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RESEARCH ARTICLE

Systematic Evaluation of *Premna barbata* Bark in STZ-induced Diabetes in Albino Wistar Rats

Monika and Neeraj Kumar*

Department of Pharmacology, School of Pharmaceutical Sciences, Shri Guru Ram Rai University, Patel Nagar, Dehradun – 248001, Uttarakhand, India; neerajkumar@sgrru.ac.in

Abstract

Background: Diabetes mellitus is a worldwide health problem that needs new therapeutics with multimodal action. *Premna barbata* has been conventionally used for its medicinal value, but its antidiabetic efficacy needs scientific authentication. **Aim:** The present study scientifically assesses the antidiabetic and antihyperlipidemic efficacy of *Premna barbata* stem bark extract in a streptozotocin (STZ)-nicotinamide (NA)-induced diabetic albino Wistar rat model. **Methods:** Type 2 diabetes was induced in rats through intraperitoneal administration of STZ (55-65 mg/kg) following NA pre-treatment. Rats were assigned to a normal control, diabetic control, PBSB-treated (200, 400, 800 mg/kg orally), and positive control (gliclazide) groups. Blood glucose, body weight, lipid profiles (total cholesterol, triglycerides), and oxidative stress markers (SOD, CAT, MDA) were measured every week for 28 days. **Results:** Data revealed dose-dependent glucose-lowering activities, lowering blood glucose levels significantly like gliclazide. The extract was found to possess strong antihyperlipidemic activity, with the highest dose significantly decreasing total cholesterol and reducing triglycerides moderately. Diabetic rats gained weight and underwent oxidative stress. PBSB increased peripheral glucose utilisation, optimised oral glucose tolerance, and reversed STZ-induced β-cell apoptosis. **Conclusion:** *Premna barbata* stem bark extract possesses strong antidiabetic and antihyperlipidaemic activities through various mechanisms such as improved glucose tolerance, modulation of lipids, and inhibition of oxidative stress. This validates its possibility as a useful complementary drug for diabetes and related metabolic disturbances.

Major Findings: Results show successful inhibition of diabetic hyperglycaemia and dyslipidemia in rats in a dose-related manner similar to reference drugs. The extract reversed diabetic weight loss and markers of oxidative stress, underscoring its therapeutic potential and affirming the traditional uses of *Premna barbata* in the control of diabetes.

Keywords: Antidiabetic Activity, HMG-CoA Reductase, Oxidative Stress, *Premna barbata*, Streptozotocin-induced Diabetes, Wistar Rats

Abbreviations: ALP – Alkaline Phosphatase; ANOVA – Analysis of Variance; b.wt– Body Weight; CAT – Catalase; CF – Charles Foster (rat strain); CMC – Carboxymethyl Cellulose; CPCSEA – Committee for the Purpose of Control and Supervision of Experiments on Animals; DM – Diabetes Mellitus; PBSB – Ethanolic Extract of **Premna barbata** Stem Bark; Glb – Glibenclamide; HDL – High-Density Lipoprotein; HMG-CoA – 3-Hydroxy-3-Methylglutaryl-Coenzyme A; i.p.– Intraperitoneal; LDL – Low-Density Lipoprotein; MDA – Malondialdehyde; MODY – Maturity-Onset Diabetes of the Young; NA – Nicotinamide; ROS – Reactive Oxygen Species; SD – Standard Deviation; SEM – Standard Error of Mean; SGOT(AST) – Serum Glutamate Oxaloacetate Transaminase; SGPT (ALT) – Serum Glutamate Pyruvate Transaminase; SGLT2 – Sodium-Glucose Cotransporter-2; SOD – Superoxide Dismutase; STZ – Streptozotocin; T2DM – Type 2 Diabetes Mellitus; TG – Triglycerides; WHO – World Health Organization

1. Introduction

Diabetes mellitus and metabolic disease are a worldwide health issue that strikes millions of people and hugely influences morbidity, mortality, and quality of life. The conditions are typified by multifactorial pathophysiological mechanisms, variable clinical manifestations, and a wide range of complications

*Author for correspondence

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affecting multiple organ systems[1-3]. Diabetes mellitus is recognised as a long-duration condition that alters metabolism, mainly typified by chronic hyperglycaemia. It arises due to problems in either insulin production, insulin effectiveness, or both. Insulin, a pancreatic hormone, has a significant impact on maintaining proper blood glucose levels. Either if the pancreas is incapable of secreting enough insulin or if the tissues become resistant to insulin action, glucose remains in the blood, and diabetes develops clinically[4-5] (Table 1).

The treatment of diabetes mellitus is complex and is directed towards achieving maximum glycaemic control with minimum risk of complications. Lifestyle adjustment, with dietary restriction, enhanced physical activity, and weight reduction, constitutes the foundation of therapy in both types (1 and 2) of diabetes mellitus[6-9]. Pharmacotherapy is individualised and might involve the use of oral hypoglycaemic medications, insulin therapy, or a combination of both[10-11].

Premna barbata, commonly known as Bearded *Premna*, is a deciduous shrub or small tree belonging to the family *Lamiaceae* (Figure 1). It is circulated across the eastern and northern parts of India, Nepal, Myanmar, Pakistan, as well as in Australia, Africa, and the Pacific Islands[21-23]. Traditionally, the plant is highly valued in ethnomedicine, especially among tribal communities in the Himalayan regions, Uttarakhand, and other parts of India, where it is known as "*Aganyo*" in folk language. The plant is used in several forms, such as powders, juices, pastes, and decoctions, for the treatment of a wide range of ailments[24-25] (Table 2).

1.1 Iridoids as a Chemical Constituent of *Premna barbata* Bark

Iridoids are a class of monoterpenoid compounds characterised by a cyclopentane-fused pyran ring structure. They are predominantly found as glycosides in plants, where a glucose moiety is attached to the core iridoid skeleton, enhancing their solubility and bioavailability[31,32]. The presence of iridoids in *Premna barbata* has been confirmed through phytochemical screening and the isolation of specific iridoid glycosides, notably premnosidic acid [33] (Table 3).

2. Materials and Methods

2.1 Plant Material

The Botanical Survey of India (BSI), Dehradun, Uttarakhand, India, authenticated the plant vide letter no.Tech./Herb (Ident.)/2022-23/518 with 1187 that was obtained from wildly grown area of Kumaon Region (Almora), Uttarakhand, India.

2.2 Preparation of Plant Extract (Freeze-dried Aqueous Plant Extract)

The dried plant material was shed, dried and converted to a coarse powder. Weighed coarse powder was soaked overnight in distilled water in a 1:4 ratio (100

Table 1. Aspects and metabolic syndromes of type 2 diabetes[12-20]

Aspect	Type 2 Diabetes	Metabolic Syndrome/Other Disorders
Onset	Predominantly after 40 years, but increasingly seen in youth	Typically, adulthood increases with age and obesity
Pathogenesis	Insulin resistance with relative insulin deficiency	Insulin resistance, central obesity, dyslipidemia, and hypertension
Prevalence	90–95% of diabetes cases	Affects >20% of adults in developed countries
Key Symptoms	Often asymptomatic; early polyuria, polydipsia, fatigue, gradual onset	Often asymptomatic; features include obesity, hypertension, dyslipidemia
Risk Factors	Obesity, sedentary lifestyle, family history, and age	Obesity, inactivity, and genetic factors
Treatment	Lifestyle modification, oral agents, and insulin if needed	Weight loss, exercise, and management of individual risk factors
Complications	Microvascular and macrovascular complications	Cardiovascular disease, fatty liver, PCOS
Diagnosis	Hyperglycaemia, insulin resistance, higher C-peptide	Clinical criteria: waist, BP, triglycerides, HDL, glucose
Other Types	Monogenic diabetes, secondary diabetes, LADA, MODY	Inherited metabolic disorders (e.g., PKU, Gaucher's), mitochondrial
Prevention	Preventable with lifestyle changes	Preventable with lifestyle changes

Table 2. Key features of *Premna barbata* bark[26-30]

Feature	Details
Botanical Family	*Lamiaceae* (Mint family)
Common Names	*Bearded Premna, Lammar, Karadi, Bakaar, Gineri, Vasuka, Ganhila*
Habit and Size	Deciduous shrub or small tree, 3–5 meters tall; bark greyish brown, rough, corky outside
Distribution	Himalayas, India, Nepal, Pakistan, Myanmar, Australia, Africa, Pacific
Bark Morphology	Outer surface greyish brown with grooves and furrows; inner surface wrinkled, yellowish white; astringent taste, no Odour.
Root System	Fibrous roots, 1–2 feet deep, spread horizontally up to 3–4 feet.
Major Uses	Anti-inflammatory, antibacterial, wound healing, fever, stomach issues
Key Phytochemicals	Iridoid glycosides, diterpenoids, flavonoids, alkaloids, terpenoids
Pharmacological Action	Antibacterial, anti-inflammatory, antioxidant, hepatoprotective
Microscopic Features	Cork cells, phelloderm, multiseriate medullary rays, fibres, secondary phloem
Pharmacological Activities	Antibacterial, anti-inflammatory, wound healing, febrifuge, analgesic
Cultivation and Lifespan	Perennial, moderate growth rate, lives 10–15 years; prefers well-drained soil and regular care.
Conservation Status	At risk in some regions; needs sustainable management.



Figure 1. Picture of plant: *Premna barbata.*

Table 3. Reported hypoglycaemic activity of iridoid present in *Premna barbata* bark[34-40]

Iridoid Name	Phyto-Chemical	Reported Hypoglycaemic Activity
Premnosidic acid	Iridoid glycoside	Reported in *Premna barbata*, potential activity
Diterpenoid iridoid glycosides	Iridoid glycoside	General antihyperglycemic activity in *Premna* spp.
Acyclicmonoterpenediols (Premnaodorosides D–G	Iridoid glycoside	Isolated from the *Premna* genus, potential activity
Flavonoid–iridoid Conjugates	Iridoid conjugate	General hypoglycaemic activity in *Premna* spp.
Geniposidic acid	Iridoid glycoside	Reported in *Premna* spp. potential activity
Lamiide	Iridoid glycoside	Present in *Premna* spp. potential activity
6-O-trans-p-coumaroyl -geniposidic acid	Iridoid glycoside	Isolated from *Premna* spp. potential activity
8-epi-kingiside	Iridoid glycoside	Isolated from *Premna* spp. potential activity
Premnacorymboside	Iridoid glycoside	Isolated from *Premna* spp. potential activity
Premnacorymboside B	Iridoid glycoside	Isolated from *Premna* spp. potential activity

gm of powder and 400 ml of distilled water). Soaked coarse powder was filtered using a muslin cloth[41-42]. The filtrate was collected and concentrated using a rotary evaporator. The concentrated extract was frozen at -20°C temperature and then freeze-dried under vacuum for over 24 hrs using the Lobconco Freeze Drying System (-42°C to -47°C temperature and 0.340 mbar pressure). After complete drying, the sample was collected[43-45].

2.3 *In Vivo* Study of Freeze-dried Plant Extract

Adult albino rats (CF Strain) were purchased from Animal House of Shri Guru Ram Rai University, Patel Nagar, Dehradun (CPCSE No. 264/CPCSEA/IAEC/2022/14). The animals were maintained at a room temperature of 22 ± 30 °C with 50 – 70% RH and 12:12 hrs. Of light and dark cycles[46-47]. The animals were provided with a pellet-form feed with the composition of protein (22–24%), fat (4–5%), crude fibre (4–5%), nitrogen free extracts, bengal gram (45–55%), phosphorus 15%(0.4–0.6%), calcium (1–1.5%), insoluble ash 8% and soaked bengal gram and water ad libitum. Weighing around 180-200g was utilised for the study.

2.4 Experimental Protocol

2.4.1 Induction of Diabetes

Streptozotocin (STZ), obtained from the store of School of Pharmaceutical Sciences, Shri Guru Ram Rai University, Patel Nagar and dissolved in 0.1 M citrate buffer (pH = 4.5) freshly for the dose of 60mg/kg body weight was injected intraperitoneal.

The STZ-NA rat model of type 2 diabetes mellitus is established by the protective actions of NA against β-cytotoxicity of STZ. Type 2 diabetes can be induced after injection of NA 110 mg/kg body weight, liquified in saline 15 min before STZ injection (65 mg/kg body weight, liquified in 0.1 M citrate buffer, pH 4.5) i.p.[48].

2.4.2 Grouping of Animals

A total of six groups were formed, each containing six rats.

Group 1: Control: Receive CMC (carboxymethyl cellulose) as a vehicle.

Group 2: Diabetic control: STZ administration (65 mg/kg body weight, dissolving in 0.1 M citrate buffer, pH 4.5) i.p. After a quarter of an hour of Nicotinamide (110 mg/kg body weight dissolving in saline) i.p.

Group 3: Active control: STZ administration (65 mg/kg body weight, dissolving in 0.1 M citrate buffer, pH 4.5) i.p. After a quarter of an hour of Nicotinamide (110 mg/kg body weight dissolving in saline) i.p. + Glibenclamide (10mg/kg body weight) for three weeks.

Group 4: Test group 1: STZ administration (65 mg/kg body weight, dissolving in 0.1 M citrate buffer, pH 4.5) i.p. After a quarter of an hour of Nicotinamide (110 mg/kg body weight dissolving in saline) i.p.+ 90% ethanolic plant extract at a dose of 125 mg/kg of body weight for three weeks.

Group 5: Test group 2: STZ administration (65 mg/kg body weight, dissolving in 0.1 M citrate buffer, pH 4.5) i.p. After a quarter of an hour of Nicotinamide (110 mg/kg body weight dissolving in saline) i.p. +90% ethanolic plant extract at a dose of 250 mg/kg of body weight for three weeks.

Group 6: Test group 3: STZ administration (65 mg/kg body weight, dissolving in 0.1 M citrate buffer, pH 4.5) i.p. After a quarter of an hour of Nicotinamide (110 mg/kg body weight dissolving in saline) i.p.+ 90%ethanolic plant extract at a dose of 500 mg/kg of body weight for three weeks[49].

Collection of Serum: Approximately 500 ml of blood was drawn from Retro Orbital Plexus of rats using Non-Heparinised Hematocrit capillaries (Himedia). Clotting of the blood was carried out at room temperature for a duration of 1 hour, and then stored at 4°C temperature for 1-2 hours and then Centrifugation was carried out at 3000 rpm for ten minutes, after which the serum-containing supernatant was isolated and kept at -20°C for later use[50].

3. Results and Discussion

3.1 Effect of *Premna barbata* Bark Extract on the Rat's Body Weight

Post 21 days of treatment, the diabetic control group experienced a significant decrease in body weight in comparison with the control group, and other groups did not show a significant reduction in their body weight, as shown in Table 4.

3.2 Effect of Plant Extract on Blood Glucose Level

According to the results, the aqueous extract showed strong blood sugar-lowering properties in STZ-diabetic

rats, closely matching the performance of Glibenclamide, which is shown in the following Table 5.

3.3 Effect of Plant Extract on Serum Level of SGOT in Rats

The diseased control group showed extremely high levels of SGOT as compared to the normal control, while the plant extract, Glibenclamide positive control groups significantly reduced the level of SGOT as compared to the diabetic control, as shown in the following Table 6.

3.4 Effect of Plant-based Extract on Serum Level of SGPT in Rats

The diabetic control group showed extremely high level of SGPT as compared to normal control while Plant extracts, and positive control groups significantly reduced level of SGPT as compared to diabetic control as shown in the following Table 7.

3.5 Effect of Plant-based Extract on ALP Serum Level

The diabetic control group showed a significant ($p<0.001$) rise in serum ALP level compared to the normal control group, while plant extracts and Glibenclamide positive groups significantly reduced the level of ALP as compared to the diabetic control, as shown in the following Table 8.

3.6 Effect of Plant-based Extract on the Serum Level of Creatinine

The diabetic control group showed extremely high levels of creatinine compared to the normal control group, while

Table 4. Impact of plant-based extract on the rat's body weight

Groups		Days after dosing			
	0	1	7	14	21
Control (Vehicle)	169.5 ±4.209	165.1667 ±4.070	169.166 ±4.743	169.833 ±6.954	169.942 ±4.435
Diabetic	162.6 ±7.860	149.2 ±14.475	146.2 ±18.813	143 ±22.814	140.6 ±24.814
Diabetic (125mg/kg b.wt)	171.8 ±6.478	144.333 ±3.242	134.333 ±4.842	142.333 ±7.535	142.62 ±5.474
Diabetic (250mg/kg b.wt)	164.8 ±2.982	146 ±4.545	135.8 ±4.088	151.67 ±7.545	153.4 ±5.545
Diabetic Positive Control (Glibenclamide)	169.1 ±5.023	133.67 ±2.813	128.2 ±1.536	139.2 ±2.083	141.23 ±3.032
Diabetic (500mg/kg b.wt)	170.5 ±7.928	144.4 ±5.680	146.75 ±8.440	153.5 ±7.006	157 ±4.220

Table 5. Impact of plant-based extract on blood sugar levels

Days	Normal Control	Diabetic Control	Diabetic 125mg/kg b.wt	Diabetic (250mg/kg b.wt)	Diabetic Positive Control (Glibenclamide)	Diabetic (500 mg/kg b.wt)
Initial day (Pre-induction)	95.333 ± 6.854	88.666 ± 9.492	84.667 ± 8.5153	84.1667 ± 4.756	90.833 ± 4.292	84.8 ± 3.611
1stDay	77.833 ± 8.627	249.1667 ± 19.00	257 ± 14.3201	232.33 ± 14.269	221.334 ± 12.5605	252.333 ± 18.689
7thDay	85.1667 ± 3.320	282.4 ± 16.113	84.667 ± 13.370	81 ± 3.714	83.8 ± 6.256	81.25 ±6.263
14thDay	80.333 ± 2.275	306.2 ± 8.569	81.667 ± 6.489	78.733 ± 12.197	82.2 ± 8.469	76 ± 3.937
21st Day	83.623 ±5.651	306.6 ±7.317	79.364 ±4.742	78.478 ±6.131	78.724 ±9.1	73.541 ±8.232

Table 6. Impact of Plant-Based Extract on SGOT serum level in rats

Groups	Normal control	Diabetic control [STZ]	Plant Ext. 125mg/kg	Plant Ext. 250 mg/kg	Positive control [Glb]	Aq. Ext. 500 mg/kg
Mean ± SEM	46.40911 ± 0.7155	67.26629 ±1.243	65.16063 ± 1.460	34.5644 ±1.010	32.73158 ±1.076	40.70558 ±1.965

plant extracts and Glibenclamide positive control groups significantly reduced the level of creatinine compared to the diabetic control, as shown in the following Table 9.

3.7 Effect of Plant Extract on the Serum Level of Urea in Rats

The diabetic control group showed an extremely high level of urea compared to the normal control. The plant extracts and Glibenclamide control groups significantly reduced the level of urea compared to the diabetic control, as shown in the following Table 10.

3.8 Effect of Plant Extract on the Serum Level of Cholesterol

Serum total cholesterol levels were detected to be significantly higher in the diabetic mellitus control

Table 7. Impact of plant-based extract on serum level of SGPT in rats

Groups	Normal control	Diabetic control [STZ]	Plant Ext. 125mg/kg	Plant Ext. 250mg/kg	Positive control [Glb]	Plant Ext. 500mg/kg
Mean ± SEM	13.437 ±1.081	33.851 ±0.376	26.197 ±3.183	17.857 ±1.258	17.892 ±0.751	21.216 ±0.352

Table 8. Impact of plant-based extract on ALP serum level

Groups	Normal control	Diabetic control [STZ]	Plant Ext. 125mg/kg	Plant Ext. 250mg/kg	Positive control [Glb]	Plant Ext. 500mg/kg
Mean ± SEM	40.425 ±2.434	91.058 ±2.361	52.433 ±5.349	54.065 ±0.745	38.523 ±2.311	67.833 ±1.492

Table 9. Impact of plant-based extract on the serum level of creatinine

Groups	Normal control	Diabetic control [STZ]	Plant Ext. 125mg/kg	Plant Ext. 250mg/kg	Positive control [Glb]	Plant Ext. 500mg/kg
Mean ± SEM	0.9061 ±0.0200	1.2223 ±0.05	0.8497 ±0.0467	0.8732 ±0.1056	0.9774 ±0.0422	0.9816 ±0.0388

Table 10. Impact of polyherbal extract on the serum level of urea in rats

Groups	Normal control	Diabetic control [STZ]	Plant Ext. 125mg/kg	Plant Ext. 250mg/kg	Positive control [Glb]	Plant Ext. 500mg/kg
Mean ± SEM	42.694 ±0.391	118.493 ±0.33	63.972 ±0.29	26.0273 ±0.9589	67.8082 ±0.2675	29.9657 ±0.3546

Table 11. Impact of plant-based extract on the serum level of cholesterol

Groups	Normal control	Diabetic control [STZ]	Plant Ext. 125mg/kg	Plant Ext. 250mg/kg	Positive control [Glb]	Plant Ext. 500mg/kg
Mean ± SEM	66.5401 ±0.7510	92.0683 ±1.294	42.7578 ±1.339	42.5047 ±1.518	36.1290 ±1.363	52.3719 ±0.7208

Table 12. Impact of plant-based extract on the serum level of LDL in rats

Groups	Normal control	Diabetic control [STZ]	Plant Ext. 125mg/kg	Plant Ext. 250mg/kg	Positive control [Glb]	Plant Ext. 500mg/kg
Mean ± SEM	75.8333 ±1.625	147.875 ±3.641	43.9833 ±0.8382	64.8375 ±3.838	60.515 ±1.318	60.8562 ±2.874

Table 13. Impact of plant-based extract on the serum level of triglyceride

Groups	Normal control	Diabetic control [STZ]	Plant Ext. 125mg/kg	Plant Ext. 250mg/kg	Positive control [Glb]	Plant Ext. 500mg/kg
Mean ± SEM	18.5477 ±1.329	32.7800 ±4.429	13.4169 ±1.559	5.3941 ±0.8229	11.3692 ±1.280	10.0622 ±0.664

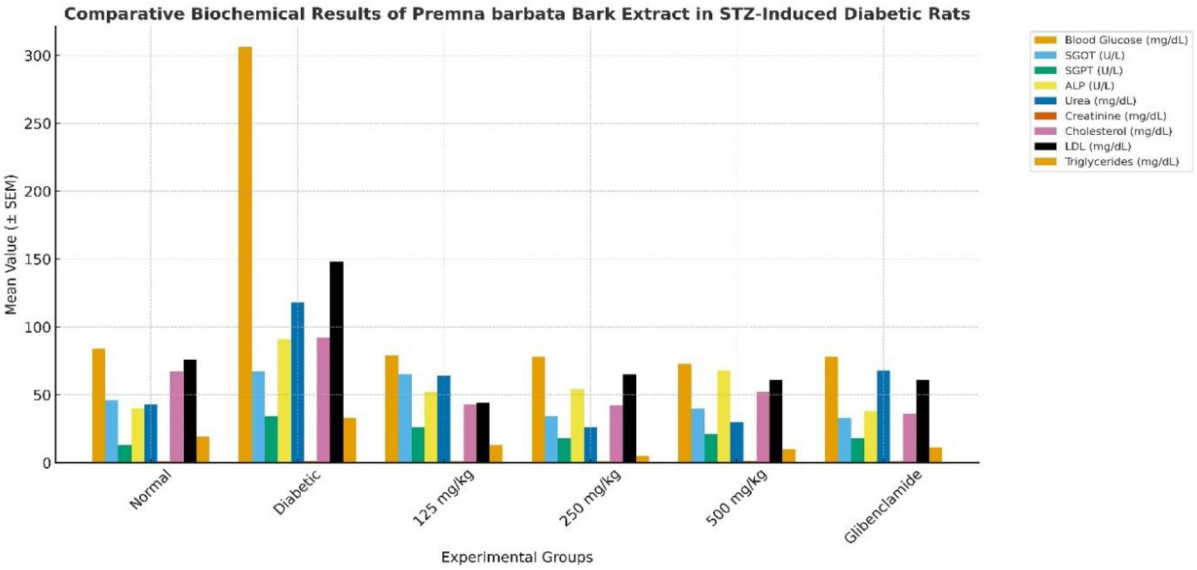


Figure 2. Showing a comparative conclusive bar chart showing the overall biochemical outcomes of *Premna barbata* bark extract in STZ-induced diabetic rats. It clearly indicates that the different doses (125, 250, and 500 mg/kg) and Glibenclamide normalise blood glucose, hepatic, renal, and lipid parameters compared with the diabetic control group.

group relative to the normal control group, while plant extracts and Glibenclamide-treated control groups significantly reduced the level of total cholesterol as compared to the diabetic control, as shown in the following Table 11.

3.9 Effect of Plant Extract on the Serum Level of LDL in Rats

The diabetic mellitus control group demonstrated elevated serum LDL levels when compared to the normal control group, while the plant extracts-treated groups and Glibenclamide control positive groups significantly reduced the LDL level in serum as compared with the diabetic control group, as shown in the following Table 12.

3.10 Effect of Plant Extract on the Serum Level of Triglyceride

The diseased control group showed a high level of triglyceride compared to the normal control, while the plant extract groups and Glibenclamide control groups significantly reduced the level of triglyceride compared to the diabetic control, as shown in the following Table 13.

4. Conclusion

The present investigation demonstrated that *Premna barbata* bark extract exerts a significant antidiabetic effect in STZ-induced diabetic rats, as evidenced by the normalisation of body weight, blood glucose, and multiple biochemical parameters when compared to the diabetic control group. Among the tested doses (125, 250, and 500 mg/kg b.wt), the 500 mg/kg dose exhibited the most pronounced improvement, showing results closely comparable to the standard drug Glibenclamide, as shown in Figure 2. Specifically, treatment with *P. barbata* extract resulted in a marked reduction in fasting blood glucose levels, with values approaching those of the normal control group by the 21st day of treatment. Similarly, serum hepatic markers such as SGOT, SGPT, and ALP-which

were significantly elevated in diabetic rats-were notably reduced following extract administration, indicating restoration of hepatic function. The extract also demonstrated nephroprotective potential by significantly lowering elevated serum creatinine and urea levels compared to the diabetic control. Lipid profile evaluation further revealed that *P. barbata* treatment effectively decreased total cholesterol, LDL, and triglyceride concentrations, reflecting an improvement in lipid metabolism and cardiovascular protection. The biochemical outcomes of *P. barbata* at higher doses paralleled those of Glibenclamide, confirming its potent antidiabetic and organ-protective efficacy.

These findings substantiate that *Premna barbata* bark extract possesses substantial hypoglycaemic, hepatoprotective, nephroprotective, and antihyperlipidemic activities, with efficacy comparable to the standard antidiabetic agent. The results support its potential as a promising natural therapeutic agent for the management of diabetes mellitus and its associated complications.

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6. Statement of Ethical Approval

All animal experimental work is done in the Department of Pharmacology, School of Pharmaceutical Sciences, Shri Guru Ram Rai University, Animal House laboratory, which is approved by CPCSEA, New Delhi.

7. Author Contribution

Neeraj Kumar: Conceptualisation, data analysis, and visualisation. Monika: Experimental work, protocol design, writing and formatting, visualisation. All authors have read and agreed to the published version of the manuscript.

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