Original article

The effect of aloin in blood glucose and antioxidants in male albino rats with Streptozoticin-induced diabetic

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ABSTRACT

The anti-diabetic effect of aloin was examined in vivo in the current study, similar to the study, which for four weeks examined how aloin affected the blood sugar, insulin, and antioxidant levels in both healthy and diabetic rats generated by streptozotocin. Adult male albino rats were experimentally given a single intraperitoneal injection of 60 mg/kg of streptozotocin to induced diabetes. The in vitro experiment utilized blood samples, and adult male albino rats' kidneys, pancreas and liver were separated. In comparison to control diabetic rats, aloin isolates (30 mg / kg) body weight for 30 days considerably decreased serum glucose and effectively boosted serum insulin levels. Liver and kidney congeners of malondialdehyde (MDA) were substantially decreased while, Catalase (CAT), superoxide dismutase (SOD) and Congeners Glutathione (GSH) were significantly boosted as contrasted to diabetic rats after aloin therapy. Moreover, a histological assessment of the pancreas was performed.

These results show the promise of aloin at a dose of 30 mg/kg body weight for 30 days as an antidiabetic and antioxidant agent.

1. Introduction

Diabetes mellitus (DM), a group of metabolic disorders with several different etiologies that are characterized by elevated serum glucose levels or persistent hyperglycemia and abnormalities of insulin hormone secretion, insulin hormone resistance, or both, is one of the biggest threats to human health in the world today (Khan, 2021). Diabetes-related metabolic disorders increase the formation of mitochondrial superoxide in the heart muscle and endothelial cells of either small and large blood arteries (Kelkar, Aditya, Jai, Mehta, & Amoaku, 2018).

Consequently, oxidative stress is a crucial factor in the emergence of microvascular and cardiovascular problems associated with diabetes mellitus. (Tabatabaei S. R., Ghaderi, Tapehebur, Farbood, & Rashno, 2017; Sha, Hu, & Bu, 2020). Studies also show available treatments for controlling diabetes and its complications have various side effects with limited benefits; therefore, the desire for herbal products with anti-diabetic properties and fewer side effects that are more cost-effective furthermore is increasing (Association, 2018). Aloin (Aloe vera L., Liliaceae family), extracted from the outer bark of the aloe vera plant, has diverse applications in medicinal products and cosmetics, while research on animals has shown that aloin can be toxic, there is little indication of this in humans. If consumed excessively, especially over a lengthy period, aloin can be toxic, which signifies that it began having adverse effects on the body that may even be life-threatening. (Zhang, Liu, Liu, Zhao, & Tian, 2016; Association, 2018). Recent approaches suggest that the treatment of diabetes should not only focus on insulin secretion but also antioxidant protection of the β-cell in the pancreas, this may facilitate the repair of β-cells undergoing damage by oxidative stress secondary to hyperglycemia (Tangvarasittichai, 2015; Xu, Li, & Li, 2017) the objective of the study was to investigate how aloin affected blood sugar, insulin, and antioxidants to healthy rats, as well as rats with streptozotocin-induced diabetes, for four weeks.

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2. Material and methods

2.1. Chemicals

Streptozotocin was supplied by Alfa Aesar USA and Aloin was supplied by Sigma Aldrich Co USA., Catalase (CAT), Superoxide dismutase activity (SOD), Kit Malondialdehyde (MDA) and Glutathione (GSH), and were also purchased from the NWLSS™.

2.2. Experimental animals

The College of Pharmacy at King Saud University provided 26 male Wistar rats for this investigation, each weighing 200–250 g. The rats were kept in polyacrylate cages with constant conditions and typical light/dark cycles. Animals were left for one month before experimentation to adapt to laboratory conditions. Throughout the experiment's acclimation phase and duration, a commercial balanced diet (General Organization for Grain Silos and Flour Mills, Riyadh) and water were provided ad libitum.

2.3. Induction of DM and study design

Rats were given intraperitoneal injections of streptozotocin after being starved for the previous night (Alfa Aesar, USA) (60 mg/kg). Throughout the first twenty-four hours following the administration of streptozotocin, mice treated with STZ were given a 5 % glucose solution rather than water to prevent hypoglycemia shock-related mortality. Fasting blood glucose was measured seventy-two hours later utilizing a One Touch glucometer (Icare TD-4279); diabetic rats were defined as those with fasting blood glucose levels>250 mg/dL. (Mestry, Dhodi, Kumbhar, & Juvekar, 2017; Elekofehinti, Onunkun, & Olaleye, 2020).

Six rats each were given to the four groups,

Group 1: was normal control rats given an aqueous solution, Group 2: The diabetic control rats were given an aqueous solution daily for 30 days, Group 3: The normal control rats were given an aqueous solution daily for 30 days, and Group 4: The diabetic rats were administered Aloin (30 mg/kg) in an aqueous solution daily for 30 days.

2.4. Sampling

In the first, second, third, and fourth weeks, a blood glucose meter (Icare TD-4279) was utilized to check the blood sugar level in the tail vein.

By the completion of the experiment phase (day 30th), The *retro*-orbital plexus was used to collect blood samples, and serum samples subsequently separated using centrifugation. (Thermo Scientific, USA) and used immediately for Insulin hormone analyses (qing Su, diWang, & yanChi, 2017).

Post-sacrificed by anesthesia, the Liver, kidneys, and pancreas were harvested and rinsed in ice-cold saline, and calculation of liver, and kidney oxidative stress concentrations (MAD, GSH, SOD, CAT) (Sun, Wang, & Lu, 2017).

2.4.1. Determination of glucose

In this experience, we estimate blood glucose based on the use of the enzyme's method (Glucose oxidase) by the blood glucose meter (Icare TD-4279) (Rahmati, Keshvari, Mirnasouri, & Chehelcheraghi, 2021).

2.4.2. Measurement of serum insulin concentration

Commercial quantitative enzyme-linked immunosorbent assay [(insulin ELISA kit) (DRG International, USA) (Jeffrey, Flier, Kahn, & Roth, 1979) was employed in a microplate reader to evaluate the optical density at an absorbance of 450 nm in order to evaluate the serum insulin levels of STZ-induced diabetic rats and also normal rats (Alborno, 2016).

2.5. Oxidative stress indicators

2.5.1. Sample preparation

Animals were anaesthetized with chloroform and slaughtered at the conclusion of the procedure right after blood was collected. Livers and kidney tissues were quickly collected, collected organs were cleaned from fatty tissues and washed with Phosphate-buffered Heparin 0.16 mg/mL is introduced to saline (PBS), pH 7.4, to eliminate any red blood cells and clots. The samples were then homogenized in cold phosphate buffer using an ultrasonic homogenizer., the homogenate was centrifuged at 4000 rpm for 10 min at 4 °C in a refrigerated centrifuge and the supernatant was collected and kept at − 20 °C and used as a sample for antioxidant assays (Al-musa & Al-hashem, 2013).

2.5.2. Determination of tissue samples

malondialdehyde (MDA), glutathione (GSH)
superoxide dismutase (SOD) and catalase (CAT)

Tissue samples MDA was estimated by the method of Janero (1990). GSH was estimated by the method of Paglia, Valentine (1967). Depending on the enzyme's capacity to prevent autoxidation using the pyrogallol methodology of Martin, Dailey, and Sugarman (1987), SOD activity was determined. Catalase was estimated by the method of Beers and Sizer (1952).

Kit Malondialdehyde (MDA), Glutathione (GSH), Superoxide dismutase activity (SOD), and Catalase (CAT) was used by the NWLSS™.

2.6. Hematoxylin and eosin staining

Procedure: The pancreas tissues were dried in ethanol at increasing concentrations (70–100 %) before being embedded in paraffin and fixed in a 10 % neutral buffered formalin solution. Using a microtome, tissues were divided into sections that were 4 μm thick, mounted on glass slides, and afterwards dried slides. Following that, routine hematoxylin and eosin staining was performed on all samples. Thereafter, sections were examined at Olympus Optical in Tokyo, Japan, using a light microscope. All groups' slides were examined and captured on camera. (Alkhudhayri, Osman, Alshammari, Al Maiman, & Yahya, 2021; Sarfraz, Khaliq, Hafizur, Raza, & Ullah, 2021).

2.7. Statistical analysis

Data were expressed as the mean ± SEM. statistically analyzed using the SPSS program (version 23) and With the use of ANOVA and the Tukey multiple comparisons test, the various groups were compared. Significance was acceptable at $P < 0.05$.

[*] Significant variance unlike the standard control.
[a] significant variance unlike the standard control.

3. Result

3.1. Effect of 30 days daily dose administration of Aloin on serum glucose and insulin levels.

Figs. 1 and 2 depict the levels of serum-glucose as well as insulin in healthy and diabetic rats caused by streptozotocin, respectively. When contrasted to the matching control group, the serum glucose level was significantly elevated during diabetes,
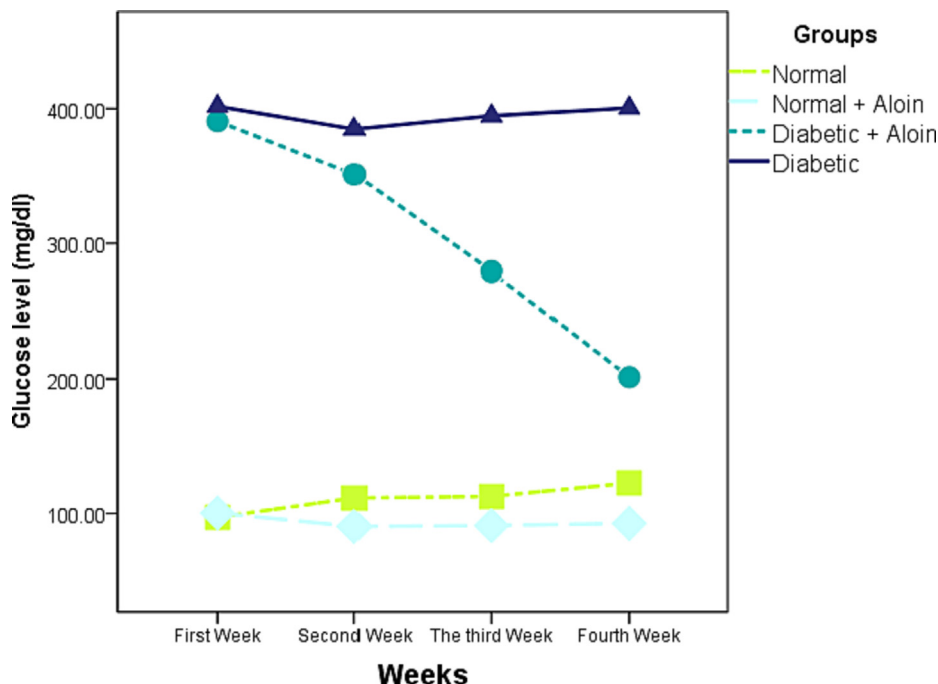
Fig. 1. Effect of Aloin on glucose level * Significant different unlike the standard control a significant different unlike the standard control ^{ns} $P < 0.05$.
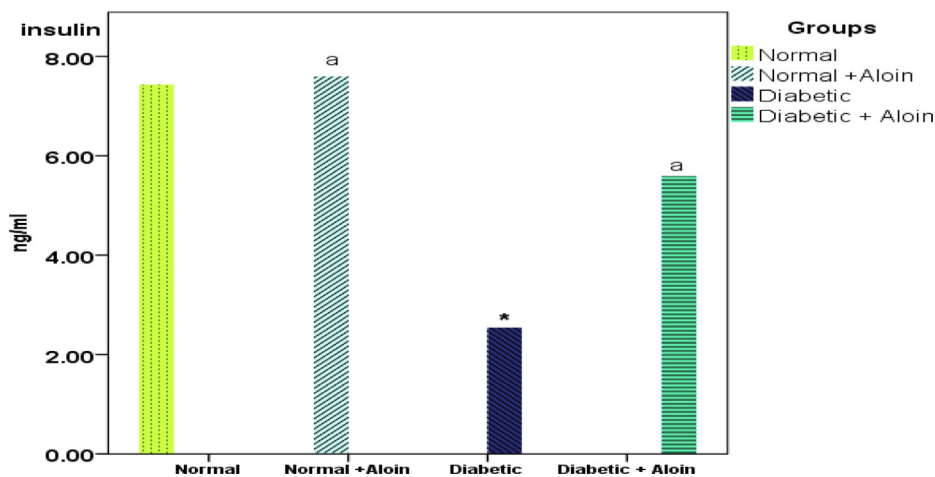

Fig. 2. Effect of Aloin on insulin level * Significantly variance unlike the standard control a significantly variance unlike the diabetic control ^{ns} $P < 0.05$.

and the serum insulin level was significantly reduced. The current study demonstrates a significantly gradual decline in the serum glucose level. In the second week in the diabetic and Aloin group compared to the diabetic control group and was significantly lower versus normal control groups in the 4th week, and the values of insulin levels and serum glucose tended to be close to normal in the aloin group.

3.2. Effect of 30 days daily dose administration of aloin on liver and kidney tissue malondialdehyde (MDA) levels

MDA level was significantly increased in the diabetic control group compared with the normal controls group, in the liver and kidney tissue re- respectively,(Fig. 3). With, MDA levels were decreased in the Diabetic + Aloin group contrast with the Diabetic control group, However, no significant ($P > 0.05$) difference in malondialdehyde level in the normal + Aloin group contrast to the normal control group.

3.3. Effect of 30 days daily dose administration of aloin on liver and kidney tissue Glutathione (GSH) levels

Liver and kidney tissue Glutathione activity were considerably lower in the Diabetic control group contrasted with the normal control group, respectively. GSH activity was significantly increased in the Diabetic + Aloin group contrast with the Diabetic control group. However no significant ($P > 0.05$) difference in GSH level in the normal + Aloin contrast to the usual control group (Fig. 4).

3.4. Effect of 30 days daily dose administration of aloin on liver and kidney tissue Superoxide dismutase (SOD) levels

Liver and kidney tissue Superoxide dismutase activity was considerably increased in the Diabetic + Aloin group contrasted with the Diabetic control group, respectively. SOD activity was significantly lower in the Diabetic control group contrast with the normal
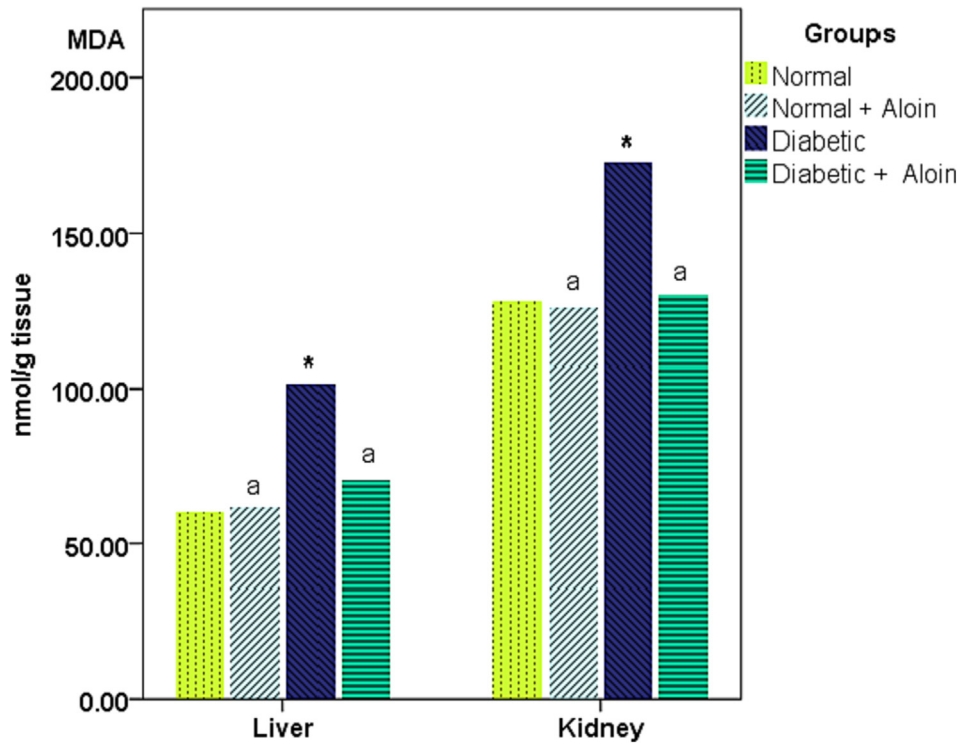
Fig. 3. Effect of Aloin on MDA * Significant variance unlike the standard control a significant variance unlike the diabetic control [ns] $P < 0.05$.
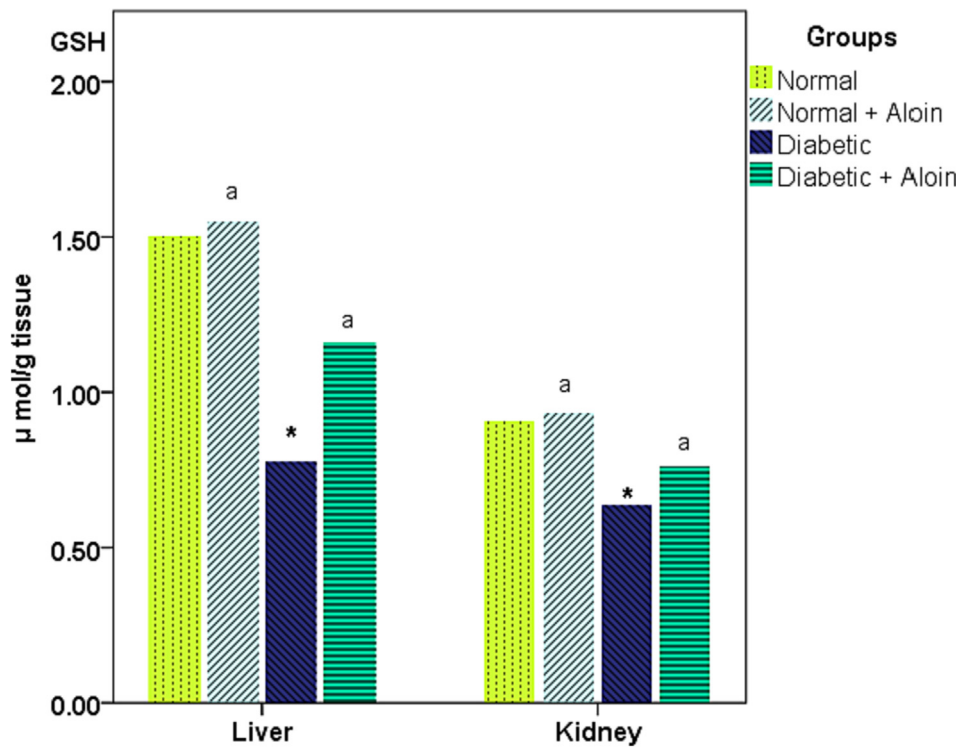

Fig. 4. Effect of Aloin on GSH * Significant variance unlike the standard control a significant variance unlike the diabetic control [ns] $P < 0.05$.
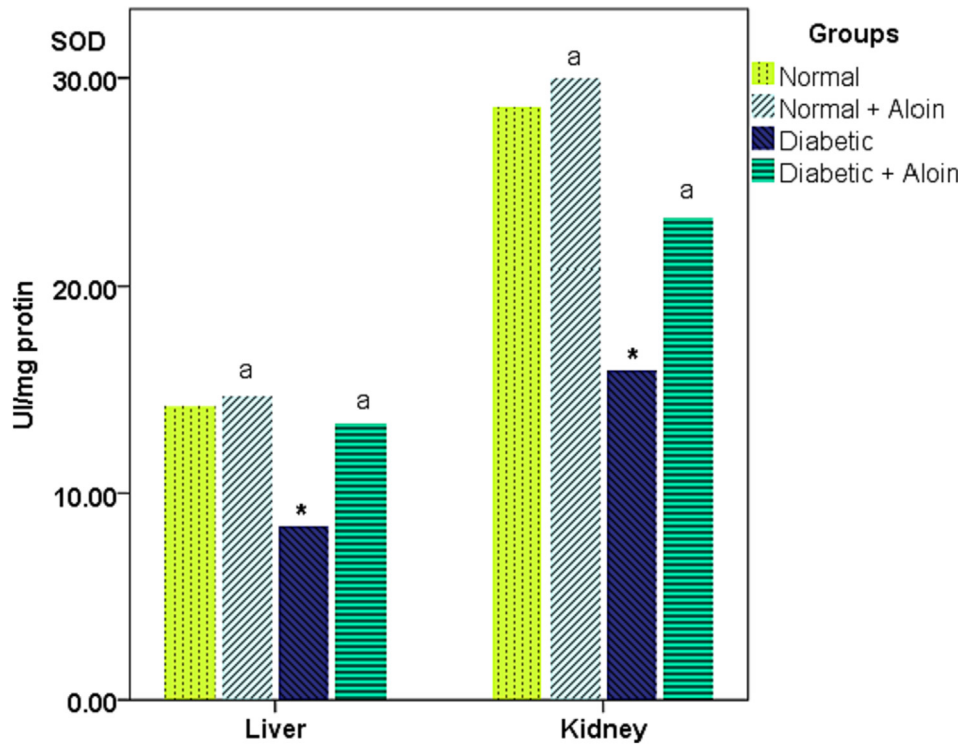
Fig. 5. Effect of Aloin on SOD * Significantly variance from the normal control. a significantly variance from the diabetic control [ns] $P < 0.05$.
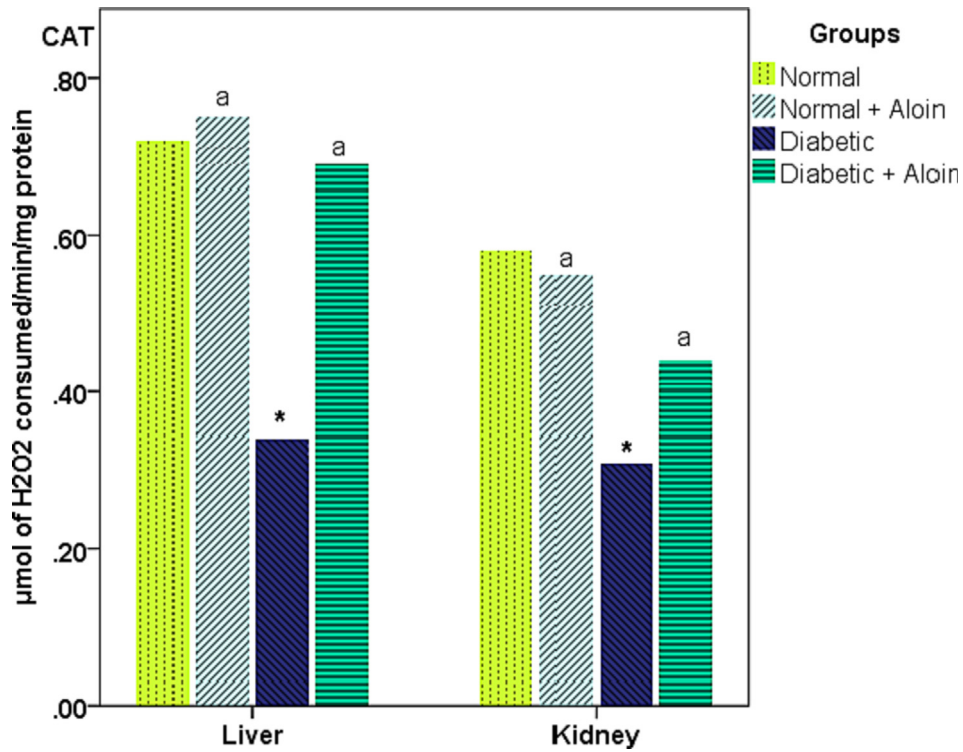

Fig. 6. Effect of Aloin on CAT * Significantly variance unlike the standard control. a significantly variance unlike the diabetic control [ns] $P < 0.05$.
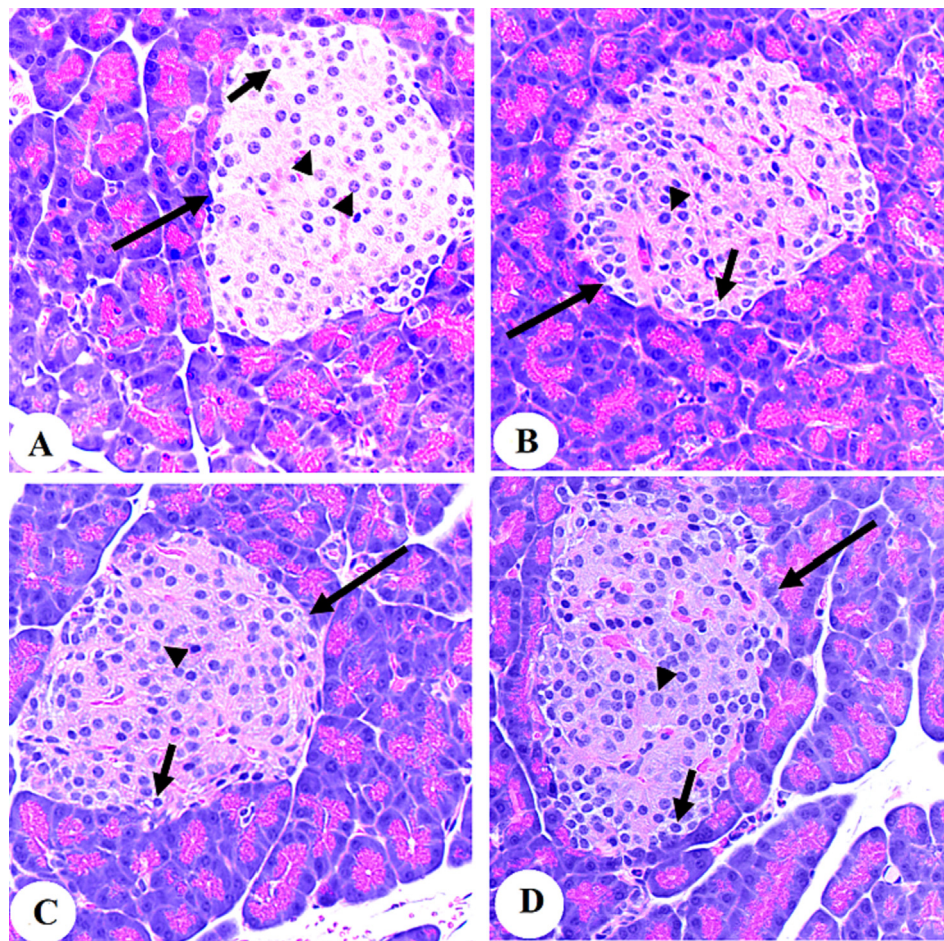
Fig. 7. Photomicrographs of the pancreases from the control (A&B) and control + Aloin (30 mg/kg)-treated rats (C&D).

control group. However no significant (P > 0.05) difference in SOD level in the normal + Aloin group contrast to the usual control group (Fig. 5).

3.5. Effect of 30 days daily dose administration of aloin on liver and kidney tissue Catalase (CAT) levels

Liver and kidney tissue Catalase level was significantly lower in the Diabetic control group compared with the normal control group, respectively. CAT level was significantly increased in the Diabetic + Aloin group contrast with the Diabetic control group. However, no significant (P > 0.05) difference in CAT level in the normal + Aloin group contrast to the usual control group (Fig. 6).

3.6. Histological results

Both groups are showing normally sized circular islets of Langerhans intact α-cells (peripheral small cells with dark nuclei (small arrow) and β-cells (central larger with light nuclei (arrowhead).

There was a severe reduction in the size of the islets of the Langerhans, with obvious cytoplasmic denegation and a reduction in the number of both α and βcell (short arrow). Note the increase in inflammatory cell infiltration (long arrow). In C and D: there was a considerably increase in the size of the islets of the Langer-hans (long arrow) with an increase in the number of both α (short arrow) and β-cell (Arrowhead).

4. Discussion

The current investigation's findings overwhelmingly point to aloin's potential as an anti-diabetic. When compared to diabetic controls, aloin-treated rats' in-vivo blood glucose and insulin levels were higher depicted in Fig. 1 and Fig. 2. (Abo-Youssef & Messiha 2013; Wexler, 2014). In conjunction, earlier writers stated that aloin had such an anti-diabetic effect in laboratory animals. (Patel & Patel, 2013).

There are many theories as to why aloin has an anti-diabetic effect.

The first theory is that Aloin's capacity to boost insulin sensitivity and encourage insulin production from the remaining β-cells may be the cause of these effects. (abatabaei, Ghaderi, Tapehebur, & Farbood, 2017).

The strong antioxidant properties of aloin extract provide the second justification. It has long been understood that aloin has antioxidant potential by reducing the production of free radicals and improving cellular thiol status. (Lee, Jeong, Chang Baek, Kwang Ku, & Sup Bae, 2019; Cichocka, Wietchy, Nabrdalik, & Gumprecht, 2016), Additionally, it is said to increase the activity of the enzyme glutathione-S-transferase. (Baruah, Bordoloi, & Baruah, 2016).

The quantitative determination of their metabolic end-product malondialdehyde (MDA), which is quantified in nmol/g utilizing the thio-barbituric acid test, is a straightforward and sensitive approach for estimating lipid peroxide concentration (TBA-test). Malondialdehyde is a very hazardous consequence of lipid oxida-
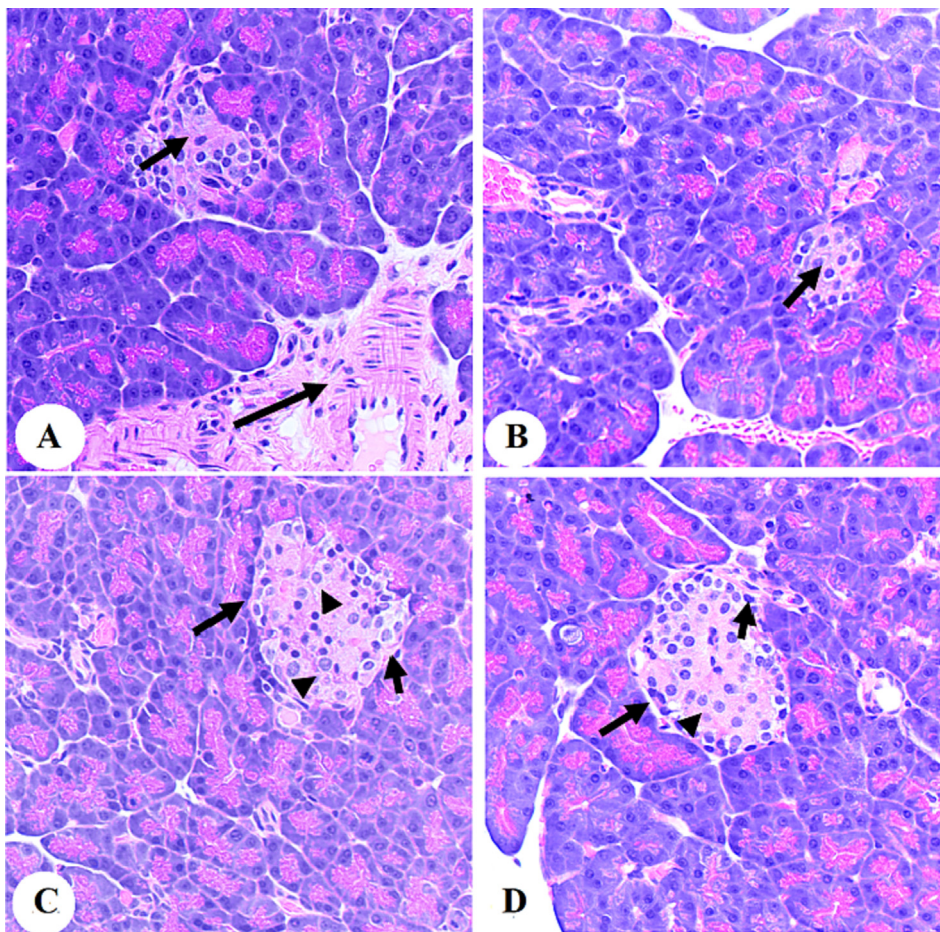
Fig. 8. Photomicrographs of the pancreases from the diabetic rats (A and B) and diabetic + Aloin (30 mg/kg)-treated rats. In C and D:

tion that is produced in part by free radicals. Its concentration is dramatically elevated in diabetes mellitus, according to numerous research. MDA combines with proteins and phospholipids in both irreversible and reversible ways, and it can have serious consequences (ManalKamal, MonaSalem, NaglaaKholousi, & KhadegaAshmawy, 2009). MDA levels in the kidney and liver of all groups were measured. When comparing the control group of diabetics to the ordinary control group, we found a substantial rise in malondialdehyde (MDA). These results are consistent with those achieved by (Gina, Aulani, & Mahdi, 2016).

Our observation significantly confirmed aloin's ability to act as an antioxidant, since it was discovered to reduce excessive levels of malondialdehyde in tissue samples and to strengthen kidney and liver tissue. Glutathione, Superoxide dismutase, and Catalase levels (Gina, Aulani, & Mahdi, 2016). Recent strategies emphasize the significance of oxidative stress in pancreatic β-cells damage (see Figs. 7 and 8).

(Bajaj & Khan, 2012; Sumi, et al., 2019; ManalKamal, MonaSalem, NaglaaKholousi, & KhadegaAshmawy, 2009). The aetiology of diabetes mellitus involves oxidative stress, however antioxidants including aloin could have a real antidiabetic impact due to their antioxidant activity (Aldayel, Grace, & Lila, 2020; Ariani, Gofur, Listyorini, & Susanto, 2015).

5. Conclusion

Antioxidant GSH, SOD, and CAT levels in the kidney and liver tissues of cured rats were significantly greater, whereas MDA levels were substantially lower after the program comparison with control rats consequently these data suggest that aloin may have promise as diabetes preventative and/or therapeutic agent, moreover, toxicological and clinical experiments are required to evaluate this plant extract and its possible applications in the medical and pharmaceutical fields.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jksus.2023.102589.

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