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Experimental Evaluation of Mehasetu RASA W.S.R. to its Anti-Diabetic Activity – An Ayurvedic Kupipakva Rasayana Approach

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ABSTRACT:

Mehasetu Rasa[1] is a novel *Sagandha Murchita Kupipakva Rasayana*, specifically indicated in *Madhumeha* (Diabetes Mellitus) as per classical Ayurvedic texts. It is prepared using *Shuddha Parada* (mercury) as *Yogavahi*, *Shuddha Gandhaka* (sulphur) as *Rasayana*, and *Shuddha Vanga* (tin), which is classified under *Pootiloha Varga* and is renowned for its potent *Pramehaghna* (antidiabetic) action. Diabetes mellitus (*Madhumeha*) is a chronic metabolic disorder described in Ayurveda under the broad category of *Prameha*, primarily caused by *Agnimandya* (digestive fire impairment) and *Kapha* vitiation leading to deranged *Medo-dhatu* metabolism. Contemporary research supports its multifactorial pathogenesis involving insulin deficiency and β-cell dysfunction. This study aimed to evaluate the antidiabetic potential of Mehasetu Rasa (MR), a classical herbo-mineral *Kupipakwa* formulation, in streptozotocin (STZ)-induced diabetic Wistar rats, with special emphasis on both Ayurvedic and pharmacological mechanisms.

KEYWORDS: Experimental Diabetes, *Kupipakwa Rasayana*, *Madhumeha*, *Mehasetu Rasa*.

INTRODUCTION:

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from impaired insulin secretion, insulin action, or both. According to the International Diabetes Federation (IDF), the global prevalence of diabetes continues to rise rapidly, posing a significant threat to public health due to its complications affecting the cardiovascular, renal, and nervous systems. While modern antidiabetic drugs offer glycemic control, they are often associated with adverse effects and fail to address long-term tissue regeneration. Hence, there is a growing interest in traditional systems of medicine for safer and holistic alternatives. In Ayurveda, diabetes is described under the umbrella term *Prameha*, with *Madhumeha* being its most severe and incurable form. The pathogenesis involves the vitiation of *Kapha dosha*, impaired *Agni* (digestive fire), and derangement of Medo dhatu (fat metabolism), leading to excessive urination with sweet taste *(Madhumeha)*. Ayurvedic management emphasizes the use of *Deepana*, *Pachana*, *Medohara*, and *Rasayana* therapies to correct the underlying metabolic dysfunctions. Among the *Chaturvidha Rasayana Kalpanas, Kupipakwa Rasayana* is considered to exhibit the highest *Rasayana* activity with a comparatively faster onset of action. Herbo-mineral formulations *(Rasaushadhis)* are known for their quick action, long shelf life, and rejuvenative properties. *Mehasetu Rasa* (MR) is a classical herbo-mineral formulation mentioned in authoritative texts, indicated for Madhumeha and related *Prameha*. It contains potent ingredients believed to enhance *Agni*, normalize *kapha-medas*, and support pancreatic function. However, there is limited scientific evidence validating its pharmacological effects in modern experimental models. Streptozotocin (STZ)-induced diabetes in rodents is a well-established experimental model to study Type 1-like diabetes as it causes selective cytotoxicity to pancreatic β-cells, leading to persistent hyperglycemia. This model allows the assessment of both glycemic control and pancreatic tissue protection offered by candidate drugs. In this context, the present study was designed to evaluate the antidiabetic potential of Mehasetu Rasa in STZ-induced diabetic Wistar rats, with assessment parameters including fasting blood glucose, body weight, and histopathological analysis of the pancreas. The study aims to bridge traditional Ayurvedic wisdom with modern pharmacological validation.

REVIEW OF LITERATURE

It is one of the potent mineral drugs and the detailed description of ingredients, usage, properties, method of preparation & therapeutic effect of *Mehasetu Rasa* is mentioned in *Rasachandamshu*.

AIMS AND OBJECTIVE

To assess the antidiabetic activity of Mehasetu Rasa at two dose levels in Streptozotocin (STZ)-induced diabetic Wistar albino rats.

MATERIALS AND METHODS

Albino wistar male rats weighing 180-200 gm were used. The animals were purchased from National Institute of Biosciences. Dhangawadi, Nigadewada Road, Pune-Bangalore highway, TAL: Bhor, DIST: Pune and maintained in the animal house of SET's College of Pharmacy, Dharwad for experimental purpose. Male Wistar albino rats (180–200 g) were rendered diabetic via a single intraperitoneal injection of STZ (55 mg/kg). Animals were randomly divided into five groups (n = 6): normal control, diabetic control, standard treatment (Metformin 5 mg/kg), and two test groups receiving MR at 125 mg and 250 mg (human-equivalent doses) respectively. All treatments were administered orally for 28 consecutive days. Fasting blood glucose levels were measured on days 0, 7, 14, 21, and 28 using a glucometer. Body weight changes were monitored. On day 28, animals were sacrificed, and pancreatic tissue was collected for histopathological analysis. All the studies conducted were approved by the Institutional Animal Ethical Committee (IAEC) of SET's College of Pharmacy, Dharwad, Karnataka (112/PO/Re/S/99/CCSEA Date: 08.02.2023) according to the prescribed guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India. SETCPD/IAEC/APR/2024/17 Date 27.04.2024**.**

INDUCTION OF DIABETES

The baseline blood glucose levels were determined before the induction of diabetes. Rats were fasted overnight and experimental diabetes induced by intraperitoneal injection of streptozotocin (STZ) with a single dose of 55 mg/kg body weight. STZ was dissolved in 0.1M citrate buffer at pH of 4.5. After three days, rats with blood glucose level greater than 250 mg/dl that exhibit hyperglycaemia were selected for the experiment. The Dr. Morepen GlucoOne blood glucose monitoring metre and test strips were used for the assay. Injection of STZ and attack on pancreas cause hypersecretion of insulin and this lead to intensive hypoglycaemia and this may cause death to many animals, to avoid this, drinking water containing 10% dextrose were given to rats directly after I.P of STZ.

DRUG PREPARATION

A weighed amount of powdered test drug MR (*Mehasetu Rasa*) was first triturated in a motor using a pestle. A small amount of tragacanthin (a suspension agent) was then added to the motor and triturated again. After adding the required amount of water, the trituration process was continued until a stable suspension was formed.

BIOCHEMICAL ANALYSIS

Collected serum was subjected for lipid parameter such as total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), very low-density lipoprotein (VLDL), high density

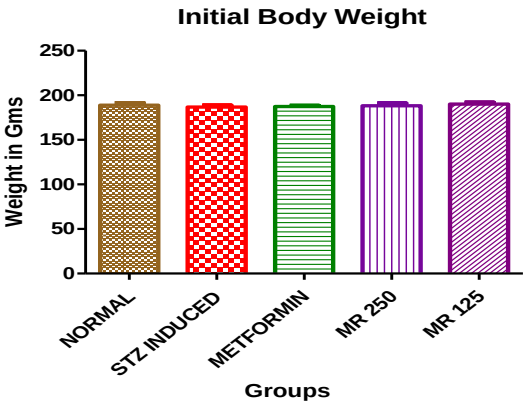
lipoprotein (HDL), were estimated by Swemed (Artos) analyzer.

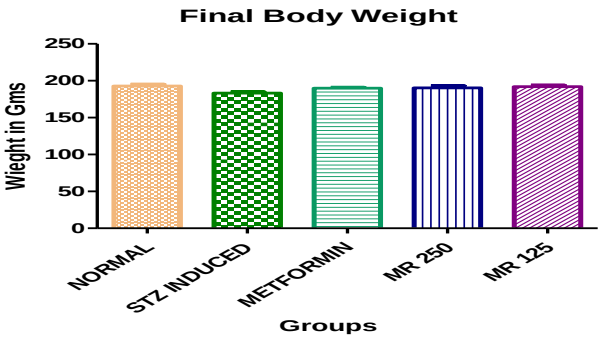
STATISTICAL ANALYSIS

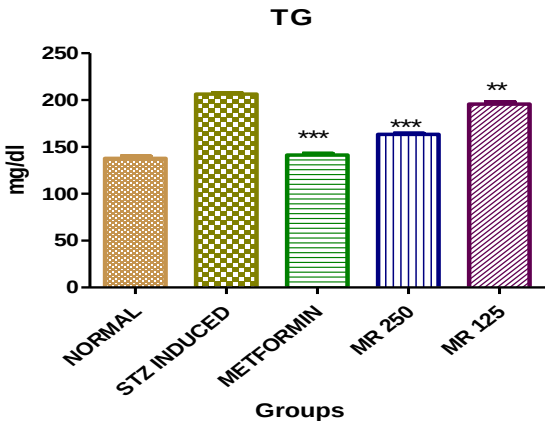
The results were expressed as the mean ± SEM and analyzed using one-way ANOVA followed by Tukey's Multiple Comparison tests. Data were computed for statistical analysis using the graph pad prism software 5.0.

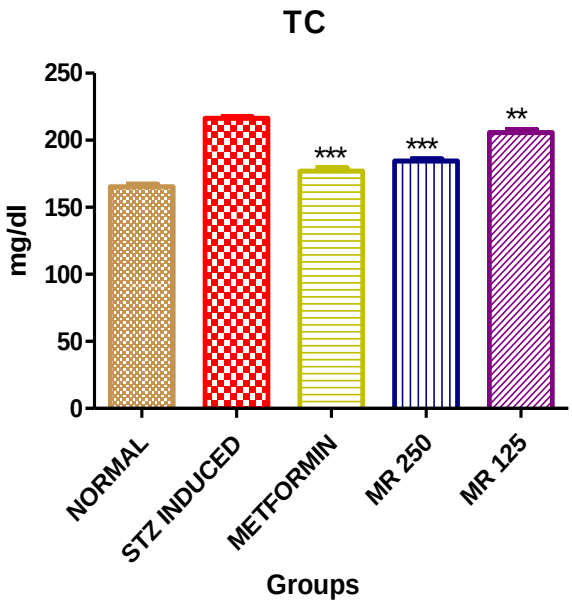
Table & Graphs showing the Experimental result of Lipid Parameters of *Mehasetu Rasa*

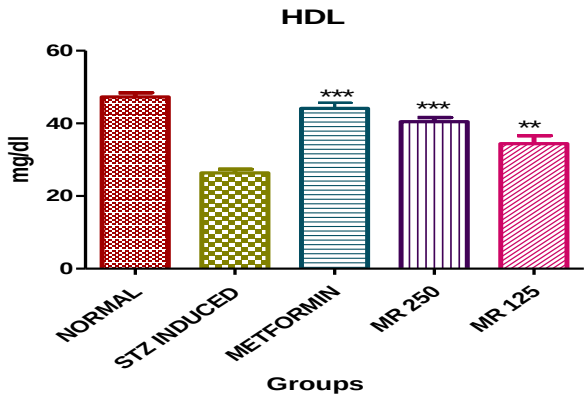
Groups	Initial BW (Gms)	Final BW (Gms)	% Change	TG (mg/dl)	TC (mg/dl)	HDL (mg/dl)	VLDL (mg/dl)	LDL (mg/dl)
Normal	188.8± 2.726	192.8±2.488	2.07%	137.7±2.319	165.3±1.886	47.30±1.134	27.54±0.4643	90.43±2.140
STZ	186.8± 2.063	183.1±1.861	-2.02%	206.3±1.593	216.3±1.138	26.36±1.030	41.24±0.3228	148.7±1.812
Metformin	187.3± 1.336	189.9±1.294	1.36%	141.3±1.789***	177.1±2.158***	44.12±1.548***	28.26±0.3579***	97.09±2.078***
MR 250	188.2± 2.856	190.3±2.641	1.103%	163.4±1.058***	184.5±1.512***	40.47±1.174***	32.67±0.2123***	101.8±2.769***
MR 125	190.0±2.098	191.9±2.117	0.99%	195.6±2.275**	205.7±2.176**	34.43±2.178**	39.13±0.4544**	130.1±2.932**


Initial Body Weight
Weight in Gms
250
200
150
100
50
0
NORMAL
STZ INDUCED
METFORMIN
MR 250
MR 125
Groups


Final Body Weight
Wieght in Gms
250
200
150
100
50
0
NORMAL
STZ INDUCED
METFORMIN
MR 250
MR 125
Groups


TG
mg/dl
250
200
150
100
50
0
***
***
**
NORMAL
STZ INDUCED
METFORMIN
MR 250
MR 125
Groups


TC
mg/dl
250
200
150
100
50
0
***
***
**
NORMAL
STZ INDUCED
METFORMIN
MR 250
MR 125
Groups


HDL
mg/dl
60
40
20
0
***
***
**
NORMAL
STZ INDUCED
METFORMIN
MR 250
MR 125
Groups

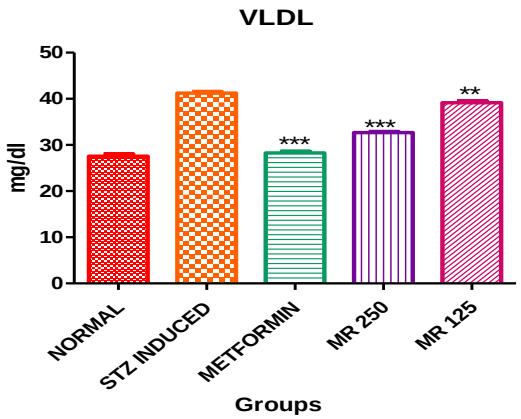
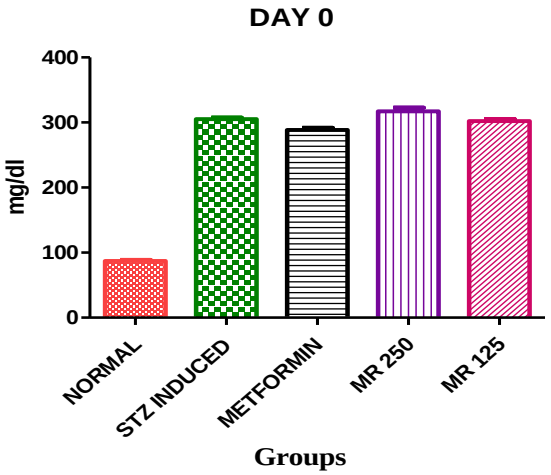
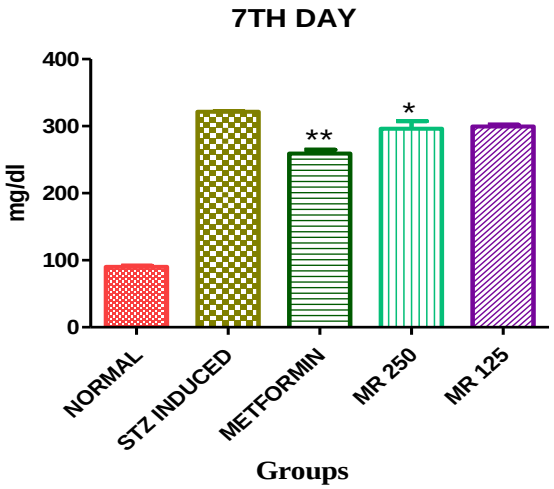

VLDL
mg/dl
50
40
30
20
10
0
***
***
**
NORMAL
STZ INDUCED
METFORMIN
MR 250
MR 125
Groups

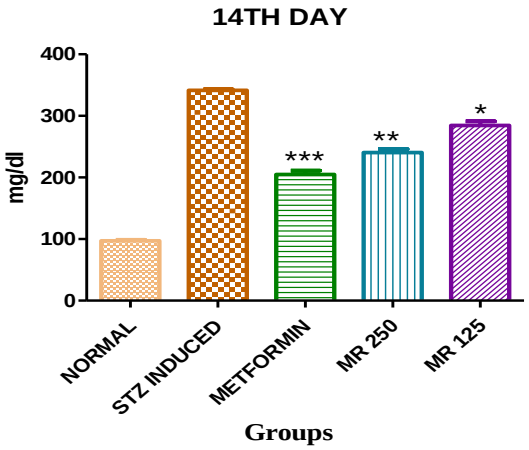
Table & Graph showing the Experimental Result of Blood Glucose Level (mg/dl) of *Mehasetu Rasa*

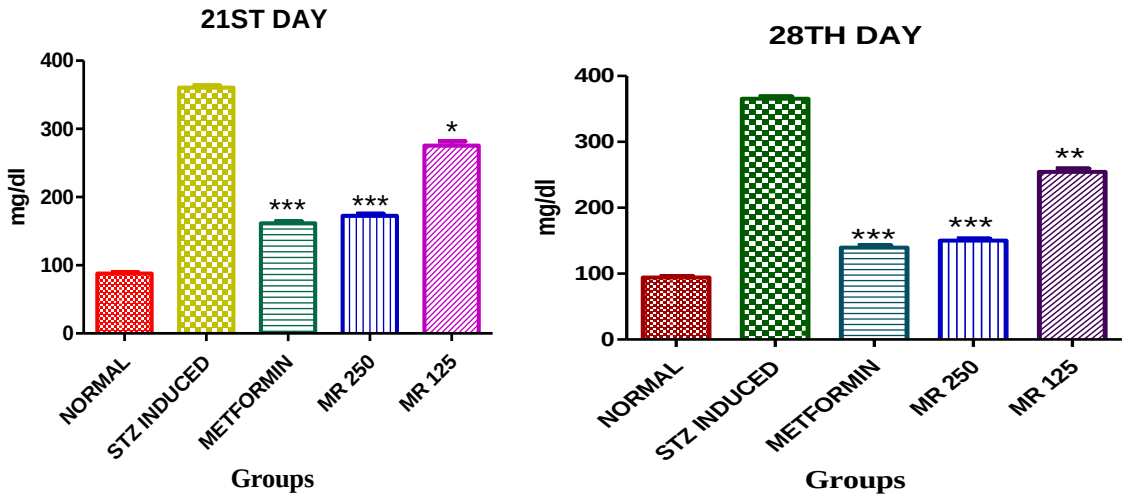
Groups	Basal	Day 0(ns)	Day 7	Day 14	Day 21	Day 28
Normal	87.0±1.844	87.2±1.655	90.0±1.732	97.0±1.844	87.8±2.035	94.2±2.083
STZ	94.4±1.364	305.0±2.345	321.4±1.03	341.4±1.778	360.6±2.874	365.6±3.187
Metformin	96.2±1.393	288.4±3.311	259.2±5.571**	204.8±6.499***	161.4±2.619***	139.4±3.415***
MR 250	100.2±1.772	317.0±5.992	296.0±6.36*	240.6±5.501**	172.4±3.01***	150.2±3.023***
MR 125	92.8±1.356	302.0±3.082	299.4±2.926ns	284.6±6.470*	275.4±6.423*	254.4±5.046**

Values are expressed as Mean±SEM for 6 animals per group *p<0.05, **p<0.01, ***p<0.001 compared with controls (ANOVA followed by post – hoc Tukey's tests for multiple comparisons)









Histopathology of Pancreas:

At the end of the study, the histopathological analysis of the pancreas from the normal control group revealed healthy pancreatic acini and islets of Langerhans with normal cellular structure

(A). In contrast, the diabetic rats exhibited a reduced number and size of pancreatic islets, along with characteristics such as vacuolation, hydropic and necrotic cells, karyopyknosis, cellular degranulation, and connective tissue invasion

(B). In Both the groups of Metformin and MR 250 (C & D) effectively restored the damaged islets of Langerhans in diabetic rats, leading to improved islet structure and integrity, as well as a increase in the number and size of the pancreatic islets. Animals treated with MR 125 showed moderate protection against STZ induced toxicity.

DISCUSSION:

The results of this study clearly demonstrate the efficacy of Mehasetu Rasa (MR) in alleviating hyperglycemia and associated lipid abnormalities in STZ-induced diabetic rats, a widely accepted model of Type 1-like diabetes. The administration of STZ caused significant β-cell damage, evident through the marked increase in fasting blood glucose, lipid derangements, and histological degeneration of pancreatic islets. These findings are in line with previous studies demonstrating STZ's cytotoxic effect on pancreatic β-cells. Treatment with MR (250 mg) significantly reduced blood glucose levels from day 7 onward, comparable to the standard drug Metformin, indicating that MR may exert insulin-mimetic or insulin-sensitizing effects. The improvement in lipid profile parameters (notably TG, TC, LDL, and VLDL) further suggests that MR has a protective effect on lipid metabolism, possibly via improved insulin sensitivity or modulation of hepatic enzymes. Histopathological analysis showed substantial regeneration and restoration of islet structure in animals treated with MR 250 mg, indicating potential β-cell protective or regenerative effects. MR 125 mg showed moderate antihyperglycemic and histological protection, implying dose-dependency in its therapeutic effects. The combined antihyperglycemic, antihyperlipidemic, and pancreatic protective actions may be attributed to the synergistic effect of ingredients in MR, which are traditionally known for *Deepana, Pachana,* and *Rasayana* properties.

CONCLUSION:

The findings suggest that *Mehasetu Rasa,* especially at the 250 mg human-equivalent dose, exhibits potent antidiabetic activity and provides histological protection to pancreatic β-cells in STZ-induced diabetic rats. These results support its traditional use in the management of *Madhumeha* (Diabetes mellitus) and lay the foundation for future clinical studies to explore its efficacy and safety in humans.

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