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Original Research Paper

The effect of Beta - aminobutyric acid on Malondialdehyde and urea levels in type 2 diabetic male rats

Shams Husham Al-Naqqash[1], Mohammed Abbas Jasim [1]

[1]*Biology Department, College of Education for Women, Al-Ramadi 30001, Al-Anbar, Iraq.*

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*Corresponding Author:,
Mohammed Abbas Jasim,
Department of biology, Faculty of Education for Women, University of Anbar, Ramadi 31001, Al-Anbar, Iraq.;
Email:
mohammed.a.jasim@uoanbar.edu.iq

Abstract: Diabetes mellitus, a complex metabolic disorder characterized by hyperglycemia. **Objective:** This study aimed to evaluate the protective effect of beta-aminobutyric acid (BABA) on streptozotocin (STZ)-induced diabetes in male rats, by studying its effect on Malondialdehyde (MDA), and urea**.** Thirty adult male albino rats models of diabetes mellitus were randomly assigned to six groups of five pets each, age of (8-10 weeks). All rats were in good health, with weights ranging from 140 to 160 grams, Positive control groups treated with normal saline, Negative control groups treated only with streptozotocin, Group A treated with 50 mg/kg of STZ then BABA, Group B treated with 100 mg/kg strptozotocin then BABA, Group C treated with 150 mg/kg of strptozotocin then BABA, and Group D treated with 200 mg/kg of strptozotocin then BABA. Enzyme-linked immunosorbent assay (ELISA) was utilized to evaluate MDA, and urea levels in serum. The results of the study show MDA levels elevated in the rats studied (Control -,A, B, C, and D) which recorded (4.47 ±1.93 mg/dl), (3.01 ±0.76 mg/dl), (3.07 ±0.41 mg/dl), and (2.04 ±0.22 mg/dl), compared control group(4.61 ±0.15 mg/dl), results indicate high levels of **urea** in the groups of rats studied (Control -,A, B, C, and D) which recorded (115.33± 39.01) mg/dl, (107.67±22.25)mg/dl, (70.67±22.06)mg/dl, (73.00±13.65)mg/dl, and (57.67±3.71) mg/dl, compared to control+ (44.33±3.48)mg/dl. The results indicated correlation coefficient between weight and sugar Level is 0.027. This indicates a very weak positive correlation between the two variables, that there is no significant linear relationship between weight and sugar level in rats studied. BABA plays an important protective role as an antioxidant against STZ-induced oxidative stress.

Keywords: Diabetes mellitus, MDA, Urea, Rats, ELISA

1. Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance, impaired glucose metabolism, and progressive pancreatic β-cell dysfunction. The global prevalence of T2DM has reached alarming levels, posing serious health, social, and economic burdens. Among the many complications associated with diabetes, oxidative stress and kidney dysfunction are particularly significant, as they contribute to the development of diabetic nephropathy and other systemic complication [1,2].

Streptozotocin (STZ) is a chemical extracted from the bacteria Streptomyces achromogenes. It is characterized by its ability to damage beta cells (β-cells) in the

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pancreas, which are responsible for producing insulin[3]. It results in a sharp decrease in insulin production due to the loss of a large number of beta cells, leading to high blood glucose levels and a disease similar to type 1 diabetes[4, 5]. Although numerous drug treatments are available, there is growing interest in researching new, more effective treatments with fewer side effects, particularly those based on bioactive and natural compounds.

Malondialdehyde (MDA), a key marker of oxidative stress, is a byproduct of lipid oxidation and an indicator of cell damage caused by reactive oxygen species (ROS). Elevated levels in diabetic patients have been closely associated with increased oxidative stress and the development of diabetic complications[6, 7]. Another important biochemical marker is urea, a nitrogenous waste product that reflects kidney function. Diabetes is often accompanied by impaired kidney function, which can lead to elevated serum urea levels and further complicate disease progression[8, 9].

Beta-amino butyric acid (BABA) has emerged as a promising compound that may play an important role in regulating metabolic and immune responses, making it a potential treatment option for diabetes[10]. Studies have shown that BABA has the ability to stimulate protective mechanisms at the cellular and molecular levels, helping mitigate damage associated with high blood glucose levels and improve insulin sensitivity[11].

2. Methodology

Subject

Thirty adult male albino rats models of diabetes mellitus were randomly assigned to six groups of five pets each, age of (8-10 weeks). All rats were in good health, with weights ranging from 140 to 160 grams. After the acclimatization period, the rats were given three doses of strptozotocin, one every three days. The rats also received oral therapeutic doses of β-aminobutyric acid, four doses every three days, and one dose via daily gavage for 30 days.

Treatments of Streptozotocin

Streptozotocin (STZ) was acquired from Sigma Chemical Company, St. Louis, Missouri, USA, in 1 g vials. Diabetes was produced by oral administration of a newly prepared solution of STZ. Administered (60 mg/kg body weight) in 0.1 M cold citrate buffer (pH 4.5) to overnight-fasted rats. Due to STZ's potential to induce lethal hypoglycemia by excessive pancreatic insulin release, the rats were maintained on a 5% glucose solution for the subsequent 24 hours to avert hypoglycemia [12].

Treatments of BABA

Beta-aminobutyric acid (BABA) acquired from Sigma-Aldrich, St. Louis, Missouri, USA, in 25 g vials, was diluted in distilled water and thereafter delivered administered to rats daily via gastric gavage at a dosage of 50, 100, 150, and 200 mg/kg body weight every day for a duration of 3 weeks.

Collection of blood samples

After completing the designated 30-day experiment period, the animals were subjected to a night of starvation lasting 10 hours. Subsequently, their final weight was measured. Following this, the animals were anesthetized using a chloroform solution. 4 ml of blood samples were collected from each animal through cardiac puncture using specialized syringes was placed into test tubes without anticoagulants. The serum was acquired by centrifugation between 2500 -3000 rpm. It was then preserved at a temperature of -20°C in fresh plastic containers until specific biochemical examinations were conducted [11].

Animals groups

The treatments administered were tailored to the specific requirements of the experiment: Groups A,B, C and treated with streptozotocin (STZ) then 50, 100, 150, 200 mg/kg of body weight of BABA respectively, a Positive control group treated with 2ml normal saline and Negative control group treated only with streptozotocin.

Blood glucose levels

Blood glucose levels were assessed utilizing an Accu-check blood glucose meter (Roche Diagnostics, Basel, Switzerland) from tail vein blood samples collected 72 hours post-STZ produced by oral administration. Equation 1 is used to estimate the glucose level per unit body weight .Rats with blood glucose levels over 250 mg/dl were classified as diabetic[11].

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$$Glucose = \frac{levels\ of\ glucose\ in\ blood\ (\frac{mg}{dl})}{Boody\ weight\ (kg)} \dots\dots\dots Eq\ 1$$

ELISA test

The enzyme-linked immunosorbent assay (ELISA) was utilized to evaluate the serum concentrations of Malondialdehyde (MDA) and urea .The antibodies for MDA and urea were precoated on the plates of the ELISA. The chromogenic response in substrate solutions is related to the concentration of MDA and urea after putting the samples on plates. The cessation of the process was achieved through the introduction of a stop solution, followed by the quantification of absorbance at a wavelength of 450 nm .The level of MDA and urea, were measured in serum by using (Sunlong, China).

Ethics approval

The Experimental protocols and animal usage (protocol number264 - 26/12/2024) have been authorized by the Institutional Animal Ethics Committee, and all procedures adhered strictly to the ethical standards established by Anbar University.

Statistical analysis

The Statistical Analysis System- SAS (2018) program was used to detect the effect of difference factors in study parameters. Chi-square test was used to significant compare between percentage (0.05 and 0.01 probability) in this study [13].

3. Results and discussion

Concentration of Malondialdehyde

Malondialdehyde (MDA) is an important biomarker that reflects the level of damage caused by oxidative stress in the body. The higher its level, the more oxidative damage there is, and the lower it is, the better the condition and less cellular damage. The results shown in Figure 1 indicate changes in MDA levels in the studied animal groups. The healthy group (Control+) recorded the lowest MDA level (2.57 ±0.17 mg/dl), reflecting the normal physiological state of the cells, free from the harmful effects of oxidative stress.

The negative group (Control-), which was treated only with streptozotocin (STZ), an oxidative stress inducer, MDA levels increased sharply to (4.61 ±0.15 mg/dl), the highest level among all groups. This increase indicates severe oxidative damage to the cells as a result of the effects of STZ.

For the groups treated with BABA after STZ administration, the results showed a gradual decrease in MDA levels with increasing BABA dose, indicating a clear protective effect. In group A (50 mg/kg), MDA levels increased to (4.47 ±1.93 mg/dl), similar to the control+. In group B (100 mg/kg), MDA levels increased to (3.01 ±0.76 mg/dl), indicating further improvement in cellular protection. Group C (150 mg/kg) showed a further increase in MDA, reaching (3.07 ±0.41 mg/dl), a level closer to the normal range. Group D (200 mg/kg) recorded (2.04 ±0.22 mg/dl), a level very close to the negative group, reflecting the significant negative effect of the high dose of STZ in increasing oxidative damage.

Streptozotocin (STZ) is responsible for causing type 2 diabetes in rats. It damages pancreatic beta cells, which secrete insulin, resulting in the production of free radicals, such as reactive oxygen species (ROS)[14]. These free radicals damage cell membranes by oxidizing lipids. When lipids in cell membranes are oxidized, MDA is produced, a key indicator of oxidative stress. Oxidative stress may be linked to hyperglycemia and the overproduction of free radicals. When rats were given a dose of STZ, there was a marked increase in free radical production, leading to a significant increase in MDA levels in serum and tissues, particularly the liver and kidneys. This increase reflects widespread oxidative damage, which is a major cause of chronic diabetic complications such as nephropathy and neuropathy. The results of the current study indicate a decrease in MDA levels upon dosing with BABA[15]. The hypothesized mechanism of action of BABA can be explained by its stimulation of endogenous antioxidant systems such as glutathione peroxidase (GPx), catalase (CAT), and SOD, which are enzymes that work to remove free radicals and reduce their toxic effects. Thus, BABA reduces damage to cell membranes and improves cellular stability in affected tissues, contributing to a reduction in biomarkers of oxidation such as MDA[16]. The results of the current study are consistent with many studies that have indicated the protective role of BABA in reducing oxidative stress induced by STZ, GABA reduces the

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content of MDA in the liver and kidney of diabetic rats [15, 17, 18].

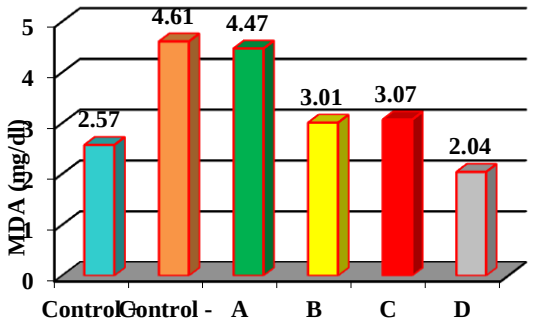

Fig 1: Comparison between difference groups in MDA

The results in Figure 2 represent serum **urea levels** in the experimental groups of rats treated with different doses of BABA following diabetes induction using STZ. The results revealed that the negative group (control-), which was treated only with STZ, showed the highest serum urea levels (115.33±39.01) mg/dl. This indicates the toxic effect of STZ on the kidneys due to oxidative stress and hyperglycemia, which leads to kidney damage and dysfunction, leading to the accumulation of metabolites such as urea in the blood. The positive group (**Control+**) showed the lowest urea levels (44.33±3.48) mg/dl, reflecting normal renal function and the absence of toxic or metabolic effects affecting nitrogen excretion. From results indicate that diabetes mellitus resulted in a significant ($p \leq 0.05$) increase in serum urea in STZ-treated animals compared to normal controls. The treated groups (A, B, C, and D), which were first induced with diabetes using STZ and then treated with increasing concentrations of BABA, showed a gradual decrease in urea levels as the BABA dose increased. Group A (50 mg/kg) recorded (107.67±22.25)mg/dl, showed a slight improvement compared to the negative group, but urea levels remained relatively high, indicating the onset of a mild protective effect. Groups B (100 mg/kg) and C (150 mg/kg) recorded (70.67±22.06)mg/dl, and (73.00±13.65)mg/dl, showed a more pronounced decrease in urea levels, indicating a better treatment response as the dose increased. Group D (200 mg/kg), recorded (57.67±3.71) mg/dl, showed the greatest degree of renal protection, with urea levels approaching those of the control group, Injecting the studied animals with BABA compound led to a significant decrease ($p \leq 0.05$) in the concentration of kidney function in the blood serum, demonstrating the potent and potential effect of BABA in mitigating the nephrotoxic effects of STZ. When blood glucose levels are consistently high, as -3particularly in the kidneys. This stress causes progressive damage to nephrons (the kidney's primary filtering units), impairing the kidney's ability to eliminate metabolic waste products, such as urea, causing a significant increase in its levels[19]. This increase is an early sign of diabetic nephropathy. In contrast, when injected with BABA, we notice a decrease in urea levels, these results suggest that BABA possesses potential antioxidant or anti-inflammatory properties that may contribute to protecting the kidneys from damage resulting from STZ-induced diabetes. The results also reinforce the hypothesis that the effect of BABA is directly dose-dependent, with the higher the dose, the better the biomarker[20].

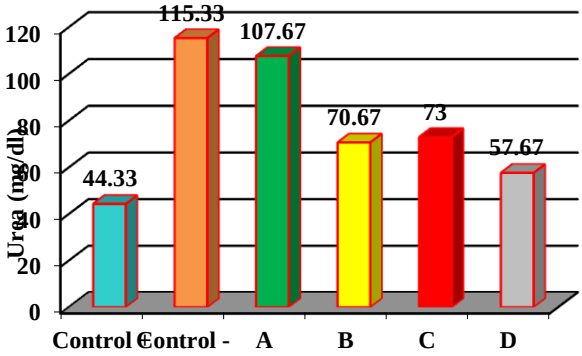

Fig 2: Comparison between difference groups in Urea

Figure 3 represents the relationship between weight and blood sugar level for the group of animals studied. From the results, we find that in some areas, especially when the weight is low (less than approximately 170 kg), we notice high sugar values, while at higher weights (between 180 - 230 kg), sugar levels mostly range between 90 - 140 mg/dl. The results indicated correlation coefficient between Weight and Sugar Level is 0.027. This indicates a very weak positive correlation between the two variables, suggesting that there is no significant linear relationship between weight and sugar level in this dataset.

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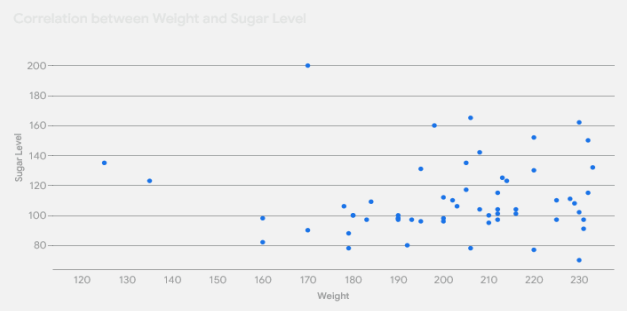

Fig 3: The relationship between sugar levels and animal body weight

Conclusion

The present study demonstrated that beta-aminobutyric acid (BABA) exhibits a protective effect against oxidative stress and renal dysfunction in male rats with type 2 diabetes induced by streptozotocin (STZ). BABA administration significantly reduced malondialdehyde (MDA) levels, indicating decreased lipid peroxidation and improved oxidative status. Additionally, a noticeable reduction in urea levels was observed, suggesting enhanced renal function. These findings highlight the potential therapeutic role of BABA in mitigating diabetes-induced biochemical alterations, particularly oxidative damage and kidney impairment. Further studies are recommended to confirm these results and explore the clinical applications of BABA in human diabetic management.

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Author's Contributions

Mohammed A. Jasim (Theory, plan, supervision, revision); Shams Al-NAqqash (Methodology, write).

Ethics

This study was conducted under approval by the medical ethics committee at the University of Anbar (2025).

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