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Therapeutic Potential of White Sweet Potato Peel in Enhancing Insulin Production and The Proliferation of Beta Cells in Diabetic Rats

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Abstract

Diabetes mellitus (DM) affects approximately 422 million people worldwide, predominantly in low- to middle-income countries, and is associated with increasing morbidity and mortality. The long-term use of conventional antidiabetic drugs may cause adverse effects, prompting interest in natural therapeutic alternatives. This study aimed to evaluate the effects of white sweet potato peel (WSPP) on glycemic control, insulin expression, and pancreatic beta-cell proliferation in streptozotocin-induced diabetic rats. Male Wistar rats were divided into five groups: diabetic control, diabetic rats treated with WSPP at doses of 400, 800, and 1600 mg/kgBW/day, and non-diabetic controls. Diabetes was induced by a single intraperitoneal injection of streptozotocin (60 mg/kgBW). Fasting blood glucose (FBG) levels were measured at baseline and during treatment. Pancreatic tissues were analyzed using immunohistochemistry to assess insulin expression, Langerhans islet area, and beta cell proliferation using anti-insulin and anti-PCNA antibodies. WSPP administration resulted in a significant, dose-dependent reduction in FBG levels compared to diabetic controls ($p < 0.05$). The highest dose (1600 mg/kgBW/day) reduced FBG from approximately 250 mg/dL to 72.22 mg/dL after four weeks ($p < 0.01$), reaching the normal range. Immunohistochemical analysis demonstrated significant increases in insulin expression scores, Langerhans islet area, and the percentage of PCNA-positive cells in the 800 and 1600 mg/kgBW/day groups compared to untreated diabetic rats. At the highest dose, these parameters approached those observed in non-diabetic controls, indicating substantial restoration of pancreatic islet structure and function. In conclusion, WSPP improves glycemic control and promotes beta-cell proliferation in diabetic rats, highlighting its potential as a natural, cost-effective therapeutic strategy for diabetes management.

Keywords: Beta cell proliferation; Diabetes mellitus; Fasting blood glucose; Insulin expression; White sweet potato peel

1. INTRODUCTION

Diabetes mellitus (DM) impacts around 422 million people globally, with most residing in developing countries. Every year, diabetes leads to 1.5 million fatalities. In recent decades, both the prevalence and incidence of DM have been on a continuous rise (World Health Organization, 2024). According to the International Diabetes Federation's 2025 Diabetes Facts

& Figures, approximately 589 million adults worldwide live with diabetes, and this number is projected to rise substantially in the coming decades (International Diabetes Federation, 2025). Diabetes mellitus is a chronic metabolic condition characterized by elevated blood sugar levels and disruptions in the metabolism of carbohydrates, proteins, and lipids due to insufficient insulin. This disorder can arise from beta cells in the pancreatic Langerhans islets producing inadequate or impaired insulin, or from the body's cells becoming less sensitive to insulin (P2PTM Kemenkes, 2024). The islets of Langerhans consist of seven different cell types, each secreting specific hormones, with beta cells making up 50-80% of the islet area and producing insulin. Pathologically, DM is associated with inflammation and beta-cell destructionue to prolonged hyperglycemia and increased Reactive Oxygen Species (ROS) (Baro et al., 2023).

The standard management of DM involves a combination of dietary planning, physical exercise, and hypoglycemic agents, including insulin (Perkumpulan Endokrinologi Indonesia (PERKENI), 2019). Commonly used medications for type 2 diabetes, such as metformin and glibenclamide, can cause various side effects with long-term use. Consequently, traditional medicine and natural remedies have emerged as alternative treatments for DM (Kinanti et al., 2023; Nabila et al., 2023; Widiastuti et al., 2023; Wijayanti et al., 2023). The "back to nature" movement has led to increased interest in over 400 plant species with documented hypoglycemic activity, including the white sweet potato (Pakaya et al., 2022).

The white skinned sweet potato, widely grown in Indonesia, is traditionally used as an alternative carbohydrate source due to its lower glycemic index and higher fiber content compared to rice. With a moderate to low glycemic index (54-68), sweet potatoes are a preferable carbohydrate source over bread, rice, and potatoes (Putri et al., 2023). The sweet potato contains sporamin, an antioxidant protein produced in response to physical damage, which plays a significant role in its healing properties. Extracts of sweet potato have been reported to enhance adiponectin levels, improving insulin metabolism in type 2 diabetes patients. Additionally, sweet potatoes are rich in essential nutrients, including vitamin A, thiamine, ascorbic acid, niacin, riboflavin, phosphorus, calcium, and iron, making them an accessible and nutritious food source for rural populations (Babasaheb et al., 2019).

Studies have shown that white sweet potato peel (WSPP) powder can reduce fasting blood glucose levels (FBG) and improve insulin sensitivity in diabetic rats. The active components identified in the peel include acidic glycoproteins (22 kDa) and arabinogalactan proteins (126.8 kDa). These components possess antidiabetic properties, while Trypsin Inhibitor Proteins (TIP) in the peel exhibit antioxidant activity against various ROS, increasing catalase, superoxide dismutase (SOD), and glutathione peroxidase activities in diabetic rats (Akomolafe et al., 2025; Arisanti et al., 2023a). Histopathological examinations of the pancreas in diabetic rats treated with sweet potato tubers and leaves for eight weeks showed improvements in the Langerhans islet area, suggesting that the antioxidants in sweet potato can trigger beta cell regeneration (C.-K. Shih et al., 2020). Streptozotocin (STZ) is also used in this study to induce Diabetes. Streptozotocin (STZ) causes necrosis in beta cells of the pancreas and inhibits the secretion of insulin (Widiastuti et al., 2023; Kinanti et al., 2023). However, hematoxylin-eosin (HE) staining

used in these studies is not specific for beta cells, as the Langerhans islets also contain other cell types.

This study aims to investigate the effects of WSPP on the histopathological characteristics of the pancreas in diabetic rats using immunohistochemical staining methods. The novelty of this research lies in exploring the potential therapeutic effects of WSPP peel. Most previous research focuses on the flesh of sweet potatoes, while this research highlights the benefits of the peel, which is often discarded. The specific objective is to provide detailed insights into the regenerative mechanisms of sweet potato peel components in mitigating hyperglycemia and promoting beta cell proliferation. This research addresses the gap in the literature by offering a more specific analysis of beta cell regeneration and insulin secretion in diabetic conditions, contributing valuable information on the potential application of natural substances in diabetes treatment and supporting the development of alternative therapeutic strategies.

2. MATERIAL AND METHODS

2.1. Materials

About 5 kg of white sweet potatoes were thoroughly washed, then peeled down to the cortex layer to a thickness of 4 mm using a disk knife, with the peel thickness measured using a caliper. The peel slices were dried using an electric oven at 40°C for 8 hours, then ground into powder using a blender.

2.2. Research design

This was an in vivo experimental study using a completely randomized design. Wistar rats (*Rattus norvegicus*), all male, aged 6 weeks, weighing between 100-160 grams, divided into 5 groups, each group consists of 6 rats: diabetic rats, diabetic rats administered with 400, 800, and 1600 mg/kgBW/day of white sweet potato cortex powder suspension, and non-diabetic rats given standardized feed. White sweet potato cortex powder suspension was prepared daily using 0.5% sodium carboxymethyl cellulose (Na-CMC) as a suspending agent. The required amount of cortex powder was weighed according to the treatment dose (400, 800, and 1600 mg/kgBW/day) and suspended in 0.5% Na-CMC solution until homogeneous. The rats were fasted overnight (10-12 hours) and subsequently injected intraperitoneally with 60 mg/kgBW streptozotocin (STZ) in citrate buffer pH 4.5, once (Harijanto et al., 2017). The non-diabetic rats were injected with citrate buffer only. One hour after STZ injection (Merck, Darmstadt Germany), 10% dextrose was given orally to prevent hypoglycaemia. Blood samples were drawn from the retro-orbital sinus to measure Fasting Blood Glucose (FBG) levels on the 3rd day post-STZ injection, and at 2 and 4 weeks post-treatment.

2.3. Immunohistochemistry staining and analysis

Pancreatic tissues were preserved in a 10% formalin buffer and then encased in paraffin. The samples were cut into of 3-4 μm thickness and placed on slides treated with poly L-lysine. Following deparaffinization, the sections were immunohistochemically stained using an anti-insulin antibody (clone INS05, Labvision corporation NeoMarkers) and anti-PCNA

(Proliferating Cell Nuclear Antibody) (LS-C9538, Lifespan Biosciences). Immunological reactions were visualized using Biotin-Streptavidine peroxidase with DAB chromogen (Ultravision Detection System Anti-Polyvalent (UDSAP) - HRP/DAB kit (TP-015-HD), Labvision corporation). In negative control slides, PBS was utilized instead of the primary antibody. Images were captured using Optilab viewer and Image Raster software (PT. Miconos, Yogyakarta Indonesia), at magnifications of 100 and 400x. Semi-quantitative assessment of insulin expression was scored as 0 (no brown colour), 1 (mild brown), 2 (average brown), and 3 (intense and very intense brown colour). This evaluation was conducted on the first 10 Langerhans islets found, and a histological score (histoscore) was calculated for each islet, averaged for each slide (Shapiro et al., 2021). Insulin expression score = {(A x 0) + (B x 1) + (C x 2) + (D x 3) }/ 10 (A, B C, and D represent the number of Langerhans islets with scores of 0, 1, 2, and 3, respectively).

The area of the Langerhans islets was measured by counting the grid boxes within the islet area (the first 10 Langerhans islets found). Images were taken with Image Raster (magnification 100x) placed under a 5x5 mm grid box (5mm = 7µm; area of one box is 49µm²). Islet area = number of boxes x 49µm². The islet of Langerhans cell proliferation was assessed by calculating the percentage of PCNA-positive cells from the first 500 cells found within the Langerhans islet (marked by a brown colour on the cell nucleus) (Zini et al., 2016).

2.4. Statistical analysis

Quantitative data on FBG levels were statistically evaluated within groups and paired t-test between groups. Changes in insulin expression intensity in Langerhans islets and proliferation of PCNA-positive Langerhans islet cells were analysed using the Kruskal-Wallis test and Mann-Whitney test between two groups.

2.5. Ethics

This research adhered to the ethical guidelines established by the Institutional Ethical Committee of YARSI University Research Centre, following the approval granted under the protocol No: 150/KEP-UY/EA.20/VI/2024. All animal-related experimental procedures were conducted in strict accordance with institutional guidelines and regulations, ensuring humane treatment and adherence to ethical principles in scientific research. The welfare of the animals was a primary consideration throughout the study, and all efforts were made to minimize suffering and stress.

3. RESULTS AND DISCUSSION

All STZ-induced rats experienced weight loss, while the normal group showed weight gain due to ad libitum feeding. The benefit of WSPP treatment on the body weight of diabetic rats is presented in Figure 1. Diabetes mellitus is characterized not only by elevated blood glucose levels but also by weight loss in rats. The non-diabetic rats naturally gained weight over the four-week period, while untreated diabetic rats experienced significant weight loss. The weight loss is attributed to STZ-induced beta cell damage, resulting in reduced insulin

production and impaired glucose uptake. When glucose is insufficiently utilized, alternative energy reserves such as fats and proteins are metabolized for energy, leading to weight loss (Rokhmah et al., 2022). After 4 weeks of treatment, all WSPP-treated rats (400, 800, and 1600 mg/kgBW per day) exhibited weight gain back to normal levels, concomitant with the reduction in FBG. However, diabetic rats treated with WSPP showed a dose-dependent improvement in body weight, indicating the potential therapeutic benefits of WSPP in managing diabetes and mitigating its symptoms. This suggests that WSPP could be a valuable natural supplement in the management of diabetes-related weight loss.

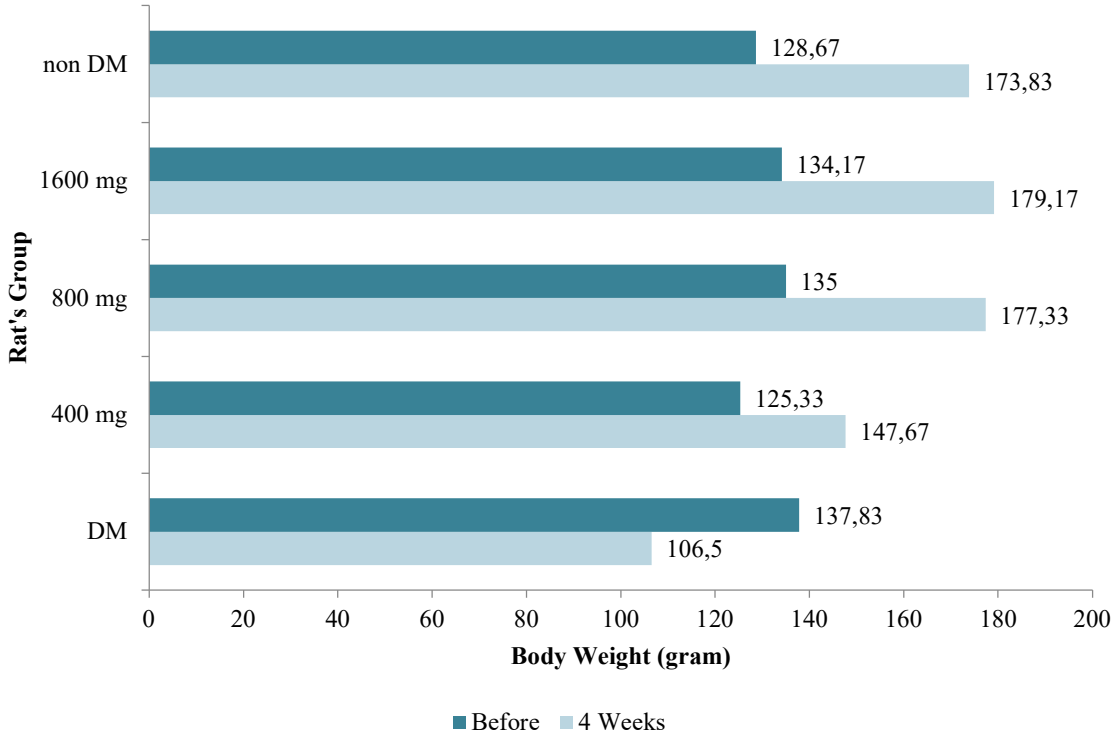

Figure 1. Rats body weight before and 4 weeks after white sweet potato peel (WSPP) treatment. *Description*: DM: diabetic rats; 400 mg: diabetic rats+400 mg/kgBW WSPP; 800 mg: diabetic rats+800 mg/kgBW WSPP; 1600 mg: diabetic rats+1600 mg/kgBW WSPP; non-DM: non diabetic rats.

Treatment with white sweet potato peel powder (WSPP) reduced fasting blood glucose (FBG) levels in diabetic rats in a dose-dependent manner ($p < 0,05$) (Figure 2). Untreated diabetic rats maintained persistently high glucose levels throughout the experimental period, while those treated with increasing doses of WSPP showed progressively lower glucose levels. After 4 weeks of treatment, the FBG levels in the 800 mg/kgBW and 1600 mg/kgBW WSPP-treated groups were normalized to 102.54 mg/dL and 72.22 mg/dL, respectively (normal FBG range for rats: 50-135 mg/dL). Moreover, administration of the highest dose (1600 mg/kgBW) brought glucose levels nearly to those of normal, non-diabetic rats. The WSPP could reduce FBG levels ($p < 0.05$) in all treatment groups.

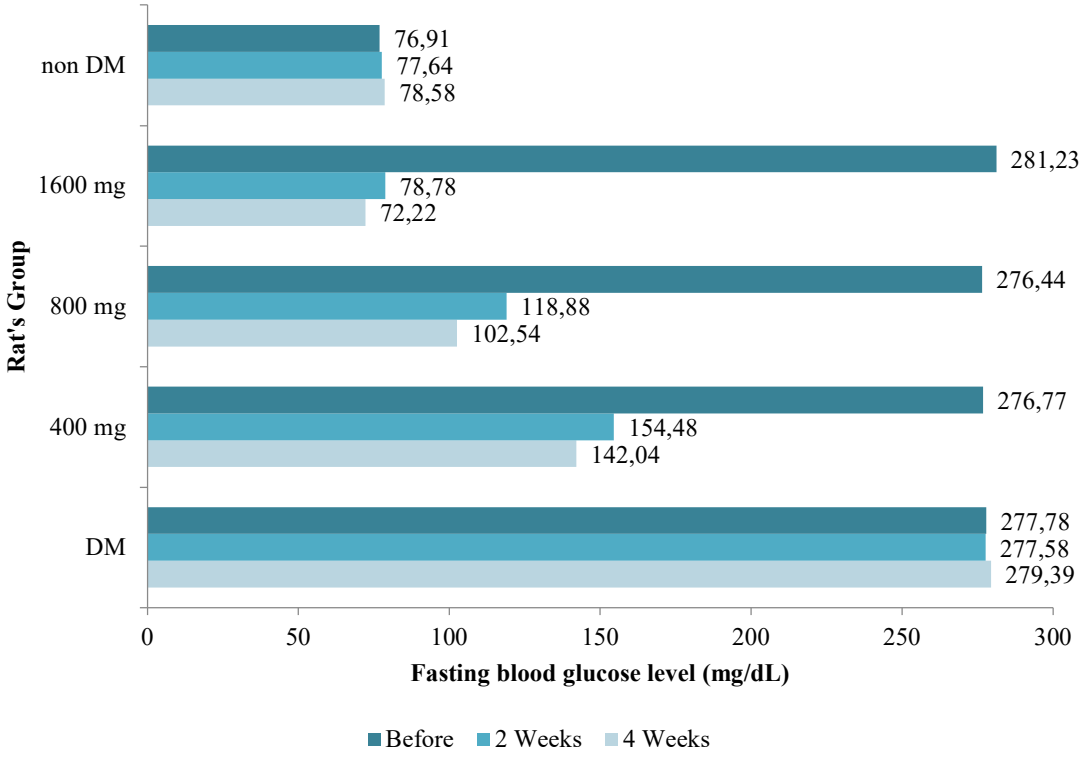

Figure 2. Fasting Blood Glucose level before, 2 weeks, and 4 weeks after white sweet potato peel (WSPP) treatment. *Description*: DM: diabetic rats; 400 mg: diabetic rats+400 mg/kgBW WSPP; 800 mg: diabetic rats+800 mg/kgBW WSPP; 1600 mg: diabetic rats+1600 mg/kgBW WSPP; non-DM: non diabetic rats.

The near normalization of FBG at the highest dose (Figure 2) suggests that WSPP improved glycemic control by enhancing insulin sensitivity and supporting endogenous insulin availability. These findings are consistent with previous reports showing that white sweet potato and its bioactive compounds exert antihyperglycemic effects by improving insulin signaling and protecting against oxidative stress–induced β-cell dysfunction (Arisanti et al., 2023b; Kinoshita et al., 2023; C. K. Shih et al., 2020) Collectively, the sustained reduction in FBG indicates that WSPP holds promise as a natural therapeutic agent for diabetes management.

Treatment with white sweet potato peel powder (WSPP) improved insulin expression and promoted regeneration of the Langerhans islets in diabetic rats in a dose-dependent manner (Figure 3). While the 400 mg/kgBW/day group showed a non-significant increase compared to diabetic controls ($p = 0.09$), significant improvements were observed in the 800 and 1600 mg/kgBW/day groups ($p = 0.02$ and 0.01, respectively). Both insulin expression scores and islet area increased with higher WSPP doses, with the highest dose nearly restoring these parameters to normal levels. This enhancement in insulin production is associated with reduced fasting blood glucose levels and is likely mediated by increased β-cell proliferation in treated diabetic rats.

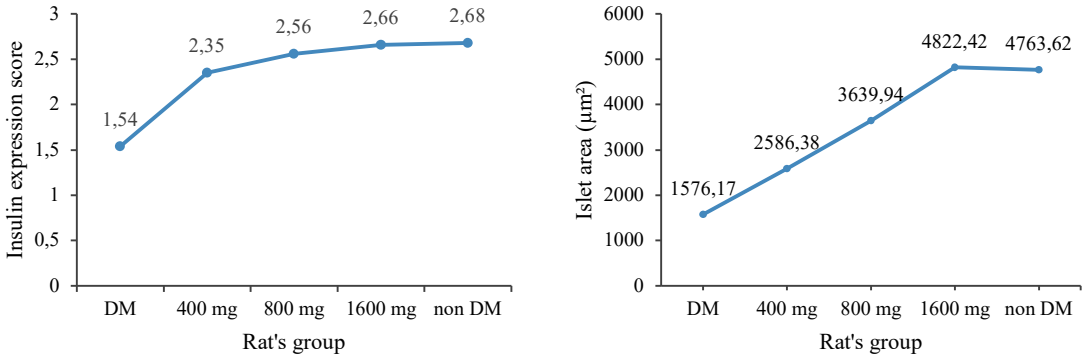

Figure 3. Insulin expression scoring and Langerhan's islet area after white sweet potato peel (WSPP) treatment. *Description*: (DM: diabetic rats; 400 mg: diabetic rats+400 mg/kgBW WSPP; 800 mg: diabetic rats+800 mg/kgBW WSPP; 1600 mg: diabetic rats+1600 mg/kgBW WSPP; non-DM: non diabetic rats).

The immunohistochemical analysis in Figure 4 demonstrate the potential of WSPP in restoring insulin expression and increasing the area of Langerhans islets of diabetic rats. The treatment shows a clear dose-dependent effect, with higher doses leading to significant improvements in insulin production. This suggests that WSPP could play a crucial role in diabetes management by enhancing the insulin-producing capacity of the pancreas.

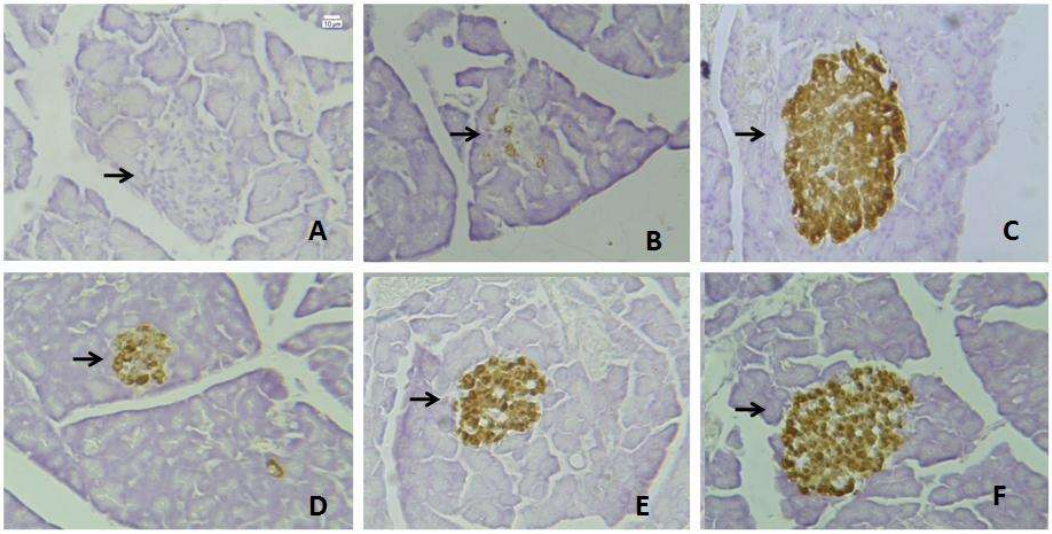

Figure 4. Insulin expression (brown color) and area of Langerhan's islet (→) after white sweet potato peel (WSPP) treatment. *Description*: (A) negative control, (B) diabetic rats, (C) non diabetic rats, (D) diabetic rats+400mg/kgBW WSPP, (E) diabetic rats+800 mg/kgBW WSPP, (F) diabetic rats +1600 mg/kgBW WSPP (immunohistochemistry staining with anti-insulin, x100).

The findings in Figures 3 and 4 are consistent with the previous reports showing that bioactive compounds in white-fleshed sweet potato, particularly polyphenols, flavonoids, and

resistant starch, exert protective effects on pancreatic β-cells by reducing oxidative stress and inflammation. The strong insulin immunoreactivity and enlarged islet area in the highest-dose WSPP group closely resembled the non-diabetic control, suggesting a regenerative or β-cell–preserving effect rather than mere glycemic compensation. Mechanistically, sweet potato–derived phytochemicals have been shown to enhance insulin secretion, suppress β-cell apoptosis, and improve insulin signaling pathways, including modulation of GLP-1 and reduction of DPP-4 activity (Akomolafe et al., 2025). In addition, antioxidant activity from phenolic-rich sweet potato extracts has been reported to mitigate streptozotocin-induced pancreatic damage and support islet regeneration (Islam, 2024; Zhang et al., 2020). Collectively, these data support the conclusion that WSPP improves both functional (insulin expression) and morphological (islet size) parameters of pancreatic islets, reinforcing its potential as a functional food–based intervention for diabetes management.

Administration of white sweet potato peel powder (WSPP) significantly increased the proliferation of Langerhans islet cells in diabetic rats, as indicated by the higher percentage of PCNA-positive cells observed in all treatment groups compared to diabetic controls (Figure 5). The diabetic rats receiving WSPP at doses of 400, 800, and 1600 mg/kgBW/day demonstrated a significantly higher percentage of PCNA-positive cells than the diabetic control rats. The Kruskal-Wallis test showed noticeable differences between the non-diabetic rats and all WSPP-treated diabetic groups when compared to the diabetic control group ($p < 0.05$). The dose-dependent increase in PCNA positive cells across the treatment groups highlights the efficacy of WSPP in enhancing regenerative activity. The findings suggest that WSPP could serve as a promising natural intervention for improving pancreatic function and managing diabetes.

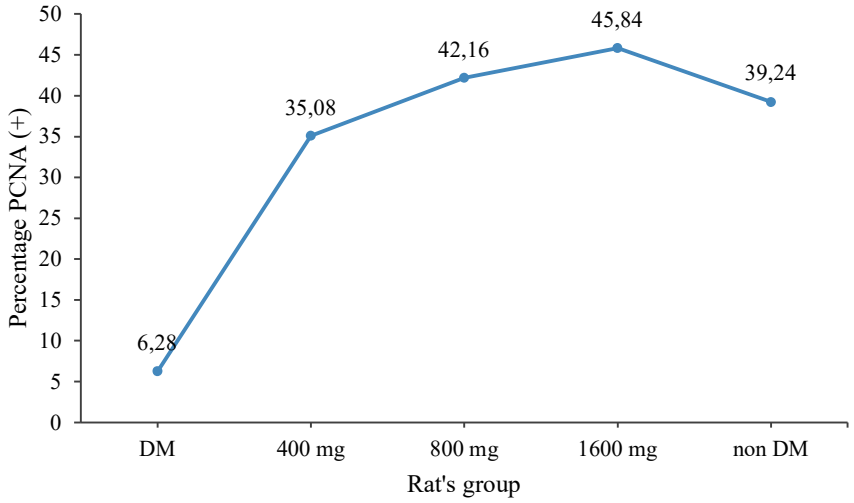

Figure 5. Percentage of anti PCNA (+) cells in Langerhan's islet after white sweet potato peel (WSPP) treatment. *Description*: DM: diabetic rats; 400 mg: diabetic rats+400 mg/kgBW WSPP; 800 mg: diabetic rats+800 mg/kgBW WSPP; 1600 mg: diabetic rats+1600 mg/kgBW WSPP; non-DM: non diabetic rats.

The immunohistochemical analysis in Figure 6 demonstrates the benefit of WSPP treatment on the growth of Langerhans islet cells in diabetic rats. The untreated diabetic rats exhibit minimal proliferative activity, while the non-diabetic rats show active cell proliferation. Treatment with WSPP leads to a dose-dependent increase in PCNA-positive cells, indicating enhanced regenerative activity in the pancreatic islets.

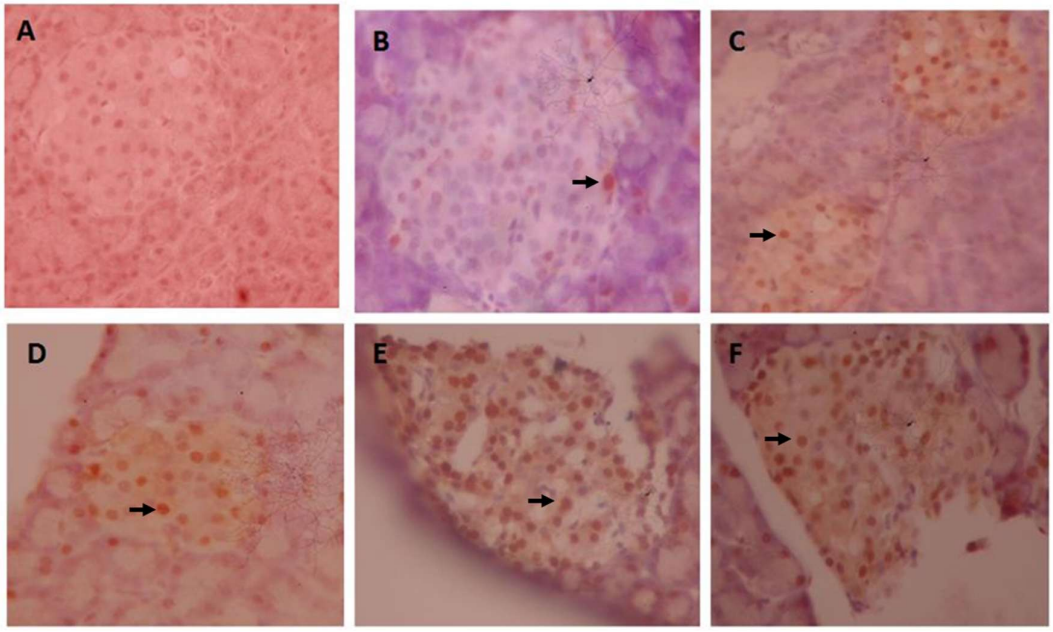

Figure 6. Proliferation of Langerhan's islet cells after white sweet potato peel (WSPP) treatment. *Description*: PCNA (+) cells (Proliferating Cell Nuclear Antibody cells) marked with brown color (→). (A) negative control, (B) diabetic rats, (C) non diabetic rats, (D) diabetic rats+400mg/kgBW WSPP, (E) diabetic rats+800 mg/kgBW WSPP, (F) diabetic rats +1600 mg/kgBW WSPP (immunohistochemistry staining with anti-PCNA, x400).

The increased percentage of PCNA-positive cells in the Langerhans islets (Figure 5 and 6) across all treatment groups suggests enhanced beta cell proliferation, likely induced by the anti-diabetic properties of WSPP. Research indicates that WSPP contains bioactive compounds like acidic glycoproteins and arabinogalactan proteins, which have been shown to lower fasting blood glucose and enhance insulin sensitivity (Pakaya et al., 2022). The antioxidant capabilities of trypsin inhibitor protein (TIP) found in WSPP, known to reduce reactive oxygen species (ROS), could mitigate oxidative stress on beta cells, enhancing their survival and function (Rokhmah et al., 2022). This aligns with findings by C.-K. Shih et al. (2020), demonstrating WSPP's potential to regenerate pancreatic islets in diabetic models by counteracting hyperglycaemia. Thus, WSPP may contribute to improved pancreatic function, supporting diabetes management through natural means.

These findings emphasize the potential of WSPP as a natural therapeutic compound for boosting beta cell proliferation, insulin production, and effectively managing diabetes mellitus by improving glycaemic control and normalizing body weight. The study's duration was limited

to a few weeks, providing a snapshot rather than long-term effects. Prolonged studies are necessary to understand the sustainability of WSPP's therapeutic benefits and any potential long-term side effects. A deeper investigation into the specific bioactive compounds in WSPP and their interactions with cellular pathways such as AMPK and PI3K/AKT would enhance the understanding of its mechanisms.

4. CONCLUSION

This study showed that white sweet potato peel (WSPP) as considerable therapeutic potential for diabetes management. through its ability to enhance insulin expression and promote the proliferation of pancreatic islet cells. These findings suggested that WSPP could serve as a novel, natural, and cost-effective treatment for diabetes, offering an alternative to conventional therapies. The dose-dependent effects observed in this study provide a foundation for optimizing WSPP dosage for therapeutic applications. The use of an agricultural by-product also highlights the potential for sustainable and eco-friendly medical solutions.

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CONFLICT OF INTEREST

All authors declared that there was no conflict of interest.

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