



Linking MDA Levels and Blood Glucose in Streptozotocin-Induced Rat Diabetes: Implications for Diabetic Complications and Therapeutic Strategies

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Abstract: Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels resulting from insulin deficiency or resistance. Streptozotocin, a potent diabetogenic agent, is commonly employed to induce experimental diabetes by selectively damaging pancreatic beta cells, resulting in insulin deficiency and hyperglycemia. Elevated Malondialdehyde (MDA) levels, indicative of oxidative stress and lipid peroxidation, are closely linked to diabetic complications. This study aimed to investigate the association between MDA levels and blood glucose in Streptozotocin-induced rat diabetes, shedding light on potential therapeutic strategies. Spectrophotometric analysis was utilized to quantify MDA levels in rat tissues, providing insights into the extent of oxidative damage. The results revealed a significant correlation between MDA levels and blood glucose, highlighting the role of oxidative stress in diabetic pathogenesis. These findings underscore the importance of targeting oxidative stress in diabetes management to prevent complications. In conclusion, the study emphasizes the relevance of monitoring MDA levels as a biomarker for assessing oxidative stress in diabetic conditions and guiding therapeutic interventions.

Keywords: Blood glucose; Diabetic complications; Diabetes melitus; MDA therapeutic strategies; Streptozotocin

Introduction

Diabetes mellitus, a chronic metabolic disorder marked by elevated blood glucose levels, presents a substantial global health concern with its increasing prevalence. Effective management strategies, comprising lifestyle adjustments, pharmacological interventions, and collaborative healthcare efforts, are essential to mitigate complications and enhance the well-being of those living with diabetes (Association, 2021). By integrating comprehensive approaches and fostering interdisciplinary cooperation, it becomes possible to address the multifaceted challenges posed by diabetes and improve overall patient outcomes.

Diabetes mellitus, a multifaceted condition characterized by impaired insulin production or utilization leading to hyperglycemia, encompasses various types, with Type 2 diabetes prevailing as the most widespread variant (Dilworth et al., 2021; Su et al., 2023). Its complications span across a spectrum, encompassing cardiovascular diseases, neuropathy, nephropathy, retinopathy, and other related ailments. Effective management strategies necessitate a multifaceted approach, incorporating lifestyle adjustments, pharmacological interventions, and vigilant monitoring of blood glucose levels to mitigate the progression and adverse effects of the disease (Joseph et al., 2022; Ramalho & Petrica, 2023).

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Streptozotocin (STZ) is a naturally occurring antibiotic compound derived from *Streptomyces achromogenes* (Zhang et al., 2020; Zhu, 2022). It is widely used in experimental models to induce diabetes due to its selective toxicity towards pancreatic beta cells. STZ selectively enters pancreatic beta cells via the glucose transporter GLUT2, leading to DNA alkylation, fragmentation, and ultimately, cellular necrosis (Wszola et al., 2021). This process mimics the pathophysiology of type 1 diabetes mellitus (T1DM), characterized by autoimmune destruction of pancreatic beta cells (Roep et al., 2021; Zhu, 2022). Malondialdehyde (MDA) is a reactive aldehyde compound generated during lipid peroxidation of polyunsaturated fatty acids (Mas-Bargues et al., 2021). Elevated MDA levels serve as a biomarker for oxidative stress, reflecting an imbalance between the production of reactive oxygen species (ROS) and antioxidant defense mechanisms. In the context of DM, chronic hyperglycemia and metabolic abnormalities contribute to increased oxidative stress, leading to cellular damage and dysfunction (González et al., 2023).

The administration of Streptozotocin (STZ) in diabetic rats models serves as a widely adopted method for inducing diabetes mellitus (DM), characterized by insulin deficiency and hyperglycemia, which closely mimics the pathophysiological features observed in humans (Quiroz & Yazdanyar, 2021). This model stands as a crucial tool for researchers to delve into the intricate mechanisms underlying diabetic complications and explore potential therapeutic interventions. Monitoring blood glucose levels provides valuable insights into the severity of hyperglycemia, a defining characteristic of DM, which contributes to the initiation and progression of various diabetic complications (Logette et al., 2021). However, alongside glucose dysregulation, researchers also scrutinize the extent of oxidative stress and lipid peroxidation within the diabetic milieu, where quantifying Malondialdehyde (MDA) levels emerges as a pivotal endeavor.

MDA, a reactive aldehyde compound formed during lipid peroxidation, stands as a reliable biomarker for oxidative stress (Sidorova & Domanskyi, 2020). When STZ-induced diabetes disrupts the delicate balance between pro-oxidants and antioxidants, it leads to heightened oxidative stress, exacerbating tissue damage and dysfunction (Arabshomali et al., 2023; Chae et al., 2023). By examining MDA levels alongside blood glucose concentrations, researchers gain a comprehensive understanding of the interplay between hyperglycemia-induced oxidative stress and diabetic pathogenesis, which could pave the way for novel therapeutic strategies targeting oxidative stress pathways alongside traditional glycemic control

measures to mitigate diabetic complications and improve overall disease management.

In the comprehensive management of diabetes mellitus (DM) and its associated complications, a multifaceted strategy is crucial for achieving optimal results. Central to this approach is the meticulous control of blood glucose levels, which serves as the foundation of DM management (Tang et al., 2023). This entails maintaining target glucose levels through dietary adjustments, regular physical activity, and appropriate medication regimens to prevent the progression of both microvascular and macrovascular complications. Additionally, an essential aspect of therapeutic interventions involves combating oxidative stress, a significant contributor to the development of diabetes-related complications (Bhatti et al., 2022).

Pharmacological agents with antioxidative properties, such as alpha-lipoic acid and angiotensin-converting enzyme (ACE) inhibitors, are commonly used to counteract oxidative damage and mitigate the harmful effects of reactive oxygen species (ROS) on cellular structures (Dugbartey et al., 2022). Simultaneously, lifestyle modifications, including quitting smoking, adopting a nutrient-rich diet with antioxidant properties, and integrating regular exercise, have shown significant effectiveness in reducing oxidative stress and lowering the risk of diabetic complications. Furthermore, emerging therapeutic strategies that focus on preserving the function of pancreatic beta cells offer promise in preventing the onset of DM-related complications (Liu et al., 2022). Approaches aimed at enhancing beta cell viability and function, such as the use of incretin-based therapies and innovative regenerative techniques, bring renewed hope to the field of diabetes treatment, potentially alleviating the burden of the disease and improving patient outcomes (Raoufinia et al., 2024).

Despite significant advancements in understanding of DM pathophysiology and therapeutic options, several gaps in research persist. Bhatti et al. (2022) studies are shows the precise mechanisms underlying STZ-induced diabetes and its correlation with oxidative stress markers such as MDA. Additionally, exploring novel therapeutic targets and evaluating their efficacy in preclinical and clinical settings are essential for advancing diabetes management strategies. Like any scientific inquiry, this study has its limitations. Experimental models using STZ-induced diabetes may not fully recapitulate the complexity of human DM, limiting the generalizability of findings. Furthermore, the interpretation of MDA levels as a biomarker for oxidative stress should consider potential confounding factors and assay variability. Despite these limitations, this study contributes to our understanding of the interplay between oxidative stress, hyperglycemia, and

diabetic complications, paving the way for future research and therapeutic innovations in diabetes management.

Method

This study employed an experimental design conducted at the Faculty of Medicine, Universitas Prima Indonesia. The research focused on investigating the effects of *Gynura procumbens* leaf extract on blood glucose levels in Streptozotocin-induced diabetic rat models. The treatment method use Twenty-eight male Wistar rats were randomly divided into four groups: Control Positive (no treatment), Control Negative (Streptozotocin-induced) for MDA levels and same groups for blood glucose. The rats were housed in wire-topped cages at the animal facility of the Faculty of Medicine, Universitas Prima Indonesia. They were acclimatized for seven days, provided with standard pellet feed, and water ad libitum. The doses were calculated based on the body weight of the rats to ensure accurate administration. In the study conducted the activities of Blood Glucose before and after induced by streptozotocin, as well as Malondialdehyde (MDA) in rat tissues, were measured using specific formulas.

Malondialdehyde (MDA) levels were measured as a marker of lipid peroxidation and oxidative stress in the rat tissues. The MDA levels were quantified to assess the extent of oxidative damage and the effectiveness of *Gynura procumbens* leaf extract in reducing oxidative stress. Furthermore, the MDA levels were determined using the formula $MDA\ concentration\ (nmol/mL) = (Absorbance\ sample - Absorbance\ blank) / (\epsilon \times l)$, where Absorbance sample and Absorbance blank are the absorbance values of the sample and blank at 532 nm, respectively, ϵ is the molar absorption coefficient of MDA ($1.56 \times 10^5\ M^{-1}\ cm^{-1}$), and l represents the path length of the cuvette in cm. These formulas were integral in assessing the antioxidant activities and oxidative stress levels in the rat tissues following treatment with *Gynura procumbens* leaf extract, providing valuable insights into the potential therapeutic effects of the extract on diabetes-induced oxidative damage.

Data collection involved recording blood glucose levels, as well as MDA levels before and after treatment with streptozotocin-*induce*. Statistical analysis, including ANOVA and post-hoc tests, was then conducted to compare the results between the treatment groups and determine the significance of the findings. This comprehensive data collection and analysis process aimed to provide a thorough evaluation of the effects of streptozotocin-*induce* on implications for diabetic complications and therapeutic strategies of rat models.

Result and Discussion

Malondialdehyde (MDA) is a commonly used biomarker for assessing lipid peroxidation and oxidative stress levels in biological samples. MDA is a reactive aldehyde formed as a byproduct of lipid peroxidation, a process that occurs when free radicals attack polyunsaturated fatty acids in cell membranes. Measurement of MDA levels provides valuable insights into the extent of oxidative stress and the efficacy of antioxidant interventions in mitigating cellular damage (Park et al., 2023; Olufunmilayo et al., 2023; Chaudhary et al., 2023).

In this study, the MDA levels in rat tissues were quantified using a spectrophotometric method. A standard curve for MDA was created to establish a linear relationship between MDA concentration and absorbance values at 532 nm. The standard curve data, presented in Table 1.

Table 1. MDA Standard Curve Creation

Concentration	Average Absorbance
5	0.14
2.50	0.07
1.25	0.035
0.62	0.01
0.31	0.01
0	0

Figure 1, visually depicting the relationship between MDA concentration (nmol/mL) and absorbance values. The spectrophotometric method allowed for accurate and precise measurement of MDA levels, enabling the assessment of lipid peroxidation and oxidative stress status in the rat tissues following treatment with *Gynura procumbens* leaf extract. The MDA standard curve served as a reference for determining the MDA concentrations in the samples and evaluating the effectiveness of the extract in reducing oxidative damage in the diabetic rat model.

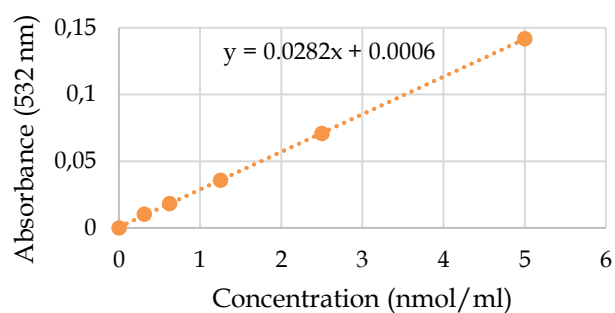


Figure 1. MDA standard curve

The MDA standard curve, as depicted in Figure 1 and detailed in Table 1, served as a crucial reference

point for quantifying MDA levels in the rat tissues. Based on the data provided in the table, it is evident that there is a clear relationship between the concentration of the solution and the absorbance readings obtained. As the concentration decreases, the absorbance also decreases proportionally. This phenomenon can be explained by the Beer-Lambert law that use on Oshina et al. (2021) study, which states that there is a linear relationship between the concentration of a solute in a solution and the absorbance of light by that solution. Mathematically, this relationship is expressed as $A = \epsilon cl$, where A is the absorbance, ϵ is the molar absorptivity (a constant specific to the absorbing species and the wavelength of light), c is the concentration of the solution, and l is the path length of the cuvette. In this experiment, since the path length and the molar absorptivity are constant, the absorbance is directly proportional to the concentration of the solution. Thus, as the concentration decreases, the number of absorbing molecules in the solution decreases, leading to a decrease in absorbance. This relationship is evident in the data provided, where as the concentration decreases from 5 to 0 units, the absorbance also decreases from 0.1417 to 0, respectively.

By correlating the absorbance values obtained from the spectrophotometric analysis with the concentrations of MDA in the standard curve, the MDA levels in the experimental samples were accurately determined. Table 2 presents the MDA levels measured using the spectrophotometer, reflecting the extent of lipid peroxidation and oxidative stress in the rat tissues following treatment with *Gynura procumbens* leaf extract.

Table 2. MDA Levels (Spectrophotometer Results)

Rat	Control (-)	Control (+)
1	0.09	2.87
2	0.22	2.69
3	0.17	2.72
4	0.14	0.31
5	0.15	0.90
6	0.18	2.79
7	0.16	0.12
Mean	0.16	1.77

The comparison between the MDA levels in the experimental groups and the control group provides

Tabel 3. Blood Glucose Levels

Groups	Results of initial blood glucose level measurements (mg/dL)	Results of measuring blood glucose levels after streptozotocin induction (mg/dL)
K (-)	81.29 ± 18.35	86.57 ± 11.38
K (+)	81.71 ± 6.12	128.57 ± 15.80

Comparing the initial blood glucose levels between the control and treatment groups revealed no significant

valuable insights into the antioxidant effects of the extract and its potential in mitigating oxidative damage associated with diabetes mellitus. Table 2 have presents the results of MDA (Malondialdehyde) Levels obtained from spectrophotometer analysis. MDA is a marker for lipid peroxidation, a process indicative of oxidative stress within cells. In the context of this study, the rat samples were divided into two groups: control (-) and control (+). The control (-) group represents the baseline MDA levels, while the control (+) group indicates MDA levels after exposure to a certain condition or treatment.

Upon analysis, it is evident that the mean MDA level for the control (-) group is 0.1620, whereas for the control (+) group, it is notably higher at 1.7757. This significant increase in MDA levels in the control (+) group suggests a heightened level of lipid peroxidation, indicating increased oxidative stress compared to the control (-) group. The interpretation of these results aligns with the theoretical understanding on (Afzal et al., 2023), that oxidative stress occurs when there is an imbalance between the production of reactive oxygen species (ROS) and the body's ability to detoxify them or repair the resulting damage. Elevated MDA levels, as seen in the control (+) group, can lead to cellular damage and dysfunction, contributing to various pathological conditions including inflammation, aging, and chronic diseases.

Overall, these findings underscore the importance of monitoring MDA levels as a marker for oxidative stress and its potential implications in biological systems (Bencivenga et al., 2023; Wróbel-Nowicka et al., 2024; Kong et al., 2024; Valavanidis et al., 2006). Further research may delve into elucidating the specific factors contributing to the observed increase in MDA levels in the control (+) group, leading to a better understanding of the underlying mechanisms and potential therapeutic interventions to mitigate oxidative stress-related damage. The increasing prevalence of diabetes mellitus has spurred in-depth research into its pathogenesis and treatment (Galicia-Garcia et al., 2020). In this context, the use of streptozotocin as an inducer of diabetes in animal models has become a significant subject of investigation. Table 3 presents the findings of recent research examining the impact of streptozotocin on blood glucose levels in a group of rats.

differences, signifying similar baseline health conditions among the rats before streptozotocin induction. This

consistency suggests a balanced distribution of health parameters at the onset of the experiment. However, post-streptozotocin administration, a notable contrast emerged in blood glucose levels between the two groups. The control group, unaffected by streptozotocin, maintained normal blood glucose levels (18.35 mg/dL), indicating stable metabolic function. Conversely, the treatment group exhibited a stark elevation in blood glucose levels (128.57 mg/dL), indicative of hyperglycemia. This significant disparity underscores the potent impact of streptozotocin on glucose regulation, implicating its role in inducing diabetic conditions within the treatment group. These findings align with Ram et al. (2023) research, that demonstrated streptozotocin's ability to disrupt glucose homeostasis, thereby substantiating its utility as an experimental model for studying diabetes pathogenesis and therapeutic interventions.

Therapeutic strategies play a pivotal role in the management of diabetic complications by specifically addressing both blood glucose levels and malondialdehyde (MDA) levels, which serve as important markers for oxidative stress and lipid peroxidation. Padhi et al. (2020) states, A variety of pharmacological interventions, including biguanides, sulfonylureas, thiazolidinediones, SGLT-2 inhibitors, and DPP-4 inhibitors, operate through distinct mechanisms to regulate glucose metabolism, insulin secretion, and inflammatory pathways. Consequently, they facilitate enhanced glycemic control and reduced oxidative stress. For instance, metformin, a biguanide, diminishes hepatic glucose production and inflammation, thereby reducing blood glucose levels and curtailing the production of reactive oxygen species (ROS).

Similarly, SGLT-2 inhibitors exhibit properties that augment urinary glucose excretion, decrease free-radical production, and alleviate inflammation, resulting in notable enhancements in cardiac and renal function. According to Caturano et al. (2023), these therapeutic modalities not only address hyperglycemia but also contribute to diminishing oxidative stress, as evidenced by the modulation of antioxidant enzymes and inflammatory pathways (Guan et al., 2024; Li et al., 2023; Liu et al., 2023). Through the effective regulation of both blood glucose levels and oxidative stress, these strategies play a vital role in mitigating diabetic complications and ultimately improving overall health outcomes for individuals with diabetes. This is underscored by Syeda et al. (2023), Klupa et al. (2023), and Shaban et al. (2024) research, which has consistently demonstrated the efficacy of these interventions in managing diabetic complications and enhancing patient well-being.

Conclusion

The research findings suggest a correlation between MDA levels and blood glucose in Streptozotocin-induced diabetic rats, indicating a potential influence of oxidative stress on diabetes complications. This highlights the importance of controlling both blood glucose levels and oxidative stress as therapeutic strategies for managing diabetes. Further research is recommended to explore the mechanism behind this relationship and test the effectiveness of therapies targeting oxidative stress reduction in diabetic patients.

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Conflicts of Interest

The authors declare no conflict of interest.

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