Effects of Aluminium Chloride Exposure on the Cerebral Cortex of Adult Wistar Rats Were Not Transferable o the Offspring

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Abstract

Aluminium is presents in many manufactured foods, medicines and is also added to drinking water for purification purposes.The cerebral cortex is a sheet of neural tissue that is outer-most to the cerebrum. This study was conducted in order to evaluate the possible effects that aluminium chloride exposure could have on the histology of cerebral cortex of wistar rats' offspring.The wistar rats were divided into five groups; group I was the control while groups II-V were given various concentrations of aluminium chloride for eight weeks; after which they were allowed to mate and their offspring (litters) were breed for another three months.The offspring were humanely sacrificed; brain was removed, fixed in bouin fluid, processed and stained with Hirano-Zimmerman's stain.Our observations showed normal appearances of the cerebral cortex of offspring.We therefore conclude that effects of aluminium chloride exposure on the cerebral cortex of adult wistar rats were not transferable to the offspring.

Key words: Effects, Aluminium Chloride, Wistar rats, Transferable, Offspring.

1. Introduction

Aluminium is a trivalent cation found in its ionic form in most kinds of animal and plant tissues and in natural waters everywhere (Jiang, et al., 2008).The almost ubiquitous presence of this element has so heavily contaminated the environment that exposure to it is virtually inescapable. The elemental aluminium does not occur in its pure state but is always combined with other elements such as chloride, hydroxide, silicate, sulphate and phosphate. The wide distribution of this element ensures the potential for causing human exposure and harm (Berthon, 1996; Candura *et al*., 1998; Williams, 1992; Zhang and Zhou, 2005). Aluminium is released to the environment by natural processes and from various anthropogenic sources. As a light weight metal with a melting point of 649.8°C., it is being used more and more for a number of different and important uses.

It is not an overstatement to aver that the modem technological age could not have occurred without the availability of aluminium. Human exposure to Aluminium has been increasing over the last decades. Patients on dialysis or on long-term treatment with total parenteral nutrition have been shown to accumulate this metal in different organs (Alfrey et al., 1976; Yokel and McNamara, 2001; Klein, 1993). It has been suggested that there is a relationship between high levels of aluminium and increased risk of a number of neurodegenerative disorders including dialysis encephalopathy, Alzheimer's disease (AD) and Parkinson's disease (PD) (Becaria et al., 2002; Berthon, 1996; Corain et al., 1996; Hughes, 1989; Yokel, 2000; Yokel, 2002).

It has been shown clearly that aluminium accumulates in various mammalian tissues such as brain, bone, liver and kidney (Wills *et al*., 1993; Sahin *et al.*, 1994) and is accompanied by renal failure (Alfrey, 1980) or associated with age (Gómez *et al*., 1997). Epidemiological studies have indicated a link between aluminium in drinking water and Alzheimer's disease; and a variety of human and animal studies have implicated learning and memory deficits after aluminium exposure (Buraimoh et al., 2011a; Exley, 2005; Yokel, 2000). Aluminium chloride was said to have negative effects on behavioural endpoints of wistar rats(i.e. alters behaviour), (Buraimoh et al., 2011b), have negative effects on anxiety-related behaviour of wistar rats as it increased the rate of anxiety in aluminium treated rats((Buraimoh et al., 2011c), had neurodegenerative effects on the histology of cerebral cortex of adult wistar rats especially at higher dose((Buraimoh et al., 2012a), have detrimental effects on the integrity of the testes of wistar rats((Buraimoh et al., 2012b), and also decrease the level of sperm count, but did not result into infertility(Buraimoh et al., 2012c).

The cerebral cortex is a sheet of neural tissue that is outer-most to the cerebral of the mammalian brain and it plays a key role in memory, attention, perceptual awareness, thought, language, and consciousness. It also integrates higher mental functions, general movement, visceral functions, and behavioural reactions. (Brodal, 1992; Cauller,1995). It consists essentially of three regions; neopallium, the paleopallium and archipallium. The neopallium is the newest portion and also the largest of the three, consisting of gyri and sulci (Sisson and Grossman, 1953). Archipallium now called "hippocampus" and the paleopallium of the pyriform lobe become the centre devoted extensively to olfactory functions. The corpus callosum arises to connect the enlarged neopallia of the two halves of the brain (Theodore and Alan, 1979).

The cerebral cortex is the biggest part of the brain. This large and complicated neural circuit is involved in most of the brain's highest functions, such as memory, language and sight. In man and higher animals, modifications of behaviour are due to cortical activity. (Pavlov, 1927). Pavlov demonstrated that conditional reflex being mediated through the cerebral cortex can be impaired or abolished in the dog by removal of appropriate cortical areas. Meyer and Woolsey (1952) also demonstrated how studies on frequency and intensity of sound can be used to study conditional reflex. Memories are stored in the cerebral cortex (Penfield, 1950).In his observation on temporal cortex in conscious patients, he made an assumption that integration of memories is not dependent on the association system of the cerebral cortex alone but also on central connections in the higher brain stem. Mettler, in 1935 explained that the two hemispheres of man are not symmetrical in their control of several functions. Speech, reading and writing for example, are vested in the left hemisphere, whereas the analysis of music is in the right (or right handed persons). These cortical areas account for most of the cortex of lower mammals (Marsupials and Insectivores), but for only one-quarter of the cortex of man.

In the parietal and occipital regions, there are secondary and tertiary projections areas that code messages, store information, combine inputs and provide spatial orientation (Milton, 1974). If these areas are impaired, a man might see well, yet confuse right and left; might walk well, yet get lost in a familial place. The frontal region of the cerebral cortex relates to programs intentions, orientation to goals and sequence in the performance of activities. The entire cortex of experimental animals becomes relatively heavy if the animals live in a relatively diverse, stimulating and enriched environment (Milton, 1974). George (1973) described the cerebral cortex as the highest center to which sensory impulse can be projected. This impulse, according to him, gives rise in the cortex to sensations of discriminative nature by recognizing minor differences in the temperature, texture or weight of an object held in the hand. It also appears to be one of the locations where past experiences are stored as memory, he explained. Drugs administered to mothers have the potential to cross the placenta and reach the fetus. Under particular circumstances, the comparison of the drug concentration in the maternal and fetal plasma may give an idea of the exposure of the fetus to the maternally administered drugs. Drugs are classified according to their type of transfer across the placenta.

Several drugs rapidly cross the placenta and pharmacologically significant concentrations equilibrate in maternal and fetal plasma. Their transfer is termed 'complete'. Other drugs cross the placenta incompletely, and their concentrations are lower in the fetal than in maternal plasma. The majority of drugs fit into 1 of these 2 groups. A limited number of drugs reach greater concentrations in fetal than maternal plasma. It is said that these drugs have an 'exceeding' transfer. The impression prevails that suxamethonium chloride (succinylcholine chloride) and doxorubicin do not cross the placenta. However, a careful analysis of the literature suggests that this impression is wrong and that all drugs cross the placenta, although the extent transfer varies considerably (Pacific and Nottoli, 1995).This study was designed in order to evaluate the possible effects that aluminium chloride exposure could have on the histology of cerebral cortex of offspring of wistar rats.

2. Materials and Methods

This work was carried out in the Department of Human Anatomy, Faculty of Medicine, Ahmadu Bello University, Samaru, Zaria, Nigeria. The rules and regulations governing animal handling of Ahmadu Bello University were strictly adhered to and the experiment was conducted in accordance to the ethical committee guidelines.

Experimental Animals

Twenty adult wistar rats were selected for this experiment. The wistar rats were housed in steel cages in the Department of Human Anatomy, Faculty of Medicine, Ahmadu Bello University, Zaria, under good ventilation, with sufficient food and water.

Experimental design

The wistar rats were divided into five groups; group I was the control, group II received 475mg/Kg, group III received 950mg/kg, group IV received 1,425mg/kg and group V received 1,900mg/kg via oral intubation for duration of eight weeks; after which they were allowed to mate freely and their litters (offspring) were breed for another three months. The offspring were humanely sacrificed; the brain was removed and immediately fixed in bouin fluid. The brain tissues were processed and stained with Hirano-Zimmerman's stain. The stained sections of the cerebral cortex were examined under the light microscope fitted to a laptop and digital camera for photomicrographs at magnifications of 100 and 250 respectively for each group.

3. Results and Discussion

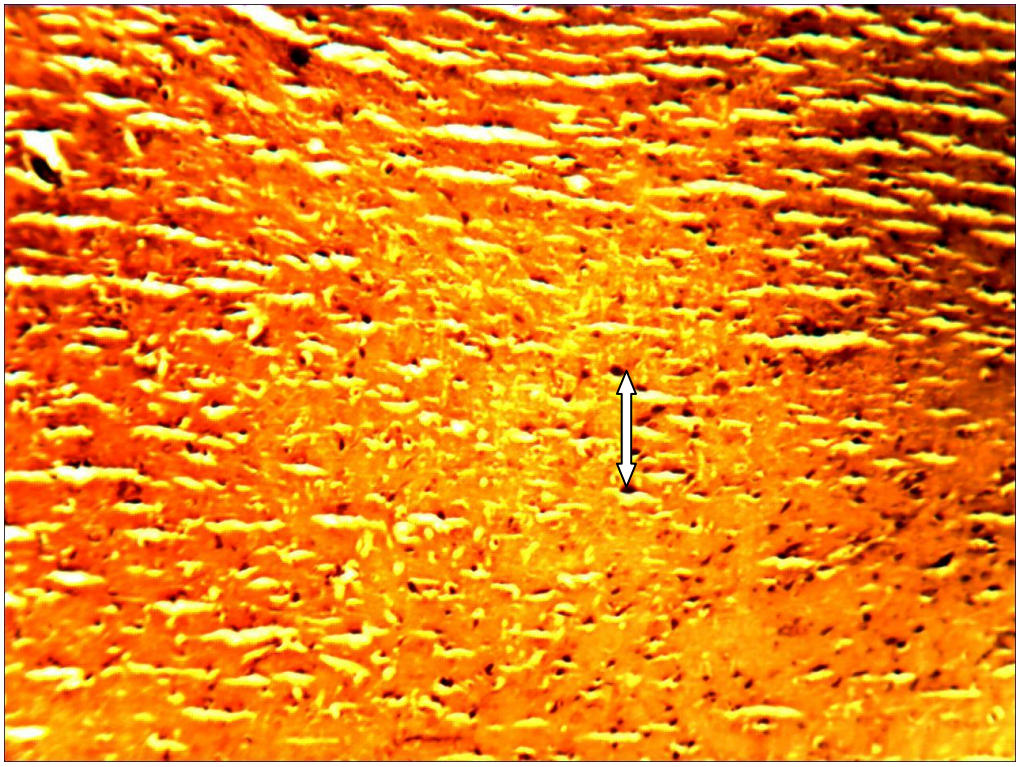


Plate 1. Normal histology of the cerebral cortex of offspring of wistar rats in group I with normal nerve cells(double arrow). Hirano-Zimmerman stain. X100

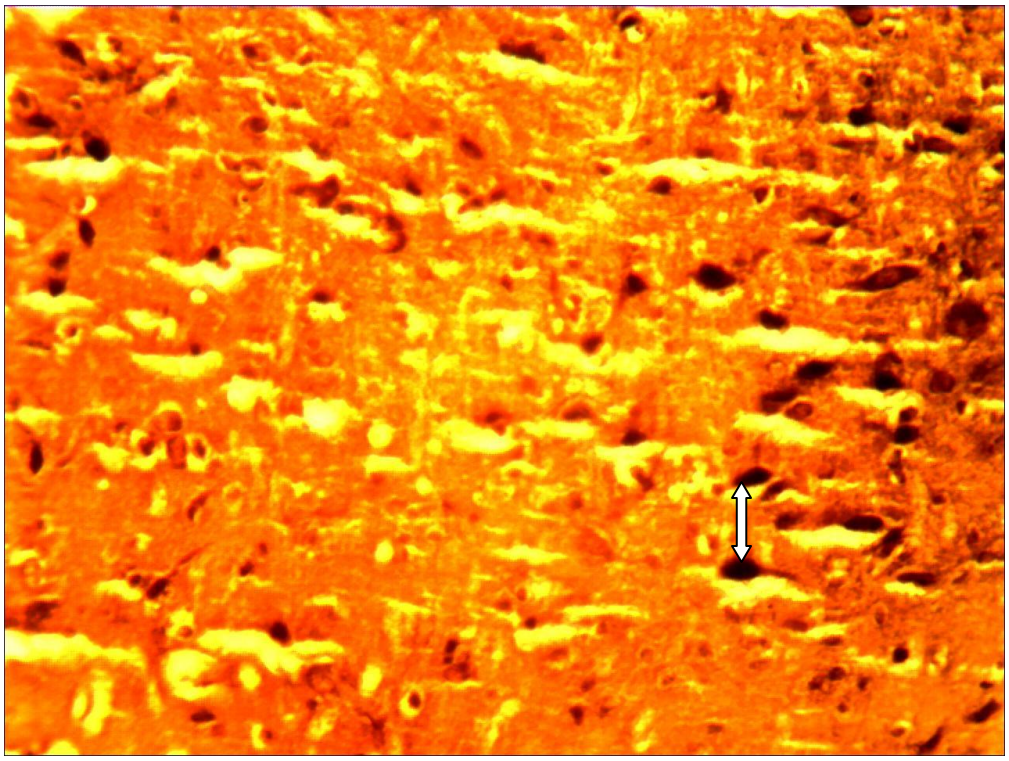


Plate 2. Normal histology of the cerebral cortex of offspring of wistar rats in group I with normal nerve cells(double arrow) . Hirano-Zimmerman stain. X250

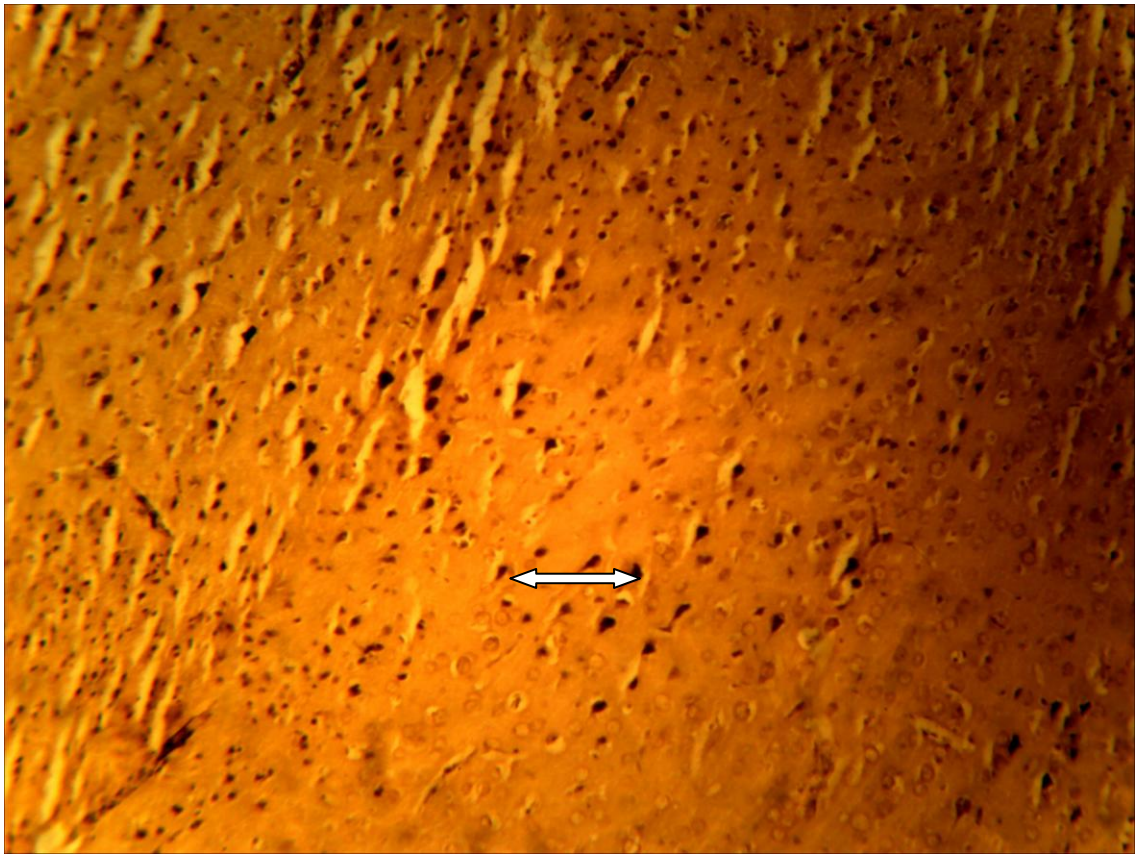


Plate 3. Normal histology of the cerebral cortex of offspring of wistar rats in group II with normal nerve cells(double arrow). Hirano-Zimmerman stain. X100

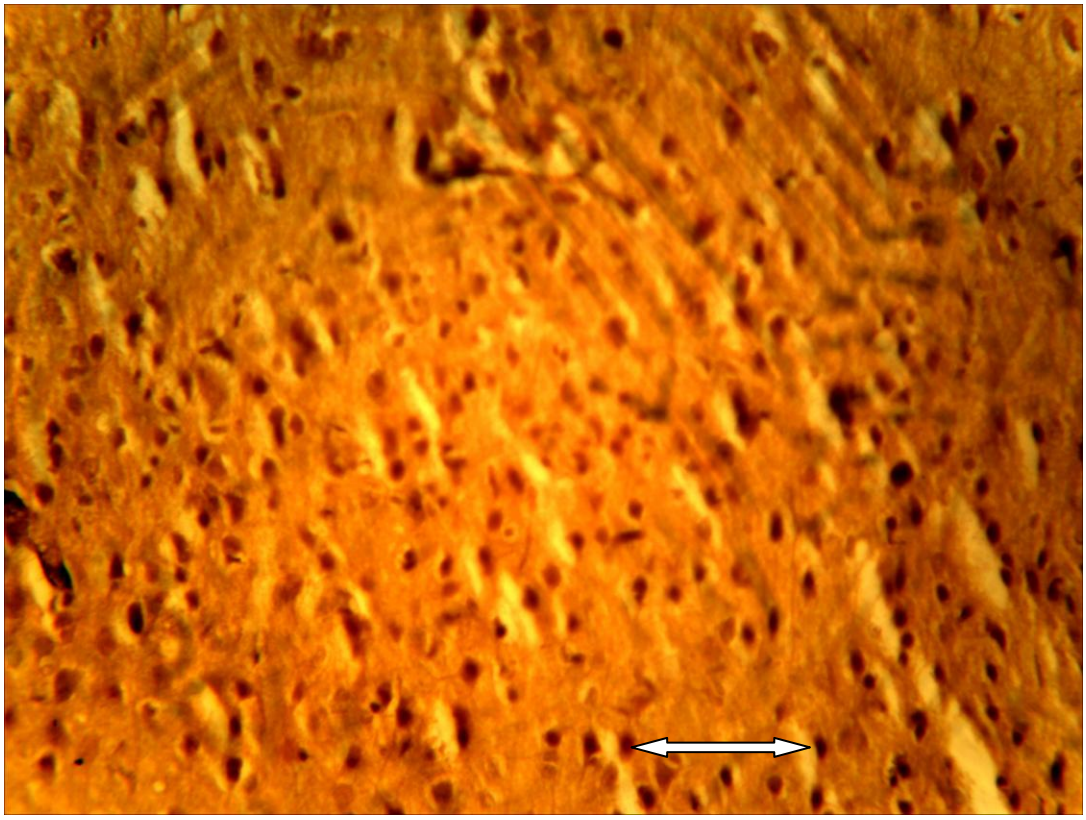
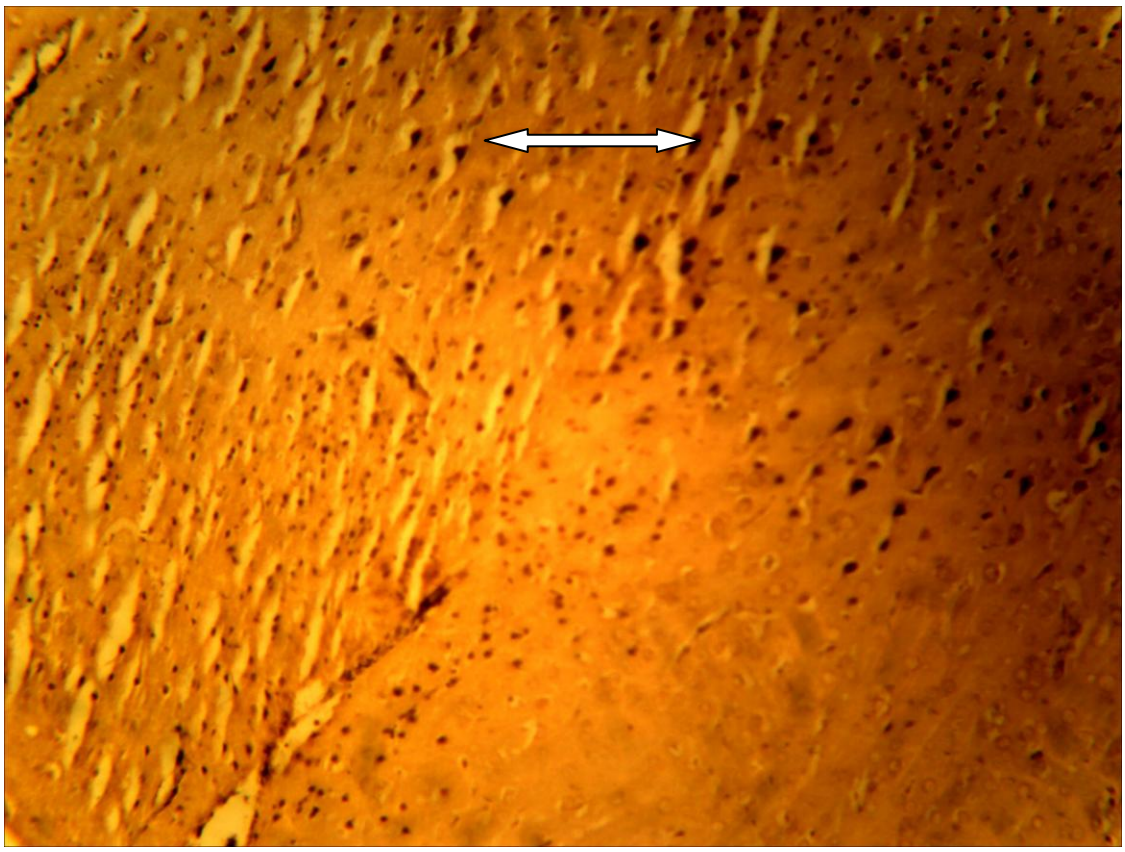


Plate 4. Normal histology of the cerebral cortex of offspring of wistar rats in group II with normal nerve cells (double arrow) Hirano-Zimmerman stain. X250.



late 5. Normal histology of the cerebral cortex of offspring of wistar rats in group III with normal nerve cells (double arrow). Hirano-Zimmerman stain.X100

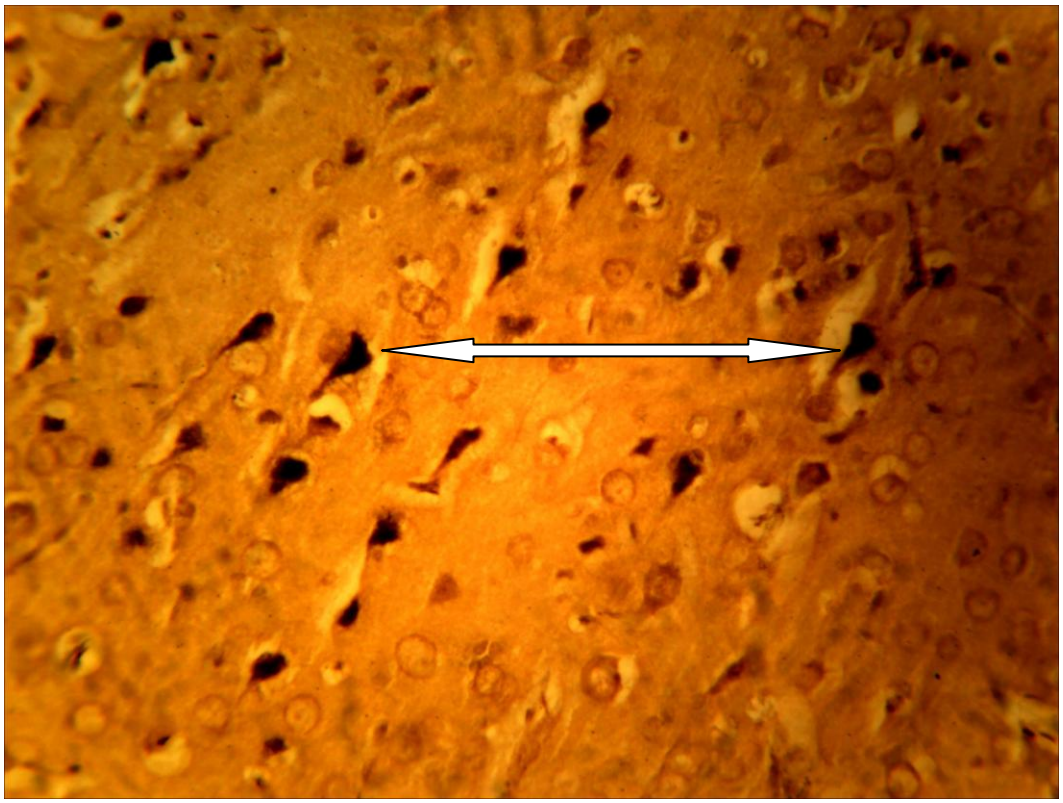


Plate 6. Normal histology of the cerebral cortex of offspring of wistar rats in group III with normal nerve cells (double arrow). Hirano-Zimmerman stain.X250

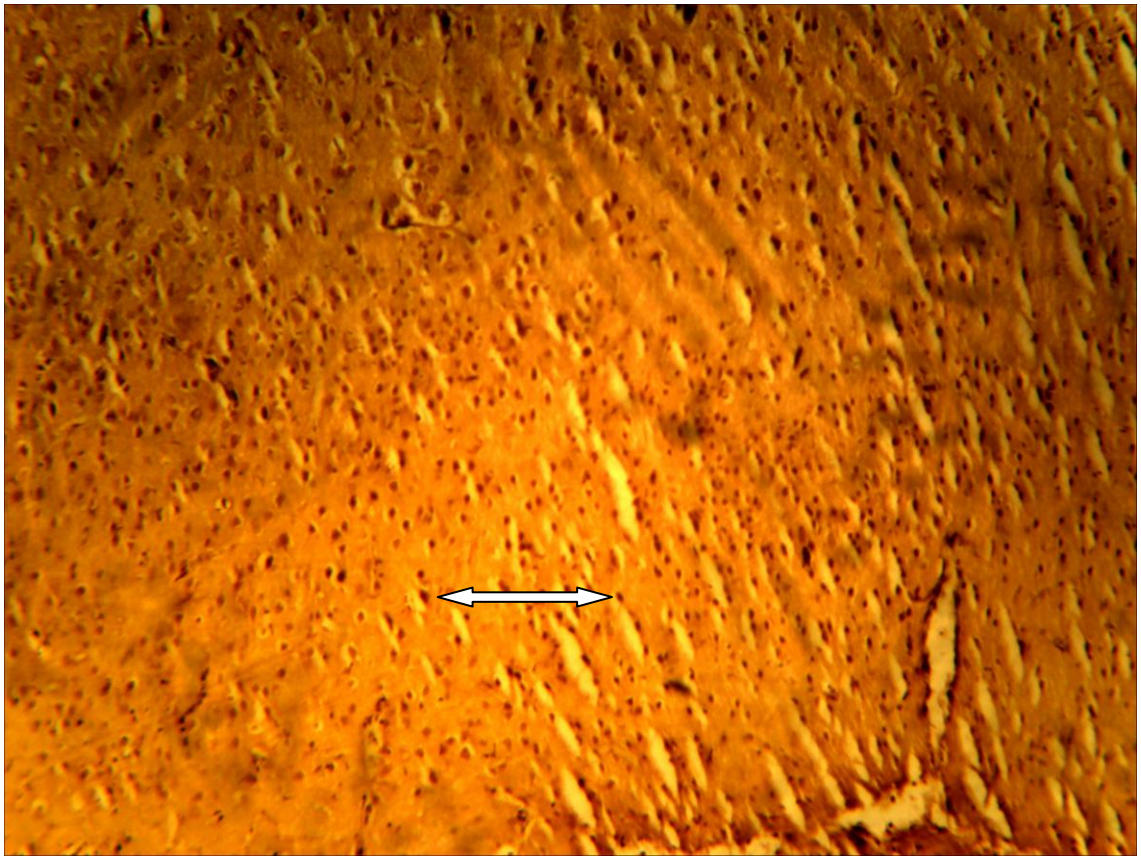


Plate 7. Normal histology of the cerebral cortex of offspring of wistar rats in group IV with normal nerve cells (double arrow). Hirano-Zimmerman stain.X100

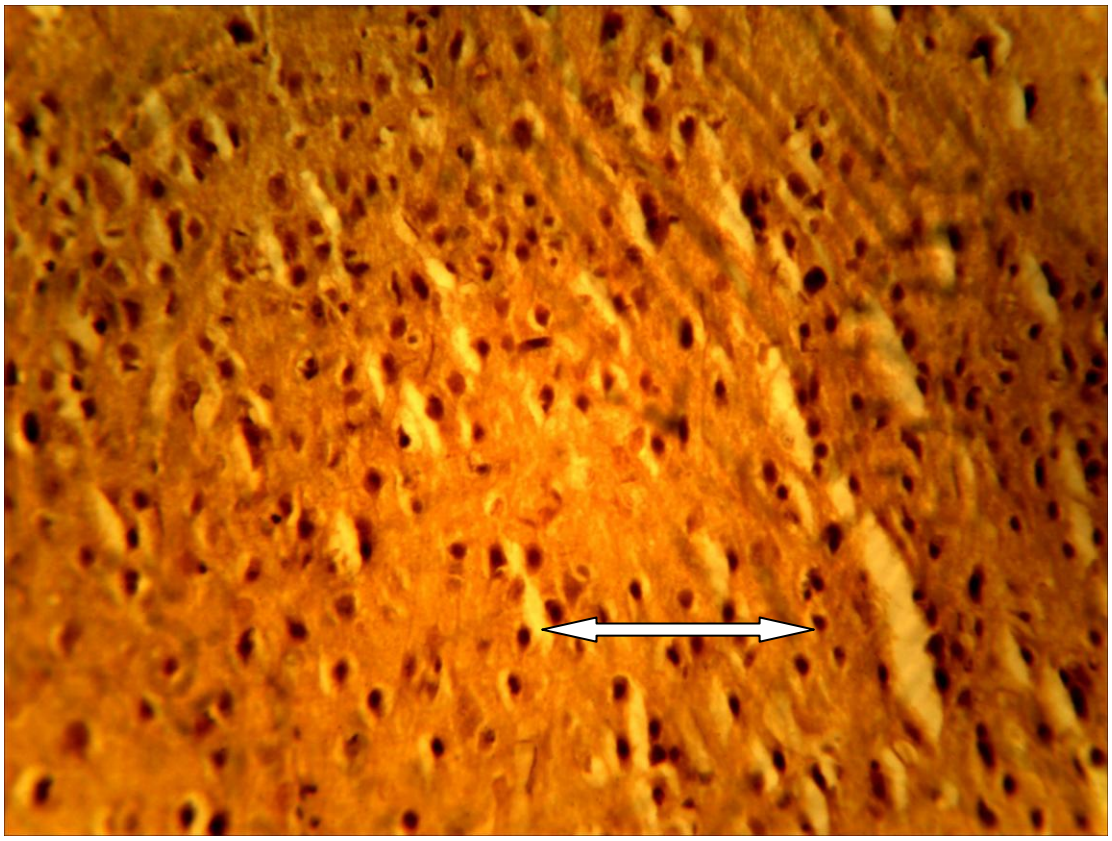


Plate 8. Normal histology of the cerebral cortex of offspring of wistar rats in group IV with normal nerve cells (double arrow). Hirano-Zimmerman stain.X250

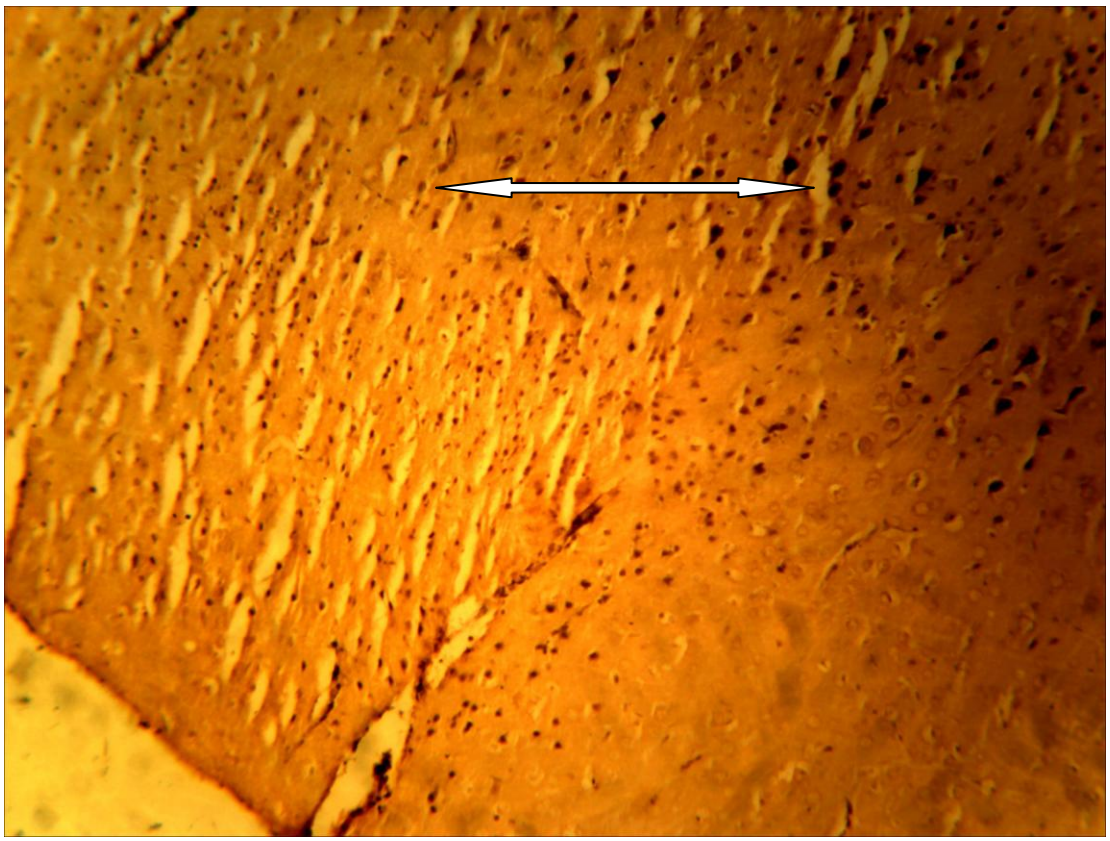


Plate 9. Normal histology of the cerebral cortex of offspring of wistar rats in group V with normal nerve cells(double arrow). Hirano-Zimmerman stain.X100

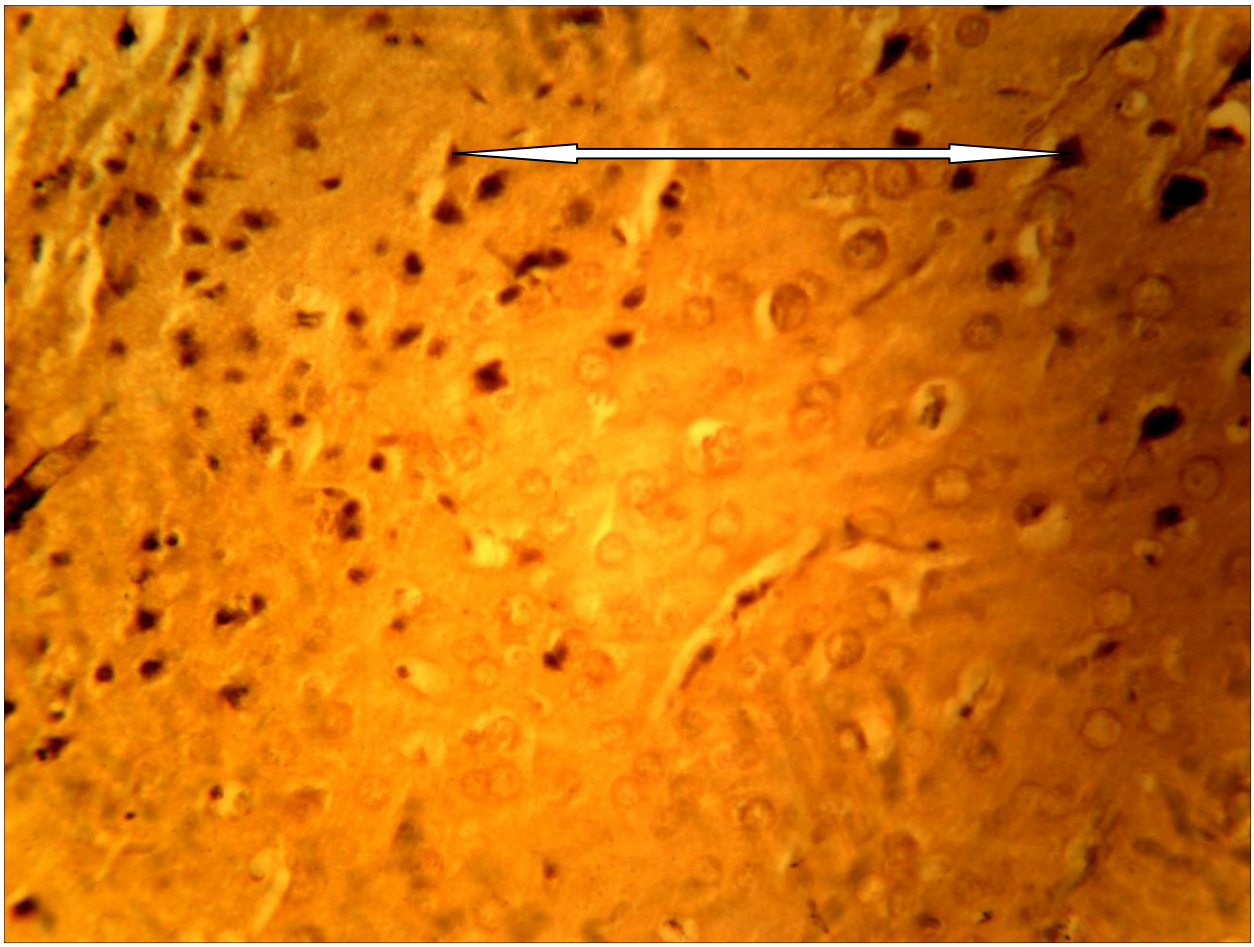


Plate 10. Normal histology of the cerebral cortex of offspring of wistar rats in group V with normal nerve cells (double arrow). Hirano-Zimmerman stain.X250

Traditionally, aluminium has been considered as nontoxic to humans. However, in recent years, increased attention is being focussed on possible adverse effects of aluminium on human health. Human exposure to aluminium is from its natural occurrence in the environment i.e. through food, water and air as well as from aluminium deliberately introduced into the environment by man. Aluminium compounds are used in pharmaceuticals (antacids, analgesics, antiperspirants) in water treatment processes (as coagulant) and as metal in consumer products. Aluminium is present in virtually all plants. Foods naturally high in aluminium include potatoes, spinach and tea. Processed dairy products, flour and infant formula may be high in aluminium, if they contain aluminium compounds as food additives (WHO, 1998).Aluminium is present in small amounts in mammalian tissues, yet there is little or scanty research work to support its physical usefulness. However, its neurotoxic effect on living organisms is becoming clear, aluminium being implicated as interfering with a variety of cellular metabolic processes in the nervous system and in other systems. Although molecular mechanisms by which aluminium exerts its neurotoxicity remain to be established, several pieces of evidence suggest that Aluminium can interfere with cellular metabolism in terms of biological stimulation, inhibition, or metal accumulation and compartmentation (Zatta *et al*., 1991).

Aluminium was said to have contributed to a variety of cognitive impairments in mice, rabbits, and rat pups (Muller et al., 1990; Yokel, 1985, Bilkei-Gorzo, 1993; Mari, 2001). Behavioural impairment has also been reported in wistar rats exposed to soluble aluminium salts (chloride) in the drinking water (Buraimoh et al., 2011b).Both rats (Connor et al., 1988) and mice (Yen-Koo, 1992) have demonstrated such impairments at doses exceeding 200 mg of aluminium per kg of body weight per day. Although significant alterations in acquisition and retention of learned behaviour were documented, the possible role of organ damage (kidney, liver, immunological) due to aluminium was incompletely evaluated in these studies (WHO, 1997).

Aluminium chloride was said to have negative effects on anxiety-related behaviour of wistar rats as indicated by increased rate of anxiety in Aluminium treated rats and that its exposure could be detrimental to the integrity of the testes of wistar rats. (Buraimoh, et al., 2011c; Buraimoh et al.,2012b). Buraimoh et al., 2012d also reported that aluminium chloride exposure was detrimental to the liver of wistar rats, as indicated by congested central vein and distorted sinusoids.

In our present study, we observed that the neurodegenerative effects of aluminium chloride exposure on the histology of cerebral cortex of adult wistar rats as reported by Buraimoh et al., 2012a, were not transferable to the offspring. This was eminent in the normal appearances of the histology of the cerebral cortex of all groups of offspring as the nerve cells were seen to be normal (See plates 1-10).

4. Conclusion

The histological observations of the offspring showed normal histological appearances of the cerebral cortex of all groups of the offspring (Plates 1-10). Based on our observations, we therefore conclude that the effects of aluminium chloride exposure on the cerebral cortex of adult wistar rats were not transferable to the offspring.

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References

Alfrey, A.C., LeGendre, G.R., & Kaehny, W.D. (1976).The dialysis encephalopathy syndrome. Possible Aluminium intoxication. N. Engl. J. Med., 294: 184-188.

Alfrey, A.C. (1980). Aluminium metabolism in uremia. Neurotoxicology 1:43–53.

Becaria, A., Campbell, A., & Bondy, S.C. (2002). Aluminium as a toxicant. Toxicol Ind Health 18:309–320.

Berthon, G. (1996). Chemical speciation studies in relation to Aluminium Metabolism and toxicity. Coord Chem Rev 149:241–280.

Bilkei-Gorzo, A. (1993). Neurotoxic effect of enteral Aluminium. Food Chem Toxicol.; 31:357–361.

Brodal, S. (1992). The Central Nervous system: Structure and Function. Oxford University Press.

Buraimoh, A.A., Ojo, S.A., Hambolu, J.O., & Adebisi, S.S. (2011a). Effects of Oral Administration of Aluminium Chloride on the Histology of the Hippocampus of Wistar Rats.*Current Research Journal of Biological Sciences*, 3(5): 509-515. ISSN: 2041-0778.

Buraimoh, A.A., Ojo, S.A., Hambolu, J.O., & Adebisi, S.S. (2011b). Behavioural Endpoints of Adult Wistar Rats, Following Aluminium Chloride Exposure. *British Journal of Pharmacology and Toxicology*, 2(5): 273-276.ISSN: 2044-2467.

Buraimoh, A.A., Ojo, S.A., Hambolu, J.O., & Adebisi, S.S. (2011c). Effects of Aluminium Chloride on Anxiety-Related Behaviour. *American Journal of Neuroscience*, 2(2): 65-69, 2011. http://dx.doi.org/10:3844/amjns.2011.

Buraimoh, A.A., Ojo, S.A., Hambolu, J.O., & Adebisi, S.S. (2012a) Effects of Aluminium Chloride Exposure on the Histology of the Cerebral Cortex of Adult Wistar Rats. Journal of Biology and Life Science@Macrothink Institute. Vol.3, No.1. ISSN 2157-6076. DOI: 10.5296/jbls.v3i1.1421.

Buraimoh, AA, Ojo, S.A., Hambolu, J.O., & Adebisi, S.S. (2012b). Histological Study of the Effects of Aluminium Chloride Exposure on the Testis of Wistar Rats. American International Journal of Contemporary Research.Vol. 2, No. 5, Pp.114-122.

Buraimoh, A.A., Ojo, S.A., Hambolu, J.O., & Adebisi, S.S. (2012c). Effects of Aluminium Chloride Exposure on the Sperm Count of Adult MaleWistar Rats. Asian J. Biol. Sci.Vol.3 (2): 435-438.

Buraimoh, A.A., Ojo, S.A., Hambolu, J.O., & Adebisi, S.S. (2012d).Effects of Aluminium chloride exposure on the Histology of the Liver of Adult Wistar Rats. IOSR Journal of Pharmacy. Vol.2 issue 3, Pp 525-533. ISSN 2250-3013.

Candura, S.M., Manzo, L., & Costa, L.G. (1998). Role of occupational neurotoxicants in psychiatric and neurodegenerative disorders.In: Costa LG, Manzo L (eds) Occupational neurotoxicology. CRC Press, Boca Raton, pp 131–167.

Cauller, L. (1995). Layer I of primary sensory neocortex: where top-down converges upon bottom-up. Behav Brain Res. 71(1-2):163-70.

Connor, D.J., Jope, R.S., & Harrell, L.E. (1988).Chronic, oral Aluminium administration to rats:Cognition and cholinergic parameters. *Pharmacology, biochemistry, and behaviour*, 31:467-474.

Corain, B., Bombi, G.G., Tapparo, A., Perazzolo, M., & Zatta, P. (1996).Aluminium toxicity and metal speciation:established data and open questions.Coord Chem Rev 149:11-22.

Exley, C. (2005). The aluminium-amyloid cascade hypothesis and Alzheimer's disease aluminium and β-amyloid. Alzheimer's Disease, 38:225-234. DOI: 10.1007/0-387-23226511.

George, C.K. (1973). Comparative Anatomy of Vertebrates. 7th edition.Pp.375-412.

Gómez, M., Sánchez, D.J., Llobet, J.M., Corbella, J., & Domingo, J.L. (1997).The effect of age on aluminium retention in rats. Toxicology 116:1–8.

Hughes, J.T. (1989). Aluminium encephalopathy and Alzhemer's diseases. Lancet, 1(8636):490-491.

Jiang, H.X., Chen, L.S., Zheng, J.G., Han, S., Tang, N., & Smith, B.R. (2008). Aluminium-induced effects on Photosystem II photochemistry in citrus leaves assessed by the chlorophyll a fluorescence transient. *Tree Physiol*. Dec 2008; 28 (12):1863-71.

Klein, G.L. (1993). Aluminium and hepatobiliary complications of total parenteral nutrition. Gastroenterology, 10: 1583-1584.

Mari, S., Golub, & Stacey, L. (2001). Long-term consequences of developmental exposure to Aluminium in a suboptimal diet for growth and behavior of Swiss Webster mice. Neurotoxicology and Teratology.; 23:365–372.

Mettler, F.A. (1935). Coticifugal fiber connections of the cortex of Macaca mulata. Journal of comparative neurology. 63: 23-47.

Meyer, D.R., & Woolsey, C.N. (1952). Effects of localized cortical destruction on auditory discriminative conditioning in cat. J. Neurophysiology, 15: 149-162.

Milton, H. (1974). Nervous System. In: Analysis of Vertebrate Structure Text. Pp.77.

Muller, G., Bernuzzi, V., Desor, D., Hutin, M.F., Burnel, D., & Lher, P.R. (1990). Developmental alteration in offspring of female rats orally intoxicated by Aluminium lactate at different gestation periods. Teratology.; 42:253–261.

Pacific, G.M., & Nottoli, R. (1995). Placental transfer of drugs administered to the mother. Clin Pharmacokinet.Mar;28(3):235-69. PMID: 7758253.

Pavlov, I.P. (1927).Conditional Reflexes. Oxford University Press, London.

Penfield, W. (1950). Observations on the anatomy of memory. Fol. Psychiat. Neurology. Neurochirurgica Nearl, 53: 349-351.

Sahin, G., Varol, I., & Temizer, A. (1994). Determination of aluminium levels in the kidney, liver, and brain of mice treated with aluminium hydroxide. Biol Trace Element Res 41:129–135.

Sisson, S., & Grossman, J.D. (1953). Nervous System. In: The Anatomy of the Domestic Animals. 4th Ed. W.B. Saunders Company. PP.788-811.

Theordore, W.T., & Alan, F. (1979). Nervous system development. In: The morphogenesis of vertebrates. 4th edition, John Wiley and Sons. Pp.457-531.

WHO, (1997). Aluminium. Geneva, World Health Organization, International Programme onChemical Safety (Environmental Health Criteria 194.

WHO, (1998). Guidelines for drinking water quality. second edition. Addendum to Vol.2., Published by World Health Organization, Geneva.

Williams, R.J.P. (1992). Aluminium and biological systems: an introduction. Coord Chem Rev 149:1–9.

Wills, M.R., Hewitt, C.D., Sturgill, B.C., Savory, J., & Herman, M.M. (1993). Long-term oral or intravenous aluminium administration in rabbits.I. Renal and hepatic changes. Ann Clin Lab Sci 23:1–16.

Yen-Koo, H.C. (1992).The effect of Aluminium on conditioned avoidance response (CAR) inmice. Toxicology and industrial health, 8:1-7.

Yokel, R.A. (1985). Toxicity of gestational Aluminium exposure to the maternal rabbit and offspring. Toxicol Appl Pharmacol.;79:121–133.

Yokel, R.A. (2000).The toxicology of Aluminium in brain:review, Neurotoxicology .21 (5): 813-828.

Yokel, R.A. (2002). Brain uptake, retention, and efflux of aluminium and manganese. Environ Health Perspect 110:699–704.

Yokel, R.A., & McNamara, P.J. (2001). Aluminium toxicokinetics: an updated minireview. Pharmacol. Toxicol., 88: 159-167.

Zattal, P.F., Nicolini, M., & Corain, B. (1991). Aluminium (III) toxicity and blood-brain barrier permeability: IN Aluminium in Chemistry, biology and medicine cortina international, Verona and Reven Press, New York Pg. 97-112.

Zhang, K., & Zhou, Q. (2005). Toxic effects of Al-based coagulants on Brassica chinensis and Raphanus sativus growing in acid and neutral conditions. Environ Toxicol 20:179–187.