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Experimental Evaluation of antidiabetic activity of Swertia Chirata – Aqueous Extract.

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Abstract

Aims : The present study evaluates the antidiabetic activity of *Swertia chirata* (aqueous extract) on the blood glucose level of streptozotocin induced diabetic rat models.

Objectives : i) To study the antidiabetic activity of aqueous extract of *Swertia chirata* in streptozotocin induced diabetes in albino rats. ii) To compare the antidiabetic activity of *Swertia chirata* extracts with that of standard drug glibenclamide used in the treatment of type 2 diabetes mellitus.

Materials and Methods: In the present study 24 male albino wistar rats divided into 4 groups with 6 animals were 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 aqueous extract (200mg/kg) daily for 21 days respectively.

Result : 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.

Key Words: antidiabetic activity, *Swertia chirata*, aqueous extract, glibenclamide.

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. India has now been declared by WHO as the 'diabetes capital of the world'[2,3,4].

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[4].The antihyperglycemic effects of the antidiabetic plants are attributed to their ability to increase insulin output from the pancreas or inhibit intestinal absorption of glucose or some other process. Several herbs have been tried in various studies to prevent or delay type2 diabetes. *Aegle marmelose, Aloe vera, Artemisia pallens, Coccinia indica, Swertia chirayita* and many others have been shown to have antidiabetic activity[5,6,7].

Among the different species of Swertia, *Swertia chirata* is considered for its medicinal properties as antihelminthic, antipyretic, hypoglycaemic and antifungal property. So this study is undertaken to evaluate the antidiabetic activity of aqueous extract *Swertia chirata* in streptozotocin induced diabetes in rats.

Aims : The present study evaluates the antidiabetic activity of *Swertia chirata* (aqueous extract) on the blood glucose level of streptozotocin induced diabetic rat models.

Objectives: i) To study the antidiabetic activity of aqueous extract of *Swertia chirata* in streptozotocin induced diabetes in albino rats. ii) To compare the antidiabetic activity of *Swertia chirata* extracts with that of 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]. In India alone the prevalence of diabetes is expected to increase from 42 million to 69.9 million by 2025[4].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.

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I. Type 1 diabetes due to β-cell destruction, usually leads to absolute insulin deficiency. Type 2 diabetes may range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretory defect with insulin resistance.

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*[8].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. Its medicinal properties, antihelminthic[19], hypoglycaemic[21,24] and antipyretic[18], are 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[16]. It is also used in the dyspepsia and diarrhoea[18]. Three main phytochemicals mangiferin, amarogentin, and swertiamarin were identified in aqueous and 12% ethanolic extracts of all plant parts. Mangiferin is reported to possess considerable hypoglycaemic property and also shows suppressive effects on blood lipid profiles in diabetes[25].

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.

Maintaince of Animals :

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.

2) Drugs :

2.1) 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[12]. STZ was purchased from Sisco Research Lab, Ahmedabad.

2.2) Sodium citrate buffer: Composition of 100 ml of 0.1M citrate buffer of pH 4.5.

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

2.4) Test drug (*Swertia Chirata*): *Swertia chirata* extracts-aqueous extract at a dose of 200 mg/kg b.w. by oral administration was used. *Swertia chirata* extract was procured from Department of Rasayanashastra, Ayurveda Mahavidyalaya; Bengeri, Hubli.

2.5) Glucometer: The Glucometer used was Accu-Chek-Active,™ Roche Group, Germany for measuring blood glucose.

Methods:

Inclusion Criteria: Animals weighing 150-250 g and healthy male rats with normal behaviour & activity. Exclusion Criteria: Animals weighing <150 g and >250 g and female rats.

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[14] in 18 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[12]. 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[14]. 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 6 groups as follows[33]. Animals not given STZ were considered as non-diabetic or normal control group.

***Swertia Chirata* Aqueous extract:**

Normal control group (A-1)

This group of animals received 0.5 ml of normal saline daily for 21 days by oral route. Blood glucose levels were

recorded before the administration of normal saline on day 0 at 9 am, then on 3rd, 7th, 14th & 21st day at 9 a.m.

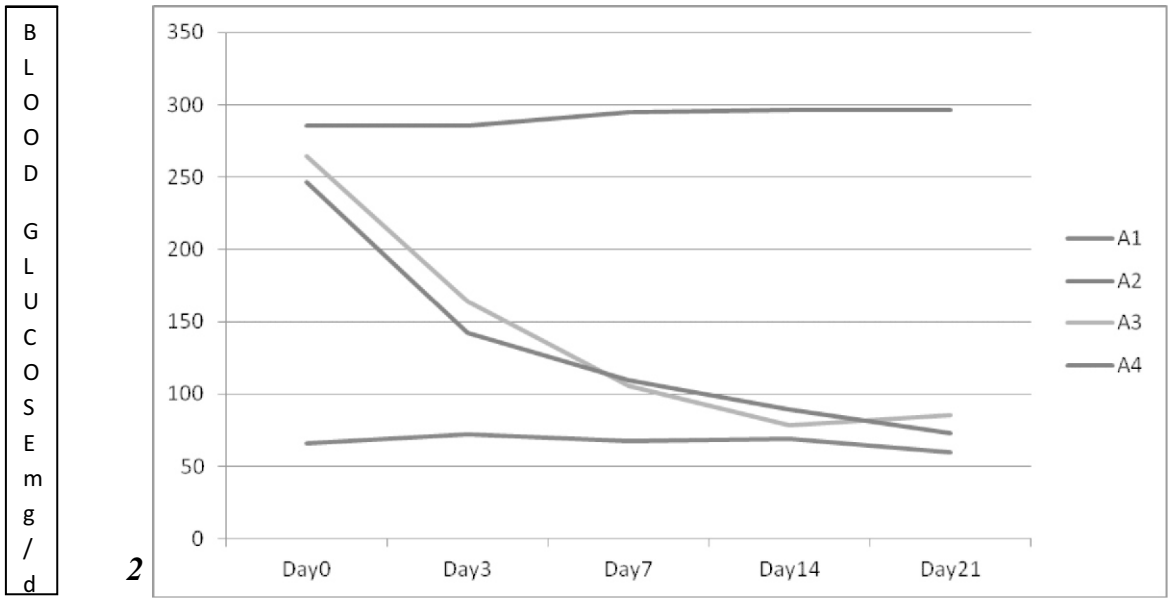
Diabetic control group (A-2) - The blood glucose levels of this group were recorded at 9 am on day 0 before administering normal saline. Later the animals were fed with 0.5 ml of normal saline daily orally for 21 days. The animals were observed for evidence of any behavioural changes, hyperglycaemia and convulsions. **Aqueous extract test group (A-3) -** The blood glucose levels of this group were recorded at 9 am on day 0 before the administration of the test drug. Then the aqueous extract at a dose of 200 mg/kg b.w. were fed to all animals orally for 21 days daily. The blood glucose levels were recorded on 3rd, 7th, 14th and 21st day. The animals were observed for any evidence of hypoglycaemia and convulsions. **Glibenclamide standard group (A-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 3rd, 7th, 14th and 21st day. They were observed carefully for evidence of hypoglycaemia and convulsions.

Statistical Analysis: 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. $p<0.001$ was considered highly significant.

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

Groups	Day0	Day3	Day7	Day14	Day21
A1	66.33 ±7.50	72.33 ±4.13	67.50 ±5.36	69.00 ±8.833	60.00 ±5.18
A2	285.17 ±12.75	285.83 ±7.17	294.50 ±14.61	296.17 ±10.80	296.17 ±12.11
A3	264.67 ±24.43	163.70 ±31.80	105.67 ±8.57	78.20 ±25.50	85.80 ±31.70
A4	246.50 ±20.83	142.00 ±14.21	109.83 ±12.91	89.33 ±11.86	73.17 ±8.01
ANOVA	p< 0.001	p< 0.001	p< 0.001	p> 0.05	p> 0.05

Fig-1: Mean Blood Glucose Levels in Different Groups of rats treated with Aqueous Extract of Swertia chirata on Days 0, 3, 7, 14,



Line diagram-1: Shows comparison of mean blood glucose levels between normal control, diabetic control, standard and test groups in aqueous extract treated rats which are recorded in the fixed intervals as detailed in Table 2. It indicates that the test drug (A3) has antidiabetic activity but less when compared to the standard group (A4). Thus an analysis of results shows that aqueous extract group (A3) of *Swertia chirata* have significant antidiabetic activity in comparison to respective control groups (A1,A2),but less marked antidiabetic activity when compared to the respective standard glibenclamide groups (A4).

Discussion:

In this study, the hypoglycaemic (antidiabetic) activity of aqueous extract of *Swertia chirata* has been evaluated & its efficacy had been compared with that of standard oral hypoglycaemic drug glibenclamide. Study done by Susanna Phoboo *et al*[16] had shown that aqueous extract of *Swertia chirata* has antidiabetic activity and is probably due to the active principle mangiferin, present in the stem of the plant.

Mangiferin has several modes of action viz

i) Direct stimulation of β cells to release insulin
ii) May be due to reduced intestinal absorption of glucose[32].
iii) Enhances glycolytic enzymes which stimulates glycogenesis in the liver and thereby contributes to reduction of blood glucose[33].
iv) Inhibiting α-glucosidase & other enzymes as maltase, sucrase, isomaltase & aldose reductase[30].
v) Enhances peripheral utilization of glucose[29].
vi) Increases hepatic and muscle glycogen content[29], promotes β cell repair and regeneration[30].
vii) Exerts insulin like action by reducing the glycated haemoglobin levels[30].
viii) Also inhibits dipeptidyl peptidase IV mediated degradation of glucagon like peptide-1(GLP-1) & increases GLP-1[33].

Swertiamarin found in roots, inflorescence & leaf mixture accounts for antidiabetic activity of aqueous extract of *Swertia chirata*. Amarogentin present in all plant parts also contributes to the antidiabetic activity[28].

Study done by Joshi and Dhawan had also showed the antidiabetic activity of *Swertia chirata*[8]. Studies done by Singh AP had shown that swerchirin, xanthone of *Swertia chirata* had antidiabetic activity[9].

- Saxena *et al* had demonstrated the blood sugar lowering effect of swerchirin found in aqueous extract of *Swertia chirata* extract in streptozotocin treated rats. Swerchirin acts by stimulating insulin release from islets of Langerhans[29].
- Arya Renu *et al* have demonstrated the antidiabetic activity of its hexane fraction of *Swertia chirata* which has active principle swerchirin[28].
- Sekar *et al* had shown that the main principle swerchirin of *Swertia chirata* induced a significant fall in blood sugar in albino rats and more effective in regulating blood sugar levels when compared to the regular drug tolbutamide[28].
- Grover J.K., Yadav S., Vats V.[27] had shown that swerchirin (a xanthone isolated from hexane fraction of the plant) showed significant blood sugar lowering effect in fasted, glucose loaded & tolbutamide pre-treated albino rats[34].
- Studies done by Bajpai *et al* has confirmed observation that swerchirin from hexane fraction of *Swertia chirata* had antidiabetic activity[28].

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 picture about 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* extract – aqueous extract at a dose of 200 mg/kg body weight, has exhibited antidiabetic activity in streptozotocin induced diabetes in rats.
- These extracts exhibited less marked antidiabetic activity when compared to standard drug glibenclamide in streptozotocin induced diabetes in rats.

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.Results have shown that *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 aqueous extract of *Swertia chirata* possess significant antidiabetic activity.

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