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Reno-pancreas protective effects of *Spirulina platensis* in alloxan induced diabetic rats

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Abstract: A large variety of herbal elements are employed in the treatment of diabetes for their better efficacy and safety compare to synthetic drugs. In this experiment Spirulina platensis was used to evaluate the antidiabetic, kidney & pancreas injury protective potential in alloxan induced diabetic rats. Male Long Evans rats having six weeks of age were used for the experiment. Diabetes was induced by intraperitoneal injection of alloxan @ 150 mg/kg and experiment was carried out for a period of six weeks. The study was conducted by dividing the animal into three groups (n=7 rats in each group) indicated as with Group-A (healthy control); Group-B (diabetic control); Group-C (Diabetic rats treated with Spirulina platensis @ 400 mg/kg). Spirulina platensis reduced blood glucose significantly (P<0.01) and improved the body weight losses significantly (P<0.05) compared to diabetic rats after six weeks treatment. The histopathological alteration was observed in the kidney of diabetic rats which was characterized by glomerular hypertrophy, tubular necrosis and interstitial fibrosis. Marked improvements in the histopathological change were noticed in the kidneys of diabetic rats treated with Spirulina platensis. Pancreatic injury was produced by alloxan induction in rats characterized by destruction of the pancreatic β cells mostly in the central portion of the islets of langerhans and lymphocytic infiltrations, atrophy, and interstitial fibrosis, which were suppressed by Spirulina platensis. In addition, alloxan induced diabetic rats showed increased plasma lipid peroxidase level which was ameliorated by *Spirulina platensis* treatment. Along with previous report the anticipated results would concluded that *Spirulina platensis* having antioxidant compounds could protect renal tissues damage, stimulate regeneration and reactivation of pancreatic β- cells in alloxan induced diabetic rats.

Keywords: *Spirulina platensis*, diabetes, kidney, pancreas, oxidative stress, rat.

INTRODUCTION

The word diabetes has been evolved from Greek Word (‘dia’ means through; ‘betes’ means pass). More specifically it has been defined as the excretion of an excessive amount of sugar rich urine having peculiar smell, in association with great thirst, dryness of skin, debility, and general emaciation (Dijkstra *et al*., 2003). The World Health Organization (WHO) defined diabetes mellitus as “a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances in carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both”.

Diabetes is recognized as the world’s fastest expanding chronic condition. The number of people with type-2 diabetes is growing in each country. In 2013, the International Diabetes Federation’s (IDF) Diabetes Atlas estimated that- 415 million of the world population were suffering from diabetes which means that one in 11 adults are suffering from diabetes. One in two (46.5%) adults with diabetes is undiagnosed and one in seven births is affected by gestational diabetes. Every six seconds a person dies from diabetes (5.0 million deaths) throughout the world (IDF, 2013). There are currently more than 3.2 million people with diabetes in Bangladesh. This number is expected to rise by more than 11 million by the year 2030.

There are three main types of diabetes mellitus (DM). Type-1 DM results from the body's failure to produce insulin, and presently requires the person to inject insulin or wear an insulin pump. This form was previously referred to as “Insulin Dependent Diabetes Mellitus” (IDDM) or “Juvenile Diabetes”. Type-2 DM results from insulin resistance, a condition in which cells fail to use insulin properly. This form was previously referred to as Non-Insulin-Dependent Diabetes Mellitus (NIDDM) or

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"Adult-Onset Diabetes". The third main form, gestational diabetes occurs when pregnant women without a previous diagnosis of diabetes develop a high blood glucose level. It may precede development of type-2 DM (Sharma *et al*., 2013).

Management of Diabetes without any side effects is still a challenge for the medical system. Traditional medicinal plants are used throughout the world for the treatment of Diabetes mellitus, because the plants are considered to be less toxic, low cost and free from side effects than the synthetic medicines (Latha *et al*., 2014). In recent years, herbal remedies for the unsolved medical problems have been gaining importance in the research field. Herbal drugs are prescribed widely because of their effectiveness, less side effects and relatively low cost (Devaki *et al*., 2011).

Spirulina is a filamentous cyanobacteria belonging to algae of the class Cyanophyta that grows vigorously in strong sunshine under high temperatures and highly alkaline conditions characterized by high protein content (60-70%). It has unique blend of nutrients that no single source can provides. It contains a wide spectrum of nutrients that include B-complex vitamins, minerals, trace elements, good quality proteins, gamma-linolenic acid and the super antioxidants, beta carotene, vitamin E, phycocyanine and chlorophyll (Layam and Reddy, 2006). In 1967, Spirulina was established as a "Wonderful future food source" in the International Association of Applied Microbiology. The United Nations world food conference declared Spirulina as "the best for tomorrow" (Anitha *et al*., 2010). Along with its high nutritional value, S. platensis has also showed immunomodulatory (Hayashi *et al*., 1994), cardio protective (Khan *et al*., 2005), reno protective (Gaurav *et al*., 2010), antioxidant (Makhlouf and Makhlouf, 2012), protective against heavy metals (Abdel-Daim *et al*., 2013), anti-diabetic (El–Baz *et al*., 2013), hepato protective (Yoshinari *et al*., 2014; Sharoud, 2015), neuroprotective (Alam and Hendawi, 2015) and antiviral (Chen *et al*., 2016) effects in different animal models. In addition, 400 mg/kg per day S. platensis was shown to produce significant analgesia (Elgendy and Diam, 2014) and anti-inflammatory effects (Joventino *et al*., 2012) after ≥3 weeks' oral administration in rats. Furthermore, no adverse effect was seen even after 5000 mg/kg per day oral S. platensis for 14 days in rats (Chen *et al*., 2016). However, to the best of our knowledge, no study has yet been reported on the effect of S. platensis available in Bangladesh on kidney protective and regeneration or reactivation of pancreatic β- cells in alloxan induced diabetic rat model.

Based on above background and discussion, the present study was designed to evaluate the beneficial effects of oral administration of *Spirulina platensis* (400 mg per kg body weight per day for 21 consecutive days in rats) on kidney and pancreas of alloxan induced diabetic rat model.

MATERIALS AND METHODS

The study was conducted in the Department of Pharmacology, Bangladesh Agricultural University (BAU), Mymensingh, the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. The study protocol was approved by the Institutional Review Board of BSMMU. All experimental procedures were performed according to the guidelines for the care and use of animals as established by Animal Welfare and Experimentation Ethics Committee, Bangladesh Agricultural University, Mymensingh.

Collection of rats

Total 21 (twenty-one) male Long evans rats having 150 to 160 gm body weight were obtained from the animal house of the Bangladesh University of health Science (BUHS), Dhaka. All the rats were kept in the Laboratory of the Department of Physiology, BSMMU, proper ventilation was maintained to the collection box and slices of cucumber was supplied to protect the animals from dehydration. Addition care was taken to the rats to prevent from heat shock or transportation stress. Immediately after reaching the destination the rats were shifted to wire cases and provided Vit-C, glucose syrup to help them to overcome the transportation stress.

Collection of feed

Rat pellet were collected from China Gift Corner, Chawkbazar, Dhaka from a reputed rat feed exporter. Pellet and water were provided *ad-libitum* during the experimental period.

Acclimatization of rats

All rats were acclimatized to new environmental conditions for two weeks, prior to initiation of experiment. The rats were randomly divided into three equal groups (n=7). All groups were housed in compartmentalized rectangular metallic cages (9× 11 ×7 cubic inches) wrapped with wire mesh. Rats were kept in separate cages according to group. Each cage was labeled. The cages were kept in well ventilated room at 28 ± 2^0C and a relative humidity of 70-80%. They were housed under standard laboratory conditions of 12 hours light and 12 hours dark cycle.

Experimental animal grouping

Twenty-one (21) adult male Long Evans rats of six weeks of age were used in the experiment. For the study rats were divided into three groups, each group containing seven (n=7) rats.

Group A*:* The rats were administered with saline water orally and fed normal diet and given water *ad-libitum*. This group was served as Healthy control group.

***Group B**:* After acclimatization alloxan monohydrate injection was given at a dose rate of 150 mg/kg in intraperitoneal route to each rat to induce diabetes. The rats were fed normal diet and given water *ad-libitum.* This group served as Diabetic control group.

***Group C**: Spirulina platensis* was fed orally at a dose rate of 400 mg/kg body weight after alloxan induce. This group served as Treatment group to find the effect of *Spirulina platensis* as antidiabetic drug. 400 mg/kg body weight (Neekhra *et al*., 2014) powder of *S. Platensis* [Bangladesh Council of Scientific and Industrial Research (BCSIR), Dhaka, Bangladesh] were dissolved in 5 ml/kg body weight of normal saline (NS) (Popular infusion limited, Bangladesh) and their solutions were prepared

Preparation and administration of alloxan solution

Alloxan monohydrate was first measured according to rat's body weight through electric balance into different amounts and was kept into different Eppendorf tubes which were previously labeled. Eppendorf tubes were kept in ice to protect from high temperature. Alloxan was dissolved in chilled saline. This solution was injected intraperitonealy to rats immediately after preparation. To induce diabetic condition in rats a dose of 150 mg Alloxan monohydrate per kg of body weight was chosen following the recommendation of works done previously (Meenakshi *et al*., 2010). The rats were then kept for the next 24 hours on 5% glucose solution bottles in their cages to prevent hypoglycemia. The blood glucose level of each animal was measured after 7 days of alloxan administration.

Collection, preservation and administration of Spirulina platensis

Spirulina platensis collected from Bangladesh Council of *Scientific* and Industrial Research (BCSIR), *Dhaka.* It was preserved at room temperature and was administered at a dose rate of 400mg/kg bwt orally for 6 weeks.

Observation of rats

During acclimatization (pre- treatment) body weight was measured at every week interval. After alloxan induction (during treatment) body weight was measured at two weeks interval. Fasting blood glucose level of each rat was measured on 15th day before alloxan injection and weeks 0, 1, 4 and 6 after alloxan induction.

Histological Examination

For histopathology, tissue samples from the pancreas were fixed in 10% buffered neutral formalin, embedded in paraffin, sectioned at 5µm and stained with Hematoxylin & Eosin (H & E) (Yazdanparast *et al.*, 2005). Haematoxylin & Eosin stains were used to stain the pancreas to demonstrate the pancreatic islets. Mallory's azan stain was also used to stain the pancreas to demonstrate the pancreatic islets and interstitial fibrosis.

For histopathology, the kidney tissues were immediately transferred to 10% formal saline for paraffin embedding and staining with Hematoxylin & Eosin (H&E) (Zafar *et al.*, 2009). Haematoxylin & Eosin stains were used to stain the kidney to demonstrate lesions in the glomerulus and tubules. Mallory's azan stain was also used to stain the kidney to demonstrate the interstitial fibrosis.

Biochemical analysis for oxidative stress

Assay of plasma lipid peroxidation: For measuring the rate of thiobarbituric acid-reactive substances (TBARS), an index of lipid peroxidation. Plasma samples were mixed with TCA (20%) and the precipitate was dispersed in H_2SO_4 (0.05 M). TBA (0.2% in sodium sulfate 2M) was added and heated for 30 min in boiling water bath as described previously (Rafiq *et al.,* 2012). TBARS adducts were extracted by *n*-butanol and the absorbance was measured at 532 nm. This reaction is formed in acidic pH and high temperature and the maximum absorption is a pink complex in 532 nm (Alam and Fareed, 2016; Istiak *et al*, 2018).

STATISTICAL ANALYSIS

The obtained data were expressed as mean ± standard deviation. The differences among the groups of animals of study were compared using student t-test (Unpaired) in GraphPad prism software (Version 6) (San Diego, CA) and applying one-way ANOVA followed by Bonferonni tests. Statistical significance was set at $P<0.05$ and it is considered significant in relation to control and standard.

RESULTS

Effect of Spirulina platensis on body weight in alloxan induced diabetic rats

The effects of *Spirulina platensis* on body weight in alloxan induced diabetic rats are presented in the fig 1. At 0 week and 6 week of treatment, average body weight of Group-A (Healthy control) were 180.71±2.02g and 202.86±1.85g, respectively. On the other hand, Group-B (Diabetic control) showed 172.85±1.84g and 192.14± 2.14g at week 0 and week 6, respectively. At week 0 and week 6 of treatment, Group-C (Diabetic+*Spirulina platensis* @ 400mg/kg bwt) showed 180±3.08g and 200±1.89g body weight, respectively. This data indicates that body weight was decreased significantly ($P<0.01$) in diabetic rat compared to healthy rat. In *Spirulina platensis* treated group improves the body weight loss in diabetic rat significantly ($P<0.01$).

Effect of Spirulina platensis on fasting blood glucose in alloxan induced diabetic rats

The effects of *Spirulina platensis* on fasting blood glucose in alloxan induced diabetic rats are presented in the fig2. At 0 week and 6 week of treatment, average fasting blood glucose level of Group-A (Healthy control) rats was

4.13±0.10 mmol/L and 4.77±0.09mmol/L, respectively. On the other hand, in the Group-B (Diabetic control) rats, after alloxan injection the blood glucose level on week 0 was 4.1±0.99 mmol/L and on week 1 was increased to 9.79±0.50 mmol/L, this value was further increased to 18.49±0.39mmol/L at week 6. The blood glucose level of Group-C (Diabetic + *Spirulina platensis* @ 400 mg/kg bwt) on week 0 was 4.41±0.30mmol/L and on 6th week was 14.97±0.39mmol/L. This data indicates that after one week of alloxan injection rats showed hyperglycemia which was further more markedly increased time dependently. *Spirulina platensis* @ 400 mg/kg bwt significantly decreased hyperglycemia in alloxan induced rat.

Figure 1

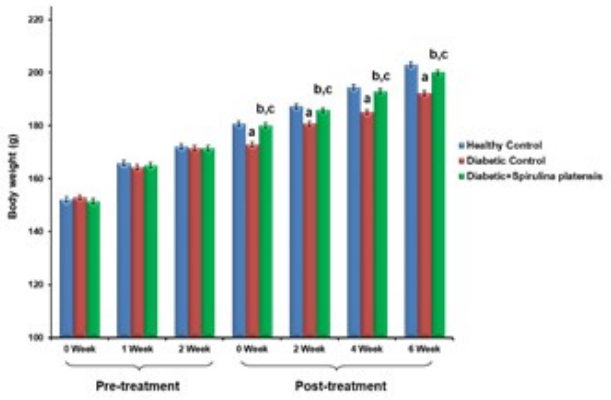

Fig. 1: Effect of *Spirulina platensis* on body weight (g) in alloxan induced diabetic rats. Data are shown as Mean±Standard Error Mean of n=7 samples per group. a, Healthy control vs Diabetic control (P<0.01); b, Diabetic control vs Diabetic+*Spirulina platensis* (P<0.05); c, Diabetic+*Spirulina platensis* vs Healthy control (P<0.01).

Figure 2

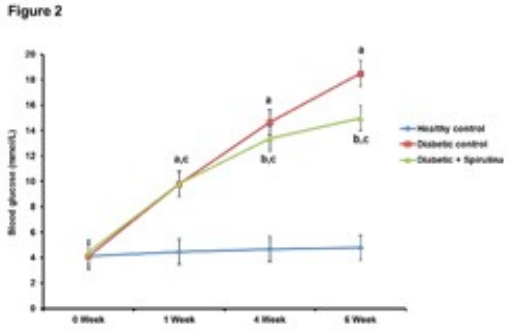

Fig. 2: Effect of *Spirulina platensis* on fasting blood glucose (mmol/dL) level in alloxan induced diabetic rats. Data are shown as Mean ± Standard Error Mean of n=7 samples per group. a, Healthy control vs Diabetic control (P<0.01); b, Diabetic control vs Diabetic+*Spirulina platensis* (P<0.05); c, Diabetic+*Spirulina platensis* vs Healthy control (P<0.05).

Figure 3

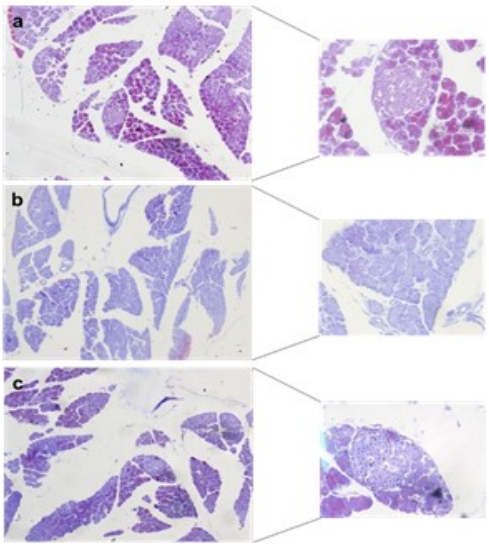

Fig. 3: Representative histopathological profiles of β-cells (arrow show one islet) of pancreas sections of normal and experimental diabetic rat. Paraffin embedded sections of pancreatic tissue were stained with hematoxilin and eosin (H&E). a) Healthy control rats shown normal histological structure of β-cells at the central zone in the islet of langerhans and normal proportion of acinar cell with prominent nuclei; b) Diabetic control rats shown atrophy, interstitial fibrosis and destruction of β cells; c) Diabetic+*Spirulina platensis* rats shown partial regeneration of β cells. Microscopic magnification (10X and 20X)

Figure 4

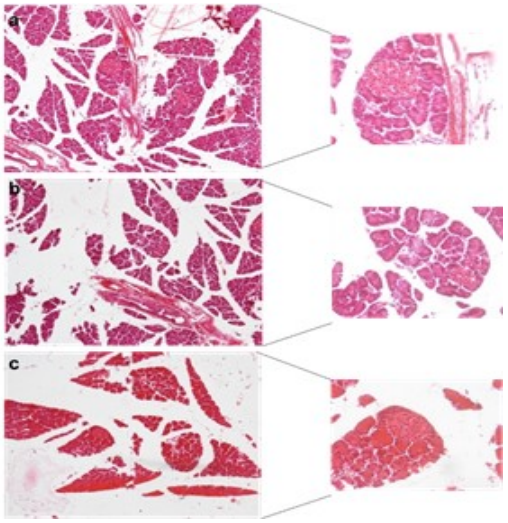

Fig. 4: Representative histopathological profiles of pancreas sections of normal and experimental diabetic rat. Paraffin embedded sections of pancreatic tissue were stained with Mallory-Azan. a) Healthy control rats shown normal histological structure of β-cells at the central zone in the islet of langerhans and normal proportion of acinar cell with prominent nuclei; b) Diabetic control rats shown atrophy, interstitial fibrosis and destruction of β cells.; c) Diabetic+*Spirulina platensis* rats shown the regeneration of β cells. Microscopic magnification (10X and 20X).

Figure 5

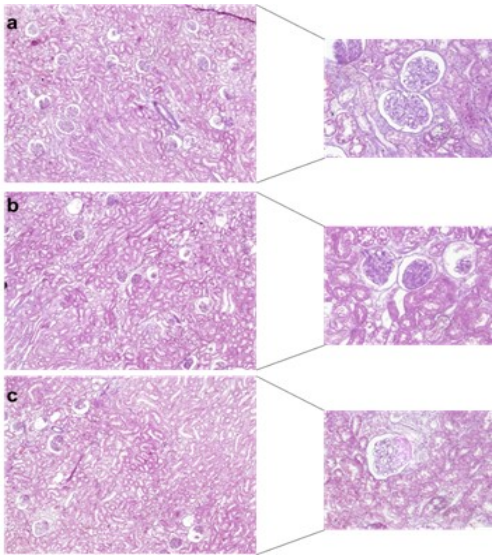

Fig. 5: Representative photomicrographs of histopathological studies of kidney sections of normal and experimental diabetic rat. Paraffin embedded sections of renal cortex were stained with hematoxilin and eosin (H&E). a) Healthy control rats shown the normal Bowman's capsule, glomerulus and tubules (proximal and distal); b) Diabetic control rats shown glomerular hypertrophy, glomerular sclerosis, tubular necrosis cast cell formation; c) Diabetic+*Spirulina platensis* rats shown partially improved renal capsular, glomerular and tubular lesions. Microscopic magnification (10X and 20X).

Figure 6

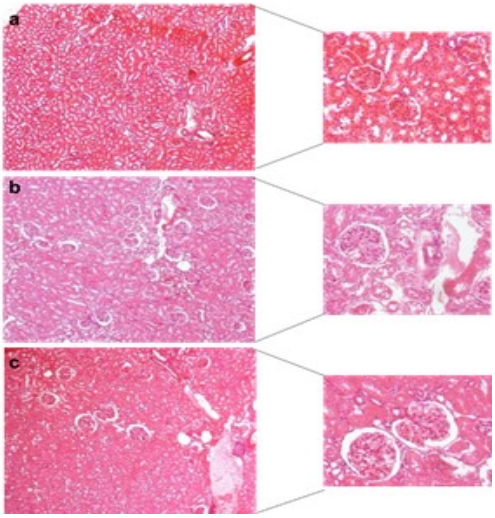

Fig. 6: Representative photomicrographs of histopathological studies of kidney sections of normal and experimental diabetic rat. Paraffin embedded sections of renal cortex were stained with Mallory-Azan. a) Healthy control rats show the normal Bowman's capsule, glomerulus and tubules (proximal and distal); b) Diabetic control rats show the glomerular hypertrophy, glomerular sclerosis, tubular necrosis, interstitial fibrosis; c) Diabetic+*Spirulina platensis* rats show the partially improved renal capsular, glomerular and tubular lesions. Microscopic magnification (10X and 20X).

Effects of Spirulina platensis on pancreatic injury in alloxan induced diabetic rats

In healthy control group, the cells of the pancreas were all present in their normal architectures. It was exhibited normal histological structure of β-cells at the central zone in the islet of langerhans in the endocrine portion and the aciner cells which stained strongly are arrange in lobules with prominent nuclei. The ilets cells seen embedded within the acinar cell and surrounded by fine capsule (fig. 3A, fig. 4A).

Figure 7

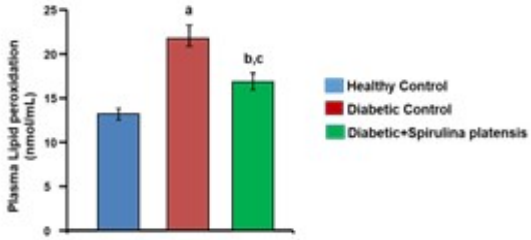

Fig. 7: Effect of *Spirulina platensis* on Plasma Lipid peroxidation (nmol/mL) in alloxan induced diabetic Rat. Data are shown as Mean ± Standard Error Mean of n=7 samples per group. a, Healthy control vs Diabetic control (P<0.05); b, Diabetic control vs Diabetic+*Spirulina platensis* (P<0.05); c, Diabetic+*Spirulina platensis* vs Healthy control (P<0.05).

In contrast, the photomicrograph of the pancreas of diabetic rats showed lymphocytic infiltrations, atrophy and destruction of beta cells mostly in the central portion of the islets of langerhans. The acinar cells around the islets through seem to be in normal proportion does not look classical compared to healthy rats by Hematoxylin & Eosin. Interstitial fibrosis was marked in renal section stained by Mallory's azan (fig. 3B, fig. 4B).

Photomicrograph of the pancreas of diabetic rats treated with Spirulina platensis (@ 400mg/kg bwt) showed that the size of cell and number of beta cells were back in almost normal position after 6 weeks of treatment. This was likely due to an increase in the β-cells, leading to increased insulin production and secretion. Hematoxylin & Eosin and Mallory's azan stained sections of the pancreas of diabetic rats treated with Spirulina platensis shows partial regeneration of β cells as well as reduction of interstitial fibrosis (fig. 3C, fig. 4C).

Effect of Spirulina platensis on renal injury in alloxan induced diabetic rats

Kidney section from healthy control rats exhibited normal distinct cortex and medulla, normal glomerulus surrounded by the Bowman's capsule, parenchyma and tubules (proximal and distal) without any inflammatory changes in Hematoxylin & Eosin stained renal section. No interstitial fibrosis was found in renal section stained

by Mallory's azan (fig. 5A, fig. 6A). In contrast, untreated diabetic control rats showed degenerated and sclerotic glomeruli infiltrated with inflammatory cells and thickening of the basement membrane; glomerular hypertrophy, glomerulosclerosis; enlarged or even disrupted Bowman capsule; tubular necrosis, interstitial fibrosis. In addition, many cortical tubules were vacuolated (fig. 5B, fig. 6B). Renal damages in alloxan induced diabetic rats were markedly improved by *Spirulina platensis* treatment. Normal glomerulus, reduction of inflammatory cells, normal basement membrane and capillaries was observed (fig. 5C, fig. 6C).

Effect of Spirulina platensis on plasma lipid peroxidation in alloxan induced diabetic rats

Alloxan induced rats showed increased plasma lipid peroxidase level indicating systemic oxidative stress. After 6 week treatment with *Spirulina platensis* markedly decreased plasma lipid peroxidase level in diabetic mice (fig. 7).

DISCUSSION

In the present study pre-treatment body weight was similar among the groups. Alloxan induced diabetes in rat was characterized by a severe loss in body weight, which has also been reported by other researchers (Erejuwa *et al*., 2010; Istiak *et al*., 2018) and this reduction in body weight is due to the loss or degradation of structural proteins, since structural proteins are known to contribute to the body weight. Previous reports show that protein synthesis is decreased in all tissues due to decreased production of ATP and absolute or relative deficiency of insulin (Erejuwa *et al*., 2010). Administration of Spirulina platensis in alloxan induced diabetic rats showed a significant (P<0.05) improvement in body weight loss when compared to diabetic control rats. This results are in agreement with our previously published report (Hussaini *et al*., 2018, Nipa *et al*., 2020).

The basal blood glucose level before treatment was similar between the groups. Alloxan @ 150 mg/kg body weight significantly (P<0.01) increased the blood glucose level in rats after one week. Alloxan causes a massive reduction in insulin release by the destruction of â cells of the islets of Langerhans and thus induces hyperglycemia (Pari *et al*., 2005). In the present study alloxan induced elevated blood glucose levels were reduced by the treatment with Spirulina platensis @ 400 mg/kg for 6 weeks. Anti-hyperglycemic effect of Spirulina platensis was also observed by previous study (Hussaini *et al*., 2018). The anti-hyperglycemic role of this medicinal herb (El-Baz *et al*., 2013) may potentiate its kidney and pancreas protective effects as shown in our present study.

In the present study, diabetes was induced in rats by intraperitoneal injection of alloxan @150 mg/kg (Meenakshi *et al*., 2010). Alloxan selectively destroy the pancreatic â cells via production of reactive oxygen species. In this experiment, histopathological examination of pancreas of diabetic rats showed degenerated islets of Langerhans and number of islets significantly decreased and atrophied with marked interstitial fibrosis. Treatment with Spirulina platensis in diabetic rats stimulate regeneration and reactivation of pancreatic â- cells regeneration partially as well as reduced pancreatic fibrosis. These results agree with Muthuraman *et al*., 2009 who reported that diabetic rats treated with marine Spirulina platensis showed an increase in the beta-cell numbers and large size islet of Langerhans. The anti-hyperglycemic action, occurred through the regeneration of â-cell potentiates pancreatic secretion of insulin from the intact beta- cells of the islets.

Nephropathy is a common chronic complication for diabetic patients. Diabetes causes glomerular lesions, atherosclerosis in renal vasculature leading to chronic diabetic nephropathy (Atalay and Laaksonen, 2002). In agreement with previous study alloxan induced rats also showed typical diabetic nephropathy which were ameliorated by Spirulina platensis treatment for six weeks. These findings of present study are in agreement with the findings of Ramesh *et al*., 2007; Kim *et al*., 2008 and Renno *et al*., 2008 who showed tubular epithelial changes, enlargement of lining cells of tubules and accumulation of glycogen in the kidney tubules. In addition, previous findings also support the present study findings by Farouk *et al*., 2013 who also observed the kidney protective effect of Spirulina platensis in diabetic rats.

Oxidative stress leads to the onset and subsequent complications of type 2 diabetes mellitus, neural damage, vascular dysfunction, cognitive decline and renal injury. In this regards previous study demonstrated that alloxan induced mice showed argumentation of plasma lipid peroxidation (Istiak *et al*., 2018). Other clinical studies also highlighted that increased oxidative stress induced by hyperglycemia may contribute to the pathogenesis of diabetic complications including nephropathy (Abe *et al*., 2011; Goodarzi *et al*., 2005). In contrast, present study demonstrated that alloxan induced rat showed argumentation of plasma lipid peroxidation. The increase in thiobarbituric acid-reactive substances (TBARS), an index of lipid peroxidation in the diabetic rat might be due to increased levels of oxygen free radicals. In animal studies, tea polyphenol administration was shown to decrease serum TBARS level due to its potential antioxidant activity (Sharifzadeh *et al*., 2018). Along with previous finding, these results suggest that argumentation of oxidative stress plays an important role in the pathogenesis of pancreas and renal injuries in alloxan induced diabetic mice (Meenakshi *et al*., 2010). Therefore, the beneficial effects of Spirulina platensis in

alloxan induced diabetic rats might be due to its antioxidative properties (Abe *et al*., 2011; Goodarzi *et al*., 2013; Sharifzadeh *et al*., 2018). Previous studies showed that Spirulina platensis inhibit peroxynitrite (ONOO-) and superoxide in mitochondria (Bhata and Madyasthab, 2001; Zheng *et al*., 2013), which inhibits expression of N-methyl-D-asparted (NMDA) receptor, tumor necrosis factor-á (TNF-á), interleukin-1á (IL-1á) and cyclooxygenase-2 (COX-2) genes in different inflamed tissues (Kumar *et al*., 2010; Hwang *et al*., 2013), to suppress the inducible nitric oxide synthase (iNOS) followed by decreased NO production, that modulates the c-Jun N-terminal kinase (JNK) and p38 mitogen-activated protein kinase (MAPK) pathways (Lee and Jeong, 2002; Khan *et al*., 2005). Therefore, this present study result coincided with Khan *et al*., 2005; Arpita Mohan *et al*., 2014 and Farouk K. *et al*., 2013 who reported that Spirulina platensis elicited significant kidney protective activity by decreasing lipid peroxidation and elevating the levels of antioxidants.

CONCLUSION

Herbal medicines are being progressively used all over the world. Nevertheless, herbal remedies are not free from hazards and some are causes adverse reactions have been described. From the current experimental data, it may conclude that Spirulina platensis have beneficial effects on glucose intolerance, pancreatic injury and renal injury in alloxan induced diabetic rats may be partially through its antioxidant properties which may reduce oxidative stress. Finally, it may state that the *Spirulina platensis* available in Bangladesh provide a new therapeutic avenue against diabetes and diabetes-related complications because of its availability, cheap rate and effectiveness. To draw a definite conclusion in this regard it demands detail study specially mechanism of action, side effect and contraindication of this newly derived herb *Spirulina platensis*.

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