Natural: Jurnal Pelaksanaan Pengabdian Bergerak bersama Masyarakat
Volume 3, Nomor.1 tahun 2025
e-ISSN: 3031-0199; p-ISSN: 3031-0202, Hal 139-147
DOI : https://doi.org/10.61132/natural.v3i1.1124
Available online at: https://journal.arikesi.or.id/index.php/Natural

Therapeutic Potential of Moringa pterigosperma Extract in Alloxan-Induced Type 2 Diabetic Rats: Endocrine and Metabolic Modulation with a Focus on LH, Testosterone, and Glucose-Insulin Homeostasis

Asia Ali Hamza
Departemen Ilmu Laboratorium Klinis, Sekolah Tinggi Farmasi, Universitas AlKafeel, Irak

*Korespondensi Penulis: asia.ali@alkafeel.edu.iq**

Article History:
Received: Januari 17, 2025;
Revised: Januari 31, 2025;
Accepted: Februari 17, 2025
Published: Februari 19, 2025

***Keywords**: Moringa pterygosperma, Type 2 Diabetes mellitus, Insulin, Luteinizing hormone,Testosterone*

Abstract.*Background: Diabetes mellitus type 2 is a chronic metabolic disorder characterized by persistent hyperglycemia and endocrine dysfunction, including disturbances in luteinizing hormone, testosterone, and insulin levels. Moringa pterygosperma, known for its antidiabetic, antioxidant, and anti-inflammatory properties, has been explored for its therapeutic potential in mitigating diabetes-induced complications.Objective: The present study aimed to estimate the effects of Moringa pterygosperma extraction on endocrine and metabolic parameters against the diabetic rats induced by alloxan, by the mensurate the on LH, testosterone, glucose, and insulin levels.Methods: Forty adult male albino Wistar rats were used in the present study which was divided into four equal groups: Control, Negative Control, Treatment one which used 100 mg/kg extract, and Treatment two which used 200 mg/kg extract). Diabetes was induced with alloxan monohydrate (100 mg/kg). After 41 days, serum samples were analyzed for testosterone, LH, glucose, and insulin concentrations. Results: The NC group showed significant reductions in testosterone (0.0926 ± 0.0081 ng/mL) and insulin (0.560 ± 0.09274 µIU/mL) levels, with increased luteinizing hormone (0.592 ± 0.03 ng/mL) and glucose (464.6 ± 18.71 mg/dL) concentrations, indicating severe endocrine and metabolic disruptions. Treatment with Moringa pterygosperma extract significantly improved these parameters in a dose-dependent manner. The T2 group exhibited near-normal levels of testosterone (0.1769 ± 0.01 ng/mL), insulin (2.140 ± 0.1435 µIU/mL), LH (0.3163 ± 0.063 ng/mL), and glucose (105.8 ± 9.34 mg/dL).*

Abstrak.

Latar Belakang: Diabetes melitus tipe 2 merupakan kelainan metabolisme kronis yang ditandai dengan hiperglikemia persisten dan disfungsi endokrin, termasuk gangguan kadar hormon luteinizing, testosteron, dan insulin. Moringa pterygosperma, yang dikenal karena sifat antidiabetik, antioksidan, dan anti-inflamasinya, telah dieksplorasi karena potensi terapeutiknya dalam mengurangi komplikasi yang disebabkan oleh diabetes. Tujuan: Penelitian ini bertujuan untuk memperkirakan efek ekstraksi Moringa pterygosperma pada parameter endokrin dan metabolik terhadap tikus diabetes yang diinduksi aloksan, dengan mengukur kadar LH, testosteron, glukosa, dan insulin. Metode: Empat puluh pria dewasa albino Wistar tikus digunakan dalam penelitian ini yang dibagi menjadi empat kelompok yang sama: Kontrol, Kontrol Negatif, Perlakuan satu yang menggunakan ekstrak 100 mg/kg, dan Perlakuan dua yang menggunakan ekstrak 200 mg/kg). Diabetes diinduksi dengan aloksan monohidrat (100 mg/kg). Setelah 41 hari, sampel serum dianalisis konsentrasi testosteron, LH, glukosa, dan insulin. Hasil: Kelompok NC menunjukkan penurunan yang signifikan pada kadar testosteron (0,0926 ± 0,0081 ng/mL) dan insulin (0,560 ± 0,09274 µIU/mL), dengan peningkatan konsentrasi hormon luteinizing (0,592 ± 0,03 ng/mL) dan glukosa (464,6 ± 18,71 mg/dL), menunjukkan endokrin dan metabolik yang parah gangguan. Pengobatan dengan ekstrak Moringa pterygosperma secara signifikan meningkatkan parameter ini dan bergantung pada dosis. Kelompok T2 menunjukkan kadar testosteron mendekati normal (0,1769 ± 0,01 ng/mL), insulin (2,140 ± 0,1435 µIU/mL), LH (0,3163 ± 0,063 ng/mL), dan glukosa (105,8 ± 9,34 mg/dL).

Kata Kunci: Moringa pterygosperma, Diabetes melitus Tipe 2, Insulin, Luteinizing hormone, Testosteron

1. INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia due to decreased insulin production or reduced insulin action, or both (Sneha, Abhinav et al. 2021). Moreover, Type 2 diabetes mellitus is considered as predominant type of diabetes characterized by insulin resistance, impaired glucose metabolism, and insufficient insulin production (Alexopoulos, Blair et al. 2019, Nakamura and Sadoshima 2020, Sneha, Abhinav et al. 2021). Besides metabolic disorder, type 2 diabetes mellitus harms endocrine function and the hypothalamic-pituitary-gonadal axis, which leads to an imbalance in luteinizing hormone, testosterone, and insulin levels (Sinha, Formica et al. 1996, Al-Saadi, Al-Charrakh et al. 2011). The Moringa pterygosperma, commonly known as Moringa oleifera or the Miracle Tree, is famous for its nutritional and medicinal properties (A'laa Hassan Abdul Hussain, Al Haideri et al. 2022). The Moringa pterygosperma is used in traditional medicine due to its antidiabetic, antioxidant, and anti-inflammatory properties, recent studies illustrated its potential in modulating metabolic and endocrine parameters, especially in diabetes-induced hormonal imbalances (Rao and Mishra 1998, kumar Bargah 2015). The study illustrated that the bioactive compounds of M. pteridosperms, including polyphenols, flavonoids, isothiocyanates, and glucosinolates, play a major role in decreased oxidative stress and enhancement the insulin sensitivity (Rao and Mishra 1998, Patil, Mohite et al. 2022).In diabetic conditions induced by alloxan, a chemical that destroys insulin-producing β-cells in the pancreas, subsequently lead to disruptions occur in glucose homeostasis and insulin secretion (Majeed and Mahmood 2024). Additionally, diabetes is associated with declines in serum testosterone levels and alterations in LH concentrations, indicative of hypothalamic-pituitary-gonadal axis dysfunction which endocrine disruptions further exacerbate the metabolic complications associated with T2DM. Thus, the present study aims to evaluate the therapeutic potential of Moringa pteridosperms extract in enchant endocrine and metabolic parameters in alloxan-induced type 2 diabetic rats by evaluating the luteinizing hormone, testosterone levels, glucose concentration, and insulin concentration (Tavafi 2013, Al-Amery, Obaid et al. 2022).

2. MATERIAL AND METHODS

Animals

Forty male albino Wistar rats, weighing between 150–200 g, were selected for the present study which was sourced from the Abo Grab animal house in Baghdad, Iraq. They were housed in standard international cages at the Faculty of Science, University of Kufa, Iraq, under

controlled environmental conditions, with a temperature range of 25–30 °C. The rats were provided with a pellet diet and water ad libitum to ensure adequate nutrition.

Experimental Design

The study has aimed to investigate the potential therapeutic effects of Moringa pterigosperma extract on endocrine and metabolic parameters in alloxan-induced diabetic rats. To this end using fourth group from forty male albino Wistar rats, was divided into four groups assigned: The C group received no treatment, serving as the control group (n=10). The N group (n=10) was administered alloxan monohydrate (100 mg/ kg body weight) intraperitoneally on the first day to induce diabetes serving as the Negative Control Group. Treatment Group 1 (T1) (n=10) received alloxan as in the NCG and was treated with an aqueous extract of Moringa pterigosperma at a dose of 100 mg/kg body weight via gavage daily for 10 days. Treatment Group 2 (T2) (n=10) was also treated with alloxan and received a higher dose of Moringa pterigosperma extract, 200 mg/kg body weight, for 10 days. Noted the glucose level was measured at the first week and second week. The experiment lasted for 41 days, after that, the animals were sacrificed for the collection of blood samples for biochemical analysis.

Sample Collection

At the end of the experimental period (41 days), all rats were sacrificed under ethical and humane conditions. Blood samples were collected via cardiac puncture for serum analysis of luteinizing hormone (LH), testosterone, glucose, and insulin concentrations (Bustani, Jabbar et al. 2022).

Insulin Measurement

The insulin levels were measured by using a wet chemistry based on the photometric principle which is applied by a liquid reagent system with an insulin kit provided by Nalondi (Iran). A UV-Spectrophotometer (VS721G Brand) manufactured in the UK was employed for these measurements.

Testosterone Hormone

An assay kit (Catalog No: SL1061Ra) from SunLong Biotech Co., Ltd., China, helped ascertain testosterone levels in rat serum. Blood samples were taken via a heart puncture and processed to provide serum. T. The extraction and measurement of testosterone were performed following the manufacturer's instructions provided with the kit.

Luteinizing Hormone

Luteinizing hormone (LH) levels in rat serum were analyzed using an assay kit (Catalog No: SL1093Ra) from SunLong Biotech Co., Ltd., China. Blood samples were obtained via cardiac puncture and processed to isolate serum. The extraction and measurement of LH were carried out following the guidelines provided by the kit's manufacturer

3. RESULTS

The results in Figure 1 illustrated the testosterone concentration which showed significant differences across the experimental groups and explained the effects of alloxan-induced diabetes and the therapeutic potential of Moringa pterigosperma extract. The C Group showed a mean testosterone level of 0.1408 ± 0.008 ng/mL; in contrast, the N group exhibited a significant reduction (0.0926 ± 0.0081 ng/mL,) indicating significant endocrine disruption due to alloxan-induced diabetes without treatment. The T1 group 1 showed an increase in testosterone levels (0.1512 ± 0.013 ng/mL), which received Moringa pteridosperms extract at 100 mg/kg, Notably, the T2 group exhibited the highest concentration of testosterone level (0.1769 ± 0.01 ng/mL) significantly surpassing all other groups which were treated with a higher dose of 200 mg/kg.

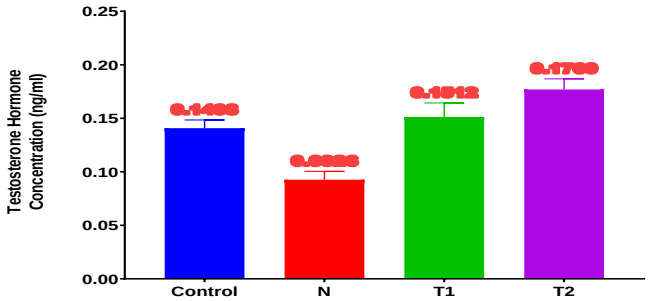

Figure (1): Testosterone Hormone: Control (C), Negative Control (NC), Treatment 1 (T1), and Treatment 2 (T2). The results are presented as the mean levels (ng/mL) with their respective standard errors.

The result in Figure 2 illustrated that the levels of luteinizing hormone showed significant differences in the experimental groups, in which the C group exhibited (0.4139 ± 0.015 ng/mL) for normal endocrine function, in contrast, the N group showed a significant increase (0.592 ± 0.03 ng/mL), indicating endocrine disruption caused by alloxan-induced diabetes, while the T1 group showed a significant reduction in LH levels to (0.3886 ± 0.01 ng/mL) which received 100 mg/kg of Moringa pterigosperma, and the T2 group, exhibited the lowest LH levels at 0.3163 ± 0.063 ng/mL, that treated with a higher dose of 200 mg/kg,

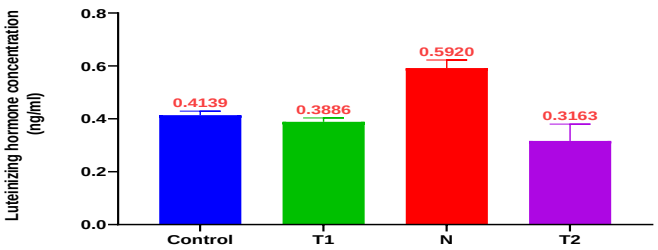

Figure (2): Luteinizing Hormone: Control (C), Negative Control (NC), Treatment 1 (T1), and Treatment 2 (T2). The results are presented as the mean levels (ng/mL) with their respective standard errors.

At the induction level, glucose concentrations were significantly higher in the Negative Control (NC) group (464.6 ± 18.71 mg/dL) compared to the Control (C) group (114.2 ± 6.583 mg/dL), indicating successful diabetes induction. The treatment groups showed reduced glucose levels, with Treatment 1 (T1) at 414.4 ± 7.118 mg/dL and Treatment 2 (T2) at 389.2 ± 10.33 mg/dL, demonstrating a slight amelioration of hyperglycemia.

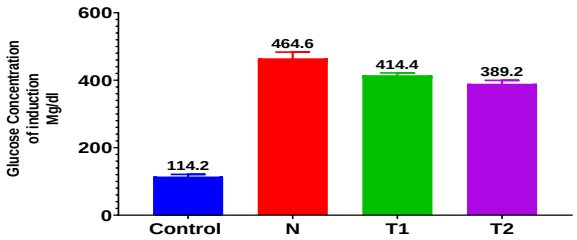

Figure (3): Glucose concentration at induction Control (C), Negative Control (NC), Treatment 1 (T1), and Treatment 2 (T2). The results are presented as the mean levels (ng/mL) with their respective standard errors.

During the first week, the glucose concentration in the NC group further elevated to 519.8 ± 32.00 mg/dL, while the C group maintained a normal level at 97.20 ± 2.728 mg/dL. Both treatment groups showed a significant reduction in glucose levels, with T1 at 234.0 ± 13.26 mg/dL and T2 at 177.0 ± 17.16 mg/dL, indicating a strong glucose-lowering effect of Moringa pterigosperma, particularly at the higher dose.

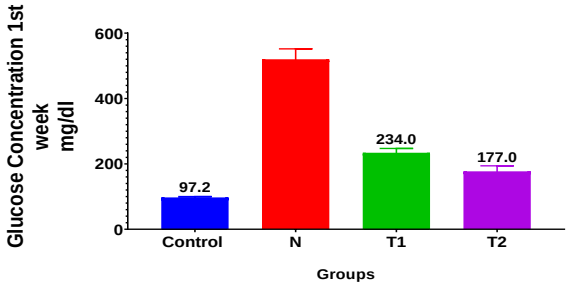

Figure (4): Glucose concentration at 1st week Control (C), Negative Control (NC), Treatment 1 (T1), and Treatment 2 (T2). The results are presented as the mean levels (ng/mL) with their respective standard errors.

By the second week, the NC group's glucose level decreased slightly to 457.2 ± 15.42 mg/dL, remaining significantly higher than the C group (100.0 ± 4.889 mg/dL). Notably, T1 and T2 showed substantial improvements, with glucose levels reduced to 128.0 ± 19.67 mg/dL and 105.8 ± 9.340 mg/dL, respectively. The T2 group nearly restored glucose levels to normal, emphasizing the dose-dependent efficacy of the treatment.

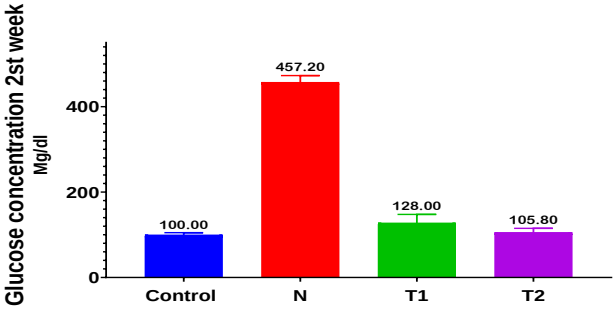

Figure (5): Glucose concentration at 2st week Control (C), Negative Control (NC), Treatment 1 (T1), and Treatment 2 (T2). The results are presented as the mean levels (ng/mL) with their respective standard errors.

The insulin concentrations varied significantly among the experimental groups. The C Group showed a mean insulin concentration of 2.560 ± 0.1887 µIU/mL. In contrast, the N group exhibited a significant reduction to 0.560 ± 0.09274 µIU/mL due to the destruction of pancreatic β-cells by alloxan, leading to severe insulin deficiency. T1 group treated with 100 mg/kg of Moringa pterygosperma, showed a insulin levels reaching 1.568 ± 0.1211 µIU/mL,. T2 Group , which received a higher dose of 200 mg/kg, showed an insulin levels of 2.140 ± 0.1435 µIU/mL.

4. DISCUSSION

The present study illestrated the therapeutic potential of Moringa pterygosperma extract in modulating endocrine and metabolic parameters in alloxan-induced diabetic rats, that focused on testosterone, luteinizing hormone , glucose concentration, and insulin levels. Diabetes mellitus type 2 (T2DM) is characterized by persistent hyperglycemia due to impaired insulin secretion or action, often accompanied by endocrine dysfunction (Nakamura and Sadoshima 2020, Sneha, Abhinav et al. 2021).that provide by present results, which alloxan-induced diabetes significantly reduced the testosterone levels, and increased luteinizing hormone concentrations, and glucose levels, consistent with the endocrine and metabolic imbalances as showed in previous (Mallick, Sinha et al. 2016, Majeed and Mahmood 2024).The findings showed the effects of diabetes on the hypothalamic-pituitary-gonadal axis,

where oxidative stress and metabolic derangements impair endocrine signaling (Al-Saadi, Al-Charrakh et al. 2011).The Moringa pterygosperma has been shown to possess potent antidiabetic, antioxidant, and anti-inflammatory properties (Rao and Mishra 1998, Adibhatla and Hatcher 2002, Patil, Mohite et al. 2022, Sarode, Sonawane et al. 2023).which improvement testosterone levels as observed in present study result, particularly in the T1 and T2 treatment groups, illustrated the role of the bioactive compounds of moringa pterygosperma, included polyphenols and flavonoids, which recover the hormonal balance (Rao and Mishra 1998, A'laa Hassan Abdul Hussain, Al Haideri et al. 2022). In other hands, higher dose (200 mg/kg) shwed a increased and benefit effect, with testosterone levels in the T2 group surpassing the control group, highlighting the dose-dependent efficacy of Moringa pterygosperma in enhancing testosterone synthesis. Similarly, the luteinizing hormone levels reflects the extract's ability to normalize endocrine signaling disrupted by diabetes. The elevated luteinizing hormone levels in the N group likely result from compensatory mechanisms triggered by testosterone deficiency. The significant reduction in luteinizing hormone levels in the treatment groups suggests that the extract alleviates the need for such compensatory responses by improving testosterone production and overall endocrine function (Bustani and Kashef Alghetaa 2024).The glucose-lowering effects of Moringa pterygosperma are consistent with its established role in improving insulin sensitivity and enhancing pancreatic β-cell function (Kumar, Kumar et al. 2015, A'laa Hassan Abdul Hussain, Al Haideri et al. 2022).The gradual reduction in glucose levels observed over the study period, particularly in the T2 group, emphasizes the extract's ability to restore glycemic control. These findings align with prior studies demonstrating the hypoglycemic properties of Moringa pterygosperma, attributed to its bioactive compounds such as isothiocyanates and glucosinolates (Patil, Mohite et al. 2022).The restoration of insulin levels in the treatment groups further underscores the therapeutic potential of Moringa pterygosperma. While the NC group exhibited severe insulin deficiency due to alloxan-induced β-cell destruction, the T1 and T2 groups showed significant improvements, with insulin levels in the T2 group nearing those of the control group. These results highlight the extract's role in promoting β-cell regeneration and enhancing insulin secretion (Jaiswal, Rai et al. 2009, Farid and Hegazy 2020).

This study demonstrates the significant therapeutic potential of Moringa pterygosperma extract in addressing endocrine and metabolic disruptions caused by alloxan-induced diabetes in rats. The extract effectively improved testosterone and luteinizing hormone (LH) levels, restored glucose-insulin balance, and exhibited a dose-dependent efficacy in normalizing endocrine function and glycemic control. The findings highlight the role of Moringa

pterygosperma's bioactive compounds, such as polyphenols, flavonoids, and isothiocyanates, in mitigating oxidative stress, enhancing insulin sensitivity, and promoting pancreatic β-cell recovery. These results provide a robust basis for the further exploration of Moringa pterygosperma as a natural therapeutic agent for managing diabetes and its complications.

CONCLUSION

Moringa pterygosperma extraction modulates endocrine and metabolic parameters, agent diabetes type 2 complications.

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