Antioxidant and hepatoprotective activity of *Aphanizomenon flos-aquae* Linn against paracetamol intoxication in rats

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Paracetamol caused liver damage as evident by significant increase in the activities of aspartate and alanine transferases. There were general statistically significant losses in the activities of superoxide dismutase, catalase, glutathione peroxidase and glutathione transferase and an increase in thiobarbituric acid reactive substances in the liver of paracetamol treated group compared with the control group. However, treatment with ethanol extract of *A. flos-aquae* (EEAFA) was able to counteract these effects. Protection offered by silymarin (standard reference drug) seemed relatively greater. The results suggest that EEAFA can act as hepatoprotective agent against paracetamol induced toxicity as an antioxidant.

**Keywords:** Antioxidants, *Aphanizomenon flos-aquae*, Hepatoprotection, Paracetamol, Reactive oxygen species

Reactive oxygen species (ROS) are generated spontaneously in cells during metabolism and are implicated in the aetiology of different degenerative diseases, such as heart diseases, stroke, rheumatoid arthritis, diabetes and cancer. In addition to chronic diseases, oxidative stress can also play a fundamental role in the acute hepatotoxicity of several drugs, including the world-widely used analgesic and antipyretic paracetamol. Acetaminophen is widely used over-the-counter drug for analgesic and antipyretic effects. Its use in overdose (suicidal or accidental) or with chronic alcohol abuse causes fulminant liver failure and contributes significantly to intensive care unit admissions and cost of hospitalization. Acetaminophen induced hepatic failure is the second leading cause of liver transplantation and accounts to considerable levels of morbidity and mortality. The hepatotoxicity is the result of the formation of a toxic metabolite, *N*-acetyl-*p*-benzoquinoneimine (NAPQI) by cytochrome P4502E1 that can induce a dose dependent depletion of intracellular glutathione and perturbations of calcium homeostasis. Presently, *N*acetylcysteine (NAC) is the treatment option since it increases glutathione levels in the hepatic cytosol and mitochondria to detoxify the highly reactive and cytotoxic NAPQI. Besides, selective inhibitors of Cytochrome P4502E1 that inhibit NAPQI formation are under investigation in managing acetaminophen-associated hepatotoxicity.

Chronic viral hepatitis B and C, alcoholic liver disease, non-alcoholic fatty liver disease, and hepatocellular carcinoma are major problems which still remain unresolved. Therapies developed along the principles of modern medicine are often limited in their efficacy, carry the risk of adverse effects, and are often too costly, especially for the developing world. Therefore, treating liver diseases with natural compounds, which are easily available and do not require laborious pharmaceutical synthesis seems highly attractive.

Increased use of synthetic drug therapy leads to many side effects and undesirable hazards. Therefore there is a worldwide trend to return to natural resources, which are culturally acceptable and economically viable. *Aphanizomenon flos-aquae*, a fresh water unicellular blue-green alga, which is consumed as a nutrient-dense food source and for its health-enhancing properties. *Aphanizomenon* is an important source of the blue photosynthetic pigment phycocyanin (PC), which has been described as a strong antioxidant and anti-inflammatory natural compound, as evidenced by *in vitro* and *in vivo* studies on PC. Mostly the species belonging to the order Nostocales and Oscillatoriales have known...
hepatoprotective and biomodulatory effects. The objective of the present work is to explore the antioxidant and hepatoprotective activity of *A. flos-aquae* against paracetamol (PCM) induced hepatopathy in rats.

**Materials and Methods**

**Maintenance of cyanobacterial strain**—Cyanobacterial strain, *A. flos-aquae*, was procured from NCCUBGA, IARI New Delhi. Stock culture of the strains was maintained in our laboratory by using BG-11 medium. Cyanobacteria (50 mL) from a mid log phase growth culture was dispersed aseptically into cotton plugged 1000 mL sterilized conical flasks. These were maintained at 25 ± 2°C under 24 h light in an illuminated chamber at 2.5 Klux. These cultures were thoroughly shaken 2-3 times daily to prevent mat formation.

**Chemicals**—1,1-diphenyl-2-pycryl-hydrazyl (DPPH) was purchased from Sigma Chemical Co. (St. Louis, MO). Paracetamol (Smith Kline Beecham, India) was suspended in pathogen-free normal distilled water before use. All other chemicals were of analytical grade.

**Preparation of the extracts of *A. flos-aquae***—The cyanobacterial culture was grown up to the mid log phase (10-14 days old culture) and was harvested by filter removing the medium through coarse filter paper. The harvested cyanobacterial mass was washed twice with distilled water for completely removing the culture medium. Approximately 8-10 mL water was used for every 1 g culture harvested. The harvested strains of *A. flos-aquae* were dried at 45-50°C for 48 h. The dried material was granular and this was macerated in liquid nitrogen in a pestle and mortar till fine powder was obtained. The powdered material was mixed with petroleum ether and sonicated to break open the cell wall. Then it was placed on the shaker platform for 24 h for cold extraction. The filtrate was collected by centrifugation and the material was repeatedly cold extracted with solvents of increasing polarity (chloroform, ethanol, methanol and distilled water). The filtrate was evaporated by rotary evaporator at 30-35°C and the mass obtained was dissolved in distilled water and employed for further experiments. The cold extraction procedure was repeated twice. Maximum dose of 100 mg of extract/kg body weight was used for treatment in experiments. Other high dose like 200 mg/kg body weight also showed almost the same results as given in the case of 100 mg of extract/kg body weight (data not given). So the lower concentration was selected for the study.

**Experimental animals**—Male albino rats of Sprague-Dawley strain weighing between 120-150 g were purchased from Small Animal Breeding Section of Kerala Agriculture University, Mannuthy, Trichur, India. The animals were maintained in an animal house with standard facilities having CPCEA approval (No732). The animals were housed in polypolyrene cages and maintained at 25°C ± 2°C under 12 h light/dark. They were fed with Amrut Laboratory Animal Feed, manufactured by Nav, Maharashtra Chakan Oil Mills Ltd Pune. Water was provided *ad libitum*. The animals were acclimatized for one week under laboratory conditions. Ethical clearance for handling the animals was obtained from the ethic committee constituted for the purpose.

**Experimental design**—Hepatoprotective activity was determined by the method of Kumar et al. Animals were divided into 5 groups of 8 animals each and treated as follows.

The animals in group I served as normal and were given distilled water for 10 days in succession. The group II rats served as control and were administered with PCM in distilled water by oral administration @ 3 g/kg body weight, 1 h after distilled water administration. The animals in group III, IV and V were served as experimental and treated orally with ethanol extract of *A. flos-aquae* 50 mg/kg body weight, 100 mg/kg body weight, and silymarin 100 mg/kg body weight respectively once in a day for 10 days followed by a single oral administration of PCM (3 g/kg body weight), 1 hour after extract administration. After 24 h of PCM administration rats of all groups were sacrificed by decapitation, and the blood was collected by cutting the jugular vein.

**DPPH free radical scavenging activity**—Reduction of 2,2’-Diphenyl-1-picrylhydrazyl radical (DPPH) to diphenylpicryl hydrazine by EEAFA was measured spectrophotometrically at 517 nm. L-Ascorbic acid was used as a reference compound (100 µg/mL) and data were expressed as the percent decrease in the absorbance compared to the control. The optical density was recorded and % inhibition was calculated using the formula:
Percent (%) inhibition of DPPH activity = [(A - B)/A]×100
where A = optical density of the blank and B = optical density of the sample.

Biochemical estimation—The level of alanine aminotransferase (ALT)\(^ {16} \) and aspartate aminotransferase (AST)\(^ {16} \) gamma glutamyl transpeptidase (GGT)\(^ {17} \) and alkaline phosphatase (ALP)\(^ {18} \) was assayed. The measurement of thiobarbituric acid reactive substances (TBARS) was done as an index of lipid peroxidation by using the method of Nichans and Samuelson\(^ {19} \). Conjugated dienes (CD) was estimated according to the method of Beuje and Aust\(^ {20} \). The protein content and bilirubin content in the serum were evaluated by using standard procedure of Lowry et al.\(^ {21} \) and Malloy and Evelyn\(^ {22} \) respectively. The concentrations of total lipids\(^ {23} \), phospholipids\(^ {24} \), triglycerides\(^ {25} \) and cholesterol\(^ {26} \) were measured by following standard procedure. Activities of superoxide dismutase (SOD)\(^ {27} \), catalase (CAT)\(^ {28} \), reduced glutathione (GSH)\(^ {29} \), glutathione peroxidase (GPX)\(^ {30} \) and glutathione transferase (GST)\(^ {31} \) were assayed.

Histopathological examination of liver—A portion of the liver in each group was fixed in 10% formosal (formalin diluted to 10% with saline) and protected for histopathology. For histopathology, serial sections of 5 µm thickness were made from the fixed liver tissues and then studied with haematoxylin and eosin to evaluate the details of hepatic architecture in each group microscopically.

Statistical analysis—The results are presented as the mean of 10 animals in each group ± SD. The data obtained by one-way ANOVA followed by Dunnett t-test. The level of significance was set at \( P < 0.01 \).

Results

The antioxidant activity of different extracts of \( A. \ flos-aquae \) was evaluated by the DPPH radical scavenging capacity. Fig. 1 shows the percent of DPPH radical scavenging capacity with L-ascorbic acid as reference. The experimental data of the variety reveal that all of these extracts at various levels are likely to have the effect of scavenging free radicals (Fig. 1). A dose-response relationship was found in DPPH radical scavenging capacity. Among the three extracts used in the experiment, 30 µg/mL of ethanol extract was the strongest one with 77.78%, then 30 µg/mL of methanol extract with 65.09% and 30 µg/mL of water extract with 62.39% of DPPH radical scavenging activity. The percent of inhibition of DPPH radical scavenging activity found to be 84%.

A significant increase in the activity of the serum enzymes AST, ALT, GGT and ALP was observed in rats receiving PCM in vehicle (Group II) when compared to normal (Group I) rats administered vehicle alone (Table 1). However, the activities of these serum enzymes were significantly (\( P < 0.01 \)) lower in rats treated with the EEAFA (Group III and IV) than in Group II rats. The protection offered by silymarin was found to be higher.

A marked increase in the mean TBARS and CD level was found in the liver of Group II (PCM exposed) rats relative to normal (Group I)

**Table 1**—Effect of ethanol extract of \( A. \ flos-aquae \) on the activities of liver function marker enzymes in serum

<table>
<thead>
<tr>
<th>Groups</th>
<th>AST</th>
<th>ALT</th>
<th>ALP</th>
<th>GGT</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Normal</td>
<td>38.36 ± 7.09</td>
<td>29.60 ± 8.35</td>
<td>89.61 ± 12.98</td>
<td>3.94 ± 0.97</td>
</tr>
<tr>
<td>II PCM</td>
<td>137.61 ± 11.54*</td>
<td>178.38 ± 9.09*</td>
<td>196.92 ± 13.92*</td>
<td>9.64 ± 1.33*</td>
</tr>
<tr>
<td>III PCM+EEAFA (50 mg)</td>
<td>90.32 ± 10.58 a</td>
<td>86.19 ± 12.45 a</td>
<td>114.69 ± 7.87 a</td>
<td>7.34 ± 0.78 a</td>
</tr>
<tr>
<td>IV PCM+ EEAFA (100 mg)</td>
<td>43.44 ± 12.94 a</td>
<td>34.15 ± 9.22 a</td>
<td>93.97 ± 9.16 a</td>
<td>4.29 ± 1.01 a</td>
</tr>
<tr>
<td>V PCM+ Silymarin</td>
<td>39.38 ± 11.24 a</td>
<td>30.17 ± 10.68 a</td>
<td>91.62 ± 6.83 a</td>
<td>3.90 ±0.85 a</td>
</tr>
</tbody>
</table>

Statistical analysis ANOVA followed by Dunnett t-test. \( P < 0.01 \) as compared with *group I, a group II

![Fig. 1—Percent DPPH radical scavenging capacity of different extracts of \( A. \ flos-aquae \) [(Ethanol extract (EEAFA), Methanol extract (MEFA) and Water extract (WEAFA)]](image-url)
rats (Table 2); this increase was statistically significant \((P < 0.01)\). Treatment with EEAFA in Group IV rats was found to result in a significant \((P < 0.01)\) lowering of the mean TBARS and CD concentration, presumably by limiting lipid peroxidation in the hepatic tissue. PCM administration in Group II rats resulted in a marked decrease (relative to normal) in the level of reduced glutathione in liver (Table 2); this decrease was statistically significant \((P < 0.01)\). Treatment with EEAFA and silymarin resulted in a significantly higher concentration of GSH \((P < 0.01)\) than that in Group II. A marked elevation in the concentration of bilirubin and decreases in protein content was observed in the PCM treated rats compared to normal animals (Table 2). In rats, which received EEAFA at a dose of 100 mg/kg body weight, the concentrations of bilirubin and total protein were maintained at near normal levels.

Table 2—Effect of ethanol extract of *A. flos-aquae* on antioxidant, protein and bilirubin status of liver in rats

<table>
<thead>
<tr>
<th>Groups</th>
<th>TBARS (mg/100 g tissue)</th>
<th>CD (mg/100 g tissue)</th>
<th>GSH (mg/100 ml serum)</th>
<th>Protein (mg/100 g tissue)</th>
<th>Bilirubin (mg/100 g tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Normal</td>
<td>1.39 ± 0.04</td>
<td>62.24 ± 10.19</td>
<td>0.94 ± 0.02</td>
<td>8.65 ± 1.20</td>
<td>1.71 ± 0.08</td>
</tr>
<tr>
<td>II PCM</td>
<td>1.68 ± 0.57*</td>
<td>80.40 ± 15.54*</td>
<td>0.45 ± 0.05*</td>
<td>6.98 ± 0.98</td>
<td>2.48 ± 0.05*</td>
</tr>
<tr>
<td>III PCM + EEAFA (50 mg)</td>
<td>1.53 ± 0.38*</td>
<td>67.14 ± 12.53*</td>
<td>0.76 ± 0.09*</td>
<td>7.11 ± 0.87</td>
<td>2.02 ± 0.75*</td>
</tr>
<tr>
<td>IV PCM + EEAFA (100 mg)</td>
<td>1.43 ± 0.07*</td>
<td>64.02 ± 9.46*</td>
<td>0.88 ± 0.09*</td>
<td>8.55 ± 1.39</td>
<td>1.79 ± 0.12*</td>
</tr>
<tr>
<td>V PCM + Silymarin</td>
<td>1.40 ± 0.34a</td>
<td>62.56 ± 7.07a</td>
<td>0.90 ± 0.04a</td>
<td>8.59 ± 0.99</td>
<td>1.74 ± 0.26a</td>
</tr>
</tbody>
</table>

Statistical analysis ANOVA followed by Dunnett t-test.

\(P < 0.01\) as compared with Group I, *group II

Table 3—Effect of ethanol extract of *A. flos-aquae* on the activity of lipid profile of liver of rats on PCM induced hepatotoxicity

<table>
<thead>
<tr>
<th>Groups</th>
<th>Total lipids (mg/100 g tissue)</th>
<th>Phospholipids (mg/100 g tissue)</th>
<th>Cholesterol (mg/100 g tissue)</th>
<th>Triglycerides (mg/100 g tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Normal</td>
<td>4375.88 ± 12.01</td>
<td>2254.64 ± 9.01</td>
<td>565.35 ± 3.16</td>
<td>447.44 ± 9.24</td>
</tr>
<tr>
<td>II PCM</td>
<td>5685.72 ± 15.29*</td>
<td>3017.41 ± 13.01*</td>
<td>784.92 ± 4.24*</td>
<td>561.23 ± 6.96*</td>
</tr>
<tr>
<td>III PCM + EEAFA (50 mg)</td>
<td>5259.89 ± 13.52*</td>
<td>2765.26 ± 11.45*</td>
<td>654.36 ± 10.45*</td>
<td>470.96 ± 9.63*</td>
</tr>
<tr>
<td>IV PCM + EEAFA (100 mg)</td>
<td>4797.71 ± 9.73*</td>
<td>2420.44 ± 10.12*</td>
<td>571.80 ± 11.25*</td>
<td>456.64 ± 14.34*</td>
</tr>
<tr>
<td>V PCM + Silymarin</td>
<td>4590.45 ± 12.44a</td>
<td>2311.69 ± 13.58a</td>
<td>569.76 ± 12.38a</td>
<td>451.82 ± 10.67a</td>
</tr>
</tbody>
</table>

Statistical analysis ANOVA followed by Dunnett t-test.

\(P < 0.01\) as compared with *group I, *group II

Table 4—Effect of ethanol extract of *A. flos-aquae* on activity of antioxidant enzymes in liver

<table>
<thead>
<tr>
<th>Groups</th>
<th>SOD (U/mg protein)</th>
<th>CAT (U/mg protein)</th>
<th>GPX (U/mg protein)</th>
<th>GST (U/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Normal</td>
<td>5.33 ± 1.10</td>
<td>2.93 ± 0.09</td>
<td>165.96 ± 10.12</td>
<td>0.34 ± 0.04</td>
</tr>
<tr>
<td>II PCM</td>
<td>4.14 ± 1.09*</td>
<td>0.54 ± 0.08*</td>
<td>142.12 ± 7.09*</td>
<td>0.24 ± 0.09*</td>
</tr>
<tr>
<td>III PCM + EEAFA (50 mg)</td>
<td>4.48 ± 0.88a</td>
<td>1.99 ± 0.09a</td>
<td>155.49 ± 12.09*</td>
<td>0.27 ± 0.06a</td>
</tr>
<tr>
<td>IV PCM + EEAFA (100 mg)</td>
<td>5.16 ± 0.56a</td>
<td>2.78 ± 0.10a</td>
<td>163.95 ± 11.43*</td>
<td>0.31 ± 0.03a</td>
</tr>
<tr>
<td>V PCM + Silymarin</td>
<td>5.30 ± 0.67a</td>
<td>2.80 ± 0.15a</td>
<td>164.84 ± 5.95*</td>
<td>0.33 ± 0.04a</td>
</tr>
</tbody>
</table>

Statistical analysis ANOVA followed by Dunnett t-test.

\(P < 0.01\) as compared with *group I, *group II

Significant increase in the lipid profile was observed in PCM intoxicated rats (Table 3). Co-administration of EEAFA were significantly prevented the PCM induced alterations in the lipid profile.

A significant decrease in antioxidant enzymes like CAT, SOD, GPX and GST activity was observed in the liver of PCM-administered (Group II) rats when compared to normal (Group I) rats that had received vehicle alone (Table 4). Treatment with the EEAFA appeared to exert a beneficial effect since the activities of these enzymes were significantly higher in the liver of Group III and IV than that of Group II rats.

The hepatoprotective effect of the test drug was further confirmed by histopathological examination of the livers of control, paracetamol treated and paracetamol plus test drug extract treated groups. The histopathological pattern of the livers of the rats

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**Table 2**—Effect of ethanol extract of *A. flos-aquae* on antioxidant, protein and bilirubin status of liver in rats

**Table 3**—Effect of ethanol extract of *A. flos-aquae* on the activity of lipid profile of liver of rats on PCM induced hepatotoxicity

**Table 4**—Effect of ethanol extract of *A. flos-aquae* on activity of antioxidant enzymes in liver
treated with paracetamol plus the extract showed minimal necrosis in centrilobular and regeneration of hepatocytes (Figs 2-5).

**Discussion**

The present study reveals the hepatoprotective activity of the EEAFA against the well known hepatotoxins, paracetamol. Paracetamol is a common antipyretic agent, which is safe in therapeutic doses, but can produce fatal hepatic necrosis in man, rats and rat with toxic doses\(^5\).

DPPH is a free radical donor that accepts an electron or hydrogen to become a stable diamagnetic molecule. The tendencies of electron or hydrogen donation are critical factors in characterizing antioxidant activity that involves free radical scavenging\(^32\). Therefore, DPPH is often used as a substrate to evaluate antioxidant activity. Different extracts significantly quenched DPPH radical with increasing concentrations, indicating that it has a good ability for electron or hydrogen donation (Fig. 1). DPPH scavenging activities of cyanobacterial extract by organic solvents have been reported\(^9\).

An obvious sign of hepatic injury is the leaking of cellular enzymes into the plasma due to the disturbance caused in the transport functions of hepatocytes\(^33\). The rat treated with an overdose of paracetamol developed significant hepatic damage, which was observed through substantial increases in the concentrations of serum parameters. Treatment

![Figs 2-5—Microphotographs of stained histological sections of liver [(2): normal rat showing central vein (CV) surrounded by normal hepatocytes; (3): rat treated with acetaminophen (3 g/kg body weight) showing centrilobular necrosis (CN), congestion and an extensive area of inflammatory cell infiltration; (4): rat treated with acetaminophen (3 g/kg body weight) + EEAFA (100 mg/kg body wt.) showing well preserved hepatocytes as well as the architecture with small areas of centrilobular necrosis (CN) and inflammatory cell infiltration; (5): rat treated with acetaminophen (3 g/kg body weight) + Silymarin (100 mg/kg body wt.) showing partially preserved hepatocytes and architecture with very small areas of necrosis. H&E ×100]
of the rats with EEFA extracts at 100 mg/kg resulted in a significant reduction of paracetamol induced elevation of serum marker enzymes and appears to be protective in reducing the injurious effect of paracetamol observed in the study. It was also reported that the alcohol extract of *Spirulina* inhibited lipid peroxidation more significantly than the chemical antioxidants like α-tocopherol and β-carotene.

Any oxidative insult to a cell induces lipid peroxidation of cell-membrane lipids. TBARS, a secondary product of lipid peroxidation, is widely used to assess lipid peroxidation in animal tissues. In the present study EEFA effectively prevented paracetamol-induced lipid peroxidation in liver cells. Antioxidant property of *Nostoc sphaeroides* and *Aulosira fertilissima* on CCl₄ induced hepatic damage in rats had been reported earlier. C-phytocyanin from *Spirulina platensis* effectively inhibited PCM induced lipid peroxidation in rat liver in vivo.

Glutathione is the main intracellular non-protein sulphydryl and it plays an important role in the maintenance of cellular proteins and lipids in their functional states. When GSH is lowered, the toxic effects of oxidative insult are exacerbated, resulting in increased membrane and cell damage. At this point, other protein and non-protein sulphydryl groups present in the cell provide an important alternate protection. Decline in the GSH content in the liver of PCM intoxicated rats, and its subsequent return towards the near normalcy in PCM+EEFA administered group also reveal anti-lipid peroxidative effect of *A. flos-aquae*.

The hepatotoxicity of paracetamol occurs because of its reactive metabolite, N-acetyl- P-benzoquinone imine (NAPQI). NAPQI exerts its toxicity primarily via its oxidative effect on cellular proteins. The site specific oxidative damage of some of the susceptible amino acids of protein is now regarded as the major cause of metabolic dysfunction during pathogenesis. The lowered level of total proteins recorded in the serum of PCM treated rats attained near normalcy. Protein content of in serum in PCM+EEFA treated rats further confirmed the anti-hepatotoxic effect of *A. flos-aquae*. The liver abnormalities may be preceded by an increase in plasma unconjugated bilirubin due to early reduction in bilirubin glucuronyltransferase activity and an even earlier inhibition of hepatic bilirubin conjugation by either paracetamol or a metabolite of paracetamol.

Endogenous defenses against free radicals include antioxidant enzymes, such as SOD, CAT, GPX and GST. When the balance between ROS production and antioxidant defenses is lost, oxidative stress results, which through a series of events deregulates the cellular functions leading to various pathological conditions. Any compound, natural or synthetic, with antioxidant properties may contribute towards the partial or total alleviation of this type of damage. In the present study, decline in the level of antioxidant enzymes observed in PCM treated rat is a clear manifestation of excessive formation of free radicals and activation of lipid peroxidation system resulting in tissue damage. The significant increase in the concentration of these constituents in liver tissues of PCM+EEFA treated animals indicate antioxidant effect of EEFA. *Dunaliella salina*, a green marine algae has the ability to protect against oxidative stress in vivo using animal models. Carotenoids from microalgae exert their action against liver injury by lipid peroxidation, either through decreased production of free radical derivatives or due to the antioxidant activity of the protective agent itself.

During toxicity, lipid profile of serum and tissues increases. Intoxication of experimental animals with PCM altered membrane structure and function as shown by the increases in cholesterol and subsequent decreases in phospholipid concentrations, hence increased cholesterol to phospholipid ratio. Pre-treatment of experimental animals with the extract of EEFA prevented the alterations of membrane fluidity with the decrease in the cholesterol to phospholipid ratio which has been elevated by PCM alone treated animals.

Histological sections of liver showed centrilobular necrosis with inflammatory cell infiltration in acetaminophen alone treated rat. Centrilobular necrosis, the pathognomonic feature of acetaminophen hepatotoxicity was strikingly reduced in EEFA pre-treated rat. Further, the congestion and inflammatory cell infiltration evoked by acetaminophen was considerably decreased by EEFA and silymarin indicating its possible anti-hepatotoxic action.

**Conclusions**

From the results, it can be concluded that the ethanol extract of *A. flos-aquae* prevents hepatic injury induced by PCM in rats by neutralizing
the oxidative stress. The hepatoprotective effect of EEFA may be due to the presence of phycocyanin pigment present in the extract. Thus the plausible mechanism of the hepatoprotective effect of EEFA may be due to its antioxidant effect. Further study is needed to identify and isolate the active principle of EEFA, which can have offer antioxidant and hepatoprotective properties. Studies in this direction are progressing in our lab, as this is the first report in the antioxidant and hepatoprotective properties about ethanol extract of A. flos-aquae. Further studies are required for its potential uses as a hepatoprotective drug in clinical practice.

References


