International Journal of Pharmacology and Clinical Research

ISSN Print: 2664-7613
ISSN Online: 2664-7621
Impact Factor: (RJIF) 8.29
IJPCR 2025; 7(2): 201-206
www.pharmacologyjournal.in
Received: 15-05-2025
Accepted: 21-06-2025

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Evaluation of antidiabetic and antioxidant potential of *Mallotus apelta* leaf extracts in streptozotocin-induced diabetic rats

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DOI: https://www.doi.org/10.33545/26647613.2025.v7.i2c.110

Abstract
Herbal medicines are increasingly explored as safe alternatives for diabetes management. *Mallotus apelta* (family *Euphorbiaceae*) has been used traditionally for inflammatory and hepatic disorders but lacks scientific validation for antidiabetic activity. To evaluate the phytochemical composition, safety profile, and antidiabetic potential of *M. apelta* leaf extracts in streptozotocin (STZ)-induced diabetic rats. Leaves were extracted using successive solvents (n-hexane, ethyl acetate, methanol, aqueous). Preliminary phytochemical analysis was performed. Acute toxicity (OECD-425) was assessed. Antidiabetic activity was evaluated in STZ-induced diabetic Wistar rats for 21 days, with glibenclamide (5 mg/kg) as standard. Biochemical markers (blood glucose, lipid profile, albumin, urea, total protein, Hb), antioxidant parameters (SOD, GSH, TBARS), and histopathology were studied.
Phytochemical screening revealed alkaloids, glycosides, flavonoids, tannins, saponins, and phenolics. Acute toxicity showed no mortality up to 2000 mg/kg. Methanolic extract significantly ($p<0.01$) reduced blood glucose, improved lipid profile, elevated serum protein and hemoglobin, and restored antioxidant enzymes compared to diabetic control. Histopathology showed protection of pancreatic β-cells.
M. apelta leaf extract, particularly the methanolic fraction, demonstrates significant antidiabetic and antioxidant activities, validating its ethnomedicinal use and suggesting its potential as a natural therapeutic for diabetes.

Keywords: *Mallotus apelta*, antidiabetic, oxidative stress, herbal medicine, STZ-induced diabetes etc.

Introduction
Diabetes mellitus is a chronic metabolic disorder of global concern, primarily characterized by persistent hyperglycaemia, impaired insulin secretion, insulin resistance, and associated oxidative stress. The condition is strongly linked to complications involving the kidneys, eyes, liver, heart, and nervous system, making it one of the leading causes of morbidity and mortality worldwide. According to the World Health Organization, the prevalence of diabetes continues to rise at an alarming rate, especially in low- and middle-income countries, creating an urgent need for safe, effective, and affordable therapeutic interventions [1].

Although synthetic drugs such as sulfonylureas, biguanides, and thiazolidinediones remain the cornerstone of diabetes management, they are often associated with limitations, including high cost, undesirable side effects, and reduced efficacy with long-term use. Consequently, considerable attention has shifted toward medicinal plants and natural products as alternative or complementary therapies. Herbal medicines have historically been used to manage metabolic disorders, and many phytochemicals such as flavonoids, tannins, and alkaloids exhibit promising antidiabetic activity through mechanisms ranging from antioxidant defence to pancreatic β-cell protection [2-3].
Mallotus apelta, a member of the *Euphorbiaceae* family, is traditionally employed in treating inflammatory and hepatic conditions. However, despite its ethnomedicinal importance, its antidiabetic potential remains scientifically underexplored. This study aims to evaluate its phytochemical composition, safety profile, and efficacy in experimental diabetic models [4-6].

Materials and Method: The *Mollugo apelta* leaf powder were purchase from online portal. Powder was dried under shed at room temperature and stored in air tight container for further use.

- **Plant Material & Extraction:** Dried leaves were subjected to successive solvent extraction (n-hexane, ethyl acetate, methanol, aqueous) [5].
- **Phytochemical Screening:** Standard qualitative tests were performed. The animal ethical committee protocol number IAEC/RKDP/10/2024-25/06 [7].
- **Animals:** Female Wistar rats (150-200 g) were used. All procedures followed CPCSEA guidelines [9].
- **Acute Toxicity:** OECD-425 guideline at 2000 mg/kg [13].
- **Induction of Diabetes:** STZ (45 mg/kg i.p.) was used; rats with fasting glucose >300 mg/dl were included [7-15].

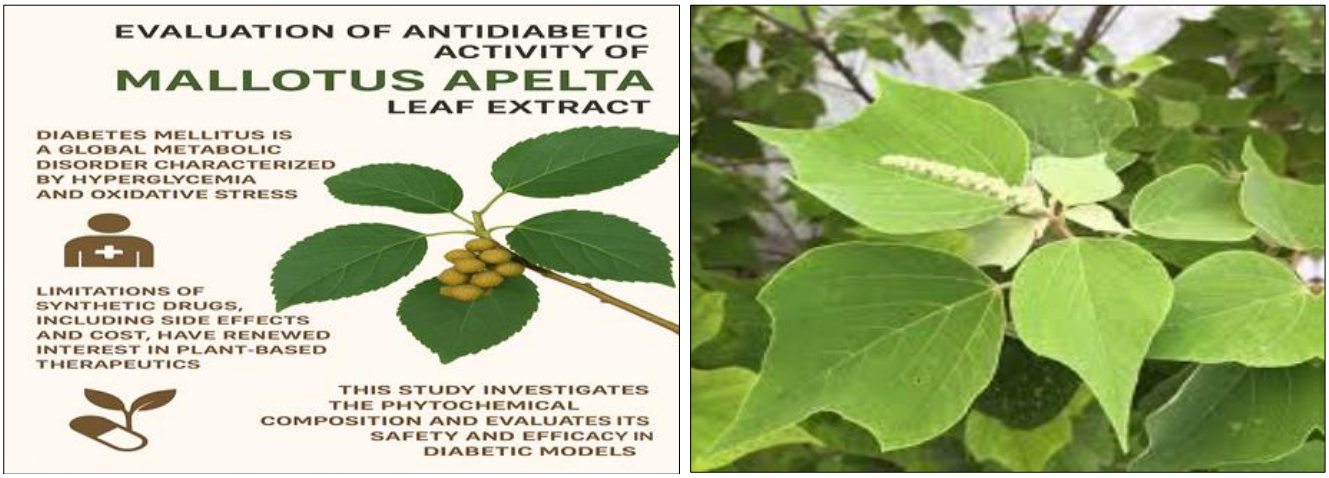

Fig 1: Pharmacological activity of *Mallotus apelta*.

Experimental Design

Table 1: pharmacological activity of *Mallotus apelta* on List of groups with their conditions:

Sr. no	Group	Condition
1.	Group-I	Normal control
2.	Group-II	Diabetic control
3.	Group-III	Standard (Glibenclamide 5 mg/kg)
4.	Group-IV	VII: Extracts (300 mg/kg, p.o.)

Parameters Assessed

Blood glucose, body & liver weight, serum albumin, urea, total protein, haemoglobin, lipid profile, antioxidant enzymes (SOD, GSH, TBARS), histopathology. [16-34]

Results: Result of Extraction Process

After the extraction of powdered drug with different solvents the percentage yield of all the extracts is given in table 6.1.

Table 2: Extractive Yield and Percentage Yield of *Mallotus apelta*:

S. No.	Extracts	Yield in gm	Percentage Yield
1.	n-Hexane	52.60	10.52%
2.	Ethyl acetate	36.82	7.36%
3.	Methanol	60.00	12.00%
4.	Aqueous	80.00	8.00%

Phytochemistry

Presence of alkaloids, glycosides, flavonoids, saponins, tannins, proteins, and phenolics confirmed.

Result of Preliminary Qualitative Phytochemical Studies: The result of phytochemical screening in given in table 3.

Table 3: Preliminary Phytochemical Screening of *Mallotus apelta* Extracts:

Sl. No.	Test	n-Hexane Extract	Ethyl acetate Extract	Methanolic Extract	Aqueous Extract
i	Alkaloids				
	A. Mayer's Test	+	-	+	-
	B. Dragandroff'sTest	-	+	+	-
	C. Wagner's Test	-	+	-	-
	D. Hager's test	+	+	+	+
ii	Carbohydrates	+	+	+	+

	A. Molish'sTest B. Barfoed'sTest C. Bendict'sTest D. Fehling, Test	- - -	- - -	- - +	+ - -
iii	Flavonoids A. Shinoda Test B. Ferric chloride Test C. Alkaline Test D. Lead acetate Test	- - + -	- - + -	+ - + -	- + - -
iv	Steroids A. Salkowski Test B. Liebermann Buchard'sTest	- -	- -	+ +	+ -
	C. Sulphur Test	+	+	+	-
v	Glycosides A. Balget'sTest B. Keller- Killani Test C. Bromine water Test D. Legal's Test	- + - -	+ + - -	+ + + -	+ - - -
Vi	Triterpenoids A. Libermann-Burchard'sTest B. Salkowski's Test	- -	- -	- -	- -
vii	Proteins A. Millon's Test B. Ninhydrin Test C. Xanthoproteic Test D. Burettes	+ + - -	+ - + -	+ - + -	+ + + -
Viii	Tannins A. Ferric chloride Test B. Gelatin Test	- +	+ -	- -	- -
ix	Saponins A. Foam Test B. HaemolysisTest	- -	- -	- -	+ -

Result of Toxicity: No mortality or abnormal behavior up to 2000 mg/kg. In both phase I and Phase II procedures, none of the animals show any toxicity upon the single administration of HEMA, EAEMA, MEMA and AEMA (2000 mg/kg). Hence the procedure is repeated by increasing the dose of extracts (3000 mg/kg). None of the animals had shown any toxicity. Thus, $1/10^{th}$ of maximum dose (300 mg/kg) tested was selected for the present study**.**

Result of Blood Glucose

Methanolic extract (MEMA) produced significant reduction over 21 days ($p<0.01$ vs diabetic control).

Table 4: Effect of *Mallotus apelta Plant* Extracts on Blood Glucose Levels in STZ Induced Diabetic Rats

Groups	Treatment	Blood Glucose Levels (mg/dl)			
		0 day	7 days	14 days	21 days
Group-I	Saline	94.82±4.58	91.67 ±5.62 ***	91.50±6.81 ***	101.0±4.13 ***
Group-II	Saline + STZ (45mg/kg)	377.2±18.41	388.7±12.90	356.5±14.30	321.7±09.19
Group-III	Glibenclamide (5mg/kg) + STZ (45mg/kg)	389.8±27.04	284.0±13.90 ***	184.0±14.06 ***	99.0±7.24 ***
Group-IV	MEMA (300mg/kg) + STZ (45mg/kg)	368.8±13.52	296.2±09.92 **	192.0±7.80 ***	108.8±5.30 ***

Values are Mean±SEM (n=6) one way ANOVA followed by Dunnett's test. Were, *** $P<0.001$, ** $P<0.01$, * $P<0.05$ and ns represents Not significant. All the values are compared with the diabetic control group, STZ- Streptozotocin, MEMA - Methanolic extract of *Mallotus apelta*.

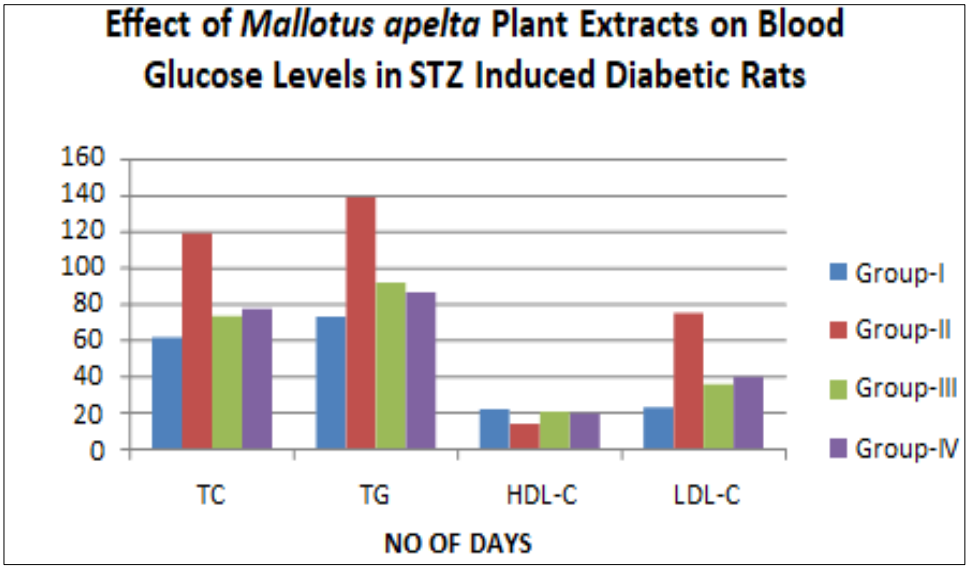

Fig 2: Effect of *Mallotus apelta* Plant Extracts on Blood Glucose Levels in STZ Induced Diabetic Rats.

Result of Biochemical Parameters: MEMA improved serum proteins, albumin, Hb, and lipid profile.

Table 5: Effect of *Mallotus apelta* Extract on Biochemical Parameters in STZ-Induced Diabetic Rats

Parameter	Group I (Normal)	Group II (Diabetic Control)	Group III (Glibenclamide)	Group IV (MEMA 300 mg/kg)
Serum Albumin (g/dl)	3.54±0.09***	1.93±0.11	3.23±0.11***	3.82±0.09***
Serum Urea (mg/dl)	31.69±0.76***	58.48±2.46	34.91±0.90***	38.49±2.89***
Serum Total Protein (g/dl)	11.04±0.31***	7.61±0.20	10.64±0.25***	9.39±0.17***
Haemoglobin (g/dl)	15.13±0.32***	11.03±0.54	14.77±0.39***	15.63±0.27***
TC (mg/dl)	60.8±1.08***	128.28±3.15	72.73±0.81***	77.22±2.82***
TG (mg/dl)	72.10±4.69***	137.68±10.03	90.89±6.88***	85.87±5.91***
HDL-C (mg/dl)	21.36±0.42***	13.65±0.72	20.11±0.82***	19.31±0.37***
LDL-C (mg/dl)	22.47±0.90***	74.47±3.21	35.44±0.62***	39.44±2.89***
VLDL-C (mg/dl)	12.72±0.92***	25.84±2.00	12.94±0.98***	14.24±0.91***

Values: Mean±SEM (n=6), ANOVA followed by Dunnett's test; ***P<0.001 vs. diabetic control.

Result of Oxidative Stress Markers: MEMA increased SOD and GSH while reducing TBARS.

Table 6: Effect of *Mallotus apelta* Extract on Antioxidant Parameters in STZ-Induced Diabetic Rats

Parameter	Group I (Normal)	Group II (Diabetic Control)	Group III (Glibenclamide)	Group IV (MEMA 300 mg/kg)
SOD (U/mg protein)	15.00±0.39***	09.68±0.46	14.02±0.40***	13.57±0.30***
TBARS (nmol MDA/100 mg tissue)	1.23±0.05***	03.97±0.26	1.57±0.08***	2.07±0.14***
GSH (mM/100 mg tissue)	44.91±0.77***	31.49±2.80	43.09±0.61***	42.57±0.58***

Values: Mean±SEM (n=6), one-way ANOVA followed by Dunnett's test. ***P<0.001 vs. diabetic control.

Result of Histopathology

Preservation of pancreatic β-cell integrity observed in MEMA-treated rats.

a) Group I (Normal control): Normal pancreatic architecture with intact lobules, well-defined islets of Langerhans, abundant β-cells (70%) and α-cells (25%).
b) Group II (Diabetic control, STZ): Marked reduction in islet number, decreased β-cells (30%), increased α-cells (65%), degenerated β-cells, and lymphocytic infiltration.
c) Group III (STZ + Glibenclamide): Improved islet structure with increased β-cells (60%) and reduced α-cells (35%); few congested vessels noted.
d) Group IV (STZ + Hexane extract): Small islets with moderate β-cells (50%) and α-cells (45%); degenerated β-cells present.
e) Group V (STZ + Ethyl acetate extract): Small islets with β-cells (55%) and α-cells (40%); some degeneration observed.
f) Group VI (STZ + Methanol extract): Large islets with marked β-cell restoration (75%) and reduced α-cells (20%); vascular congestion seen.
g) Group VII (STZ + Aqueous extract): Islets with increased β-cells (65%) and α-cells (30%); vascular spaces present.

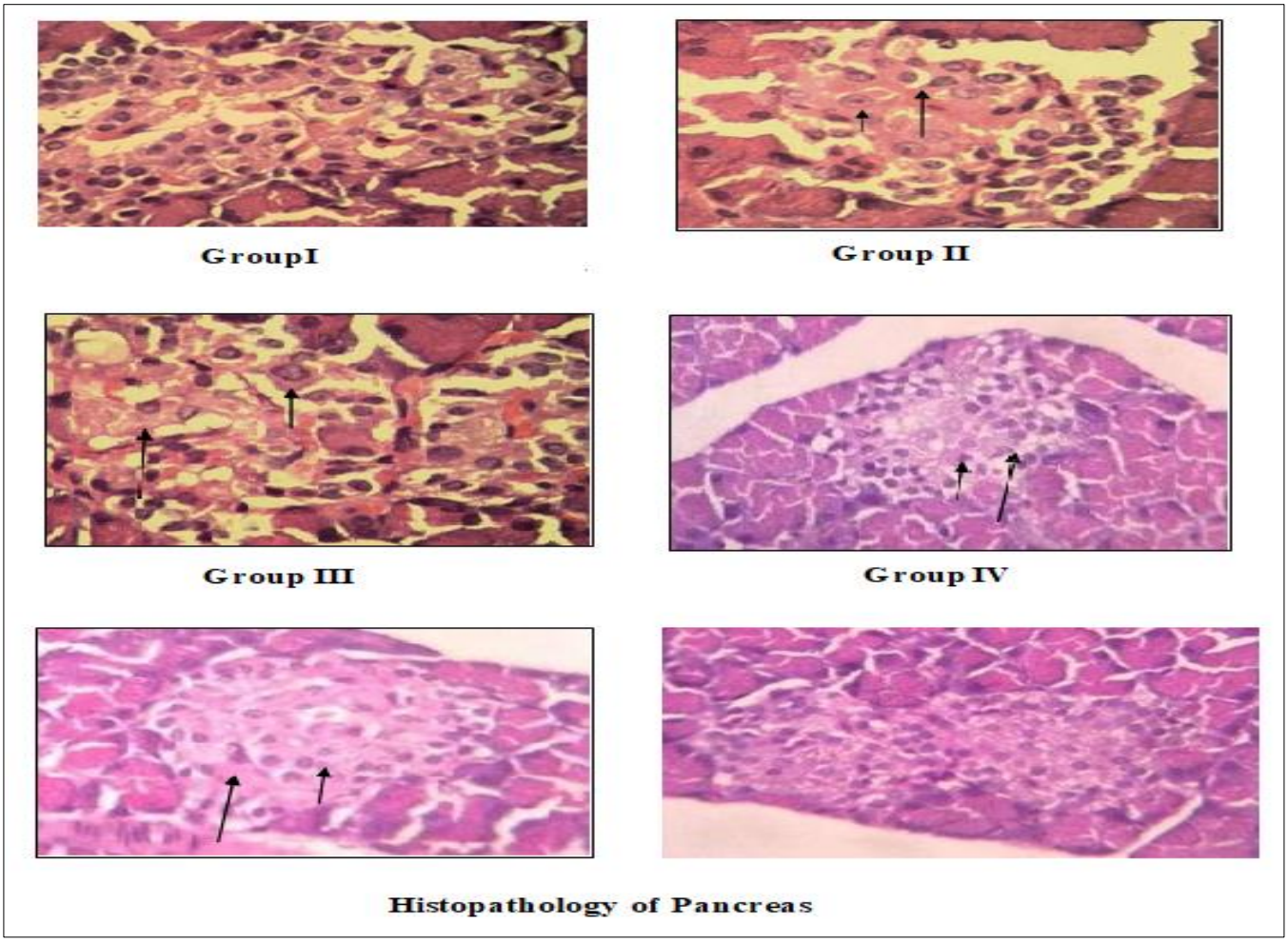

Fig 3: Result of Histopathology of four different groups.

Discussion

The study demonstrates that *M. apelta* leaf extracts, especially methanolic, possess strong antihyperglycemic and antioxidant activity. The effect may be attributed to flavonoids, glycosides, and tannins, known for β-cell protection and insulin sensitivity enhancement. Improvement in oxidative stress markers suggests dual action: glycemic control and antioxidant defense.

Conclusion: Methanolic extract of *M. apelta* leaves shows promising antidiabetic and antioxidant potential in STZ-induced diabetes, supporting its traditional use and warranting further isolation of bioactive compounds and clinical studies.

Acknowledgments

The authors thank Vedica College of B. Pharmacy, RKDF University, for providing facilities.

- **Conflict of Interest:** Authors doesn't have any conflict of interest.
- **Funding: NA**

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