Pakistan J. Zool., vol. 56(2), pp 703-710, 2024 **DOI**: https://dx.doi.org/10.17582/journal.pjz/20221010041029

The Hypoglycaemic Mechanism of Camel Placenta Powder on Streptozotocin Induced Type 2 Diabetic Rats

Xiangmei Chen, Burie Bao* and Mo Degema

Traditional Mongolian Medicine College of Inner Mongolia Minzu University, Tongliao, No.996, West Ramulun Street (West), Horqin District, Tongliao City, 028000, Inner Mongolia Autonomous Region, China 028000, China.

ABSTRACT

The objective of this study was to explore the effects of camel placenta powder on associated symptoms, signs and indicators in type 2 diabetic rats. For this study sixty male Wistar rats were randomly divided into a normal group, model group, metformin group, and low-, medium- and high-dose camel placenta groups. A high-fat and high-sugar feed combined with intraperitoneal injection of STZ dissolved in a citric acid-sodium citrate buffer was used to establish a rat model of hyperglycaemia. Metformin hydrochloride tablets were used as a positive control to detect fasting blood glucose. The contents of glycated haemoglobin (HbALc), insulin (INS) and glucose (GLUC3) as well as the protein expression and mRNA levels of sodium-glucose co-transporter 2 (SGLT2) and glucose transporter 2 (GLUT2) were used to study the mechanism of the hypoglycaemic effect of CPP on diabetic rats. We found that camel placenta produced no meaningful changes in the weight of hyperglycaemic rats or the weight of the liver, kidney, or pancreas. After STZ modelling, the blood glucose levels of rats noticeably increased. However, the blood glucose values of rats decreased substantially due to camel placenta treatment from the 4th to the 6th week. Camel placenta dramatically reduced the serum HbALc and GLUC3 content in hyperglycaemic rats. Dry CPP had a down-regulating effect on the levels of SGLT2 and GLUT2 protein, SGLT2 mRNA and GLUT2 mRNA in the kidneys of hyperglycaemic rats. However, there was no meaningful difference between the metformin group and the high- and medium-dose camel placenta groups. To conclude camel placenta has a notable hypoglycaemic effect on diabetic rats induced by STZ with a high-fat and high-sugar feed.

Article Information
Received 10 October 2022
Revised 20 November 2022
Accepted 17 December 2022
Available online 13 May 2023
(early access)
Published 27 January 2024

Authors' Contribution
XC conceived of the study. BB participated in its design and coordination. MD helped to draft the manuscript. All authors read and approved the final manuscript.

Key words
Camel placenta, Type 2 diabetic, Hypoglycaemic effect, SGLT2; GLUT2

INTRODUCTION

In an aging global society, diabetes places a heavy burden on individual and public health in terms of the number of patients with the disease, diabetes-related complications (including frailty and disability) and expenditures for national health and social care systems (Sinclair *et al*., 2019). The prevalence of diabetes is rising rapidly around the world, as recently confirmed by the finding that, in 2019, 9.5% of 488 million adults around the world aged 20–99 years have diabetes (Saeedi *et al*., 2019).

Although various therapeutic medicines are commonly used to relieve diabetes, this problem has still not been fully resolved by currently available treatments. Antidiabetic medicine like sulfonylureas show limited efficacy in many diabetic conditions and is severely limited by adverse effects (Gloyn *et al*., 2018). Therefore, this unmet clinical need reflects a demand to develop novel classes of antidiabetic drugs than those currently available.

In Mongolian medicine, xiherixijing refers to a prolonged disease characterised by polydipsia, polyuria and emaciation. It is equivalent to diabetes in modern medicine. The treatment principle is to regulate three roots (heyi, xila and badagan) and tonify the kidney (Bai *et al*., 1990). Modern medical and biological research has shown that the placenta contains a variety of hormones, immunoglobulins, growth factors, enzymes, interferons, lipopolysaccharides and other substances that have complex bioactive components and positive medicinal value (Nagae *et al*., 2022; Prince *et al*., 2018; Heo *et al*., 2018). The placenta is non-toxic, non-irritating, convenient to consume and has meaningful efficacy on human immunity, antioxidant capacity and disease treatment (Zhang and Huang, 2018; Choi and Kim, 2019). Camel placenta is recommended for the treatment of diabetes in pastoral areas where camels are bred in large numbers and to have a

* Corresponding author: burie202010@126.com
0030-9923/2024/0002-0703 $ 9.00/0

preventive and therapeutic effect on some diabetic patients (Ao *et al*., 2019). Previous studies indicated that the dried powder of camel placenta can noticeably reduce food intake, inhibit appetite, improve abdominal obesity and reduce blood glucose in spontaneous diabetic mice (Bao *et al*., 2022). However, the hypoglycaemic mechanism of CPP remains unclear. By assessing the contents of HbALc, INS and GLUC3, as well as the protein expression and mRNA levels of SGLT2 and GLUT2, we aim to reveal the mechanisms and characteristics of CPP on associated symptoms, signs and indicators in STZ-induced type 2 diabetic rats, providing a theoretical basis for exploring novel therapies for diabetic patients.

MATERIALS AND METHODS

Experimental animals

Specific pathogen-free (SPF) male Wistar rats weighing 180–200 g were purchased from Changchun Yisi Experimental Animal Technology Co., Ltd. (SCXK Ji –2018–0003) were housed in the animal room of key laboratory of the Ministry of Education of the State People's Committee. These rats were fed in standard cages (5 mice per cage) for 1 week under standard conditions (temperature: 22±2°C; humidity: 30–40% relative humidity; 12 h light/dark cycle) with free access to food and water prior to the experiment (Cui, 2016).

Main instruments, reagents and drugs

H-2050R centrifuge (Cence), sunrise multiscan spectrum (Tecan), fluor chem HD2 chemiluminescent imaging system (Protein Simple), ABI 7500 fast real-time polymerase chain reaction (RT-PCR) (Applied Biosystems) (Dai *et al*., 2021).

CPP (batch number: 20181024, provided by the Preparation Department of Alashan Mongolian Medical Hospital); metformin hydrochloride tablets (batch number: 14880466, Youcare Pharmaceutical); STZ (batch number: 917L038, Solarbio); rat HbALc ELISA kit (batch number: 201904) and rat INS ELISA kit (201905) were purchased from Mlbio; glucose detection kit (batch number: 40879901, Sandhofer Strasse 116, 68305 Mannheim); anti-SGLT2 antibody (batch number: GR3211034-2) and anti-glucose transporter GLUT2 antibody (batch number: GR3249968-12) were purchased from Aibio; FastStart Universal SYBR Green Master (ROX; batch number: 41472600, Tiangen Biotech Co., Ltd.) (Dai *et al*., 2021).

Preparation of camel placenta powder (CPP)

A healthy camel placenta was selected according to the standardisation requirements of placenta products proposed by the Ministry of Health, and impurities, such as foreign bodies and surface fat, were removed, and the blood attached to its surface was washed. The placenta was cut into small pieces and dried in a microwave oven until slightly yellow (dry) before being crushed with a medicinal pulveriser (Chen *et al*., 2019).

Animal grouping and treatment

Sixty male Wistar rats were randomly divided into a normal group, model group, metformin group, and low, medium and high-dose camel placenta groups. There were 10 rats in each group, and modelling began after 1 week of adaptive feeding. The normal group continued to be given a normal diet, and the other 5 groups were given a high-fat and high-sugar diet and were fasted for 12 h after 4 weeks (Zhang *et al*., 2019). The normal group was administered a 30 mg/kg sodium citrate buffer intraperitoneally, and the other 5 groups were given STZ intraperitoneally for 3 consecutive days. Fasting blood glucose was measured after 3 days and again after 1 week of feeding. The fasting glucose should be >10.0 mmol/L (Lin *et al*., 2021).

The positive control group (metformin hydrochloride tablets 120 mg/kg) was administered by gavage. The low-dose camel placenta group was administered 2.5 g/kg camel placenta. The medium-dose camel placenta group were administered with 5.0 g/kg and the high-dose camel placenta group were administered with 7.5 g/kg. The normal control group and model group were given an equal volume of saline. The experimental plan is shown in Figure 1.

Observed indices and methods of detection

Experiments were performed according to the manufacturer's instructions and standard procedures, as previously described (Wen *et al*., 2018). The rats weight was measured weekly. After 6 weeks of administration, the rats were anesthetised by intraperitoneal injection of 30 mg/kg chloral hydrate. Blood was collected from the abdominal aorta, the serum was centrifuged at 3,000 rpm for 15 min, and the liver, kidney and pancreas were weighed and stored at –80°C. The rats were observed for the following general conditions: Activity, mental status, appetite, hair growth and presence of faecal matter. A drop of blood was taken from the tail vein each week to measure fasting blood glucose using a blood glucose meter, and the rats' weight change was measured. Serum triglyceride (TG), total cholesterol (TCHO), high-density lipoprotein (HDL-C), low-density lipoprotein (LDL-C), and glucose tolerance, 3 h (GLUC3) levels were measured with a biochemical instrument. The levels of glycosylated haemoglobin and insulin in the serum were detected by enzyme-linked immunosorbent assay. The effect of camel placenta on the sodium-glucose cotransporter (SGLT2) and

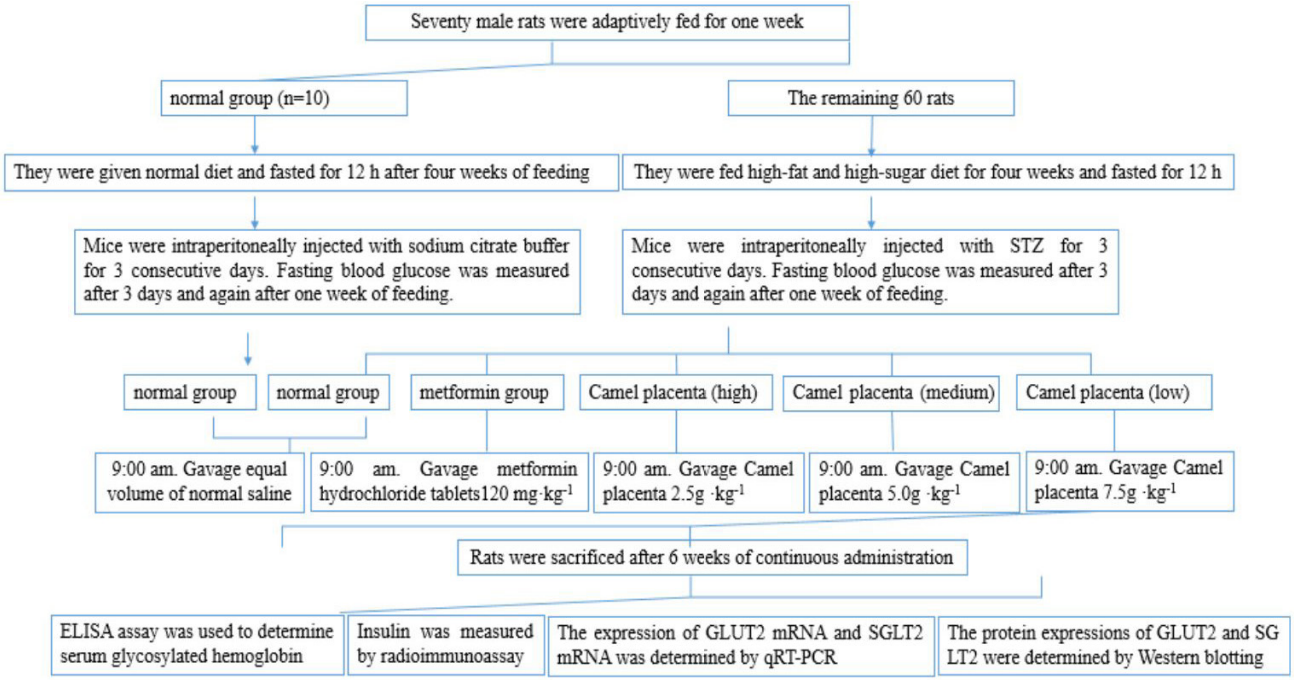

Fig. 1. Experimental plan of work.

Table I. Effect of CPP on the body weight of diabetic rats ($\bar{x}$±s, n = 10).

Groups	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11
Normal group	416.2±19.3	430.3±16.2	442.5±16.7	459±16.5	474.4±18.8	490.7±15.0
Model group	331.2±19.0**	341.1±17.3**	353.2±21.4**	358.4±16.9**	366.4±15.0**	372.9±18.2**
Metformin group	324.5±14.3**	334.5±19.4**	345.8±17.0**	354.5±20.3**	359.7±16.6**	364.8±14.9**
Camel placenta (high)	322.3±16.3**	334.8±16.5**	347.8±18.4**	358.2±19.0**	361.1±17.2**	368.3±15.5**
Camel placenta (medium)	333.8±10.3**	343.6±17.4**	355.8±12.8**	354.1±20.9**	358.8±14.3**	360.2±13.9**
Camel placenta (low)	334.5±14.7**	344.5±19.6**	348.9±12.3**	357.5±12.0**	368.2±19.6**	366.4±19.1**

Compared with normal group, $^{**}P < 0.01$, $^{*}P < 0.05$; Compared with model group, $^{\#\#}P < 0.01$, $^{\#}P < 0.05$.

rat kidney was detected by Western blot. The effect of the camel placenta on the expression of SGLT2 mRNA and GLUT2 mRNA in the diabetic rat kidney was detected by quantitative fluorescence PCR (QF-PCR). The primer sequences are as follows.

SGLT2 F 5'-TCTGAACTTGGGGAGCAGAAG-3`
R 5'-AACACCAATGACCAGCAGGAA-3`

GLUT2 F 5'-CAACATGTTCAGAAGACAAGATCAC-3`
R 5'-CACACCGATGTCATATCCGAACT-3`

ACTB F 5`-TCAGCAAGCAGGAGTACGATG-3`
R 5`-GTGTAAAACGCAGCTCAGTAACA

Statistical analysis

Statistical analyses were conducted with SPSS19.0. Continuous variables were expressed as the means ± standard deviations, and categorical variables were expressed as numbers and percentages. A one-way analysis of variance was conducted for continuous variables, while analyses for categorical variables were performed using the x^2 test or Fisher exact test. $P < 0.05$ was statistically significant.

RESULTS

Effect of CPP on the weight of diabetic rats

The body weight of rats in the model group after intraperitoneal injection of STZ decreased to varying degrees compared with the normal group ($P < 0.01$). Compared with the model group, there was no relevant difference between the body weight of rats in the metformin group and the high-, medium-, and low-dose camel placenta treatment groups (Table I). Camel placenta and metformin had no demonstrable effect on the body weight of STZ-induced diabetic rats.

Table II. Effect of CPP on blood glucose in diabetic rats ($\bar{x}$ ±s, n = 10).

Groups	Week 1	Week 2	Week 3	Week 4	Week 15	Week 6
Normal group	5.4±1.3	4.0±0.2	4.5±0.7	4.9±1.5	4.4±0.8	5.6±1.0
Model group	18.2±3.0**	18.1±4.3**	19.6±2.4**	19.4±16.9**	18.4±15.0**	19.9±18.2**
Metformin group	17.5±4.3**	14.5±3.6**	12.8±3.7$^{\#**}$	10.3±2.3$^{\#**}$	8.7±2.1$^{\#\#**}$	7.2±1.2$^{\#\#**}$
Camel placenta (high)	17.3±1.3**	17.8±5.5**	17.8±5.1**	18.2±4.3**	16.1±17.2**	16.3±4.2**
Camel placenta (medium)	18.8±4.3**	16.2±3.4**	13.1±2.5$^{\#**}$	13.0±2.9$^{\#**}$	1`3.4±4.0$^{\#**}$	11.2±3.1$^{\#**}$
Camel placenta (low)	15.5±3.7**	14.5±1.6**	12.9±2.3$^{\#**}$	11.5±1.1$^{\#**}$	11.2±1.6$^{\#**}$	9.8±2.7$^{\#**}$

Compared with normal group, $^{**}P < 0.01$, $^{*}P < 0.05$; Compared with model group, $^{\#\#}P < 0.01$, $^{\#}P < 0.05$.

Effect of CPP on blood glucose in diabetic rats

Changes in the rats' blood glucose were measured weekly before and after modelling, as well as after treatment with camel placenta and metformin (Table II). After STZ sadiminstration, the blood glucose level of each group rose noticeably compared with the normal group ($P < 0.05$). Compared with the model group, the blood glucose value of the metformin treatment group decreased steadily from the 1st week to the 6th week of treatment, and dropped markedly from the 3rd week to the 6th week of treatment ($P < 0.05$). After treatment with camel placenta, the blood glucose values of the low- and medium-dose group dropped noticeably from the 4th to the 6th week compared with the model group ($P < 0.05$).

Effect of CPP on organ weights of diabetic rats

The weight of the liver, kidney and pancreas in the model and treatment groups was lower than that of rats in the normal group to varying degrees, but the difference was not statistically significant (Table III).

Effect of CPP on blood lipids and serum glucose in diabetic rats

Compared with the normal group, the levels of TG, TCHO and LDL-C of each model group increased to different degrees ($P < 0.05$), while HDL-C was dramatically decreased ($P < 0.05$). Compared with the model group, the TG, TCHO and LDL-C values of the treatment group all went down, and HDL-C meaningfully increased ($P < 0.05$). This indicates that both camel placenta and metformin tablets have hypolipidemic effects. The results of the serum glucose measurement showed that GLUC3 in the serum of each model group increased to varying degrees compared with the normal group ($P < 0.05$). Compared with the model group, GLUC3 in the serum of the metformin group, mid- and low-dose camel placenta group decreased demonstrably ($P < 0.05$) (Table IV). The metformin and low-dose CPP treatments were effective in reducing blood glucose in STZ-induced diabetic rats.

Table III. Effect of CPP on the weight of liver, kidney and pancreas of diabetic rats ($\bar{x}$ ±s, *n*= 10).

Groups/ Organ weight	Liver	Kidney	Pancreas
Normal group	4.11±0.61	14.79±2.49	2.92±0.46
Model group	3.20±0.80	11.74±2.11	2.09±0.46
Metformin group	3.69±0.48	12.48±1.20	2.85±0.22
Camel placenta (high)	3.91±0.59	12.20±1.55	2.57±0.13
Camel placenta (medium)	3.79±0.48	12.44±0.49	2.48±0.13
Camel placenta (low)	3.88±0.54	11.74±2.11	2.51±0.14

Compared with normal group, $^{**}P < 0.01$, $^{*}P < 0.05$; Compared with model group, $^{\#\#}P < 0.01$, $^{\#}P < 0.05$.

Table IV. Effect of CPP on blood lipids and serum glucose in diabetic rats ($\bar{x}$ ±s, n = 10, nmol/L).

Groups	TG	TCHO	LDL-C	HDL-C	GLUC3
Normal group	2.51±0.12	0.62±0.02	0.41±0.03	1.82±0.42	4.68±1.06
Model group	4.76±1.11*	2.81±0.53*	2.36±0.69**	0.96±0.06*	21.84±5.0**
Metformin group	2.70±0.78$^{\#*}$	1.56±0.44$^{\#*}$	1.18±0.26$^{\#**}$	1.37±0.23$^{\#}$	7.77±2.1$^{\#\#**}$
Camel placenta (high)	3.28±1.13$^{\#*}$	2.11±0.55*	1.33±0.16$^{\#**}$	1.32±0.13$^{\#}$	16.1±4.2*
Camel placenta (medium)	3.16±1.02$^{\#*}$	1.95±0.46$^{\#*}$	1.47±0.21$^{\#**}$	1.44±0.19$^{\#}$	11.4±4.0$^{\#*}$
Camel placenta (low)	2.89±0.90$^{\#}$	1.78±0.52$^{\#*}$	1.26±0.21$^{\#**}$	1.64±0.30$^{\#}$	7.2±2.0$^{\#}$

Compared with normal group, $^{**}P < 0.01$, $^{*}P < 0.05$; Compared with model group, $^{\#\#}P < 0.01$, $^{\#}P < 0.05$. TG, triglycerides; TCHO, total cholesterol; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; GLUC3, glucose tolerance, 3 h.

Effect of CPP on HbALc and INS in the serum of diabetic rats

The HbALc level in each model group rose to varying degrees compared with the normal group, while the HbALc level in each treatment group fell to varying degrees compared with the model group, among which the metformin and high-, medium- and low-dose camel placenta groups all decreased distinctively ($P < 0.01$). The fasting INS level in each model group increased to varying degrees compared with the normal group ($P < 0.05$), while metformin and camel placenta did not affect the INS after treatment ($P > 0.05$) (Table V).

Table V. Effect of CPP on GHbALc and INS in diabetic rats ($\bar{x}$ ±s, n = 10).

Groups	GHbALc (nmol·L^{-1})	INS (mU·L^{-1})
Normal group	900.2±219.5	15.8±3.2
Model group	3284.76±311.3*	44.6±5.3*
Metformin group	992.3±178.0$^{\#\#}$	39.1±4.2*
Camel placenta (high)	1401.7±111.3$^{\#\#*}$	43.4±5.5*
Camel placenta (medium)	1136±152.0$^{\#\#}$	45.7±9.6*
Camel placenta (low)	1010.9±209.4$^{\#\#}$	38.8±7.2*

Compared with normal group, $^{**}P < 0.01$, $^{*}P < 0.05$; Compared with model group, $^{\#\#}P < 0.01$, $^{\#}P < 0.05$. GHbALC, glycated hemoglobin A1c; INS, insulin (?).

Table VI. Effect of CPP on the expression of SGLT2 and GLUT2 proteins and mRNA levels in the kidney of diabetic rats ($\bar{x}$±s, n = 10).

Groups	SGLT2	GLUT2
Expression of proteins		
Normal group	0.42±0.05	0.68±0.21
Model group	2.18±0.30**	2.66±0.34*
Metformin group	1.83±0.41**	2.81±0.82*
Camel placenta (high)	1.73±0.43**	2.14±0.53*
Camel placenta (medium)	0.96±0.30$^{\#\#}$	1.37±0.26$^{\#}$
Camel placenta (low)	0.66±0.24$^{\#\#}$	1.08±0.25$^{\#}$
mRNA levels		
Normal group	11.54±3.01	3.87±1.21
Model group	24.18±6.23**	9.66±3.18*
Metformin group	24.93±8.11**	9.57±2.06*
Camel placenta (high)	17.32±5.48*	7.89±2.43*
Camel placenta (medium)	15.77±6.02*	8.22±2.62*
Camel placenta (low)	10.66±3.05$^{\#\#}$	5.08±2.15$^{\#}$

Compared with normal group, $^{**}P < 0.01$, $^{*}P < 0.05$; Compared with model group, $^{\#\#}P < 0.01$, $^{\#}P < 0.05$.

Effect of CPP on the expression of SGLT2 and GLUT2 protein in the diabetic rat kidney

SGLT2 and GLUT2 protein expression in each model group expanded to varying degrees compared with the normal group and decreased markedly in the medium- and low-dose camel placenta treatment groups compared with the model group ($P < 0.05$) (Table VI, Fig. 2). There was no statistically significant difference between the high-dose camel placenta and metformin groups ($P > 0.05$).

Effect of CPP on the expression of SGLT2 and GLUT2 mRNA in the diabetic rat kidney

The expression of SGLT2 mRNA and GLUT2 mRNA in the model and treatment groups was reduced to varying degrees compared with the normal group ($P < 0.05$) (Table VI). Compared with the model group, the low-dose camel placenta group showed a statistical reduction ($P < 0.05$). There was no notable difference between the metformin group and the high- and medium-dose camel placenta groups.

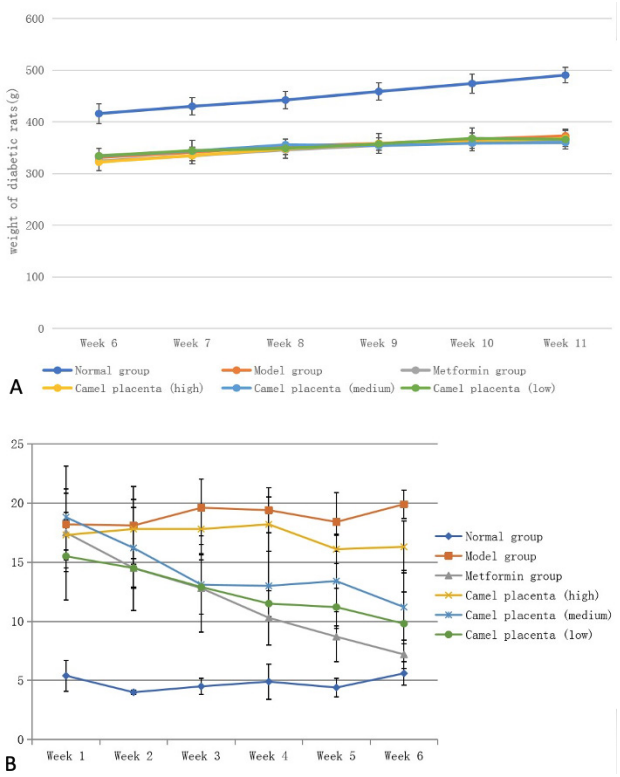

Fig. 2. Effect of CPP on the expression of SGLT2 and GLUT2 proteins in the kidney of diabetic rats.
A: Compared with normal group, $^{**}P < 0.01$, $^{*}P < 0.05$; Compared with model group, $^{\#\#}P < 0.01$, $^{\#}P < 0.05$.

DISCUSSION

Previous studies indicated that STZ combined with high-fat and high-sugar diets can establish a more stable animal model of type 2 diabetes (Gan *et al*., 2020; Sang and Zhang, 2019; Li *et al*., 2019). Our studies indicate that the rats represented a higher food intake and urine output as well as less weight with mental depression and a slightly yellowish coat, consistent with the symptoms of type 2 diabetic patients.

The pathogenesis of T2DM has not been fully clarified. The main pathophysiological changes associated with T2DM include β cell dysfunction and insulin resistance; glucose metabolism disorder, elevated blood glucose and multiple organ system damage are the main manifestations (Bian *et al*., 2019). STZ leads to pancreatic cancer by reactive oxygen species mechanism, oxidative damage of cells and nitric oxide β cell cytotoxicity, resulting in β cell dysfunction and influencing insulin secretion (Rao and Mohan, 2017).

The kidney also plays an important role in blood glucose control (Pecoits-Filho *et al*., 2016). Three membrane proteins are responsible for glucose absorption from the glomerular filtrate of the proximal tubule: the sodium-glucose cotransport proteins SGLT1 and SGLT2 in the parietal membrane and the single transporter GLUT2 in the basolateral membrane (Ghezzi *et al*., 2018). SGLT1 is a glucose transporter in the apical membrane of the small intestine, which is responsible for transporting glucose from the intestinal cavity, while SGLT2 and GLUT2 in the proximal renal tubule play a key role in glucose reabsorption and are associated with the development of type 2 diabetes (Dalli *et al*., 2021; Jiang *et al*., 2019).

The study of Hussain *et al*. (2021) revealed that camel milk could act as an alternative treatment regimen for diabetes therapy. Previous studies indicated that dried CPP can dramatically reduce food intake, inhibit appetite, improve abdominal obesity and reduce blood glucose in spontaneous diabetic mice (Bao *et al*., 2022). The results of our group show that STZ-induced type 2 diabetic rats treated with CPP meaningfully reduced blood glucose, glycated haemoglobin and renal SGLT2 and GLUT2 protein expression. Compared with the model group, both SGLT2 mRNA and GLUT2 mRNA expression within the treatment group were distinctively down-regulated, especially in the low-dose group. Notably, camel placenta fostered the analogous efficacy and characteristics to metformin in STZ-induced diabetic rats. The results of the present study suggest that CPP can effectively reduce blood glucose in STZ-induced experimental diabetic rats, and its hypoglycaemic mechanism may be related to the down-regulation of the expression of glucose transporter proteins SGLT2 and GLUT2 in the kidney, specifically reducing the blood glucose by lowering the glucose reabsorption.

This study has some limitations, i.e., the mechanism is an animal experiment. In addition, a study showed that patients given SGLT2 inhibitors developed phenomena such as high anion gap acidosis, despite being in a normal glycaemic state (Wang and Isom, 2020). Therefore, in order to ensure the safety of clinical use, the question of lowering blood glucose through CPP causing a similar high anion gap acidosis, its specific dose and side effects need to be further studied. To sum up, this study provides a new idea and theoretical basis for the treatment of type 2 diabetes.

CONCLUSION

In conclusion, this study shows that CPP has a hypoglycaemic effect, and its hypoglycaemic mechanism may reduce glucose reabsorption by inhibiting the expression of SGLT2 and GLUT2. Considering its satisfactory efficacy and hypoglycaemic mechanism, it is necessary to promote follow-up studies on clinical translation of CPP and explore novel therapies for diabetic patients. As a whole, we provided a novel theoretical basis for the application of CPP in reducing blood glucose.

Funding

Inner Mongolia Minzu University Phd Research start-up Fund Project (BS454).

Ethical statement

The study was approved by the Ethics Committee of Inner Mongolia Minzu University.

Data availability

All data generated or analyzed during this study are included in this published article.

Statement of conflict of interest

The authors have declared no conflict of interest.

REFERENCES

Ao, D.D., Lg, A., and Chen, W.Y., 2019. Advance of *Mongolian medicine* Haliyasu in preventing and treating diabetes mellitus. *J. Med. Pharm. Chin. Minorities,* **25**: 49-51.

Bai, Q.Y., Su-Rong, Z.B., and Su-He, B.L., 1990. Encyclopedia of Chinese medicine (Mongolian medicine). *Shanghai Sci. Technol. Press*, **1990**: 89.

Bao, S., Wang, X., Ma, Q., Wei, C., Nan, J., and Ao,

W., 2022. Mongolian medicine in treating type 2 diabetes mellitus combined with nonalcoholic fatty liver disease via FXR/LXR-mediated P2X7R/NLRP3/NF-κB pathway activation. *Chin. Herb. Med*., **14**: 367–375. https://doi.org/10.1016/j.chmed.2022.06.003

Bian, C., Bai, B., Gao, Q., Li, S., and Zhao, Y., 2019. 17β-estradiol regulates glucose metabolism and insulin secretion in rat islet β cells through GPER and Akt/mTOR/GLUT2 pathway. *Front. Endocrinol.* (Lausanne), **10**: 531. https://doi.org/10.3389/fendo.2019.00531

Chen, W.Y., Alaga, Wuriga, and Odede. 2019. Research progress and clinical application of Mongolian medicine camel placenta dry powder. *J. Med. Pharma. Chin. Minorit*., **25**: 56-58.

Choi, S.J., and Kim, D.I., 2019. To evaluate the efficacy and safety of PLC in perimenopausal or postmenopausal women with Hot Flashes: Study protocol for a randomized controlled trial. *Trials*, **20**: 415. https://doi.org/10.1186/s13063-019-3482-5

Cui, Y., 2016. *The research of effect of Fufang Tangyisheng on type 2 diabetic and Ki67/INS in islet β cells of mouse*. Shandong University of Traditional Chinese Medicine, https://kns.cnki.net/kcms/detail/detail.aspx?FileName=1016321332.nhandDbName=CMFD2017

Dai, Y.L., Chen, X.H., Ding, H.L., Li, M.L., Pang, S.Q., and Liu, W.N., 2021. Effects of Shuyu gruel on the glucose metabolism and islet function of type 2 diabetic model rats. *J. Tradit. Chin. Med*., **18**: 1628-1634.

Dalli, M., Daoudi, N.E., Azizi, S.E., Benouda, H., Bnouham, M., and Gseyra, N., 2021. Chemical Composition analysis using HPLC-UV/GC-MS and inhibitory activity of different *Nigella sativa* fractions on pancreatic α-amylase and intestinal glucose absorption. *Biomed. Res. Int*., **2021**: 9979419. https://doi.org/10.1155/2021/9979419

Gan, Y.L., Han, X.C., Liu, C.H., Wang, Y., Wang, S.J., and Liu, L.Q., 2020. Progress in the establishment of rat models of type 2 diabetes. *West. J. Tradit. Chin. Med*., **33**: 152-154.

Ghezzi, C., Loo, D.D.F., and Wright, E.M., 2018. Physiology of renal glucose handling via SGLT1, SGLT2 and GLUT2. *Diabetologia*, **61**: 2087-2097. https://doi.org/10.1007/s00125-018-4656-5

Gloyn, A.L., and Drucker, D.J., 2018. Precision medicine in the management of type 2 diabetes. *Lancet Diabetes Endocrinol*., **6**: 891–900. https://doi.org/10.1016/S2213-8587(18)30052-4

Heo, J.H., Heo, Y., Lee, H.J., Kim, M., and Shin, H.Y., 2018. Topical anti-inflammatory and anti-oxidative effects of porcine placenta extracts on 2, 4-dinitrochlorobenzene induced contact dermatitis. *BMC Complement. Altern. Med*., **18**: 331. https://doi.org/10.1186/s12906-018-2396-1

Hussain, H., Wattoo, F.H., Wattoo, M.H.S., Gulfraz, M., Masud, T., Shah, I., Ali, S., and Alavi, S.E., 2021. Camel milk as an alternative treatment regimen for diabetes therapy. *Fd. Sci. Nutr*., **9**: 1347-1356. https://doi.org/10.1002/fsn3.2078

Jiang, Y.K., Xin, K.Y., Ge, H.W., Kong, F.J., and Zhao, G., 2019. Upregulation of renal GLUT2 and SGLT2 is involved in high-fat diet-induced gestational diabetes in mice. *Diabetes Metab. Syndr. Obes*., **12**: 2095-2105. https://doi.org/10.2147/DMSO.S221396

Li, S., Huang, Q., Zhang, L., Qiao, X.F., Zhang, Y.Y., and Tang, F.S., 2019. Effect of CAPE-pNO2 against type 2 diabetes mellitus via the AMPK/GLUT4/ GSK3β/PPARα pathway in HFD/STZ-induced diabetic mice. *Eur. J. Pharmacol*., **853**: 1-10. https://doi.org/10.1016/j.ejphar.2019.03.027

Lin, H.B., Lin, Y.H., Zhang, J.Y., Guo, W.J., Ovcjak, A., You, Z.J., Feng, Z.P., Sun, H.S., Li, F.X., and Zhang, H.F., 2021. NLRP3 inflammasome: A potential target in isoflurane pretreatment alleviates stroke-induced retinal injury in diabetes. *Front. Cell Neurosci*., **15**: 697449. https://doi.org/10.3389/fncel.2021.697449

Nagae, M., Nishio, T., Ohnuki, K., and Shimizu, K., 2022. Effects of oral administration of equine placental extract supplement on the facial skin of healthy adult women: A randomized, double-blind, placebo-controlled study. *Hlth. Sci. Rep*., **5**: e522. https://doi.org/10.1002/hsr2.522

Pecoits-Filho, R., Abensur, H., Betônico, C.C., Machado, A.D., Parente, E.B., Queiroz, M., Salles, J.E.N., Titan, S., and Sergio, V., 2016. Interactions between kidney disease and diabetes: Dangerous liaisons. *Diabetol. Metab. Syndr*., **8**: 50. https://doi.org/10.1186/s13098-016-0159-z

Prince, C.S., Maloyan, A., and Myatt, L., 2018. Tropomyosin receptor kinase B agonist, 7, 8-dihydroxyflavone, improves mitochondrial respiration in placentas from obese women. *Reprod. Sci*., **25**: 452-462. https://doi.org/10.1177/1933719117716776

Rao, P.S., and Mohan, G.K., 2017. *In vitro* alpha-amylase inhibition and *in vivo* antioxidant potential of Momordica dioica seeds in streptozotocin-induced oxidative stress in diabetic rats. *Saudi J.*

biol. Sci., **24**: 1262-1267. https://doi.org/10.1016/j.sjbs.2016.01.010

Saeedi, P., Petersohn, I., Salpea, P., Malanda, B., Karuranga, S., Unwin, N., Colagiuri, S., Guariguata, L., Motala, A.A., Ogurtsova, K., Shaw, J.E., Bright, D., Williams, R. and IDF Diabetes Atlas Committee. 2019. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res. Clin. Pract*., **157**: 107843. https://doi.org/10.1016/j.diabres.2019.107843

Sang, Y.X., and Zhang, J.J., 2019. Establishment of insulin resistance rat model induced by diet combined with STZ. *J. Guangdong Pharm. Univ*., **35**: 789-792+808.

Sinclair, A.J., Abdelhafiz, A.H., Forbes, A., and Munshi, M., 2019. Evidence based diabetes care for older people with Type 2 diabetes: A critical review. *Diabet Med*., **36**: 399–413. https://doi.org/10.1111/dme.13859

Wang, K.M., and Isom, R.T., 2020. SGLT2 Inhibitor induced euglycemic diabetic ketoacidosis: A case report. *Kidney Med*., **2**: 218-221. https://doi.org/10.1016/j.xkme.2019.12.006

Wen, L.M., Xu, Y.L., Li, Z., Zheng, Y.J., and Guo, W.F., 2018. Study on the effects and mechanism of astragalus liuyi decoction on type 2 diabetes mellitus rats. *J. Chin. Med. Mater*., **3**: 699-702.

Zhang, S.W., and Huang, D.P., 2018. Effects of pig placenta powder on reproductive performance, serum immunity, reproductive hormone and milk composition of lactating sows. *Anim. Nutr*., **30**: 4113-4120. https://kns.cnki.net/kcms/detail/detail.aspx?FileName=DWYX201810037andDbName=CJFQ2018

Zhang, X.M., He, J.R., Hu, C.H., and Xu, K., 2019. The effects of hedysarum polybotyssaccharide joined with irbesartan on myocardial fibrosis of type two diabetic rats. *West. J. Tradit. Chin. Med*., **11**: 12-16. https://kns.cnki.net/kcms/detail/detail.aspx?FileName=GSZY201911004andDbName=CJFQ2019