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Anti-Diabetic Effect of Phytochemicals of Azadirachta Indica (Neem)

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Abstract

Diabetes mellitus is a condition characterized by elevated blood glucose levels as well as anomalies in carbohydrates, amino acids, and lipid metabolism, which are connected to an absolute or relative lack of insulin production or activity. Chronic diabetes causes secondary complications that affect the arteries, nerves, bladder, and eyes. Diabetes is a severe health condition that is rapidly expanding over the world. Diabetes incidence is currently on the increase to epidemic proportions over the world. Diabetes affects an estimated 170 million people globally, and this figure is expected to quadruple by 2030. When the illness is common and treatment is often excessively expensive or unavailable, it constitutes a severe public health risk in developing countries. Diabetes and its myriad complications have a negative impact on nations' health and economics all around the world. Diabetes along with additional chronic diseases are going to become an increasingly expensive issue that healthcare systems must address if not properly handled. Due to the apparent inability of existing modern medications to effectively treat all the clinical features of the disorder, as well as their exorbitant cost and restricted availability for many rural communities in developing countries, alternative approaches to current modern pharmacotherapy of diabetes syndrome are urgently required.

Keywords: Anti Diabetic, Azadirachta Indica

Introduction

Traditional herbal treatments derived from herbal remedies have long been used in areas where there is no access to official healthcare. [1]These natural plant-based medications have minimal toxicity and a favourable safety profile, with few side effects reported [2]. Given the potential usefulness of plant-based medicines for diabetes therapy, there has recently been an eruption of interest in their use. In fact, many conventional medications are derived from the earliest chemicals identified in these therapeutic plants.[3]

As a result, traditional herbs that are used to treat insulin resistance may be an effective option for managing this illness. Azadirachta indica (Neem) was first used to treat diabetes, which laid the groundwork for its development.[4]

In India and its neighbouring countries, A. Indicaa A. Juss (family Meliaceaee) is well known as one of the most versatile medicinal plants with a wide spectrum of biological activity. Every single part of the neem plant has medicinal properties, making it profitable [5, 6]. A. indica'santipyretic, anti-inflammatory, antibacterial, antidiabetic, and other pharmacological effects have been thoroughly reported [7,8].

The Neem tree, which grows mostly in southern Asia and Africa, has a long history of use in traditional medicine. The leaves, timber, fruit, flowers, oil, and gum of the Neem tree have all been woven into medicinal folklore, and they have shown promise in the treatment of a variety of medical ailments, including cancer, hypertension, heart disease, and diabetes. [9]The observed effects of using these compounds can be related to complex cellular and molecular processes. These mechanisms include free radical scavenging, purification, DNA repair, cell cycle modification, prevention of programmed cell death and autophagy, improved immune surveillance, anti-inflammatory benefits, anti-angiogenic effects, anti-metastatic actions and the ability to affect various signalling pathways.[10,11]

Significant advances have been achieved in the biological activities and therapeutic applications of A. indica A Juss (Neem) over the last 50 years. Since prehistoric times, the

Indian health care system has frequently used A. indica to treat diabetes. Numerous testimonies suggest to A. indica's danger of hypoglycemia [12,13]. Extracts from A. indica leaves and bark have been shown in the liver and kidney parts of female alloxan-diabetic rats to reduce blood glucose levels and oxidation of lipids while enhancing antioxidant enzymes such as catalase, superoxide dismutase and glutathione peroxidase. Treatment of high-fat diet-induced diabetic Charls Foster rats with A. indica leaf liquid extract for 30 days dramatically boosted enzymatic antioxidant activity in hepatic tissues, demonstrating that A. indica leaf extract possesses both antidiabetic and antioxidant properties [14]. Furthermore, investigations involving diabetic mice generated by streptozotocin showed that sustained administration using an ethanol-based extract of A. indica led to a decrease in plasma glucose levels and a decline in pancreatic islet lesions [15,16].

Methodology

Study Design

The examination will be carried out as a clinical trial. In this study, we will look at anti-diabetic properties of phytochemicals found in various parts of Azadirachtaindicaa.

Study Location

The study will be conducted in department of Pharmaceutical science.

Collection of Plant materials

The fresh and healthy leaves, barks, seeds, and roots of Azadirachta indica will be taken from planting region of Sangli, Maharashtra. Botanical Research Division of Sangali, Maharashtra, will taxonomically identify plants.

Experimental design

In Vitro Anti-Diabetic Activity:

The in vitro anti-diabetic efficacy of phytochemical extracts from various sections of Azadirachta indica will be evaluated largely using enzyme inhibition tests, as specific enzymes play an important role in diabetes treatment.[17]

The two most popular targets are:

α-Amylase inhibition assay (prevents starch breakdown → reduces glucose spikes)

α-Glucosidase inhibition assay (delays glucose absorption in intestine)

- **Sample Preparation:**

Collect several components of Azadirachta indica, including foliage, growl, seeds, and flowers. Wash, dry (in shade), and powder up plant materials.[18]

Soxhlet's extraction or maceration can be used with appropriate solvents (for example, ethanol, methanol, or another solvent or aqueous extraction).

Concentrate extracts with a rotary evaporator.

- **Phytochemical Screening:**

Conduct preliminary phytochemical screening to identify alkaloids, flavonoids, terpenoids, tannins, and saponins.

- **In Vitro Anti-Diabetic Tests:**

a. α-Amylase Inhibition Assay:

b. α-Glucosidase Inhibition Assay:

- **Controls:**

Positive control: Use a regular anti-diabetic medication (e.g., Acarbose).

Negative control: Solution of enzymes without extract.

Blank: every ingredient except enzyme.

- **Statistical Analysis:**

Experiment in triplicate.

Analyse findings using statistical software (ANOVA) to see whether there are any significant differences between portions.

Determine IC_{50} values for comparison.[19, 20]

Result and Discussion

Establishment of animal model of diabetes

To create an animal model of diabetes, a single intraperitoneal injection of STZ (60 mg/kg BW) has been used. As a result, blood glucose levels begin to rise; on the third day following STZ treatment, they were higher than 250 mg/dl. However, the glucose level in these animals was determined to be approximately 400 mg/dl after seven days of STZ injection, and it was nearly constant at 410 mg/dl for the next fourteen days.

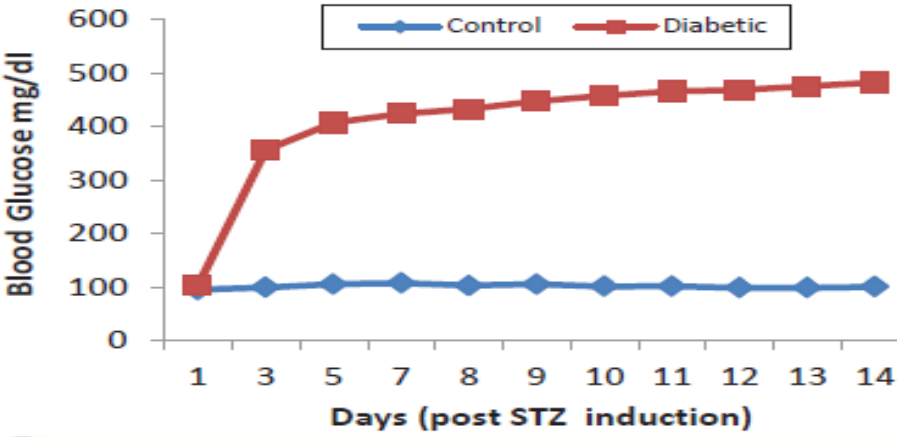

Figure 1: Blood glucose levels changes with STZ treatment.

Standardization of effective dose of ALE

Based on the blood glucose-lowering response and the accompanying adverse effects on animal physiology, the optimal dosage of ALE has been determined.

Dose dependent response of ALE

After creating the diabetic model, ALE's effects on the diabetic mice were noted seven days after they were treated with STZ. Fig. shows that blood glucose levels significantly increased to around four times the control level after the seventh day of STZ treatment. Blood glucose levels in several groups of diabetic rats (G3) have decreased in a dose-dependent manner after receiving oral ALE at varying concentrations (200–1000 mg/kg BW.) every day for seven days in a row. At lower dosages, such as 200–400 mg/kg BW, the magnitude of ALE's glucose-lowering action remained low (~16%), as seen in Figure 4.2. However, compared to the diabetic group (G2), ALE concentrations increased further, from 500 to 1000 mg/BW, and this resulted in a considerable drop in blood glucose levels, which were ~29% at 500 mg, 50% at 600 mg, and 60% at 1000 mg.

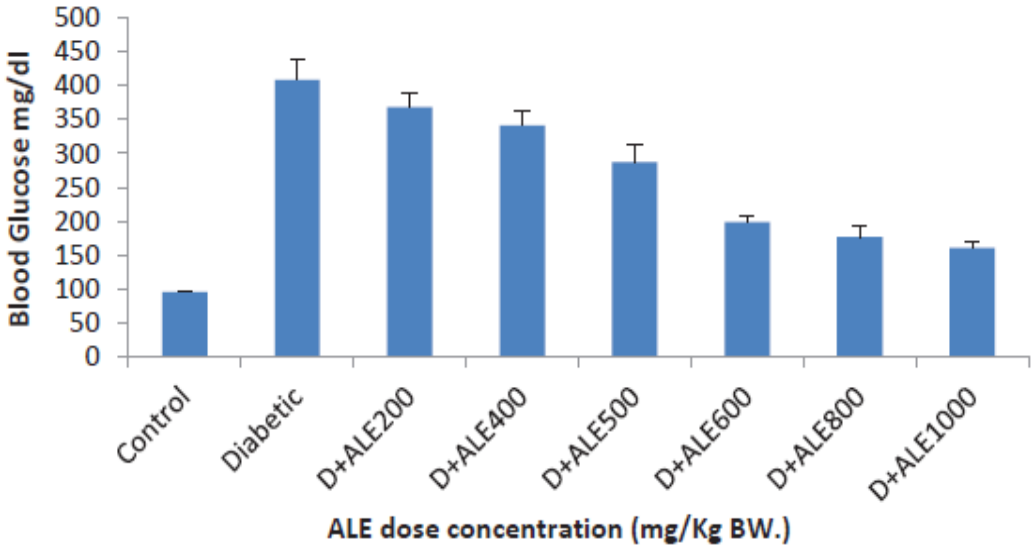

Figure 2: Blood glucose lowering effect of ALE treatment.

Animal response towards ALE treatment

The concentrations of ALE that lower blood glucose levels by greater than 50% (500, 600, 800, and 1000 mg/kg BW) have been tested for any adverse effects after the efficiency of ALE in lowering blood glucose levels has been noted. The change in behavioral and physiological observations made daily after giving these animals ALE served as the basis for these effects. None of the ALE concentrations have resulted in any deaths during the experiment; however, some of the animals that received ALE concentrations of 800 mg and 1000 mg/Kg BW showed clear behavioral changes, including decreased food intake, general lethargies, and decreased activity, along with a decrease in body weight. Rats given a 600 mg/kg dosage of ALE, however, showed a rise in body weight in comparison to the control group. These rats also continued to exhibit typical activity levels with regard to food and water consumption. As a result, ALE at a dose of 600 mg/kg BW has been employed for additional experimental research because it is both effective and free of noticeable side effects.

Analysis of body weight with an effective dose of ALE

Following the selection of an effective ALE dosage, the entire experimental protocol was conducted with the same concentration (600 mg/kg BW). First, the difference in body weight between diabetic, D+ALE-treated, and control rats has been examined. All animals' body weight has been measured on a regular basis for this purpose. The changes in body weight at two and four weeks of diabetic investigations are shown in Figures 4.3 and 4.4, respectively.

For the first two to three days, there was no discernible variation in the groups' body weights. Nevertheless, following a week of STZ treatment, there has been determined to be important. Throughout the ALE treatment, consistent weight shifts have also been documented. In comparison to their starting body weights, the controls, diabetic, and D+ALE animals' body weights changed by 24 g (raised), 20 g (decreased), and 13 g (decreased) during the course of the two-week trial. For the control, diabetic, and D+ALE-treated rats, the corresponding changes in body weight over the course of the four-week research were 33g (raised), 32g (decreased), and 27g (decreased). However, compared to D+ ALE treated animals (5.5 g, or 4.4% in two weeks of diabetes) and 2.2 g, or 1.4% in four weeks of diabetes, the untreated diabetic animals (group 2) had a greater reduction in body weight during the ALE treatment period, down 11 g (~9% in two weeks of diabetes) and 8.8 g (~5.6 % in four weeks of diabetes). The outcome shows that, in comparison to control mice, both diabetic and D+ALE animals have significantly decreased their body weight. ALE therapy for seven days in a row, however, has partially stopped the D+ALE animals' body weight from decreasing at the end of two and four weeks, respectively.

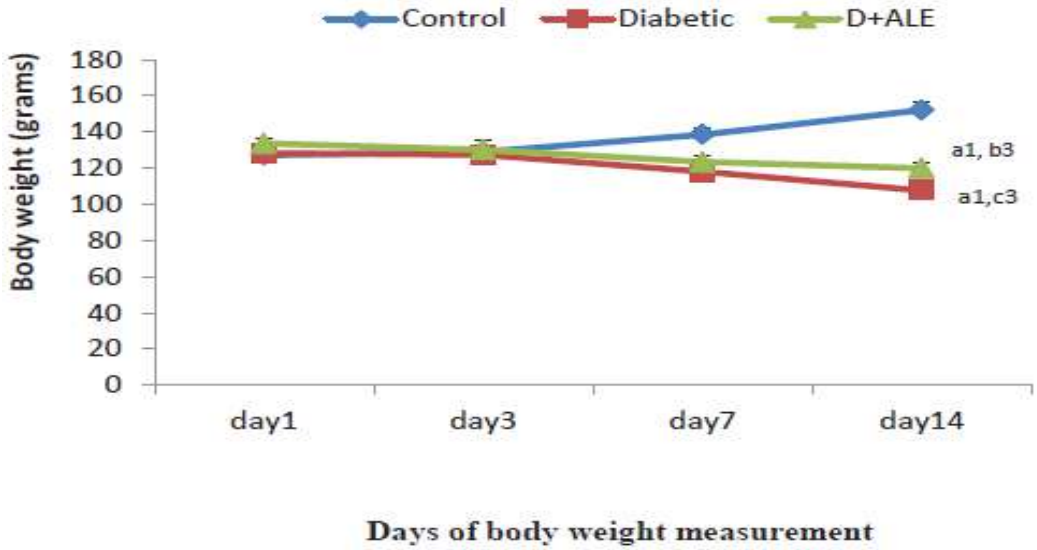

Figure 3: Change in body weight and effect of ALE treatment in two weeks study.

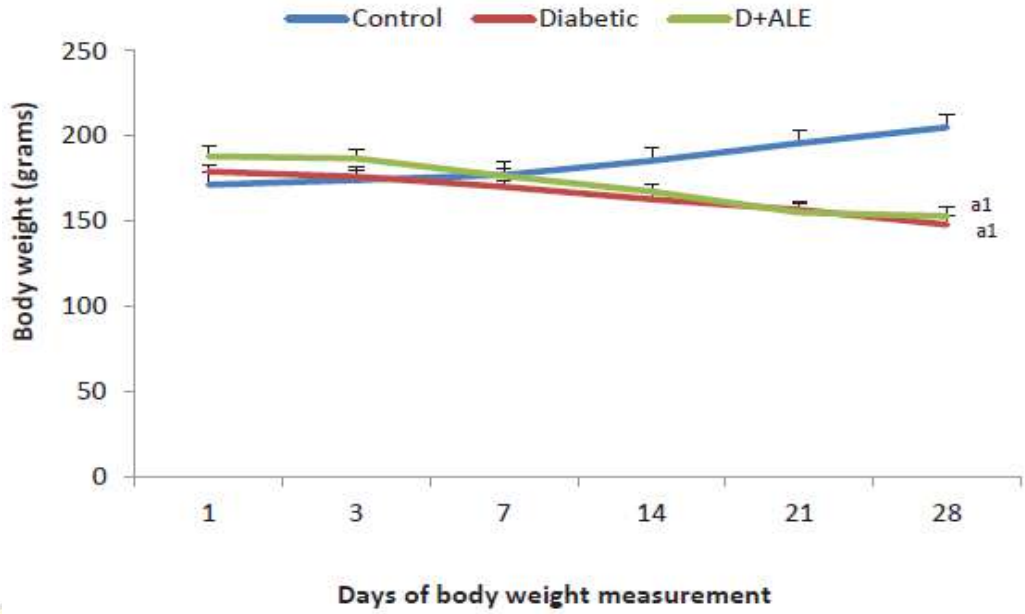

Figure 4: Change in body weight and effect of ALE treatment in four weeks study.

Biochemical Analysis

Analysis of blood glucose profile

To determine the severity of the diabetes and the impact of ALE treatment on the diabetic rats, blood glucose levels have been examined. After 72 hours of STZ treatment, the glucose level began to rise and was found to be approximately 3.6 times ($p \leq .001$) greater than in control rats. The blood glucose levels of the seventh day (before to ALE therapy) and the fourteenth day (post-ALE treatment) have been compared in Fig., which shows the blood glucose levels during the two-week study. Fig. compares the blood glucose levels on the 21st day (before to ALE treatment) and the 28th day (post-treatment) in order to evaluate the impact of ALE therapy throughout the course of a four-week trial. The blood glucose levels of group 2 animals showed a substantial increase ($p \leq .001$) at the end of two and four weeks. However, at the end of two and four weeks, respectively, the group 3 animals (D+ALE animals) had significantly lower blood glucose levels ($p \leq .001$) by about 61% and 58% compared to the untreated diabetic rats (group 2).

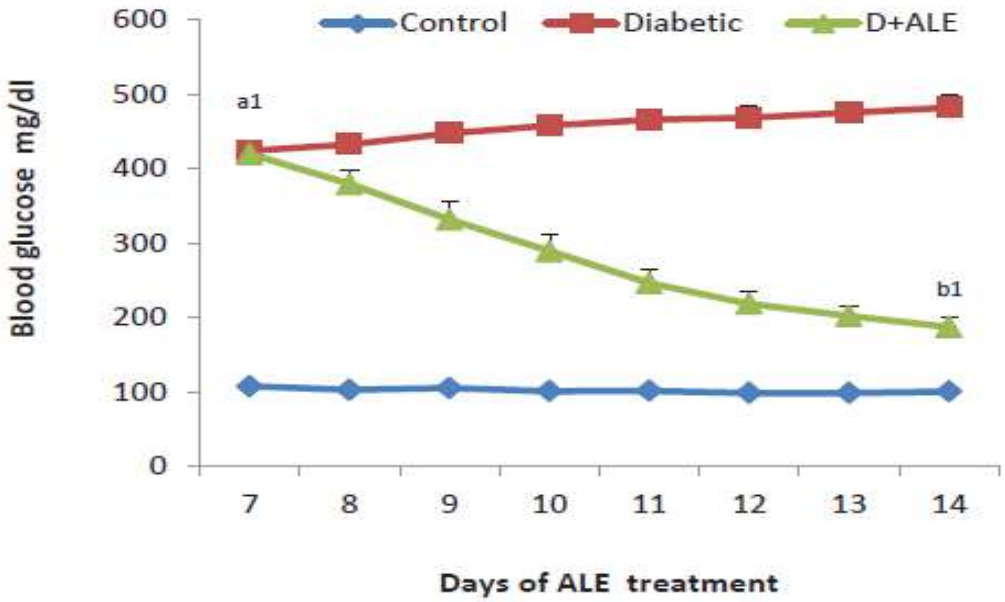

Figure 5: Blood glucose profile with effective dose of ALE in two weeks study.

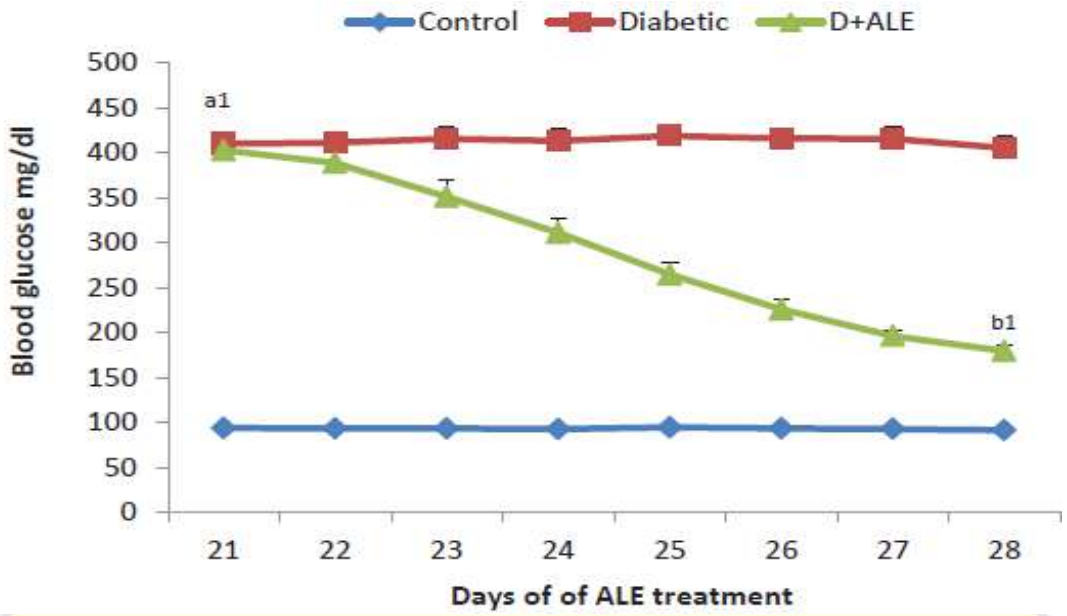

Figure 6: Blood glucose profile with effective dose of ALE in four weeks study.

Analysis of lipid profile levels

The lipid profile estimation has been carried out by measuring the levels of total cholesterol, triglyceride, LDL and VLDL and HDL cholesterol in all the three groups of animals. Lipid profile levels at the end of two and four weeks are shown in Fig, respectively. After two weeks, diabetic rats (group 2) showed significantly higher levels of total cholesterol, triglycerides, LDL, and VLDL cholesterol ($p \leq 0.001$) than control rats. In contrast, diabetic animals have been shown to have lower HDL cholesterol levels ($p \leq 0.001$). One week of ALE therapy resulted in a significant reduction in total cholesterol ($p \leq 0.001$), triglycerides ($p \leq 0.01$), LDL ($p \leq 0.001$), and VLDL cholesterol ($p \leq 0.01$) in D+ALE animals (group 3). In addition, there has been a notable improvement in HDL ($p \leq 0.001$) levels as compared to the animals in group 2. Similarly, in diabetic mice with four weeks of diabetes, ALE therapy significantly reduced total cholesterol ($p \leq 0.001$), LDL cholesterol ($p \leq 0.001$), and VLDL cholesterol ($p \leq 0.05$). However, it has been determined that there is no substantial difference in the levels of HDL and triglycerides.

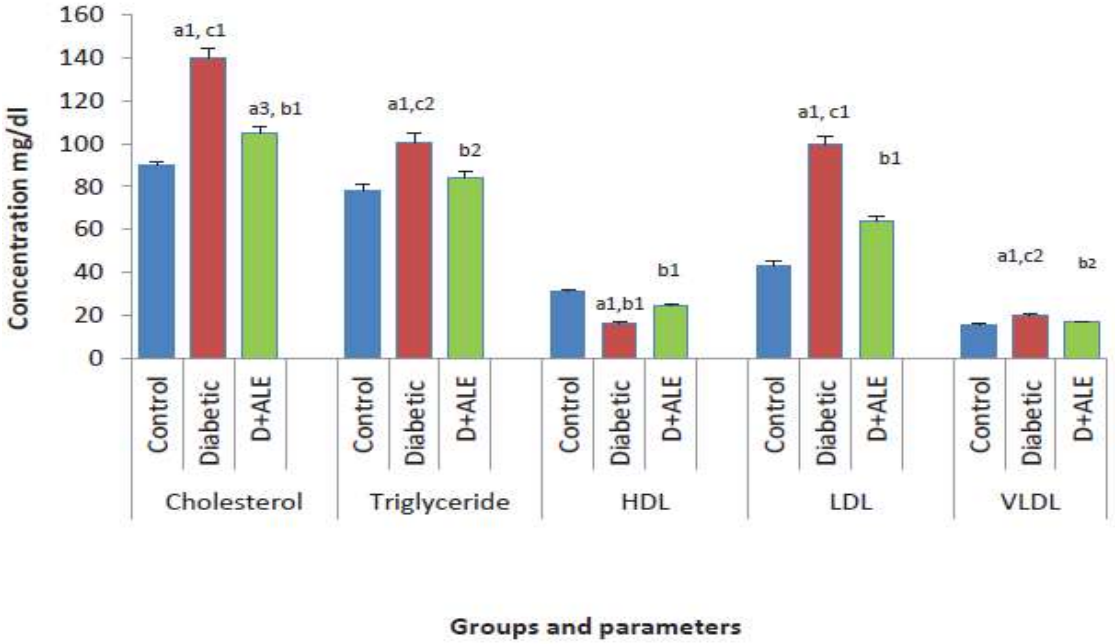

Figure 7: Evaluation of serum lipid profile levels in two weeks study.

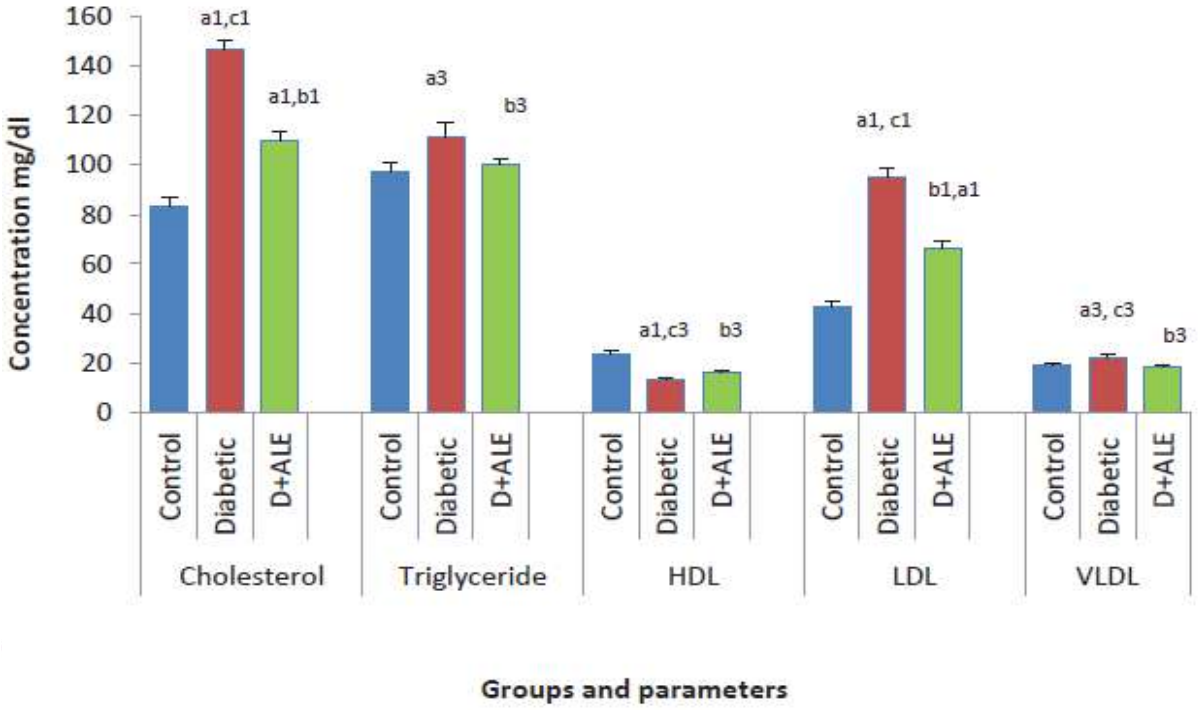

Figure 8: Evaluation of serum lipid profile levels in four weeks study.

Estimation of plasma insulin levels

Since beta cells secrete insulin, which is crucial for glucose metabolism, plasma insulin levels have been calculated to assess the pancreatic beta cell health. At two and four weeks, respectively, the diabetic rats' plasma insulin concentrations were found to be approximately 163% and 52% lower than those of the control rats (Figure 4.9 and 4.10). However, diabetic rats' insulin status has not improved after receiving ALE treatment for seven days in a row.

Even after receiving ALE therapy, the insulin levels in the rats in groups 2 and 3 were found to be comparable in both the two-week and four-week tests. Additionally, at the conclusion of four weeks, it was found that the insulin levels of the animals in groups two and three were worse than those in the two-week diabetes. Therefore, the overall outcome showed that insulin levels following ALE therapy did not alter significantly.

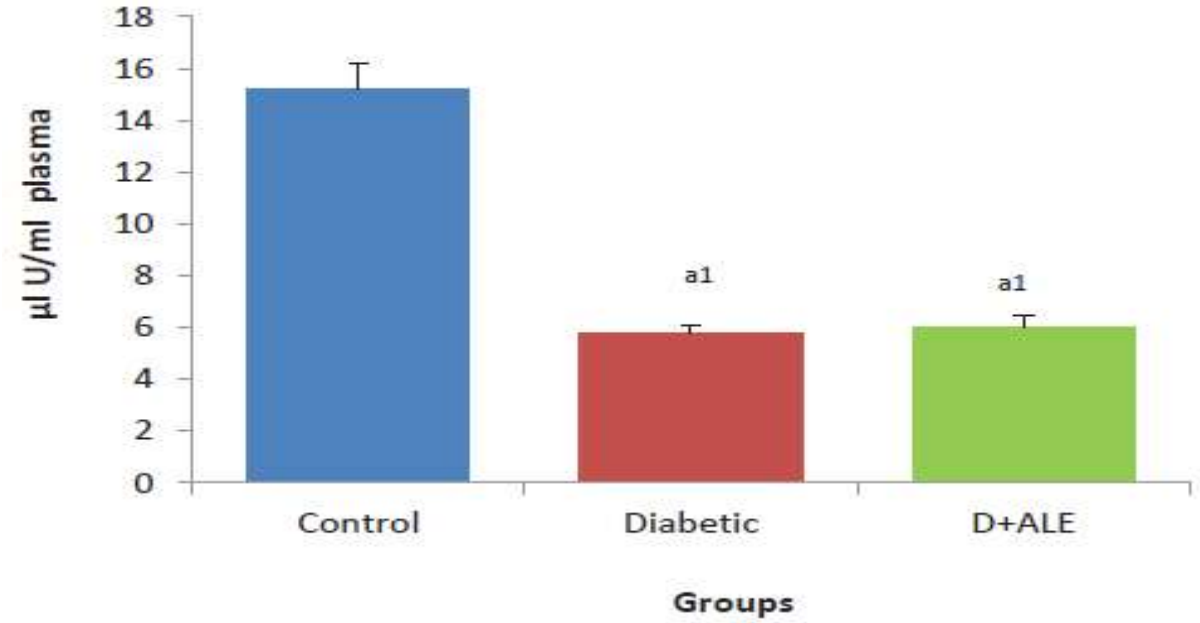

Figure 9: Estimation of plasma insulin levels at the end of two weeks.

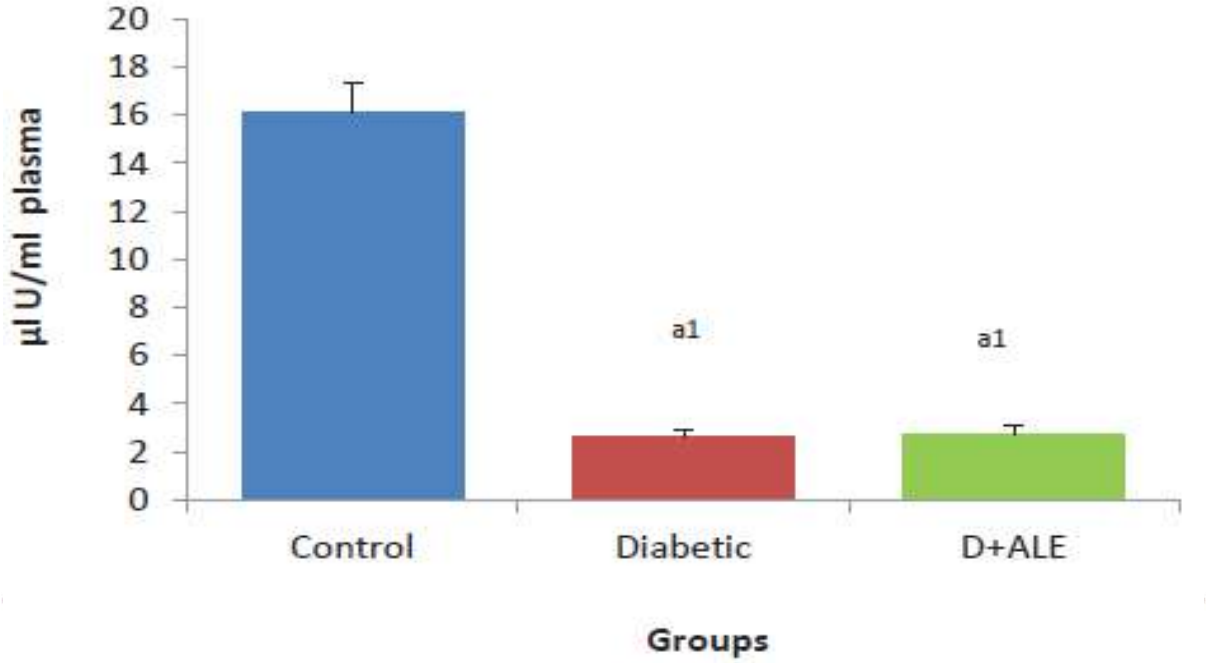

Figure 10: Estimation of plasma insulin levels at the end of four weeks.

Analysis of pro oxidants/antioxidants biomarkers in tissues

Since beta cells secrete insulin, which is crucial for glucose metabolism, plasma insulin levels have been calculated to assess the pancreatic beta cell health. At two and four weeks, respectively, the diabetic rats' plasma insulin concentrations were found to be approximately 163% and 52% lower than those of the control rats. However, diabetic rats' insulin status has not improved after receiving ALE treatment for seven days in a row.

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Analysis of LPO levels in Liver, Kidney, Heart and Brain tissues

An essential part of the plasma membrane, lipids experience oxidation reactions in a variety of clinical circumstances. As a result, it is a crucial technique for identifying the tissue-damaging effects of diabetes and assessing the protective effects of ALE. After two weeks of diabetes, the LPO levels in the liver, kidney, and heart tissue were determined, and after four weeks of diabetes, neurological investigations were conducted.

The liver ($p \leq 0.001$), kidney ($p \leq 0.01$), and heart ($p \leq 0.001$) tissues of diabetic rats exhibited considerably higher levels of lipid peroxidation than those of control rats. Compared to the liver and kidney, the heart tissue has been found to have the greatest peroxidation levels among the three tissues. Among the tissues, the liver has demonstrated the least amount of lipid peroxidation. Although the degree varies by tissue, the administration of ALE to diabetic rats has reduced LPO levels in every tissue. In comparison to untreated diabetic mice (group 2), Figure clearly shows that ALE treatment dramatically reduced lipid peroxidation in the liver ($p \leq 0.01$), kidney ($p \leq 0.05$), and heart ($p \leq 0.001$) of D+ALE treated animals (group 3).

However, after receiving STZ, it was shown that the LPO levels in brian tissue were noticeably higher. Compared to control rats, the diabetic rats' LPO levels were noticeably ($p \leq 0.001$) higher. The brain had the highest levels of peroxidation of any tissue; however, when compared

to untreated diabetic rats (group 2 animals), ALE therapy dramatically decreased ($p \leq 0.01$) these levels in brain tissue.

Peroxidation levels in the liver, kidney, heart, and brain tissues of diabetic rats have significantly increased as a result of LPO, and ALE treatment has successfully decreased these raised levels in treated rats (D+ALE).

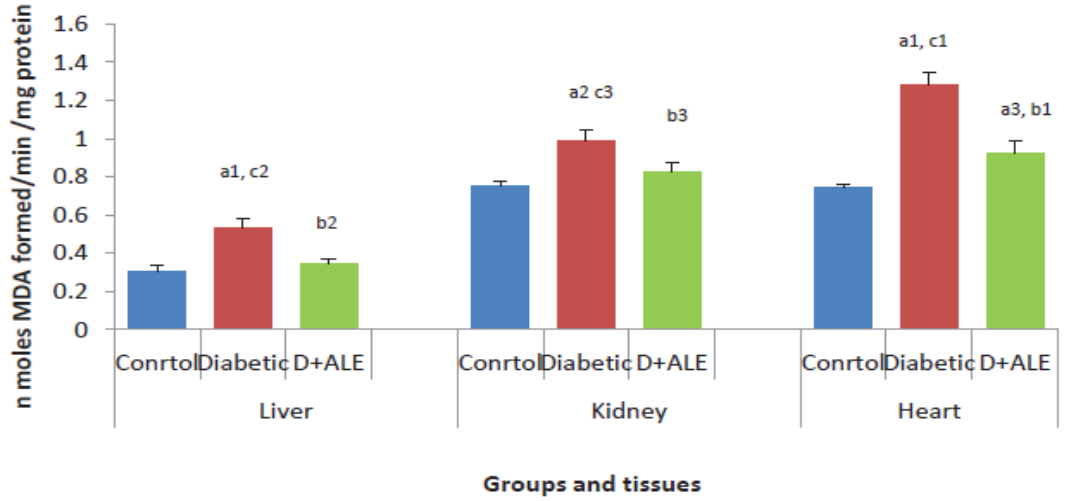

Figure 11: Evaluation of LPO levels in liver, kidney and heart tissues.

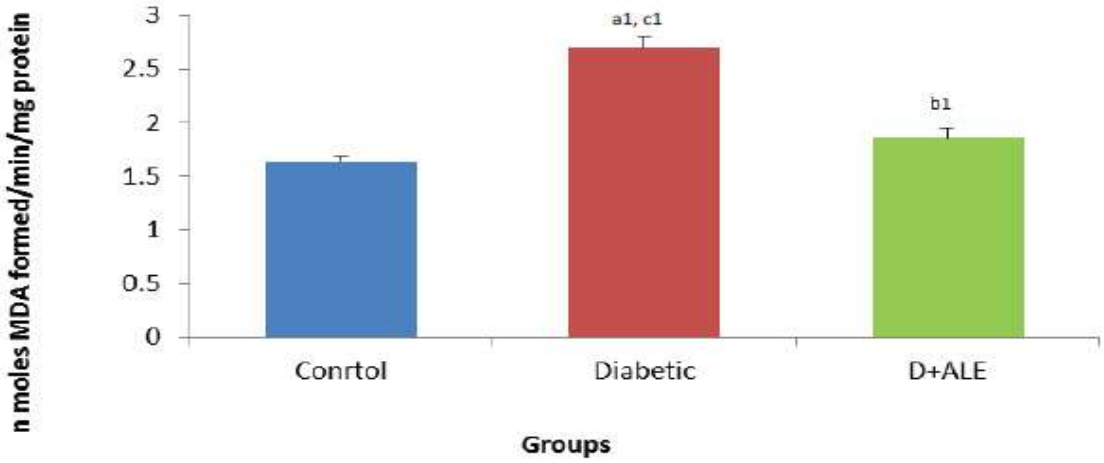

Figure 12: Evaluation of LPO levels in brain tissue.

Analysis of GSH levels in Liver, Kidney, Heart and Brain tissues

Estimating GSH levels indicates the degree of cellular protection since GSH, an intracellular antioxidant, plays a critical function in shielding cells from reactive oxygen species. The liver, kidney, heart, and brain tissues of diabetic, D+ALE-treated, and control rats were examined for GSH levels. Compared to diabetic and ALE-treated rats, control rats had significantly greater levels of GSH in their liver ($p \leq 0.001$), kidney ($p \leq 0.001$), and heart ($p \leq 0.001$). It has been found that the liver contains the highest GSH concentration, whereas the kidney has the lowest. For seven days in a row, D+ALE (group 3) rats were given ALE orally, which significantly raised the levels of cellular GSH in the liver ($p \leq 0.001$) and heart ($p \leq 0.01$) tissues. In contrast to diabetic rats, the alterations in kidney tissue have been minimal, and the GSH content has not changed much.

Although the GSH levels in the brain tissue have changed, the control brain's GSH level was determined to be the lowest when compared to the other tissues employed in this investigation. When compared to control brains, the GSH levels in the rats treated with STZ were significantly lower ($p \leq 0.01$). When compared to untreated diabetic rats, the GSH status of group 3 animals was considerably ($p \leq 0.05$) enhanced by oral ALE treatment.

The GSH analysis's overall findings show that the GSH content has dramatically dropped in diabetic liver, kidney, heart, and brain tissues. However, with the exception of the kidney, all tissues improved equally well with the ALE treatment.

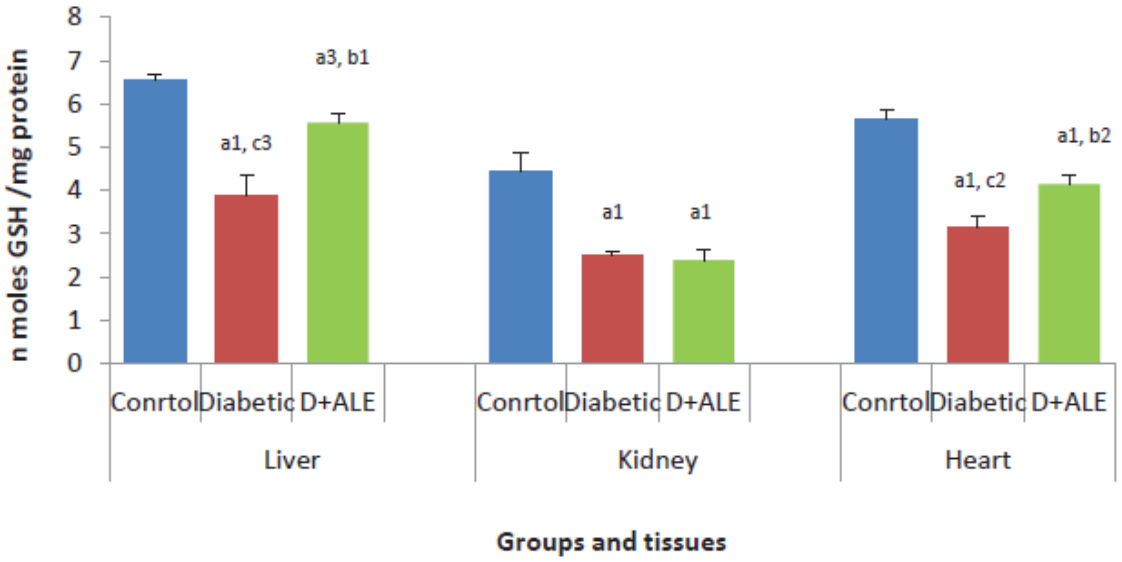

Figure 13: Estimations of GSH levels in liver, kidney and heart tissues.

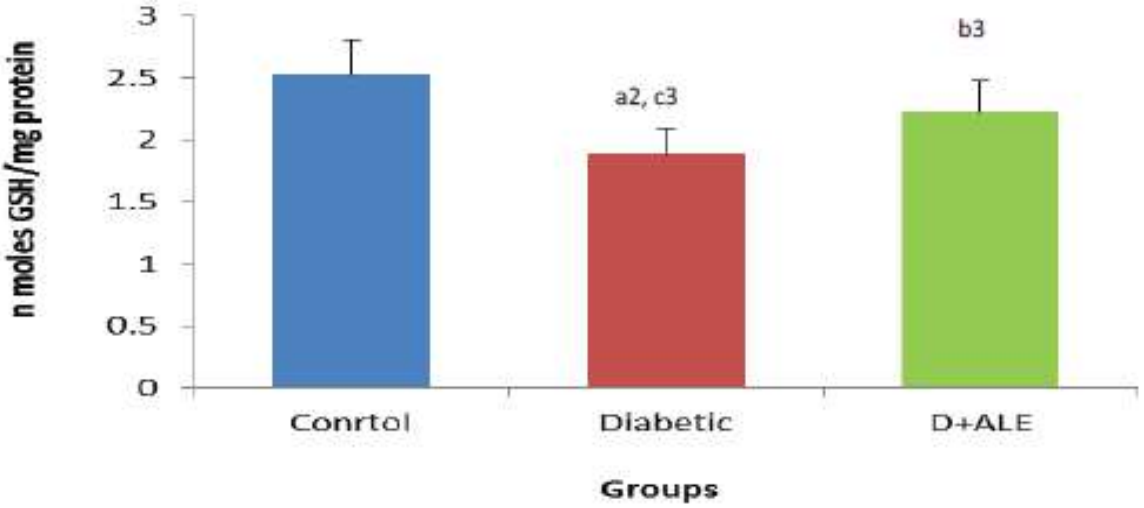

Figure 14: Estimations of GSH levels in brain tissue.

Analysis of CAT activity in Liver, Kidney, Heart and Brain tissues

It has been discovered that different tissues exhibit different levels of CAT activity. The CAT enzyme's activity in the liver, kidney, heart, and brain tissues is shown in Fig, respectively. When compared to control animals, diabetic animals' liver and heart tissues exhibit higher levels of CAT activity, as seen in Fig. Compared to the kidney and heart, the liver had the highest CAT activity among the diabetes tissues. It has been determined that the diabetic liver and heart have considerable levels of ($p \leq 0.001$) and ($p \leq 0.001$), respectively, in comparison to controls.

Although there has been no discernible difference in the enzyme activity between diabetes and control kidney tissue, diabetic mice have shown a modest decrease in CAT activity. In the liver and heart tissues of diabetic mice (group 3), ALE therapy significantly reduced increased CAT activity and brought it back to normal ($p \leq 0.001$). Similar alterations in CAT activity have been observed in the diabetic brains of both untreated (group 2) and ALE-treated (group 3) mice. When compared to age-matched controls, diabetic rats' brains have much higher CAT activity. However, ALE therapy brought the increased activity back to levels that were within control.

Overall, it was discovered that the CAT activity in diabetic tissues differed from control levels; however, group 3 animals' CAT activity returned to control levels after receiving ALE treatment.

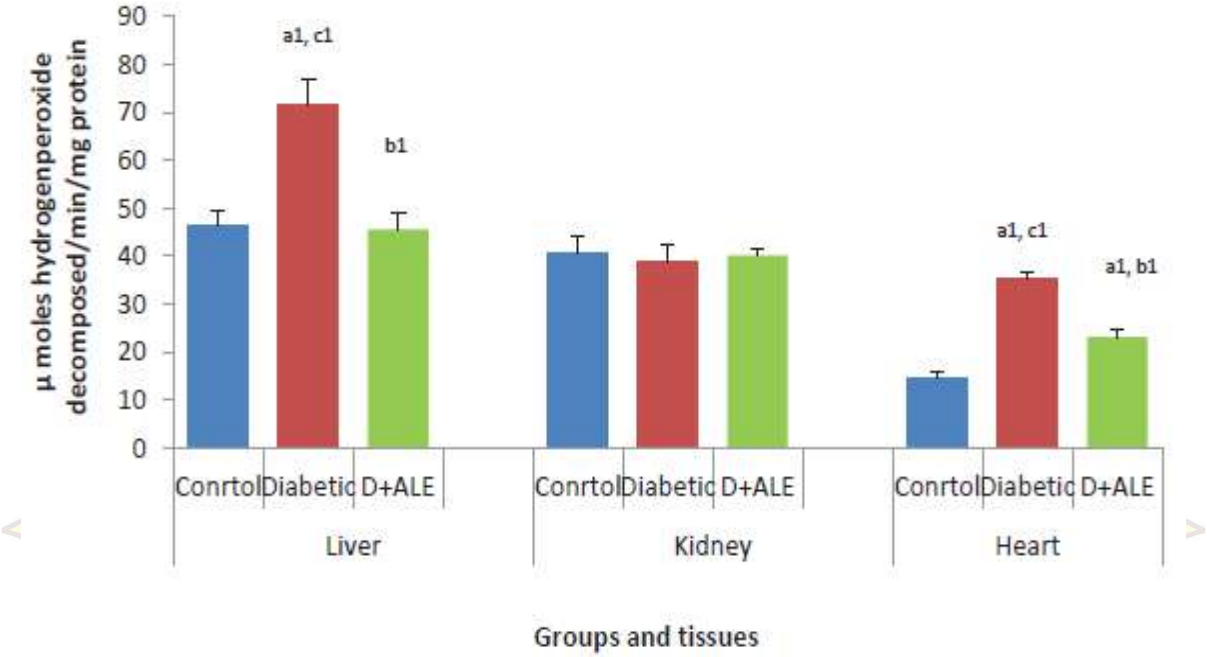

Figure 15: Analysis of CAT activity in liver, kidney and heart tissues.

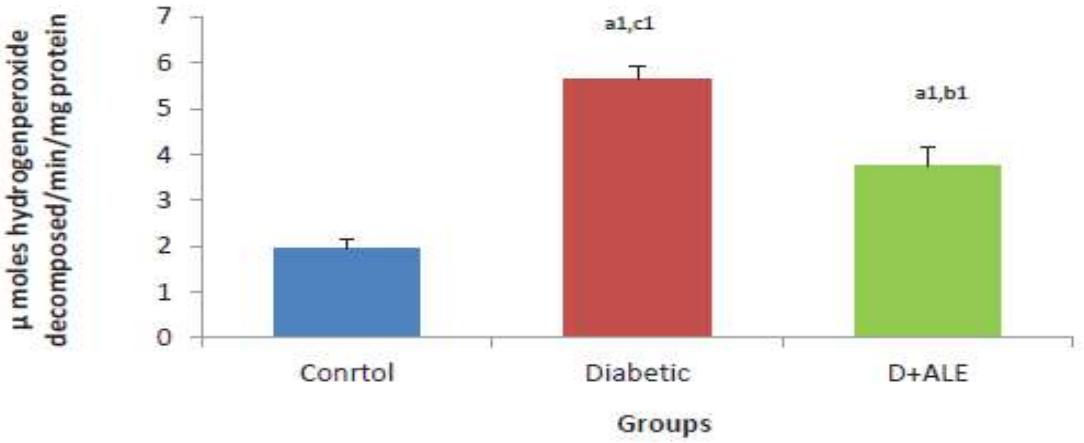

Figure 16: Analysis of CAT activity in brain tissue.

Analysis of SOD activity in Liver, Kidney, Heart and Brain tissues

The examination of SOD activity in liver, kidney, heart, and brain tissues is shown in Figures. SOD activity has been discovered to be elevated in the heart, kidney, and brain tissues of diabetic rats (group 2 animals), as seen in the comparative examination of liver, kidney, and heart tissues. In contrast to the control, the increase in heart tissue was found to be extremely significant ($P \leq 0.001$), whilst the rise in kidney tissue was determined to be non-significant. Compared to controls, the liver tissue of diabetic rats exhibits a significant decrease in activity ($p \leq 0.05$).

However, diabetic rats (group 3) treated with ALE showed an improvement in SOD activity in their cardiac tissues ($p \leq 0.001$) compared to control levels. On the other side, a minor but less substantial improvement has been noted in the liver and kidney tissues.

The SOD activity in the brain tissue of each of the three animal groups is shown in Figure 4.18. In a diabetic state, there is a significant ($p \leq 0.001$) increase in SOD activity. When ALE was administered to diabetic animals (group 3 animals), the enzyme activity was significantly

(p≤0.001) lower than in the untreated diabetic animals and returned to the control groups. In conclusion, once ALE was administered, the SOD activity returned to normal levels after exhibiting variability in various tissues during the diabetes state.

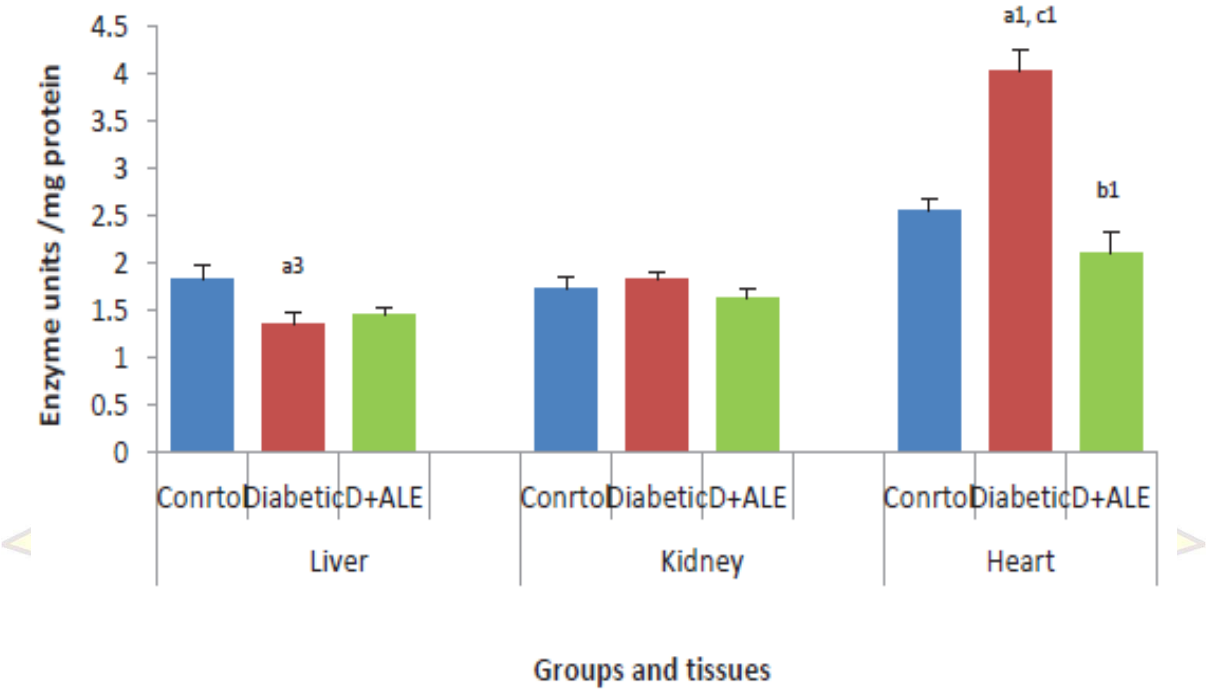

Figure 17: Analysis of SOD activity in liver, kidney and heart tissues.

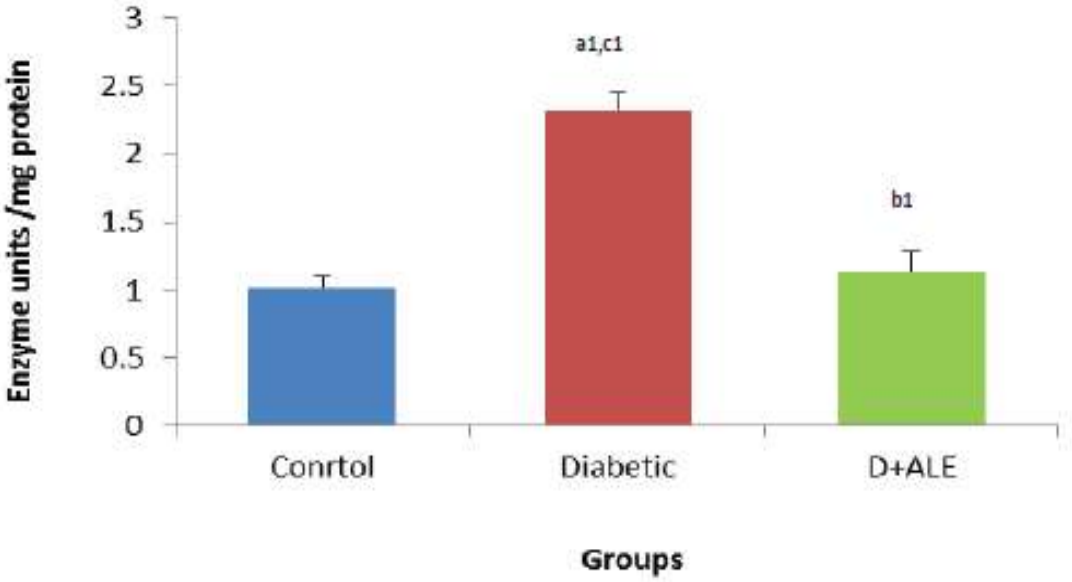

Figure 18: Analysis of SOD activity in brain tissue.

Analysis of GPX activity in Liver, Kidney, Heart and Brain tissues

Enzymatic activity has been observed to be higher in heart tissue and decreased in liver and kidney tissues of group 2 (diabetic) mice after diabetes, as illustrated in Figure. It has been determined that these alterations in diabetes tissues relative to control tissues are substantial in all organs, including the liver (p≤0.001), kidney (p≤0.001), and heart (p≤0.05). The liver had the highest GPX activity among the control tissues, followed by the kidney and heart. In contrast to untreated diabetic rats (group 2 animals), ALE treatment of diabetic rats (group 3) resulted in a substantial decrease in GPX activity in the heart (p≤0.05) and an increase in the liver (p≤0.01) and kidney (p≤0.05) tissues. The brain tissue has shown the lowest GPX activity when compared to the liver, kidney, heart, and brain tissues of the control mice. In contrast to

controls, diabetic mice have been shown to exhibit considerably higher ($p \leq 0.001$) GPX activity. When ALE is given orally to diabetic rats for seven days in a row, the GPX activity is markedly reversed and returned to control levels.

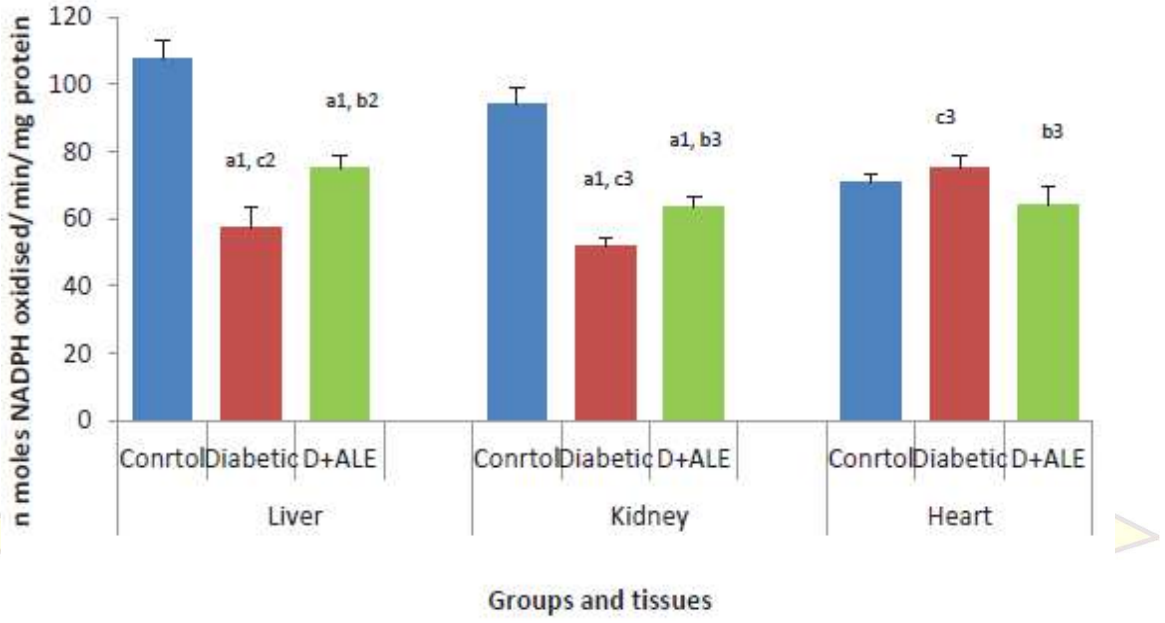

Figure 19: Analysis of GPX activity in liver, kidney and heart tissues.

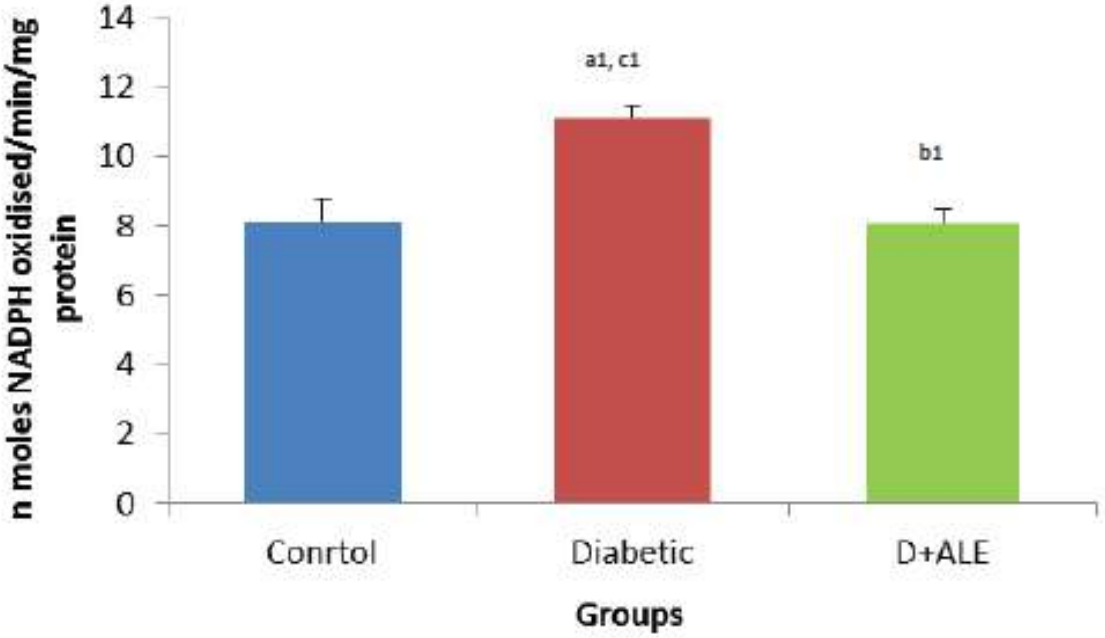

Figure 20: Analysis of GPX activity in brain tissue.

Analysis of GR activity in Liver, Kidney, Heart and Brain tissues

The activity of the enzyme GR in the liver, kidney, and cardiac tissues is depicted in the data. The control heart displayed the least amount of GR activity, whereas the control liver displayed the most. Furthermore, Figure shows that the GR activity in the liver and renal tissues of diabetics has significantly decreased ($p \leq 0.001$) when compared to the corresponding controls. However, compared to the control, the diabetic heart has demonstrated a substantial increase ($p \leq 0.05$) in activity. The GR activity in the liver ($p \leq .001$), kidney ($p \leq .05$), and heart ($p \leq .001$) tissues have been dramatically restored in diabetic rats (group 3 animals) treated with ALE.

In comparison to age-matched controls, diabetic mice exhibit a significant ($p \leq 0.001$) decrease in GR activity in brain tissue, as illustrated. When compared to untreated diabetic rats, the GR

activity level of diabetic animals treated with ALE improved, indicating a significant shift ($p \leq 0.01$).

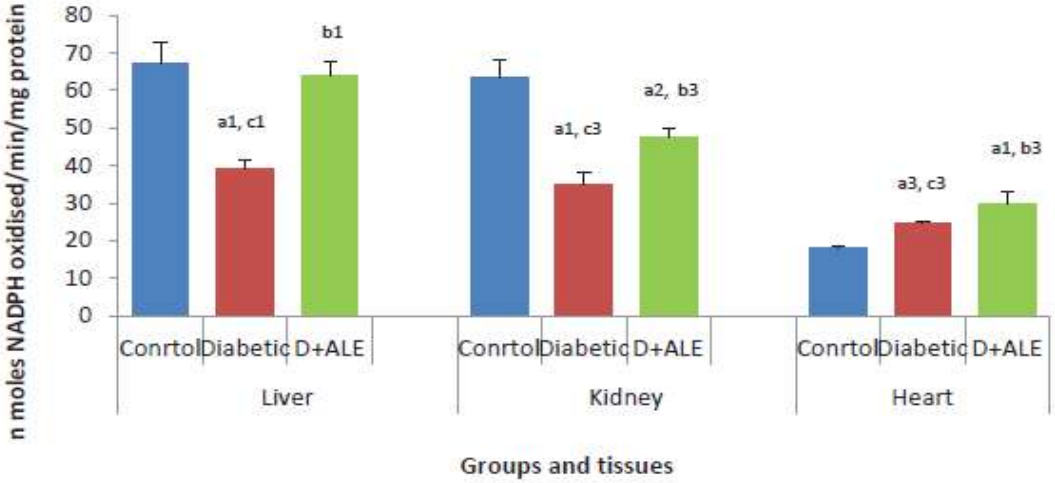

Figure 21: Analysis of GR activities in liver, kidney and heart tissues

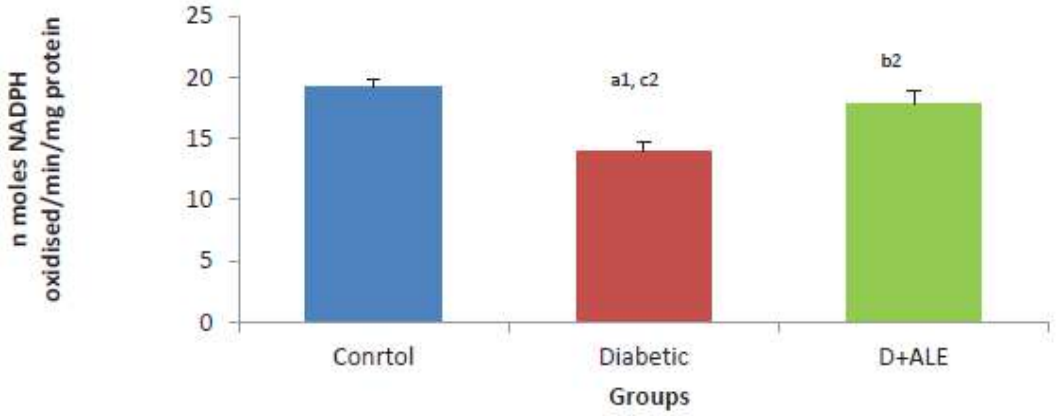

Figure 22: Analysis of GR activity brain

Analysis of GST activity in Liver, Kidney, Heart and Brain tissues

Like other enzymes, the activity of GST has also been assessed in tissues such as the liver, kidney, heart, and brain. The activity of the enzyme GST in the tissues of the liver, kidney, and heart is shown in Figure. According to reports, the control liver exhibits the highest activity of this enzyme, whilst the control heart exhibits the lowest.

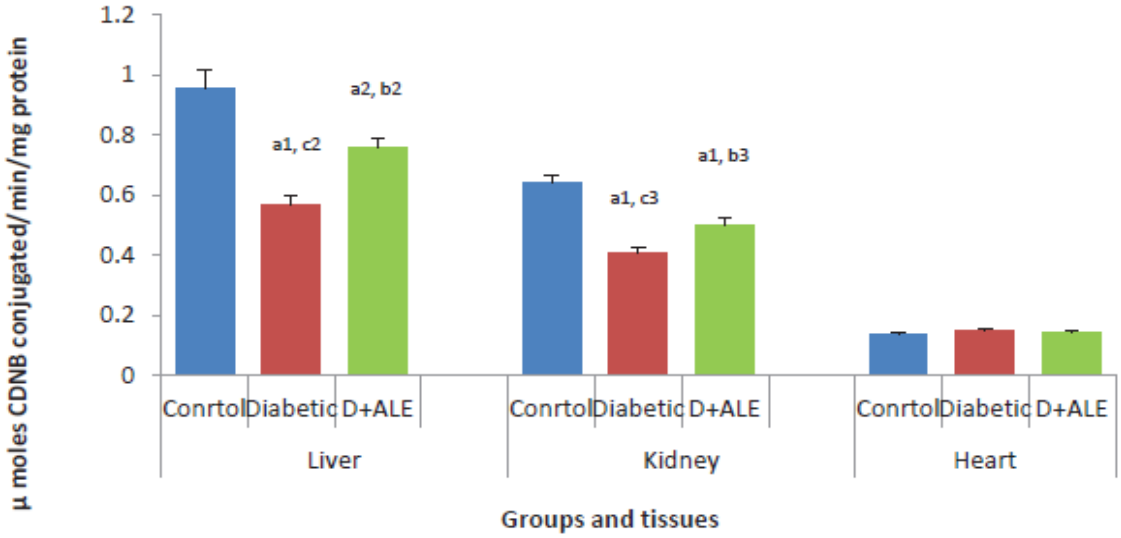

Figure 23: Analysis of GST activity in liver, kidney and heart tissues.

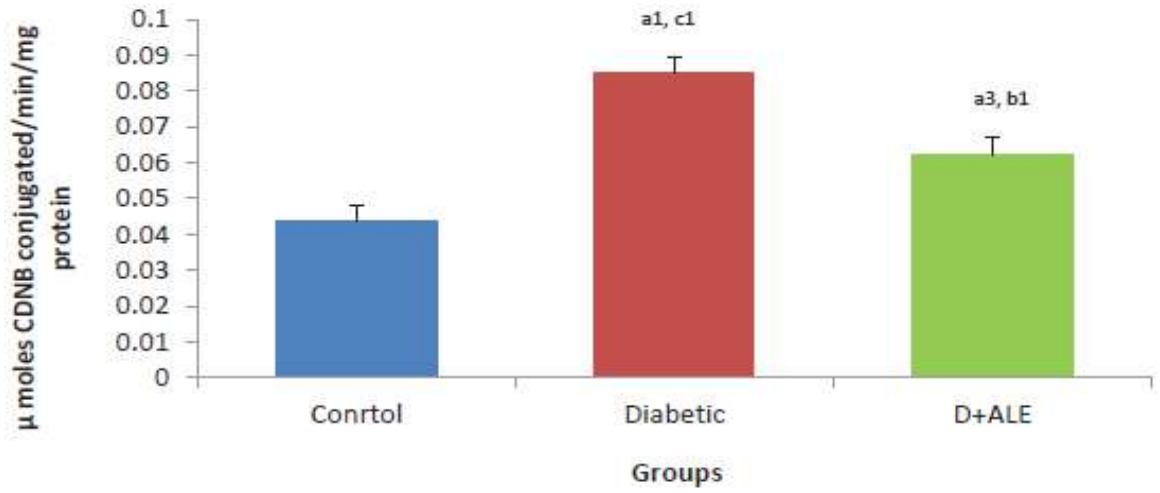

Figure 24: Analysis of GST activity in brain.

However, it has been discovered that the activity of this enzyme is dramatically ($p \leq 0.001$) reduced in liver and kidney tissue when STZ therapy or diabetes is administered. Furthermore, it has been determined that there is no discernible difference in the activity of diabetic and ALE-treated hearts in heart tissue. Compared to untreated diabetic rats, the oral administration of ALE to group 3 rats resulted in improved GST activity in the liver ($p \leq 0.01$) and kidney ($p \leq 0.05$) tissue.

In addition, Figure shows that the activity of GST is more low in brain tissue than in other tissues. It has also been discovered that diabetic animals have higher levels of GST activity in their brains when compared to control animals. ALE therapy, however, has considerably decreased ($p \leq 0.01$) this increased GST activity and brought it back to control levels.

Analysis of inflammatory markers

Many diabetic animals have been shown to have inflammation. Thus, TNF α and C reactive protein (CRP), two inflammatory markers, have been measured in diabetic rats.

Estimation of CRP

The study of CRP levels in the plasma of control, diabetic, and ALE-treated mice. It has been discovered that diabetic animals have considerably higher levels of CRP ($p \leq 0.001$) than control animals. Compared to controls, diabetic animals have been shown to have a ~97% increase in CRP levels. In contrast to diabetic animals that were not treated, these levels have dropped to about 28% in the D+ALE group of mice that received ALE treatment. Therefore, it has been determined that ALE therapy is effective since it significantly ($p \leq 0.001$) alters the CRP levels in group 3 animals compared to diabetic animals.

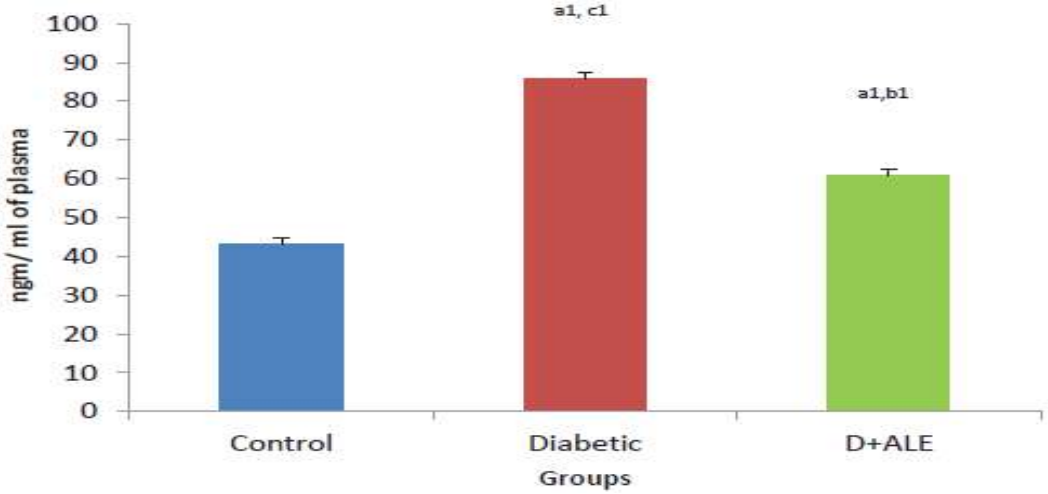

Figure 25: Estimations of CRP levels in plasma of three groups of animals.

Estimation of TNF α

The western blot examination of TNF α in the blood of control, diabetic, and D+ALE mice is shown in Figure. In all three animal groups, there was a single TNF α band (26 kDa) that was enhanced in comparison to the β actin control band (43 kDa). Compared to the diabetes (lane 2) and D+ALE (lane 3) groups, the control group's (lane 1) immunoblot intensity was found to be lower. It was discovered that the diabetes group's band intensity (1.36 ± 0.16) was approximately 1.34 times greater than that of the control group (0.58 ± 0.14). However, compared to the untreated diabetic group, the D+ALE group (1.05 ± 0.1) treated with ALE showed a decrease in band intensity of about 0.22 times.

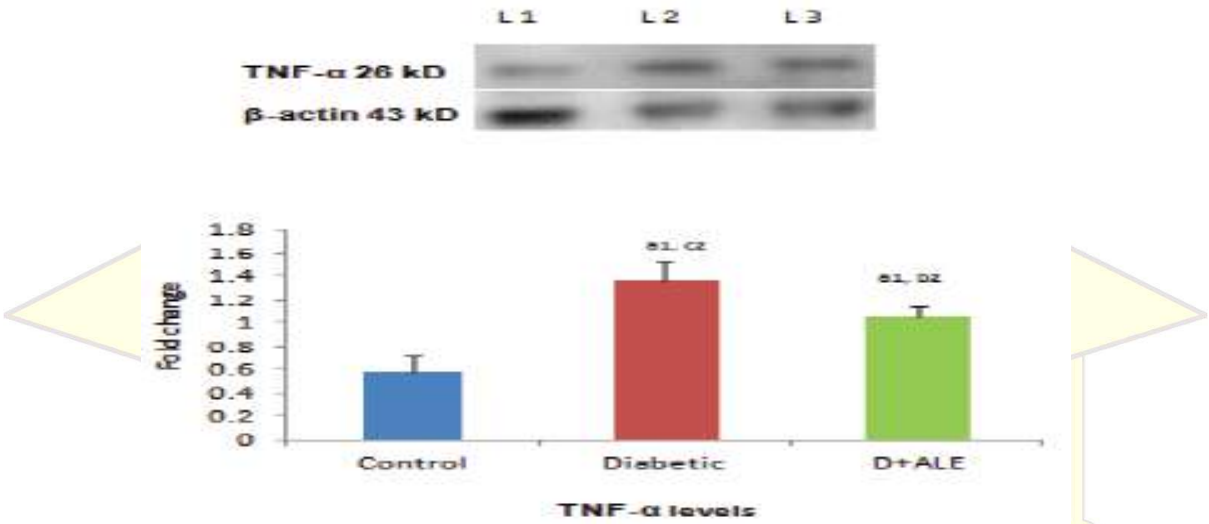

Figure 26: Estimations of TNF α levels (Western blot) in the blood of three groups of animals.

Conclusion

Diabetes mellitus is a chronic endocrine condition characterised by impaired insulin production, action, glucose transport, and/or utilisation. It may be identified using its defining trait, hyperglycemia. destructive effects of hyperglycemia increase incidence of death and morbidity by causing related complications. Thus, related issues put a lot of strain on practically every organ, including kidney, liver, heart, and brain, resulting in diabetic neuropathy, nephropathy, cardiac difficulties, microangiopathic alterations, and stroke. Several research organisations are investigating diabetes-induced problems in experimental diabetic animals in attempt to create new treatments for illness.

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