66	78.17±10.48	75.50±8.38	62.67±6.62
M2	285.33±11.84	290.00±11.93	292.67±11.78	295.00±11.78	295.0011.15
M3	278.17±11.39	151.67±23.36	92.00±13.13	83.3±25.6	83.17±18.78
M4	266.50±19.34	175.33±12.99	109.83±8.86	89.33±11.86	73.17±8.01
M1vsM2, M1vsM3,M1vsM4	p<0.001	p<0.001	p<0.001	p>0.05	p>0.05

ANOVA-Analysis of Variance $p < 0.0001$-HighlySignificant, $p > 0.05$-Not significant

The results have been statistically analyzed for significance by using one way analysis of variance (ANOVA) for multiple group comparisons followed by Post Hoc Tukey's test.Thus an analysis of results shows that methanolic extract group (M3) of *Swertia chirata* have significant antidiabetic activity in comparison to respective control groups (M1,M2)but less marked antidiabetic activity when compared to the standard glibenclamide group (M4).

DISCUSSION

In this study, the antidiabetic activity of methanolic extract of *Swertia chirata* has been evaluated & its efficacy had been compared with that of standard oral hypoglycaemic drug glibenclamide.

Suryawanshi *et al* had shown that methanolic extract of *Swertia chirata* which has antidiabetic activity contains mangiferin, amarogentin, amaroswerin, sweroside & swertiamarin as active constituents [8].

Mangiferin has several modes of action vizDirect stimulation of β cells to release insulin [9] May be due to reduced intestinal absorption of glucose [10].

Enhances glycolytic enzymes which stimulates glycogenesis in the liver and thereby contributes to reduction of blood glucose [14].

Inhibiting α-glucosidase & other enzymes as maltase, sucrase, isomaltase & aldose reductase.

Enhances peripheral utilization of glucose [13].Increases hepatic and muscle glycogen content, promotes β cell repair and regeneration [11].

Exerts insulin like action by reducing the glycatedhaemoglobin levels. Also inhibits dipeptidyl peptidase IV mediated degradation of glucagon like peptide-1(GLP-1) and increases GLP-1 [12].

Study done by Joshi and Dhawan had also showed the antidiabetic activityof *Swertia chiratta [5].*

The present study has several limitations. The study has been carried out only in one species of animal i.e. rats and needs to be extended to other animals as well. Only the fasting blood glucose was estimated in this study which does not give a clear pictureabout the effect of *Swertia chirata* on other parameters of diabetes mellitus. No attempt has been made to establish exact mechanism of antidiabetic activity and β cell pathology. In order to establish the exact mechanism of antidiabetic activity further investigations are also required to standardize the composition of extracts of *Swertia chirata*.

CONCLUSION

At the end of the study it can be concluded that *Swertia chirata* (methanolic extract at a dose of 50 mg/kg body weight) has exhibited antidiabetic activity in streptozotocin induced diabetes in rats. This extract exhibits less marked antidiabetic activity when compared to standard drug glibenclamide in streptozotocin induced diabeticrats. However extensive studies have to be undertaken to establish this activity in animal models as well as human subjects.

Further investigations are also required to standardize the composition of extracts.

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SUMMARY

Methanolic extract of *Swertia chirata* (at a dose of 50 mg/kg body weight) has been investigated in streptozotocin induced diabetic rats for its antidiabetic activity. The results were compared with the standard drug glibenclamide (0.5 mg/kg body weight). The results obtained were statistically analyzed by calculating the mean values, the standard deviation, ANOVA and post hoc Tukey's test.Results have shown that methanolic extract of *Swertia chirata* has significant antidiabetic activity which is statistically significant as compared to control groups but has less marked antidiabetic activity when compared to the standard drug glibenclamide. Thus, this study concludes that methanolic extract of *Swertia chirata* possess significant antidiabetic activity.

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