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RESEARCH ARTICLE

Unraveling the Pharmacodynamic Aspects of *Mucuna pruriens* Seed Extract on Metabolic Parameters and Organ Weights in Streptozotocin Induced Diabetic Rats

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Abstract

Background: Diabetes mellitus, a chronic metabolic disorder, affects millions worldwide. *Mucuna pruriens*, a traditional medicinal plant, shows antidiabetic potential. However, the pharmacodynamic aspects of *M. pruriens* seed extract on metabolic parameters and organ weights in diabetic rats remain least explored. **Aim:** The study aims to assess the changes in metabolic parameters, including body weight, relative and absolute organ weights (Liver and pancreas), water consumption, and food intake in diabetic rats following *M. pruriens* seed extract treatment for 12 weeks, comparing it with Glibenclamide. **Methods:** In this study, 72 neonatal Wistar rats were used, with 54 made diabetic using intraperitoneal administration of Streptozotocin. After 4 weeks, diabetic rats were divided into 3 groups: Positive control, Test drug (*M. pruriens* extract, 200 mg/kg), and Standard drug (Glibenclamide, 1 mg/kg). 18 rats served as Normal control. Parameters like fasting plasma glucose, body weight, organ weights, food and water consumption were measured and statistically analyzed using one-way ANOVA. **Results:** Over 12 weeks, normal control rats steadily gained weight, while positive control rats showed slower gain. *M. pruriens*-treated rats went from 115 g to 222 g, surpassing the standard drug group after 6 weeks. Pancreas weight in the Test drug group decreased insignificantly. Diabetic rats showed polydipsia and Polyphagia; however, both test and standard drug groups showed a significant decrease in food and water intake compared to positive controls. Fasting Plasma Glucose (FPG) in the *Mucuna pruriens* treated group reduced by 65.4 %, and the standard drug by 53.3 %, but FPG levels in *M. pruriens* treated group were higher than the standard drug in weeks 9-12. **Conclusion:** The administration of *M. pruriens* seed extract in diabetic rats effectively regulates abnormal metabolic parameters and body weight.

Major Findings: *Mucuna pruriens* seeds helps to reduce increased cholesterol level. *Mucuna pruriens* seeds helps to reduce liver weight gain in metabolic diseases. *Mucuna Pruriens* seeds helps in body weight regulation in dyslipidemia.

Keywords: Body Weight Gain, Diabetes Mellitus, Food and Water Consumption, *Mucuna pruriens*, Wistar Rats

1. Introduction

Diabetes Mellitus (DM) is a metabolic disorder marked by persistent high blood sugar levels due to impaired insulin secretion or action. It has a substantial impact on global health. As of 2023, over half a billion people worldwide live with diabetes, affecting individuals of all ages across countries. Projections indicate that this number will surpass 1.3 billion within the next three decades[1]. Managing and preventing diabetes remain critical endeavors. Diabetes, especially type 2, is associated with weight loss, polydipsia, and polyphagia. Weight loss serves both as a symptom and a therapeutic strategy in diabetes. Early weight loss often occurs in individuals with diabetes due to impaired glucose utilization, particularly in type 1 diabetes. In this case,

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muscle protein is used as an alternate energy source instead of glucose[2]. Maintaining a healthy weight through regular exercise remains crucial for effective weight management in individuals with diabetes. Increased appetite is another hallmark symptom of diabetes, which tends to consume more food, possibly due to inefficient glucose utilization. Polydipsia, characterized by excessive thirst, occurs when a person with diabetes develops high blood sugar levels. The kidneys cannot reabsorb all the sugar passing through, leading to excess sugar in the urine and subsequent increased urination (polyuria)[3].

Diabetes affects almost all organs in the body. It has a long-term impact on reducing the mean weight of the liver and pancreas[4]. Additionally, it is a major risk factor for Cardiovascular Disease (CVD) and can lead to Coronary Artery Disease (CAD) due to plaque buildup in arteries. People with Diabetes are twice as likely to develop heart disease. Persistent blood glucose levels damage both large (macrovascular) and small (microvascular) blood vessels in the kidneys, leading to nephritis over time[5]. Apart from these effects, it is well-known that the oxidative stress induced in diabetes can cause diabetic retinopathy, affecting blood vessels in the retina and potentially leading to vision loss. Diabetes also induces nerve damage (neuropathy), affecting sensation in the feet. Poor circulation due to damaged blood vessels can lead to foot ulcers and infections[6]. Therefore, early treatment of the disease is crucial. Regular physical exercises and proper medications are the treatment options to mitigate these problems.

Besides regular exercise, maintaining a proper dietary regimen is crucial for effective diabetes management[7]. From a nutritional perspective, several factors contribute to regulating diabetes through dietary control. One key factor is the inclusion of staple foods. Legumes and beans, which provide essential protein, play a pivotal role in preventing muscle mass loss—a common cause of weight reduction in diabetes. While common medications like sulfonylureas are helpful for short-term diabetes management, long-term usage may lead to side effects.

Plant-derived secondary metabolites have been extensively studied for their diverse biological effects, laying the scientific groundwork for the utilization of various herbal medicines in traditional and folklore practices[8]. Traditional pulses and legumes, rich in nutrients, antioxidants, and phytonutrients, possess significant medicinal properties. They aid in regulating metabolic diseases such as diabetes, hyperlipidemia, and dyslipidemia, which are associated with diabetes[9]. Numerous studies have investigated the impact of pulses on diabetes management. Evidence suggests that long-term consumption of pulses (approximately 5 cups per week) consistently improves glycemic control[8]. Consuming pulses can enhance satiety, reduce overall food intake, and help regulate body weight, thereby lowering the risk of obesity and improving diabetes management.

Legume seeds offer numerous health benefits, particularly in managing diabetes, promoting heart health, and aiding in weight management due to their complex carbohydrates. Legumes, such as lentils, chickpeas, and beans, have a low glycemic index, which means they digest slowly and help regulate blood sugar levels, making them advantageous for individuals with diabetes[9]. These legumes are rich in essential nutrients such as fiber, protein, and vitamins, contributing to overall health[10]. The high fiber content in legumes also helps lower cholesterol levels. Furthermore, legumes are abundant in potassium, magnesium, and folate, which are crucial for cardiovascular health. They also contain antioxidants that help reduce inflammation and oxidative stress[11].

As legumes are filling and promote satiety, they aid in weight control. Their protein content supports muscle health and metabolism. Legumes have been part of human diets for centuries and are an excellent source of protein. Their consumption is associated with various health benefits, including a reduced risk of cardiovascular diseases, Type 2 Diabetes mellitus, and certain cancers. Furthermore, the high fiber content in legumes promotes digestive health[12].

Mucuna pruriens, also known as velvet bean or cowitch, is a member of the Fabaceae family. This legume boasts a wealth of nutritional and medicinal benefits. The seeds of *M. pruriens* are primarily composed of proteins and starch. Moreover, they contain l-Dopa (3,4-dihydroxy-l-phenylalanine), a compound known for its numerous medicinal properties[13]. *M. pruriens* offers a variety of health benefits, such as anticholesterolemic, anti-Parkinson, antioxidant, sexual-enhancing, anti-inflammatory, antimicrobial, and antivenomous effects. These impressive properties arise from the legume's

phytochemical constituents, including alkaloids, glycosides, saponins, reducing sugars, and tannins[14,15].

This plant, with traditional Ayurvedic uses, shows promise in Diabetes management. It is a rich source of carbohydrates and soluble fibers. Therefore, supplementing *M. pruriens* as both a dietary component and a medicinal option could provide a balanced treatment approach for individuals with metabolic distress. The active medicinal ingredients in *M. pruriens* may effectively reduce the metabolic derangements associated with Diabetes and metabolic syndrome. The present study aims to provide valuable insights into the therapeutic potential of *M. pruriens* in Diabetes management, and its potential as a complementary or alternative treatment strategy for this disease.

2. Materials And Methods

In this study, seventy-two neonatal albino rats of the Wistar strain (Rattus norvegicus), including both sexes, were used. The study received approval from the Institutional Animal Ethics Committee of Mahatma Gandhi Medical College and Research Institute, SBV University, Puducherry (CPCSEA (686/02/a/CPCSEA/IAEC/JULY 28/2011), and the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA).

Fifty-four neonatal rats, aged five days, were given a single intraperitoneal injection of Streptozotocin (STZ) (Sigma Aldrich – USA) at a dose of 65 mg/kg to induce Type 2 diabetes. Additionally, 18 pups were designated as the normal control group. Four weeks post-STZ injection, fasting blood glucose (FPG) levels were measured using an Accu-Chek glucometer from Roche Diagnostics. Rats with FPG levels exceeding 180 mg/dL were identified as diabetic and selected for further studies. These neonatal rats were housed with their mothers for four weeks in a controlled environment with a temperature of 23 ± 2°C, humidity, and a 12-hour light-dark cycle.

Twelve weeks post-injection, the subjects were divided into four groups: Normal control, Positive control, Test drug group, and Standard drug group. The grouping of animals was depicted in Table 1. The positive control group consisted of diabetic uncontrolled rats, while the test drug group received

Table 1. Grouping of animals

Group	Name	Particulars
Group I	Normal Control	Non diabetic rats
Group II	Positive Control	STZ induced diabetic rats.
Group III	Test Drug	STZ induced diabetic rats orally treated with ethanolic extract of *M.pruriens* (200mg/kg b.w)
Group IV	Standard Drug	STZ induced rats orally treated with Glibenclamide (1mg/kg b.w.)

200 mg/kg body weight of *M. pruriens* seed extracted orally. The standard drug group was treated orally with Glibenclamide at a dose of 1mg/kg body weight.

The drug study lasted 12 weeks, with 6 animals from each group being sacrificed every 4 weeks to assess the progression of disease and to compare the ameliorative effects of the test drug and standard drugs at different stages of etiopathogenesis. For the assessment of metabolic parameters, six animals from each group were placed in separate cages for two days prior to sacrifice. To evaluate food consumption, rats were individually housed in cages and provided with 40 g of dry pellet food per day to ensure maximum consumption according to their capacity. After 24 hours, the residual food pellets were weighed to determine the amount consumed by each animal. Absolute food consumption was calculated by subtracting the residual food weight from the initial 40 g. Water intake was monitored once every four weeks from the beginning of the drug study. Rats were individually housed in cages with 100 ml of drinking water. After 24 hours, the remaining water in the bottle was noted, and the total water intake for each animal was calculated by subtracting the remaining water from the initial 100 ml.

Body weight assessments were performed once a week in all groups, using a standard weighing machine. After every four weeks 6 animals from each group were sacrificed for the harvesting of liver and pancreas tissues. The collected organs were washed in normal saline, wiped with tissue paper, and accurately weighed using a digital weighing machine to obtain their absolute weights. To calculate the relative weight percentage of the organs, the following formula was used[16].

Relative weight = Absolute Organ weight ÷ Body weight ×100

3. Statistical Analysis

The data was presented as Mean ± Standard Deviation. Statistical significance was evaluated using Analysis of Variance (ANOVA), followed by Tukey's HSD post hoc test for pairwise comparisons. A p-value of less than 0.05 was deemed significant. All statistical analyses were conducted using SPSS version 16.

4. Results

4.1 Body Weight Assessments

The data showing total body weight and percentage of body weight gain in animals of different groups are depicted in Table 2 and 3 respectively. Normal control rats showed a steady increase in weight as they aged. At the beginning of the drug study, the mean weight recorded among the group was 140 ± 5 g. By the end of the drug study, it reached 243.5 ± 16.43 g. In contrast, weight gain in the positive control group rats occurred at a slower rate compared to normal control rats. The body weight gradually increased among Test drug group rats, specifically from 115 g ± 18 g to 222 g ± 16 g over 12 weeks. When compared with test drug group, the standard drug group showed increased values in the first 6 weeks of the study. However, from the 7th to the 12th week, the test drug group rats exhibited higher values than the standard drug group ($P < 0.05$).

4.2 Food and Water Intake Assessments

The data showing food and water intake in animals of different groups and the percentage changes are depicted in Table 4 and Table 5 respectively. The diabetic animals exhibited polydipsia and polyphagia. The positive control group showed significantly higher mean water and food consumption compared to the normal control rats (Table 3). However, food and water intake significantly decreased in the test and standard drug groups compared to the positive control rats ($p < 0.01$). No statistical significance was observed between the test drug and Standard drug groups ($p > 0.05$).

4.3 Organ Weight Changes

The data showing Absolute and relative organ weight of pancreas and liver in animals of different groups are depicted in Table 6. No statistically significant weight changes were observed in the Liver of positive control and experimental drug groups. The organ weight analysis of the pancreas in the *M. pruriens* group

Table 3. Body Weight Gain (in Percentage)

Group	4th week	8th week	12th week
Positive control	-26.50%	-35.74%	-40.7%
Test drug	+15.57%	+39.09%	+54.16%
Standard Drug	+14.75%	+33.08%	+45.83%

*Positive Control compared with the Normal Control, test drug and Standard drug groups

Table 2. The effect of *Mucuna pruriens* seed extract on total body weight

PERIOD	NORMAL CONTROL	POSITIVE CONTROL	TEST DRUG	STANDARD DRUG
1st week	145 ±6.6 g	114 ±12.56g^{a}	115 ± 9.44 g^{b}	116 ± 6.93 g
2nd week	150 ±7.8	117 ±13.65g^{a}	124 ±9.34 g^{b}	121 ± 6.974 g
3rd week	157 ± 9.9g	119 ±16.67g^{a}	133 ±8.23 g^{b}	130 ± 7.07 g
4th week	166 ±12.4g	122 ±15.98g^{a}	141 ±9.45 g^{b}	140 ± 6.99 g
5th week	178 ±12.7g	126 ±16.76g^{a}	149 ±9.34 g^{b}	151 ± 7.55 g
6th week	186 ±13.65g	129 ±16.77g^{a}	158.5±11.76g^{b}	160 ± 8.88 g
7th week	196 ±14.9 g	131 ±17.87g^{a}	170 ± 11.54 g^{b}	169 ± 8.9 g
8th week	207 ±14.89g	133 ±16.54g^{a}	185 ±12.99 g^{bc}	177 ± 9.4 g
9th week	216 ±15.54g	136 ±16.87g^{a}	192 ± 13.65 g^{bc}	184 ± 9.8 g
10th week	226.5=±15.6g	139 ± 16.7g^{a}	201 ±16.67 g^{bc}	193 ± 9.7 g
11th week	235.5 ±16.4g	141 ±16.76g^{a}	212.2±18.43 g^{bc}	201 ± 9.55 g
12th week	243 ±16.43g	144 ±17.65g^{a}	222.5 ±18.6 g^{bc}	210 ± 9.48 g

All values were expressed as Mean ± SD. Different alphabets between groups denote significance at $p < 0.05$, using Tukey's HSD test. Specifically: 'a': Positive Control compared with Normal control 'b': test drug group compared with Positive Control. 'c': test drug group compared with Standard Drug group.

Table 4. Food and water consumption assessments

Group	4th WEEK		8th WEEK		12th WEEK	
	Feed (g)	Water(ml)	Feed (g)	Water(ml)	Feed (g)	Water(ml)
Normal control	10.2±0.8	30±1	10.6±0.6	30.2± 0.9	11.1±0.6	29.4±1
Positive control	34.5±2.7	49±1.8	34±2.4	48±1.1	32±2.2	47± 1.5
Test drug	18.16±1.5[b]	40.4±0.9[b]	17.16±1.5[b]	35.4±0.7b	15.16±1.5[b]	32.4±0.9[b]
Standard Drug	18.33±1.5	40.5±1.2	17.38±1.8	36.5±1.2	15.33±1.5	31.5±1.2

All values were expressed as Mean ± SD. Different alphabets between groups denote significance at $p < 0.05$, using Tukey's HSD test. Specifically: 'a': Positive Control compared with Normal Control 'b': test drug compared with positive control 'c': Test Drug compared with Glibenclamide.

Table 5. Changes in percentage of water and food consumption

Group	4th week		8th week		12th week	
	Feed	**Water**	**Feed**	**Water**	**Feed**	**Water**
Positive control	23.8%	63.3%	22.4%	58.94%	18.2%	59.86 %
Test Drug	-46.8%	-17.34%	-48.9%	-23.9%	-52.62%	-39.19%
Standard drug	-47.36%	-17.55%	-51.15%	-26.25	52.09%	-32.97%

*Positive Control group compared with the Normal control

*Test drug and Standard drug groups were compared with the Positive control

Table 6. Absolute and relative organ weight of pancreas and liver

Organ	Groups	4th week		8th week		12th week	
		Abs(g)	Rel (%)	Abs(g)	Rel (%)	Abs(g)	Rel (%)
Pancreas	**Normal control**	0.72±0.04	0.43 ±0.03	0.91±0.05	0.43±0.03	1.11±0.10	0.44±0.03
	Positive control	0.46±0.09[a]	0.38 ±0.08[a]	0.49±0.03[a]	0.39±0.03[a]	0.51±0.08[a]	0.38±0.02[a]
	Test Drug	0.58±0.03[b]	0.41 ±0.03[b]	0.74±0.03 [b]	0.42±0.03	0.92±0.09	0.42±0.03
	Standard Drug	0.57±0.08	0.42 ± 0.07	0.73±0.08	0.42±0.09	0.89±0.05	0.41±0.03
Liver	**Normal Control**	4.6± 0.95	2.77 ± 0.93	5.67± 0.97	2.74±0.93	6.8± 0.92	2.79±0.62
	Positive Control	4.31±0.91	3.52 ±0.92	5.1±0.98	3.8±0.95	5.7±0.9	3.96±0.71
	Test Drug	4.38 ±0.94	3.1 ±0.93	5.6±0.88	3.02±0.83	6.65±0.6	2.99±0.77
	Standard Drug	4.4 ±0.70	3.14 ±0.7	5.5±.71	3.11±0.73	6.52±0.7	3.1±0.72

All values were expressed as Mean ± SD. Different alphabets between groups denote significance at $p < 0.05$, using Tukey's HSD test. Specifically: 'a': Positive Control compared with Normal Control 'b': Test drug compared with positive control 'c': Test Drug compared with Standard Drug.

revealed a statistically insignificant decrease in both absolute and relative organ weight when compared with the Positive control and Standard drug groups ($p > 0.05$).

5. Discussion

The study revealed distinct weight patterns in various rat groups. Normal control rats consistently gained weight over time whereas positive control rats exhibited slower weight gain. Interestingly, test drug group rats demonstrated a gradual weight increase, suggesting a potential positive effect of *M. pruriens* on body weight regulation. Initially, the standard drug group outperformed the Test Drug group rats, but the latter surpassed them in later weeks.

Previous researchers, such as Wahono *et al.*, and Barragán *et al.*, reported weight loss due to Streptozotocin (STZ) toxicity in rats[16]. Several factors contribute to body weight loss in diabetic animals such

as, incapability of Cells to Use Glucose, Consumption of Muscle Protein and Adipose Tissues to compensate for energy deficits, Caloric Loss from Glycosuria[17]. Despite increased appetite, diabetic animals still experience weight loss due to these factors.

Treatment with *M. pruriens* seed extract effectively improved weight gain in diabetic rats. After 12 weeks of treatment, these rats showed a remarkable +54.16 % weight gain, which was distinctly higher than that observed in Standard Drug group rats (+45.83 %). In a similar study by Majekodunmi *et al.*, a 40 % weight gain was reported with *M. pruriens* (100 mg/kg), while Glibenclamide resulted in an 18 % weight gain over 12 weeks in experimental rats[18]. The differences in weight gain may be attributed to variations in the dosage of *M. pruriens* seed extract or ethnobotanical factors[19].

The change in absolute liver weight observed among the positive control and experimental groups was not statistically significant. Regardless of reduced mean body weight, a significant upsurge in relative liver weight was observed in Positive control group rats. This increase may be attributed to the amplified hepatic influx of fatty acids due to hypoinsulinemia, leading to triglyceride accumulation in the liver. The results of this study align with findings by Mohammad Zafar *et al.*, who reported that STZ treatment significantly increases absolute and relative liver weight[20]. Notably, *M. pruriens* treatment appeared effective in decreasing relative liver weight, possibly due to the strong antioxidant properties of *M. pruriens* seeds, which might have ameliorated abnormalities in liver function.

6. Conclusion

In conclusion, *M. pruriens* seed extract holds promise as a potential therapeutic agent for managing weight gain in type 2 diabetes. Test Drug rats demonstrated gradual weight increase, suggesting a positive effect on body weight regulation. Despite initial differences, *M. pruriens* outperformed the standard drug group in weight gain. The relative liver weight also decreased, possibly due to its phytonutrients and antioxidants. These findings highlight *M. pruriens* as a potential therapeutic agent for managing weight gain in type 2 diabetes. Further research is warranted to explore optimal dosages and long-term effects.

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8. Author Contribution

Rajesh Raveendra: Principal Author and PI of this work; Sreekala V.: Manuscript drafting, subject expert (Ayurvedic Pharmacology); Shomi Anand: Statistical analysis and referencing; Dhananjay S. Kotasthane: Guided the research work; Sanjay Kumar Singh: Critical review of the manuscript. All authors have read and agreed to the published version of the manuscript.

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