PROCEEDING
5th International Conference of Health Polytechnic of Jambi 2025
icon@poltekkesjambi.ac.id
http://journal.poltekkesjambi.ac.id/index.php/ICoHPJ
doi.org/10.35910/icohpj.v5i0

YELLOW SWEET POTATO (YSP) ENHANCES INSULIN SENSITIVITY AND REDUCES TYPE 2 DIABETES RISK IN OBESE RATS

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ABSTRACT

Background: *YSP (Ipomoea batatas) shows potential as a rice substitute due to its lower glycemic index, higher fiber content, and reduced caloric density. This study aimed to evaluate the effects of a YSP-based diet on biomarkers of insulin resistance in obese rats.*
Method: *A randomized controlled trial was conducted using 28 rats, all rendered obese through a high-fat diet for 3 weeks, resulting in a Lee index greater than 310 g. The rats were then divided into four dietary groups and treated for an additional 3 weeks. The control group (K−) received standard AIN-93M feed. The positive control group (K+) received a modified standard feed in which 100% of the corn starch was replaced with rice. Group K1 was given 100% steamed YSP, while group K2 received 100% twice-steamed YSP. Blood samples were analyzed using SPSS software version 25.0. The K2 group demonstrated the most significant improvements across all measured parameters.*
Results: *Total antioxidant levels increased by 5.11 U/mL, while HOMA-IR and glycated albumin decreased by 5.67 and 3.83 pmol/mL, respectively. Post-prandial glucose levels also dropped significantly by 184 mg/dL. Furthermore, the K2 group exhibited the highest concentrations of GLUT4 (25.12 ng/mL), acetic acid (150.31 mmol/L), propionic acid (53.20 mmol/L), and butyric acid (27.18 mmol/L). Levels of PPAR-α and PPAR-γ were also highest in the K2 group at 1.94 ng/mL and 0.78 ng/mL, respectively. In contrast, glucose-6-phosphatase (G6P) reached its highest level in the K− group at 9.91 mIU/mL.*
Conclusion: *A twice-steamed YSP diet significantly improved insulin sensitivity in obese rats. These findings suggest that YSP may serve as a functional food promoting metabolic health.*

Keywords: *Antioxidant, post-prandial glucose, GLUT4, Glycated albumin, HOMA-IR, PPAR, Insulin resistance, SCFA, Obese rats, Yellow Sweet Potato*

INTRODUCTION

The incidence of obesity in developing countries has tripled over the past 20 years, with Southeast Asia experiencing one of the highest increases in obesity rates(Askari et al., 2022). Central obesity, in particular, is associated with an elevated risk of non-communicable diseases such as type 2 diabetes mellitus, cardiovascular disease, cancer, and osteoarthritis, all of which contribute to increased morbidity and mortality(Harbuwono et al., 2018) (Yumuk et al., 2015) (Awasthi et al., 2023). According to the Diabetes Prevention Program (DPP), type 2 diabetes mellitus can be prevented in high-risk populations through weight loss and lifestyle modifications, including dietary regulation and increased physical activity(National Institute of Diabetes and Digestive and Kidney Disease, 2021).

One of the major consequences of central obesity is insulin resistance, a condition in which the body's cells become less responsive to insulin. Adipose tissue stores lipids in the form of triacylglycerols, derived from chylomicron absorption, and releases non-esterified fatty acids to meet increased energy demands. A prolonged positive energy balance results in fatty acid accumulation that exceeds the adipose tissue's storage capacity, leading to dysfunction. This impairment reduces the availability of insulin needed to facilitate

triacylglycerol uptake and suppress endogenous lipolysis. As a compensatory mechanism, insulin secretion increases, resulting in hyperinsulinemia. Excess fatty acids subsequently accumulate in peripheral tissues such as muscle, liver, and pancreas due to impaired lipid buffering(Pramono, 2020). The accumulation of fatty acids and elevated blood glucose levels induce oxidative stress, which arises from an imbalance between the production and neutralization of reactive oxygen species (ROS). Excessive ROS damages cellular components, including proteins, lipids, and DNA. Inadequate antioxidant defenses further exacerbate oxidative stress(Mahat et al., 2019).

To measure insulin resistance, several biomarkers and assessment tools are available. One widely used method is the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), which estimates insulin sensitivity and β-cell function based on fasting glucose and insulin levels. Central obesity is strongly associated with elevated HOMA-IR values, even in individuals not yet diagnosed with diabetes(Pramono, 2020) (Kurniawan et al., 2020) (Mayerhofer et al., 2020). In addition to HOMA-IR, glycated albumin (GA) is a valuable marker of insulin resistance. Unlike hemoglobin A1c (HbA1c), GA is unaffected by hemoglobin metabolism disorders and reflects glycemic control over the previous 2–4 weeks(Kohzuma et al., 2021).Post-prandial glucose levels also play a critical role in identifying individuals at risk of developing diabetes and its complications. The utility of fasting plasma glucose and HbA1c, with 2-hour post-prandial plasma glucose serving as a primary criterion for diagnosing prediabetes and diabetes(Fauziah et al., 2017).

Despite the availability of these biomarkers, dietary interventions targeting insulin resistance have yielded mixed results. Although numerous studies have explored the effects of diet on insulin resistance in both animal models and humans, many interventions have proven to be less effective or difficult to implement in real-world settings. For instance, a study by Utari et al. (2019) demonstrated that low-calorie and low-glycemic index diets were ineffective in significantly reducing insulin resistance (as measured by HOMA-IR), primarily due to limited monitoring of dietary intake among participants(Utari et al., 2019).

Given these limitations, there is a growing interest in identifying local, accessible food sources that are rich in fiber, have a low glycemic index, and can serve as viable alternatives to staple foods like rice. One such candidate is sweet potato (*Ipomoea batatas*), which contains approximately one-third the calories of rice, a lower glycemic index (46 vs. 79.6), ten times more fiber, and bioactive compounds such as β-carotene that possess antidiabetic properties(Kementrian Kesehatan Republik Indonesia, 2018) (Houston, 2023) (Nayar and Madhu, 2020).

Therefore, this study aims to investigate the potential of yellow sweet potato as a functional food to improve insulin resistance and oxidative stress in obesity. Specifically, we evaluate the effects of yellow sweet potato consumption on total antioxidant capacity, insulin resistance (HOMA-IR), glycated albumin (GA), post-prandial glucose, GLUT4 expression, glucose-6-phosphatase (G6P), short-chain fatty acids (SCFA), and the expression of peroxisome proliferator-activated receptors (PPAR-α and PPAR-γ).

METHODS

Materials

Yellow sweet potatoes (*Ipomoea batatas L.*), Sari variety, were obtained from CV Arindo Makmur, Malang, East Java, Indonesia. The tubers were harvested at 3–4 months of age and certified under variety purification certificate No. Ubjl.R.3514010.0288.0068/PV. For the steamed yellow sweet potato (SYSP) preparation, the tubers were peeled, sliced into 4 cm pieces, and steamed at approximately

70°C for 15 minutes. Meanwhile, for the resistant starch-rich SYSP (SYSP-RS), the sweet potatoes underwent steaming for 15 minutes at 70°C, followed by cooling at 4°C for 24 hours, and were subsequently re-steamed for 15 minutes under the same temperature condition. The processed sweet potatoes were then incorporated into the experimental diet.

Biochemical analysis of steamed yellow sweet potato

Proximate composition and functional components of the steamed yellow sweet potato and SYSP-RS were analyzed in duplicate following standard methods by AOAC. The nutrient composition of the steamed yellow sweet potato (SYSP) and the high-resistant starch yellow sweet potato (SYSP-RS) diets was calculated based on their formulated feed ingredients (Table 1).

Table 1. Composition of Standard Feed Ingredients AIN 93(26) and Yellow Sweet Potato Feeding

Material	Standar Feed (%)	Feed High Fat (%)	SYSP (%)	SYSP-RS (%)	Rice Feed (%)
Corn Starch-dextrin	62	1,6	-	-	-
Dextrin	-	15,5	15,5	15,5	15,5
Casein	14	14	14	14	14
Sucrose	10	10	10	10	10
Powdered cellulose	5	5	5	5	5
Soybean oil	4	46,9	4	4	4
AIN-93 mineral mix	3,5	3,5	3,5	3,5	3,5
AIN 93 vitamin mix	1	1	1	1	1
Choline bitartrate	0,25	0,25	0,25	0,25	0,25
L-cystine	0,18	0,18	0,18	0,18	0,18
t-Butylhydroquinone	0,0008	0,0008	0,0008	0,0008	0,0008
Cholesterol	-	2	-	-	-
Rice	-	-	-	-	46,6
Total	99,93	99,93	100,03	100,03	100,03
Energy (kcal)	4000	6241	4004	4004	4004
Protein (%)	14	14	14	14	14
Fat (%)	4	48.9	4	4	4
Carbohydrate (%)	77	32	77.1	77.1	77.1

Animal Handling

This study utilized male Sprague Dawley rats aged approximately 8 weeks. All animals were obtained in a healthy and active condition and were maintained in individual cages to monitor dietary intake and avoid feed competition. The animals underwent a 7-day acclimatization period under controlled conditions, including a room temperature of 25°C, 12-hour light/dark cycle, and free access to water and standard AIN-93M chow. During acclimatization, behavioral observations were performed to assess animal health status. Inclusion criteria included a Lee Index >310, indicating an obese phenotype, while exclusion criteria were mortality or abnormal behavioral signs during the acclimatization and intervention period.

Ethical approval

All experimental procedures involving animals were conducted at the Animal Experiment Laboratory of the Center for Nutrition and Food Studies, Universitas Gadjah Mada. The study protocol was reviewed and approved by the Health Research Ethics Committee of the Faculty of Medicine, Diponegoro University, Semarang, Indonesia. Ethical approval was granted under the reference number 075/ECH/KEPK/FK-UNDIP/VII/2024. All research activities were conducted in accordance with the principles outlined in the Declaration of Helsinki and the guidelines set forth by the Council for International Organizations of Medical Sciences (CIOMS).

Experimental design

The minimum number of animals per group was determined using the Federer formula, resulting in six rats per group, with an additional rat included per group as a reserve (n=7). After acclimatization, obesity was induced using a high-fat diet administered for three weeks, composed of 48.9% fat, 32% carbohydrates, and 19.1% protein. Cholesterol powder (Sigma-Aldrich) was used as the primary lipid source. Rats were randomly assigned into four experimental groups. Group K1 (Treatment Group 1) was provided with a diet in which 100% of the corn starch was substituted with steamed yellow sweet potato. Group K2 (Treatment Group 2) received a diet where all corn starch was replaced by yellow sweet potato rich in resistant starch, processed using a steam–cool–steam method. The K+ group (Positive Control) was given a diet with complete replacement of corn starch by rice (Platinum Raja brand), while the K− group (Negative Control) was maintained on a standard AIN-93M chow diet. All diets were provided at a fixed quantity of 15 g/rat/day, and water was available ad libitum throughout the intervention period. Body weight and naso-anal length were recorded weekly to calculate the Lee Index as a measure of obesity progression and intervention efficacy.

Blood and caecum samples collection

Blood samples were collected on Day 0 and Day 22 of the intervention period. Rats were anesthetized using ketamine (60 mg/kg BW) during the light phase, and approximately 3 mL of blood was drawn via the orbital sinus using glass capillary tubes. Samples were centrifuged at 4000 rpm for 15 minutes at 4°C to separate the serum. The supernatant was aliquoted and stored at –80°C for further biochemical analyses. At the end of the intervention, rats were sacrificed, and both cecal contents and adipose tissue were collected. Luminal contents of the caecum were obtained by rinsing with phosphate-buffered saline (1X PBS, pH 7.4) and stored at –80°C for short-chain fatty acids (SCFAs) analysis using gas chromatography. Adipose tissue samples were preserved for post-intervention evaluation of insulin signaling and metabolic-related protein expressions.

Biomedical analysis of blood and caecum samples

Fasting blood glucose was measured using an enzymatic photometric test based on the glucose oxidase-peroxidase (GOD-PAP) method (Glucose GOD FS, DiaSys Diagnostic Systems GmbH, Germany). Serum insulin levels were determined using a sandwich ELISA kit (FineTest® Rat Insulin ELISA Kit, Wuhan Fine Biotech Co., Ltd., China). HOMA-IR was calculated using the formula: (fasting glucose (mg/dL) × fasting insulin (µU/mL)) / 405, with HOMA-IR values above 3.9 considered indicative of insulin resistance in rats. Glycated albumin was analyzed using the FineTest® Rat GA QuickTest ELISA Kit (Wuhan Fine Biotech Co., Ltd., China). Total antioxidant capacity (TAC) was evaluated using the Trolox Equivalent Antioxidant Capacity (TEAC) method with ABTS (2,2-azino-bis-3-ethylbenzthiazoline-6-sulphonic acid) as the radical source, and absorbance was measured using a UV-Vis spectrophotometer (Genesys 150, Thermo Fisher Scientific, USA). Post-prandial glucose levels were assessed 120 minutes after feeding on Day 0 and Day 22 using the same GOD-PAP enzymatic method. The normal post-prandial glucose level for rats was set at 5.65 mmol/L (218.5 mg/dL). SCFAs including acetate, propionate, and butyrate were analyzed from the caecum samples after the intervention. The concentrations were measured using gas chromatography.

Protein Expression Analysis for GLUT4, G6P, PPAR-α, and PPAR-γ

The expression levels of GLUT4 and PPAR-γ proteins were analyzed from adipose tissue samples, while G6P and PPAR-α proteins were measured from liver tissue. All protein expression levels were determined using sandwich enzyme-linked immunosorbent

assay (ELISA) kits (FineTest® Rat ELISA Kits: GLUT4, G6P, PPAR-α, and PPAR-γ; Wuhan Fine Biotech Co., Ltd., China), following the manufacturer's protocols.

Statistical analysis

Statistical analysis was performed using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA), while graphical illustrations were generated using GraphPad Prism version 9.0 (GraphPad Software Inc., USA). All data were expressed as mean ± standard deviation (SD). The normality of data distribution was assessed using the Shapiro–Wilk test, considering that the number of subjects in each group was fewer than 50. For intra-group comparisons, the paired t-test was used for normally distributed data. Between-group comparisons were conducted using one-way ANOVA, followed by Bonferroni or Tamhane's T2 post hoc test depending on the homogeneity of variance based on Levene's test results. Non-normally distributed variables were analyzed using the Kruskal–Walls test followed by the Mann–Whitney U test for pairwise comparisons. Correlations between variables after the intervention were assessed using Spearman's rank correlation test. A p-value of <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

RESULTS

Baseline characteristics

A total of 28 Wistar rats with diet-induced obesity were included in this study, with seven rats in each group. No significant differences were observed at baseline among the groups for body weight, Lee index, antioxidant total, glycated albumin, and post-prandial glucose levels ($p > 0.05$). However, a significant difference was found in HOMA-IR values between groups at baseline ($p = 0.026$), although the overall mean values remained indicative of insulin resistance in all groups (Table 2).

Effects of SYSP intervention on lee index

The Lee index, was significantly affected by the intervention across all groups. As presented in Table 1, the K1 and K2 groups exhibited markedly lower Lee index values post-intervention compared to both control groups. Specifically, the K1 group showed a Lee index of 309.59 ± 3.03, while the K2 group demonstrated an even lower value of 308.02 ± 2.47. In contrast, the negative control (K−) and positive control (K+) groups maintained higher indices of 331.16 ± 1.36 and 331.02 ± 2.00, respectively. The change (Δ) in Lee index post-treatment was −13.55 in the K1 group and −17.35 in the K2 group, indicating a significant reduction in body fat accumulation compared to the K− ($\Delta = 5.44$) and K+ ($\Delta = 5.32$) groups. The statistical analysis confirmed that these differences were highly significant, with $P < 0.000$ for both within-group and between-group comparisons. These findings suggest that the intervention effectively reduced adiposity in a dose-dependent manner, with the greatest improvement observed in the K2 group.

Effects of SYSP intervention on antioxidant total, glycated albumin, homa-ir, and post-prandial glucose

The effect of the intervention on antioxidant status and metabolic parameters was evaluated by comparing post-intervention values among groups.

As shown in Figure 1A, total antioxidant levels were significantly higher in both intervention groups (K1 and K2) compared to the negative control (K−) and positive control (K+). The K2 group exhibited the highest antioxidant capacity (6.69 ± 0.10 U/mL), followed by K1 (5.93 ± 0.20 U/mL), with both showing statistically significant differences from K− and K+ ($P < 0.0001$). There was also a significant difference between K1 and K2, indicating a dose-dependent effect.

Table 2. Baseline characteristics

Parameter	Group				p
	K-	K+	K1	K2	
Bodyweight (g)	275.00±11.31	265.85±21.58	269.14±16.92	270.57±23.56	0.839
Lee index	325.72±1.43	325.70±2.26	323.14±3.32	325.37±3.18	0.238
Antioxidant total (U/mL)	1.59±0.01	1.56±0.04	2.57±0.03	1.58±0.03	0.545
HOMA-IR	9.32±0.14	9.29±0.21	9.06±0.08	9.14±0.20	0.026
Glycated albumin (%)	7.34±0.34	7.33±0.49	7.34±0.27	7.33±0.37	0.901
Post-prandial Glucose (mg/dL)	290.61±2.11	289.43±3.13	289.08±2.62	288.26±1.53	0.357

Data were expressed as mean ± standard deviation (SD) and measured before the treatment period; K1 (Treatment Group 1): normal diet + 100% of corn starch replaced by SYSP; K2 (Treatment Group 2): normal diet + 100% of corn starch replaced by SYSP-RS; K+ (Positive Control): normal diet + 100% of corn starch replaced by rice; K− (Negative Control): standard AIN-93M chow; n: 7; $p < 0.05$ was considered significant with One Way ANOVA test.

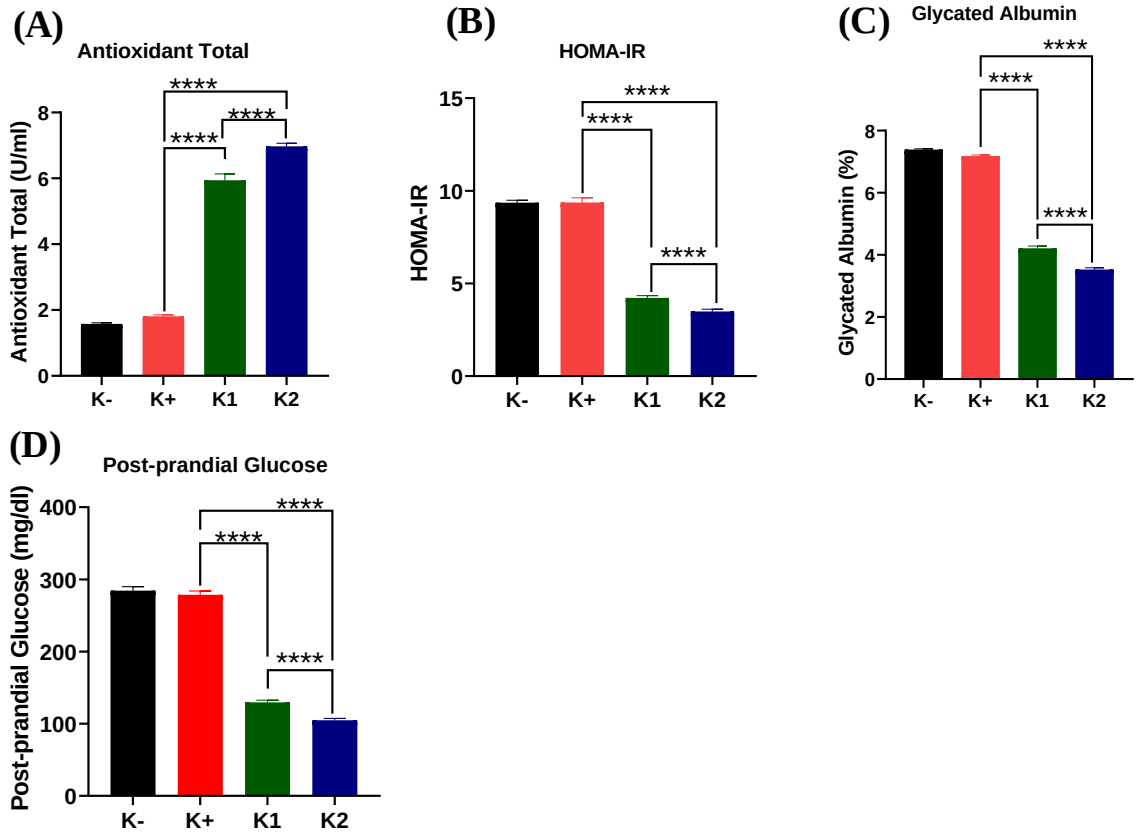

Figure 1. Effects of SYSP on antioxidant capacity and metabolic parameter. (A) Total antioxidant capacity, (B) HOMA-IR (insulin resistance), (C) Glycated albumin (%), and (D) Post-prandial glucose levels (mg/dL) in each experimental group after the intervention. Data are presented as mean ± SD. Significant differences were observed between the positive control group (K^+) and both intervention groups (K1; K2), as well as between K1 and K2, as indicated by **** ($P < 0.0001$). One-way ANOVA followed by Tukey's post hoc test was used for statistical analysis.

In terms of insulin resistance (Figure 1B), post-intervention HOMA-IR values were markedly lower in the K1 (4.21 ± 0.13) and K2 (3.47 ± 0.12) groups compared to K− (9.35 ± 0.13) and K+ (9.36 ± 0.26) groups ($P < 0.0001$). Furthermore, K2 demonstrated significantly lower HOMA-IR than K1, suggesting a more pronounced improvement in insulin sensitivity with higher intervention dose. Similarly, glycated albumin levels (Figure 1C) were significantly reduced in K1 (4.20 ± 0.79%) and K2 (3.51 ± 0.66%) groups

compared to the control groups (K−: 7.38 ± 0.31%; K+: 7.17 ± 0.45%), with $P < 0.0001$ for all comparisons. K2 group exhibited the lowest level of glycated albumin, indicating better long-term glycemic control. Post-prandial glucose concentrations (Figure 1D) were also substantially decreased in both intervention groups. The K2 group had the lowest glucose level (104.55 ± 2.75 mg/dL), followed by K1 (129.41 ± 3.30 mg/dL), both of which were significantly lower than the values observed in K− (284.19 ± 5.65 mg/dL) and K+ (278.49 ± 5.36 mg/dL) groups ($P < 0.0001$). The reduction in post-prandial glucose was greater in K2 compared to K1, highlighting a dose-dependent glycemic-lowering effect.

Effects of SYSP intervention on adipose tissue GLUT4 and PPAR-γ

The SYSP intervention significantly altered the expression levels of GLUT4 and PPAR-γ in adipose tissue across all treatment groups (Figure 2A–B).

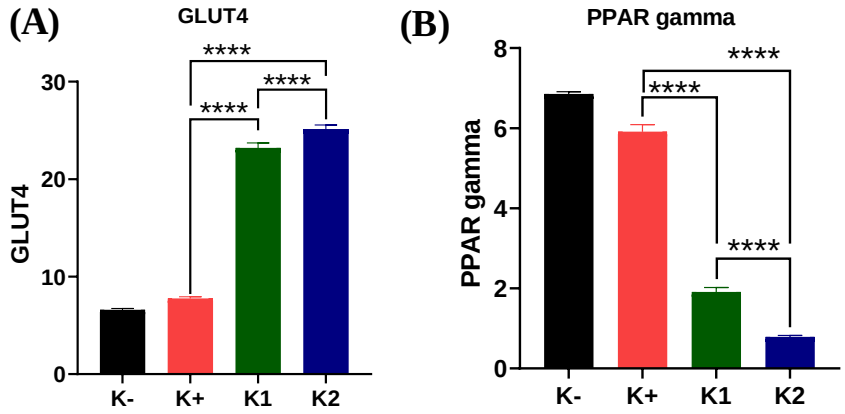

Figure 2. SYSP intervention modulates expression of glucose transport and insulin sensitivity markers in adipose tissue. (A) GLUT4 and (B) PPAR-γ expression levels post-intervention. Data are shown as mean ± SD. SYSP treatment significantly increased GLUT4 expression and decreased PPAR-γ expression in a dose-dependent manner, with **** indicating $P < 0.0001$ for comparisons between K^+ and K1/K2, and between K1 and K2. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test.

Post-intervention analysis revealed a marked increase in GLUT4 expression in the K1 and K2 groups compared to both the negative control (K−) and positive control (K+) groups. Specifically, GLUT4 levels were significantly higher in K1 (23.19 ± 0.51) and K2 (25.12 ± 0.43) groups than in K− (6.58 ± 0.15) and K+ (7.74 ± 0.18) groups ($P < 0.000$). Notably, the highest GLUT4 expression was observed in the K2 group, suggesting a dose-dependent effect of the SYSP intervention (Figure 2A). Conversely, the expression of PPAR-γ was significantly reduced in the K1 and K2 groups compared to the K− and K+ groups. The PPAR-γ levels in the K2 group (0.78 ± 0.03) were significantly lower than in K1 (1.90 ± 0.11), K+ (5.90 ± 0.17), and K− (6.84 ± 0.06) groups ($P < 0.000$), with the K2 group showing the most substantial suppression (Figure 2B). These findings suggest that SYSP intervention may enhance insulin sensitivity and glucose transport activity in adipose tissue via upregulation of GLUT4 and downregulation of PPAR-γ in a dose-dependent manner.

Effects of SYSP intervention on liver tissue G6P and PPAR-α

Post-intervention analysis demonstrated significant differences in liver G6P and PPAR-α levels across all groups (Figure 3A–B). G6P expression was markedly decreased in the K+ group (0.80 ± 0.02) compared to the K− group (9.91 ± 0.48). Interestingly, administration of SYSP in both treatment groups (K1 and K2) restored G6P levels to values significantly higher than K+ (7.76 ± 0.22 and 8.67 ± 0.41,

respectively; $P < 0.000$), although not fully to the level of the K− group (Figure 3A). Among the treatment groups, K2 exhibited the highest G6P level, indicating a possible dose-dependent effect of SYSP intervention. In contrast, hepatic PPAR-α levels were significantly downregulated in the K1 and K2 groups (2.93 ± 0.11 and 1.94 ± 0.08, respectively) when compared to K− (9.38 ± 0.08) and K+ (8.06 ± 0.25) groups ($P < 0.000$). The lowest expression was observed in the K2 group, suggesting that the SYSP intervention suppressed PPAR-α more effectively at the higher dose (Figure 3B). This pattern may reflect a modulatory role of SYSP in hepatic lipid metabolism through downregulation of PPAR-α expression.

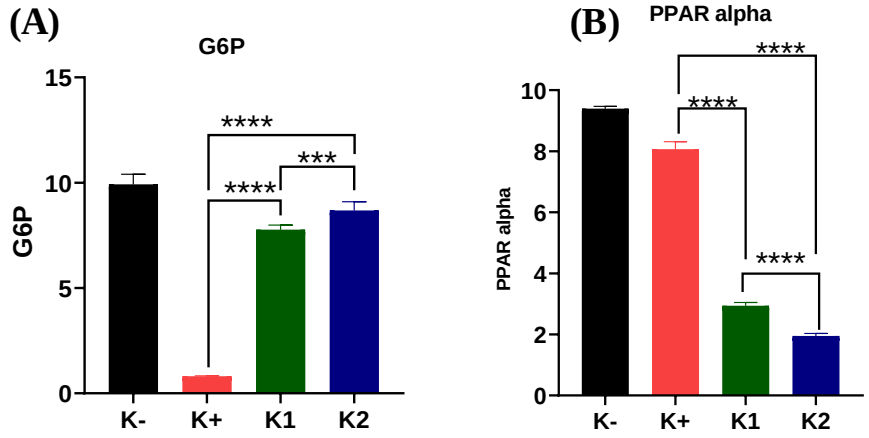

Figure 3. Liver expression of G6P and PPAR-α following SYSP intervention. (A) G6P and (B) PPAR-α levels post-intervention. Data are expressed as mean ± SD. SYSP treatment restored G6P levels and suppressed PPAR-α expression significantly, with K2 showing the most prominent effect. Asterisks (****) indicate $P < 0.0001$ for all significant group comparisons (K^+ vs K1/K2 and K1 vs K2). One-way ANOVA with Tukey's post hoc test was applied.

Effects of SYSP intervention on Caecum SCFAs

Post-intervention analysis revealed significant differences in caecal short-chain fatty acid (SCFA) concentrations among groups ($P < 0.000$), as shown in Figures 4A–C.

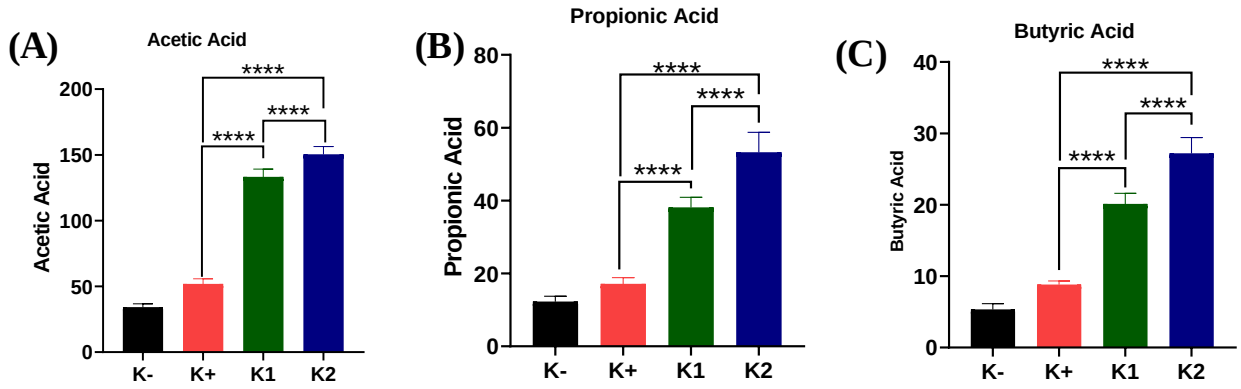

Figure 4. SYSP enhances caecal SCFA concentrations in a dose-dependent manner. Concentrations of (A) Acetic acid, (B) Propionic acid, and (C) Butyric acid measured in caecal samples post-intervention. Results are presented as mean ± SD. SYSP intervention significantly increased SCFA levels, particularly in the K2 group. Significant differences between K^+ and both K1/K2, as well as between K1 and K2, are denoted by **** ($P < 0.0001$). Data were analyzed using one-way ANOVA with Tukey's post hoc test.

The K2 and K1 groups, which received SYSP intervention, exhibited markedly higher levels of acetic acid, propionic acid, and butyric acid compared to the K− and K+ groups. Specifically, acetic acid levels were highest in the K2 group (150.31 ± 6.08 mmol/kg),

followed by K1 (133.16 ± 5.98 mmol/kg), K+ (51.82 ± 4.01 mmol/kg), and K− (34.18 ± 1.06 mmol/kg) (Figure 4A). A similar trend was observed for propionic acid, with concentrations in K2 (53.20 ± 5.54 mmol/kg) and K1 (38.10 ± 2.78 mmol/kg) substantially surpassing those in K+ (17.09 ± 1.75 mmol/kg) and K− (12.23 ± 1.52 mmol/kg) (Figure 4B). Likewise, butyric acid levels were significantly elevated in the SYSP-treated groups, with the highest level observed in K2 (27.18 ± 2.23 mmol/kg), followed by K1 (20.09 ± 1.50 mmol/kg), K+ (8.80 ± 0.52 mmol/kg), and K− (5.32 ± 0.81 mmol/kg) (Figure 4C). These findings suggest that SYSP supplementation enhances microbial SCFA production in a dose-dependent manner, particularly in the caecum.

DISCUSSION

The present study provides compelling evidence that supplementation with SYSP significantly enhances insulin sensitivity and improves glycemic control, as evidenced by reductions in glycated albumin, fasting glucose, and post-prandial glucose levels. These findings contribute to a growing body of literature supporting the metabolic benefits of dietary interventions targeting gut microbiota metabolites and host metabolic pathways. In this discussion, we examine the mechanistic underpinnings of these effects, focusing on the role of short-chain fatty acids (SCFAs) in the caecum and the regulation of key metabolic genes, including GLUT4, PPAR-α, PPAR-γ, and G6P.

The reduction in fasting glucose and post-prandial glucose levels following SYSP administration clearly indicates improved glucose homeostasis. Fasting glucose reflects the baseline regulation of hepatic glucose production and peripheral glucose uptake, while post-prandial glucose levels are influenced by both insulin secretion and tissue insulin responsiveness(Jorgensen et al., 2021). Glycated albumin, a marker of short-term glycemic control over 2 to 3 weeks, further substantiates the effectiveness of SYSP in reducing circulating glucose levels(Kohzuma et al., 2021).

The amelioration of these glycemic indices strongly suggests an improvement in insulin sensitivity. Insulin resistance, characterized by impaired insulin signaling in skeletal muscle, adipose tissue, and liver, is a hallmark of type 2 diabetes mellitus (T2D)(Wondmkun, 2020). Thus, the observed improvements highlight the potential of SYSP to function as a therapeutic agent for preventing or managing insulin resistance and early-stage T2D.

One of the notable findings in the current study is the increased concentration of SCFAs in the caecum. SCFAs, including acetate, propionate, and butyrate, are the primary end-products of microbial fermentation of dietary fibers in the colon(Vinelli et al., 2022). These metabolites are critical in modulating host energy metabolism, gut barrier integrity, and immune responses.

Increased SCFA levels have been associated with improved insulin sensitivity through multiple mechanisms. Butyrate, for instance, serves as an energy source for colonocytes and exhibits anti-inflammatory properties, thereby reducing metabolic endotoxemia—a contributor to systemic insulin resistance(van Deuren et al., 2022). Propionate and acetate also influence hepatic gluconeogenesis and lipid metabolism, partly through the activation of G-protein-coupled receptors (GPR41 and GPR43)(Lee et al., 2024).

Furthermore, SCFAs enhance the secretion of glucagon-like peptide-1 (GLP-1) and peptide YY (PYY), which play roles in satiety signaling and insulin secretion. GLP-1, in particular, enhances glucose-dependent insulin secretion and delays gastric emptying, thereby improving post-prandial glucose control(Jalleh et al., 2024). Therefore, the increased caecal SCFA concentration observed in this study likely played a pivotal role in

improving insulin sensitivity and glycemic control.

The observed upregulation of GLUT4, PPAR-α, PPAR-γ, and G6P protein in response to SYSP administration provides mechanistic insight into the pathways through which SYSP exerts its metabolic effects. These genes are critical glucose and lipid metabolism regulators and are closely linked to the pathophysiology of insulin resistance and metabolic syndrome. GLUT4 is an insulin-responsive glucose transporter expressed in adipose tissue and skeletal muscle. It facilitates glucose uptake into cells, a process impaired in insulin-resistant states(Chadt and Al-Hasani, 2020). Upregulation of GLUT4 suggests enhanced peripheral glucose disposal, contributing to improved glycemic control. Prebiotic and polyphenol-rich diets have previously been shown to upregulate GLUT4 expression via AMPK and PPAR signaling(Fotschki et al., 2022). PPAR-α is primarily involved in hepatic lipid metabolism. Its activation promotes fatty acid β-oxidation, reducing lipid accumulation in tissues and ameliorating lipotoxicity-induced insulin resistance. SYSP-induced PPAR-α upregulation may reduce hepatic steatosis and improve systemic metabolic parameters. PPAR-γ regulates adipocyte differentiation and lipid storage and maintains insulin sensitivity(Bougarne et al., 2018). The ability of SYSP to modulate this pathway suggests a potential for similar benefits with a more favorable safety profile. G6P catalyzes the final step in gluconeogenesis and glycogenolysis, influencing hepatic glucose output. While overactivation may contribute to hyperglycemia, its regulation in this study may indicate a balanced adaptation in response to improved peripheral glucose uptake(Rajas et al., 2019). Additional studies are warranted to characterize the context-specific role of G6P modulation by SYSP.

The gut-metabolic axis offers a framework through which microbiota, dietary components, and host metabolism interact. SYSP appears to modulate this axis favorably by enhancing SCFA production and regulating host gene expression. This dual mechanism improves systemic metabolism and reinforces intestinal integrity, reducing low-grade inflammation—a known contributor to insulin resistance(Ariyoshi et al., 2021).

Recent studies suggest that microbial shifts induced by dietary interventions can influence host gene expression via epigenetic and metabolite-mediated pathways(Gerhauser, 2018). SYSP may promote the growth of beneficial bacterial taxa, such as *Akkermansia muciniphila* and *Faecalibacterium prausnitzii*, associated with improved mucosal health and metabolic outcomes(Verhoog et al., 2019). Future metagenomic and metabolomic studies are necessary to delineate these microbial shifts and their impact on host physiology. Unfortunately, in this study, we did not analyze the gut microbiome, which might be interesting to be studied further.

Compared to pharmacological agents like metformin or thiazolidinediones, SYSP offers a promising dietary approach with potentially fewer side effects. While traditional medications remain foundational in T2D treatment, adjunctive nutritional strategies that target both the microbiota and host metabolic genes hold great promise(Vandeputte, 2020).

Interventions that modulate PPARs and GLUT4 expression have demonstrated synergistic benefits in metabolic disease models(Loza-Rodríguez et al., 2020). The multifactorial effects of SYSP underscore its potential as a holistic intervention targeting diverse aspects of metabolism. However, translating preclinical findings into clinical practice necessitates rigorous trials to assess long-term safety, efficacy, and optimal dosing in human populations.

Despite the strengths of this study, several limitations warrant discussion. First, the causal relationship between SCFAs and the regulation of genes involved in glucose and lipid metabolism has not yet been directly

established. Although the association is biologically plausible, future studies involving receptor antagonists or germ-free models could validate causality.

Second, the active compounds within SYSP responsible for these effects remain to be identified. It is unknown whether the observed benefits stem from specific polysaccharides, polyphenols, or their fermentation products. Isolation and characterization of these components would enhance reproducibility and therapeutic targeting.

Third, the analysis focused on gene expression without measuring protein abundance or activity. Since gene transcription does not always correlate with protein function, complementary proteomic and phosphoproteomic analyses are needed to fully understand SYSP's effects on insulin signaling and glucose metabolism.

CONCLUSION

This study demonstrated that consumption of steamed yellow sweet potato, particularly when steamed twice to enhance its resistant starch content, significantly improved metabolic health in obese rats. The intervention led to increased total antioxidants, GLUT4, and SCFAs, while reducing insulin resistance (HOMA-IR), glycated albumin, post-prandial glucose, and PPAR-α/γ levels. These results highlight the potential of yellow sweet potato as a functional food for improving insulin sensitivity and reducing metabolic risk factors, suggesting its use in dietary interventions aimed at managing obesity and related conditions.

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