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Evaluation of the Glucose-Regulating Function of a Momordica charantia Compound Capsule

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Abstract

Background: *Diabetes mellitus is a prevalent metabolic disorder characterized by impaired glucose regulation and insulin resistance. Developing functional foods with blood glucose–modulating potential is crucial for diabetes prevention and management.*

Methods: *A diabetic rat model was induced by intraperitoneal injection of streptozotocin (STZ, 65 mg/kg) combined with nicotinamide (230 mg/kg) to evaluate the hypoglycemic effects of a Momordica charantia compound capsule. Sixty male Sprague-Dawley rats (8 weeks old) were randomly divided into a control group and diabetic groups (DM, DM-1X, DM-2X, and DM-5X). The treatment groups received oral supplementation for eight weeks. Fasting blood glucose, oral glucose tolerance test (OGTT), serum insulin, 24-hour urine volume, and urinary glucose were assessed.*

Results: *STZ/NA-induced diabetic rats exhibited significantly elevated fasting blood glucose, reduced insulin secretion, and impaired glucose tolerance ($p < 0.05$). After eight weeks of supplementation, all treatment groups showed significant decreases in fasting blood glucose and OGTT area under the curve, along with improved insulin sensitivity and glucose tolerance ($p < 0.05$).*

Conclusion: *The Momordica charantia compound capsule significantly improved glycemic control and insulin resistance in diabetic rats, demonstrating its potential as a functional food for blood glucose regulation. The recommended adult dosage is four capsules per day (497 mg per capsule), which may help support glycemic balance and metabolic health.*

Keywords: *Momordica Charantia, Blood Glucose Regulation, Insulin Resistance, Streptozotocin, Functional Food.*

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder primarily characterized by dysregulated blood glucose levels, accompanied by impaired insulin secretion or action. Although hyperglycemia itself can lead to metabolic disturbances, the most severe consequences are derived from chronic complications such as retinopathy, nephropathy, peripheral neuropathy, and cardiovascular and cerebrovascular diseases. These complications substantially impair patients' quality of life and reduce life expectancy (Forbes & Cooper, 2013).Current strategies for diabetes management include dietary regulation, regular physical activity, and pharmacological interventions, with dietary management being considered one of the most fundamental and crucial approaches. Evidence indicates that more than 50% of patients achieve improved glycemic control through proper dietary management (Evert et al., 2019).However, as the prevalence of diabetes continues to rise globally, reliance solely on conventional pharmacotherapy and lifestyle modifications may not be sufficient. Therefore, there has been increasing interest in exploring functional foods and complementary and alternative medicine (CAM) with glucose-regulating potential as adjunctive or alternative therapeutic strategies. These approaches are gaining importance in both clinical practice and research, particularly for their potential in improving glycemic control and preventing diabetes-related complications (Li et al., 2022).

Among numerous studies on blood glucose regulation, natural plant-derived compounds such as *Momordica charantia*, Citrus bergamia, and sesame have been recognized for their

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significant potential. Notably, *Momordica charantia* has received extensive attention for its hypoglycemic potential due to its richness in various bioactive constituents. Extracts from its fruit and leaves have been reported in multiple animal and clinical studies to significantly reduce fasting plasma glucose (FPG), postprandial glucose (PPG), and glycated hemoglobin (HbA1c), serving as an adjunct for type 2 diabetes management (Liu et al., 2021; Laczkó-Zöld et al., 2023).The major bioactive compounds of M. charantia include charantin, polypeptide-P, alkaloids (e.g., momordicine I and other momordicines), and flavonoids (e.g., quercetin), which exert multi-targeted mechanisms of glucose regulation (Kao et al., 2024; Çiçek et al., 2022). The potential mechanisms of glycemic control involve stimulation of pancreatic β-cell insulin secretion, enhancement of glucose uptake and oxidation in peripheral tissues such as muscle and adipose tissue, upregulation of GLUT4 expression, inhibition of hepatic gluconeogenesis, promotion of glycogen synthesis in the liver, and improvement of insulin resistance through antioxidative and anti-inflammatory effects (Singh et al., 2011; Liu et al., 2024). These mechanisms collectively indicate that M. charantia possesses the potential for systemic modulation of glucose metabolism and could serve as a key component in adjunctive therapy or functional foods for diabetes management in the future.

Citrus bergamia (bergamot) is rich in polyphenolic compounds, particularly flavonoids. Evidence from multiple clinical and animal studies indicates that bergamot can improve insulin resistance, slow postprandial glucose elevation, and enhance lipid metabolism (Musolino et al., 2020). Previous studies have reported that dietary supplementation with bergamot significantly reduces HOMA-IR, an indicator of insulin resistance, and improves both fasting and postprandial blood glucose levels (F Fogacci et al., 2023). Furthermore, bergamot extract polyphenols may exert hypoglycemic and insulin-sensitizing effects by activating the AMPK pathway, promoting glucose uptake, inhibiting hepatic gluconeogenesis, and enhancing hepatic glucose storage (Janda et al., 2016).

Sesame (Sesamum indicum) and its bioactive components, such as lignans including sesamin, sesamolin, and sesamol, have demonstrated potential for glycemic control in multiple animal and human studies. In human studies, sesame intake has been reported to reduce fasting blood glucose, improve insulin sensitivity, and lower HbA1c levels (Yargholi et al., 2021; Atefi et al., 2025). In animal models, sesamin administration has been shown to decrease blood glucose and glycated hemoglobin, while protecting pancreatic β-cells. The underlying mechanisms include enhancement of hepatic glycogen synthesis (via glycogen synthase activity), reduction of inflammatory responses and oxidative stress, improvement of insulin signaling pathways, and promotion of GLUT4 translocation in peripheral tissues (Huang et al., 2023).

The nutritional role of chromium has received considerable attention, and both animal and clinical studies have shown that chromium yeast supplementation can improve carbohydrate and lipid metabolism abnormalities (Lai et al., 2006) and protect pancreatic β-cells from inflammatory infiltration and fibrosis (Weksler-Zangen et al., 2012). In clinical trials involving patients with type 2 diabetes, supplementation with chromium yeast powder significantly reduced fasting blood glucose levels (Sharma et al., 2011) by enhancing insulin action and improving glycemic control (Ghosh et al., 2002). The underlying mechanisms may involve stimulation of insulin receptor phosphorylation, increased insulin sensitivity, and promotion of glucose uptake and utilization (Brautigan et al., 2006; Wang et al., 2009).

Based on the aforementioned background, the *Momordica charantia* compound capsule, which contains bitter melon and other bioactive components, is hypothesized to possess blood glucose–regulating potential. However, there is currently a lack of direct experimental evidence validating its physiological effects. Therefore, it is necessary to evaluate its efficacy through scientific experimentation and literature integration. This study aims to investigate the glycemic regulatory effects of the *Momordica charantia* compound capsule using an animal model and relevant analytical methods. Additionally, existing literature is referenced to provide guidance on dosage selection and to infer potential mechanisms. The findings are expected to offer a scientific basis for the development of this compound capsule as a functional food with commercial and clinical application potential.

MATERIALS AND METHODS

Experimental Supplement

The Momordica charantia compound capsule, provided by SummitBio Co., Ltd., included bitter melon extract, Glycostat®, bergamot extract, zinc yeast, chromium yeast, vitamin E, and sesame extract.

Animal and Study Design

A total of 60 male Sprague–Dawley (SD) rats, 8 weeks old with an average body weight of approximately 260 g, were used in this study. The animals were obtained from Lesco Biotechnology Co., Ltd. All rats were housed at the Animal Facility of the Institute of Sports Science, National Taiwan Sport University, under controlled conditions of 24 ± 2 °C, 65 ± 5% relative humidity, and a 12-hour light/dark cycle. Standard laboratory chow (Chow 5001) and water were provided ad libitum.

The animal study protocol was approved by the Institutional Animal Care and Use Committee (IACUC) of National Taiwan Sport University (Approval No.: IACUC-11007). Diabetes was induced using streptozotocin (STZ, 65 mg/kg) combined with nicotinamide (NA, 230 mg/kg). On day 1 and day 8 of induction, rats were first intraperitoneally injected with NA

(230 mg/kg BW), followed 15 minutes later by STZ (65 mg/kg BW), which was dissolved in physiological saline buffered with 10 mM sodium citrate. Fasting blood glucose (GLU-AC) was measured on day 15 of induction. Rats with blood glucose ≥ 230 ± 10 mg/dL (13 mM) were considered successfully diabetic, while those failing to meet this criterion were excluded. Normal control rats received only physiological saline.

Following screening, rats were randomly divided into five groups (n = 10 per group, 2 rats per cage):

1. Normal control (NC, n = 10): Non-diabetic rats;
2. Diabetic control (DM, n = 10): Successfully induced diabetic rats without treatment;
3. DM-1X (n = 10): Diabetic rats administered 1× the recommended human dose of *Momordica charantia* compound capsule;
4. DM-2X (n = 10): Diabetic rats administered 2× the human dose;
5. DM-5X (n = 10): Diabetic rats administered 5× the human dose.

Oral supplementation was conducted for 8 weeks. During the experiment, fasting blood glucose (GLU-AC) and oral glucose tolerance tests (OGTT) were performed. The dosage design of the *Momordica charantia* compound capsule was based on the recommended daily human intake (33.1 mg per capsule). Low (1×), medium (2×), and high (5×) doses were tested and compared.

To ensure each rat received the precise dose according to body weight, the capsule powder was suspended in distilled water and administered via oral gavage. Because metabolic rates differ between humans and test animals, human doses were converted to rat equivalent doses based on the literature (Nair & Jacob, 2016) and the 2005 U.S. FDA guidelines for estimating maximum safe starting doses in initial clinical trials (US FDA, 2005). Using a human-to-rat conversion factor of 6.2, the daily doses for 1×, 2×, and 5× groups were 61.6 mg, 123.1 mg, and 307.8 mg per day rat, respectively.

Physiological Measurements

(A) Body Weight: The body weight of the rats was measured regularly throughout the experimental period, and comparisons were made between the initial and final body weights.

(B) Water Intake: Daily water consumption was recorded to assess changes in

drinking behavior.

Fasting Blood Glucose Measurement

After 8 weeks of treatment with the test compound (time points determined based on experimental data), blood samples were collected at weeks 0, 2, 4, 6, and 8 to measure overnight fasting blood glucose. Rats were fasted for 18 hours prior to tail vein sampling. Following proper restraint, approximately 5 μL of blood was collected from the tail vein using a blood collection needle. Fasting blood glucose was measured using a OneTouch® UltraEasy™ glucometer (Johnson, TX, USA) with manufacturer-supplied test strips.

Oral Glucose Tolerance Test, OGTT

OGTT was performed at weeks 0 and 8 of test compound intervention. All animals were fasted for 18 hours with free access to water. On the day of the test, baseline blood glucose was obtained via tail vein sampling (used as both fasting and 0-minute glucose values). Subsequently, glucose solution (10% w/v) was orally administered at 1 g/kg body weight via gavage. Blood samples were collected from the tail vein at 30, 60, 90, 120, and 180 minutes post-administration. Blood glucose was measured immediately, and both the area under the curve (AUC) and the incremental area under the curve (ΔAUC) were calculated.

Urine Analysis

At week 8 of test compound intervention, all animals were placed in metabolic cages for 24 hours, with water provided ad libitum but food restricted. Total urine volume was recorded. Urinary glucose concentration was measured using a glucose assay kit (item no. 10009582, Cayman Chemicals, Ann Arbor, MI, USA) and an ELISA reader at 510 nm. Concentrations were calculated based on a standard curve.

Serum Insulin Measurement

At weeks 0 and 8 of test compound intervention, all animals were fasted for 18 hours with free access to water. On the day of the experiment, blood samples were collected from the facial vein to measure serum insulin levels. Serum insulin concentrations were determined using a rat insulin ELISA kit (Catalog Number: 10-1250-01, Mercodia AB, Sylveniusgatan 8A, Sweden) and an ELISA reader at 450 nm. Concentrations were calculated based on a standard curve.

Insulin Resistance Index(HOMA-IR index)

At weeks 0 and 8 of test compound intervention, all animals were fasted for 18 hours with free access to water. Blood samples were collected from the facial vein to measure serum insulin and blood glucose concentrations. Insulin resistance was calculated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) formula: HOMA-IR = [fasting blood glucose (mg/dL) × fasting insulin (μIU/mL)]/405 (Matthews et al., 1985).

Statistical Analysis

The data are expressed as the mean ± standard deviation (SD). Statistical comparisons among groups were made using one-way analysis of variance (ANOVA), followed by Duncan's post hoc test. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were done using SAS software (SAS Institute, Cary, NC, USA).

RESULTS

Changes in Body Weight During the Experimental Period

Weekly body weight changes for each group during the experimental period are shown in Figure 1. Two weeks after DM induction, prior to test compound administration, the initial body weights of the NC, DM, DM-1X, DM-2X, and DM-5X groups were 321 ± 17.2, 304.0 ± 14.0, 301.1 ± 16.6, 299.7 ± 18.3, and 296.8 ± 18.9 g, respectively. Body weights of the DM, DM-1X, DM-2X, and DM-5X groups were significantly lower than those of the NC group ($p < 0.001$), while no significant differences were observed among the DM, DM-1X, DM-2X, and DM-5X groups ($p > 0.05$).

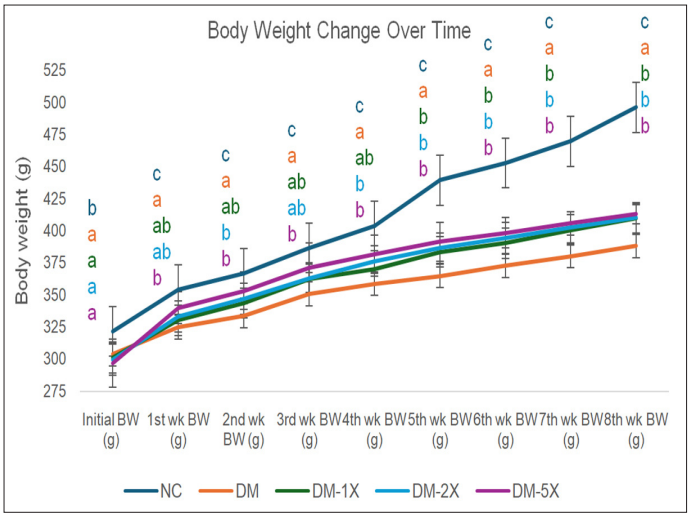

Figure 1. Changes in Body Weight During the Experimental Period

The experimental animals were divided into five groups, with ten rats in each group, as follows:(1) Normal control group (NC);(2) Diabetic control group (Diabetes mellitus, DM);(3) Diabetic group administered with 1× dose (DM-1X);(4) Diabetic group administered with 2× dose (DM-2X);(5) Diabetic group administered with 5× dose (DM-5X).All data are expressed as mean ± standard deviation (Mean ± SD).

During the 8-week intervention period, body weights of the DM, DM-1X, DM-2X, and DM-5X groups remained significantly lower than those of the NC group ($p < 0.05$), demonstrating the typical clinical physiological phenomenon of diabetes-induced weight loss. From week 1 of intervention, body weight in the DM-5X group was significantly higher than that in the DM group ($p < 0.05$). From week 5 onwards, body weights of the DM-1X, DM-2X, and DM-5X groups were significantly higher than those of the DM group. Therefore, continuous 8-week supplementation with 1X, 2X, and 5X doses of *Momordica charantia* complex capsules significantly alleviated diabetes-induced weight loss.

Furthermore, trend analysis revealed a significant dose-dependent effect, indicating that increased doses of *Momordica charantia* complex capsules were associated with greater body weight improvement (Trend analysis, $p = 0.0456$).

Changes in Water Intake of Animals in Each Group During the Experimental Period

The daily average water intake of animals in each group during the experimental period is presented in Table 1. Over the 8-week intervention, the daily average water intake for the NC, DM, DM-1X, DM-2X, and DM-5X groups was 44.1 ± 2.0, 154.5 ± 8.8, 144.8 ± 12.3, 139.3 ± 11.0, and 132.2 ± 7.8 mL, respectively. The DM, DM-1X, DM-2X, and DM-5X groups showed a significant increase in daily water intake compared to the NC group by 3.50-fold ($p < 0.0001$), 3.28-fold ($p < 0.0001$), 3.16-fold ($p < 0.0001$), and 3.00-fold ($p < 0.0001$), exhibiting polydipsia, a clinical symptom of diabetes.

Table 1. Changes in Water Intake of Animals in Each Group During the Experimental Period

Characteristics	NC	DM	DM-1X	DM-2X	DM-5X
1st wk Water (mL/rat/day)	44.4 ± 2.6^{a}	155.6 ± 7.3^{c}	146.7 ± 13.1^{c}	148.0 ± 11.9^{c}	134.0 ± 6.1^{b}
2nd wk Water (mL/rat/day)	43.4 ± 2.7^{a}	151.7 ± 8.4^{d}	142.7 ± 8.0^{c}	142.8 ± 7.3^{c}	132.1 ± 9.6^{b}
3rd wk Water (mL/rat/day)	44.8 ± 2.4^{a}	156.6 ± 11.8^{d}	145.4 ± 5.3^{c}	139.5 ± 9.4^{bc}	134.5 ± 8.9^{b}
4th wk Water (mL/rat/day)	44.6 ± 1.8^{a}	157.1 ± 6.5^{c}	158.9 ± 9.5^{c}	135.6 ± 11.3^{b}	129.8 ± 10.3^{b}
5th wk Water (mL/rat/day)	43.6 ± 1.1^{a}	153.0 ± 11.2^{d}	139.4 ± 8.9^{c}	128.7 ± 4.7^{b}	131.2 ± 6.2^{b}
6th wk Water (mL/rat/day)	43.8 ± 0.8^{a}	151.5 ± 8.0^{d}	134.1 ± 13.3^{bc}	142.4 ± 11.7^{cd}	130.3 ± 6.9^{b}
7th wk Water (mL/rat/day)	42.5 ± 2.2^{a}	162.7 ± 15.4^{c}	132.3 ± 12.7^{b}	133.9 ± 8.0^{b}	128.8 ± 6.3^{b}
8th wk Water (mL/rat/day)	44.2 ± 1.1^{a}	169.9 ± 15.9^{c}	139.7 ± 13.9^{b}	135.2 ± 10.9^{b}	129.3 ± 8.7^{b}
Water (mL/rat/day)	44.1 ± 2.0^{a}	154.7 ± 8.8^{e}	144.8 ± 12.3^{d}	139.3 ± 11.0^{c}	132.2 ± 7.8^{b}

The experimental animals were divided into five groups, with ten rats in each group, as follows: (1) Normal control group (NC); (2) Diabetic control group (Diabetes mellitus, DM); (3) Diabetic group administered with 1× dose (DM-1X); (4) Diabetic group administered with 2× dose (DM-2X); (5) Diabetic group administered with 5× dose (DM-5X). All data are expressed as mean ± standard deviation (Mean ± SD).

Different superscript letters (a, b, c, d) within the same row indicate significant differences among groups ($p < 0.05$).

Water intake in the DM-1X, DM-2X, and DM-5X groups was significantly lower than that of the DM group by 6.28% ($p < 0.0001$), 9.84% ($p < 0.0001$), and 14.43% ($p < 0.0001$), respectively. Moreover, the DM-5X group showed 8.70% ($p = 0.0291$) and 5.10% ($p < 0.0001$) lower water intake than the DM-1X and DM-2X groups, respectively. These results indicate that continuous supplementation with 1X, 2X, and 5X doses of *Momordica charantia* complex capsules for 8 weeks significantly reduced diabetes-induced polydipsia.

Furthermore, trend analysis revealed a significant dose-dependent effect of the *Momordica charantia* complex capsules on reducing water intake (Trend analysis, $p < 0.0001$).

Changes in Fasting Blood Glucose Levels During the Experimental Period

The changes in fasting blood glucose (FBG) levels of rats in each group during the experimental period are shown in Table 2.

Table 2. Changes in Fasting Blood Glucose Levels During the Experimental Period

Characteristics	NC	DM	DM-1X	DM-2X	DM-5X
Baseline (mg/dL)	81.2 ± 3.5[a]	245.0 ± 8.8[b]	243.9 ± 6.3[b]	243.8 ± 11.3[b]	244.5 ± 8.1[b]
2nd wk (mg/dL)	84.1 ± 5.0[a]	295.5 ± 15.5[b]	294.8 ± 18.6[b]	293.4 ± 19.7[b]	291.7 ± 19.2[b]
4th wk (mg/dL)	82.7 ± 6.2[a]	349.8 ± 16.3[c]	320.0 ± 12.8[b]	318.8 ± 17.8[b]	319.9 ± 19.3[b]
6th wk (mg/dL)	83.5 ± 4.5[a]	385.5 ± 13.6[d]	352.9 ± 14.6[c]	336.2 ± 12.7[b]	329.1 ± 19.3[b]
8th wk (mg/dL)	85.0 ± 3.9[a]	464.8 ± 9.3[e]	407.0 ± 16.0[d]	375.8 ± 18.9[c]	343.3 ± 10.2[b]

The experimental animals were divided into five groups, with ten rats in each group, as follows: (1) Normal control group (NC); (2) Diabetic control group (Diabetes mellitus, DM); (3) Diabetic group administered with 1× dose (DM-1X); (4) Diabetic group administered with 2× dose (DM-2X); (5) Diabetic group administered with 5× dose (DM-5X). All data are expressed as mean ± standard deviation (Mean ± SD).

Different superscript letters (a, b, c, d, e) within the same row indicate significant differences among groups ($p < 0.05$).

Before the experiment, the FBG levels of the NC, DM, DM-1X, DM-2X, and DM-5X groups were 81.2 ± 3.5, 245.0 ± 8.8, 243.9 ± 6.3, 243.8 ± 11.3, and 244.5 ± 8.1 mg/dL, respectively. Compared with the NC group, the FBG levels of the DM, DM-1X, DM-2X, and DM-5X groups were significantly increased by 3.01-fold ($p < 0.0001$), 3.00-fold ($p < 0.0001$), 3.00-fold ($p < 0.0001$), and 3.01-fold ($p < 0.0001$), confirming the successful induction of diabetes by STZ + NA. However, no significant differences were observed among the DM, DM-1X, DM-2X, and DM-5X groups ($p > 0.05$).

At week 2, the FBG levels of the NC, DM, DM-1X, DM-2X, and DM-5X groups were 84.1 ± 5.0, 295.5 ± 15.5, 294.8 ± 18.6, 293.4 ± 19.7, and 291.7 ± 19.2 mg/dL, respectively. The FBG levels of the DM, DM-1X, DM-2X, and DM-5X groups were significantly higher than that of the NC group by 3.51-fold ($p < 0.0001$), 3.51-fold ($p < 0.0001$), 3.49-fold ($p < 0.0001$), and 3.47-fold ($p < 0.0001$). No significant differences were observed among the four diabetic groups ($p > 0.05$), and no dose-dependent effects were found at this stage.

At week 4, the FBG levels of the NC, DM, DM-1X, DM-2X, and DM-5X groups were 82.7 ± 6.2, 349.8 ± 16.3, 320.0 ± 12.8, 318.8 ± 17.8, and 319.9 ± 19.3 mg/dL, respectively. Compared with the DM group, the FBG levels of the DM-1X, DM-2X, and DM-5X groups were significantly reduced by 8.52% ($p < 0.0001$), 8.86% ($p < 0.0001$), and 8.55% ($p < 0.0001$), respectively. Trend analysis further revealed a significant dose-dependent reduction in FBG levels with increasing doses of the *Momordica charantia* complex capsules ($p = 0.0010$).

At week 6, the FBG levels of the NC, DM, DM-1X, DM-2X, and DM-5X groups were 83.5 ± 4.5, 385.5 ± 13.6, 352.9 ± 14.6, 336.2 ± 12.7, and 329.1 ± 19.3 mg/dL, respectively. Compared with the DM group, the FBG levels of the DM-1X, DM-2X, and DM-5X groups were significantly decreased by 8.46% ($p < 0.0001$), 12.79% ($p < 0.0001$), and 14.63% ($p < 0.0001$). Trend analysis again demonstrated a significant dose-dependent hypoglycemic effect ($p < 0.0001$).

At week 8, the FBG levels of the NC, DM, DM-1X, DM-2X, and DM-5X groups were 85.0 ± 3.9, 464.8 ± 9.3, 407.0 ± 16.0, 375.8 ± 18.9, and 343.3 ± 10.2 mg/dL, respectively. Compared with the DM group, the FBG levels of the DM-1X, DM-2X, and DM-5X groups were significantly reduced by 12.44% ($p < 0.0001$), 19.15% ($p < 0.0001$), and 26.14% ($p < 0.0001$), respectively. These findings indicate that continuous supplementation with the *Momordica charantia* complex capsules for 8 weeks significantly reduced fasting blood glucose levels. Moreover, trend analysis confirmed a pronounced dose-dependent reduction ($p < 0.0001$), demonstrating that the hypoglycemic effect was positively correlated with the dosage administered.

Changes in Oral Glucose Tolerance Test (OGTT) among Experimental Groups during the Study Period

The oral glucose tolerance test (OGTT) is an important method for evaluating glucose metabolic function and is widely used in the diagnosis and research of diabetes and impaired glucose tolerance. This test involves the oral administration of a fixed dose of glucose solution, followed

by blood glucose measurements at specific time intervals to assess insulin secretion and glucose regulatory capacity (Matthews et al., 1985; Nathan et al., 2007).

Before the intervention, the OGTT results, including the area under the curve (AUC) of glucose changes and the change in AUC (ΔAUC), are shown in Figure 2. As shown in Figure 2B, the AUC values of the NC, DM, DM-1X, DM-2X, and DM-5X groups were 21,794 ± 1,454, 59,594 ± 3,462, 59,558 ± 3,763, 59,682 ± 3,944, and 59,697 ± 3,601 mg/dL×180 min, respectively. The AUCs of the DM, DM-1X, DM-2X, and DM-5X groups were significantly higher than that of the NC group by 2.73-fold ($p < 0.0001$), 2.73-fold ($p < 0.0001$), 2.74-fold ($p < 0.0001$), and 2.74-fold ($p < 0.0001$), respectively. However, no significant differences were observed among the diabetic groups ($p > 0.05$).

As shown in Figure 2C, the ΔAUC values before the intervention for the NC, DM, DM-1X, DM-2X, and DM-5X groups were 6,998 ± 970, 16,034 ± 2,147, 16,160 ± 2,492, 16,104 ± 2,363, and 16,065 ± 2,768 mg/dL×180 min, respectively. The ΔAUCs of the DM, DM-1X, DM-2X, and DM-5X groups were significantly higher than that of the NC group by 2.29-fold ($p < 0.0001$), 2.31-fold ($p < 0.0001$), 2.30-fold ($p < 0.0001$), and 2.30-fold ($p < 0.0001$), respectively, with no significant differences among diabetic groups ($p > 0.05$).

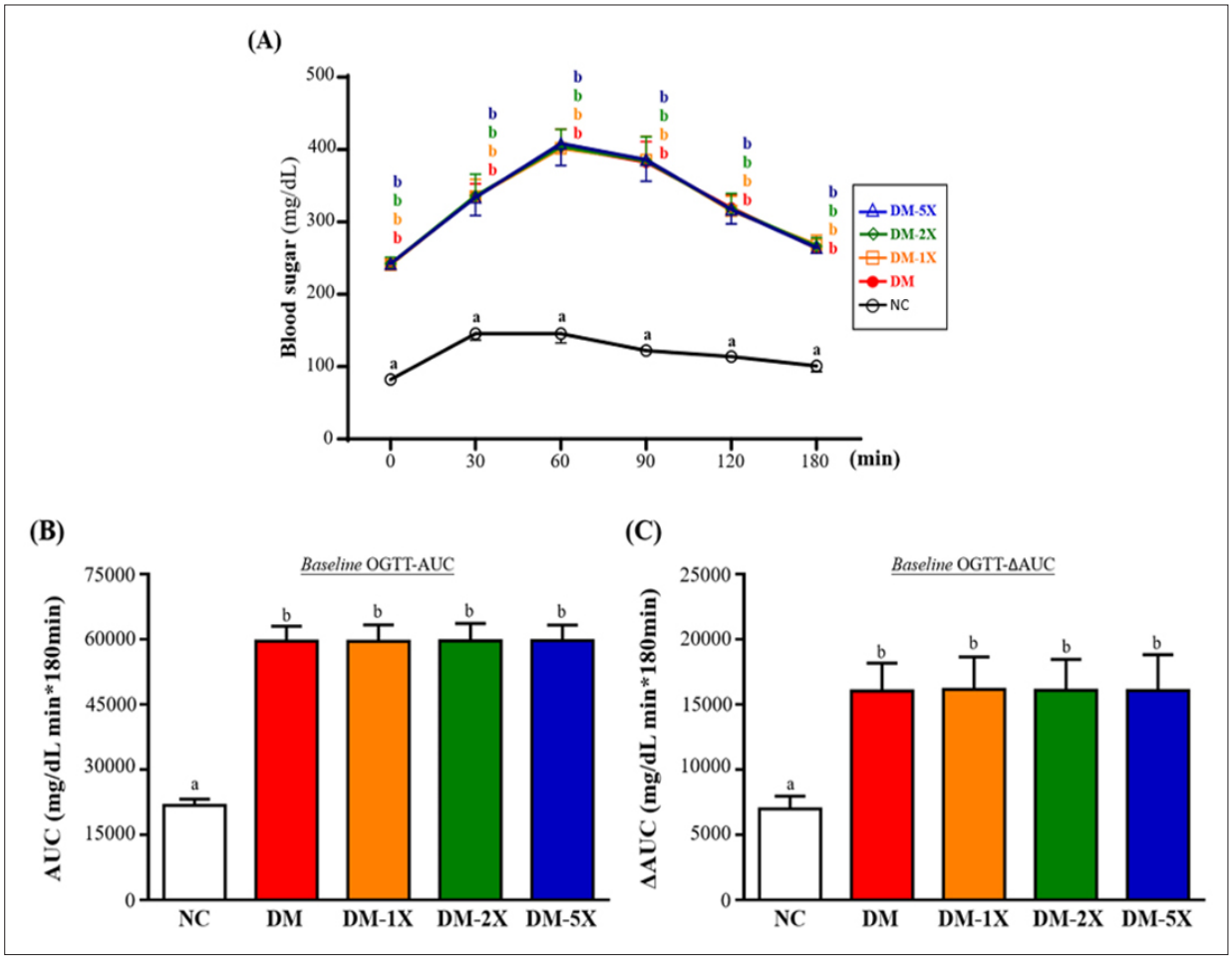

Figure 2. Changes in Oral Glucose Tolerance Test Parameters of Each Group before Intervention (Baseline) (A) Blood glucose changes during the oral glucose tolerance test (OGTT) (B) Area under the curve (AUC) of blood glucose in the OGTT.(C) Incremental area under the curve (ΔAUC) of blood glucose during the OGTT.

The experimental animals were divided into five groups, with ten rats in each group, as follows: (1) Normal control group (NC); (2) Diabetic control group (Diabetes mellitus, DM);(3) Diabetic group administered with 1× dose (DM-1X); (4) Diabetic group administered with 2× dose (DM-2X); (5) Diabetic group administered with 5× dose (DM-5X). All data are expressed as mean ± standard deviation (Mean ± SD).

After 8 weeks of intervention, the OGTT results, AUC, and ΔAUC of each group are shown in Figure 3. As shown in Figure 3B, the AUC values of the NC, DM, DM-1X, DM-2X, and DM-5X groups were 21,099 ± 1,967, 95,349 ± 3,189, 81,993 ± 3,763, 75,351 ± 4,044, and 71,651 ± 4,051 mg/dL×180 min, respectively. The AUCs of the DM, DM-1X, DM-2X, and DM-5X groups were significantly higher than that of the NC group by 4.52-fold ($p < 0.0001$), 3.89-fold ($p < 0.0001$), 3.57-fold ($p < 0.0001$), and 3.40-fold ($p < 0.0001$), respectively. Compared with the DM group, the AUCs of the DM-1X, DM-2X, and DM-5X groups were significantly reduced by 14.01% ($p < 0.0001$), 20.97% ($p < 0.0001$), and 24.85% ($p < 0.0001$), respectively.

As shown in Figure 3C, the ΔAUC values at week 8 for the NC,

DM, DM-1X, DM-2X, and DM-5X groups were 6,051 ± 1,280, 15,375 ± 1,385, 11,073 ± 1,858, 8,517 ± 1,435, and 8,057 ± 810 mg/dL×180 min, respectively. The ΔAUCs of the DM, DM-1X, DM-2X, and DM-5X groups were significantly higher than that of the NC group by 2.54-fold ($p < 0.0001$), 1.83-fold ($p < 0.0001$), 1.41-fold ($p = 0.0003$), and 1.33-fold ($p = 0.0024$), respectively. Compared with the DM group, the ΔAUCs of the DM-1X, DM-2X, and DM-5X groups were significantly reduced by 27.98% ($p < 0.0001$), 44.60% ($p < 0.0001$), and 47.60% ($p < 0.0001$), respectively.

Therefore, continuous supplementation with 1×, 2×, and 5× doses of *Momordica charantia* complex capsules for 8 weeks significantly improved glucose utilization. Furthermore, trend analysis revealed a clear dose-dependent effect on the reduction of both AUC and ΔAUC values (trend analysis, $p < 0.0001$).

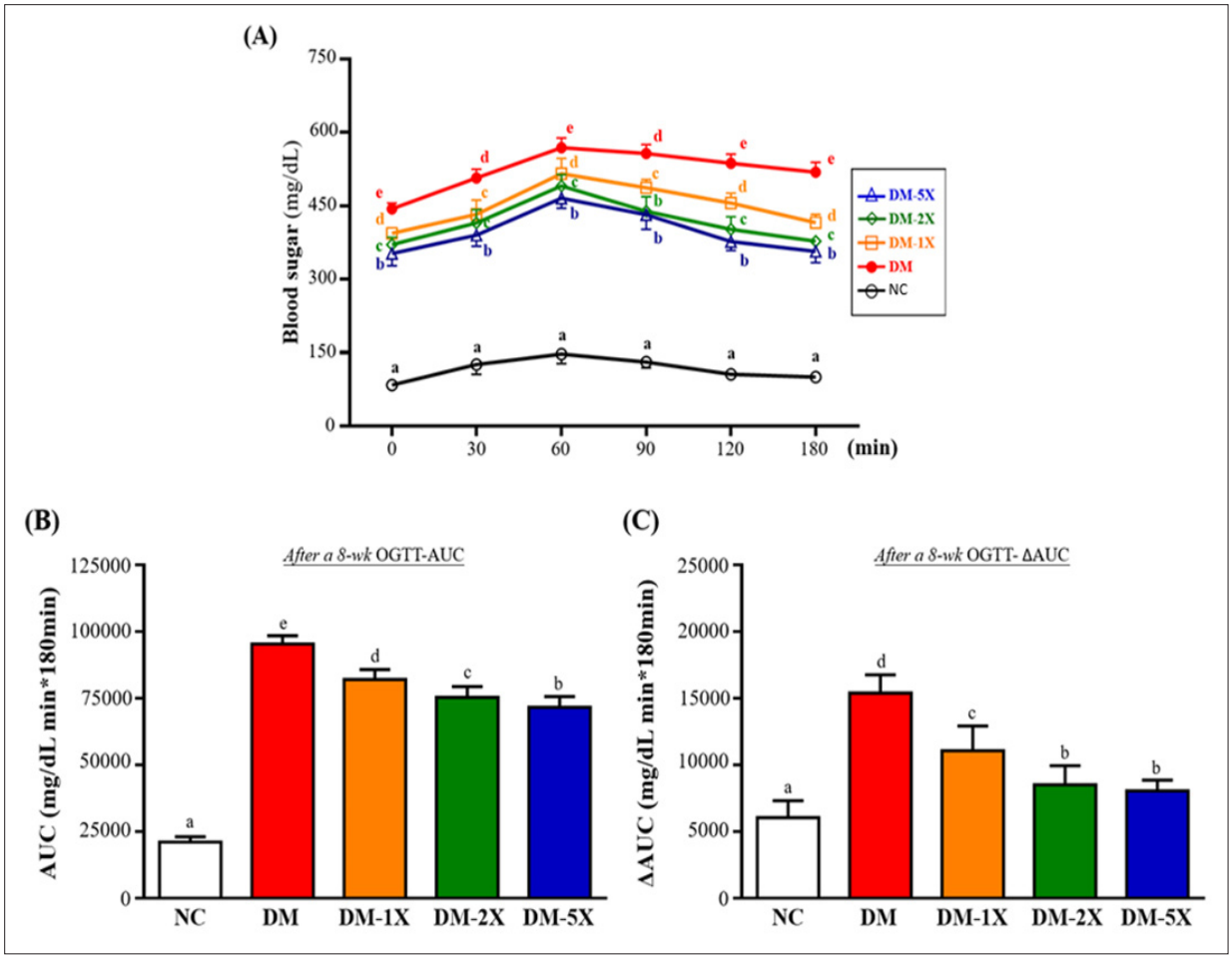

Figure 3. Changes in Oral Glucose Tolerance Test Parameters of Each Group after 8th week (A) Blood glucose changes during the oral glucose tolerance test (OGTT). (B) Area under the curve (AUC) of blood glucose in the OGTT. (C) Incremental area under the curve (ΔAUC) of blood glucose during the OGTT.

The experimental animals were divided into five groups, with ten rats in each group, as follows: (1) Normal control group (NC); (2) Diabetic control group (Diabetes mellitus, DM); (3) Diabetic group administered with 1× dose (DM-1X); (4) Diabetic group administered with 2× dose (DM-2X); (5) Diabetic group administered with 5× dose (DM-5X). All data are expressed as mean ± standard deviation (Mean ± SD).

Different superscript letters (a, b, c, d, e) within the same row indicate significant differences among groups ($p < 0.05$).

Changes in Serum Insulin Levels among Experimental Groups during the Study

As shown in Figure 4A, the baseline serum insulin concentrations in the NC, DM, DM-1X, DM-2X, and DM-5X groups were 42.7 ± 2.9, 37.1 ± 2.1, 37.4 ± 3.6, 37.0 ± 3.3, and 37.1 ± 2.4 (uIU/ml), respectively. Compared with the NC group, serum insulin levels in the DM, DM-1X, DM-2X, and DM-5X groups were significantly reduced by 13.11% ($p < 0.0001$), 12.41% ($p = 0.0002$), 13.35% ($p < 0.0001$), and 13.11% ($p < 0.0001$), respectively. However, there were no significant differences ($p > 0.05$) in serum insulin levels among the DM, DM-1X, DM-2X, and DM-5X groups.

As shown in Figure 4B, after 8 weeks of intervention, the serum insulin concentrations in the NC, DM, DM-1X, DM-2X, and DM-5X groups were 42.9 ± 2.5, 25.2 ± 1.6, 26.8 ± 1.6, 28.0 ± 1.2, and 29.3 ± 1.6 (uIU/ml), respectively. Compared with the NC group, insulin levels in the DM, DM-1X, DM-2X, and DM-5X groups were significantly decreased by 41.26%

($p < 0.0001$), 37.53% ($p < 0.0001$), 34.73% ($p < 0.0001$), and 31.70% ($p < 0.0001$), respectively. Moreover, the serum insulin concentrations in the DM-1X, DM-2X, and DM-5X groups were 1.06-fold ($p = 0.0428$), 1.11-fold ($p = 0.0008$), and 1.16-fold ($p < 0.0001$) higher than that in the DM group, respectively.

Therefore, continuous supplementation with 1X, 2X, or 5X doses of the *Momordica charantia* compound capsule for 8 weeks significantly improved serum insulin concentrations. Furthermore, trend analysis indicated a dose-dependent increase in serum insulin levels with higher supplementation doses ($p < 0.0001$).

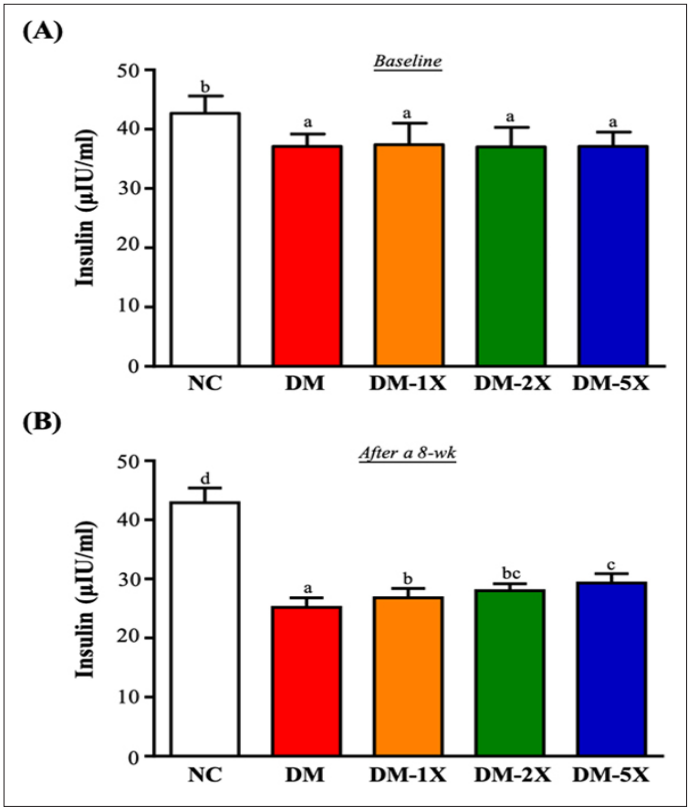

Figure 4. Serum insulin changes of each group during the experiment:(A) Serum insulin levels before intervention (Baseline).(B) Serum insulin levels after 8 weeks of intervention (8th wk).

The experimental animals were divided into five groups, with ten rats in each group, as follows: (1) Normal control group (NC); (2) Diabetic control group (Diabetes mellitus, DM); (3) Diabetic group administered with 1× dose (DM-1X); (4) Diabetic group administered with 2× dose (DM-2X); (5) Diabetic group administered with 5× dose (DM-5X). All data are expressed as mean ± standard deviation (Mean ± SD).

Different superscript letters (a, b, c, d) within the same row indicate significant differences among groups ($p < 0.05$).

Changes in 24-hour Urine Volume and Urinary Glucose Concentration During the Experimental Period

Urine volume and urinary glucose concentration are important indicators for evaluating renal glucose reabsorption capacity and glycemic control. Under hyperglycemic conditions, excessive glucose is filtered by the glomerulus; when the filtered load exceeds the tubular reabsorption threshold, unabsorbed glucose is excreted in the urine, resulting in glucosuria and osmotic diuresis (American Diabetes Association, 2024). Therefore, monitoring urine volume and urinary glucose concentration serves as an important reference for early detection of diabetes and its complications, such as diabetic nephropathy, as well as metabolic status assessment (Vallon &Komers, 2011).

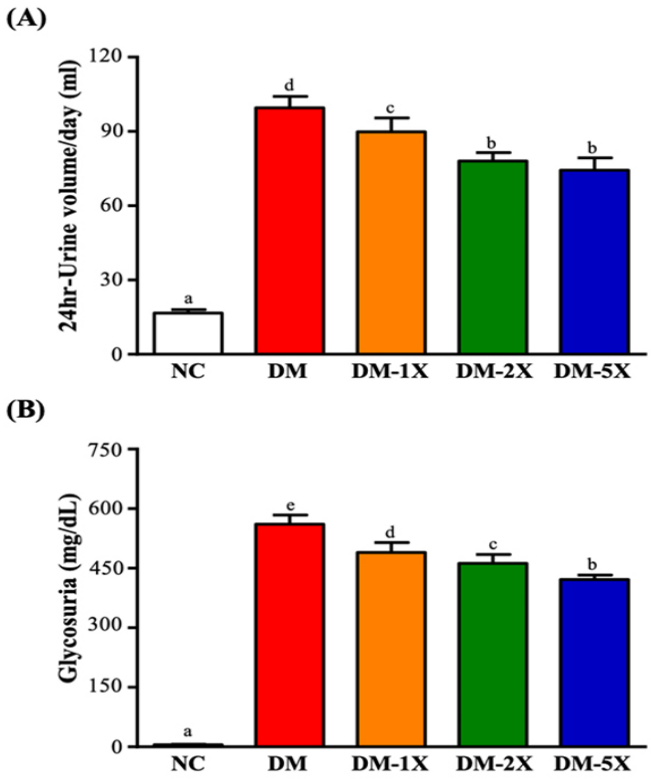

Figure 5. Changes in 24-hour Urine Parameters of Each Group after the 8th Week Intervention(A) Changes in 24-hour urine volume (B) Changes in urinary glucose concentration

The experimental animals were divided into five groups, with ten rats in each group, as follows: (1) Normal control group (NC); (2) Diabetic control group (Diabetes mellitus, DM); (3) Diabetic group administered with 1× dose (DM-1X); (4) Diabetic group administered with 2× dose (DM-2X); (5) Diabetic group administered with 5× dose (DM-5X). All data are expressed as mean ± standard deviation (Mean ± SD).

Different superscript letters (a, b, c, d, e) within the same row indicate significant differences among groups ($p < 0.05$).

As shown in Figure 5, 24-hour urine volume and urinary glucose concentration were measured in all groups at week 8 of supplementation. As shown in Figure 5A, the 24-hour urine volumes in NC, DM, DM-1X, DM-2X, and DM-5X groups were 16.6 ± 1.4, 99.6 ± 4.6, 89.8 ± 5.6, 78.0 ± 3.4, and 74.3 ± 5.0 mL, respectively. Compared with NC, DM, DM-1X, DM-2X, and DM-5X groups showed significantly increased urine volumes by 6.00-fold ($p < 0.0001$), 5.41-fold ($p < 0.0001$), 4.70-fold ($p < 0.0001$), and 4.48-fold ($p < 0.0001$), reflecting polyuria, a

typical clinical manifestation of diabetes. Furthermore, DM-1X, DM-2X, and DM-5X groups showed significantly reduced 24-hour urine volumes compared with the DM group by 9.84% ($p < 0.0001$), 21.69% ($p < 0.0001$), and 25.40% ($p < 0.0001$), respectively.

As shown in Figure 5B, urinary glucose concentrations at week 8 were 5.3 ± 1.3, 561.1 ± 23.1, 489.7 ± 25.2, 462.0 ± 22.9, and 421.3 ± 11.7 mg/dL for NC, DM, DM-1X, DM-2X, and DM-5X groups, respectively. DM, DM-1X, DM-2X, and DM-5X groups exhibited significantly higher urinary glucose than NC by 105.87-fold ($p < 0.0001$), 92.40-fold ($p < 0.0001$), 87.17-fold ($p < 0.0001$), and 79.49-fold ($p < 0.0001$). Compared with DM, DM-1X, DM-2X, and DM-5X groups showed significantly reduced urinary glucose concentrations by 12.73% ($p < 0.0001$), 17.66% ($p < 0.0001$), and 24.92% ($p < 0.0001$), respectively.

Taken together, continuous supplementation with 1X, 2X, and 5X doses of *Momordica charantia* compound capsules for 8 weeks significantly reduced diabetes-induced polyuria and urinary glucose concentration. Trend analysis further revealed that the reductions in urine volume and urinary glucose concentration were dose-dependent, showing significant dose-response effects (Trend analysis, $p < 0.0001$).

Changes in Insulin Resistance (HOMA-IR) in Each Group during the Experimental Period

Insulin resistance (IR) is one of the key pathological mechanisms in the development of diabetes, and the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) is a widely used method for evaluating insulin sensitivity and β-cell function (Matthews et al., 1985). This index, calculated from fasting blood glucose and fasting insulin levels, reflects changes in hepatic and peripheral tissue responses to insulin (Wallace et al., 2004). HOMA-IR is extensively applied in both diabetic animal models and clinical studies to assess the degree of insulin resistance and the effectiveness of metabolic improvement (American Diabetes Association, 2024).

As shown in Figure 6A, the pre-intervention HOMA-IR values for NC, DM, DM-1X, DM-2X, and DM-5X groups were 8.6 ± 0.6, 22.4 ± 1.1, 22.5 ± 2.4, 22.4 ± 2.5, and 22.4 ± 1.7, respectively. Compared with the NC group, HOMA-IR values were significantly higher in the DM, DM-1X, DM-2X, and DM-5X groups, by 2.60-fold ($p < 0.0001$), 2.62-fold ($p < 0.0001$), 2.60-fold ($p < 0.0001$), and 2.60-fold ($p < 0.0001$), respectively.

As shown in Figure 6B, after 8 weeks of intervention, the HOMA-IR values for NC, DM, DM-1X, DM-2X, and DM-5X groups were 9.0 ± 0.7, 28.9 ± 1.2, 26.9 ± 0.8, 26.0 ± 0.9, and 24.8 ± 1.0, respectively. Compared with the NC group, HOMA-IR values in the DM, DM-1X, DM-2X, and DM-5X groups were significantly increased by 3.21-fold ($p < 0.0001$), 2.99-fold ($p < 0.0001$), 2.89-fold ($p < 0.0001$), and 2.76-fold ($p < 0.0001$), respectively. Compared with the DM group, HOMA-IR values were significantly reduced by 6.92% ($p < 0.0001$), 10.03% ($p < 0.0001$), and 14.19% ($p < 0.0001$) in the DM-1X, DM-2X, and DM-5X groups, respectively.

These results indicate that continuous supplementation with 1X, 2X, and 5X doses of the bitter melon (*Momordica charantia*) compound capsules for 8 weeks significantly reduces insulin resistance. Moreover, trend analysis further demonstrated a dose-dependent effect of bitter melon compound supplementation on decreasing HOMA-IR (Trend analysis, $p < 0.0001$).

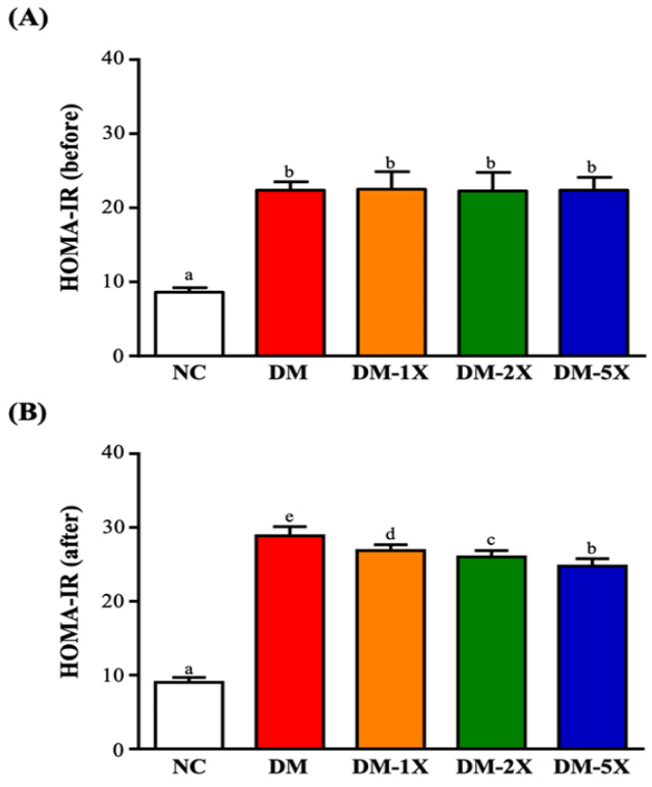

Figure 6. Changes in Insulin Resistance (HOMA-IR) of Each Group (A) HOMA-IR at baseline (before intervention) (B) HOMA-IR after 8 weeks of intervention (8th week)

The experimental animals were divided into five groups, with ten rats in each group, as follows: (1) Normal control group (NC); (2) Diabetic control group (Diabetes mellitus, DM); (3) Diabetic group administered with 1× dose (DM-1X); (4) Diabetic group administered with 2× dose (DM-2X); (5) Diabetic group administered with 5× dose (DM-5X). All data are expressed as mean ± standard deviation (Mean ± SD).

Different superscript letters (a, b, c, d, e) within the same row indicate significant differences among groups ($p < 0.05$).

DISCUSSION

The study employed Streptozotocin (STZ, 65 mg/kg) combined with Nicotinamide (NA, 230 mg/kg) to induce a diabetes model in male SD rats, simulating the hyperglycemia and impaired insulin secretion characteristic of human diabetes. The results demonstrated that rats treated with STZ+NA exhibited significantly elevated fasting blood

glucose, decreased serum insulin, and typical diabetic symptoms including weight loss, polyphagia, polydipsia, and polyuria. The oral glucose tolerance test (OGTT) further indicated impaired glucose responsiveness. These findings are consistent with previous studies, confirming that STZ+NA can reliably establish a stable diabetic animal model (Zhu et al., 2020; Szkudelski et al., 2012; Chen et al., 2008; Barragán-Bonilla et al., 2019; Andrade-Cetto et al., 2013).

After 8 weeks of supplementation with *Momordica charantia* (bitter melon) complex capsules at 1X, 2X, and 5X human recommended doses, diabetic rats showed a significant reduction in fasting blood glucose, indicating a hypoglycemic effect of the product. This effect may be attributed to the bitter melon extract within the formulation. *Momordica charantia* contains multiple bioactive compounds, among which charantinis a major steroidal saponin, and polypeptide-P can mimic insulin activity, promoting cellular glucose uptake and enhancing insulin sensitivity (Sun et al., 2023; Ali et al., 2022).

Previous studies have indicated that charantin exerts hypoglycemic effects through multiple mechanisms, including stimulating insulin secretion from pancreatic β-cells, upregulating GLUT4 expression in skeletal muscle to enhance glucose uptake, activating the AMPK pathway to inhibit hepatic gluconeogenesis, and potentially inhibiting intestinal enzymes such as α-glucosidase and DPP-4 to reduce postprandial glucose (Tan et al., 2008; Laczkó-Zöld, Eszter, et al., 2024). Animal studies have shown that administration of charantin-rich bitter melon extract can significantly improve pancreatic function and glucose tolerance in high-fat diet-induced diabetic rats (Tan et al., 2008). Clinical studies have also observed that supplementation with bitter melon extract reduces fasting blood glucose in patients with type 2 diabetes (Kim, Soo Kyoung et al., 2020).

In addition, chromium yeast included in the product can enhance insulin signaling and regulate blood glucose by stimulating insulin receptor activation and increasing insulin receptor tyrosine kinase (IRTK) activity (National Institute of Health, 2013; Molz et al., 2021). Studies indicate that chromium acts as a cofactor for insulin, promoting the binding of insulin to its receptor, enhancing downstream PI3K/Akt signaling, and increasing GLUT4 translocation to the plasma membrane, thereby facilitating glucose uptake in skeletal muscle and adipose tissue (Hua, Yinan et al., 2012). Multiple clinical studies have also demonstrated that chromium yeast supplementation effectively improves insulin sensitivity and reduces fasting blood glucose and HbA1c levels, showing beneficial effects in patients with type 2 diabetes and individuals with insulin resistance (Asbaghi, Omid, et al., 2020; Georgaki, Maria-Nefeli et al., 2024). Animal studies further reveal that chromium yeast can suppress hepatic gluconeogenic enzyme expression and reduce oxidative stress-induced damage to pancreatic β-cells, thereby enhancing insulin secretion and glucose tolerance (Feng, Weiwei et al., 2015; Abdourahman, Aicha, & John G. Edwards, 2008).

Results from the oral glucose tolerance test (OGTT) demonstrated that supplementation with the *Momordica charantia* compound capsules significantly improved glucose tolerance in diabetic rats, showing lower blood glucose levels and faster recovery compared with untreated groups. This effect may be attributed to the flavonoid-rich Citrus bergamia extract contained in the product. These bioactive compounds, such as hesperidin, naringin, and eriocitrin, can stimulate insulin secretion, promote pancreatic β-cell proliferation, and enhance peripheral glucose uptake (Vinayagam & Xu, 2015; Graf et al., 2005; Cai et al., 2017). Several studies indicate that citrus flavonoids upregulate GLUT4 expression in skeletal muscle and activate AMPK signaling pathways, thereby increasing cellular glucose uptake, while simultaneously inhibiting hepatic gluconeogenic enzymes such as PEPCK and G6Pase, reducing endogenous glucose production (Li, Sen et al., 2019; Jung, Un Ju et al., 2004). Animal experiments further demonstrate that hesperidin and naringin markedly improve glucose tolerance and insulin sensitivity in type 2 diabetic rats while reducing oxidative stress and lipid peroxidation (Jung, Un Ju et al., 2006; Prasatthong, Patoomporn et al., 2021).

Moreover, sesame extract exhibits antioxidant and anti-inflammatory properties that may attenuate oxidative stress-mediated interference with insulin action, further improving glucose tolerance (Sankar et al., 2011; Haidari et al., 2016).

Studies have indicated that the bioactive components in sesame can enhance insulin sensitivity and reduce the expression of hepatic gluconeogenic enzymes, such as glucose-6-phosphatase, thereby decreasing glucose production (Dalibalta, Sarah et al., 2020). Its antioxidant and anti-inflammatory properties may mitigate the interference of oxidative stress on insulin action, further improving glucose tolerance (Freise, Christian et al., 2012; Nakano, Daisuke et al., 2006). Moreover, both animal studies and limited clinical trials have demonstrated that sesame extract can improve fasting blood glucose, HbA1c, and lipid metabolism in diabetic models or prediabetic populations, while exhibiting antioxidant activity and reducing the risk of diabetes-related complications (Mohammad Shahi, Majid et al., 2017; AN, Jianbo&Ruijuan ZHANG, 2010).

Following 8 weeks of supplementation with the *Momordica charantia* compound capsules, diabetic rats exhibited marked improvements in polyphagia, polydipsia, and polyuria, with a slower decline in body weight. These improvements are likely attributable to the synergistic effects of the formulation's components—including bitter melon, bergamot extract, sesame, zinc yeast, chromium yeast, and vitamin E—which collectively enhance insulin sensitivity, promote insulin secretion, and reduce blood glucose, thereby alleviating typical physiological symptoms of diabetes.

Taken together, the hypoglycemic effects of the *Momordica*

charantia compound capsules may be achieved through the following mechanisms: 1) enhancement of insulin secretion and β-cell regeneration; 2) activation of insulin receptor function and signaling pathways; 3) mitigation of oxidative stress and inflammation; and 4) regulation of glucose metabolism and glucose tolerance. Therefore, this study confirms that *Momordica charantia* compound capsules can effectively stabilize blood glucose, improve glucose tolerance, and alleviate diabetes-associated physiological symptoms, suggesting their potential as a complementary functional food for diabetes management.

CONCLUSION

The results of this study indicate that STZ + NA injection successfully induced diabetes in rats, with fasting blood glucose levels exceeding 230 mg/dL (approximately 13 mmol/L). Continuous administration of *Momordica charantia* (bitter melon) compound capsules for 8 weeks in STZ + NA-induced diabetic rats significantly reduced fasting blood glucose, alleviated polydipsia, and improved glucose intolerance and insufficient insulin secretion. These findings suggest that *Momordica charantia* compound capsules may serve as an adjunctive intervention for individuals with elevated fasting blood glucose, contributing to blood glucose regulation. Based on dosage conversion, the recommended daily intake for adults is 4 capsules (497 mg per capsule), which may help support blood glucose control and promote metabolic health.

ACKNOWLEDGMENT

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