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Preclinical Evaluation Of Antidiabetic Properties Of Murraya Koenigii And Abelmoschus Esculentus In Diabetic Rats

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Abstract
The present study deals with the antidiabetic and antihyperlipidemic activities of Murraya koenigii, commonly known as curry leaves, extract on STZ-induced diabetic rats. The given dose of the extract to the rats in this study was 500 mg/kg body weight for 37 days and then estimated its effects on blood glucose and HbA1c levels and lipid profile. Results: The results indicated that Murraya koenigii has significant hypoglycemic activity since the blood glucose and HbA1c levels of the treated group were significantly reduced compared with the diabetic control group. The extract has also been found to possess antihyperlipidemic activity as there is a significant reduction in triglyceride levels and an increase in the level of HDL cholesterol, respectively. In addition, biochemical markers and histopathological examinations revealed no effect on the pancreas, liver, or kidneys due to this extract. These findings could suggest the possibility of using Murraya koenigii as a natural safe and effective treatment of diabetes mellitus, alongside its complications. Further studies should be recommended to validate these results in clinical trials.

Keywords: Murraya koenigii, antidiabetic, antihyperlipidemic, streptozotocin, blood glucose, glycosylated hemoglobin, lipid profile, histopathology, diabetes management.

1. INTRODUCTION

1.1. Background of Diabetes Mellitus

Diabetes mellitus is defined as a metabolic disease arising due to elevated blood glucose levels. This elevated blood glucose level may be the consequence of impaired insulin production, impaired action of insulin, or both parts of the insulin [1]. Diabetes is progressively being increased in number all over the world, which threatens public health due to its complications. Such complications include cardiovascular disease, nephropathy, neuropathy, and retinopathy. Two reasons for the more normal type of the infection, known as type 2 diabetes, are insulin obstruction and relative insulin deficiency. Type 1 diabetes is totally ailing in insulin and is frequently immune system.

Lifestyle factors are among the most common causes to the development of type 2 diabetes and these include a poor diet, obesity, and a general lack of physical exercise. Diabetes is characterized by persistently high levels of blood sugar that can cause damage to other body systems [2] [3]. As such, diabetes is a chronic condition that needs to be managed over an extended period of time. Even with significant advancements in the field of pharmacotherapy, the side effects and the limitations of conventional drugs for diabetes have provided alternative medicines, especially those based on medicinal plants. These therapies offer safer, more cost-effective, and more culturally acceptable approaches to the treatment of diabetes [4].

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Figure 1: Diabetes Mellitus

1.2. Importance of Medicinal Plants in Managing Diabetes

Ayurveda and Traditional Chinese Medicine are ancient medicine practices which have been using medicinal plants for the treatment of hundreds of diseases, including diabetes [5]. In a composite disease like diabetes, oxidative stress, inflammation, and metabolic dysfunction all play significant roles, and therefore the bioactive chemicals that are often found in these plants and contain multiple pharmacological effects make them useful. Medicinal plants can act through a wide range of mechanisms, which may include stimulation of the secretion of insulin, enhancement of insulin sensitivity, and/or inhibition of the enzymes responsible for carbohydrate metabolism [6]. Besides, the number of adverse effects, compared with synthetic pharmaceuticals, is usually much lower; hence, an attractive option for long-term usage. Many plant species have been reported to be hypoglycemic, and thus explained that plants have a potential therapeutic role in the prevention and treatment of diabetes, based on research done on the blood glucose lowering capacity of plants.

1.3. Overview of *Murraya koenigii* and *Abelmoschus esculentus* as Potential Antidiabetic Agents

Two of the medicinal plants studied include curry leaves, Murraya koenigii, and okra, Abelmoschus esculentus, which have been suspected to produce anti-diabetic properties. One of the most widely used herbs in South Asian food preparations, Murraya koenigii has especially high levels of alkaloids, flavonoids, among other bioactive compounds with antioxidant, anti-inflammatory, and hypoglycemic properties [7] . Several studies have shown that curry leaves are believed to enhance insulin production, reduce blood glucose levels, and protect the pancreatic β-cells from oxidative stress action. In a similar manner, Abelmoschus esculentus, also known as okra, is one of the fibrous, polysaccharide-rich, and flavonoid-rich vegetables that have been evidenced to reduce diabetes [8] . There are several studies that have shown that okra modifies glucose absorption, enhances insulin sensitivity, and reduces hyperglycemia through its effect on critical enzymes that catalyze various steps in glucose metabolism [9] [10]. Individually and collectively, these plants offer a range of interesting natural candidates to be considered for the regulation of diabetes due to the variety of mechanisms of action that they possess.

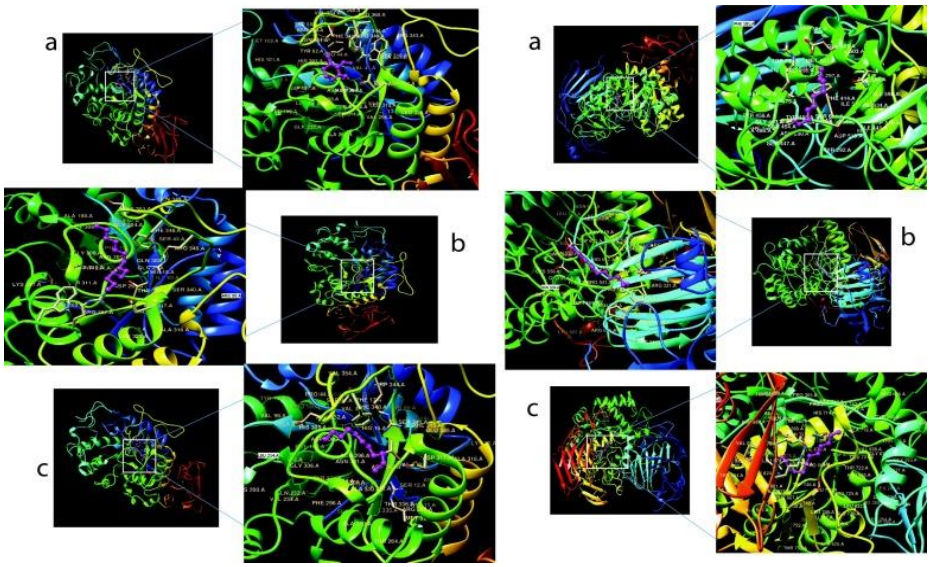

Figure 2: Antidiabetic and antioxidant potentials of Abelmoschus esculentus

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2. PHYTOCHEMICAL COMPOSITION

2.1. Bioactive Compounds of *Murraya koenigii*

A number of bioactive compounds have been reported abundant in the leaves of Murraya koenigii, including carbazole alkaloids such as mahanimbine, murrayanol, and koenimbine, that have been known to produce anti-diabetic activity [11] [12]. These have the effect of enhancing sensitivity through an increase in glucose uptake in peripheral tissues, consequently enhancing the uptake of glucose. In addition to this, flavonoids, which include quercetin and rutin, are present in the leaves and show high antioxidant activity, reducing oxidative stress that seems to be a major cause for progression of diabetes [13]. Terpenoids and phenolic compounds, obtained from the essential oils extracted from Murraya koenigii, may be responsible for the hypoglycemic and anti-inflammatory properties documented in the essential oils [14] [15]. These bioactive compounds therefore, as a collection, help modulate different metabolic pathways for an integrative approach to managing hyperglycemia and preventing problems in diabetes.

2.2. Bioactive Compounds of *Abelmoschus esculentus*

Okra, or Abelmoschus esculentus, is rich in bioactive components, which makes it valuable in the treatment of diabetes mellitus. Laboratory studies have proven that the polysaccharides in okra, such as pectin and mucilage, significantly reduce the blood glucose level following a meal by slowing down the absorption of carbohydrates from the gut lumen during digestion. Flavonoids quercetin and rutin are among those found in okra [16]. These flavonoids exhibit antioxidant and anti-inflammatory activities, which have made them part and parcel of the healing process regarding mitigating the oxidative stress that is linked with diabetes. In addition, the seeds and pods of okra are rich in saponins and tannins, both of which might be implicated in the improved mechanisms whereby insulin sensitivity is increased and hyperglycemia is reduced [17]. Because okra contains bioactive substances with synergistic effects on glucose metabolism, it might be an effective dietary adjuvant for the management of diabetes [18].

2.3. Potential Mechanisms of Action in Diabetes

Both Abelmoschus esculentus and Murraya koenigii control the blood sugar; it can be obtained in various ways. The main system of activity for Murraya koenigii is the excitement of insulin discharge delivered by the pancreatic β-cells and expanded glucose utilization in fringe tissues. Its antioxidant property will help protect the pancreas against oxidative stress, which is important for preserving its ability to synthesize insulin. Other enzymes that break down carbohydrates, such as α-amylase and α-glucosidase, are also inhibited by curry leaves, hence reducing subsequent rises in glucose after meals [19]. Similarly, Abelmoschus esculentus slows down glucose release into the circulation by regulating glucose absorption within the stomach. This is due to the presence of numerous fibres it possesses. In addition, the bioactive chemicals present in okra enhance insulin sensitivity through altered signalling pathways of the insulin receptors leading to better glucose uptake and utilization. For example, both plants have anti-inflammatory properties, which aid in the prevention of the chronic inflammation that is also fueled by insulin resistance in type 2 diabetes [20]. The pharmacologic management of diabetes may therefore be improved and more holistic through these plants because they impact several elements of glucose homeostasis.

3. METHOD

3.1. Experimental Animals

Twenty-four mature male Wistar rats were selected for the study. For this purpose, three groups of rats were randomly selected as follows:
Sham Group (Healthy control, n = 8)
Control Group (Diabetic control, n = 8)
Test Group (Treated with Murraya koenigii extract, n = 8)
The creatures were kept on a 12-hour light-dim cycle with controlled temperature scope of 22 to 25°C. Taking care of and drinking were given whenever during the review. The experimental procedure was approved by the Ethical Committee after examination.

3.2. Induction of Diabetes

The Control and Test bunches were directed a solitary intraperitoneal infusion of 55 mg/kg body weight of STZ to instigate diabetes. The component of the impact of STZ is the specific obliteration of pancreatic β-cells, consequently insulin inadequacy. The Hoax bunch was given an equivalent volume of saline as vehicle control. Blood glucose levels were estimated utilizing a glucometer following 72 hours post-STZ infusion. Creatures with glucose levels at in excess of 250 mg/dl were viewed as diabetic and remembered for the trial.

3.3. Preparation of Plant Extract

New leaves of Murraya koenigii were gathered, washed, and dried in the shade. Fine powder was ready by crushing the dried leaves. A fluid concentrate was ready by bubbling 100 g of powdered leaves in 500 ml of refined water for a specific time frame period, which was then sifted and focused with the assistance of a revolving evaporator. The ready extract

was stored in the refrigerator at 4°C for further use. Test group rats received an oral dose of Murraya koenigii extract every day for 37 continuous days at a level of 500 mg/kg body weight.

3.4. Measurement of Blood Glucose and HbA1c Levels

For the points in the experiment, blood glucose was measured three times: at baseline (pre-treatment), on day 22, and on day 37. Glucometer measurement of glucose present in blood samples drawn from the tail vein estimated blood glucose. HbA1c measurement at baseline and on the 37th day was made to monitor long-term control of blood glucose. Blood glucose concentrations (mg/dl) noted were as follows:

- Sham Group: 100 (Baseline), 100 (22nd Day), 100 (37th Day)
- Control Group: 100 (Baseline), 300 (22nd Day), 350 (37th Day)
- Test Group: 100 (Baseline), 200 (22nd Day), 150 (37th Day)

Percentages of HbA1c recorded by observation were the following

- Sham Group: 5.8 (Baseline), 5.5 (37th Day)
- Control Group: 5.4 (Baseline), 11.2 (37th Day)
- Test Group: 5.8 (Baseline), 6.4 (37th Day)

3.5. Lipid Profile Analysis

On the 37th day of the experiment, all groups were bleed to obtain blood samples for lipid profile studies. For, plasma levels of triglycerides (TG) and high-density lipoprotein (HDL) cholesterol were assayed. The triglyceride values (mg/dl) obtained were:

- Sham Group: 60 (Day 0) and 60 (22nd Day), 60 (37th Day)
- Control Group: 60 (Baseline), 100 (22nd Day), 120 (37th Day)
- Test Group: 60 (Base line), 80 (22nd Day), 60 (37th Day)

For example, at day 37, it has been seen that HDL cholesterol of the Experimental group was evidently higher than that in the Benchmark group. This further connects with the antihyperlipidemic impact of the Murraya koenigii remove.

3.6. Biochemical Marker Analysis

Biochemical indicators were used to evaluate the safety of Murraya koenigii extract on vital organs, namely the liver, kidneys, and pancreas. The measured markers included

- Pancreatic Lipase (U/L): An enzyme activity that indicates the function of the pancreas.
- Serum Glutamic-Pyruvic Transaminase (SGPT, U/L): presents the extent of liver function.
- Creatinine (mg/dl) It is the measure of renal function.

The Murraya koenigii extricate bunch was contrasted and the Benchmark group, and it showed that the concentrates had a specific safeguarding activity on these organs. There was no appreciable side effects observed in the treated group. The treated group showed minimal damaging effects on the liver, kidneys, and pancreas, which was a testimony for the safety of the extract by histopathological evaluation.

4. RESULTS AND DISCUSSION

4.1. Impact of M. koenigii leaf extract on glycosylated hemoglobin and blood glucose levels

While contrasting the blood glucose levels of the STZ Control Gathering (Diabetic Control) to the Joke Gathering (Wellbeing Control), the outcomes showed a significant increment on days 22 and 37. When contrasted with the benchmark group, the blood glucose focus was extensively lower in the gathering treated with Murraya koenigii. While contrasting the treatment bunch with the benchmark group, the Murraya koenigii moreover decisively diminished the Glycosylated Hemoglobin level. The hypoglycemic impact of Murraya koenigii is affirmed by these discoveries.

Table 1: Time point Changes in Blood Glucose Level

Group	Baseline (mg/dl)	22nd Day (mg/dl)	37th Day (mg/dl)
Sham	100	100	100
Control	100	300	350
Test	100	200	150

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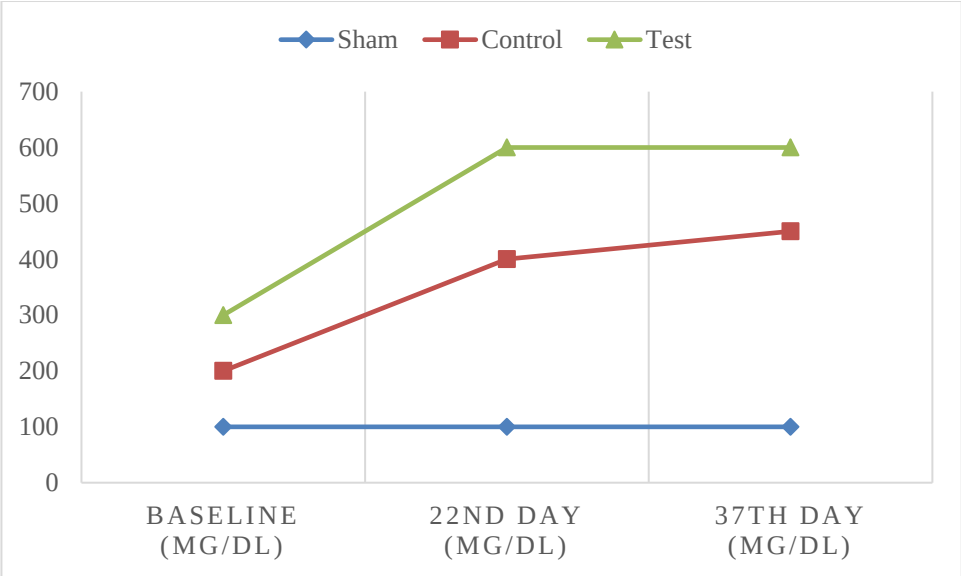

Figure 3: Time point Changes in Blood Glucose Level

Table 2: Hba1c Level Among Experimental Groups

Group	Baseline (percentage)	37th Day (percentage)
Sham	5.8	5.5
Control	5.4	11.2
Test	5.8	6.4

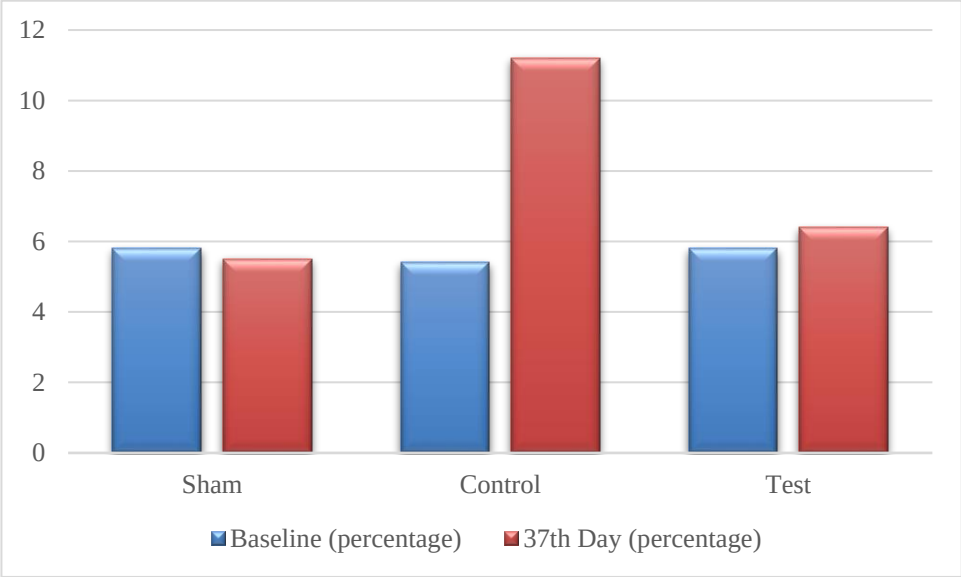

Figure 4: Hba1c Level Among Experimental Groups.

4.2. Murraya koenigii extract's impact on the lipid profile of plasma.

When contrasted with the benchmark group on day 37, the treated gathering's fatty substance level was impressively lower, demonstrating that the Murraya koenigii treatment had antihyperlipidemic activity. On the other hand, there was a huge ascent in high thickness lipoprotein (HDL) cholesterol in the treated gathering contrasted with the benchmark group. As indicated by biochemical outcomes and a histological investigation, Murraya koenigii treatment is ok for the kidney, liver, and pancreas. (Figure 6, Table 4).

4.3. Histopathological assessments

Plate 1: A: Sham group rat liver slices are shown on a photomicrograph, displaying normal architecture. B: The control group rat's liver exhibits increased inflammatory infiltration and blood vessel congestion in the central vein. C: The livers

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of the test group of rats show reduced vascular congestion, less inflammatory infiltration, and normal peripheral and central vein architecture (Figure 6a).

Table 3: Level Of Triglycerides in Different Experimental Groups

Group	Baseline	22nd Day	37th Day
Sham	60	60	60
Control	60	100	120
Test	60	80	60

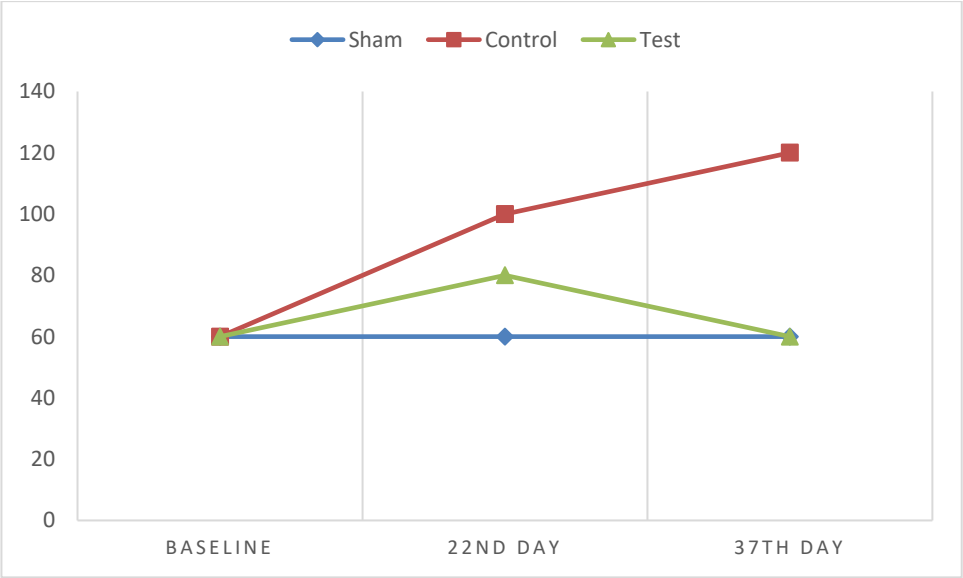

Figure 5: Level Of Triglycerides in Different Experimental Groups

Table 4: Various Experimental Groups' Safety Marker

Sr. No.	Variable	Sham Group	Control Group	Test Group
1	**Pancreatic Marker**			
	Pancreatic Lipase (U/L)	30.66 ± 2.10	48.26 ± 9.36	36.83 ± 1.50*
2	**Liver Marker**			
	SGPT (U/L)	61.25 ± 8.68	99.85 ± 10.38	77.42 ± 7.20**
3	**Kidney Marker**			
	Creatinine (mg/dl)	0.32 ± 0.07	1.27 ± 0.43	0.51 ± 0.06*

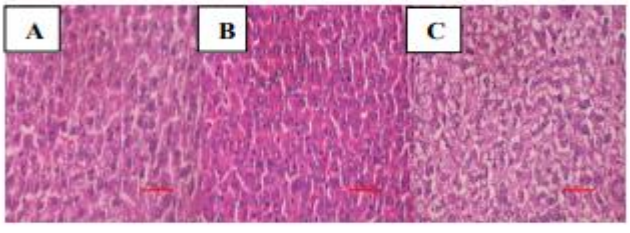

Figure 6(a): Histopathological Assessment of Liver Tissue

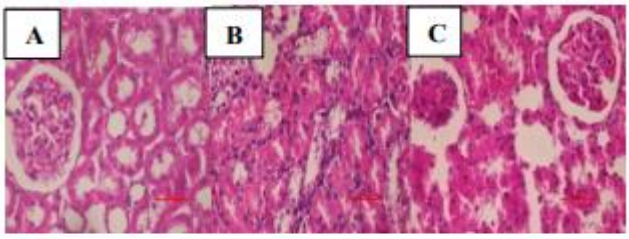

Figure 6(b): Histopathological Assessment of Kidney Tissue

Plate 2: A: A photomicrograph of the kidney sections from rats in the Sham group demonstrates the kidney's normal anatomy. B: The rats in the control group showed inflammation, hazy degeneration, tubular necrosis, and glomerular blood vessel congestion. C: The kidney of the test group exhibits decreased tubular necrosis, inflammation, and glomerular blood vessel congestion (Figure 6b).

The leaves of Murraya koenigii are accounted for to contain unpredictable oils, iron, calcium, lysine, carbs, and niacin. Following two months of treatment with fluid and methanol concentrates of Murraya koenigii, the insulin focuses in the diabetic T1 and T2 gatherings, separately, essentially expanded. The presence of alanine, leucine, starches, niacin, and press might be the reason for the raised insulin discharge in the diabetes T1 and T2 gatherings.. The longer-lasting stimulating impact on pancreatic islets' β-cells or the regeneration of pancreatic β-cells by Murraya koenigii may also be responsible for the rise in plasma insulin concentration.

A β-cytotoxin, streptozotocin causes chemical diabetes in a range of animal species, including rats, by specifically harming the pancreatic β-cells that secrete insulin.

The rationale for selecting streptozotocin as a diabetes inducer was its ability to cause irreversible diabetes mellitus with only one intraperitoneal injection by a relative necrotic impact on the pancreatic β-cells, resulting in insulin insufficiency. By impressively bringing down blood glucose and glycosylated hemoglobin in diabetic rodents treated with Murraya koenigii leaves separate (500 mg/kg body weight) comparative with untreated diabetic rodents, the ongoing examination showed the hypoglycemic activity of the test medication. Comparable examination using Murraya koenigii (200-600 mg/kg) by Venuthanet al. (2004) shown that the concentrate diminishes blood glucose levels; however, glycosylated hemoglobin levels were not measured. The current research's findings are comparable to those of the Dinesh Kumar et al. study.

5. CONCLUSION

The present research findings indicate that Murraya koenigii extract from curry leaves possessed important antihyperglycemic and antihyperlipidemic activity in STZ-induced diabetic rats. Apart from increasing HDL cholesterol, this extract proved to be effective in lowering triglycerides and enhancing HbA1c while reducing blood sugar levels. Such results show that Murraya koenigii possesses an important potential as a natural medicinal agent in the therapeutic management of diabetes along with associated lipid disorders. Histopathology studies and biochemical marker safety evaluation further confirmed the innocuous nature of the extract as no appreciable organ damage was accounted for extended periods of usage. Overall, this study presents compelling evidence that suggests Murraya koenigii may be utilized as a useful additive in the management of diabetes but more research is needed to be conducted on the efficacy of the plant in treating human patients.

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