Journal of Pharmaceutical Research International

25(3): 1-18, 2018; Article no.JPRI.46699
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Modulation the Neuro-toxicity Induced by Aluminum Chloride in Rats Using Beetroots and Broccli Extracts

Abeer Ali Al-Balawi[1], Yousri Mohamed Ahmed[1,2,3], Ashwag Albukhari[1], Shareefa A. ALGhamdi[1], Mustafa A. Zeyadi[1], Morog R. Maddah[1], Etimad H. Huwait[1], Soad Ali[4], Taha A. Kumosani[1,2] and Said S. Moselhy[1,5,6*]

[1]Department of Biochemistry, Faculty of Science, King Abdulaziz University, Jeddah, Saudi Arabia.
[2]Production of Bioproducts for Industrial Applications Research Group and Experimental Biochemistry Unit, King Fahd Medical Research Center, King Abdulaziz University, Saudi Arabia.
[3]Department of Microbial Biotechnology, Genetic Engineering and Biotechnology Research Division, National Research Center, Dokki–Cairo, Egypt.
[4]Department of Anatomy, Yousef Abdullatif Jameel Chair of Prophetic Medical Applications (YAJCPMA), Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia.
[5]Bioactive Natural Products Research Group, King Abdulaziz University, Saudi Arabia.
[6]Department of Biochemistry, Faculty of Science, Ain Shams University, Cairo, Egypt.

Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2018/v25i330100
Editor(s):
(1) Dr. Jinyong Peng, Professor, College of Pharmacy, Dalian Medical University, Dalian, China.
Reviewers:
(1) Vijaya Krishnan, MGM College of Physiotherapy, India.
(2) Eman A. Mohamed, Kafrelsheikh University, Egypt.
Complete Peer review History: http://www.sdiarticle3.com/review-history/46699

Original Research Article

Received 08 November 2018
Accepted 21 January 2019
Published 21 February 2019

ABSTRACT

Backgound: The generation of oxidative stress can be referred to Aluminium toxic effect in animals and humans. This study aimed to evaluate the role of broccoli (Br) and beetroot (Be) extarcts as antioxidant that prevents oxidative stress that associated with aluminum toxicity. **Materials and Methods:** Fifty Wister female rats were grouped into five groups (each 10 rats): Group 1: control group, administered drinking water only. Group 2: (Neurogenerative) which were induced by oral administration of aluminum chloride (20 mg/kg b.w) daily for one month. Group 3:

**Corresponding author: E-mail: moselhy6@hotmail.com, seldesouky@kau.edu.sa;*

Rats given aluminum chloride were treated with Rivastigmine (Ri) (1 mg/kg b.w) as a reference drug daily for five weeks. Group 4: Rats given aluminum chloride were treated with beet root extract (50 mg/kg b.w) daily for six weeks. Group 5. Rats given aluminum chloride were treated with broccoli extract (50 mg/kg b.w) daily for five weeks.

Results: ($AlCl_3$) group showed a significant increase in Ach level ($P<0.05$) and a non-significant change in DOP and NE levels compared to control. ($AlCl_3$+Be) was non-significant ($P<0.05$) change in Ach, DOP and NE levels compared to ($AlCl_3$) group and showed a significant ($P<0.05$) increase in Ach level compared to control. ($AlCl_3$+Br) showed a significant ($P<0.05$) increase in NE level and non-significant ($P<0.05$) change in Ach and DOP levels compared to ($AlCl_3$) group. ($AlCl_3$+Ri) showed a significant ($P<0.05$) increase in Ach, DOP and NE levels compared to ($AlCl_3$) group. Also, showed a significant ($P<0.05$) increase in Ach and NE compared to control.

Conclusion: Neuroprotective role of broccoli in the present study which may result from its antioxidant properties due to its bioactive content such as glucosinolate, isothiocyanate, Sulforaphane, and flavonoids. Therefore, Broccoli can have a favorable effect on neurotoxicity due to their antioxidant and anti-inflammatory properties.

Keywords: Neurotoxicity; Brocolli; beetroots; antioxidants.

1. BACKGROUND

Aluminium (Al) is the most abundant metal on earth and it was also known as a neurotoxicant [1]. Several studies have indicated neurobehavioral, neuropathological, neuro-chemical and neurophysical effects following Al exposure. It can react with other metals in the environment to form various complexes. The widely spread use of products that contain or made from Alensures its presence within our body [2]. Algets access to the human body through the environment, food or drugs. However, there is no recognized physiological function for Alinside the body and as a result, this metal can also produce reverse physiological effects [3]. The generation of oxidative stress can be referred to Altoxic effect in animals and humans. The oxidative stress has been involved in the pathogenesis of various neurodegenerative conditions including Alzheimer's disease and Parkinson's disease [4]. Dueto the easy access of Alto the central nervous system under normal physiological conditions and its accumulation in the brain, Al has been reported to alter the blood-brain barrier (BBB) [5]. The main toxic effects of Al occur in the brain, the nervous system and the kidney. The brain is sensitive to oxidative stress due to the low levels of antioxidants and high levels of free radicals following toxicity and therefore, it is considered as the most susceptible organ to Al toxic effect [6]. Oxidants and antioxidants play a significant role in maintaining the balance between the antioxidant system of the body and free radicals that are produced by body metabolism or derived from environmental sources [7]. Different antioxidant compounds that were extracted from natural products (nutraceuticals) have shownneuroprotective activity from neuronal cell death and neurodegeneration using different *in vitro* and *in vivo* experimental models [8]. Nutraceuticals that are extracted from therapeutic plants have shown an essential role in drug discovery due to the complexity and abundance of secondary metabolites composition with the unique structure of the molecular composition bearing a significant amount of stereo-centres revealing high specificity connected to biological activity. Different extraction techniques are used for the extraction of natural products that aim to separate certain class of compounds from a very complex matrix [9]. A variety of natural products which contain bioactive nutrients play a critical role in prevention and cure of various neurodegenerative diseases and other neuronal dysfunctions [10]. Because the plants are important components in the dietary food chain, the nutritional health is completely dependent on plant-based food. Plants provide all the mineral, organic and almost all essential nutrients to humans and therefore, they are good sources of chemicals that promote health [11].

Recently, red beetroot (*Beta vulgaris* rubra) has been attracting the attention as a functional food due to its biological activity and its potential role in improving health and preventing disease [12]. Its native is the Mediterranean and is widely cultivated in America, Europe and throughout India. Several parts of this plant are used in traditional Indian medicine for numerous therapeutic properties [13]. The researchers studied free radical scavenging activities which revealed that they are rich in antioxidants due to the presence of compounds such as carotenoids, folic acids, phenols and flavonoids [14].

Commonly known by Broccoli (*Brassica oleracea* L. var. Italica), a plant that known by its benefits in health improvement, contains high amount of nutrients such as vitamins, phenolic compounds, and dietary essential minerals. However, the interest into the benefits of broccoli that exceeded its role as a basic nutrition has been raised over the years [15]. Broccoli was shown to prevent oxidative stress that is associated with many diseases. This study aimed to evaluate the role of broccoli and beetroot extracts as antioxidants in preventing the oxidative stress associated with Altoxicity.

2. MATERIALS AND METHODS

All chemicals and drugs, which were used in this study, were of analytical grade and were supplied from different companies for medical and commercial services.

2.1 Plant Material and Extract Preparation

The beetroot and broccoli were procured from the supermarket in Jeddah.

Preparation of beetroot and broccoli Extracts was done as described in [16]. Briefly, 100 g of fresh Broccoli or beetroots samples were homogenized and extracted with 1L of 70% methanol at room temperature for 120 min with stirring to ensure the extraction, followed by centrifugation (10 min, 4°C). The supernatants were collected and methanol was completely removed using a rotary evaporator. Then, the aqueous fractions containing bioactive compounds were lyophilized and used as dry broccoli extracts.

2.2 Animals and Experimental Design

Fifty Wister female rats weighing between 100 to 150 gm were obtained from King Fahd Medical Research Center (KFMRC), King Abdul-Aziz University, Jeddah, Saudi Arabia. Ethical approval for the current study was obtained from the animal house at KFMRC. Rats were randomly grouped into five groups (each 10 rats) as following

- Group 1 (control group): Rats were administered drinking water only.
- Group 2 (Neurogenerative): Rats were orally administrated aluminum chloride (20 mg/kg b.w) daily for one month.
- Group 3 ($AlCl_3$+Bi): Rats were given aluminum chloride and treated with Rivastigmine (1 mg/kg b.w) as a reference drug daily for five weeks.
- Group 4 ($AlCl_3$+Be): Rats were given aluminum chloride and treated with beet root extract (50 mg/kg b.w) daily for five weeks.
- Group 5 ($AlCl_3$+Br): Rats were given aluminum chloride were treated with broccoli extract (50 mg/kg b.w) daily for five weeks.

At the end of the treatment, animals were euthanized by cardiac puncture under thiopental general anesthesia and death was confirmed by cervical dislocation. Blood was collected from the inner can thus of the eye using heparinized capillary tube and centrifuged for 15 min at 3000×g to separate blood plasma for the estimation of biochemical parameters.

2.3 Estimation of Plasma Biochemical Parameters

For the assessment of liver functions, kinetic methods for the determination of activities of aspartate aminotransferase (AST) and alanine aspartate aminotransferase (ALT) were used according to the recommendation of the Expert Panel of the IFCC (International federation of clinical chemistry). Alkaline phosphatase (ALP) activity was determined according to the recommendation of the German Clinical Chemistry Association. While the plasma total protein concentration was estimated by biuret method as described in [17].

2.4 Oxidative Stress Biochemical Assays

The following biochemical markers were measured in the liver and kidney homogenates according to the manufacturers' instructions (All kits were purchased from Elabscience company): reduced glutathione (GSH) assay kit (Catalog No: E-BC-K05), glutathione peroxidase (GSH-PX) assay kit (Catalog No: E-BC-K096), total antioxidant capacity assay kit (Catalog No: E-BC-K136).

2.5 Estimation of Plasma Aluminum Level

Plasma collected from rats were mixed with an equal volume of 0.2% HNO3 to eliminate the problems of organic residue accumulation in the furnace. Aluminum was determined using calorimetric method with aluminon (triammonium salt of aurintricarboxylic acid) [18], a dye commonly used to detect the presence of aluminum ion in an aqueous solution. The compound aluminum forms a red lake color with aluminum in neutral solution.

2.6 Estimation of Plasma Acetylcholinesterase (AChE) Level

The Competitive AChE ELISA Kit (Catalog No: E-EL-R0355- Elabscience) was used to determine AChE level according to the manufacturer's instructions.

2.7 Estimation of Brain Neurotransmitters

The following neurotransmitters were measured in the brain according to the manufacturers' instructions. All kits were purchased from Elabscience company: Acetylcholine (ACH) ELISA Kit (Catalog No: E-EL-0081- Elabscience). Dopamine(DA) ELISA Kit (Catalog No: E-EL-0046-Elabscinence).
Noradrenaline/Norepinephrine (NA/NE) ELISA Kit (Catalog No: E-EL-0047- Elabscience).

2.8 Histological Examination

Brain tissue was initially fixed with 10% neutral buffered formalin solution, embedded in paraffin, sectioned at 4 µm thickness, and stained with hematoxylin and eosin (H&E). Sections were stained with hematoxylin and eosin.

2.9 Statistical Analyses

The statistical analyses were performed using the (SPSS program for Windows, version 20). Add details here about the statistical tests that were used (t test, ANOVA etc) plus the P values.

3. RESULTS

As indicated in Table 1, $AlCl_3$ group showed non-significant (P>0.05) changes in Hb level and RBCs count compared with control group. On the other hand, there was a significant (p<0.05) decrease in platelets level and WBCs count compared with control group. For ($AlCl_3$+Be) group, there was a significant (P<0.05) decrease in RBCs count and platelets level compared to control and a non-significant (P>0.05) increase in WBCs compared with ($AlCl_3$) group. While showing a non-significant (P>0.05) change in Hb, RBCs count, and platelets levels compared to group of ($AlCl_3$). In ($AlCl_3$+Br) group, there was a significant (P<0.05) increase in Hb level and WBCs count and a significant (P<0.05) decrease in platelets level compared to ($AlCl_3$) group and anon-significant (P>0.05) change in RBCs count compared to ($AlCl_3$) group. For ($AlCl_3$+Ri) group, there was a significant (P<0.05) increase in Hb level, RBCs, platelets WBCs count compared to ($AlCl_3$) group.

In (Table 2) Fig. 1 showed a significant (P<0.05) increase in Allevel ($AlCl_3$) group compared with control. While treatment groups showed a significant (P<0.05) decrease and a significant (P<0.05) increase in Allevel compared to ($AlCl_3$) and control group, respectively.

In Table 3, ($AlCl_3$) group showed a significant (P<0.05) increase in ALT, AST levels and a significant (P<0.05) decrease in albumin level compared to control group. Additionally, ($AlCl_3$) group showed a non-significant (P>0.05) changes in ALP and protein levels compared to control.

All treatment groups showed a significant (P<0.05) increase in ALT level compared to ($AlCl_3$) and control groups.

($AlCl_3$+Be) group showed a significant (P>0.05) decrease in ALP and increase in protein compared to ($AlCl_3$) group. Furthermore, there was a significant (P>0.05) increase in AST and was a significant (P>0.05) decrease ALP and albumin levels compared to control group.

($AlCl_3$+Br) group showed a significant (P>0.05) decrease in ALP and anon-significant (P>0.05) change in protein compared to ($AlCl_3$) group. Also, there was a significant (P<0.05) increase in AST and a decrease in albumin level compared to control group.

($AlCl_3$+Ri) group showed a significant (P<0.05) increase in AST level and a decrease in ALP and protein levels compared to ($AlCl_3$) group. For albumin level, there was a non-significant (P>0.05) change compared to ($AlCl_3$) group and a significant (P<0.05) decrease compared to control.

Data in Table 4 revealed a significant (P<0.05) increase in uric acid and creatinine levels ($AlCl_3$) group and non-significant (P>0.05) decrease in urea level compared to control group.

($AlCl_3$+Be) and ($AlCl_3$+Ri) groups showed non-significant (P>0.05) changes in uric acid, urea and creatinine levels compared to ($AlCl_3$) group and showed a significant (P<0.05) increase in uric acid compared to control.

($AlCl_3$+Br) group showed a significant (P<0.05) decrease in uric acid and a non-significant (P>0.05) changes in urea and creatinine levels compared to ($AlCl_3$) group.

Table 1. Comparison of blood indices in different studied groups

Parameters \ Groups	Control	AlCl3	AlCl3+Be	AlCl3+Br	AlCl3+Ri
HB (g/dL)	14.66±0.33	14.31±0.63	14.64±0.93	15.04±0.79	15.74±0.66
P1		0.397	0.960	0.371	**0.012**
P2		-	0.334	**0.048**	**0.0001**
P3		-	-	0.259	**0.002**
P4		-	-	-	0.054
RBCs (10^6 cells/ml)	7.78±0.55	7.48±0.86	6.76±1.11	7.12±1.12	8.30±0.24
P1		0.538	**0.039**	0.185	0.278
P2		-	0.072	0.374	**0.041**
P3		-	**-**	0.373	**0.0001**
P4		-	**-**	-	**0.005**
Platelets (cells/ml)	803.60±134.36	634.80±125.21	559.50±100.97	506.22±106.01	791.10±142.53
P1		**0.015**	**0.001**	**0.0001**	0.852
P2		-	0.174	**0.027**	**0.007**
P3		-	-	0.347	**0.0001**
P4		-	-	-	**0.0001**
WBCs (10^3cells/ml)	10.10±0.81	3.93±0.81	10.02±1.47	5.29±1.31	8.60±1.49
P1		**0.0001**	0.910	**0.0001**	**0.035**
P2		-	**0.0001**	**0.024**	**0.0001**
P3		-	-	**0.0001**	**0.015**
P4		-	-	-	**0.0001**

Data is expressed as mean+/- standard deviation (STD), P1: significance versus control; P2: significance versus ALCL3; P3: significance versus AlCl3 + Be; P4: significance versus ALCL3+ Br. Comparison between groups was made using OneWay ANOVA (LSD) test

Table 2. Comparison of aluminum level in different studied groups

Parameters \ Groups	Control	ALCL3	AlCl3+Be	AlCl3+Br	AlCl3+Ri
Aluminum (mg/ml)	0.17±0.02	0.32±0.04	0.24±0.03	0.22±0.03	0.26±0.05
P1		**0.0001**	**0.0001**	**0.002**	**0.0001**
P2		**-**	**0.0001**	**0.0001**	**0.0001**
P3		**-**	**-**	0.330	0.231
P4		**-**	**-**	**-**	**0.039**

Data is expressed as mean+/- standard deviation (STD), P1: significance versus control; P2: significance versus AlCl3; P3: significance versus AlCl3 + Be; P4: significance versus AlCl3+ Br. Comparison between groups was made using OneWay ANOVA (LSD) test

Table 3. Comparison of liver function tests in different studied groups

Groups / Parameters	Control	ALCL3	AlCl3+Be	AlCl3+Br	AlCl3+Ri
ALT (U/L)	10.10±1.81	15.77±2.29	16.03±2.44	21.45±3.93	16.57±4.91
P1		**0.0001**	**0.007**	**0.038**	**0.015**
P2		-	**0.006**	**0.001**	**0.003**
P3		-	-	0.535	0.760
P4		-	-	-	0.745
AST (U/L)	21.65±3.49	43.56±7.28	39.96±9.21	49.31±10.95	27.74±7.23
P1		**0.0001**	**0.0001**	**0.0001**	0.095
P2		-	0.331	0.133	**0.0001**
P3		-	-	**0.014**	**0.001**
P4		-	-	-	**0.0001**
ALP (U/L)	163.67±30.53	179.77±38.03	128.84±23.04	82.81±27.16	146.67±39.90
P1		0.298	**0.020**	**0.0001**	0.224
P2		-	**0.002**	**0.0001**	**0.036**
P3		-	-	**0.003**	0.222
P4		-	-	-	**0.0001**
Protein (g/dl)	9.71±1.34	8.74±1.45	9.86±0.98	9.56±0.96	6.78±0.72
P1		0.061	0.774	0.768	**0.0001**
P2		-	**0.036**	0.122	**0.0001**
P3		-	-	0.570	**0.0001**
P4		-	-	-	**0.0001**
Albumin (g/dl)	4.81±0.89	4.12±0.46	4.05±0.74	4.07±0.44	4.05±0.58
P1		**0.024**	**0.013**	**0.022**	**0.013**
P2		-	0.812	0.870	0.819
P3		-	-	0.951	0.992
P4		-	-	-	0.959

Data is expressed as mean+/- standard deviation (STD), P1: significance versus control; P2: significance versus ALCL3; P3: significance versus AlCl3 + Be; P4: significance versus ALCL3+ Br. Comparison between groups was made using OneWay ANOVA (LSD) test

Table 4. Comparison of kidney function tests in different studied groups

Groups / Parameters	Control	ALCL3	AlCl3+Be	AlCl3+Br	AlCl3+Ri
Uric acid (mg/dl)	4.82±1.32	6.10±1.41	6.28±1.47	4.84±1.41	6.49±1.08
P1		**0.039**	**0.019**	0.978	**0.008**
P2		**-**	0.766	**0.047**	0.518
P3		**-**	-	**0.024**	0.726
P4		**-**	-	-	**0.010**
Urea (mg/dl)	40.93±5.74	37.66±5.10	41.98±8.24	37.50±4.81	34.72±2.97
P1		0.214	0.687	0.205	**0. 021**
P2		-	0.094	0.952	0.251
P3		-	-	0.091	**0.006**
P4		-	-	-	0.289
Creatinine(mg/dl)	1.33±0.42	2.48±1.66	1.76±0.72	2.34±1.00	1.67±0.83
P1		**0.016**	0.351	0.168	0.477
P2		**-**	0.123	0.383	0.091
P3		**-**	-	0.477	0.843
P4		**-**	-	-	0.477

Data is expressed as mean+/- standard deviation (STD), P1: significance versus control; P2: significance versus ALCL3; P3: significance versus AlCl3 + Be; P4: significance versus ALCL3+ Br. Comparison between groups was made using OneWay ANOVA (LSD) test

Table 5. Comparison of oxidative stress markers in liver homogenate in different studied groups

Groups / Parameters	Control	ALCL3	AlCl3+Be	AlCl3+Br	AlCl3+Ri
GSH-L (mmol/l)	5.08±1.99	6.70±1.17	7.34±1.75	7.69±0.79	8.55±1.31
P1		**0.018**	**0.001**	**0.0001**	**0.0001**
P2			0.330	0.151	**0.007**
P3				0.616	0.075
P4					0.211
GPX-L (mmol/l)	0.181±0.005	0.185±0.003	0.174±0.009	0.175±0.004	0.176±0.003
P1		0.191	**0.010**	**0.002**	**0. 037**
P2		-	**0.0001**	**0.0001**	**0.001**
P3		-	-	0.806	0.631
P4		-	-	-	0.819
TA-L (mg/l)	2.38±0.38	2.06±0.79	2.32±0.81	2.48±0.48	2.61±0.50
P1		0.247	0.829	0.738	0.409
P2			0.344	0.146	0.051
P3				0.587	0.299
P4					0.637

Data is expressed as mean+/- standard deviation (STD), P1: significance versus control; P2: significance versus ALCL3; P3: significance versus AlCl3 + Be; P4: significance versus ALCL3+ Bri. Comparison between groups was made using OneWay ANOVA (LSD) test

Table 6. Comparison of oxidative stress markers in kidney homogenate in different studied groups

Groups / Parameters	Control	ALCL3	AlCl3+Be	AlCl3+Br	AlCl3+Ri
GSH-K (mmol/l)	6.43±1.51	5.04±1.56	5.68±0.97	6.31±0.58	5.59±0.91
P1		**0.012**	0.164,	0.829	0.121
P2		**-**	0.232	**0.024**	0.301
P3		**-**	**-**	0.252	0.868
P4		**-**	**-**	**-**	0.193
GPX-K (mmol/l)	0.175±0.007	0.180±0.005	0.175±0.005	0.160±0.013	0.167±0.008
P1		0.207	0.968	**0.001**	**0.045**
P2		**-**	0.170	**0.0001**	**0.001**
P3		**-**	**-**	**0.0001**	**0.037**
P4		**-**	**-**	**-**	0.079
TA-K (mg/l)	1.04±0.22	1.78±0.47	1.85±0.41	2.07±0.66	2.60±0.23
P1		**0.0001**	**0.0001**	**0.0001**	**0.0001**
P2		**-**	0.737	0.144	**0.0001**
P3		**-**	**-**	0.252	**0.0001**
P4		**-**	**-**	**-**	**0.009**

Data is expressed as mean+/- standard deviation (STD), P1: significance versus control; P2: significance versus ALCL3; P3: significance versus AlCl3 + Be; P4: significance versus ALCL3+ Br. Comparison between groups was made using OneWay ANOVA (LSD) test

Table 7. Comparison of Acetylcholinesterase level in different studied groups

Groups / Parameters	Control	ALCL3	AlCl3+Be	AlCl3+Br	AlCl3+Ri
AChE(ng/ml)	5.47±0.35	4.60±0.65	5.26±0.96	5.56±0.81	4.87±0.70
P1		**0.015**	0.543	0.781	0.081
P2		**-**	0.059	**0.007**	0.412
P3		**-**	**-**	0.377	0.252
P4		**-**	**-**	**-**	**0.044**

Data is expressed as mean+/- standard deviation, a: significance versus control; b: significance versus ALCL3; d: significance versus AlCl3+ Br. Comparison between groups was made using OneWay ANOVA (LSD) test

Table 8. Comparison of neurotransmitters levels in different studied groups

Groups / Parameters	Control	ALCL3	AlCl3+Be	AlCl3+Br	AlCl3+Ri
Ach (ng/ml)	2.35±0.08	2.44±0.10	2.48±0.10	2.47±0.08	2.53±0.07
P1		**0.029**	**0.002**	**0.004**	**0.0001**
P2		-	0.321	0.408	**0.032**
P3		-	-	0.888	0.233
P4		-	-	-	0.194
DOP (ng/ml)	0.56±0.02	0.55±0.01	0.56±0.01	0.57±0.02	0.57±0.01
P1		0.279	0.78	0.554	0.259
P2		-	0.428	0.107	**0.035**
P3		-	-	0.401	0.174
P4		-	-	-	0.596
NE (ng/ml)	0.031±0.004	0.028±0.007	0.025±0.005	2.311±0.423	1.878±0.564
P1		0.982	0.971	**0.0001**	**0.0001**
P2		-	0.988	**0.0001**	**0.0001**
P3		-	-	**0.0001**	**0.0001**
P4		-	-	-	**0.008**

Data is expressed as mean+/- standard deviation (STD), P1: significance versus control; P2: significance versus ALCL3; P3: significance versus AlCl3 + Be; P4: significance versus ALCL3+ Br. Comparison between groups was made using OneWay ANOVA (LSD) test

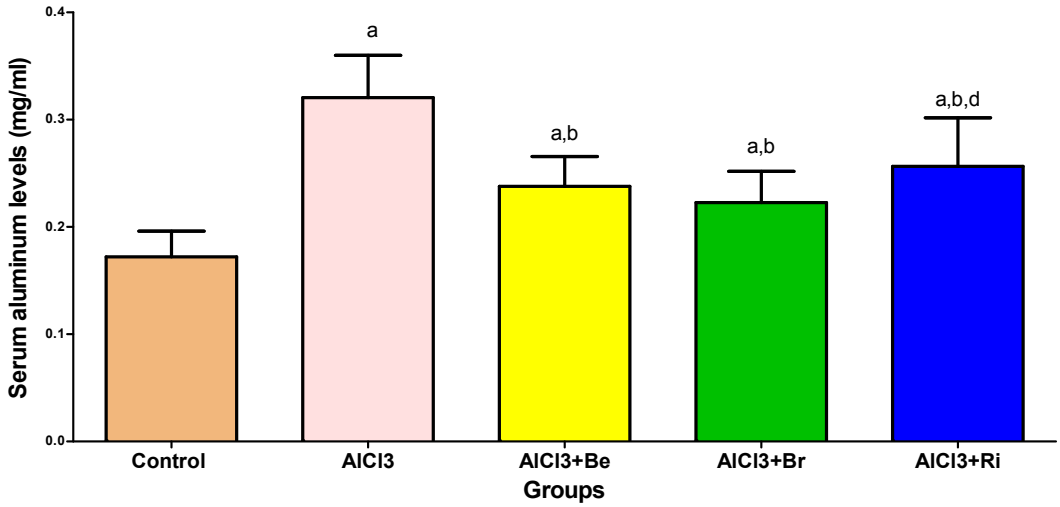

Fig. 1. Comparison of plasma aluminum level in different studied groups

Control: Control group, $AlCl_3$: group exposure to Aluminium chloride, $AlCl_3$+Be: group treated with beetroot extract, $AlCl_3$+Br: group treated with broccoli extract, $AlCl_3$+Ri: group treated with Rivastigmine

In Table 5, data indicated a significant (P<0.05) increase in GSH level and a non-significant (P<0.05) change in GPX and TA in the liver homogenate of ($AlCl_3$) group compared to control group.

($AlCl_3$+Ri) group showed a significant (P<0.05) increase in GSH level and a non-significant (P<0.05) change for groups of ($AlCl_3$+Be) and ($AlCl_3$+Br) compared to ($AlCl_3$) group.

All treatment groups showed a significant (P<0.05) decrease in GPX level and a non-significant (P<0.05) change in TA level compared to ($AlCl_3$) and control groups.

In Table 6 For kidney homogenate, ($AlCl_3$) group showed a significant (P<0.05) decrease in GSH level and an increase in TA level compared to control group and a non-significant (P<0.05) change for GPX level compared to what?? .($AlCl_3$+Be) group showed a non-significant (P<0.05) change in GSH,GPX and TA levels compared to ($AlCl_3$) group and a significant (P<0.05) increase in TA level compared to control.

($AlCl_3$+Br) group showed a significant (P<0.05) increase in GSH level compared to ($AlCl_3$) group and a significant (P<0.05) increase TA level compared to control group.

($AlCl_3$+Br) and ($AlCl_3$+Ri) showed a significant (P<0.05) decrease in GPX level compared to ($AlCl_3$) and control groups.

($AlCl_3$+Ri) group showed a significant (P<0.05) increase in TA level compared to ($AlCl_3$) and control groups and a non-significant (P<0.05) change in GSH level compared to both groups.

As shown in Table 7 and Fig. 2, there was a significant (P<0.05) decrease in AChE level in ($AlCl_3$) group compared to control group. On the other hand, ($AlCl_3$+Br) group showed a significant (P<0.05) increase in AChE level compared to ($AlCl_3$) group.($AlCl_3$+Be) and ($AlCl_3$+Ri) showed non-significant (P<0.05) changes in AChE level compared to ($AlCl_3$) group.

In Table 8, ($AlCl_3$) group showed a significant (P<0.05) increase in Ach level and non-significant (P<0.05) changes in DOP and NE levels compared to control.

($AlCl_3$+Be) group showed anon-significant (P<0.05) change in Ach, DOP and NE levels compared to ($AlCl_3$) group but a significant (P<0.05) increase in Ach level compared to control group.

($AlCl_3$+Br) group showed a significant (P<0.05) increase in NE level and non-significant (P<0.05) change in Ach and DOP levels compared to ($AlCl_3$) group.

($AlCl_3$+Ri) showed a significant (P<0.05) increase in Ach, DOP and NE levels compared to ($AlCl_3$) group. Also, it showed a significant (P<0.05) increase in Ach and NE compared to control group.

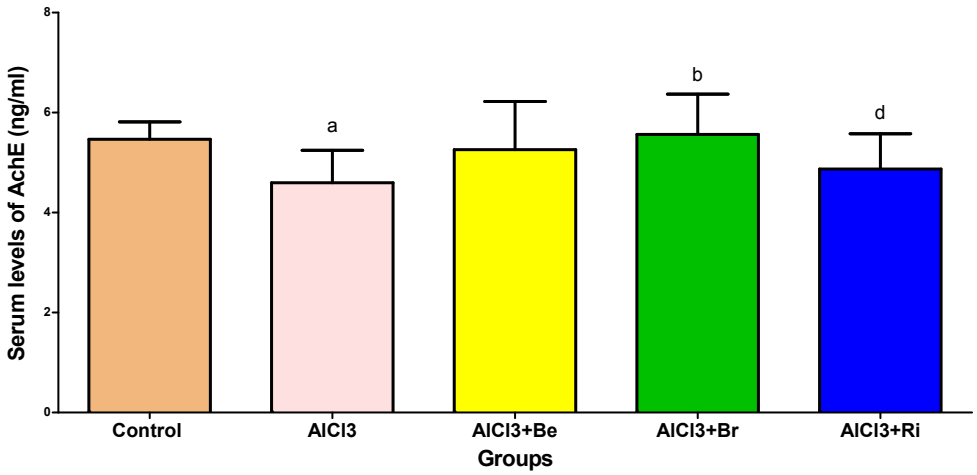

Fig. 2. Comparison of serum levels of AChE in different studied groups

Control: Control group, AlCl3: group exposure to Aluminium chloride, AlCl3+Be: group treated with beetroot extract, AlCl3+Br: group treated with broccoli extract, AlCl3+Ri: group treated with Rivastigmine

3.1 Histological Examination

Fig. 3 showed that, (AlCl3) group: showing a few normal neurons (black arrows). Most cells are shrunken and showed dark stained cytoplasm and nuclei (white arrows). Glia cells with small dark nuclei are also increased (dotted arrows). C1. reg. (AlCl3+Be): showing marked protection of hippocampal neurons. Cells looked normal with active large nuclei (black arrows). Degenerated shrunken apoptotic cells are few (white arrows). Glia cells with dark nuclei are also few (dotted arrows). C1. reg. (AlCl3+Br): showing marked protection of hippocampal neurons. Cells looked normal with active large nuclei (black arrows). Degenerated shrunken apoptotic cells are few (white arrows). Glia cells with dark and nuclei are also few (dotted arrows) C1. reg. (AlCl3+Ri): showing marked protection of hippocampal neurons. Cells looked normal with active large nuclei (black arrows). Degenerated shrunken apoptotic cells are few (white arrows). Glia cells with dark and nuclei are also few (dotted arrows).

4. DISCUSSION

Alis recognized as a neurotoxic element in animals and humans, and it is considered as a causative agent in a range of neurodegenerative disorders. Natural antioxidants, such as those found in plants, proved to be useful in reducing the progression of various pathologies associated with oxidative stress including neurodegeneration [19]. The use of plant extracts has been observed to be as effective as antioxidants in Al-induced neurotoxicity [20].

The decrease in the level of hemoglobin and RBCs in Al-treated group in our study was similar to previously published observation [21], but this decrease was not statistically significant. The age of animals at the time of exposure, different duration of chronic administration and different animal species might explain this variation between the present and previous studies. One of the basic mechanisms of the toxic action of heavy metal on mammals is erythrocyte destruction [22]. Erythrocyte is one of the major target cells for Altoxicities [23], and a hemolytic effect of $AlCl_3$ is an indicator of a decline in RBC count [24]. Al can inhibit the activity of enzymes that are involved in the haem biosynthetic pathway or interfere with cellular iron uptake and utilization and that can affect in hemoglobin which leads to the reduction of synthesis and this can cause anemia [25]. Because the content of rare natural pigments (betalains), polyphenols, antioxidants, vitamins, minerals, and fiber in the beetroot, it was considered the most important vegetable in the world [26]. Also, broccoli is useful to health because of its high content of health-enhancing compounds such as glucosinolate, vitamins, phenolic compounds, and dietary essential minerals [27]. Vitamins and minerals found in beetroot and broccoli are most likely active ingredients responsible for its increase in the amount of hemoglobin in the blood and improvement of white blood cells. Rats treatment with rivastigmine showed a significant

elevation in Hb and RBCs, this is due to rivastigmine may chelate aluminum chloride and ameliorate toxic effect or stimulate enzyme involved in hemoglobin synthesis.

Aluminum (Al) is known as a toxicant agent. It linked to many neuro-disorders diseases and other serious neurodegenerative diseases [28].

The result of obtained showed that the Aluminium exposure group had a significant increase in its serum level. Aluminium interferes with most physical and cellular processes. The aluminum as a toxicant agent especially with respect to the bone, blood, and the nervous system when finding in high doses in circulation. Increased Aluminium levels in organs and

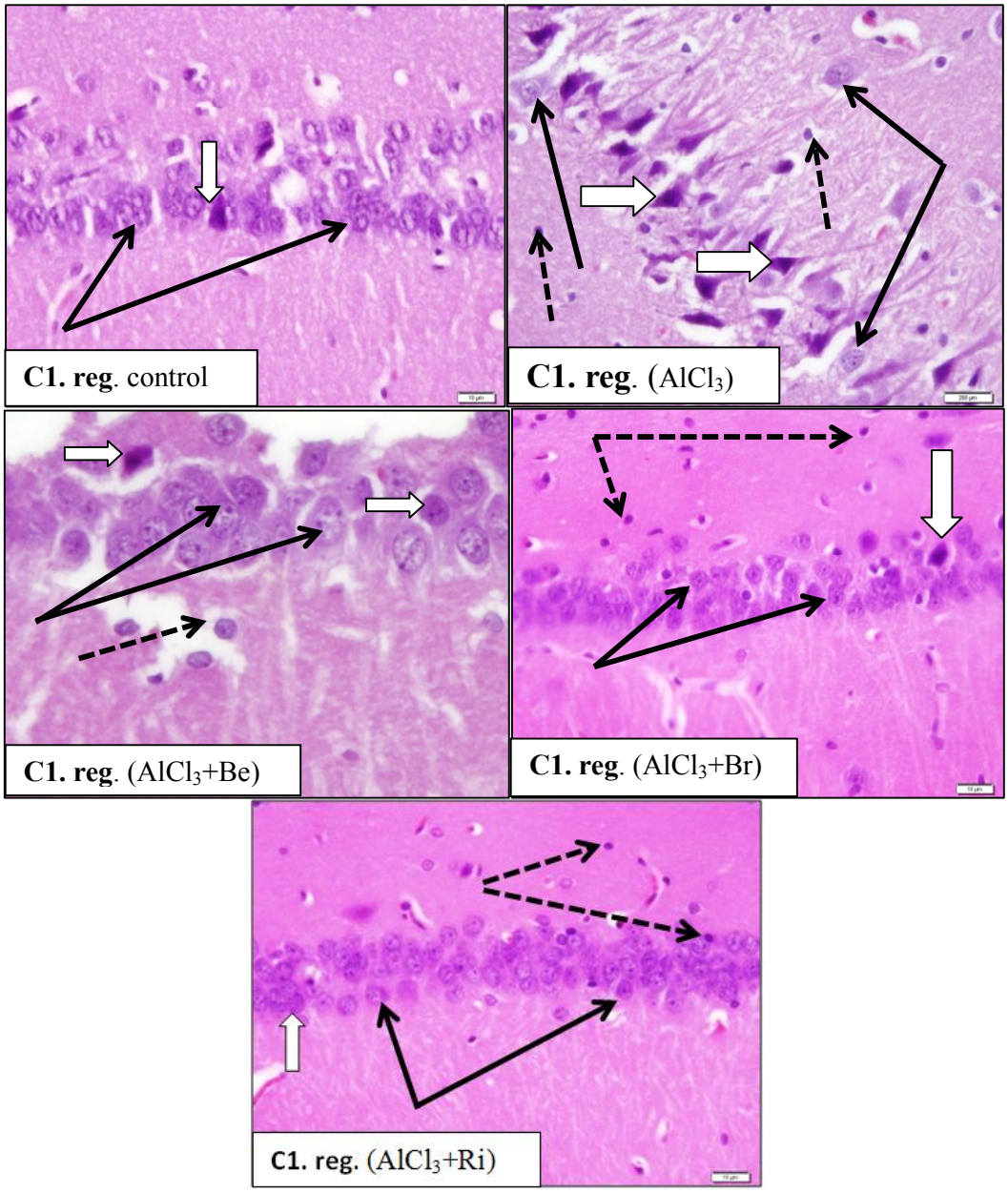

Fig. 3. Sections in rat hippocampus (c1. region) stained by H&E to show

Control: Showing normal hippocampal neurons with rounded nuclei and prominent nuclei (black arrows). Dark degenerated or apoptotic cells are few (white arrows). The dark small nuclei of glial cells are also few (dotted arrow)

tissues can lead to toxicity and dysfunction, the effects of the metal are usually linked with the local concentration. The blood-brain barrier has an active efflux through a monocarboxylate transporter in order to avoid aluminum deposition in the brain. However, this system can be affected by increasing the concentration of aluminum in the blood Reduction in serum aluminum concentration in treated group could be as a result of beetroot or broccoli extract interaction with the aluminum possibly by chelation to cause its elimination from the blood [29].

Increased hepatic enzyme levels may indicate cellular degeneration or destruction. In this study, a significant increase in serum ALT, AST were reported in Aluminium-exposure group compared to control. Similar results have been reported by other studies [30]. The increase in enzymes activity may be due to an indicator of liver injury or dysfunction [31]. Aluminum exposure can result in its accumulation in the liver and leads to liver damage because of increased enzymes levels in the serum [32]. The present data showed that serum creatinine and uric acid levels increased in Aluminium exposure group, which is accurately linked with the renal function dysfunction.

Treatment with beetroot showed improvement AST level compared with untreated group. Based previous study showed beetroot juice has an effect in reducing the level of creatinine which considers the marker of kidney damage. Beetroot feeding can induce metabolic alterations to protect against liver injury by preserving the integrity of the plasma membrane suppresses the leakage of enzymes and proteins [33].

Treated with broccoli extract showed improvement in serum liver enzymes and creatinine. It was concluded to that broccoli extract has the effect on liver injuries and on oxidative stress, which resulted to ameliorated serum biochemical parameters such as AST, ALP, and ALT. Also, this study indicated that the broccoli extract may be useful for the prevention of hepatotoxicity induced by oxidative stress.

Aluminum causes oxidative injury in the brain, liver and kidney. It can change the activity of antioxidant enzymes by inducing the production of free radical. Conversely, the antioxidant enzymes are active in defense against oxidative stress because it considers as free radical scavengers. In liver, Aluminium exposure group showed a significant increase in the activity of GSH while no significant changes were recorded in level of GPx and TA in aluminum chloride group. In kidney, Aluminium exposure group showed significant decrease in the activity of GSH and increase in TA level in Aluminium exposure group compared with control. Glutathione (GSH) acts as an antioxidant and a detoxifying agent [34]. Glutathione is important to counteract the damaging effects of oxidative stress and to preserve the normal reduced state of cells. Glutathione has an important role in the detoxification and metabolism of many xenobiotic compounds. The increased levels of reduced glutathione in Aluminium exposure animals would suggest an increased detoxification capacity of the liver. The changes in GSH may also reflect a response to aluminum-induced oxidative stress [35]. Glutathione is known to be one of the important components of an intracellular protective mechanism present in the cell and thus is an important determinant for the threshold of tissue damage caused by environmental chemicals. High doses of aluminum are able to reduce GSH levels and stimulate free radicals. Also, decreasing glutathione levels may cause by aluminum which effects in glutathione synthesis by reducing glutathione synthase activity [36].

The GPx is important antioxidant enzymes that constitute a supportive defense mechanism against free radical [37]. It plays an important role in protects of cells from oxidative stress by inhibiting lipid peroxidation. The increase of GPx in group exposure to aluminum chloride may due to as a response to oxidative stress.

It was found that, increased total antioxidant capacity in rats treated with aluminum considered as a compensatory response against oxidative stress. Rats treatment with beetroot and broccoli extracts resulted in a partial recovery in reduced glutathione and glutathione peroxidase activity. This is due to the active components of beet roots and broccoli which prevent Free radicals production. Beetroot and broccoli consider a rich source of antioxidant compounds [38]. Free radical scavenging property of antioxidants compounds can lead to delay or inhibit of cellular damage. Beetroot juice can prevent oxidative stress induced by xenobiotic in rats. Betalains classified as one of the highest antioxidant activity in beetroot. The betalain in beetroot has been shown it protect cellular components from oxidative injury [39].

Broccoli has been found to have stronger antioxidant. It contains numerous bioactive substances with health-promoting properties including vitamins, glucosinolate and phenolic compounds [40]. Glucosinolate have effect in protection from oxidative stress through the elimination of ROS). In addition, Sulforaphane is one of broccoli component, is an antioxidant agent. In different in vivo and in vitro experiments was found that effective to reduce oxidative stress and damage of cell/tissue. Also, it has been reported to have potent neuroprotective effects [41-44].

Acetylcholinesterase an enzyme that breaks down the neurotransmitter acetylcholine. In this study Aluminium treated group showed a significant decrease in AChE activity in serum. The results agree with previous studies that demonstrated a decreased activity of AChE. It was reported a reduction in AChE activity in the brain as a response to Aluminium intoxication. Loss of cholinergic markers enzymes such as AChE is correlating with the degree of cognitive and loss of this enzymes is considered the most severe and the earliest of the biochemical changes to occur. Chronic Aluminium exposure has choline toxic effects and significant reduction of AChE activity is seen with Aluminium [45-47]. Aluminum can result in the production of free radicals which lead to oxidative damage, and this may be responsible for the decreased AChE enzyme activity. On the other hand, Treatment with beetroot and broccoli showed improvement in AChE level compared with untreated group.

Neurotransmissions in the central nervous system are associated with learning and memory and consequently, changes in the neurotransmission would absolutely affect the behavioral responses [48-50].

The results of biochemical markers were supported wit histological examination that showed improvement in the rats treated with beet root or broccoli compred with untreated.

The functions of Cholinergic in the central nervous system depend principally on acetylcholine. The change in the function of cholinergic neurotransmission can be due to aluminum chloride [51]. In this study, a significant increase in Acetylcholine level was reported in Aluminium-exposure group compared to the control group while the non-significant change in dopamine and norepinephrine was record in Aluminium exposure group. The high level of acetylcholine may be due to the low level of acetylcholinesterase that responsible for hydrolysis of acetylcholine to acetate and choline as shown in the results.

Rivastigmine previously showed to be beneficial in preventing neuronal degeneration by increasing regional cerebral blood flow in animal model [52].

5. CONCLUSION

Neuroprotective role of broccoli in the present study which may result from its antioxidant properties due to its bioactive content such as glucosinolate, isothiocyanate, Sulforaphane, and flavonoids. Therefore, Broccoli can have a favorable effect on neurotoxicity due to their antioxidant and anti-inflammatory properties.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard ethical approval has been collected and preserved by the authors.

ACKNOWLEDGEMENT

This project was funded by the Deanship of Scientific Research at King Abdulaziz University, Jeddah, under grant no.(HiCi-3-141-36).The authors, therefore, acknowledge with thanks DSR for technical and financial support.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
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