pISSN 1978-2071 | eISSN 2580-5967
Jurnal Ilmiah Kedokteran Wijaya Kusuma 15 (1): Page 67-76, Maret 2026

Comparative Effects of Garlic and Bitter Melon Extracts on Kidney Histopathological Changes in Hyperglycemic White Rats

Rafidah Nur Hidayati[1], Noer Kumala Indahsari [2], Ayu Cahyani Noviana[3], Ayly Soekanto[4]

Abstract

Background: Hyperglycemia in diabetes mellitus is known to induce renal damage through oxidative stress, inflammatory pathways, and tubular cell degeneration. Herbal plants with antihyperglycemic and antioxidant properties have attracted considerable attention as potential therapeutic agents. Garlic (*Allium sativum* L.) and bitter melon (*Momordica charantia*) contain bioactive compounds that may reduce blood glucose levels and provide nephroprotective effects. **Objective:** To determine and compare the effects of garlic and bitter melon extracts on the kidney histopathology of hyperglycemic white rats (*Rattus norvegicus*). **Methods:** This experimental laboratory study employed a *post-test only control group design* using 35 rats (*Rattus novergicus)* divided into four groups: normal control (K-), hyperglycemic control (K+), garlic extract treatment P1 and P2), and bitter melon extract treatment (P3 and P4). Hyperglycemia was induced using alloxan monohydrate (150 mg/kg BW). Blood glucose levels were measured using a glucometer, and kidney tissues were examined histopathologically using Hematoxylin–Eosin staining under 400× magnification. **Results:** The results showed that both garlic and bitter melon extracts significantly reduced blood glucose levels ($p < 0.05$) compared with the hyperglycemic control group. Histopathological evaluation revealed decreased tubular degeneration and inflammatory cell infiltration in the treatment groups. Among the treatments, bitter melon extract at 150 mg/kg BW demonstrated the most prominent improvement in renal tubular morphology. **Conclusion:** These findings indicate that both garlic and bitter melon extracts possess antihyperglycemic and nephroprotective properties in hyperglycemic rats, with bitter melon extract showing a slightly stronger protective effect on kidney histological structure.

Keywords: *Allium sativym, Momordica charantia, Rattus novergicus*

ARTICLE INFO

AUTHOR'S AFFILIATIONS
Faculty of Medicine, Wijaya Kusuma University, Surabaya, Indonesia[1], Departement of Biochemistry, Fakultas of Medicine, Wijaya Kusuma University, Surabaya[2] Departement of Public Health, Faculty of Medicine, Wijaya Kusuma University, Surabaya[3], Departement of Anatomy, Faculty of Medicine, Wijaya Kusuma University, Surabaya[4].

CORRESPONDING AUTHOR
Noer Kumala Indahsari
Department of Biochemistry, Faculty of Medicine, Wijaya Kusuma University, Surabaya.
Email: noerkumala2023@gmail.com

Article history

Received	17-10-2025
Revised	05-02-2026
Accepted	16-03-2026
Available online	31-03-2026

Please cite this article in APA 7 th edition style as:
Hidayati, R. F., Indahsari, N.K., Noviana, A.C., & Soekanto, A. (2026). Comparative Effects of Garlic and Bitter Melon Extracts on Kidney Histopathological Changes in Hyperglycemic White Rats. *Jurnal Ilmiah Kedokteran Wijaya Kusuma, 15(1), 67-76*

https://doi.org/10.30742/jikw.v15i1.4943

Original Research Article

INTRODUCTION

Hyperglycemia is a medical condition characterized by an increase in blood glucose levels above the normal range, which is a hallmark of diabetes mellitus. This condition occurs when the body is unable to produce sufficient insulin or when insulin cannot be used effectively. Insulin functions to regulate blood glucose levels to remain within the normal range, and impairment of this function leads to glucose accumulation in the bloodstream. Factors that contribute to hyperglycemia include insufficient insulin production, insulin resistance, high-sugar and high-carbohydrate dietary patterns, lack of physical activity, and stress, which elevates adrenaline and cortisol levels (Ariqoh *et al*., 2022). In addition, hyperglycemia can also be caused by hormonal disorders such as *Cushing's syndrome*, hypothyroidism, and polycystic ovary syndrome (PCOS) (Yuniastuti et al., 2018).

Chronic hyperglycemia primarily induces microvascular injury in the glomeruli, leading to mesangial expansion, thickening of the glomerular basement membrane, and eventual glomerulosclerosis, which are hallmark features of diabetic nephropathy. Persistent metabolic and oxidative stress may subsequently contribute to tubulointerstitial injury, including tubular degeneration and inflammatory cell infiltration (Jin et al., 2023a). Therefore, although glomerular damage represents the principal pathological hallmark, tubular alterations may occur as secondary changes associated with sustained hyperglycemic conditions. If left untreated, progressive structural damage may impair renal filtration and ultimately lead to chronic kidney failure requiring dialysis or transplantation (Elendu et al., 2023).

Kidney disorders have become an increasing health concern in Indonesia. Data from the Ministry of Health of the Republic of Indonesia (2023) show a continuous rise in the number of kidney disease patients, particularly among those with diabetes and hypertension. Diabetic nephropathy is one of the leading causes of chronic kidney failure, significantly increasing healthcare costs. Many patients become aware of kidney disorders only at advanced stages, as the symptoms develop gradually—unlike type 2 diabetes mellitus, which begins with mild and progressive symptoms (Dewi et al., 2021). In addition to medical factors, unhealthy lifestyle habits such as excessive salt intake, lack of exercise, and unsupervised drug use exacerbate the condition (Rosa Tiurma, 2021).

The increasing prevalence of chronic kidney disease highlights the importance of preventive efforts and the exploration of herbal-based alternative treatments. Herbal plants have long been used to lower blood glucose levels and protect organs from the effects of hyperglycemia (Putri *et al*., 2023). Garlic contains active compounds such as *allicin* and *flavonoids*, which function as antioxidants and anti-inflammatory agents, enhance insulin sensitivity, and protect pancreatic β-cells. Meanwhile, bitter melon contains *charantin* and *polypeptide-P*, which have hypoglycemic effects by increasing glucose uptake and stimulating insulin secretion (Jin et al., 2023a). In addition, bitter melon can inhibit the *α-glucosidase enzyme* (Sun et al., 2022)

Previous investigations have demonstrated the antihyperglycemic properties of garlic (Allium sativum L.) and bitter melon (Momordica charantia). Although numerous studies have demonstrated the antihyperglycemic effects of garlic and bitter melon, most investigations have focused primarily on blood glucose reduction. Studies evaluating their comparative nephroprotective effects on kidney histopathological changes in hyperglycemic conditions remain limited. Therefore, this study aims to compare the effects of garlic and bitter melon extracts on renal histopathological alterations in hyperglycemia-induced white rats (*Rattus norvegicus*).

MATERIALS AND METHODS

Experimental Design

This study employed a true experimental laboratory design with a post-test only control group approach. The experiment was conducted in the Animal Laboratory and Biochemistry Laboratory of the Faculty of Medicine, Wijaya Kusuma University Surabaya

Animal Model

A Total samples used in this study were 35 male white rats (*Rattus norvegicus*) aged 8-12 weeks and weighing 150–200 grams. The animals were acclimatized for seven days before the experiment under controlled environmental conditions (temperature 22-25°C, 12-hour light/dark, cycle) with free access to standard laboratory feed and water.

Induction of Hyperglycemia

Hyperglycemia was induced using alloxan monohydrate (150 mg/kg BW) administered intraperitoneally. Alloxan selectively destroys pancreatic β-cells through the generation of reactive oxygen species, leading to insulin deficiency and hyperglycemic conditions (Šoltésová & Herichová, 2011)

Blood glucose levels were measured after 72 hours using a glucometer. Rats with fasting blood glucose levels ≥200 mg/dL were considered hyperglycemic and included in the treatment groups.

Treatment Groups

The rats were randomly divided into seven groups:
K- : Normal control
K+: Hyperglycemic control
P0: Glibenclamide 0.45 mg/kg BW
P1: Garlic extract 100 mg/kg BW
P2: Garlic extract 150 mg/kg BW
P3: Bitter melon extract 100 mg/kg BW
P4: Bitter melon extract 150 mg/kg BW
All treatments were administered orally once daily for 14 days.

Histopathological Examination

At the end of the treatment period, rats were sacrificed under anesthesia, and kidney tissues were collected. Tissue samples were fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned at 5 µm thickness, and stained with Hematoxylin–Eosin (HE)**.** Microscopic observations were performed using a light microscope at 400× magnification. Histopathological parameters evaluated included:

A. Normal renal tubules
B. Inflammatory cell infilttation
C. Tubular degeneration

Scoring was conducted using a semi-quantitative histopathological scoring system.

Procedure Study

Hyperglycemia was induced by *intraperitoneal* injection of alloxan at a dose of 150 mg/kg BW. Blood glucose levels were measured from tail vein blood samples using a portable glucometer based on the glucose oxidase enzymatic method. Measurements were performed after 8–10 hours of fasting to ensure standardization. Hyperglycemia was confirmed when fasting blood glucose levels were ≥200 mg/dL three days after alloxan induction. Subsequently, garlic and bitter melon extracts were administered orally for 14 consecutive days. Histopathological examination was conducted only at the end of the experimental period. No renal biopsy was performed in living animals prior to treatment. At the end of the treatment period, the rats were sacrificed, and their kidneys were collected for histopathological examination. Tissue samples were prepared using the paraffin method and stained with *Hematoxylin-Eosin* (HE). The slides were observed under a light microscope at 400× magnification.

Data analysis

The histopathological data of the kidney were analyzed descriptively to assess the degree of tubular cell degeneration and necrosis in each treatment group. The results were presented in tables and figures. Statistical analyses were conducted using SPSS software, including the *Kolmogorov–Smirnov normality test, Levene's homogeneity test, Paired Sample T-Test,* and *LSD test.*

Eligibility Ethics

This study was approved by the Research Ethics Committee of the Faculty of Medicine, Universitas Wijaya Kusuma Surabaya, under ethical clearance number 86/SLE/FK/UWKS/2025.

RESULTS

This study aimed to compare the effects of garlic extract (*Allium sativum* L.) and bitter melon extract (*Momordica charantia*) on the histopathological features of the kidneys in hyperglycemia-induced white rats (*Rattus norvegicus*).

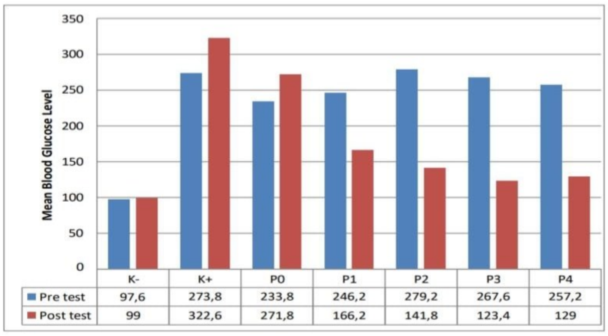

Figure 1. Blood Glucose Levels of Male White Rats Before and After Treatment

The negative control group (K−) showed stable and low glucose levels between *pretest* and *posttest* (approximately 97–100 mg/dL), indicating normal metabolic function without disturbance. The positive control group (K+) exhibited a significant increase in glucose levels from *pretest* to *posttest* (rising from approximately 270 to above 320 mg/dL), demonstrating successful induction of hyperglycemia through a high-fat and high-sugar diet.

The P0 group, which did not receive any extract treatment, also showed an increase in glucose levels similar to the K(+) group. Meanwhile, the P1–P4 groups, treated with a combination of Allium sativum and Momordica charantia extracts, showed a significant reduction in *posttest* glucose levels compared to *pretest* values. The most prominent decrease was observed in the P2, P3, and P4 groups, approaching or even surpassing the glucose-lowering effect of P1. These findings indicate the efficacy of the herbal extracts in reducing blood glucose levels in hyperglycemic rats.

Table 1. Blood Sugar Level Normality Test

Code	*p-value*	Information
K-	0.113*	Normal
K+	0.200*	Normal
P0	0.200*	Normal
P1	0.200*	Normal
P2	0.030	Abnormal
P3	0.200*	Normal
P4	0.200*	Normal

Most groups had p-values greater than 0.05 in the *Kolmogorov–Smirnov normality test*, indicating that data from K(−), K(+), P0, P1, P3, and P4 were normally distributed. However, the P2 group showed a p-value of 0.030, which is less than 0.05, indicating that its blood glucose data were not normally distributed.

Table 2. Homogeneity Test

Parameter	*Levene Statistics*	p-value
Pre-test	2.574	0.041
Post test	6.678	0.000

The Levene's test results for both pretest and posttest glucose levels were 0.041 and 0.000, respectively. Homogeneity is assumed when $p > 0.05$; thus, since both values were less than 0.05, the assumption of homogeneity of variances was not met. Therefore, the analysis was continued using paired tests to evaluate changes in blood glucose levels before and after treatment within each group.

Table 3. paired test

Code	*p-value*	Information
K-	0.063	Not significant
K+	0.001	Significant increase
P0	0.007	Significant down
P1	0.001	Significant down
P2	0.001	Significant down
P3	0.001	Significant down
P4	0.001	Significant down

The paired test was conducted to evaluate differences in blood glucose levels before and after treatment within each group. The K− group showed no significant change ($p = 0.063$), indicating stable metabolic conditions. In contrast, the K+ and P0 groups exhibited significant increases in blood glucose levels ($p < 0.05$). Meanwhile, treatment groups P1–P4 demonstrated significant reductions in blood glucose levels ($p = 0.001$), indicating the antihyperglycemic effects of garlic and bitter melon extracts.

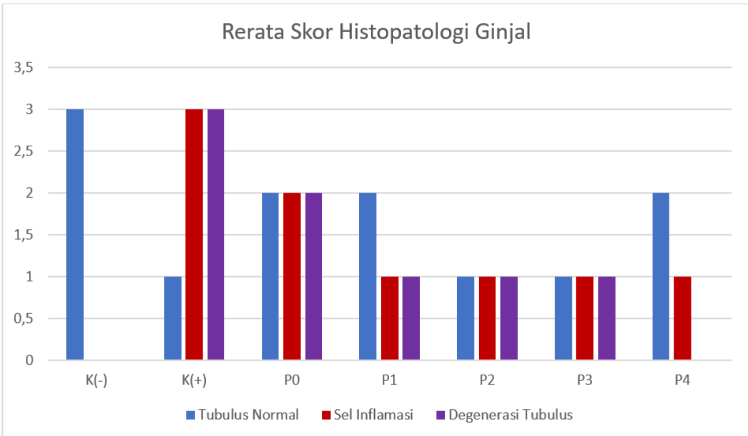

Figure 2. Scoring measurement histopathology in mice white male *posttest*

The negative control group (K−) exhibited the highest scores for normal tubules and no evidence of cellular damage, reflecting healthy kidney morphology without structural alterations. Conversely, the positive control group (K+) displayed the highest scores for tissue damage, including tubular degeneration and inflammation cell, indicating severe kidney injury due to a high-fat and high-sugar diet without treatment. Groups P0–P4 showed progressive histological improvement, with the P4 group demonstrating the highest normal tubular scores and the lowest damage scores among all treated groups. These results suggest a protective effect of *Allium sativum* and *Momordica charantia* combination extracts against hyperglycemia-induced kidney injury.

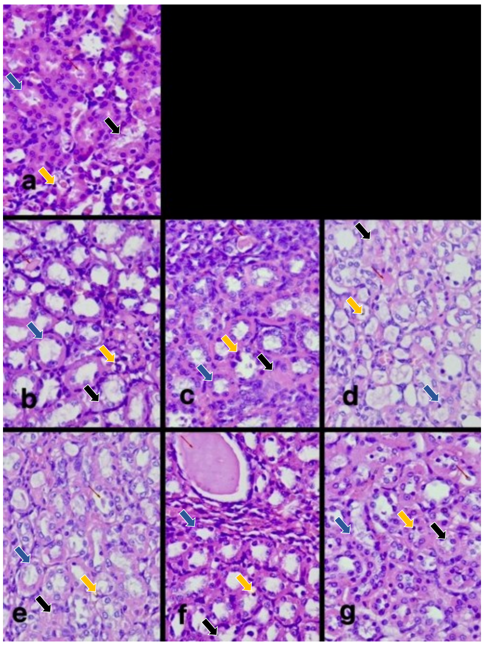

Figure 3. Histopathological image of the kidneys of the experimental group with HE examination using a light microscope with 400x magnification. (a) group K-, (b) group K+, (c) group P0, (d) group P1, (e) group P2,(f) group P3,(g) group P4. Note: Blue arrows indicate normal renal tubules; yellow arrows indicate inflammatory cell infiltration; and black arrows indicate tubular degeneration.

Histopathological examination of kidney tissue (Hematoxylin–Eosin, 400×) showed distinct morphological differences among experimental groups. In the negative control group (K−), renal tubules were predominantly normal, with mild and evenly distributed inflammatory cell infiltration, and limited tubular degeneration. In contrast, the positive control group (K+) exhibited diffuse inflammatory infiltration, and dominant, extensive tubular degeneration, indicating severe renal damage due to hyperglycemia. The P0 group demonstrated predominantly normal tubules with mild, scattered inflammation, and limited degeneration. In the P1 group, a moderate number of normal tubules were observed alongside active and diffuse inflammatory infiltration, and extensive tubular degeneration. The P2 group showed predominantly normal renal tubules with mild and evenly distributed inflammatory cells, and limited tubular degeneration. In the P3 group, normal tubules were limited, while inflammatory infiltration was active and diffuse, and dominant, extensive tubular degeneration. The P4 group demonstrated variable numbers of normal tubules with mild to moderate inflammatory infiltration, and dominant tubular degeneration.

DISCUSSION

The present study demonstrated that administration of garlic and bitter melon extracts significantly reduced blood glucose levels and improved kidney histopathological structures in hyperglycemic rats. These findings support previous studies reporting that plant-derived bioactive compounds possess both antihyperglycemic and organ-protective properties (El-Saber Batiha et al., 2020; Jin et al., 2023b; Šoltésová & Herichová, 2011).

Alloxan-induced diabetes is widely used in experimental animal models because alloxan selectively destroys pancreatic β-cells through oxidative stress mechanism (Rais et al., 2021; Rohilla & Ali, 2012; Sheriff et al., 2020). The resulting insulin deficiency leads to persistent hyperglycemia, which subsequently causes metabolic disturbances and tissue damage in various organs, including the kidneys(system (Alharbi et al., 2022; Grey Venyo, 2023; Upadhyay, 2020) Šoltésová & Herichová, 2011)

Chronic hyperglycemia promotes oxidative stress through excessive production of reactive oxygen species (ROS). Elevated ROS levels damage renal cells, particularly tubular epithelial cells, leading to inflammation, apoptosis, and structural degeneration of renal tissue (Gianchandani et al., 2020; Nasuno et al., 2022) These ROS can damage renal cells, particularly tubular epithelial cells, leading to inflammation, apoptosis, and structural degeneration of renal tissue (Gambhir, 2015; Nct, 2024; Jin et al., 2023b).

Based on the *paired sample t-test*, there was a reduction in mean blood glucose levels from 315.85 mg/dL (*pre-test*) to 219.87 mg/dL (*post-test*), with a significance value of $p < 0.001$ and an *effect size (Cohen's d)* of 1.031, indicating a large effect. These findings support the theory that proper blood glucose management can prevent and reduce the risk of kidney complications, particularly diabetic nephropathy. Chronic hyperglycemia is known to increase oxidative stress, form advanced glycation end products (AGEs), and activate inflammatory pathways that can damage renal tubular cells and trigger degeneration (Afra et al., 2023; Hushmandi et al., 2025; Lee et al., 2025; Parwani & Mandal, 2024).

Garlic (*Allium sativum*) contains several bioactive compounds such as allicin, diallyl disulfide, and flavonoids, which exhibit antioxidant and anti-inflammatory activities. Allicin has been reported to stimulate insulin secretion from pancreatic β-cells and enhance glucose metabolism in peripheral tissues (El-Saber Batiha et al., 2020; ; Chen et al., 2022). In addition, it contains *flavonoids* that help improve kidney function, reduce inflammation, and enhance antioxidant enzyme activity (Jin et al., 2023a). Similarly, bitter melon (*Momordica charantia*) has demonstrated significant antidiabetic effects. Charantin and polypeptide-P present in bitter melon act as insulin-like molecules that increase glucose uptake in peripheral tissues and reduce blood glucose levels(Prasangika, 2025). Furthermore, bitter melon extracts contain polyphenols and flavonoids that exhibit strong antioxidant properties, which may contribute to renal tissue protection (Ansari et al., 2024; Liu et al., 2025; Vesa et al., 2026).

Histopathological observations revealed that kidney tissue changes were consistent with blood glucose levels. In the untreated group, there was a drastic reduction in the number of normal tubules and an increase in inflammation and tubular degeneration. ANOVA results showed significant differences between groups in normal tubules ($p < 0.001$; $\eta^2 = 0.84$), inflammatory cells ($p = 0.005$), and tubular degeneration ($p < 0.001$). The highest mean of normal tubules was found in the healthy control group (20.55), while the diabetic control group showed the lowest value (1.33). Likewise, inflammatory cell infiltration was markedly higher in the untreated group and decreased in the treated groups, indicating that the treatment was able to reduce inflammation triggered by elevated glucose levels.

Tubular degeneration, which reflects structural and functional kidney damage due to glucotoxicity, decreased significantly in the treated groups. The untreated group had a mean degeneration score of 19.33, while the treated groups showed much lower means ranging from 1.33 to 5.00. This suggests that the treatment agents possess nephroprotective effects, likely due to active compounds such as flavonoids, saponins, or other antioxidants. Previous research by Kumar *et al*. (2021) in *Phytomedicine Reviews* stated that these compounds play a role in reducing oxidative stress and preventing cellular damage caused by chronic inflammation (Abdul-Hamid et al., 2023; Alsawaf et al., 2022).

Treatment with bitter melon (*Momordica charantia*) and garlic (*Allium sativum*) showed varying effectiveness in lowering blood glucose levels in hyperglycemic white rats (*Rattus norvegicus*). The highest reduction was observed in group P3 (bitter melon 100 mg/kg BW) at 53.9%, followed by P4 (bitter melon 150 mg/kg BW) at 49.8%, and P2 (garlic 150 mg/kg BW) at 49.2%. In contrast, the negative (K–) and positive (K+) control groups experienced increased glucose levels, indicating no therapeutic effect. Interestingly, glibenclamide (P0), as the standard drug, showed a 16.3% increase in glucose levels, possibly indicating resistance or suboptimal dosing in the animal model used.

These results were further supported by the finding that group P4 (bitter melon 150 mg/kg BW) demonstrated the most optimal histopathological kidney repair compared to other groups. All parameters of kidney damage—including inflammatory cells, and tubular degeneration—decreased by 66.7%, while the number of normal renal tubules increased significantly. On the other hand, the positive control group (K+) showed the most severe kidney damage, with the highest scores across all histopathological indicators. This indicates that bitter melon, particularly at a dose of 150 mg/kg BW, has strong potential as an effective nephroprotective and antidiabetic agent that improves kidney structure and function under hyperglycemic conditions. Additionally, garlic (*Allium sativum L.*) enhances immune function and possesses antibacterial properties (Moutia et al., 2018).

Overall, the treatments demonstrated potential as phytotherapeutic agents that not only reduce blood glucose levels but also provide nephroprotective effects on kidneys exposed to diabetes-induced stress.

CONCLUSION

Based on the histopathological findings of the kidneys of hyperglycemic white rats (*Rattus norvegicus*), extracts of garlic (*Allium sativum L.)* and bitter melon (*Momordica charantia*) were proven to improve kidney damage by reducing tubular degeneration, decreasing inflammatory cells, and increasing the number of normal tubular cells. The kidney tissue repair effect was more pronounced in the group treated with bitter melon extract compared to the garlic extract group. Further studies are recommended to identify the active compounds contained in both treatment materials to determine more specific mechanisms of action related to blood glucose reduction and kidney structure improvement, as well as to use a larger sample size with varied dosages and treatment durations to obtain more comprehensive and accurate results.

This study has several limitations, including a relatively small sample size and a short treatment duration, which limit the generalizability of the findings. In addition, biochemical blood examinations such as urea, creatinine, and MDA levels were not conducted, so the nephroprotective effects could not be fully explained.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest in this study.

ACKNOWLEDGEMENTS

The author would like to express sincere gratitude to the Faculty of Medicine, Wijaya Kusuma University Surabaya, for providing facilities and support during the implementation of this research. Special thanks are also extended to the supervisor and all parties who have contributed to the successful completion of this study.

REFERENCES

Abdul-Hamid, M., Galaly, S. R., Mohamed, H. M., Mostafa, F., & Abdel-Moneim, A. (2023). Polydatin nanoparticles attenuate oxidative stress and histopathological changes in streptozotocin model of diabetic nephropathy: targeting Nrf2/HO-1/NF-κβ signaling pathways. *Beni-Suef University Journal of Basic and Applied Sciences*, *12*(1), 99. https://doi.org/10.1186/s43088-023-00441-1

Afra, F., Mahboobipour, A. A., Salehi Farid, A., & Ala, M. (2023). Recent progress in the immunotherapy of hepatocellular carcinoma: Non-coding RNA-based immunotherapy may improve the outcome. *Biomedicine & Pharmacotherapy*, *165*, 115104. https://doi.org/10.1016/j.biopha.2023.115104

Alsawaf, S., Alnuaimi, F., Afzal, S., Thomas, R. M., Chelakkot, A. L., Ramadan, W. S., Hodeify, R., Matar, R., Merheb, M., Siddiqui, S. S., & Vazhappilly, C. G. (2022). Plant Flavonoids on Oxidative Stress-Mediated Kidney Inflammation. *Biology*, *11*(12), 1717. https://doi.org/10.3390/biology11121717

Ansari, P., Khan, J. T., Soultana, M., Hunter, L., Chowdhury, S., Priyanka, S. K., Paul, S. R., Flatt, P. R., & Abdel-Wahab, Y. H. A. (2024). Insulin secretory actions of polyphenols of *Momordica* *charantia* regulate glucose homeostasis in alloxan-induced type 2 diabetic rats. *RPS Pharmacy and Pharmacology Reports*, *3*(1). https://doi.org/10.1093/rpsppr/rqae005

Dewi, N. H., Rustiawati, E., Sulastri, T., Studi, P., Keperawatan, D., Sultan, U., & Tirtayasa, A. (2021). ANALISIS FAKTOR-FAKTOR YANG BERPENGARUH TERHADAP KEJADIAN HIPERGLIKEMIA PADA PENDERITA DIABETES MELLITUS TIPE 2 DI POLIKLINIK PENYAKIT DALAM RSUD DR. DRADJAT PRAWIRANEGARA SERANG. *Jurnal Ilmiah Keperawatan*, *2*(3), 27–34.

Elendu, C., Elendu, R. C., Enyong, J. M., Ibhiedu, J. O., Ishola, I. V., Egbunu, E. O., Meribole, E. S., Lawal, S. O., Okenwa, C. J., Okafor, G. C., Umeh, E. D., Mutalib, O. O., Opashola, K. A., Fatoye, J. O., Awotoye, T. I., Tobih-Ojeanelo, J. I., Ramon-Yusuf, H. I., Olanrewaju, A., Afuh, R. N., … Yusuf, A. (2023). Comprehensive review of current management guidelines of chronic kidney disease. *Medicine (United States)*, *102*(23), E33984. https://doi.org/10.1097/MD.0000000000033984

El-Saber Batiha, G., Magdy Beshbishy, A., G. Wasef, L., Elewa, Y. H. A., A. Al-Sagan, A., Abd El-Hack, M. E., Taha, A. E., M. Abd-Elhakim, Y., & Prasad Devkota, H. (2020). Chemical Constituents and Pharmacological Activities of Garlic (Allium sativum L.): A Review. *Nutrients*, *12*(3), 872. https://doi.org/10.3390/nu12030872

Gianchandani, R., Esfandiari, N. H., Ang, L., Iyengar, J., Knotts, S., Choksi, P., & Pop-Busui, R. (2020). Managing Hyperglycemia in the COVID-19 Inflammatory Storm. *Diabetes*, *69*(10), 2048–2053. https://doi.org/10.2337/dbi20-0022

Hushmandi, K., Klionsky, D. J., Farahani, N., Reiter, R. J., Imani Fooladi, A. A. I., Alimohammadi, M., & Aref, A. R. (2025). Regulation of pyroptosis in diabetic nephropathy by long non-coding and circular RNAs. *Clinical and Experimental Medicine*, *25*(1), 208. https://doi.org/10.1007/s10238-025-01740-w

Jin, Q., Liu, T., Qiao, Y., Liu, D., Yang, L., Mao, H., Ma, F., Wang, Y., Peng, L., & Zhan, Y. (2023a). Oxidative stress and inflammation in diabetic nephropathy: role of polyphenols. *Frontiers in Immunology*, *14*, 1–17. https://doi.org/10.3389/fimmu.2023.1185317

Jin, Q., Liu, T., Qiao, Y., Liu, D., Yang, L., Mao, H., Ma, F., Wang, Y., Peng, L., & Zhan, Y. (2023b). Oxidative stress and inflammation in diabetic nephropathy: role of polyphenols. *Frontiers in Immunology*, *14*. https://doi.org/10.3389/fimmu.2023.1185317

Lee, H.-W., Gu, M. J., Kim, D., Han, E. H., Kim, Y., & Ha, S. K. (2025). Effect of advanced glycation end products formed methylglyoxal, a food-borne dicarbonyl precursor, on the exacerbation of diabetic kidney disease by NOX4/Nrf2/NLRP3 inflammasome signaling pathway in db/db mice. *Applied Biological Chemistry*, *68*(1), 38. https://doi.org/10.1186/s13765-025-01011-y

Liu, L., Lin, Z., Cai, X., Zhang, Y., Yang, Y., Yang, C., & Liang, D. (2025). The bitterness, biosynthesis, chemical transformation, and antidiabetic activity of cucurbitane-type triterpenoids from bitter gourd (Momordica charantia L.). *Food Chemistry*, *497*, 147081. https://doi.org/10.1016/j.foodchem.2025.147081

Moutia, M., Habti, N., & Badou, A. (2018). In Vitro and In Vivo Immunomodulator Activities of Allium sativum L. *Evidence-Based Complementary and Alternative Medicine*, *2018*. https://doi.org/10.1155/2018/4984659

Nasuno, R., Yoshikawa, Y., & Takagi, H. (2022). Acetaldehyde reacts with a fluorescent nitric oxide probe harboring an o-phenylenediamine structure that interferes with fluorometry. *Free Radical Biology and Medicine*, *187*, 29–37. https://doi.org/10.1016/j.freeradbiomed.2022.05.014

Parwani, K., & Mandal, P. (2024). *Advanced glycation end products and insulin resistance in diabetic nephropathy* (pp. 117–148). https://doi.org/10.1016/bs.vh.2024.02.007

Prasangika, F. N. (2025). Computational Insights into the Comparative Analysis of Insulin- like Compounds in Bitter Melon: Targeting GSK-3 Protein and Insulin Receptor. *Biology, Medicine, & Natural Product Chemistry*, *14*(2), 1105–1110. https://doi.org/10.14421/biomedich.2025.142.1105-1110

Rais, N., Ved, A., Ahmad, R., Parveen, K., Gautam, G. K., Bari, D. G., Shukla, K. S., Gaur, R., & Singh, A. P. (2021). Model of Streptozotocin-nicotinamide Induced Type 2 Diabetes: a Comparative Review. *Current Diabetes Reviews*, *18*(8). https://doi.org/10.2174/1573399818666211117123358

Rohilla, A., & Ali, S. (2012). Alloxan Induced Diabetes: Mechanisms and Effects. *International Journal of Research in Pharmaceutical and Biomedical Science*, *3*(2).

Rosa Tiurma, J. (2021). HIGEIA JOURNAL OF PUBLIC HEALTH RESEARCH AND DEVELOPMENT Obesitas Sentral dengan Kejadian Hiperglikemia pada Pegawai Satuan Kerja Perangkat Daerah. *HIGEIA JOURNAL OF PUBLIC HEALTH RESEARCH AND DEVELOPMENT*, *5*, 354–363. https://doi.org/10.15294/higeia/v5i3/39786

Sheriff, O. L., Olayemi, O., Taofeeq, A. O., Riskat, K. E., Ojochebo, D. E., & Ibukunoluwa, A. O. (2020). A New model for Alloxan-induced diabetes mellitus in rats. *Journal of Bangladesh Society of Physiologist*, *14*(2). https://doi.org/10.3329/jbsp.v14i2.44785

Šoltésová, D., & Herichová, I. (2011). On the mechanisms of diabetogenic effects of alloxan and streptozotocin. In *Diabetologie Metabolismus Endokrinologie Vyziva* (Vol. 14, Number 3).

Sun, K., Fu, C., Li, P., Li, T., Fang, L., Xu, J., & Zhao, Y. (2022). *Effects of dietary wild bitter melon (Momordica charantia var. 2 abbreviate Ser.) extract on glucose and lipid metabolism in HFD/STZ-induced type 2 diabetic rats regulating AMPK/PI3K signaling pathway. On the other hand, the content of total*. https://ssrn.com/abstract=4142030

Vesa, C. M., Ghitea, T. C., Radu, A., Radu, A. F., Bodog, T. M., Bodog, R. F., Brata, R. D., & Bustea, C. (2026). Phytotherapeutic Supplementation with Momordica charantia: Beneficial Effects in Patients with Suboptimal Glycemic Control on Double Antidiabetic Therapy—A Real-World Evidence Observational Study. *Nutrients*, *18*(2), 309. https://doi.org/10.3390/nu18020309

Yuniastuti, A., Susanti, R., & Iswari, R. S. (2018). Efek Infusa Umbi Garut (Marantha arundinaceae L) Terhadap Kadar Glukosa dan Insulin Plasma Tikus yang Diinduksi Streptozotocyn Info Artikel. *Jurnal MIPA*, *41*(1), 34–39. http://journal.unnes.ac.id/nju/index.php/JM