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Effects of herbal tea (*Platostoma palustre*) on blood glucose regulation *in vivo*

Hsing-Tan Liu [1, #], Yun-Xuan Chang [2, #], Tzu-Yun Chi [2, #], Ya-Peng Wang [2], Tsung-Han Wu [2], Yen-Jung Lu [2], Pi-Hsin Chen [2], Ya-Ling Cyue [2], Shih-Yi Guo [2], Suz-Ching Ke [2], Tseng-Han Chou [2], Chien-Chao Chiu [2], Ching-Feng Chiu [3], Hsuan-Wen Chiu [4], Wei-Huang Tsai [5], Yu-Hsing Lin [6], Chia-Chi Chen [2, #] and Shao-Wen Hung [2, 7, *]

[1] *Yueta Agricultural Biotechnology Inc., Hsinchu 306, Taiwan.*
[2] *Division of Animal Industry, Animal Technology Research Center, Agricultural Technology Research Institute, Hsinchu 300, Taiwan.*
[3] *Graduate Institute of Metabolism and Obesity Sciences, College of Nutrition, Taipei Medical University, Taipei 110, Taiwan.*
[4] *Department of Biotechnology and Bioindustry Sciences, College of Bioscience and Biotechnology, National Cheng Kung University, Tainan 701, Taiwan.*
[5] *Department of Science and Technology, Council of Agriculture, Executive Yuan, Taipei 100, Taiwan.*
[6] *Department of Pet Healthcare, Yuanpei University of Medical Technology, Xiangshan, Hsinchu 300, Taiwan.*
[7] *Department of Nursing, Yuanpei University of Medical Technology, Hsinchu 300, Taiwan.*
[#] *Contributed equally to this work.*

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Abstract

Platostoma palustre jelly is a traditional food. *Platostoma palustre* has been used as folk medicine and is effective against heat-shock, hypertension and diabetes. Therefore, the aim of *in vivo* study was to determine the effects of herbal tea (*Platostoma palustre*) on blood glucose regulation. The commercial herbal tea (*Platostoma palustre*) was kindly provided by Yueta Agricultural Biotechnology Inc. Adult male 18 Institute of Cancer Research (ICR) mice [8 weeks old; body weight (BW) between 31-33 g] with specific pathogen-free conditions were used for this study. All ICR mice were divided respectively the normal control group (n = 6), the negative control group (n = 6), and the herbal tea group (n = 6). The ICR mice (the negative control group and the herbal tea group) were intraperitoneally injected with streptozotocin (65 mg/kg BW) and nicotinamide (230 mg/kg BW) for inducing the symptoms of hyperglycemia. In the herbal tea group, the herbal tea (10 mL/kg BW) was administrated to ICR mice by gavage. To monitor the blood glucose levels in ICR mice, blood was obtained from the tail of ICR mice, and blood glucose levels were determined using the external glucometer. Blood glucose measurements were conducted once in ICR mice before the experiment and were detected once per month after the experiment. Additionally, the change of ICR mice' BW, the blood glucose of ICR mice, and the observation of ICR mice' behavior were monitored and detected during the experiment. The results of this experiment showed

- Weight change: the weight gain of the negative control group and the herbal tea group were significantly lower than those of the normal control group and there was no significant difference between the negative control group and the herbal tea group.
- Fasting blood glucose and postprandial blood glucose: the fasting blood glucose of the negative control group was significantly higher than that of the normal control group, while the herbal tea group had a tendency to lower the fasting blood glucose, but there was no significant difference compared with the negative control group. The postprandial blood glucose level results showed that the negative control group was significantly higher than the normal control group. The postprandial blood glucose level of the herbal tea group was between the normal control group and the negative control group at the 4th week administration with the herbal tea. At

* Corresponding author: Shao-Wen Hung

the 8th week administration with the herbal tea, there was a significant difference compared with the negative control group.

- Oral glucose tolerance test (OGTT): 4 to 12 weeks after hyperglycemia was induced, the blood glucose levels of the negative control group at each OGTT test point were significantly higher than those of the normal control group.

The blood glucose level at the test point tended to decrease, but there was no significant difference from the negative control group. By calculating the area under the OGTT curve, it was found that the area under the curve of the negative control group was significantly higher than that of the normal control group, while the results of the herbal tea group at the 8th and 12th weeks were significantly lower than those of the negative control group. Taken all results together, the hyperglycemia was successfully induced in the experimental ICR mice. After administrating with the herbal tea, the fasting blood glucose level of the ICR mice tended to improve. In addition, a significant improvement was seen in the results of postprandial blood sugar and oral glucose tolerance test effectiveness. Therefore, based on the results of this experiment, it is speculated that drinking the herbal tea for 3 months has considerable potential for blood glucose regulation, which can be used as the basis for the development of related products of the herbal tea in the future.

Keywords: Blood glucose; Herbal tea; *In vivo*; *Platostoma palustre*; Regulation

1. Introduction

Diabetes is one of the top ten causes of death among Taiwanese. Nearly, 10,000 people die of diabetes every year in Taiwan. According to the statistics, there are more than 2 million diabetic patients in the country, and the number continues to increase at a rate of 25,000 cases per year. Diabetes and its related complications affect Taiwanese's health and cannot be underestimated, and the medical burden is quite huge. Diabetes can be divided into type 1 diabetes (destroyed islet cells, resulting in insulin deficiency), type 2 diabetes (insulin resistance, and combined relative insulin deficiency), other types of diabetes, gestational diabetes, etc. Its diagnostic criteria include the following 4 items [(1) Glycosylated hemoglobin (HbA1c)≧6.5%; (2) Fasting plasma glucose ≧126 mg/dL; (3) Plasma blood glucose ≧200 mg/dL in the second hour of oral glucose tolerance test (OGTT); (4) Typical symptoms of hyperglycemia (eating, drinking, polyuria and weight loss) and random plasma glucose ≧200 mg/dL], as long as one of the items is met in non-pregnancy conditions, it can be diagnosed as diabetes (the first three items need to be verified more than 2 times). Diabetes is a complex chronic disease. Diabetes lovers should receive regular treatment and follow-up, and learn to implement a good lifestyle and manage their own blood sugar. This is the only way to delay and avoid complications [1-3].

When the blood glucose is high, the body is usually asymptomatic. Usually, it is only known by means of blood glucose testing, or when there are symptoms of three excesses and one deficiency (eating too much, drinking too much, urinating too much, and losing weight), you will doubt whether you have diabetes. Diabetic patients are also less prone to symptoms of physical discomfort when their blood glucose is not well controlled, because of this makes it easy for diabetics to ignore blood glucose control [1-2].

Platostoma palustre is an annual plant that is mainly distributed in tropical and subtropical regions, including Taiwan, Indonesia, Vietnam, southern China, and Burma [4-7]. The related food with *Platostoma palustre* as tea, herbal jelly, and sweet soup with herbal jelly are popular during the summer. Additionally, the heated herbal jelly with *Platostoma palustre* is admired by many Taiwanese in winter. *Platostoma palustre* has been used as folk medicine. *Platostoma palustre* has been verified that possessed many functional compounds such as polysaccharides (gum) with a unique aroma and texture, sterol compounds, stigmasterol, α-sitosterol, tripterpene compounds, oleanolic acid, volatile compounds (caryophyllene oxide, α-caryophyllene, eugenol, benzene acetaldehyde, and 2,3-butanedione etc), essential oil (n-hexadecanoic acid, linoleic acid, and linolenic acid), volatile oil (chavibetol, n-hexadecanoic acid, and α-cadinol), and ursolic acid [4-8]. Therefore, theses functional compounds of *Platostoma palustre* have indicated that many biological effects is effective against and attenuating the metabolic syndrome, heat-shock, hypertension, diabetes, liver disease, muscle and/or joint pains, hyperglycemia, inflammation, oxidant activity, free radical scavenging effects, acute and chronic hepatitis, and caner growth [9-12]. Therefore, the objective of this study was to evaluate the *in vivo* effects of the commercial herbal tea (*Platostoma palustre* water extracts) on the regulation of blood glucose.

2. Material and methods

2.1. Chemicals and Reagents

Phosphate-buffered saline (PBS; Sigma-Aldrich, Cat. No. P3813), saline (Taiwan Biotech Co., LTD, Cat. No. 100-120-1101), and Zoletil 50 (Virbac, Carros, France) were applied in this experiment.

2.2. Source of Herbal Tea

The herbal tea (*Platostoma palustre*) were kindly provided by Yueta Agricultural Biotechnology Inc. (Guanxi, Hsinchu, Taiwan). Yueta® herbal tea has been passed the SGS pesticide test, and is cooked through high-temperature cooking. The operation process of machinery and equipment is consistent, and it is sterilized by high-temperature sterilizing kettle, without adding preservatives.

2.3. Experimental Animals and Experimental Design

Adult male 18 ICR mice [8 weeks old; body weight (BW) between 31-33 g] with specific pathogen-free conditions were used for this study, were purchased from BioLASCO Taiwan Co., Ltd. (Yilan, Taiwan). Before the experiment, all mice were housed in the animal room for 7 days. The environment was maintained room temperature (24-27°C) and 60%-70% humidity with a photoperiod of 12-hr light/12-hr dark cycle. The study will begin after a week acclimation. The Institutional Animal Care and Use Committee (IACUC) of Agricultural Technology Research Institute inspected all animal experiments and this study comply with the guidelines of protocol IACUC 111045 approved by the IACUC ethics committee. The male 18 ICR mice were divided respectively the normal control group (n = 6), the negative control group (n = 6), and the herbal tea group (n = 6). In the herbal tea group, the herbal tea (10 mL/kg BW) was administrated to ICR mice by gavage. All ICR mice were fed with standard laboratory diet (No. 5053, LabDiet®; PMI Nutrition International, St. Louis, MO, USA) ad libitum during the experimental period. The change of ICR mice' BW, the blood glucose of ICR mice, and the observation of ICR mice' behaviors were monitored and detected during the experiment (Fig. 1).

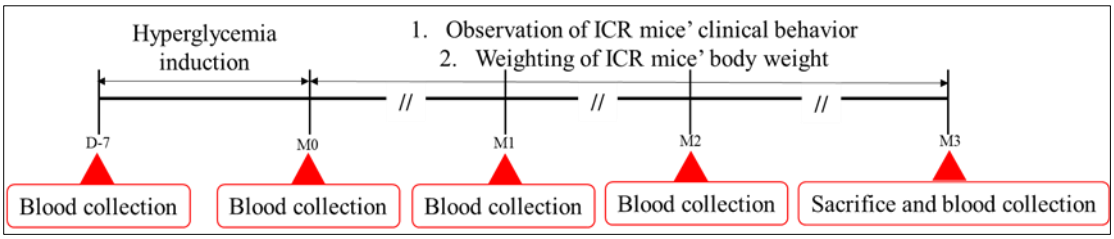

Figure 1 Experimental designs and the change of ICR mice' BW, the blood glucose of ICR mice, and the observation of ICR mice' behaviors were monitored and detected during the experiment

2.4. Induction of Hyperglycemia Animal Model

The ICR mice were intraperitoneally injected with streptozotocin (65 mg/kg BW) and nicotinamide (230 mg/kg BW) for inducing the symptoms of hyperglycemia.

2.5. Blood Glucose Detection in ICR Mice

To monitor the blood glucose levels in ICR mice, blood was obtained from the tail of ICR mice, and blood glucose levels as the levels of fasting blood glucose and postprandial blood glucose and oral glucose tolerance test (OGTT) were determined using the external glucometer. Blood glucose measurements were conducted once in ICR mice before the experiment and were detected once per month after the experiment.

2.6. OGTT

Mice were fast for 16 hours before starting OGTT. The 200 μL heparinized blood was collected from the tail vein of mice and the 0-minute blood glucose levels of mice were measured. Later, the glucose solution (1 g/10 mL/kg BW) was given by gavage to mice. At 15, 30, 60, 90, 120, and 180 minutes after glucose administration, blood glucose was measured and the results are represented by the area under the curve, cut into several trapezoids according to each blood collection time point, and then calculated and summed up the areas of the trapezoids. The unit was expressed in g × min × dL.

2.7. Statistical Analysis

The data were expressed as mean ± SD (standard deviation). All comparisons were made by one-way ANOVA and all significant differences are reported at $^{*/\#}p < 0.05$, $^{**/\#\#}p < 0.01$, and $^{***/\#\#\#}p < 0.001$.

3. Results

In this experiment, ICR mice were injected intraperitoneally with streptozotocin (65 mg/kg BW) and nicotinamide (230 mg/kg BW) to induce hyperglycemia in the negative control group and herbal tea group mice. After the mice were induced with hyperglycemia, the mice in the negative control group were given drinking water by gavage every day, and the mice in the herbal tea group were given the herbal tea (administration dose 10 mL/kg BW) by gavage every day. Fasting blood glucose, postprandial blood glucose and oral glucose tolerance test were performed before hyperglycemia induction (Week 0, W0) and after hyperglycemia induction (W4, W8, and W12), and weighed weekly.

3.1. BW Change of Mice in Each Group during the Experiment

The results were shown that the average BW of the mice in the negative control group (Negative control) and the herbal tea group (Herbal tea) was significantly lower than that of the mice in the normal control group (Normal control) during W6-W12 hyperglycemia induction. There was no significant difference between the negative group and the herbal tea group (Fig. 2).

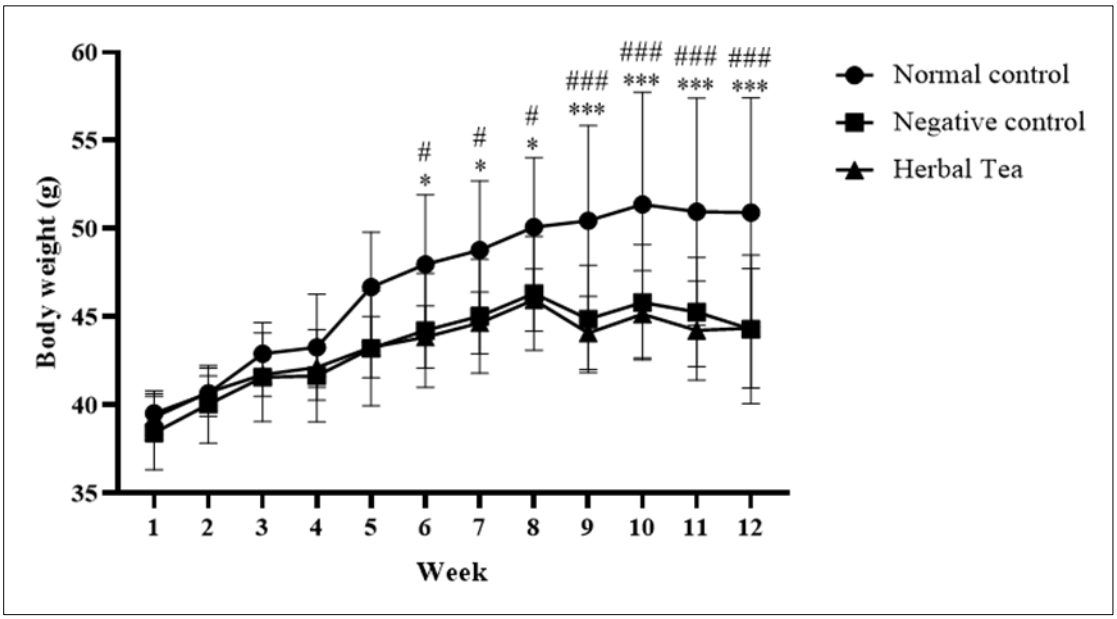

Figure 2 BW change of mice in each group during the experiment. Data are presented as Mean ± SD. * indicates the normal control group vs. the negative control group, # indicates the normal control group vs. the herbal tea group. $^{*/\#}p < 0.05$; $^{***/\#\#\#}p < 0.001$

3.2. Detection of the Levels of Fasting Blood Glucose and Postprandial Blood Glucose in Mice:

To compare the fasting blood glucose level and postprandial blood glucose level at each experimental point in the normal control group, the negative control group and the herbal tea group. The results were shown that (1) the level of fasting blood glucose: the fasting blood glucose level of mice in the negative control group was significantly higher than that of mice in the normal control group at the 8th and 12th weeks-experiment. The fasting blood glucose level of mice in the herbal tea group was between the negative control group and the normal control group and there were no significant differences between groups (the herbal tea group and the negative control group) (Fig. 3A). (2) the level of postprandial blood glucose: the fasting blood glucose level of mice in the negative control group was significantly higher than that of the normal control group at the 4th week-, 8th week- and 12th week-experiment. At the 4th and 8th weeks-experiment, the fasting blood glucose levels of mice in the herbal tea group were significantly lower than that of the negative control group, and had no significant difference with the normal control group at the 12th weeks-experiment (Fig. 3B).

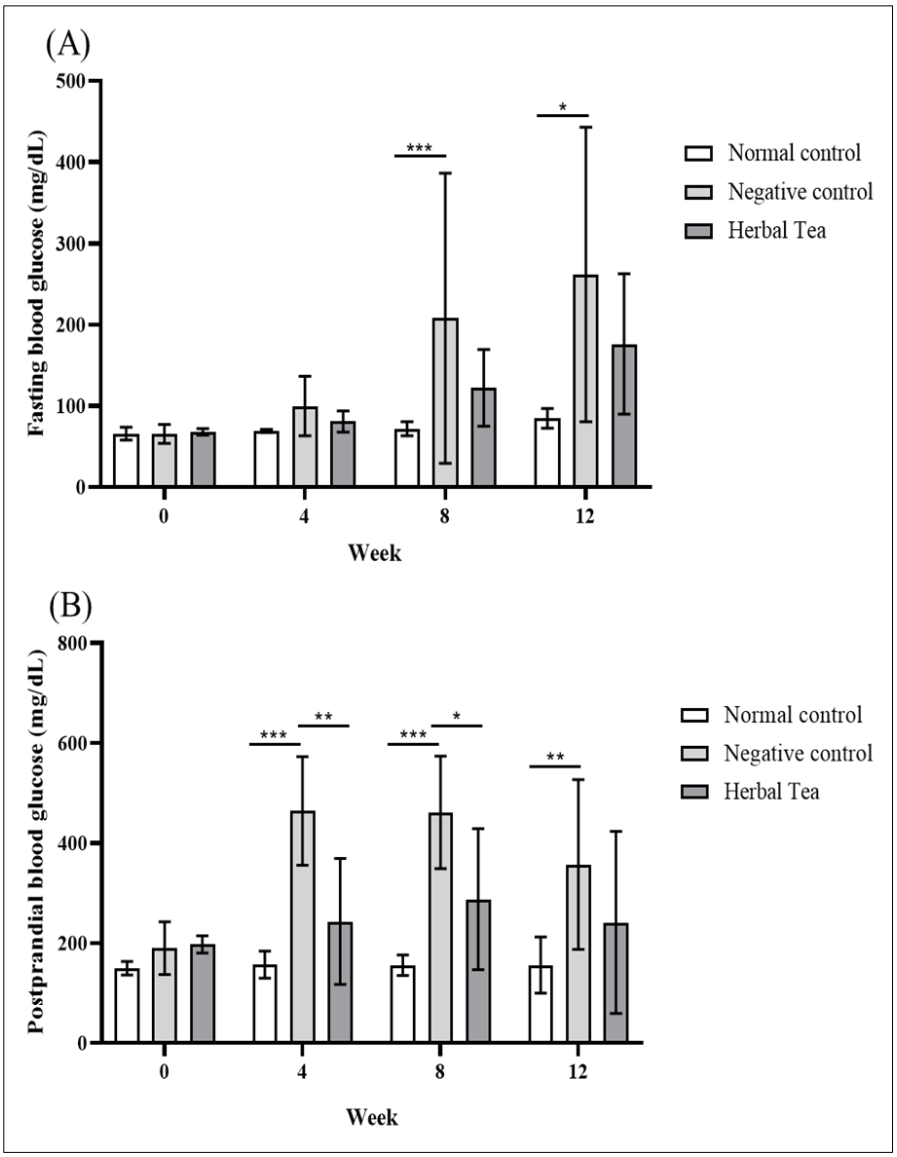

Figure 3 Detection of the levels of fasting blood glucose and postprandial blood glucose in mice. (A) The level of fasting blood glucose at each experimental point. (B) The level of postprandial blood glucose at each experimental point. Data were presented as mean ± SD. $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$

3.3. OGTT

The results of OGTT at each experimental point were compared among the normal control group, the negative control group and the herbal tea group. It can be seen from the results that (1) the changes in blood glucose in OGTT: At W0 experiment, there was no significant difference in blood glucose at each experimental point in each group. At W4 experiment (15 minutes-180 minutes), the blood glucose of mice in the negative control was significantly higher than that in the normal control group and at W4 experiment (30 minutes-180 minutes), the blood glucose of mice in the herbal tea group was also significantly higher than that in the normal control group. There were no significant differences between the negative control group and the herbal tea group at W4 experiment.

At W8 experiment, the blood sugar level of the negative control group was significantly higher than that of the normal control group from the 15th minute to the 180th minute, while the blood sugar level of mice in the herbal tea group was between the negative control group and the normal control group, and there was no significant difference between the herbal tea group and the normal control group.

At W12 experiment, the blood sugar level of mice in the negative control group was significantly higher than that of the normal control group from the 30th minute to the 120th minute, while the blood sugar level of mice in the herbal tea group was between the negative control group and the normal control group, and there was no significant difference

between the groups (Fig. 4A). (2) The area under the curve of OGTT: at the 4th week, the 8th week, and the 12th week experiment, the area under the curve of OGTT of mice in the negative control group was significantly higher than that of the normal control group. The area under the curve of OGTT of mice in the herbal tea group was significantly lower than the negative control group at the 8th and 12th week experiment, and there was no significant difference between the normal control group and the herbal tea group during the experiment (W0, W4, W8, and W12) (Fig. 4B).

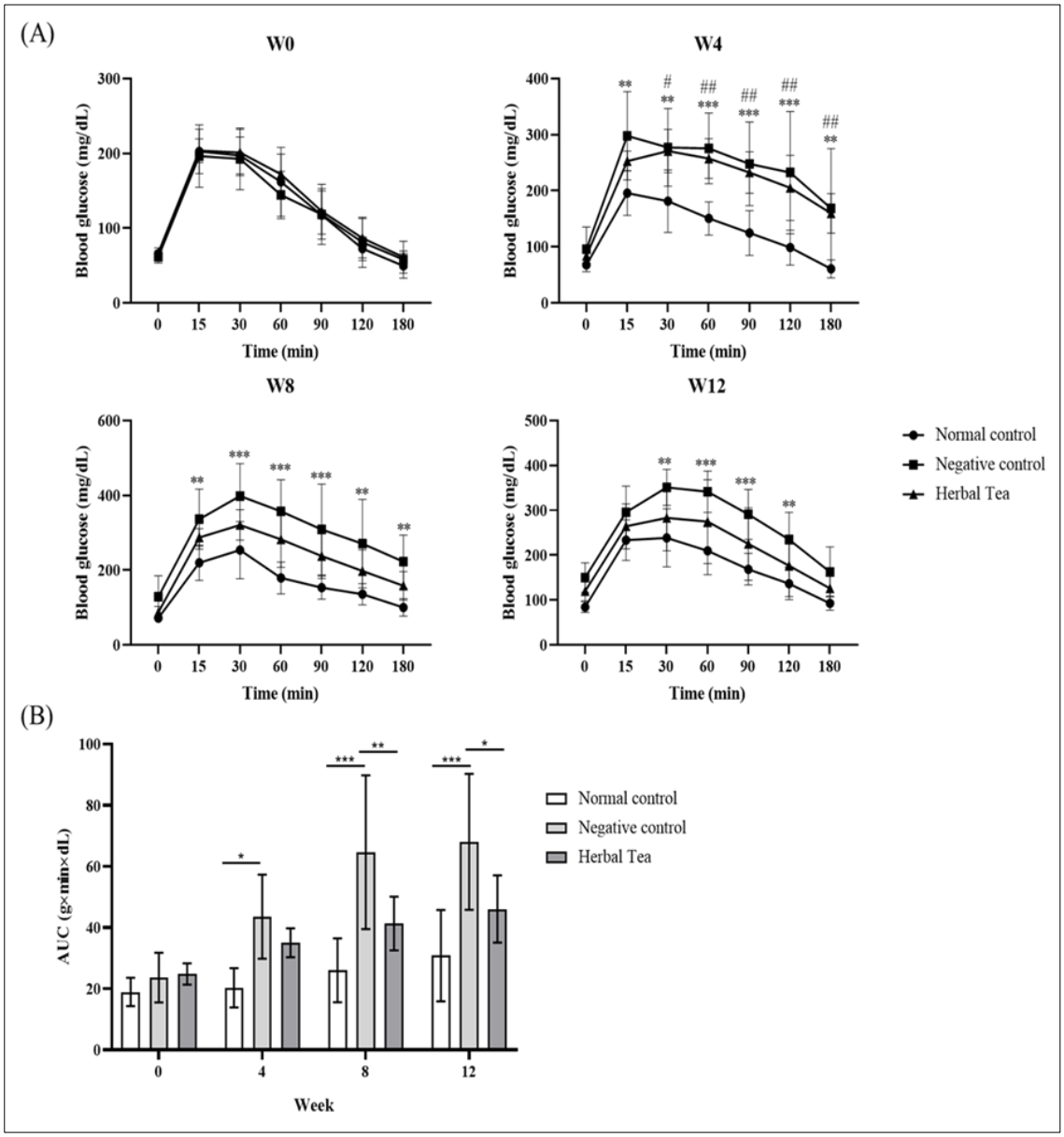

Figure 4 Changes in blood glucose and the area under the curve of an oral glucose tolerance test. (A) Blood glucose changes of OGTT at each experimental point, (B) the area under the curve of OGTT at each experimental point. Data were presented as mean ± SD. * indicates the normal control group vs. the negative control group, # indicates the normal control group vs. the herbal tea group. $^{*/\#}p < 0.05$; $^{**/\#\#}p < 0.01$; $^{***}p < 0.001$

4. Discussion

Why control of blood glucose is very important myself and why so much emphasis and attention to diabetes treatment in the recent years? In fact, the diabetes itself is not terrible, but high blood glucose will destroy the endothelial cells of all blood vessels in the body, and then destroy the function of organs, so it will cause many acute and chronic complications. These complications are often irreversible and progressive, culminating in complete loss of organ function and death. Therefore, it is the importance of blood glucose control to avoid complications as ketoacidosis, hyperglycemic, hyperosmolar coma, eye diseases (cataract, glaucoma, retinopathy, etc.), kidney diseases (edema,

proteinuria, increased blood pressure, and even kidney failure can cause uremia and require life-long dialysis), cardiovascular diseases (80% of diabetic patients have coronary artery problems), neuropathy (motor, sensory, and autonomic neuropathy), foot lesions (the loss of the sensation of vibration, temperature, and pain, and finally completely lose the sensation. If the bacterial infection occurred and finally leads to ulcers, gangrene, and wounds that are difficult to heal, resulting in the tragedy of amputation) [1-3, 13-16].

Previously, the effect of different ethanolic concentrations on antioxidant properties and cytoprotective activities of *Platostoma palustre* has been verified. The antioxidant activities of *Mesona procumbens* ethanolic extracts which displayed variable antioxidant levels. The 60% *Mesona procumbens* ethanolic extracts exhibited higher antioxidant activities that possessed a protective capability for the biological membrane system to prevent and treat oxidative stress-related disorders [13-16]. According to our previous results [6-7], 90% *Platostoma palustre* ethanolic extracts were detected the components. The bio-functional indexes and concentrations of 90% *Platostoma palustre* ethanolic extracts were chlorogenic acid (0.30 mg/mg 90% *Platostoma palustre* ethanolic extracts), caffeic acid (0.70 mg/mg 90% *Platostoma palustre* ethanolic extracts), rutin (0.80 mg/mg 90% *Platostoma palustre* ethanolic extracts), astragaloside IV (7.50 mg/mg 90% *Platostoma palustre* ethanolic extracts), and rosmarinic acid (15.90 mg/mg 90% *Platostoma palustre* ethanolic extracts). Among of these bio-functional indexes of 90% *Platostoma palustre* ethanolic extracts, the contents of astragaloside IV and rosmarinic acid were higher than others [16-18]. In this study, the herbal tea was via water extraction and the bio-functional indexes and concentrations of the herbal tea were also detected out. The rosmarinic acid and caffeic acid were the major components in this herbal tea (data not shown).

Additionally, the results of this experiment showed the mouse model with hyperglycemia was successfully established. The weight gains of mice in the negative control group and the herbal tea group were significantly lower than those of the normal control group. The fasting blood glucose of mice in the negative control group was significantly higher than that of the normal control group, while the herbal tea group had a tendency to lower the fasting blood glucose. The postprandial blood glucose level results showed that the herbal tea group was administered with herbal tea for 8 weeks, the postprandial blood glucose level was significant difference with the negative control group. The OGTT results were showed that the blood glucose levels of mice in the negative control group were significantly higher than those of the normal control group. By calculating the area under the OGTT curve, it was found that the area under the curve of the negative control group was significantly higher than that of the normal control group, while the results of the herbal tea group at the 8^{th} and 12^{th} weeks were significantly lower than those of the negative control group.

5. Conclusion

In this experiment, the mice in the negative control group and the herbal tea group were injected intraperitoneally with streptozotocin (65 mg/kg BW) and nicotinamide (230 mg/kg BW) to induce hyperglycemia. During the 12-week experimental period, the negative control group was given drinking water by gavage every day, and the herbal tea group was given herbal tea (administration dose: 10 mL/kg BW) by gavage every day. During the experimental period, the BW was measured once a week, and the fasting blood glucose level, the postprandial blood glucose level, the blood sugar level, and OGTT were measured before hyperglycemia induction (W0) and after hyperglycemia induction (W4, W8, and W12). Taken all results together, the hyperglycemia mice were successfully induced. During the experimental period, the fasting blood sugar level of the mice in the herbal tea group tended to improve. In addition, a significant improvement was found in the results of postprandial blood sugar level and OGTT effectiveness. Therefore, it is speculated that drinking herbal tea for 3 months has considerable potential for the blood sugar regulation, which can be used as the basis for the development of related products of herbal tea in the future.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

The Institutional Animal Care and Use Committee (IACUC) of Agricultural Technology Research Institute inspected all animal experiments and this study comply with the guidelines of protocol IACUC 111045 approved by the IACUC ethics committee.

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