Available Online at www.ijpscr.info
International Journal of Pharmaceutical Sciences and Clinical Research 2021; 1(1):52-67

RESEARCH ARTICLE

Antidiabetic Activity of Methanolic Extract of *Searsia mysorensis* in Alloxan Induced Diabetic Rats

Gaddamedi Narender[1], A. Lakshmana Rao[2], N. V. Satish kumar[3], Nayudu Teja[4], Tera Sandhya[5], Pasumarthy Sree Mahalakshmi[5]

[1]Department of Pharmaceutical Analysis, Career Point University, Kota, Rajasthan, India, [2]Department of Pharmaceutical Analysis, V. V. Institute of Pharmaceutical Sciences, Gudlavalleru, Andhra Pradesh, India, [3]Department of Analytical Chemistry, Andhra University, Andhra Pradesh, India, [4]Department of Pharmaceutics, V. V. Institute of Pharmaceutical Sciences, Gudlavalleru, Andhra Pradesh, India, [5]Department of Pharmacology, Institute of Pharmaceutical Technology, Sri Padmavathi Mahila Viswavidyalayam, Tirupathi, Andhra Pradesh, India

Received: 10-12-2020; Revised: 15-01-2021; Accepted: 31-01-2021

ABSTRACT

This dreadful disease is found in all parts of the world and is becoming a serious threat to the mankind. There are a lot of chemical agents available to control and to treat diabetic patients but total recovery from diabetes has not been reported up to this date. Alternative to these synthetic agents' plants provide a potential source of hypoglycemic drugs and are used widely in several traditional systems of medicine to prevent diabetes. The aim of the present study was to evaluate the antidiabetic activity of methanolic leaf extract of *Rhus mysorensis* in alloxan-induced diabetic rats.

Keywords: Antidiabetic, Methanolic, Searsia mysorensis

INTRODUCTION

Traditional medicine is looked on as an alternative or supplement to modern medicine and has made significant contributions to the healthcare of the world over the past decades. Various diseases such as diarrhea, skin problems, headache, fever, cough, wounds, hypertension, diabetes, and rheumatism are treated with herbal medicine. Traditional medicines continue to be practiced by the community to treat disease and maintain health especially in remote areas where modern facilities are not readily available. Most of the medicinal plant species are collected from the wild, a few are being cultivated.[1]

***Corresponding Author:**
Gaddamedi Narender,
E-mail: gnarendergoud@gmail.com

DIABETES MELLITUS

Diabetes mellitus commonly known as diabetes is a group of metabolic disorder characterized by high glucose blood level over a prolonged period of time.[2] Diabetes is due to either pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced.[3]

Types of diabetes mellitus

WHO classified diabetes mellitus into three types based on the etiology.[4]

- Type 1 diabetes (Insulin Dependent Diabetes Mellitus [IDDM])
- Type 2 diabetes (Non-IDDM)
- Gestational diabetes.

Type 2 diabetes

- In type 2 diabetes, body's cells are not capable to react to insulin as required. In later phases of the disease, body may perhaps not secrete adequate insulin too.
- Uncontrolled type II diabetes may perhaps lead to chronically high blood glucose amounts, causing numerous symptoms, and potentially foremost to severe complications.[5]

Symptoms of type II diabetes

In type II diabetes, body is not capable to efficiently make use of insulin to transport glucose into cells.[6-11] This basis for body to rely on substitute energy sources in muscles, tissues, and organs. This is a chain response that may perhaps cause a range of symptoms.[12-25]

Type II diabetes may perhaps progress slowly. The symptoms may perhaps be mild and simple to dismiss at initial.

Blood glucose levels have been elevated for an extended time, the symptoms may perhaps include:

1. Slow-healing cuts or sores
2. Yeast infections
3. Foot pain
4. Dark patches on skin
5. Feelings of numbness in extremities, or neuropathy.

If have two or more of these symptoms, we should go to hospital. Without treatment, diabetes may perhaps become life-threatening. Discover other symptoms of type II diabetes.[26-28]

Causes of type II diabetes

Insulin is a naturally occurring hormone. Pancreas secretes it and releases it when eat.[29] Insulin helps transport glucose from bloodstream to cells throughout body, where its used for energy.

In type II diabetes, body develop into which is resistant to insulin. Body is no longer by means of the hormone proficiently. This condition forces pancreas to work harder to construct more amount of insulin.

Over time, this may perhaps injure cells in pancreas. Ultimately, pancreas may perhaps not be capable to generate any insulin.

If body does not secrete adequate insulin or if body does not employ it efficiently, glucose accumulates in bloodstream. This leaves cells of human body's hungry for energy. It may perhaps have to do with cell dysfunction in the pancreas or with cell signaling and regulation. In some people, the liver secretes too much glucose. There may perhaps be a genetic predisposition to on the rise type II diabetes. There's definitely a predisposition of genetic to obesity, augment the danger of insulin resistance and diabetes. There could too be an environmental elicit.

Most probably, it is a combination of aspects that augment the risk of type II diabetes.[30,31]

Medications for type II diabetes

In few instances, lifestyle alterations are adequate to keep up type II diabetes under management.[32] If not so, there are quite a few medications that may perhaps be of assistance a few of these medications are:

Class	Drug
Dipetidylpeptidase-4 inhibitors	Alogliptin, linagliptin, saxagliptin, sitagliptin, vildagliptin
Glucagon-like peptide-1 receptor agonists	Dulaglutide, exenatide, liraglutide, lixisenatide (albiglutide not included)
Insulin release stimulators	Nateglinide, repaglinide
Intestinal alpha-glucosidase inhibitor	Acarbose
Sodium-glucose co-transporter 2 inhibitors	Canagliflozin, dapagliflozin, empagliflozin
Thiazolidinedione	Pioglitazone

Every one of these medications may perhaps produce side effects. It may perhaps take some time to discover the best medicament or combination of medicament to treat diabetes.

If the blood pressure or cholesterol level are a concern, it may perhaps medications to deal with those requires too.

If body may perhaps it create adequate insulin, may perhaps require insulin therapy too. May perhaps merely require a long acting injection may perhaps take at night, or may perhaps require taking insulin a number of times per day.[33-35]

Diet for type II diabetes

Diet is a chief tool to keep up heart healthy and levels of blood glucose inside a safe and healthy

range. The diet suggested for people with type II diabetes is the same diet merely about everyone should follow. These few key actions:[34,35]

Consume meals and snacks on schedule
1. Choose an array of foods that are lofty in nutrients and stumpy in empty calories
2. Be cautious not to eat too much
3. Examine food labels intimately

PLANT PROFILE

Introduction to plant

Plant Botanical Name: *Rhus mysorensis* Don.
Family: Anacardiaceae (Cashew family).
Common name: Mysore Sumac.

Taxonomical classification

Synonym: *Searsia mysorensis*
Family: Anacardiaceae
Kingdom: Plantae
Phylum: Magnoliophyta
Class: Magnoliopsida
Order: Sapindales
Genus: Rhus
Species: *Rhus mysorensis*

Vernacular names

The vernacular name of plant is Dasni, Dansara, Darsan, Amboni, and Chippamaram.

Distribution

Usually widespread in foothills, scrub jungle up to 900 m, northwest to the peninsular region in India.

Description

Perennial, indigenous, and shrub. It is a tiny aromatic, frequently gregarious shrub with a slim brown bark and bristly branches
Leaves are subdivided into three leaflets Leaflets are extremely toothed, or lobed, the middle one 1–1.5 in long, the lateral ones lesser The leaflets are almost stalking less
Flowers are tiny, white, or greenish, bear in panicles at the ending of branches or in leaf axils. Sepal is tiny, 4–5-parted, seen still in fruit Petals are 5, ovate, falling off premature Disk plump, vaguely 5-lobed. Ovary 1-celled; styles 3 in number.
Fruit is a tiny, dry, compacted drupe, 3 mm in diameter.
The wood is hard, reddish yellow, close up grained and weighty, is merely employed for fuel, and the twigs for fencing ground[36]

Flowering: February–June

Chemical constituents

The preliminary phytochemical screening indicates the presence of flavonoids in ethanolic extract of *R. mysorensis*.[37]

Traditional uses

The stem, root, and leaf are by tradition employed in management of diabetes.[38]
Young shoots prepared into paste, and applied externally on spots of psoriasis.[39]

Pharmacological activities

A variety of flavonoids have been accounted for their hepatoprotective action.[40]

Antidiabetic

The constituents isolated from the *R. mysorensis* demonstrate the antidiabetic effect tested *in vitro* and *in vivo*.[41]

Hypolipidemic

The exploration of *R. mysorensis* proved hypolidemic effect,[42] plant extract also exhibited antimicrobial and antioxidant activity.

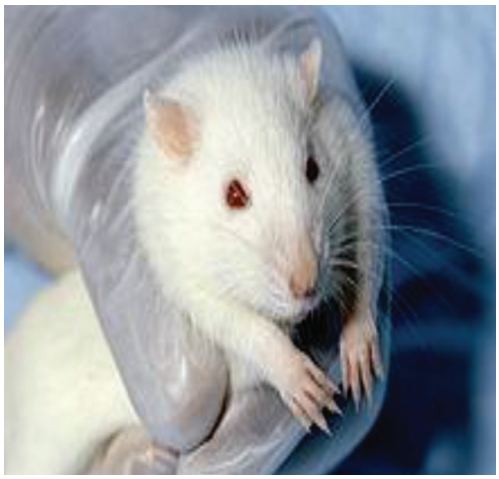
Antiurolithiatic

Antiurolithiatic activity of *R. mysorensis* against ethylene glycol induced urolithiasis in Wistar rats was proved effective in treatment.[43]

PLAT MATERIAL

The plant of *R. mysorensis* was collected from hilly province of Chittoor district, Tirupathi area, Andhra Pradesh, India. The plant was authentified by Dr. K. Madhav Chetty, Asst. Professor, Botany Dept, S V U, Tirupathi.

EXPERIMENTAL ANIMALS



Male wistar rats

Rats of Male Wistar weighing amid 180–220 g were making available by animal house of Sigma Institute of Clinical Research and Administration (SICRA Labs), Kukatpally, Hyderabad, India. They were accommodation in ventilated rooms at a temperature of 24 ± 2°cm, 54 ± 5% relative humidity and in the midst of a 12h light/dark cycle, keep up on standard pellet diet and water to labium rats all the way through the experimental phase. The animals were get used to for a phase of 1 week. The experiments were executed on the basis of the guidelines of CPCSEA, the committee for the purpose of control and supervision of experiments on animals, New Delhi, India, and permitted by IAEC, the Institutional Animal Ethical Committee of SICRA Pvt. Ltd. Hyderabad.

DRUGS AND CHEMICALS

Glibenclamide, alloxan monohydrate, all other chemicals and diagnostic kits were making available by SICRA.

PREPARATION OF EXTRACT

The gathered medicinal plant was dried under shade for about 1 month and was crushed to course powder employing commercial mixer grinder. The powdered material of medicinal plant (250 g) was extracted with methanol (80% v/v) by process of soxhlation. Finally, methanolic extract was dried by means of air at room temperature (RT). 4.2% w/w extract as a result obtained was subjected for evaluation of antidiabetic effectiveness in rats of alloxan-induced diabetic. The test sample of extract of methanolic was prepared in apt concentrations employing distilled water former to its implication for animal investigations.

PHYTOCHEMICAL SCREENING

Preliminary phytochemical analysis was done by means on 80% methanolic extract of *R. mysorensis* (80% v/v multiple reaction monitoring [MRM]) for revealing of various phytochemicals by standard methods and procedures.[44]

Detection of carbohydrates

Small quantity of extract was dissolved in distilled water and filtered. The filtrate was subjected to.

Molisch's test

To the filtrate few drops of alcoholic α-naphthol were added and 2 ml of concentrated sulfuric acid was added slowly through the sides of the test tube. No purple color ring was found at the junction of the two layers, which indicates the absence of carbohydrates.

Test for starch

A small amount of powdered drug was treated with dilute iodine solution. No blue color was observed, which indicates the absence of starch.

Detection of proteins and amino acids

Small quantity of extract was dissolved in few milliliter of water and was subjected to Millon's, biuret and ninhydrin test.

Millon's test

The extract was treated with Millon's reagent. No white precipitate was produced, which shows the absence of proteins and amino acids.

Biuret test

To the extract equal volume of 5% w/v NaOH and 4 drops of 1% w/v $CuSO_4$ solution were added. No pink or purple was formed indicating the absence of proteins.

Ninhydrin test

The extract was treated with ninhydrin reagent. No purple color was produced, indicating the absence of proteins.

Detection of phenolic compounds and tannins

The extract was diluted with distilled water and filtered. The filtrate was treated with following tests.

Ferric chloride test

The filtrate was treated with 5% ferric chloride solution. No black precipitate was formed, indicating the absence of tannins and phenolics compounds.

Test with lead acetate solution

Few milliliter of filtrate was treated with lead acetate solution. No white precipitate was produced.

Test for phytosterols

Small quantity of extract was dissolved in 5 ml of chloroform separately. Then, these chloroform layer was subjected to.

Salkowski test

To the 1 ml of the above prepared chloroform solution, few drops of concentrated H_2SO_4 were added. Red color was produced in the lowered layer, shows the presence of phytosterols.

Liebermann–Burchards test

The above chloroform solution was treated with few drops of concentrated H_2SO_4 followed by 1 ml of acetic anhydride solution. Green color was produced, shows the presence of phytosterols.

Test for fixed oils and fats

A small quantity extract was pressed between two filter papers. Oil stain observed, shows the presence of fixed oils.

Saponification

Few drops of 0.5 N alcoholic potassium hydroxide were added to the extract along with a few drops of phenolphthalein. The mixture was heated on a water bath for about 1–2 h. Formation of soap or a partial neutralization of alkali indicates the presence of fixed oils and fats.

Test for alkaloids

Small amount of the extract was stirred with a few milliliter of dilute hydrochloric (HCL) and filtered. The filtrate was tested with various alkaloid reagents.

Mayer's test

To the small amount of filtrate add few drops of Mayer's reagent. A white precipitate was formed, indicating the presence of alkaloids.

Dragendroff's test

To the small amount of the filtrate add few drops of Dragendroff's reagent. An orange red color

precipitate was formed, indicating the presence of alkaloids.

Wagner's test

To the small amount of the filtrate add few drops of Wagner's reagent. A brown color precipitate was formed, indicating the presence of alkaloids.

Test for glycosides

A small amount of the extract was hydrolyzed with HCL for 1 h on a water bath and hydrolyzed solution was subjected to

Legal's test

To the solution 1 ml pyridine and few drops of sodium nitroprusside solution were added and then made alkaline with NaOH solution. Pink color was obtained showing the presence of glycosides.

Balget's test

To the solution sodium picrate solution was added. Yellowish orange color was obtained showing the presence of glycosides.

Borntrager's test

Hydrolyzed solution was treated with chloroform and the chloroform layer was separated. To this equal quantity of ammonia solution was added. Pink color was observed in ammonical layer, confirms the presence of glycosides.

Test for flavonoids

The extract was dissolved in ethanol and then subjected to the following tests.

Ferric chloride test

To the small quantity of ethanolic solution of extract, few drops of ferric chloride were added. Blackish red color was observed, showing the presence of flavonoids.

Fluorescence test

Alcoholic solution was seen under Ultraviolet (UV) light. Green color florescence was observed, indicating the presence of flavonoids.

Reaction with alkali and acid

With sodium hydroxide solution the extracts gave yellow color. Extract gave orange color with conc. H_2SO_4 indicating the presence of flavonoids.

Detection of saponins

The extract was diluted with 20 ml of distilled water and it was agitated in a graduated cylinder for 15 min. A 1 cm layer of foam was produced, indicating the presence of saponins.

Detection of coumarins

A small quantity of extract was dissolved in alcohol and exposed to UV light, shows green color. A small quantity of extract was dissolved in alcohol and adds ferric chloride solution shows green color, indicating the presence of coumarins.

DETERMINATION OF ACUTE ORAL TOXICITY

Studies of acute toxicity were executed according to acute toxic class method, category IV substance of OECD-423 guidelines. Albino rats (n = 3) of each sex preferred by random sampling practice were employed in this screening. The animals were maintained for fasting for 4 h with free admittance to water lone. The medicinal plant extract of *R. mysorensis* was administering orally with utmost dose of 2000 mg/kg body weight (b.w). The mortality was kept under observation for 3 days. If mortality was watchable in 2/3 or 3/3 of animals, rats, then the dose administering was considered as a dose of toxicity. On the other hand, if the death was observed merely one rat out of three rats then the identical dose was repetitive again to validate the toxic effectively. If death was not observed, the method was then repetitive with superior dose.[45]

ORAL GLUCOSE TOLERANCE TEST (OGTT)

The OGTT dealings the body's capacity to exercise a type of sugar, termed as glucose that is the human

body's key source of energy. OGTT, a test of enormous value and attitude in favors of by means of fasting plasma glucose concentration lone was observable as a practical way to make simpler and assist the diabetes diagnosis. Hyperglycemia is the chief factor in the progress and development of the complications of diabetes mellitus.

Oral glucose tolerance test on normal rats (OGTT)

The overnight hungered rats kept of every single one of the groups were loaded with glucose (2 g\kg orally) 30 min subsequent to drug administration. Blood samples were collected from the method of puncture of tail vein former to drug administering and at 1\2, 1, 2 h subsequent to glucose loading. Serum glucose was measured right away. The glucose level was estimate by means of digital glucometer.[46]

6 fasted animals were employed in each group.

Rats were subdivided into following groups.

Group- I – administering Vehicle- Distilled water(Control –ve)

Group-II – administering 2 g/kg glucose p.o. (Control+ve)

Group-III – administering standard drug glibenclamide (10 mg/kg), p.o.

Group-IV – administering methanolic extract of plant of *Rhus mysorensis*, dose 200 mg/kg, p.o.

Group-V – administering methanolic extract of the plant of *Rhus mysorensis*, dose 400 mg/kg, p.o.

INDUCTION OF EXPERIMENTAL DIABETES[47]

Blood glucose of fasting was determined subsequent to depriving foodstuff for 16 h with free accessibility of drinking water. Hyperglycemia was produced by a single i.p. injection of 120 mg/kg of alloxan in saline of sterile following injection of 5 days of alloxan; the hyperglycemic rats (level of glucose >200 mg/dl) were alienated and categorized into diverse groups consisting of six rats each for the antidiabetic exploration. The treatment (p.o) was initiated from the same day excluding groups of normal, control, and diabetic control for a phase of 21 days. During this phase, animals in all groups had free accessibility to standard diet and distilled water. B.W. and blood glucose levels were measured on 1st, 7th, 14th, and 21st days of the treatment on the last day of 21st day.

EXPERIMENTAL PROCEDURE

The rats were at random categorized into five of six each group.[47]

Group I – Vehicle-Distilled water (1 ml/kg, p.o)

Group II- Diabetic control administering Streptozotocin (120 mg/kg, i.p)

Group III – Standard Single dose of Streptozotocin (120 mg/kg, i.p) and Glibenclamide (10 mg/kg. p.o.) from 5th day till 21stdays

Group IV – Single dose of Streptozotocin (120 mg/kg, i.p) and MRM (200 mg/kg, p.o) from 5thday till 21st day

Group V – Single dose of Streptozotocin (120 mg/kg, i.p) and MRM (400 mg/kg, p.o) from 5th day till 21st day

Collection blood and serum samples

Samples of blood were collected from the plexus of retro orbital by implication of mild ether anesthesia for biochemical assessment. The samples of blood were permitted to clot for 30 min at RT and then they were centrifugal at 5000 RPM for 15 min. The resulting superior serum layer was collected in labeled properly in clean and dry microcentrifuge tubes. The samples of the serum were examined straight away.[48,49]

The parameters studied were as follows

Biochemical parameters such as Naito and Tietz:[48,49]

a. Blood glucose

b. Cholesterol of Total type

c. Cholesterol of high-density lipoprotein type

d. Cholesterol of low density lipoprotein and very low density lipoprotein type

e. Triglycerides

f. SGOT

g. SGPT

Morphological parameter include

A. Body weight

B. Histopathological investigation

HISTOPATHOLOGICAL STUDIES

The pancreas from every animal was detached instantly and kept up in solution of 10% formalin for histopathological assessment.[49]

Statistical analysis

All obtained data were expressed as the Avg ± SEM. To do statistical analysis of the data, group means were contrast by one-way analysis of variance (ANOVA) immediately followed by Dunnet test $P < 0.05$ was taken as significance.

RESULTS AND DISCUSSION

Preliminary phytochemical screening

Results of the preliminary phytochemical investigation on 80% methanolic extract of *R. mysorensis* (80% ERM) are shown in Table 1 Percentage yield of crude extract of *R. mysorensis* leaves is shown in [Tables 2,3,5-8].

Table 1: Preliminary phytochemical screening of 80% MRM

Phytochemical constituents	80%Methanolic extract
Alkaloids	+++
Glycosides	++
Carbohydrates	+
Flavonoid	+++
Saponins	+++
Tannins	++
Steroids	+++
Proteins and amino acids	_
Phytosterols	++
Phenols	+++
Triterpenoids	+++

_: Absent, + +: More clarity, +: Indicates presence, + + +: Better response

Table 2: Percentage yield of crude extract of *Rhus mysorensis*

S. No.	Solvent	Color and consistency	Percentage yield
1	Methanol 80%	Dark brown sticky	8.2%

Determination of acute oral toxicity of 80% MRM

The plant extract of *R. mysorensis* did not show any mortality and toxicity even at highest dose of 2000 mg/kg b.w employed. The present research study was carried out using two different doses (200 mg/kg; 400 mg/kg) for antidiabetic activity. Toxicity record sheet: The toxicity record sheet is as follows.

OGTT on normal rats

The effect of Methanolic extract of *R. mysorensis* on glucose tolerance test in normal fasted rats is shown in Table 4.

Methanolic extract of *R. mysorensis* (400 mg/kg) significantly decreased blood glucose level in glucose feeded rats at 120 min when compared with the control group. It also decreased the elevated blood glucose at 60 min after the glucose administration. Methanolic extract of *R. mysorensis* (200 mg/kg) also showed marked decrease in glucose level when compared with control group. The control group showed significant increase in blood glucose level when compared with the normal group.

Glibenclamide showed its potent antidiabetic activity at 120 min. Furthermore, the reduction in elevated blood glucose level at 30 and 60 min after the administration of glucose was significant when compared to the control group.

These data suggested that treatment with methanolic extract of *R. mysorensis* showed better tolerance to exogenously administered glucose.

Antidiabetic study on alloxan monohydrate-induced diabetic rats

Repeated administration of methanolic extract of *R. mysorensis* (200 mg/kg B.W.) for 21 days showed significant reduction in serum glucose levels compared to basal value (0 day). However, more marked reduction in blood glucose was observed with a dose of 400 mg/kg B.W. The control group showed increased blood glucose levels which were found to be significantly higher when compared with the normal rats. These elevated serum glucose levels were found to have been maintained throughout the treatment period indicating that the rats are rendered diabetic. On 21st day higher dose of the extract (400 mg/kg) showed greater reduction in glucose levels when compared to control and their potency is comparable to standard (GLB) treated diabetic rats.

Subacute study of 21 days suggested that methanolic extract (400 mg/kg B.W.) showed better antidiabetic activity.

Effect of methanolic extracts of *rhus mysorensis* on lipid profile in alloxan induced

Diabetic rats

Animals treated with methanolic extract of *R. mysorensis* (200 and 400 mg/kg) showed significant reduction in serum concentration of total cholesterol, TG, LDL, and very LDL (VLDL) also showed significant increase in serum concentration of HDL when compared with control group.

Effect of *R. mysorensis* on biochemical (liver) parameters

The biochemical parameters such as serum SGOT and SGPT are significantly increased in control compared to normal group. Animals treated with methanolic extract of *R. mysorensis* (200 and 400 mg/kg) showed significant reduction in all these parameters when compared to the control group.

Effect of methanolic extract of *rhus mysorensis* on B.W. In alloxan induced

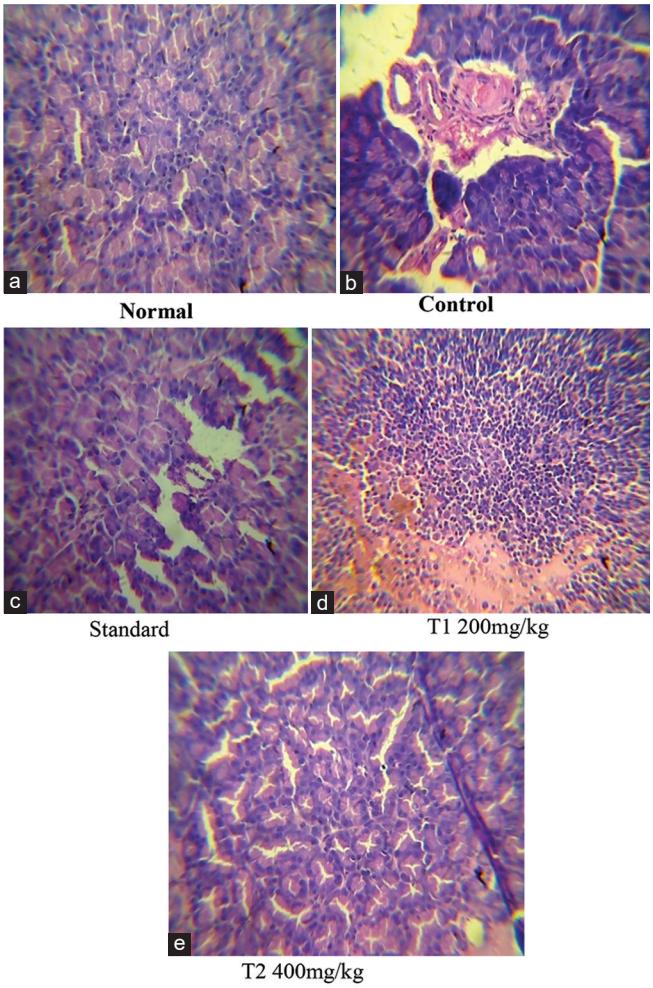
Diabetic rats

The change in b.w of the different groups of animals during the period of study is recorded, which shows an increase in b.w of normal rats. This shows that the group of normal rats gained b.w during the treatment period of 21 days. During the same period of treatment the control group of rats has shown a progressive loss of b.w significantly during the 21 days of treatment period as against the gain in b.w seen in normal group of rats.

The Glibenclamide (10 mg/kg) treated group of rats shown a b.w loss relatively less when compared with the control group. This shows that glibenclamide treatment has protected the diabetic rats from losing the b.w in a significant manner when compared with the control group.

Similarly, the MRM (200 mg/kg; 400 mg/kg) shows a reduction in b.w during the treatment period. In these groups, the reduction of weight is less when compared to control group. This shows that the extract treatment has protected diabetic rats from losing b.w in a significant manner when compared with the control group of rats.

HISTOPATHOLOGICAL STUDIES



In Figure, slides a and b represent islets of Langerhans from normal and rats of alloxan-induced diabetic, correspondingly. Comparison of these two slides evidently indicates the drop in the number of β-cells in the islet of Langerhans of pancreas of rats of diabetic. As it is obvious from slide B the islet is erratically shaped, moderately small, and atrophic. The majority cells of the islets are degranulated, small, and dark with insufficient cytoplasm. yet, contrast to the untreated rats of diabetic, histophatological assessment of the medicinal plant *R. mysorensis* extract-treating rats of diabetic exposed an augment in the number of β-cells within the islets of pancreatic, along with a drop in the vacillation (slides C, D, and E). In other terms, the medicinal plant extract treated samples of diabetic histopathologically be apt to advance the histopathology of the samples of healthy pancreatic. The standard treating group

Table 3: Observation of skin color

S. No.	Code	Toxicity		Time of death	Observation									
		Onset	Stop		Skin colour	Eyes	Resp	CNS	Tre	Con	Sali	Diah	Sleep	Let
1	MRM	x	X	X	X	X	X	X	X	X	x	X	X	x

TRE: Tremor, CON: Convulsions, SALI: Salivation, Diah: Diarrhea, LET: Lethargy. ×: Negetive, Ø: Positive

Table 4: Effect of methanolic extracts of *Rhus mysorensis* on oral glucose tolerance test in normal rats

Groups	Blood glucose level mg/dl			
	0 min	30 min	60 min	120 min
Normal	80.12±0.89	82.11±1.32	85.11±0.65	88.29±0.99
Control (Glucose 2 g/kg)	91.32±0.95	161.31±1.03[a]	182.87±0.56[a]	215.87±1.06[a]
Standard (GLB 10 mg/kg)	73.49±1.03	132.32±1.28***	105.18±0.98***	91.48±1.23***
Methanolic (200 mg/kg)	99.03±1.39	167.98±1.96	156.90±0.23***	118.32±0.86***
Methanolic (400 mg/kg)	84.97±1.45	150.67±0.84	126.88±0.69***	101.45±0.99***

All the values are expressed as Mean±SEM, n=6, One-way analysis of variance followed by multiple comparison Dunnet's test, * P<0.05, ** P<0.01 and ***P<0.001 as compared to control and [a]P<0.001, [b]P<0.01, and [c]P<0.05 when compared to normal group

Table 5: Effect of methanolic extract of *Rhus mysorensis* on blood glucose level in alloxan-induced rats

Groups	Blood glucose level mg/dl			
	0 day	7th day	14th day	21st day
Normal	95.69 ± 1.51	85.95 ± 1.37	93.83 ± 0.94	94.51 ± 0.99
Control (120 mg/kg)	264.84 ± 1.26[a]	277.01 ± 1.19[a]	269.86 ± 1.01[a]	260.18 ± 1.12[a]
Standard (GLB 10 mg/kg)	275.45 ± 1.52	203.01 ± 1.39***	159.72 ± 1.05***	118.39 ± 1.04***
MRM (200 mg/kg)	273.02 ± 1.43	217.67 ± 1.60***	197.94 ± 1.22***	134.64 ± 0.89***
MRM (400 mg/kg)	283.03 ± 1.21	213.49 ± 1.34***	178.02 ± 1.18***	126.15 ± 1.03***

All the values are expressed as Mean ± SEM, n = 6, One-way analysis of variance followed by multiple comparison Dunnet's test, *P < 0.05, **P < 0.01, and ***P < 0.001 as compared to control and [a]P < 0.001, [b]P < 0.01, and [c]P < 0.001 when compared to normal group

Table 6: Effect of methanolic extract of *Rhus mysorensis* on lipid profile in streptozotocin induced rats

Groups	Lipid profile (mg/dl)				
	Cholesterol	TG	HDL	LDL	VLDL
Normal	67.33±1.145	75.6±1.24	43.61±0.75	18.43±1.14	15.12±0.24
Control (ALX 120 mg/kg)	160.5±1.258[a]	157.18±1.07[a]	19.71±1.08[a]	109.42±1.66[a]	31.43±0.21[a]
Standard (GLB10 mg/kg)	80.16±1.16***	86.4±0.99***	40.68±1.05***	22.20±1.71***	17.28±0.19***
MRM (200 mg/kg)	98.16±0.94***	102.8±1.07***	28.81±1.09***	48.93±1.19***	20.41±0.21***
MRM (400 mg/kg)	86±1.06***	94.84±1.18***	35.75±0.77***	31.28±0.95***	18.96±0.23***

All the values are expressed as Mean±SEM, n=6, One-way analysis of variance followed by multiple comparison Dunnet's test, *P<0.05, **P<0.01, and ***P<0.001 as compared to control and [a]P<0.001, [b]P<0.01, and [c]P<0.001 when compared to normal group

Table 7: Effect of methanolic extract of *Rhus mysorensis* on liver parameters in streptozotocin-induced rats

Groups	Liver parameters (U/L)	
	SGOT	SGPT
Normal	62.02±1.28	40.81±1.12
Control (ALX 120 mg/kg)	130.68±1.17[a]	84.49±1.16[a]
Standard (GLB 10 mg/kg)	74.23±1.14***	47.19±0.91***
MRM (200 mg/kg)	94.9±1.21***	53.97±1.45***
MRM (400 mg/kg)	78.63±1.24***	49.83±1.13***

All the values are expressed as Mean±SEM, n=6, One-way analysis of variance followed by multiple comparison Dunnett's test,*P<0.05, **P<0.01, and ***P<0.001 as compared to control and [a]P<0.001, [b]P<0.01, and [c]P<0.001 when compared to normal group

also illustrates recovery and be apt to approach the histopathology of the pancreas of normal rat.

DISCUSSION

The end result of this investigation demonstrated that oral administering of methanolic extract of the plant of *R. mysorensis* had an advantageous effectiveness on the diabetic circumstances by means of drop off of hyperglycemia. The extract of RM at dosing levels of 200 and 400 mg/kg b.w.

Table 8: Effect of methanolic extract *Rhus mysorensis* on body weight in alloxan-induced rats

Groups	Body weight of the animal (g)	
	Initial	Final B.W. (21st day)
Normal	194.84 ± 1.13	209.27 ± 1.45
Control (120 ALX mg/kg)	205.49 ± 1.31	178.15 ± 1.39[a]
Standard (GLB 10 mg/kg)	210.95 ± 1.20	200.56 ± 1.67**
MRM (200 mg/kg)	214.25 ± 1.38	190.93 ± 1.17*
MRM (400 mg/kg)	217.91 ± 1.75	204.91 ± 1.79**

All the values are expressed as Mean ± SEM, $n = 6$, One-way analysis of variance followed by Multiple comparison Dunnet's test, *$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$ as compared to control. And [a]$P < 0.001$, [b]$P < 0.01$, and [c]$P < 0.001$ when compared to normal group.

grounds a statistically significant ($P < 0.05$) drop off in blood glucose in rats of alloxan-induced diabetic. Alloxan is an oxidation produce of uric acid, extensively employed for pharmacological stimulation of diabetes and more employed in manifold aspects of the diabetes disease.

From the outcome of clinical investigations, it is apparent devoid of any doubt that the drop off of hyperglycemia is the most chief factor in the avoidance of chronic microvascular complications of diabetes mellitus such like

1. Retinopathy,
2. Neuropathy,
3. Poor wound healing
4. Nephropathy,
5. Diabetic foot and
6. As well as in the avoidance of accelerated atherosclerosis-related circumstance (a) Myocardial infarction, Stroke, etc.

The accurate mechanism implicated in the hypoglycemic action is not apparent. The extract may perhaps stimulate insulin production by means of the pancreas or/and augment insulin sensitivity in a range of organs in particular the muscles by means of encourage glucose uptake and metabolism hinder hepatic gluconeogenesis.

Phytochemical test of methanolic extract of the medicinal plant of *R. mysorensis* exposed the accessibility of:

I. Flavonoids,
II. Glycosides,
III. Alkaloids,
IV. Triterpenoids,
V. Tannins,
VI. Steroids,
VII. Saponins,
VIII. Phenols, and
IX. Phytosterols.

Flavonoids have been made known to put forth their antioxidant effectiveness by means of a variety of mechanisms by means of scavenging or quenching free radicals and or by means of inhibiting enzymatic accountable for free-radical creation.[50,51]

Apart from as antioxidants, flavonoids have been accountable to inhibit

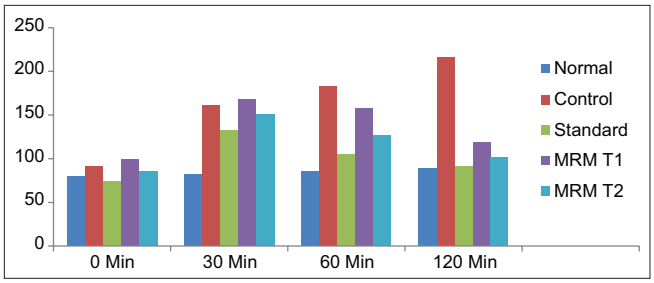
I. Glucose transport Is form 2 (Glut 2),
II. Sodium-dependent vitamin C transporter 1 and the intestinal transporter for vitamin C and
III. Glucose, leading to a decrease in the intestinal absorption of glucose,

For this, reason diminish in the blood glucose amount.[52] Quite a lot of researches have also confirmed that flavonoids act as dropper of hyperglycemia by means of causing inhibition of reabsorption of renal glucose via inhibition of the sodium-glucose symporters positioned in the proximal renal convoluted tubule.[53,54]

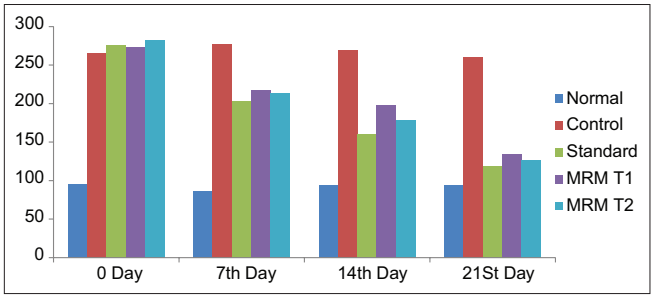
Previous investigations have accounted a few of these phytocomponents to bring out a wide range of biological effectiveness inclusive of hypoglycemic, and hypolipidemia amid others (Oladele *et al*., 1995). Exclusively, saponin is acknowledged to bring out serum cholesterol drop off activity by means of grounds resin-like actions, thereby means of dropping the enterohepatic circulation of bile acids (Topping *et al*., 1980). In the course, the conversion of cholesterol to bile acid is improved in the liver consequential in concomitant hypocholesterolemia.[55,56]

The medicinal plant extract of *R. mysorensis* did not illustrate any death and toxicity even at uppermost dose of 2000 mg/kg b.w employed. Hence, present research study was carried out using 2 dissimilar doses 2g/kg; 400 mg/kg b.w.

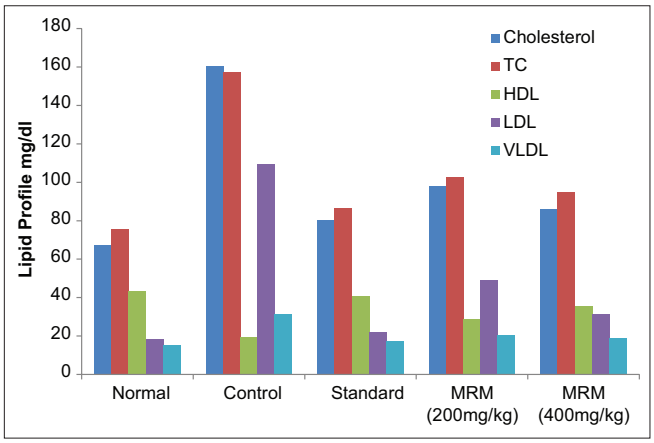
OGTT abbreviates form of the OGTT, dealings the body's capability to metabolize glucose, or eliminate it out of the stream of blood. The test exposes how does speedily glucose is metabolized from the stream of blood for utilization by means of cells as a source of energy. The methanolic extract of the medicinal plant of *R. mysorensis* formed



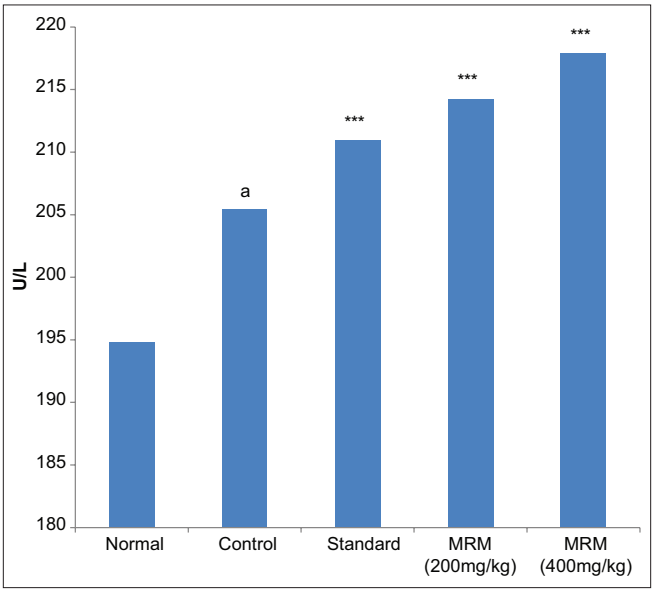
Graph 1: Effect of methanolic extracts of *Rhus mysorensis* in oral glucose tolerance test in normal rats



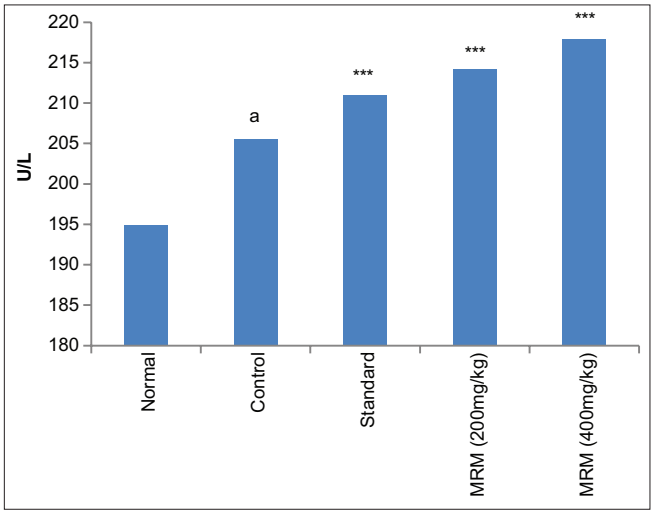
Graph 2: Effect of methanolic extract of *Rhus mysorensis* on blood glucose level in alloxan-induced rats



Graph 3: Effect of methanolic extract of *Rhus mysorensis* on lipid profile in alloxan-induced rats



Graph 4: Effect of methanolic extract of *Rhus mysorensis* on SGOT in alloxan-induced rats

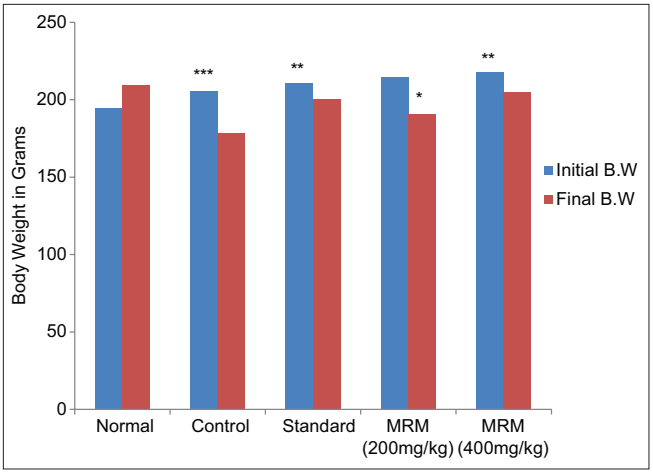


Graph 5: Effect of methanolic extract of *Rhus mysorensis* on SGPT in alloxan-induced rats. All the values are expressed as Mean ± SEM, $n = 6$, One-way analysis of variance followed by multiple comparison Dunnet's test, $^{*}P < 0.05$, $^{**}P < 0.01$ and $^{***}P < 0.001$ as compared to control and $^{a}P < 0.001$, $^{b}P < 0.01$, and $^{c}P < 0.001$ when compared to normal group

hypoglycemia and enhanced glucose tolerance in normal rat's in spite of counter regulatory features avoiding drop off in levels of blood glucose.

For that reason, hypoglycemic doings of MRM could be intervened by means of stimulus of surviving beta cells to discharge more insulin and may perhaps be through extra-pancreatic means. The MRM (200 mg/kg; 400 mg/kg) dose illustrated promising outcome [Graphs 1-6].

The diabetic rats as treated with the *R. mysorensis* extract exhibited significant ($P < 0.05$) drop off in level of blood glucose on 21st day. Level of serum glucose in group of diabetic control stay put elevated during the whole study phase, whereas in groups of treated, displayed progressive decline in level of glucose was found, and at the finish of the experiment both groups treated with 200 mg/kg and 400 mg/kg MRM displayed significant lessen in blood glucose contrast with control group. Like the plant extract, Glibenclamide also caused a significant drop off in the level of blood glucose of diabetic rats. Glibenclamide put forth its action



Graph 6: Effect of methanolic extract of *Rhus mysorensis* on body weight in streptozotocin-induced rats. All the values are expressed as Mean ± SEM, $n = 6$, One-way analysis of variance followed by multiple comparison Dunnet's test, $^{*}P < 0.05$, $^{**}P < 0.01$, and $^{***}P < 0.001$ as compared to control and $^{a}P < 0.001$, $^{b}P < 0.01$, and $^{c}P < 0.001$ when compared to normal group

mainly by means of mounting the discharge of insulin.[57]

The analogous effectiveness of the RM plant extract with Glibenclamide in this investigation may perhaps suggest related mechanism of action. These findings come into view to be in consonance with the former suggestion of Jackson and Bressler (1981) that sulfonylurea's such like Glibenclamide have extra-pancreatic hypoglycemic means of action secondary to their grounds insulin discharge and the attendant glucose uptake into and consumption by means of the tissues.

Levels of high cholesterol and hyperlipidemia are connected consequences of diabetes.[58]

There were statistically significant differences in serum cholesterol, TG, HDL, VLDL, and LDL levels when diabetic rats received MRM. The observed significant drop off in lipid profile could also be due to depressed hepatic gluconeogenesis by means of MRM, although this claim remains a speculation until it is subjected to further scientific validation by means of the key enzymes regulating this pathway. The levels of serum lipids are usually elevated in diabetes mellitus and such an elevation represents risk factor for coronary heart diseases.

The deficient of insulin and elevation of the oppose regulatory hormones direct to activation of enzymes (lipase of hormone-sensitive) that stimulate lipolysis and improved discharge of free fatty acids from tissue of adipose.[59,60] The fatty acids from tissues of adipose are mobilized for energy rationale and surplus fatty acids are amass in liver, are transformed to triglyceride.

The noticeable hyperlipidemia that typify the diabetic state may perhaps thus be considered as an outcome of unlimited events of lipolytic hormones on the fat depositories. In this exploration, management of methanolic extracts of the plant of *R. mysorensis* significantly

a. Dropped off in serum amounts of
1. Total cholesterol,
2. Triglycerides,
3. Low density lipoprotein (LDL) and

b. Increased serum levels of cholesterol of high-density lipoprotein (HDL) in rats of alloxan induced diabetic.

The drop off of b.w. and augment in fluid and food intake of rats of diabetic contrast to that of control group of experimental rats may perhaps be due to emaciation of skeletal muscles, dehydration, and catabolism of proteins and fats. The control group of experimental rats has revealed a progressive drop off of b.w. significantly contrast to the group of normal. The MRM (200 mg/kg; 400 mg/kg) displayed a drop in b.w. and this lessening of weight is less contrast to group of control. This illustrates that the treatment with extract has protected rats of diabetic from losing b.w. in a significant ($P < 0.05$) way contrast to the control group of rats.

As a result, it can be long-established that, in present investigation considerable antidiabetic potential of *R. mysorensis* leaves may perhaps be because of

I. Flavonoids,
II. Alkaloids,
III. Saponins,
IV. Tannins,
V. Phenols,

Phytosterols constituent, which were long-established by preliminary phytochemical assessment. The investigation was executed to uncover out the advantageous possessions of methanolic extract of *R. mysorensis* medicinal plant in rats of normal glycaemia and alloxan-induced diabetic. Moreover, the outcome discloses

that the medicinal plant has advantageous effects on levels of blood glucose of normal along with streptozotocin-induced rats of diabetic. The outcomes disclosed that the medicinal plant extracts significantly protect from other metabolic aberrations institute in diabetes, biochemical as well as physiological aberrations too.

The outcomes uncover that the methanol extract of medicinal plant is the majorly potent in drop the level of fasting blood glucose of the rats of diabetic followed the effect is dose dependent manner. [61-63]

Furthermore, the extract illustrates enhancement in parameters such like

1) B.W.,
2) food intake,
3) fluid intake and
4) Urine excreted.

The extracts also dropped the levels of serum lipids such like

1) Triglycerides,
2) LDL,
3) VLDL and
4) Cholesterol and
5) Increase HDL.

Histopathological assessment of pancreas uncovers the revival of damaged tissue as sections of groups of treated are contrast to diabetic control. From the toxicity investigations, it was accomplished that the extracts are safer and do not uncover any sort of toxic reply up to the oral doses of g/kg of b.w.

The plant extract uncover augment in the glucose tolerance of the experimental rats and diminish in the level of fasting blood glucose of rats of normal group, uncovering the hypoglycemic effect of the medicinal plant, mainly pronounced in highest dose.

Outcome from the phytochemical scrutiny of *R. mysorensis* exposed the presence of

1) Saponins,
2) Terpenoids,
3) Alkaloids,
4) Tannins,
5) Phenolics,
6) Flavonoids, and
7) Glycosides as the promising biologically active values, been isolated from the other plants and found to have ant diabetic activity too.

In nutshell the extract of *R. mysorensis* possesses significant hypoglycemic and antidiabetic effect, is the first claim in this esteem.

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