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ANTIDIABETIC ACTIVITY OF RHUS AROMATICA MOTHER TINCTURE ON DIABETIC MALE WISTAR ALBINO RATS

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ABSTRACT

Objectives: The aim of this study was to assess the antidiabetic effect of *Rhus arom Q* mother tincture on diabetic wistar albino rats. **Methods:** Diabetic induction in wistar albino rats was performed as per standard method using alloxan at the dose 150mg/kg body weight. After overnight fasting diabetes was induced in rats by single intraperitoneal injection of Alloxan monohydrate dissolved in normal saline at a dose of 150mg/kg body weight. Dose of the mother tincture(1ml/kg) were administered to normal and experimental diabetic rats for 14 days. The blood samples were withdrawn from the retro orbital sinus on 1,7 and 14th days of mother tincture administration. Fasting blood glucose level and change in body weight also examined on these days. OGTT and histopathological studies of Pancreas, liver and kidney were also performed. Serum lipid profiles were also performed. **Results and Discussion**: In in vivo study, *Rhus arom Q* mother tincture showed a decrease in fasting blood glucose levels. All these effects compared with Syzigium jambolanum MT(Homeopathic standard) and Glibenclamide 0.6mg/kg as a reference drug. The administration resulted in significant decrease in level of blood glucose and lipid profile. The total cholesterol and serum triglycerides levels were also reduced and the HDL cholesterol level were increased upon treatment with the *Rhus arom Q* mother tincture thus providing the potent antidiabetic property of the mother tincture. Recovery of body weight of mother tincture treated diabetic rats gave further evidence for dose related antidiabetic activity of *Rhus arom Q*. The mechanism involves potentiation of the insulin effect to plasma by increasing pancreatic secretion of insulin from the existing beta cells and it also inhibited cholesterol and triglyceride synthesis. The mother tincture of *Rhus arom Q* significantly

increases glucose tolerance of normal animals, which further confirms the safety and antidiabetogenic action of the *Rhus arom Q* mother tincture. **Conclusion:** The in vivo study confirmed the antidiabetic activity of *Rhus aromatica* mother tincture.

KEYWORDS: Diabetes, Mothertincture, Rhus aromatica, Lipid profile.

INTRODUCTION

Diabetes mellitus is a group of metabolic disorder characterized by hyperglycemia; altered, metabolism of lipids, carbohydrates and proteins; and an increased risk of vascular complications. Diabetes occurs when the pancreas is not producing insulin or produced insulin cannot be used by the body, these may lead to raise blood glucose levels. Hyperglycemia for the long-term are associated with damage to the various organs and tissues. Blood glucose level is maintained within a range of 80-120mg/dl. Elevation of the blood sugar is known to bring about an increase in the secretion of insulin which results in an increased uptake of glucose by the cells and also its conversion into glycogen within the cells that results in the reduction of the blood sugar level.[1] Diabetes mellitus is a disease that prevents your body from properly using the energy from the food you eat. Diabetes occurs in one of the following situations:

The pancreas (an organ behind your stomach) produces little insulin or no insulin at all. (Insulin is a naturally occurring hormone, produced by the beta cells of the pancreas, which helps the body use sugar for energy.)-Or-The pancreas makes insulin, but the insulin made does not work as it should. This condition is called insulin resistance. To better understand diabetes, it helps to know more about how the body uses food for energy (a process called metabolism).[2] Your body is made up of millions of cells. To make energy, the cells need food in a very simple form. When you eat or drink, much of your food is broken down into a simple sugar called glucose. Glucose provides the energy your body needs for daily activities.

Rhus aromatica is a deciduous shrub in the family Anacardiaceae native to Canada and the United states. It is a woody plant that can grow to around 2-4 meters tall with a rounded form. It is also known as fragrant sumac. It contained a wide range of constituents including flavonoids, sterols, alkaloids, tannins, glycosides, carbohydratesetc. *Rhusaromatica* exerted antiviral, antihaemorragic and antidiabetic effects. Homeopathy is a holistic method of treatment that uses microdoses of natural substances originating from plants, minerals or animal parts.[3] Homeopathic mothertincture is a combination of botanical extract with

specified amount of alcohol. At present, the treatment of diabetes mainly involves some synthetic hypoglycemic agents and the hormone insulin. Among the synthetic agents, biguanides, thiazolidinediones and a-glucosidase inhibitors are very commonly used. However, many of the oral antihyperglycemic drugs being used have some undesirable side-effects.8–10 Therefore, less toxic natural products having little or no side-effects are now being preferred to synthetic products as a remedy by many for treating various diseases including diabetes.

The global prevalence of diabetes is likely to rise from 200 million in 2017 to 366 million in 2030. The greatest absolute increase in the number of people with diabetes will be in India, which will lead India to become the 'diabetes capital of the world'.[4] The oxidative stress impairs various cellular functions and plays important roles in the pathophysiology of many diseases. In type 1 diabetes, reactive oxygen species generated by macrophages and participate in the toxic actions that lead to necrosis or apoptosis of the insulin producing cells.[5] In type 2 diabetes, chronic hyperglycemia leads to overproduction of reactive oxygen species and the high reactivity of reactive oxygen species caused cellular injury through nonspecific modification and disruption of proteins, phospholipids and nucleic acids.

Alloxan monohydrate

Alloxan is most prominent chemical compound used in diabetogenic research. In research it is used for induction of Type 1 diabetes. Alloxan is a urea derivative which causes selective necrosis of the β- cells of pancreatic islets. It has been widely used to induce experimental diabetes in animals such as rabbits, rats, mice and dogs with different grades of disease severity by varying the dose of alloxanused. The chemical name of alloxan is 2,4,5,6 tetraoxypyrimidine; 2, 4, 5, 6- pyrimidinetetrone, which is an oxygenated pyrimidine derivative which is present as alloxan hydrate in aqueous solution Alloxan was prepared by the oxidation of uric acid by nitric acid and the monohydrate form is simultaneously prepared by oxidation of barbituric acid by chromium trioxide. The drug has been noted to its diabetogenic action when administered parenterally, i.e., intravenously, intraperitoneally or subcutaneously. The dose of alloxan required for inducing diabetes depends on the animal species and route of administration. Moreover, alloxan has been demonstrated to be non-toxic to the human beta-cells, even in very high doses, because humans have different glucose uptake mechanisms as compared to rodents.[6]

Mechanism of action

Alloxan treatment evokes a sudden rise in insulin secretion in the presence or absence of glucose and this insulin release occurs for short duration followed by the complete suppression of the islet response to glucose even when high concentrations of glucose were used Further, important feature of alloxan action in pancreas is preceded by its rapid uptake by pancreatic beta cells. Moreover, in pancreatic beta cells, the reduction process occurs in the presence of reducing agents like reduced glutathione (GSH), cysteine, ascorbate and protein-bound sulfhydryl (-SH) groups. Alloxan reacts with two - SH groups in the sugar binding site of glucokinase and results in inactivation of the enzyme. As a result dialuric acid is formed which is then re-oxidized back to alloxan establishing a redox cycle and generates reactive oxygen species (ROS) and superoxide radicals The superoxide radicals liberate ferric ions from ferritin and reduce them to ferrous and ferric ions and also undergo dismutation to yield hydrogen peroxide (H2O2). As a result, highly reactive hydroxyl radicals are formed in the presence of ferrous and H2O2. Another mechanism that has been reported is the effect of ROS on the DNA of pancreatic islets. In the beta cells alloxan causes DNA fragmentation and damage. Antioxidants like superoxide dismutase, catalase and the non enzymatic scavengers of hydroxyl radicals have been found to protect against alloxan toxicity.[7]

MATERIALS AND METHODS

Mother tincture was collected from Central Research Institute homeopathy Kurichi and diluted with distilled water to prepare 1m/kg body weight of the animals.

Acute toxicity study

Acute oral toxicity test was performed as per OECD (Organisation for Economic Co-operation and Development) -423 guidelines. 3 female rats were used for this study. Following the fasting period, the rats were weighed and the dose was calculated in reference to the body weight. For the main test, a single dose of 4 ml/kg body weight of each mother tincture was administered to rats in the treatment groups, whereas the control groups received vehicle (the respective percentage of alcohol) at dose of 4 ml/kg body weight by oral route. Food was provided to the rats approximately an hour after treatment. The animals were observed 30 min after dosing followed by hourly observation for 8 hours till 14 days. Once daily, cage side observations included changes in skin and fur, eyes and mucous membrane (nasal) and also respiratory rate, circulatory (heart rate and blood pressure), autonomic (salivation, lacrimation, perspiration, piloerection, urinary incontinence, and defecation) and

central nervous system (drowsiness, gait, tremors, and convulsion) changes. Mortality, if any, was determined over a period of 2 weeks.[8]

Animals: Healthy adult Wistar male albino rats weighing about180-300g were used for the study. Animals were procured from the animal house of Mannuthy Veterinary Sciences. Housed in polypropylene cages at a temperature of 25-30°C and relative humidity 35-45% light and dark cycles of 12 and 12h respectively for one week before and during the experiments. Animals were provided with standard rodent pellet diet (Dayal industries Banglore) and the food was withdrawn 12-18h before the experiment though water was allowed ad libitum.[9] All studies were performed in accordance with the guide for the care and use of laboratory animals and approved by the Institutional Animal Ethical Committee of Department of Pharmaceutical Sciences Cheruvandoor, Kottayam, India.

1. Effect of *Rhus aromatica* mother tincture in Normoglycemic rats

For normoglycemic study, over night fasted animals were randomly divided into four groups of six animals each.

Group I – Normal control rats received vehicle solution

Group II – Normal rats treated with Rhus aromatic mother tincture 1ml/kg body weight

Group III- Normal rats treated with Syzigium jambolanum MT 1ml/kg body weight

Group IV –Normal rats treated with Glibenclamide 0.6mg/kg body weight

The vehicles and drug/ Mother tincture were administered orally using intra gastric tube daily for 2 weeks. The blood samples were withdrawn from the tail vein on 1,7 and 14th days of mother tincture administration. The fasting blood glucose levels were estimated by glucose oxidase –peroxidase reactive strips and a glucometer.[1]

2. Oral Glucose Tolerance Test (OGTT)

The oral glucose tolerance test was performed in over night fasted normal rats(18h). Rats divided into four groups, each group contains six animals.

Group I – Normal control rats received vehicle solution

Group II – Normal rats treated with Rhus aromatic mother tincture 1ml/kg body weight

Group III- Normal rats treated with Syzigium jambolanum MT 1ml/kg body weight

Group IV –Normal rats treated with Glibenclamide 0.6mg/kg body weight suspended in Vehicle solution.

Glucose (3g/kg) was fed 30 min after the administration of mother tincture and drugs. Blood was withdrawn from the retro orbital sinus at 0,30,60,90, and 180 min of glucose administration and glucose levels were estimated using a glucose oxidase- peroxidase reactive strips and a glucometer.[10]

3. Effect of Rhus aromatic mother tincture in Alloxan monohydrate type 2 diabetic rats

Induction of Non insulin dependent diabetes mellitus (NIDDM)

NIDDM was induced in over night fasted adult Wistar strain albino male rats by a single intraperitoneal injection of 150mg/kg Alloxan monohydrate. Alloxan monohydrate was dissolved in normal saline. Hyperglycemia was confirmed by the elevated glucose levels greater than 200mg/dl in plasma, determined at 48 h and after 2 days injection.

Experimental design

Animals were divided into five groups of six rats each and mother tincture was administered for 14 days.

Group I: Normal control (diluted ethanol).

Group II: Alloxan treated control (150mg/kg.ip).

Group III: Alloxan (150 mg/kg.ip) + Standard drug, Glibenclamide (0.6mg/kg, p.o).

Group IV: Alloxan(150 mg/kg.ip) + *Syzigiumjambolanum* mother tincture standard (1ml/kg)

Group V: Alloxan (150mg/kg.ip) + *Rhusaromatica* mother tincture (1ml/kg)

Collection of Blood Sample and Blood Glucose Determination

Blood samples was drawn from tail tip of rat at weekly intervals till the end of study (i.e., 2 weeks). Fasting blood glucose estimation and body weight measurement was done on day 1, 7, 14 of the study. Blood glucose estimation could be done by one touch electronic glucometer using glucose test strips. On day 14, blood was collect from retro-orbital plexus under anesthesia from overnight fasted rats and fasting blood sugar was estimated Serum is separate and analyze for serum cholesterol, serum triglycerides by enzymatic DHBS colorimetric method, serum HDL, serum LDL was estimated.

Histopathological examination of liver and pancreas

The organs from each animal was removed after sacrificing the animal and was collected in 10% formalin solution, and immediately processed by the paraffin technique. Sections of 5μ thickness are cut and stain by haematoxylin and eosin for histological examination.

Statistical analysis

Data were statistically evaluated using two way ANOVA, followed by Bonferroni post test using Graph Pad Prism 5 version computer software.

RESULTS

1. Effect of Rhus aromatica mothertincture on blood glucose level (mg/dl) of normoglycemic rats

Blood glucose level of animals in all groups was recorded at 1st, 7th and 14th day. Data obtained were tabulated in the table 1.

Groups	Day1	Day 7	Day 14
Group I Diluted ethanol 0.6ml/kg	**87.5±0.83**	**86.5±1.51**	**85.83±1.47**
Group II Syzigium MT 1ml/kg	**86±1.26**	**85.83±1.32**	**84.83±1.60**
Group III Rhus aromatica MT1ml/kg	**85.16±0.983**	**84.83±0.752**	**83.5±1.224**
Group IV Glibenclamide0.6mg/kg	**84.83±1.16**	**84.66±1.032**	**83.33±1.032**

Values are statistically evaluated by Two Way Anova followed by Bonferroni post test.

* Represents ststistical significance of treatment group vs normal control group ($p < 0.05$).

From the above tabulated data it is clear that, in normal animals treated with Rhus aromatica mother tincture 1ml/kg body weight, no significant reduction in the blood glucose level was observed as compared to the normal control group.

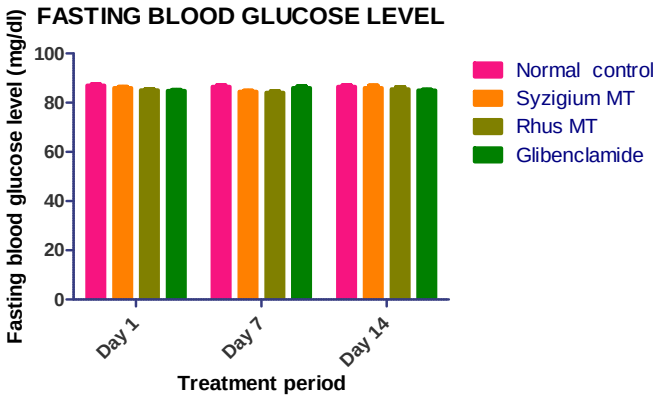


Figure 1.

2. Effect of Rhus aromatica mother tincture on OGTT (normoglycemic animals)

Table 2.

Groups	0 min	30 min	60 min	90 min	120min
GroupI(Normal control)	104.33±5.75	122.33±6.71	127.33±3.66	102.83±6.73	103.33±6.21
GroupII(Syzigium MT)	83.83±4.44***	114.66±3.72***	123.33±4.45	85.5±2.50***	83.5±3.78***
Group III(Rhus aromatica MT)	86.33±2.58***	120.33±6.65	125.88±2.99	87.16±4.40***	85.66±2.50***
Group IV(Glibenclamide)	87.66±3.01***	123.83±4.75	126±3.68	87±2.097***	87.16±3.06***

Values are statistically evaluated by Two Way Anova followed by Bonferroni post test.

*** Represents statistical significance of treatment groups vs Normal Control ($p<0.001$).

n =6 values are expressed as mean± SEM. The serum glucose levels of normal rats reached a peak at 60 min after the oral administration of glucose (3 g/kg) and gradually decreased to 87mg/dl in 2 hours.

In this study, it was observed that within 30 minutes of starting the glucose tolerance test, blood glucose concentration almost doubled from its initial level of control. This hyperglycemia was maintained until 90 minutes and then began to decrease. The three treatment groups(Group II, III, and IV) significantly blocked the deviation in blood glucose level after glucose administration. Glibenclamide blocked the hyperglycemia significantly ($p <0.001$) at 90 and 120 minutes of glucose administration as compared to normal control. Rhus aromatica mother tincture 1ml/kg blocked the hyperglycemia significantly ($p <0.001$) at 90 and 120 minutes of glucose administration as compared to normal control. Syzigium jambolanum MT 1ml/kg blocked hyperglycemia significantly ($p <0.001$) at 90 and 120 minutes of glucose administration as compared to normal control.

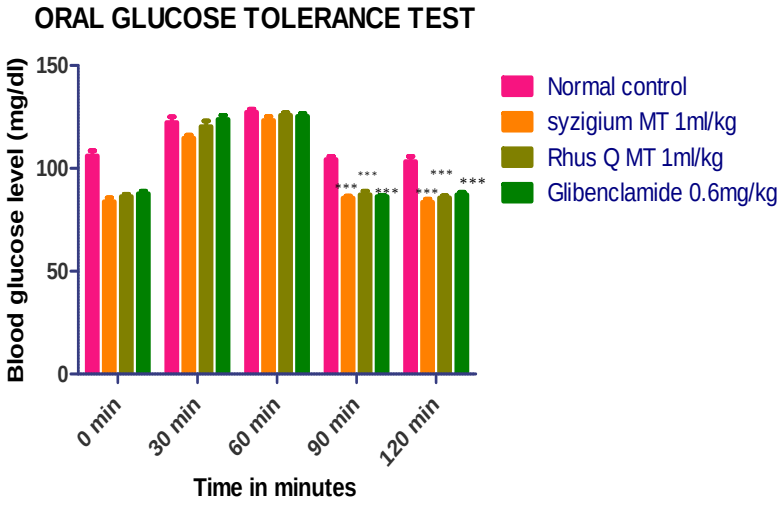
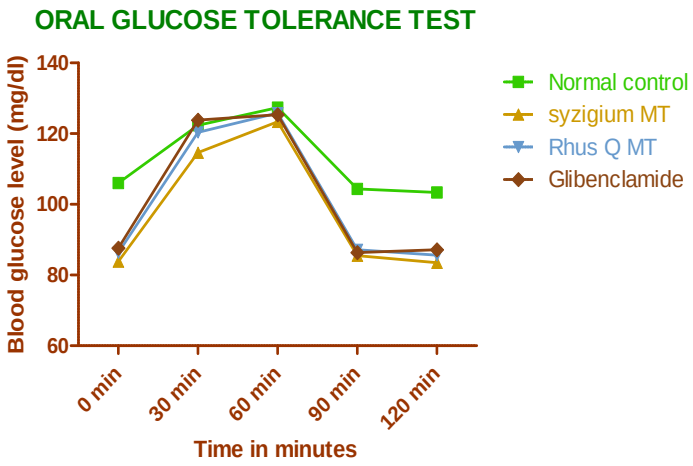


Figure 2.

Effect of Rhus aromatica mother tincture on OGTT

Statistical summary of oral glucose tolerance test showed that F value = 0.6037, R^2 =0.1017.



Fgure 3.

3. Effect of Rhus aromatic mother tincture in Alloxan monohydrate induced type II diabetic rats

a. Effect on blood glucose level

Blood glucose level of animals in all groups were recorded on 1st, 7th and 14th day. Data obtained were tabulated in the table 7.3.

Groups	Day 1	Day7	Day 14
Group I (Normal control)	106.33±1.36***	105.5±1.04***	102.16±5.60***
Group II (Diabetic rats + vehicle)	270.50±23.32	272.83±28.70	273.83±28.40
Group III(Diabetic rats+Syzigium MT1ml/kg)	260.83±12.23	186.83±4.66***	112.33±4.96***
Group IV (Diabetic rats + Rhus aromatica MT 1ml/kg)	250.66±16.08	140.16±10.88***	95.33±2.42***
Group V (Diabetic rats + Glibenclamide 0.6mg/kg)	259.16±8.35	141.16±10.40***	94.33±15.05***

***Represents statistical significance of treatment groups vs Diabetic control(p<0.05)**

****Represents statistical significance of treatment groups vs Diabetic control (p<0.01)**

*****Represents statistical significance of treatment groups vs Diabetic control (p<0.001)**

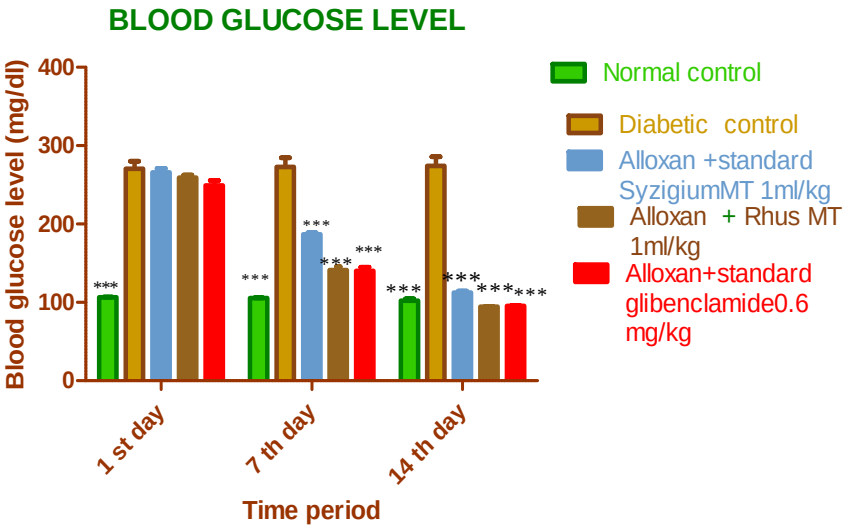
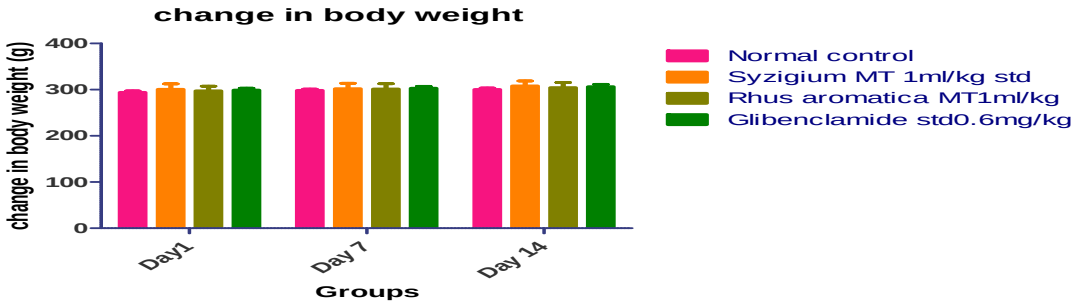


Figure 4.

Progressive decrease in blood glucose level was found in all three treatment groups during study. On day 7 of mother tincture/drug administration, in Syzigium jambolanum 1ml/kg treated group, Rhus aromatic 1ml/kg treated group and Glibenclamide 0.6mg/kg treated group, blood glucose level was decreased significantly ($p<0.001$, $p<0.001$ and $p<0.001$ respectively) as compared to diabetic control group. At the end of the experiment (on day 14), all the three treatment groups (Group II, III and IV) showed a significant ($p<0.001$) reduction in the fasting blood glucose level as compared to diabetic control rats (Group II).

b. Effect of Rhus aromatica mother tincture in change in body weight in normoglycemic rats (Table 4)

Groups	Day 1	Day7	Day 14
GroupI	294.16±3.02	299.60±3.42	301.83±3.27
Group II	300.83±11.70	304.50±11.34	308.50±11.32
Group III	297.5±10.07	301.83±11.23	304.50±11.05
Group IV	299±4.32	303.83±4.29	308.66±5.59



c. Effect of Rhus aromatica mother tincture in change in body weight diabetic rats

Table 5.

Groups	Day 1	Day 7	Day 14
Group I	296.66±6.17	306.66±3.79**	313±2.86***
Group II	290±6.28	282.33±5.39	269.5±3.71
Group III	290.33±6.39	292.5±7.1	296.16±7.37**
Group IV	295.33±4.51	298±4.75	300.66±4.01***
Group V	295.83±3.93	296.5±4.19	299.16±4.72***

**Represents statistical significance of treatment groups vs Diabetic control ($p<0.01$)

***Represents statistical significance of treatment groups vs Diabetic control ($p<0.001$)

Significant change in body weight during study period was found to be in diabetic control group which decreased significantly as compared to normal control group. In animals treated with Rhus aromatica MT (1ml/kg) and Glibenclamide (0.6mg/kg) the body weight increased significantly ($p<0.001$, $p<0.001$ respectively) by 14th day as compared to diabetic control group. In animals treated with Syzigium MT (1ml/kg) standard the body weight increased significantly ($p<0.01$) by 14th day as compared to diabetic control group. Rhus aromatica MT treated group animals showed a non significance increase in the body weight when compared with Group I animals.

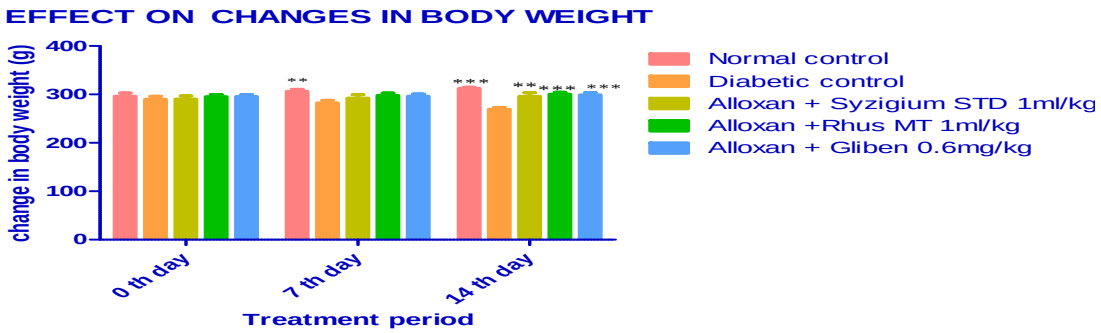


Figure 5.

d. Effect on serum lipid profile

In the Diabetic control group, total cholesterol and triglycerides, increased and HDL level decreased when compared to normal group. In the Rhus aromatica MT1ml/kg, Syzigium MT 1ml/kg and Glibenclamide 0.6mg/kg treated groups total cholesterol and triglycerides decreased significantly.

d.1. Effect on Triglycerides level

Table 6.

Sl No	Group I Normal control	Group II Diabetic control	Group III Diabetic rats+ Syzigium MT 1ml/kg	Group IV Diabetic rats+ Rhus aromatica MT 1ml/kg	Group V Diabetic rats+ Glibenclamide 0.6mg/kg
Mean±SEM	81.16±1.42***	270.2±2.63	129.3±0.988***	142.7±1.60***	145.3±1.33***

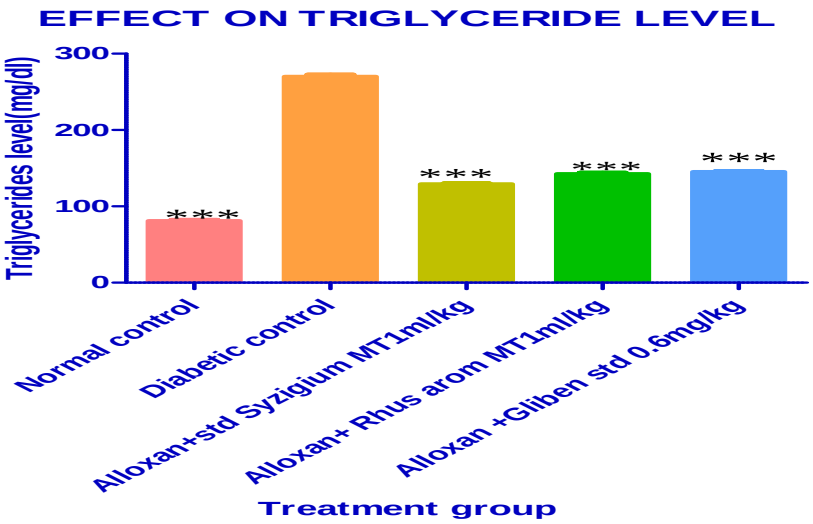


Figure 6.

In the Diabetic induced group triglycerides level increased significantly with respect to normal control group. In the Rhus aromatica MT1ml/kg, Syzigium MT 1ml/kg and Glibenclamide 0.6mg/kg treated groups triglycerides decreased significantly ($p<0.001$).

d.2. Effect of Rhus aromatica mother tincture on Total cholesterol level (mg/dl) of diabetic rats

Table 7.

Sl No	Group I Normal control	Group II Diabetic control	Group III Diabetic rats+ Syzigium MT 1ml/kg	Group IV Diabetic rats+ Rhus aromatica MT 1ml/kg	Group V Diabetic rats+ Glibenclamide 0.6mg/kg
Mean±SEM	85.16±1.42***	271.8±4.56	129.3±0.98***	142.7±1.60***	140.50±0.885***

*** Represents statistical significance of Treatment groups vs Diabetic control group

In the Diabetic induced group total cholesterol level increased significantly with respect to normal control group. In the Rhus aromatica MT1ml/kg, Syzigium MT 1ml/kg and Glibenclamide 0.6mg/kg treated groups total cholesterol level decreased significantly ($p<0.001$).

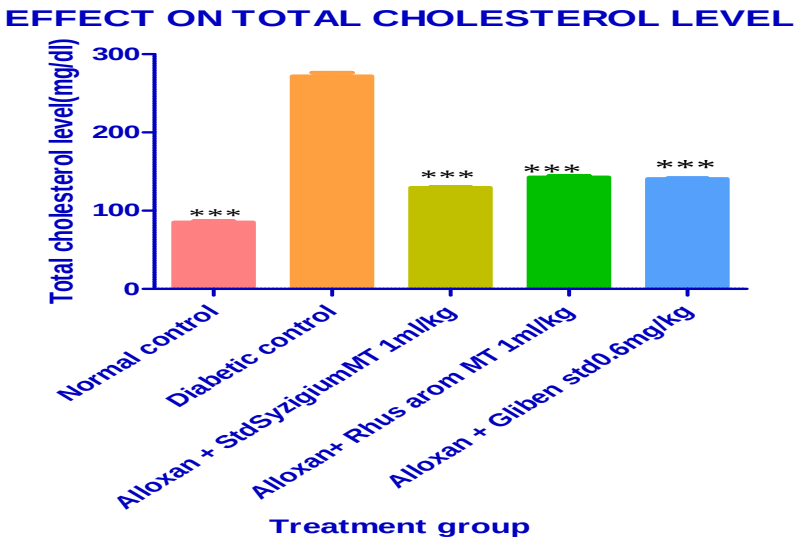


Figure.7

d.3. Effect on HDL Level

Table 8.

Sl No	Group I Normal control	Group II Diabetic control	Group III Diabetic rats+ Syzigium MT 1ml/kg	Group IV Diabetic rats+ Rhus aromatica MT 1ml/kg	Group V Diabetic rats+ Glibenclamide 0.6mg/kg
Mean±SEM	40±1.15***	19.83±1.10	45.33±0.95***	44.83±1.27***	35.17±0.83***

***Represents statistical significance difference between Treatment group vs Diabetic control group

In the Diabetic induced group HDL level decreased significantly with respect to normal control group. In the Rhus aromatica MT1ml/kg, Syzigium MT 1ml/kg and Glibenclamide 0.6mg/kg treated groups HDL level increased significantly ($p<0.001$).

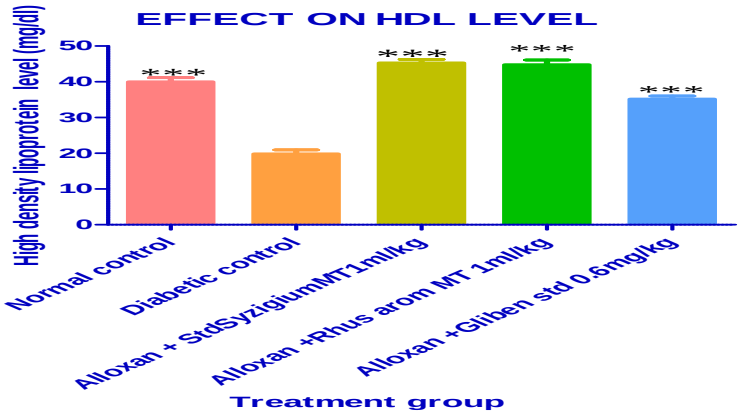


Figure 8.

d.4. Effect on Low density lipoprotein level

Table 9.

Sl No	Group I Normal control	Group II Diabetic control	Group III Diabetic rats+ Syzigium MT 1ml/kg	Group IV Diabetic rats+ Rhus aromatica MT 1ml/kg	Group V Diabetic rats+ Glibenclamide 0.6mg/kg
Mean±SEM	19.17±1.04***	152.8±2.61	39.83±0.74***	35.50±2.12***	41±1.03***

***Represents statistical significance difference between Treatment group vs Diabetic control group.

In the Diabetic induced group LDL level increased significantly with respect to normal control group. In the Rhus aromatica MT1ml/kg, Syzigium MT 1ml/kg and Glibenclamide 0.6mg/kg treated groups LDL level decreased significantly ($p<0.001$).

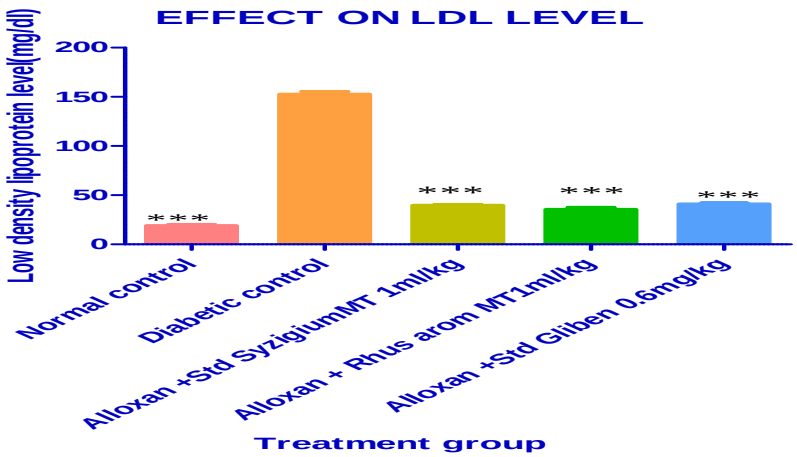


Figure.9

d.5. Effect on Very low density lipoprotein level

Table 10.

Sl No	Group I Normal control	Group II Diabetic control	Group III Diabetic rats+ Syzigium MT 1ml/kg	Group IV Diabetic rats+ Rhus aromatica MT 1ml/kg	Group V Diabetic rats+ Glibenclamide 0.6mg/kg
Mean±SEM	21.83±0.833***	54.17±1.32	23.50±1.45***	24.17±1.10***	26±1.48***

***Represents statistical significance difference between Treatment group vs Diabetic control group.

In the Diabetic induced group V LDL level increased significantly with respect to normal control group. In the Rhus aromatica MT1ml/kg, Syzigium MT 1ml/kg and Glibenclamide 0.6mg/kg treated groups VLDL level decreased significantly ($p<0.001$).

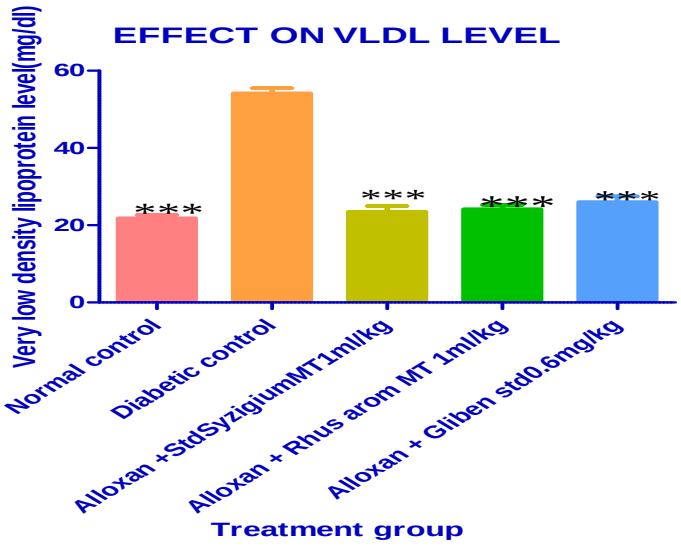


Figure 10.

Histopathological evaluation of liver

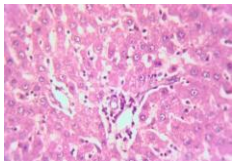


Figure 11: Shows In normal control group animal the histopathology of liver showed portal triad surrounded by cords of hepatocytes.

Figure.11

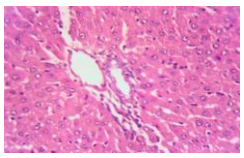


Figure 12 Shows Alloxan induced diabetic rat showed no periportal inflammation

Figure.12

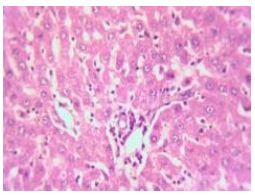


Figure 13 Shows *Syzigium MT* treated animals showed very mild periportal inflammation compared with diabetic rat.

Figure.13

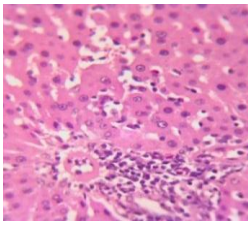


Figure. 14 Shows *Rhus aromatica MT* treated animals showed mild periportal inflammation when compared with normal control as well as standard drug.

Figure.14

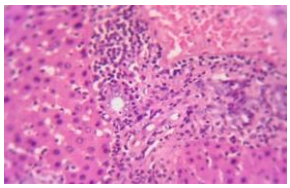


Figure.15 shows Glibenclamide treated animal the histology of liver showed moderate periportal inflammation when compared with normal control.

Figure.15

Histopathology of Pancreas

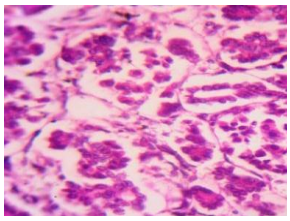


Figure. 16 Shows The pancreatic islets of langerhans of normal rat showing alpha cells and beta cells.

Figure.16

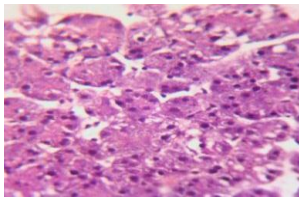


Figure. 17 Shows Alloxan induced diabetic damaged pancreatic islets showing reduced size and increased damaged beta cells.

Figure.17

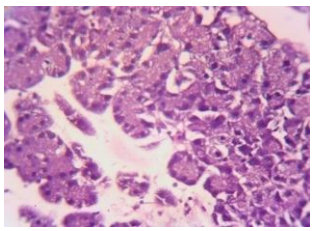


Figure.18 Shows *Syzigium MT* treated pancreatic islets partial restoration of beta cells. The animals revealed better restoration from the Alloxan induced damage when compared to control and disease control as well as Rhus MT treated animal.

Figure.18

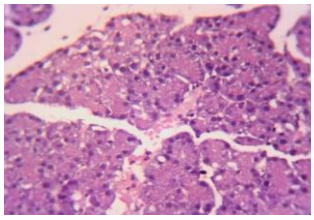


Figure. 19 Shows *Rhus aromatica MT* treated pancreatic islet showed partial better restoration, when compared to the alloxan induced diabetic rats.

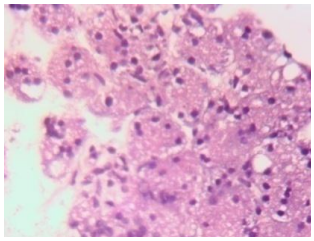


Figure. 20 Shows Glibenclamide (0.6mg/kg) treated pancreatic islet showed better restoration, when compared to the alloxan induced diabetic control rats.

Figure 20.

DISCUSSION

In in vivo study, *Rhus aromatica* mother tincture showed a decrease in fasting blood glucose levels. All these effects compared with Syzigium jambolanum MT (Homeopathic standard) and Glibenclamide 0.6mg/kg as a reference drug. The administration resulted in significant decrease in level of blood glucose and lipid profile. The total cholesterol and serum triglycerides levels were also reduced and the HDL cholesterol level were increased upon treatment with the *Rhus aromatica* mother tincture thus providing the potent antidiabetic property of the mother tincture. Recovery of body weight of mother tincture treated diabetic rats gave further evidence for dose related antidiabetic activity of *Rhus aromatica*.

The mechanism involves potentiation of the insulin effect to plasma by increasing pancreatic secretion of insulin from the existing beta cells and it also inhibited cholesterol and triglyceride synthesis. The mother tincture of *Rhus aromatica* significantly increases glucose tolerance of normal animals, which further confirms the safety and antidiabetogenic action of the *Rhus aromatica* mother tincture. Control animal were found to be almost stable in their body weight but diabetic induced rats showed significant reduction in body weight. The administration of *Rhus aromatica MT, Syzigium MT* and Glibenclamide (0.6mg/kg) to the diabetic rats restored the changes in the body weight. There was a significant difference in body weight **($p< 0.001$)** was observed. The dose dependant antidiabetic property of the Rhus aromatica MT exhibited slight improvement in body weight.

Diabetes induce hyperlipidemia due to excess mobilization of fats from adipose tissue to the under utilization of glucose. High levels of triglyceride, LDL and VLDL also reported and have been associated with heart disease, insulin resistance and diabetes mellitus.

The levels of total serum cholesterol and triglycerides were raised in diabetic rats which were lowered significantly with the treatment of Glibenclamide, Rhus aromatica MT and Syzigium MT. On comparing groups 3,4,5 with group 2 there was a significant reduction in total cholesterol, triglyceride and HDL levels **($p<0.001$)** in Alloxan induced diabetic rats and its hypolipidemic effect could represent a protective mechanism against the development of atherosclerosis which is usually associated with diabetes.

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