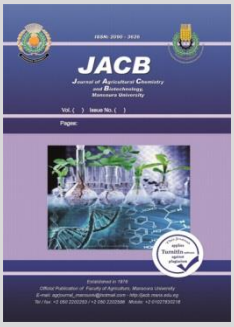
**Journal of Agricultural Chemistry and Biotechnology**

**Journal homepage & Available online at: www.jacb.journals.ekb.eg**

# Genetic Impact of Flavonoids Derived from Onion (*Allium cepa* L.) Peels on Hepatic Tissue in Type II Diabetes Mice Model

**Abd EL-Aziz, M. H.[1]; M. A. Taher[2]; Ghada H. ELnady[3] and Alshaimaa G. Fathallah[1*]**

[1]Dept. of Genetics, Fac. of Agric., Mansoura University. EGYPT
[2]Dept. of Chemistry, Fac. of Agric., Mansoura University. EGYPT
[3]Medical Genetics Centre, Faculty of Medicine, Ain Shams university, Egypt




**Article Information**
**Received 24/ 8 /2025**
**Accepted 22/ 9/2025**

## ABSTRACT

Type 2 Diabetes Mellitus (T2DM) accounts for over 90% of global diabetes cases and results from complex interactions between genetic and environmental factors. Growth hormone (GH) is essential for glucose metabolism, and its dysregulation contributes to diabetic complications. This study evaluated the effects of onion peel flavonoid extracts on hepatic GH gene expression in streptozotocin (STZ)-induced diabetic mice.Twenty-five male albino mice were divided into five groups: normal control (C), diabetic control (D), diabetic treated with metformin 200 mg/kg (D+M200), diabetic treated with flavonoid extract 100 mg/kg (D+F100), and diabetic treated with flavonoid extract 200 mg/kg (D+F200). Diabetes was induced with STZ (40 mg/kg). Blood glucose levels were monitored weekly for four weeks, and HbA1c was assessed at study completion. Hepatic GH gene expression was analyzed using qRT-PCR. Groups treated with flavonoid extracts demonstrated progressive improvements in glycemic control . By week 4, blood glucose levels were significantly reduced in D+F100 (104.4±1.69 mg/dl) and D+F200 (88.4±2.93 mg/dl) compared to D (242±12.9 mg/dl). HbA1c levels were also reduced in D+F100 (6.93±0.15) and D+F200 (6.6±0.1) relative to D (7.86±0.25). GH expression was markedly downregulated in D (0.2±0.002), but flavonoid treatment restored expression, with D+F200 showing near-normalization (FC=0.97±0.04) and D+F100 showing moderate improvement (FC=0.7±0.06).Onion peel flavonoids produced significant glucose-lowering effects superior to metformin, with the higher dose achieving near-normal glycemia. These findings suggest that flavonoids may restore hepatic metabolic balance by normalizing GH gene expression, offering therapeutic potential for T2DM management

***Keywords***: Type 2 diabetes, flavonoids, gene expression, onion peels, growth hormone

## INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) represents one of the most significant global health challenges of our time, accounting for over 90% of all diabetes diagnoses worldwide (Zakaria *et al.,* 2021). This chronic metabolic disorder is characterized by persistent hyperglycemia resulting from a complex interplay between genetic predisposition and environmental factors (Geng and Huang 2020). The condition's insidious nature often leads to delayed diagnosis, as many individuals remain asymptomatic during the early stages of disease development (Djamil *et al.,* 2017).

The development of T2DM involves multiple pathophysiological mechanisms, Including insulin resistance in target tissues, inadequate insulin production by pancreatic beta cells, and dysregulated glucagon secretion (Djamil *et al.,* 2017). While genetic factors play an important role, as evidenced by the 40% lifetime risk in offspring of diabetic parents, the rapid global increase in T2DM prevalence over recent decades highlights the critical influence of lifestyle changes (Varshney *et al.,* 2019). Modern Western lifestyles, characterized by reduced physical activity and increased caloric intake, create an environment that promotes the development of diabetes in genetically susceptible individuals (Nachawi *et al.,* 2022).

Uncontrolled diabetes leads to serious complications affecting both small and large blood vessels (microvascular and macrovascular systems). Which significantly increase morbidity and mortality rates among diabetic patients (Singh, 2015). Current management strategies combine lifestyle modifications with various pharmacological interventions, including metformin, sulfonylureas, and newer agents like GLP-1 receptor agonists (Said *et al.,* 2024). However, no single treatment provides a complete cure, emphasizing the need for novel therapeutic approaches.

Metformin is the most widely prescribed oral antihyperglycemic agent for Type 2 Diabetes. It is recommended as the first-line treatment alongside diet and exercise at the time of diagnosis. The drug can be safely and effectively combined with other oral antihyperglycemic agents and insulin, offering synergistic effects Metformin is considered an excellent choice for both specialized and primary healthcare settings .Metformin's primary mechanisms include reducing appetite, decreasing intestinal carbohydrate absorption, inhibiting hepatic gluconeogenesis, and increasing glucose uptake by peripheral tissues It also promotes free fatty acid esterification, inhibits lipolysis in adipose tissue, and protects β-cells from glucose toxicity and lipotoxicity .Recent findings suggest that increased secretion of glucagon-like peptide-1 (GLP-1) may also contribute to its efficacy The diverse and collective cellular actions lead to its characterization as a 'multitasking medication'(Papana and Maltezos 2009)

Growth hormone (GH) is a key regulator of metabolism and plays a complex role in glucose homeostasis.

* **Corresponding author.**
**E-mail address: Shaimaagamal462@gmail.com**
**DOI: 10.21608/jacb.2025.415145.1121**

Under normal conditions, GH is produced by the pituitary gland and stimulates the liver to produce insulin-like growth factor-1 (IGF-1) (Al-Massadi *et al*., 2022). This GH/IGF-1 axis is crucial for maintaining proper metabolic function. In healthy individuals, GH helps regulate blood sugar levels through several mechanisms. It promotes glucose production in the liver during fasting periods and influences how cells respond to insulin (Blum *et al* ., 2018). However, in diabetic conditions, this system becomes disrupted. Studies have shown that chronic elevation of GH can contribute to insulin resistance, particularly in liver tissue (Kim and Park 2017). The relationship between GH and diabetes is bidirectional. Diabetes can alter GH secretion patterns, while abnormal GH levels can worsen diabetic control (Sharma *et al*.,2020). In diabetic patients, GH gene expression in the liver may be altered, contributing to metabolic dysfunction. Understanding how to modulate GH expression could provide new therapeutic targets for diabetes management (Weber *et al .,* 2017 ).

Portal insulin delivery also plays a crucial role in controlling the GH/IGF-1 system. Insulin directly affects how the liver responds to GH by influencing GH receptor production (Nijenhuis *et al.,* 2024). When insulin levels are abnormal, as occurs in diabetes, this can lead to imbalanced GH and IGF-1 levels, further complicating metabolic control (Yuen *et al.,* 2024).

Flavonoids are natural compounds found abundantly in fruits, vegetables, and medicinal plants. These polyphenolic molecules have gained considerable scientific attention due to their potential health benefits (Panche *et al*., 2016). Research has shown that flavonoids possess multiple properties that may be beneficial for diabetes management, including antioxidant, anti-inflammatory, and direct metabolic regulatory effects (Manavi SP, Amiri T, Mozafaryan MJ (2021).

Onion peels, typically discarded as waste, are surprisingly rich sources of bioactive flavonoids. The main compounds include quercetin and its derivatives, along with organosulfur compounds (Rodrigues *et al*., 2017). These substances have demonstrated various beneficial effects on glucose metabolism in experimental studies.

Several mechanisms explain how onion peel flavonoids may help manage diabetes. First, they provide strong antioxidant protection, which is important because diabetes is associated with increased oxidative stress (Joković *et al.*, 2024). Second, these compounds can reduce inflammation, which contributes to insulin resistance (Jung *et al*., 2011). Third, some studies suggest that onion peel extracts can inhibit enzymes involved in carbohydrate digestion, helping to control post-meal blood sugar spikes (Poonia, 2023).

Animal studies have shown that onion peel extracts can improve insulin sensitivity, increase glucose storage in muscles and liver, and protect organs from diabetes-related damage (Saleh *et al*., 2023). However, the specific effects of these flavonoids on hepatic GH gene expression have not been thoroughly investigated. Therefore, this study aimed to investigate the genetic impact of flavonoids derived from onion (*Allium cepa*) peels on hepatic tissue in STZ-induced type 2 diabetic mice, with particular focus on growth hormone gene expression. Specifically, we aimed to evaluate the effects of different doses of onion peel flavonoid extracts on blood glucose levels, HbA1c, and hepatic GH gene expression compared to standard metformin treatment.

# MATERIALS AND METHODS

**Preparation of Flavonoid Extract**

Red onion peels were collected and processed to obtain flavonoid-rich extracts. The peels were dried and ground into fine powder. The powder was extracted using 70% methanol (1:10 weight/volume ratio) at room temperature for 48 hours (Nan *et al.,* 2018). The mixture was filtered and concentrated under reduced pressure. The concentrated extract was further purified using ethyl acetate to isolate the flavonoid-rich fraction ( Haggag, M. I. (2021). The final extract was standardized based on total flavonoid content before use in experiments.

**Experimental Animals and Study Design**

All studies that involve the use of animals were authorized by the Agriculture Sector Committee of the Mansoura University Committee on Experimental Animal Care and Studies Ethics ( No AGR.MS.25.08.8 )

Twenty-five male albino mice (local strain) weighing 20-30 grams , age 6_8 weeks were obtained from the animal house at the National Centre of Research, Cairo. The mice were acclimatized for one week in well-ventilated polypropylene cages (20×25×15 cm) with five mice per cage under natural light-dark cycles.

The animals were randomly divided into five groups of five mice each:

- Group 1 (C): Normal control group
- Group 2 (D): Diabetic control group (STZ-induced, untreated)
- Group 3 (D+M200): Diabetic mice treated with metformin (200mg/kg body weight/day) (Darwish et al., 2022)
- Group 4 (D+F100): Diabetic mice treated with flavonoid extract (100mg/kg body weight/day) (klaudia *et al* ., 2025 )
- Group 5 (D+F200): Diabetic mice treated with flavonoid extract (200mg/kg body weight/day) (klaudia *et al* ., 2025 )

Treatment began one week after diabetes induction and continued for four weeks. Both flavonoid extract and metformin were administered orally.

**Induction of Type 2 Diabetes**

Type 2 diabetes was induced using a single intraperitoneal injection of streptozotocin (STZ) at 40mg/kg body weight. STZ was prepared in cold citrate buffer (pH 4.5) and administered after overnight fasting (Darwish et al., 2022) Seven days after injection, blood glucose levels were measured from the tail vein using a glucometer. Mice with fasting blood glucose levels ≥180 mg/dL were considered diabetic and included in the study.

**Animal sacrifice and sample handling**

**Blood samples:**

Collected via tail vein sampling weekly for glucose monitoring and via cardiac puncture at euthanasia for comprehensive biochemical analyses

**Tissue samples:**

Liver was rapidly excised, weighed, and was saves in snap-frozen in liquid nitrogen and stored at -80°C for gene expression analysis

**Biochemical Analysis**

During the experimental period, blood glucose levels were monitored weekly starting seven days after diabetes induction. Measurements were taken from fasted mice by snipping the tail with a sharp razor and using a rapid glucometer (RIGHT TEST wiz plus blood glucose

monitoring system, JIANGSU, CHINA). Blood glucose was measured at weeks 1, 2, 3, and 4 of the treatment period to assess the progressive effects of the interventions. HbA1c levels were measured at the end of the experimental period using an immunoassay kit (Human Biochemical and Diagnostic, Germany)(Thomas 2012) on a semi-automated biochemistry analyzer (BIOELAB ES-102).

**Gene Expression Analysis**

Total RNA was extracted from liver tissues using TRIzol reagent (Qiagen, USA) following the manufacturer's protocol. RNA quality and concentration were assessed using a Nanodrop spectrophotometer. 1000 ng of total RNA was reverse transcribed complementary DNA (cDNA). conversion using a First-strand Synthesis Kit (GeneDirex, Cat. MB310-T100)

Quantitative real-time PCR (qRT-PCR) was performed to analyze GH gene expression using Xpert fast SYBR (uni) (GRISP, Cat: #GE20.0100). The primer sequences used were listed in Table (1). Relative gene expression was calculated using the $2^{-\Delta\Delta Ct}$ method (Livak and Schmittgen, 2001) with β-actin as the reference gene.

Reaction conditions : Initial activation at 95°C for 12 min, one cycle, and 40 cycles as follows: denaturation at 95°C for 15 s, annealing at 60°C for 20 s, elongation at 72°C for 20 s, the temperature was raised from 63 to 95 °C for melting curve analysis at the end of the last cycle.

**Table 1. Primer sequences used for qRT-PCR analysis**

| Gene | Accession No | Nucleotide Sequence 5′-3′ | Amplicon Size (bp) | Amplicon Tm | Ref. |
|---|---|---|---|---|---|
| GH | NM_008117.3 | F.5'GGTCGAGGAAAACAGGTAGGG-3′<br>R.5′-GCTCGGAGCACAGCATTAGA-3′ | 240 | 79.578 | AlSuhaymi *et al* ., 2021 |
| β actin | NM_007393.5 | F 5′-GGCACCACACCTTCTACAATG-3′<br>R 5′-GGGGTGTTGAAGGTCTCAAAC-3′ | 133 | 80.162 | Darwish *et al.,* 2022 |

**Statistical Analysis**

Statistical analysis was performed using SPSS software version 22. Data are presented as mean ± standard error (SE). One-way analysis of variance (ANOVA) was used for group comparisons, followed by Tukey's post hoc test. Statistical significance was set at $p<0.05$.

## RESULTS AND DISCUSSION

**Results**

In this study examined the effects of onion peel flavonoid extracts on glucose metabolism and hepatic gene expression in STZ-induced diabetic mice. The results are presented in two main sections: biochemical analysis of glucose control parameters and molecular analysis of hepatic GH gene expression.

**Biochemical Analysis**

The biochemical analysis focused on evaluating the antidiabetic effects of flavonoid extracts by measuring key glucose control parameters, including blood glucose and HbA1c levels in all experimental groups.

**Blood Glucose and HbA1c Levels**

STZ injection successfully induced diabetes in the experimental mice. The diabetic control group (G2) exhibited significantly elevated blood glucose levels (242±12.9 mg/dL) compared to the normal control mice (G1: 88.2±0.97 mg/dL). Similarly, HbA1c levels were markedly increased in diabetic mice (G2: 7.86±0.25) compared to controls (G1: 4.06±0.05) (Figure 1).

Treatment with flavonoid extract resulted in significant improvements in both parameters. The low-dose treatment group (G4: 100mg/kg) showed a reduction in blood glucose levels (122.65±7.67 mg/dL) (Figure 1) and HbA1c (6.93±0.15) (Figure 2). The high-dose treatment group (G5: 200mg/kg) demonstrated even better results, with blood glucose levels of 107.55±6.23 mg/dL and HbA1c of 6.6±0.1 (Figure 2).

Metformin treatment (G3) also improved glucose control (134.15±8.62 mg/dl glucose, 7.63±0.15 HbA1c) (Figure 2), but the improvements were less pronounced than those achieved with the higher dose of flavonoid extract.

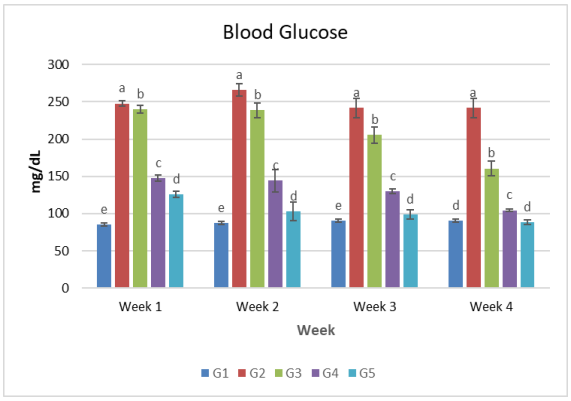



**Figure 1. Blood glucose levels (mg/dL) recorded weekly during the treatment duration. The values are the mean ± SE (n=5). Statistically significant differences between groups ($p<0.05$) are denoted by different letters (a, b, c, d). G1: Normal control, G2: Diabetic control, G3: Diabetic + metformin (200 mg/kg), G4: Diabetic + flavonoid extract (100 mg/kg), and G5: Diabetic + flavonoid extract (200 mg/kg).**

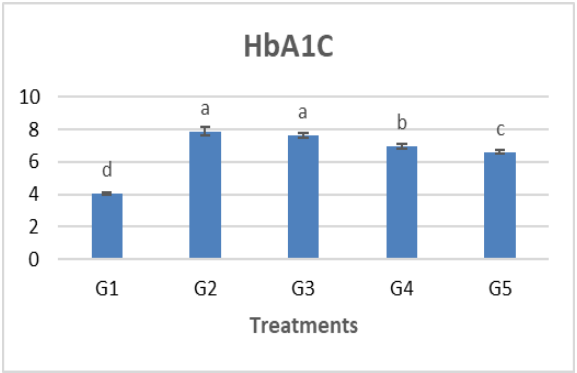



**Figure 2. HbA1c levels showing a significant reduction in flavonoid-treated groups. The values are the mean ± SE (n=5). Statistically significant differences between groups ($p<0.05$) are denoted by different letters (a, b, c, d). G1: Normal control, G2: Diabetic control, G3: Diabetic + metformin (200 mg/kg), G4: Diabetic + flavonoid extract (100 mg/kg), and G5: Diabetic + flavonoid extract (200 mg/kg).**

**Gene Expression Analysis**

Gene expression analysis was performed to investigate the molecular effects of flavonoid treatment on hepatic metabolism, with a specific focus on growth hormone gene expression as a key regulator of glucose homeostasis.

**Relative Hepatic *GH* Gene Expression**

All samples exhibited melting curve peaks at approximately the same Tm for the target sequence of target and reference gene. *GH* gene expression analysis revealed interesting patterns across the experimental groups. In the diabetic control group (G2), GH gene expression was downregulated (0.2±0.002) compared to normal controls (G1: 1±0.03) (Figure 3).

Metformin treatment (G3) significantly increased GH gene expression (0.4±0.04) compared to diabetic controls. Similarly, flavonoid extract treatment resulted in a distinctive elevation in GH gene expression. Interestingly, the high-dose group (G5) showed the most pronounced suppression with expression levels of 0.97±0.04, while the low-dose group (G4) demonstrated more moderate normalization with expression levels of 0.7±0.06 (Figure 3).

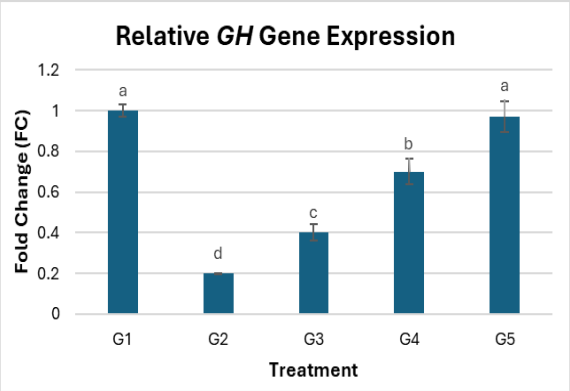



**Figure 3. G2 (Diabetic): Notable downregulation (0.2 FC) G3 (Metformin): Partial recovery (0.4 FC) G4 (Low-dose flavonoid): Moderate recovery (0.7 FC) G5 (High-dose flavonoid): Almost complete recovery (0.97 FC, not significantly different from normal) High-dose flavonoid therapy (G5: 200mg/kg) showed almost total normalization of GH expression (0.97±0.04 FC ), with no significant difference compared to normal controls (p>0.05), suggesting complete therapeutic restoration of hepatic GH gene expression.**

**Discussion**

This study investigated the potential therapeutic effects of onion peel flavonoid extracts on glucose metabolism and hepatic GH gene expression in a mouse model of type 2 diabetes. Our findings demonstrate that flavonoid treatment significantly improved glucose control and modulated hepatic GH gene expression in diabetic mice.

**Glucose Control and Metabolic Improvements**

The weekly glucose monitoring revealed important insights into the kinetics of treatment responses. Flavonoid extracts demonstrated a rapid onset of action, with significant glucose reductions observed as early as week 1. This rapid response contrasts with metformin, which showed a more gradual effect over the treatment period. The sustained glucose-lowering effects throughout the four-week period suggest that flavonoids may provide consistent metabolic benefits without tolerance development.

The superior performance of the higher flavonoid dose in achieving near-normal glucose levels indicates a dose-response relationship for glucose control, although this pattern was not observed for GH gene expression modulation. This differential response suggests that glucose control and GH expression regulation may involve distinct molecular pathways activated by flavonoids (Lu *et al* ., 2024).

The results clearly show that onion peel flavonoid extracts have potent antidiabetic effects. Both doses of flavonoid extract significantly reduced blood glucose and HbA1c levels compared to untreated diabetic mice. Notably, the higher dose (200mg/kg) achieved better glucose control than the standard diabetes medication metformin.

These improvements can be attributed to several mechanisms. Flavonoids, particularly quercetin found abundantly in onion peels, have been shown to enhance insulin sensitivity and improve glucose uptake by peripheral tissues (Mendes and Gunes 2022). Additionally, these compounds can inhibit intestinal α-glucosidase activity, reducing post-meal glucose spikes (Ansari *et al*, 2022). The antioxidant properties of flavonoids may also protect pancreatic beta cells from oxidative damage, helping preserve insulin production capacity (Jomova *et al* ., 2025).

**Effect of flavonoid treatment on hepatic *GH* gene**

One of the most significant findings of this study is the effect of flavonoid treatment on hepatic GH gene expression. In diabetic mice, GH gene expression was downregulated compared to normal controls. This downregulation likely represents a disruption of normal metabolic signaling, as diabetes can impair the liver's ability to maintain proper GH expression patterns (List *et al.,* 2014).

The reduction in GH expression in diabetic conditions may contribute to metabolic dysfunction and impaired glucose homeostasis. Our results showed that both flavonoid extract treatments effectively restored GH gene expression levels toward normal. This suggests that part of their therapeutic benefit may involve normalizing GH signaling in the liver.

The dose-dependent restoration effect of flavonoid treatment on GH expression is particularly noteworthy. The higher dose (200mg/kg) resulted in near-complete normalization of GH expression with an insignificant fold change (FC= 0.97±0.04), while the lower dose (100mg/kg) showed moderate restoration (FC= 0.7±0.06). This pattern suggests that higher doses of flavonoids may be more effective in restoring normal GH expression patterns.

**Proposed mechanisms of flavonoid action**

The beneficial effects of onion peel flavonoids likely involve multiple pathways. Quercetin and other flavonoids can directly activate insulin signaling pathways, improving glucose uptake and utilization (Kumar *et al* ., 2022). They also possess strong anti-inflammatory properties, which help reduce chronic inflammation that contributes to insulin resistance (Cordeiro GS 2023 ).

At the molecular level, flavonoids may influence gene expression through various mechanisms. They can modulate transcription factors involved in metabolic regulation and affect epigenetic modifications that control gene expression (Cazarolli *et al* ., 2008). The normalization of GH gene

expression observed in our study may result from these molecular effects.

**Clinical Implications**

These findings have important implications for diabetes management. Onion peels are readily available agricultural waste products that could be developed into cost-effective therapeutic supplements. The superior glucose-lowering effects compared to metformin suggest that flavonoid extracts could serve as adjunct therapy or even alternative treatments for some patients.

The modulation of GH gene expression represents a novel mechanism of action that distinguishes flavonoid therapy from conventional diabetes medications. This could be particularly beneficial for patients who do not respond adequately to standard treatments.

## CONCLUSION

This study demonstrates that onion peel flavonoid extracts have significant antidiabetic effects in STZ-induced diabetic mice. The treatment improved glucose control more effectively than metformin and normalized hepatic GH gene expression. These findings suggest that onion peel flavonoids could represent a promising natural therapeutic approach for type 2 diabetes management. The modulation of GH gene expression represents a novel mechanism that may contribute to the therapeutic benefits observed. Further research is needed to fully explore the clinical potential of these natural compounds.

## REFERENCES


Al-Massadi O, Parini P, Fernø J, Luquet S, Quiñones M (2022). Metabolic actions of the growth hormone-insulin growth factor-1 axis and its interaction with the central nervous system. Rev Endocr Metab Disord. doi: 10.1007/s11154-022-09732-x.

AlSuhaymi, N., Darwish, A. M., & Khattab, A. E. (2021). Protective and therapeutic effects of two novel strains of Lactobacilli on diabetes-associated disorders induced by a high level of fructose. Molecular Biology Reports, 48(6), 4333–4340. https://doi.org/10.1007/s11033-021-06448-0

Ansari P, Choudhury ST, Seidel V, Rahman AB, Aziz MA, Richi AE, Rahman A, Jafrin UH, Hannan JMA, Abdel-Wahab YHA (2022). Therapeutic potential of quercetin in the management of type-2 diabetes mellitus. Life. 12:1146.

Blum WF, Alherbish A, Alsagheir A, El Awwa A, Kaplan W, Koledova E, Savage MO (2018). The growth hormone–insulin-like growth factor-I axis in the diagnosis and treatment of growth disorders. Endocr Connect. 7:R212-R222. doi: 10.1530/EC-18-0099.

Cazarolli LH, Zanatta L, Alberton EH, Figueiredo MSRB, Folador P, Damazio RG, Pizzolatti MG, Silva FRMB (2008). Flavonoids: cellular and molecular mechanism of action in glucose homeostasis. Mini Rev Med Chem. 8(9):1032-1038.

Cordeiro GS, Santos LS, Vieira GP, Espírito-Santo DA, Teixeira RS, Matos RJB, Costab CAS, Deiróa TCBJ, Barreto-Medeiros JM (2023). Antioxidant, anti-inflammatory and anti-obesity effects of onion and its by-products in high-fat fed rodents: a systematic review. Braz J Biol. 83:e266108. doi: 10.1590/1519-6984.266108.

Darwish, A. M., Khattab, A.-E.-N. A., Sharaf, H. A., Abdelhafee, M. A., & Abd El-Razik, K. A. (2022). Improvement of male mice fecundity by using two new Lactobacillus strains. Egyptian Journal of Chemistry, 65(8), 317–321. https://doi.org/10.21608/ejchem.2022.109966.5012

Djamil R, Winarti W, Zaidan S, Abdillah S (2017). Antidiabetic activity of flavonoid from Binahong leaves (Anredera cordifolia) extract in alloxan induced mice. J Pharmacogn Nat Prod. 3(2). doi: 10.4172/2472-0992.1000139.

Furman BL (2021). Streptozotocin-induced diabetic models in mice and rats. Curr Protoc. 1:e78. doi: 10.1002/cpz1.78.

Geng T, Huang T (2020). Gene-environment interactions and type 2 diabetes. Asia Pac J Clin Nutr. 29(2):220-226.

Haggag, M. I. (2021). Extraction, separation, and identification of two flavonoids from leaves of Catharanthus roseus (L.) G. Don. Journal of Basic and Environmental Sciences, 8, 91–96. https://journals.ekb.eg/article_371208.html

Joković N, Matejić J, Zvezdanović J, Stojanović-Radić Z, Stanković N, Mihajlov-Krstev T, Bernstein N (2024). Onion peel as a potential source of antioxidants and antimicrobial agents. Agronomy. 14(2):453. doi: 10.3390/agronomy14030453.

Jomova K, Alomar SY, Valko R, Liska J, Nepovimova E, Kuca K, Valko M (2025). Flavonoids and their role in oxidative stress, inflammation, and human diseases. Chem Biol Interact. 413:111489.

Jung J, Young Y, Sun Moon M, Jeon Kim J, Kwon O (2011). Onion peel extracts ameliorate hyperglycemia and insulin resistance in high fat diet/streptozotocin-induced diabetic rats. Nutr Metab (Lond).

Kim SH, Park MJ (2017). Effects of growth hormone on glucose metabolism and insulin resistance in human. Ann Pediatr Endocrinol Metab. 22(3):145-152. doi: 10.6065/apem.2017.22.3.145.

Kumar M, Barbhai MD, Hasan M, Punia S, Dhumal S, Radha R, Rais N, Chandran D, Pandiselvam R, Kothakota A, Tomar M, Satankar V, Senapathy M, Anitha T, Dey A, Sayed AS, Gadallah FM, Amarowicz R, Mekhemar M (2022). Onion (*Allium cepa* L.) peels: a review on bioactive compounds and biomedical activities. Biomed Pharmacother. 146:112498.

L.,HbA1C , Labor and Diagnose,8 ed ., 236-242 (2012)Varshney R, Mishra R, Das N, Sircar D, Roy P (2019). A comparative analysis of various flavonoids in the regulation of obesity and diabetes: an in vitro and in vivo study. J Funct Foods. 59:194-205.

List EO, Berryman DE, Funk K, Jara A, Kelder B, Wang F, Stout MB, Xu Zhi X, Sun L, White TA, LeBrasseur NK, Pirtskhalava T, Tchkonia T, Jensen EA, Zhang W, Masternak MM, Kirkland JL, Miller RA, Bartke A, Kopchick JJ (2014). Liver-specific GH receptor gene-disrupted (LiGHRKO) mice have decreased endocrine IGF-I, increased local IGF-I, and altered body size, body composition, and adipokine profiles. Endocrinology. 155(5):1793-805.

Livak KJ, Schmittgen TD (2001). Analysis of relative gene expression data using real time quantitative PCR and the 2^(-ΔΔCT) method. Methods. 25:402-408.

Lu C, Wolfs D, El Ghormli L, Levitsky LL, Katz LEL, Laffel LM, Patti M, Isganaitis E (2024). Growth hormone mediators and glycemic control in youths with type 2 diabetes: a secondary analysis of a randomized clinical trial. JAMA Netw Open. 2024;7(2):e240447. doi: 10.1001/jamanetworkopen. 0447.

Manavi SP, Amiri T, Mozafaryan MJ (2021). Role of flavonoids in diabetes. J Rev Med Sci. 1(3):e149. doi: 10.5281/zenodo.5211371.

Mendes B, Gunes-Bayir A (2022). The role of quercetin in diabetes mellitus. K Int J Health Sci. 5(3):74-78.

Nachawi N, Rao PP, Makin V (2022). The role of GLP-1 receptor agonists in managing type 2 diabetes. Cleve Clin J Med. 89(8):457- 464.

Nan L, Huang J, Li Y, Cui C, Peng G, Xie B, Liu H, Liu Y (2018). Study on the extraction and antioxidant properties of flavonoids from onion. In: 2018 International Conference on Biotechnology and Bioengineering (8th ICBB). AIP Publishing; p. 020005-1. doi: 10.1063/1.5092383.

Nijenhuis-Noort EC, Berk KA, Neggers SJCMM, van der Lely AJ (2024). The fascinating interplay between growth hormone, insulin-like growth factor-1, and insulin. Endocrinol Metab. 39:83-89. doi: 10.3803/EnM.2024.101.

Panche AN, Diwan AD, Chandra SR (2016). Flavonoids: an overview. J Nutr Sci. 5:e47. doi: 10.1017/jns.2016.41.

Papana, N., & Maltezos, E. (2009). Metformin: A review of its use in the treatment of type 2 diabetes. Clinical Medicine: Therapeutics, 1, 1367–1381. https:// doi.org/ 10.4137/CMT.S1725

Poonia P (2023). Utilization of onion peel as a functional food. Pharma Innov J. 12(8):419-426.

Rodrigues AS, Almeida DPF, Simal-Gándara J, Pérez-Gregorio MR (2017). Onions: a source of flavonoids. In: IntechOpen; doi: 10.5772/intechopen.69896.

Said AB, Ibrahim IA, Bahr HI, El-Beltagy MA (2024). Biochemical evaluation of metformin and GLP-1 therapy in amelioration metabolic disturbance in rats induced type II diabetes. SCVMJ. 29(2):403.

Saleh El-Marasy SE, Abd El-Aziz AA, Abd El-megeid Doaa AA, Mandor BM (2023). The effect of red onion peel and fortified bread with these peels on kidney function, liver enzymes, and antioxidant enzymes in diabetic rats. Egypt J Nutr. 38(2).

Sharma R, Kopchick JJ, Puri V, Sharma VM (2020). Effect of growth hormone on insulin signaling. Mol Cell Endocrinol. 518:111038. doi: 10.1016/j.mce.111038.

Singh S (2015). Genetics of type 2 diabetes: advances and future prospect. J Diabetes Metab. 6(4). doi: 10.4172/2155-6156.1000519.

Weber MM, Biller BMK, Pedersen BT, Pournara E, Christiansen JS, Höybye C (2017). The effect of growth hormone (GH) replacement on blood glucose homeostasis in adult nondiabetic patients with GH deficiency: real-life data from the NordiNet® International Outcome Study. Clin Endocrinol (Oxf). 86(2):192-198. doi: 10.1111/cen.13256.

Yuen KCJ, Hjortebjerg R, Ganeshalingam AA, Clemmons DR, Frystyk J (2024). Growth hormone/insulin-like growth factor I axis in health and disease states: an update on the role of intra-portal insulin. Front Endocrinol (Lausanne). 15:1456195. doi: 10.3389/fendo.2024.1456195.

Zakaria ZZ, Ahmad MN, Qinna NA (2021). Animal models in type 2 diabetes mellitus research: pros and cons. Jordan J Agric Sci. 17(4). doi: 10.35516/jjas.v17i4.95.

# الأثر الوراثي للفلافونويدات المستخلصة من قشور البصل (*Allium cepa* L.) على أنسجة الكبد في نموذج الفئران المصابة بمرض السكرى من النوع الثاني

**محمد حسن عبد العزيز[١]، محمد عبد الحميد طاهر[٢]، غادة حمدي النادي[٣] و الشيماء جمال فتح الله[١]***

[١]قسم الوراثة – كلية الزراعة – جامعة المنصورة- مصر
[٢]قسم الكيمياء - كلية الزراعة - جامعة المنصورة - مصر
[٣]مركز البحوث الوراثية الطبية - كلية الطب - جامعة عين شمس - مصر

## الملخص

يُصيب مرض السكري من النوع الثاني أكثر من ٩٠٪ من مصابى السكري في العالم مشتملا تفاعلات معقدة بين الوراثية والبيئية. لهرمون النمو دورًا حاسمًا في أيض الجلوكوز، ويؤدى اختلال تنظيمه إلى مضاعفات مرض السكري. هدفت الدراسة إلى بحث تأثيرات المستخلصات الفلافونويدية لقشر البصل على التعبير الجيني لهرمون النمو في كبد الفئران المصابة بالسكري ، إجريت التجربة على ٢٥ فأرًا ألبينو ذكر قسموا إلى خمس مجموعات: مجموعة طبيعية ككنترول سلبى ، مجموعة مصابة بالسكري ككنترول إيجابى ، مجموعة مصابة ومُعالجة بالميتفورمين ٢٠٠ملجم\كج وح ، مجموعة مصابة ومُعالجة بالمستخلص ١٠٠ملجم\كج وح، ومجموعة مصابة ومُعالجة بالمستخلص ٢٠٠ ملجم\كج وح. قدرت مستويات جلوكوز الدم أسبوعيًا خلال فترة العلاج التي استمرت أربعة أسابيع، بعدها قيست مستويات الهيموجلوبين وتم تحليل التعبير الجيني لهرمون النمو في الكبد باستخدام تقنية qRT-PCR. أظهرت النتائج تحسنًا تدريجيًا في التحكم بالجلوكوز بالدم، حيث انخفضت مستوياته في المجموعتين المعالجتين بالمستخلص ١٠٠ملجم\كج وح (١٠٤،٤mg/dl) و٢٠٠ملجم\كج وح (٨٨،٤mg/dl) مقارنةً بالمجموعة المصابة(٢٤٢mg/dl)، كما انخفضت مستويات الهيموجلوبين في المجموعتين المعالجتين بالمستخلص ١٠٠ملجم\كج وح(6.93) و ٢٠٠ملجم\كج وح (6.6) مقارنةً بالمجموعة المصابة (7.86). كان التعبير الجيني المقارن لجين هرمون النمو منخفضًا في الفئران المصابة عن الفئران الطبيعية لكنه عاد إلى طبيعته بعد العلاج بالمستخلص ٢٠٠ ملجم\كج وح ، حيث أظهرت فئران هذه المعاملة تغييرًا طفيفًا وغير معنوى في متوسط التعبير الجينى المقارن، بينما أظهرت المجموعة المعاملة بالمستخلص ١٠٠ملجم\كج وح تغيرا بسيطا معنويا في متوسط التعبير الجينى المقارن.مما يشير إلى أن المستخلص قد يساعد في استعادة التوازن الأيضي في الكبد لدى مرضى السكري الأمر الذى يؤهلها لتقديم فوائد علاجية محتملة لمرض السكري من النوع الثاني.