Journal of Clinical and Nursing Research, 2025, Volume 9, Issue 10
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

Study on the Correlation between Irisin Expression and the Healing of Diabetic Skin Injury

Xuefeng Yu[1], Xi Jiang[2]

[1]Zhejiang Pharmaceutical University, Ningbo 315100, Zhejiang, China
[2]Ningbo Mingzhou Hospital, Ningbo 315100, Zhejiang, China

Abstract: A diabetic skin ulcer model was established by combining streptozotocin (STZ) administration with full-thickness skin defect surgery to evaluate the changes in irisin levels during the healing process. The experiment was divided into 2 groups, with 6 mice in each group: the normal control group and the diabetic skin injury group. Compared with the normal group, the model injury group showed a significant increase in blood glucose ($p < 0.001$), a significant decrease in healing rate ($p < 0.001$), and a significant decrease in irisin levels ($p < 0.001$) after 14 days. Irisin levels were positively correlated with blood glucose and positively correlated with wound healing rate. In conclusion, irisin may be a potential therapeutic target for the treatment of diabetic skin injury.

Keywords: Diabetes mellitus; Skin healing; Irisin; Blood glucose

Online publication: Nov 3, 2025

1. Introduction

Diabetes mellitus is one of the common chronic metabolic disorders [1]. It is accompanied by a series of complications, such as diabetic nephropathy, diabetic encephalopathy, and diabetic foot [2]. These complications affect the quality of life of diabetic patients, and severe complications can even be life-threatening. Among them, difficult-to-heal diabetic wounds, such as diabetic foot ulcers, are a major concern. Due to significant impairment of vascular microcirculation in diabetic patients, wounds are difficult to heal. Once induced by factors such as wound infection or low immunity, these wounds can develop into diabetic skin ulcers [3]. At present, there are still no effective treatment methods for diabetic skin ulcers, and in-depth research on the pathological mechanism of diabetic skin ulcers is lacking, which hinders the identification of specific targets for drug development.

Irisin, a myokine-derived protein, is closely related to tissue metabolism in the body [4]. In recent years, more scholars have focused on the role of irisin in metabolic diseases, such as its effect on diabetes mellitus [5,6]. Relevant studies have found that irisin can significantly improve body metabolism, promote blood glucose utilization, and alleviate diabetes [7]. Meanwhile, irisin also exhibits certain anti-inflammatory and antioxidant effects [8]. However, whether the expression of irisin in the body, especially in skin tissue, is correlated with diabetic skin ulcers remains unclear.

In this study, an animal model of diabetic skin injury was established to detect irisin levels in blood and skin tissue, and to explore its correlation with the healing of diabetic skin ulcers. This study aims to provide a theoretical basis for determining whether irisin can be a potential effective target for the treatment of diabetic skin ulcers in future research.

2. Materials and methods

2.1. Experimental animals

Adult male ICR mice, 8–10 weeks old (n = 24), weighing between 20 and 24 g, were purchased from the Hangzhou Medical Experimental Animal Center.

2.2. Experimental equipment and reagents

Irisin (ThermoFisher Scientific); Streptozotocin (ThermoFisher Scientific); High-fat diet (ThermoFisher Scientific); Blood glucose meter and test strips (Roche); Ultrapure water system (Millipore); Analytical balance with a precision of 0.01 mg (1/100,000 balance, ThermoFisher Scientific); Irisin detection kit (ThermoFisher Scientific).

2.3. Animal grouping

The experiment was divided into two groups: the normal control group and the diabetic skin ulcer group, with 6 mice in each group (n = 6 per group).

2.4. Animal model establishment

First, a diabetic animal model was established by intraperitoneal injection of streptozotocin at a dose of 50 mg/kg [9]. Seventy-two hours later, blood samples were collected from the tail vein for the first time, and subsequent blood glucose monitoring was conducted continuously. A blood glucose level ≥ 16.7 mmol/L was considered a successful establishment of the diabetic model. On the basis of the successfully established diabetic model, a skin ulcer model was constructed. Specifically, mice were anesthetized by isoflurane inhalation, and their dorsal hair was removed using depilatory cream. A circular wound with a diameter of 20 mm was created on the dorsal skin of the mice. Mice in the normal control group only underwent the skin wound creation procedure without being induced to develop diabetes.

2.5. Evaluation of wound area in diabetic skin ulcers

On days 3, 7, and 14, the ulcer wounds of mice in both groups were photographed using a camera to measure the wound area. The wound healing rate was calculated using the formula: Wound healing rate = [(Original wound area - Unhealed wound area) / Original wound area] × 100%.

2.6. Tissue sample collection

On days 7 and 14 after wound creation, blood samples were collected from the tail vein of mice in both groups for blood glucose detection. Fourteen days after wound healing, 6 mice in each group were sacrificed, and dorsal skin tissue samples were collected.

2.7. Irisin detection using the kit

Skin tissue samples were lysed, followed by ultrasonic homogenization. The homogenate was centrifuged, and

the supernatant was collected for sample loading. After adding the antibody, a stop solution was added. The absorbance value was measured at a wavelength of 540 nm, and the irisin content in the samples was calculated by referring to the standard curve.

2.8. Statistical analysis

Experimental data were expressed as mean ± standard error (mean ± SE). Statistical analysis was performed using GraphPad Prism software, and the unpaired t-test was used for comparisons between the two groups. A p-value < 0.05 was considered to indicate a statistically significant difference.

3. Experimental results

3.1. Changes in body weight and blood glucose

Compared with the normal group (32.4 ± 2.1 g), the body weight of mice in the model group (24.1 ± 1.0 g) was significantly decreased 14 days later ($p < 0.01$); the blood glucose level of mice in the model group (12.6 ± 0.8 mmol/L) was significantly higher than that in the normal control group (4.2 ± 0.5 mmol/L, $p < 0.001$) (see **Table 1**).

Table 1. Changes in body weight and blood glucose levels of mice

Group	Body Weight (g)	Blood Glucose Level (mmol/L)
Normal Control Group	32.4 ± 2.1	4.2 ± 0.5
Model Group	24.1 ± 1.0**	12.6 ± 0.8***
t-value	3.568	8.904
p-value	0.0051	< 0.0001

Data from 6 mice in each group were expressed as mean ± standard error of the mean (SEM). Student's *t*-test was used for data analysis. ** indicated a significant difference compared with the control group at $p < 0.01$; *** indicated a significant difference compared with the control group at $p < 0.001$.

3.2. Changes in wound area

The wounds of mice in both groups gradually narrowed over time. At 7 days after wound creation, the wound healing rate of mice in the model group (22.3 ± 0.9%) was significantly lower than that in the normal control group (36.8 ± 1.8%). A similar trend was also observed in mice at 14 days after model establishment (see **Table 2**).

Table 2. Changes in wound healing rate of mice

Group	3 days after wounding	7 days after wounding	14 days after wounding
Normal Control Group	12.8 ± 0.5	36.8 ± 1.8	81.8 ± 2.2
Model Group	9.3 ± 0.7**	22.3 ± 0.9***	44.3 ± 2.3
t-value	3.995	7.348	11.860
p-value	0.0025	< 0.0001	< 0.0001

Data from 6 mice in each group were expressed as mean ± standard error of the mean (SEM). Student's *t*-test was used for data analysis. ** indicated a significant difference compared with the control group at $p < 0.01$; *** indicated a significant difference compared with the control group at $p < 0.001$.

3.3. Changes in irisin level

At 14 days after model establishment, compared with the normal control group (2.2 ± 0.3 nmol/L), the irisin level in the skin tissue of mice in the model group (0.7 ± 0.1 nmol/L) was significantly decreased ($t = 4.743$, $p < 0.001$).

3.4. Results of correlation analysis

The irisin level showed a negative correlation with blood glucose ($R = -0.755$, $R^2 = 0.57$, $p < 0.01$) and a positive correlation with wound healing rate ($R = 0.821$, $R^2 = 0.67$, $p < 0.01$) (see **Table 3**).

Table 3. Correlation analysis of variables in mice at 14 days after wounding

Variable	Irisin level	Blood glucose level	Wound healing rate
Irisin Level	1	-0.755**	0.821**
Blood Glucose Level	-0.755**	1	-0.902***
Wound Healing Rate	0.821**	-0.902***	1

The data represent Pearson correlation coefficients. ** indicates that the result of the correlation analysis between the two groups has a statistical significance of $p < 0.01$; *** indicates that the result of the correlation analysis between the two groups has a statistical significance of $p < 0.001$. The "-" symbol represents a negative correlation between the two sets of data.

4. Discussion

This study found that the expression level of irisin in the skin tissue of diabetic mice may be associated with wound healing. An increase in irisin level can accelerate the healing of diabetic wounds. The irisin level in the skin tissue of diabetic mice is significantly lower than that of mice in the normal group, which may be one of the reasons for the difficulty in wound healing. Irisin has anti-inflammatory and antioxidant effects, and can improve nerve and tissue functions [10]. However, no studies have shown so far that it can promote skin tissue repair. The latest relevant research has detected the expression of irisin in dermal tissue. Combined with the biological activity of irisin, this suggests that irisin may have the effect of promoting tissue repair [11].

This study also has certain limitations. Correlation research results indicate that there is a correlation between irisin, blood glucose, and wound healing rate; however, it remains unclear whether irisin directly promotes skin healing or improves skin healing by regulating blood glucose. It cannot be ruled out that irisin improves the local tissue microenvironment with high glucose levels, thereby alleviating microcirculatory disorders and further promoting tissue repair.

Through literature research, it is hypothesized that irisin may improve wound repair through the following pathways.

(1) It may inhibit inflammatory mechanisms, such as the Nuclear Factor kappa-B (NF-κB) signaling pathway, thereby optimizing the inflammatory phase of skin healing [12].

(2) It may activate the AMP-activated protein kinase/Phosphatidylinositol-3-kinase (AMPK/PI3K) signaling pathway to promote the secretion of growth factors, thus facilitating the formation of new blood vessels [13].

(3) It may activate oxidative stress-related mechanisms such as Nuclear Factor Erythroid 2-Related Factor 2 (Nrf2) to exert antioxidant effects and protect cells [14].

(4) It may regulate the metabolism of the microenvironment and improve microcirculation [15].

5. Conclusion

In conclusion, irisin may be a potential therapeutic target for diabetic skin ulcers, but further experiments are required to verify its mechanism of action.

Funding

Ningbo Yinzhou District Agricultural and Social Development Technology Plan Project for Jiang Xi (Project No.: 2022AS036); Zhejiang Provincial Science Foundation of China, Yu Xuefeng (Project No.: LTGY24H150003)

Disclosure statement

The authors declare no conflict of interest.

Reference

[1] Priyanka M, Faustina A, Dinesh E, et al., 2023, Pharmacological Approaches to the Prevention of Type 2 Diabetes Mellitus. Front Endocrinol (Lausanne), 14: 1118848.

[2] Papatheodorou K, Banach M, Bekiari E, et al., 2018, Complications of Diabetes 2017. J Diabetes Res, 2018: 3086167.

[3] Holl J, Kowalewski C, Zimek Z, et al., 2021, Chronic Diabetic Wounds and Their Treatment with Skin Substitutes. Cells, 10(3): 655.

[4] Cheng Z, Huang L, Xiao X, et al., 2021, Irisin in Atherosclerosis. Clin Chim Acta, 522: 158–166.

[5] Marrano N, Biondi G, Borrelli A, et al., 2021, Irisin and Incretin Hormones: Similarities, Differences, and Implications in Type 2 Diabetes and Obesity. Biomolecules, 11(2): 286.

[6] Sousa R, Improta-Caria A, Souza B, 2021, Exercise-Linked Irisin: Consequences on Mental and Cardiovascular Health in Type 2 Diabetes. Int J Mol Sci, 22(4): 2199.

[7] Wang K, Song F, Xu K, et al., 2019, Irisin Attenuates Neuroinflammation and Prevents the Memory and Cognitive Deterioration in Streptozotocin-Induced Diabetic Mice. Mediators Inflamm, 2019: 1567179.

[8] Zhu D, Wang H, Zhang J, et al., 2015, Irisin Improves Endothelial Function in Type 2 Diabetes through Reducing Oxidative/Nitrative Stresses. J Mol Cell Cardiol, 87: 138–147.

[9] Dong Q, Han Z, Gao M, et al., 2024, FNDC5/Irisin Ameliorates Bone Loss of Type 1 Diabetes by Suppressing Endoplasmic Reticulum Stress-Mediated Ferroptosis. J Orthop Surg Res, 19(1): 205.

[10] Maak S, Norheim F, Drevon C, et al., 2021, Progress and Challenges in the Biology of FNDC5 and Irisin. Endocr Rev, 42(4): 436–456.

[11] Tarakçı B, Girgin A, Timurkaan S, et al., 2016, Immunohistochemical Localization of Irisin in Skin, Eye, and Thyroid and Pineal Glands of the Crested Porcupine (Hystrix cristata). Biotech Histochem, 91(6): 423–427.

[12] Li Q, Tan Y, Chen S, et al., 2021, Irisin Alleviates LPS-Induced Liver Injury and Inflammation through Inhibition of NLRP3 Inflammasome and NF-κB Signaling. J Recept Signal Transduct Res, 41(3): 294–303.

[13] Rabiee F, Lachinani L, Ghaedi S, et al., 2020, New Insights into the Cellular Activities of FNDC5/Irisin and Its Signaling Pathways. Cell Biosci, 10: 51.

[14] Tu Y, Liu J, Kong D, et al., 2023, Irisin Drives Macrophage Anti-Inflammatory Differentiation via JAK2-STAT6-Dependent Activation of PPARγ and Nrf2 Signaling. Free Radic Biol Med, 201: 98–110.

[15] Darkwah S, Park E, Myint P, et al., 2021, Potential Roles of Muscle-Derived Extracellular Vesicles in Remodeling

Cellular Microenvironment: Proposed Implications of the Exercise-Induced Myokine, Irisin. Front Cell Dev Biol, 9: 634853.