OPEN ACCESS

Current Research in Complementary & Alternative Medicine

Chung H-Y, et al., Curr Res Complement Altern Med 8: 243.

www.doi.org/10.29011/2577-2201.100243

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Research Article

Exercise-Drug Interaction in Blood Sugar Regulation: Insights from α-Glucosidase Inhibitors and Postprandial Exercise

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Citation: Chung H-Y, Li P-Y, Chen T-C, Huang K-E, Chen F-S, et al. (2024) Exercise-Drug Interaction in Blood Sugar Regulation: Insights from α-Glucosidase Inhibitors and Postprandial Exercise. Curr Res Cmpl Alt Med 8: 243. DOI: 10.29011/2577-2201.100243

Received Date: 11 May 2024; **Accepted Date:** 20 May 2024; **Published Date:** 23 May 2024

Abstract

Background: The global population is aging, and the diseases of these aging people are related to their living habits. Implementing a healthy diet, physical activity, and appropriate medication is equally important. This study explores the impact of 60% Maximum Heart Rate (MHR) exercise on blood sugar after taking α-glucosidase inhibitors-Nangapiry (α-GI-N) to explore optimal blood sugar control management. **Methods:** Seven healthy male college students participated in four experiments involving Group A (Control group), Group B (α-GI-N group, 2.5mg/kg), Group C (Exercise group, a 30-minute bicycle test at 60% MHR) and Group D (α-GI-N + Exercise group). The groups were compared using statistical tests to identify any differences. **Results:** According to the OSTT test, there were notable variations between groups B and D compared to the control group A after taking α-GI-N for 30 minutes. When exercise was added 30 minutes after consuming the α-GI-N, the exercise intensity of groups C and D was 63 ± 4% MHR, decreasing blood glucose to resting levels. Interestingly, the exercise test results showed no significant differences in heartbeat, oxygen uptake, and respiratory quotient collection between groups C and D. Additionally, α-GI-N did not affect exercise capacity or cause hypoglycaemia. **Conclusion:** A well-rounded lifestyle entails the proper medication, a nutritious diet, and consistent physical activity. An up-to-date study suggests that merging medication with exercise can effectively manage blood sugar levels. This approach presents a fresh avenue for regulating blood sugar and improving overall health by exercising after 30 minutes of eating.

Keywords: Diabetes; Exercise-drug interaction; Exercise therapy; α-glucosidase inhibitors-Nangapiry (α-GI-N); Drug safety

Introduction

The global population of people aged 65 and over is expected to increase from 10% to 16% in 2050, presenting a challenge [1]. While global life expectancy has increased markedly, there has also been a significant rise in chronic illnesses and population aging [2]. Noncommunicable diseases (NCDs) account for 74% of global deaths annually, with cardiovascular disease being the primary cause of death from NCDs, followed by cancer, chronic respiratory diseases, and diabetes [3]. These conditions are closely linked to lifestyle choices and are frequently referred to as lifestyle diseases. Medications alone cannot completely treat these illnesses, and they must be managed through a combination of diet control and exercise therapy. Promoting healthy aging is crucial for individual and societal well-being [4].

It is important to note that exercise and diet can impact how the body processes drugs [5]. This means that combining basic treatment with drug therapy can sometimes result in interactions like those that can occur between different drugs [5]. A deeper understanding of the interactions between specific antidiabetic agents and various forms and intensities of exercise is critical to optimizing glycaemic control while minimizing the potential for blood glucose level disturbances [6].

Alpha-glucosidase inhibitors (AGIs), also known as acarbose and miglitol, slow down the occurrence of postprandial blood sugar by inhibiting the intestinal processing of carbohydrates. Patients with impaired glucose tolerance can also use it to delay the onset of type 2 diabetes [7]. Absorption of sugar occurs in the small intestine and requires the breakdown of disaccharides into simple sugars. α-Glucosidase is the enzyme that performs this decomposition. Inhibiting this enzyme can reduce sugar absorption, which prevents blood sugar levels from rising after meals. However, the most common side effect of AGIs is gastrointestinal disturbances [7]. AGIs are helpful for blood sugar control and are contained in many natural foods, such as peppers [8], tomatoes [9], onion [10] and bitter melon [11], has been studied for its 50% inhibitory effect on sucrase activity, which is helpful for blood sugar control. In addition, Nangapiry is a plant that grows in South America, Paraguay, Brazil, Argentina and Southeast Asia, and its naturally dried leaves are used for medicinal purposes. In Paraguay, Nangapiry is widely used in natural medicine, especially to treat diabetes [12] and hypertension [13].

Nangapiry can delay the mechanism of postprandial hyperglycaemia through its AGIs effect [14]. Compared with oral hypoglycaemic drugs, Nangapiry can also reduce blood sugar fluctuations throughout the day [12]. Therefore, this study aims to gain a deeper understanding of the interaction between α-glucosidase inhibitor drugs, dietary control, and exercise to find safe and effective methods of glycaemic control through exercise.

Materials and Methods

Participants

This research involved the voluntary participation of seven healthy male college students between 18 and 25. Before implementation, the research plan was submitted for review and approval by Donghua University's Human Experiment Ethics Committee, and an IRB number 2010003 was assigned. The recruitment of subjects will not commence until later, at which point all participants will be asked to complete a consent form and health questionnaire. Additionally, each participant takes a comprehensive physical examination and questionnaire to ensure their suitability for the study.

Material

Blood Glucose Machine

This research employs the Roche-Active Blood Glucose Machine (GC model) from Germany to detect blood glucose levels. The machine's cutting-edge patent features a gentle and painless method, which utilizes glucose dehydrogenase to place the collected blood on the test paper and then analyse it in the blood glucose machine. Only 1-2 μL (0.001~ 0.002 CC) of blood is needed for collection, and the measurable range is between 10 and 600 mg/dl. The blood collection site can be located on the side of the fingertips or other appropriate areas.

Cycling exercise machine

The cycling exercise test utilizes relative intensity to determine exercise intensity, which is adjusted to the absolute exercise intensity of the LODE ERGOMETRY MANAGER bicycle from Nichilong Instrument Company.

Cardiopulmonary function

To assess cardiopulmonary function, the test method for oxygen uptake measures the efficiency of oxygen absorption and utilization. The Vmax gas analysis software collects and analyses gas, including VO2, VO2/kg, VCO2, and RQ.

Heart rate

To monitor heart rate, this study employs four inductions of ECG100C and attaches conductive electrodes next to the left and right clavicle and under the left and right ribs. The chest inductions are then placed on the subjects.

α-glucosidase inhibitors -Nangapiry(α-GI-N)

This study delves into α-GI-N, primarily used to prevent disaccharides from converting into monosaccharides, thereby slowing the increase in blood sugar levels [15]. The α-GI-N used in this study was the product "Nangapiry Ypacarai" standardized by Professor Yasutoku Momose, Faculty of Pharmacy, Toho University. (October 2005). The extract, obtained from Nangapiry dry leaves and processed using Amberlite IR-120 ion exchange resin column for extraction [12,14], has an inhibition rate on maltose and sucrose, as well as an IC50 of maltose-inhibiting effect.

Intervention

All participants take an exercise intensity test and four sets of formal tests scheduled one week apart. It is recommended that participants abstain from alcohol and caffeine 24 hours before each session. A preliminary exercise test was conducted two weeks before the official experiment test, identified by PWC170, to determine individual load differences. The exercise intensity was established at 60% of the maximum heart rate (MHR).

Every participant will take part in four separate experimental groups labelled A, B, C, and D. Here are the details of each group's activities:

• Group A(Control) will undergo an Oral Sucrose Tolerance Test (OSTT).

• Group B (α-GI-N) will take an OSTT test 10 minutes after ingesting maltose and α-GI-N.

• Group C (Exercise)will perform a 60% MHR bicycle test at the 30-minute mark during the OSTT test.

• Group D (α-GI-N+ Exercise) will take an OSTT test 10 minutes after ingesting maltose and α-GI-N, followed by a 60% MHR bicycle test 30 minutes later.

Before the examination, participants were instructed to abstain from eating for 8 hours. Following this, sucrose was orally administered at a rate of 1.5g/kg, and they were permitted to drink water at their discretion. The research was conducted in the morning. In Groups B and D, α-GI-N (2.5mg/kg) was administered 10 minutes before maltose consumption.

Measurement

Prior to the morning testing, height and weight anthropometric measurements were taken. Participants were required to sit for at least five minutes before administering two fasting blood samples. Five blood collections were performed before and after the experiment, including fasting, 30, 60, 90, and 120 minutes. Furthermore, the exercise test group's data collected included blood sugar, heartbeat, oxygen uptake, and respiratory quotient, all of which will be closely monitored. Finally, statistical analysis will be conducted.

Statistical Analysis

Use Two Way ANOVA to detect the differences between groups A, B, C, and D, and use Duncan's Method to compare time and groups. The comparison results of Group C and Group D exercise physiological responses were subjected to the T-test, and the significance level was $\alpha < 0.05$.

Results

Basic information

The seven subjects had an average age of 19.71±0.29 years, a height of 176.43±2.73 cm, a weight of 78.43±4.38 Kg, and a BMI of 23.96±0.76 Kg/M2.

Blood glucose test

Group A (Control)

Individuals in Group A(Control) had a fasting blood glucose level of 91.71 ± 0.84 mg/dl. After consuming maltose, their blood glucose levels were measured at 191.71 ± 14.21 mg/dl at 30 minutes, 166.57 ± 14.66 mg/dl at 60 minutes, 132.43 ± 5.79 mg/dl at 90 minutes, and 122.00 ± 6.13 mg/dl at 120 minutes (Table 1).

Group B (α-GI-N)

The individuals in Group B (α-GI-N) underwent an oral sucrose tolerance test ten minutes after consuming Nangapiry(2.5mg/kg), followed by maltose intake (1.5 g/kg). Before the test, their fasting blood glucose was recorded at 91.00 ± 2.44 mg/dl. The results showed that after 30 minutes, the blood glucose level increased to 148.00 ± 6.83 mg/dl. After 60 minutes, it was measured at 131.43 ± 9.01 mg/dl; after 90 minutes, it was 121.14 ± 5.39 mg/dl. Finally, after 120 minutes, it was 103.14 ± 8.58 mg/dl (Table 1).

Group C (Exercise)

Before consuming maltose (1.5 g/kg), the fasting blood glucose levels were 96.71 ± 2.1 mg/dl. After consuming maltose, the levels increased to 191.14 ± 12.03 mg/dl at the 30-minute mark, then decreased to 101.43 ± 7.19 mg/dl after 60 minutes and increased again to 129.71 ± 5.14 after 90 minutes. Finally, at the 120-minute mark, the levels were 118.57 ± 9.12 mg/dl (Table 1).

Group D (α-GI-N+ Exercise)

The fasting blood glucose concentration of subjects in this group was 90.00 ± 2.37 mg/dl, with levels of 153.25 ± 10.48 mg/dl at 30 minutes after taking maltose (1.5 g/kg), 101.88 ± 5.89 mg/dl at 60 minutes, 126.50 ± 5.55 mg/dl at 90 minutes, and 115.50 ± 9.6 mg/dl at 120 minutes (Table 1).

	0 minutes	30 minutes	60 minutes	90 minutes	120 minutes
Group A (Control)	91.7±2.2	191.7±37.6	166.6±38.8	132.4±15.3	122.0±16.2
Group B (α-GI-N)	91.0±6.4	148.0±18.1 +++	131.4±23.9 ++	121.1±14.3	103.1±22.7
Group C (Exercise)	96.7±5.6	191.1±31.8 ###	101.4±19.0 +++, ###	129.7±13.6	118.6±24.1
Group D (α-GI-N+ Exercise)	91.3±6.6	157.4±32.9 ++	103.6±13.8 +++, ###	127.6±16.4	114.4±21.5

Observations were made on changes in blood glucose levels of four groups over time. Significant levels were reached at both the 30-minute and 60-minute marks. + We were comparing Group A (Control) with Group B (α-GI-N), Group C (Exercise), and Group D (α-GI-N+ Exercise) at 30 and 60 minutes. Significant level. P<0.05. Significant differences were found between Group A(Control) and Group B (α-GI-N) at 30 and 60 minutes, between Group A(Control) and Group C (Exercise)at 60 minutes, between Group A(Control) and Group D (α-GI-N+ Exercise) at 30 and 60 minutes. + α<.05 ++ α<.01 +++ α<.001. # We were comparing Group B (α-GI-N) with Group C (Exercise) and Group D (α-GI-N+ Exercise) at 30 and 60 minutes. Significant level. P<0.05. Significant differences were found between Group B (α-GI-N) and Group C (Exercise) at 30 and 60 minutes and between Group B (α-GI-N) and Group D (α-GI-N+ Exercise) at 60 minutes. α<.05 ## α<.01### α<.001

Table 1: The table provides information on the mean and standard deviation for each group, analyzed four groups using Two-Way ANOVA (Duncan's Method).

A Two-Way ANOVA (Duncan's Method) was used to compare four groups over time

The study analyzed four groups using Two-Way ANOVA (Duncan's Method). The findings indicated a significant difference between Group A (Control) and Group B (α-GI-N), Group C (Exercise), and Group D (α-GI-N+ Exercise) at P<0.05. Specifically, significant differences were observed between Group A (Control) and Group B (α-GI-N) at 30 and 60 minutes (Figure 1), between Group A(Control) and Group C (Exercise) at 60 minutes (Figure 2), between Group A (Control) and Group D (α-GI-N+ Exercise) at 30 and 60 minutes (Figure 3), and Group B (α-GI-N), and Group C (Exercise)at 30 and 60 minutes (Figure 4), between Group B (α-GI-N) and Group D (α-GI-N+ Exercise) at 60 minutes (Figure 5), and between Group C (Exercise) and Group D (α-GI-N+ Exercise) at 30 minutes (Table 1).

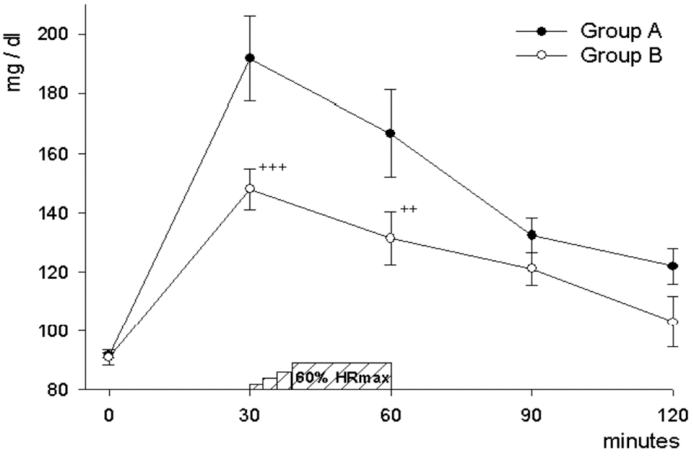

Figure 1: Changes in blood glucose levels over time were compared between Group A(Control) and Group B (α-GI-N) Significant differences were observed at 30 and 60 minutes.

+ α<.05 ++ α<.01 +++ α<.001

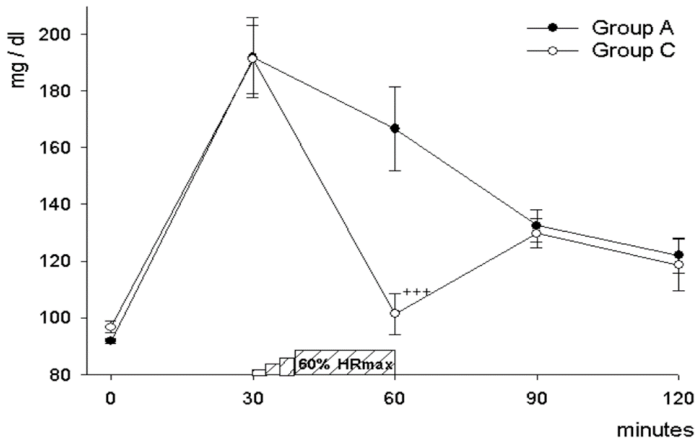

Figure 2: Changes in blood glucose values over time were observed in the Group A(Control) and Group C (Exercise) group. The significant level was reached after 30 minutes of exercise.

+ α<.05 ++ α<.01 +++ α<.001

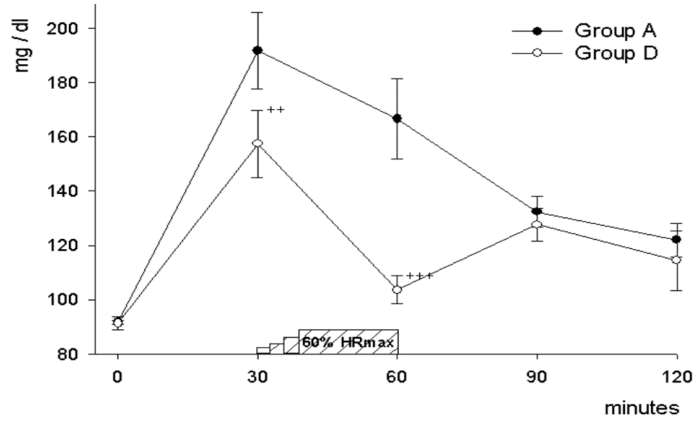

Figure 3: Changes in blood glucose levels over time in groups Group A (Control) and Group D (α-GI-N + Exercise) Significant levels were reached at 30 minutes and 60 minutes.

+ α<.05 ++ α<.01+++ α<.001

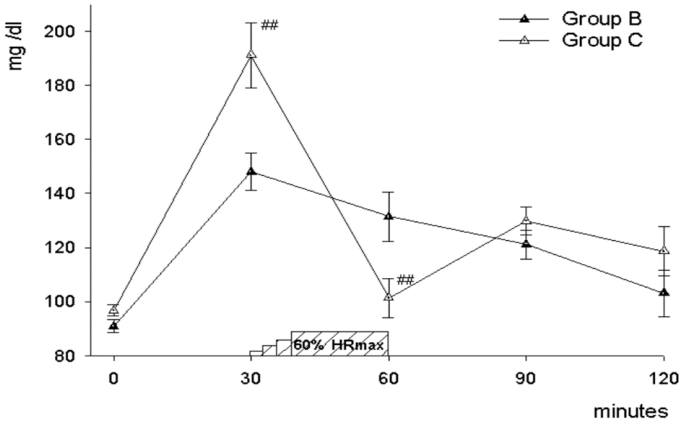

Figure 4: Changes in blood glucose levels over time in groups Group A (Control) and Group B (α-GI-N) Significant levels were reached at 30 minutes and 60 minutes.

α<.05 ## α<.01 ### α<.001

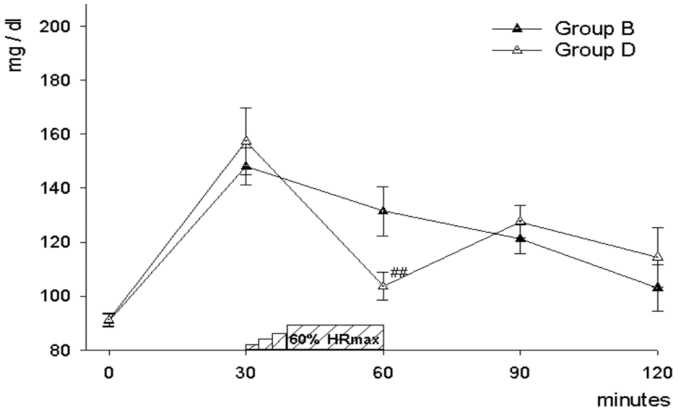

Figure 5: Changes in blood glucose levels over time in groups Group B (α-GI-N) and Group D (α-GI-N + Exercise) Significant levels were reached at 30 minutes and 60 minutes.

α<.05 ## α<.01 ### α<.001

Comparative results of exercise performance between Group C (Exercise)and Group D (α-GI-N+ Exercise)

Group C (Exercise) and α Group D (α-GI-N+ Exercise) showed no significant change in the HR, VO2, VO2/KG/VCO2, and RQ during exercise after the T-test. The values for both groups remained consistent, as shown in Table 2.

	HR	**$\dot{V}O_2$**	**$\dot{V}O_2$ /KG**	**$\dot{V}CO_2$**	**RQ**
Group C (Exercise)	126.7 ± 3.4 (63.6% ± 5.5%)	1.26 ±0.27	16.41±4.85	1.16±0.24	0.93±0.05
Group D (α-GI-N+ Exercise)	127.5 ±11.0 (63.1%±1.7%)	1.37±0.22	17.19±3.66	1.28±0.23	0.93±0.05
T-Test P	0.79	0.51	0.73	0.51	0.70
* The table provides the Exercise Group and α-GI-N+ Exercise Group after T-test data					

Table 2: The mean, standard deviation, and significance of each indicator for Group C (Exercise) and Group D (α-GI-N+ Exercise).

Discussion

In many cases, chronic diseases are closely related to lifestyle habits, especially in patients with chronic diseases. In many cases, especially in patients with chronic diseases, these diseases are often closely related to lifestyle habits. These patients require continued medical treatment, but the disease often cannot be cured entirely under medical treatment [5]. The patient's condition must be improved by changing lifestyle habits and significantly increasing physical activity and nutritional control. There is a potential for danger due to the interaction of medication, diet, and physical activity. This study aims to understand the interaction between alpha-glucosidase inhibitor drugs and exercise and to find a safe and effective way to control blood sugar.

The role of exercise

PA and exercise can be as effective as medications in managing health, and like medications, they should be prescribed with dosage considerations in mind [16]. A notable difference was observed between the Group A(Control) and Group C (Exercise), and Group A(Control) and Group D (α-GI-N+ Exercise) regarding the reduction in blood sugar levels 30 minutes after exercising (Figure 2, 3). Waiting 30 minutes after eating before engaging in physical activity may be the optimal time to regulate blood sugar response [17]. Previous research has indicated that high-intensity exercise (80% $\dot{V}O_2$max-Max % $\dot{V}O_2$max) can trigger excessive epinephrine stimulation, which leads to a higher rate of glucose regeneration after exercise than utilization. This can result in post-exercise hyperglycaemia and is detrimental to blood sugar control. At 60% $\dot{V}O_2$ max, the benefits are at their highest [18]. The same metabolic situation occurs during exercise intensity of 60% HRmax (Table 2). Therefore, engaging in physical activity at 60% HRmax 30 minutes after eating can benefit blood sugar regulation.

However, after exercise, blood glucose dropped to the resting normal blood glucose range, no hypoglycaemia was observed, and blood glucose levels increased 30 minutes after exercise (Figure 2, 3). Studies have observed that blood glucose transport activity increases with strenuous exercise, and gluconeogenesis may still be activated for a long-time during recovery. The reduced use of glycogen after exercise causes glucose production to exceed demand, resulting in at least an increase in blood glucose concentration [19, 20]. In addition, studies have pointed out that glycogen resynthesis increases rapidly after exercise, which occurs independently of insulin concentration and lasts 30-60 minutes after exercise [21, 22].

According to Hirsch et al., the secretion of adrenaline can prevent hypoglycaemia during exercise by preventing changes in glucose levels [23]. This suggests that strenuous exercise can affect the body's metabolic processes through various factors, including increased glucose transport activity, gluconeogenesis activation, and hepatic glucose resynthesis rate increase. Such changes may lead to fluctuations in blood sugar levels, necessitating counterregulatory factors like epinephrine to maintain stability. Although a rise in blood sugar after a meal is average, the continued presence of high blood sugar can cause glycation of substances in the blood, such as red and white blood cells and proteins. The physical deterioration of diabetic patients is triggered by fluctuations in blood sugar levels, making it crucial to swiftly return to normal levels after meals and extend the quiet time between meals to maintain stability. To this end, exercise can play a crucial role, mainly if done for 30-60 minutes following

a meal. While exercising before meals can lower blood sugar levels, eating afterwards may cause them to spike again, rendering exercise therapy ineffective.

Interactions between exercise and α-glucosidase inhibitors-Nangapiry (α-GI-N)

Taking α-GI-N can effectively inhibit the digestion and absorption of blood sugar after meals and prevent blood sugar levels from rising. Engaging in moderate-intensity exercise training under these conditions will not lead to a dangerous hypoglycaemia situation.

The findings suggest that following a moderate-intensity exercise regimen while taking α-GI-N can swiftly restore normal blood sugar levels and avoid any adverse effects of hypoglycaemia, conversely, Group D (α-GI-N+ Exercise) is better than Group B (α-GI-N) (Figure 5). The exercise test group's heartbeat, oxygen uptake, and respiratory quotient were also monitored, revealing significant differences in exercise intensity between the two groups (Table 2). The study indicates that α-GI-N has no impact on exercise capacity and does not cause any hypoglycaemia. Furthermore, research suggests that relying solely on exercise to manage poorly controlled patients may be ineffective [24]. As a result, we recommend α-GI-N in combination with exercise as a safe and efficient approach to managing blood sugar levels. It is worth noting that fulfilling the requirements of the 2018 Physical Activity Guidelines for Americans is challenging for the average individual in practical settings [25]. Patients with diabetes may find engaging in enjoyable exercise three times a week challenging. However, chronic hyperglycemia, or persistent high blood sugar levels, poses one of the most significant issues for these patients. This condition can cause irreversible cell damage or glucose toxicity [26]. To counteract this, it is essential to rapidly restore normal blood sugar levels and increase the average blood glucose time. A combination of α-GI-N medication, postprandial exercise, and a healthy diet can effectively reduce the symptoms of chronic hyperglycemia.

Conclusions

The global population is aging, and the diseases of these aging people are related to their living habits. Implementing a healthy diet, physical activity, and appropriate medication is equally important. Despite the benefits of exercise on glycemic control, optimal exercise recommendations still need to be made more apparent when considering the timing of exercise versus medication, diet, or other behaviours.

This study combined the exercise test of taking α-GI-N 2.5 mg/kg and 60% HRmax intensity to understand that 30 minutes after eating is the best time to exercise, and it is also a safe and effective method for people who have difficulty controlling blood sugar. This may be an effective management strategy in humans and raises the idea of exercise alongside pharmacotherapy.

Author Contributions: Conceptualization: HC, FC. Methodology: HC. Validation: HC and FC. Formal analysis: HC, FC, and PL. Investigation: HC, PL, TC, and FC. Data curation: HC, PL,TC, and FC. Writing – Original Draft: HC. Writing – Review & Editing: HC, KH, IA, FC Visualization: HC. Supervision: AI. Project administration: FC.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: All data presented in the study are available to the editors upon request.

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