Evaluation of the effect of Spirulina against Gamma irradiation-induced oxidative stress and tissue injury in rats

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Abstract: Many antioxidants have been investigated as hepato-protectors against ionizing radiation induced injury since they reduce the oxidative effect of the reactive oxygen species on normal cells. Spirulina is a potent scavenger of a variety of free radicals. The aim of this study was to investigate the radio-protective effect of Spirulina algae against oxidative stress and tissue injury caused by gamma radiation. Rats were irradiated at two doses of 2 and 4Gy from cesium-137 source. Ten days prior to irradiation, animals received Spirulina daily (300mg/kg body weight i.p.). In the irradiated animal group, the oxidative stress markers malondialdehyde (MDA) was significantly increased in the liver, while a marked decrease in hepatic contents of DNA, and glutathione (GSH). The level of cholesterol, triglyceride (TG), low density lipoprotein (LDL), as well as activity of aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT), were significantly increased in sera of the irradiated rats. This was coupled with a decreased serum level of high-density lipoprotein (HDL) and total serum protein by irradiation. The administration of Spirulina alone daily for 10 days caused a significant decrease in MDA and produced significant elevation of liver GSH. Moreover, a significant decrease occurred in cholesterol, and TG level with no change in serum LDL or HDL levels in serum. Treatment of rats with Spirulina for 10 days before acute irradiation significantly abolished radiation induced elevation in liver MDA level and significantly maintained hepatic GSH content and CAT activity close to the control values. Pre-irradiation treatment of rats with Spirulina showed a significantly higher hepatic DNA content compared to that of irradiated rats. The level of cholesterol, TG, HDL, LDL as well as the activity of AST, ALT, and GGT in serum was significantly ameliorated when Spirulina was injected before irradiation. In conclusion, the increase in oxidative stress markers and the concomitant change in antioxidant levels indicate the role of oxidative stress in radiation-induced tissue damage. It was concluded that administration of Spirulina algae possess a radio protective capacity against ionizing-radiation induced oxidative stress and organ injury.

Keywords: Spirulina, radiation, radioprotection, antioxidants, oxidative stress, liver.

1. Introduction

Exposure to ionizing radiation represents a genuine, increasing threat to mankind and our environment. The steadily increasing applications of radiation in clinical practice, industrial and agricultural activities, on top of residual radio-activity resulting from nuclear test explosions, have a measurable impact contributing to possible radiation hazards in humans. Control of radiation hazards is considered as one of the most important challenges in order to protect our lives from radiation damage (Edrees et al., 2008). Ionizing radiations interact with biological systems through free radicals generated by water radiolysis. This indirect action plays an important role in the induction of oxidative stress leading to cellular damage and organ

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dysfunction (Berroud et al., 1996). The deleterious effects of ionizing radiation in biological systems are mainly mediated through the generation of reactive oxygen species (ROS) in cells as a result of water radiolysis (Kamat et al., 2000). Among them, particularly, the highly damaging hydroxyl radical (OH·) can cause injury by reacting with biomolecules (Breen and Murphy, 1995; Jagetia et al., 2003). ROS and oxidative stress may contribute to radiation-induced cytotoxicity and to metabolic and morphologic changes in animals and humans during radiotherapy, experimentation, or even space flight (Fang et al., 2002).

Against oxidative stress, cells are equipped with several natural enzymatic and non enzymatic antioxidant defenses (Halliwell, 1992). The exposure to ionizing radiation leads to depletion of these endogenous antioxidants (Koc et al., 2003a, b) and ultimately to the development of systemic disease. Irradiation up to 14.4 Gy caused marked decrease in serum enzymes and its pineal biosynthesis 3 and 5 days after radiation exposure (Ahlersova et al., 1998). In addition, total antioxidant capacity of plasma was reduced in patients exposed to whole body irradiation for the purpose of reducing tumor growth. Consequently, the cellular antioxidant capacity is decreased and the organs become more susceptible to the deleterious effects of ROS (Karbownik and Reiter, 2000).

Spirulina is a blue-green microalgae has a spiral cellular structure, and has an extraordinary capacity to survive under conditions that are much too harsh for other algae. Habitats with extensive Spirulina growth include the Pacific Ocean near Japan and Hawaii, large fresh water lakes in Africa, North America, Mexico, and South America. Two species of Spirulina that are most commonly used in nutritional supplements are Spirulina platensis and Spirulina maxima (Khan et al., 2005). Spirulina, contains large amounts of protein (70% dry weight)( Dillon, and Phan 1993), carotenoid (4000 mg/kg) (Kapoor, R. and Mehta, 1993) (omega-3 and omega-6 polyunsaturated fatty acids γ-linolenic acid (GLA), sulfolipids, glycolipids, polysaccharides, provitamins; vitamin A (Annapurna et al 1991) vitamin E, (Mitchell, et al., 1990) various B vitamins; and minerals, including calcium, iron, magnesium, manganese, potassium, zinc,( Khan et al., 2005) and selenium (Cases, J. et al., 2002). It is, therefore, a potential therapeutic agent for treating oxidative-stress-induced diseases (Bhat, and Madyastha 2000). Recent findings concerning the antioxidant, anti-inflammatory, immune-enhancing, antiviral, anticancer, and hepato-protection properties of Spirulina, with reference to the potential advantages of Spirulina as a regular nutritious supplement in the prevention of various disorders that are associated with oxidative stress, inflammation, cancer, and liver-malfunctioning diseases.

2. Materials and methods

2.1 Chemicals

All reagents were of the highest purity available. Spirulina powder was purchased from DXN company in Malaysia. All chemicals for measurement of antioxidants, lipid peroxidation, and chemical for biochemical analysis were purchased from Sigma Chemical Co. (St. Louis, MO).

2.2 Animals

Male Westar rats weighing 150–180 g, were used in the present experiments. Experimental animals were housed in cages with free access to drinking water and diet and maintained in the animal care facility throughout the duration of the experiment. The animals were kept at 22–24°C with the 12 h light/dark cycle. Animal husbandry and experimentation were consistent with the Public Health Guide for the Care and Use of Laboratory Animals (National Research Council, 1996) and in accordance with protocols approved by

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the local experimental animal ethics committee.

3. Experimental Design

Animals were divided into four groups, each group containing six rats. Animals in group 1 were served as control group and no treatment was given to these rats. Animals in group 2 were given Spirulina daily by gavages for 45 consecutive days at dose level of 300 mg/kg dissolved in water (Simsek et al., 2009). Group 3 gamma irradiated rats, the animals were divided into two subgroup: Six rats were whole body irradiated at dose level of 2Gy while other six rats were exposed to the dose of 4Gy radiation. Animals in group 4 were given Spirulina (300 mg/kg) by gavages for 10 consecutive days before radiation exposure and continued up to 45 days after radiation exposure

3.1 Irradiation

Animals were placed in a specially designed well-ventilated acrylic container and the whole body of the animals were exposed to either 2 or 4 Gy, given at a dose rate of 0.84 Gy/min from the biological irradiator gamma cell-40, cesium-137 source (Atomic Energy Agency, Canada), belonging to National Center for Radiation Research and Technology (NCRRT), Cairo.

3.2 Collection samples

Animals were sacrificed at the end of the experiment (12 h after over night fasting). Blood samples were collected and put into chilled non-heparinized tubes, which were centrifuged at 3000 rpm for 10 min at 4 °C. The sera were frozen at -20 °C for the following measurements. The serum levels of cholesterol, triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDH) and total protein, as well as the activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyltransferase (GGT), were estimated using kits from bio-Merieux, France. HDL and LDL were separated from serum by precipitation of lipoproteins of lower densities with polyethylene glycol (PEG 20 000, Fluka, Switzerland), a method originally developed for separation of HDL, and cholesterol was determined in lipoprotein fractions. A tissue sample from a known portion of the liver was accurately weighed and homogenized (Potter-Elvehjem) in a 10-fold volume of ice cold (20mM) tris-HCl buffer, pH 7.4. The homogenates were subjected to the following biochemical analysis. Lipid peroxidation product, malondialdehyde (MDA), was measured by thiobarbituric acid assay, which is based on MDA reaction with thiobarbituric acid to give thiobarbituric acid reactive substances (TBARS), a red species that absorbs at 535nm (Ohkawa et al., 1979). The GSH content was determined by using spectrophotometer at 412nm using 5, 5-dithiobis-2-nitrobenzoic acid (Beutler, 1982). Catalase (CAT) activity was assayed as suggested by Bock et al. (1980). The method is based on the rate of H2O2 degradation by the action of CAT contained in the examined samples. DNA content was assayed by quantitative determination of nucleic acids through the reaction of its sugar components with diphenylamine reagent (Burton, 1956; Thoresen et al., 1983).

3.3 Statistical Analysis

Statistical significance of the data was analyzed using Student’s t-test. Data are shown as means ± SD and the level for statistical significance was P<0.05 Snedecor and Cochran (1980).

4. Results and discussion

The administration of Spirulina (300 mg/kg) alone for 45 days caused significant decreases in TBARS paralleled with significant elevations of GSH content activity in the liver. Hepatic CAT activity as well as
DNA contents were not changed after *Spirulina* treatment (Table 1). Exposure of rats to gamma- radiation resulted in a significant increase in lipid peroxidation, as measured by the formation of TBARS in the rat liver after whole body γ-irradiation (Table 1). Such an increase occurred at the two doses examined. The lower dose (2 Gy) caused the 44% increase, while the higher dose (4 Gy) was effective in further increasing (97%) the extent of lipid peroxidation (Table 1). The formation of TBARS at 2 and 4Gy was quite considerable and therefore protective effect of *Spirulina* was examined at these doses. Daily treatment with *Spirulina* for 10 days before acute irradiation significantly abolished these radiation-induced elevations in TBARS level in the liver (Table 1).

Hepatic GSH content was significantly decreased following irradiation when compared with the control group. The reduction in GSH level observed at 2 Gy, was further enhanced at 4 Gy. On the other hand, *Spirulina* treatment before irradiation markedly maintained hepatic GSH levels close to the control level and showed insignificant changes compared to control and irradiated groups (Table 1). Hepatic CAT activity of both irradiated groups was significantly increased when compared with the control group. In contrast, *Spirulina* pretreatment significantly protected CAT activity in the liver of rats exposed to gamma radiation. The protective action of *Spirulina* on CAT activity was complete in case of rats subjected to 2Gy but not to 4Gy, where it showed activity intermediate between the control and irradiated group levels (Table 1). In 2 and 4Gy-irradiated groups, there were significant decreases in hepatic DNA content. Daily treatment with *Spirulina* for 10 days before irradiation showed significantly higher DNA content in the liver of *Spirulina*-treated+ irradiated groups than irradiated rats (Table 1). On its own, *Spirulina* treatment daily for 45 days produced significant decreases in cholesterol, and TG levels, while it did not affect LDL or HDL levels in serum. *Spirulina* also showed insignificant changes in total protein levels as well as ALT and AST activities in serum (Table2). The levels of cholesterol, TG, and LDL in serum were significantly higher in 2 and 4Gy irradiated groups after radiation exposure than those of the control group. Treatment with *Spirulina* before irradiation significantly ameliorated the elevation in the levels of lipid profile (Table 2).

On the other hand, radiation exposure resulted in a significant decrease in HDL level in serum of the irradiated rats. This effect is significantly prevented by daily treatment with *Spirulina* for 10 days before acute irradiation (Table 2). In addition, serum total proteins contents were lower in 2 and 4Gy irradiated groups after radiation exposure than that of the control group. This effect was statistically significant when rats were exposed to the 4Gy dose. Treatment with *Spirulina* before irradiation significantly ameliorated the decline in the contents of serum protein content (Table 2).

The activities of ALT, AST, ALP and GGT in serum showed a significant rise following 2- or 4Gy irradiation doses. The treatment with *Spirulina* before irradiation displayed significant amelioration in the elevation of these enzyme activities in serum (Table 2).

**Table 1:** Serum activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST), Alkaline phosphatase(ALP) , Gamma- glutamyl transferase (GGT) and total protein (T. protein) in various animal groups

<table>
<thead>
<tr>
<th></th>
<th>ALT (u/l)</th>
<th>AST (u/l)</th>
<th>ALP (u/l)</th>
<th>GGT (u/l)</th>
<th>T. protein (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>23.22±1.52</td>
<td>28.77±1.95</td>
<td>66.20±1.60</td>
<td>40.0±1.50</td>
<td>8.12±0.37</td>
</tr>
<tr>
<td>Spirulina group</td>
<td>25.32±1.66</td>
<td>29.80±2.71</td>
<td>65.30±1.00</td>
<td>39.0±1.00</td>
<td>8.53±0.23</td>
</tr>
<tr>
<td>Irradiated group 2Gy</td>
<td>41.07±3.98</td>
<td>46.80±1.52</td>
<td>150.03±2.70</td>
<td>65.0±2.00</td>
<td>7.50±0.17</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Irradiated group 4 Gy</th>
<th>53.50±2.10</th>
<th>59.80±0.53</th>
<th>163.18±1.50</th>
<th>73.0±1.00</th>
<th>6.50±0.21</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spirulina + 2 Gy + Spirulina</td>
<td>39.21±0.30</td>
<td>40.90±2.10</td>
<td>82.21±3.60</td>
<td>45.0±1.60</td>
<td>8.20±0.38</td>
</tr>
<tr>
<td>Spirulina + 4 Gy + Spirulina</td>
<td>42.10±0.42</td>
<td>44.50±0.52</td>
<td>109.30±2.70</td>
<td>53.0±1.10</td>
<td>7.30±0.29</td>
</tr>
</tbody>
</table>

Table 2: Serum levels of cholesterol, Triglyceride, HDL, LDL in various animal groups

<table>
<thead>
<tr>
<th></th>
<th>Cholesterol (mg/dl)</th>
<th>Triglyceride (mg/dl)</th>
<th>HDL (mg/dl)</th>
<th>LDL (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>138.60±6.52</td>
<td>130.77±3.95</td>
<td>49.20±0.28</td>
<td>40.0±1.50</td>
</tr>
<tr>
<td>Spirulina group</td>
<td>126.32±7.66</td>
<td>81.80±4.71</td>
<td>49.10±0.22</td>
<td>39.0±1.00</td>
</tr>
<tr>
<td>Irradiated group 2 Gy</td>
<td>176.07±13.98</td>
<td>162.80±2.52</td>
<td>150.03±2.70</td>
<td>46.90±0.59</td>
</tr>
<tr>
<td>Irradiated group 4 Gy</td>
<td>229.50±10.13</td>
<td>267.80±5.53</td>
<td>163.18±1.50</td>
<td>34.80±0.77</td>
</tr>
<tr>
<td>Spirulina + 2 Gy + Spirulina</td>
<td>141.21±5.30</td>
<td>145.90±2.10</td>
<td>82.21±3.60</td>
<td>48.00±0.27</td>
</tr>
<tr>
<td>Spirulina + 4 Gy + Spirulina</td>
<td>151.10±10.42</td>
<td>188.50±4.52</td>
<td>109.30±2.70</td>
<td>47.90±1.00</td>
</tr>
</tbody>
</table>

Table 3: Hepatic levels of glutathione (GSH), malonaldehyde dismutase (MDA), catalase (CAT) as well as the content of DNA in various animal groups

<table>
<thead>
<tr>
<th></th>
<th>GSH (µg/mg tissue)</th>
<th>MDA (ng/g tissue)</th>
<th>CAT (µmol H₂O/min/g)</th>
<th>DNA (mg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>21.60±1.52</td>
<td>86.56±3.62</td>
<td>5.21±0.43</td>
<td>28.1±1.85</td>
</tr>
<tr>
<td>Spirulina group</td>
<td>24.32±1.66</td>
<td>70.50±1.18</td>
<td>4.60±0.83</td>
<td>28.1±1.03</td>
</tr>
<tr>
<td>Irradiated group 2 Gy</td>
<td>17.07±0.98</td>
<td>198.40±2.52</td>
<td>8.60±0.92</td>
<td>18.5±0.68</td>
</tr>
<tr>
<td>Irradiated group 4 Gy</td>
<td>15.50±1.13</td>
<td>382.50±3.53</td>
<td>10.50±0.55</td>
<td>12.8±0.63</td>
</tr>
<tr>
<td>Spirulina + 2 Gy + Spirulina</td>
<td>19.21±1.30</td>
<td>118.34±2.10</td>
<td>5.40±0.31</td>
<td>23.7±1.13</td>
</tr>
<tr>
<td>Spirulina + 4 Gy + Spirulina</td>
<td>18.10±1.42</td>
<td>296.50±4.52</td>
<td>6.40±0.39</td>
<td>20.3±0.73</td>
</tr>
</tbody>
</table>

Radiations are commonly used in a number of medical and industrial situations; however, their pro-oxidative effects limit their applications. The present study demonstrates that administration of Spirulina prior to gamma irradiation protected rats against the oxidative stress and tissue damage produced by sub-lethal doses of gamma radiation. The major forms of cellular damage induced by radiation are DNA damage, lipid peroxidation, and protein oxidation. The present study demonstrates increased concentration of TBARS and nucleic acid in the rat liver, indicating high level of oxidative stress, which markedly enhanced with increasing radiation dose (Table 1). Similar observations were reported on radiation-induced oxidative damage in several organs (Bhatia and Manda, 2004; Sener et al., 2003) and mitochondrial...
membranes (Kamat et al., 2000). Ionizing radiation generates ROS as a result of water radiolysis. In actively metabolizing cells, there is considerable water apart from the target macromolecules. These ROS can induce oxidative damage to vital cellular molecules and structures including DNA, lipids, proteins, and membranes (Cadet et al., 2004; Esterbauer, 1996). Products of lipid peroxidation such as MDA and 4NHE (4-hydroxynonenal) have the ability to interact with and alter macromolecules, possibly resulting in diseases (Box and Maccubbin, 1997; Petersen and Doorn, 2004). Oxidative damage to proteins, as assessed by formation of carbonyl groups is a highly damaging event, and may occur in the absence of lipid peroxidation (Dean et al., 1997; Stadtman and Berlett, 1997). Thus, modification of lipids and proteins by ROS is implicated in the etiology of radiation-induced physiological disorders and diseases. The present results show that low-energy γ-radiation from cesium-137 source produced a significant oxidative damage in rats after whole body exposure. It is reported that whole-body exposure of rats to high energy radiation from Co-60 causes tissue damage in several organs, as assessed by increased lipid peroxidation, 2, 12, and 72 h after irradiation (Koc et al., 2003a; Sener et al., 2003, 2004). Thus, radiation-induced damage might result in adverse health effects within hours to weeks or delayed effects observable many months after exposure (Vijayalaxmi et al., 2004). Recently, emerging evidence suggests that oxidative stress is possibly involved in the pathology of some diseases and other inborn errors of lipid and protein metabolism (Onody et al., 2003). Significant increase in the levels of serum lipid profile and LDL are demonstrated post radiation exposure of rats, possibly as a result of liver injury (Table 2). These changes are in agreement with previous studies on Syrian hamsters (Feurgard et al., 1999) and on mice (Agrawal et al., 2001). This indicates that ionizing-radiation-induced oxidative stress which might altered hepatic lipid metabolism and serum lipoproteins. It seems that there is an association between radiation-induced oxidative stress and elevated levels of lipid fractions and LDL (Onody et al., 2003). This association is similarly observed in other conditions characterized by increased oxidative stress (Baynes, 1991; El-Missiry et al., 2004; Zwirska-Korczala et al., 2003). Therefore, it is suggested that oxidative stress might be an important determinant of altered lipid metabolism due to radiation exposure.

The above mentioned effects were accompanied by elevated activity of ALT, AST and ALP and increased level of total serum proteins of irradiated rats with cesium-137 source, indicating occurrence of liver injury. These conclusion are in accordance with those of other studies (Bhatia and Manda, 2004) using high-energy radiation from cobalt source. Therefore, it is proposed that oxidative stress is linked to the organ damage following exposure to ionizing radiation. It is hypothesized that if the oxidative stress is involved in the origin of tissue damage, then successful antioxidant treatment should delay or prevent the onset of that damage (Halliwell and Whiteman, 2004). The present result demonstrate that *Spirulina* treatment of rats before irradiation induced protection against oxidative stress, evidenced by decreased TBARS and production in the liver compared to the irradiated non-treated rats. The protective role of *Spirulina* may be attributed to the presence of β-carotene (Luxia et al., 1996), enzyme superoxide dismutase or selenium (Henrikson, 1989) and blue pigment phycocyanin (Bhat and Madyastha, 2001). Luxia et al.(1996) reported that β-carotene of *Spirulina* may reduce cell damage, especially the damage to DNA molecules, thus playing a role in the repair of damaged liver cells. It also prevented the loss of DNA from rat liver.

This interpretation seems to be in accordance with that of recent studies in mouse bone marrow- cells, *spirulina* extract reduced the number of micronuclei from oxidative damage. Since 70% of cellular damage produced by ionizing radiation is due to ºOH formed from water radiolysis (Ward, 1988), the protective action of *Spirulina* might be attributed to its ability to scavenge this damaging radical (Wu et al., 2005). Ionizing radiation causes oxidative damage to tissues within an extremely short period, and possible
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protection against it would require the rapid transfer of antioxidants to the sensitive sites in cells. At this point, *Spirulina* seems unique among cellular antioxidants because of its physical and chemical properties; it can easily cross biological membranes and reach the cytosol, nucleus, and cellular compartments (Matsuo et al., 1989). The effect of *Spirulina* in maintaining normal hepatic functions is well documented (Dhu et al., 2004). The decrease in protein level may be due to inhibition of amino acid transporter (Brookes and Kristt, 1989) or RNA synthesis (Sarafian and Verity, 1983). The protective action of *Spirulina* against lipid and protein oxidation as a factor of modifying membrane organization may also be related to *Spirulina*’s ability to scavenge the oxidation-initiating agents, which are produced during the oxidation of proteins and lipids. Since membrane functions and structure are influenced by proteins in membranes and radiation is known to damage thiol proteins (Stacey and Kappus, 1982), it is possible that the protective action of *Spirulina* against membrane damage may be related partially to the ability of *Spirulina* to prevent protein damage. Changes in membrane structure and fluidity due to ROS reactivity after irradiation of rats could also be attributed to graded alterations in the lipid bi-layer environment (Karbownik and Reiter, 2000). Such alterations result in the disruption of membrane potential and enhanced permeability hence altered cellular function. It seems that treatment with *Spirulina* before irradiation protects against these changes. This is indicated by a significant reduction in radiation-induced hepatic injury because the biochemical parameters as well as the hepatic function tests approached control levels (Table 2). These data imply that *Spirulina* offers radioprotection at molecular and biochemical levels by protecting membranes, from breaking and consequent alteration of biochemical status of cellular functions.

At sufficiently high radiation doses, GSH becomes depleted, leaving highly reactive ROS, beyond the immediate and normal needs of the cell, to react with critical cellular biomolecules and cause tissue damage. The concentration of intracellular GSH, therefore, is the key determinant of the extent of radiation-induced hepatic injury. Thus, interest has been focused on *Spirulina*, which acts as an antioxidant and is capable of stimulating GSH synthesis. *Spirulina* is demonstrated to increase hepatic GSH content, and hence to inhibit formation of extracellular and intracellular ROS (Dasgupta, et al. 2001). It is also proposed that prevention of GSH depletion is the most efficient method of direct protection against radiation-induced oxidative toxicity. GSH depletion is prevented when *Spirulina* was administered before irradiation (Table 1). Thus, *Spirulina* has an important role in maintaining this crucial antioxidant in the liver and increasing the antioxidant capacity of hepatocytes. CAT is an inducible enzyme, decomposes H2O2, and is involved in the antioxidant defense mechanisms of mammalian cells. Thus it is an index of increased H2O2 production (Meneghini, 1997). This might explain the higher CAT activity demonstrated in the livers of irradiated rats compared to that of controls. Although it is probable that antioxidant enzymes provide important protection from radiation exposure (Sun et al., 1998), the proper balance of the enzymes, in specific cells and in the whole organism, required for maximum radioprotection is far from clear. For example, a large increase in manganese superoxide dismutase activity in some model systems may have a radio sensitizing effect rather than a radio protective effect (Scott et al., 1989), which is probably related to the inability of the cell to cope with over production of H2O2 or °OH (Weiss et al., 2003). The activity of CAT was maintained within control level by pretreatment of rats with *Spirulina*, indicating controlled H2O2 generation in the liver or its scavenging directly by *Spirulina* (Xue et al., 2010). This effect might result in reduced accumulation of lipid and protein oxidation products and ameliorated oxidative stress in the liver and presumably other tissues.

Like cholesterol, TG, LDL, and free radicals are also risk factors that tend to damage arteries, leading to heart disease. In the current study, administration of *Spirulina* to rats was found to reduce serum cholesterol, TG, and LDL levels in serum, indicating modulation of cholesterol and lipid metabolism in cell...
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(Ray, 1991). The hypocholesterolemic effect of Spirulina on rabbits fed on diet enriched with cholesterol has also been reported (Colla et al., 2008). According to Hill and McQueen (1997), HDL-C has known to be protective against the development of atherosclerosis. There is an inverse relationship between HDL-C concentration and the incidence of coronary heart disease. HDL reverse cholesterol transport whereby cholesterol synthesized is returned to the liver for reuse or re-excretion into the bile resulting in a decrease of cholesterol level. Moreover, the hypotriglyceridemic effect of Spirulina may be through its effect on the increased the activity of lipase (Iwata et al., 1990). The presence of antioxidant compounds like phycocyanin and β-carotene, linolenic acid and sulfated polysaccharide in Spirulina could be the cause of the properties and action of Spirulina on the decrease of plasma lipids levels. According to Nagaoka et al. (2005), phycocyanin cause hypocholesterolemic activity in rats. They hypothesized that phycocyanin binds to bile acids in the jejunum, this binding affects the micellar solubility of cholesterol and then suppresses cholesterol absorption. Seo et al. (2004) reported that β-carotene reduced the elevation of cholesterol and triglycerides of diabetic rats. Both sulfated polysaccharides and linolenic acid showed hypolipidemic effect (Godard et al., 2009; Serougne et al., 2004). Moreover, Kim et al. (2004) found that feeding of rats with linolenic acid rich oil lowers plasma triacylglycerol and inhibits hepatic fatty acids synthesis which may result in a hypolipidemic effect, and control hyperlipidaemia (Mary et al., 2002).

The hypocholesterolemic effect of Spirulina in humans has been reported by reducing serum cholesterol (4.5%), triacylglycerol and LDL were observed when Spirulina (4.2 g/day) was added for 8 weeks to the diet of thirty Japanese males with high cholesterol, mild hypertension, and hyperlipidemia (Khan et al., 2006). Becker et al. (1986) evaluated clinical and biochemical outcomes following the application of Spirulina to treat obesity. They found weight loss accompanied by reduced cholesterol level. This might potentiate anti-atherogenic effects of antioxidants including Spirulina. Therefore, the present data suggest that supplementation with Spirulina appears to be hypolipidemic which might potentate its beneficial use before radiation exposure.

The present study also demonstrated a significant increase in serum GGT activity after exposure of rats to ionizing radiation. GGT is a key enzyme in the catabolism of GSH (Djavaheri-Mergny et al., 2002; Lee et al., 2002). Recently, it has been reported that the extracellular cleavage of GSH by GGT induces the production of ROS, suggesting that GGT plays a pro-oxidant role (Lee et al., 2004a). Therefore, the present results suggest that serum GGT might be one of the enzymes related to oxidative stress after exposure to γ-irradiation. These associations suggest that the net result of high serum GGT activity was the increased, rather than decreased oxidative stress and damage. GGT is inversely associated with antioxidants (Brown et al., 1998; Kilanczky and Bryszewska, 2003), while Spirulina treatment stimulates several antioxidants that raise the total antioxidant capacity of the body (Gini and Muraleedhara 2010). Thus, besides its direct effect, Spirulina may protect against oxidative stress by modulating GGT level in serum by acting as antioxidant and working cooperatively with other antioxidants.

5. Conclusion

Spirulina properties and its constituents give the impression of being a radioprotective agent against gamma irradiation induced oxidative stress. This might be through stimulating GSH, modulating serum GGT activity and exerting hypolipidemic impact. Thus, supplementation with Spirulina may have a benefit for safe application of radiation technology in medicine and industry.

Acknowledgement

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6. References


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