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Research Article

Evaluation of aqueous extracts of *Musa acuminata* (Banana) peels on the liver of streptozotocin induced diabetic Wistar rats

Sharon Kaundu[1,2], Kombe Mwitwa[1,2], Lukundo Mulambia Siame[1], Isabel Namfukwe Luambia[1], Ally Siabwacha[1] and Uthman Ademola Yusuf[1]

1. Department of Human Anatomy, School of Medicine and Health Sciences, Mulungushi University, Livingstone Campus, Zambia.
2. Department of Clinical sciences, School of Medicine, Eden University, Lusaka, Zambia.

Abstract

Banana peels (BP) have numerous therapeutic and nutritional benefits**.** This study aimed to investigate the effects of Banana peels aqueous extract on the liver of diabetic Wistar rats. 36 male Wistar rats (*Rattus norvegicus*) were grouped into six, each containing six Wistar rats. Control, Banana peels-only, diabetic + banana peels, diabetic + insulin, diabetic + metformin and diabetic-only. Diabetes was induced with streptozotocin (STZ) 70 mg/kg BW and sustained an increase in blood glucose levels after 72 hours. Treatment with banana peels aqueous extract 100mg/kg BW orally, insulin 4IU/Kg BW intraperitoneally and metformin 100mg/kg BW orally were given for four weeks. The diabetic+ banana peels attained normoglycemic at week 3, while the other treated groups attained normoglycemic at week 4. The treated groups (body weight and relative weight of the liver) are higher than the diabetic group ($p < 0.05$). Histological studies showed disrupted liver histoarchitecture in the diabetic only group while the treated groups were almost comparable to the control group. The glucose-6-phosphate dehydrogenase (G-6-PDH) activities in the liver were similar in the control and treated groups, while the diabetic-only group was the lowest when compared to the other groups. The lactate dehydrogenase (LDH) activities in the diabetic-only group were significantly higher compared to other groups. The reduced glutathione (GSH) and superoxide dismutase (SOD) in the liver showed similar activities in the three treated groups when compared to control. The study's findings revealed that an aqueous extract of banana peels reduced liver fat in diabetic Wistar rats.

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Corresponding Author
Dr. Uthman Ademola Yusuf
E-mail: uthmanademola@yahoo.com, uademola@gmail.com
Tel: +260967682170

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1. Introduction

Diabetes mellitus is characterized by hyperglycemia with disturbance of carbohydrates, fat, and protein metabolism, which is a result of defects in insulin secretion, insulin action, or both [1]. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs, including the liver [2]. In 2021, globally about 536.6 million people were estimated to be diabetic within the age range of 20—79 [3]. Herbal remedies are becoming an increasingly important component of contemporary, high-tech medicine since they have long been a highly regarded kind of medicine [4]. In this context, studies on the potential antidiabetic properties of a variety of plants have revealed the presence of antidiabetic

properties in plant compounds, including carotenoids, flavonoids, polyphenols, terpenoids, alkaloids, and glycosides [5]. Because *Musa acuminata* are readily available and grown almost in every country worldwide, they have traditionally been used to treat illnesses [6-7].

Banana peel's phenolics have been connected to several health advantages and have been shown to have strong antioxidant and are linked with various health benefits like anti-inflammatory, antidiarrheal, antihypertension, anti-obesity, antitumor, anticancer, and cytotoxic agents [8]. Despite banana fruit and its peels having a high-calorie content, they are said to have antidiabetic properties, which include gallo catechin, tannins, phlobatann, alkaloids, glycosides, anthocyanins and terpenoids [9]. This study aimed to investigate the effects of banana peel aqueous extract on the liver of diabetic Wistar rats.

2. Materials and methods

2.1 Study area

The study was conducted at Mulungushi University School of Medicine and Health Sciences, Department of Human Anatomy, Livingstone, Southern province, Zambia.

2.2 Plant materials

The bananas (Fig 1) were bought from a Shoprite in the Matero Lusaka province of Zambia. Before the start of the study, the peels were taken for identification at the Department of Biological Sciences at the University of Zambia School of Natural Sciences. The peels were washed three times in clean tap water and wiped, they were air-dried at room temperature and when they were completely dried, they were pounded and sieved to create a uniform powder of 300 g. The extraction method used was the Soxhlet extraction method [10].

Figure 1. Banana fruits and peel [10].

2.3 Animals and animal management

Thirty-six adult male Wistar rats (*Rattus norvegicus*) presumably in good health were used. The animals' body weight ranged from 160 to 200 g, and they were 8 to 10 weeks old. The animals were housed in the animal holdings of the Mulungushi University School of Medicine and Health Sciences Department of Anatomy, divided into six cages with six rats per cage. They were given access to clean water, regular feedings (ad libitum) and standard animal feeds (Wealth-gate pelletized feeds).

2.4 Induction of diabetes

The rats were weighed to get the baseline weight, and then they were fasted for about 8 to 10 h. After the overnight fast, their baseline glucose level was measured. The animals were returned to the regular feeding cycle after receiving an injection of streptozotocin (STZ) at a dose of 70 mg/kg body weight intraperitoneal [11]. After 72 hours of receiving (STZ) the blood glucose was checked and the ones that had measurements of more than 7 mmol/l or ≥ 250 mg/dl were considered diabetic.

2.5 Experimental design

Thirty-six adult male Wistar rats were randomly selected into six groups of six per cage.

Group A: normoglycemic
Group B: received banana peel extract only
Group C: diabetic + banana peel extract
Group D: diabetic + insulin
Group E: were diabetic + metformin
Group F: were diabetic only.

2.6 Banana peels mode of administration

The banana peels aqueous extracts were dissolved in physiological saline daily [12]. It was administered orally with the use of an Oro-gastric cannula to Group B and C rats at 100 mg/kg body weight daily for a maximum period of four weeks, Group D rats were given insulin at a dose of 4IU/kg body weight intraperitoneal and Group E rats were receiving 100 mg/kg of metformin orally daily for the maximum period of 4 weeks [13]. Group A and F rats received 2 mL physiological saline daily orally for four weeks.

2.7 Measurement of blood glucose

The blood glucose was evaluated in overnight fasted rats using the glucose oxidase method of one-touch

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ultra 2 glucometers (Accu-Chek Compact Plus). Blood was obtained from the median caudal vein of the tail by snipping the tip of the tail. The blood glucose level was monitored weekly for two weeks (acclimatization period) before the induction of diabetes and for four weeks of treatment [14].

2.8 Measurement of the body weight (g)

The body weight (g) of the rats was recorded weekly for two weeks (acclimatization period) before the induction of diabetes and every week during the experimental treatment for four weeks. Body weight was taken with a weighing scale (Venus VT 30 SL) [14].

2.9 The relative organ weight (%)

A sensitive weighing balance (SonyF3G brand) was used to record the relative organ weight of the liver of the rat as a percentage (%) based on the ratio of the weight of the liver to the terminal body weight of the same rat [14].

2.10 Histological and histochemical studies

At the end of the study, euthanasia was used to sacrifice the animals. The animals were placed on the dissection board in a supine position and they had their back and paws pinned. Using a scalpel coupled with a surgical blade, the animals' abdomens were dissected and the livers were carefully removed and weighed. To observe changes in cellular morphology, the tissues for histological studies were fixed in freshly prepared formal saline for 72 hours before being processed for routine histological examinations with Hematoxylin and Eosin (H&E) and some specialized staining techniques such as Periodic Acid-Schiff (PAS) stain for seeing the glycogen stores in the liver and Masson trichome stain for collagen fibers was exploited. The tissues for enzymes of glucose metabolism (G6PD and LDH) and oxidative stress markers (GSH and SOD) studies were immediately placed in 0.1 M of phosphate buffer solution (pH = 7.4) for homogenization.

2.11 Photomicrography

Photomicrography of histological sections of the liver was taken with an Olympus Microscope (New York, United States of America) coupled with a camera at the Department of Human Anatomy, Mulungushi University School of Medicine and Health Sciences, Livingstone Campus, Zambia.

2.12 Statistical analysis

Data was presented as mean ± standard error of the mean (mean ± SEM); analyzed using one-way ANOVA and all graphs were drawn using Excel. P values less than 0.05 ($p < 0.05$) were taken to be statistically significant.

3. Results and discussion

3.1 Average blood glucose levels every week (mmol/L)

Fig. 2 illustrates the weekly changes in average blood glucose levels across the different Wistar rat groups.

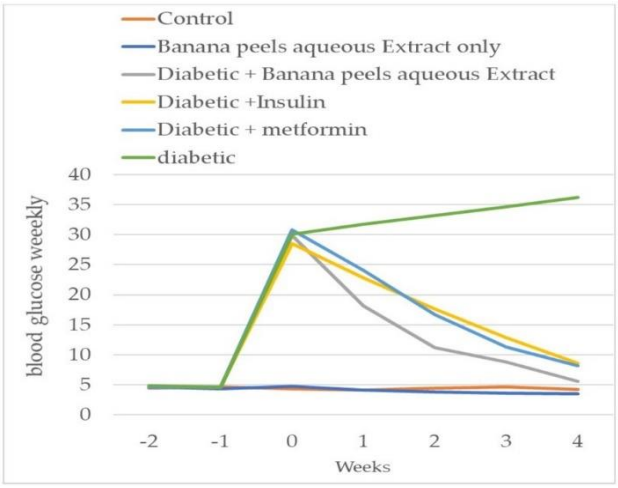

Figure 2. Blood glucose every week (mmol/L). (Data was analyzed using MEAN ± SEM and $p < 0.05$ was considered significant).

In the acclimatization weeks (-1 and -2), the average glucose levels of the rats across all the groups were similar with no significant differences ($p > 0.05$). From weeks 0 to 4, the control and banana peel extract-only groups showed normal glucose levels. The diabetic + banana peel extracts, diabetic+ insulin, and diabetic + metformin groups showed high glucose levels in week 0 and started to decline from week 1 through to week 4. The diabetic-only group showed an increase in glucose levels from week 0 to week 4, and the increase in the glucose levels was significant when compared to other groups ($p<0.05$). The blood glucose levels in the diabetic group Wistar rats revealed a marked hyperglycemic state compared to other groups, this can be due to the destruction or dysfunction of pancreatic beta cells, which leads to decreased insulin production [15]. Since insulin is essential for the uptake of glucose by cells, its deficiency results in elevated blood glucose levels, a

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condition known as hyperglycemia, this also leads to unregulated gluconeogenesis in the liver, further contributing to elevated blood glucose levels [15]. The Wistar rats treated with banana peel extract attained normoglycemic levels in week 3 while the diabetic + insulin and diabetic + metformin attained normoglycemic levels in week 4. The findings elucidated that the Wistar rats treated with banana peel extract had a faster decrease in blood glucose levels when compared to the diabetic Wistar rats treated with insulin and metformin. It might be due to the presence of phenolic compounds such as flavonoids, which have proven to possess strong antioxidant activity, which makes them act as a good antioxidant by reducing blood glucose [16] and It was also reported that banana peel extract has the potential antidiabetic effects due to its rich polyphenol and antioxidant content, which may enhance insulin sensitivity and glucose uptake [18]. This study is in line with Luambia *et al* [17] which indicates that the insulin-related signaling pathways that encourage the uptake of glucose by hepatocytes, which in turn results in enhanced glucose metabolism.

3.2 Average body weight every week (g)

Fig. 3 illustrates the weekly changes in average body weight among the different Wistar rat groups. In the acclimatization weeks (-1 and -2), the average body weights of the rats across all the groups were similar with no significant difference ($p > 0.05$).

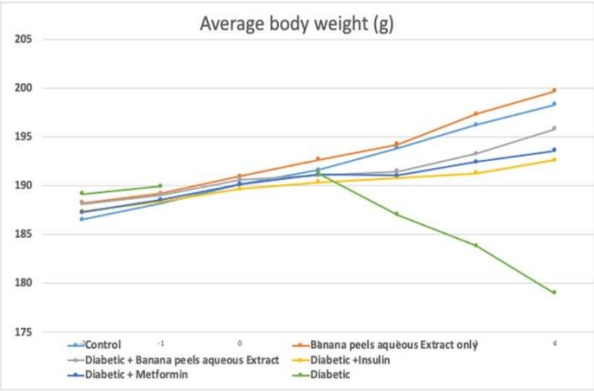

Figure 3. Average body weight every week (g). (Data was analyzed using MEAN ± SEM and $p < 0.05$ was considered significant).

A week beginning 0 and 1 post-induction, the average body weights of the Wistar rats across all groups were similar with no significant difference ($p > 0.05$). From week 2 to week 4, the control, banana peels only and diabetic+ banana peels groups showed a steady increase in the body weight though not significant ($p > 0.05$). The diabetic + insulin and the diabetic + metformin groups maintained their body weight when compared to the control, banana peel aqueous extracts only, and diabetic + banana peels groups which are not significant ($p > 0.05$). However, from week 2 to week 4, the body weights of the diabetic groups declined when compared to other groups and the decline was significant ($p < 0.05$). This study revealed that from weeks 2-4 of post diabetes mellitus induction, there was significant body weight loss in the diabetic group compared to the control and banana peels-only groups. This reduction indicates the adverse impact of uncontrolled diabetes on body weight, which is attributed to several factors, including impaired glucose utilization and increased catabolism of fat and muscle tissue [18]. The diabetic + banana peels showed higher weight at week 4 compared to diabetic + insulin and diabetic + metformin groups, this was due to their richness in polyphenols, which have antioxidant properties. Polyphenols, such as flavonoids and tannins, can help regulate glucose metabolism, reduce fat accumulation, and improve insulin sensitivity [19]. These findings agree with Mohapatra *et al* [20] which indicate that banana peels are rich in dietary fiber, which helps regulate blood sugar levels by slowing glucose absorption. High fiber intake can also promote satiety, potentially reducing overeating and helping with weight management and banana peels also contain antioxidants, which may improve insulin sensitivity and help combat oxidative stress, a common issue in diabetes. The weight of the rats in the diabetic + insulin and diabetic + metformin groups also stayed constant as the drugs suppressed gluconeogenesis, decreased glucose output, elevated glucose uptake and utilization in peripheral tissues, and enhanced the energy metabolism in organs such as muscle, fat, and liver by activating adenosine monophosphate activated protein kinase [21].

3.3 Relative liver weight (%)

Fig. 4 shows the relative weight of the livers from the different Wistar rats' groups. The control (6.35) and the banana peel only (6.23) groups show similar weights. The diabetic + banana peels (5.51), diabetic +

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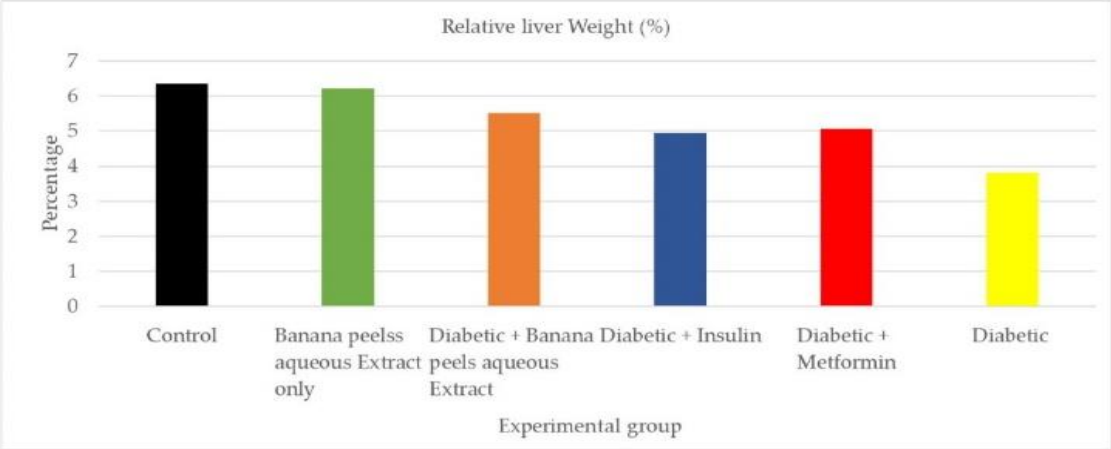

Figure 4. Relative liver weight (%) (Data was analyzed using MEAN ± SEM and $p < 0.05$ was considered significant).

insulin (4.95) and diabetic + metformin (5.07) groups showed a reduction in weights when compared to the control (6.35) and banana peels aqueous extracts (6.23) groups, but there was no significant difference ($p > 0.05$). However, the diabetic group (3.82) liver shows a significant reduction in relative weight when compared to all the other groups ($p < 0.05$). In this present study, the diabetic-only group showed a significant reduction in the relative liver weight compared to all other groups. The significant reduction in liver weight observed in the diabetic group is attributed to chronic hyperglycemia and altered metabolic processes associated with diabetes, like increased catabolism of liver glycogen, lipid metabolism disturbances, and protein degradation. which often results in liver dysfunction and changes in liver morphology [22]. This aligned with the findings of Younossi *et al.* [23] and Hanhineva K, *et al.* [24] which indicate that diabetes can lead to liver atrophy or reduced liver size due to various metabolic disturbances. The relative liver weight of the diabetic + banana peels aqueous extracts, diabetic + insulin, and diabetic + metformin groups are similar to the control group. The similarity of relative liver weight seen in the diabetic + banana peel extract group to that of the control group was due to antioxidants such as flavonoids and phenolic compounds, which can reduce oxidative stress in diabetic conditions by neutralizing free radicals. These antioxidants help protect liver cells from apoptosis and necrosis, thereby maintaining liver mass [21]. These findings align with Mohapatra *et al* [20]. This indicates that dietary fiber in banana peels may help prevent excessive fat accumulation in the liver, potentially stabilizing or even reducing liver weight over time in diabetics. The diabetic + insulin and diabetic + metformin groups have similarities to the control group. Conventional drugs such as insulin and metformin have been reported to help promote the uptake of glucose into the liver cells, where it is converted into glycogen for storage**.** This helps maintain liver mass by preventing glycogen depletion, which is often observed in untreated diabetes. Insulin also suppresses the breakdown of fats (lipolysis) in adipose tissue, reducing the influx of free fatty acids to the liver and metformin improves insulin sensitivity in peripheral tissues, including the liver. This leads to better glucose uptake and utilization, reducing the metabolic stress on the liver and supporting its normal function and weight [25].

3.4 Histological Findings

3.4.1 Hematoxylin and eosin stain of the liver

The liver in the normal control and banana peel only groups showed normal histoarchitecture with many healthy hepatocytes (Figs. 5 A and B). The diabetic + banana peel group was similar to the control (Fig. 5 C), diabetic + insulin and diabetic + metformin groups showed few disruptions in their histoarchitectures and there are both healthy and necrotic hepatocytes present (Figs. 5 D and E). The diabetic group showed that the histoarchitecture was disrupted with numerous necrotic hepatocytes (Fig. 5 F). The photomicrograph of the Wistar rats in the diabetic group displayed significant histoarchitectural

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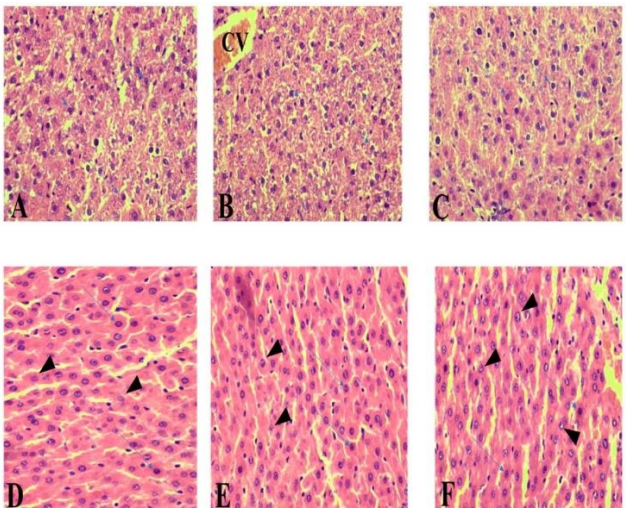

Figure 5. Photomicrograph showing the liver at day 28. H&E stain X400 (A-Normal control, B – Banana Peel only, C – Diabetic+ Banana Peel, D – Diabetic + insulin E- Diabetic + Metformin and F- Diabetic only. Arrow – hepatocyte, Arrow head – Necrotic hepatocyte, CV – Central vein).

disruption that was characterized by numerous necrotic hepatocytes, which can be due to impaired mitochondrial function in hepatocytes [25]. Mitochondrial dysfunction reduces ATP production and increases ROS production, contributing to cellular energy failure and necrotic cell death [26]. The normal control, banana peel-only groups and the diabetic + banana peel extract group exhibited normal histoarchitecture with abundant healthy hepatocytes. diabetes +banana peel extract exerted protective effects against liver damage, potentially through its antioxidant and anti-inflammatory properties found in flavonoids [27-28]. The diabetic + insulin and diabetic + metformin groups demonstrated some disruption in histoarchitecture, with a mixture of healthy and necrotic hepatocytes, this was due to incomplete glycemic control with insulin and metformin treatment. Persistent or intermittent hyperglycemia can continue to generate reactive oxygen species (ROS) and cause oxidative stress in hepatocytes, leading to cellular damage and necrosis. Also, persistent accumulation of fatty acids in hepatocytes can lead to ongoing lipotoxicity, causing mild but persistent hepatocyte necrosis [29]. This is in line with Paczkowska *et al*. [30], indicating that while insulin and metformin provide some level of therapeutic benefit, they may not completely prevent histological damage.

3.4.2 Periodic acid-schiff (PAS) stain of the liver

In Figs. 6: A and B (normal control and banana peel only groups) the PAS demonstrated normal a reaction. The diabetic+ banana peel group was similar to the control (Fig. 6 C), while diabetic + insulin and diabetic + metformin groups (Figs. 6: D and E) showed a bit of a positive reaction.

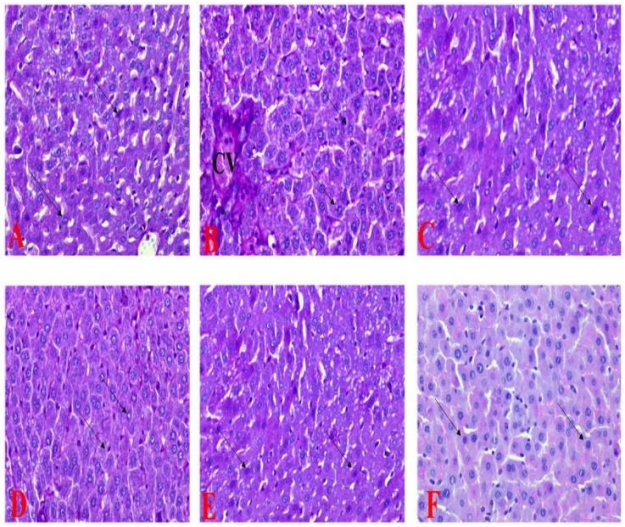

Figure 6. Photomicrograph showing the liver at day 28 (PAS stain X400. A-Normal Control, B – Banana Peel only, C – Diabetic+ Banana Peel, D - Diabetic + insulin E-Diabetic + Metformin and F- Diabetic only. Arrow - hepatocyte, Arrow head - Necrotic hepatocyte, CV Central vein).

Diabetic only group showed positive reaction (Fig. 6 F). The photomicrograph of the Wistar rats in the diabetic group showed a strong positive PAS reaction, which may be due to altered glycogen storage or increased glycoprotein deposition as a result of metabolic disturbances associated with diabetes [31]. PAS staining demonstrated normal glycoprotein content in the normal control, banana peel aqueous extracts only and diabetic + banana peels aqueous extract groups. This normal glycoprotein in diabetes + banana peel is due to its antioxidant and anti-inflammatory properties found in flavonoids and carotenoids, which help to reduce oxidative stress in the liver. This protects liver cells and preserves their normal function, leading to a healthy PAS staining response [32]. This agrees with Amini Khoozani *et al* [33], attributing to the fact that banana peels contain fibers that may help in reducing abnormal glycogen storage in the liver. In the diabetic + insulin and diabetic + metformin groups, the PAS reaction was

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slightly positive due to partial improvement or restoration of glycogen storage or glycoprotein levels, which may be a result of the blood glucose-lowering effects of these treatments but may not fully normalize liver metabolism. Metformin improves insulin sensitivity and enhances peripheral glucose uptake, which lowers blood glucose levels. As a result, more glucose is available for glycogen storage in the liver [34].

3.4.3 Masson trichome stain of the liver

In the normal control and banana peel only groups showed normal distribution of collagen (Figs. 7: A and B). The diabetic+ banana peel group was similar to the control (Fig. 7: C), diabetic + insulin and diabetic + metformin groups showed a few collagen depositions (Figs. 7: D and E). Diabetic group showed a lot of collagen deposition (Fig. 7: F). The photomicrograph in the diabetic group revealed a Masson Trichrome stain with substantial collagen deposition due to chronic inflammation, oxidative stress, and metabolic disturbances associated with diabetes. These factors lead to the activation of hepatic stellate cells, which produce excess collagen and other extracellular matrix components, resulting in fibrosis. Hyperglycemia-induced oxidative stress leads to the production of reactive oxygen species (ROS) in the liver. ROS can directly damage liver cells and further stimulate the activation of HSCs, promoting collagen synthesis and deposition [35]. The normal control, banana peel-only groups and the diabetic + banana peel aqueous extract groups exhibited similar collagen distribution. The diabetic + banana peel aqueous extract had normal collagen deposition because of the help of the antioxidant compounds like dopamine in the banana peel, which may help reduce oxidative stress in the liver and prevent or reduce collagen deposition, thus potentially protecting against liver fibrosis [36]. The diabetic + insulin and diabetic + metformin groups showed some collagen deposition but were less pronounced compared to the diabetic group. This is due to chronic inflammation in diabetes, even with insulin and metformin treatment, the inflammatory processes associated with diabetes might not be eliminated. Chronic low-grade inflammation can lead to liver fibrosis, where collagen deposition is a hallmark. Inflammation triggers the activation of hepatic stellate cells, which are responsible for producing extracellular matrix components, including collagen [36- 37].

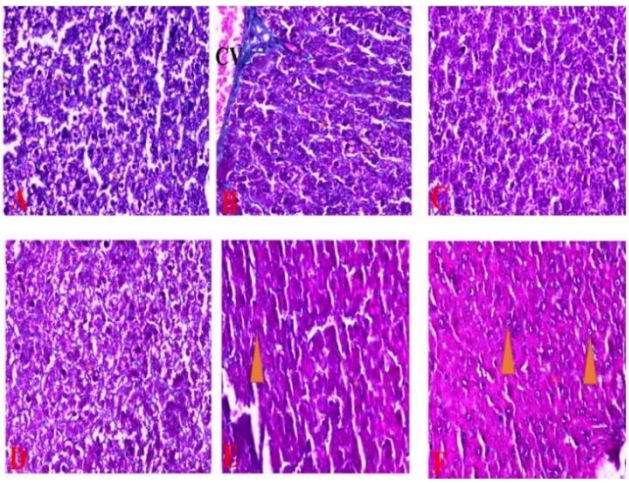

Figure 7. Photomicrograph showing the liver at day 28. (Masson stain X400. A- Normal control, B – Banana Peel only, C – Diabetic + Banana Peel, D –Diabetic+insulin, E- Diabetic+Metformin and F- Diabetic only. Arrow – hepatocyte, Arrow head-Necrotic hepatocyte, CV – Central vein).

3.5 Histochemical findings

3.5.1 Glucose 6 phosphate dehydrogenase (G6PDH) activity level in the liver (IU/L)

Fig. 8 shows the activities of the glucose-6-phosphate dehydrogenase enzyme (G6PDH) levels in the liver across different experimental groups of the Wistar rats. The banana peels aqueous extracts only (3210) group exhibited the highest G6PDH activity level, while the diabetic only (1856) group exhibited the lowest activity, when compared with the two groups that was a significant statistical difference ($p < 0.05$). In the diabetic + banana peels aqueous extracts (2947), diabetic + insulin (2735) and diabetic + metformin (2690) groups when compared to the control (3110) and the banana peels only (3210) groups there were no significant differences ($p > 0.05$). In this study, the histochemical analysis showed that the banana peel aqueous extract group exhibited the highest G6PDH activity level, while the diabetic-only group had the lowest. The diabetic-only group showed significantly lower G6PDH activity due to increased oxidative stress and impaired metabolic pathways [38-39]. This finding agrees with Sharma *et al* [36], indicating that diabetes often leads to reduced G6PDH activity, which contributes to elevated oxidative stress and cellular damage. The diabetic + banana peels aqueous

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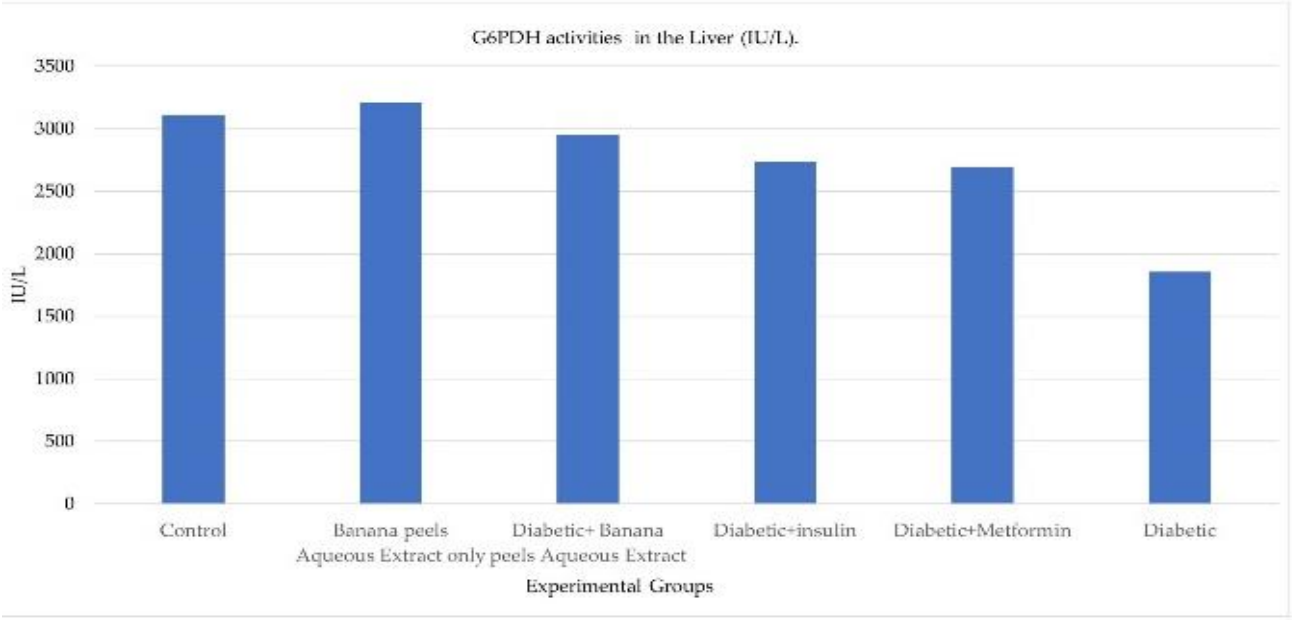

Figure 8. Glucose 6 phosphate dehydrogenase (G6PDH) activity level in the liver at the end of the fourth week. Data are expressed as Mean ± SEM ($P < 0.05$).

extract, diabetic + insulin and diabetic + metformin groups showed no significant differences in G6PDH activity compared to the control and banana peels aqueous extract-only groups. The increased G6PDH activity in the diabetic + banana peel aqueous extract group is due to its antioxidant properties, such as flavonoids, polyphenols, and vitamin C, which protect against oxidative stress that comes as a result of the normal metabolism process. Higher G6PDH activity helps protect cells by maintaining adequate levels of reduced glutathione and other antioxidants, preventing oxidative damage to DNA, proteins, and lipids. G6PDH plays a crucial role in the pentose phosphate pathway (PPP), which generates NADPH, an important molecule for maintaining the antioxidant glutathione in its reduced form. This finding is consistent with Alakbaree *et al*., [39], indicating that the increased G6PDH activity is a response to support enhanced antioxidant defenses, protecting hepatocytes from oxidative damage. Diabetic +insulin and diabetic + metformin groups the activities of G6PDH were similar to control due to their influence on glucose metabolism and insulin sensitivity but their effects on G6PDH activity are not as pronounced as those observed with the banana peel aqueous extract alone, these findings agree with Tongxin *et al.,* [40]. That insulin activates the pentose phosphate pathway (PPP), where G6PDH is the key enzyme. The increased flux through this pathway provides reducing power (in the form of NADPH). It helps in the synthesis of nucleotides and fatty acids, which may support cellular repair and energy balance in diabetic individuals. At the same time, metformin indirectly affects the activity of G6PDH by improving cellular insulin signaling and reducing oxidative stress. The exact impact on G6PDH is less direct compared to insulin but can still help in reducing overall oxidative damage, which is particularly beneficial in diabetes.

3.5.2 Lactate dehydrogenase (LDH) activity level in the liver (IU/L)

Fig. 9 shows the activities of lactate dehydrogenase in the liver of different experimental groups of Wistar rats. The diabetic-only (1634) group showed significantly higher activities compared to the other groups, it was significant ($p < 0.05$). The diabetic + banana peels aqueous extract (974), diabetic + insulin (1017) and diabetic + metformin (1083), when compared to the banana peels aqueous extract only (928) and control (906) which was not statistically significant ($p > 0.05$). LDH is an enzyme involved in the conversion of pyruvate to lactate during anaerobic glycolysis and is widely distributed in tissues throughout the body. In this current study, the activities of LDH were higher in the diabetic-only group compared to the other groups. This could be

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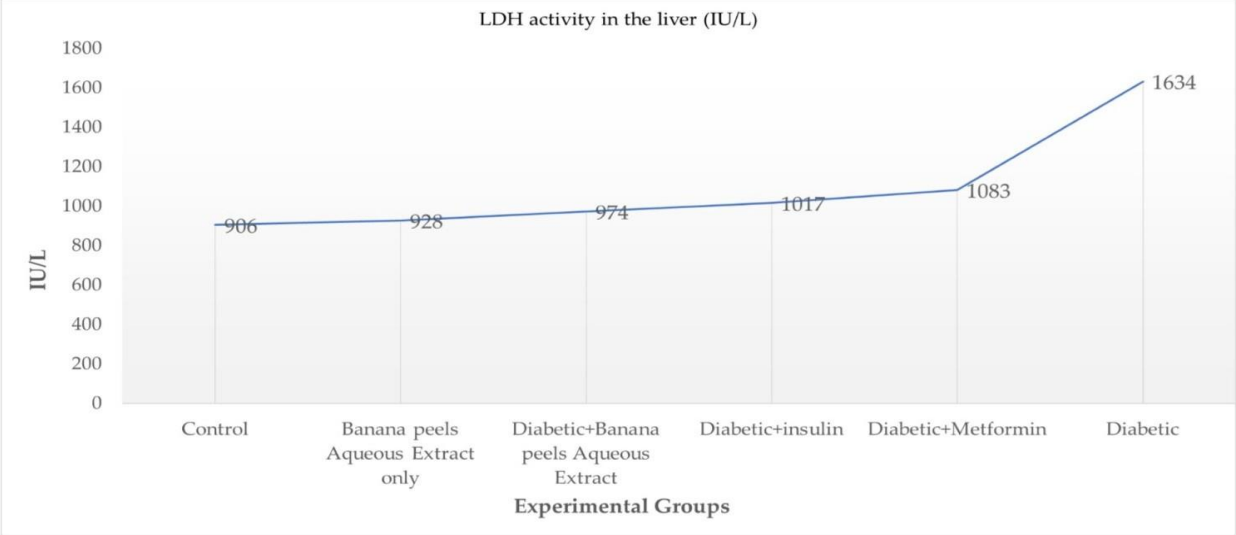

Figure 9. Lactate dehydrogenase (LDH) activity level in the liver (IU/L). Data are expressed as EAN ± SEM ($p < 0.05$).

due to impaired glucose utilization as a result of insulin resistance, which impairs the efficient utilization of glucose by cells [19]. The diabetic + banana peels aqueous extract, diabetic + insulin and diabetic + metformin groups showed no significant differences when compared to the banana peels aqueous extract only and control groups. The results in the diabetes + banana peel extract was due to the antioxidants such as flavonoids and polyphenols that help to reduce oxidative stress in the liver by mitigating oxidative damage. These antioxidants can prevent cellular injury and reduce the release of LDH from damaged cells [16]. These findings are consistent with Yusuf *et al* [13], indicating that the reduction of oxidative stress is due to the antioxidants in banana peels, which reduce liver cell damage, potentially leading to a decrease in LDH levels and Improved liver function, banana peels may support liver regeneration and reduce inflammation, which could stabilize or reduce elevated LDH levels in diabetics. The activities seen in diabetes + insulin were due to the ability of insulin to facilitate glucose uptake into cells, while in diabetes + metformin was due to the enhancement of insulin sensitivity and decrease in hepatic glucose production, thereby decreasing the production of lactate and the associated LDH activity [18].

3.5.3 Reduced glutathione (GSH) activity level in the liver (IU/L)

Fig. 10 depicts the activity of reduced glutathione (GSH) in the liver of various groups of Wistar rats. Notably, the diabetic (293) group exhibited the lowest GSH activity, while the banana peel aqueous extract (355) displayed the highest activity level. When the diabetic (293) group was compared with other groups, the difference was statistically significant ($p < 0.05$). Diabetic group + banana peels aqueous extract (323), diabetic + insulin (314), and diabetic + metformin (302) when compared to control (349) and banana peels aqueous extract (355) groups there were no significant statistical differences ($p < 0.05$). Reduced glutathione (GSH) plays an important role in maintaining cellular health and protecting against oxidative stress [24]. In this study, the diabetic group exhibited the lowest GSH activity compared to the control. This could be due to elevated reactive oxygen species (ROS) production, hyperglycemia and associated metabolic disturbances. Excessive ROS overwhelms the antioxidant defenses, leading to its GSH depletion [41]. The diabetic + banana peels aqueous extract, diabetic + insulin and diabetic + metformin groups exhibited similar activities when compared to the control and banana peel extract-only groups showed no significant differences in GSH activity. The activities seen in the diabetes + banana peel aqueous extract group resulted from its antioxidant properties found in flavonoids, which help to reduce oxidative stress in the liver by mitigating oxidative damage [42]. GSH is depleted in diabetics due to the heightened oxidative stress and replenishing GSH can reduce

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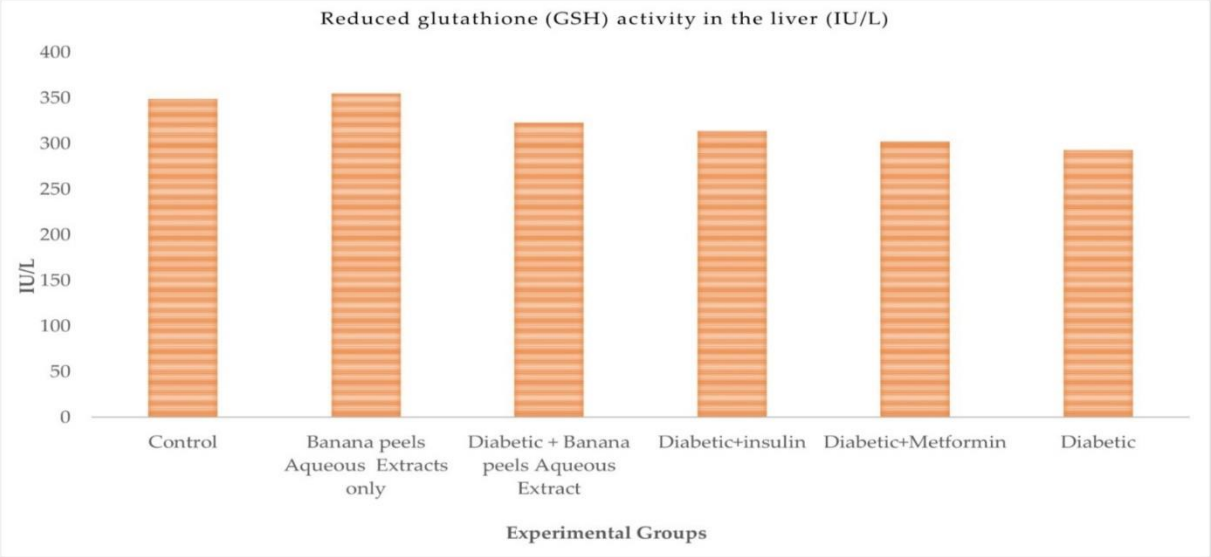

Figure 10. Reduced glutathione (GSH) activity level in the liver(IU/L). (Data are expressed as MEAN ± SEM ($p < 0.05$).

oxidative damage to cells and improve insulin sensitivity. This is consistent with Luambia et al. [18]. indicating that the bioactive compounds in banana peels may help reduce oxidative stress, potentially supporting the antioxidant defenses of the body, which includes GSH activity. The activities seen in diabetes + Insulin and diabetic + metformin were due to the regulation of blood glucose levels by facilitating the uptake of glucose into cells and promoting the uptake of cysteine. One of the key amino acids needed for the synthesis of GSH, thus restoring the levels of GSH, helping to maintain antioxidant defenses. Metformin helps reduce oxidative stress in diabetes, indirectly preserving GSH levels by lowering blood glucose [43].

3.5.4 Superoxide dismutase (SOD) activity level in the liver (IU/L)

Fig. 11 shows the activity level of superoxide dismutase (SOD) in various Wistar rats groups. Notably, the banana peels aqueous extract (318) group indicated higher SOD activity levels as compared to the diabetic group (196) with a significant statistical difference ($p < 0.05$). Further, the diabetic + banana peels aqueous extracts (268), diabetic + insulin (253) and diabetic + metformin (244) showed similar result when compared to the control (283) and banana peels aqueous extract (318) showed no significant difference ($p>0.05$). There was a close similar increase of the SOD activities in the control and banana peels only groups compared to the diabetic only group. The diabetic group had significantly lower SOD activity, due to oxidative stress, impaired synthesis, glycation, and degradation of the enzyme, as well as mitochondrial dysfunction and chronic inflammation [44]. The diabetic + banana peels aqueous extract, diabetic + insulin, and diabetic + metformin groups showed no significant differences in SOD activity when compared to the control and banana peels aqueous extract groups. The diabetes + banana peels were high due to being rich in antioxidants, such as flavonoids, polyphenols, and vitamins, which can reduce oxidative stress in diabetic conditions. These antioxidants can help preserve and even boost the activity of endogenous antioxidant enzymes like SOD and they may upregulate the expression of genes encoding antioxidant enzymes. This can lead to an increase in SOD activity, helping to neutralize superoxide radicals more effectively [45]. This finding is consistent with Balajee V *et al* [46], indicating that the antioxidant properties of banana peel aqueous extracts improve SOD activity and reduce oxidative damage. Both insulin and metformin work together to improve blood glucose control. By reducing hyperglycemia, these treatments lower the production of reactive oxygen species (ROS) that are typically elevated in diabetes. This reduction in ROS can decrease the oxidative burden on cells, allowing SOD levels to recover and increase [47].

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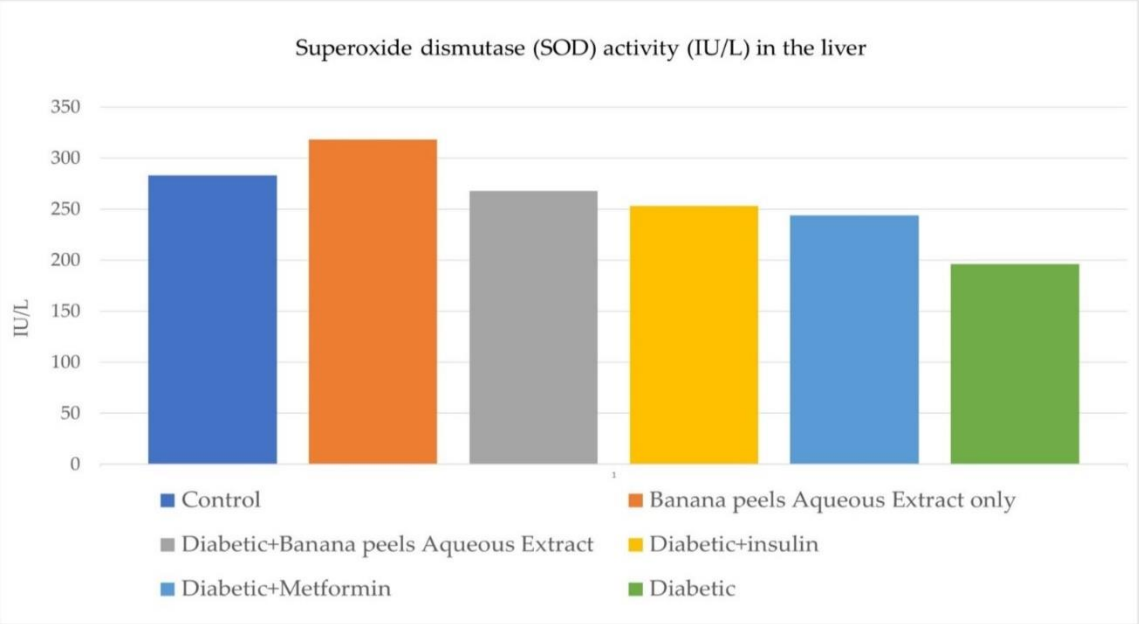

Figure 11. Superoxide dismutase (SOD) activity level in the liver (IU/L). (Data expressed as MEAN ± SEM $p < 0.05$).

4. Conclusions

Based on the findings, the banana peel aqueous extract was more effective than metformin and insulin at lowering blood glucose levels, maintaining histoarchitecture of the liver, reversing the effects of oxidative stress on the liver and averting the disturbance of glucose metabolism. To strengthen these findings, we recommend that the liver function tests, aldolase B, catalase and phosphoglycerate kinase should be carried out.

Ethical statement

Ethical clearance was sorted and received from the Ethics Committee on Animal Use and Care of the Mulungushi University School of Medicine and Health Sciences (MUSoMHS) with the approval number SMHS-MU4-2023-038.

Authors' contributions

Design and coordination, S.K.; Responsible for animal holding and cares, K.M.; Responsible for preparation of extract and data analysis, L.M.S.; Responsible for preparing tissue homogenate and enzyme assays, I.N.L.; Incharge of animal euthanasia and dissection, A.S.; Tissue processing and histological slides interpretation, U.A.Y.

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Availability of data and materials

All data will be made available on request according to the journal policy.

Conflicts of interest

All the authors declare no conflict of interest.

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