Research Paper

Analysis of the Effect of Grain Amaranth Hypoglycemic Powder in Type 2 Diabetes Mellitus

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This study was to analyze the effects of grain amaranth hypoglycemic powder on blood glucose and oxidative stress in patients with type 2 diabetes mellitus. A total of 100 type 2 diabetes mellitus patients admitted to our hospital from March 2020 to March 2021 were randomly divided into an observation group and a control group, with 50 patients in each group. The control group was treated with metformin tablets orally and the observation group was additionally treated with grain amaranth hypoglycemic powder and both were treated for 3 mo. Fasting plasma glucose, hemoglobin A1c, 2 h postprandial blood glucose, total cholesterol, triglyceride, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, homeostatic model assessment for insulin resistance, fasting insulin, homeostasis model assessment-beta, malondialdehyde, reactive oxygen species, glutathione peroxidase, risk of complications and adverse reactions were observed. After 1 mo and 3 mo of treatment, fasting plasma glucose, hemoglobin A1c, 2 h postprandial blood glucose, total cholesterol, triglyceride, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, homeostatic model assessment for insulin resistance, fasting insulin, homeostasis model assessment-beta, malondialdehyde and reactive oxygen species in the observation group were lower, whereas high-density lipoprotein cholesterol, homeostatic model assessment for insulin resistance and glutathione peroxidase were higher than those in the control group. After 3 mo of treatment, the observation group was at low risk of developing complications and had no difference in the incidence of adverse reactions. Grain amaranth hypoglycemic powder can effectively reduce oxidative stress, improve insulin resistance, regulate glucose and lipids, and reduce the risk of complications in patients with type 2 diabetes mellitus.

Key words: Grain amaranth hypoglycemic powder, type 2 diabetes mellitus, blood glucose, oxidative stress, insulin

In recent years, Diabetes Mellitus (DM) has become the third largest chronic non-communicable disease after cardiovascular and cerebrovascular diseases and tumors. Type 2 Diabetes Mellitus (T2DM) accounting for more than 90 % of diabetes is increasing year by year[1,2]. The relationship between oxidative stress and insulin resistance and islet beta (β)-cell damage in patients with T2DM has attracted much attention[3]. Studies have reported that oxidative stress can stimulate and inhibit the activity of the insulin gene promoter, damage mitochondria and islet β-cells, affect insulin synthesis and signaling pathways, and cause islet beta cell dysfunction[4,5]. Inhibiting the oxidative stress-inflammatory state in patients with diabetes can effectively improve insulin resistance, abnormal glucose metabolism and vascular function[6]. Plants are rich in a variety of antioxidant active substances, which can reduce the levels of lipid peroxidation and oxidative stress markers in diabetic patients[7]. Grain amaranth belongs to the amaranth plant and its active ingredients, polyphenols, have the functions of lowering blood glucose, anti-oxidation, and regulating blood lipids[8]. Grain amaranth hypoglycemic powder is a hypoglycemic preparation composed of grain amaranth, aweto, common yam rhizome and lobed kudzuvine root, which can inhibit oxidative stress and reduce the generation of metabolites and oxygen free radicals. In view of this, this study observed the efficacy and safety of grain amaranth hypoglycemic powder in the treatment of T2DM patients.

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MATERIALS AND METHODS

General information:

This study was approved by the hospital ethics committee (No: 2019-241) and 100 patients with T2DM who were admitted to our hospital from March 2020 to March 2021 were selected and randomly divided into an observation group and a control group, with 50 patients in each. The two groups had no significant difference in general data as shown in Table 1.

Selection criteria:

Inclusion criteria: Patients are diagnosed for the first time; good compliance and cooperation with treatment and follow-up; have never taken grain amaranth hypoglycemic powder before and patients have signed informed consent.

Exclusion criteria: Patients who participate in other experimental studies during the same period to affect the curative effect; a history of hyperosmolar coma or ketoacidosis in the past 4 w; a history of T2DM complications; any serious heart, liver, kidney dysfunction and malignant tumor; have treated with estrogen, glucocorticoid drugs or immunosuppressive drugs; allergic constitution and contraindications to the drugs used in this study.

Methods:

All were given health education, including lifestyle adjustment, moderate-intensity aerobic exercise, diabetic diet, weight control, drinking and smoking prohibition and staying in a good mood.

Control group: Oral metformin tablets (Bristo-Myers Squibb Company, No. H20023370, specification 0.5 g), 0.5 g/time, 2 times/d, for 3 mo.

Observation group: Oral metformin tablets combined with oral grain amaranth hypoglycemic powder (Wuhan GuangAo Technology Co., Ltd., production license number: SC10642112200062, implementation standard: GB7101-2015, specification 30 g), 1 pack/time, 2 times/d, for 3 mo.

Indicators:

Laboratory indicators: Fasting venous blood was collected before treatment and after 3 mo of treatment, respectively. Fasting Plasma Glucose (FPG), Hemoglobin A1c (HbA1c), 2 h Postprandial Blood Glucose (2hPG), Total Cholesterol (TC), Triglyceride (TG), Low-Density Lipoprotein Cholesterol (LDL-C) and High-Density Lipoprotein Cholesterol (HDL-C) were measured by an automatic biochemical analyzer. Reactive Oxygen Species (ROS) was tested by the chemical colorimetric method, Malondialdehyde (MDA) was tested by the thiobarbituric acid method and Glutathione Peroxidase (GSH-Px) was tested by enzyme-linked immunosorbent assay. Fasting Insulin (FINS) was determined by radioimmunoassay and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR)=(FPG×FINS)/22.5 and Homeostasis Model Assessment-β (HOMA-β)=20×FINS/(FPG-3.5) were calculated. GSH-Px, MDA and ROS detection kits were purchased from Nanjing Jiancheng Biological Co., Ltd.

Risk of complications: After 3 mo, the risk of complications in patients was assessed using the EzScan human biostimulation feedback instrument. High-intensity exercise was stopped 2 h before the examination. The electrodes are placed on the soles of the feet and palms of the patient, and the patient stands still for 2-3 min. Risk of peripheral nerve damage includes mild (41 %-60 %), moderate (61 %-80 %), high (81 %-100 %); risk of renal dysfunction includes mild (89 %-60 %), moderate (59 %-30 %), high (29 %-0 %) and risk of vascular complications includes mild (26 %-50 %), moderate (51 %-75 %) and high (76 %-100 %).

Observation of adverse reactions: The adverse reactions caused by drug use were summarized and the major adverse reactions include gastrointestinal symptoms, hypoglycemia and itchy skin.

Statistical analysis:

All data were statistically analyzed by Statistical Package for the Social Sciences (SPSS) 22.0 software and processed with SPSS 23.0 software. Measurement data ($\bar{x}\pm s$) were evaluated by t-test, count data (n [%]) were evaluated by χ^2 test and rank data were evaluated by Relative to an Identified Distribution (RIDIT) analysis and $p<0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

Comparison of blood glucose levels between the two groups was shown in Table 2. Discrepancies in FPG, HbA1c and 2hPG levels were not significant before administration, but the three were lower after combined administration than single administration (fig. 1).

Comparison of blood lipid levels between the two groups was shown in Table 3. TC, TGs, LDL-C and HDL-C exhibited no significant difference before administration, but the former three were reduced and the last was enhanced after combined administration with oral grain amaranth hypoglycemic powder.

Comparison of islet function between the two groups was shown in Table 4. Before treatment, islet function suggested no difference between the two groups. FINS and HOMA-IR were decreased and HOMA-β was promoted more effectively after combined administration with oral grain amaranth hypoglycemic powder.

Comparison of oxidative stress between the two groups was shown in Table 5. Oxidative stress was not significant between the two groups before administration. GSH-Px was more effectively elevated and MDA and ROS were suppressed after combined administration with oral grain amaranth hypoglycemic powder.

Comparison of the risk of complications between the two groups was shown in Table 6. After 3 mo, combined administration with oral grain amaranth hypoglycemic powder caused a lower risk of complications in patients than single administration.

Comparison of adverse reactions between the two groups was shown in Table 7. Combined administration and single administration caused no significant difference in the incidence of adverse reactions.

At present, metformin is the basic drug for the treatment of diabetes to effectively control blood glucose and insulin resistance and achieve an anti-glycemic effect[9,10]. Fundamentally solving the causes of diabetes, restoring pancreatic islet function and reducing oxidative stress are potentially effective to control blood glucose and reduce insulin usage[11-13]. Therefore, it is imperative to find a safe and effective new therapy for T2DM patients.

Grain amaranth hypoglycemic powder is a

TABLE 1: COMPARISON OF GENERAL INFORMATION BETWEEN THE TWO GROUPS

Project	Observation group (n=50)	Control group (n=50)	t	p
Male/Female	28/22	26/24	0.161	0.688
Age (Year)	20~69 (50.23±7.45)	21~72 (52.11±8.36)	1.187	0.238
Education			0.038	0.97
Junior high school and below	9 (18.00)	7 (14.00)		
High school or technical secondary school	17 (34.00)	20 (40.00)		
College degree and above	24 (48.00)	23 (46.00)		
History of chronic disease			0.657	0.418
Yes	27 (54.00)	31 (62.00)		
No	23 (46.00)	19 (38.00)		
Risk of complications			0.599	0.549
Mild	13 (26.00)	10 (20.00)		
Moderate	20 (40.00)	21 (42.00)		
High	17 (34.00)	19 (38.00)		
Body Mass Index (BMI, kg/m^2)			0.592	0.554
18.5-23.9	23 (46.00)	26 (52.00)		
24.0-27.9	16 (32.00)	15 (30.00)		
≥28.0	11 (22.00)	9 (18.00)		
Smoking			0.644	0.422
Yes	29 (58.00)	25 (50.00)		
No	21 (42.00)	25 (50.00)		
Drinking			0.649	0.42
Yes	26 (52.00)	30 (60.00)		
No	24 (48.00)	20 (40.00)		

TABLE 2: COMPARISON OF BLOOD GLUCOSE LEVELS BETWEEN THE TWO GROUPS

Time	Group	n	FPG (mmol/l)	HbA1c (%)	2hPG (mmol/l)
Before treatment	Observation group	50	9.66±1.43	9.25±0.78	13.27±2.13
	Control group	50	9.88±1.47	9.14±0.73	13.22±2.10
	t		0.289	0.648	0.602
	p		0.736	0.591	0.564
1 mo after treatment	Observation group	50	8.13±0.95[a]	8.07±0.67[a]	11.30±1.60[a]
	Control group	50	9.12±1.15[a]	8.62±0.73[a]	12.14±1.67[a]
	t		5.169	3.169	2.166
	p		<0.001	<0.001	<0.001
3 mo after treatment	Observation group	50	6.13±0.91[a]	7.11±0.75[a]	8.60±1.11[a]
	Control group	50	7.16±0.94[a]	8.04±0.77[a]	9.96±1.30[a]
	t		6.798	5.984	6.853
	p		<0.001	<0.001	<0.001

Note: Compared with the same group before treatment, [a]p<0.01

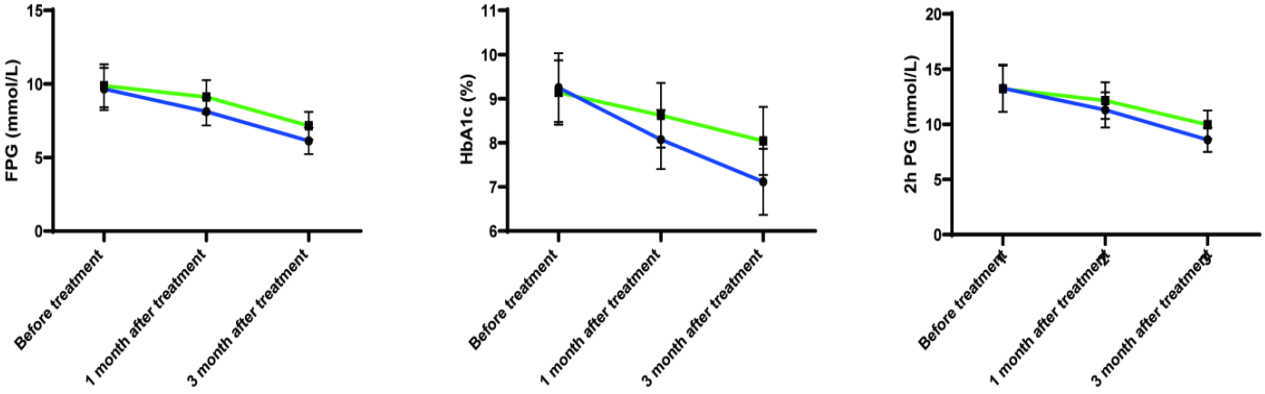

Fig. 1: Changes in blood glucose levels between the two groups, ( ) Observation group and ( ) Control group

TABLE 3: COMPARISON OF BLOOD LIPID LEVELS BETWEEN THE TWO GROUPS (mmol/l)

Time	Group	n	TC	HDL-C	LDL-C	TGs
Before treatment	Observation group	50	6.00±2.12	1.15±0.30	4.15±0.75	3.48±0.85
	Control group	50	6.15±1.99	1.13±0.31	4.05±0.68	3.60±0.92
	t		0.365	0.282	0.699	0.732
	p		0.716	0.779	0.457	0.401
1 mo after treatment	Observation group	50	4.56±1.32[a]	1.28±0.20[a]	3.00±0.70[a]	1.85±0.63[a]
	Control group	50	5.36±1.41[a]	1.20±0.20a	3.74±0.62a	2.39±0.80[a]
	t		2.929	1.948	5.596	3.75
	p		0.004	0.048	<0.001	<0.001
3 mo after treatment	Observation group	50	3.43±1.11[a]	1.35±0.23[b]	2.30±0.51[a]	1.50±0.42[a]
	Control group	50	4.48±1.24[a]	1.26±0.20[b]	2.91±0.83[a]	1.96±0.56[a]
	t		4.461	2.088	4.248	4.467
	p		<0.001	0.039	<0.001	<0.001

Note: Compared with the same group before treatment, [a]p<0.01 and [b]p<0.05

TABLE 4: COMPARISON OF ISLET FUNCTION BETWEEN THE TWO GROUPS (mmol/l)

Time	Group	n	FINS	HOMA-IR	HOMA-β
Before treatment	Observation group	50	7.65±1.65	3.33±1.32	24.36±5.33
	Control group	50	7.75±1.44	3.39±1.25	24.41±4.85
	t		0.323	0.233	0.049
	p		0.748	0.816	0.961
1 mo after treatment	Observation group	50	6.62±1.00[a]	2.43±0.98[a]	29.09±5.10[a]
	Control group	50	7.10±1.04[a]	2.87±0.92[a]	25.36±5.65[a]
	t		2.675	2.315	3.465
	p		0.014	0.023	0.002
3 mo after treatment	Observation group	50	6.08±1.12[b]	1.66±0.73[b]	45.89±4.32[b]
	Control group	50	6.76±1.03[b]	2.21±0.82[ab]	35.03±5.98[b]
	t		3.165	3.542	10.409
	p		0.002	0.001	<0.001

Note: Compared with the same group before treatment, [a]p<0.05 and [b]p<0.01

TABLE 5: COMPARISON OF OXIDATIVE STRESS BETWEEN THE TWO GROUPS

Time	Group	n	MDA (nmol/ml)	ROS (U/ml)	GSH-Px (U/ml)
Before treatment	Observation group	50	3.63±1.25	503.25±42.32	68.56±5.78
	Control group	50	3.57±1.36	506.47±45.78	70.12±6.63
	t		0.23	0.365	1.254
	p		0.819	0.716	0.213
1 mo after treatment	Observation group	50	2.66±1.01[a]	423.69±35.54[a]	79.86±6.10[a]
	Control group	50	3.11±0.98[a]	477.52±32.10[a]	75.32±5.66[a]
	t		3.124	7.948	3.858
	p		<0.001	<0.001	<0.001
3 mo after treatment	Observation group	50	2.45±0.74[a]	365.25±24.26[a]	84.32±4.78[a]
	Control group	50	2.98±0.63[a]	401.22±29.74[a]	79.55±5.10[a]
	t		3.856	6.627	4.825
	p		<0.001	<0.001	<0.001

Note: Compared with the same group before treatment, [a]p<0.05

TABLE 6: COMPARISON OF THE RISK OF COMPLICATIONS BETWEEN THE TWO GROUPS [n (%)]

Group	n	Risk of peripheral nerve damage			Risk of renal dysfunction			Risk of vascular complications		
		Mild	Moderate	High	Mild	Moderate	High	Mild	Moderate	High
Observation group	50	32 (64.00)	10 (20.00)	8 (16.00)	36 (72.00)	8 (16.00)	6 (12.00)	30 (60.00)	15 (30.00)	5 (10.00)
Control group	50	15 (30.00)	22 (44.00)	13 (26.00)	17 (34.00)	23 (46.00)	10 (20.00)	20 (40.00)	20 (40.00)	10 (20.00)
χ^2		2.785			3.09			1.915		
p		0.003			0.002			0.046		

TABLE 7: COMPARISON OF ADVERSE REACTIONS BETWEEN THE TWO GROUPS [n (%)]

Group	n	Gastrointestinal symptoms	Hypoglycemia	Itchy skin	Incidence
Observation group	50	2 (4.00)	1 (20.00)	3 (6.00)	6 (12.00)
Control group	50	3 (6.00)	2 (4.00)	2 (4.00)	7 (14.00)
χ^2					0.088
p					0.766

hypoglycemic preparation developed by the Radiation Processing Research Institute of Hubei Academy of Agricultural Sciences in 2003. It is suitable for diabetic patients by exerting a hypoglycemic effect. This study applied it to patients with T2DM and the results showed that after 3 mo of treatment, the blood glucose and blood lipid levels were effectively regulated, suggesting that grain amaranth hypoglycemic powder has a good glucose and lipid regulation effect. Grain amaranth has the characteristics of high quality, high yield, fast growth rate and strong stress resistance. It contains lysine, protein, unsaturated fatty acids and starches necessary for the human body. It is also rich in a variety of physiologically active substances, which can scavenge free radicals in the body and has the effect of delaying aging, regulating fat and glucose, etc.[14]. Thanks to the development of emerging genomics and biotechnology, amaranth is gradually widely used in medicine, food and other fields, and has become an important alternative medicinal plant in some developing countries. Tang *et al.*[15] pointed out that the S100 Calcium Binding Protein A1 (S100A1) and calcium content in the liver tissue, kidney and blood of T2DM patients are lower, resulting in the decrease of GSH-Px and MDA activity, and grain amaranth as an alternative drug can improve calcium homeostasis through the calcium signaling pathway to exert its anti-glycemic effect. Velarde-Salcedo *et al.* confirmed that the phenolic compounds in amaranth have the strongest anti-radical properties against 2,2-diphenyl-1-pyridohydrazino radicals, reducing the damage of abnormal blood glucose to the body[16]. In addition, the active ingredient lobed kudzuvine root in grain amaranth hypoglycemic powder is rich in puerarin, which is effective to reduce insulin resistance, improve insulin sensitivity, scavenge free radicals in the body and control blood glucose[17-19]. This study showed that combined administration with grain amaranth hypoglycemic powder lowered FINS and HOMA-IR and heightened HOMA-β.

Oxidative stress is closely related to insulin resistance and islet β-cell damage in patients with T2DM. Oxidative stress can increase the activity of inhibiting the insulin gene promoter, damage mitochondria and islet β-cells, affect the signaling pathway of insulin secretion and synthesis, cause insulin synthesis to decline, cause irreversible damage to islet β-cell function, and ultimately lead to abnormal blood glucose[20,21]. MDA is a product of lipid peroxidation, which affects mitochondrial phosphorylation and electron transport, and is used to reflect the degree of oxidative stress and membrane lipid peroxidation in the body[22]. ROS can scavenge oxygen free radicals, inhibit oxidative stress and protect the stability of cell structure and function. GSH-Px is an enzyme with a free radical-scavenging function and has a strong antioxidant effect[23]. T2DM patients show responses to oxidative stress MDA, ROS and GSH-Px can accurately reflect the oxidative stress status of the body and evaluate T2DM[24]. In this study, the dynamic assessment found that the above oxidative stress factors were gradually improved after combined administration with grain amaranth hypoglycemic powder. In addition, grain amaranth hypoglycemic powder has the functions of lowering blood pressure, improving microcirculation, inhibiting platelet aggregation, reducing plasma endothelin, etc., and can improve insulin sensitivity in patients with T2DM, reduce vascular endothelial cell apoptosis, thereby inhibiting chronic complications of diabetes. In view of this, the EzScan system in this study found that the risk of complications was significantly lower after 3 mo of combined administration with grain amaranth hypoglycemic powder. The use of grain amaranth hypoglycemic powder can help to reduce the risk of diabetes complications, reduce the possibility of diabetes involving other organs and will not significantly increase adverse drug reactions.

To sum up, grain amaranth hypoglycemic powder is a relatively safe hypoglycemic food, as it does not cause complications and adverse reactions. It can improve oxidative stress, effectively control blood glucose and will not cause major damage to the body. However, the sample size of this study is small and the research period is short. In the future, the

sample size can be expanded and the follow-up time of the study can be extended to comprehensively and deeply analyze the hypoglycemic effect of grain amaranth hypoglycemic powder.

Funding:

This study was supported by National Natural Science Foundation of China with approval number of 81673657 and Wuhan Medical Research Project with approval number of WZ20Z08.

Conflict of interests:

The authors declared no conflict of interest.

REFERENCES

1. Kolb H, Martin S. Environmental/lifestyle factors in the pathogenesis and prevention of type 2 diabetes. BMC Med 2017;15(1):1-11.
2. Ojo O. Dietary intake and type 2 diabetes. Nutrients 2019;11(9):2177.
3. Yong J, Han XL, Yong XW. Analysis of pathogen distribution, the oxidative stress index and related factors in patients with type 2 diabetes and a urinary tract infection. J Parasit Biol 2019;14(10):1219-22.
4. Rong XZ, Lin SJ, Wang R. Intervention of total flavonoids of rattan tea on glucose and lipid metabolism and oxidative stress injury in type 2 diabetic rats based on the PI3K/Akt signaling pathway. World J Integr Tradit West Med 2020;15(11):2041-8.
5. Wu XY. Regulatory effect of tetragenous viable *Bifidobacterium* tablets adjuvant therapy on serum inflammatory factors and oxidative stress in newly diagnosed type 2 diabetic patients. Chin J Microecol 2020;32(6):680-3.
6. Wang R, An JL, Zhu YY, Tian YM, Wang R. Correlation between oxidative stress and blood glucose and islet function among patient with different glucose tolerance. Label Immunoassay Clin Med 2019;26(1):23-7.
7. He Y, Huang Y, Guan HY, Wang XM, Luo JJ, Jin W, *et al.* Effect of compound long-qi decoction on peripheral neuropathy in type 2 diabetic rats. Chin Arch Tradit Chin Med 2019;37(11):2694-8.
8. Peng J. Extraction, purification, physicochemical properties and *in vitro* antioxidant activity of polysaccharides from *Amaranthus hybridus* L. Sichuan Agricultural University; 2017.
9. Sanchez-Rangel E, Inzucchi SE. Metformin: Clinical use in type 2 diabetes. Diabetologia 2017;60(9):1586-93.
10. Vallianou NG, Stratigou T, Tsagarakis S. Metformin and gut microbiota: Their interactions and their impact on diabetes. Hormones 2019;18(2):141-4.
11. Linli JH, Wang JP. Research progress on the relationship between sodium-glucose co-transporter 2 inhibitors and oxidative stress in diabetic macrovascular. Chin J Diabetes Mellitus 202;13(1):98-102.
12. Hou LM, Li X, Huo C, Jia X, Yang J, Lei YZ, *et al.* Effects of chronic inflammation and oxidative stress on skeletal muscle mass and strength in elderly patients with type 2 diabetes mellitus. Chin J Geriatr 2021;40(1):39-42.
13. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol 2018;14(2):88-98.
14. Xue LZ. Discuss the studying process and prospect of amaranth grain in food industry briefly. Food Ind 2016;296(5):257-60.
15. Tang Y, Tsao R. Phytochemicals in quinoa and amaranth grains and their antioxidant, anti-inflammatory and potential health beneficial effects: A review. Mol Nutr Food Res 2017;61(7):1568-9.
16. Velarde-Salcedo AJ, Regalado-Rentería E, Velarde-Salcedo R, Juárez-Flores BI, Barrera-Pacheco A, González de Mejía E, *et al.* Consumption of amaranth induces the accumulation of the antioxidant protein paraoxonase/arylesterase 1 and modulates dipeptidyl peptidase IV activity in plasma of streptozotocin-induced hyperglycemic rats. J Nutrigenet Nutrigenomics 2018;10(5):181-93.
17. Zhang C, Wang X, Wang LY, Xu L, Xu C, Zhao SD, et al. Effects of puerarin combined with atorvastatin on adiponectin, inflammatory factors and myocardial fibrosis in rats with type 2 diabetic cardiomyopathy. Mod J Integr Tradit Chin West Med 2020;29(11):1167-71.
18. Tang QL, Gao ZY, Zheng JY, Liao WS, Cao YN. The effect of *Pueraria* alcohol extract on postprandial glycaemia in mice. China Prescr Drug 2019;17(4):36-7.
19. He GX, Ma YH, Liu HY, Zhong Y. Clinical study of puerarin combined with α-lipoic acid in the treatment of diabetes mellitus with carotid atherosclerosis. China Med Herald 2020;17(10):82-5.
20. Lou SX, Liu XY, Zheng WY. Effects of intensive insulin therapy on serum inflammatory factors and oxidative stress in newly diagnosed type 2 diabetic mellitus patients. Chin J Pharmacoepidemiol 2019;28(12):792-5.
21. Poblete-Aro C, Russell-Guzmán J, Parra P, Soto-Muñoz M, Villegas-González B, Cofré-Bola-Dos C, *et al.* Effect of physical exercise on oxidative stress markers in patients with type 2 diabetes mellitus. Rev Med Chil 2018;146(3):362-72.
22. Zhao YP, Sun Z, Liu J, Yuan FY, Sun MM, Su H, *et al.* Protective effect of valsartan combined with alprostadil in the vascular endothelium of patients with T2DM and hypertension and the effect on oxidation substances. Med J Chin People Armed Police Forces 2019;30(10):829-33.
23. Chai SB, Si FC, Wang ZT, Zhang SJ, Liu SY. Yiqi-Yangyin recipe attenuates myocardial ischemia-reperfusion injury in diabetic rats by activation of ERK/Nrf2/HO-1 pathway. Chin J Pathophysiol 2019;35(10):1743-52.
24. Wang Dc, Xiao H, Shu Q .Effects of Bailing capsule combined with simvastatin on oxidation and anti-oxidation imbalance and inflammatory mediator's levels in patients with type 2 diabetic nephropathy. Med Pharma J Chin People Liber Army 2020;32(9):45-9.

This article was originally published in a special issue, "New Research Outcomes in Drug and Health Sciences" Indian J Pharm Sci 2023:85(6) Spl Issue "25-31"