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Evaluation Of Antidiabetic Activity Of Ethanolic Extract Of *Mesua Ferrea* Leaves In Experimental Animal

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Abstract: This research investigates the potential antidiabetic properties of the ethanolic extract derived from the leaves of *Mesua ferrea* L in a rat model. The study extracted *Mesua ferrea* L. (MFLE) leaves using ethanol, followed by phytochemical analysis. Diabetes was induced in Wistar albino rats using Alloxan (100 mg/kg) and Streptozotocin (50 mg/kg) via intraperitoneal injection. Two oral doses of MFLE (250 mg/kg and 500 mg/kg) were tested, with a control group receiving Glibenclamide (5 mg/kg). The effects were assessed by fasting blood glucose levels, serum lipid profiles, and histopathological examination of pancreatic tissues. Phytochemical screening showed the presence of several bioactive compounds, including flavonoids, alkaloids, glycosides, and triterpenoids. Diabetic rats treated with both doses of MFLE had a significant drop in blood glucose levels, showing a dose-dependent effect. Microscopic examination revealed clear regeneration of pancreatic β-cells in the MFLE-treated groups, suggesting a healing effect similar to Glibenclamide. The results of this study indicate that the ethanolic extract of *Mesua ferrea* L leaves has promising antidiabetic activity, suggesting its potential as a therapeutic agent for managing diabetes mellitus induced by Alloxan and Streptozotocin.

Keywords: Alloxan, Antidiabetic activity, *Mesua ferrea* L, Streptozotocin

I. INTRODUCTION

Diabetes mellitus is defined by the American Diabetes Association (ADA) Expert Committee in their 1997 recommendations as “a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycaemia is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidney, nerves, heart and blood vessels.” [1] Thus, diabetes covers a wide range of heterogeneous diseases. Recent data from the International Diabetes Federation and WHO indicate that the number of people affected by diabetes worldwide is set to rise sharply, growing from 382 million in 2013 to an estimated 592 million by 2035. India faces a significant challenge, with 65.1 million individuals currently managing diabetes, placing it second only to China, where 98.41 million people are affected by the disease. [2]

Diabetes mellitus (DM) is primarily classified into three distinct types. Type 1 diabetes is a condition where the pancreas is unable to produce adequate insulin due to the autoimmune destruction of beta cells, necessitating lifelong insulin therapy. Conversely, Type 2 diabetes results from the body's reduced sensitivity to its own insulin, often managed through a combination of dietary adjustments, physical activity, and pharmacological interventions. This form of diabetes is the most widespread, accounting for approximately 90-95% of all diagnosed cases. The third type, gestational diabetes, emerges during pregnancy and demands meticulous management to ensure the well-being of both the mother and the developing foetus. [3]

For many years, medicinal plants have played a crucial role as sources of effective antidiabetic substances. In numerous developing countries, these plants are widely utilized to manage diabetes, providing a cost-effective alternative to standard medications. Nowadays, there is a growing recommendation to use medicinal plants for diabetes treatment, as they contain various bioactive compounds like flavonoids, terpenoids, saponins, carotenoids, alkaloids, and glycosides, which are believed to have antidiabetic effects. This natural approach offers an accessible and economical way to manage diabetes, particularly in regions where the expense of conventional drugs is burdensome. [4]

The increasing prevalence of diabetes has become a significant concern for both healthcare professionals and the public. While there are numerous pharmaceutical treatments available, the use of medicinal plants for managing diabetes has proven to be highly effective. These natural remedies, characterized by their low toxicity and absence of side effects, offer a promising alternative for diabetes treatment worldwide. [5]

Herbal medicine is seeing a rise in popularity across both developing and developed countries, largely due to its natural basis and reduced side effects. Many of today's traditional treatments come from medicinal plants, which are favored for their lower toxicity, minimal adverse reactions, cost-efficiency, and greater accessibility compared to conventional drugs. [6] One such ancient medicinal plant with significant value in many cultures is *Mesua ferrea* L, locally known as Nageswar or Nagkesar. *Mesua ferrea* L are worthy for advance study as it predominantly contains flavonoids and triterpenoids which is a major phytoconstituent in any antidiabetic study, with low toxicity and limited research on invivo animal study. However, intensive survey revealed an inadequacy of reported scientific data for the antidiabetic activity of leaves of *Mesua ferrea*. [7] Hence, the present study has been designed to evaluate *Mesua ferrea* leaf extract for the antidiabetic potential using experimental animal models.

II. MATERIALS AND METHODS

2.1 Drugs and Chemicals:

Chemicals such as Alloxan monohydrate, Streptozotocin and Glibenclamide were of pure analytical grade and procured from a local supplier.

2.2 Preparation of ethanolic extract of root

The collected leaves will be dried in shade and crushed to coarse powder, extracted by maceration with ethanol (95%) followed by occasional stirring and allow to stand at room temperature for at least 3-7days. After 72 hours, the mixture will be filtered and the residue will be re-macerated twice for the same duration of hours and the mixture is filtered again. The combined filtrate will be dried and the residue is discarded. The dried extract will be then stored in a refrigerator until further use. [8]

2.3 Dose selection of *Mesua ferrea* L. leaf ethanolic extract (MFLE): [9]

The dose selected for the study is 250mg/kg and 500mg/kg of the ethanolic extract of leaves of *Mesua ferrea* L, based on a prior study that assessed acute toxicity at a maximum dose of 2000 mg/kg. The body weight of the rats used in the experiment was taken into consideration when determining these dosages.

2.4 Preliminary phytochemical screening of alcoholic extract

The ethanolic extract of *Mesua ferrea* L was subjected to preliminary phytochemical screening as per the standard procedure.

2.5 Experimental Animals

Wistar Albino rats (175 to 225 g) of either sex was used for this study. They were maintained under standard conditions (temperature 22 ± 2°C, relative humidity 60±5% and 12 h light/dark cycle) and had free access to standard pellet diet and water and libitum. The animals were housed in sanitized polypropylene cages containing sterile paddy husk as bedding. The Institutional Animal Ethics Committee reviewed and approved the experimental protocol (**Approval no: SCP/IAEC/F150/P220/2023**). All the procedures were performed in accordance with Institutional Animal ethics committee constituted as per the direction of the Committee for the Control and Supervision of Experiments on Animals (CCSEA). [10]

III. EVALUATION OF ANTIDIABETIC ACTIVITY

3.1 ALLOXAN INDUCED DIABETIC ACTIVITY IN RATS:

The Wistar albino rats (175-225g) of either sex were randomly divided into five groups of six each. The different groups were assigned as follows.

Group I: Normal control (Vehicle)
Group II: Diabetic control (Alloxan 100 mg/kg, i.p on 1st day)
Group III: Alloxan 100 mg/kg, i.p on 1st day + standard Glibenclamide 5 mg/kg, p.o
Group IV: Diabetic animals (Alloxan 100 mg/kg, i.p on 1st day + Mesua ferrea leaf extract 250 mg/Kg, p.o)
Group V: Diabetic animals (Alloxan 100 mg/kg, i.p on 1st day + Mesua ferrea leaf Extract 500 mg/Kg, p.o)

Treatment:

All the animals except group I was made diabetic by a single intra peritoneal injection of Alloxan monohydrate (100mg/kg body weight) in normal saline. After two days of Alloxan injection the blood glucose level was assessed using glucometer and the animals having blood sugar level >200 mg/dl were selected for the study. Plant extract was given orally. All the treatment was given orally once daily for entire 30 days.

Evaluation:

Starting from the first day of treatment, blood glucose levels will be checked weekly (on days 0, 7, 14, and 21) through tail vein puncture using a glucometer. Body weight, as well as food and water intake, will also be recorded every week throughout the entire experimental period. On the 30th day of treatment, all animals will be anesthetized using ether, and blood will be collected via cardiac puncture. The blood will then be centrifuged at 2500 rpm for 15 minutes and analyzed for biochemical parameters such as fasting glucose, total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol using specific kits. The color intensity of the complexes formed with these reagents will be measured using a semi-automated analyzer. At the end of the experiment, after collecting blood for biochemical analysis, all animals will be sacrificed, and their pancreases will be removed for histopathological examination.

Histopathological studies:

Pancreas was allowed to fix in 10% formalin. Washed in running water followed by dehydration with isopropyl alcohol and impregnated with paraffin wax. Section was made using microtome. After staining with eosin, the different histopathological indices were determined.

3.2 STREPTOZOTOCIN INDUCED DIABETIC ACTIVITY IN RATS [10,11]:

The Wistar albino rats (175-225 g) of either sex were randomly divided into five groups of six each. The different groups were assigned as follows

Group I: Normal control (Vehicle)
Group II: Diabetic control (Streptozotocin 50 mg/kg, i.p on 1st day)
Group III: (Streptozotocin 50 mg/kg, i.p on 1st day + Standard Glibenclamide 5 mg/Kg, p.o)
Group IV: Diabetic animals (Streptozotocin 50 mg/kg, i.p on 1st day + Mesua ferrea leaf Extract 250mg/Kg, p.o)
Group V: Diabetic animals (Streptozotocin 50mg/kg, i.p on 1st day + Mesua ferrea leaf Extract 500mg/Kg, p.o)

Treatment

All the animals except group I was made diabetic by a single intra peritoneal injection of Alloxan monohydrate (100mg/kg body weight) in normal saline. After two days of Alloxan injection the blood glucose level was assessed using glucometer and the animals having blood sugar level >200 mg/dl were selected for the study. Plant extract was given orally. All the treatment was given orally once daily for entire 30 days.

Evaluation

Starting from the first day of treatment, blood glucose levels will be checked weekly (on days 0, 7, 14, and 21) through tail vein puncture using a glucometer. Body weight, as well as food and water intake, will also be recorded every week throughout the entire experimental period. On the 30th day of treatment, all animals will be anesthetized using ether, and blood will be collected via cardiac puncture. The blood will then be centrifuged at 2500 rpm for 15 minutes and analyzed for biochemical parameters such as fasting glucose, total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol using specific kits. The color intensity of the complexes formed with these reagents will be measured using a semi-automated analyzer. At the end of the experiment, after collecting blood for biochemical analysis, all animals will be sacrificed, and their pancreases will be removed for histopathological examination.

Histopathological studies:

Pancreas was allowed to fix in 10% formalin. Washed in running water followed by dehydration with isopropyl alcohol and impregnated with paraffin wax. Section was made using microtome. After staining with eosin, the different histopathological indices were determined.

3.3 Methods for estimation of biomarkers

The biochemical parameters were estimated as per the standard procedure prescribed by the manufacturer's instruction manual provided in the kit using semi-autoanalyzer [12,13].

3.4 Statistical analysis

All data were expressed as Mean ± SEM. The statistical significance between groups were compared using one-way ANOVA, followed by Dunnett's multiple comparison test.

IV. RESULTS

Preliminary phytochemical screening

The preliminary phytochemical test of *Mesua ferrea* leaf extract is performed and the results showed the presence of Carbohydrates, alkaloids, flavonoids, glycosides, Triterpenoids, Coumarin, Phytosterols, Volatile oil, and Resins.

Alloxan induced antidiabetic activity:

At the start of the study (day 0), all groups had fasting blood glucose (FBG) levels between 70-100 mg/dl. However, administering alloxan (100 mg/kg, i.p.) in normal saline caused FBG levels to rise above 200 mg/dl within 48 hours. Table 1 summarize the changes in FBG levels across the groups after repeated treatments. The diabetic control group experienced a consistent and significant rise in FBG over the study period. In contrast, repeated doses of glibenclamide (5 mg/kg) led to a notable ($p<0.01$) reduction in FBG compared to the diabetic control group. Additionally, MFLE treatment at 250 mg/kg and 500 mg/kg showed a significant ($p<0.01$) decrease in FBG on days 7, 14, 21, and 30 when compared to the diabetic control group.

Table no 1: Effect of ethanolic extract of leaves of *Mesua ferrea* L on blood glucose level in alloxan induced diabetic rat.

Groups	Blood glucose level (mg/dL)				
	Initial	Day 7	Day 14	Day 21	Day 30
Normal	89.167±1.132	89.667± 1.205	90.667± 1.195	89.833± 1.191	90.333± 1.887
Diabetic control	293.667± 1.311$^{\#}$	299.167± 1.295$^{\#}$	305.667± 1.309$^{\#}$	311.167± 1.265$^{\#}$	317.167± 1.345$^{\#}$
Glibenclamide (5 mg/kg)	288.0± 1.987***	197.333± 1.876***	182.5± 1.999***	154.167± 2.006***	132.167±2.013***
MFLE (250mg/kg)	294.0± 1.782*	261.167± 1.872*	249.5± 1.954*	231.167± 1.655**	182.0± 1.731*
MFLE (500mg/kg)	292.167± 1.702**	249.167±1.688**	234± 1.437**	217.167± 1.598**	155.167± 1.632**

Values are expressed as mean± S.E.M, n=6 in all group except in diabetic control, one way ANOVA followed by Dunnette's test *p<0.05. **p<0.01, ***p<0.001 when compared with diabetic control rats, # p<0.001 which is compared with normal control rats. Values are significantly different from normal with control group.

STZ induces anti diabetic activity

At the beginning of the study (day 0), all groups had fasting blood glucose (FBG) levels between 70-100 mg/dl. Following treatment with STZ (50 mg/kg, i.p.) in normal saline, FBG levels increased beyond 200 mg/dl within 48 hours. The alterations in FBG after repeated drug dosing are detailed in Table 2. The diabetic control group demonstrated a notable rise in FBG throughout the experiment. On the other hand, glibenclamide (5 mg/kg) significantly ($p<0.01$) lowered FBG compared to the diabetic control. Additionally, MFLE at 250 mg/kg and 500 mg/kg doses significantly ($p<0.05$) decreased FBG levels on days 7, 14, 21, and 30 when compared to the diabetic control group.

Table no 2: Effect of ethanolic extract of leaves of *Mesua ferrea* L on blood glucose level in STZ induces diabetic rats.

Groups	Blood glucose level (mg/dL)				
	Initial	Day 7	Day 14	Day 21	Day 30
Normal	91.167± 1.032	88.176± 1.132	90.667± 1.209	89.722± 1.197	91.767± 1.884
Diabetic control	292.833± 1.431$^{\#}$	301.433± 1.356$^{\#}$	306.733± 1.398$^{\#}$	312.455± 1.265$^{\#}$	319.877± 1.402$^{\#}$
Glibenclamide (5 mg/kg)	294.333±1.875***	205.544±1.988***	185.577± 2.03***	159.5± 1.998***	135.411± 2.133***
MFLE (250mg/kg)	299.0± 1.769*	266.777± 1.987*	251.167± 1.854*	239.988± 1.734*	189.0± 1.667*
MFLE (500mg/kg)	297.167± 1.668**	248.5± 1.659**	231.0± 1.437**	215.167± 1.498*	159.766± 1.632**

Values are expressed as mean± S.E.M, n=6 in all group except in diabetic control, one way ANOVA followed by Dunette's test *p<0.05. **p<0.01, ***p<0.001 when compared with diabetic control rats, # p<0.001 which is compared with normal control rats. Values are significantly different from normal with control group.

Effect of ethanolic extract of leaves of *Mesua ferrea* L on serum cholesterol, triglycerides, HDL and LDL in alloxan and STZ induced diabetic rats:

All doses of MFLE showed a significant ($p<0.05$) reduction in the elevated levels of total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL) in diabetic rats. Additionally, HDL levels were significantly increased. When compared to the diabetic control group, these changes in lipid profile were notably different ($p<0.05$) in the MFLE-treated diabetic rats. Results are summarized in Table No. 3 and 4 and respectively.

Table no 3: Effect of *Mesua ferrea* L leaf extract on serum cholesterol, triglycerides, HDL, and LDL, in Alloxan induced diabetic rats.

Groups	Serum Biochemical Parameters (mg/dL)			
	Cholesterol	Triglyceride	HDL	LDL
Normal	65.43± 1.257	136.75± 1.097	43.9± 1.164	27.8± 1.229
Diabetic control	187.79± 1.98$^{\#}$	205.3± 2.008$^{\#}$	30.58± 1.998$^{\#}$	79.93± 1.897$^{\#}$
Glibenclamide (5 mg/kg)	76.58± 1.887***	115.7± 1.799***	45.98± 1.761***	33.81± 1.814***
MFLE (250mg/kg)	139.87± 2.05*	169.56± 1.985*	32.99± 2.003**	52.59± 1.901**
MFLE (500mg/kg)	102.31± 1.765**	144.67± 1.699**	37.8± 1.701**	41.11± 1.811**
Values are expressed as Mean± S.E.M (n=6). One way ANOVA followed by Dunette's test. *p<0.05, **p<0.01, ***p<0.001 when compared with diabetic control rats, # p<0.001 which is compared to normal control rats. Values are significantly different from normal with control group.				

Table no 4: Effect of *Mesua ferrea* L leaf extract on serum cholesterol, triglycerides, HDL, and LDL in STZ induced diabetic

Groups	Serum Biochemical Parameters (mg/dL)			
	Cholesterol	Triglyceride	HDL	LDL
Normal	78.65± 1.307	143.77± 1.113	54.31± 1.199	23.79± 1.257
Diabetic control	197.41± 2.008$^{\#}$	206.9± 1.973$^{\#}$	29.89± 2.073$^{\#}$	81.88± 1.921$^{\#}$
Glibenclamide (5 mg/kg)	99.8± 1.899***	114.45± 1.802***	47.11± 1.754***	34.76± 1.814***
MFLE (250mg/kg)	141.87± 1.985*	173.54± 2.043*	33.47± 2.003**	57.9± 1.922**
MFLE (500mg/kg)	109.55± 1.785**	148.9± 1.711**	38.99± 1.643*	43.31± 1.811**
Values are expressed as Mean± S.E.M (n=6). One way ANOVA followed by Dunette's test. *p<0.05, **p<0.01, ***p<0.001 when compared with diabetic control rats, # p<0.001 which is compared to normal control rats. Values are significantly different from normal with control group.				

Table no 5: Bodyweight in Alloxan induced diabetic rats

Groups	BODY WEIGHT (g)				
	Initial	Day 7	Day 14	Day 21	Day 30
Normal	215.0± 1.561	216.4± 1.478	215.7± 1.498	217.8± 1.506	219.5± 1.511
Diabetic control	235.5± 1.975$^{\#}$	227.8± 1.876$^{\#}$	223.5± 2.155$^{\#}$	220.2± 2.079$^{\#}$	214± 1.999$^{\#}$
Glibenclamide (5 mg/kg)	225.0± 1.657***	221.5± 1.711***	223.7± 1.789***	225.6± 1.611***	227.2± 1.699***
MFLE (250mg/kg)	210.5± 2.008*	206.5± 1.99*	205.6± 2.011*	205.9± 1.899*	208.9± 2.015*
MFLE (500mg/kg)	220.8± 1.756**	210.4± 1.801**	213.2± 1.709**	218.7± 1.699*	221.9± 1.678*
Values are expressed as mean± S.E.M, n=6 in all group except in diabetic control, one way ANOVA followed by Dunette's test *p<0.05. **p<0.01, ***p<0.001 when compared with diabetic control rats, # p<0.001 which is compared with normal control rats.					

Table no 6: Bodyweight in STZ induced diabetic rats.

Groups	BODY WEIGHT (g)				
	Initial	**Day 7**	**Day 14**	**Day 21**	**Day 30**
Normal	235.0± 1.299	236.5± 1.478	238.2± 1.509	238.7± 1.315	241.9± 1.511
Diabetic control	250.5± 2.114$^{\#}$	245.9± 1.987$^{\#}$	243.7± 1.879$^{\#}$	240.9± 2.079$^{\#}$	236.8± 1.902$^{\#}$
Glibenclamide (5 mg/kg)	243.2± 1.799***	237.8± 1.765***	238.9± 1.699***	240.9± 1.611**	245.7± 1.781***
MFLE (250mg/kg)	233.7± 2.05*	225.6± 1.988*	226.7± 2.011*	224.9± 1.877*	227.2± 2.011**
MFLE (500mg/kg)	228.4± 1.699**	214.6± 1.701*	217.3± 1.811**	224.7± 1.674*	230.1± 1.765**
Values are expressed as mean± S.E.M, n=6 in all group except in diabetic control, one way ANOVA followed by Dunette's test *p<0.05. **p<0.01, ***p<0.001 when compared with diabetic control rats, # p<0.001 compared to normal control.					

V. Histopathological studies:

Normal Control:

The photomicrograph shows healthy acini and a normal cellular population within the islets of Langerhans in the pancreas (Refer to Fig. 1A and 2A).

Diabetic Control:

The diabetic control group shows significant damage to the islets of Langerhans, with reduced size of the islets (Refer to Fig. 1B and 2B) in both the alloxan and STZ models.

Standard:

The standard indicates the restoration of the normal cellular size of the islets (Refer to Fig. 1C and 2C) in both the alloxan and STZ models.

MFLE Treatment in Alloxan and STZ Induced Diabetes:

This suggests potential recovery through cellular repair within the islets of Langerhans, with partial preservation of the cells (Refer to Fig. 1D and 2D).

MFLE Treatment in Alloxan and STZ-Induced Diabetes:

This implies a lesser degree of restoration of the islets of Langerhans, with the cells appearing shrunken and degenerated (Refer to Fig. 1E and 2E).

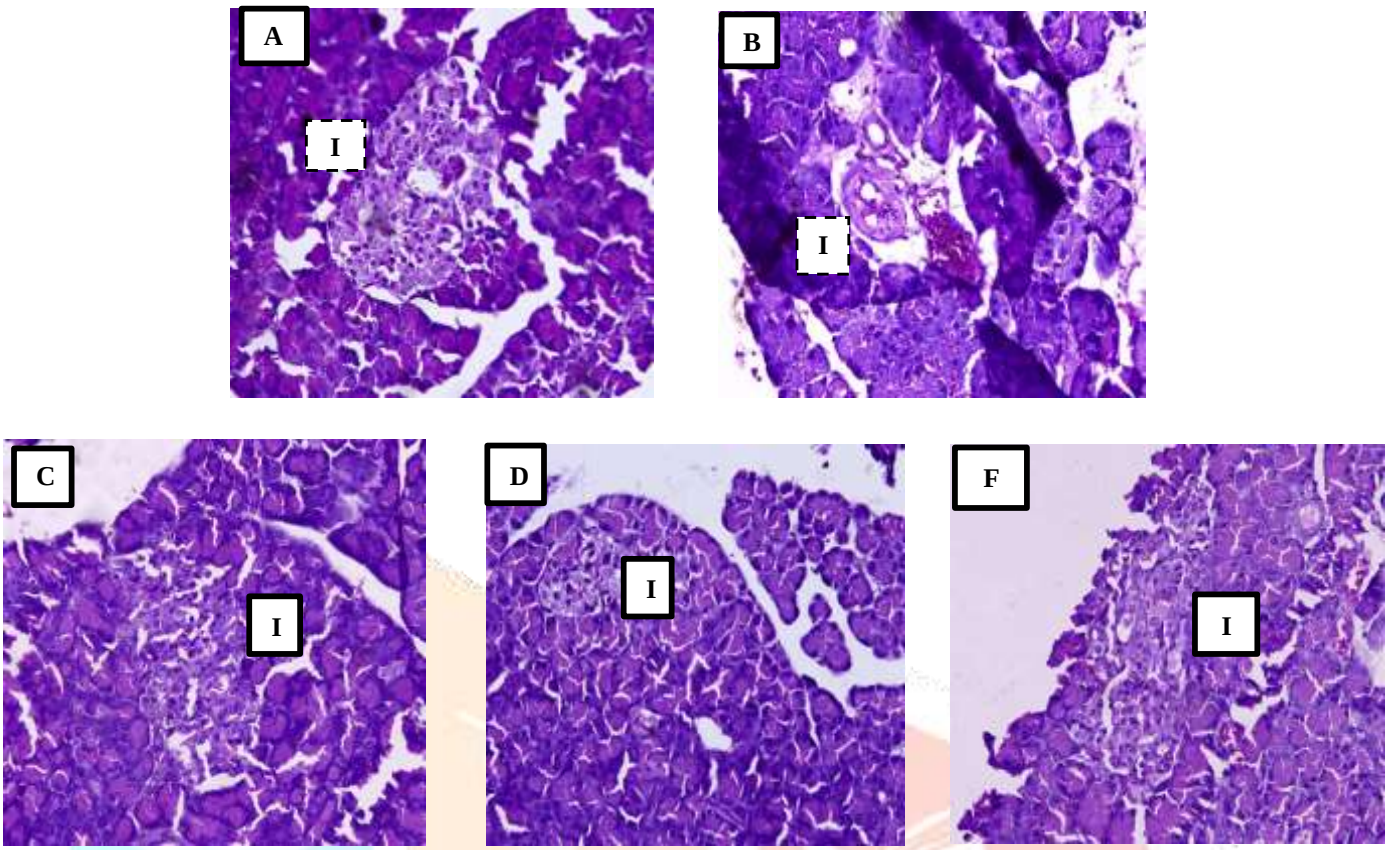

FIG 1: Histopathological analysis of Pancreas in Alloxan induced diabetic Rats (I – Pancreatic islet cells.)

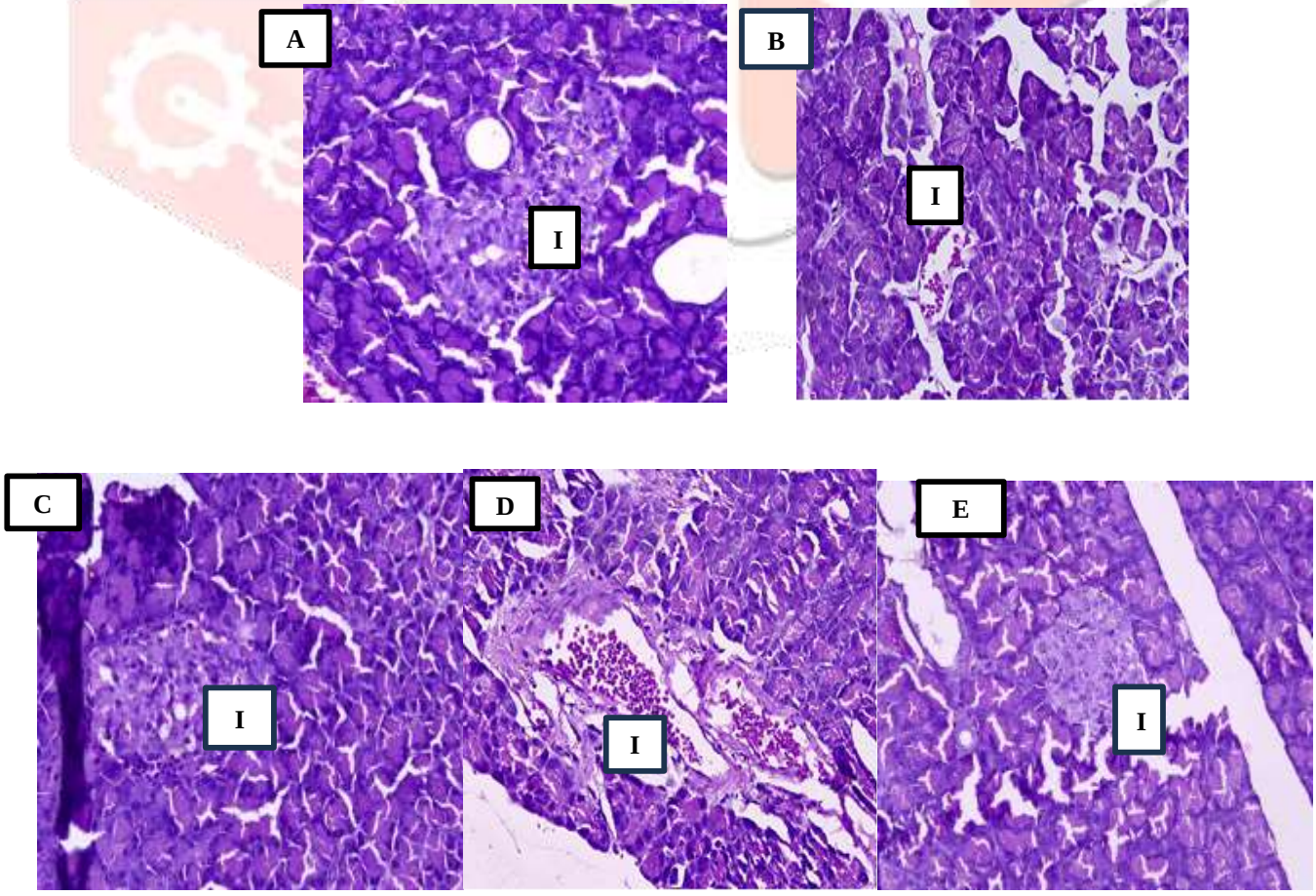

FIG 2: Histopathological analysis of Pancreas in Streptozotocin induced diabetic Rat (I – Pancreatic islet cells)

(A) Normal control **(B)** Diabetic control **(C)** Standard (5mg/kg) **(D)** MFLE (250mg/kg) **(E)** MFLE (500mg/kg)

VI. DISCUSSION

Diabetes mellitus is a long-term metabolic disorder marked by elevated levels of glucose in the blood, both during fasting and after meals. This occurs due to the body's resistance to insulin or an insufficient amount of insulin production. [14] The results demonstrated that Alloxan monohydrate specifically targeted and destroyed the pancreatic beta cells, causing significant damage to the islets of Langerhans. This led to decreased insulin secretion and a slower rate of glucose conversion into glycogen. As a result, there was a sharp increase in blood sugar levels (hyperglycemia) in the diabetic rats. These findings are consistent with existing research, which shows that Alloxan induces diabetes by selectively damaging beta cells responsible for insulin production, storage, and release. [15,16] Streptozotocin (STZ) induces diabetes by selectively destroying pancreatic beta cells, which are responsible for insulin production. [17,18]

Glibenclamide is a second-generation sulfonylurea, commonly used as an oral hypoglycemic agent. It is effective in diabetic rats with functioning pancreatic beta cells. Its primary mechanism of action is stimulating beta cells to produce and release more insulin. [19]

The ethanolic extract of leaves of *Mesua ferrea* L exhibited notable antidiabetic activity ($p<0.01$) in both experimental diabetes models, showing comparable results to the standard drug Glibenclamide. This study's outcomes suggest that the extract effectively managed diabetes by reducing blood glucose level in diabetic induced animals. However, treatment with different doses of *Mesua ferrea* L and Glibenclamide in these diabetic rats resulted in improved body weight, likely due to enhanced glycemic control.

In diabetic control rats, elevated levels of total cholesterol, triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) were observed, along with reduced high-density lipoprotein cholesterol (HDL-C). Treatment with various doses of *Mesua ferrea* L and Glibenclamide significantly ($p<0.05$) lowered cholesterol, triglycerides, and LDL-C, while increasing HDL-C in the diabetic rats. These findings suggest that *Mesua ferrea* leaf extract has a hypolipidemic effect in managing lipid abnormalities associated with diabetes.

The phytochemical screening of *Mesua ferrea* leaf extract revealed the presence of alkaloids, flavonoids, glycosides, triterpenoids, Carbohydrates, Phytosterols, Resins, Coumarins and volatile oils. Previous studies on diabetes have indicated that triterpenoids, flavonoids and alkaloids contribute to antidiabetic effects. Flavonoids and triterpenoids are recognized for their antidiabetic bioactivity, while alkaloids may stimulate hepatic glycogen production. Therefore flavonoids, triterpenoids and alkaloids in the leaves of *Mesua ferrea* are likely responsible for its observed antidiabetic properties. [7]

Histopathological analysis of the pancreas further validated our results. In the photomicrographs, normal control rats displayed healthy acini and a typical cellular population within the islets of Langerhans. In contrast, the diabetic control group exhibited significant islet damage and shrinkage. The group treated with Glibenclamide showed a recovery of normal islet cell size. Similarly, treatment with both doses of *Mesua ferrea* leaf extract appeared to promote partial restoration of the islet cells in the pancreas.

The precise mechanism behind the antidiabetic effects of *Mesua ferrea* L leaf extract remains unclear. However, its significant antidiabetic activity may be attributed to enhancing serum insulin levels, possibly by stimulating pancreatic insulin secretion from the existing beta cells or by improving peripheral glucose utilization. Additionally, it may inhibit glucose transport activity in the intestine. Further research is necessary to isolate and characterize the active compounds and to elucidate the exact mechanisms responsible for its antidiabetic properties.

VII. CONCLUSION

Numerous botanical remedies have been traditionally recommended for managing diabetes. In the current study, the leaf extract of *Mesua ferrea* L. was evaluated for its anti-hyperglycemic potential. The preliminary phytochemical analysis of the extract revealed the presence of various active compounds, including alkaloids, flavonoids, glycosides, triterpenoids, carbohydrates, phytosterols, resins, coumarins, and volatile oils. These phytoconstituents are believed to contribute to the observed blood sugar-lowering effects.

Experimental results demonstrated that the *Mesua ferrea* L. leaf extract showed a significant, dose-dependent reduction in blood glucose levels in diabetic models induced by alloxan and streptozotocin. The possible mechanism of action may involve the regeneration of pancreatic beta cells, as indicated by histopathological findings, which could enhance insulin secretion. Additionally, the extract may improve glucose utilization at the cellular level, aiding in better glycemic control. While these findings indicate a

promising hypoglycemic effect, further research is needed to isolate the specific bioactive compounds responsible and to fully understand the underlying mechanisms. This suggests that *Mesua ferrea* may serve as a potential therapeutic adjunct and a valuable natural resource for diabetes treatment.

VIII. ACKNOWLEDGMENT

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