Toxicological Communication

Biosci. Biotech. Res. Comm. 8(2): 197-203 (2015)

BBRC Bioscience Biotechnology Research Communications

Aloe vera protects aluminium induced changes in brain enzyme activity of albino rats, *Rattus norvegicus*

Laxman Kumar and Sharique A. Ali*

Department of Biotechnology Saifia Science College, Bhopal-MP-462001, India

ABSTRACT

The current study was carried out to investigate the protective role of *Aloe vera* plant extract on aluminium induced changes in brain enzymes of albino rats. *Aloe vera* is a medicinal plant belonging to the family –Liliaceae, which has a wide range of therapeutic applications such as wound healing, diabetes, burns, for easing intestinal, curing ulcers and arthritic swellings. 30 adult rats were taken and divided into 3 groups 10 (5+5) for each. Control group animals were fed with normal diet and water adlibitum, as Group I or control group. Group II animals were fed with normal diet and received aluminium in a dose of 98 mg/kg of body weight orally for 30 and 60 days. Group III were fed with normal diet and received aloin (100mg/kg body weight) and aluminium sulphate (98 mg/kg body weight) for 30 and 60 days. On the last day of the experiment animals were sacrificed by cervical dislocation on 30th and 60th days respectively. Brain was removed and homogenized with 5 volume of ice cold 5mM Tris HCL ph 7.4 containing 30 mM sucrose. The results of the present study clearly indicated that aluminium sulphate has significantly altered the normal levels of acetyl cholinesterase, sodium potassium ATPase and glutathione of rat brain. The levels of brain enzymes were found to be highly decreased in both the alumiuium treated groups. But in contrast to this, elevated levels of acetyl cholinesterase, sodium potassium ATPase and glutathione were noticed in aloin and aluminium sulphate co treated groups, indicating the protective role of aloin against aluminium sulphate toxicity.

KEY WORDS: ALUMINIUM, TOXICITY, *ALOE VERA*, RAT BRAIN ENZYMES

INTRODUCTION

Aluminium (Al), the third most common element approximately 8% of total mineral components in the earth's crust found combination with oxygen, silicon, fluorine and other elements in the soil, rocks, clays and gems has a significant toxic potential for humans (Verstraeten *et al.*, 2008). Aluminium enters the human body via food, air, water and drugs, and is present in many manufactured foods such as processed cheese, baking

ARTICLE INFORMATION:

**Corresponding Author: drshariqali@yahoo.com*
Received 5th August, 2015
Accepted after revision 28th November, 2015
BBRC Print ISSN: 0974-6455
Online ISSN: 2321-4007 NAAS Journal Score : 3.48

Online Contents Available at: http//www.bbrc.in/

powders, cake mixes, frozen dough, pancake mixes (Levesque *et al.,* 2000) and pharmaceutical products, especially antacids (Wang, *et al.,* 2000). Chronic exposure to aluminium is involved in neuro-degenerative disorders, such as Alzheimer's disease (Flora *et al.,* 2005) dialysis, Parkinson's dementia (Hirsch *et al.,* 1991) and hepatotoxicity (Yumoto *et al.,* 1993, Muhammad *et al*, 2014 Crane *et al* 2014).

It has the potential to cause neurological disorders in human and animals, it's accumulation in the brain has been linked to various neurodegenerative diseases (Yokel, 2002; Zatta *et al.,* 2003). Aluminium ions alter the structure of cellular membranes, inhibit many enzymes like alkaline phosphatase and acetylocholinesterase, and adenyl cyclise (Zatta *et al.,* 2002; Platt *et al.,* 2001). Aluminium forms complex with ATP (Al-ATP) as it has strong affinity for phosphate ion, which is 107 times stronger than Mg 2+ ion. Therefore, it can be hypothesized that the synthesis of GSH hindered due to the less availability of ATP by altering the synthesis of g-Glutamylcysteine (g-GluCys) synthetase and glutathione synthetase, enzymes involved in GSH synthesis. Thus decreased activity of glutathione synthetase leads to reduced GSH level (Nehru *et al.,* 2005).

Salt *et al.,* (1998) reported that plant extracts detoxify various kinds of environmental pollutant. Plants have been used to treat various diseases and have been an exemplary source of medicine over the years (Ates *et al.,* 2003). *Aloe vera* is one such ancient plant whose medicinal properties have been known since centuries and has wide range of therapeutic applications such as wound healing effect, reduction of blood sugar in diabetes, for soothing burns, for easing intestinal, for curing ulcers and for reducing arthritic swellings (Shelton 2003; Davis *et al.,* 1994). *A. vera* gel contains anthroquinones (aloin, aloe-emodin) which may have a variety of properties of anti oxidant agent, including the protective role for heavy metal toxicity (Flora *et al.,* 2005; Yadav *et al.,* 2009; Zubaydi *et al.,* 2009). The goal of this study was to investigate the protective role of *Aloe vera* on aluminium induced changes in brain enzymes of albino rats.

MATERIALS AND METHODS

Healthy adult albino rats (*Rattus norvegicus*) weighing 175 ± 5 gm were used for the experiments, procured from Mhow, Bhopal (MP) India, and maintained in our laboratory. The rats were acclimatized in laboratory conditions for two weeks and were maintained at 28 ± 2^{0}C room temperature and relative humidity (60 ± 10%) with a 12 hours light-dark cycle in the animal house of biotechnology laboratory, Saifia Science College, Bhopal. Food and water were provided *ad libitum* throughout the experiment to avoid effects of starvation. No mortality was observed during the acclimatization period and during whole experimentation period up to 60 days.

Aloe vera plant leaves were used for the present study. Leaves of *A. vera* were collected in and around the Bhopal. Preparation of *A. vera* (leaf gel) extracts was done according to the method of Arunkumar *et al*., (2009) with slight modifications. Skin of the leaves were pealed and the gel inside was used for extraction. 100 gms of the gel was added to 250 mL of ethanol and extracted using the Soxlet assembly. Later on, the solvent of the extracted material was removed at low temperature in a rotary vacuum evaporator and the resulting dried extract was lyophilized in a freeze dryer.

All the experimental animals were divided into three groups as group I, II and III.

Group I: - This group of 10 (5+5) animals was fed with normal diet and water *ad libitum*, as control group. Group II: - This group of 10 (5+5) animals was fed with normal diet and aluminium in a dose of 98 mg/kg of body weight orally for 30 and 60 days. Group III: - This group of 10 (5+5) animals was fed with normal diet and received aloin (100mg/kg body weight) and aluminium sulphate (98 mg/kg body weight) for 30 and 60 days. Animals were sacrificed by cervical dislocation on 30th and 60th days respectively. Liver and kidney were isolated and kept in ice cold conditions for experiment.

Brain tissue was homogenized with 5 volume of ice cold 5mM Tris HCL ph 7.4 containing 30 mM sucrose. The homogenate was centrifuged at 1500 xg for 10 minutes to remove nuclei and cell debris. The resultant supernatant was used for further analysis. The experimental chemicals were obtained from Sigma Chemical Co. USA of analytical grade. The following Brain enzymes i.e. Acetylcholinesterase, Sodium Potassium ATPase and Reduced glutathione from rat brain of aluminium sulphate per se exposed and *Aloe vera* plus aluminium sulphate exposed and non exposed (Control) was assayed as per the following standard procedures.

Acetylcholinesterase activity of control as well as experimental rats were assayed as per the method of Ellman *et al.,* (1961).Sodium Potassium ATPase Sodium Potassium ATPase (Na+K+ATPase activity was assayed as per the method of Svoboda *et al.,* (1984).Glutathione (GSH) Reduced glutathione was determined by the method of Moron *et al*., (1979)

RESULTS AND DISCUSSION

In the present investigation, analyses of brain enzyme were done in albino rats subjected to different durations of aluminium sulphate administration. The values of brain enzymes (i.e. acetyl cholinesterase, Sodium Potas-

sium ATPase and Glutathione) of rats exposed to aluminium sulphate *per se* and in combination with aloin for a period of 30 days and 60 days with well matched controls are reported here (table 1 to 6 and figure 1 to 6).

The effects of aluminium sulphate and in combination with standard aloin on acetyl cholinesterase (AChE) activity during the 30 days and 60 days experimental period were showed in table 1,2 and figure 1,2. There was no much fluctuation in the AChE activity in the brain tissue of control animals throughout the experimental period. The data indicated that aluminium sulphate caused significant decrease in acetyl cholinesterase activity as compared to control animals after 30 days of exposure period. The value decreased from the control value of 41.80 ± 1.985µmol/min/mg protein to16.38 ± 0.4954µmol/min/mg protein (Table 1; Figure 1).

While, in combination of aluminium sulphate with standard aloin did not show as much significant reduction in acetyl cholinesterase activity where the value was found to be 27.02 ± 1.0740 µmol/min/mg protein as compared to the aluminium sulphate *per se* value of 16.38 ± 0.4954 µmol/min/mg protein and control value of 41.80 ± 1.985 µmol/min/mg protein (Table 1; Figure 1). When the period of exposure was further increased

Table 1: Showing values of acetylcholinesterase of brain of rats exposed to aluminium sulphate (98 mg /kg of body weight) *per se* and in combination with aloin for a period of 30 days with well matched controls.

Variables (N)	Mean ± SE	P-Value
Control	41.80 ± 1.9850	
Alum Per se	16.38 ± 0.4954	<0.0001****
Aloin +Alum	27.02 ± 1.0740	0.0002***

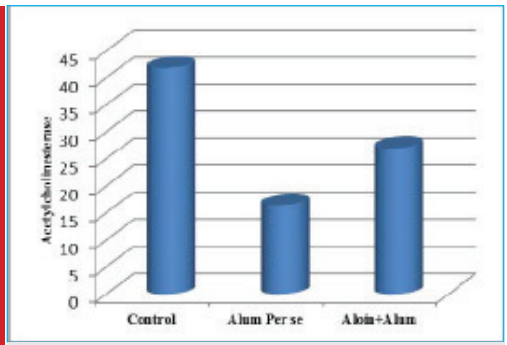

FIGURE 1: Showing values of acetylcholinesterase of brain of rats exposed to aluminium sulphate (98 mg /kg of body weight) *per se* and in combination with aloin for a period of 30 days with well matched controls.

Table 2: Showing values of acetylcholinesterase of brain of rats exposed to aluminium sulphate (98 mg /kg of body weight) per se and in combination with aloin for a period of 60 days with well matched controls.

Variables (N)	Mean ± SE	P-Value
Control	40.00 ± 0.7071	
Alum Per se	14.01 ± 0.8765	<0.0001****
Aloin +Alum	34.64 ± 1.9380	0.0317*

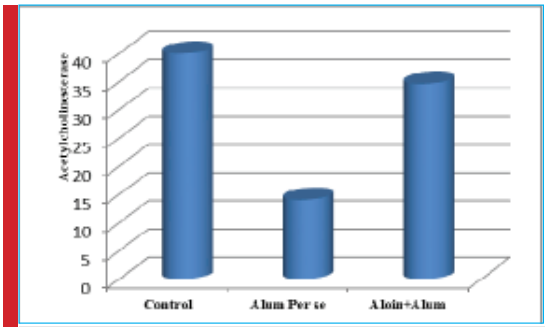

FIGURE 2: Showing values of acetylcholinesterase of brain of rats exposed to aluminium sulphate (98 mg /kg of body weight) *per se* and in combination with aloin for a period of 60 days with well matched controls.

up to 60 days the activity of acetyl cholinesterase was decreased drastically from the control value 40.00 ± 0.7071 µmol/min/mg protein to 14.01 ± 0.8765 µmol/min/mg protein which is more prominent in compared to the 30 days treated group. But when aloin was given to rats after aluminium sulphate intoxication for 60 days the value was elevated up to 34.64 ± 1.9380 µmol/min/mg protein in comparison to the *per se* value of 14.01 ± 0.8765 µmol/min/mg protein (Table 2; Figure 2).

The effects of aluminium sulphate and in combination with standard aloin on enzyme Na^+/K^+ ATPase activity during the 30 days and 60 days experimental period are shown in table 3, 4 and figure 3,4. The data obtained from the experiments clearly indicated that after aluminium sulphate intoxication Na^+/K^+ ATPase activity was decreased in 30 days exposed animals where the value was found to be 43.52 ± 1.066 nm/mg/protein which is quite less than the control value of 63.71±.6665 nm/mg/protein (Table 3; Figure 3).

On the other hand after co treatment of aloin and aluminium sulphate, decline in Na^+/K^+ ATPase activity was further continued where the value was found to be 36.71±1.099 nm/mg/protein which is also less than the control value as well as aluminium sulphate per se treated value (Table 3, Figure 3).

Table 3: Showing the effect of Aluminium sulphate (98 mg /kg of body weight) on the brain enzyme, Na^+/K^+ ATP ase activity (nm/mg/protein) of albino rats along with treatment of Aloin (100 mg /kg of body weight) plus aluminium (98 mg /kg of body weight) for 30days of exposure along with well matched control animals.

Variables (N)	Mean ± SE	P-Value
Control	63.71±.6665	
Alum Per se	43.52 ± 1.066	<0.0001****
Aloin +Alum	36.71±1.099	<0.0001****

Table 4: Showing the effect of Aluminium sulphate (98 mg /kg of body weight) on the brain enzyme, Na+/K+ ATP ase activity (nm/mg/protein) of albino rats along with treatment of Aloin (100 mg /kg of body weight) plus aluminium (98 mg /kg of body weight) for 60days of exposure along with well matched control animals.

Variables (N)	Mean ± SE	P-Value
Control	63.71±.6665	
Alum Per se	34.23±1.982	<0.0001****
Aloin +Alum	42.71±1.443	<0.0001****

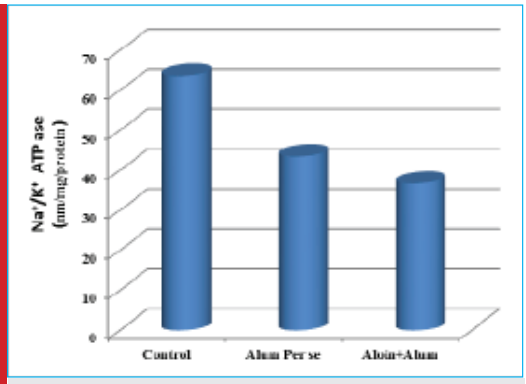

FIGURE 3: Showing the effect of Aluminium sulphate (98 mg /kg of body weight) on the brain enzyme, Na^+/K^+ ATP ase activity (nm/mg/protein) of albino rats along with treatment of Aloin (100 mg /kg of body weight) plus aluminium (98 mg /kg of body weight) for 30days of exposure along with well matched control animals.

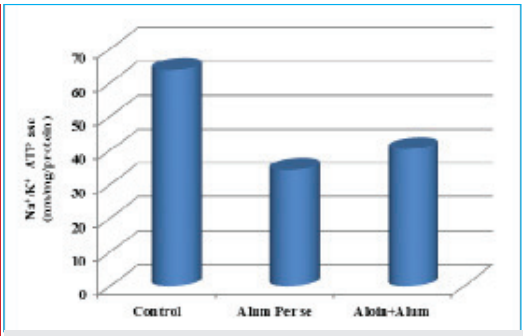

FIGURE 4: Showing the effect of Aluminium sulphate (98 mg /kg of body weight) on the brain enzyme, Na+/K+ ATP ase activity (nm/mg/protein) of albino rats along with treatment of Aloin (100 mg /kg of body weight) plus aluminium (98 mg /kg of body weight) for 30 days of exposure along with well matched control animals.

When the period of exposure was further increased up to 60 days the activity of Na^+/K^+ ATPase was drastically reduced from the control value 63.71±.6665 nm/mg/protein to 34.23±1.982 nm/mg/protein which is more prominent in compared to the 30 days treated group. But when aloin was given to rats after aluminium sulphate intoxication for 60 days the value was elevated up to 42.71±1.443 nm/mg/protein in comparison to the *per se* value of 34.23±1 nm/mg/protein (Table 4, Figure 4).

Reduced glutathione (GSH) contents in brain tissue homogenates were estimated using a colorimetric technique. As indicated by the data showed in table and figure 5, 6. Aluminium sulphate alone caused significant reduction in reduced glutathione level in both 30 and 60 days treated animals. In 30 days intoxicated animals the level of glutathione was reduced from the control value of 7.040 ± 0.1691 m mole g^{-1} to 4.060 ± 0.1806 m mole g^{-1} (Table 5; figure 5).

When the duration of exposure was increased up to 60 days the reduction of glutathione level was reduced more drastically in comparison to the 30 days treated animals where the level of glutathione was found to be 2.780 ± 0.2627 mmole g^{-1} which is quite low in comparison to the control value of 7.160 ± 0.1077 mmole g^{-1} (Table 5; figure 5).

Table 5: Showing glutathione of rat brain tissue (m mole g-l) in aluminium sulphate per se and Aluminium sulphate (98 mg /kg of body weight) with aloin exposed rats along with a period of 30 days of exposure with control values.

Variables (N)	Mean ± SE	P-Value
Control	7.040 ± 0.1691	
Alum Per se	4.060 ± 0.1806	<0.0001****
Aloin +Alum	3.526 ± 0.1911	<0.0001****

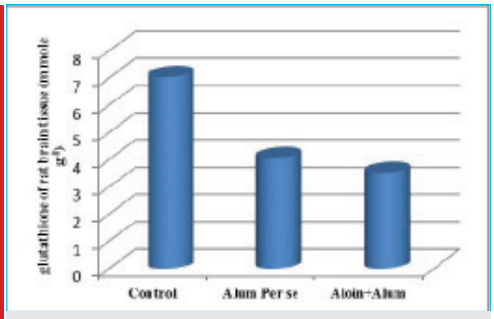

FIGURE 5: Showing glutathione of rat brain tissue (m mole g-l) in aluminium sulphate (98 mg /kg of body weight) *per se* and aluminium sulphate with aloin exposed rats along with a period of 30 days of exposure with control values.

Table 6: Showing glutathione of rat brain tissue (m mole g-l) in Aluminium per se and aluminium sulphate (98 mg /kg of body weight) with aloin exposed rats along with a period of 60 days of exposure with control values.

Variables (N)	Mean ± SE	P-Value
Control	7.160 ± 0.1077	
Alum Per se	2.780 ± 0.2627	<0.0001****
Aloin +Alum	5.296 ± 0.2180	<0.0001****

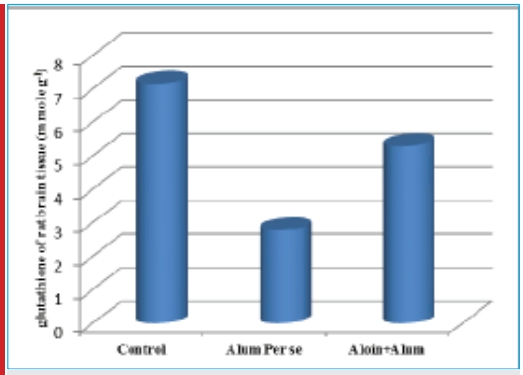

FIGURE 6: Showing glutathione of rat brain tissue (m mole g-l) in aluminium sulphate (98 mg /kg of body weight) *per se* and aluminium sulphate with aloin exposed rats along with a period of 60 days of exposure with control values.

In an another set of experiment when rats were co treated with aloin and aluminium sulphate, aloin almost nullify the toxic effect of aluminium sulphate as indicated by the glutathione level which is now found to be near about control range. In this set of experiment the level of reduced glutathione was found to be 3.526 ± 0.1911 mmole g^{-1} in 30 days exposed animals and 5.296 ± 0.2180 mmole g^{-1} in 60 days exposed animals (Table and figure 6, 6).

Acetyl cholinesterase is found at mainly neuromuscular junctions and cholinergic brain synapses, where its activity serves to terminate synaptic transmission. Acetylcholine is a neurotransmitter which enables chemical communication to occur between a nerve cell and a target cell. This target cell may be another nerve cell, muscle fiber or gland (Richetti et al 2011). The results of the present study thus have clearly indicated that aluminium sulphate significantly altered the level of acetyl cholinesterase activity in rat brain where the level was found to be highly decreased in both the treated groups. In contrast to this elevated level of acetyl cholinesterase was noticed in aloin and aluminium sulphate co treated groups, indicating the protective role of aloin against aluminium sulphate toxicity.

Several plant extracts do have enzyme protective effects and can reverse the alterations caused by the metals (Muhammad *et al*., 2014). The neuroprotective efficacy of *Cucumis melo seed oil* in protecting the cadmium induced changes in acetyl cholinesterase (AChE) activity was investigated in the rat brain. The results showed that rats intoxicated with cadmium for 4 weeks significantly reduced the AChE levels in brain, also observed that administration of oil for 4 weeks in cadmium intoxicated rats significantly elevated the activity of AChE (Somade *et al*., 2014).

Sodium, potassium-adenosine 5'-triphosphatase is an ion-transporting enzyme. Na^+/K^+-ATPase is a transmembrane protein found in higher eukaryotes that transports Na^+ and K^+ across the plasma membrane to maintain ionic gradients. These gradients, in turn, facilitate other secondary active transport systems such as Na+/amino acid and Na+/glucose cotransport in animals, Na^+/K^+-ATPase is very important for the proper functioning of cells and tissues and in the induction of cytotoxicity, especially in nerve cells (Crane *et al*., 2014; Wright *et al*., 1989). Above results of present study clearly demonstrated that aluminium sulphate significantly inhibited Na^+, K^+-ATPase activity where the level of this enzyme was dropped down in quit significant way in both 30 as well as 60 days treated group. It is also interesting to note that aloin counter balanced the toxic effect of aluminium sulphate which is indicated by the above data where level of Na^+, K^+-ATPase enzyme was found to be near as the control rats in both 30 and 60 days treated groups. Alcoholic seed extract of *Celastrus paniculatus* could potentially prevent aluminium induced neurotoxicity in the cerebral cortex, hippocampus and cerebellum of the rat brain. It was found that aluminium administration significantly decreased the level of GSH and the activities of Na^+/K^+ ATPase, Ca2+ ATPase and

Mg2+ ATPase as compared with control rats (Thangarajan Sumathi *et al*., 2013).

Glutathione (GSH) plays an essential role in the intracellular antioxidant defense against oxidant radicals, especially the OH radical. The GSH level in the brain provides indirect information on oxidative stress of the brain. It is the major free radical scavenger in the brain. Diminished GSH levels elevate cellular vulnerability towards oxidative stress; characterized by accumulating reactive oxygen species (Dringen *et al*., 2000; Pravat *et al*., 2012). In interpretation of the above data, it has been found that there is a clear cut inhibition of GSH values in all the rats exposed to aluminium sulphate in all durations of treatments, whether of short or long term exposures. In the present study, aluminium has strongly altered the normal values of GSH in brain tissues of all exposed rats, however interestingly it has been observed that co treatment with aloin markedly, counter acted the toxic effects of aluminium sulphate, by a synergistic action of ain at the cellular levels.

Ogungbe and Lawal, (2008) reported marked protective effects of ethanolic extracts of garlic, *Allium sativum* and ascorbic acid on cadmium-induced oxidative stress in rats, which had induced reduced glutathione levels. It was observed that there was significant increase in GSH content in the liver and kidney of ethanolic extract garlic pretreated rats as compared to controls. Similarly, supporting the data of our present work, Sharmila *et al*., (2009) have shown that there is a significant therapeutic efficacy of oral administration of *Ocimum sanctum* (200 mg/kg, once daily), post arsenic exposure (100 ppm in drinking water) in rats. They observed that animals exposed to arsenic showed a significant inhibition of GSH activity in blood, where as administration of *O. sanctum* post arsenic exposure, exhibited significant recovery and restored blood GSH levels, as seen in the present findings.

The results of the present study clearly indicated that aluminium sulphate has significantly altered the normal levels of acetyl cholinesterase, Sodium Potassium ATPase and glutathione of rat brain enzymes, where the levels were found to be highly decreased in both the treated group. But in contrast to this elevated level of acetyl cholinesterase, sodium potassium ATPase and glutathione were noticed in aloin and aluminium sulphate co treated groups, indicating protective role of aloin against aluminium sulphate toxicity.

ACKNOWLEDGEMENT

Authors are grateful to Principal Saifia College of Science Bhopal and Secretary, Saifia Education Society Bhopal, for providing necessary facilities and encouragement.

REFERENCES

Arunkumar, S., Muthuselvam M (2009). Analysis of phytochemical constituents and antimicrobial activities of *Aloe vera* L. against clinical pathogens. World J. Agril. Sc., 5(5): 572-576.

Ates DA, Erdogrul OT.(2003) Antimicrobial activities of various medicinal and commercial plant extracts. Turk J Biol 27:157-162.

Crane, R. K. (2014), Na+-gradient hypothesis, Rev. Physiol. Biochem. Pharmacol. 78,99-159

Dringen,R., J.M. Gutterer, J. Hirrlinger (2000), Glutathione metabolism in brain metabolic interaction between astrocytes and neurons in the defense against reactive oxygen species, Eur. J. Biochem. 267 4912–4916

Davis RH Davis, JJD,Donato, GM Hartman, RC Haas (1994) Anti-inflammatory and wound healing activity of a growth substance in *Aloe vera*. Journal of the American Pediatric Medical Association, 84 pp. 77–81.

Ellman, L., Courtey, K.D., Andreas J .V. and Featherstone, R.M. (1961). A new rapid colorimetric determination of cholinesterase activity. Biochem. Pharmacol., 7, 88e95.

Flora S., Richa Gupta and Swaran J. S. (2005): Protective Value of *Aloe vera* against Some Toxic Effects of Arsenic in Rats, Published in Wiley InterScience, Res. 19, 23–28.

Hirsch EC, Brandel JP, Galle P, Javoyagid F, Agid Y.(1991)Iron and aluminium increase in the substantia nigra of patients with Parkinson's disease: an x-ray microanalysis. J Neurochem 56: 446-451.

Levesque, S., Mizzen, CA., McLachlan, DR.,Fraser, PE.,. (2000) Ligand specific effects on aluminium incorporation and toxicity in neurons and astrocytes. Brain Res. 877: 191-202,

Muhammad, A., O. A. Odunola, M. A. Gbadegesin, A. M. Adegoke, J. O. Olugbami, and N. S. Uche (2014), Modulatory role of *Acacia* honey from north-west Nigeria on sodium arsenite-induced clastogenicity and oxidative stress in male Wistar rats, Natural Product Research 29, 4, 321–326.

Moron MS, Dipierre JW, Mannervik B. (1979) Levels of glutathione reductase and glutathione-S-transferase activities in rat lung and liver. Biochem Biophy Acta 582: 67-8.

Nehru B, Anand P. (2005) Oxidative damage following chronic aluminium exposure in adult and pup rat brains. J Trace Elem Med Biol.19(2–3):203–208.

Ogungbe, I.V. and A.O. Lawal, (2008). The protective effect of ethanolic extract of garlic and ascorbic acid on cadmium-induced oxidative stress. J. Biol. Sci., 8: 181-185.

Platt B, Fiddler G, Riedel G, Henderson Z.(2001) Aluminium toxicity in the rat brain histochemical and immunocytochemical evidence.Brain Res Bull. 55:257-267.

Pravat K. Mandal A, Manjari Tripathi, Sreedevi Sugunan (2012), Brain oxidative stress: Detection and mapping of anti-oxidant marker 'Glutathione' in different brain regions of healthy male/female, MCI and Alzheimer patients using non-invasive magnetic resonance spectroscopy, Biochemical and Biophysical Research Communications 417 43–48

Richetti, S.K., Rosemberg,D.B., Ventura-Lima, J.,Monserrat,J.M., Bogo, M.R. and Bonan C.D.(2011). Acetylcholinesterase activity and antioxidant capacity of zebrafish brain is altered by heavy metal exposure. Neurotoxicol., 32, 116–122.

Salt, D.E., R.D. Smith and I. Raskin (1998) Phytoremediation. Annu. Rev. Plant Physiol. Plant Mol. Biol., 49, 643-668

Sharmila, G., G Kumar, A.G. Murugesan (2009), Effects of leaves extract of *Ocimum sanctum* L. on arsenic-induced toxicity in Wistar albino rats, Food and chemical toxicology: 47(2):490-5.

Somade PM, R. S. Adnaik, S. K. Mohite, C. S Magdum (2014), Protective role of *Curcumis melo* against cadmium -induced oxidative neurotoxicity in mice, International Journal of Universal Pharmacy and Bio Sciences 3(4): p269-279

Shelton RM. (1991) *Aloe vera:* its chemical and therapeutic properties. Int J Dermatol 30:679-683.

Svoboda P, Svartengren J, Naprstek J & Jirmanova I (1984) The functional and structural reorganisation of the plasma membranes of brown adipose tissue induced by cold acclimation of the hamster. Changes in catecholamine sensitive adenylate cyclase activity. Molecular Physiology 5197–210.

Sumathi, T., Chandrasekar Shobana, Varadharajan Mahalakshmi, Ramachandran Sureka, Manogaran Mubathra (2013), Oxidative stress in brains of male rats intoxicated with aluminium and neuromodulating effect of *Celastrus paniculatus* alcoholic seed extract, Asian J Pharm Clin Res, Vol 6, suppl 3, 2013, 80-90

Verstraeten, S.V., Aimo, L., Oteiza, P.I., (2008). Aluminium and lead: molecular mechanisms of brain toxicity.Archives of Toxicology. 82, 789–802.

Wang, M., Ruan, D., Chen, J., Xu, Y., Lack of effects of vitamin E on aluminium-induced deficit of synaptic plasticity in rat dentate gyrus in vivo . Food Chem. Toxicol. 40: 471-478, (2002).

Wright SH, Manahan DT (1989) Integumental nutrient uptake by aquatic organisms.Annu Rev Physiol 51(1):585–600.

Yadav M R Sanath DS Singh (2009): Heavy metals toxicity in plants: An overview on the role of glutathione and phytochelatins in heavy metal stress tolerance of plants, South African-Journal of Botany Volume 76, Issue 2: 167-179.

Yokel RA. (2002)Aluminium chelation principles and recent advances. Coord Chem Rev; 228:97–113.

Yumoto S, Ohashi H, Nagai HS, Kakimi A, Ishikawa K, Kobayashi(1998) Aluminium toxicity in the rat liver and brain. Nucl Instrum Methods Phys Res B 1993; 75: 188-190.

Zatta P. Ibn-Lkhayat-Idrissi M, Zambenedetti P, Kilyen M, Kiss T. (2002) In vivo and in vitro effects of aluminium on the activity of mouse brain acetylcholinesterase. Brain Res Bull. 59(1):41–45.

Zatta P, Lucchini R. van Rensburg SJ. Taylor A.(2003)The role of metals in neurodegenerative processes: Aluminium, manganese, and zinc. Brain Res Bull. 62:15–28.

Zubaydi S R., Maetham A Al- and Shyma A J. Raesan (2009): Antibacterial effect of some medicinal plant extracts against some pathogenic bacterial strains. J Duhok Univ;.12:244-249.