



## Role of *Spirulina platensis* on some Physiological Aspects in Paracetamol-Induced Subacute Toxicity in Male Rats

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### ABSTRACT

The last two decades witnessed focusing on the role of *spirulina* in protecting organs against oxidative stress and toxic metabolites. Therefore, this study aimed to detect its potential protection influence on the brain, liver, and kidney in paracetamol-induced subacute toxicity in male rats. Animals were administered paracetamol 500mg/kg body weight, 500 and 1000mg/kg body weight *Spirulina* in set with paracetamol for 28 constitutive days. *Spirulina* tablets were grounded and dissolved in distilled water then administered to rats 3 days before starting with paracetamol. Open field was used to probe neurotoxicity effects of paracetamol treated group and the combination of *Spirulina* and paracetamol treated groups in day 14<sup>th</sup> and 28<sup>th</sup> of treatment. Liver and kidney functions were tested at the end of treatment on day 29<sup>th</sup>; aspartate aminotransferase AST, alanine transaminase ALT, gamma-glutamyl transferase GGT, creatinine, and blood urea nitrogen BUN. Histopathological changes were tested in brain, liver, and kidney. High concentration of *spirulina* markedly affected on neurobehavioral activity represented by increasing number of rearing, grooming, and square crossing compared to paracetamol treated group. Liver enzymes levels in *Spirulina* and paracetamol treated animals were significantly decreased compared with only paracetamol treated animals. Kidney function in *Spirulina* and paracetamol treated animals was also noticeably decrease in comparison with only paracetamol treated animals. Histopathological changes caused by paracetamol in brain, liver, and kidney were reduced in animals received *Spirulina* 1000mg/kg body weight. The results of the current study detected that *Spirulina* has capacity to protect organs; including brain, liver, and kidney against paracetamol induced toxicity. This may due to *spirulina* richness with variety of nutrients, in particular, antioxidants.

**Keywords:** Hepatic cells, Neurons, Paracetamol, Rats, Renal cells, *Spirulina platensis*.

## INTRODUCTION

*Spirulina platensis* is a blue-green algae that possesses a filamentous spiral appearance. It is multi-cellular algae which revives in alkaline watery environments, in particular tropical regions. It gains its two colors, blue and green from existence of two compounds in these cells, phycocyanin and chlorophyll, respectively (Dillon *et al.*, 1995; Soni *et al.*, 2017). There is evidence that this alga was used as a source of food by an ancient Aztec civilization in Mexico about four centuries ago, and still producing *Spirulina* in the lake Chad for nutritional purposes (Abdulqader *et al.*, 2000). Within two recent decades, it has been explained that *Spirulina* is composed of diverse important nutrients including; protein, carbohydrates, essential amino acid, lipid, vitamins, minerals, antioxidants, and pigments. All these macro and micro-nutrients give significant characteristics to *Spirulina*, so it is broadly used in different life fields, including dietary supplementation and therapeutic purposes (Kay and Barton, 1991; Belay, 2002; Seyidoglu *et al.*, 2017; Anvar and Nowruzi, 2021).

Many studies including the utilization of rodents and in vitro the models have attributed that the antioxidant effects of *Spirulina* is due to its content of c-phycocyanin which resulted from scavenging free radicals produced by some chemicals including carbon tetrachloride (Romay *et al.*, 1998; Hirata *et al.*, 2000; Bhat and Madyastha, 2000).

*Spirulina* has also been shown to exhibit antioxidant properties in rats exposed to lead acetate for four weeks (El-Tantawy, 2016). Additional studies have also demonstrated *Spirulina* capacity in the maintenance of antioxidants level and inflammatory markers in treated rats with D-galactosamine, diclofenac, and kainic acid (Pérez-Juárez *et al.*, 2016; Rajbanshi *et al.*, 2016; Al-Qahtani and Binobead, 2019). These results explained an obvious association between antioxidant and anti-inflammatory effects of *Spirulina* against liver injury. By administration of Cyclophosphamide to rat, it has also been demonstrated that *Spirulina* displayed renal protection effects (Sinanoglu *et al.*, 2012).

Many chemicals and clinically used drugs characterized by being hepatotoxic, one of these drugs is paracetamol. Paracetamol is a broadly used all over the world as an analgesic and antipyretic drug. It has been demonstrated that paracetamol toxicity is linked to its metabolite, N-acetyl-p-benzoquinoneimine (NAPQI). NAPQI toxic effect is detoxified by an antioxidant glutathione when its level is low, however, high concentration of the metabolite results in engaged with cellular protein leading to liver damage (Henderson *et al.*, 2000).

Damage of hepatic cell is not only targeted by paracetamol but also kidney and brain are influenced by its toxicity. Two studies showed that paracetamol is toxic to renal tissue (Canayakin *et al.*, 2016; Hegazy *et al.*, 2021). It has also pointed out that paracetamol caused behavioral changes and pathological alteration comparing to control group in chicks and rats, respectively (Oksuz *et al.*, 2020; Al-Zubaidy, 2021). In the current study we aimed to investigate the potential protection role of *Spirulina* on hepatic, renal and neuronal tissue in male rats administered paracetamol for 28 constitutive days.

## MATERIALS AND METHODS

### Animals

Twenty male albino Wistar rats weighing 150-200g were obtained from animal house, college of pharmacy, Hawler Medical University, Erbil, Iraq. Rats were kept in plastic cages and added wood sawdust in an environment provided with standardized requirements including temperature 23°C, supplied with pellets of food and tap water. Also, they were provided with normal cycle light, 12 hrs. light and 12 hrs. dark. Ethical approval regarding treating lab animal was confirmed by Scientific and Ethic Committee members in the college of Health sciences on 31/10/2022, No 2D.

### Experiments Protocol

After adaptation of animals to standardized needs, they were randomly divided to 4 groups, each consisted of 5 rats. These groups included: (1) Control group; (2) Group received only

500mg/kg body weight of paracetamol; (3) Group received 500mg/kg body weight of *Spirulina* and 500mg/kg body weight of paracetamol; (4) Group received 1000mg/kg body weight of *Spirulina* and 500mg/kg body weight of paracetamol.

The control group was given distilled water containing propylene glycol. The second and third groups were administered *Spirulina* three days earlier before giving paracetamol. After dissolving 500mg or 1000mg in 10ml of distilled water, animal was administered *Spirulina* and 2 hours later were followed by administration of paracetamol for twenty-eight constitutive days. Last group was received only paracetamol (Rajbanshi *et al.*, 2016). Open field was conducted on day 14<sup>th</sup> and 28<sup>th</sup> day of administration (Alrawe and ALzubaidy, 2022). Blood samples and tissues were collected after 24 hours of fasting, on 29<sup>th</sup> day of experiment.

### **Chemical Substances and Material**

The required chemicals for the current study were purchased from different companies and these included, Acetaminophen as a powder form (paracetamol), Propylene Glycol, *Spirulina* as a tablet, each 250mg, Diethyl ether, Ketamine, and Xylazine.

### **Open Field**

A wooden box (100x100x50cm), consisting of 25 squares; each 20 cm was used to measure neurobehavioral activity of rats in two different periods of treatment, on day 14<sup>th</sup> and 28<sup>th</sup> of administration (Koob *et al.*, 2006). The test was carried out after 2 hours of paracetamol administration. The animal was placed in middle of the box for 5 minutes and was recorded by a camera. Parameters were taken represented; latency, square crossed, rearing, grooming, and number of defecations during the limited time.

### **Biochemical Parameters**

Rats were anesthetized with diethyl ether and blood samples were collected on day 29<sup>th</sup>, 24 hrs. after the last administration of *Spirulina* and paracetamol. By using separation gel coagulant tube, approximately 2 ml of blood was collected from retro-orbital plexus. The samples were centrifuged 5000 round per minute for 12 minutes. Thereafter serum was used for measuring ALT, AST, GGT, UBN, and creatinine with ALTL kit (Roche, Germany) via analyzer (Cobas c 111, Germany).

### **Histopathological Examination**

After 5 hrs. of blood collection, rats were again anesthetized with ketamine and xylazine with 50mg/kg body weight. and 5mg/kg body weight, respectively (Struck *et al.*, 2011). They were dissected for collection of brain, liver, and kidney to be prepared for histopathological examination. The target organs were placed in 10% neutral buffered formalin for 72hrs. This buffered formalin was prepared from the following substances with their quantities, 100 ml of formaldehyde (37%), 900ml of distilled water, 4.0 g of sodium phosphate monobasic NaH<sub>2</sub>P<sub>04</sub>, and 6.5 g of sodium phosphate dibasic (Na<sub>2</sub>HP<sub>04</sub>). The next step was embedding them in paraffin wax. Sections for each organ were deparaffinized, and dehydrated in descending grade of alcohol, 4 $\mu$  sections were prepared. The sections then stained with Hematoxylin and Eosin (H and E) (Luna, 1968). Histopathological changes were identified and reported for all samples using microscope (40x10X).

### **Statistical Analysis**

Data were analyzed by one-way analysis of variance (ANOVA) by using Statistical Package for the Social Sciences (SPSS for windows, release 17.0.1, 2008, SPSS Inc., Chicago, IL).

## **RESULTS**

### **Effect of *Spirulina* on Open Field Activity in Paracetamol Induced Neurotoxicity**

Paracetamol exhibited no significant alterations in neurobehavioral activity in treated rats compared to the control group on day 14<sup>th</sup> of the treatment as shown in (Table 1). Paracetamol caused significant decrease in number of squares crossed, rearing, and grooming in comparison to the control group (Table 2). On the 28<sup>th</sup> day of treatment, *Spirulina* at dose 1000mg/kg body weight caused restoration of neurobehavioral activity regarding rearing, grooming and crossed square compared with paracetamol treated rats (Table 2). No significant changes were observed in defecation and latency as shown in (Table 2). Surprisingly, on the last day of administration *Spirulina* at dose 500 mg/kg body weight, a significant decrease in number of rearing, grooming and square crossed to the control group was recorded (Table 2).

**Table 1: Effect of *Spirulina* (500 and 1000 mg/kg body weight in 5-minutes open field activity in paracetamol induced neurotoxicity in rats in the 14<sup>th</sup> day of treatment (n=5).**

Variables	Control	PAR 500 mg/kg	SPR 500mg/kg+ PAR 500 mg/kg	SPR 1000mg/kg+ PAR 500 mg/kg
Latency	1.4 ± 0.2	1.4 ± 0.2	1.6 ± 0.19	2.4 ± 0.43
Square Crossed	134 ± 5.32	132 ± 3.04	90 ± 2.15 <sup>*,a</sup>	144.2 ± 5.22 <sup>b</sup>
Rearing	12.0 ± 0.54	17.6 ± 0.73	10.8 ± 0.69 <sup>a</sup>	17.2 ± 0.95 <sup>b</sup>
Grooming	3.8 ± 0.42	3.6 ± 0.30	4.8 ± 0.29	2.8 ± 0.33 <sup>b</sup>
Defecation	1.4 ± 0.30	0.8 ± 0.11	1 ± 0.13	1.4 ± 0.30

Values represent means ± Slander error (n=5 animals per group). (\*) indicate a significant difference with control group (P≤0.05). (a) indicate a significant difference with group administered only paracetamol (P≤0.05). (b) indicate a significant difference with group treated with paracetamol and *Spirulina* 500mg/kg (P≤0.05). SPR stand for *Spirulina* and PAR stand for paracetamol.

**Table 2: Effect of *Spirulina* (500 and 1000 mg/kg body weight in 5-minutes open field activity in paracetamol induced neurotoxicity in rats in the 28<sup>th</sup> day of treatment (n=5).**

Variables	Control	PAR 500 mg/kg	SPR 500mg/kg + PAR 500 mg/kg	SPR1000mg/kg+ PAR 500 mg/kg
Latency	1.32 ± 0.69	0.475 ± 0.14	0.6 ± 0.10	0.6 ± 0.10
Square Crossed	110 ± 11.13	8 ± 0.37 <sup>*</sup>	34.6 ± 6.17 <sup>*</sup>	141 ± 8.51 <sup>a,b</sup>
Rearing	14.6 ± 4.25	1.25 ± 0.36 <sup>*</sup>	5.6 ± 2.54 <sup>*</sup>	12.8 ± 1.28 <sup>a</sup>
Grooming	2.8 ± 0.20	1 ± 0.22 <sup>*</sup>	3.6 ± 0.25 <sup>*,a</sup>	4.6 ± 0.31 <sup>*,a,b</sup>
Defecation	1.2 ± 0.74	0	1.2 ± 0.74	1.2 ± 0.74

Values are means ± Slander error (n=5 animals per group). (\*) indicate a significant difference with control group (P≤0.05). (a) indicate a significant difference with group administered only paracetamol (P≤0.05). (b) indicate a significant difference with group treated with paracetamol and *Spirulina* 500mg/kg (P≤0.05). SPR stand for *Spirulina* and PAR stand for paracetamol.

### **Effect of *Spirulina* on Liver and Kidney Function in Paracetamol Induced Liver and Kidney Damage**

Paracetamol at a dose of 500 mg/kg body weight caused significant increase in liver enzymes activities (AST, ALT, and GGT) compared to control group as shown in (Table 3). *Spirulina* at dose 500mg/kg body weight caused encore in liver enzymes activities including AST and ALT. *Spirulina* at 1000mg/kg body weight showed restoration of liver enzymes activities of GGT and

ALT compared to paracetamol treated animals (Table 3). Paracetamol also caused significant increase in kidney function represented by high level of urea in comparison to control group as mentioned in (Table 4). *Spirulina* at 500 and 1000mg/kg body weight caused decrease in urea level similar to that recorded in control group as shown in (Table 4). No significant alterations were observed for creatinine (Table 4).

**Table 3: Effect of *Spirulina* (500 and 1000 mg/kg body weight on liver enzymes in paracetamol induced hepatic toxicity (n=5).**

Groups	GGT	AST	ALT
Control	1.56 ± 0.19	150.70 ± 9.26	46.82 ± 0.72
PAR 500 mg/kg	2.54 ± 0.34 *	172.34 ± 4.04 *	65.34 ± 5.11 *
SPR 500mg/kg+ PAR 500 mg/kg	2.14 ± 0.37	150.24 ± 3.34 <sup>a</sup>	51.00 ± 1.17 <sup>a</sup>
SPR 1000mg/kg+ PAR 500 mg/kg	1.50 ± 0.30 <sup>a</sup>	156.38 ± 2.21	52.62 ± 4.09 <sup>a</sup>

Values are means ± Slandered error (n=5 animals per group). (\*) indicate a significant difference with control group (P≤0.05). (a) indicate a significant difference with group treated with only paracetamol (P≤0.05). SPR stand for *Spirulina* and PAR stand for paracetamol.

**Table 4: Effect of *Spirulina* (500 and 1000 mg/kg body weight on kidney function in paracetamol induced renal toxicity (n=5).**

Groups	Urea	Creatinine
Control	34.18 ± 0.84	0.32 ± 0.02
PAR 500 mg/kg	39.29 ± 1.27 *	0.38 ± 0.03
SPR 500mg/kg + PAR 500 mg/kg	35.23 ± 1.67	0.33 ± 0.03
SPR 1000mg/kg + PAR 500 mg/kg	35.08 ± 2.48	0.33 ± 0.02

Values are means ± Slandered error (n=5 animals per group). (\*) indicate a significant difference with control group (P≤0.05). (a) indicate a significant difference with group treated with only paracetamol (P≤0.05). SPR stand for *Spirulina* and PAR stand for paracetamol.

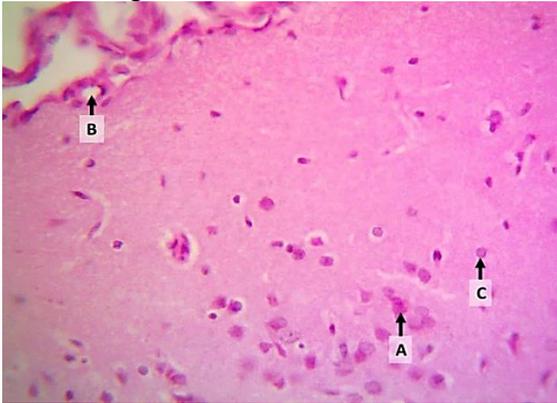
### Effect of *Spirulina* on Histopathological Changes Induced by Paracetamol

Fig. (1) shows the histological section of the brain of the control group which is represented by normal features of brain. Fig. (2) shows histological changes in brain of animals treated with only paracetamol which represented by vacuolization, perivascular edema, and gliosis. Fig. (3) represents the brains of animals treated with *Spirulina* at 500mg/kg body weight and paracetamol 500mg/kg body weight which showed cuffing, perivascular edema, and satellitosis. Fig. (4) represents the brain tissue in animals treated with *Spirulina* at 1000mg/kg body weight and paracetamol 500mg/kg body weight elucidated vacuolization, perivascular edema and satellitosis.

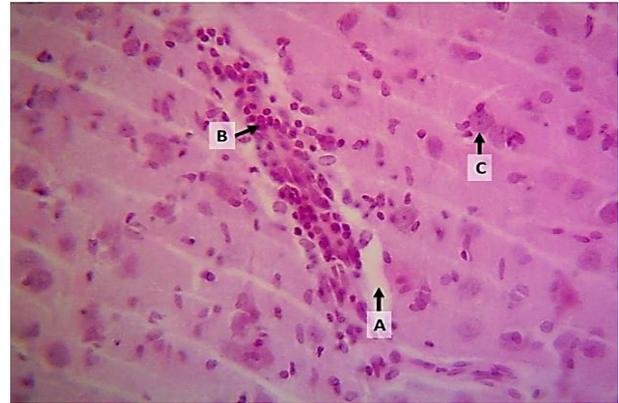
Fig. (5) exhibits histological section of rat liver of the control which is represented by normal features of liver. Fig. (6) shows histological changes in liver of animals treated with only paracetamol which is represented by necrosis of hepatocytes, inflammatory cells in the portal area, and hyperemia in the blood vessels. Histological section of animal treated with *Spirulina* at 500mg/kg body weight and paracetamol 500mg/kg body weight displayed hepatocyte necrosis, expansion of the sinusoids, and congestion of central vein Fig. (7). Histological examination of animals treated with *Spirulina* at 1000mg/kg body weight and paracetamol 500mg/kg body weight elucidated vacuolar degeneration and necrosis of hepatocytes Fig. (8).

Fig. (9) shows histological section of kidney of control group which is represented by normal architecture of renal tissue. The histological section of animal treated with only paracetamol showed atrophy of glomeruli, dilation of Bowman's space, degeneration, and necrosis of renal epithelial cells Fig. (10). Histological changes in animal treated with *Spirulina* at 1000mg/kg body weight and paracetamol 500mg/kg body weight demonstrated intact glomeruli, single cell degeneration and

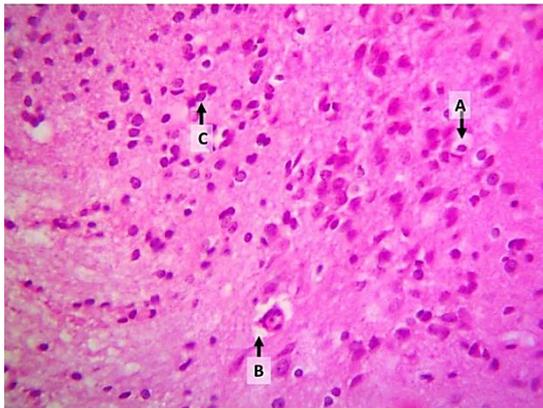
necrosis of renal epithelial cells Fig. (11). Renal section of *Spirulina* treated animals at 1000mg/kg body weight showed atrophy of glomeruli, dilation of Bowmans space, degeneration of renal epithelial cells Fig. (12).



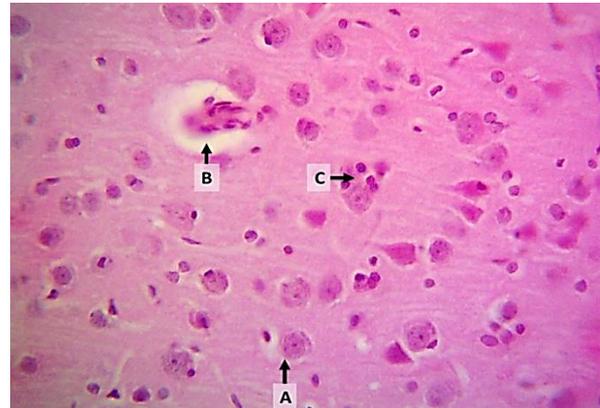
**Fig. 1:** Histological section of rat brain of the control group showing normal architecture of neurons(A), glial cells(B) and blood vessels(C). HE, 40×10X



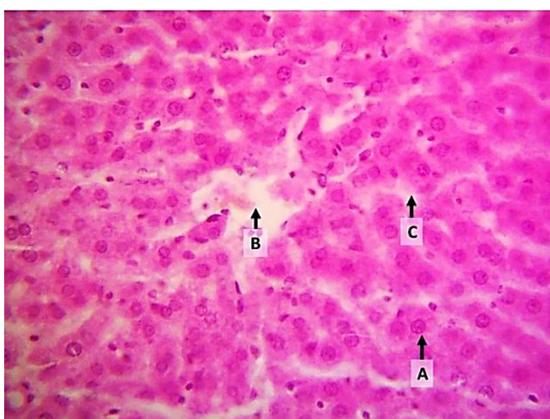
**Fig. 3:** Histological section of rat brain treated with *spirulina* 500mg and paracetamol 500mg/kg body weight showing cuffing(A), perivascular edema(B) and satellitosis(C). HE, 40×10X



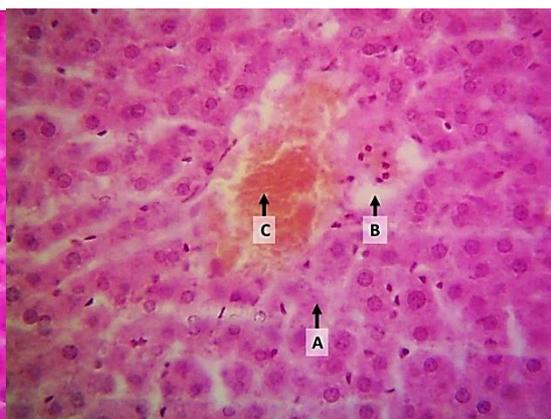
**Fig. 2:** Histological section of rat brain treated with paracetamol 500mg/kg body weight showing vacuolization(A), perivascular edema(B) and gliosis (C). HE, 40×10X



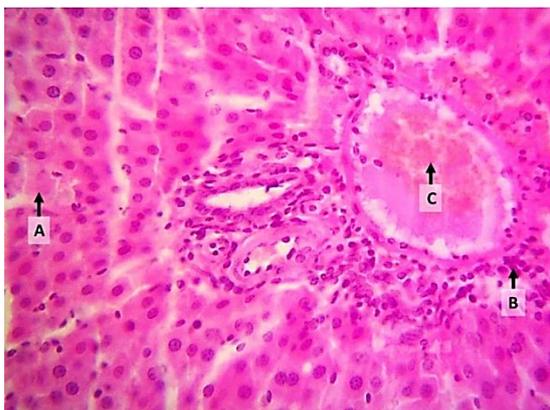
**Fig. 4:** Histological section of rat brain treated with *spirulina* 1000mg and paracetamol 500mg/kg body weight showing vacuolization(A), perivascular edema(B) and satellitosis(C). HE, 40×10X



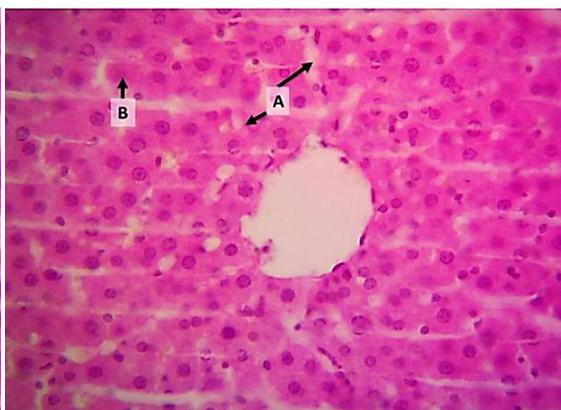
**Fig. 5:** Histological section of rat liver of the control group showing normal architecture represented by hepatocytes(A), central vein(B) and sinusoids(C). HE, 40×10X



**Fig. 7:** Histological section of rat liver treated with *Spirulina* 500mg and paracetamol 500mg/kg body weight showing necrosis of the hepatocytes(A), inflammatory cells in the portal area(B) and hyperemia in the blood vessels(C). HE, 40×10X



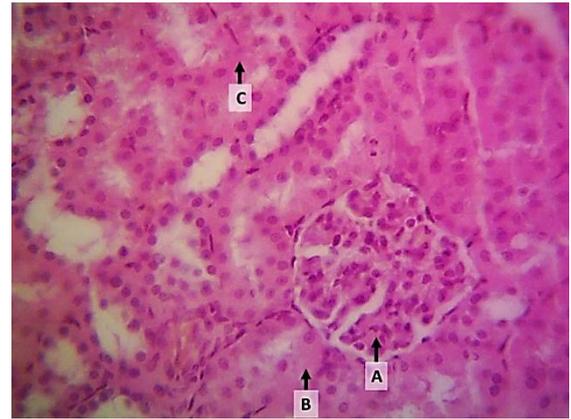
**Fig. 6:** Histological section of rat liver treated with paracetamol 500mg/kg body weight showing necrosis of the hepatocytes(A), inflammatory cells in the portal area(B) and hyperemia in the blood vessels(C). HE, 40×10X



**Fig. 8:** Histological section of rat liver treated with *Spirulina* 1000mg and paracetamol 500mg/kg body weight showing vacuolar degeneration(A) and necrosis(B) of the hepatocytes. HE, 40×10X



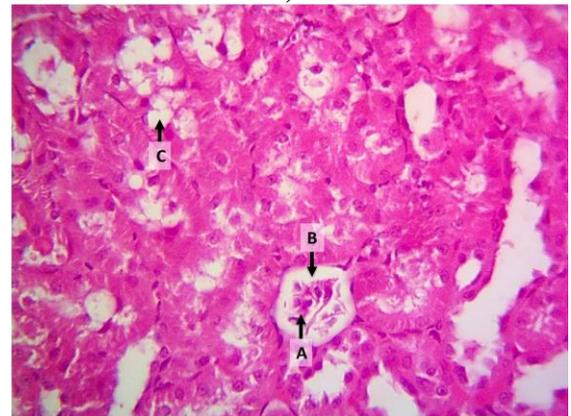
**Fig. 9:** Histological section of rat kidney of the control group showing normal architecture of glomeruli(A), proximal renal tubules(B) and distal renal tubules(C). HE, 40×10X



**Fig. 11:** Histological section of rat kidney treated with *spirulina* 500mg and paracetamol 500mg/kg body weight showing intact glomeruli(A), single cell degeneration(B) and necrosis(C) of epithelial cells lining renal tubules. HE, 40×10X



**Fig. 10:** Histological section of rat kidney treated with paracetamol 500mg/kg body weight showing atrophy of glomeruli(A), dilatation of Bowman's space(B), degeneration(C) and necrosis(D) of epithelial cells lining renal tubules. HE, 40×10X



**Fig. 12:** Histological section of rat kidney treated with *spirulina* 1000mg and paracetamol 500mg/kg body weight showing atrophy of glomeruli(A), dilatation of Bowman's space (B), degeneration of epithelial cells lining renal tubules (C). HE, 40×10X

## DISCUSSION

As a natural anti-oxidant source and rich with variety of nutrients, *Spirulina* has been widely used in diverse fields including food industry and pharmaceutical preparations. The objective of this research was to detect protection role of *Spirulina* in rats administered paracetamol for 28 continuous days.

It has been shown that paracetamol caused damage to some organs including liver, kidney and brain (Elkomy *et al.*, 2016; Essawy *et al.*, 2017; El Menyiy *et al.*, 2018). Therefore, it was administered to male rats to induce toxicity.

Among crucial neurobehavioral tests to examine rodent exploratory activity and chicks which are subjected to various drugs induce neurons toxicity, is an open-field test (Abawy and Alzubaidy, 2023; ALzubaidy *et al.*, 2023). On the 28<sup>th</sup> day of treatment, paracetamol treated animals showed alteration in their behavior in the open field test. These results reflect that paracetamol can cross blood brain barrier and trigger depressive effects by altering neurotransmitter in the brain. A study has demonstrated that paracetamol caused an increase in level of inhibitory amino acid, gamma amino butyric acid in cortex of rat brain, which interprets its effect on animal behavior (Blecharz-Klin *et al.*, 2014). In agreement with our study, a recent study has expounded that paracetamol caused behavioral changes in some variables in an open-field test in a7-day old chicks treated with 100 and 200mg/kg (Al-Zubaidy, 2021). No effect was observed in behavioral changes in this group on 14<sup>th</sup> day of treatment, which might be due to ability of rat liver to effectively excrete paracetamol metabolite. This toxic effect of paracetamol on rat brain may be due to accumulation of paracetamol metabolites and inability to effectively excreted.

*Spirulina* treated animals with 1000mg/kg body weight demonstrated restoration of neurobehavioral activity in comparison to paracetamol treated group. This may be attributed to *Spirulina* richness with antioxidant activity that neutralized the effect of paracetamol metabolite NAPQI. A couple of studies have revealed that *Spirulina* ability in exhibiting neuron protection effect in rabbit brain against aspartame induced oxidative stress through its antioxidant and anti-inflammatory properties (Attiya *et al.*, 2019; Attiya, 2022). These results were consistent with results of the current study in term of neuroprotection effects. *Spirulina* protection effect on neurons cell was also confirmed by decreasing inflammatory mediator's interleukin IL-1 $\beta$  and TNF- $\alpha$  in microglia cell culture of one-day rat poppies exposed to lipopolysaccharide (Piovan *et al.*, 2021).

In term of the biochemical parameters, paracetamol treated animals have shown liver damage which characterized by significant increase in enzyme activities (GGT, AST, and ALT). Paracetamol also caused kidney damage which represented by increased level of urea compared to the control animals. The activities of liver enzymes were restored by *Spirulina* indicating its hepatoprotection effect. Urea also was modulated in animals administered *Spirulina* confirming its renal protection role against paracetamol induced toxicity. The results of current research were supported by an investigation demonstrated that *Spirulina* effectively reversed liver enzyme activities (ALT, AST, and AIP) in diclofenac-induced hepatotoxicity in rats (Rajbanshi *et al.*, 2016). A recent study has also revealed that liver enzyme activities were restored by spirulina depending on its concentration. *Spirulina* also showed its capacity to normalize kidney function by decreasing urea level in comparison to paracetamol-induced toxicity animals (Bin-Jumah *et al.*, 2021). The powerful effect of *Spirulina* in reversing liver injury and kidney damage may attribute to its compositions of antioxidant compounds including phycocyanin and other related compounds.

Regarding histopathological results, paracetamol caused histopathological alteration in the rat brain. (Posadas *et al.*, 2010) have shown that paracetamol caused neuronal death in rat cortex as a result of increase releasing of neuronal cytochrome P450 in particular CYP2E1. Neuron death was found to be due to release of cytochrome C and activation of caspase 3 via mitochondria. An additional study has demonstrated paracetamol overdose triggered histopathological changes in rat brain (Essawy *et al.*, 2017). *Spirulina* treated animals have revealed improvement in the brain sections compared to paracetamol treated animal. The findings of the current study were consistent with group of researchers who confirmed that *Spirulina* decreased neuronal death in CA3 hippocampal part of mice brain treated with kainic acid (Pérez-Juárez *et al.*, 2016). A recent investigation has also shown that *Spirulina* reversed brain damage in Alzheimer's induced rats (Abdelghany *et al.*, 2023). *Spirulina* neuroprotective property may be due to its content of antioxidant substance.

Liver and kidney histological sections showed that paracetamol triggered injury in hepatic and renal cells. From previous studies, it is obvious that paracetamol displayed histopathological alterations on rat liver and kidney (Mahmood *et al.*, 2014; Hegazy *et al.*, 2021). *Spirulina* high dose

has elucidated its ability to improve histopathological sections of the rat liver and kidney treated with paracetamol indicating its protection role against paracetamol metabolites. *Spirulina* hepatoprotection role in our work was supported by an investigation that demonstrated *Spirulina* effectiveness in improving liver histological sections of animal injected with diclofenac sodium (Rajbanshi *et al.*, 2016). Our finding was in agreement with a study demonstrated that 6% and 9% *Spirulina* extraction improved damaged hepatic cells in comparison to rat liver treated with D-galactosamine (Al-Qahtani and Binobead, 2019). An additional recent study has also confirmed *Spirulina* capacity to provide hepatoprotection effect in rat liver treated with ethanol (Pérez-Juárez *et al.*, 2022).

Similarly, to hepatic protection properties of *Spirulina*, it also exhibited renal protection as well in the current study. The results of this work were in agreement with two studies that found *Spirulina* amelioration effects in renal histopathological alterations in rats administered cyclophosphamide medicine, and against  $\gamma$ -irradiation and thioacetamide (Sinanoglu *et al.*, 2012; Salem and Ismail, 2021). Depending on the results of the current study, *Spirulina* can protect organs damage against the toxic metabolite of paracetamol.

### CONCLUSIONS

Administration of *Spirulina* in paracetamol-induced toxicity in the rat brain, liver, and kidney exhibited its capacity to protect these tissues against oxidative stress produced by paracetamol overdose. *Spirulina* was able to restore behavioral activity, biochemical parameters, and histopathological alterations. As a results of *Spirulina* protection role, it can be used in paracetamol toxicity for its antioxidant activity and anti-inflammatory properties.

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## دور السبيرولينا بلاتينسيس في بعض الجوانب الفسلجية في ذكور الجرذان المعرضة لسمية تحت الحادة المستحثة بالباراسيتامول

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### الملخص

في العقدين الاخيرين تم التركيز على دور السبيرولينا في حماية الاعضاء ضد الجهد التاكسدي والنواتج الايضية السامة بسبب امتلاكها خصائص مضادة للاكسدة. ولذلك هدفت الدراسة الحالية الى الكشف الوقائي للسبيرولينا على بعض النواحي الفسلجية من خلال حماية كل من وظائف الدماغ، الكبد، والكلية ضد السمية تحت الحادة والمستحثة بالباراسيتامول. اعطاء السبيرولينا بتركيز عالي 1000ملغم/ كغم وزن الجسم أثر بشكل واضح على النشاط السلوكي العصبي، تمثلت بزيادة عدد مرات الوقوف، الحكة، والمربعات التي تم اجتيازها مقارنة مع المجموعة المعاملة بالباراسيتامول فقط. أثرت السبيرولينا ايضا بشكل ملحوظ على فعالية انزيمات الكبد والتي تمثلت بانخفاض مستوياتها في الحيوانات المعاملة بالسبيرولينا مع الباراسيتامول مقارنة مع الحيوانات المعاملة بالباراسيتامول فقط. كذلك بالنسبة لوظائف الكلية، الحيوانات المعاملة بالسبيرولينا والباراسيتامول اظهرت انخفاضا ملحوظا في مستوى اليوريا مقارنة مع المجموعة المعاملة بالباراسيتامول فقط. اظهرت السبيرولينا ايضا تحسن في المقاطع النسيجية المرضية لكل من انسجة الدماغ، الكبد، والكلية مقارنة مع المقاطع النسيجية المرضية للحيوانات المعاملة مع الباراسيتامول فقط. النتائج في الدراسة الحالية اثبتت بان السبيرولينا اظهرت حماية في كل من الدماغ، الكبد، والكلية ضد سمية الباراسيتامول، وقد يرجع ذلك الى غنى السبيرولينا بمجموعة متنوعة من العناصر الغذائية، وخاصة، مضادات الاكسدة.

**الكلمات الدالة:** خلايا الكبد، الخلايا العصبية، باراسيتامول، الجرذان، خلايا الكلية، سبيرولينا بلاتينسيس.