JOURNAL OF NATURAL REMEDIES
DOI: 10.18311/jnr/2025/44454
RESEARCH ARTICLE

Evaluation of Antihyperglycemic Effect of Pectolinarigenin in Experimentally Induced Type 2 Diabetes Mellitus in Rats

Samiksha Jayswal[1*] and Snigdha Das Mandal[2]

[1]Department of Pharmacology, Parul College of Pharmacy and Research, Parul University, Ahmedabad - 380058, Gujarat, India; samikshajayswal1107@gmail.com

[2]Department of Pharmacology, Parul Institute of Pharmacy and Research, Parul University, Vadodara - 391760, Gujarat, India

Abstract

Background: Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disease of insulin resistance with insufficient insulin secretion, in addition to chronic inflammation and impaired glucose metabolism. Finding new therapeutic uses of drugs that can target multiple pathways will serve an important role in disease management. The possible pharmacological effects of pectolinarigenin merit further investigation for its antidiabetic activity. **Aim:** Evaluation of the therapeutic impact of pectolinarigenin on the major molecular targets linked to T2DM via computational and experimental techniques. **Methods:** The interaction of pectolinarigenin with key T2DM targets was explored in silico using molecular docking simulations of Peroxisome Proliferator-Activated Receptor (PPAR), Dipeptidyl Peptidase 4 (DPP4) and Sulphonylurea Receptor 1 (SUR1). **Animal Experimental Design:** Animals (Sprague-Dawley male rats) were divided into five categories: normal, disease control, reference standard (glibenclamide), and pectolinarigenin at doses of 20 and 50 mg/kg, respectively (oral experiment). Different metabolic and biochemical parameters were measured over five weeks, including serum glucose fasting, insulin sensitivity, oxidative stress, inflammatory markers, lipid profiles, and HbA1c levels. **Results:** Docking analysis showed significant binding affinities of pectolinarigenin with diverse T2DM-associated targets, indicating its potential for multi-target therapy. Furthermore, treatment with pectolinarigenin improved glucose tolerance, markedly decreased fasting blood glucose levels, and increased insulin sensitivity *in vivo* compared to the disease control and reference standard groups. Compared to rats who received 50 mg/kg, rats who received 50 mg/kg and rats who lost a significant amount of weight had improved lipid profiles, maintained weight better, and had improved antioxidant defences and inflammation markers, as well as significantly lower HbA1c levels. These findings highlight the compound's effectiveness for glycemic control and prevention of diabetes-related complications. **Conclusion:** Pectolinarigenin exhibited significant antidiabetic activity in both computational and experimental strategies, enhancing metabolic markers and alleviating inflammation. These findings underscore its potential as a therapeutic candidate for the treatment of diabetes. Additional research, including clinical trials, is needed to prove its effectiveness in people.

Major Findings: Pectolinarigenin markedly enhanced glucose tolerance, insulin sensitivity, lipid profiles and oxidative stress parameters, with the 50 mg/kg dose-related effects being the most evident. This information further describes its potential for use as a novel antidiabetic agent and prevention of diabetes-related complications.

Keywords: DPP4, Diabetes Mellitus, Flavonoid, *in silico* Studies, PPAR, T2DM

1. Introduction

Beta-cell failure in insulin production, insulin resistance, or both can result in persistently elevated blood sugar levels, which is the hallmark of Diabetes Mellitus (DM), a varied chronic metabolic disorder[1]. Being a major cause of death in Western countries, its incidence is increasing globally and is linked

*Author for correspondence

Article Received on: 12.06.2024 Revised on: 21.03.2025 Accepted on: 02.04.2025

to sedentary lifestyles, obesity, and food habits[2]. Increased cellular oxidative damage is a major factor in chemically induced diabetes, and it appears that this is also the primary cause of beta-cell degeneration in T2DM is yet unknown[3]. Since Streptozotocin (STZ) is cytotoxic and nicotinamide partially protects beta cells, the combination of the two has been used for many years to produce type-2 diabetes[4-5]. Diabetes results in an imbalance between pro-oxidants and antioxidants, which can be caused by reduced antioxidant enzyme activity or increased generation of Reactive Oxygen Species (ROS)[6]. This imbalance leads to cellular oxidative stress.

Free radical production is encouraged and the antioxidant defence mechanism is compromised by chronic hyperglycemia in diabetes, according to numerous studies[7]. The role that persistent hyperglycemia plays in causing anomalies in the metabolism of lipids and proteins in diabetics has been highlighted by earlier epidemiological and clinical research[8]. Except for High Density Lipoprotein (HDL)[7], all lipid parameters (Very Low Density Lipoprotein (VLDL), total cholesterol, Low Density Lipoprotein (LDL) and triglycerides) are raised in diabetes, which is associated with a high incidence of lipoprotein fluctuations. Disorders such as hypertriglyceridemia, insulin resistance, metabolic syndrome and type-2 diabetes are largely brought on by these changes in lipid levels. Instances of severe hyperglycemia and hyperlipidaemia should be highlighted.

As an alternative to manufactured medications for the treatment of many ailments, natural products and their bioactive components have drawn more attention recently. Diabetes control and the management of its consequences make special use of those with the ability to scavenge free radicals[9]. Making use of naturally occurring substances that possess antioxidant properties could encourage the regeneration of beta cells and protect against cytotoxic agents-induced degenerative modifications[10-11]. One possible way that natural products and their active ingredients may manage diabetes and its related issues is by increasing antioxidative potential and decreasing lipid peroxidation[7].

Pectolinarigenin, identified as a methoxyflavonoid, occurs naturally in diverse botanical sources like *Cirsium japonicum* and *Anemarrhena asphodeloides*. Renowned for its unique chemical composition and pharmacological attributes, pectolinarigenin has attracted considerable interest in the realm of pharmaceutical investigation. Research endeavours have underscored its diverse therapeutic potentials, encompassing antioxidant, anti-inflammatory, and anticancer properties[12].

In silico docking investigations were conducted to examine how pectolinarigenin interacts with crucial molecular targets involved in both type 2 (T2DM). SUR1, PPAR and DPP4 were among these targets. From these simulations, we designed the current study to investigate whether pectolinarigenin supplementation affects hyperglycemia, HbA1c, liver glycogen, lipid profile, insulin level, oxidative and inflammatory biochemical markers, and histological changes in the b-cells of the pancreas and liver of type 2 diabetic rats. This suggests that pectolinarigenin may be a multi-targeted therapeutic agent for DM by affecting multiple pathways related to glucose metabolism and insulin sensitivity.

2. Materials and Methods

For the investigation, 250–300 g of Sprague Dawley rats, weighing between two and three months, were chosen. Nestled into separate polypropylene cages, each animal was kept in normal settings with 12 hours of light and darkness, 25 ± 30 ◦C, 35–60 % humidity. The study received approval from the Institutional Animal Ethics Committee of Parul Institute of Pharmacy and Research, Parul University, Vadodara (PIPR 984/2023/02/03).

15 minutes after the intraperitoneal injection of 120 mg/kg of nicotinamide, adult male Sprague Dawley rats weighing 250–300 g were starved overnight, and a single intraperitoneal dose of 60 mg/kg streptozotocin was used to induce Non-Insulin Dependent Diabetes Mellitus (NIDDM)[13]. Normal saline was used to dissolve nicotinamide, whereas citrate buffer (pH 4.5) was used to dissolve STZ. NIDDM[14] has been induced before using this approach. The higher plasma glucose levels, which were measured 72 hours and again on day 7 following injection, were measured using an Accu-Chek glucometer from Roche Diagnostics. Rats with FPG levels exceeding 180 mg/ dL were identified as diabetic and selected for further studies.

Five groups of diabetic rats were randomly assigned to them. Group 1 (control) received saline for 28 days. Group 2, who were untreated diabetics, received citrate buffer for 28 days. For 28 days, glibenclamide (10 mg/kg, orally) was administered to Group 3 (diabetic, treated standard). Group 4 (diabetes treated, test) given pectolinarigenin (20 mg/kg, orally) for 28 days. Group 5 (treated diabetic, test) was given pectolinarigenin (50 mg/kg, orally) for 28 days as shown in Table 1.

The drug study lasted 4 weeks, with regular monitoring of blood glucose levels to assess the progression of disease and to compare the ameliorative effects of the test drug and standard drugs at different stages. Blood sample from each rat was collected on the 28th day of the research to acquire serum, which was then tested for several biochemical characteristics. A diagnostic kit based on the concepts of glucose oxidase and peroxidase was used to assess the levels of glucose. Using an ELISA kit and the ELISA sandwich method, the levels of insulin were measured. The HOMA-IR index, which is computed as [fasting insulin (μU/ml) × fasting glucose (mmol/l)]/22.5, was utilised to evaluate peripheral insulin resistance. Diagnostic kits were also used to assess the amounts of triglycerides, total cholesterol, HDL and LDL cholesterol in serum samples. Serum IL-6 levels as a sign of inflammatory stress were evaluated. Also, the amount of liver glycogen was measured. After the collection of blood, the rats were slaughtered, and the liver and pancreas were removed, cleaned in ice-cold saline, and utilised to estimate oxidative biochemical markers. Using pancreas tissue homogenate, the erythrocyte osmotic fragility test and oxidative stress indicators, such as Superoxide Dimutase (SOD), Malondialdehyde (MDA), Reduced Glutathione (GSH) and catalase were measured.

After the completion of treatment, animals were sacrificed, the pancreas was taken out of the rats and cleaned well with saline solution while being kept on ice at a low temperature. The pancreatic tissues were then preserved by immersing them in a 10% formalin solution. The tissues were then sliced to the appropriate size and fixed in paraffin to form blocks. Then, using these paraffin-embedded blocks, sections varying in thickness from 3 to 5mm were created. For a histological analysis, the slices were put on slides and stained with H and E. Ultimately, the slides were covered with Dibutylphthalate Polystyrene Xylene (DPX) media to enable further tissue morphology observation using a light microscope.

2.1 Statistical Analysis

Every result was recorded for every parameter and displayed as mean ± SEM. One-way ANOVA and Dunnett's multiple comparison test were used to statistically analyse the results to identify any significant differences in group averages. It was considered statistically significant to analyse findings at p values less than 0.5.

3. Results

3.1 Effect of Pectolinarigenin on Body Weight

As seen in Figure 1, group II rats had a substantial reduction in body weight relative to group I rats, whereas group I rats saw a rise in body weight throughout the same time frame. Conversely, after the treatment period, diabetic rats treated with Pectolinarigenin (20 and 50 mg/kg) had a considerable increase in body weight compared to group II (Figure 1).

Table 1. Grouping of animals

Group	Name	Particulars
Group I	Normal Control	Non diabetic rats
Group II	Disease Control	STZ and NIC induced diabetic rats
Group III	Standard Control	STZ and NIC induced diabetic rats orally treated with Glibenclamide (10mg/kg b.w)
Group IV	Test Drug (Low Dose)	STZ and NIC induced diabetic rats orally treated with Pectolinarigenin (20mg/kg b.w)
Group V	Test Drug (High Dose)	STZ and NIC induced diabetic rats orally treated with Pectolinarigenin (50mg/kg b.w)

3.2 Effect of Pectolinarigenin on Fasting Blood Glucose

Rats in all diabetes groups had beginning Fasting Blood Glucose (FBG) levels that were significantly greater than those of rats in group I. In contrast to group II, the FBG levels were considerably lower following pectolinarigenin administration. In groups III, IV, and V, the FBG decrease was 65%, 69%, and 60%, respectively (Figure 2).

3.3 Effect of Pectolinarigenin on IPGTT

Throughout the trial (0–120 minutes following intraperitoneal glucose injection), group II's blood glucose level in the Intraperitoneal Glucose Tolerance Test (IPGTT) was continuously higher. On the other hand, as compared to group II, the blood glucose levels were considerably lower in the *Pectolinarigenin*-treated groups at all time points examined (Figure 3).

3.4 Effect of Pectolinarigenin on Serum Insulin Level

A decrease in serum insulin levels was observed in group II ($p<0.0001$). However, towards the end of treatment significant increase in serum insulin levels in group III ($p<0.0001$), group IV($p<0.001$) and group V($p<0.0001$)were observed when compared to group II, as shown in Figure 4.

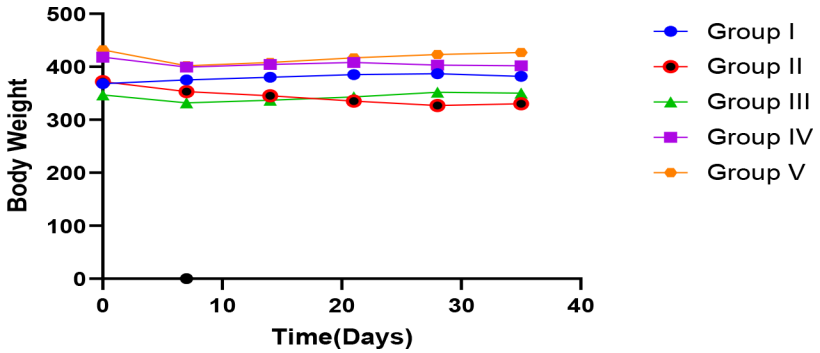


Figure 1. Effect of Pectolinarigenin on body weight at six different time points: day 0, 7, 14, 21, 28 and 35th.

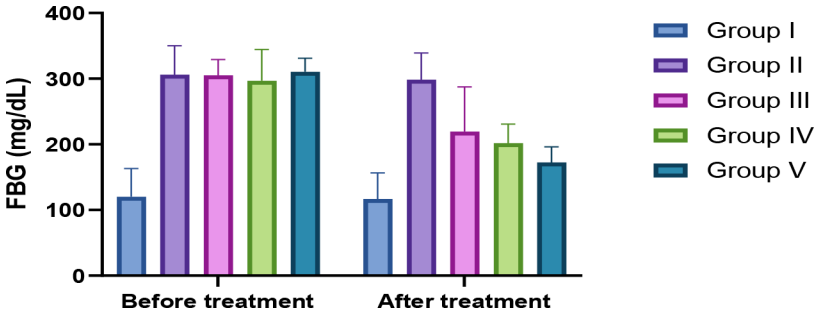


Figure 2. Effect of Pectolinarigenin on changes in fasting blood glucose.

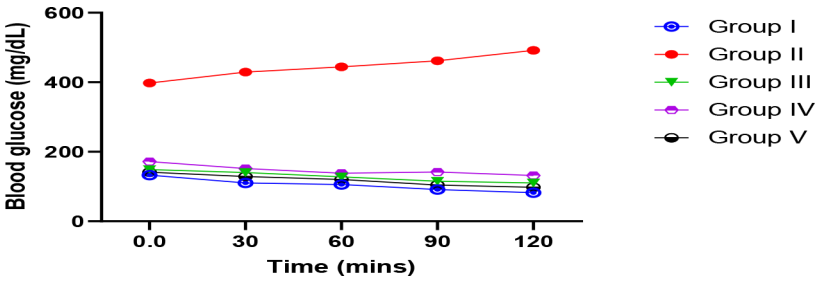


Figure 3. Effect of Pectolinarigenin on changes in IPGTT at five different time points.

3.5 Effect of Pectolinarigenin on HOMA IR

A decrease in HOMA IR levels was observed in group II when compared with group I. However, towards the end of treatment significant increase in HOMA IR levels in group III ($p<0.05$), group IV($p<0.001$) and group V ($p<0.05$) were observed when compared to group II, as shown in Figure 5.

3.6 Effect of Pectolinarigenin on HbA1c

An increase in HbA1c levels was observed in group II when compared with group I ($p<0.0001$). However, significant decreases in HbA1c levels were observed in group III ($p<0.0001$), group IV($p<0.001$) and group V ($p<0.0001$) when compared to group II, as shown in Figure 6.

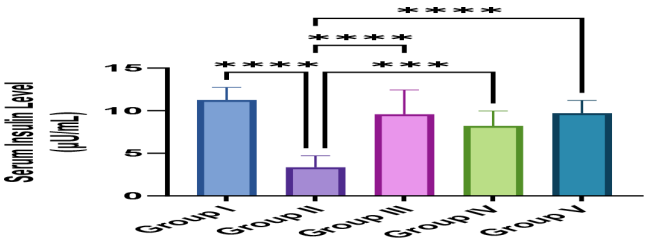


Figure 4. Effect of Pectolinarigenin on serum insulin level.

Statistical analysis was performed by ANOVA followed by Dunnet's multiple comparisons test to compare each group to Group II (Disease Control). Significance levels were denoted as ns (no significance), * ($p<0.05$), ** ($p<0.01$), and *** ($p<0.001$).

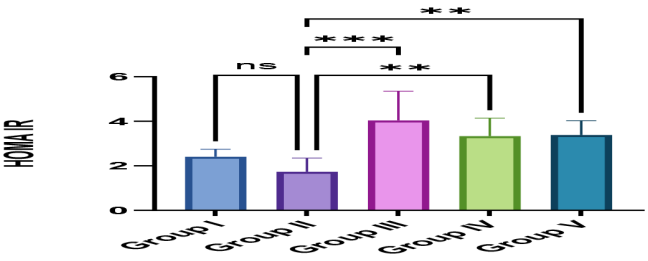


Figure 5. Effect of Pectolinarigenin on HOMA IR.

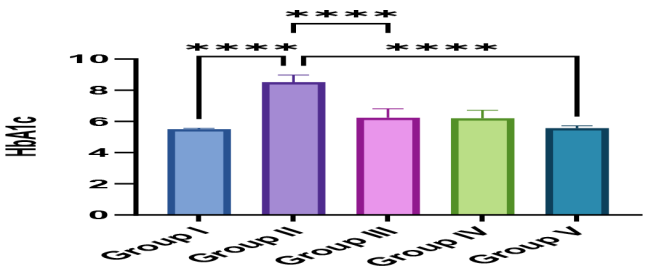


Figure 6. Effect of Pectolinarigenin on HbA1c.

3.7 Effect of Pectolinarigenin on Lipid Profile

Increase in total cholesterol and triglyceride levels and decrease in HDL-C levels were observed in group II when compared with group I ($p<0.0001$) as shown in Figure 7a, 7b and 7c. However, significant decrease in TC levels were observed in group III ($p<0.001$), group IV($p<0.01$) and group V ($p<0.01$) when compared to group II and significant decrease in TG levels were observed in group III ($p<0.01$), group IV($p<0.01$) and group V ($p<0.0001$) when compared to group II. Group V showed a better result compared to groups III and IV. However, a significant increase in HDL-C levels was

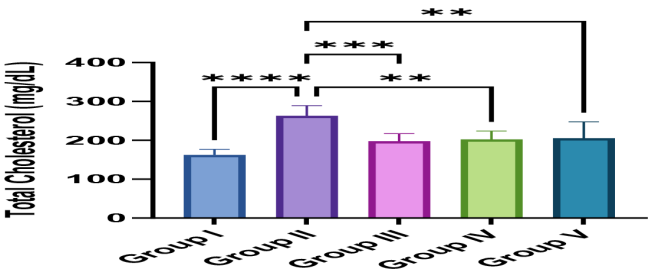


Figure 7a. Effect of Pectolinarigenin on total cholesterol.

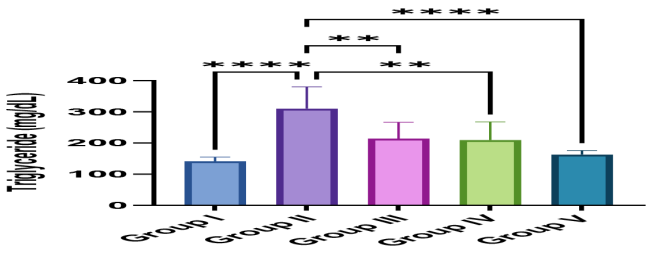


Figure 7b. Effect of Pectolinarigenin on triglyceride levels.

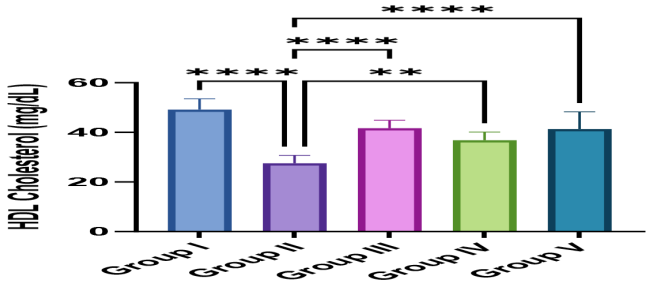


Figure 7c. Effect of Pectolinarigenin on HDL levels.

Statistical analysis was performed by ANOVA followed by Dunnet's multiple comparisons test to compare each group to Group II (Disease Control). Significance levels were denoted as ns (no significance), * ($p<0.05$), ** ($p<0.01$), and *** ($p<0.001$).

observed in group III (p<0.0001), group IV(p<0.01) and group V (p<0.0001) when compared to group II. Group V showed a better result compared to group IV.

3.8 Effect of Pectolinarigenin on Erythrocyte Osmotic Fragility Test

Erythrocyte osmotic fragility at various NaCl concentrations in diabetic and normal control groups found significant differences. Complete haemolysis was observed at 0.0% and 0.1% NaCl in both groups. Significant increases in fragility were noted in group II compared to group I at higher NaCl concentrations, as shown in Figure 8. Treatment with pectolinarigenin and glibenclamide reduced fragility, with pectolinarigenin showing better efficacy, especially at 0.7% NaCl. Overall, both treatments lowered fragility compared to group II (p<0.05) across various NaCl concentrations.

3.9 Effect of Pectolinarigenin on Oxidative Stress-related Enzymes in Pancreatic Tissue

Significant decrease in SOD and CAT levels were observed in group II when compared with group I (p<0.0001). However, increase in SOD levels were observed in group III (p<0.0001), group IV(p<0.0001) and group V (p<0.0001) when compared to group II. An increase in CAT levels was observed in group III (p<0.0001), group IV(p<0.001) and group V (p<0.0001) when compared to group II. Groups III and V showed equally significant results as given in Table 1. An increase in MDA levels was observed in group II when compared with group I (p<0.0001). However, a decrease in MDA levels was observed in group III (p<0.0001) and group V (p<0.0001) when compared to group II. Group IV did not show any significance when compared to group II, whereas group V showed better results compared to group III. A decrease in GSH levels was observed in group II when compared with group I (p<0.0001). However, significant increases in levels were observed in group III (p<0.0001), group IV(p<0.0001) and group V (p<0.001) when compared to group II. Group IV showed a more significant increase in GSH compared to group V, as shown in Table 2.

3.10 Effect of Pectolinarigenin on Interleukin-6

An increase in IL-6 levels was observed in group II when compared with group I (p<0.0001). However, a significant decrease in IL-6 levels was observed in group III (p<0.0001), group IV(p<0.05) and group V (p<0.0001) when compared to group II. Group III showed a better result compared to IV and V, as shown in Figure 9.

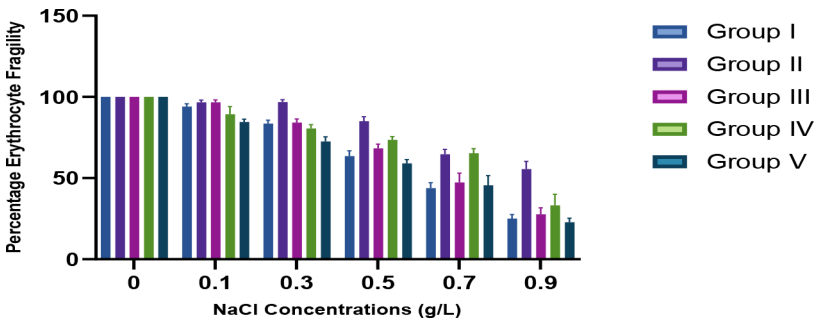


Figure 8. Effect of Pectolinarigenin on changes in the erythrocyte osmotic fragility test.

Table 2. Effect of Pectolinarigenin treatment on SOD, MDA, CAT and GSH in pancreatic tissue of experimental rats

	SOD Activity	MDA Activity	GSH Activity	CAT Activity
Group I	106.5± 2.88	0.71± 0.11	64.15± 4.15	9.13± 0.44
Group II	80.50± 6.05	11.92± 1.82	18.55± 1.86	4.71± 0.66
Group III	108.3± 4.13	1.81± 0.18	57.03± 3.52	7.80± 0.88
Group IV	96.0± 6.63	4.76± 2.44	52.83± 3.79	6.40± 0.42
Group V	111.8± 5.07	1.39± 0.32	43.74± 2.98	7.70± 0.62

Statistical analysis was performed by ANOVA followed by Dunnet's multiple comparisons test to compare each group to Group II (Disease Control). Values are expressed as mean ± SD (n=6).

3.11 Effect of Pectolinarigenin on Liver Glycogen

A significant decrease in liver glycogen levels was observed in group II when compared with group I ($p<0.0001$). However, a significant increase in liver glycogen levels was observed in group III ($p<0.0001$), group IV($p<0.0001$) and group V ($p<0.0001$) when compared to group II. Group III and V showed equally significant results, as shown in Figure 10.

3.12 Effect of Pectolinarigenin on Histological Examination of Pancreas

Image of pancreas H/E stained 40X showing normal beta cells (Figure 11a). Image of Pancreas H/E stained 40X showing degeneration of islets, increase in lobes and beta cells with saturated vacuoles (Figure 11b). Image of Pancreas H/E stained 40X showing normal islets of beta cells. Some degeneration of vacuoles is seen (Figure 11c). Image of Pancreas H/E stained 40X showing normal islets of beta cells. Normal arrangement of islets is seen, beta cell count is more (Figure 11d).

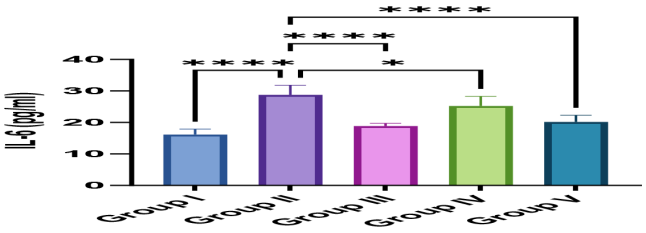


Figure 9. Effect of Pectolinarigenin treatment on IL-6.

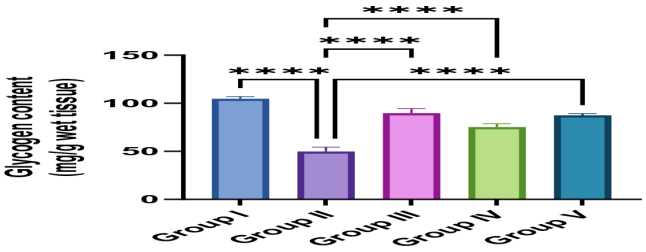


Figure 10. Effect of Pectolinarigenin treatment on liver glycogen.

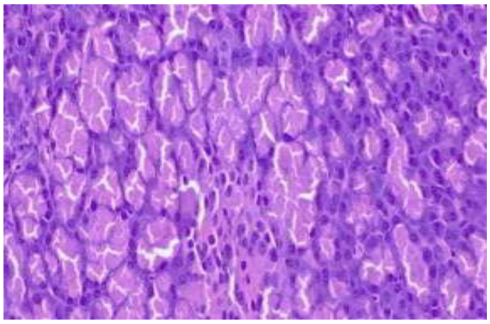


Figure 11a. Group I (NC).

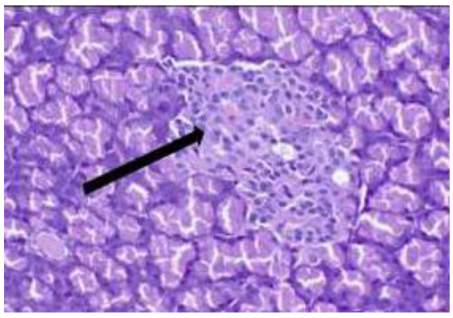


Figure 11b. Group-II (DC).

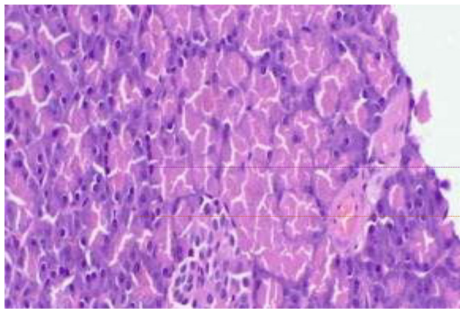


Figure 11c. Group-III (SC).

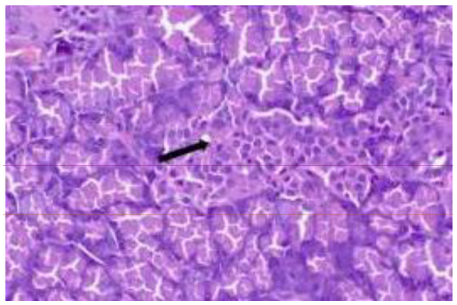


Figure 11d. Group-IV (T1).

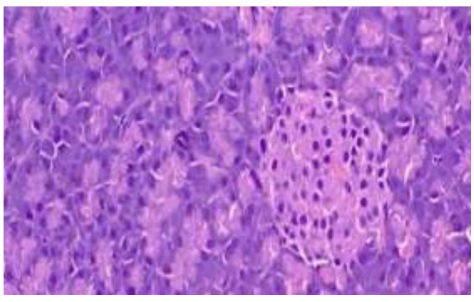


Figure 11e. Group-V (T2).

Image of Pancreas H/E stained 40X showing normal islets of beta cells. No signs of degeneration in beta cells (Figure 11e).

4. Discussion

The outcomes showed that supplementing with pectolinarigenin decreased body weight increase and fasting blood glucose levels while also enhancing glucose tolerance. Additionally, the rats that were administered the treatment exhibited favorable modifications in their lipid profiles, increased levels of blood insulin, and a drop in HOMA-IR values, which indicated improved insulin sensitivity. Significantly, lower IL-6 levels and decreases in HbA1c and erythrocyte osmotic fragility suggested better long-term glycemic management and reduced inflammation. In pancreatic tissues, lower MDA levels and higher antioxidant enzyme activity suggested improved antioxidant defenses and decreased oxidative stress. Significance was defined as p values<0.05. To sum up, research conducted both *in vitro* and *in silico* has demonstrated *pectolinarigenin's* therapeutic potential in the management of type 2 diabetes. Its promise for controlling DM is highlighted by its multi-targeted actions, which include anti-diabetic, anti-inflammatory and antioxidant capabilities.

5. Conclusion

In conclusion, there is substantial evidence to support the therapeutic efficacy of pectolinarigenin in the treatment of type 2 diabetes mellitus from both *in vivo* tests and in silico docking studies combined. The potential of pectolinarigenin as a flexible therapeutic agent was shown by its considerable binding affinity towards essential molecular targets implicated in the etiology of diabetes. Pectolinarigenin supplementation led to significant improvements in several diabetes-related parameters, including body weight, blood glucose levels, lipid profiles, insulin sensitivity, and inflammation markers, according to *in vivo* studies on Sprague Dawley rats. Furthermore, as assessed by SOD, MDA, CAT, and GSH, pectolinarigenin demonstrated an antioxidant action in pancreatic tissues. The importance of these findings was further validated by statistical analysis. In comparison to disease control, histological alterations also revealed normal islet beta cells in the pancreas. Pectolinarigenin is a viable option for the treatment of DM and associated consequences, according to these data. The results of this study indicate that pectolinarigenin may be a promising new therapy option for diabetes, however, more experimental validation is needed.

6. Author Contribution

Samiksha Jayswal, as the principal author, played a key role in conducting in silico molecular docking studies, performing *in vivo* experiments, analysing biochemical and metabolic parameters, and drafting the manuscript. Snigdha Das Mandal provided essential guidance throughout the research, supervising the experimental design, interpreting data, and offering critical insights into diabetes pathophysiology. She also thoroughly reviewed the manuscript to ensure scientific accuracy. Both authors have read and approved the final version of the manuscript.

7. References

1. Alam MF, Safhi MM, Anwer T, Siddiqui R, Khan G *et al.* Therapeutic potential of Vanillylacetone against CCl4 induced hepatotoxicity by suppressing the serum marker, oxidative stress, inflammatory cytokines and apoptosis in Swiss albino mice. Exp Mol Pathol. 2018; 105(1):81-88. https://doi.org/10.1016/j.yexmp.2018.06.001 PMid:29909158.
2. Jané-Salas E, Estrugo-Devesa A, Segura-Egea JJ, López-López J. Correlation between periodontal disease management and metabolic control of type 2 diabetes mellitus. A systematic literature review. Medicina Oral Patologia Oral y Cirugia Bucal. 2016; 21(4):e440.
3. Anwer T, Sharma M, Pillai KK, Haque SE, Alam MM *et al.* Protective effect of bezafibrate on streptozotocin-induced oxidative stress and toxicity in rats. Toxicology. 2007; 229(1-2):165-172. https://doi.org/10.1016/j.tox.2006.10.016 PMid:17145126.
4. Answer T, Sharma M, Pillai KK, Khan G. Protective effect of *Withania somnifera* against oxidative stress and pancreatic beta-cell damage in type 2 diabetic rats. Acta Pol Pharm. 2012; 69(6):1095-1101.
5. Berrougui H, Ettaib A, Gonzalez MH, De Sotomayor MA *et al.* Hypolipidemic and hypocholesterolemic effect of argan oil (*Argania spinosa* L in Merioneshawi rats. J Ethnopharmacol. 2003; 89(1):15-18. https://doi.org/10.1016/S0378-8741(03)00176-4 PMid:14522427.
6. Barham D, Trinder P. An improved colour reagent for the determination of blood glucose by the oxidase system.

Analyst. 1972; 97(1151):142-145. https://doi.org/10.1039/an9729700142 PMid:5037807.
7. Bucolo G, David H. Quantitative determination of serum triglycerides by the use of enzymes. Clin Chem. 1973; 19(5):476-482. https://doi.org/10.1093/clinchem/19.5.476 PMid:4703655.
8. Chahil TJ, Ginsberg HN. Diabetic dyslipidemia. Endocrinol Metab Clin. 2006; 35(3):491-510. https://doi.org/10.1016/j.ecl.2006.06.002 PMid:16959582.
9. Greenwald RA. Catalase activity. CRC Handbook of Methods for Oxygen Radical Research. 1985; p. 1-447.
10. Cui Y, Shi Y, Bao Y, Wang S, Hua Q, Liu Y. Zingerone attenuates diabetic nephropathy through inhibition of nicotinamide adenine dinucleotide phosphate oxidase 4. Biomed Pharmacother. 2018; 99:422-430. https://doi.org/10.1016/j.biopha.2018.01.051 PMid:29367111
11. Cruz KJ, Oliveira AR, Marreiro D. Antioxidant role of zinc in diabetes mellitus. World J Diabetes. 2015; 6(2):333. https://doi.org/10.4239/wjd.v6.i2.333 PMid:25789115 PMCid:PMC4360427.
12. Chen Y, Li H, Tang Y, Ren J. Pectolinarigenin inhibits lipopolysaccharide-induced inflammatory response by down-regulating MAPK, AKT, and NF-κB pathways in Raw 264.7 cells. Int Immunopharmacol. 2018; 61:310-317.
13. Pellegrino M, Meldolesi J, Avogaro A. Induction of non-insulin-dependent diabetes in adult rats by high-fat diet and low doses of streptozotocin: An animal model for study of lipid-induced diabetes. Int J Exp Diabetes Res. 1998; 1(2):121-131.
14. Shirwaikar A, Rajendran K, Barik R, Shirwaikar A. Antinflammatory activity of *Plectranthus amboinicus* on aspirin-induced ulcerated gastric mucosa. Inflammopharmacol. 2014; 12(6):41-48.