

Research Article

Does Filgrastim, a Granulocyte-Colony Stimulating Factor, Potentiate the Glycemic Effect of Glimepiride? Evidence from an HFD/STZ Rat Model

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Article Info

Keywords: Type2 Diabetes Mellitus, Glimepiride, Filgrastim, Glycemic control.**Received:** 10.09.2026;**Accepted:** 01.10.2026;**Published:** 06.10.2026 © 2026 by the author's. The terms and conditions of the Creative Commons Attribution (CC BY) license apply to this open access article.

Abstract

Background: Type 2 diabetes mellitus is a chronic inflammatory metabolic disorder. Glimepiride, a sulfonylurea, has been separately reported to have anti-inflammatory properties. At the same time, granulocyte-colony stimulating factor (Filgrastim) has been proposed to modulate inflammatory pathways relevant to glucose homeostasis. Whether combining Filgrastim with glimepiride confers additional glycemic benefit over glimepiride alone has not been established. **Aim:** To evaluate and compare the glycemic effects of glimepiride, Filgrastim, and their combination in a rat model of type 2 diabetes. **Methods:** Twenty-five adult male albino rats were assigned to five groups (n=5): normal control, untreated DM, glimepiride (0.5 mg/kg oral), Filgrastim (70 µg/kg subcutaneous), and glimepiride+Filgrastim. T2DM was induced by two weeks of high-fat diet followed by a single low dose of streptozotocin (35 mg/kg i.p.). Treatments were given for 28 days. Endpoints were fasting blood glucose (FBG) and glycated hemoglobin (HbA1c); group differences were evaluated by one-way ANOVA with post hoc tests. **Results:** All HFD/STZ groups developed hyperglycemia and elevated HbA1c versus normal controls. Compared with untreated T2DM, glimepiride monotherapy and the glimepiride+Filgrastim combination produced significant reductions in FBG and HbA1c. Filgrastim alone did not significantly alter either glycemic measure. Although the combination group showed numerically lower FBG and HbA1c than glimepiride alone, the difference was not statistically significant. The study did not measure inflammatory mediators, limiting conclusions about mechanisms. **Conclusion:** In summary, glimepiride improved glycemic control in this rat DM model; Filgrastim alone had no glucose-lowering effect at the tested dose and duration. Adding Filgrastim produced only a non-significant numeric improvement over glimepiride, providing limited support for an inflammation-mediated synergistic benefit and highlighting the need for direct measurement of inflammatory markers in future work.

1. Introduction

Type 2 diabetes mellitus is increasingly recognized as a chronic, low-grade inflammatory condition, in which pro-inflammatory cytokines contribute to the development of insulin resistance and impaired glycemic control [1, 2]. This has prompted growing interest in whether

agents with incidental anti-inflammatory or immunomodulatory properties might confer glucose-lowering benefits beyond their primary indications [3].

Glimepiride, a third-generation sulfonylurea used primarily to stimulate pancreatic insulin secretion in type 2 diabetes, has been reported to exert effects that extend beyond glycemic control [4]. In addition to its role as a K-ATP channel modulator, glimepiride has been shown to influence plasma membrane dynamics, pro-inflammatory cytokine secretion, and peroxisome proliferator-activated receptor- γ (PPAR- γ) activation [5]. In a clinical study of patients with type 2 diabetes, 24 weeks of glimepiride treatment produced significant decreases in toxic advanced glycation end products, eotaxin, and fibroblast growth factor-2, together with a trend toward increased granulocyte-colony stimulating factor (G-CSF) and granulocyte-macrophage colony-stimulating factor (GM-CSF) [6], and decreases in fractalkine, soluble CD40 ligand, macrophage inflammatory protein- β , vascular endothelial growth factor, and soluble receptor for advanced glycation end products; the authors concluded that glimepiride may possess anti-oxidative, anti-inflammatory, and angiogenic properties with potential to repair tissue damage [4]. Separately, at the cellular level, glimepiride has been reported to suppress macrophage-derived cytokine release: treatment reduces membrane-associated CD14 on macrophages by shedding it into a soluble form, and pretreated cells produce significantly less tumor necrosis factor- α , interleukin- 1β , and interleukin-6 in response to inflammatory stimuli, an effect attributed to glimepiride's activation of glycosylphosphatidylinositol-specific phospholipase C (GPI-PLC) and consequent CD14 shedding [6]. Collectively, these findings have led to the characterization of glimepiride as a novel anti-inflammatory agent.

Filgrastim, a recombinant form of granulocyte-colony stimulating factor (G-CSF), is best known for stimulating neutrophil production [7], but has also been investigated for metabolic and vascular effects relevant to diabetes. In a rat model of alloxan-induced diabetes with superimposed glucose fluctuations, subcutaneous Filgrastim (200 $\mu\text{g/kg/day}$) raised circulating insulin levels relative to untreated diabetic animals, although levels remained below those of non-diabetic controls, and treatment mitigated the endothelial and structural damage to the aortic wall associated with fluctuating hyperglycemia [8]. These findings support a possible protective role for G-CSF in the vascular and, potentially, metabolic derangements associated with glucose instability.

Taken together, these observations raise the hypothesis that Filgrastim may lower blood glucose, at least in part, through modulation of inflammatory pathways, and that this effect could be potentiated when combined with glimepiride given its independently reported anti-inflammatory actions. It should be noted, however, that the broader literature on G-CSF and glucose metabolism is not uniformly supportive of this direction of effect: G-CSF has also been characterized as a saturated-fatty-acid-induced myokine with insulin-desensitizing properties in humans, with data showing that G-CSF inhibits insulin-stimulated signaling and glycogen synthesis in human myotubes and adipocytes, and that a functional CSF3 gene variant is associated with adipose tissue and whole-body insulin resistance and impaired glucose tolerance in individuals with elevated circulating free fatty acids [9]. This suggests that the net effect of G-CSF on glucose homeostasis may be context- and dose-dependent, differing between acute pharmacologic administration in a setting of vascular injury and chronic, lipid-driven elevation as part of an inflammatory myokine response. This apparent discrepancy underscores the need for direct experimental testing of the proposed glimepiride-Filgrastim combination, with explicit attention to dosing, duration, and the metabolic context in which G-CSF is administered.

2. Methods

2.1. Materials

Drugs and chemicals

- Streptozotocin (STZ) (Sigma-Aldrich, St. Louis, MO, USA).
- Glimepiride (Amaryl) (Sanofi Arabia -Egypt).
- Filgrastim (Fil) (AMGEN, California, USA)

Animals

Rats were obtained from the animal unit of the Faculty of Medicine, University of Benghazi, and housed in the care of the laboratory. All experiments in this study were done according to the ethics guidelines of the University of Benghazi. A total of 25 adult male albino rats weighing 200–250 g were housed under regulated standard environmental conditions ($25\pm 1^\circ\text{C}$, $50\pm 2\%$ humidity), with 12-hour light/dark cycles, and allowed free access to commercial rat chow and tap water ad libitum.

Experimental protocol

The rats were randomly divided into five groups ($n=5$ rats/group). The control group (G1) was fed normal feed. The rest of the rats were fed a high-fat diet for two weeks [10]. The high-fat diet (HFD) employed was adapted from Abd-Eldaim's study [11], with some modifications. The chemical composition of the HFD is described in Table 1. A single dose of streptozotocin was administered intraperitoneally (35 mg/kg body weight) to animals fasted for 12 h, and the control animals received only vehicle [12]. After 3–7 days, blood glucose was measured to confirm the establishment of diabetes.

Rats in the DM group (G2) did not receive any medical intervention. Rats in the Glim-treated group (G3) received Glimepiride (0.5 mg/kg/day, PO) concurrently for 28 days [13]. Rats in the Fil-treated group (G4) received filgrastim (70 $\mu\text{g/kg/day}$, subcutaneously (SC) for 28 days [14]. Rats in the Glim-Fil-treated group (G5) received the same doses of Glimepiride and filgrastim for 28 days.

Table 1: Compositions of the standard and high-fat diets

	Standard diet		HFD	
	Energy Kcal/100 g	%	Energy Kcal/100 g	%
Protein	96.14	25.3	62	12
Fat	49.4	13	303.5	57
Carbohydrates	228	60	161.5	30.5
Fiber	6.46	1.7	3	0.5
Total	380	100	530	100

Blood Collection

Animals were euthanized with a high dose of urethane (1.5 mg/kg, i.p.) (UNTHSC, 2020). Blood samples were obtained for fasting blood glucose and HbA1c measurement.

2.2. Statistical Analysis

The obtained results were tabulated as means $\pm$ standard error of the mean (SEM). GraphPad Prism computer software (version 8) was used to carry out the statistical analysis. Comparisons between different groups were made using one-way analysis of variance (one-way ANOVA) followed by post hoc (least significant difference “LSD”) tests as described by [15]. The differences between different groups were considered to be statistically significant when $p < 0.05$.

3. Results

FBG and HbA1c were measured in five experimental groups. The Control group had a mean FBG of 61 ± 1.8 mg/dL and a mean HbA1c of $3.75 \pm 0.1\%$. The Diabetes (DM) group showed markedly higher glycemic values, with a mean FBG of 199.4 ± 2.5 mg/dL and a mean HbA1c of $8.6 \pm 0.1\%$. The Glimepiride (Glim) group had a mean FBG of 134.7 ± 0.5 mg/dL and a mean HbA1c of $6.3 \pm 0.2\%$. The Filgrastim (Fil) group recorded a mean FBG of 185.8 ± 1.5 mg/dL and a mean HbA1c of $8.1 \pm 0.05\%$. The combined Filgrastim and Glimepiride (Fil-Glim) group showed a mean HbA1c of 123.4 ± 1.1 mg/dL and a mean HbA1c of $5.9 \pm 0.04\%$.

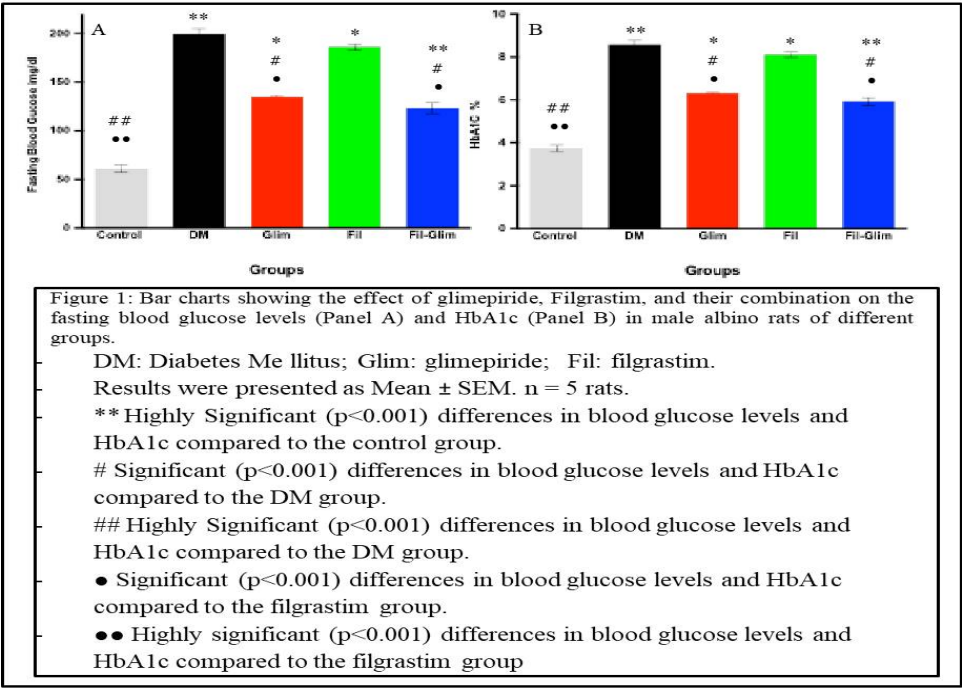


Figure 1: Bar charts showing the effect of glimepiride, Filgrastim, and their combination on the fasting blood glucose levels (Panel A) and HbA1c (Panel B) in male albino rats of different groups

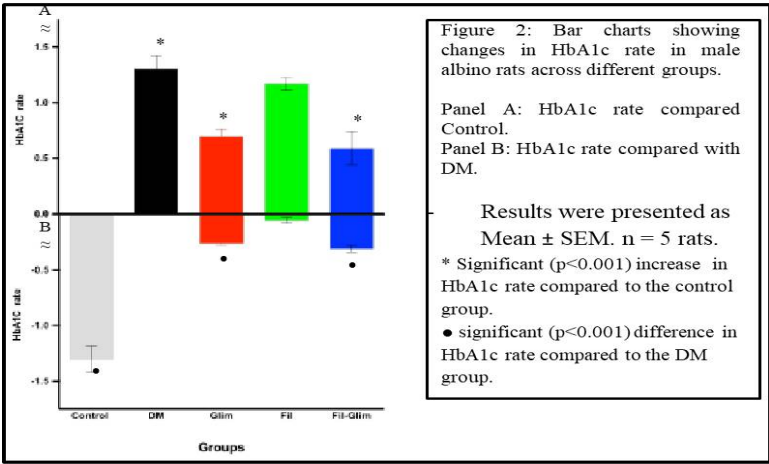


Figure 2: Bar charts showing changes in HbA1c rate in male albino rats across different groups

Compared with the Control group, all other groups (DM, Glim, Fil, and Fil-Glim) showed statistically significant differences in the reported outcomes (all $p < 0.0001$) Figure 1. It was notable that the rate of HbA1c increased in the DM and treatment groups (Glim, Fil, and Fil-Glim) by 1.3 ± 0.05 ; 0.7 ± 0.03 ; 1.2 ± 0.03 ; and 0.6 ± 0.03 , respectively, in relation to the control group, with a significant statistical difference (all $p < 0.0001$). Thus, each treatment and the diabetic condition differed markedly from the healthy Control group Figure 2, Panel A. Comparing the diabetes group with the treatment groups, the Fil group did not differ significantly in glycemic control ($p = 0.1027$ in FBG and HbA1c) Figure 1. It was also found that its HbA1c ratio was comparable with the DM group (0.00 vs 0.05 ± 0.01), which was not statistically significant ($p = 0.9564$) Figure 2, Panel B. Conversely, the DM group differed significantly from Glim and Fil-Glim ($p < 0.0001$) Figure 1, and both groups decreased the rate of HbA1c by 0.26 ± 0.007 and 0.31 ± 0.006 , respectively, which were statistically significant ($p = 0.0218$, 0.0057) Figure 2, Panel B, indicating that each intervention produced values significantly different from the untreated diabetic state.

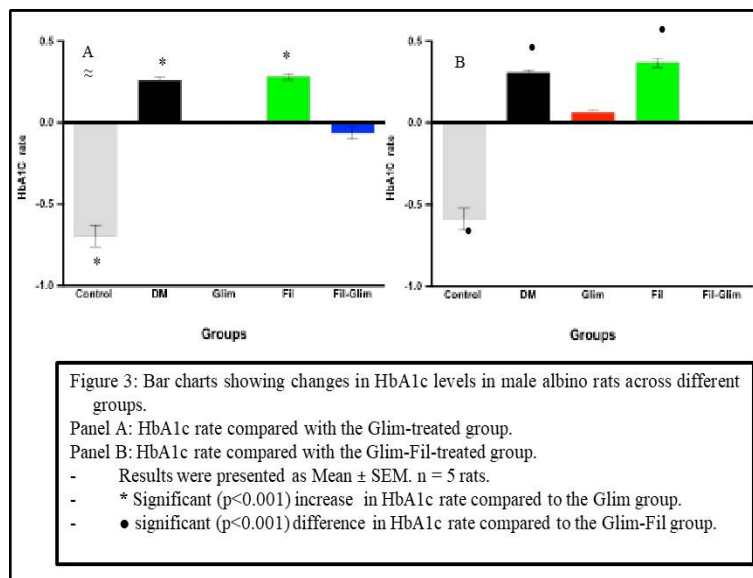


Figure 3: Bar charts showing changes in HbA1c levels in male albino rats across different groups

When comparing with the Glimepiride-treated group, the Fil group had a statistically significant increase ($p < 0.0001$) in both FBG and HbA1c Figure 1. The rate of HbA1c increased significantly by 0.28 ± 0.01 ($p < 0.0001$) Figure 3, Panel A. Although there were no statistically significant differences between Glim and Fil-Glim ($p = 0.2153$), the glycemic measures were slightly reduced in the Fil-Glim group (FBG = 134.7 ± 0.5 vs 123.4 ± 1.1 ; HbA1c = 6.3 ± 0.2 vs 5.9 ± 0.04) Figure 1. Additionally, the rate of HbA1c was reduced in the Fil-Glim group by 0.06 ± 0.008 ; However it was not statistically significant ($p = 0.672$) Figure 3, Panel A. The comparison between Fil and Fil-Glim produced a high statistical significance in their glycemic control ($p < 0.0001$) Figure 1. The rate of HbA1c was reduced in Glim-Fil by 0.37 ± 0.01 , which was statistically significant ($p < 0.0001$) Figure 3, Panel B. These results suggest that while Filgrastim alone did not affect glycemic control, adding Glimepiride to Filgrastim produced a slight reduction in these values; however, they were not significant. Suggesting the minor effect of the filgrastim combination.

In conclusion, induction of diabetes produced marked increases in FBG and HbA1c compared with Control. Treatment with Filgrastim alone could not affect glycemic measures, while Glimepiride and the combination treatment significantly differed from untreated diabetic animals, lowering glycemic parameters versus DM. However, there were no significant differences between these two treatment groups themselves (Glimepiride vs Fil-Glim), indicating comparable effects on FBG and HbA1c across these interventions in this study.

4. Discussion

Glimepiride and filgrastim have different primary pharmacological actions, but both may influence inflammatory processes. Glimepiride is a second-generation sulfonylurea that lowers blood glucose mainly by stimulating insulin secretion from pancreatic β -cells. It has been reported that glimepiride modulates inflammatory mediators [6]. Filgrastim is a recombinant granulocyte colony-stimulating factor that promotes the proliferation, maturation, and mobilization of neutrophils. However, filgrastim is not primarily an antihyperglycemic drug, and its potential effect on glucose metabolism would be expected to occur indirectly through immune or inflammatory mechanisms [16].

In the present study, two weeks of high-fat diet feeding followed by a single dose of streptozotocin produced a T2DM phenotype, reflected in significantly elevated FBG and HbA1c relative to control across all manipulated groups. This combined dietary/chemical protocol is a well-established means of reproducing the insulin resistance-plus-relative-insulin-deficiency pattern seen in human T2DM, in contrast to high-dose STZ alone, which more closely mimics type 1 diabetes [12, 17]. The consistent hyperglycemia and elevated HbA1c observed in this study across the T2DM, glimepiride, Filgrastim, and combination groups relative to control confirms that the model was successfully established before treatment effects were assessed [18].

Although there was a significant difference between the glimepiride and control groups, a reduction in the glycemic values was noticed. This aligns well with the results of Bhateja and Singh, in which glimepiride failed to normalize blood glucose in rat-induced type 2 DM [19]. In contrast, glimepiride treatment significantly reduced both FBG and HbA1c compared with the DM group, confirming its antihyperglycemic effect. This result is consistent with previous studies showing the glimepiride could lower fasting glucose and HbA1c by stimulating pancreatic insulin secretion and improving overall glycemic control [19, 20]. Clinical evidence has shown meaningful reductions in FBG and HbA1c with glimepiride monotherapy, supporting the pattern observed in the present study. This indicates that glimepiride is highly effective

but may not always return glycemic markers completely to baseline, depending on disease severity and experimental conditions [21]. The filgrastim-treated group showed a more limited metabolic response. Its glycemic values differed significantly from the control, glimepiride, and combination groups; they were not significantly different from the DM group. This indicates that filgrastim alone did not produce a robust glucose-lowering effect in this model. This outcome is not unexpected because filgrastim is primarily a recombinant granulocyte colony-stimulating factor used to modulate neutrophil production and immune recovery rather than to directly correct hyperglycemia [22]. This was consistent with other studies. In one study, the G-CSF injection failed to promote physiologically significant regeneration of pancreatic islets in post-irradiated diabetic mice [23]. Lee and colleagues also reported that G-CSF injection did not lower FBG and HbA1c in type 2 Diabetic rats [24]. Nevertheless, inflammation is now recognized as a major contributor to insulin resistance and beta-cell dysfunction in diabetes, and colony-stimulating factor pathways may influence immune activation in diabetic states [25]. Reports linking inflammatory cytokines and diabetic dysregulation [26, 27] suggest that filgrastim may have exerted only an indirect or partial metabolic effect through immune modulation, which would explain why its impact on FBG and HbA1c was weaker than that of glimepiride [28]. Therefore, the present results suggest that filgrastim alone is insufficient to normalize glycemia, even if it may contribute to inflammatory regulation.

Although the combined filgrastim-glimepiride group showed significant improvement compared with the DM group, it was not statistically significant compared with the control group, indicating an overall beneficial effect on glycemic control. However, the combined treatment did not outperform glimepiride alone; indeed, FBG and HbA1c reductions were slightly lower than in the glimepiride group, and the difference between these two groups was not significant. This suggests that glimepiride remained the principal agent responsible for glucose lowering, while filgrastim added a minor metabolic advantage under the present conditions. One possible explanation is that filgrastim influenced the inflammatory environment without sufficiently enhancing insulin sensitivity or beta-cell function to improve glycemic indices beyond glimepiride monotherapy [29]. Another interpretation is that the anti-inflammatory effect, although biologically relevant, may not translate into superior FBG or HbA1c reduction when combined with an already potent hypoglycemic drug [30].

In conclusion, glimepiride, alone or in combination with Filgrastim, effectively improved glycemic control in this HFD/STZ rat model of T2DM, while Filgrastim alone did not. The combination showed a non-significant numerical advantage over glimepiride monotherapy. These findings do not provide direct support for the proposed inflammation-mediated glucose-lowering mechanism of Filgrastim, and dedicated measurement of inflammatory mediators is required before this hypothesis can be adequately tested.

Article Information

Ethical Approval: The study was approved by the University of Bengazi Ethics Committee.

Informed Consent: Written informed consent was obtained from all participants before their inclusion in the study.

Data Availability: The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of Interest: The authors declare that they have no conflict of interest.

Funding: No external funding was received for this study.

Author Contributions: H.M.G. - Conceptualization, Methodology, Data curation, Formal analysis, Writing – review & editing, Supervision; K.R.A. - Methodology, Data curation, Writing – original draft.

Acknowledgments: The authors thank the technical staff of the departments of clinical pharmacology, and of the animal housing.

AI Use Disclosure: No generative artificial intelligence tools were used in the preparation of this manuscript.

References

- [1] M. Donath and S. Shoelson. Type 2 diabetes as an inflammatory disease. *Nature reviews.Immunology*, 11(2):98–107, 2011.
- [2] G. S. Hotamisligil. Inflammation and metabolic disorders. *Nature*, 444(7121):860–867, 2006.
- [3] D. Li, J. Zhong, Q. Zhang, and J. Zhang. Effects of anti-inflammatory therapies on glycemic control in type 2 diabetes mellitus. *Frontiers in immunology*, 14:1125116, 2023. URL <https://doi.org/10.3389/fimmu.2023.1125116>.
- [4] I. Nakamura, J. Oyama, H. Komoda, A. Shiraki, Y. Sakamoto, I. Taguchi, A. Hiwatashi, A. Komatsu, M. Takeuchi, S. Yamagishi, T. Inoue, and K. Node. Possible effects of glimepiride beyond glycemic control in patients with type 2 diabetes: a preliminary report. *Cardiovascular Diabetology*, 13(1):15, 2014. URL <https://doi.org/10.1186/1475-2840-13-15>.
- [5] J. Rojas, R. Añez, M. S. Martínez, M. Ochoa, J. Salazar, M. J. Calvo, and V. Bermúdez. A tale about perfect partners: New horizons in glimepiride and metformin Mechanisms of action. *Revista Venezolana de Endocrinología y Metabolismo*, 14(2), 2016. URL https://saber.ucv.ve/ojs/index.php/rev_aavft/article/view/11943.
- [6] V. Ingham, A. Williams, and C. Bate. Glimepiride reduces CD14 expression and cytokine secretion from macrophages. *Journal of Neuroinflammation*, 11:115, 2014. URL <https://doi.org/10.1186/1742-2094-11-115>.
- [7] D. C. Dale, J. Crawford, Z. Klippel, M. Reiner, T. Osslund, E. Fan, P. K. Morrow, K. Allcott, and G. H. Lyman. A systematic literature review of the efficacy, effectiveness, and safety of filgrastim. *Supportive Care in Cancer*, 26(1):7–20, 2018. URL <https://doi.org/10.1007/s00520-017-3854-x>.
- [8] I. Jafri, G. Alsharif, W. Al Zamzami, M. El-Sharnouby, A. S. Abdel Monsef, M. M. Khalifa, O. M. Mehanna, M. A. M. Abbas, A. I. Sharahili, and A. El Askary. The Influence of Blood Glucose Instability on Aortic Health in Diabetes: Evaluating the Role of G-CSF Therapy. *Vivo*, 39(6):3351–3357, 2025. URL <https://doi.org/10.21873/invivo.14132>.

- [9] A. M. Ordelheide, N. Gommer, A. Böhm, C. Hermann, I. Thielker, F. Machicao, A. Fritsche, N. Stefan, H. U. Häring, and H. Staiger. Granulocyte colony-stimulating factor (G-CSF): A saturated fatty acid-induced myokine with insulin-desensitizing properties in humans. *Molecular metabolism*, 5(4):305–316, 2016. URL <https://doi.org/10.1016/j.molmet.2016.02.001>.
- [10] D. A. Magalhães, W. T. Kume, F. S. Correia, T. S. Queiroz, E. W. Allebrandt Neto, M. P. D. Santos, N. H. Kawashita, and S. A. França. High-fat diet and streptozotocin in the induction of type 2 diabetes mellitus: a new proposal. *An Acad Bras Cienc*, 91(1):e20180314, 2019. URL <https://doi.org/10.1590/0001-3765201920180314>.
- [11] M. A. Abd Eldaim, F. M. Ibrahim, S. H. Orabi, A. Hassan, and H. S. El Sabagh. l-Carnitine-induced amelioration of HFD-induced hepatic dysfunction is accompanied by a reduction in hepatic TNF- α and TGF- β 1. *Biochemistry and Cell Biology*, 96(6):713–725, 2018. URL <https://doi.org/10.1139/bcb-2018-0074>.
- [12] P. L. Guerra-Ávila, T. J. Guzmán, B. Vargas-Guerrero, J. A. Domínguez-Rosales, A. B. Cervantes-Garduño, A. M. Salazar-Montes, L. V. Sánchez-Orozco, and C. M. Gurrola-Díaz. Comparative Screening of the Liver Gene Expression Profiles from Type 1 and Type 2 Diabetes Rat Models. *International Journal of Molecular Sciences*, 25(8), 2024. URL <https://doi.org/10.3390/ijms25084151>.
- [13] J. Kakadiya and S. P. Rathod. Protective Effect of Glimepiride Alone and Its Combination With Metformin on Serum Glucose, Hba1c and Liver Functions in Nondiabetic and Diabetic Rats. *Pharmacologyonline*, 2:261–272, 2009.
- [14] A. Prakash, B. Medhi, and K. Chopra. Granulocyte colony stimulating factor (GCSF) improves memory and neurobehavior in an amyloid- β induced experimental model of Alzheimer’s disease. *Pharmacology, biochemistry, and behavior*, 110:46–57, 2013. URL <https://doi.org/10.1016/j.pbb.2013.05.015>.
- [15] P. Armitage and G. Berry. *Statistical Methods in Medical Research*. Blackwell, Scientific Publications, 3rd edition, 1994.
- [16] Y. Lee, Y. S. Song, C. H. Fang, B. I. So, J. Y. Park, H. W. Joo, I. H. Park, G. Y. Shen, J. H. Shin, H. Kim, Y. H. Ahn, and K. S. Kim. Anti-obesity effects of granulocyte-colony stimulating factor in Otsuka-Long-Evans-Tokushima fatty rats. *PLoS One*, 9(8):e105603, 2014. URL <https://doi.org/10.1371/journal.pone.0105603>.
- [17] K. Srinivasan, B. Viswanad, L. Asrat, C. L. Kaul, and P. Ramarao. Combination of high-fat diet-fed and low-dose streptozotocin-treated rat: a model for type 2 diabetes and pharmacological screening. *Pharmacological research*, 52(4):313–320, 2005. URL <https://doi.org/10.1016/j.phrs.2005.05.004>.
- [18] A. Guo, N. A. Daniels, J. Thuma, K. D. McCall, R. Malgor, and F. L. Schwartz. Diet is critical for prolonged glycemic control after short-term insulin treatment in high-fat diet-induced type 2 diabetic male mice. *PLoS One*, 10(1):e0117556, 2015. URL <https://doi.org/10.1371/journal.pone.0117556>.
- [19] P. K. Bhateja and R. Singh. Antidiabetic Activity of Acacia tortilis (Forsk.) Hayne ssp. raddiana Polysaccharide on Streptozotocin-Nicotinamide Induced Diabetic Rats. *BioMed research international*, 8(3):152–162, 2016. URL <https://doi.org/10.1155/2014/572013>.
- [20] J. Kakadiya and N. Shah. Effect of Glimepiride on Serum Glucose, Hba1c and Lipid Profile in Normal and Type 2 Diabetic Rats. *Pharmacologyonline*, 1:176–182, 2010.
- [21] A. Basit, M. Riaz, and A. Fawwad. Glimepiride: evidence-based facts, trends, and observations (GIFTS). [corrected]. *Vascular health and risk management*, 8:463–472, 2012. URL <https://doi.org/10.2147/HIV.S33194>.
- [22] Z. Cantürk, N. Z. Cantürk, B. Cetinarıslan, O. Sentürk, C. Ercin, and C. Yenise. Effect of G-CSF on ethanol-induced hemorrhagic gastritis model in diabetes mellitus-induced rats. *Endocrine Research*, 27(1-2):191–201, 2001. URL <https://doi.org/10.1081/erc-100107180>.
- [23] L. E. Logdberg, A. M. Adon, M. B. Singer, T. Vikulina, and C. D. Hillyer. Failure of G-CSF Mobilization of Hematopoietic Stem Cells To Prevent or Reverse STZ-Induced Hyperglycemia in Mice. *Blood*, 104(11):4183, 2004. URL <https://doi.org/https://doi.org/10.1182/blood.V104.11.4183.4183>.
- [24] K. A. Lee, K. T. Park, . H. M. Yu, H. Y. Jin, H. S. Baek, and T. S. Park. Effect of Granulocyte Colony-Stimulating Factor on the Peripheral Nerves in Streptozotocin-Induced Diabetic Rat. *Diabetes & Metabolism Journal*, 37(4):286–290, 2013. URL <https://doi.org/10.4093/dmj.2013.37.4.286>.
- [25] P. V. Dlodla, S. E. Mabhidia, K. Ziqubu, B. B. Nkambule, S. E. Mazibuko-Mbeje, S. Hanser, A. K. Basson, C. Pheiffer, and A. P. Kengne. Pancreatic β -cell dysfunction in type 2 diabetes: Implications of inflammation and oxidative stress. *World Journal of Diabetes*, 14(3):130–146, 2023. URL <https://doi.org/10.4239/wjd.v14.i3.130>.
- [26] Y. H. Lim, J. H. Joe, K. S. Jang, Y. S. Song, B. I. So, C. H. Fang, J. Shin, J. H. Kim, H. K. Lim, and K. S. Kim. Effects of granulocyte-colony stimulating factor (G-CSF) on diabetic cardiomyopathy in Otsuka Long-Evans Tokushima fatty rats. *Cardiovascular Diabetology*, 10:92, 2011. URL <https://doi.org/10.1186/1475-2840-10-92>.
- [27] T. V. Velikova, P. P. Kabakchieva, Y. S. Assayov, and T. Georgiev. Targeting Inflammatory Cytokines to Improve Type 2 Diabetes Control. *BioMed Research International*, 2021. URL <https://doi.org/10.1155/2021/7297419>.
- [28] J. Surendar, V. Mohan, N. Pavankumar, S. Babu, and V. Aravindhan. Increased levels of serum granulocyte-macrophage colony-stimulating factor is associated with activated peripheral dendritic cells in type 2 diabetes subjects (CURES-99). *Diabetes Technology & Therapeutics*, 14(4):344–349, 2012. URL <https://doi.org/10.1089/dia.2011.0182>.

- [29] M. J. Haller, M. A. Atkinson, C. H. Wasserfall, T. M. Brusko, C. E. Mathews, M. Hulme, M. Cintron, J. Shuster, K. McGrail, A. Posgai, and D. Schatz. Mobilization without immune depletion fails to restore immunological tolerance or preserve beta cell function in recent onset type 1 diabetes. *Clinical and Experimental Immunology*, 183(3):350–357, 2016. URL <https://doi.org/10.1111/cei.12731>.
- [30] A. Lin, J. A. Mack, B. Bruggeman, L. M. Jacobsen, A. L. Posgai, C. H. Wasserfall, T. M. Brusko, M. A. Atkinson, S. E. Gitelman, P. A. Gottlieb, M. J. Gurka, C. E. Mathews, D. A. Schatz, and M. J. Haller. Low-Dose ATG/GCSF in Established Type 1 Diabetes: A Five-Year Follow-up Report. *Diabetes*, 70(5):1123–1129, 2021. URL <https://doi.org/10.2337/db20-1103>.