

***Effect of Spirulina (Spirulina platensis) on Blood Glucose Level and Renal Impairment in Diabetic Rats***

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***Abstract***

Spirulina (*S. platensis*) is a blue-green alga with medicinal and nutritional interest due to its richness in nutrients as well as its hepatoprotective, nephroprotective, and antioxidant activities. This study aimed to examine the effect of spirulina against streptozotocin (STZ) induced hyperglycemic associated with kidney impairment in rats. Thirty-five rats were randomly divided into two main groups: The first main group (n= 7) were fed on basal diet only during the experiment and kept as the negative control group (-ve), the second main group " induced diabetic rats" (n=28) were divided into four subgroups as follow: the first subgroup was fed on basal diet and served as a positive control group (+ve). Groups (2, 3 and 4) were fed on basal diet supplemented with dried spirulina at the level of 2.5%, 5% and 7 %, respectively. At the end of the experimental period (8 weeks), rats were sacrificed and blood samples were collected to obtain serum. The results indicated that spirulina contains proteins (56.80 %) and fat (8.16 %) in addition to several minerals and vitamins. Spirulina supplementation significantly increase the final body weight, feed efficiency ratio and body weight gain % values compared to the +ve control rats. Diabetic treated rats had a significant increase (P<0.05) in insulin concentration and lower glucose levels as well as an improvement in kidney functions. Besides, spirulina significantly (P<0.05) reduced serum lipid profile, diminished the Malondahyde and enhanced glutathione peroxidase concentrations. Conclusion: The findings suggest that oral spirulina platensis could have a potential protective role for managing induced painful diabetic neuropathy in rats.

**Keywords:** Spirulina, diabetes, oxidative stress, glucose, lipid profile

***Introduction***

Diabetes mellitus (DM) is a multifactorial disease characterized by hyperglycemia and increased basal metabolic rate (**Bos and Agyemang, 2013**). High blood glucose levels damage the cell membranes and generate reactive oxygen species (ROS) (**Ha and Kim, 1999**). As the prevalence of this disease increases, there is a need to look for more efficient drugs with fewer side effects. Currently available drugs may lead to obesity and hyperandrogenemia even though they bring down the glucose levels (**Latha et al., 2014**).

The number of people with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity. The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. (**Wild et al.,**

2004). Diabetes is a leading cause of vision loss in Egypt. It is estimated that 42% of patients with diabetes in Egypt have diabetic retinopathy, 5% are legally blind, and 22% had peripheral neuropathy. Diabetes is also the major cause of end-stage renal disease and leg amputation in Egypt (**Hegazi et al., 2015**).

Kidneys are one of the important organs that are involved in diabetes. Diabetes is the most common cause of chronic kidney disease and end-stage renal disease in most parts of the world (**Shahbazian and Rezaii, 2013**). The kidney is an extremely complex organ with broad ranging functions in the body, including, but not restricted to, waste excretion, ion and water balance, maintenance of blood pressure, glucose homeostasis and generation of erythropoietin or activation of vitamin D (**Mihaescuet et al., 2012**). Kidney disease that occurs as a result of diabetes is the diabetic nephropathy. It is occurring as a result of an interaction between hemodynamic and metabolic factors (**Risović and Pejicic, 2011**).

Hyperglycemia, either acute or chronic, leads to oxidative stress and microvascular consequences in the peripheral nerves and initiates diabetic neuropathy. Diabetic neuropathy is a common microvascular disease that estimated recently, approximately 10–20% in diabetic subjects who exhibit painful neuropathy (**Rudroju et al., 2013**).

Medicinal plants have long been used against life threatening diseases including diabetes. Some of these plants have been shown to possess antioxidant activities, which could help improving diabetes inconveniences (**Gargouriet al., 2016**). Spirulina (SP) is a blue-green algae belonging to the Cyanobacteria family that is rich in bioactive compounds such as proteins, lipids, carbohydrates, trace elements, pigments (phycocyanin,  $\beta$ -carotene) riboflavin, tocopherol and  $\alpha$ -linoleic acid (**Yusuf et al., 2016**). Spirulina is the world's largest natural protein source and an important medicinal herb (**Tietze, 2004**). Two species of this Blue green algae are most commonly used as nutritional supplements, spirulina platensis (*S. Platensis*) and spirulina maxima (*S. maxima*) (**Sixabela et al., 2011 and Tefera et al., 2016**).

Spirulina species can regulate diabetic processes, hypercholesterolemia activity, have antioxidative effects, and radical scavenging properties (**Pankaj and Varma, 2013 and Abdel-Daimet al., 2016**). The potential health and nutritional benefits of spirulina must therefore be adequately recognized and utilized, thus making full use of this nature's gift to humanity (**Barnabas et al., 2020**). Moreover, **Hussainiet al., (2018)** showed that oral administration of spirulina platensis (400mg/kg body weight) for 6 weeks could reduce the adverse effect of alloxan induced diabetes in rats.

## **Materials and Methods**

### **Materials:**

Chemicals: Casein, vitamins, minerals, cellulose and Streptozotocin (STZ) were purchased from El-Gomhoria Company, Cairo, Egypt. Kits for blood analysis were purchased from Alkan Company for Biodiagnostic Reagents, Dokki, Cairo, Egypt. Spirulina: spirulina platensis samples were obtained from the Biotechnology Unit, National Research Centre, Dokki-Cairo, Egypt.

### **Experimental animals:**

Adult male albino rats (Sprague- Dawley strain) (n=35 rat) weighing approximately (190 g.) were purchased from Helwan Experimental Animals Farm.

**Methods:**

1. Identification of *Spirulina platensis* was carried out at the National Research Center, **Kingdom:** Bacteria, **Subkingdom:** Gracilicutes, **Phylum:** Cyanobacteria, **Class:** Cyanophyceae, **Subclass:** Oscillatoriothycideae, **Order:** Spirulinales, **Family:** Spirulinaceae, **Genus:** *Spirulina* spp.

2. **Chemical composition:**

Analysis of spirulina powder macro and micronutrients contents were assessed according to the method of (AOAC, 2019).

3. **Induction of animal model of diabetes:** Diabetes was induced by a single intraperitoneal injection of freshly prepared (STZ) (60 mg/kg BW) of rat. Three days later, random blood samples were taken from the eye of rat, then the level of the blood glucose was assessed and the level  $\geq 250$  mg/dl was considered as diabetic (Sarkar et al., 1996).

4. **Preparation of Spirulina powdered:** After collection, spirulina platensis samples were washed with fresh water several times to remove salts and debris, then it was air dried at Solar Energy Unit, at the National Research Centre.

5. **Biological study:** This study was carried out at the Postgraduate Lab of Home Economics Faculty, Helwan University. Thirty-five adult male Sprague-Dawley rats were fed on standard diet according to Reeves et al (1995) for one week for adaptation. Rats then were randomly divided into two main groups as follow: The first main group (n= 7) were fed on basal diet only and served as the negative control group (-ve), the second main group "induced diabetic rats by (STZ)" (n=28) were fed on basal diet and were divided into four subgroups as follow: the first subgroup was fed on basal diet and served as positive control group (+ve). Groups (3, 4 and 5) were fed on basal diet and supplemented with dried spirulina at the level of 2.5%, 5% and 7 %, respectively.

All rats were observed each day. Their feed intake (FI) was determined daily and body weights were obtained every week throughout the whole experimental period. Body weight gain (BWG%) and feed efficiency ratio (FER) were calculated according to the method of (Chapman et al., 1959) using the following equation:

$$\text{BWG\%} = \frac{\text{intial body weight (IBW)} - \text{final body weight (FBW)}}{\text{initial body weight}} \times 100$$

$$\text{FER} = \frac{\text{Body weight gain (g/d)}}{\text{Feed intake (g/d)}}$$

At the end of the experimental period (8 weeks), rats were fasted over night before sacrificing, blood samples were collected into a centrifuge tube without any anticoagulant and were centrifuged to obtain serum which was stored at -20°C until used for subsequent analysis.

**5. Biochemical analysis:** serum glucose level was determined according to Asatoor and King, (1954). Serum total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C) were determined according to Richmond, (1973), Wahlefeld, (1974) and Albers et al., (1983), respectively. Regarding to serum low density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) were calculated according to Friedewald et al., (1972).

Serum urea was determined according to the method of Tabacco (1979), uric acid was assayed in serum according to the method of Jelikić-Stankov et al., (2003) serum level of creatinine was determined according to the method described by Burtiset et al., (1999) and Young (2001). Serum Glutathione peroxidase (GPx) and Malondahyde (MDA) were determined according to Hissin and Hilf, (1976) and Draper and Hadley, (1990), respectively. Insulin activity was estimated using enzyme linked immunosorbent assay ELISA method as described by Clark and Hales, (1994).

**6. Statistical Analysis:**

The obtained results were analyzed according to SPSS program (Statistical Package for the Social Sciences) program. ANOVA (Analysis of Variance) test was used to compare results among different groups according to (**Armitage and Berry, 1987**). All differences were considered significant if p-values were ( $P \leq 0.05$ ).

**Table (1):  
Chemical composition of Spirulina**

Nutrient	(g/100 g)	Minerals (mg/100g)		Vitamins (mg/100g)	
Moisture	6.90	Calcium	288.80	Vitamin E	55.98
Protein	56.80	Phosphorus	117.92	Vitamin A (as $\beta$ -Carotene)	69.10
Fat	8.16	Potassium	183.52	Vitamin B1	3.85
Ash	10.5	Iron	11.85	Vitamin B2	3.90
Fibre	4.23	Zinc	2.75		
Carb.	13.41	Manganese	9.10		
		Sodium	220.25		
		Copper	5.70		

**Results and Discussion**

Spirulina is a bluish green algae rich in many active biological substances that have many medicinal uses. The results of this study showed that spirulina contains 56.80 % of its dry weight proteins which is considered a high protein value, while it contains only 8.16% of its dry weight fats. Spirulina contains several minerals mostly calcium, potassium, and phosphorus. Moreover, it contains high amount of vitamin E (alpha tocopherol) and vitamin A ( $\beta$ -carotene) (Table 1).

This study pursued to evaluate the nutritional contents of spirulina besides evaluating the protective impacts of the algae on blood glucose level and renal impairment in diabetic rats. The findings of the instant study agreed with the results of (**Ragheb and Aljehany, 2020**) who reported that spirulina contains high protein percent (57.30 %) of its dry weight.

Moreover, (**Sharoba, 2014**) found that spirulina is a rich source of protein as it contains 62.84% of its weight protein mostly essential amino acids. Besides, spirulina is a perfect source of beta-carotene and vitamin E (**Gutiérrez-Salmeán et al., 2015 and Wang, et al., 2007**).

**Table (2):  
Effect of Spirulina on body weight status in diabetic rats**

Parameters Groups	IBW(g)	FBW (g)	BWG (g)	BWG %	FI (g/d/rat)	FER
Control (-ve)	191.5±0.76a	210.16±1.42a	18.67	9.75±0.76a	16.0	0.026±0.02a
Control (+ve)	194.0±1.73a	178.3±0.88d	-	-8.06±0.38d	13.0	-0.027±0.01c
Spirulina 2.5%	191.6±1.20a	199.3±1.20c	7.66	4.00±0.64c	13.7	0.012±0.01b
Spirulina 5%	193.0±1.00a	203.6±0.88bc	10.67	5.53±0.98bc	14.0	0.017±0.02b
Spirulina 7%	193.3±1.45a	205.8±2.24ab	12.48	6.46±0.51b	14.8	0.019±0.01b

Results are expressed as mean ±SE.

Values in each column which have different letters are significantly different at(P<0.05).

The results also revealed that FI(g/d/rat) was decreased in the positive control group compared to the negative control group. Spirulina supplementation at different levels enhanced the feed intake compared to the positive control group. Regarding FER, there was no significant difference in the mean value of FER among the rats that fed on 2.5%, 5% or 7% of spirulina, compared to each other.

It was noticed that the higher the percentage of spirulina supplementation in the diet, the higher the FBW, BWG%, FI and FER. The results of this study found that the injection of rats with STZ reduced the FBW, FI, and BWG% while treatment with spirulina reversed all these vital changes. Like these findings, previous results have documented the decreased body weight associated with STZ (**Negm, 2020**). In this connection, diabetic rats treated with spirulina maxima showed a regain in their body weight which may be explained by the increased insulin secretion or the increased feed consumption (**Pandey et al., 2010**).

Likewise, oral administration of *S. platensis* aqueous extract to diabetic rats for 50 days led to an obvious regain in their body weight loss, suggesting general health status and metabolic mechanisms improvement by effective control glycemia or reversing of gluconeogenesis (**Abdel-Daim 2014; Yusuf et al. 2016; Aissaoui et al., 2017 and Hussaini et al., 2018**). In addition, **Ragheb and Aljehany, (2020)**. **Ismail et al., (2020)** showed that *Spirulina platensis* reduced blood glucose and improved the body weight losses compared to diabetic rats after six weeks' treatment.

**Table(3):  
Effect of Spirulina on insulin level, and glucose in diabetic rats**

Parameters Groups	Insulin (ng/ml)	Glucose (mg/dl)	% reduction
Control (-ve)	35.20±1.79a	113.83±1.72e	-
Control (+ve)	8.53±1.28e	296.66±2.97a	-
Spirulina 2.5%	17.83±0.89d	240.67±1.28b	18.87
Spirulina 5%	23.96±0.86c	190.15±1.95c	35.90
Spirulina 7%	31.17±0.82b	136.20±2.90d	54.08

Results are expressed as mean ±SE.

Values in each column which have different letters are significantly different at(P<0.05).

Results recorded in Table(3) revealed that there was a significant increase ( $p < 0.05$ ) in the mean value of blood glucose in the positive control group compared to the negative control group, due to STZ injection. In addition, blood glucose level was significantly decreased, as a result of spirulina supplementation at the different tested levels compared to the positive control group and among the three tested levels.

Supplementation with spirulina at 2.5% caused glucose reduction by 18.8% while 5% spirulina caused a 35.9% reduction, and the highest glucose reduction was recorded at the group fed 7% spirulina by (54.08%). Results also indicated that there was a significant decrease ( $p < 0.05$ ) in the mean value of insulin in the positive control group compared to the negative control group. Rats fed on 2.5%, 5% and 7% of spirulina had a significant increase ( $p < 0.05$ ) in the mean value of insulin, as compared to the positive control group. There was a significant difference in insulin level among the three tested levels of spirulina.

Our findings agreed with that of (**Estrada et al., 2001; Nasirian et al., 2019 and Negm, 2020**) who showed that administration of STZ increased glucose due to the decreased insulin concentration in rats. In the present study, we found that spirulina reversed the diabetic effects of glycemia and insulinemia. Similar results were reported by **Muthuraman et al., (2009) and Aissaoui et al., (2017)**. The hypoglycemic effect of spirulina platensis powder aids in the diabetes treatment by controlling the increased blood glucose levels in the STZ induced diabetic animals (**Pandey et al., 2011 and Ripa et al., 2018**). Moreover, the administration of 400 mg/Kg of *S. platensis* powder could reduce the adverse effect of plasma hyperglycemia in the alloxan induced diabetic rats as recommended by **Hussaini et al., (2018) and Okechukwu et al., (2019)**.

**Gargouri et al., (2012)** also showed that receiving 5% spirulina-enriched diet for 21 days could reduce serum glucose level. Spirulina and Chlorella alone and in combination exerted anti-hyperglycemic effect, which has been reported by (**Gargouri et al., 2016 and Mehdinezhad et al., 2021**). Also, **Gargouri et al., (2018)** indicates that supplementation with spirulina (5%) for 3 weeks is efficient in inhibiting hyperglycemia and oxidative stress induced by diabetes, and suggested that the administration of this algae may be helpful in the prevention of diabetic complications. This amelioration was even more pronounced than that caused by insulin injection.

**Gheda et al., (2021)** showed that administration of *S. platensis* methanolic extract (at 15 and 10 mg/Kg BW) caused anti-hyperglycemic activity by reducing the elevated blood glucose level. The possible mechanism through improving the pancreatic secretion of insulin from  $\beta$ -cell islets or due to enhanced transportation of blood glucose to the peripheral tissue in the spirulina -treated diabetic rats (**El-Baz et al., 2013**).

**Table(4):  
Effect of Spirulina on kidney functions of the diabetic adult male rats**

Parameters Groups	Urea (mg/dl)	Uricacid (mg/dl)	Creatinine (mg/dl)
Control (-ve)	40.61±0.85e	1.20±0.02e	0.388±0.08e
Control (+ve)	70.83±0.88a	1.62±0.02a	0.928±0.01a
Spirulina 2.5%	61.06±2.51b	1.47±0.01b	0.806±0.06b
Spirulina 5%	53.60±2.43c	1.33±0.02c	0.689±0.02c
Spirulina 7%	47.10±1.16d	1.26±0.01d	0.543±0.05d

Results are expressed as mean ±SE.

Values in each column which have different letters are significantly different at (P<0.05).

Results of Table (4) showed that there was a significant increase (p<0.05) in the mean value of urea, uric acid and creatinine in the positive control group compared to the negative control group. Spirulina supplementation at different levels significantly (P<0.05) decreased the urea, uric acid and creatinine level compared to the positive control group. There was a significant difference (P<0.05) in kidney functions among the three tested levels of spirulina. It was noticed that the higher percent age of spirulina supplementation in the diet, the lower urea, uric acid and creatinine level.

These findings were in convention with those reported by **Salem et al., (2014) and Abbas et al., (2015)**. Addition of spirulina supplementation improved kidney functions which was in agreement with **Gargouri et al., (2018)** who demonstrated that treatment with spirulina (5%) for 3 weeks or insulin significantly ameliorated renal dysfunction by reducing oxidative stress, while rats recovered normal kidney histology. Also, **Ragheb and Aljehany, (2020)** demonstrated that treatment with spirulina resulted in a marked improvement in kidney function. In agreement with the present results, the researchers reported preventive effect of feeding spirulina and its active ingredient Phycocyanin on chronic renal toxicity model in rats (**Memije-Lazaro et al., 2018**).

Moreover, **Ripa et al., (2018)** indicated that, the mitigation effect may be due to the potential antioxidant properties of *S. platensis* extract that improved the renal function via attenuation of the oxidative stress mediated decline in kidney function. This was in agreement with **Okechukwu et al., (2019)** who reported that, diabetic rats treated with spirulina showed a pronounced reduction in the renal functions through decreasing lipid peroxidation, thus considerably modify the renal damage.

Also, **Ismail et al., (2020) and Hossain et al., (2020)** concluded that *Spirulina platensis* (400 mg/kg diet) having antioxidant compounds could protect renal tissues damage, stimulate regeneration and reactivation of pancreatic β- cells in alloxan induced diabetic rats. **Gabr et al., (2021) and Gheda et al., (2021)** reported that spirulina could be used as alternative treatments as anti-hyperlipidemic and antidiabetic agent as well as in liver and kidney protective.

**Table(5):  
Effect of Spirulina on Lipid profile in diabetic rats:**

Parameters Groups	TG (mg/dl)	TC (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)
Control (-ve)	49.36±1.90e	87.50±3.02e	54.40±2.45a	23.22±5.36e	9.87±0.38e
Control (+ve)	90.53±2.16a	126.93±2.07a	25.13±1.02e	83.69±2.58a	18.10±0.43a
Spirulina 2.5%	78.53±3.11b	118.43±0.70b	36.03±0.93d	66.69±1.16b	15.70±0.62b
Spirulina 5%	66.36±0.52c	107.46±1.72c	41.76±1.35c	52.42±2.95c	13.27±0.10c
Spirulina 7%	56.20±1.84d	99.53±1.00d	49.56±0.81b	38.72±1.32d	11.24±0.36d

Results are expressed as mean ±SE.

Values in each column which have different letters are significantly different at (P<0.05).

Results recorded in Table (5) revealed a significant increase (p<0.05) in the mean value of TG, TC, LDL-C, VLDL-C, and significant decrease in HDL-C in the positive control group compared to the negative control group. Rats had a significant decrease in the mean value of lipid profile, and significant increase in HDL-c when they were fed on 2.5%, 5% and 7% of spirulina, as compared to the positive control group. In addition, there was a significant difference in lipid profile level among the three tested levels of spirulina. The highest reduction in lipid profile was recorded at the group fed spirulina at 7%.

Diabetes mellitus may be accompanied by significant increase in TG levels, which leads to lipid breakdown and obesity (*Hoseini et al., 2013 and EL-Sabagh et al., 2014*). Evidence suggests that consumption of spirulina as a dietary supplement prevents hypercholesterolemia due to the large amount of cysteine in spirulina (*Cheong et al., 2010*). The addition of this alga into the diet diminished the intestinal absorption of cholesterol as well as the re-absorption of bile acids in the ileum. Thus, spirulina can be considered a functional food capable of weight reduction according to *Joventino et al., (2012) and Gargouri et al., (2016)*.

Similar results were obtained by *Salem et al., (2014)* when they orally administered 15 mg/kg BW of *S. platensis* powder for diabetic rats. Moreover, *Ragheb and Aljehany, (2020) and Mehdinezhad et al., (2021)* demonstrated that treatment with spirulina resulted in a marked improvement in lipid profile. In agreement with the results of the current study, consuming spirulina supplement was associated with a decreased concentration of blood fat (*Ferreira-Hermosillo, 2010; Mazokopakis et al., 2014 and Gheda et al., 2021*). The lipid-lowering mechanism for this Algae lies in its ability to reduce the level of triglycerides as studies have proven to contain a high level of protein and very little of fat (*Nagaoka et al., 2005; Browning et al., 2006 and Ragheb and Aljehany, 2020*).



Table(6):  
Effect of Spirulina on GPx and MDA in diabetic adult male rats

Parameters	GPx (U/mg)	MDA ( $\mu$ mol/dl)
Control(-ve)	60.65 $\pm$ 0.65 <sup>a</sup>	10.44 $\pm$ 0.30 <sup>e</sup>
Control(+ve)	32.13 $\pm$ 1.26 <sup>e</sup>	25.26 $\pm$ 0.83 <sup>a</sup>
Spirulina 2.5%	38.50 $\pm$ 1.11 <sup>d</sup>	19.93 $\pm$ 0.52 <sup>b</sup>
Spirulina 5%	48.66 $\pm$ 1.61 <sup>c</sup>	15.93 $\pm$ 0.61 <sup>c</sup>
Spirulina 7%	56.73 $\pm$ 1.43 <sup>b</sup>	13.06 $\pm$ 0.41 <sup>d</sup>

Results are expressed as mean  $\pm$ SE.

Values in each column which have different letters are significantly different at (P<0.05).

Results of Table (6) showed that there was a significant decrease (p<0.05) in the mean value of GPx in the positive control group as compared to the negative control group. Rats had a significant increase (p<0.05) in the mean value of GPx, when they were fed on 2.5%, 5% and 7% of spirulina supplementation as compared to the positive control group. Moreover, there was a significant difference in GPx among the three tested levels, in addition, the higher percentage of spirulina supplementation in the diet, the higher GPx concentration.

It also revealed that there was a significant increase (p< 0.05) in the mean value of MDA in the positive control group as compared to the negative control group. Diabetic rats fed on different levels of spirulina supplementation (2.5%, 5% and 7%) had a significant decrease (p<0.05) in the mean value of MDA, also, there was a significant difference among the three tested levels, the higher the percentage of spirulina supplementation in the diet, the lower the MDA.

Similar results were noted by **Abdel-Daim et al., (2015)**. Treatment with spirulina offered protection through attenuation of lipid peroxidation and decreased production of free-radical derivatives, as evident from the decreased levels of serum MDA (**Abdel-Daim, 2014 and Aissaoui et al., 2017**). Diabetics models exhibit high oxidative stress due to persistent and chronic hyperglycaemia as well as hyperlipidaemia, which blocks the antioxidative defense system and thus promotes de novo free radical generation (**Vijayaraj et al., 2013**). Spirulina supplementation enhanced all altered serum biochemical parameters and antioxidant biomarkers (**Abdelkhalek et al., 2014 and Aissaoui et al., 2017**). The results of the present study showed an increase in the level of antioxidant levels (GPX), and decrease in the product of oxidative stress (MDA) in rats. These results were confirmed by **Aissaoui et al., (2017) and Ragheb and Aljehany, (2020)**. **Gargouri et al., (2018)** reported that spirulina is efficient in inhibiting hyperglycemia and oxidative stress induced by diabetes. On conclusion, the study suggests that oral spirulina platensis could have a potential protective role for managing induced painful diabetic neuropathy in rats and recommends its trial on diabetic patients.

## References

- Abbas, A.; Shazly, M.; Ahmed, K.; Abdel-Mawla, E. and Ibrahi, K.A. (2015):**  
Therapeutic effects of *Spirulina platensis* on streptozotocin-induced diabetic rats. Egyptian Journal of Comparative Pathology and Clinical Pathology, 28:18-31.
- Abdel-Daim M.; El-Bialy B.E.; Rahman H.G.; Radi A.M.; Hefny H.A. and Hassan A.M. (2016):**  
Antagonistic effects of *Spirulina platensis* against sub-acute deltamethrin toxicity in mice: biochemical and histopathological studies. Biomed Pharmacother. 77:79–85.
- Abdel-Daim M. (2014):**  
Pharmacodynamic interaction of *Spirulina platensis* with erythromycin in Egyptian Baladi bucks (*Capra hircus*). Small Rumin Res. 120:234–241.
- Abdel-Daim M.; Farouk S.; Madkour F. and Azab S. (2015):**  
Antiinflammatory and immunomodulatory effects of *Spirulina platensis* in comparison to *Dunaliella salina* in acetic acid-induced rat experimental colitis. Immunopharmacol Immunot. 37:126–139.
- Abdelkhalek N.; Ghazy E. and Abdel-Daim M. (2014):**  
Pharmacodynamic interaction of *Spirulina platensis* and deltamethrin in freshwater fish Nile tilapia, *Oreochromis niloticus*: impact on lipid peroxidation and oxidative stress. Environ Sci Pollut Res Int. 22:3023–3031.
- Aissaoui, O.; Amiali, M.; Bouzid, N.; Belkacemi, K. and Bitam, A. (2017):**  
Effect of *Spirulina platensis* ingestion on the abnormal biochemical and oxidative stress parameters in the pancreas and liver of alloxan-induced diabetic rats. Pharmaceutical biology, 55(1):1304-1312.
- Albers, N.; Benderson, V. and Warnick, G. (1983):**  
Enzymatic determination of high density lipoprotein cholesterol, Selected Methods. Clin. Chem, 10(5):91-99.
- AOAC. (2019):**  
Association of Official Agricultural Chemists. Official Methods of Analysis, 21st Edition; 2019.
- Artimage, G. and Berry, W. (1987):**  
Statistical Methods 7th Edition. Ames, Iowa State University, 39-63.
- Asatoor, A., & King, E. (1954):**  
Simplified colorimetric blood sugar method. The Biochemical Journal, 56(325th Meeting), xlv.
- Barnabas, A.; Asogwa, S. and Omaha, C. (2020):**  
The nutritional and health potentials of *spirulina plantensis*. Department of food science and technology, University of Nigeria Nsukka, Enugu State.

**Bos M. and Agyemang C. (2013):**

Prevalence and complications of diabetes mellitus in Northern Africa, a systematic review. *BMC Public Health*. 13:1–7.

**Browning J.; Davis J.; Saboorian M. and Burgess S. (2006):**

A low-carbohydrate diet rapidly and dramatically reduces intrahepatic triglyceride content. *Hepatology*.; 44(2):487–8.

**Burtis, C. A., Ashwood, E. R., &Tietz, N. W. (1999):**

Tietz textbook of clinical chemistry. Philadelphia, London Pub Saunders WB & CO, 1917.

**Chapman, D.; Castillo, R. and Campbell, J. (1959):**

Evaluation of protein in foods: 1. A method for the determination of protein efficiency ratios. *Canadian Journal of Biochemistry and Physiology*, 37(5):679-686.

**Cheong, S.; Kim, M.; Sok, D.; Hwang, S.; Kim, J.; Kim, H.; Lee, J.; Kim, Y.; and Kim, M. (2010):**

Spirulina prevents atherosclerosis by reducing hypercholesterolemia in rabbits fed a high-cholesterol diet. *Journal of Nutritional Science and Vitaminology*, 56(1):34–40.

**Clark, P. and Hales, C. (1994):**

How to measure plasma insulin. *Diabetes/metabolism reviews*, 10(2):79-90.

**Draper, H. and Hadley, M. (1990):**

Malondialdehyde determination as index of lipid Peroxidation. *In Methods in enzymology*. Academic press, 186:421-431.

**El-Baz, F.; Aly, H. and Mohamed, A. (2013):**

Role of Spirulina platensis in the control of glycemia in DM2 rats. *International Journal of Scientific and Engineering Research*, 4(12):1731-1740.

**EL-Sabagh M.; Eldaim M.; Mahboub D. and Abdel-Daim M. (2014):**

Effects of Spirulina platensis algae on growth performance, antioxidative status and blood metabolites in fattening lambs. *J Agric Sci*.;6(3):92.

**Estrada J.; Bescós P. and Fresno A. (2001):**

Antioxidant activity of different fractions of Spirulina platensis protean extract. *II Farmaco*, 56:497-500.

**Ferreira-Hermosillo A.; Torres-Duran P. and Juarez-Oropeza M. (2010):**

Hepatoprotective effects of Spirulina maxima in patients with non-alcoholic fatty liver disease: A case series. *Journal of Medical Case Reports*; 4:103.

**Friedewald, W.; Levy, R. and Fredrickson, D. (1972):**

Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical chemistry*, 18(6):499-502.

**Gabr G.; El-Sayed S.; Hikal M. and El-Assar M. (2021):**

Ameliorative effect of spirulina platensis bioactive compounds on oxidative stress lipid profile kidney and liver function markers of streptozotocin-induced diabetic rats., *Fresenius Environmental Bulletin*.

**Gargouri, M.; Ghorbel-Koubaa, F.; Bonenfant-Magné, M.; Magné, C.; Dauvergne, X.; Ksouri, R.; Krichen, Y.; Abdelly, C. and Feki, A. (2012):**

Spirulina or dandelion-enriched diet of mothers alleviates lead-induced damages in brain and cerebellum of newborn rats. *Food and Chemical Toxicology*, 50(7):2303–2310.

**Gargouri, M.; Hamed, H.; Akrouti, A.; Dauvergne, X.; Magné, C. and El Feki, A. (2018):**

Effects of Spirulina platensis on lipid peroxidation, antioxidant defenses, and tissue damage in kidney of alloxan-induced diabetic rats. *Applied Physiology, Nutrition, and Metabolism*, 43(4):345-354.

**Gargouri, M.; Magné, C. and El Feki, A. (2016):**

Hyperglycemia, oxidative stress, liver damage and dysfunction in alloxan-induced diabetic rat are prevented by Spirulina supplementation. *Nutrition research*, 36(11):1255-1268.

**Gheda, S.; Abo-Shady, A.; Abdel-Karim, O. and Ismail, G. (2021):**

Antioxidant and Antihyperglycemic Activity of *Arthrospira platensis* (*Spirulina platensis*) Methanolic Extract: *In vitro* and *in vivo* Study. *Egyptian Journal of Botany*, 61(1):71-93.

**Gutiérrez-Salmeán G.; Fabila C. and Chamorro-Cevallos G. (2015):**

nutritional and toxicological aspects of Spirulina (*Arthrospira*). *Nutr Hosp.*;32(1):34– 40. 37.

**Ha H. and Kim K. (1999):**

Pathogenesis of diabetic nephropathy: the role of oxidative stress and protein kinase C. *Diabetes Res Clin Pract.* 45:147–151.

**Hegazi, R.; El-Gamal, M.; Abdel-Hady, N. and Hamdy, O. (2015):**

Epidemiology of and risk factors for type 2 diabetes in Egypt. *Annals of global health*, 81(6):814-820.

**Hissin, P. and Hilf, R. (1976):**

A fluorometric method for determination of oxidized and reduced glutathione in tissues. *Analytical biochemistry*, 74(1):214-226.

**Hoseini S.; Khosravi-Darani K. and Mozafari M. (2013):**

Nutritional and medical applications of spirulina microalgae. *Mini-Rev Med Chem.*13(8):1231–7.

**Hossain, M.; Akter, S.; Nipa, N.; Chowdhury, U.; Bhuiyan, A.; Ali, T. and Rafiq, K. (2020):**

Reno-pancreas protective effects of Spirulina platensis in alloxan induced diabetic rats. *Pakistan Journal of Pharmaceutical Sciences*, 33(6).

**Hussaini, S.; Hossain, M.; Islam, M. and Rafiq, K. (2018):**

Effects of *Spirulina platensis* on alloxan induced diabetic rats. *Progressive Agriculture*, 29(2):139-146.

**Ismail H.; Sakila A.; Nahida S.; Ummal W.; Abdus Sattar B.; Taskina A. and Kazi R. (2020):**

Reno-pancreas protective effects of *Spirulina platensis* in alloxan induced diabetic rats. *Pak J Pharm Sci.*,33(6):2511-2519.

**Jelikić-Stankov, M.; Đurđević, P. and Stankov, D. (2003):**

Determination of uric acid in human serum by an enzymatic method using N-Methyl-N-(4-aminophenyl)-3-methoxyaniline reagent. *Journal of the Serbian Chemical Society*, 68(8-9):691-698.

**Joventino, I.; Alves, H.; Neves, L.; Pinheiro-Joventino, F.; Leal, L.; Neves, S.; Ferreira, F.; Brito, G. and Viana, G. (2012):**

The microalga *Spirulina platensis* presents anti-inflammatory action as well as hypoglycemic and hypolipidemic properties in diabetic rats. *Journal of Complementary & Integrative Medicine*, 9(1).

**Latha, S., Rajaram, K., & Suresh Kumar, P. (2014):**

Hepatoprotective and antidiabetic effect of methanol extract of *Caralluma fimbriata* in streptozotocin induced diabetic albino rats. *International Journal of Pharmacy and Pharmaceutical Sciences*, 6(1), 665–668.

**Mazokopakis E.; Papadomanolaki M.; Foustieris A.; Kotsiris D.; Lampadakis I. and Ganotakis E. (2014):**

The hepatoprotective and hypolipidemic effects of *Spirulina* (*Arthrospira platensis*) supplementation in a Cretan population with non-alcoholic fatty liver disease: A prospective pilot study. *Annals of Gastroenterology.*; 27(4):387–94.

**Mehdinezhad, N.; Aryaeian, N.; Vafa, M.; Saeedpour, A.; Ebrahimi, A.; Mobaderi, T.; Fahimi, R. and SajadiHezaveh, Z. (2021):**

Effect of spirulina and chlorella alone and combined on the healing process of diabetic wounds: an experimental model of diabetic rats. *Journal of Diabetes and Metabolic Disorders*, 20(1):161–169

**Memije-Lazaro I.; Blas-Valdivia V.; FrancoColín M. and Cano-Europa E.(2018):**

*Arthrospira maxima* (*Spirulina*) and C-phycocyanin prevent the progression of chronic kidney disease and its cardiovascular complications. *Journal of Functional Foods*; 43:37–43.

**Mihaescu, R.; Serban, M.; Dragan, S.; Timar, R.; Mozos, I; Craina, M. and Schiller, A. (2012):**

Diabetes and Renal Disease. University of Medicine and Pharmacy, Victor Babeş” Timișoara Romania.

**Muthuraman P.; Senthilkumar R. and Srikumar K. (2009):**

Alterations in beta-islets of Langerhans in alloxan-induced diabetic rats by marine *Spirulina platensis*. *J Enzyme Inhib Med Chem.*; 24:1253–1256.

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**Nagaoka, S.; Shimizu, K.; Kaneko, H.; Shibayama, F.; Morikawa, K.; Kanamaru, Y.; Otsuka, A.; Hirahashi, T. and Kato, T. (2005):**

A novel protein C-phycoerythrin plays a crucial role in the hypocholesterolemic action of *Spirulina platensis* concentrate in rats. *Journal of Nutrition*, 135(10): 2425–2430.

**Nasirian, F.; Sarir, H. and Moradi-kor, N. (2019):**

Antihyperglycemic and antihyperlipidemic activities of *Nannochloropsis oculata* microalgae in Streptozotocin-induced diabetic rats. *Biomolecular Concepts*, 10(1):37-43.

**Negm, H. (2020):**

Study of Glycemic Control by Ketogenic Diet Supplemented with Different Oils in Type II Diabetic Rats. *Home Econ. J.* 36(2):20-39.

**Okechukwu, P.; Ekeuku, S.; Sharma, M.; Nee, C.; Chan, H.; Mohamed, N. and Anisah Froemming, G. (2019):**

In vivo and in vitro antidiabetic and antioxidant activity of spirulina. *Pharmacognosy Magazine*, 15(62):17–29.

**Pandey, J.; Tiwari, A. and Mishra, M. (2010):**

Evaluation of Biomass Production of *Spirulina maxima* on Different Reported Media. *Journal of Algal Biomass Utilization*, (1):70–81.

**Pandey, J.; Tiwari, A.; Mishra, G. and Mishra, R. (2011):**

Role of *Spirulina maxima* in the control of blood glucose levels and body weight in streptozotocin induced diabetic male Wistar rats. *Journal of Algal Biomass and Utilization*, 2: 35-37.

**Pankaj P. and Varma M, (2013):**

Potential role of *Spirulina platensis* in maintaining blood parameters in alloxan-induced diabetic mice. *Int J Pharm Pharm Sci.* 5:450–456.

**Ragheb A. and Aljehany G. (2020):**

Evaluation of the Ameliorative Effects of *Spirulina* in Propylthiouracil Induced Hyperlipidaemia, Liver and Kidney Toxicity in Rats, *Journal of Pharmaceutical Research International* 32(26): 21-3.1.

**Reeves, P. G., Nielsen, F. H., & Fahey, G. C. (1993):**

AIN-93 purified diets for laboratory rodents: final report of the American Institute of Nutrition ad hoc writing committee on the reformulation of the AIN-76A rodent diet. *The Journal of Nutrition*, 123(11), 1939–1951.

**Richmond, N. (1973):**

Colorimetric determination of total cholesterol and high density lipoprotein cholesterol (HDL-c). *Clin. Chem*, 19, 1350-1356.

**Ripa, S.; Aziz, F.; Islam, R.; Hasan, M.; Misrat, M.; Parvez, M.; Jubayar, T. and Roy, M. (2018):**

Antidiabetic effect of spirulina (*Spirulina platensis*) in an alloxan-induced rabbit model. *International Journal of Natural and Social Sciences*, 5(4):48–53.

**Risović, I. and Pejičić, S. (2011):**

Renal function in diabetes mellitus. *Current topics in neurology, psychiatry and related disciplines*. 19(3):23-27.

**Rudroju, N.; Bansal, D.; Teja Talakokkula, S; Gudala, K.; Hota, D.; Bhansali, A. and Ghai, B. (2013):**

Comparative efficacy and safety of six antidepressants and anticonvulsants in painful diabetic neuropathy: A network meta-analysis. *Pain Physician*, 16(6): E705-E714.

**Salem, S.; Ibrahim, A.; El-Olemy, K. and Mosleh, M. (2014):**

Clinicopathological studies on the use of *Spirulina platensis* as a modern food supplement in alloxan-induced diabetic rats. *Egyptian Journal of Comparative Pathology and Clinical Pathology*, 27(1):55-72.

**Sarkar S.; Pranava M. and Marita R.A. (1996):**

Demonstration of the hyperglycemic action of *Momordica charantia* in a validated animal model of diabetes". *Pharmacol. Res*; 33: 1-4.

**Shahbazian, H. and Rezaii, I. (2013):**

Diabetic kidney disease; review of the current knowledge. *Journal of renal injury prevention*, 2(2):73-80.

**Sharoba, A. (2014):**

Nutritional value of spirulina and its use in the preparation of some complementary baby food formulas. *Journal of Agroalimentary Processes and Technologies*.;20(4):330–50.

**Sixabela P.; Chivandi E.; Badenhorst M. and Erlwanger K. (2011):**

The effects of dietary supplementation with *Spirulina platensis* in growing rats. *Asian Journal of Animal and Veterinary Advances*, 6(6): 609-617.

**Tabacco, A. (1979):**

Quantitative enzymatic colorimetric determination of blood urea nitrogen in serum or plasma. *Clin. Chem*, 25, 336-338.

**Tefera G.; Hailu D. and Tsegaye Z. (2016):**

Importance of arthrospira 8 (*Spirulina*) in sustainable development. *International Journal of Current Trend in Pharmacobiology and Medical Sciences* 1: 60-68.

**Tietze H. (2004):**

Micro Food Macro Blessing. 4th ed.India (New Delhi): *Jain Publishers*; p.7-48.

## **Naeem M. Rabeh et al**

---

**Vijayaraj P.; Muthukumar K.; Sabarirajan J. and Nachiappan V. (2013):**

Antihyperlipidemic activity of *Cassia auriculata* flowers in Triton WR 1339 induced hyperlipidemic rats. *Exp Toxicol Pathol*.

**Wahlefeld, A. (1974):**

Triglycerides determination after enzymatic hydrolysis. *In Methods of enzymatic analysis*. Academic Press, 4(2):1831-1835.

**Wang L.; Pan B.; Sheng J.; Xu J. and Hu Q. (2007):**

Antioxidant activity of *Spirulina platensis* extracts by supercritical carbon dioxide extraction. *Food Chemistry*.;105(1):36–41.

**Wild, S.; Roglic, G.; Green, A.; Sicree, R. and King, H. (2004):**

Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes care*, 27(5):1047-1053.

**Young, D. (2001):**

Effects of disease on clinical Lab. tests, AACC. *Press*, Washington, DC.

**Yusuf M.; Hassan M.; Abdel-Daim M.; El Nabtiti A.; Ahmed A.; Moawed S.; El-Sayed A. and Cui H. (2016):**

Value added by *Spirulina platensis* in two different diets on growth performance, gut microbiota, and meat quality of Japanese quails. *Vet World*. 9:1287– 1293.



تأثير السيبرولينا على مستوى جلوكوز الدم والقصور الكلوي في الفئران المصابة  
بداء السكري

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الملخص العربي

السيبرولينا هي طحالب خضراء مزرققة اللون لها فوائد طبية وغذائية بسبب العناصر الغذائية الغنية بها كما تعمل السيبرولينا كمنشطات كبدية ، وقائية من أمراض الكلى وكمضادات للأكسدة. هدفت هذه الدراسة إلى معرفة تأثير السيبرولينا على مستوى السكر في الدم الناتج عن الحقن بمادة الاستربتوزوتوسينالتي تؤثر على الكلى في الفئران. تم تقسيم 35 فأرا بشكل عشوائي إلى مجموعتين رئيسيتين: المجموعة الرئيسية الأولى (ن = 7) تم تغذيتها على النظام الغذائي الأساسي فقط لنهاية التجربة بمثابة مجموعة ضابطة سالبة ، المجموعة الرئيسية الثانية "تم إحداث داء السكري لها عن طريق الحقن بمادة STZ" (ن = 28) ثم تقسيمها إلى أربع مجموعات فرعية على النحو التالي: المجموعة الفرعية الأولى تم تغذيتها على النظام الغذائي الأساسي كمجموعة ضابطة موجبة. تم تغذية المجموعات 2 ، 3 ، 4) على النظام الغذائي الأساسي المدعم بالسيبرولينا المجففة بنسبة 2.5% و 5% و 7% على التوالي. في نهاية فترة التجربة (8 أسابيع) تم ذبح الفئران وتم جمع عينات الدم للحصول على سيرم الدم. أشارت النتائج إلى أن السيبرولينا تحتوي على بروتينات (56.80%) ودهون (8.16%) بالإضافة إلى العديد من المعادن والفيتامينات. التدعيم بالسيبرولينا ادي الي حدوث زيادة معنوية ( $P < 0.05$ ) في وزن الجسم النهائي ، معدل كفاءة الطعام ، معدل الزيادة في الوزن المكتسب مقارنة بفئران المجموعة الضابطة الموجبة. سجلت الفئران المعالجة بالسيبرولينا زيادة معنوية ( $P < 0.05$ ) في تركيز الأنسولين وانخفاض مستويات الجلوكوز بالإضافة إلى تحسن في وظائف الكلى. إلى جانب ذلك لوحظ انخفاض معنوي ( $P < 0.05$ ) في دهون الدم و المالونداهيد وعززت بشكل معنوي ( $P < 0.05$ ) تركيز الجلوتاثيون . الخلاصة: تشير النتائج إلى أن السيبرولينا يمكن أن يكون لها دور وقائي للاعتلال الكلوي الناتج عن مرض السكر .

الكلمات المفتاحية: السيبرولينا ، السكري ، الإجهاد التأكسدي ، الجلوكوز ، صورة الدهون