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***Research Paper***

# AMELIORATION OF THE TOXIC EFFECTS OF ALUMINIUM INDUCED NEURODEGENERATIVE CHANGES IN BRAIN OF ALBINO RATS BY *Aloe vera*

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**Abstract**

The current study was carried out to investigate the protective role of *Aloe vera* plant extract on aluminium induced neuro-degenerative changes in brain 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 30$^{th}$ and 60$^{th}$ days respectively. While examination of brain sections, aluminium treated group *per se* showed abnormal characteristic architecture compared with the control group. Rats exposed to precalculated dose of aluminium sulphate for 30 days did not show any notable alterations in brain histology, whereas rats exposed to the same dose for 60 days intoxication showed significant neurodegenerative changes in the hippocampus, amygdala, motor cortex, and cerebellum. It was also observed that supplementation of *A. vera* extract noticeably reduced degenerative changes caused by aluminium and improved the architectural histology of brain and significantly reduced brain damage and improved functional outcome.

Key words: Aluminium Toxicity, Aloe vera, Albino Rats, Brain and Histopathology.

## 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[1].

Aluminium enters the human body via food, air, water and drugs, and is present in many manufactured foods such as processed cheese, baking powders, cake mixes, frozen dough, pancake mixes [2] and pharmaceutical products, especially antacids[3]. 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 [4,5]. The pathologic defects due to aluminium toxicity in rats to be included spongioform changes in the neurons specially those of hippocampus, nuclear deformity, and neurofibrillary degeneration similar to neurofibrillary tangles in Alzheimer's disease [6]. The toxic effects of chronic aluminium intoxication could be mediated through modifications in the intracellular calcium homeostasis, which may lead to impaired neuronal function [7]. Chronic exposure to aluminium is involved in neuro-degenerative disorders, such as Alzheimer's disease[8] dialysis, Parkinson's dementia,[9] and hepatotoxicity [10]. The toxic effects of aluminium appear to be mediated, at least in part, by free-radical generation [11]. The treatment commonly used in aluminium disorders is desferrioxamine[12] However, desferrioxamine therapy is associated with undesirable side effects, it is very expensive, and it is only efficient when applied intravenously or subcutaneously[13].

Plants have been used to treat various diseases and have been an exemplary source of medicine over the years [14]. It has been reported that plant extracts detoxify various kinds of environmental pollutant [15]. *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 [[16, 17]. *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 [18,19,20] The goal of this study was to investigate the protective role of *Aloe vera* on aluminium induced neuro-degenerative changes in Rat brain.

## 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 *adlibitum* 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.

### Collection and preparation of plant materials for experiment

*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 and Muthuselvam [21] 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.

### Experimental design

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 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. Animals were sacrificed by cervical dislocation on $30^{th}$ and $60^{th}$ days respectively. Brain was isolated and kept in ice cold conditions for experiment.

**Histopathological work**

Samples of rat brain of both control and treated with aluminium sulphate *per se* treated and aluminium sulphate plus aloin treated rats were immediately excised, fixed in Bouins fixative followed by standard procedures of paraffin embedding and were sectioned at 5-6 microns. Sections were stained with haematoxylin and eosin and mounted with Canada balsam/DPX abd were examined by Olympus light microscope to evaluate histological changes. The experimental chemicals were obtained from Sigma Chemical Co. USA of analytical grade.

**RESULTS**

In the present investigation, histological analyses of brain was done in albino rats subjected to different durations of aluminium sulphate administration. Photomicrographs were taken for histopathology of the brain tissue sections at 10X and 40X magnification and reported here. H&E stained sections displayed restoration of the pyramidal cells to nearly their normal structure.

**Brain**

Nervous system is a vulnerable target for toxicants due to critical voltages which must be maintained in the cells and the all responses when voltages reach threshold levels. Aluminium (Al) has the potential to be neurotoxic in human and animals.

Section of control rat brain showed the typical layered appearance of the cerebral cortex labelled 1-6 as follows: 1 - molecular layer; 2 - external granular layer; 3 - pyramidal cell layer; 4 - internal granular layer;5 - ganglionic layer; 6 - multiform layer. Section of the brain of rats fed aluminium sulphate showed disorganization of normal architecture. The histopathology of brain tissue has been demonstrated that rats exposure to aluminium sulphate for duration of 30 and 60 days intoxication resulted into neuronal vacuolation and necrosis of the cerebral cortex which are form of neuro-degeneration.

Rats exposed to precalculated dose of aluminium sulphate for 30 days did not show any notable alterations in brain histology, whereas rats exposed to the same dose for 60 days intoxication showed significant neurodegenerative changes in the hippocampus, amygdala, motor cortex, and cerebellum. Changes included decrease in size and number of neurons in all the regions, decrease in the number of Purkinje cells in the cerebellum, and signs of chromatolysis and gliosis in the motor cortex.

It was also observed that supplementation of *A. vera* extract noticeably reduced degenerative changes caused by aluminium and improved the architectural histology of brain and significantly reduced brain damage and improved functional outcome. H&E stained sections displayed restoration of the pyramidal cells to nearly their normal structure.

**DISCUSSION:**

**Brain**

In the present study, rats exposed to precalculated dose of aluminium sulphate for 30 days did not show any notable alterations in brain histology, whereas rats exposed to the same dose for 60 days intoxication showed significant neurodegenerative changes in the hippocampus, amygdala, motor cortex, and cerebellum. Changes included decrease in size and number of neurons in all the regions, decrease in the number of Purkinje cells in the cerebellum, and signs of chromatolysis and gliosis in the motor cortex. Sections of control rat brain showed the typical layered appearance of the cerebral cortex as follows: cellular layer; external granular layer; pyramidal cell layer; internal granular layer, ganglionic layer and the multiform layer (See Photomicrography plate).

On the other hand, section of the brain of rats fed aluminium sulphate showed disorganization of normal architecture. The histopathology of brain tissue has demonstrated that rats exposed to aluminium sulphate for longer duration of 60 days resulted into marked neuronal vacuolation and necrosis of the cerebral cortex which are some forms of neuro-degeneration (Photomicrography plate).

The role of green tea in protection against neurotoxicity induced by lead acetate was investigated in rats [22]. In this study, lead acetate was given orally at a dose of 100 mg/kg body

weight, while green tea was given in drinking water at a concentration of 5 g/L to experimental rats. Their histopathological studies of brain, showed normal histopathological structure in control and green tea treated groups, while in lead treated rats, oedema was observed in the hippocampus area and between the cells associated with focal gliosis in the cerebrum, as seen with aluminium sulphate. Their findings are in corroboration with the present work under taken on the effects of alumiunim *per se* and its counter action by aloin.suggested that co-administration of green tea with lead acetate significantly alleviated these adverse effects[22].

The data of our work in relation to damages caused by alumiuim and phyto protection by aloin the extract of *Aloe vera* has considerable similarity with the work of Tandon *et al.,* (2012), who have evaluated the protective effect of aqueous extract of *Psidium guajava* leaves against sodium arsenite induced toxicity in experimental rats. Histopathological results revealed mild to severe type of necrosis and degenerative changes with cytological alteration in brain tissues. Neurons were shrunken due to necrosis that indicated a metal induced degenerative process. The data of the present work in relation to the amelioration of the damages by aloin are in full corroboration with this above cited reference, where the workers had observed that treatment with aqueous extract of *P. guajava* had significantly restored activities of oxidative stress but with the limited protective activity on tissue architecture. Therefore they have concluded that prophylactic co-administration of plant extract could provide specific protection from oxidative injury and to some extent on tissue damage as well [23].

Recently Shrivastava (2013), have demonstrated the ameliorative effect of garlic extract against aluminium nitrate induced toxicity in rat brain tissue quite similar to what we have observed presently with aloin . He observed neuronal degeneration and glial cell (microglia) proliferation in brain and pyknotic neurons along with cerebellar atrophy, which was also observed in aluminium treated rats. He further reported that garlic extract of 25 mg/kg showed mild improvement in Purkinje cells. Astrocytes led to scattered neurons with reduced vacuolation in granule cell layer. The oligodendrites were reduced in size. Astrocytes, oligodendrites and Purkinje cells were maintained at a 50 mg/Kg dose of garlic extract but still vacuoles in endoneurium were seen. While treatment with higher dose of garlic resulted in almost normal histoarchitecture depicting by all normal layers and Purkinje neurons. By these observations he concluded that garlic can counteract the deleterious effects of aluminium very similar to what we have observed with aloin [24].

Recently, Adikwu *et al.,* (2014) have suggested that in brain, lead induces cerebellar edema, cerebral satellitosis and encephalomalacia with impairments in cortex, hippocampus and cerebellum. They have also reported that the toxicological effects of lead were mitigated by vitamin C, vitamin E, selenium, zinc and calcium. Some extracts of plant origin also ameliorated the toxicological effects of lead. Some of these mitigating agents may require further evaluation if they could be of clinical application[25].

Thus it is concluded that these above quoted references and the data of the presently carried out investigation, clearly showed that the herbal extracts of certain indigenous plants possesses considerable protective effects against metal induced augmented oxidative stress in rat's brain. In the present study, aluminium sulphate induction also caused histopathological changes in the cerebral cortex, cerebellum and hippocampus of rat brain which was reverted by pre-treatment with aloin treatment.

Thus the above interpretation from our studies clearly indicates the potential of plant extracts like that of *Aloe vera* in negating the neuro-toxicological manifestations of aluminium, which can be a potential candidate for protecting the onset of dreadful neurological disorders like Alzheimer's and Parkinsons, which are on an alarming rise due to excessive anthropogenic use of aluminium.

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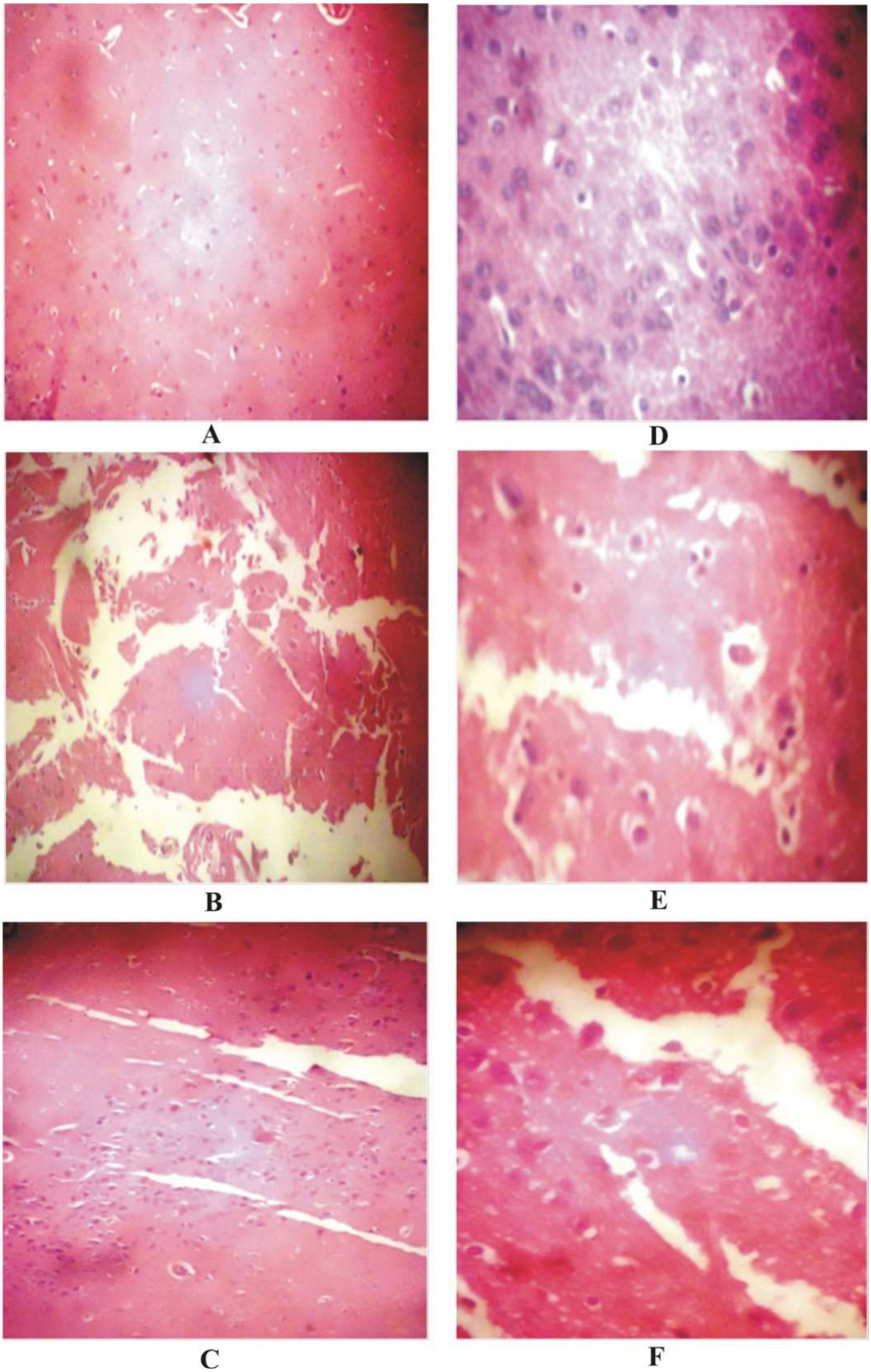


**Photomicrograph plate :** Histopathology of the brain tissue showing **A.** Control, **B.** Aluminium Sulphate *Per se* treated, **C.** Aluminium Sulphate + Aloin co-treated sections at10X magnification and **D.** Control, **E.** Aluminium Sulphate *Per se* treated, **F.** Aluminium Sulphate + Aloin co-treated sections at40X magnification.

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