EXPLORE ANTI-DIABETIC ACTIVITY OF *PLECTRANTHUS MOLLIS* LEAVES EXTRACT, STREPTOZOCIN –INDUCED ON DIABETIC RAT

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Abstract

Diabetes mellitus is a chronic condition causing high blood sugar levels due to inadequate insulin production or resistance. It can lead to severe complications like cardiovascular issues and neuropathy. Effective management involves lifestyle changes, regular monitoring, and medication. This study investigates the phytochemical and pharmacological properties of the leaves of *Plectranthus mollis*, a member of the Lamiaceae family. Preliminary phytochemical analysis revealed the presence of carbohydrates, flavonoids, steroids, phenolic compounds, terpenoids, and tannins. The ethanolic extract of *Plectranthus mollis* demonstrated significant α-glucosidase inhibitory activity in a dose-dependent manner, showing effects comparable to the standard drug acarbose across concentrations from 10 to 200 µg/mL. These findings suggest that the phytochemicals in the leaves effectively inhibit α-glucosidase, thereby indicating potential anti-hyperglycemic properties. Further pharmacological assessment, The biologically effective doses of 200 mg/kg and 400 mg/kg were selected for in-vivo studies on diabetic Sprague Dawley rats, revealing significant antidiabetic effects. Histopathological examination of the pancreas indicated that the extract reversed diabetes-induced histological changes, restoring normal pancreatic architecture. In conclusion, the ethanolic extract of *Plectranthus mollis* exhibits potent antidiabetic activity, likely attributable to its flavonoid content, suggesting its potential as a natural therapeutic option for diabetes management.

Key words: Diabetes mellitus, neuropathy, antidiabetics and *Plectranthus mollis*

Introduction:

Medicinal Plants are helping humanity for millions of years since they contain vital therapeutic components and aid in the treatment of chronic illnesses. The past was termed the synthetic age since the pharmaceutical industry commercially produced a broad variety of synthetic drugs.[1]Furthermore, the high cost of these treatments renders them unavailable to a substantial portion of the population. In recent decades, there has been a global shift toward green medications, which are preferred due to their decreased side effects and cost effectiveness. Medicinal plants are widely acknowledged for their role in the development of modern herbal therapies, particularly for cancer, liver disease, and arthritis, which frequently lack effective treatments in mainstream medicine.[2]The bioactive chemicals present in medicinal plants operate as anti-diabetic, chemotherapeutic, anti-inflammatory, and anti-arthritic agents, particularly throughout circumstances where modern medicine fails to provide a sufficient treatment.[3]Diabetes mellitus is a long-term endocrine condition that disrupts the metabolism of carbohydrates, proteins, fats, electrolytes, and water, encompassing a range of metabolic disorders marked by elevated blood sugar levels. Recently, there has been an increasing focus on herbal treatments as an alternative, largely due to the adverse effects linked to conventional oral hypoglycemic medications used in managing diabetes mellitus.[4]Free radicals are believed to play a significant role in the development of various diseases, including liver cirrhosis, atherosclerosis, cancer, and diabetes, among others. Compounds that possess the ability to neutralize free radicals show considerable promise in mitigating the progression of these health conditions.[5]Antioxidants are essential in safeguarding the human body from the harmful effects caused by reactive oxygen species. These compounds help neutralize free radicals, thereby preventing cellular damage and contributing to overall health and well-being.[6]Elevated oxidative stress is believed to be a significant factor in the diabetic condition. The activity of oxygen free radicals can trigger lipid peroxidation, which subsequently promotes the glycation of proteins, leading to the inactivation of enzymes and modifications in the structure and functionality of collagen, basement membranes, and other cellular membranes. This cascade of events is thought to contribute to the long-term complications associated with diabetes.[7]Oxidative stress in individuals with diabetes is often accompanied by a decline in antioxidant levels, which can exacerbate the harmful impacts of free radicals. Research has demonstrated that alloxan primarily exerts its diabetogenic effects by generating oxygen free radicals, leading to pancreatic damage.[8-9]Medicinal plants that contain non-toxic antioxidants could play a significant role in providing chemoprotection for individuals with diabetes. These natural compounds may help mitigate oxidative stress and inflammation, which are often associated with the disease, thereby potentially improving overall health outcomes for diabetic patients. By harnessing the therapeutic properties of these plants, it may be possible to develop complementary strategies that enhance traditional diabetes management and promote better metabolic control.[10]In the current investigation; we assessed the antidiabetic properties of *Plectranthus mollis* and explored the correlation between these properties and their antioxidant activity[11].

Numerous medicinal plants have been evaluated and shown to possess active compounds with healing properties for various ailments. Anticancer agents are substances that can potentially reduce resistance to cancer treatments. The phytochemicals and their derivatives found in these plants offer promising avenues to enhance treatment efficacy for cancer patients while minimizing side effects. Many of these phytochemicals are naturally occurring biologically active substances with notable antitumor capabilities. The journey toward developing effective, side-effect-free phytochemical-based anticancer therapies starts with assessing natural extracts from both dry and wet plant materials for their anticancer biological activity, followed by the purification of active compounds through bioassay-guided fractionation and subsequent in vitro and in vivo testing. *Plectranthus mollis*, in particular, contains a wealth of phytochemical constituents such as alkaloids, flavonoids, tannins, saponins, and cyanogenic glycosides. The essential oils derived from its leaves are recognized for their antioxidant[11], anti-inflammatory[12], antimicrobial[13], cytotoxic, and antitumor properties[14]. Nevertheless, there has been a lack of comprehensive studies to confirm the biological effects of *Plectranthus mollis* in preventing Diabetes mellitus.

Materials and Methods:

Plant Extraction:

After the *Plectranthus mollis* plant was collected from Meppadi hills area, wayanad dt, kerala, and its identity was verified by Dr. V. Aravindhan, an assistant professor in the Department of Botany at Kongunadu Arts and Science College in Coimbatore, leaves were taken from mature specimens at the same spot and thoroughly cleaned under running tap water removing any remaining materials before being dried in the shade.[15]

Chemicals:

Streptozotocin (LOBA Chemie, Mumbai, India) was acquired and stored at 25ºC. Acarbose, an oral antidiabetic agent with effective hypoglycemic properties, was sourced from the market and is produced by Aventis Pharma Ltd. in Goa, India, and was kept at room temperature for this study.

Prepare of Extraction:

The dried leaves of *Plectranthus mollis* were ground into a powder and subjected to Soxhlet extraction using petroleum ether and ethanol. The resulting extracts were concentrated using a rotary vacuum evaporator at 45°C until all solvents were completely removed, yielding a semisolid mass of crude extracts. These extracts were then collected and incubated in a hot air dryer at 52°C to produce powdered forms. The yields of the various extracts will be assessed for preliminary evaluation and pharmacological studies related to in-vivo anti-diabetic activity.[16]

Phytochemical screening:

The ethanolic extract of the plant *Plectranthus mollis* leaves was investigated top preliminary phytochemical studies.[17]

***In-vitro* Studies:**

Evaluation of *In-vitro* α-Glucosidase Inhibitory Activity of *Plectranthus mollis* leaves extract:

The inhibitory activity of α-glucosidase was assessed using a standardized protocol. An enzyme solution was created by dissolving 0.5 mg of α-glucosidase in 10 ml of phosphate buffer (pH 7.0) with 20 mg of bovine serum albumin, which was then diluted to a 1:10 ratio with phosphate buffer prior to use. Test samples at concentrations of 5%, 10%, 15%, and 25% were prepared, and 5 µL of each sample or DMSO (as a blank) was added to 250 µL of 20 mM p-nitrophenyl-α-D-glucopyranoside and 495 µL of 100 mM phosphate buffer (pH 7.0). The mixture was pre-incubated at 37°C for 5 minutes, after which 250 µL of the enzyme solution was added to initiate the reaction, which was allowed to proceed for 15 minutes at the same temperature. For the blank, 250 µL of phosphate buffer was used instead of the enzyme. The reaction was terminated by adding 1000 µL of 200 mM Na2CO3 solution, and the release of p-nitrophenol was quantified by measuring the absorbance at 400 nm using a UV-visible spectrophotometer, with results reported as percentage inhibition.[18]

The percentage inhibition was calculated by following formula:

$$\text{Enzyme inhibition (\%)} = \frac{\text{Absorbance}_{\text{negative control}} - \text{Absorbance}_{\text{reaction}}}{\text{Absorbance}_{\text{negative control}}} \times 100$$

***In-vivo* Studies:**

Animals:

Male Sprague Dawley rats, weighing between 180-250g, were utilized in this study. The rats were housed at a controlled room temperature of 22-25ºC within the animal facility. All procedures adhered to internationally recognized ethical standards for laboratory animal care. To acclimate to the laboratory environment, the rats were fed standard food for one week before the experiments commenced.

Determination of LD_{50}value of ethanolic extract of *Plectranthus mollis*

Twelve Sprague Dawley rats, weighing between 180-250 grams, were chosen for the study. An initial dose of ethanolic extracts of *Plectranthus mollis* at 300 mg/kg body weight was administered orally. Most of the crude extracts exhibited an LD50 value exceeding 2000

mg/kg of the rats' body weight. The dose volume given was 0.1 ml per 100 grams of body weight via the oral route. Toxic signs were noted within 3-4 hours post-administration. Observations included changes in body weight before and after dosing, onset and signs of toxicity such as alterations in skin, fur, eyes, and mucous membranes, as well as effects on the respiratory, circulatory, autonomic, and central nervous systems, along with somatomotor activity and behavioral patterns. Signs of tremors, convulsions, salivation, diarrhea, lethargy, sleep, and coma were also monitored, with toxic effects or mortality assessed over a 14-day period.[19]

Oral Glucose Tolerance Test (OGTT):

Normal rats that had undergone an overnight fast of 18 hours were divided into four groups, each consisting of six animals, and were given only drinking water. Group I received normal saline solution, while Group II was administered Acarbose at a dosage of 25 mg/kg (3 mg/kg body weight) as a standard treatment. Groups III and IV were given *Plectranthus mollis* ethanol extract at doses of 200 and 400 mg/kg, respectively, via oral administration. A glucose load of 2 mg/kg was provided 30 minutes after the extracts were administered.[20] Blood samples were collected from the tail vein under mild ether anesthesia at baseline, and at 30, 60, and 90 minutes post-glucose administration, with glucose levels measured using glucose strips and a glucometer from Standard Diagnostics Ltd. The blood glucose levels were recorded and analyzed.

Induction of Experimental Diabetes:

Adult Sprague Dawley rats weighing between 180 and 250 grams were subjected to an overnight fast to assess their fasting blood glucose levels. Following this, blood glucose measurements were taken from the selected animals, with the exception of those in group I, which were induced with diabetes through a single intraperitoneal injection of 55 mg/kg of streptozotocin, prepared in citrate buffer at pH 4.5. Hyperglycemia was confirmed by measuring elevated blood glucose levels at 72 hours post-injection and again on day 0. A fasting blood glucose threshold of greater than 200 mg/dl was established to classify the rats as diabetic, and those with persistent diabetes were utilized for the antidiabetic study.[21]

Anti-Diabetic Activity:

The study used Sprague Dawley rats, kept at room temperature and following ethical guidelines. They were fed standard food for a week before experiments to adapt to laboratory conditions.

Experimental design:

Experimental rats were categorized into five groups, each consisting of six animals, with all groups except the control being induced with diabetes and treated over a period of 21

days. Group I served as the normal control, receiving only vehicle treatment (normal saline with 1% CMC). Group II comprised diabetic control rats that were administered streptozotocin at a dosage of 55 mg/kg via a single intraperitoneal injection. Group III included diabetic rats treated with the standard drug Acarbose at a dosage of 25 mg/kg, administered orally. Group IV consisted of diabetic rats receiving an ethanolic extract of *Plectranthus mollis* at 200 mg/kg, also given orally and dissolved in 1% carboxymethyl cellulose (CMC). Finally, Group V involved diabetic rats treated with a higher dosage of the ethanolic extract of *Plectranthus mollis* at 400 mg/kg, administered orally and similarly dissolved in 1% CMC. Fasting blood glucose (FBG) levels were measured in all rats prior to the commencement of the experiment.[22] Blood samples were taken weekly via tail vein puncture until the study concluded. Throughout the 21 days of continuous drug treatment, blood glucose levels for all animals were assessed on days 0, 7, 14, and 21 using the One Touch glucometer (SD Check) method. Following blood sampling for biochemical analysis, the animals were euthanized, rapidly dissected, and small pieces of the pancreas were collected and preserved in 10% formalin. The specimens underwent dehydration through increasing concentrations of ethanol, were cleared with xylene, and subsequently embedded in paraffin wax. Thin sections, measuring 6µm, were prepared, stained with Haematoxylin and Eosin, and then analyzed under a microscope.

Result and discussion:

Preliminary studies:

The preliminary Phytochemical studies were done in the ethanolic extract of *Plectranthus mollis* Leaves result suggest that presence ofCarbohydrate, flavanoids, Steroids, phenolic compounds, Terpenoids and tannins.

***In-vitro* studies:**

The inhibitory effects of the ethanolic leaves extract of *Plectranthus mollis* against α-glucosidase were thoroughly examined and compared to the effects of the standard drug acarbose. The results show a clear dose-dependent relationship, where the α-glucosidase inhibitory activity increased steadily as the concentration of both the plant extract and acarbose was ramped up from 10 to 200 µg/mL. Notably, at each and every concentration level tested, the ethanolic extracts of *Plectranthus mollis* demonstrated a statistically significant inhibitory effect on α-glucosidase that was comparable, and in some cases even superior, to the potent pharmaceutical drug acarbose. This indicates that the phytochemicals present in the *Plectranthus mollis* leaves are highly effective at blocking the activity of the α-glucosidase enzyme, which plays a crucial role in carbohydrate digestion and the regulation of postprandial blood glucose levels. The results conclusively reveal that the ethanolic extract of *Plectranthus mollis* possesses potent anti-hyperglycemic properties stemming from its ability to inhibit α-glucosidase enzyme. **(Table: 1 & Fig. no. 1)**

Effect on Glucose Tolerance:

In the OGTT, administering EEPM at doses of 200 mg/kg and 400 mg/kg enhanced glucose tolerance, indicating improved peripheral glucose utilization. The decrease in blood glucose levels was observed to be dose-dependent. The results were given in **(Table No.: 2 & Fig. No.: 2)**

Evaluation of Parameters:

Animals in the vehicle control group maintained stable body weight, whereas a significant decrease was observed in the diabetic control group over the 21-day period (Table 6.7). Streptozotocin administration led to a reduction in body weight, which was partially mitigated in the groups treated with ethanolic extract of *Plectranthus mollis* at doses of 200 mg/kg and 400 mg/kg after 21 days. Furthermore, a significant increase in body weight ($p<0.01$, $p<0.001$) was noted in rats receiving the ethanolic extract, with the group treated at 400 mg/kg showing a slight increase in body weight levels and and showed in **(Table No: 3 & Fig No: 3).**

Determination in blood glucose changes:

A notable rise in blood glucose levels was detected in diabetic control rats compared to the control group. The treatment of diabetic rats with EEPM and Acarbose at a dosage of 25 mg/kg resulted in a significant reduction of blood glucose levels, bringing them close to those of the control group. **(Table No: 4 & Fig No: 4).**

Lipid Profile:

The serum lipid levels of total cholesterol (TC) and triglycerides (TG) in subjects treated with EECA extract approached those of the control group. In comparison to the control animals, diabetic subjects exhibited elevated cholesterol and triglyceride levels. The results indicated that treatment with EEPM at doses of 200 mg/kg and 400 mg/kg significantly improved the lipid profile in rats induced with diabetes by Streptozotocin, with a p-value of less than 0.001. **(Table No: 5 & Fig No: 5).**

Changes in HDL, LDL and VLDL:

The plasma lipid profiles of HDL, LDL, and VLDL in subjects treated with EECA extract approached levels similar to those of the control group. Diabetic animals exhibited a reduction in HDL levels, which were significantly restored to near-normal levels in the groups treated with EECA. Conversely, LDL and VLDL levels were elevated in diabetic animals compared to controls. Following treatment with EEPM, the elevated levels of both LDL and VLDL were reduced to levels close to those of the control group. The results indicated that treatment with EEPM at doses of 200 mg/kg and 400 mg/kg significantly

improved the lipid profile in rats induced with diabetes by Streptozotocin, with a p-value of less than 0.001. **(Table No: 6 & Fig No: 6).**

Changes in Total protein and Albumin:

The plasma lipid levels of total protein and albumin in subjects treated with EECA extract approached those of the control group. In diabetic animals, there was an increase in total protein and albumin levels. In the diabetic groups treated with EEPM, total protein and albumin levels were significantly restored to near-normal values. **(Table No: 7 & Fig No: 7).**

Changes in Alkaline Phospahtase and Uric acid:

The plasma lipid values of Alkaline Phosphatase of those were treated with EEPM extract returned to values near to control group. The level of Alkaline Phosphatase in serum of diabetic animals was increased. Total protein and Albumin were restored significantly near to normal in EEPM treated diabetic groups. **(Table No: 8 & Fig No: 8).**

Histopathology Observation:

Group I: The normal control group exhibits pancreatic cells with intact architecture and appropriate proportions. Acinar cells, which display strong staining, are organized into lobules, while islet cells are situated among the acinar cells and encased in a thin fibrous capsule. There are no signs of inflammation or malignancy.

Group II: In the diabetic control group, pancreatic tissue reveals hyalinization of the islets of Langerhans, accompanied by mild focal degenerative changes. The interstitial area shows mild fibrosis, with dilated, thick-walled, congested blood vessels and localized chronic inflammatory cell infiltration.

Group III: The diabetes group treated with Acarbose demonstrates significant atrophy of pancreatic islet cells and minimal degenerative changes in the acinar cells. The tissue contains eosinophilic material, pericapsular fibrosis, congested blood vessels, and scattered mononuclear inflammatory cell infiltration, all surrounded by a thin fibrous capsule. No signs of inflammation or malignancy are present.

Group IV: This group shows mild atrophy of pancreatic islet cells and minimal degenerative changes in the acinar population. The acinar cells exhibit dark staining and are arranged in lobules, with islet cells embedded within them. There is minimal pericapsular fibrosis, congested blood vessels, and scattered mononuclear inflammatory cell infiltration, all encased in a thin fibrous capsule, with no evidence of inflammation or malignancy.

Group V: In the diabetes group receiving 400 mg/kg EEPM, pancreatic cells show mild atrophy of islet cells while the acinar population remains normal. The acinar cells are darkly stained and organized in lobules, with islet cells embedded within them. There is minimal

pericapsular fibrosis, edema, congested blood vessels, and very few scattered mononuclear inflammatory cells, all surrounded by a thin fibrous capsule, with no signs of inflammation or malignancy

Table No.1: Evaluation of *In-vitro* α-Glucosidase Inhibitory Activity of *Plectranthus mollis* leaves extract.

Concentration (µg/ml)	*Plectranthus mollis* ethanolic extract % inhibition	Agarbose as standard
10	52.15±0.360	80.21±0.044
20	56.52±0.052	82.15±0.050
40	59.26±0.065	84.86±0.048
80	62.20±0.070	88.59±0.028
120	71.26±0.036	94.60±0.360
160	74.39±0.142	96.48±0.028
200	76.27±0.201	98.54±0.032

Values are expressed as Mean ± Standard deviation

Fig No.1: Evaluation of *In-vitro* α-Glucosidase Inhibitory Activity of *Plectranthus mollis* leaves extract

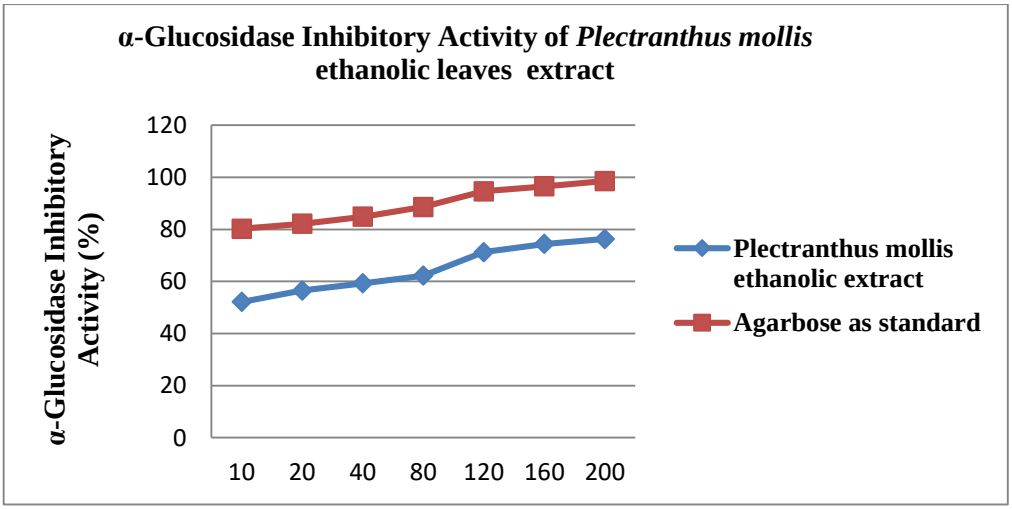


Table No.: 2 Effect of Ethanolic extract of *Plectranthus mollis* and Acarbose *25mg/kg* on glucose tolerance of diabetic rats.

Groups	Treatment	Change in blood glucose levels(mg/dL)			
		Fasting	After 30 Minutes	After 60 minutes	After 90 minutes
I.	Glucose 2mg/kg	84.33±3.80	126±3.04	127.35±2.25	108. 5±3.69
II.	Glucose + Acarbose 25mg/kg	66.67±4.33	83.35±2.58 a	63.88±2.47 a	52.7±4.40 a
III.	EEPM 200mg/kg	65.85±1.52	110.69±6.28 a	112.38±12.00 a	96.65±6.89 a
IV.	EEPM 400mg/kg	78±3.18	99.67±2.41 c	105.17±8.91 b	92.67±3.95 a

Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at a=*** = p<0.001; b= ** = p<0.01; c= *

=p<0.05. EEPM. (Analyzed by one-way analysis of variance (ANOVA) followed by Tukey-Kramer multiple comparison tests). Normal control group- I was compared with extract treated groups III and IV.

Figure No.2: Effect of Ethanolic extract of *Plectranthus mollis* and *Acarbose 25mg/kg* on glucose tolerance of diabetic rats.

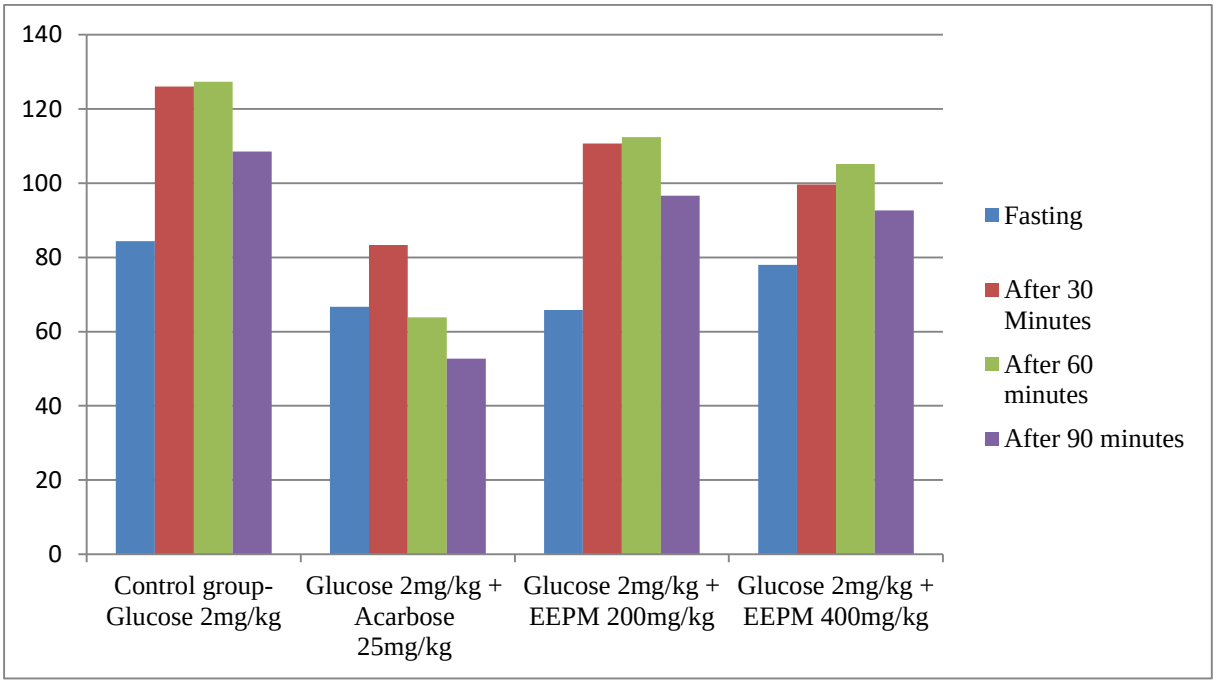


Table No: 3 Body weight changes in ethanolic extract of *Plectranthus mollis* and Acarbose 25mg/*kg* on control and experimental groups of rats

Group	Treatment	Body weight changes (g)	
		Day 0	Day 21
I	Normal control rats (vehiclesonly)	145±7.67	204.16± 11.94
II	Diabetic control rats	162.5±8.54 b	127.19± 7.67 b
III	Diabetic group + Acarbose 25mg/kg	150±6.44 a	208.39± 12.37 a
IV	Diabetic group + EEPM(200/kg)	154.18±7.67 b	200± 6.46 b
V	Diabetic group + EEPM (400mg/kg)	162.7 ±14.05 c	187.7± 17.98 c

Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at a=*** = p<0.001; b=** = p<0.01; c=*=p<0.05.

Figure: 3 Body weight changes in ethanolic extract of and *Plectranthus mollis* and Acarbose 25mg/kg on control and experimental groups of rats

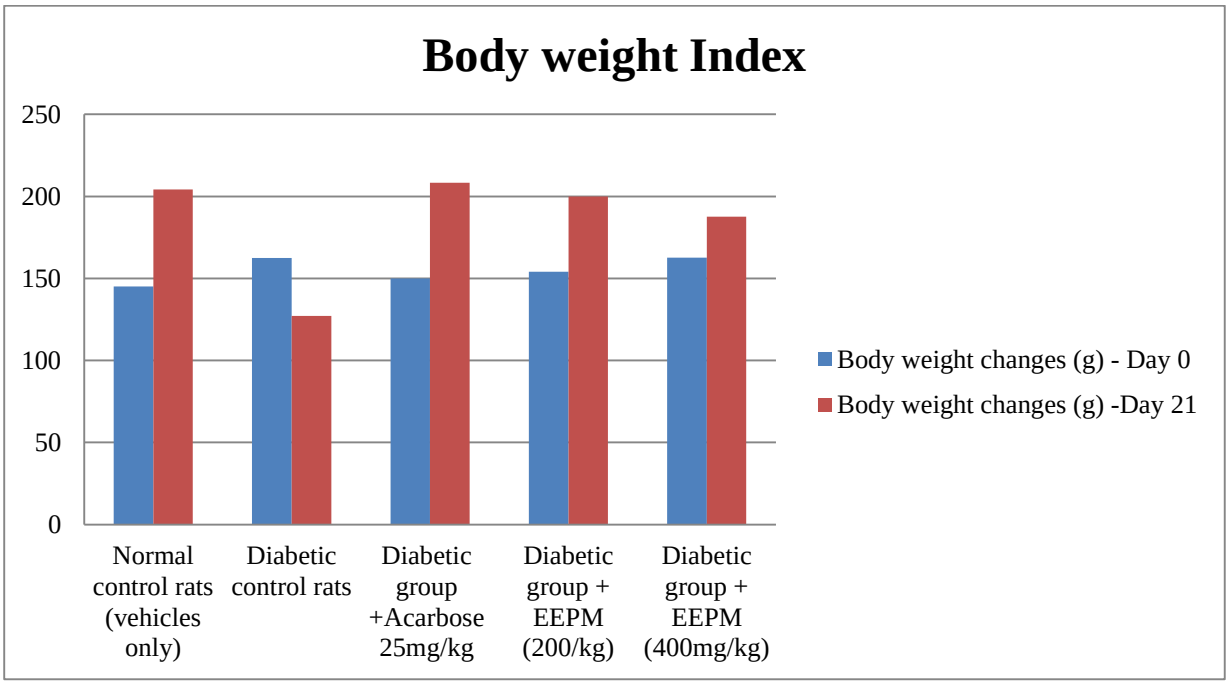


Table No. 4. Effect of *Plectranthus mollis* Ethanolic extract and Acarbose 25mg/kg on blood glucose level

Groups	Treatment	Blood glucose level (mg/dL)			
		Day 0	Day 7	Day 14	Day 21
I	Normal control rats (vehicles only)	71.37 ± 1.42	80±2.34	77.85 ± 2.36	71.34 ±1.82
II	Diabetic control rats	379.7±13.57 a	335.82±7.18 a	353.85±10.81 a	370.31±12.91 a
III	Diabetic group + Acarbose 25mg/kg	312.9±9.09 a	280.33±9.56 a	234.66±5.42 a	148.69±8.05 a
VI	Diabetic group + EEPM (200mg/kg)	335.18±8.90 c	286±13.26 a	173.84±8.91 a	163±10.81 a
V	Diabetic group + EEPM (400mg/kg)	319.15±12.16 b	288±5.08 b	158.82±7.30 a	162.6±7.74 a

Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at a=*** = p<0.05; b=** = p<0.01; c=* =p<0.001.

Figure No: 4 Effect of ethanolic extract of *Plectranthus mollis* and Acarbose 25mg/kg on blood glucose level.

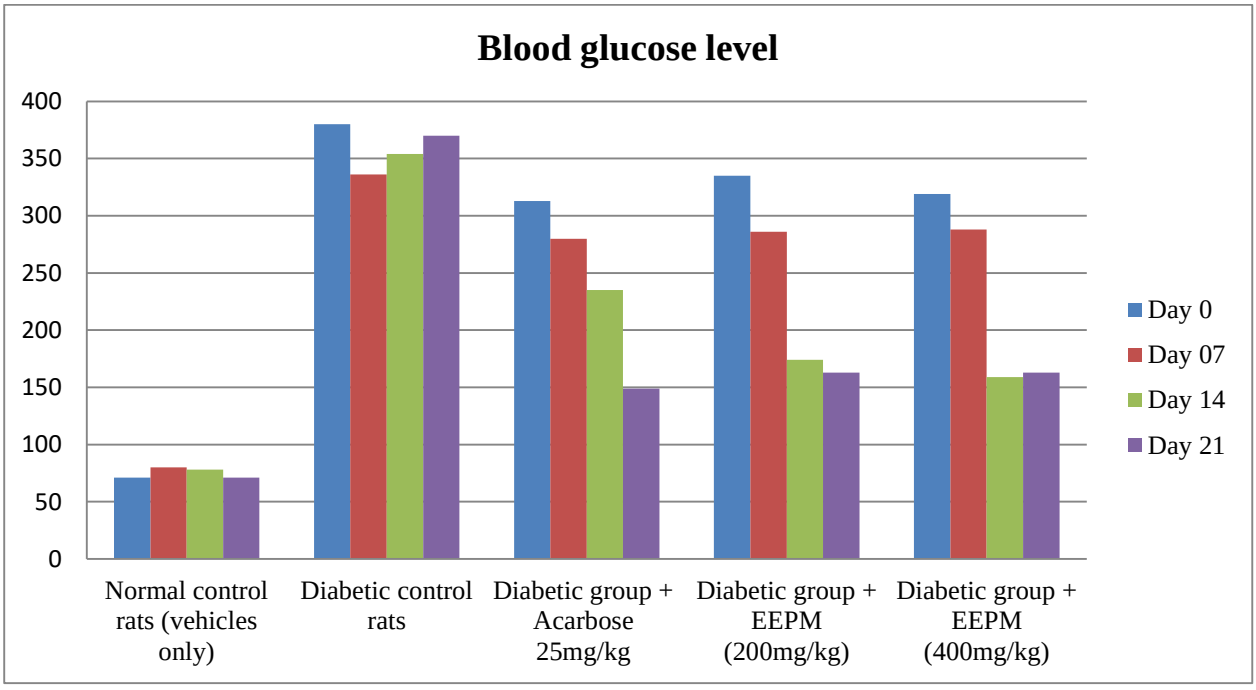


Table No: 5. Effect of ethanolic extract of *Plectranthus mollis* and Acarbose 25mg/*kg* in total cholesterol, triglycerides levels on control and experimental groups of rats.

Group	Treatment	Total Cholesterol (mg/dl)	Triglycerides (mg/dl)
I	Normal control group (vehicles only)	110.14±0.47	90.18±1.71
II	Diabetic control rats	213.23±1.84 [a]	185±2.63 [a]
III	Diabetic group + Acarbose 25mg/kg	123.17±1.94 [a]	131±2.63 [a]
IV	Diabetic group + EEPM (200mg/kg)	135.3±2.11 [a]	63.52±1.45 [a]
V	Diabetic group + EEPM (400mg/kg)	133.79±2.94 [b]	82.45±2.11 [a]

Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at a=*** = p<0.001; b=** = p<0.01; c=*=p<0.05.

Figure No. 5: Effects of ethanolic extract of *Plectranthus mollis* and Acarbose 25mg/*kg* on total cholesterol, triglycerides level s on control and experimental groups of rats.

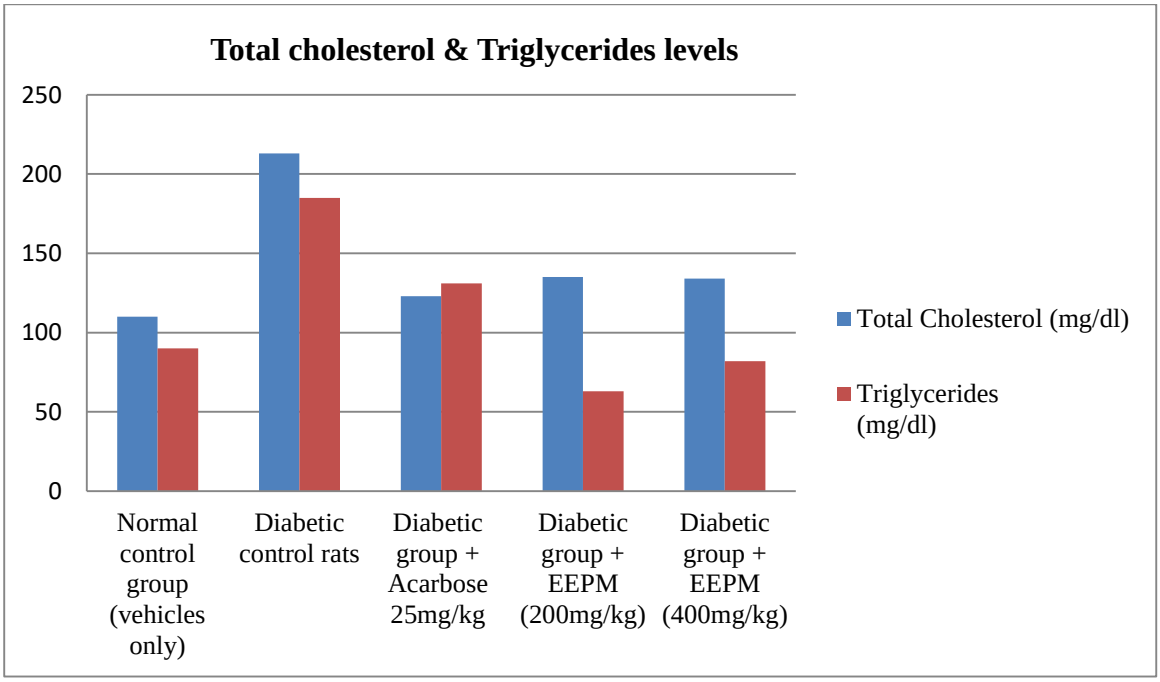


Table No 6: Effect of ethanolic extract of *Plectranthus mollis* and Acarbose 25mg/*kg* on LDL, VLDL, HDL of control and experimental group of rats

Group	Treatment	LDL Cholesterol (mg/dl)	VLDL Cholesterol (mg/dl)	HDL Cholesterol (mg/dl)
I	Normal control group (vehicles only)	50.94±1.19	19.23±0.34	42.66±0.87
II	Diabetic control rats	154.3±2.15 [a]	34.7±0.52 [a]	22±1.06 [a]
III	Diabetic group + Acarbose 25mg/kg	57.73±1.67 [a]	28.54±0.52 [a]	40.83±1.07 [a]
IV	Diabetic group + EECA (200mg/kg)	82.1±2.80 [b]	14.56±0.27 [a]	39.83±1.07 [a]
V	Diabetic group + EECA (400mg/kg)	84.34±1.85 [a]	17.18±0.44 [a]	30.85±0.82 [a]

Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at a=*** = p<0.001; b=** = p<0.01; c=* =p<0.05.

Figure No: 6 Effects of ethanolic extract of *Plectranthus mollis* and Acarbose 25mg/*kg* on LDL cholesterol, VLDL cholesterol, HDL cholesterol of control and experimental groups

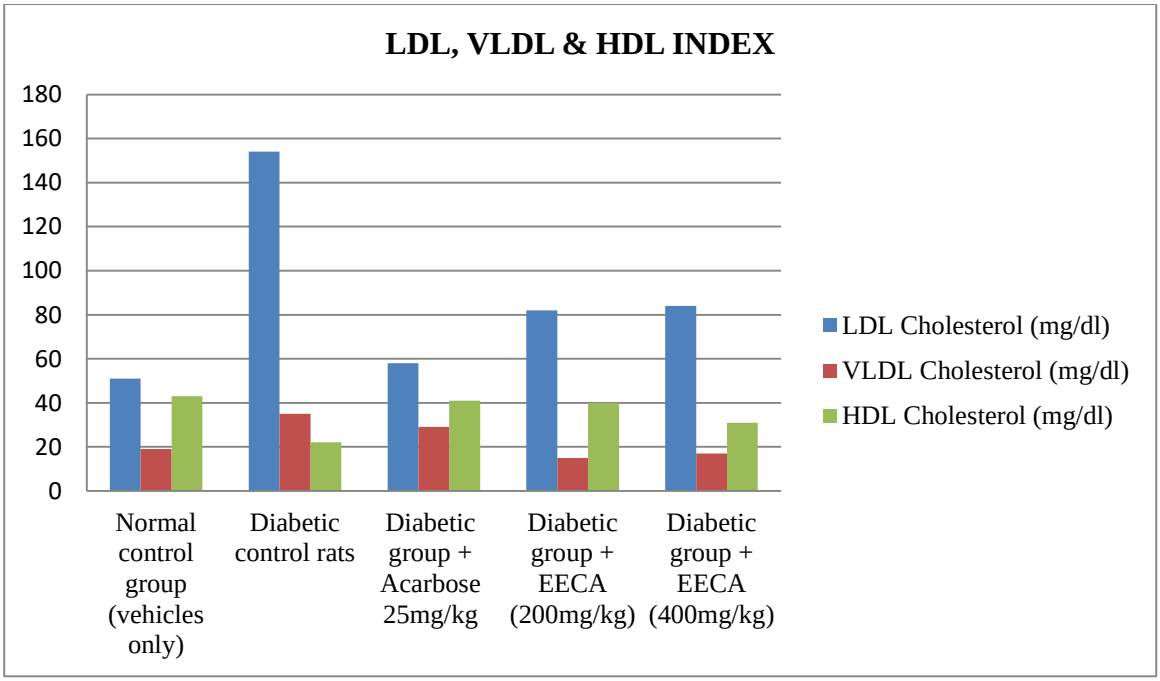


Table No. 7: Effect of ethanolic extract of *Plectranthus mollis* and Acarbose 25mg/kg in Total Protien, Albumin of control and experimental groups of rats

Group	Treatment	ɔtein	ɯmin(mg/dl)
I	Normal control group (vehicles only)	8.1±0.13	5.167±0.10
II	Diabetic control rats	5.82±0.19 a	2.29±0.11 a
III	Diabetic group + Acarbose 25mg/*kg*	8.1977±0.14 a	3.22±0.12 a
IV	Diabetic group + EEPM(200mg/kg)	8.1±0.13 a	3.09±0.09 a
V	Diabetic group + EEPM (400mg/kg)	8.1±0.18 a	3.28±0.08 a

Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at a=*** = p<0.001; b=** = p<0.01; c=* =p<0.05

Figure No. 7: Effect of ethanol extract of *Plectranthus mollis* and*Acarbose 25mg/kg* on Total protein and Albumin levels on control and experimental groups of rats.

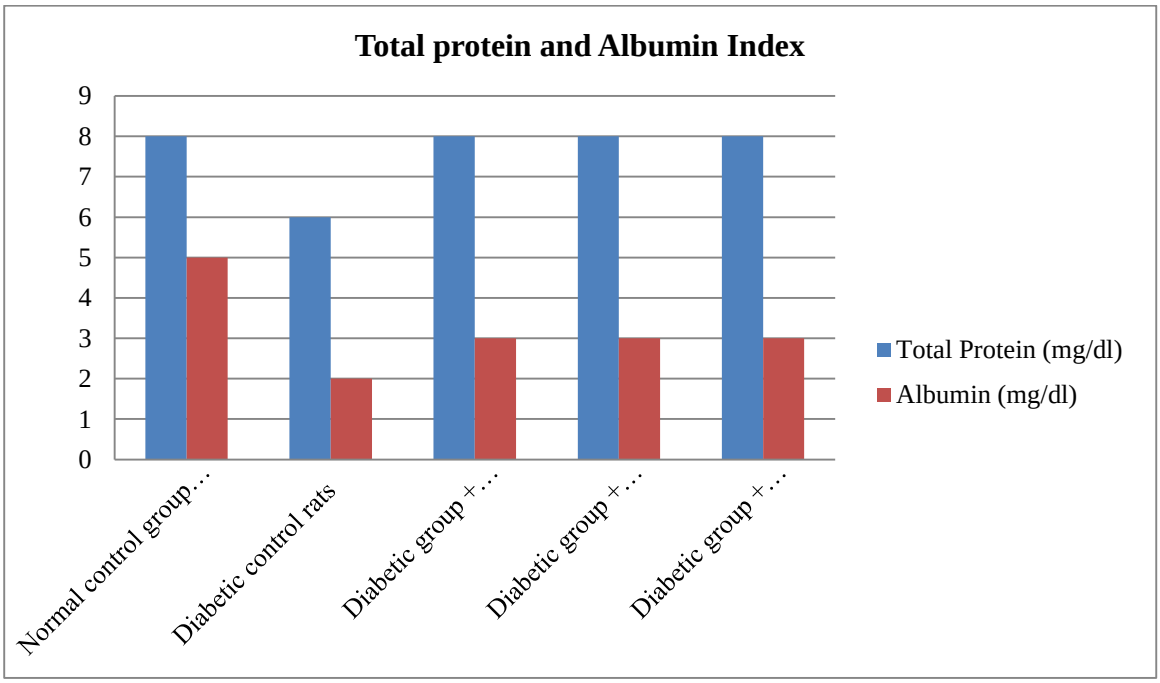
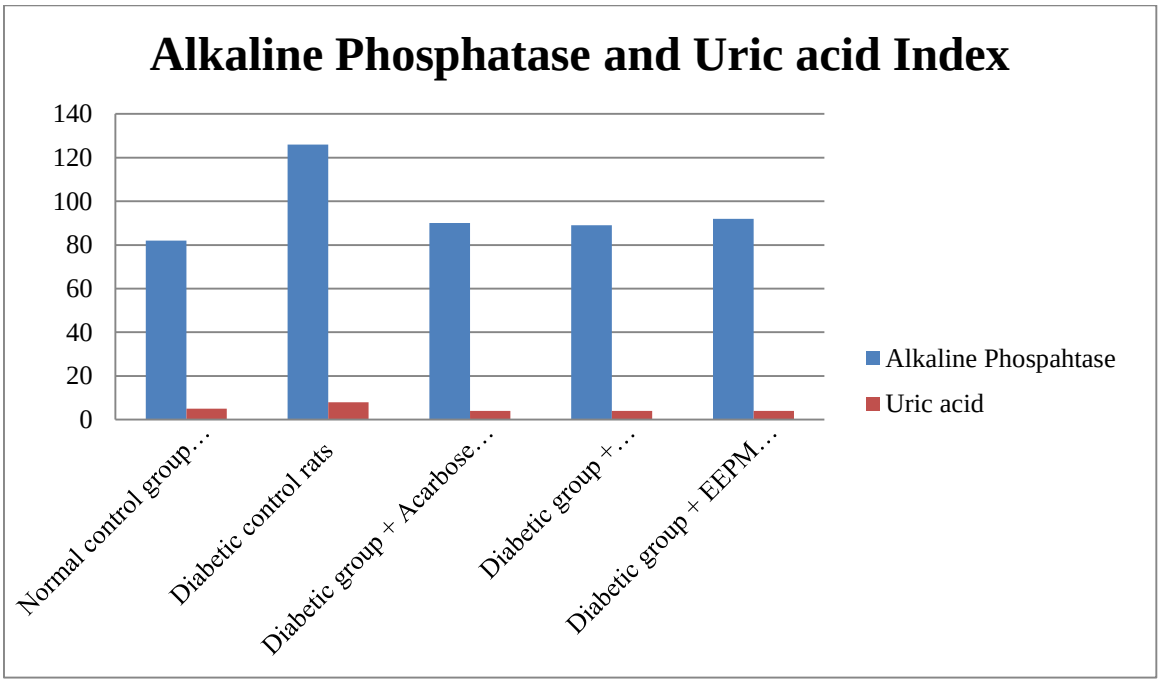


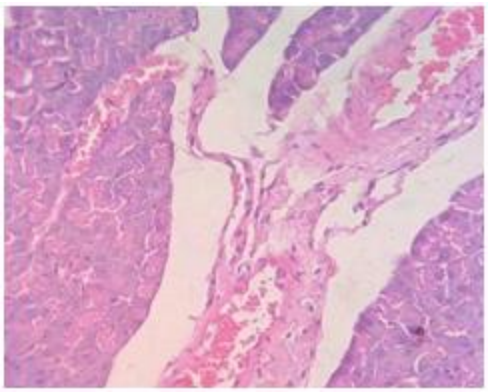
Table No. 8: Effect of ethanolic extract Plectranthus mollis and Acarbose 25mg/kg in Alkaline Phosphatase and uric acid on control andexperimental groups of rats.

Group	Treatment	Alkaline Phospahtase	Uric acid
I	Normal control group (vehicles only)	81.7±1.05	4.71±0.12
II	Diabetic control rats	125.6±1.95 [a]	8.16±0.14 [a]
III	Diabetic group + Acarbose 25mg/kg	90.3±0.99 [a]	4.07±0.10 [a]
IV	Diabetic group + EEPM(200mg/kg)	89.1±1.28 [a]	4.08±0.08 [a]
V	Diabetic group + EEPM (400mg/kg)	92.35±0.85 [a]	4.27±0.11 [a]

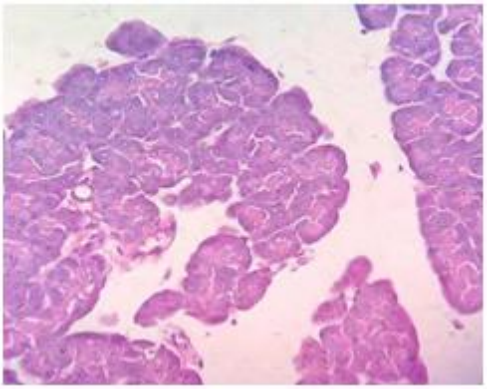
Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at a=*** = p<0.001; b=** = p<0.01; c=* =p<0.05.

Figure No. 8: Effect of ethanol extract *Plectranthus mollis* and Acarbose 25mg/kg on Alkaline Phosphatase and Uric acid levels on controland experimental groups of rats.

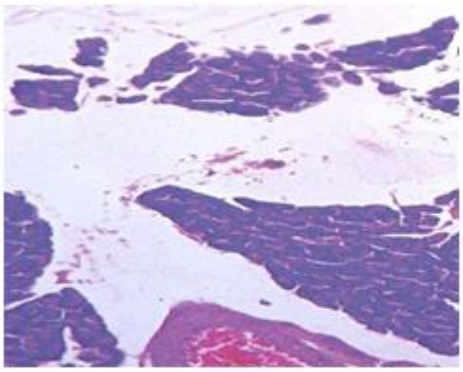




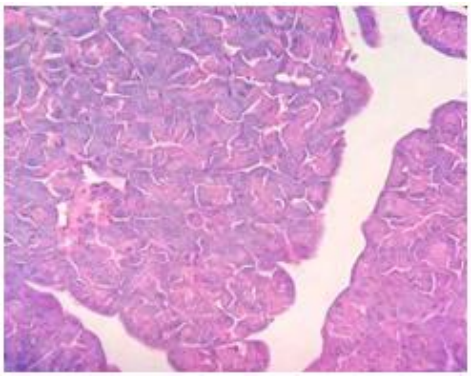
Group I – Normal Control



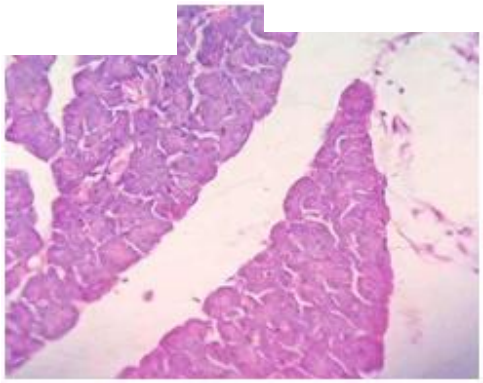
Group II – Diabetic Control



Group III – Diabetic group + Acarbose 25mg/kg



Group IV – Diabetic group + EEPM 200mg



Group V – Diabetic group + EEPM 400mg

Figure No. 9: Histopathological Studies

Conclusion:

The leaves of *Plectranthus mollis*, a member of the Laminaceae family, have been studied to understand their phytochemical and pharmacological properties. Preliminary investigations revealed the presence of carbohydrates, flavonoids, steroids, phenolic compounds, terpenoids, and tannins. The ethanolic extract of *Plectranthus mollis* was

evaluated for its inhibitory effects on α-glucosidase, with results compared to the standard drug acarbose. A clear dose-dependent relationship was observed, with α-glucosidase inhibition increasing as the concentration of both the plant extract and acarbose from 10 to 200 µg/mL. At all tested concentrations, the ethanolic extracts exhibited a statistically significant inhibitory effect on α-glucosidase, often surpassing that of acarbose. This suggests that the phytochemicals in *Plectranthus mollis* are effective in inhibiting the α-glucosidase enzyme, which is essential for carbohydrate digestion and the management of postprandial blood glucose levels. The findings indicate that the ethanolic extract possesses strong anti-hyperglycemic properties, highlighting its potential as a natural alternative or complementary therapy for diabetes and metabolic disorders. Consequently, we plan to conduct in vivo anti-hyperglycemic activity studies using diabetic Sprague Dawley rats. This study on the ethanolic extract of *Plectranthus mollis* leaves demonstrates significant antidiabetic activity, comparable to that of Acarbose. The presence of flavonoids in the extract is likely linked to its anti-hyperglycemic effects. Histopathological examinations of the isolated pancreas indicated that the ethanolic extract of *Plectranthus mollis* effectively reversed diabetes-induced changes caused by Streptozotocin, restoring the normal histological structure of the pancreas.

Acknowledgement

"We acknowledge Department of Pharmacology, JKKMMRFs Annai JKK Sampoorani Ammal College of Pharmacy, B. Komarapalayam, Namakkal (D.T), Tamil Nadu, India.

Conflicts of interest: The authors declare that they have no conflict of interests.

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