S-Allyl-Cysteines Reduce Amelioration of Aluminum Induced Toxicity in Rats
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Abstract: Problem statement: Aluminum (Al) is a trivalent cation found in its ionic form in most kinds of animal tissues and in natural waters everywhere. Approach: It is a potent neurotoxin and has been associated in the pathogenesis of several clinical disorders including Alzheimer’s disease.

Results: The aim of the study was to demonstrate the protective effect of S-Allyl-Cysteines (SAC) against Al-induced toxicity in rat model on certain biochemical parameters, lipid peroxidation and oxidative stress enzymes of white albino rats. Six rats per group were divided into various treatment groups. Group one rats were given normal saline and served as control group. Group two animals received Al as aluminum nitrate 32.5 mg (i.p.) for the induction of toxicity. Group three to five received different doses of SAC (25, 50 and 100 mg kg\(^{-1}\)) for 3 days after 24 h of Al toxicity. Rats were orally administered their respective doses every day for 3 days. Evaluations were made in blood and tissues. The activity of Acetylcholinesterase (AchE) was inhibited in all the parts of brain after Al intoxication. Significant rise were observed the activities of Serum Transaminases (AST and ALT) after toxicant exposure. The activity of δ-Aminolevulinic acid Dehydratase (ALAD) in blood and δ-Aminolevulinic Acid Synthetase (ALAS) in brain was decreased after Al exposure. Al significant increased cholesterol, triglyceride, creatinine and urea level in serum. TBARS level was significantly higher and GSH content were significantly lower during toxicity. Total and esterified cholesterol in liver, kidney and brain were increased after Al exposure. Histopathological changes in liver, kidney and brain were also recouped with the therapy.

Conclusion/Recommendations: Our data proved that SAC which is a bioactive and bioavailable component of garlic has organosulfur compounds which regulates the thiol status of the cell and scavenges free radicals and work as an antioxidant. Thus SAC effectively reduces cognitive dysfunction and oxidative damage induced by Al.

Key words: S-Allyl-Cysteines (SAC), aluminum, oxidative stress, liver, kidney and brain

INTRODUCTION
Recent trends in controlling and treating diseases tend to favor natural antioxidant compounds rather than synthetic ones. Garlic (Allium sativum) is a commonly worldwide used food and its medical properties have been well recognized since the ancient times (Craig and Beck, 1999). Many beneficial health properties of garlic are attributed to organosulfur compounds, particularly to sulfur-bearing compounds such as allicin, S-Allyl-Cysteines (SAC), Diallyl-Di-Sulfide (DADS) and Diallyl-Sulfide (DAS). The protective actions of SAC in the basal memory responses, ischemic brain, brain edema, on learning defects (Nishiyama et al., 2001) and neurons against TM-induced neurotoxicity is reported (Kosuge et al., 2006). It also protects the Abeta-induced neuronal cell death (Ishige et al., 2007). Garlic is also one of the well known plants with multiple beneficial effects such as antimicrobial (Johnson and Vaughn, 1969), antithrombotic, hypolipidemic (Bordia et al., 1975), antiarthritic, hypoglycemic (Jain and Vjas, 1975) anticarcinogenic (Hussain et al., 1990), antifungal (Amer et al., 1980), anti-atherosclerotic (Bordia and Verma, 1980) an antioxidant against free radicals (Morihara et al., 2006; Banerjee et al., 2003). It has been shown to be significantly effective against lead, cadmium, nickel, chromium, arsenic and mercury poisoning (Senapati et al., 2001; Tandon et al., 2001; Das et al., 2009; 2008; Kalayarasan et al., 2008; Lee et al., 1999; Metwally et al., 2009).

Aluminium (Al) is a ubiquitous element and has been proposed as an environmental factor that may contribute to some neurodegenerative diseases and affects several enzymes and other biomolecules relevant to Alzheimer’s disease. It is present in many manufactured foods, medicines, cheese, tea, cosmetics and is also added to drinking water during purification purposes (Al-Hashem, 2009a; 2009b; Newairy et al., 2009; Yousef and Salama, 2009). Different forms of Al are environmental xenobiotics that induce free radical-
mediated cytotoxicity and neurotoxicity (Yousef and Salama, 2009; Prakash and Kumar, 2009; Kan et al., 2010; Bihagi et al., 2009). Also, increased aluminium burdens, can cause neurological symptoms, biochemical responses leading to unhealthy bone metabolism and learning disabilities in children (Isaacson and Jensen, 1994). The high aluminium diet led to increased central nervous system aluminium concentration and altered concentrations of the essential trace elements iron and manganese (Goulb et al., 1995), neutrophilic inflammation and oxidative stress in welders of aircraft plant (Stark et al., 2009), deregulation of cell signaling thus impairment of neurotransmission (Verstraeten et al., 2008). Aluminum may have a direct effect on iron metabolism; it influences absorption of iron via the intestine, it hinders iron’s transport in the serum and it displaces iron’s binding to transferring (Mostaghie and Skillen, 1986)

The aim of the study was to evaluate the anti-oxidant potential of S-Allyl-Cysteines (SAC) against aluminium-induced toxicity in rat model by evaluating antioxidant enzymes activities, markers of haem synthesis, acetycholenistrase in brain, LFT’s and KFT’s. The changes were substantiated by histopathological findings.

**MATERIALS AND METHODS**

Experimental animals: Sprague Dawley female albino rats weighing 160 ± 10 g from department animal facility were selected. They received a standard pellet diet (Pranav Agro Industries, New Delhi, India having metal contents in ppm dry weight Cu, 10; Mn, 33; Zn, 45; and Co, 5) and drinking water ad libitum. Animals used in this study were treated and cared for in accordance with the guidelines recommended by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India, Ministry of Culture, Chennai.

Chemicals: Aluminium nitrate (Qualigens), other analytical grade laboratory reagents were procured from Merck (Germany) HiMedia and Glaxo chemical (India) and SAC was procured from Prof Xiong.

Experimental design:

Group 1: Were control rats received a single daily
dose of normal saline orally.

Group 2: Were rats given a daily single dose of
aluminum nitrate at 32.5 mg Kg⁻¹ (1/2LD₅₀
i.p. once only) and name Al treated rats.

Group 3-5: Were rats given a dose of SAC at 25, 50 and 100 mg Kg⁻¹, p.o. for 3 days

Animals of all the groups were sacrificed after 48 hours of last treatment and different biochemical analyses were performed.

Biochemical assays: Blood was collected directly
from the heart by puncturing the retro-orbital venous
sinus (Riley, 1960) and serum was isolated for the
estimation of AST and ALT (Reitman and Frankel,
1957) and δ-Aminolevulinic Acid Dehydratase (ALAD)
(Berlin and Schaller, 1974). Serum cholesterol, Triglyceride (TG), creatinine and urea (kit method)
were estimated by autoanayler. The activity of
Acetylcholinesterase (AChE) was determined in
different parts of brain (Ellman et al., 1961). Homogenate in an isotonic solution was processed for
total and esterified cholesterol (Zlatkis et al., 1953). Hepatic, renal and cerebral LPO (Sharma and Krishna Murthy, 1968) and GSH (Brehe and Burch, 1976) was also estimated. The activity of 6-Aminolevulinic Acid Synthetase (ALAS) was also determined in brain (Maines, 1980).

Histopathological assays: Liver, kidney and brain
were dissected out washed in saline and fixed in
Bouin’s fluid, embedded in paraffin, sectioned at 6µm
and stained with haemotoxylin and eosin for
examination by light microscopy.

Statistical analysis: P values at the level of ≤ 0.05
were evaluated by student’s t test. Significance of
the difference among various groups was evaluated by one
way Analysis of Variance (ANOVA) @ F=Ps≤0.05
(Snedecor and Cochran, 1989).

RESULTS

Biochemical observations: The results demonstrates
that the toxicity produced by Al was associated with a
variety of biochemical abnormalities and these could
usually be attributed to the release of intracellular
constituents in to the circulation, following loss of
integrity of the cell membrane or interference with
normal metabolism and function. Table 1 and 2 depicts
that administration of Al elevated the activity of serum
AST, ALT and LDH where as serum protein was found
to be depleted. These results indicate a protective effect
of S-allylcysteine (P ≤ 0.05) on the membrane by virtue
of its antioxidant property. Toxicant induced depletion
in the activity of ALAD and serum proteins. SAC
therapy showed recovery pattern, this was significant at
higher doses. The serum profile of Al exposed rats reveals significant rise in triglyceride, cholesterol, creatinine and urea as kidney markers ($P < 0.05$). SAC therapy showed values near to the control at higher doses (Table 2). Al is highly neurotoxic element and has been suggested to play a role in degeneration of nerve cells in the brain of human and experimental animals. It reduced the AChE activity of cerebellum (hind brain) when compared to controls. At the same time the mid-brain and cortex (for brain) enzyme activity was also reduced ($P < 0.05$). Toxicant also caused depletion in ALAS in brain. Treatment of SAC significantly restored these parameters (Table 3).

Further, we assessed oxidative stress parameters and antioxidant activity in the liver and the kidney and the results are summarized in Table 4. Hepatic, renal and cerebral (brain) LPO was significantly increased after Al exposure whereas hepatic, renal and cerebral GSH was significantly decreased. However, combination of garlic extract reduced TBARS concentration and restored the levels of GSH. Results show that total cholesterol and esterified cholesterol in the liver, kidney and brain was increased after toxicant administration. These results show that, SAC has a protective effect on the Al induced changes in the lipid levels (Table 5). Control rats had extremely small amount of Al in liver, kidney and brain. Exposure led to a pronounced increase in Al body burden ($P < 0.05$) in all the organs. The accumulation of Al was in the order liver>kidney>brain. Therapy of SAC was significantly effective ($P \leq 0.05$) in removing Al from all the organs significantly ($P \leq 0.05$) (Table 6). An overview of the effect of extract treatment in aluminium intoxicated rats reveals that higher dose were significantly effective when compared with other doses.

**Histopathological observations:** Aluminum exposure showed, disturbed chord arrangement, enlargement in sinusoidal spaces, hypertrophy of hepatocytes with hyperchromatic nuclei. Kupffer cells were increased in number (Fig. 1). At places bile duct proliferation and inflammatory cells were seen. At low doses therapy showed mild cytoplasmic vacuolation and granulation in hepatocytes. However the highest dose showed hexagonal hepatocytes with clear nucleus (Fig. 2). Al treatment showed higher degree of degeneration in cortex and medullary region. Bowman’s capsules showed hypertrophy, disturbed endothelial lining and cytoplasmic vacuolation was observed (Fig. 3). At low dose therapy improvement was seen, however at the highest dose endothelial lining was maintained, Bowman’s capsules was recouped (Fig. 4).

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**Fig. 1:** Hypertrophy of hepatocytes, hyperchromatic nuclei with fluid filled sinus was seen in liver after Al exposure (X400)

**Fig. 2:** Al ($\text{NO}_3^-\text{SAC}_{100}$) showed hexagonal hepatocytes and clear sinus (X400)

**Fig. 3:** Al exposure increased cellularity in glomeruli and distorted endothelial lining (X400)
<table>
<thead>
<tr>
<th>Treatments</th>
<th>SAC</th>
<th>ALAD (n mol min⁻¹ mL⁻¹ erythrocytes)</th>
<th>AST (IU L⁻¹)</th>
<th>ALT (IU L⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td>7.80±0.43</td>
<td>67.3±3.72</td>
<td>41.2±2.27</td>
</tr>
<tr>
<td>Al</td>
<td></td>
<td>3.20±0.17*</td>
<td>157.0±8.67*</td>
<td>127.0±7.02*</td>
</tr>
<tr>
<td>Al + SAC₀₅</td>
<td></td>
<td>4.23±0.23*</td>
<td>122.0±6.74*</td>
<td>66.9±3.69*</td>
</tr>
<tr>
<td>Al + SAC₁₀₀</td>
<td></td>
<td>4.91±0.27*</td>
<td>116.0±6.41*</td>
<td>66.0±3.64*</td>
</tr>
<tr>
<td>Al + SAC₁₀₀</td>
<td></td>
<td>5.96±0.32*</td>
<td>116.0±6.41*</td>
<td>55.6±3.07*</td>
</tr>
<tr>
<td>Anova (F-Value)</td>
<td>40.80*</td>
<td>28.2*</td>
<td></td>
<td>70.9*</td>
</tr>
</tbody>
</table>

Values are mean ± S.E., N = 6. *: p<0.05 vs control group; #: p<0.05Vs Al administered group. ANOVA (F-values) @: Significant at 5 % level

<table>
<thead>
<tr>
<th>Treatments</th>
<th>SAC</th>
<th>Liver (µ mole min⁻¹ mg⁻¹protein)</th>
<th>Kidney (µ mole min⁻¹ mg⁻¹protein)</th>
<th>Brain (µ mole min⁻¹ mg⁻¹protein)</th>
<th>Liver (µ mole g⁻¹ protein)</th>
<th>Kidney (µ mole g⁻¹ protein)</th>
<th>Brain (µ mole g⁻¹ protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td>19.8±1.09</td>
<td>0.43±0.02</td>
<td>68.0±3.80</td>
<td>46.9±2.59</td>
<td>11.8±1.22</td>
<td>2.9±0.12</td>
</tr>
<tr>
<td>Al</td>
<td></td>
<td>55.8±3.08*</td>
<td>0.50±0.02</td>
<td>94.2±5.20*</td>
<td>75.0±4.14</td>
<td>20.3±1.22</td>
<td>4.0±0.22</td>
</tr>
<tr>
<td>Al + SAC₀₅</td>
<td></td>
<td>42.6±2.35*</td>
<td>0.45±0.02*</td>
<td>84.0±4.66*</td>
<td>53.2±2.94</td>
<td>26.2±1.44</td>
<td>4.9±0.52</td>
</tr>
<tr>
<td>Al + SAC₁₀₀</td>
<td></td>
<td>42.0±1.32*</td>
<td>0.44±0.02*</td>
<td>77.0±4.25*</td>
<td>51.8±2.86</td>
<td>28.3±1.56</td>
<td>4.9±0.52</td>
</tr>
<tr>
<td>Al + SAC₁₀₀</td>
<td></td>
<td>41.3±2.28*</td>
<td>0.44±0.02*</td>
<td>72.3±3.99*</td>
<td>48.1±2.65</td>
<td>30.5±1.68</td>
<td>10.2±0.56</td>
</tr>
<tr>
<td>Anova (F-Value)</td>
<td>37.3*</td>
<td>1.47*</td>
<td></td>
<td></td>
<td>6.35*</td>
<td>21.0*</td>
<td>38.7*</td>
</tr>
</tbody>
</table>

Values are mean ± SE, N = 6. *: p<0.05 Vs control group; #: p<0.05 Vs Al administered group; ANOVA (F-values) @: Significant at 5 % level

<table>
<thead>
<tr>
<th>Treatments</th>
<th>SAC</th>
<th>Acetyl Cholinesterase (µ mole min⁻¹ mg⁻¹ brain protein)</th>
<th>ALAS (µ mole min⁻¹ mg⁻¹ protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td>40.0±2.21</td>
<td></td>
</tr>
<tr>
<td>Al</td>
<td></td>
<td>17.6±0.97</td>
<td>9.4±0.52</td>
</tr>
<tr>
<td>Al + SAC₀₅</td>
<td></td>
<td>27.6±1.53</td>
<td>11.9±0.65</td>
</tr>
<tr>
<td>Al + SAC₁₀₀</td>
<td></td>
<td>29.6±1.63</td>
<td>12.7±0.70</td>
</tr>
<tr>
<td>Al + SAC₁₀₀</td>
<td></td>
<td>30.6±1.69</td>
<td>15.3±0.84</td>
</tr>
<tr>
<td>Anova (F-Value)</td>
<td>37.3*</td>
<td>1.47*</td>
<td></td>
</tr>
</tbody>
</table>

(F-Value) Values are mean ± SE, N = 6. *: p<0.05 Vs control group; #: p<0.05 Vs Al administered group; ANOVA (F-values) @: Significant at 5 % level

<table>
<thead>
<tr>
<th>Treatments</th>
<th>SAC</th>
<th>Lipid Peroxidation (n mole MDA g⁻¹ protein)</th>
<th>Glutathione (µ mole g⁻¹ protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td>0.45±0.02</td>
<td>7.2±0.39</td>
</tr>
<tr>
<td>Al</td>
<td></td>
<td>1.31±0.07*</td>
<td>5.02±0.27*</td>
</tr>
<tr>
<td>Al + SAC₀₅</td>
<td></td>
<td>0.67±0.03*</td>
<td>6.50±0.35*</td>
</tr>
<tr>
<td>Al + SAC₁₀₀</td>
<td></td>
<td>0.65±0.03*</td>
<td>6.70±0.37*</td>
</tr>
<tr>
<td>Anova (F-Value)</td>
<td>70.60</td>
<td>28.80*</td>
<td>6.41*</td>
</tr>
</tbody>
</table>

(F-Value)Values are mean ± SE, N = 6. *: p<0.05 Vs control group; #: p<0.05 Vs Al administered group. ANOVA (F-values) @: Significant at 5 % level

<table>
<thead>
<tr>
<th>Treatments</th>
<th>SAC</th>
<th>Total Cholesterol (mg/100 mg)</th>
<th>Esterified Cholesterol (mg/100 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td>0.12±0.006</td>
<td>0.08±0.003</td>
</tr>
<tr>
<td>Al</td>
<td></td>
<td>1.21±0.060*</td>
<td>0.20±0.011*</td>
</tr>
<tr>
<td>Al + SAC₀₅</td>
<td></td>
<td>0.49±0.027*</td>
<td>0.15±0.008*</td>
</tr>
<tr>
<td>Al + SAC₁₀₀</td>
<td></td>
<td>0.47±0.025*</td>
<td>0.14±0.008*</td>
</tr>
<tr>
<td>Anova (F-Value)</td>
<td>148.00</td>
<td>41.10*</td>
<td>53.30*</td>
</tr>
</tbody>
</table>

(F-Value): Values are mean ± SE, N = 6. *: p<0.05 Vs control group; #: p<0.05 Vs Al administered group. ANOVA (F-values) @: Significant at 5 % level
Table 6 Effectiveness of SAC against aluminum treated rats in Metal concentration (µg/g) in tissues

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Liver</th>
<th>Kidney</th>
<th>Brain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>12.50 ±.91</td>
<td>16.40 ±0.90</td>
<td>13.20±0.71</td>
</tr>
<tr>
<td>Al</td>
<td>34.10 ±1.88 *</td>
<td>42.20 ±2.32*</td>
<td>37.61±2.07*</td>
</tr>
<tr>
<td>Al+SAC25</td>
<td>21.76 ±1.20</td>
<td>38.62 ±2.13</td>
<td>36.42 ±2.01</td>
</tr>
<tr>
<td>Al+SAC50</td>
<td>19.51 ±1.07*</td>
<td>29.76±1.64*</td>
<td>30.00±1.65*</td>
</tr>
<tr>
<td>Al+SAC100</td>
<td>13.90 ±0.76*</td>
<td>20.91±1.15*</td>
<td>28.76 ±1.58*</td>
</tr>
<tr>
<td>Anova (F Value)</td>
<td>61.1 @</td>
<td>49.4 @</td>
<td>40.1 @</td>
</tr>
</tbody>
</table>

Values are mean ± S.E., N = 6. * P < 0.05 vs control group, * P < 0.05 vs Al administered group. ANOVA (F values) @ = Significant at 5 % level

DISCUSSION

The present study was undertaken to determine whether SAC can prevent and/or reduce Al-induced oxidative stress by examining different biochemical parameters of oxidative damage in the serum, the liver, kidney and brain in rats.

Our results clearly showed that there was a significant biochemical and histopathological changes suggesting strong prooxidant activity inspite of its non-redox status (Exley, 2004). Its toxicity may be mediated by free radical generation and alterations in antioxidant enzymes in vivo and in vitro (Tabaldi et al., 2009), which caused neurotoxicity (Kumar et al., 2009; Rodella et al., 2008), nephrotoxicity (Mahieu et al., 2009) and hepatotoxicity (Kutlubay et al., 2007).

Activities of serum AST, ALT, LDH, urea and creatinine were increased after toxicant administration. Changes in these enzymatic activities may be due to the leakage of these enzymes from the liver cytosol into the blood stream and/or liver dysfunction. These abnormalities were prevented by supplementation of SAC, perhaps due to its role in stabilizing the cell membrane and protect the liver from free radical-mediated liver cell toxicity various authors (Al-Hashem, 2009a; Yousef, 2004; Nayak et al., 2006). Mohamed and Awad (2008) reported similar findings after Al exposure. LDH is a hydrogen transfer enzyme is used in the diagnosis of liver damage. Other metals like cadmium also increased the serum transaminases (Al-Hashem et al., 2009; Amin et al., 2006). Results
of the present study clearly depicted that Al administration enhanced concentration of this soluble enzyme significantly. The activity of this enzyme is also increased by feedback mechanism as it is involved in glucose metabolism. It is used as marker of Al toxicity. Similar finding was noted by El-Demerdash (2004); Yousef (2004) and Anane and Creppy (2001). These values were restored near to control after SAC treatment. SAC restored the values of AST, ALT, LDH in serum along with improved histological and transmission electron microscopic structure against chromium and acetaminophen induced toxicity (Kalayarasan et al., 2008; Hsu et al., 2006).

Cholesterol, TG and creatinine were increased after toxicant exposure. The increase in serum TG is possibly due to hypoactivity of lipoprotein lipase in blood vessels which breaks up TG. High serum cholesterol level may be due to hepatic dysfunction (Al-Hashem, 2009a; Kojima et al., 2004; Kantola et al., 1998). The cholesterol content in brain was higher in Al fed rats (Pandya et al., 2004). The decreased value of lipid levels on the administration of SAC may be due to hypolipidemic effect (Chang and Johnson, 1980). The elevation in creatinine and urea levels in Al treated rats in the present study reveals significant damage in kidney. These findings are supported by various authors (Afifi, 2010; Mahieu et al., 2009; Al-Hashem et al., 2009; Rudenko et al., 1998). Toxicant administration enhanced the LPO in liver, kidney and brain but caused a significant decline in the GSH level. Elevation of LPO in liver, brain and kidney was evident by the increased production of TBARS, which suggests participation of free-radical induced oxidative cell injury in mediating the toxicity of Al (Al-Hashem, 2009a; Newairy et al., 2009; Anane and Creppy, 2001). GSH play an important role in the detoxification and metabolism of many xenobiotic compounds. Several pathologies that affect the nervous system involve oxidative stress, possibly associated with the decrease in glutathione content. The decrease in SH group of GSH content was also found in the studies of Dua and Gill (2001). GSH is the brain masters antioxidant and protect neurons from the harmful effects of free radicals. Al caused significant decrease in the GSH in brain and liver. Metals like as Cadmium, Cisplatin, lead and mercury induced oxidative stress by depleting the major intracellular antioxidant, glutathione in liver, kidney and brain (Afifi, 2010; Al-Hashem et al., 2009; Amin et al., 2006) therapy SAC provoked considerable recovery. SAC restored activities of enzymic antioxidants (SOD, CAT, GPx), non-enzymic antioxidants (vitamin C and vitamin E), GSH, LPO and reactive oxygen species in liver and serum of against chromium, alcohol and acetaminophen induced group (Kalayarasan et al., 2008; Yan and Yin 2007; Hsu et al., 2006).

Aluminum neurotoxicity is due to the contribution of the Al3+ ion to iron-induced neuronal oxidative damage. The two metals are expected to act synergistically, aluminum coordination to the neuronal membrane facilitating attacks by iron-induced free radicals, whereas membrane oxidation in turn increases aluminum binding, thus, aggravating oxidation (Berthon, 2002). Brain membranes are not only based on the presence of polysaturated fatty acids and phospholipids components, but also that of molecules with a high content of lipid/protein ratio (like e.g., myelin) supporting the fact that ions without redox capacity can stimulate lipid peroxidation by promoting phase separation and membrane rigidification (Christen, 2000).

A significant decrease was observed in the AchE of fore, mid and hind brain after Al exposure which may interfere with either synthesis of AchE or inhibit choline uptake by synaptosomes. The higher reduction in AchE activity of brain may suggest that this part of brain is much more susceptible to metal intoxication. Al also may bind with the active site of AchE hence, decreases the activity of AchE in all parts of the brain. When this enzyme is inhibited Ach is not hydrolized and accumulates in cholinergic sites causing alteration in the normal nervous system function (Moshtaghi et al., 1999). Kumar et al. (2009) reported a significant decrease in the AchE activity in brain of rats after Al exposure. Treatment with extract showed neuroprotection by enhancing AchE in all parts of brain.

Activity of ALAD in blood and ALAS in brain was significantly decreased after Al exposure. The ALAS, is first and the rate-limiting enzyme of heme biosynthesis which is localized in mitochondria. The enzyme requires glycine and succinyl Coenzyme A (CoA) as substrates and pyridoxal 5'-phosphate as a cofactor. ALAD activity is second enzyme of the haem biosynthesis pathway. The reduced level of Hb can be associated with hemolysis or disturbances in heme biosynthesis as a result of inhibit linking of iron with heme and drop in activity of ALAD and ALAS taking part in heme biosynthesis. Lead and mercury also inhibited ALAD and cause neurotoxicity (Rose et al., 2008). SAC therapy improved the activity of ALAD blood and ALAS by protecting dysfunction of mitochondria, ER, disruption of calcium homeostasis and preventing its accumulation in macrophages in hepatocyte organelles such as lysosomes vesicles (Bogdanovic et al., 2008).
The efficiency of SAC was perhaps due to the presence of these sulfur-containing biologically active lipophilic compounds, which might have chelated Al by the formation of ionic bonds between sulfur containing compounds and enhanced its excretion from the body. These easily permeate through phospholipid membranes (Miron et al., 2000) and reduce intracellular Al thus enhancing the endogenous antioxidant defenses thereby preventing reactive oxygen species formation and lipid peroxidation. It also protects histological structure thereby depleting functional improvement to some extent. The present study indicates that SAC extracted from garlic has antioxidant and hypolipidemic effects. Sulphocysteine, such as its high water solubility and stability, suggest a broad spectrum of potential therapeutic actions in different experimental models of systemic and central diseases, this aged garlic extract compound is a promising candidate to be clinically and experimentally tested in neurological degenerative events with oxidative components.

CONCLUSION

Aluminum has adverse effects on human health. Our results demonstrate that Al alters biochemical parameters induces oxidative stress and histopathological alterations Consequently, attention should be paid to the sources of aluminum in food, water and medical drugs. SAC therapy after Al exposure, minimized Al-associated hazards. Therefore, SAC could be beneficial for reducing aluminium toxicity. Further studies are required using a human population, to confirm these protective effects.

ACKNOWLEDGMENT

This study was supported by DST, New Delhi for financial assistance (SR/WOS-A/LS-153/2007). The author is thankful to Prof. Sangeeta Shukla, Dr. Monika Bhadauria, Jiwaji University, Gwalior (MP) for lab facility.

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