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ASSESSMENT OF ELEMENT CONCENTRATION DISTRIBUTION IN DIFFERENT RAT ORGANS BY WAVELENGTH DISPERSIVE X-RAY FLUORESCENCE: EFFECTS OF ALUMINUM CHLORIDE

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ABSTRACT

Aluminum (Al) is present on earth surface has different chemical forms. It is a toxic metal and it may cause different disorders such as osteomalacia, microcytic anemia, Alzheimer and Parkinson's disease. Thus, it is very important to understand the effects of Al on different organs. In order to examine its accumulation, rats (male Wistar) were exposed to 5 mg/kg/day $AlCl_3$ through gavage method for 30 days. At the end of the process, heart, brain, kidney and skin were removed and dried under sunlight. The samples were analyzed on a sequential Wavelength Dispersive X-ray Fluorescence (WDXRF) spectrometer. The results indicate that Al accumulates significantly in the brain. These results can be associated with neurotoxin effects. Although this study focused on the accumulation of Al, the concentration changes of detected elements from Beryllium (Be) to Uranium (U) accumulations were analyzed. The current study has proved that the WDXRF method is a quick, inexpensive and effective method in toxicological studies.

KEYWORDS:
Aluminum, Bio-distribution, Wistar Rat, WDXRF

INTRODUCTION

Aluminum (Al) is the third most abundant element and the most common metal on earth's crust, existing primarily as polymorphous aluminum-silicate (Al_2O_5Si) in rocks and soils [1]. Al is used in several manufactured foods and medicines as well as in water purification [2]. This metal is widely used in daily life and this use leads to environmental release [3]. Al may accumulate in human body from diet, occupations, and the use of cosmetics, medications, and adjuvant exposure [4]. The toxicity of Al was shown in many experimental studies and this effect attracted growing concern in the field of human and animal health as the immune system appears to be most sensitive to Al exposure [5]. For human, Al is a well-known neurotoxin and a possible candidate being of hepatotoxins [6]. It can accumulate in the liver as a low toxicological metal, and toxic effects of Al is linked to the development of dialysis dementia, osteomalacia, Alzheimer's and Parkinson's diseases [7-10]. Al is reported to accelerate oxidative damage to the biomolecules and it can accumulate in central nervous system (CNS) easily [11, 12]. Exposure to Al neurotoxicity is accompanied by the perikaryal accumulation of tangles of the phosphorylated neurofilaments (NFs) [13]. The toxic effects of Al on nervous system especially occur at high concentration such as causing loss of memory, speech disturbances, dysparaxia, tremors, jerking movements, impaired muscular coordination, and paralysis [14-16]. Al exposure and its toxicity to reproductive system have also been investigated and some damage to the reproductive system of aluminum deposits has been identified [17, 18]. The molecular mechanisms causing these symptoms may include oxidative stress induction, membrane function disruption, gene structure impairment and disruption of mineral metabolism of several metals [19, 20]. Exposure of Al can cause free radical-mediated cytotoxicity, lipid peroxidation and altered protein phosphorylation and these generate reactive oxygen species resulting in oxidative deterioration of lipids, proteins and DNA. Therefore, the estimation of free radical generation and antioxidant defense has become an important aspect of investigating Al toxicity [21, 22]. Al accumulates in the organs of the organism including spleen which is peripheral organ of the immune system and the accumulated Al may alter the immune function. There is remarkable and considerable evidence to demonstrate that the accumulation of Al in body tissues is associated with the damage for the target organs [23, 24].

As can be understood from the above information, Al is an element affecting human and ani-

mal health negatively and it takes a great place in our daily lives. A great numbers of studies regarding the Al effect on immune function have demonstrated that Al suppressed immune function and the association of Al with the immune system has resulted in allergy or autoimmunity [5]. Some of the research on this issue reveals that acid-suppressing drugs in mice can cause allergic response, and $AlCl_3$ also has a mutagenic potential. Based on these investigations, researchers observed that $AlCl_3$ is clastogenic and indirectly affects the construction of mitotic fuse in all the tested concentrations [25]. It has been deduced that $AlCl_3$ has unfavorable effects on the male rats' testicular function where $AlCl_3$ can change the balance of trace element decreases the spermatogenesis and the activities of testicular enzymes [26]. Furthermore, Al accumulates in the ovary could damage the ovarian structure of the female mice and it can result in ovulatory disorders with disturbed hormone profiles and this damaged ovary structure can lead to infertility [27, 28]. Exposure to Al impair the secretory function of reduce the levels of FSH and LH in rat serum that Al is a potential risk to female infertility [10]. Moreover, $AlCl_3$ can damage the BCL-W gene, an anticancer gene belong to the DNA repair system in brain cells, and can regulate R-spondin and inositol polyphosphate 4-phosphatase genes that have a role in cell proliferation [29]. The effect of iron deficiency and iron load on Al deposition was also investigated by the researchers. Based on the findings it was ascertained that in case of iron deficiency, high aluminum uptake was determined in the intestines of rats. In addition, high aluminum storing was observed in the spleen, lungs and blood plasma of the rats. In contrast, it was detected that aluminum deposition decreased in the tissues in the case of iron overload [37].

In toxicology studies, a number of analytical methods such as Atomic Absorption Spectroscopy (AAS), Inductively Coupled Plasma – Mass Spectrometer (ICP-MS), High-Performance Liquid Chromatography (HPLC) and X-Ray Fluorescence (XRF) can be used for elemental analysis. XRF is either wave dispersive X-ray fluorescence (WDXRF) or energy dispersive X-ray fluorescence (EDXRF). In this study, WDXRF technique was used. There are a number of advantages over other techniques. For example, many elements can be determined simultaneously, it is non-destructive, simple, fast and less expensive than other techniques. As such, it has been used for the analysis of biological, chemical and geological samples within ranges from parts-per-billion (ppb) to 100% [38-41].

Consequently, the aim of the present study was to examine elemental change in different organs of rats subjected to $AlCl_3$ by using a quick and inexpensive analysis technique (WDXRF). Since Al is widely used in daily life, there are many different studies about aluminum. These studies give us some insights about the negative effects of Al toxicity on neural, immune and reproduction system. That's why it is crucial to understand the effects of Al accumulation in various organs and tissues. Apart from Al, other elements (C, O, Cl, Na, Mg, Al, Si, P, S, K, Ca, Ti, Mg, Fe, Cu, Zn, As, Rb, Sr and Pb) were analyzed, and concentrations were compared in the hearts, brains, kidneys and skin of rats according to the control group.

MATERIALS AND METHODS

Instruments. In this study, an agate mortar, a digital scale (Ohous TS 120), a hydraulic press ($SpexP_{max}$ =3.5×10^7 kg/m^2), a WDXRF spectrometer (ZSX-100e with Rhodium target X-ray controlled by ZSX software) were used. This system analyzes the elements from Be (Beryllium) to U (Uranium). WDXRF instrument consist of a detector, an amplifier, a discriminator, a counter and printer units. The system includes a 4 kW 70 kV end-windows X-ray tube. The detector converts the falling X-rays to measurable pulse. It has the property of the micro area mapping down to 0.5 mm. The X-ray detector is used in the following three spectrometers: proportional, gas flow and scintillation detectors. The other features of the system are included up to five primary beam filters, 10 analyzing crystals, eight limiting area diaphragms, optional secondary collimators, automatic sample changer, compact design and multi-window, multi-function fundamental parameters software. The discriminator filters the pulses coming from the detector, and allows them to pass through certain height pulses. These pulses are saved in a recorder. If required, the system can show the number of pulses (of violence) as a function of the wavelength and the angle of the reflection spectrum in diagrams. Matrix-correction process is conducted automatically by this system including line overlaps. Rigaku has improved their semi-quantitative software package further with the introduction of SQX can also correct the secondary excitation effect by photoelectrons (light and ultra-light elements), varying atmospheres, impurities and different sample sizes. Increased accuracy is achieved using Matching Library and Perfect Scan Analysis Programs. The Fundamental Parameter Method is used to determine the mass concentration by using measured counts. This method is a kind of compensation analysis method X-Ray Fluorescence Analysis and mathematically compensates the matrix-effects overlapped effects [38]. WDXRF is a unique technique to use when fast and accurate elemental analysis is needed. The equipment ensures qualified results to be obtained from the rat tissues without needing advanced analytical skills. [38- 42].

Experimental Section. The study protocol was approved by the Ethical Committee of Atatürk University, Erzurum, Turkey, according to the principles of laboratory animal care. The study was carried out with 12 certified male Wistar rats (mean initial weight of 253±14 g). The rats were supplied by Atatürk University Experimental Medical Research and Application Center, Erzurum, Turkey. The rats were kept in standard glass cages at room temperature. They were maintained in normal daily light cycle (at room temperature, with sun cycle). The rats were randomly divided into two groups with each group containing six rats: control group (G1) and $AlCl_3$ diet group (G2). In the group G2, the rats were orally fed with $AlCl_3$ for 30 days with 5 mg/kg/day by gavage method. During this period, 15-25 g daily commercial laboratory chow and 13-17 ml water was given to each rat. This commercial chow comprises oats, barley flour, meat, milk powder and fish oil. At the end of this period, the rats were sacrificed the different organs (heart, brain, kidney and skin) were excised and they were dried under sunlight for 2-3 days [to prevent the system from being affected by humidity (the vacuum condition of the sample chamber of the system is affected by humidity)]. During drying procedure, the organs were placed over a tulle-covered glass container to prevent cross-contamination of the organs. Nevertheless, possible sample contamination has been evaluated in systematic errors. After drying the organs were separately ground in an agate mortar. Six samples were prepared for each tissue from both groups. These samples were then pressed into uniform pellets of 20 mm diameter and ~2.0 mm thickness using a hydraulic press machine (SPEX, P = 25 tons/cm^2) with a standing time of 120s. After the beam from the X-ray tube passes a primary beam filter with a 20 mm diameter, it is reflected on the sample.

The beam affects the surface of the whole sample. Since the pellets were easily formed and not scattered, a bonding material (e.g. cellulose microcrystalline) was not used to glue the sample powders and the average weights of the pellets are given in Table 1. These pellets were analyzed on a WDXRF spectrometer equipped with the Rh X-ray tube. The measurement room temperature was 20-21°C, and it was a relatively dry environment. The experimental geometry was the same for all the samples. The basic differences between the G1 and G2 were examined. The obtained spectra were drawn via the Origin 7.0 software. By using a spectroscopic technique, the current study examined whether the employed $AlCl_3$ diet actually influences the organ content of the rats. These graphs were plotted with the average of 6 samples. In this study four different organ tissues were investigated separately.

TABLE 1
Weight of pellets

Organ	Weight (g)	
	G1	G2
Heart	0.25±0.010	0.29±0.035
Brain	0.30±0.115	0.34±0.030
Kidney	1.32±0.020	1.27±0.035
Skin	1.83±0.025	1.88±0.015

G1: control group; G2: experimental group

Statistical Analysis. To see whether there is a significant difference between groups; Mann-Whitney-U Test has been applied for all the measurements using SPSS-17. Results are given in Table 2.

RESULTS AND DISCUSSION

Results. Al exposure caused significant changes in elemental concentrations especially in brain and skin tissue of the rat. In brain, Al increased when compared to G1 values. Also while Mg and Na increasing, Ca decreased. It was observed that K, Si, Ca, Mg, Al concentration ratios increased in heart samples after the $AlCl_3$ diet. Especially the increase in K is remarkable. The elements of C, Cl, P, S, K, Ca, Al, Br, Zn and Fe were found in higher amounts in the skin tissue of the G2 rats. Finally, K, Si, Mg, Fe, Ca, Al, Cl and P elements increased in kidney following the dietary $AlCl_3$ although there were no significant decreases in terms of specific elements after spectroscopic investigations.

TABLE 2
p values between two groups for each element of all the tissues

Tissues	ELEMENTS (p-value)								
	O	C	Cl	P	S	Si	K	Ca	Fn
Brain	0,050	0,275	0,050	0,653	0,077	0,050	0,077	0,034	1,000
Kidney	0,827	0,050	0,317	0,317	0,099	0,046	0,046	0,037	0,114
Skin	0,050	0,043	0,025	0,037	0,046	0,507	0,043	0,046	1,000
Heart	0,050	0,275	0,513	0,268	0,376	0,046	0,000	0,034	1,000
Tissues	ELEMENTS (p-value)								
	Zn	Na	Mg	Al	Rb	Fe	Cu	Se	Br
Brain	1,000	0,037	0,037	0,037	1,000	1,000	1,000	1,000	1,000
Kidney	0,121	1,000	0,011	0,045	1,000	0,034	1,000	1,000	1,000
Skin	0,037	1,000	0,317	0,037	1,000	0,037	1,000	1,000	0,037
Heart	1,000	1,000	0,037	0,037	1,000	1,000	1,000	1,000	1,000

*If the $p < 0, 05$, there is a significant difference between the groups G1 and G2 in terms of elements.

TABLE 3
Percent mass ratios from all samples obtained by WDXRF spectrometer.

Tissues	Groups	Elements (%Mass)								
		O	C	Cl	P	S	Si	K	Ca	Fn
Brain	G1	99.312 ±0.015	0.6145 ±0.019	0.0508 ±0.026	0.0115 ±0.024	0.0057 ±0.000**	0.0026 ±0.016	0.0018 ±0.031	0.0006 ±0.003	0.0000 ±0.000**
	G2	99.264 ±0.025	0.6220 ±0.073	0.0611 ±0.064	0.0116 ±0.008	0.0056 ±0.031	0.0021 ±0.026	0.0018 ±0.003	0.0002 ±0.001	0.0000 ±0.000**
Kidney	G1	99.032 ±0.022	0.9639 ±0.017	0.0000 ±0.000**	0.0000 ±0.000**	0.0001 ±0.000	0.0012 ±0.004	0.0017 ±0.003	0.0001 ±0.000	0.0000 ±0.000**
	G2	99.049 ±0.025	0.9440 ±0.023	0.0001 ±0.000	0.0001 ±0.000	0.0002 ±0.000	0.0017 ±0.007	0.0021 ±0.005	0.0015 ±0.010	0.0000 ±0.000**
Skin	G1	96.022 ±0.008	1.2300 ±0.012	0.0001 ±0.000	0.0001 ±0.000	0.0002 ±0.000	0.0033 ±0.001	0.0001 ±0.000	0.0001 ±0.000	0.0000 ±0.000**
	G2	97.324 ±0.011	1.5780 ±0.016	0.0030 ±0.010	0.0340 ±0.031	0.0023 ±0.019	0.0050 ±0.027	0.0003 ±0.001	0.0013 ±0.006	0.0000 ±0.000**
Heart	G1	99.234 ±0.009	0.6110 ±0.032	0.1351 ±0.021	0.0072 ±0.018	0.0096 ±0.001	0.0014 ±0.003	0.0034 ±0.011	0.0001 ±0.000**	0.0000 ±0.000**
	G2	99.353 ±0.010	0.6057 ±0.012	0.0155 ±0.021	0.0073 ±0.022	0.0087 ±0.004	0.0022 ±0.006	0.0058 ±0.01	0.0004 ±0.001	0.0000 ±0.000**

Tissues	Groups	Elements (%Mass)								
		Zn	Na	Mg	Al	Rb	Fe	Cu	Se	Br
Brain	G1	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**
	G2	0.0000 ±0.000**	0.0306 ±0.012	0.0011 ±0.007	0.0005 ±0.002	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**
Kidney	G1	0.0001 ±0.000	0.0000 ±0.000**	0.0006 ±0.002	0.0001 ±0.000	0.0000 ±0.000**	0.0001 ±0.000	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**
	G2	0.0001 ±0.000	0.0000 ±0.000**	0.0008 ±0.003	0.0015 ±0.001	0.0000 ±0.000**	0.0003 ±0.001	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**
Skin	G1	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**
	G2	0.4017 ±0.034	0.0000 ±0.000**	0.0000 ±0.000**	0.0098 ±0.017	0.0000 ±0.000**	0.5610 ±0.005	0.0000 ±0.000**	0.0000 ±0.000**	0.0229 ±0.041
Heart	G1	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**
	G2	0.0000 ±0.000**	0.0000 ±0.000**	0.0015 ±0.001	0.0002 ±0.001	0.0000 ±0.000**	0.0001 ±0.000	0.0000 ±0.000**	0.0000 ±0.000**	0.0000 ±0.000**

**The amount of the element is below the detection limit of the system

Shortly, as can be seen in Table 2, Table 3, and Figure 1 the significant differences between G1 and G2 have been observed in all the tissues in terms of the elements of Ca, Mg, and Al. In the kidney tissues for Si, K, Ca elements, the significant value differences have been found. Especially in skin tissues for C, Cl, P, S, K, Ca, Zn, Fe and Br elements, the value differences have emerged. In heart tissues for Si, K, Ca, Mg and Al elements, remarkable differences between the groups have been determined.

DISCUSSION

The presented results show that Al and Cl increased in all the tissues after $AlCl_3$ administrations with the exception of Cl in heart tissue. Significant increases were especially observed in the skin and brain for both Al and Cl elements. When we consider the variation of Al in various organs, it can be seen that skin has the most increase, with 0.0098% mass, brain comes second with 0.0005% mass increase in Al amount heart and kidney have the same amount of Al concentration with 0.0002% mass after Al intoxication. The present results can explain why Al affects neurons and cause nervous system diseases. Thus, our findings indicated that Al could easily accumulate in the brain after 30 days with $AlCl_3$ dietary, and it could probably pollute the central nervous system (CNS) with its high neurotoxin potential. In accordance to this finding, previous studies showed that immune system could also be affected from Al exposure, and the analysis of Al accumulation in spleen, which is a peripheral organ of the immune system, showed that the accumulated Al can alter immune function [24]. Also, it was demonstrated that the accumulation Al in body tissues damaged the target organs severely [23]. Different researchers also have found that the Al exposure disturb the secretory function of the ovary, reduce levels of FSH and LH in the rat serum. Moreover, $AlCl_3$ exposure changed the balance of trace element, decreased the spermatogenesis and the activities of testicular enzymes [10-26].

The molecular mechanisms of Al accumulation causing symptoms on the nervous system, include oxidative stress induction, membrane function delay, interfering of gene expression and mineral metabolism disruption on several metals [19-

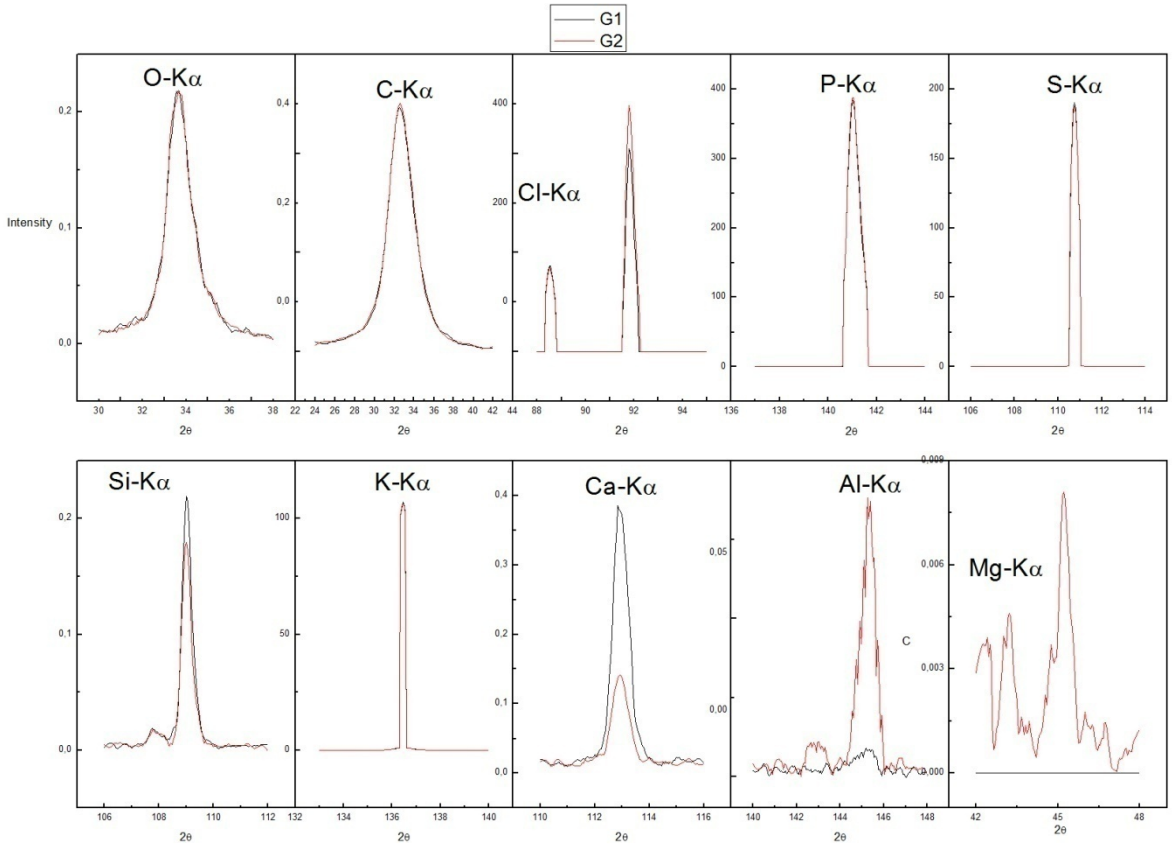

FIGURE 1
Element analysis results of brain sample obtained by WDXRF spectrometer as an example.

20]. One of the element that accumulates according to the Al concentration is Cl. As a matter of the fact, Cl amount increased significantly in the brain, kidney and skin; yet, the concentration of Cl interestingly decreased in the heart. In addition, the obtained results showed that there were significant changes in the concentration of certain elements that are very important for the body. For example, Ca is very important for gene regulations and cell biochemical activities; hence, a little change in Ca concentration causes the vital results in all cell types [39]. It appears that $AlCl_3$ dietary affect Ca concentration in the brain, heart, skin and kidney as Ca increased in all the organs. Furthermore, it could be argued that the Al exposure led to alterations in one of the most important element for organisms, phosphor (P).

P has many roles in cells such as protein activation, gene silencing, and pathway regulation [40]. The present results indicate that the P concentration increases significantly in the skin. Some other elements (K, Si, Mg, Fe, O, C, Na, S, Zn and Br) could be affected by Al, and some of them increased in concentration while some others decreased. The biggest element change has occurred in the skin tissues.

CONCLUSION

The present study shows that after rats orally administration of $AlCl_3$ to rats for 30 days, accumulation of Al was evident in skin and brain. The study indicates that WDXRF is a reliable and sensitive analysis method for toxicokinetic and biodistribution studies.

REFERENCES

[1] Wang, M., Chen, J.T., Ruan, D.Y., Xu., Y.Z. (2002) The influence of developmental period of aluminum exposure on synaptic plasticity in the adult rat dentate gyrus in vivo. Neuroscience. 113, 411-419.

[2] Türkez, H., Yousef M.I., Geyikoglu, F. (2010) Propolis prevents aluminium-induced genetic and hepatic damages in rat liver. Food. Chem. Toxicol. 48, 2741-2746.

[3] Cabrera, W.E., Schrooten, I., De Broe, M.E., D'Haese, P.C. (1999) Strontium and bone. J. Bone. Miner. Res. 14, 661-668.

[4] Guo, C.H., Liao, S.Y., Yuan, C.Y., Hsu, G.S.W. (2006) Effects of peritoneal aluminum overload on polyamines and nitric oxide contents of testes and epididymis in the mice. Environ. Toxicol. Pharmacol. 21, 1-7.

[5] Zhu, Y.Z., Liu, D.W. Liu Z.Y., Li, Y.F. (2013) Impact of Aluminum Exposure on the Immune System: a Mini Review. Environ. Toxicol. Pharmacol. 35, 82-87.
[6] El-Sayed, W.M., Al-Kahtani, M.A., and Abdel-Moneim, A.M. (2011) Prophylactic and therapeutic effects of taurine against aluminum-induced acute hepatotoxicity in mice. J. Hazard. Mater. 192, 880-886.
[7] Zhu, Y., Han, Y., Zhao, H. (2013) Suppressive effect of accumulated aluminum trichloride on the hepatic microsomal cytochrome P450 enzyme system in rats. Food. Chem. Toxicol, 51, 210-214.
[8] Halici, Z., Borekci, B., Ozdemir, Y., Cadirci, E., Suleyman, H. (2008) Protective effects of amlodipine and lacidipine on ovariectomy-induced bone loss in rats. Eur. J. Pharmacol. 579, 241-245.
[9] Gong, Q.H., Wu, Q., Huang, X.N., Sun, A.S., Shi, J.S. (2005) Protective effects of Ginkgo biloba leaf extract on aluminum-induced brain dysfunction in rats. Life Sci. 772, 140-148.
[10] Fu, Y., Jia, F.B., Wang, J. (2014) Effects of sub-chronic aluminum chloride exposure on rat ovaries. Life Sci. 100, 61-66.
[11] Thippeswamy, A.H., Rafiq, M. Viswantha, G. L.S., Kavya, K.J., Anturlikar, S.D., Patki, P.S. (2013) Evaluation of Bacopa monniera for its synergistic activity with rivastigmine in reversing aluminum-induced memory loss and learning deficit in rats. J. Acupunct. Meridian. Stud. 6, 208-213.
[12] Kakkar, V., Kaur, I.P. (2011) Evaluating potential of curcumin loaded solid lipid nanoparticles in aluminium induced behavioural, biochemical and histopathological alterations in mice brain. Food Chem. Toxicol. 49, 2906-2913.
[13] Kushkuley, J., Metkar, S., Chan, W.K.H., Lee, S., Shea, T.B. (2010) Aluminum induces neurofilament aggregation by stabilizing cross-bridging of phosphorylated c-terminal side-arms. Brain Res. 1322, 118-23.
[14] Drago, D., Bolognin, S., Zatta, P. (2008) Role of Metal Ions in the Aβ Oligomerization in Alzheimer's Disease and in Other Neurological Disorders. Curr. Alzheimer. Res. 5, 500-507.
[15] Walton, J.R. (2006) Aluminum in hippocampal neurons from humans with Alzheimer's disease. Neurotoxicology. 27, 385-394.
[16] Exley, C., Esiri, M.M. (2006) Severe cerebral congophilic angiopathy coincident with increased brain aluminium in a resident of Camelford, Cornwall, UK. J. Neurol. Neurosurg. Psychiatry. 77, 877-879.
[17] Guo, C.H. Hsu, G.S.W. Chuang, C.J. Chen, P.C. (2009) Aluminum accumulation induced testicular oxidative stress and altered selenium metabolism in mice. Environ. Toxicol. Pharmacol. 27, 176-181.
[18] Yousef, M.I., Kamel, K.I.M., El-Guendi, I., El-Demerdash, F.M. (2007) An in vitro study on reproductive toxicity of aluminium chloride on rabbit sperm: the protective role of some antioxidants. Toxicology. 239, 213-223.
[19] Perez-Granados, A.M., Vaquero, M.P. (2002) Silicon, aluminium, arsenic and lithium: essentiality and human health implications. J. Nutr. Health. Aging. 6, 54-162.
[20] Kumar, V., Gill, K.D., (2009) Aluminium neurotoxicity: neurobehavioural and oxidative aspects. Arch. Toxicol. 83, 965-978.
[21] Viezeliene, D., Jansen, E., Rodovicius, H., Kasauskas, A., Ivanov, L. (2011) Protective effect of selenium on aluminium-induced oxidative stress in mouse liver in vivo. Environ. Toxicol. Pharmacol. 31, 302-306.
[22] Strong, M.J., Garruto, R.M., Joshi, J.G., Mundy, W.R., Shafer, T.J. (1996) Can the mechanisms of aluminum neurotoxicity be integrated into a unified scheme? J. Toxicol. Environ. Health. A. 48, 599-614.
[23] Zhu, Y., Li, X., Chen, C. (2012) Effects of aluminum trichloride on the trace elements and cytokines in the spleen of rats. Food. Chem. Toxicol. 50, 2911-2915.
[24] Becaria, A., Campbell. A., Bondy, S.C. (2002) Aluminum as a toxicant. Toxicol. Ind. Health. 18, 309-320.
[25] Lima, P.D.L., Leite, D.S., Vasconcellos, M.C. (2007) Genotoxic effects of aluminum chloride in cultured human lymphocytes treated in different phases of cell cycle. Food. Chem. Toxicol. 45, 1154-1159.
[26] Zhu, Y.Z., Sun, H., Fu, Y. (2014) Effects of sub-chronic aluminum chloride on spermatogenesis and testicular enzymatic activity in male rats. Life Sci. 102, 36-40.
[27] Kuohung, W., Hornstein, M. (2011) Causes of female infertility. UpToDate Sist. http://46.4.230.144/web/UpToDate.v19.2/contents/f25/31/26603.htm?/abstract/1. (Accessed August 11, 2014)
[28] Chinoy, N.J., Patel, T.N. (2001) Effects of sodium fluoride and aluminium chloride on ovary and uterus of mice and their reversal by some antidotes. Fluoride. 34, 9-20.
[29] Shati, A.A., Elsaid, F.G., Hafez, E.E. (2011) Biochemical and molecular aspects of aluminum chloride-induced neurotoxicity in mice and the protective role of Crocus sativus L. extraction and honey syrup. Neuroscience. 175, 66-74.

[30] Yousef, M.I., El-Morsy, A.M.A., Hassan, M.S. (2005) Aluminium-induced deterioration in reproductive performance and seminal plasma biochemistry of male rabbits: protective role of ascorbic acid. Toxicology. 215, 97-107.
[31] Singla, N., Dhawan, D.K. (2013) Zinc protection against aluminum induced altered lipid profile and membrane integrity. Food Chem. Toxicol. 55, 18-28.
[32] Marguí, E., Queralt, I., Hidalgo, M. (2009) Application of X-ray fluorescence spectrometry to determination and quantitation of metals in vegetal material. TrAC Trends Anal Chem. 28, 362-372.
[33] Coudron, T A. L., Mitchell, C., Sun, R. Robertson, J.D., Pham, N.V., Popham, H.J.R. (2012) Dietary composition affects levels of trace elements in the predator Podisus maculiventris (Say) (Heteroptera: Pentatomidae). Biol. Control. 61, 141-146.
[34] Kurudirek, M., Topcuoglu, S. (2011) Investigation of human teeth with respect to the photon interaction, energy absorption and buildup factor. Nucl Instruments Methods Phys Res Sect B Beam Interact with Mater Atoms. 269, 1071-1081.
[35] Dyck, K.V., Robberecht, H., Cauwenbergh, R.V., Deelstra, H., Arnaud, J., Willemyns, L., Benijts, F.J., Centeno, A., Taylor, H., Soares, M.E., Bastos, M.L., Ferreira, M.A., D'Haese P. C., Lamberts, L.V., Hoenig, M., Knapp, G., Lugowski, S.J., Moens, L., Riondato, J., Grieken, R.V., Claes, M., Verheyen, R., Clement, L., Uytterhoeven, M. (2000) Spectrometric determination of silicon in food and biological samples: an inter laboratory trial. J. Anal, 15, 735-741.
[36] Akbaba, U., Şahin, Y., Türkez, (2012) H. Element content analysis by WDXRF in pistachios grown under organic and conventional farming regimes for human nutrition and health. Toxicol. Ind. Health. 28, 783-788.
[37] Winklhofer, C., Steinhausen, C. and Beck E. (2000) Effect of iron status on the absorption, speciation and tissue distribution of aluminium in rats. Nucl. Instrum. Methods Phys. Res. Sect. B. 172, 920-924.
[38] Dumlupinar, R., Demir, F., Budak, G., Karabulut, A., Kadic, N., Karakurt, H., Erdal, S. (2007) Determination of replacement of some inorganic elements in pulvinus of bean (Phaseolus vulgaris cv. Gina 2004) at chilling temperature by the WDXRF spectroscopic technique. J. Quant. Spectrosc. Radiat. Transfer. 103, 331–339.
[39] Stewart, T.A., Azimi, I., Thompson, E.W., Roberts-Thomson, S.J., Monteith, G.R. (2015) A role for calcium in the regulation of ATP-binding cassette, sub-family C, member 3 (ABCC3) gene expression in a model of epidermal growth factor-mediated breast cancer epithelial–mesenchymal transition. Biochem. Biophys. Res. Commun. 458, 509-514.
[40] Chien, W., Sun, Q.Y., Lee, K.L., Ding, L.W., Wuensche, P., Torres-Fernandez, L.A., Tan, S.Z., Tokatly, I., Zaiden, N., Poellinger, L., Mori, S., Yang, H.J. Tyner, W., Koeffler, H.P. (2015) Activation of protein phosphatase 2A tumor suppressor as potential treatment of pancreatic cancer. Mol. Oncol. 9, 889-905.
[41] Özdemir, Y., Börekci, B., Levent, A., Kurudirek, M. (2009) Assessment of trace element concentration distribution in human placenta by wavelength dispersive X-ray fluorescence: Effect of neonate weight and maternal age. Appl. Radiat. Isot. 67, 1790-1795.
[42] Çakır, C., Gürol, A. (2007) Semi-quantitative analysis of trace elements in Acanthoscelides obtectus (Say.) by using WDXRF Spectrometer. J. Fac. Agric. Atatürk Univ. 38, 41-47.

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