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Protective Role of Gum Arabic against miR-21 Dysregulation and Insulin Resistance in Diabetic Male White Rats

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Abstract

Dysregulation of blood glucose is considered the primary cause of insulin resistance, as it results from complex metabolic disorders and molecular changes that affect cellular functions in the human body, thereby triggering the environmental and genetic factors that lead to type 2 diabetes.

Previous studies have indicated that Gum Arabic has a beneficial effect in experimental models of type 2 diabetes, owing to its role in improving metabolic disorders as well as its role in reducing oxidative stress and inflammatory mediators; however, its effect on the molecular regulation associated with miR-21 remains unclear.

Therefore, the present study aims to evaluate the protective role of gum Arabic on miR-21 expression and insulin resistance in male rats in which type 2 diabetes was induced by streptozotocin (STZ). We used 32 male white rats weighing between (200–250) g. These were randomly allocated to four groups in which type 2 diabetes was induced by streptozotocin(STZ)at a concentration of 40 mg/kg, except the first group: (C), which comprised animals administered an oral dose of streptozotocin(STZ) dissolved in distilled water at a concentration of 0.5 throughout the duration of the experiment and served as the negative control group; and the second group: T1 comprised animals in which diabetes had been induced and which served as the positive control group; the third group, T2, comprised animals administered gum Arabic at a concentration of 10 mg/kg of body weight for a period of 30 days; and the fourth group: T3 comprised animals administered gum Arabic at a concentration of (25 mg/kg) of body weight for a period of 30 days. At the end of the experiment, the following parameters were analysed: miR-21 expression, glucose, insulin, TNF-α, IL-6, MDA, SOD, and GSH.

The results showed that rats administered doses of 10 and 25 mg/ kg of gum Arabic exhibited a change in the expression of miR-21 at the 25 mg/kg dose compared with the 10 mg/kg dose, which showed improvement, as well as improvements in the

levels of glucose, insulin, inflammatory markers, and antioxidants compared with the negative and positive control groups.

keyword
Gum Arabic, miR-21 expression, streptozotocin(STZ), Oxidative stress, Antioxidant, Inflammatory cytokines.

Introduction:

Type 2 diabetes is one of the most common metabolic disorders, resulting from elevated blood glucose levels and the consequent impairment of insulin's regulatory function, which affects its secretion into the bloodstream, leading to insulin resistance or a relative deficiency of insulin [9]. Persistently high blood glucose levels lead to impaired insulin action, resulting either in reduced secretion from the pancreas or resistance to insulin by tissue cells; both causes may occur simultaneously, making it more difficult to diagnose the underlying aetiology. The long-term complications associated with diabetes vary from retinopathy, neuropathy and nephropathy to diseases affecting the blood vessels [10].

Recent studies have confirmed that 80 per cent of patients with chronic diseases have turned to alternative medicine to prevent complications associated with these conditions, as well as to improve the functioning of the affected organs [6].

Previous studies have examined the effects of numerous medicinal plants rich in active compounds such as flavonoids, alkaloids, carotenoids, glycosides, and phenolic acids, which help to lower blood sugar levels whilst regulating insulin function in the pancreatic beta cells; this, in turn, stimulates insulin secretion whilst reducing glucose absorption in the intestine [3].

Gum Arabic is a natural substance rich in soluble fibre, extracted from the stems and branches of Acacia seyal or Acacia senegal, and is used in traditional medicine to treat digestive problems andvaginal infections, as well as diabetes [5].

MicroRNAs (miRNAs) are small, non-coding RNA molecules that play an active role in regulating post-transcriptional gene expression by binding to messenger RNA (mRNA) at specific sequences, thereby inhibiting or stimulating translation. Studies have confirmed that dysregulation of miRNA expression is directly associated with insulin resistance [8], dysfunction of pancreatic beta cells, as well as inflammation and oxidative stress. One of the most important of these molecules is miR-21, owing to its regulatory role in various cellular pathways; Studies have confirmed an association between altered miR-21 levels and diabetes mellitus; its dysregulation may cause disruption of the P13/AKT pathway as well as the regulation of the PTEN protein, both of which are directly linked to insulin-mediated metabolic signalling [11].

An animal study confirmed that elevated miR-21 levels were present in the pancreatic tissue of rats with induced diabetes and high levels of oxidative stress; whilst following treatment, its levels decreased in conjunction with a reduction in MDA and

caspase-3, alongside an improvement in insulin levels, confirming the effect of miR-21 on the molecular changes associated with beta-cell dysfunction in the pancreas [8,11]. A study also examined the direct role of miR-21 on the PTEN/AKT pathway in diabetic rats and confirmed that modulating the miR-21 molecular pathway contributed to improved markers of oxidation and insulin secretion, alongside regulation of the PTEN/AKT pathway [11].

Although previous studies have addressed the association of miRNA-21 with pancreatic function and oxidative stress, the effect of gum Arabic on the miRNA-21 molecular pathway has not been directly investigated.

Therefore, this study examined the effect of gum Arabic on miRNA-21 level dysregulation in rats in which diabetes was induced by streptozotocin(STZ), whilst determining its relationship with changes in markers of inflammation and oxidative stress. Infections, as well as diabetes.

Materials and methods

The experiment was conducted in the Animal House laboratory at the Faculty of Science, University of Al-Qadisiyah. The ARRIVE (Animal Research: Reporting of in Vivo Experiments) guidelines were followed, and we adhered to the institution's regulations on the care of laboratory animals. The experiment was conducted on 32 healthy adult male white rats weighing between 190 and 220 g and aged between 3 and 4 months. They were housed in a laboratory environment at a temperature of 22 ± 2 °C and a humidity level of 5 ± 55, with light/ dark cycles ranging from 14 to 10 hours. The animals were provided with water and feed throughout the experiment and were allowed to acclimatise to the new environmental conditions for 15 days prior to the start of the experiment. They were then randomly divided into four groups, each comprising eight animals, in which diabetes was induced using streptozotocin(STZ) at a concentration of 40 mg/kg.

, with the exception of the control group, which was administered a streptozotocin solution dissolved in distilled water at a concentration of 0.5 throughout the duration of the experiment. Following the induction of diabetes, groups (T2) and (T3) were administered gum Arabic at varying doses over 30 days during the experiment.

Induction of diabetes:

Streptozotocin(STZ) was purchased in powder form from Solgar, Inc. (Leonia, NJ, USA) and subsequently used to induce diabetes in rats at a concentration of 40 mg/kg dissolved in freshly prepared cold citrate buffer, pH 4.5 [7]; the disease was induced in groups (T1, T2, T3). Blood glucose levels were then measured to confirm the onset of the condition before the start of the experiment in the treated animals.

Extraction of gum Arabic:

A 40 g sample of Gum Arabic was ground and placed in 200 mL of water; it was heated in an oven for 30 minutes at 30 °C, and then left for 24 hours, with shaking every 3–4 hours. Ultrasound was applied for 30 minutes to enhance the release of the active compounds. A centrifuge was used at a speed of 6,000 revolutions per minute for 12 minutes; the resulting liquid was then dried in Petri dishes at room temperature for 4 days. Finally, the Gum Arabic was selectively isolated after complete drying,

yielding a fine powder ready for use [8] It was administered at doses of (10 mg/kg) [1] and (25 mg/kg) [7] of body weight.

Experimental design:

The experimental animals were randomly allocated to four groups, each comprising eight animals:

The first group was the control group (C), comprising animals administered an oral dose of streptolactin dissolved in distilled water at a concentration of 0.5 throughout the duration of the experiment; this was considered a negative control group. In groups (T1, T2, T3), diabetes was induced using streptozotocin(STZ) at a concentration of 40 mg/kg; Group 2 (T1) was in which diabetes was induced only for the duration of the experiment and was designated as the positive control group; Group 3 (T2), following induction,

was administered Gum Arabic at a concentration of 10 mg/kg body weight for 30 days. The fourth group (T3) was administered Gum Arabic at a concentration of 25 mg/kg body weight for 30 days following the induction of diabetes.

Sample collection:

At the end of the experiment, blood serum was collected via cardiac puncture from the animals, which had been anaesthetised with chloroform, in order to carry out the necessary physiological tests. The animals were then sacrificed to obtain pancreatic tissue and to measure the level of miR-21 in it. It should be noted that no unexpected deaths occurred during the experiment.

Measurement of microRNA-21 (miR-21) levels:

MicroRNA (miRNA) was extracted from pancreatic tissue using the miRcute miRNA Isolation Kit in accordance with the manufacturer's instructions; the extracted RNA was then converted into first-strand cDNA using the miRcute miRNA First-strand cDNA Synthesis Kit from TIANGEN, China, in accordance with the protocol supplied with the kit. To determine the relative expression level of rno-miR-21-5p, real-time quantitative polymerase chain reaction (qRT-PCR) was performed using the miRcute Plus miRNA qPCR Detection Kit (TIANGEN, China), which utilises SYBR Green dye. The mature rno-miR-21-5p sequence was adopted after verification in the NCBI/GenBank database:

5′-UAGCUUAUCAGACUGAUGUUGA-3′

The corresponding DNA sequence was used as the basis for the forward primer for rno-miR-21-5p:

5′-TAGCTTATCAGACTGATGTTGA-3′

using the universal reverse primer supplied with the TIANGEN kit. U6 small nuclear RNA (U6 snRNA) was used as an internal reference to normalise expression data.

The relative expression level of rno-miR-21-5p was calculated using the $2^{-}\Delta\Delta Ct$ method, after normalising the cycle threshold (Ct) values for rno-miR-21-5p to those of U6 and comparing them with the control group. The measurement is interpreted as reflecting the total/predominant relative expression of miR-21-5p within the limits of the assay's sensitivity.

The relative expression level of miR-21-5p was calculated using the $2^{-}\Delta\Delta Ct$ method, after normalising the Ct values for miR-21-5p to U6 and comparing them with the control group.
U6 primers compatible with the TIANGEN system used in this study."
Forward/ Reverse
U6 snRNA

Target	Primer	Sequence(5'-3')
mo-miR-21-5p	Forward	TAGCTTATCAGACTGATG
miR-21-5p	Reverse	Universal Reverse Primer provided with the TIANGEN miRcute Plus miRNA qPCR Detection Kit
U6 snRNA	Forward/ Reverse	U6 primers compatible with the TIANGEN system used in this study."

The rno-miR-21-5p (MIMAT0000790) sequence was obtained from the miR Base/NCBI database and
subsequently used in accordance with the primer design system described in [7].
TIANGEN

Measurement of glucose levels:

Glucose levels were measured using a glucometer in accordance with the manufacturer's instructions, using a capillary blood sample. Measurements were taken before and after the animals were administered streptozotocin(STZ), following a 13-hour fast to ensure the induction of diabetes in the treated groups. Glucose levels were also measured after treatment with gum Arabic in groups (T2, T3).

Hormonal, Inflammatory and Antioxidant Parameters

The following parameters were measured in rat serum using kits from (Sunlong Biotech Co).

Insulin No:(SL0373Ra), TNF-α No:(SL0722Ra), IL-6 No:(SL0411Ra), and malondialdehyde (MDA) No:(SL0475Ra) and superoxide dismutase (SOD) No:(SL0664Ra), in accordance with the manufacturer's instructions.

Statistical Analysis

The mean ± standard deviation (SD) was used to express the data. Data analysis was carried out using SPSS software, specifically version 25.0, developed in the USA. The one-way analysis of variance (ANOVA) and Tukey's post hoc test for multiple comparisons were used to examine group differences. We considered p .05 to be statistically significant.

Results and Discussion

Table (1). Relative gene expression of pancreatic miR-21-5p in induced diabetic rats treated with Gum Arabic.

Groups / Parameters	C	T1	T2	T3	LSD
miR-21-5p (2^-ΔΔCt)	1.02±0.16 ^d	4.03±0.6 ^a	2.32. ±0.42 ^b	1.50±0.25 ^c	0.405

Values are expressed as mean ± standard deviation (n=8). Means with different superscript letters within the same row are significantly different (p < 0.05). C: negtive Control group. group; T1: posetive Control group induced diabetes. group; T2: induced diabetes then given AG concertation 10ml/kg. group; T3 induced diabetes then given AG concertation 25ml/kg .

The results in Table (1) showed the change in the level of miR-21-5p in pancreatic tissue from the experimental animals; it was found to be (4.03±0.6) in the positive control group (T1) and (1.02 ± 0.16) in the negative control group (C), which recorded a statistically significant increase in values in group (T1), whilst the results showed an improvement in miR-21-5p levels in the groups treated with AG, with group (T2) recording a level of (2.32. ±0.42), whilst the (T3) group showed a marked improvement to a level of (1.50±0.25) compared with the (T1) group.

This may be attributed to the protective effect of gum Arabic on improving the structure of pancreatic beta cells, inhibiting PTEN, as well as activating AKT/p-AKT, which contributed to the improvement in miR-21-5p levels [11].It may also be due to the protective role of gum Arabic in modulating inflammatory mediators, as well as its role in reducing oxidative stress, as confirmed by the results of our current study [1].

Table (2) shows the effect of Gum Arabic on (glucose &insulin) in the serum of male rats in deferent concentration of AG.

Group / Parameters		C	T1	T2	T3	LSD
Glucose(mg/dL)	Pre	103.4±9.3 ^a	252.8±16.3 ^a	245.9±17.2 ^a	250.4±12.5 ^a	14.52
	Post	105.2±7.3 ^d	310.3±12.1 ^a	195.7±12.4 ^b	170.4±15.3 ^c	12.41
Insulin(mU/L)	Pre	6.61±0.53 ^a	4.17±0.18 ^b	4.12±0.43 ^b	3.87±0.32 ^b	
	Post	5.87±0.12 ^a	4.12±0.10 ^c	3.69±0.12 ^b	4.98.±0.16 ^b	0.130

Values are expressed as mean ± standard deviation (n=8). Means with different superscript letters within the same row are significantly different (p < 0.05). C: negtive Control group. group; T1: posetive Control

group induced diabetes. group; T2: induced diabetes then given AG concertation 10ml/kg. group; T3 induced diabetes then given AG concertation 25ml/kg.

The results in Table (2) show the glucose and insulin levels before and after treatment with gum Arabic. The results confirmed a statistically significant increase in glucose levels in group (T1) at (252.8 ± 16.3) compared with group (C) at (103.4 ± 9.3); after treatment, the results were (310.3 ± 12.1) and (105.2 ± 7.3), respectively. This is attributed to the induction of diabetes by streptozotocin(STZ).
Meanwhile, the results showed a statistically significant decrease in glucose levels in groups (T2) and (T3) after treatment compared with (T1), (T2), and (T3) before treatment, and group (T1) after treatment. The results also showed an improvement in insulin levels in groups (T2) and (T3) after treatment, which is attributed to the role of the active compounds in gum Arabic in regulating blood glucose levels and the levels of insulin secreted by the beta cells of the pancreas [1].

Table (3) shows the effect of Gum Arabic on (TNF-a &IL6) the serum of male rats in deferent concentration of AG.

Parameter	C	T1	T2	T3	$LSD_{0.05}$
TNF-α (pg/mL)	15.4 ± 1.5^c	55.2 ± 2.5^a	43.2± 2.4^b	25.0± 3.0^c	10.0
IL-6 (ng/mL)	14.9 ± 1.3^c	35.6 ± 3.1^a	29.1 ±4.5^ab	19.0 ±2.0^c	8.0

Values are expressed as mean ± standard deviation (n=8). Means with different superscript letters within the same row are significantly different (p < 0.05). C: negtive Control group. group; T1: posetive Control group induced diabetes. group; T2: induced diabetes then given AG concertation 10ml/kg. group; T3 induced diabetes then given AG concertation 25ml/kg .

The results in Table (3) showed a statistically significant difference in the levels of TNF-α and IL-6 in group (T1), with a tumour necrosis factor level of (55.2 ± 2.5) and an IL-6 level of (35.6 ± 3.1) compared with the negative control group (C), whilst groups (T2) and (T3) showed an improvement in TNF-α levels, at (43.2 ± 2.4) and (25.0±3.0) compared with group (T1); and when measured, IL-6 levels were (29.1 ± 4.5) and (19.0 ± 2.0) compared with group (T1).
This is attributed to the chemical compounds in gum Arabic and their protective role in shielding cells from the effects of pro-inflammatory factors resulting from the onset of diabetes [7].

Table (4) shows the effect of Gum Arabic on (MDA&SOD) of male rats in deferent concentration of AG.

Parameter	C	T1	T2	T3	$LSD_{0.05}$
MDA (ngl/mL)	1.3 ± 0.2^d	9.2± 0.8^a	6.2 ± 1.7^b	3.2 ± 1.3^c	1.20
SOD (pgl/mL)	45.1 ± 1.5^a	23.4 ± 2.3^d	31.4 ± 1.2^c	39.3±1.4b	1.69

Values are expressed as mean ± standard deviation (n=8). Means with different superscript letters within the same row are significantly different (p < 0.05). C: negtive Control group. group; T1: posetive Control group induced diabetes. group; T2: induced diabetes then given AG concertation 10ml/kg. group; T3 induced diabetes then given AG concertation 25ml/kg

The results in Table (4) showed a statistically significant increase in MDA levels and a decrease in SOD levels in the diabetes group (T1) compared with the control group; conversely, there was a statistically significant decrease in MDA levels, which were recorded as (6.2 ± 1.7) and (3.2 ± 1.3), whilst SOD levels were higher, at (31.4 ± 1.2) and (39.3 ± 1.4) in the (T2) and (T3) groups respectively, compared with the (T1) group.

This is attributed to the role of Gum Arabic in activating antioxidants and inhibiting oxidants by regulating the gene expression of antioxidants and the levels of oxidative stress markers [1].

Conclusion

The results of our current study confirmed that gum Arabic has a protective effect in rats with streptozotocin(STZ)-induced diabetes; it contributed to improving blood glucose and insulin levels whilst regulating the expression of miR-21-5p in pancreatic tissue. The protective role of gum Arabic, as confirmed by the results of our current study, is evidenced by its effect in improving levels of pro-inflammatory mediators, as well as an increase in SOD levels coupled with a decrease in MDA in serum. This confirms the positive effect of Gum Arabic on the miR-21-5p pathway in the pancreas, thereby contributing to the improvement of pancreatic beta-cell function in the context of diabetes and the effects of inflammatory factors resulting from the onset of diabetes [8].

Refrenens

1-Adam, S. Y.., Eltahir, H. A.., Ismaeel, F. A. M.., Abdallah, R. H.., Abaker, A. O.., Musa, H. H.., Husien, H. M.., Mohammed, L. A.., Cai, D., andAhmed, A. A. (2025). Gum arabic regulates glucose metabolic enzymes through modification of hepatic phosphoenolpyruvate carboxykinase expression in diabetic rats. Bioactive Carbohydrates and Dietary Fibre, 100490. https://doi.org/10.1016/j.bcdf.2025.100490

2-Adam, S. Y.., Musa, T. H.., Musa, H. H.., Saleh, A. A., andAhmed, A. A. (2026). Does gum arabic alter gene expression? Diabetic and obesity as models: A mini review. Modern Agriculture, 4(1), e70042. https://doi.org/10.1002/moda.70042

3-Akram, M.., Rashid, A.., Zainab, R.., Laila, U.., Khalil, M. T.., Anwar, H.., Thotakura, N., andRiaz, M. (2023). Application and research of natural products in modern medical treatment. J Mod Pharmacol Pathol, 1(7), 2. https://doi.org/10.53964/jmpp.2023007.

4-Carmo de Carvalho e Martins, M. d.., Martins., da Silva Santos Oliveira, A. S.., da Silva, L. A. A.., Primo, M. G. S., andde Carvalho Lira, V. B. (2022). Biological indicators of oxidative stress [malondialdehyde, catalase, glutathione peroxidase, and superoxide dismutase] and their application in nutrition. In Biomarkers in nutrition (pp. 1-25). Springer. https://doi.org/10.1007/978-3-030-81304-8_49-1

5-Cissé, K.., Gassama, D.., Diagne, A. A., andBadji, M. (2020). Influence of the inhibition of corrosion of s235 steel in a solution of perchloric acid by gum arabic. American Journal of Materials Science and Engineering, 8(1), 17-21. http://pubs.sciepub.com/ajmse/8/1/3

6-Hossain, M. J.., Al-Mamun, M., andIslam, M. R. (2024). Diabetes mellitus, the fastest growing global public health concern: Early detection should be focused. Health science reports, 7(3), e2004. https://doi.org/10.1002/hsr2.2004.

7-Jabbar, R. A.., Al-Hayder, M. N., andIbrahim, M. A. (2026). A comparative assessment on the protective effect of boswellia serrata, arabic gum extracts, and their combination in streptozotocin(STZ)-induced diabetic rats. Palestinian Medical and Pharmaceutical Journal (Pal. Med. Pharm. J.), 9999(9999), None-None. https://doi.org/10.59049/2790-0231.a2883

8-Monfared, A. L., andMenatnia, A. (2024). Evening primrose oil ameliorates tissue architecture, apoptosis, and oxidative stress in the pancreas of diabetic rats: Possible role of mir-21. Iranian Journal of Basic Medical Sciences, 27(12), 1558. https://doi.org/10.22038/ijbms.2024.78604.17007

9-Ojo, O. A.., Ibrahim, H. S.., Rotimi, D. E.., Ogunlakin, A. D., andOjo, A. B. (2023). Diabetes mellitus: From molecular mechanism to pathophysiology

and pharmacology. Medicine in Novel Technology and Devices, 19, 100247. https://doi.org/10.1016/j.medntd.2023.100247

10-Pavithra, V.., Chinthu, K. K. S., andSolomon, M. C. (2025). Diabetes mellitus, obesity and periodontitis–a three way interconnection. Obesity Medicine, 55, 100615. https://doi.org/10.1016/j.obmed.2025.100615.

11-Thabet, E. H.., Khalil, N. A.., Essawy, M. M.., Harby, S. A.., Solaiman, A. A.., El Gazaerly, H. M., andKhalifa, Y. H. (2025). Mirna-21-loaded chitosan nanoparticles ameliorate pancreatic apoptosis and oxidative stress in diabetic rats. Life Sciences, 366, 123471. https://doi.org/10.1016/j.bcdf.2025.100490