

# **Renal Protective**

Fundam Clin Pharmacol. 2006 Apr;20(2):121-8.

## **Effect of Spirulina, a blue green algae, on gentamicin-induced oxidative stress and renal dysfunction in rats.**

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Gentamicin (GM), an aminoglycoside, is widely employed in clinical practice for the treatment of serious Gram-negative infections. The clinical utility of GM is limited by the frequent incidence of acute renal failure. Experimental evidences suggest that oxidative and nitrosative stress play an important role in GM nephrotoxicity. Spirulina fusiformis is a blue green algae with potent free radical scavenging properties. The present study was designed to investigate renoprotective potential of *S. fusiformis*, against GM-induced oxidative stress and renal dysfunction. Spirulina fusiformis (500, 1000, 1500 mg/kg, p.o.) was administered 2 days before and 8 days concurrently with GM (100 mg/kg, i.p.). Renal injury was assessed by measuring serum creatinine, blood urea nitrogen and creatinine clearance and serum nitrite levels. Renal oxidative stress was determined by renal malondialdehyde levels, reduced glutathione levels and by enzymatic activity of superoxide dismutase (SOD) and catalase. Chronic GM administration resulted in marked renal oxidative and nitrosative stress and significantly deranged renal functions. Treatment with *S. fusiformis* significantly and dose-dependently restored renal functions, reduced lipid peroxidation and enhanced reduced glutathione levels, SOD and catalase activities. The results of present study clearly demonstrate the pivotal role of reactive oxygen species and their relation to renal dysfunction and point to the therapeutic potential of *S. fusiformis* in GM-induced nephrotoxicity.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 16573712 [PubMed - indexed for MEDLINE]

## **Salubrious effect of C-phycoyanin against oxalate-mediated renal cell injury.**

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**BACKGROUND:** C-phycoyanin, a biliprotein pigment found in some blue green algae (*Spirulina platensis*) with nutritional and medicinal properties, was investigated for its efficacy on sodium oxalate-induced nephrotoxicity in experimentally induced urolithic rats. **METHODS:** Male Wistar rats were divided into four groups. Hyperoxaluria was induced in two of these groups by intraperitoneal infusion of sodium oxalate (70 mg/kg), and a pretreatment of phycocyanin (100 mg/kg) as a single oral dosage was given to one of these groups by 1 h prior to sodium oxalate infusion challenges. The study also encompasses an untreated control group and a phycocyanin-alone treated drug control group. The extent of lipid peroxidation (LPO) was evaluated in terms of renal concentrations of MDA, conjugated diene and hydroperoxides. The following assay was performed in the renal tissue (a) antioxidant enzymes such as superoxide dismutase (SOD) and catalase, (b) glutathione metabolizing enzymes such as glutathione peroxidase (GPx), glutathione reductase (GR), glutathione-S-transferase (GST) and glucose 6-phosphate dehydrogenase (G6PD), (c) the low molecular weight antioxidants (GSH, vitamins E and C) and protein carbonyl content. **RESULTS:** The increased concentrations of MDA, conjugated diene and hydroperoxide (index of the lipid peroxidation) were controlled ( $P < 0.001$ ) in the phycocyanin-pretreated group. At the outset, the low molecular weight antioxidants were appreciably increased ( $P < 0.001$ ), whereas the tissue protein carbonyl concentration was decreased ( $P < 0.001$ ), suggesting that phycocyanin provides protection to renal cell antioxidants. It was noticed that the activities of antioxidant enzymes and glutathione metabolizing enzymes were considerably stabilized in rats pretreated with phycocyanin. **CONCLUSION:** We suggest that phycocyanin protects the integrity of the renal cell by stabilizing the free radical mediated LPO and protein carbonyl, as well as low molecular weight antioxidants and antioxidant enzymes in renal cells. Thus, the present analysis reveals that the antioxidant nature of C-phycoyanin protects the renal cell against oxalate-induced injury and may be a nephroprotective agent.

Publication Types:

- Comparative Study
- Research Support, Non-U.S. Gov't

PMID: 15369755 [PubMed - indexed for MEDLINE]

Renal Protective

## **Prophylactic role of phycocyanin: a study of oxalate mediated renal cell injury.**

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Oxalate induced renal calculi formation and the associated renal injury is thought to be caused by free radical mediated mechanisms. An in vivo model was used to investigate the effect of phycocyanin (from *Spirulina platensis*), a known antioxidant, against calcium oxalate urolithiasis. Male Wistar rats were divided into four groups. Hyperoxaluria was induced in two of these groups by intraperitoneal infusion of sodium oxalate (70 mg/kg) and a pretreatment of phycocyanin (100 mg/kg) as a single oral dosage was given, 1h prior to sodium oxalate infusion. An untreated control and drug control (phycocyanin alone) were also included in the study. We observed that phycocyanin significantly controlled the early biochemical changes in calcium oxalate stone formation. The antiurolithic nature of the drug was evaluated by the assessment of urinary risk factors and light microscopic observation of urinary crystals. Renal tubular damage as divulged by urinary marker enzymes (alkaline phosphatase, acid phosphatase and gamma-glutamyl transferase) and histopathological observations such as decreased tubulointerstitial, tubular dilatation and mononuclear inflammatory cells, indicated that renal damage was minimised in drug-pretreated group. Oxalate levels ( $P < 0.001$ ) and lipid peroxidation ( $P < 0.001$ ) in kidney tissue were significantly controlled by drug pretreatment, suggesting the ability of phycocyanin to quench the free radicals, thereby preventing the lipid peroxidation mediated tissue damage and oxalate entry. This accounts for the prevention of CaOx stones. Thus, the present analysis revealed the antioxidant and antiurolithic potential of phycocyanin thereby projecting it as a promising therapeutic agent against renal cell injury associated kidney stone formation.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 15294440 [PubMed - indexed for MEDLINE]

**Oxalate mediated nephronal impairment and its inhibition by c-phycocyanin: a study on urolithic rats.**

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The assumption of oxidative stress as a mechanism in oxalate induced renal damage suggests that antioxidants might play a beneficial role against oxalate toxicity. An in vivo model was used to investigate the effect of C-phycocyanin (from aquatic micro algae; *Spirulina* spp.), a known antioxidant, against calcium oxalate urolithiasis. Hyperoxaluria was induced in two of the 4 groups of Wistar albino rats (n = 6 in each) by intraperitoneally injecting sodium oxalate (70 mg/kg body weight). A pretreatment of phycocyanin (100 mg/kg body weight) as a single oral dosage was given, one hour prior to oxalate challenge. An untreated control and drug control (phycocyanin alone) were employed. Phycocyanin administration resulted in a significant improvement (p < 0.001) in the thiol content of renal tissue and RBC lysate via increasing glutathione and reducing malondialdehyde levels in the plasma of oxalate induced rats (p < 0.001), indicating phycocyanin's antioxidant effect on oxalate mediated oxidative stress. Administering phycocyanin after oxalate treatment significantly increased catalase and glucose-6-phosphate dehydrogenase activity (p < 0.001) in RBC lysate suggesting phycocyanin as a free radical quencher. Assessing calcium oxalate crystal retention in renal tissue using polarization microscopy and renal ultrastructure by electron microscopy reveals normal features in phycocyanin--pretreated groups. Thus the study presents positive pharmacological implications of phycocyanin against oxalate mediated nephronal impairment and warrants further work to tap this potential aquatic resource for its medicinal application.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 16477383 [PubMed - indexed for MEDLINE]

## **Evaluation of protective efficacy of *Spirulina fusiformis* against mercury induced nephrotoxicity in Swiss albino mice.**

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The toxicity of mercury to animals and man is well established and this depends greatly on the form of the mercury compounds. In most animals' species, including man, the kidney is the main site of deposition of inorganic mercury and target organ for its toxicity. In the present study *Spirulina fusiformis* (a cyanobacterium, belongs to family--Oscillatoriaceae) has been investigated as a possible modifier of mercury induced renal damages in Swiss albino mice. Animals were divided into four groups. (i) Control group--only vehicle (0.9% NaCl) was administered as i.p. (ii) HgCl<sub>2</sub> treated group--5.0 mg/kg b.wt. HgCl<sub>2</sub> was administered as i.p. (iii) *Spirulina* treated group--800 mg/kg b.wt. *Spirulina* extract was administered orally. (iv) Combination group--*S. fusiformis* was administered 10 days before mercuric chloride administration and continued upto 30 days after mercuric chloride administration (5.0 mg/kg b.wt.). The animals were autopsied on 1, 3, 7, 15 and 30 days after treatment and the activity of alkaline phosphatase (ALP), acid phosphatase (ACP), lactate dehydrogenase (LDH) and MDA (malondialdehyde) level were measured in kidney homogenates. The results indicated that there was a time-dependent significant enhancement in MDA content and ACP activity and decrease in LDH and ALP activity observed after HgCl<sub>2</sub> treatment. Mercury intoxication also induces pathological alterations in the kidney such as degeneration of glomerulus, proximal and distal tubules. A dose-dependent mortality was also observed following administration of different doses of HgCl<sub>2</sub>. In combined treatment of *Spirulina* with HgCl<sub>2</sub>, a significant decrease in MDA content and ACP activity and elevation in LDH and ALP activity was observed as compared to HgCl<sub>2</sub> treated group. *Spirulina* pre- and post-treatment with mercury also significantly reduces pathological alterations in kidney. Thus, the results from the present study suggest that *S. fusiformis* can significantly modify the renal damages against mercuric chloride induced toxicity.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 17215067 [PubMed - indexed for MEDLINE]

**Spirulina attenuates cyclosporine-induced nephrotoxicity in rats.**

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Cyclosporine (CsA) causes a dose-related decrease in renal function in experimental animals and humans. The generation of reactive oxygen species (ROS) has been implicated in CsA-induced nephrotoxicity. It was previously shown that Spirulina, a blue-green algae, with antioxidant properties effectively attenuated the doxorubicin-induced cardiotoxicity in mice and cisplatin-induced nephrotoxicity in rat. The present study investigated the nephroprotective role of Spirulina against CsA-induced nephrotoxicity in rats. Spirulina (500 mg kg<sup>-1</sup> b.w.) was administered orally for 3 days before and 14 days concurrently with CsA (50 mg kg<sup>-1</sup> b.w.). Rats treated with CsA showed nephrotoxicity as evidenced from a significant elevation in plasma urea, creatinine, urinary N-acetyl-beta-D-glucosaminidase (beta-NAG) and a decrease in creatinine and lithium clearance. Pretreatment with Spirulina protected the rats from CsA-induced nephrotoxicity. The CsA-induced rise in plasma urea and creatinine and the decrease in creatinine and lithium clearance were attenuated by Spirulina. There was a significant increase in plasma and kidney tissue MDA with CsA. Spirulina prevented the rise in plasma and kidney tissue MDA. Histopathology of the kidney from CsA-treated rats showed severe isometric vacuolization and widening of the interstitium. However, pretreatment with Spirulina prevented such changes, and the kidney morphology was comparable to that of the control. Spirulina treatment did not alter the blood CsA levels. These results suggest that Spirulina has a protective effect against nephrotoxicity induced by CsA. This study further supports the crucial role of the antioxidant nature of Spirulina in protecting against CsA-induced oxidative stress. Copyright 2006 John Wiley & Sons, Ltd.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 16858688 [PubMed - indexed for MEDLINE]

Ren Fail. 2006;28(3):247-54.

**Renoprotective effect of *Spirulina fusiformis* on cisplatin-induced oxidative stress and renal dysfunction in rats.**

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Cisplatin is an effective chemotherapeutic agent used in the treatment of a wide array of both pediatric and adult malignancies. Dose-dependent and cumulative nephrotoxicity is the major toxicity of this compound, sometimes requiring a reduction in dose or discontinuation of treatment. Recent evidences have implicated oxidative and nitrosative stress in cisplatin-induced nephrotoxicity. *Spirulina fusiformis*, blue-green algae, is claimed to be a potential antioxidant. The present study was designed to explore the renoprotective potential of *Spirulina fusiformis* against cisplatin-induced oxidative stress and renal dysfunction. *Spirulina fusiformis* (500,1000,1500 mg/kg(-1) p.o.) was administered 2 days before and until 3 days after cisplatin challenge (5 mg/kg(-1) i.p.). Renal injury was assessed by measuring serum creatinine, blood urea nitrogen, creatinine and urea clearance, and serum nitrite levels. Renal oxidative stress was determined by renal TBARS levels, reduced glutathione levels, and by enzymatic activity of superoxide dismutase and catalase. A single dose of cisplatin produced marked renal oxidative and nitrosative stress and significantly deranged renal functions. Chronic *Spirulina fusiformis* treatment significantly and dose-dependently restored renal functions, reduced lipid peroxidation, and enhanced reduced glutathione levels, superoxide dismutase, and catalase activities. The results of the present study clearly demonstrate the pivotal role of reactive oxygen species and their relation to renal dysfunction and point to the therapeutic potential of *Spirulina fusiformis* in cisplatin-induced nephrotoxicity.

PMID: 16703798 [PubMed - indexed for MEDLINE]

## **Protection against cisplatin-induced nephrotoxicity by Spirulina in rats.**

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**PURPOSE:** Cisplatin (CP)-induced nephrotoxicity is associated with the increased generation of reactive oxygen metabolites and lipid peroxidation in kidney, caused by the decreased levels of antioxidants and antioxidant enzymes. The purpose of this study was to evaluate the role of Spirulina, blue-green alga with antioxidant properties, in the protection of cisplatin-induced nephrotoxicity in rat. **METHODS:** Rats were treated with CP (6 mg/kg bw, single dose, intraperitoneally). Spirulina (1,000 mg/kg) was administered orally for 8 days and CP treatment was given on day 4. Nephrotoxicity was assessed, 6 days after the CP treatment, by measuring plasma urea, creatinine, urinary N-acetyl-(D-glucosaminidase) (beta-NAG) and histopathology of kidney. **RESULTS:** Rats treated with CP showed marked nephrotoxicity as evidenced from the significant elevation in plasma urea, creatinine and urinary beta-NAG. Histological assessment revealed marked proximal tubular necrosis and extensive epithelial vacuolization in the kidney of CP-treated rats. Superoxide dismutase, catalase and glutathione peroxidase were decreased and lipid peroxidation was increased in kidney tissue. Pretreatment with Spirulina protected the rats from CP-induced nephrotoxicity. The rise in plasma urea, creatinine, urinary beta-NAG, plasma and kidney tissue MDA and histomorphological changes were significantly attenuated by Spirulina. In vitro studies using human ovarian cancer cells revealed that Spirulina did not interfere with the cytotoxic effects of CP on tumor cells. **CONCLUSIONS:** In summary, Spirulina significantly protected the CP-induced nephrotoxicity through its antioxidant properties.

Publication Types:

- Research Support, N.I.H., Extramural

PMID: 16552571 [PubMed - indexed for MEDLINE]

**Spirulina platensis protects against renal injury in rats with gentamicin-induced acute tubular necrosis.**

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The present study was carried out to evaluate the renoprotective antioxidant effect of *Spirulina platensis* on gentamicin-induced acute tubular necrosis in rats. Albino-Wistar rats, (9male and 9 female), weighing approximately 250 g, were used for this study. Rats were randomly assigned to three equal groups. Control group received 0,9 % sodium chloride intraperitoneally for 7 days at the same volume as gentamicin group. Gentamicin group was treated intraperitoneally with gentamicin, 80 mg/kg daily for 7 days. Gentamicin+spirulina group received *Spirulina platensis* 1000 mg/kg orally 2 days before and 7 days concurrently with gentamicin (80 mg/kg i.p.). Nephrotoxicity was assessed by measuring plasma nitrite concentration, stabile metabolic product of nitric oxide with oxygen. Plasma nitrite concentration was determined by colorimetric method using Griess reaction. For histological analysis kidney specimens were stained with hematoxylin-eosin (HE) and periodic acid-Schiff (PAS) stain. Plasma nitrite concentration and the level of kidney damage were significantly higher in gentamicin group in comparison both to the control and gentamicin+spirulina group. *Spirulina platensis* significantly lowered the plasma nitrite level and attenuated histomorphological changes related to renal injury caused by gentamicin. Thus, the results from present study suggest that *Spirulina platensis* has renoprotective potential in gentamicin-induced acute tubular necrosis possibly due to its antioxidant properties.

PMID: 19125703 [PubMed - indexed for MEDLINE]

## **Spirulina platensis protects against gentamicin-induced nephrotoxicity in rats.**

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The present study aimed to investigate the protective effect of *Spirulina platensis* (SP) on gentamicin sulphate (GS)-induced changes in the levels of lipid peroxidation and endogenous antioxidants in the kidney of rats. Sprague-Dawley rats were treated in separate groups as follows for 7 consecutive days: control (C), gentamicin sulphate (100 mg/kg i.p.) (GS), *Spirulina platensis* (1000 mg/kg orally) (SP) and *Spirulina platensis* (1000 mg/kg orally) plus gentamicin sulphate (100 mg/kg i.p.) (SP + GS). The degree of protection was evaluated by determining the effects of *Spirulina platensis* on malondialdehyde (MDA), glutathione (GSH), superoxide dismutase (SOD), glutathione peroxidase (GPX) and nitric oxide (NO), and plasma creatinine and urea levels were estimated in kidney homogenates to evaluate antioxidant activity, and the kidney was histologically examined as well. *Spirulina platensis* elicited significant nephroprotective activity by decreasing lipid peroxidation (MDA) and elevated the levels of GSH, SOD, GPX, NO, creatinine and urea. Furthermore, these biochemical observations were supplemented by histological examination of the rat kidneys. In conclusion, the present study indicates a very important role of reactive oxygen species (ROS) and the relation to renal dysfunction and point to the therapeutic potential of *Spirulina platensis* in gentamicin sulphate induced nephrotoxicity.

PMID: 18690652 [PubMed - indexed for MEDLINE]