Review: Hepatoprotective activity of *Spirulina* species.

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Abstract— Spirulina is a filamentous, photosynthetic, spirally-shaped, multicellular cyanobacteria. The most important species of Spirulina are *Spirulina maxima, Spirulina fusiformis* and *Spirulina platensis*. Its chemical composition includes proteins (55%-70%), carbohydrates (15%-25%), essential fatty acids (18%) minerals, vitamins and pigments like phycocyanin, carotenes, chlorophyll a etc. Spirulina is considered as consisting hepatoprotective agents against toxicants such as CCl_4, alcohol, acetaminophen etc. Carbontetrachloride is known to produce free radicals and to induce cirrhosis, steatosis and necrosis in hepatic and renal cells. Our present study summarizes the hepatoprotective activity of spirulina against acute CCl_4 exposure in rats.

Index Terms— Antioxidants, carbontetrachloride, Hepatotoxicant, Hepatoprotective agents, lipid peroxidation, oxidative stress.

1 INTRODUCTION

Liver is one of the largest organs in the human body and is the main site for intense metabolism and excretion. It has astounding role in the performance, maintenance, and regulating the homeostasis in the body which is engaged in almost all the biochemical pathways to growth, fights against diseases, nutrient supply, energy provision and reproduction [15]. The major functions of liver are carbohydrate, fat and protein metabolism, detoxification, secretion of bile, and storage of vitamin. Liver is continuously and variedly exposed to environmental toxins and abused by poor drug habits and alcohol and prescribed the over-the-counter drug which can eventually lead to various liver ailments like cirrhosis, hepatitis and alcoholic liver diseases [16], [14].

In today's context, the liver diseases are some of the fatal diseases in the world. Hence it poses a serious challenge to international public health. However modern medicines have little to offer for elevation of hepatic diseases and it is chiefly the plant based preparations which are employed for the treatment of liver diseases [13], [12]. Hence many folk remedies from plant origin are tested for its potential hepatoprotective and antioxidant liver damage in experimental animal model.

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Carbon tetrachloride induced hepatotoxicity model is widely used for the study of hepatoprotective drugs and plant extract [26]

Scientific procedures of investigation reveal that *Spirulina* does not contain stimulants; it simply reduces fatigue and stress by acting as a profound antioxidant [7]. It is also has a uniquely powerful effect on the immune system, which in the majority of cases is highly beneficial [10], [8], [22]. No other substance we can swallow has such an important health effect, yet is so nontoxic. In the United States *Spirulina* is generally recognized as safe for use as food through scientific procedures with FDA review [22]. No other microalgae and few dietary supplements have that safety status.

Why does *Spirulina* have such a profound effect? The answer is very basic to metabolic and cellular functions. It is because of the bilin.

Spirulina, a blue-green algae (cyanophytes /cyanobacteria), grows as microscopic, corkscrew-shaped multicellular filaments and is now classified as a distinct genus, Arthrospora. A. plantensis is found in Africa and Asia, and A. maxima is found in Central America [40], [42]. Free growing, spirulina exists only in high-salt alkaline water in subtropical and tropical areas, sometimes imparting a dark-green color to bodies of water [42] Spirulina is noted for its characteristic behavior in carbonated water and energetic growth in laboratory cultures [43]. It is commercially grown in the United States and has been proposed as a primary foodstuff to be cultivated during long-term space missions because it withstands extreme conditions [44]. Due to its unique growth requirements, contamination of open pond cultures of spirulina by other microorganisms is usually slight, with the alga growing as a relatively pure culture.

2. HISTORY

Spirulina has been described in literature since the 16th century. Spanish explorers observed the Aztecs harvesting a blue mud that probably consisted of spirulina [41]. The mud, which was dried to form chips or flavored loaves, was obtained from Lake Texcoco near Mexico City. Spirulina was similarly harvested in the Sahara Desert from small lakes near Lake Chad, where it was called dihe. Thus, 2 cultures approximately 10,000 km apart, independently discovered and utilized the nutritional properties of spirulina [42]. Currently, spirulina is actively marketed by numerous companies as a nutritional supplement [45].

3. CHEMISTRY

Spirulina is composed of approximately 65% crude protein, high levels of B-complex vitamins [46] vitamin E [47] beta-carotene [48] and zeaxanthin [43], [49]. The protein content includes 22 essential amino acids [41], [50] and the total protein is nutritionally superior to legume protein, but inferior to meat protein [41]. The proteins C-phycocyanin and allophycocyanin in spirulina have been the focus of much research [51], [52]. High levels of gamma linolenic acid, a polyunsaturated fatty acid, are present [53]. An assay for spirulina lipids using high-pressure liquid chromatography-mass spectrometry has been developed [54]. Spirulina preparations contain 300 to 400 ppm iron (dry weight), and unlike many forms of plant iron, has high bioavailability when ingested by humans. A dosage of 10 g/day can contain 1.5 to 2 mg of absorbable iron, similar to that of standard ferrous sulfate. Trace elements present at high levels include manganese, selenium, and zinc. Calcium, potassium, and magnesium are also concentrated in the organism [55], [56]. Calcium spirulan, a sulfated polysaccharide, was characterized from A. platensis [57], [58]. Our body produces unconjugated biliverdin, which is transported into the cytoplasm of every cell in our body [27]. There, an enzyme called biliverdin reductase, converts the biliverdin to unconjugated bilirubin. The bilirubin quickly oxidizes back into biliverdin, and just as quickly biliverdin reductase recycles it back again into bilirubin. The recycling process is very fast. This form of bilirubin, (not exactly like the bilin in hemoglobin or bile.), has been shown to be 10,000 times as powerful an antioxidant as is glutathione. The unconjugated bilirubin is also a powerful inhibitor of NADPH Oxidase [5], [6], [25]. This enzyme is a major source of Super Oxide in the body, and is involved in dozens of degenerative processes involved in aging. There is now strong evidence that *Spirulina* supplements the amount of unconjugated biliverdin which we inherent from our parents providing profound protection from oxidative stress. Through regular use of 2 to 30 grams per day, a higher level of protection from oxidative stress may be achieved. High levels of protection from oxidative stress are one of the primary goals in the quest for good health and longevity.

Recent research reveals that free bilirubin functions physiologically as a potent inhibitor of NADPH oxidase activity. The chromophore phycocyanobilin (PCB), found in blue-green algae and cyanobacteria such as *Spirulina*, also has been found to be a potent inhibitor of this enzyme complex, likely because in mammalian cells it is rapidly reduced to phycocyanorubin, a close homolog of bilirubin. In light of the protean roles of NADPH oxidase activation in pathology, it thus appears likely that PCB supplementation may have versatile potential in prevention and therapy, particularly in light of rodent studies demonstrating that orally administered *Spirulina* or Phycocyanin (the *Spirulina* holoprotein that contains PCB) can exert a wide range of anti-inflammatory effects. Until PCB enriched *Spirulina* extracts or synthetically produced PCB are commercially available, the most feasible and least expensive way to administer PCB is by ingestion of whole *Spirulina*. A heaping tablespoon (about 15 g) of *Spirulina* can be expected to provide about 100 mg of PCB. By extrapolating from rodent studies, it can be concluded that an intake of 2 heaping tablespoons daily would be likely to have important antioxidant activity in humans, assuming that humans and rodents digest and absorb *Spirulina*-bound PCB in a comparable manner. An intake of this magnitude can be clinically feasible if *Spirulina* is incorporated into "smoothies" featuring such ingredients as soy milk, fruit juices, and whole fruits. Such a regimen should be evaluated in clinical syndromes characterized and in part mediated by NADPH oxidase over activity in affected tissues [5].

In studies carried out [30] effect of C-phycocyanin (from *Spirulina* platensis) pretreatment on carbontetrachloride and pulegone-induced hepatotoxicity in rats was studied. Intraperitoneal administration of a single dose of Phycocyanin to rats, one or three hours prior to pulegone or carbontetrachloride challenge, significantly reduced the hepatotoxicity caused by these chemicals. For instance, serum glutamate pyruvate transaminase (SGPT) activity was almost equal to control values. The losses of microsomal cytochrome P450, glucose-6-phosphatase and aminopyrine-N-demethylase were significantly reduced, suggesting that phycocyanin provides protection to liver enzymes. It was noticed that the level of menthofuran, the proximate toxin of pulegone was nearly 70% more in the urine samples collected from rats treated with pulegone alone than rats treated with the combination of phycocyanin and pulegone [30]. The spirulina protein phycocyanin in pure form was active in 4 different cell-free radical-scavenging assays; however, phycocyanin-containing selenium was more effective [32]. In cellular assays of antioxidant activity, 4 commercial spirulina preparations were also active [33]. Spirulina supplementation of rats did not increase plasma or liver alpha-tocopherol levels **(**Garcia-Martinez et al, 2007**)**; whereas another studies reported effective antioxidant activity using combinations of whey protein and spirulina [35]. C-phycocyanin from spirulina reduced oxidative stress in hamsters fed an atherogenic diet [25]. Similarly, rabbits fed a high-cholesterol diet were protected from oxidative stress by 4 to 8 weeks of spirulina in feed at 1% or 5% [59]. Other studies sug-

gest spirulina as an antioxidant [36]. But clinical importance has not been demonstrated [37], [38] and 1 small clinical study showed spirulina to be without effect on plasma antioxidant status [39].

The capacity of *Spirulina* maxima to prevent fatty liver development induced in rats by an intraperitoneal single dose (1 ml/kg) of carbon tetrachloride was done. Liver and serum lipids were quantified two or four days after treatment with this agent. Liver lipid concentration did not differ in rats fed on a purified diet with or without *Spirulina*. However, after carbon tetrachloride treatment, liver triacylglycerols are to be significantly lower in rats fed on a diet with *Spirulina* 5% than in rats without *Spirulina* in their diet ($P < 0.05$). Furthermore, the increased liver cholesterol values, induced by carbon tetrachloride treatment, were not observed in rats that received *Spirulina*. These results support the potential hepatoprotective role of *Spirulina* [28].

Later on the work was carried out to assess the feeding of either the oil extract of *Spirulina* maxima or of its defatted fraction would prevent fatty liver development; induced in rats by a single intraperitoneal dose of carbon tetrachloride (CCl_4) was done. Liver and serum lipids were evaluated after treatment with carbon tetrachloride hepatotoxic agent. Concentration of liver lipids did not differ in rats fed on a purified diet either without or with one of the fractions of *Spirulina*, except for total cholesterol, which showed a slight increase in the group receiving the oil extract of *Spirulina*.

However, after CCl_4 treatment, liver total lipids and triacylglycerols were significantly lower in rats fed on a diet containing any fraction of *Spirulina* (defatted or the oil fraction) than in rats without *Spirulina* in their diet. Furthermore, the increased liver cholesterol values, induced by CCl_4 treatment, were not observed in rats receiving *Spirulina*. In addition, rats receiving whole *Spirulina* in their diet and treated only with the vehicle showed an increase in the percentage of HDL values. The changes in VLDL and LDL induced by CCl_4 treatment were not observed in the whole *Spirulina* group. Furthermore, after CCl_4treatment the values of the liver microsomal thiobarbituric acid-reactive substances were lower in the whole *Spirulina* group than in the control group. These results support the potential hepatoprotective role of *Spirulina* [29].

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In an other study Cyanobacteria *Spirulina* maxima from Texcoco Lake in Mexico was administered as a component of a purified diet, to Wistar rats together with a high percentage of fructose and its effect on several lipid fractions of plasma and liver was studied and compared to those of rats fed purified diets containing glucose or fructose. A preventive effect of *Spirulina* maxima on the fructose-induced increase of the liver triglycerides level was observed together with an elevation of the phospholipid concentration in this tissue. On the other hand *Spirulina* maxima produced a plasma cholesterol level even lower than that observed in the control group [23]. Later on an evident fatty liver was shown , corroborated morphologically and chemically, was produced in CD-1 mice after five daily doses of simvastatin, a hypercholesterolemic diet and 20 percent ethanol in the drinking water. After treating the animals, they presented serum triacylglycerols levels five times higher than the control mice, total lipids, cholesterol and triacylglycerols in the liver were 2, 2 and 1.5 times higher, respectively, than in control animals. When Arthrospira maxima was given with diet two weeks prior the onset of fatty liver induction, there was a decrement of liver total lipids, liver triacylglycerols and serum triacylglycerols compared to the animals with the same treatment but without Arthrospira maxima. In addition to the mentioned protective effect, the administration of this alga produced a significant increase in serum high density lipoproteins. The mechanism for this protective effect was not established in these experiments [19].

4 HEPATOTOXICANT

The burden of metabolism and exposure to dangerous chemicals make liver vulnerable to a variety of disorders such as acute and chronic inflammation, toxin- / drug- induced hepatitis, cirrhosis and hepatitis after viral infection. Oxidative stress is one out of several etiological and pathophysiological factors implicated in various diseases. Exposure of biological systems to xenobiotics, ionizing radiations and certain normal metabolic processes in the body leads to overproduction of reactive oxygen species (ROS) that overwhelms the antioxidant armory. Recent studies have demonstrated that overproduction of ROS can further aggravate the oxidative stress and result in the unifying mechanism of injury that occurs in many developments of clinical disease processes, such as Heart diseases, diabetes, liver injury, cancer, ageing, etc [9]. Maintaining the balance between ROS and antioxidant enzyme such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) is therefore crucial and could serve as a major mechanism in preventing damage by oxidative stress. The central role played by the liver and the clearance and transformation of chemicals also makes it susceptible to drug induced injury. Smooth endoplasmic reticulum in liver is the principle "metabolic clearing house" for both endogenous chemicals (eg. Cholesterol, steroid hormones, fatty acids and proteins), and exogenous substances. A group of enzyme located in the endoplasmic reticulum, known as cytochrome P-450, is the most important family of metabolizing enzyme in the liver.

4.1 Carbontetrachloride (CCl_4)

Carbon tetrachloride in known as a model toxicant to be hepatotoxic as well as nephrotoxic to humans. It is may be used to define the nature of chemically induced cytotoxicity for its site specific and has a well documented mechanism of toxicity. It is considered as a standard chemical agent whose hepatotoxictiy through various routes has been well established by various workers [3], [60]. Experimentally induced cirrhotic response in the rats by CCl_4 is shown to be superficially similar to human cirrhosis of the liver [1], [21], [24], [2], [61], [31], [62], [20].

Mechanistic study provides evidence that metabolism of carbontetrachloride via CYP2E1 to highly reactive free radical metabolites play a critical role in the postulated mode of action. The primary metabolites trichloromethyl and trichlromethyl peroxy free radicals, are highly reactive are capable of covalently binding locally to cellular macromolecules, with preference for fatty acids from membrane phospholipids. The free radical initiate lipid peroxidation by attacking polyunsaturated fatty acids in membranes, setting of a free radical chain reaction sequence. Lipid peroxidation is known to cause membrane disruption, resulting in the loss of membrane integrity and leakage of microsomal enzymes. By products of lipid peroxidation include reactive aldehydes that can form protein and DNA adducts and may contribute to hepatotoxicity and carcinogenicity, respectively. Natural antioxidants including glutathione are capable of quenching the lipid peroxidation reaction. When glutathione and other antioxidants are depleted, however, opportunities for lipid peroxidation are enhanced. Weakened cellular membranes allow sufficient leakage of calcium into cytosol to disrupt the intracellular calcium homeostatis. High calcium levels in the cytosol activate calcium dependent protease and phopholipase that further increase the breakdown of the membranes. Similarly the increase in intracellular calcium can activate endonuclease that can acuse chromosomal damage and also contribute to cell death. Sustained cell regeneration and prolifertation following cell death may increase the likelihood of unpaired spontaneous, lipid peroxidation- or endonuclease derived mutations that can lead to cancer [63].

Many investigators have established that the industrial solvent, CCl_4 is a potent environmental hepatotoxin [64], [65]. A number of recent reports clearly demonstrated that in addition to hepatic disorders, CCl_4 also causes disorder in kidneys, lungs, testis and brain as well as in blood by generating free radicals [66]. The CCl_4 - induced hepatotoxicity was higher in females than in males [67].

The invitro study revealed that CCl_4 cause damage in primary hepatocytes [68] and increased leakage of LDH, ALT and AST into the media. Administration of CCl_4 increased lipid peroxidation and reduced level of antioxidant enzymes SOD and CAT in the liver [18], [69], [68]. CCl_4 induced hepatic pathological damage cytochrome P4502E1 (CYP2E1) protein expression in hepatic samples and decrease the activities of SOD, CAT and GPx in erythrocytes [70], [71], [62], [72], [73].

Mehmetcik et. al., (2008) reported that glutathione peroxidase (GSH-Px) and glutathione transferase (GST) activities were decreased after CCl_4 treatment. Quantitative and qualitative analysis of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx) and glutathione-S-transferase (GST) revealed lower activities of the antioxidant enzymes in the kidneys, heart and brain of rats exposed to CCl_4 [75],[74], [77] reported the activities of ATPase and succinic dehydrogenase (SDH) inhibited significantly in liver kidney after acute exposure of CCl_4.

It has been report that CCl_4 increased LPO levels in serum and microsomes. Furthermore its intoxication significantly decreased the activities of microsomal glucose-6-phosphatase, aniline hydroxylase, amidopyrine N-demethylase and cytosolic glutathione-S-transferase (GST) [4]. Induction of CYP2E1 by CCl_4 is one of the central pathway by which CCl_4 generates oxidative stress in hepatocytes.

Toxic effect of CCl_4 was evident on was evident on CYP2E1 activity by increased hexobarbitone induced sleep time and bromosulphalien retention [4]. This is also sustained by many authors [76] **&** [73]. Khorshid et. al., 2008 observed that administration of CCl_4 induced changes in body weight gain, liver morphology, bile flow, concentration and increased in narcotic-induced sleeping time in male Wistar rats.

A pathological examination showed that lesions, including ballooning, degeneration, necrosis, hepatitis and portal triaditis where induced by CCl_4 [75], [71], [74], [69].

Vinitha et. al. (2007) found CCl_4 induced DNA stand breaks in hepatocytes, as measured by single cell gel electrophoresis. CCl_4 (Single injection at a dose of 20µl and 50µl Kg-1 b. w.) induced hepatic necrosis and caused DNA damage (Strand breaks). In hepatocytes of Swiss albino mice invivo. CCl_4 drastically decreased CYP2E1, CYP2B, CYP3A2, CYP2C11, and CYP1A2 mRNA and protein expressions. Moreover, CCl_4 increased iNOS and TNF-α mRNA [78], [76] reported that expressions of TNF-α, IL-1 beta, IL-6 and iNOS where increased by CCl_4 in rats. Exposure of CCl_4 induced apoptosis and necrosis, as indicated by a liver histopathologic study and DNA laddering. It also induced Fas/FasL protein expression levels and enhanced caspase-3,8 activities in mouse livers [76]. The spirulina protein phycocyanin in pure form was active in 4 different cell-free radical-scavenging assays; however, phycocyanin-containing selenium was more effective [32].In cellular assays of antioxidant activity, four commercial spirulina preparations were also active [33]. Spirulina supplementation of rats did not increase plasma or liver alpha-tocopherol levels [34]; however, another study reported effective antioxidant activity using combinations of whey protein and spirulina [35] C-phycocyanin from spirulina reduced oxidative stress in hamsters fed an atherogenic diet [25]. Similarly, rabbits fed a high-cholesterol diet were protected from oxidative stress by 4 to 8 weeks of spirulina in feed at 1% or 5%. 86 Other studies suggest spirulina as an antioxidant [59], but clinical importance has not been demonstrated, [36], [38] and 1 small

clinical study showed spirulina to be without effect on plasma antioxidant status [39].

5 Spirulina platensis

Cyanobacteria are a known as Blue-Green algae, blue green algae and cyanophyta. The name cyanobacteria comes from the bacteria (Greek kyanos = blue) they are significant component of the marine nitrogen cycle and an important primary producer in many areas of ocean, but are also found in habitats other than a marine environment [17]. The primary species of *Spirulina* are *Arthrospira platensis* and *Arthrospira maxima*.

Another species is *Spirulina fusiformis*; it is a freshwater alga as opposed to Marine/Saltwater species of the commonly harvested/ aqua cultured species noted earlier. It used to be classified as *Spirulina platensis*. *Arthrospira fusiformis* is capable of a great deal of polymorphism; it changes its shape, color and other characteristics in adapting to its environment. This freshwater species thrives in waters that are loaded with various minerals such as sodium, magnesium, carbonates, sulfates and chlorides. It does not usually thrive in water which is suitable for watering crops, drinking or raising fish. Most commercial *Spirulina* used for human and fish food consumption primarily is grown in the USA, Thailand, India and China.

Spirulina fusiformis has been shown to provide Antioxidant/Hepatoprotective (Liver function) in a study VIT University evaluated the hepatoprotective and antioxidant effects of *Spirulina* fusiformis against acetaminophen-induced hepatotoxicity in mice. For comparison purpose, results were compared with those for silymarin, a standard hepatoprotective drug. The study clearly demonstrated that *Spirulina fusifomis* shows hepatoprotective effect through its antioxidant activity on acetaminophen-induced hepatotoxicity.

Spirulina is not Chlorella; Chlorella is a green micro-alga and does not have the same anti-viral, anti-cancer and immune stimulating properties of *Spirulina*. The Chlorella cell wall is made of indigestible cellulose, just like green grass, while the cell wall of *Spirulina* is made of complexes proteins and sugars.

The previous knowledge of medicinal organism such as *Arthrospira* significantly contributed in discovering many important drugs of the modern system of medicine. Most developing countries are completed with vast resources of medicinal organism. In fact modern pharmaceuticals still contain at least 25% drugs derived from these organisms. Traditional medicines are used by about 60% of the world's population. Use of plants *Arthrospira* as a source of medicine has been inherited and is an important component of the healthcare system in India. There are more than 15 species in world with known medicinal uses and are an essential part of traditional health care systems.

Cyanobacteria have an impressive ability to colonies infertile substrate such as volcanic ash, dessert sand and rocks. They are extraordinary excavators, boring hollows into limestone and special type of sandstone. In the assessment of liver damage by CCL_4, the determination of enzymes levels such as AST and ALT is largely used. AST is an enzyme which takes part in transamination of liver. This enzyme is localized in hepatic cells and their levels rise in the circulation when the hepatic cells are damaged. Therefore higher levels of this enzyme indicate liver damage [79]. High levels of AST indicate liver damage, such as that due to viral hepatitis, cardiac infarction and muscle injury. ALT catalyses the conversion of alanine to pyruvate and glutamate. Necrosis or membrane damage releases the enzyme into circulation; therefore, it can be measured in serum. Therefore, ALT is more specific to the liver, and is thus a better parameter for detecting liver injury [80]. Proteins are synthesized in liver and inhibition indicates liver damage. A high bolus dose of CCL_4 results in significant loss of protein content in liver. It may be due to lipid peroxidation of cell membrane which results in loss in cytosolic proteins. A reduction in protein synthesis during toxicity may also be due to the decreased ATP production. In hepatotoxicity, a depression in total protein is due to the disruption and dissociation of polyribosomes from ER or imposed biosynthesis. Albumin is the most abundant circulatory protein and its synthesis is a typical function of normal liver cells.

Lipid peroxidation is a molecular mechanism of cell injury leading to the generation of cytotoxic products such as malondialdehyde (MDA) and 4-hydroxynonenal. Toxicity is attributed to generate reactive oxygen species which causes peroxidation of membrane lipids [81] and induces a plethora of alteration in structure and function of cellular membranes. It has been postulated to the destructive process of liver injury due to CCl_4. The increase in malondialdehyde (MDA) levels in liver suggests enhanced lipid peroxidation leading to tissue damage and failure of anti oxidant defense mechanism to prevent formation of excessive free radicals [82].

Glutathione is one of the most abundant tripeptide, non-enzymatic biological antioxidants present in the liver. Its functions are concerned with the removal of free radical species such as hydrogen peroxide, superoxide radicals, alkoxy radicals, and maintenance of membrane protein thiols and as a substrate for glutathione peroxidase (GPx) and GST. Under conditions of NAPQI formation following toxic CCL_4 doses, GSH concentrations may be very low in the centrilobular cells, and the major peroxide detoxification enzyme, GSH peroxidase, which functions very inefficiently under conditions of GSH depletion [83] is expected to be inhibited. Glutathione scavenges free radicals generated in the body and renders protection against lipid peroxidation and cell membrane damage [84]. When the lipid peroxidation rate is very high, the store of GSH gets depleted because high rate of scavenging and antioxidant system loses its control over free radicals. This leads to disruption of cell membranes and

finally the cell death. In this case, low levels of GSH indicates high rate of lipid peroxidation.

6 Conclusion

Numerous evidences have shown hepatotoxicity of carbontetrachloride. The utilization of cyanobacteria has been demonstrated by a large number of studies applying this hepatotoxin and by the variety of areas that apply therapeutic agents such as cyanobacteria. Spirulina have proven to be an important therapeutic agent cure and treatment of diseases and disorders of liver, kidney and other vital organs of the body. Furthermore, cyanobacteria are rich in many essential nutrients and show very striking effect as Hepatoprotective agents.

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