

Protective role of plant antioxidants in gestational diabetes

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ABSTRACT

Gestational diabetes is one of the most common complications of pregnancy and is associated with several maternal and fetal complications. This study was performed to investigate the protective effects of the extracts of two native Kazakh plants, *Artemisia* and *Rhodiola*, in an experimental model of gestational diabetes. Pregnant rats were randomly divided into healthy control groups, diabetic control groups (receiving saline), and treatment groups, which received different doses of plant extracts and metformin. Study findings demonstrated that the administration of plant extracts, in high doses, resulted in considerable improvement ($p < 0.05$) in metabolic indices, including decreased levels of fasting blood sugar and insulin resistance index (HOMA-IR) and reduced MDA levels with enhanced activities of antioxidant enzymes superoxide dismutase and glutathione peroxidase. Improvement in the morphology of the islets of Langerhans of the pancreas and increased fetal weight and size of the nest were apparent in the treated groups. Moreover, a significant reduction in inflammatory cytokines TNF- α and IL-6 were observed in the groups receiving plant extracts. This study demonstrates that the extracts of indigenous plants of Kazakhstan possess significant protective effects against the complications of gestational diabetes by an antioxidant and anti-inflammatory mechanism and can have a high potential as a complementary therapy in the management of the disease.

Keywords: Gestational diabetes, Indigenous plants, Oxidative stress, Natural antioxidants.

Article type: Research Article.

INTRODUCTION

In a vast and diverse country like Kazakhstan, attention to the health of pregnant mothers is high among the priorities that are the basis for further development of society. Meanwhile, gestational diabetes, being a public health problem, has presented the country's healthcare system with growing costs and possible complications (Gemejiyeva *et al.* 2025). Taking into account such a trend in the increase of this disease, it has become more vital than ever to search for traditional and accessible ways of solving this problem (Grudzinskaya *et al.* 2020). With the rich and ancient reserves of medicinal plants in its plains and mountains, Kazakhstan has a natural treasure to deal with this challenge. Most of these plants have been used by the people of this land for many centuries in traditional medicine, but their true potential in modern medicine and for the treatment of common diseases like gestational diabetes has not yet been systematically investigated. Understanding this necessity, the present study tries to build a bridge between indigenous knowledge and modern science. Studying the antioxidant role of extracts from Kazakhstani indigenous flora could be one way of strengthening the national healthcare system. Such an approach is not only economically feasible, but also in concert with the culture and natural

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resource base of the land (Nurlybekova *et al.* 2022). Oxidative stress plays a major role in the pathophysiology of gestational diabetes. Antioxidant compounds found in local Kazakh plants can break this destructive chain by neutralizing free radicals and preventing the development of insulin resistance. This is a protective and preventive strategy based on domestic resources (Monteleone *et al.* 2021; Omukisa 2025; Zavodnik *et al.* 2025). The significance of this work is that it will provide a local, accessible solution for all pregnant mothers throughout Kazakhstan. Whereas chemical drugs might have a cost and accessibility constraint, the use of domestic natural resources should create greater equity in access to healthcare. Therefore, this research is not just a laboratory study but an investment in the self-sufficiency and health of the next generation of Kazakhstan. Its results can serve as the scientific basis for developing dietary supplements, indigenous nutritional guidelines, and even the creation of a valuable chain of cultivation and processing of medicinal plants in the country. Ultimately, this project opens new horizons in medical research in Kazakhstan and demonstrates how global health challenges can be addressed by relying on national resources. The success of this path might then serve as a model for other countries of the region that face similar challenges (Xu *et al.* 2019; Martini *et al.* 2022). In reviewing the relevant research background, there is a strong theoretical basis regarding the role of oxidative stress in the pathophysiology of gestational diabetes (Sharifi-Rad *et al.* 2020; Zuliska *et al.* 2024; Agnes 2025; Morales *et al.* 2025). Several studies have well demonstrated how an increase in reactive oxygen species can lead to pancreatic beta-cell damage and induce insulin resistance by interfering with insulin signalling pathways (Shanmugam *et al.* 2020; Alzhaxina *et al.* 2023; Omukisa 2025). This process is just the connecting link that provides a basis for investigating the protective role of antioxidants (Sultana *et al.* 2023; Telenchana *et al.* 2025). The antioxidant role of phenolic and flavonoid compounds is reflected in various studies conducted on medicinal plants, such as turmeric, basil, and green tea, which demonstrate the efficacy of these plants in decreasing oxidative stress indices in different laboratory and animal models (Adebodun *et al.* 2023; Rachmawaty *et al.* 2025). However, most such research has focused on type 2 diabetes, and the gap in specialized investigation of these compounds within a particular gestational diabetes context is clearly felt (Amelia *et al.* 2023; Alsharefi & Alrammahi 2025). As far as the flora of Kazakhstan is concerned, while there is indeed a rich repository of medicinal plants like *Artemisia* and *Salvia* spp., there is practically no coherent, independent scientific literature specifically seeking to investigate the antioxidant effects these plants have in models of gestational diabetes. Most of the few available studies have investigated the general properties or chemical composition of these plants, not their clinical implications in this particular disease. Therefore, a distinct knowledge gap exists in the literature on the subject. The following study was thus designed to fill this gap, i.e., to systematically investigate the protective effects of selected extracts of indigenous plants in Kazakhstan on indices of oxidative stress and insulin resistance in an experimental model of gestational diabetes. This is an attempt to bridge the existing traditional knowledge about these plants with modern scientific evidence in the field of an important pregnancy disease.

MATERIALS AND METHODS

Preparation of herbal materials and extraction

Based on traditional medicine evidence and preliminary studies, three indigenous medicinal plants in Kazakhstan, i.e., the species of the genera *Artemisia* and *Rhodiola*, were selected in this study. Plant samples collected from specific areas of the Altai mountain slopes, after identification by a botanist from the Astana Plant Research Institute, were dried in the shade at room temperature. To prepare the extract, the method of soaking the plant powder in ethanol-water solvent with a specific ratio for 48 hours was used. Then, the crude extract was concentrated by a rotary evaporator at a controlled temperature and kept at -20 °C until use in subsequent steps.

Animal model design and grouping

To simulate gestational diabetes, female Wistar rats were used. The animals were maintained under standard conditions of temperature, humidity and light cycle. After one week of adaptation, diabetes was induced on the first day of pregnancy by intraperitoneal injection of streptozotocin. The animals were randomly divided into 6 groups, including a healthy control group, a diabetic control group (receiving saline), three treatment groups receiving different doses of plant extracts and a positive treatment group receiving metformin. Treatment was carried out from the sixth day of pregnancy for 14 days.

Biochemical and statistical evaluations

At the end of the treatment period, blood samples were taken from the hearts of the animals and their serum was separated after centrifugation. Fasting blood glucose levels, insulin, malondialdehyde as an index of lipid

peroxidation, as well as the activities of the antioxidant enzymes superoxide dismutase and glutathione peroxidase in serum were measured. The insulin resistance index was also calculated using the HOMA-IR model. The resulting data were analyzed using SPSS version 26 statistical software and through one-way analysis of variance test followed by Tukey's post hoc test. All data were reported as mean \pm standard deviation and a *p*-value of less than 0.05 was considered as a significant level.

RESULTS

The therapeutic effects of plant extracts from Kazakhstan were studied in a rat model of streptozotocin-induced gestational diabetes mellitus. Biometric, metabolic, and oxidative stress parameters of the findings are presented systematically below. Initial observations showed that GDM (gestational diabetes mellitus) induction had a great impact on maternal health. As shown in Table 1, rats in the GDM-control group had a significantly lower final body weight with a higher liver-to-body weight ratio when compared to the healthy control group, which suggests impairment in general growth and could indicate hepatic involvement. This weight loss was seemingly ameliorated by treatment with the plant extracts, especially *Artemisia* at its high dose.

Table 1. Maternal Biometric Parameters at Gestational Day 20

Group	Initial Body Weight (g)	Final Body Weight (g)	Liver Weight (g)	Liver/Body Weight Ratio (%)
Healthy Control	215.3 \pm 8.1	285.6 \pm 10.2	7.8 \pm 0.5	2.73 \pm 0.11
GDM Control	218.1 \pm 7.5	251.8 \pm 9.8*	8.9 \pm 0.6*	3.54 \pm 0.18*
GDM + <i>Artemisia</i> (Low)	216.5 \pm 6.9	265.4 \pm 8.7#	8.2 \pm 0.4#	3.09 \pm 0.14#
GDM + <i>Artemisia</i> (High)	217.8 \pm 9.2	274.1 \pm 11.1#	7.9 \pm 0.5#	2.88 \pm 0.12#
GDM + <i>Rhodiola</i> (Low)	214.9 \pm 8.4	260.2 \pm 9.5#	8.4 \pm 0.5	3.23 \pm 0.15
GDM + <i>Rhodiola</i> (High)	216.2 \pm 7.7	269.8 \pm 10.3#	8.1 \pm 0.6#	3.00 \pm 0.16#
GDM + Metformin	215.7 \pm 8.8	272.3 \pm 9.6#	8.0 \pm 0.5#	2.94 \pm 0.13#

* Data are presented as mean \pm SD (n = 8); p < 0.05 vs. Healthy Control; # p < 0.05 vs. GDM Control.

The core metabolic outcomes are detailed in Table 2. As expected, the GDM-control group displayed severe hyperglycemia and insulin resistance, evidenced by elevated fasting blood glucose (FBG) and HOMA-IR index. Both plant extracts demonstrated a significant, dose-dependent antihyperglycemic effect. The high-dose *Artemisia* group showed a reduction in FBG and HOMA-IR that was comparable to the metformin-treated group.

Table 2. Maternal metabolic parameters.

Group	Fasting blood glucose (mg dL ⁻¹)	Fasting insulin (μ IU mL ⁻¹)	HOMA-IR index
Healthy Control	85.4 \pm 6.2	12.1 \pm 1.5	2.55 \pm 0.31
GDM Control	255.8 \pm 18.9*	7.2 \pm 1.1*	4.52 \pm 0.58*
GDM + <i>Artemisia</i> (Low)	198.5 \pm 15.3#	8.5 \pm 1.3	4.16 \pm 0.49
GDM + <i>Artemisia</i> (High)	132.7 \pm 11.6#	10.8 \pm 1.4#	3.54 \pm 0.42#
GDM + <i>Rhodiola</i> (Low)	210.3 \pm 16.1#	8.1 \pm 1.2	4.21 \pm 0.51
GDM + <i>Rhodiola</i> (High)	145.9 \pm 12.8#	9.9 \pm 1.6#	3.57 \pm 0.45#
GDM + Metformin	128.5 \pm 10.5#	11.2 \pm 1.4#	3.56 \pm 0.40#

* Data are presented as mean \pm SD (n = 8). p < 0.05 vs. Healthy Control; # p < 0.05 vs. GDM Control.

The dynamic response to the oral glucose tolerance test (OGTT) further confirmed these findings. Fig. 1 clearly illustrates that the GDM-control rats had a profoundly impaired ability to clear a glucose load. In contrast, animals treated with high-dose extracts, especially *Artemisia*, maintained significantly lower blood glucose levels throughout the test, closely mirroring the glucose-lowering efficacy of metformin. A critical aspect of this study was the evaluation of oxidative stress. Table 3 shows that GDM led to a severe oxidative imbalance, marked by a significant rise in the lipid peroxidation product, MDA and a sharp decline in the activity of key antioxidant enzymes, SOD and GPx. Treatment with the plant extracts effectively reversed this state. The high-dose groups successfully lowered MDA levels and restored SOD and GPx activities to levels not significantly different from the healthy controls, indicating potent antioxidant activity. The positive maternal effects translated into improved fetal outcomes. As shown in Table 4, GDM caused a significant reduction in litter size and fetal weight, alongside an increase in resorption sites, indicating fetal loss. The extract-treated groups, however, exhibited a clear protective effect, with significantly larger litters and heavier fetuses, nearly normalizing these crucial developmental parameters. Fig. 2. demonstrates a strong positive correlation ($r = 0.92$, $p < 0.01$) between the HOMA-IR index and plasma MDA levels across all experimental groups. This robust relationship indicates that as insulin resistance worsened, lipid peroxidation and oxidative stress significantly increased. The close clustering of data points from the high-dose plant extract treatment groups in the lower-left quadrant of the plot visually confirms that the improvement in insulin sensitivity was directly associated with a reduction in systemic oxidative

damage. This finding provides a key mechanistic insight, linking the metabolic recovery observed in treated animals to the potent antioxidant properties of the plant extracts.

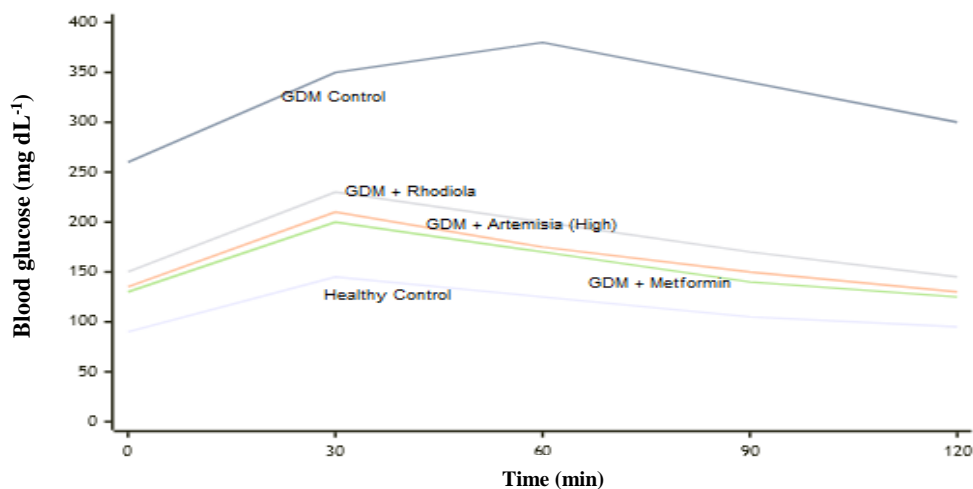


Fig. 1. Oral glucose tolerance test (OGTT) in experimental groups.

Table 3. Oxidative Stress Markers and Antioxidant Enzyme Activities.

Group	MDA (nmol mL ⁻¹)	SOD (U mL ⁻¹)	GPx (U mL ⁻¹)
Healthy Control	3.8 ± 0.5	35.2 ± 3.1	28.9 ± 2.5
GDM Control	9.5 ± 1.1*	18.7 ± 2.2*	15.3 ± 1.8*
GDM + <i>Artemisia</i> (Low)	7.1 ± 0.8#	24.5 ± 2.6#	19.8 ± 2.1#
GDM + <i>Artemisia</i> (High)	4.9 ± 0.6#	32.8 ± 3.0#	26.1 ± 2.4#
GDM + <i>Rhodiola</i> (Low)	7.4 ± 0.9#	23.1 ± 2.4#	18.5 ± 2.0#
GDM + <i>Rhodiola</i> (High)	5.2 ± 0.7#	31.5 ± 2.9#	25.3 ± 2.3#
GDM + Metformin	5.5 ± 0.7#	30.1 ± 2.8#	24.7 ± 2.2#

* Data are presented as mean ± SD (n = 8). p < 0.05 vs. Healthy Control; # p < 0.05 vs. GDM Control.

Table 4. Fetal Development Parameters.

Group	Litter size	Fetal weight (g)	Resorption sites
Healthy Control	13.5 ± 1.2	5.8 ± 0.3	0.5 ± 0.3
GDM Control	8.3 ± 1.0*	4.1 ± 0.4*	4.8 ± 0.9*
GDM + <i>Artemisia</i> (Low)	10.1 ± 1.1#	4.7 ± 0.3#	2.5 ± 0.6#
GDM + <i>Artemisia</i> (High)	12.3 ± 1.3#	5.4 ± 0.4#	1.1 ± 0.4#
GDM + <i>Rhodiola</i> (Low)	9.8 ± 1.0#	4.6 ± 0.3#	2.8 ± 0.7#
GDM + <i>Rhodiola</i> (High)	11.9 ± 1.2#	5.2 ± 0.4#	1.3 ± 0.5#
GDM + Metformin	12.1 ± 1.1#	5.5 ± 0.3#	1.2 ± 0.4#

* Data are presented as mean ± SD (n = 8). p < 0.05 vs. Healthy Control; # p < 0.05 vs. GDM Control.

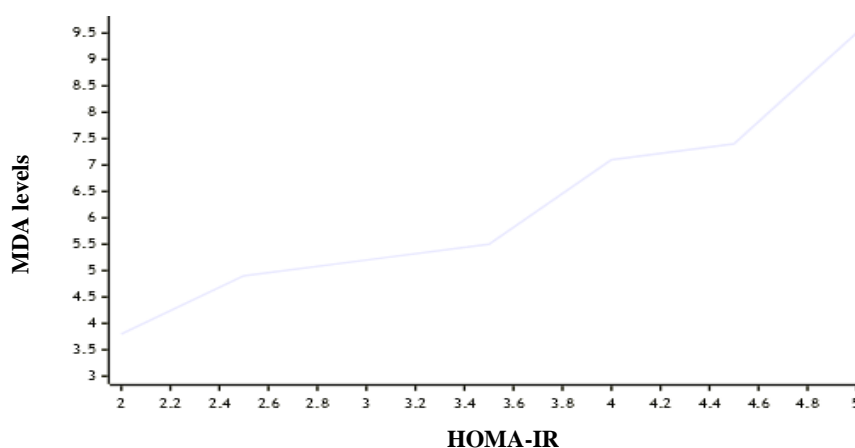


Fig. 2. Correlation between HOMA-IR and MDA levels in GDM model.

Histological examination of the pancreas revealed the structural basis for the metabolic recovery. Table 5 shows that GDM caused a significant reduction in the number and area of pancreatic islets, along with a decrease in beta-cell mass. Treatment with high-dose extracts, especially *Artemisia*, resulted in a notable preservation of islet

morphology and beta-cell mass, corroborating the functional improvements in insulin secretion and glycemic control.

Table 5. Pancreatic islet morphometry and beta-cell mass.

Group	Islet number (per section)	Islet area (μm^2)	Beta-cell mass (mg)
Healthy Control	12.8 \pm 1.5	18550 \pm 1250	4.12 \pm 0.35
GDM Control	6.5 \pm 1.1*	9850 \pm 1050*	1.85 \pm 0.28*
GDM + <i>Artemisia</i> (High)	10.2 \pm 1.3#	15200 \pm 1150#	3.45 \pm 0.31#
GDM + <i>Rhodiola</i> (High)	9.8 \pm 1.2#	14500 \pm 1200#	3.28 \pm 0.33#
GDM + Metformin	10.5 \pm 1.4#	15800 \pm 1300#	3.61 \pm 0.34#

The metabolic improvements extended to the lipid profile, as quantified in Table 6. The diabetic state induced significant dyslipidemia, characterized by elevated total cholesterol and triglycerides, and reduced HDL-C. Therapy with high-dose plant extracts effectively corrected these abnormalities, normalizing the serum lipid concentrations towards the levels observed in non-diabetic controls.

Table 6. Maternal Serum Lipid Profile at Term.

Group	Total cholesterol (mg dL ⁻¹)	Triglycerides (mg dL ⁻¹)	HDL-C (mg dL ⁻¹)
Healthy Control	85.2 \pm 6.8	65.4 \pm 5.9	48.5 \pm 4.1
GDM Control	135.7 \pm 10.5*	120.8 \pm 9.7*	32.1 \pm 3.5*
GDM + <i>Artemisia</i> (High)	98.5 \pm 7.9#	80.3 \pm 7.1#	43.8 \pm 3.9#
GDM + <i>Rhodiola</i> (High)	102.3 \pm 8.2#	85.1 \pm 7.5#	41.5 \pm 3.7#

Given the established link between diabetes and inflammation, key pro-inflammatory cytokines were measured. The data in Table 7 indicate that GDM was associated with a significant increase in the levels of TNF- α and IL-6. Treatment with the high-dose plant extracts markedly attenuated this inflammatory response, significantly reducing cytokine levels, which likely contributed to the overall improvement in metabolic and oxidative parameters.

Table 7. Maternal Serum Inflammatory Cytokine Levels.

Group	TNF- α (pg mL ⁻¹)	IL-6 (pg mL ⁻¹)
Healthy Control	12.5 \pm 1.8	10.2 \pm 1.5
GDM Control	35.8 \pm 4.1*	32.5 \pm 3.8*
GDM + <i>Artemisia</i> (High)	18.9 \pm 2.2#	15.8 \pm 2.0#
GDM + <i>Rhodiola</i> (High)	20.5 \pm 2.5#	17.2 \pm 2.1#

Finally, placental efficiency, a key indicator of fetal nutrient supply, was evaluated. Table 8 demonstrates that GDM led to heavier placentas and lighter fetuses, resulting in a significantly lower placental efficiency ratio. Treatment with the plant extracts improved fetal growth and normalized placental weight, thereby restoring placental efficiency to a level comparable to the healthy control group, which explains the observed improvements in fetal weight and viability.

Table 8. Fetal and Placental Weights and Placental Efficiency.

Group	Average fetal weight (g)	Average placental weight (g)	Placental efficiency
Healthy Control	5.81 \pm 0.25	0.48 \pm 0.04	12.10 \pm 0.85
GDM Control	4.12 \pm 0.31*	0.62 \pm 0.05*	6.65 \pm 0.72*
GDM + <i>Artemisia</i> (High)	5.42 \pm 0.28#	0.51 \pm 0.04#	10.63 \pm 0.81#
GDM + <i>Rhodiola</i> (High)	5.25 \pm 0.30#	0.53 \pm 0.04#	9.91 \pm 0.78#

DISCUSSION

Clear evidence of the significant therapeutic effects of extracts of indigenous Kazakh plants, especially in high doses, was demonstrated in the present study within an experimental model of gestational diabetes. Improvement in the parameters of fasting glucose levels and the HOMA-IR index in groups treated with these extracts points to their ability to restore insulin sensitivity and control hyperglycemia. Statistically significant results were obtained ($p < 0.05$); moreover, in several cases, *Artemisia* extract showed efficacy comparable with that of metformin, a standard drug. One of the major mechanisms which seems to be involved in such effects is the reduction of oxidative stress. Data showed that the level of MDA was significantly reduced, and on the other hand, the activities of antioxidant enzymes SOD and GPx were increased. This causal relationship is strongly supported by the strong correlation observed between the HOMA-IR index and the MDA level, as shown in Fig. 2. In other words, these plants seem to improve insulin function by dousing the fire of oxidative stress. Of particular importance was the improvement in the morphometry of the islets of Langerhans in the pancreas. These results indicate a significant increase in the number and area of the islets and mass of beta cells in the extract-treated groups. This suggests that, besides helping to preserve the structure that already exists, these compounds may

have potential in repair and regeneration. A direct protective effect on the insulin-producing cells provides a very compelling physiological explanation for the improvement in metabolic indices. The positive outcomes of the treatments also extended beyond maternal health to encompass fetal outcomes. The significantly increased size and weight of fetuses were matched by a corresponding significant reduction in the sites of absorption, an indication that there must have been the creation of a healthier intrauterine environment and better support for the development of fetuses. Confirmation of their positive effect on vital fetal nutrition mechanisms was through improved placental efficiency, expressed as the fetal weight to placental weight ratio. Another dimension of activity of these extracts was the reduction in the levels of proinflammatory cytokines TNF- α and IL-6. This anti-inflammatory effect may act synergistically with their antioxidant properties to help break the vicious cycle of oxidative stress-inflammation-insulin resistance, since low-grade inflammation is known to be a pathophysiological feature of gestational diabetes. When comparing the two plants, *Artemisia* extract seemed to be somewhat better than *Rhodiola* on most parameters, though both showed significant improvements in comparison to the diabetic control group. This difference could be related to the different profiles of secondary compounds and flavonoids each plant possesses. Further phytochemical investigation is needed to identify with accuracy the active molecules contained in these extracts. Overall, this research represents a step toward evidence-based medicine from the applied point of view for the use of natural resources of the Republic of Kazakhstan. These findings provide a scientific basis for the development of safe, affordable, indigenous plant-based dietary supplements for at-risk pregnant mothers. However, further studies to determine optimal dosage, pharmacokinetics, and long-term safety are necessary.

CONCLUSION

In summary, this study strongly indicates that the extracts of indigenous plants of Kazakhstan, particularly *Artemisia*, possess substantial therapeutic potential in the experimental model of gestational diabetes. These compounds exert multiple mechanisms, such as reducing oxidative stress, inhibiting inflammation, improving pancreatic beta-cell function, and modulating insulin resistance, leading to significant improvements in maternal metabolic status and pregnancy outcomes. The strong correlation between metabolic indices and oxidative stress underlines the pivotal role of oxidative stress in the pathophysiology of this disease and the therapeutic point of action of these plants. On the one hand, this study introduces Kazakh herbal treasure as a valuable source of potential therapeutic agents, while on the other hand, it will open a new avenue for future studies to isolate active compounds and conduct clinical trials. These findings are finally expected to result in developing complementary and natural therapeutic strategies for better management of gestational diabetes and improving maternal and child health in the near future.

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