Journal of Biosciences and Medicines, 2025, 13(4), 115-127
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Evaluation of Hypoglycemic Effects of a Variety of Chinese Herbal Medicines Based on Silkworm (*Bombyx mori*) Model

Cheng Tan[1], Huani Chen[1], Rong Li[1], Jiaming Hou[1], Nan Chen[1], Li Qian[1,2*]

[1]Graduate School, Youjiang Medical University for Nationalities, Baise, China
[2]Drug and Food Vocational College, Guangxi Vocational University of Agriculture, Nanning, China
Email: tcheng324@163.com, *qianli1656@126.com

How to cite this paper: Tan, C., Chen, H.N., Li, R., Hou, J.M., Chen, N. and Qian, L. (2025) Evaluation of Hypoglycemic Effects of a Variety of Chinese Herbal Medicines Based on Silkworm (*Bombyx mori*) Model. *Journal of Biosciences and Medicines*, **13**, 115-127.
https://doi.org/10.4236/jbm.2025.134011

Received: March 6, 2025
Accepted: April 11, 2025
Published: April 14, 2025

Copyright © 2025 by author(s) and Scientific Research Publishing Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
http://creativecommons.org/licenses/by/4.0/
Open Access

Abstract

Objective: To establish a low-cost way to evaluate the efficacy of hypoglycemic herbs. **Methods:** The silkworms were divided into control group, model group, metformin group, and various herbal extracts group, and were reared at 16˚C - 20˚C until the sixth day of modeling, and blood glucose was detected in all silkworms on the sixth day. **Results:** High-jasmine crude polysaccharide (H-JCP), total flavonoids of *Paederia scandens* (TFPS), total flavonoids of hibiscus flowers (TFHF), low-total flavonoids of chamomile (L-TFC), high-total flavonoids of chamomile (H-TFC), low-total flavonoids of potentilla discolor (L-TFPD), high-total flavonoids of potentilla discolor (H-TFPD), low-golden flowers tea extract (L-GFTE), high-golden flowers tea extract (H-GFTE), low-guava extract (L-GE) and high-guava extract(H-GE) had different hypoglycemic effects in the silkworm, respectively, H-JCP, TFPS, TFHF, H-TFC had a certain inhibitory effect on α-glucosidase activity, while crude polysaccharide of *Polyporus umbellatus* (CPPU), buckwheat shell total flavonoids (BSTF), low-hawthorn leaves flavonoids (L-HLF) and high-hawthorn leaves flavonoids (H-HLF) were not as effective in lowering the hypoglycemic effect. **Conclusion:** A model of diabetes in the silkworm, established at low temperatures, allowed a preliminary evaluation of the hypoglycemic effect of the herbal extracts.

Keywords

Silkworm, Diabetes, Chinese Herbs, α-Glycosidase

1. Introduction

Diabetes mellitus (DM) has become a major public health problem that cannot be ignored globally, according to the International Diabetes Federation (IDF) survey, more than 1.31 billion people are expected to have diabetes by 2050, with the majority having type 2 diabetes [1]. The establishment of diabetic animal model is an important basis for the study of the occurrence and development of diabetes, and it is also a key link in the study of new therapeutic drugs [2]. In order to find therapeutic countermeasures for diabetes and develop new hypoglycemic drugs, researchers have used a large number of mammals to model diabetes, such as mice, rats, pigs, etc. However, these mammals inevitably suffer from the problems of high cost and long modeling period [3]. In our previous report, stable diabetes could be modeled by rearing domestic silkworms at low temperatures through high-sugar mulberry leaves [4]. In addition, the silkworm has pharmacokinetic and pharmacodynamic properties similar to those of mammals, which makes the silkworm potential as an animal model for large-scale drug screening [5] [6]. China has rich resources of Chinese herbal medicine, flavonoids [7], polysaccharides [8], saponins [9], and triterpenoids [10] components in Chinese herbal medicines may have hypoglycemic effects, and those treated with herbal medicines also have the advantages of good safety and few side effects. Guava and hibiscus flowers contain abundant flavonoids, which may have potential hypoglycemic effects. In addition, plants from natural sources such as golden flowers tea and jasmine were selected, among which polysaccharides and other bioactive components may also have potential hypoglycemic effects. We envisioned that the silkworm, as an animal model of diabetes mellitus, was given herbal extracts as well as metformin for preliminary evaluation of the hypoglycemic effect of other herbal extracts using the hypoglycemic criteria of metformin. In addition, alpha-glucosidase inhibitors (AGIs) are effective in lowering blood glucose levels and have attracted much attention in diabetes research [11]. Due to the advantages of low cost of silkworm rearing, simple operation and short molding time, several herbs with good hypoglycemic effect in silkworms were selected for the study of α-glucosidase inhibitory activity, which may provide a low-cost way to screen hypoglycemic drugs in the future.

2. Materials and Methods

2.1. Animals

The domestic silkworm variety selected for this experiment was Liangguang II, purchased from Shanglin County, Guangxi, China. It was reared by sericulturists until the end of the fourth year of age before purchase, and then reared to the fifth year of age in a room-temperature environment after transferring to the laboratory.

2.2. Preparation of Chinese Herbs

Jasmine, hawthorn leaves, *Paederia scandens*, *Polyporus umbellatus*, buckwheat shell, hibiscus flowers, Golden flowers tea, Guava, Chamomile, etc. were purchased in China National Pharmaceutical Group Corporation. With the help of the members of this research group, the Chinese herbal medicine was dried after cleaning to remove the dust, and the dried Chinese herbal medicine was crushed, and then concentrated using a rotary evaporator to obtain a concentrated extract. Finally, the concentrated extract was cooled and placed in a refrigerator at 4˚C for use.

2.3. Feed Preparation

The rhizomes of the freshly picked mulberry leaves were subtracted, and only the leaves were retained, and subsequently stored in a 4˚C refrigerator. A 20% glucose solution was prepared by weighing 20 g of anhydrous glucose and adding 80 ml of water. A sufficient amaount of 20% glucose solution was configured according to the above ratio, and then different doses of metformin as well as herbal extracts were added directly and mixed thoroughly to configure different concentrations of drug-containing glucose solutions (Table 1). Fresh leaves were weighed 20 g each and sprayed with sugar solution and drug-containing sugar solution at a distance of 10 - 20 cm from the back of the leaves until the final weight was 25 g. Afterwards, half of the leaves were fed on the same day, and the remaining half was put into the refrigerator at 4˚C for storage, and the mulberry leaves had to be dried again before feeding on the second day.

Table 1. Drug ratios for each experimental group.

Group	20% glucose solution (ml)	Extract mass (mg)	Final concentration (mg/ml)
Metformin	200	100	0.5
Low-jasmine crude polysaccharide (L-JCP)	100	1	0.01
High-jasmine crude polysaccharide (H-JCP)	100	50	0.5
Low-hawthorn leaves flavonoids (L-HLF)	100	1	0.01
High-hawthorn leaves flavonoids (H-HLF)	100	50	0.5
Low-total flavonoids of potentilla discolor (L-TFPD)	200	5	0.025
High-total flavonoids of potentilla discolor (H-TFPD)	200	20	0.1
Low-golden flowers tea extract (L-GFTE)	200	5	0.025
High-golden flowers tea extract (H-GFTE)	200	20	0.1
Low-guava extract (L-GE)	200	10	0.05
High-guava extract (H-GE)	200	20	0.1
Low-total flavonoids of chamomile (L-TFC)	200	20	0.1
High-total flavonoids of chamomile (H-TFC)	200	100	0.5
Total flavonoids of *Paederia scandens* (TFPS)	200	100	0.5
Crude polysaccharide of *Polyporus umbellatus* (CPPU)	200	100	0.5
Buckwheat shell total flavonoids (BSTF)	200	100	0.5
Total flavonoids of hibiscus flowers (TFHF)	200	100	0.5

2.4. Environment

The silkworms were placed individually in biodegradable plastic tubs with a layer of absorbent paper at the bottom to facilitate daily clean up. To prolong the survival period of 5-year-old silkworms without affecting their normal physiological functions, this leads to a better observation of the changes after eating herbs. Consequently, the plastic pots were placed in a constant temperature and humidity cabinet (Curtis Chao Cheng XR-245L, China) for 6 days at a constant temperature of 16˚C - 18˚C and relative humidity of 65% - 75%.

2.5. Animal Modeling and Treatment

Fifth instar silkworm larvae (both male and female) weighing 0.9 g to 1.0 g, which were in good growth condition and healthy, were randomly selected and divided into 28 groups (n = 20), the control group was fed with fresh mulberry leaves, the model group was fed with sugar-containing solution, the metformin group was fed with sugar solution containing metformin, and the rest of the herbal groups were fed with sugar solution containing the corresponding herbs, respectively. According to the experimental groups were fed mulberry leaves until the sixth day, and the blood glucose levels of all silkworms were measured 3 h after feeding on the sixth day.

2.6. Glucose Determination

The silkworms were unfolded in the palm of the hand, fixed with the index finger and thumb of the left hand respectively, with the head of the silkworms facing the tiger's mouth, and a disposable blood needle was inserted about 0.5 cm above the first leg of the silkworms to collect about 20 μL of hemolymph fluid from the silkworms, and glucose content in the hemolymph fluid of the silkworms was detected by using a glucometer.

2.7. Detection of Alpha-Glucosidase Inhibition Rate

Referring to the method of literature [12], the herbal extracts were assayed for α-glucosidase inhibitory activity using the 96-microwell plate method, with a total reaction system of 240 uL. First, 120 μL of PBS (pH 6.8, 0.1 mmol/L) was added to a 96-microwell plate, and 20 μL of 0.2 U/mL α-glucosidase (Yuanye China) was added to the plate with 20 μL of sample and incubated for 10 min at 37˚C. Subsequently, 20 μL of 20 mM substrate 4-nitrophenyl α-D-glucopyranoside (pNPG, Yuanye China) was added and incubated for another 20 min at 37˚C. Finally, 60 μL of 0.1 mM Na_2CO_3 (Yuanye China) was added to terminate the reaction. Subsequently, 20 μL of 20 mM pNPG substrate was added and incubated at 37˚C for another 20 min. Finally, the reaction was terminated by adding 60 μL of 0.1 mM sodium carbonate, sealing the plate membrane, and then placed in Microplate Reader (Thermo Fisher, USA), and the absorbance was read at the wavelength of 405 nm. Three replicate wells were set up for each group and repeated three times (**Table 2**).

Table 2. *α*-glucosidase activity inhibition reaction system (μL).

Group	Sample	PBS	*α*-glucosidase	pNPG	Na_2CO_3	6% DMSO-PBS
A_1	20	120	20	20	60	-
A_2	20	120	-	20	60	20
A_3	-	120	20	20	60	20
A_4	-	120	-	20	60	40

Note: The inhibition rate of samples against *α*-glucosidase is calculated by this formula: Inhibition rate (%) = $1 - (A_1 - A_2)/(A_3 - A_4) \times 100$. A_1: Sample Group; A_2: Sample Control Group; A_3: Experimental Control Group; A_4: Blank Background Group.

2.8. Statistical Analysis

SPSS 24 software was used for statistical analysis. Comparisons between groups were made using one-way ANOVA (one-way ANOVA) and LSD method when the data met normality and Chi-square; when equal variance was not assumed, comparisons between groups were made using Games-Howell to determine statistical significance. In each case, the significance level was set at $p < 0.05$.

3. Results

3.1. Effects of Chinese Herbal Extracts on Body Weight and Blood Glucose of Silkworms

At day 6, the body weight of control silkworms was significantly higher than that of the model group, Body weight of L-JCP, M-JCP and L-HLF, M-HLF decreased compared with the model group, with the increase of dosage, the weight loss of silkworm seems to be greater. The metformin group had the greatest effect on the body weight of silkworm, and the body weight was significantly lower than that of the model group, which may be related to the effect of metformin on reducing body weight (Figure 1(A)). In previous studies, we found that the blood glucose was relatively stable when the silkworm was raised to the sixth day of the fifth instar. Therefore, we chose to detect the blood glucose changes of all silkworms on the sixth day. Results showed that, The L-HLF and H-HLF did not reduce the blood glucose level in the silkworm, but made the blood glucose level in the silkworm higher than that in the model group, The L-JCP did not improve the blood glucose level in the silkworm. However, H-JCP can significantly reduce blood glucose levels in silkworms, although not as significantly as metformin, by comparison, the hypoglycemic effect of H-JCP is verifiable (Figure 1(B)).

We found that the body weight of the model group was significantly lower than that of the control group on the sixth day, body weight of L-TFPD was higher than those in the model group, with the increase of dosage, the body weight will decrease, the difference was not significant when compared to the modeling group. Compared with the model group, the body weight of the L-GFTE had a downward trend, but there is no statistical significance between the two. However, the H-GFTE significantly reduced the body weight of silkworm. In the L-GE and H-GE, the dose of extract was proportional to the weight gain of silkworm (Figure 2(A)). When the silkworm was reared to the sixth day, the L-GE and H-GE could significantly reduce the blood glucose level of the silkworm, and with the increase of the dose, the blood glucose level in the silkworm decreased more obviously. In the L-GFTE, the blood glucose level in silkworm was significantly lower than that in the model group. With the increase of dose, the effect of reducing blood glucose was more obvious. The L-GE and H-GE can significantly reduce the blood glucose

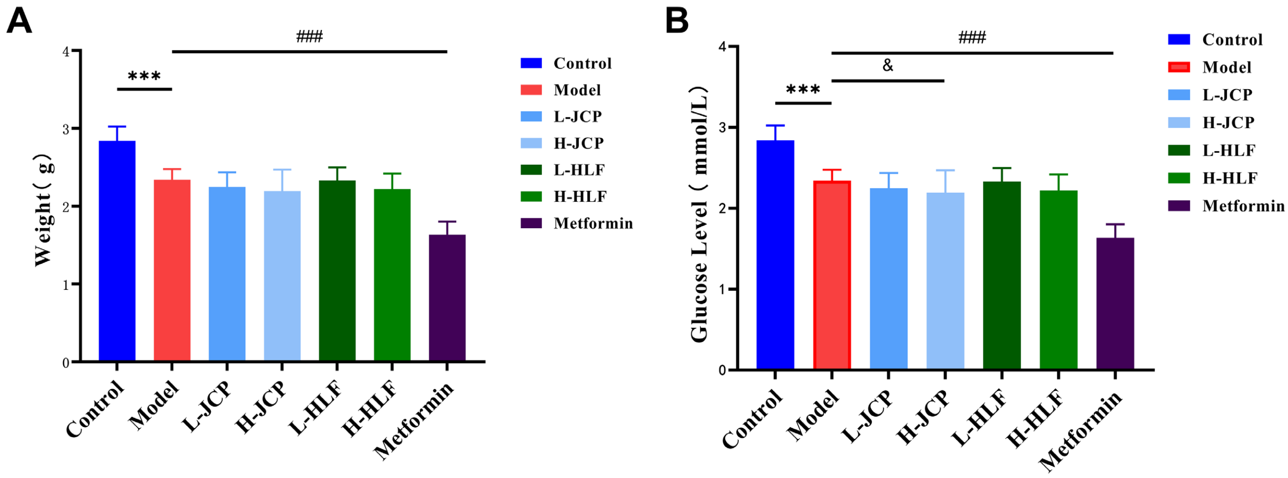

Figure 1. Silkworm numerical data after treatment: (A) Changes in body weight of silkworms after treatment of JCP, HLF, and metformin treatment. Data are presented as mean ± SEM. Control vs Model, $^{***}p < 0.001$, Model vs Metformin, $^{\#\#\#}p < 0.001$. (B) Changes in blood glucose of silkworms after treatment of JCP, HLF, and metformin. Data are presented as mean ± SEM. Control vs Model, $^{***}p < 0.001$, Model vs H-JCP, $^{\&}p < 0.05$, Model vs Metformin, $^{\#\#\#}p < 0.001$.

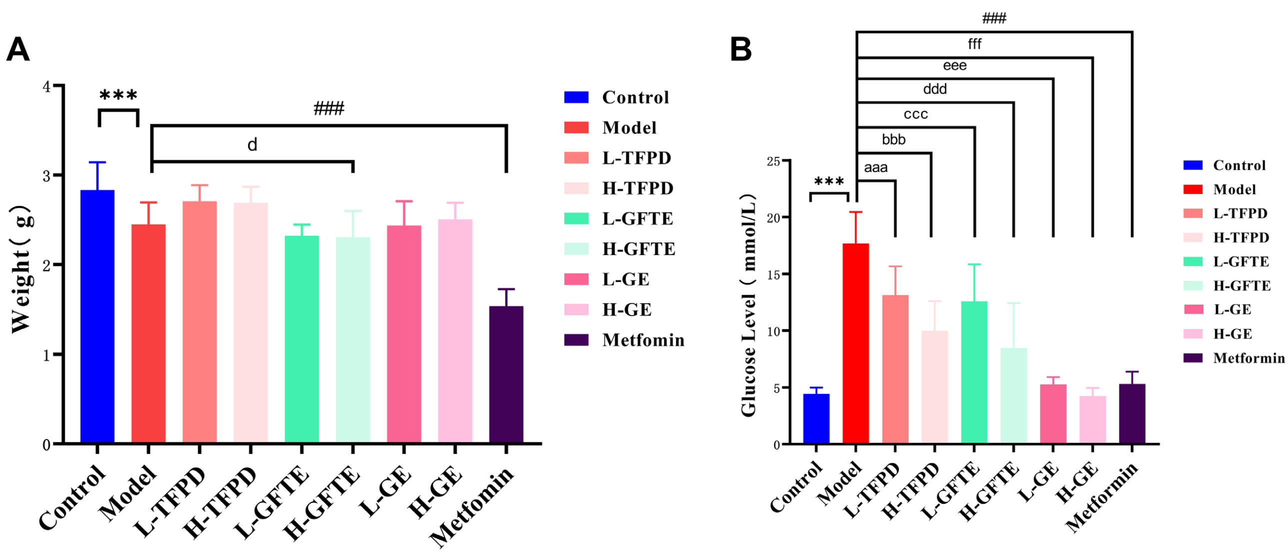

Figure 2. Silkworm numerical data after treatment. (A) Changes in body weight of silkworms after treatment of TFPD, GFTE, GE and Metformin treatment. Data are presented as mean ± SEM. Control vs Model, $^{***}p < 0.001$; Model vs H-GFTE, $^{d}p < 0.05$; Model vs Metformin, $^{\#\#\#}p < 0.001$. (B) Changes in blood glucose of silkworms after treatment of TFPD, GFTE, GE and Metformin treatment. Data are presented as mean ± SEM. Control vs Model, $^{***}p < 0.001$; Model vs L-TFPD, $^{aaa}p < 0.001$; Model vs H-TFPD, $^{bbb}p < 0.001$; Model vs L-GFTE, $^{ccc}p < 0.001$; Model vs H-GFTE, $^{ddd}p < 0.001$; Model vs L-GE, $^{eee}p < 0.001$; Model vs H-GF, $^{fff}p < 0.001$; Model vs Metformin, $^{\#\#\#}p < 0.001$.

level in the silkworm. With the increase of the dose, the blood glucose level in the silkworm will be significantly reduced, and is statistically significant compared with the model group (Figure 2(B)).

The body weight of silkworm in the L-TFC increased compared with the model group, and with the increase of the dose of chamomile, the body weight of silkworm showed a downward trend (Figure 3(A)). The total flavonoids of chamomile had a significant effect on the blood glucose in silkworm, and with the increase of dose, the blood glucose level in silkworm decreased more obviously, and the high dose group had the greatest degree of hypoglycemic effect (Figure 3(B)).

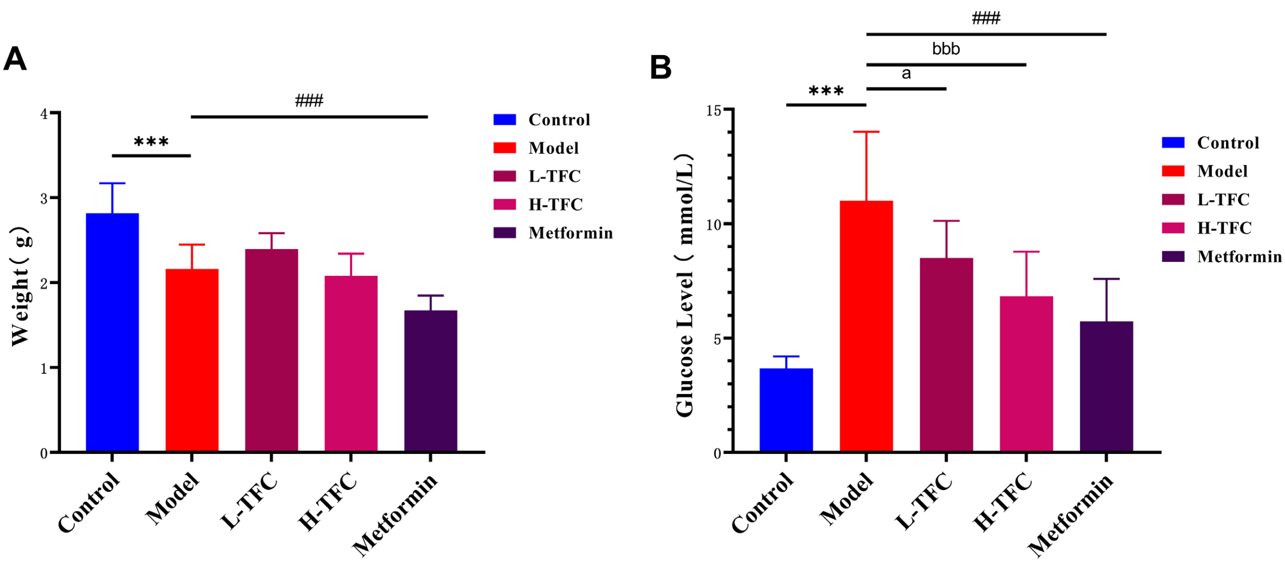

Figure 3. Silkworm numerical data after treatment. (A) Changes in body weight of silkworms after treatment of TFC and Metformin treatment. Data are presented as mean ± SEM. Control vs Model, $^{***}p < 0.001$; Model vs Metformin, $^{\#\#\#}p < 0.001$. (b) Changes in blood glucose of silkworms after treatment of TFC and Metformin treatment. Data are presented as mean ± SEM. Control vs Model, $^{***}p < 0.001$; Model vs L-TFC, $^{a}p < 0.05$; Model vs H-TFC, $^{bbb}p < 0.001$; Model vs Metformin, $^{\#\#\#}p < 0.001$.

The administration group was set to the same dose. The body weight of silkworms in the TFPS, CPPU, BSTF and TFHF was generally lower than that in the model group, and all of them were statistically significant (Figure 4(A)). The TFPS and the TFHF significantly reduced the blood glucose level in silkworm, while the CPPU and the BSTF did not reduce the blood glucose level in silkworm. Under the same dose condition, TFHF in Chinese herbal medicine extract had the most obvious effect on reducing blood glucose (Figure 4(B)).

3.2. Studies on the Inhibitory Activity of Herbal Extracts on α-Glucosidase

The extracts with better hypoglycemic efficiency tested on the silkworm diabetes model were selected and after a comprehensive evaluation with reference to other literature, these extracts were selected and again validated for *in vitro* α-glucosidase inhibition assay. Using acarbose (0.5 mg/ml) as a positive control, we set the total flavonoids of hibiscus flowers (TFHF), total flavonoids of chamomile (TFC), total flavonoids of *Paederia scandens* (TFPS) and jasmine crude polysaccharide (JCP) as the same concentration (0.5 mg/ml) to detect the inhibitory activity of α-glucosidase. Results showed that under the same conditions, acarbose inhibited α-glucosidase by 99.98%, The inhibition rate of TFHF on α-glucosidase was 86.75%, the inhibition rate of TFC on α-glucosidase was 88.71%, the inhibition rate of TFPS on α-glucosidase was 81.38%, and the inhibition rate of JCP on α-glucosidase was 10.72% (Figure 5).

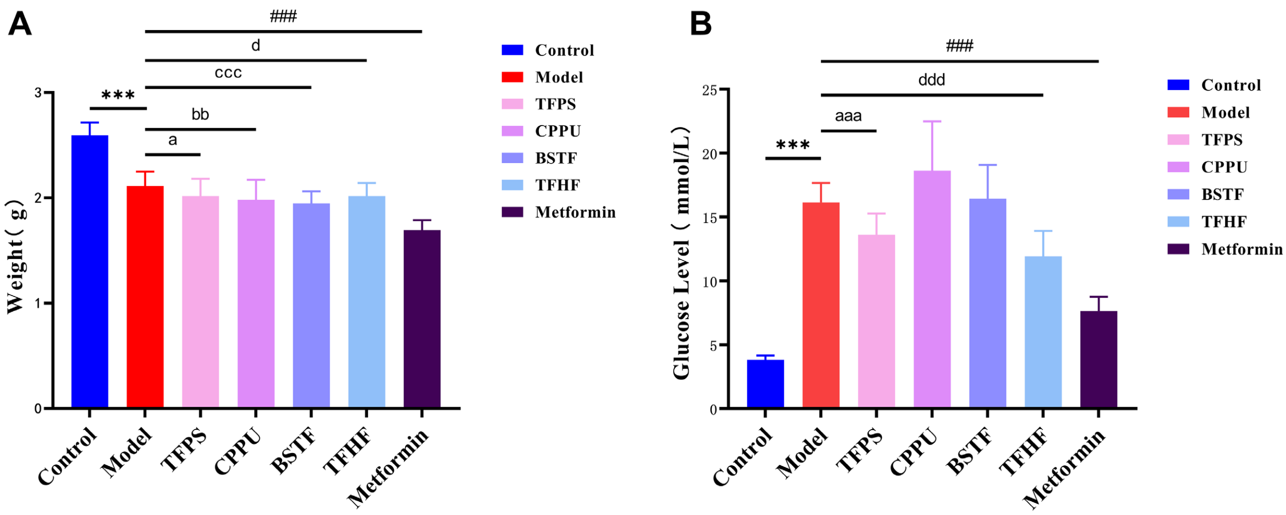

Figure 4. Silkworm numerical data after treatment. (A) Changes in body weight of silkworms after treatment of TFPS, CPPU, BSTF, TFHF and Metformin treatment. Data are presented as mean ± SEM. Control vs Model, $^{***}p < 0.001$; Model vs TFPS, $^{a}p < 0.05$; Model vs CPPU, $^{bb}p < 0.01$; Model vs BSTF, $^{ccc}p < 0.001$; Model vs TFHF, $^{d}p < 0.05$, Model vs Metformin, $^{\#\#\#}p < 0.001$. (B) Changes in blood glucose of silkworms after treatment of TFPS, CPPU, BSTF, TFHF and Metformin treatment. Data are presented as mean ± SEM. Control vs Model, $^{***}p < 0.001$; Model vs TFPS, $^{aaa}p < 0.001$; Model vs TFHF, $^{ddd}P < 0.001$; Model vs Metformin, $^{\#\#\#}p < 0.001$.

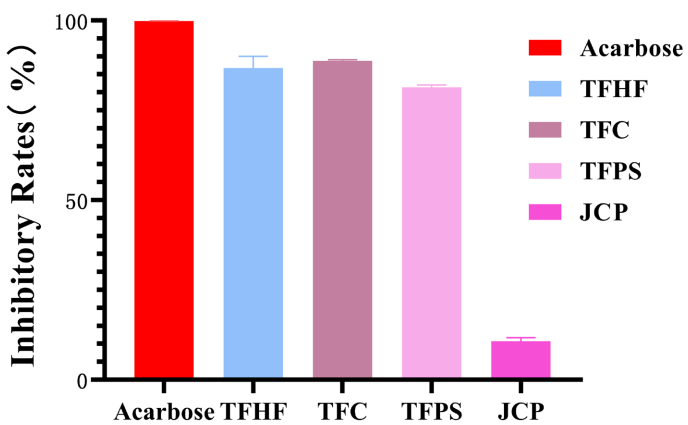

Figure 5. Effect of various herbs on the inhibitory activity of α-glucosidase.

4. Discussion

As researchers delve deeper into invertebrates, the silkworm as an alternative model can also be used as a gout [13], anti-infective [14], anti-fungal [15] research area, The use of the silkworm as a model animal can reduce the cost of scientific research to some extent. Japanese scholar Matsumoto has shown that, silkworm can be used to screen diabetes drugs [16], but it may cause some harm to experimental animals by injection, if improperly operated, it may also cause harm to researchers. Unlike mammals, the hemolymph of silkworm is mainly trehalose, which is a non-reducing disaccharide, accounting for more than 90% of the total sugar content, so it is called the "blood sugar" of insects [17]. In contrast, glucose accounts for only 4% of the total sugar content, and after the silkworm eats glucose, the glucose titer in the hemolymph will change significantly [18]. The choice of 20% glucose solution allows for better observation of the performance of silkworms after feeding on herbs without affecting their normal physiological state. The silkworm can also synthesize an insulin-like peptide similar to human insulin, which is 40% similar to human insulin, and can regulate the metabolism of trehalose and glycogen in the silkworm [19]. Silkworm feeds on mulberry leaves. This is because the GR66 gene in silkworm is encoded as a hypothetical bitter taste receptor, which makes silkworm have a special preference for mulberry leaves [20]. Therefore, in this experiment, we established a diabetic model by spraying drugs on the surface of mulberry leaves and feeding mulberry leaves, which not only reduced the damage to experimental animals by gavage and injection, but also made it easier for silkworms to accept drugs and better observe the efficacy of drugs. In addition, rearing silkworms in low-temperature environment prolonged the 5th instar survival of silkworms [4]. It can better observe the changes in silkworms after eating hypoglycemic drugs, which may reduce the development cycle of hypoglycemic drugs, making it possible to screen more natural products or synthetic drugs with hypoglycemic effects in a relatively short period of time.

Metformin is the first choice for the treatment of type 2 diabetes. However, there are inevitably adverse reactions such as gastrointestinal tract and allergy. In severe cases, it may even cause lactic acidosis [21]. Thanks to our rich Chinese herbal medicine resources, it is feasible to find effective hypoglycemic components in Chinese herbal medicines with lower side effects. Recent research has shown that AGI can inhibit the release of α-D glucose, thereby delaying the absorption of carbohydrates in the small intestine, avoid a sharp rise in postprandial blood glucose, reduce blood glucose fluctuations, thereby reducing the generation and absorption of glucose into the blood, The use of this drug alone has a low risk of hypoglycemia and has attracted widespread attention in diabetes research [22]. AGI may also stimulate the secretion of glucagon-like peptide-1 (GLP-1) in the intestine. Long-term use can increase insulin sensitivity and reduce postprandial insulin secretion, thereby reducing insulin resistance and further regulating blood glucose balance [23]. Common AGI drugs include acarbose, voglibose and miglitol. Although these highly effective AGIs are available, regular consumption of these drugs may lead to side effects such as diarrhea and allergic reactions. Researchers are still studying new AGIs with inhibitory potential and less side effects [24]. The detection of α-glucosidase inhibitory activity of Chinese herbal medicines in the silkworm, and provide *in vivo* data reference for the future clinical development of new AGI, which can not only reduce costs, but also may help to develop new AGI in the future. Silkworm has unique advantages as an experimental animal, but there are still many differences with mammals, Glucose is a common nutritional signal that induces insulin release in mammals and insects as a messenger of the body's "eating" state. Mammals maintain blood glucose levels mainly through glycogen decomposition and gluconeogenesis [25]. The role and regulation mechanism of insulin-like peptides released in the brain of silkworm larvae may be different in mammals. The difference in metabolic pathways may affect the effect of drugs, which may lead to differences in the distribution, absorption and metabolism of drugs in the body. So, it cannot completely replace mammals for drug testing. However, through the preliminary drug efficacy verification of the silkworm, it provides a reference for subsequent verification experiments in mammals, which can reduce the consumption of mammals in the experiment.

Based on our study, some Chinese herbal extracts such as JCP, TFPS, TFHF and TFC can inhibit the activity of *α*-glucosidase, thereby reducing the blood glucose level in silkworm, which may provide a reference for the development of new AGI. In addition, TFPD, GFTE and GE also have hypoglycemic effects in silkworm, which may be due to the potential hypoglycemic mechanism of flavonoids, stimulating the release of insulin-like peptides in silkworm, thus effectively reducing the blood glucose level in silkworm. Of course, in order to further study its hypoglycemic function, this is the direction that needs to be focused on in the future. In addition, the silkworm treated with Chinese herbal medicine extracts may reduce the blood glucose level in the body through the insulin signaling pathway. It is our focus in the follow-up study to verify whether these Chinese herbal medicine extracts can effectively reduce blood glucose through the insulin signaling pathway. We hope that the hypoglycemic drugs screened by the silkworm model can provide a reference for clinical medication and promote the application as an alternative model in future disease exploration.

5. Conclusion

In this research, JCP, TFPS, TFHF, TFPD, GFTE, TFC, and GE all have good hypoglycemic effect in silkworm. Especially after *in vitro α*-glucosidase activity test, it was confirmed that JCP, TFPS, TFHF and TFC had different degrees of inhibition. Therefore, as a new type of diabetes model, silkworm has the potential to screen hypoglycemic drugs. This may inform the search for new therapeutic countermeasures for diabetes and the development of new hypoglycemic drugs.

6. Limitation

In this study, we recognize that there are still some areas that deserve further improvement. The diabetes model was established by using silkworm, by comparing the blood glucose level after feeding the drug-containing mulberry leaves with the blood glucose level after feeding the high-sugar mulberry leaves, and according to the blood glucose level in the silkworm after feeding the fresh mulberry leaves, the hypoglycemic effect of a certain Chinese herbal medicine was preliminarily explored. Although we have preliminarily explored that some extracts do have hypoglycemic effects, the mechanism of how to produce hypoglycemic effects has not been explored in depth. For example, JCP has a significant hypoglycemic effect, but has a low inhibitory activity on α-glucosidase, which may be caused by other ways, it may stimulate the release of insulin-like peptide in silkworm brain, thereby reducing blood glucose. In addition, in order to better understand how the crude extract of traditional Chinese medicine reduces blood sugar and is applied to treatment in the future, it is necessary to further study its potential mechanism. In the future, we plan to further explore the mechanism of Chinese herbal medicine in reducing blood glucose in silkworms in subsequent studies to improve the current research results.

Funding

National Natural Science Foundation of China (NSFC) (81660145).

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Ong, K.L., Stafford, L.K., McLaughlin, S.A., *et al.* (2023) Global, Regional, and National Burden of Diabetes from 1990 to 2021, with Projections of Prevalence to 2050: a Systematic Analysis for the Global Burden of Disease Study 2021. *The Lancet*, **402**, 203-234.

[2] Pandey, S., Chmelir, T. and Chottova Dvorakova, M. (2023) Animal Models in Diabetic Research—History, Presence, and Future Perspectives. *Biomedicines*, **11**, Article 2852. https://doi.org/10.3390/biomedicines11102852

[3] Lutz, T.A. (2023) Mammalian Models of Diabetes Mellitus, with a Focus on Type 2 Diabetes Mellitus. *Nature Reviews Endocrinology*, **19**, 350-360. https://doi.org/10.1038/s41574-023-00818-3

[4] Hou, J., Tan, C., Chen, N., Zhou, Y., Huang, S., Chen, H., *et al.* (2024) Establishment of Diabetes Mellitus Model Using *Bombyx mori* Silkworms in a Low-Temperature Environment. *Archives of Insect Biochemistry and Physiology*, **115**, e22083. https://doi.org/10.1002/arch.22083

[5] Aznar-Cervantes, S.D., Monteagudo Santesteban, B. and Cenis, J.L. (2021) Products of Sericulture and Their Hypoglycemic Action Evaluated by Using the Silkworm, *Bombyx mori* (*Lepidoptera*: *Bombycidae*), as a Model. *Insects*, **12**, Article 1059. https://doi.org/10.3390/insects12121059

[6] Nwibo, D.D., Hamamoto, H., Matsumoto, Y., Kaito, C. and Sekimizu, K. (2015) Current Use of Silkworm Larvae (*Bombyx mori*) as an Animal Model in Pharmaco-Medical Research. *Drug Discoveries & Therapeutics*, **9**, 133-135. https://doi.org/10.5582/ddt.2015.01026

[7] Chen, J., Mangelinckx, S., Adams, A., Wang, Z., Li, W. and De Kimpe, N. (2015) Natural Flavonoids as Potential Herbal Medication for the Treatment of Diabetes Mellitus and Its Complications. *Natural Product Communications*, **10**, 187-200. https://doi.org/10.1177/1934578x1501000140

[8] Wu, J., Shi, S., Wang, H. and Wang, S. (2016) Mechanisms Underlying the Effect of Polysaccharides in the Treatment of Type 2 Diabetes: A Review. *Carbohydrate Polymers*, **144**, 474-494. https://doi.org/10.1016/j.carbpol.2016.02.040

[9] Lyu, H., Chen, J. and Li, W. (2016) Natural Triterpenoids for the Treatment of Diabetes Mellitus: A Review. *Natural Product Communications*, **11**, 1579-1586. https://doi.org/10.1177/1934578x1601101037

[10] Xi, M., Hai, C., Tang, H., Chen, M., Fang, K. and Liang, X. (2008) Antioxidant and Antiglycation Properties of Total Saponins Extracted from Traditional Chinese Medicine Used to Treat Diabetes Mellitus. *Phytotherapy Research*, **22**, 228-237. https://doi.org/10.1002/ptr.2297

[11] Tan, K., Tesar, C., Wilton, R., Jedrzejczak, R.P. and Joachimiak, A. (2018) Interaction of Antidiabetic α-Glucosidase Inhibitors and Gut Bacteria α-Glucosidase. *Protein Science*, **27**, 1498-1508. https://doi.org/10.1002/pro.3444

[12] Liu, S., Li, D., Huang, B., Chen, Y., Lu, X. and Wang, Y. (2013) Inhibition of Pancreatic Lipase, α-Glucosidase, α-Amylase, and Hypolipidemic Effects of the Total Flavonoids from *Nelumbo nucifera* Leaves. *Journal of Ethnopharmacology*, **149**, 263-269. https://doi.org/10.1016/j.jep.2013.06.034

[13] Zhang, X., Xue, R., Cao, G., Pan, Z., Zheng, X. and Gong, C. (2012) Silkworms Can Be Used as an Animal Model to Screen and Evaluate Gouty Therapeutic Drugs. *Journal of Insect Science*, **12**, Article 4. https://doi.org/10.1673/031.012.0401

[14] Hamamoto, H., Horie, R. and Sekimizu, K. (2019) Pharmacokinetics of Anti-Infectious Reagents in Silkworms. *Scientific Reports*, **9**, Article No. 9451. https://doi.org/10.1038/s41598-019-46013-1

[15] Ishii, M., Matsumoto, Y., Yamada, T., Abe, S. and Sekimizu, K. (2017) An Invertebrate Infection Model for Evaluating Anti-Fungal Agents against Dermatophytosis. *Scientific Reports*, **7**, Article No. 12289. https://doi.org/10.1038/s41598-017-12523-z

[16] Matsumoto, Y. (2020) Facilitating Drug Discovery in Human Disease Models Using Insects. *Biological and Pharmaceutical Bulletin*, **43**, 216-220. https://doi.org/10.1248/bpb.b19-00834

[17] Shukla, E., Thorat, L.J., Nath, B.B. and Gaikwad, S.M. (2015) Insect Trehalase: Physiological Significance and Potential Applications. *Glycobiology*, **25**, 357-367. https://doi.org/10.1093/glycob/cwu125

[18] Matsumoto, Y., Ishii, M., Hayashi, Y., Miyazaki, S., Sugita, T., Sumiya, E., *et al.* (2015) Diabetic Silkworms for Evaluation of Therapeutically Effective Drugs against Type II Diabetes. *Scientific Reports*, **5**, Article No. 10722. https://doi.org/10.1038/srep10722

[19] Iwami, M., Kawakami, A., Ishizaki, H., Takahashi, S.Y., Adachi, T., Suzuki, Y., *et al.* (1989) Cloning of a Gene Encoding Bombyxin, an Insulin-Like Brain Secretory Peptide of the Silkmoth *Bombyx mori* with Prothoracicotropic Activity. *Development, Growth & Differentiation*, **31**, 31-37. https://doi.org/10.1111/j.1440-169x.1989.00031.x

[20] Zhang, Z., Zhang, S., Niu, B., Ji, D., Liu, X., Li, M., *et al.* (2019) A Determining Factor for Insect Feeding Preference in the Silkworm, *Bombyx mori*. *PLOS Biology*, **17**, e3000162. https://doi.org/10.1371/journal.pbio.3000162

[21] Nasri, H., Rafieian-Kopaei, M. (2014) Metformin: Current Knowledge. *Journal of Research in Medical Sciences*, **19**, 658-664.

[22] Lu, H., Xie, T., Wu, Q., Hu, Z., Luo, Y. and Luo, F. (2023) Alpha-Glucosidase Inhibitory Peptides: Sources, Preparations, Identifications, and Action Mechanisms. *Nutrients*, **15**, Article 4267. https://doi.org/10.3390/nu15194267

[23] Kalra, S. (2014) Incretin Enhancement without Hyperinsulinemia: α-Glucosidase In-

hibitors. *Expert Review of Endocrinology & Metabolism*, **9**, 423-425. https://doi.org/10.1586/17446651.2014.931807

[24] Kashtoh, H. and Baek, K. (2022) Recent Updates on Phytoconstituent Alpha-Glucosidase Inhibitors: An Approach towards the Treatment of Type Two Diabetes. *Plants*, **11**, Article 2722. https://doi.org/10.3390/plants11202722

[25] Han, H., Kang, G., Kim, J.S., Choi, B.H. and Koo, S. (2016) Regulation of Glucose Metabolism from a Liver-Centric Perspective. *Experimental & Molecular Medicine*, **48**, e218. https://doi.org/10.1038/emm.2015.122