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Research Article

Protective Effects of the Polyphenolic-Rich Fraction of Cornsilk against Oxidative Stress in Streptozotocin-Induced Diabetic Rats

Nurraihana Hamzah[1], Sabreena Safuan[2], Wan Rosli Wan Ishak[1*]
[1]Nutrition Programme, School of Health Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia
[2]Biomedicine Programme, School of Health Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

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[*]**Corresponding Author:**
tel: +6097677649
email: wrosli@usm.my

ABSTRACT

The current study investigated the anti-hyperglycemic and antioxidative properties of the Phenolic-Rich Fraction of Cornsilk (PRF-CS) in Streptozotocin (STZ)-induced diabetic rats. Five groups of 30 male Sprague Dawley rats were employed in this study. A sample size of six rats each is placed in five groups: Normal-Control (NC), Diabetic-Control (DC), Diabetic-PRF-CS treated 100 mg/kg (DPRF100) and 200 mg/kg (DPRF200), and Diabetic-Metformin Treated (Dmet) groups. The PRF-CS was administered at 100 and 200 mg/kg doses for 28 consecutive days to the diabetic rats. Treatment with both doses of PRF-CS (DPRF100 and DPRF200) significantly decreased the blood glucose levels of the rats ($p<0.05$). Additionally, the PRF-treated rats demonstrated significantly decreased ($p<0.05$) lipid peroxidation (3.60±0.23 and 3.31±0.56 µmol/g, respectively). The hepatic antioxidant enzyme activities of Superoxide Dismutase (SOD) (169.35±4.75 and 175.30±3.69 U/mg, respectively), Catalase (CAT) (1,457.51±152.74 and 2,011.99±396.96 U/mg), and Glutathione Peroxidase (GSH-Px) (63.43±2.99 and 78.47±4.51 U/mg) were also elevated in contrast to the DC group. Furthermore, the PRF-CS administration improved the histological alterations in the liver tissues of the DPRF100 and DPRF200 rats. In conclusion, PRF-CS treatment exhibited protective effects in the diabetic rat model by decreasing oxidative stress and preserving liver integrity.

INTRODUCTION

Hyperglycemia is when blood sugar or glucose levels are higher than normal. The condition can be caused by several factors, including pancreatic cancer, cystic fibrosis, chronic pancreatitis, pheochromocytoma, acromegaly, and Cushing syndrome, but Diabetes Mellitus (DM) is the most common cause of hyperglycemia (Winter *et al.* 2021). Diabetes has a strong connection with oxidative stress as hyperglycemia stimulates the production of free radicals, leading to oxidative stress (Asmat *et al.* 2016). The imbalance between antioxidants and free radical production is known as oxidative stress. The phenomenon is caused by the inability of the body's defense system to counteract the increased radical generation, leading to high levels of free radicals and weaker antioxidant defense mechanisms (Golbidi *et al.* 2011).

Prolonged hyperglycemia induces liver disease because the escalated generation of Reactive Oxygen Species (ROS) during oxidative stress damages liver tissues (Ramu *et al.* 2016). Several studies suggested that diabetes patients suffer a higher standardized mortality rate from terminal liver disease than cardiovascular disease (Zhang *et al.* 2012). Therefore, effective antioxidant therapy is necessary in order to counteract the negative effects of ROS as antioxidants have been proven to be effective in scavenging ROS and reducing

diabetic complications (Bajaj & Khan 2012). Consuming plenty of vegetables, fruits, and other plants on a consistent basis, which are all high in different kinds of natural antioxidants, has been linked to lowering the risk of developing diabetes (Zhang *et al.* 2015). In addition, it has been found that agricultural by-products which some are commonly recognized as waste have substantial antioxidative activity. Hence, there is a growing interest in using agricultural by-products as food additives or supplements due to their specific nutritional and pharmacological properties (Faustino *et al.* 2019).

The agricultural by-products such as peels, pomace, seeds, stalks, and pulp were proved to contain various functional compounds, where some of these by-products contained the same amount or more bioactive compounds than the finished product (Silva *et al.* 2014). Bioactive compounds such as vitamins, carotenoids, phenolics, and other essential nutrients are abundant in agricultural by-products. Among these bioactive compounds, phenolics are recognized for their anti-diabetic and antioxidant activities (Lin *et al.* 2016). Recently, plant-derived phenolic compounds have gained considerable interest due to a wide range of pharmacological properties, including anti-microbial, hepatoprotective, antioxidant, anti-diabetes, and anti-inflammatory activities. In this context, the Phenolic-Rich Fraction (PRF) is beneficial due to its powerful free radicals scavenging and antioxidant actions (Dragan *et al.* 2015).

Cornsilk (CS) is a by-product or agricultural waste of maize farming since it is not edible. Each year, approximately 50,000 tonnes of CS are disposed of in Malaysia alone (Nurhanan *et al.* 2012). Cornsilk is a bundle of silky, long, and yellowish strands on top of a maize fruit that could grow to 10 to 20 cm as the fruit develops (Rahman & Wan Rosli 2014). Apart from functioning as a stigma for the female flower, CS is also rich in phenolic compounds, such as flavonoids (Liu *et al.* 2011). A few studies demonstrated that CS from baby corn (young maize) contained higher antioxidant activities than CS from mature maize fruits (Rahman & Wan Rosli 2014; Sarepoua *et al.* 2013). Hence, the PRF of CS from baby corn could potentially be the source of natural antioxidants to hinder oxidative stress. The current investigation examined the protective effects of PRF of CS from baby corn (PRF-CS) on lipid peroxidation and antioxidative actions in diabetic rats induced with Streptozotocin (STZ). The effects of PRF-CS treatment on the liver damage generated by STZ were also highlighted in this study. This present study will foster the use of agro-residue from corn as a new functional food ingredient that can assist our health-conscious population, which places an emphasis on well-being and wellness.

METHODS

Design, location, and time

The study was a randomized experimental study. The study was carried out in the Animal Research and Service Centre (ARASC), Health Campus, Universiti Sains Malaysia (USM), Kelantan, Malaysia. The study was carried out from January to April 2019 and the procedures related to the animals' section of the current study use were outlined and carried out based on the approval of the Animal Ethics Committee, USM (USM/IACUC/2017/(832)).

Materials and tools

The main material for this study was cornsilk from fresh baby corn (*Zea mays* L.). Fresh baby corn harvested 45–55 days post-planting was bought from a farm in Kampung Tendong, Pasir Mas, Kelantan, Malaysia. Two to three months old male Sprague Dawley rats weighing 250 to 300 g were employed for this study. The ARASC, Health Campus, USM supplied all 30 rats for this experiment. Chemicals and reagents used in this study were: 10% neutral buffered formalin, 1,1,3,3-tetraethoxypropane,T hiobarbituric acid (TBA), and Tris-Hydrochloric Acid (Tris-HCl) buffers were obtained from Sigma (Saint Louis, Missouri (MO), United States of America (USA)), acetic acid, ethyl acetate, hexane, and ethanol were from HmbG (Hamburg, Germany), and Albumin (BSA) were by Amresco (Solon, USA). The CAT, SOD, and GSH-Px assay kits were produced by Elabscience (Texas, USA). The phosphate buffer solution was obtained from the 1st Base (Singapore Science Park II, Singapore), n-butanol was from Fisher (Waltham, United Kingdom (UK)), metformin from Metcheck 850 (India), sodium citrate buffer solution from R & M (Essex, UK), STZ was bought from Merck (Darmstadt, Germany), and trichloroacetic acid (TCA) was obtained from Fisher (Waltham, UK).

Procedures

Preparation of the PRF-CS. The PRF from the CS of the baby corn was prepared based on the methodology reported in the study by Nurraihana *et al.* (2018).

Animal study. Subsequently, 30 diabetic rats were arbitrarily grouped into five clusters of six rats. Group I housed Non-Diabetic rats (NC), group II contained Diabetic Untreated rats (DC), groups III, IV, and V comprised diabetic rats treated with PRF-CS at 100 (DPRF100), PRF at 200 (DPRF200) and metformin at 150 (Dmet) mg/kg/day, respectively. The treatments were administered once a day for four weeks (day 28) through oral gavage.

Induction of experimental diabetes. On the first day of administration (Day 0), STZ was dissolved in 0.1 M sodium citrate buffer (pH 4.5) and administered intraperitoneally (i.p.) to the rats at a dose of 55 mg/kg. Food and water intake were closely monitored, and diabetes was validated by checking the fasting blood glucose (FBG) level using a glucose strip on the third and seventh-day post-STZ injection. Rats with FBG levels of ≥13 mmol/L were regarded as diabetic (Rahman 2016).

Determination of body weight and FBG. The body weight of each rat was recorded weekly for four weeks. The rats fasted overnight prior to the FBG test. Blood samples from the rats were collected from the veins at the tip of their tails by employing the Accu-Chek glucometer (Roche, Germany) on the dosing days and every subsequent week for FBG estimation.

Determination of lipid peroxidation and antioxidant enzymes activities. The rats were terminated after four weeks while under anesthesia. The livers of the rats were swiftly removed, weighed, and washed twice with a cold phosphate buffer solution. Subsequently, the liver tissues were split into two parts. One part was subjected to histopathological studies, while the other was used for enzymatic studies. The rat liver tissues were minced, weighed, and homogenized at a weight-to-volume ratio of 1:9 in Tris-HCl buffer (pH 7.4). The temperature was kept as low as possible by placing the homogenate on ice. The tissues homogenate was then centrifuged (1,041 g, 10 min) (Hettich, Germany) and the supernatant was collected and preserved at a -80^{O}C deep freezer (ilShin, South Korea) for the total protein and enzymatic tests, including SOD, CAT, GSH-Px, and lipid peroxidation activities. Protein concentrations were established according to the Bradford method. The amount of Malondialdehyde (MDA) that reacted with TBA in the homogenates was determined based on the technique reported by Angirekula *et al.* (2018). The SOD, CAT, and GSH-Px activities were assessed by employing a commercial assay kit from Elabscience (Texas, USA) following the guidelines provided by the manufacturer.

Histopathological study. The liver samples were fixed in 10 % formalin for two weeks before being processed into wax blocks and sectioned to a thickness of 4 µm. Tissue sections were placed on silane-coated slides and stained with hematoxylin and eosin. The stained tissues from every group were evaluated for histopathological alterations through the light microscope (Leica, Germany) at 10× and 40× magnifications, and an image analyzer captured the photomicrographs. Additionally, the tissues were assessed by a blind histologist. Any morphological alterations were observed, and the severities of each histopathological change were denoted as not (−), mildly (+), moderately (++), or severely (+++) damaged.

Data analysis

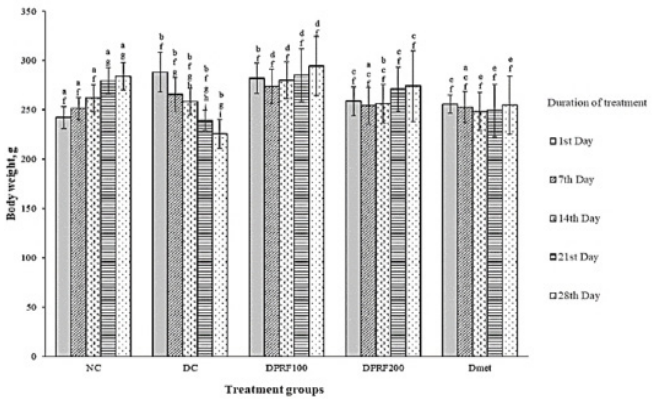
The results were evaluated for statistical significance using the IBM Statistical Package of Social Sciences (SPSS) Statistics Data Editor Version 24. The results were conveyed as means±standard error of the means (S.E.M). A p-value of less than 0.05 was deemed significant. The differences between the means were analyzed for significance using a one-way analysis of variance (ANOVA) test by employing the Post-hoc Tukey test.

RESULTS AND DISCUSSION

The effects of PRF-CS on the rat body weight

The changes in body weights observed in NC and DC groups are displayed in Figure 1. The STZ-induced rats exhibited a considerable weight loss ($p<0.05$) compared to Normal rats (NC group). The DC group lost weight throughout the study, while the DPRF100, DPRF200, and Dmet groups exhibited significant improvements in body weight compared to the DC group.

The DPRF100 and DPRF200 groups demonstrated a significant body weight elevation compared to the NC and DC groups from the second to the fourth week of treatment. The Dmet



The values indicated by the different letters are statistically significant ($p<0.05$). Letters a–e each represents pairwise comparisons among different groups based on time, while f–i are pairwise comparisons within each group based on time ; NC: Normal-Control; DC: Diabetic-Control; DPRF100: Diabetic-PRF-CS Treated (100 mg/kg); DPRF200: Diabetic-PRF-CS Treated 200 mg/kg; Dmet: Diabetic-Metformin Treated (150 mg/kg)

Figure 1. The body weights of phenolic-rich fraction of cornsilk- and metformin-treated streptozotocin-induced diabetic rats

group exhibited a significantly increased weight starting from the third week of treatment. After 28 days, the weight of the NC group significantly increased by 17.34% compared to the baseline. Conversely, the weight of the rats in the DC group was significantly reduced at 21.73% compared to the baseline. PRF-CS-treated groups showed no notable difference in the percentage of body weight increment as compared to the baseline.

A loss in body weight characterized the STZ-induced diabetic rat. The weight loss was due to the extreme breakdown of tissue proteins and fatty acids. Diabetic cells are unable to properly utilize glucose to produce energy due to inadequate insulin (Codella *et al.* 2017), causing the body to break down protein (proteolysis) and lipid (lipolysis) for energy (Syamsudin *et al.* 2010). Other than β-cells functions and insulin resistance defects, type II diabetes is also correlated to α-cells disabilities which are linked to relative glucagon hypersecretion (Lund *et al.* 2011). Glucagon resists the effects of insulin, elevating the glucose concentration in the bloodstream, inhibiting the storage of metabolic fuels, and activating gluconeogenesis (Coelho *et al.* 2013). Consequently, the condition might prevent fat and protein storage, inducing weight loss in diabetic rats (Martínez *et al.* 2014).

Studies indicated that untreated STZ-induced diabetic rats exhibited a markedly reduced body weight (Rahman 2016), which is consistent with the findings of the present study. Nevertheless, the PRF-CS treatments increased the body weight of diabetic rats. The increment might be related to increased muscle glucose uptake, preventing tissue loss. The treatments enable body tissues to access glucose to obtain energy and build necessary tissue materials for growth.

The effects of PRF-CS on the FBG levels

The effects of PRF-CS treatment on the FBG level of STZ-induced diabetic rats are displayed in Table 1. The diabetic rats demonstrated a significant increase in FBG levels than normal rats.

After four weeks, the diabetic rats administered with 100 and 200 mg/kg of PRF-CS experienced significantly diminished blood glucose levels, which were reduced by 67.45% and 66.85%, respectively, compared with the DC rats. The Dmet group also demonstrated a significant decrease of 66.76 % in blood glucose level compared with the DC group.

The diabetic rats demonstrated a high level of FBG, which is a crucial indicator of the disease. After the STZ injection, FBG levels in the DC group were notably elevated in contrast to those in the NC group, indicating that a DM model was successfully induced via STZ injection. Furthermore, the administration of PRF-CS significantly lowered the FBG level in diabetic rats, which is consistent with the studies by Ghada *et al.* (2013) that demonstrated that FBG levels decreased significantly with a crude extract of CS from mature corn fruits.

Table 1. The effects of Phenolic-Rich Fraction of Cornsilk (PHRF-CS) on Fasting Blood Glucose (FBG) levels

Groups	Blood glucose level				
	0 day	7 day	14 day	21 day	28 day
NC	5.5±0.19[a]	5.4±0.14[a]	5.53±0.35[a]	5.5±0.1[a]	5.17±0.45[a]
DC	22.38±4.13[b]	20.3±2.21[b]	27.9±3.18[b]	31.85±1.45[b]	33.33±1.08[b]
DPRF100	19.85±2.13[b]	10.23±3.36[a,b]	14.73±6.26[a,b]	11.53±3.55[a,c]	10.85±3.31[a,c]
DPRF200	17.25±2.33[b]	10.7±3.05[a,b]	15.95±5.12[a,b]	12.23±4.41[a,c]	11.05±4.53[a,c]
Dmet	18.13±3.73[b]	10.8±1.79[a,b]	13.45±5.52[a,b]	12.5±3.26[a,c]	11.08±3.79[a,c]

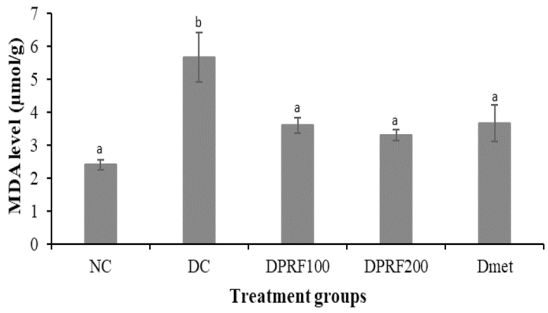
The values indicated by the different letters are statistically significant ($p<0.05$) by one-way ANOVA; NC: Normal-Control; DC: Diabetic-Control; DPRF100: Diabetic-PRF-CS treated (100 mg/kg); DPRF200: Diabetic-PRF-CS treated 200 mg/kg; Dmet: Diabetic-Metformin treated (150 mg/kg)

The phytochemical evaluation of the PRF-CS demonstrated the presence of phenolic compounds (Nurraihana *et al.* 2018). Phenolic compounds display various biological characteristics, where some are potent antioxidants, and several display anti-diabetic properties (Sarian *et al.* 2017). Jassim *et al.* (2016) reported that phenolic substances from Solanum melongena peel demonstrated remarkable hypoglycemic and hypolipidemic properties in rats that are alloxan-induced diabetics. Therefore, phenolics, especially flavonoids in PRF-CS, might induce hypoglycemic actions. Nonetheless, the potential of phenolic compounds as a Reactive Oxygen Species (ROS) scavenger could excise the toxic effects of STZ on β-cells and lower the blood glucose level in rats treated with PRF-CS (El Hawary *et al.* 2016).

Effect of PRF-CS on oxidative stress markers

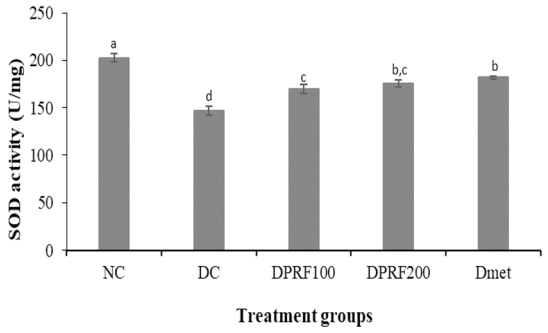
The MDA level in the DC group was significantly elevated compared to the NC group (Figure 2). Nonetheless, the DPRF100, DPRF200, and Dmet administrations exhibited significantly reduced MDA levels than the DC group.

Figure 3 displays the SOD activities in the liver of negative control, treated, and untreated diabetic rats. The SOD activity of the DC rats was significantly diminished than in the NC rats. Furthermore, the rats treated with PRF-CS and metformin demonstrated significantly enhanced



The data are expressed as mean±S.E.M. (n=6). The values indicated by the different letters are statistically significant ($p<0.05$); NC: Normal-Control; DC: Diabetic-Control; DPRF100: Diabetic-PRF-CS Treated (100 mg/kg); DPRF200: Diabetic-PRF-CS Treated 200 mg/kg; Dmet: Diabetic-Metformin Treated (150 mg/kg)

Figure 2. The malondialdehyde levels (umol/g) of each group



The data are expressed as mean±S.E.M. (n=6). The values indicated by the different letters are statistically significant ($p<0.05$); NC: Normal-Control; DC: Diabetic-Control; DPRF100: Diabetic-PRF-CS Treated (100 mg/kg); DPRF200: Diabetic-PRF-CS Treated 200 mg/kg; Dmet: Diabetic-Metformin Treated (150 mg/kg)

Figure 3. The superoxide dismutase activity levels (U/mg) of each group

SOD activities when compared to the DC rats. Nevertheless, the SOD level of activities of the DPRF100, DPRF200, and Dmet groups was significantly less in contrast to the NC group.

Based on Figure 4, significantly reduced CAT activity levels in the DC, DPRF200, DPRF100, and Dmet groups were observed when juxtaposed with the NC group. But, there was no significant elevation of the activity levels in the DPRF100, DPRF200, and Dmet groups compared to the DC group.

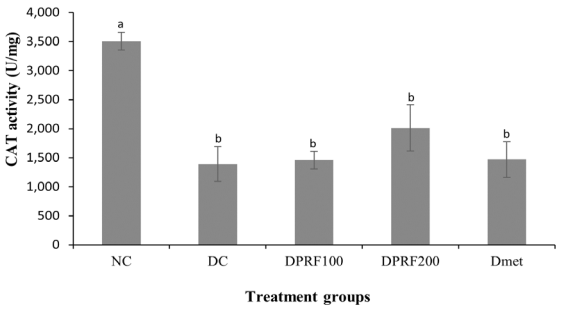
Figure 5 demonstrates the GSH-Px activities of the rats in each group. Compared to the GSH-Px activity level of the NC group, the DC and the DPRF100 groups exhibited significantly reduced activity levels. Nonetheless, the GSH-Px activities of the rats treated with DPRF200 and Dmet were significantly diminished compared to the DC group. Moreover, the diabetic group administered with 200 mg/kg of PRF-CS had a considerable elevation in GSH-Px activity in contrast to those administered with the lower dose.

The liver is the main organ responsible for the free radical reactions and oxidation and detoxification processes. In various diseases, the liver displays increased levels of oxidative stress indicators at the beginning stages (Sanchez-Valle *et al.* 2012). Since the liver was susceptible to ROS-imparted injuries, the present study investigated the effects of PRF-CS on antioxidant enzyme activities and lipid peroxidation in the liver of diabetic rats to determine if the substance could alleviate oxidative stress.

In DM, hyperglycemia induces excessive ROS production. The ROS reacts with unsaturated lipids present in cell membranes, resulting in lipid peroxidation. In lipid peroxidation, increased MDA level damages cell membranes from the inactivation of numerous cellular proteins and receptors (Birben *et al.* 2012). Lipid peroxidation is commonly measured in terms of MDA. A significant increment in MDA concentration in the STZ-induced diabetic rats reflected elevated lipid peroxidation, which led to tissue injury. The observation also suggested that the endogenous antioxidant defense mechanisms were incapable of preventing free radical overproduction. The PRF-CS treatment impeded hepatic lipid peroxidation in diabetic rats, as demonstrated by the reduction of the MDA concentration to the normal level. The findings suggested that the PRF-CS could protect tissues from lipid oxidation-induced damage.

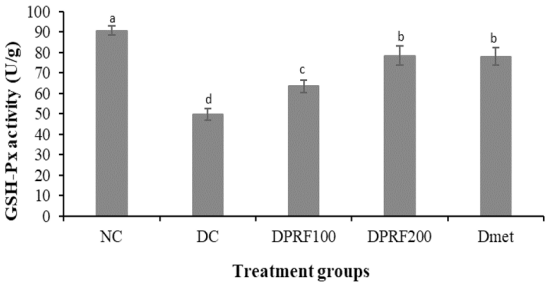
DM is linked with escalated oxidative stress (Asmat *et al.* 2016). The increment resulted from an impaired body antioxidant system. Jayaraman *et al.* (2018) indicated that diabetic rats had lower levels of antioxidant enzymes. Similar findings were obtained in the DC group in the present study.

The SOD is the frontline enzyme that converted superoxide radicals into less reactive substances, such as hydrogen peroxide (H_2O_2).



The data are expressed as mean±S.E.M. (n=6). The values indicated by the different letters are statistically significant ($p<0.05$); NC: Normal-Control; DC: Diabetic-Control; DPRF100: Diabetic-PRF-CS Treated (100 mg/kg); DPRF200: Diabetic-PRF-CS Treated 200 mg/kg; Dmet: Diabetic-Metformin Treated (150 mg/kg)

Figure 4. The catalase activity levels (U/mg) of each group



The data are expressed as mean±S.E.M. (n=6). The values indicated by the different letters are statistically significant ($p<0.05$); NC: Normal-Control; DC: Diabetic-Control; DPRF100: Diabetic-PRF-CS Treated (100 mg/kg); DPRF200: Diabetic-PRF-CS Treated 200 mg/kg; Dmet: Diabetic-Metformin Treated (150 mg/kg)

Figure 5. The Glutathione Peroxidase activity levels (U/g) of each group

Enzymes called CAT and GSH-Px, which are part of the antioxidant system's second line of defense, are responsible for the transformation of H_2O_2 into molecules of oxygen and water (Alatawi *et al.* 2018). Therefore, a decrease in SOD activity may result in an accumulation of free radicals, which may in turn induce oxidative stress, tissue damage, and metabolic abnormalities. GSH-Px is the primary enzyme that protects cells from the damage that ROS can cause when oxidative stress is low (Tiwari *et al.* 2013). The PRF-CS-treated diabetic groups in the current investigation demonstrated marked increased hepatic SOD and GSH-Px actions when juxtaposed to the DC groups. Parallel effects were observed in metformin-treated diabetic rats.

The improved antioxidant enzyme activities demonstrated by the PRF-CS indicated that this fraction might prevent enzymes from glycating or decrease reactive oxygen free radicals and enhance the antioxidant enzyme's activities. The observation demonstrated the free radicals scavenging activity abilities of the PRF-CS, exerting an advantageous action through protection against pathogenic changes generated by superoxide radicals and H2O2 radicals (Andrestian *et al.* 2019). The PRF-CS activities observed might be due to the phenolic compounds. Therefore, the PRF-CS was a significantly successful treatment in STZ-induced diabetic rats, potentially by enhancing the endogenous antioxidative actions.

The effects of PRF-CS on histological damage of the rat livers

The H & E stain was employed to analyze the pathological observations of the liver, which were assessed through a light microscope. The histopathological liver alterations in the experimental groups were scored against the control, as shown in Table 2.

Resultantly, the liver sections from the NC group exhibited normal hepatocytes with well-spaced sinusoids and the central vein (Figure 6A). The liver morphology of the rats in the DC group demonstrated moderate histopathological changes, denoted by the degeneration of hepatocytes. The degenerative modifications included the formation of fatty vacuoles, revealing fatty alterations (Figure 6B).

Diabetic rats from the DPRF100 group exhibited no significant variations, and no improvements were detected in contrast to the DC group (Figure 6C). Nonetheless, the rates from DPRF200 and Dmet groups exhibited mild histopathological improvements (Figure 6D and Figure 6E, respectively). The hepatocytes and blood sinusoidal space in both groups' livers gradually returned to near-normal morphology.

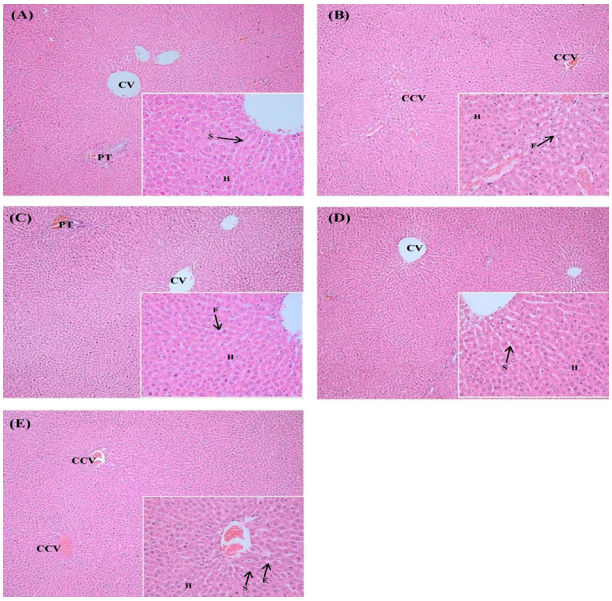
The initiation of oxidative stress caused by the exhaustion of the antioxidant scavenger system was among the diabetogenic characteristic of STZ, mediated via the destruction of pancreatic β-cell. Enhanced oxidative stress indicated an elevated generation of free radicals. The phenomenon could cause tissue damage and histopathological alterations in the organs. Since the liver plays a prominent and crucial role in controlling carbohydrate metabolism, several structural and functional abnormalities that influence glycogen and lipid metabolism can occur in the liver due to diabetes. Degeneration of hepatocytes, dilated sinusoids, and steatosis were the histological findings that were identified in the STZ-induced diabetes study (Al-Ani *et al.* 2017). Similar findings were obtained in the DC group in this investigation.

This study demonstrated that both the PRF-CS (200 mg/kg) and metformin treatments improved the morphological changes in the liver, where a marked restoration of hepatocytes and blood sinusoids was observed. The results

Table 2. The grading of the morphological changes in the liver of the rats

Histopathological changes	Groups				
	NC	DC	DPRF100	DPRF200	Dmet
Sinusoidal space	-	++	++	+	+
The density of fatty vacuoles formed	-	++	++	+	+
The presence of degeneration changes in hepatocytes	-	++	++	+	+

(–): Represent none; (+): Mild; (++): Moderate; (+++): Severe damage
NC: Normal-Control; DC: Diabetic-Control; DPRF100: Diabetic-PRF-CS Treated (100 mg/kg); DPRF200: Diabetic-PRF-CS Treated 200 mg/kg; Dmet: Diabetic-Metformin Treated (150 mg/kg)



(A): Normal-Control (NC); (B): Diabetic-Control (DC); (C): Diabetic-PRF-CS Treated (100 mg/kg) (DPRF100); (D): Diabetic-PRF-CS treated 200 mg/kg (DPRF200); (E): Diabetic-Metformin Treated (150 mg/kg) (Dmet); All figures are in 10× magnification with 40× inserts; CV: Represents the central vein; CCV: Congestion of the Central Vein; PT: The Portal Triad; S: The Sinusoid; H: The Hepatocyte; F: The Fatty Vacuole

Figure 6. The hematoxylin and eosin-stained liver images

indicated that the treatments had protective effects against the hepatic alterations correlated with diabetes. The hepatoprotective effects of the PRF-CS were associated with its antioxidant effects as it was rich in phenolic compounds, particularly flavonoids. Flavonoids, an example of phytoconstituents, are known for their hepatoprotective actions (Kumar & Pandey 2013).

CONCLUSION

Anti-hyperglycemic and anti-hyperlipidemic activities were demonstrated by PRF extracted from CS. Additionally, the PRF-CS exhibited possible antioxidant properties against free radical damage. The favorable effects of PRF-CS in diminishing lipid peroxidation and oxidative stress were observed from the reduced MDA quantities and improved antioxidant enzyme activities, such as SOD, CAT, and GSH-Px. Furthermore, biochemical, and histopathological analyses suggested that PRF-CS impeded liver damage due to antioxidant activity. The current investigation proposed that DM-induced oxidative stress might be impeded or terminated by consuming the PRF-CS.

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DECLARATION OF CONFLICT OF INTERESTS

The authors have no conflict of interest.

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