IOSR Journal of Pharmacy
Vol. 2, Issue 3, May-June, 2012, PP.525-533

EFFECTS OF ALUMINIUM CHLORIDE EXPOSURE ON THE HISTOLOGY OF THE LIVER OF ADULT WISTAR RATS

*Adebayo Adekunle Buraimoh, Samuel Adeniyi Ojo, Joseph Olajide Hambolu, Sunday Samuel Adebisi,

Department of Human Anatomy, Faculty of Medicine, Department of Veterinary Anatomy, Faculty of Veterinary Medicine, Department of Veterinary Anatomy, Faculty of Veterinary Medicine, Department of Human Anatomy, Faculty of Medicine, Ahmadu Bello University, Zaria, Nigeria.

ABSTRACT:

Aluminium is presents in many manufactured foods, medicines and is also added to drinking water for purification purposes. It presence has so heavily contaminated the environment that exposure to it is virtually inescapable. The liver is the largest gland of the body that processes blood and breaks down nutrients, drugs into forms that are easier to use for the rest of the body. This study was aimed at evaluating the possible effects that aluminium chloride exposure could have on the histology of the liver. Ten wistar rats were used and were divided into five groups; group I was the control, group II received 475mg kg^{-1}, group III received 950mgkg^{-1}, group IV received 1,425mg kg^{-1} and group V received 1,900mg kg^{-1} via oral intubation for duration of eight weeks. The liver tissues was fixed, processed, stained in H&E and slides viewed under light microscope. Our observations showed that aluminium chloride exposure was detrimental to the liver of wistar rats, as indicated by congested central vein and distorted sinusoids.

Keywords: Effects, Aluminium Chloride, Histology, Liver, Wistar Rats.

INTRODUCTION:

The liver is the largest gland of the body, weighing 1200 -1600g; it is wedge-shaped, and covered by a network of connective tissue (Glisson's capsule). Situated in the upper right portion of the abdominal cavity, the liver is divided by fissures (*fossae*) into four lobes: the right (the largest lobe), left, quadrate and caudate lobes. The liver is located in the upper right-hand portion of the abdominal cavity, beneath the diaphragm, and on top of the stomach, right kidney and intestines. Shaped like a cone, the liver is a dark reddish-brown organ.

Venous blood from the entire gastrointestinal tract (containing nutrients from the intestines) is brought to the liver by the hepatic portal vein. Branches of this vein pass in between the lobules and terminate in the sinusoids. Oxygenated blood is supplied in the hepatic artery. The blood leaves the liver via a central vein in each lobule, which drains in the hepatic vein. Microscopic structure of the liver consists of the following:

I. **Lobules -** hexagonally shaped functional units of the liver, made up of liver cells arranged in one-cell-thick plate-like layers that radiate from the central vein to the edge of the lobule.
II. **Sinusoids** - small blood vessels between the radiating rows of hepatocytes. They receive oxygen-rich blood from the hepatic artery and nutrients from the intestines via the portal vein. Oxygen and nutrients diffuse through the capillary walls into the liver cells.
III. **Portal area** - situated at the corner of each lobule, it is a complex composed of branches of the hepatic portal vein, hepatic artery, bile duct and nerve.
IV. **Bile ducts** - any of the ducts that convey bile from the liver. Bile is drained from the liver cells by many small ducts that unite to form the main bile duct of the liver, the hepatic duct. This joins the cystic duct, which leads from the gallbladder, to form the common bile duct, which drains into the duodenum.
V. **Central vein** - a blood vessel in the middle of each lobule which receives blood from the hepatic portal vein and hepatic artery via the sinusoids and drains the blood into the hepatic vein [1-3].

The liver is our greatest chemical factory, it builds complex molecules from simple substances absorbed from the digestive tract, it neutralizes toxins, it manufactures bile which aids fat digestion and removes toxins through the bowels [4]. But the ability of the liver to perform these functions is often compromised by numerous substances we are exposed to on a daily basis; these substances include certain medicinal agents which when taken in over doses and sometimes when introduced within therapeutic ranges injures the organ [5].

The liver regulates most chemical levels in the blood and excretes a product called bile, which helps carry away waste products from the liver. All the blood leaving the stomach and intestines passes through the liver. The liver processes this blood and breaks down the nutrients and drugs into forms that are easier to use for the rest of the body. More than 500 vital functions have been identified with the liver. Some of the more well-known functions include the following:

- Production of bile, which helps carry away waste and break down fats in the small intestine during digestion
- Production of certain proteins for blood plasma
- Production of cholesterol and special proteins to help carry fats through the body
- Conversion of excess glucose into glycogen for storage (glycogen can later be converted back to glucose for energy)
- Regulation of blood levels of amino acids, which form the building blocks of proteins
- Processing of hemoglobin for use of its iron content (the liver stores iron)
- Conversion of poisonous ammonia to urea (urea is an end product of protein metabolism and is excreted in the urine)
- Clearing the blood of drugs and other poisonous substances
- Regulating blood clotting
- Resisting infections by producing immune factors and removing bacteria from the bloodstream.

Aluminium is ubiquitous element and the third most prevalent (abundant) element in the earth's crust, comprising approximately 8% of the earth's crust, exceeded only by oxygen (47%) and silicon (28%). 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 [6-9].Evidence for contribution of aluminium to Alzheimer's disease remains contradictory [10-11]. Epidemiological studies have indicated a link between aluminium in drinking water and Alzheimer's disease (AD) and a variety of human and animal studies have implicated learning and memory deficits after aluminium exposure [12-15]. Aluminium chloride was implicated to have negative effects on behavioural endpoints of wistar rats(i.e. alters behaviour), have negative effects on anxiety-related behaviour of wistar rats as it increased the rate of anxiety in aluminium treated rats, had neurodegenerative effects on the histology of cerebral cortex of adult wistar rats especially at higher dose, was also said to have detrimental effects on the integrity of the testes of wistar rats , and also decrease the level of sperm count, but did not result into infertility. [16-20].*This study was aimed at evaluating the possible effects that aluminium chloride could have on the histology of the liver of adult wistar rats.*

MATERIALS AND METHODS:

This experiment was conducted in the Department of Human Anatomy, Faculty of Medicine, Ahmadu Bello University, Samaru, Zaria, Nigeria.

Experimental Animals:

Ten adult wistar rats were used for this experiment. The wistar rats were housed in steel cages in the animal house of Department of Human Anatomy, Faculty of Medicine, Ahmadu Bello University, Zaria, Nigeria; they were given sufficient food, water and kept under good ventilation. The wistar rats were kept for two weeks before commencement of aluminium chloride administration. This was to enable the wistar rats acclimatized to the environment.

Experimental Design:

The wistar rats were divided into five groups; group I was the control, group II received 475mg Kg^{-1}, group III received 950mg kg^{-1} , group IV received 1,425mg kg^{-1} and group V received 1,900mg kg^{-1} via oral intubation for duration of eight weeks.

Tissue processing and staining:

The wistar rats were humanely sacrificed by anesthetizing them in a suffocating chamber using chloroform, after the end of eight weeks of administrations of various concentrations of aluminium chloride except the control group I that received distil water only. The abdominal region was dissected and the liver tissues were removed, and immediately fixed in 10% formalin. After fixation, the tissues were transferred into an automatic processor where they went through a process of dehydration in ascending grades of alcohol (ethanol) 70%, 80%, 95% and absolute alcohol for 2 changes each. The tissues were then cleared in xylene and embedded in paraffin wax. Serial sections of 5 micron thick were obtained using a rotary microtome. The tissue sections were deparaffinised, hydrated and stained using the routine haematoxylin and eosin staining method (H&E). The stained sections were examined under the light microscope fitted to a digital camera and lap top.

RESULTS AND DISCUSSION:

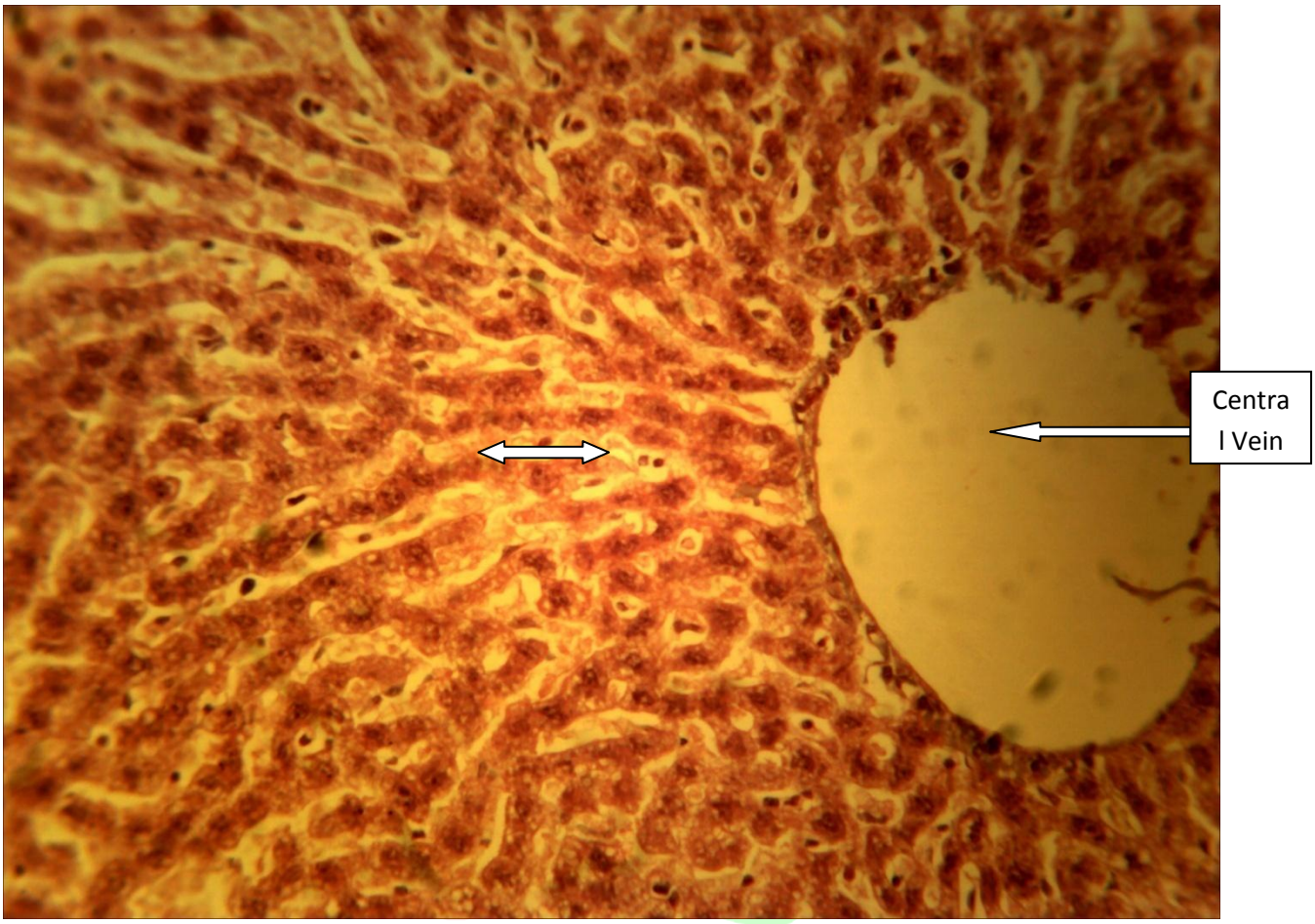

Plate 1.Histology of the normal liver (control group I) of wistar rats showing the central vein and radially arranged sinusoids (double arrow) .X400 H&E stain.

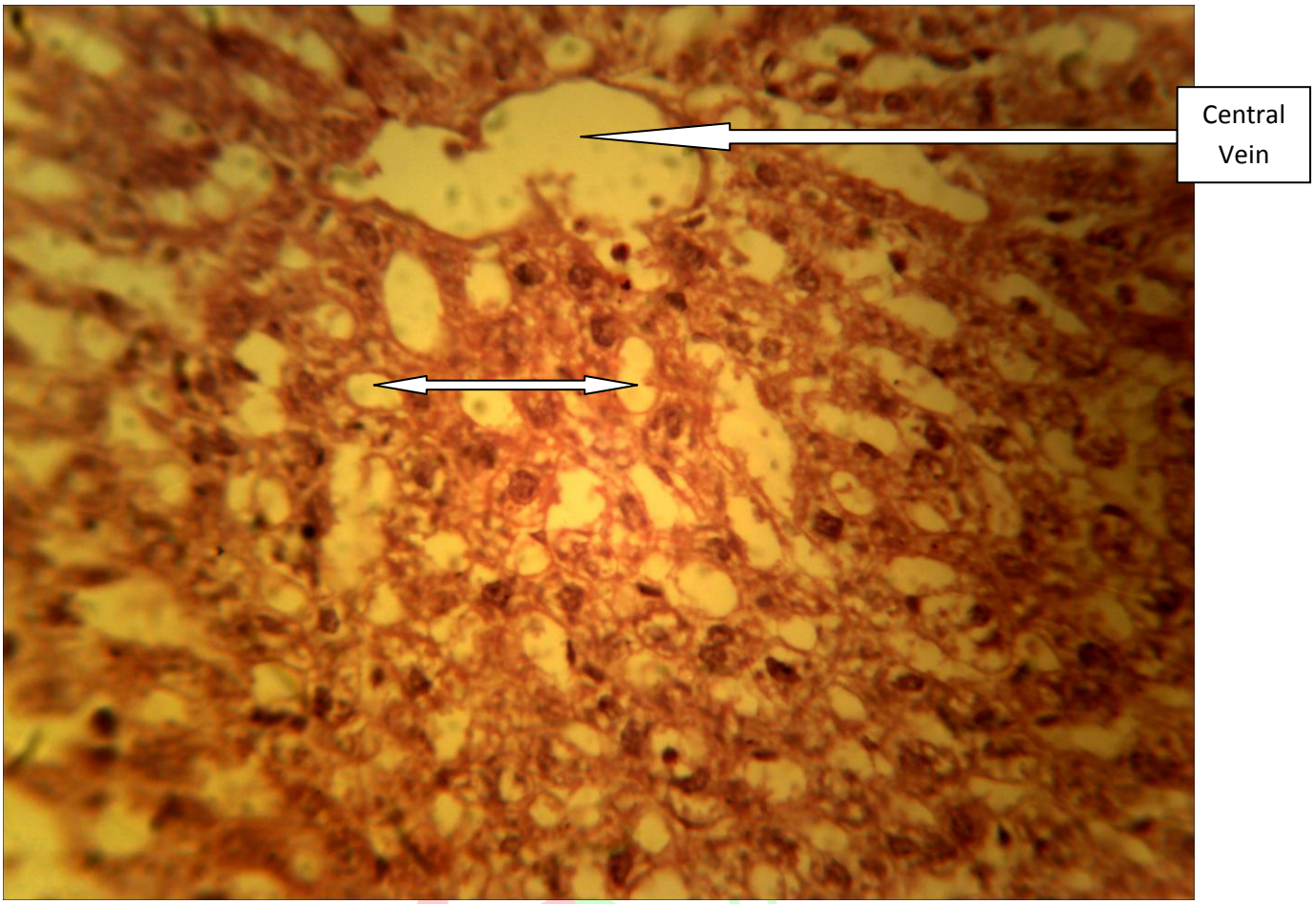

Plate 2. Histology of the liver of wistar rats of group II showing central vein and Distorted sinusoids (double arrow). X400 H&E stain.

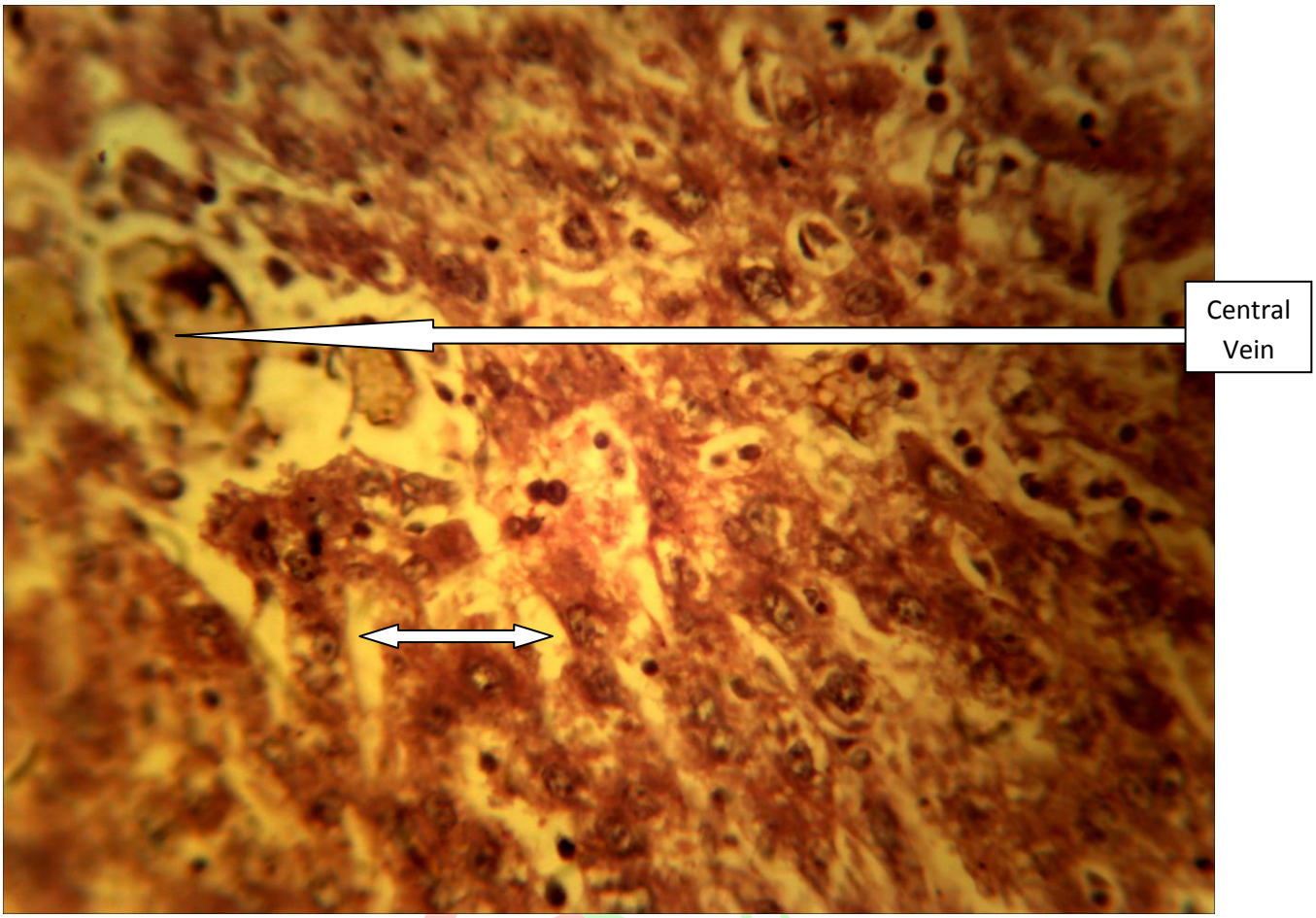

Plate 3. Histology of the liver of wistar rats of group III showing congested central vein and Distorted sinusoids (double arrow) .X400 H&E stain

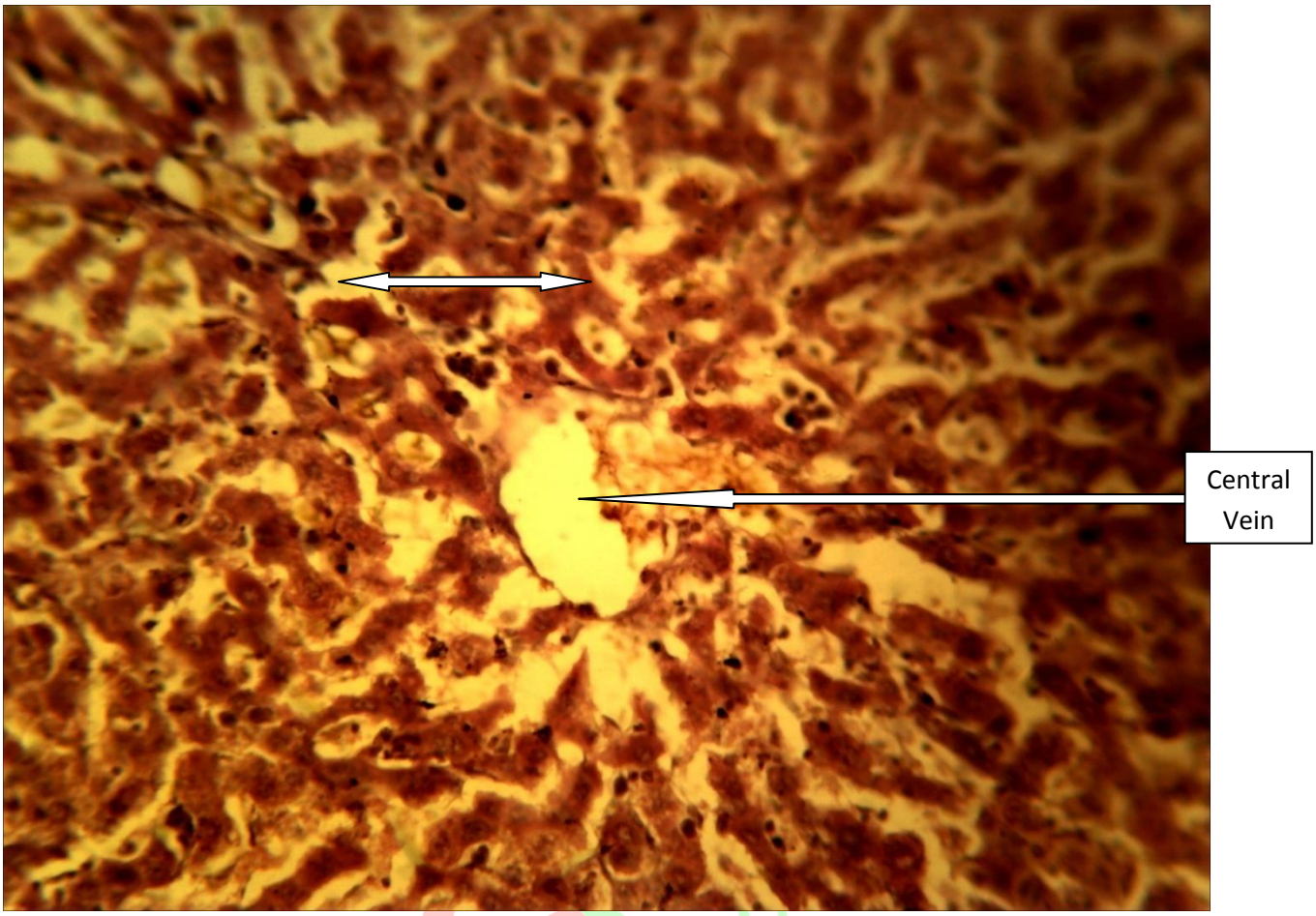

Plate IV. Histology of the liver of wistar rats of group IV showing congested central vein and Distorted sinusoids (double arrow) .X400 H&E stain.

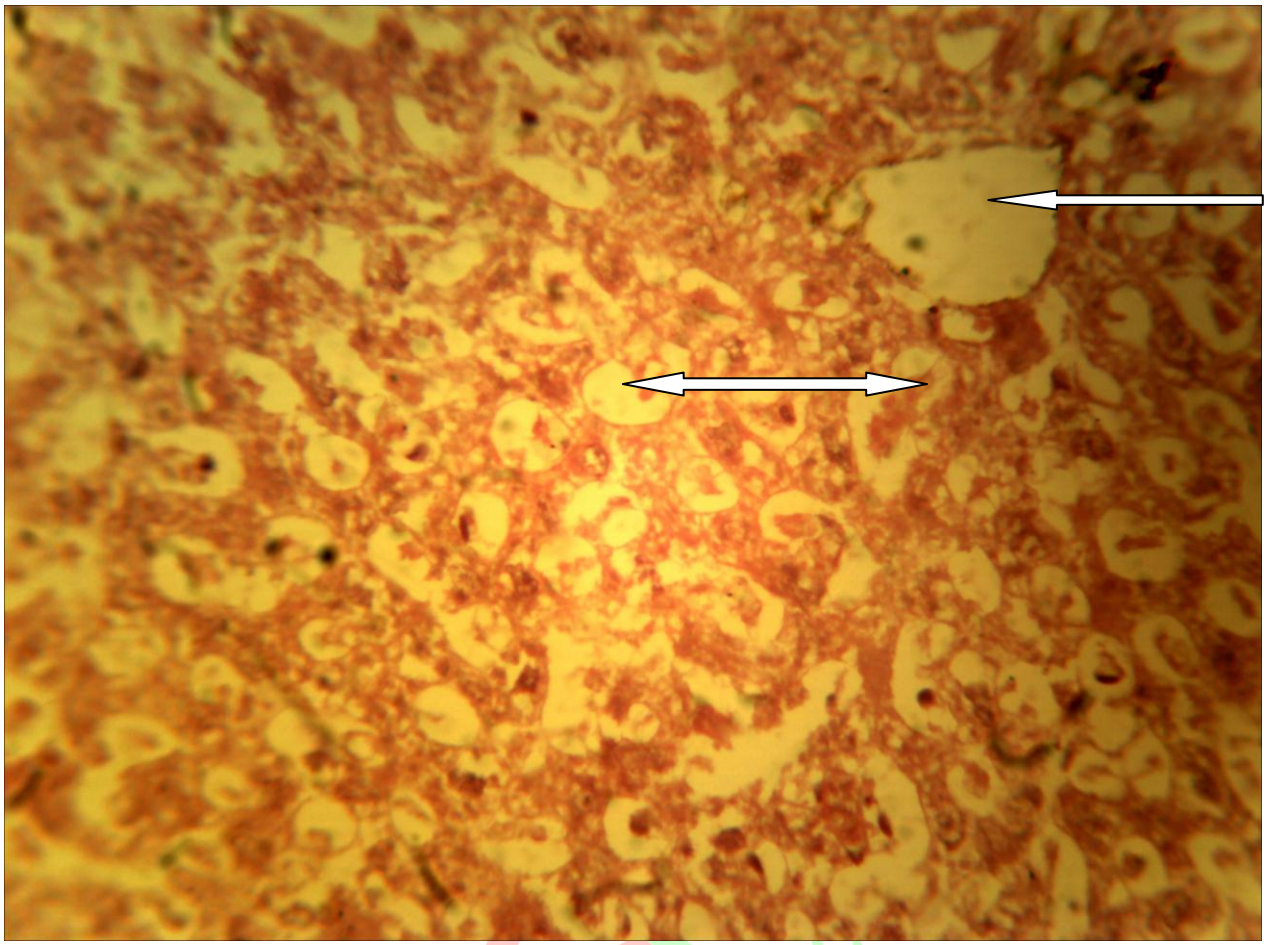

Plate V. Histology of the liver of wistar rats of group V showing central vein but Distorted sinusoids (double arrow) X.400 H&E stain.

Humans are uniformly exposed to aluminium that is present in the soil, food and drinking water [10]. Aluminium is potentially neurotoxic although its biological effects are not yet well known [21]. There are several data linking elevated Al^{3+} levels to neurological pathologies such as multiple sclerosis, Guam Parkinson dementia, Parkinson's disease and Alzheimer's disease [22]. It was reported that prolonged aluminium sulphate intake accelerate features of senescence in the adult mice liver. In Aluminium treated mice as in senescent mice, endothelial thickness was increased and porosity was decreased like perisinusoidal actin. Furthermore, aluminium stimulated the deposition of collagen and laminin, mainly in acinar zones 1 and 3. Pseudocapillarization and periportal laminin in senescent mice were similar to aluminium treated adult liver and latter concluded that prolonged aluminium sulphate intake accelerates features of senescence in the adult mice liver [23]. In our study, there was normal histology of the liver with radially arranged sinusoids from the central vein and the hexagonal shape of the hepatocytes was maintained with viable hepatic cell (plate 1). There was distorted sinusoids (see Plates 2-5) and congested central vein (Plates 3and 4) of the liver of the aluminium treated rats.

This was contrary to a report that stated that aluminium given in pharmacologic doses is absorbed but does not accumulate in the liver [24]. Prolonged aluminium exposure accelerates ageing changes in the adult rat brain [25] and enhanced aluminium deposition in the brain is a shared characteristic of progressive neurological diseases that are common in aged populations [26]. The deposition of aluminium in non nervous organs and its subsequent effects are less known. It was previously described that the effects of aluminium in the rat kidney and liver, where it induces lysosomal activation, increases iron deposition [27] and hence the liver was involved in aluminum absorption and excretion through biliary flux [28].

During ageing of the liver, besides parenchymal cells (reviewed by [29]), morphological changes involved the endothelium, bile duct cells and non parenchymal cells [30-31]. In particular, alterations in microvascular hemodynamic in rats [32] and age related sinusoidal thickening ("pseudocapillarization") has been reported in humans [33],rats [34] and mice [35-36]. These findings were similar to our observations of distorted sinusoids of the aluminium treated wistar rats (Plates 2-5).

CONCLUSION:

The aluminium treated wistar rats showed distortion of the arrangement of parenchyma of the liver, loss of radial arrangement of sinusoids from the central vein of the liver and loss of hexagonal shape of the hepatocytes (plate 2-5) when compared with the control(plate 1). Based on our histological observations, we therefore conclude that aluminium chloride exposure was detrimental to the liver of adult wistar rats and hence caution should be taken in its usage.

ACKNOWLEDGEMENT:

The Authors wish to thank the management of Ahmadu Bello University, Zaria, for supporting this research work.

REFERENCES:

[1]. Guyton AC, Hall JE, Textbook of Medical Physiology. 9th edition, W.B.Saunders Company ;1995.
[2]. Henry G**,** Lawrence, HB, Martin MB, Peter LW, Gray's Anatomy: The Anatomical Basis of Medicine and Surgery. 38th edition, Churchill Livingstone Publication;1995.
[3]. Steve P, Giuliano F, The Body Atlas: A complete Map of Human Body.Dorling Kindersley Publishers Ltd.Amazon.Co.Uk; 1993.
[4]. Maton A, Jean H, McLaughlin CW, Warner MQ, Lattart D, Wright JD, Human Biology and Health. Eaglewood Cliffs, New Jersey, Prentice Hall, USA;1993.
[5]. Gagliano N, Grizzi F, Annoni G, Mechanism of aging and liver functions. Digest. Dis. Sci; 2007, 25:118-123.
[6]. Berthon G, Chemical speciation studies in relation to aluminum Metabolism and toxicity. Coord Chem Rev; 1996, 149:241–280.
[7]. Candura SM, Manzo L, Costa LG, Role of occupational neurotoxicants in psychiatric and neurodegenerative disorders.In: Costa LG, Manzo L (eds) Occupational neurotoxicology. CRC Press,Boca Raton; 1998, pp 131-167.
[8]. Williams RJP, Aluminium and biological systems: an introduction. Coord Chem Rev; 1996, 149:1–
[9]. Zhang K, Zhou Q,Toxic effects of Al-based coagulants on *Brassica chinensis* and *Raphanus sativus* growing in acid and neutral conditions. Environ Toxico; 2005, l 20:179–187.
[10]. Flaten T, Aluminium as a risk factor in Alzheimer's disease, with emphasis on drinking water. Brain Res. Bull, 55; 2001, pp. 187–196.
[11]. Gupta VB, Anitha G, Hegda ML, Zecca L, Garruto RM, Ravid R, Shankar SK, Stein R, Hanmugavelu P, Jagannatha Rao KS, Aluminium in Alzheimer's disease: are we still at a crossroad? Cell. Mol. Life Sc; 2005, 62: 143-158.

[12]. Buraimoh AA, Ojo SA, Hambolu JO, Adebisi SS, Effects of oral administration of aluminium chloride on the histology of the hippocampus of wistar rats. Curr. Res. J. Biol. Sci.; 2011a, 3: 509-515.
[13]. Exley C, The aluminium-amyloid cascade hypothesis and Alzheimer's disease aluminium and β-amyloid. Alzheimer's Disease; 2005, 38:225-234. DOI: 10.1007/0-387-23226511.
[14]. Schmidt ML, Zhukavera V, Perl DP, Sheridan SK, Schuck T, Spinal cord neurofibrillary pathology in alzheimer disease and guam parkinsonism-dementia complex. J. Neuropathol. Exp. Neurol.; 2001, 60: 1075-1086.
[15]. Yokel RA, The toxicology of Aluminium in brain:review, Neurotoxicology; 2000, 21 (5): 813-828.
[16]. Buraimoh AA, Ojo SA, Hambolu JO, Adebisi SS, Behavioural endpoints of adult wistar rats, following aluminium chloride exposure. Br. J. Pharmacol. Toxicol ; 2011b, 2: 273-276. ISSN: 2044-2467.
[17]. Buraimoh AA, Ojo SA, Hambolu JO, Adebisi SS, Effects of Aluminium Chloride on Anxiety-Related Behaviour. American Journal of Neuroscience, Science Publication; 2011c, 2(2): 65-69, ISSN 1948-9900.
[18]. Buraimoh AA, Ojo SA, Hambolu JO, Adebisi SS, Effects of Aluminium Chloride Exposure on the Histology of the Cerebral Cortex of Adult Wistar Rats. Journal of Biology and Life Science@Macrothink Institute; 2012a, Vol.3, No.1. ISSN 2157-6076. DOI: 10.5296/jbls.v3i1.1421.
[19]. Buraimoh AA, Ojo SA, Hambolu JO, Adebisi SS, Histological Study of the Effects of Aluminium Chloride Exposure on the Testis of Wistar Rats. American International Journal of Contemporary Research; 2012b, Vol. 2, No. 5.
[20]. Buraimoh AA, Ojo SA, Hambolu JO, Adebisi SS, Effects of Aluminium Chloride Exposure on the Sperm Count of Adult MaleWistar Rats. Asian J. Biol. Sci; 2012c, Vol.3 (2): 435-438.
[21]. Walton J, A longitudinal study of rats chronically exposed to aluminium at human dietary levels. Neurosci. Lett., 412; 2007, pp. 29–33.
[22]. Nayak P, Aluminum: impacts and disease. Environ. Res., 89; 2002, pp. 101–115.
[23]. Alessandra S, Antonio L, Matteo F, Giorgio S, Rossella B, Rita R, Luigi FR, Effects of aluminium sulphate in the mouse liver: Similarities to the aging process. Experimental Gerontology; 2008, Vol.43, Issue 4; Pp330-338.
[24]. Klein GL, Lee TC, Mann PA, Miller NL, Alfrey AC, Effects of Aluminum on the Liver Following High-Dose Enteral Administration to Rats. Journal of Pediatric Gastroenterology & Nutrition; 1989, Volume 9, issue1.
[25]. Deloncle R, Huguet F, Fernandez B, Quellard N, Babin P, Guillard O, Ultrastructural study of rat hippocampus after chronic administration of aluminuml-glutamate:an acceleration of the aging process.Exp. Gerontol, 36; 2001, pp. 231–244.
[26]. Miu AC, Olteanu A, Miclea M, A behavioural and ultrastructural dissection of the interference of aluminium with aging. J. Alzheimers Dis., 6 ; 2004, pp. 315–328.
[27]. Stacchiotti A, Rodella LF, Ricci F, Rezzani R, Lavazza A, Bianchi R, Stress proteins expression in rat kidney and liver chronically exposed to aluminium sulphate. Histol. Histopathol., 21; 2006, pp. 131–140.
[28]. Gonzales M, Alvarez Mdel L, Pisani G, Bernal C, Roma M, Carrillo M, Involvement of oxidative stress in the impairment in biliary secretory function induced by intraperitoneal administration of aluminium to rats. Biol. Trace Elem. Res., 116; 2007, pp. 329–342.
[29]. Schmucker D, Hepatocyte fine-structure during maturation and senescence. J. Electron Microsc. Tech., 14; 1990, pp. 106–125.
[30]. Kmiec Z, Cooperation of liver cells in health and disease. Adv. Anat. Embryol. Cell Biol., 161; 2001, pp. 1–151.
[31]. Schmucker D, Age-related changes in liver structure and function: implications for disease? Exp.Gerontology, 40 ;2005, pp. 650–659.
[32]. Vollmar B, Pradarutti S, Richter S, Menger M, In vivo quantification of ageing changes in the rat liver from early juvenile to senescent life. Liver, 22; 2002, pp. 330–341.
[33]. Mc Lean A, Cogger V, Chong G, Ewarren A, Markus A, Dahlstrom J, Le Couter D, Age-related pseudocapillarization of the human liver. J. Pathol., 200; 2003, pp. 112–117.
[34]. Le Couter D, Cogger V, Markus A, Harvey P, Yin Z, Ansselin A, McLean A, Pseudocapillarization and associated energy limitation in the aged rat liver.Hepatology, 33; 2001, pp. 537–543.
[35]. Warren A, Bertolino P, Cogger V, Mc Lean A, Fraser R, Le Couter D, Hepatic pseudocapillarization in aged mice Exp. Gerontol., 40 ;2005, pp. 807–812.
[36]. Ito Y, Sorensen K, Bethea N, Svistounov D, Mc Cuskey M, Smedsrod B, Mc Cuskey R, Age-related changes in the hepatic microcirculation in mice. Exp. Gerontol., 42; 2007, pp. 789–797.