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Exploring Antidiabetic Effects of Enriched Mocaf Noodles: A Combined Computational and *In Vivo* Study

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Abstract

Diabetes is a critical global health issue, necessitating sustainable dietary interventions with minimal side effects. This study explores the antidiabetic potential of modified cassava flour (mocaf) noodles enriched with Latoh (*Caulerpa lentillifera*) using both computational and *In Vivo* methods. Bioactive compounds in Latoh were identified through Swiss Target Prediction and PASS Online, predicting activities such as oxidative stress reduction, glucose modulation, and Dipeptidyl Peptidase IV (DPP-IV) inhibition. Male Wistar rats (n=24) aged 2-3 months were divided into four groups: healthy control (AIN-96M diet), diabetic control, and two diabetic groups supplemented with mocaf noodles containing Latoh or carboxymethyl cellulose (CMC) as binders. Diabetes was induced using nicotinamide and streptozotocin, with blood samples collected weekly for fasting glucose, insulin, and malondialdehyde (MDA) analysis. Results demonstrated that mocaf-Latoh noodles significantly reduced fasting blood glucose levels from >250 mg/dL to 105 mg/dL, lowered MDA levels by 45%, and increased serum insulin levels by 30%, indicating enhanced beta-cell function and reduced oxidative stress. These results indicate decreased oxidative stress and enhanced beta-cell activity in the pancreas. According to the findings, mocaf-Latoh noodles have the potential as a functional food for managing diabetes and should be investigated further in human trials.

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Introduction

The global and national rise in diabetes prevalence has prompted urgent efforts to find effective, sustainable interventions for managing this chronic disease. Diabetes has reached epidemic proportions globally, affecting approximately 425 million people as of 2017, with estimates suggesting that this percentage may increase to 10.2% by 2030 and 10.9% by 2045.[1] Currently, 537 million individuals aged 20–79 are living with diabetes worldwide, and the disease is directly responsible for up to 6.7 million fatalities annually. In Indonesia, diabetes is a growing public health, significantly influenced by dietary and lifestyle choices. According to data from IDF (2021),[2] Indonesia ranks among the top ten nations with the highest number of diabetics. Although standard pharmacological treatments effectively manage blood glucose, they often come with adverse side effects, highlighting the need for safer and more sustainable alternative approaches. Functional foods rich in resistant starch and dietary fiber have shown potential in diabetes prevention and management by regulating blood glucose through mechanisms that slow glucose absorption and enhance insulin sensitivity.[3–5]

One promising product in this field is mocaf-based noodles enriched with Latoh (*Caulerpa lentillifera*). *Caulerpa lentillifera*, commonly known as Latoh, is a green seaweed with promising nutritional and therapeutic benefits, particularly in metabolic health and potential antidiabetic effects.[6,7] Latoh, a lesser-known ingredient, has been studied for its nutritional benefits and potential role in improving metabolic health, though its specific antidiabetic effects remain underexplored. Mocaf (modified cassava flour), derived from cassava, has a naturally low glycemic index (GI), making it a suitable wheat substitute for individuals with diabetes, as it aids in controlling blood glucose levels.[5] When paired with latoh, a seaweed high in dietary fiber (more than 50% of dry weight)[8] and bioactive compounds like phenolics, antioxidants, and bioactive proteins, mocaf provides a potent nutritional profile that is ideal for diabetes-friendly foods.[9] The dietary fiber and bioactive properties of Latoh further enhance the antidiabetic potential of the noodles, potentially improving both their nutritional and functional benefits.[10] The integration of mocaf and Latoh in noodle production not only offers a low-GI, high-fiber alternative to conventional noodles but also introduces antidiabetic properties through the action of bioactive compounds. Mocaf-Latoh noodle is a viable contender as a functional meal for diabetes treatment because of these ingredients, which are thought to help regulate blood glucose through processes like Dipeptidyl Peptidase IV (DPP-IV) inhibition, increasing insulin release, and supporting glucose reduction.[11,12]

Several studies have highlighted the potential of functional foods in managing diabetes, with various natural ingredients showing promising antidiabetic effects, suggesting that the incorporation of novel ingredients, like Latoh, could be beneficial in diabetes prevention and treatment. Incorporating computational methods to model the interaction of bioactive compounds in foods offers a cutting-edge approach to identifying promising antidiabetic properties, which can complement traditional *In Vivo* experiments and provide deeper mechanistic insights.[13] Recent *In Vivo* studies have demonstrated the effectiveness of functional foods, such as whole grains and fiber-rich noodles, in reducing blood glucose levels, suggesting that similar benefits might be achievable with Mocaf-enriched noodles.[14,15] As the role of diet in managing diabetes becomes increasingly important, it is crucial to investigate and validate the effects of functional foods through both computational models and well-designed *In Vivo* experiments to better understand their potential in diabetes intervention.

This study aims to evaluate the antidiabetic potential of mocaf-Latoh noodles through both in silico (computational) predictions and *In Vivo* testing on diabetic rat models. The primary objectives are to analyze the functional properties of these noodles, investigate their potential to inhibit dipeptidyl peptidase-IV (DPP-IV) through computational modelling and assess their effects on blood glucose levels and insulin response *In Vivo*. By exploring these mechanisms, this research aims to provide comprehensive insights into the therapeutic potential of mocaf noodles enriched with Latoh for diabetes management, positioning them as an innovative, health-promoting dietary intervention.

Material and Methods

Materials

The materials used in this study included modified cassava flour (Mocaf), which was made from cassava produced by local farmers through the fermentation of cassava using a Mocaf starter. The mocaf starter used for this process was sourced from tapioca waste derived from local rural products. Additionally, Latoh (*Caulerpa lentillifera*) was used as an additive. The Latoh, approximately one month old, was obtained from local farmers in Jepara, Central Java, Indonesia. The DiaSys GOD-PAP Pack (Germany) was used for blood glucose analysis, while the FineTest Rodent INS ELISA Unit (China) was used to measure serum insulin levels. Additional reagents, including paraformaldehyde for sample fixation and antibodies for immunohistochemical staining, were obtained from ScyTek Research Facilities, Inc. (USA) and Thermo Fisher Logical (USA), respectively.

Preparation of Noodles

The noodle preparation followed a modified version of the method described by Wahjuningsih *et al*.[39] A blend consisting of 63% mocaf flour, 36% wheat flour, and 1% binding agent (either Latoh or CMC) was combined in a bowl. The process involved mixing the dry ingredients with water at a ratio of 1:0.3 (w/v) to create a homogenous mixture. The mixture was then steamed for 15 minutes before being extruded into moist noodles. These moist noodles were further dried at 50°C for 12 h to produce the final dry noodle product.

Computational Analysis

A Thermo Scientific™ Q Exactive™ High-Resolution Mass Spectrometer and a Thermo Scientific™ Dionex™ Ultimate 3000 RSLCnano UHPLC system were used to evaluate bioactive peptides. Solvents A and B, which contained 0.1% formic acid in water and 0.1% formic acid in acetonitrile, respectively, made up the mobile phase. A 100 mm × 2.1 mm Phenyl Hexyl column was used for separation, and gradient specifications described in the experimental protocol were used. A flow rate of 0.20 mL/min, an injection volume of 5 µL, and a 30-minute run time were the chromatographic conditions. The mass spectrometry features included a Data-Dependent MS2 resolution of 17,500 FWHM and a full MS resolution of 70,000 FWHM. The ionization was carried out using a Heated Electrospray Ionization (H-ESI) source that could operate in positive as well as negative ion modes. Thermo ScientificTM Compound Discoverer software made it easier to identify the compound. Additionally, the Swiss Target Prediction.ch and PASSOnline platforms were used for computational analyses.

Animal Studies

In this investigation, male Wistar rats that were two to three months old were employed. The rats were kept in well-ventilated cages with natural light exposure and a regulated ambient temperature of about 25°C. The ethics commission approved this study under Dr. Moewardi General Hospital No. 2.906 / XII / HREC / 2024. Throughout the investigation, the animals' welfare was maintained by the housing conditions, which guaranteed proper lighting, ventilation, and temperature.

***In Vivo* Bioassay Assessment**

Four groups of 24 male Wistar rats were randomly selected. The healthy group (HG), or Group I, was given AIN-96M, a typical diet. The normal diet was given to Group II, also known as the diabetic group (DG). DG+MN1 refers to the diabetic group provided with a regular diet supplemented with mocaf noodles using CMC as the binder, while DG+MN2 represents the diabetic group fed a standard diet supplemented with mocaf noodles using Latoh as the binder. All groups had unrestricted access to food and water during the trial.

An intraperitoneal injection of 230 mg/kg of nicotinamide (NA) dissolved in 0.9% saline was used to induce diabetes. A 60 mg/kg intraperitoneal injection of streptozotocin (STZ) was given to rats 15 minutes after NA was administered. The rats were given a 5% glucose solution in their drinking water for 24 hours after the injection to avoid hypoglycemia. Five days following induction, malondialdehyde (MDA), insulin, and glucose levels were assessed using microcapillary tubes to draw blood samples from the retro-orbital vein. Rats were deemed diabetic if their blood glucose levels were greater than 200 mg/dL. Throughout the four weeks of the meal intervention, blood glucose levels were measured once a week for four weeks. Insulin levels were monitored in the initial and final weeks of the trial to monitor the development of diabetes and treatment effects.

Blood Glucose Analysis

With minor adjustments, blood glucose is measured using the glucose GOD-PAP DiaSys kit and the enzymatic-photometric method described by

Economou *et al.*[16] Reagents and standard solutions are the two types of solutions included in the kit. After mixing the solution, it was incubated at 37°C for 10 minutes. One hour after mixing, the absorbance was measured at a wavelength of 500 nm.

Glucose (mg/dL) = (Δ Sample Abs)/(Δ Standar Abs) x standard concentration (mg/dL)

Insulin Level Analysis

Using the FineTest Rat INS (Insulin) Enzyme-Linked Immunosorbent Assay (ELISA) kit, serum insulin levels were determined. The plate was filled with 50 µL of serum and incubated at 37°C for 90 minutes. Following the addition of 50 µL of biotin-labeled antibody, the incubation is maintained at the same temperature for an additional hour. 50 µL of the Horseradish Peroxidase (HRP)-Streptavidin Conjugate (SABC) solution was added, and the mixture was once more incubated for 30 minutes at 37°C. The reaction was maintained at 37°C for 15 minutes after 90 µL of 3,3',5,5'-Tetramethylbenzidine (TMB) substrate was added. At 450 nm, the absorbance was measured using a microplate reader.

Lipid Peroxidation (MDA)

MDA analysis refers to Yagi[17] with modification. First, the thiobarbituric acid (TBA) reagent is made by dissolving 0.67 TBA in 100 mL of distilled water, followed by the addition of 100 mL of glacial acetic acid. Labeled centrifuge tubes containing 100 µL of blood serum or standard were used. After adding 4 mL of distilled water to each tube and 1 mL of TBA reagent, the solution in the test tube was heated for one hour at 95°C in a water bath, and then centrifuged for 10 minutes at 4000 rpm. Using a spectrophotometer set to 532 nm, the absorbance of the resultant supernatant was measured. Results were indicated by the formation of malonaldehyde (nmol/mL serum). Standard 1,1,3,3-tetraethoxypropane was prepared in the concentration range of 0-3 nmol/mL.

Immunohistochemical Staining of Insulin

For immunohistochemical staining of insulin according to previous study Newkirk *et al*. [18] with slight modification, pancreatic organs were fixed in 4% paraformaldehyde for 24 h, dehydrated in graded alcohol (80% to absolute), cleaned with xylol, and embedded in paraffin. A microtome (Leica Biosystems, Germany) was used to cut the sections to a thickness of 3 µm. They were then deparaffinized and rehydrated in phosphate-buffered saline (PBS, pH 7.4) and alcohol. The samples underwent a series of incubations using insulin Ab-5 mouse monoclonal antibody (Thermo Fisher Scientific, USA), peroxidase block, super block, UltraTek anti-polyvalent, and horseradish peroxidase (HRP). Following 3,3-diaminobenzidine (DAB) chromogen staining and hematoxylin counterstaining, slides were examined under an Olympus light microscope fitted with an analysis camera.

Data Analysis

The study employed a randomized block design with a single factor: the treatment differences among the groups of mice. The groups included healthy mice, diabetic mice fed a standard diet, diabetic mice fed a standard diet supplemented with Mocaf noodles using CMC as a binder, and diabetic mice fed a standard diet supplemented with Mocaf noodles using Latoh as a binder. The findings were shown using the mean value and standard deviation. The data were statistically analyzed using analysis of variance (ANOVA) at a significance level of α = 5% using IBM version 25 of the SPSS software. Data analysis was conducted using Duncan's Multiple Range Test (DMRT) if there were significant differences ($p<0.05$) between treatments.

Results

Computational Analysis

Based on Table 1. from the results of the analysis of computational studies - bioactive compounds that have antidiabetic properties according to PASSOnline and swisstargetprediction.ch on the sample obtained bioactive peptide sequence GLPISFHK at monocytopic m/z 300.17636 Da and RT 18.4293 min. Glycine (G), leucine (L), proline (P), isoleucine (I), serine (S), phenylalanine (F), histidine (H), and lysine (K) are the eight amino acids that make up the GLPISFHK bioactive peptide sequence.

Table 1. Computational study analysis results - Bioactive compounds that have antidiabetic properties according to PASSOnline and Swisstargetprediction.ch

Sequence Bioactive Peptides	Monoisotopic m/z (Da)	RT (min)	Bioactivity prediction in silico*
GLPISFHK	300.17636	18,4293	a. Dipeptidyl peptidase inhibitor b. Antidiabetic (type 2) c. Dipeptidyl peptidase IV inhibitor d. Antidiabetic e. Dipeptidyl peptidase VIII inhibitor f. Dysmenorrhea treatment g. Cancer associated disorders treatment h. Retino protector i. Pancreatic disorders treatment j. HMG-CoA reductase treatment k. Angiotensin-converting enzyme treatment

Fasting Glucose Level

Figure 1 illustrates changes in the average blood serum glucose levels for each group throughout the intervention. According to the test results, blood glucose levels rose to more than 250 mg/dL following the induction of diabetes. The tube feeding was used to provide the noodle intervention every day. When diabetic rats were fed Latoh instead of mocaf noodles after the intervention period, their blood glucose levels significantly decreased. This decrease is likely due to the bioactive compounds contained in mocaf noodles with Latoh enrichment, including dietary fiber, phenolics, and bioactive peptides, which are known to have antidiabetic properties.[32] These findings suggest the potential of mocaf noodles with Latoh substitution as a functional food alternative in diabetics through mechanisms involving improved metabolic health.

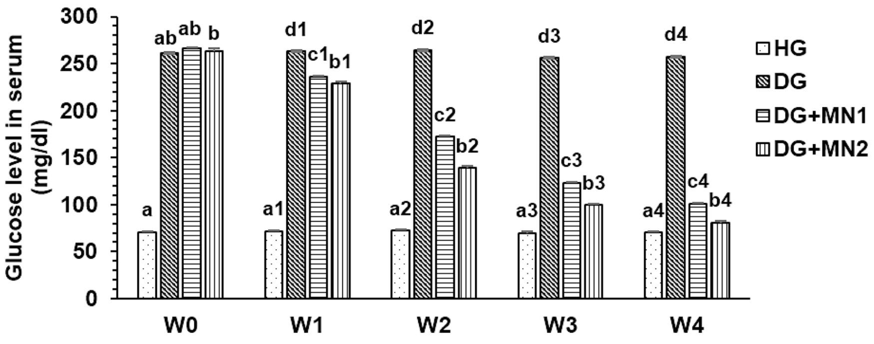

Fig. 1: Glucose levels (mg/dl) in rat blood serum

Notes: Statistically significant differences ($p < 0.05$) are shown by different letters in superscript above each value

Insulin Levels

The antidiabetic effect is further supported by the increase in blood serum insulin levels observed after intervention with the mocaf noodle diet supplemented with Latoh (Figure 2). This suggests an improvement in the function of damaged pancreatic beta cells, leading to increased insulin secretion. Research by Bommel *et al* [36] showed that increased insulin levels can occur due to improved beta cell function, which is often impaired in type 2 diabetes.

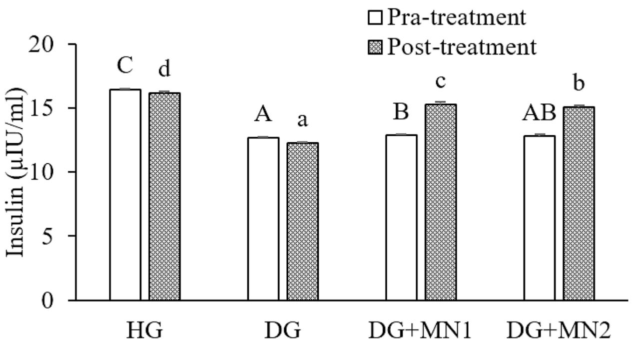

Fig. 2: Insulin levels (µIU/ml) in rat blood serum

Notes: Statistically significant differences ($p < 0.05$) are shown by different letters in superscript above each value.

Oxidative Stress (MDA) Levels

Elevated MDA levels are closely linked to beta-cell dysfunction, resulting in decreased insulin secretion and elevated blood glucose levels. Thus, assessing MDA levels provides insights not only into oxidative stress levels but also into the overall metabolic health, particularly in diabetic patients.[41] In contrast to the positive and negative control groups, which demonstrated little to no decrease in MDA levels following the intervention period, the diabetic groups receiving dietary interventions with mocaf noodles supplemented with Latoh or CMC-binding mocaf flour had significantly lower MDA levels ($P < 0.05$), as illustrated in Figure 3. This suggests that in diabetes settings, the mocaf-Latoh diet successfully decreased oxidative stress, hence reducing cellular damage and enhancing pancreatic beta-cell function. These results demonstrate the potential of mocaf-Latoh noodles as a functional diet for improving metabolic health and reducing oxidative stress in the treatment of diabetes.

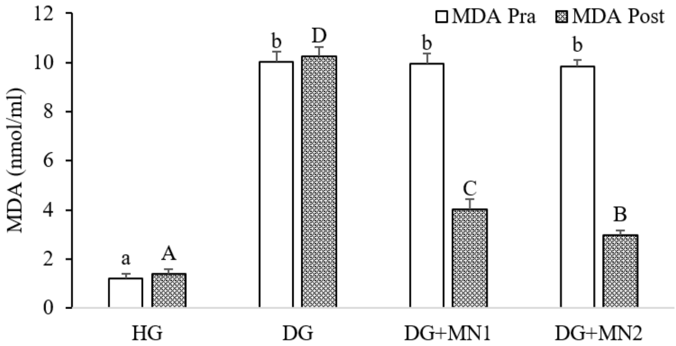

Fig. 3: MDA levels (nmol/ml) in rat blood serum

Notes: Statistically significant differences ($p < 0.05$) are shown by different letters in superscript above each value.

Immunohistochemical of Insulin

Insulin expression in pancreatic beta cells was analyzed using the immunohistochemistry (IHC) technique with an insulin-specific antibody. The beta cells, located within the islets of Langerhans, were quantified to determine the number of cells expressing insulin, indicated by the formation of a brown coloration. This brown staining in the IHC results arises from the interaction between the applied antibody and insulin proteins in the tissue.[40] Photomicrographic observations of the islets of Langerhans in the experimental rat groups are presented in Figure 4.

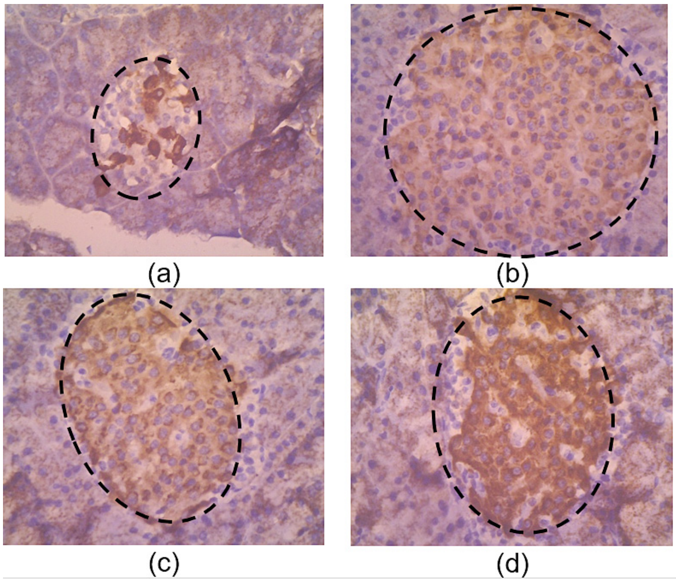

Fig. 4. Photomicrograph of immunohistochemical staining in rat pancreatic islets. Notes: (a) HG= healthy group with standard diet, (b) DG= diabetic group with standard diet, (c) DG+MN1= diabetic group fed the standard diet supplemented with mocaf noodles using CMC as the binder, (d) DG+MN2= diabetic group fed the standard diet supplemented with mocaf noodles using Latoh as the binder

Discussion

This study employs a computational technique using two platforms, Swiss Target Prediction.ch and PASSOnline, to find bioactive compounds with antidiabetic qualities. For instance, in studying mocaf-Latoh noodles, these tools can help identify potential antidiabetic effects by predicting the interactions of bioactive molecules in Latoh with biological targets relevant to diabetes management. PASSOnline allows researchers to forecast biological activities, such as Dipeptidyl Peptidase IV (DPP-IV) inhibition or antioxidant impacts, based on the structural similarities of Latoh compounds to known antidiabetic agents.[18] Similarly, SwissTargetPrediction can determine specific protein targets of these compounds by comparing them with documented bioactive substances in the ChEMBL database.[19] The combined application of these two platforms offers a thorough method for comprehending the medicinal potential of bioactive substances.[20] This study intends to find compounds with high potential as antidiabetic medicines while expanding our knowledge of the interactions between compounds by combining data from both sources.

Glycine (G), leucine (L), proline (P), isoleucine (I), serine (S), phenylalanine (F), histidine (H), and lysine (K) are the eight amino acids that make up the GLPISFHK bioactive peptide sequence. These structures' capacity to interact with biological membranes or proteins may be attributed to the combination of polar and hydrophobic amino acids they contain.[21] Hydrophobic amino acids tend to interact with the lipid portion of cell membranes, whereas polar amino acids can form hydrogen bonds with surrounding proteins or water molecules.[22] This is important in the context of the biological function of peptides, such as in the regulation of glucose metabolism or insulin response.[23] GLPISFHK peptides are predicted to have potential bioactive activities, including antidiabetic properties that may improve insulin sensitivity and regulate glucose metabolism, which have been demonstrated in several previous studies.[24,25] Furthermore, the presence of specific amino acids, such phenylalanine, may suggest potential antioxidant activity that could aid in the defence against oxidative stress in cells. The study of Bala *et al.*[26] mentioned that Patients with type 2 diabetes who are under a lot of oxidative stress have much higher levels of cysteine, phenylalanine, and tyrosine, while their levels of citrulline are lower. GLPISFHK peptides can also be utilized in functional food products to improve health benefits, especially related to metabolic health, and have potential in drug development for conditions such as diabetes and metabolic syndrome.[27]

Dipeptidyl Peptidase IV (DPP-IV), which is known to have antidiabetic characteristics, particularly for type 2 diabetes, is one of the compounds that work as dipeptidyl peptidase inhibitors, according to the results of in silico bioactive prediction. DPP-IV inhibitors prevent the breakdown of incretin hormones, which helps raise insulin levels and decrease blood glucose levels.[28] Along with DPP-IV, Dipeptidyl Peptidase VIII (DPP-VIII) inhibitors have also shown potential in the treatment of dysmenorrhea and cancer-related disorders, providing hope for new therapies in the management of these conditions.[29] Research has also shown that these compounds can function as retinol protectors, protecting the retina from damage that can be caused by various medical conditions. On the other hand, Dipeptidyl Peptidase inhibitors can have positive effects in the treatment of pancreatic disorders, as well as in the management of diseases related to HMG-CoA reductase, which is involved in cholesterol synthesis. These compounds may also affect the angiotensin-converting enzyme (ACE) pathway, contributing to blood pressure regulation and cardiovascular health.[30] The computational analysis revealed multiple bioactive substances in Latoh with potential antidiabetic effects, such as DPP-IV inhibition, glucose metabolism regulation, and oxidative stress reduction. Palmitic acid and arachidonic acid are among these substances, and they are known to aid glucose metabolism and enhance insulin sensitivity.

One of the most crucial test parameters for diabetes is blood glucose analysis. It gauges blood glucose levels, which can reveal important details about a person's blood sugar regulation. High glucose levels often indicate diabetes, while low levels may indicate hypoglycemia.[31] Previous studies have demonstrated the beneficial effects of bioactive compounds in food on blood glucose levels, supporting the findings that mocaf noodles enriched with Latoh can effectively reduce blood glucose in diabetic rats. For instance, Gustini *et al* [33] reported that soluble fiber consumption reduces postprandial glucose responses by slowing carbohydrate absorption, aiding in blood glucose regulation. Similarly, Krawczyk *et al* [34] highlighted that phenolic compounds found in plants can regulate glucose metabolism and exhibit antidiabetic effects. Javed *et al* [35] further emphasized the role of bioactive peptides from plant-based proteins in enhancing insulin secretion and improving glucose control. These observations are supported by the *In Vivo* data (Figure 1), which revealed that the DG+MN2 group (diabetic rats given Latoh-supplemented mocaf noodles) had significantly lower fasting blood glucose levels than the diabetic control group (DG). This reduction likely stems from the synergistic effects of dietary fiber, phenolic compounds, and bioactive peptides in Latoh, which collectively contribute to improved metabolic health and diabetes management.

The complex interaction between enhanced pancreatic beta-cell function, decreased oxidative stress, and decreased inflammation is highlighted by the considerable rise in serum insulin levels ($p < 0.05$) shown in the DG+MN2 group after the intervention with mocaf noodles enriched with Latoh. The hormone insulin, which is vital for controlling blood sugar, is produced and secreted by beta cells. Beta-cell activity is frequently compromised in type 2 diabetes, which results in inadequate insulin production and high blood glucose levels.[37] A diet rich in dietary fiber and bioactive compounds, as provided by mocaf-Latoh noodles, can enhance insulin sensitivity by slowing glucose absorption in the digestive tract. This steady glucose release reduces the workload on beta cells, allowing them to function more efficiently in insulin production.[38] Additionally, the antioxidant compounds in Latoh help mitigate oxidative stress, which is a major contributor to beta-cell dysfunction. Oxidative stress disrupts signaling pathways necessary for insulin secretion, but by alleviating this stress, the diet supports increased insulin production and secretion.[39] Furthermore, reducing chronic inflammation, another factor affecting beta-cell function and insulin sensitivity, may also contribute to improved outcomes. Together, these factors likely explain the significant enhancement of insulin levels in the DG+MN2 group, underscoring the therapeutic potential of mocaf-Latoh noodles in managing diabetes. This is further supported by the role of DPP-IV inhibitory compounds in Latoh, which preserve and enhance insulin secretion in diabetic conditions.

A crucial step in assessing oxidative stress, a major contributor to the etiology of diabetes, is MDA testing. Lipid peroxidation's byproduct, MDA, is a sign of oxidative stress-induced cellular damage.[40] The reduction in MDA levels observed after the intervention period indicates a significant decrease in oxidative stress under diabetic conditions. According to previous research, lower MDA levels are linked to improved antioxidant capacity and less oxidative stress-induced cellular damage, which is a prevalent problem in diabetes.[42] When compared to the diabetic control group, the group that received mocaf noodles enriched with Latoh had considerably reduced MDA levels (Figure 3). This decrease emphasizes Latoh's antioxidant qualities, which are essential for preventing oxidative damage, a major cause of pancreatic beta-cell malfunction and decreased insulin output. This is in agreement with a previous study by Wahjuningsih *et al* [43] which showed that Latoh possesses a phenolic content ranging from 2.04 to 5.47 mg GAE/g and a flavonoid concentration of approximately 4.93 mg QE/g, indicating its potential to scavenge free radicals effectively. The presence of these compounds helps in neutralizing reactive oxygen species (ROS), which can damage pancreatic cells and impair insulin secretion.[44] These findings suggest that the mocaf-Latoh diet not only improves insulin secretion but also reduces oxidative stress, offering a comprehensive approach to better diabetes management.

The STZ-NA-induced diabetic rat group showed degenerative alterations in the islets of Langerhans, which were linked to beta-cell destruction in the pancreas. The findings showed that the healthy group's insulin expression was higher than that of the diabetes group caused by STZ-NA. Beta-cell damage and elevated oxidative stress can result from exposure to hyperglycemia.[41] This result is consistent with Jeong *et al*.[42] who found that STZ-NA induction results in hyperglycemia and fewer beta cells in the islets of Langerhans that express insulin. The inclusion of DG+MN1 and DG+MN2 diets enhanced insulin expression in the STZ-NA-induced diabetic rat group, according to this study's findings (Figure 4).

Conclusion

This study demonstrates the potent antidiabetic effects of mocaf noodles enriched with Latoh in diabetic rats, as shown by a reduction in fasting blood glucose levels to 105 mg/dL, an approximately 30% increase in insulin secretion, and 45% decrease in oxidative stress markers (MDA). The bioactive peptide GLPISFHK, found in mocaf-latoh noodles and composed of glycine, leucine, proline, isoleucine, serine, phenylalanine, histidine, and lysine, was computationally studied for its antidiabetic potential. The results indicate that GLPISFHK may inhibit dipeptidyl peptidase IV (DPP-IV) activity, potentially enhancing insulin sensitivity and regulating glucose levels. Furthermore, the presence of phenylalanine suggests antioxidant activity, which may help mitigate oxidative stress. The results emphasize the potential of mocaf-Latoh noodles as an innovative functional food for improving metabolic health and managing type 2 diabetes. Further studies, including clinical trials, are recommended to validate these findings and explore their practical applications in human diets.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

This statement does not apply to this article.

Ethics Statement

The ethics commission approved this study under Dr. Moewardi General Hospital No. 2.906 / XII / HREC / 2024.

Informed Consent Statement

This study did not involve human participants, and therefore, informed consent was not required.

Clinical Trial Registration

This research does not involve any clinical trials.

Permission to Reproduce Material from other Sources

Not Applicable.

Author Contributions

- **Sri Budi Wahjuningsih:** Conceptualized the study, supervised the research, and critically reviewed and edited the manuscript for intellectual content.
- **Dian Anggraeni:** Designed the study methodology, conducted data analysis, and contributed to manuscript preparation.
- **Zulhaq Dahri Siqhny:** Collected and analyzed data and performed statistical analysis.
- **Agus Triputranto:** Supervised the study, interpreted the results, and critically reviewed the manuscript.
- **Maela Rizky Kusumastuti:** Assisted in data collection and contributed to the initial manuscript drafting.
- **Mita Nurul Azkia:** Conducted experiments, prepared data visualizations, and finalized the manuscript as the corresponding author.

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