Journal of Anatomical Sciences

Email:anatomicaljournal@gmail.com

J Anat Sci 10 (2)

Cardiotoxicity Induced Lead Acetate: The Role of *Ficus Vogelii* Extract

[1]Uchewa OO, [2]Okornkwo SO, [1]Egwu JA, [2]Okoronkwo AC and [1]Chukwu AM

[1] Department of Anatomy, Faculty of Basic Medical Sciences, College of Medicine, Alex Ekwueme Federal University Ndufu- Alike, Ikwo (AE-FUNAI), Ebonyi State.

[2] Department of Anatomy, Faculty of Basic Medical Sciences, Ebonyi State University (EBSU), Abakaliki, Ebonyi State

Corresponding Author: Uchewa, OO.

ABSTRACT

The heart as it is one of the major organs that sustain the part of human body because the contractility of its muscles helps to supply blood that maintains them. To investigate the effects of lead acetate on the cardiac muscles and the potency of the extract of *Ficus vogelii* as a useful herb. The 48 Wistar rats used for this work were purchased and acclimatized for 7 days and were divided into 12 groups of 6 rats per group. Group A (Control group) received normal saline and water *ad libitum*. The animals were given lead acetate in a dose of 2mg/kg body weight. Group B was further divided into B1-B4 (aqueous extract groups). Group C also further regrouped into C1-C4 (ethanolic extract groups). Even though the heart is one of the hardest organ to be affected by toxicity, our result showed that lead acetate causes the following on the myocardial necrosis, oedema, optical empty spaces, fatty changes, hemorrhages, myocardial cell death, etc. The groups that received the extract show little effect of lead acetate on the myocardium, this could be as a result of the therapeutic potency of the herb. Ficus vogelii leave can be used as an herbal remedy in tackling myocardial toxicity. With this our little result we recommend the herb for use.

Keywords: Cardiotoxicity, Lead acetate, Extract, Role; Morbidity.

INTRODUCTION

Exposure to environmental toxicant such as lead and many other heavy metals have been implicated in the aggravation of some pathological processes.[1] The report of WHO.[2] stated that cardiovascular diseases have become one of the leading causes of morbidity and mortality. Lead is a constituent of many home products which humans are in need of. In view of the above, we may always be in contact with the products of lead and those products will always release lead to pollute the environment. Environmental lead is present everywhere and everyone has certain amount of it in their blood stream.[3,4,5] According to Pokras *et al*.,[6] and Ekanem *et al*.,[3]), lead presents one of the largest environmental problems because of the number of people being exposed. Wright *et al*., [7] conducted a surveyed on lead toxicity in Jos, Nigeria and they reported a mean blood lead concentration of 8.7 µg/dl with a range of 1-34 µg/dl were and about 34 % of the subjects had concentrations of 10 µg/dl or greater. Because lead cannot be degraded, it remains longer on the earth's crust to contaminate it and drinking water thereby exposing the populace both non human and human to its epidemiological impacts.[1,8,9]

Many researchers were able to find out that chronic exposure to lead is one of the major risk factor for the development of hypertension. [10,11,12] In recent years, researchers like Fiorim *et al* .,[13] and Simoes *et al*.,[14]; reported that even exposure to low level of lead for even a very short period of time also leads to increase in arterial pressure in animals. Death toll from cardiovascular diseases has increased sharply in the low and middle-income countries by 12.5% in 2005 to 2015. [15] This would have been due to the less attention paid to lead's contribution to cardiovascular mortality as a broader disregard of what all forms of pollution contribute to mortality. According to Den, [16] and Weinhold, [17]; these environmental pollution are preventable in all ramification which may lead to a reduced general effect of lead in the body including cardiovascular diseases. With the emergence of all these reports suggesting that there is a huge link between lead exposure and cardiovascular disease for over 100 years.[18]

It is still difficult for us to completely elucidate the contribution of lead to cardiovascular disease.[19] It is on this note that we decided to design a work that will look into the alterations caused on the histology of the myocardial. This is because anything that affects the muscles of the heart affects its functionality which will lead to impaired heart function.

MATERIALS AND METHODS

Ethical clearance: During this experiment, we respected and strictly observed the following councils directive on the use of experimental animals. They are; Directive 2010/63/Eu, 2010 of the European Parliament and the European Council as passed on 22

September, 2010 on the use and protection of experimental animals[20]; and The Organization of Economic Co-operation Development (OECD), Paris, Guideline for Testing of Chemical usage in Experiment.[21] These animals were fed with standard rat feed and allowed water *ad libitum*.[22,23] We also sort for and obtained the ethical clearance from the Faculty of Basic Medical Sciences University of Nigeria Enugu Campus.

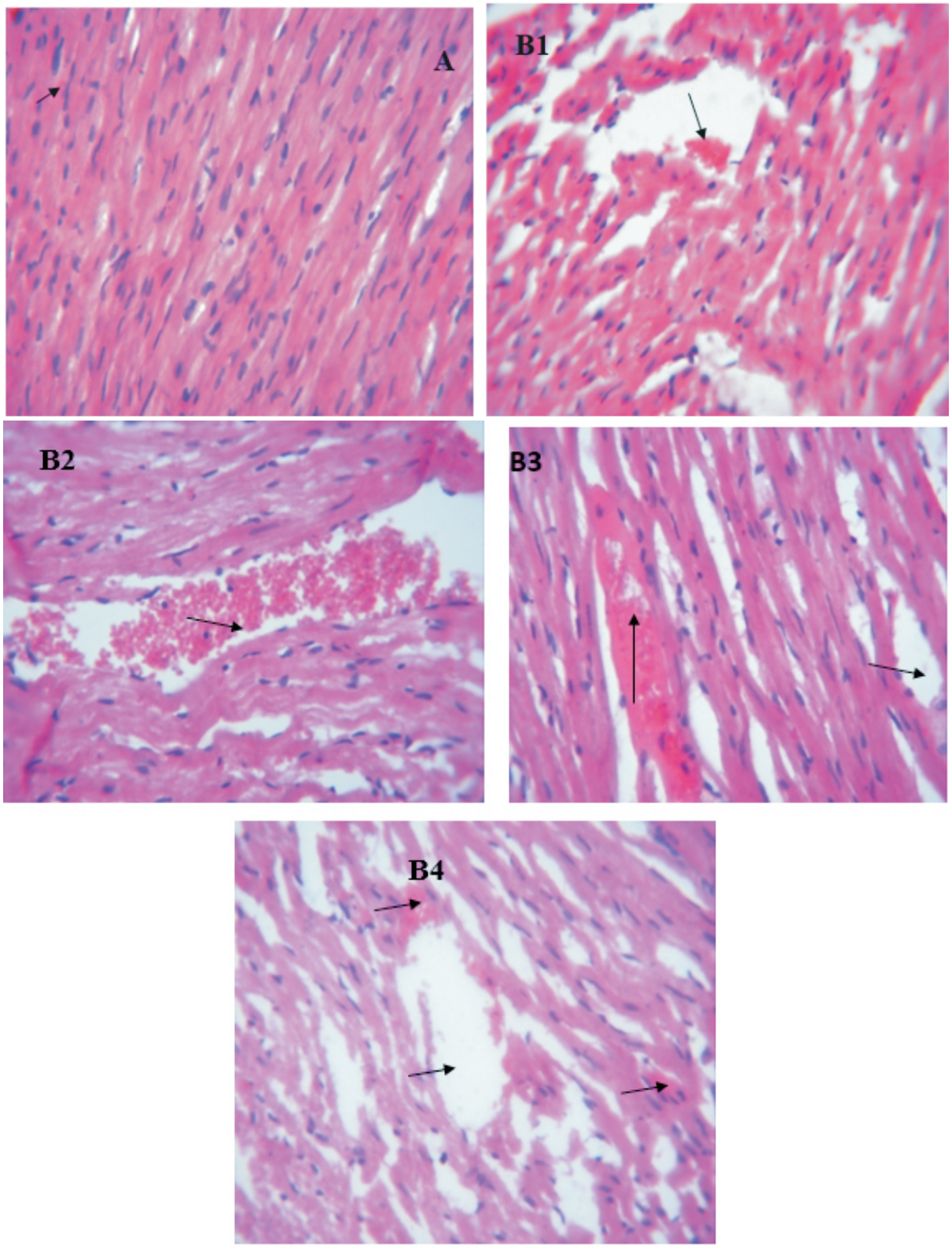
Experimental protocol: The forty eight (48) healthy adult Wistar rats used for this present research were acclimatized for 7 days and randomly assigned into 12 groups of six (6) rats each. Group A (Control) received normal saline and water *ad libitum*. The animals were given lead acetate in a dose of 2mg/kg body weight. Group B was further divided into B1-B4 (received the aqueous extract). Group C also further regrouped into C1-C4 (received ethanolic extract). They were made of both currative and protective groups. Group D was given only lead acetate of the same dosage. Group E was given aqueous extract while F received ethanolic. All the administrations were done orally using orogastric tube and it lasted for 28 days. [24]

Leaves collection and extraction: Fresh leaves of *F. vogelii* were collected from Enyibichiri Ndufu-Alike in Ikwo Local Government Area of Ebonyi State. The leaves were dried in ventilated room after they were washed. Thereafter, it was crushed into powder using electronic blender and passed through mesh sieve to get the fine powders. Five hundred grams (500g) of the powder was weighed using an electronic weighing balance and soaked in 1200mL of water. The same quantity was also soaked in ethanol. The mixture was agitated using an electric blender to enhance proper mixing of the solvent with the powder and then poured into air-tight plastic containers. The container with the mixture was kept in a refrigerator for 48hours.[25] The mixtures were filtered first with cheese cloth and then with Whiteman No 1 filter paper (24cm). The filtrates were separated and concentrated in vacuum using Rotary Evaporator to 10% of their original volumes at 37^{o}C - 40^{o}C. These were concentrated using a water bath until a sticky paste was gotten. The extracts were stored in a refrigerator until it is required for use.

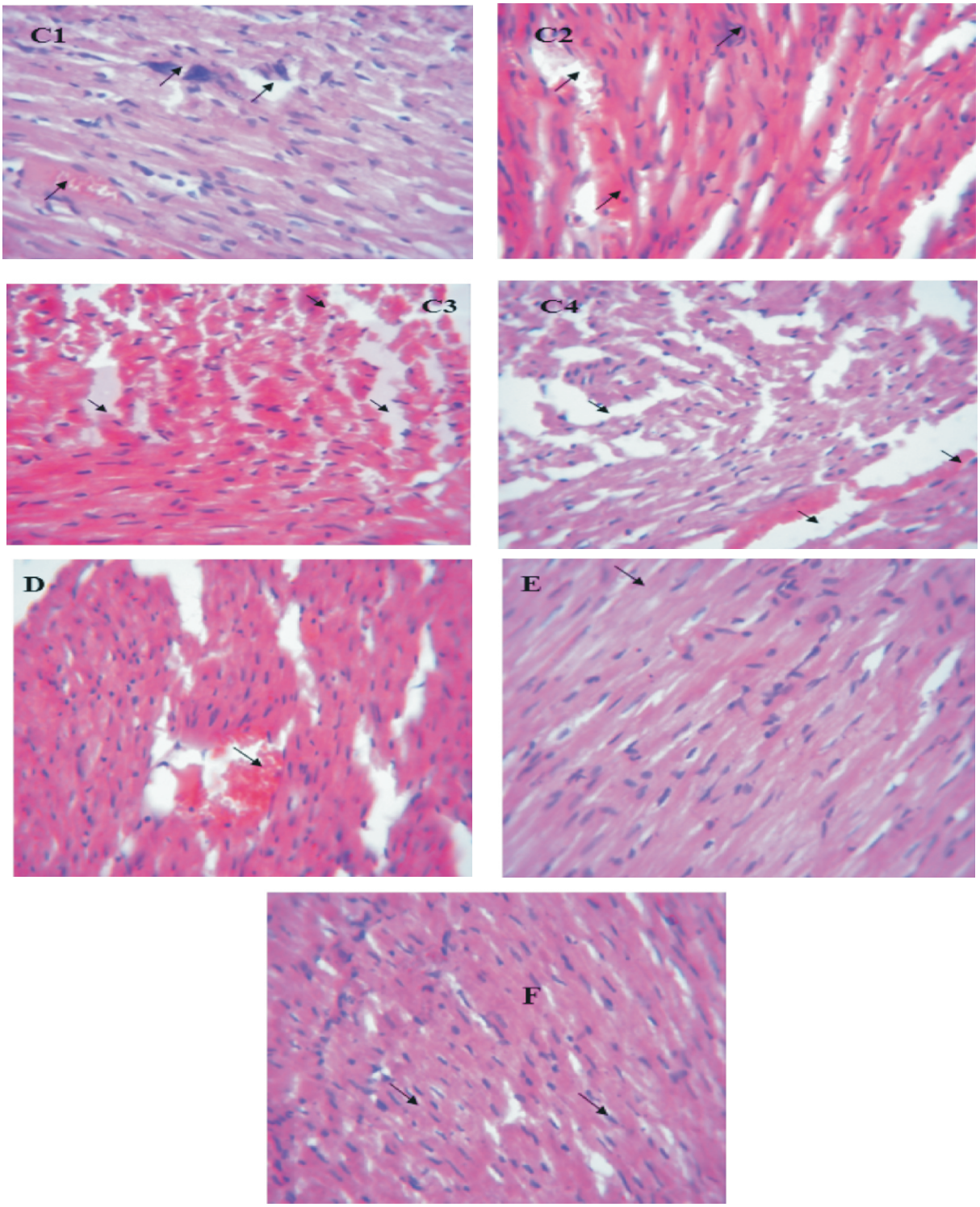
Histological Study: At the end of the experiment, the rats were starved for 24 hours and anaesthetized and then decapitated. [26] The animals were dissected and the heart was removed and quickly fixed in 10 % formalin for routine histological procedures.

RESULTS

Lead as a metal has been implicated in so many ways and its effects on exposed organs varies depending on the extent of exposure. To the animal as a whole, it could result to gain/loss of body weight [27]. The tissues were studied under the light microscope to ascertain the level of damage or alterations inflicted in the histoarchitecture of the myocardium. The study revealed that the myocardial was affected at various points and degrees even though the heart is one of the most difficult and last organs to be affected by toxicity. [19] As presented below the effects of lead in the myocardial include necrosis, oedema, optical empty spaces, fatty changes, hemorrhages, myocardial cell death, etc.



Photomicrographs of the heart Negative control group with normal muscle fibres and cytoplasm. The entire group B's received lead acetate and treated with aqueous extract ranging from 100 to 300ml/kg. Fig.1 (A): Normal histological features such as myocardial, vessels, etc. Fig. 2: (B1) Necrosis, Oedema. Fig. 3: (B2) oedema, hemorrhage. Fig. 4: (B3) hemorrhages, myocardial cell death Fig.5: (B4) Necrosis, Optical empty spaces, fatty changes



Photomicrograph of the heart of the entire group C's received lead acetate and treated with ethanolic extract ranging from 100 to 300ml/kg. Fig.6: (C1) Necrosis, Oedema. Fig.8: (C2) Oedema, haemorrhage. Fig.9: (C3) haemorrhages, myocardial cell death. Fig.10: (C4) Reduced, Optical empty spaces, fatty changes. Fig.11: (D) lead acetate group shows myocardial degeneration, Cell death, necrosis, oedema and haemorrhage. Fig.12: (E) received only aqueous extract and shows healthy cytoplasm, myofibrils and nucleus. Fig.13: (F) received only ethanolic extract and shows cytoplasm, myofibrils and nucleus

DISCUSSION

The heart is the most difficult organ is the body to be affected by toxicity of any type. It is also still under investigation the mechanisms that protect the heart muscles from being destroyed by toxicity. Studies carried out by various researchers have shown that lead is able to induce hypertension and arteriosclerosis in animals at various level of toxicity [28,29,30,31]. The mechanism of induction that leads to arteriosclerosis is still under investigation by researchers even till date.

In this experiment, the cardiac muscles of the negative control group is intact without any damage while the positive control showed signs of edema, necrosis and vessel constriction. This constriction is a sign of hypertension. It has been discovered that both acute and chronic lead poisoning has much contributions in vascular and cardiac damage and other deleterious effects such as cardiovascular illnesses and hypertension [19, 32]. According to ATSDR, [33] report, exposure to low level of any form of lead has been implicated in hypertension in both humans and animals and this research shows a sign of it in the sense that there were signs of vessel dilation in the heart. The little signs of edema recorded in this work could be a sign of a more deleterious heart disease such as congestive heart failure. This is a chronic condition in which the heart does not pump blood normally as it should and it is normally caused but not limited to narrowing of the artery. In this research we discovered that major cardiac vessels were affected which may lead to Cerebro-vascular accidents, peripheral vascular disease and ischemic coronary heart disease as a major disorders that may be accompany toxicity of the heart. This agrees with the report of Assi *et al*., [32] and Navas-Acien *et al*., [19]. The necrosis that is seen in the muscles of the heart in this work could be an indication that lead toxicity may be responsible for heart failure because the necrotized muscle does not have any power to pump blood. With the indications of vascular constriction as seen in the figures above, the relationship of hypertension and lead exposure is becoming clearer that lead toxicity may be implicated in hypertension. The above disagrees with Navas-Acien *et al*.,[19] when they reported that cardiovascular outcomes cases of toxicity of lead are only applied. Our result is totally in agreement with the experiment conducted by Vaziri and Sica, [34] when they recently studied the effects of lead exposure cardiovascular system. Our results also have a very strong correlation with the result of Kilikdar *et al*.,[35] which showed that the lead acetate administered in the rats caused heart damage.

REFERENCES

1. Fioresi M, Simo˜ es MR, Furieri LB, Broseghini-Filho GB, Vescovi MVA, *et al*., Chronic Lead Exposure Increases Blood Pressure and Myocardial Contractility in Rats. 2014; 9(5): e96900. doi:10.1371/journal.pone.0096900
2. World Health Organization (WHO). Cardiovascular Diseases; 2011 Available at http://www.who.int/cardiovasculardiseases/en/. Accessed 29 August, 2018.
3. Ekanem AU, Kwari HD, Garba SH, Salami HA. Effects of Lead Acetate on Spleen and Blood Parameters in Albino Rats. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS).* 20145; *14(3); 43-49 www.iosrjournals.org*
4. Hu, H., Shih, R., Rothenberg, S. and Schwartz, B. S. The epidemiology of lead toxicity in adults: Measuring dose and consideration of other methodologic issues. *Environmental Health Perspectives.* 2007; 115(3), 455-462.
5. Karri, S. K., Saper, R. B. and Kales, S. N. Lead encephalopathy due to traditional medicines. Current Drugs Safety. 2008; 3(1), 54-59.
6. Pokras MA and Kueeland MR. Lead poisoning: Using Transdisciplinary Approaches to Solve Ancient Problem. *EcoHealth*. 2008; 5(3), 379-385.
7. Wright NJ, Thacher TD, Pfitner, MA, Fischer PR and Pettifo, J and M. Causes of lead toxicity in a Nigerian city. *Archive of Disease in Childhood*. 2005; 90(3), 262-266.
8. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Lead. Atlanta GA: U.S. Department of Health and Human Services, Public Health Service. 2005.
9. Ministe´rio da sau´de, Brasil. Atenc¸a˜o a` sau´de dos trabalhadores expostos ao chumbo meta´lico. Sau´de do trabalhador. Protocolos de complexidade diferenciada. Normas e manuais te´cnicos. Brası´lia: Editora do Ministe´rio da Sau´de, 2006.
10. Vaziri ND, Ding Y, Ni Z, Gonick HC. Altered nitric oxide metabolism and increased oxygen free radical activity in lead-induced hypertension: Effect of lazaroid therapy. *Kidney Int.* 1997; 52: 1042–1046.
11. Farmand F, Ehdaie A, Roberts CK, Sindhu RK. Lead-induced dysregulation of superoxide dismutases, catalase, glutathione peroxidase, and guanylatecyclase. Environl Res. 2005; 98: 33–39.
12. Sharifi AM, Darabi R, Akbarloo N, Larijani B, Khoshbaten A. Investigation of circulatory and tissue ACE activity during development of lead-induced hypertension. *Toxicol Lett.* 2004; 153: 233–238.
13. Fiorim J, Ribeiro Ju´nior RF, Silveira EA, Padilha AS, Vescovi MV, *et al*. Low-level lead exposure increases systolic arterial pressure and endothelium derived vasodilator factors in rat aortas. *PLoS One*. 2011; 10.1371/journal.-pone.0017117.
14. Simo˜es MR, Ribeiro Ju´nior RF, Vescovi MV, de Jesus HC, Padilha AS, et al. Acute lead exposure increases arterial pressure: role of the Renin Angiotensin system. *PloS One* 2011; 10.1371/journal.pone.0018730.
15. GBD. Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and

occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; 388: 1659–724.
16. Den HE, Nawrot T, Staessen JA. The relationship between blood pressure and blood lead in NHANES III. *J Hum Hypertens.* 2006; 16: 563–568.
17. Weinhold B. Environmental cardiology: getting to the heart of the matter. *Environ Health Perspect*. 2004; 112:A880–A887.
18. Lorimer G. Saturnine gout and its distinguishing marks. BMJ. 1886; 2:163.
19. Navas-Acien A, Guallar E, Silbergeld EK, Rothenberg SJ. Lead exposure and cardiovascular disease–a systematic review. *Environ Health Perspect.* 2007; 115:472–482.
20. European Commission. Directive 2010/63/EU of the European Parliament and the Council on the Protection of Animals used for Scientific Purposes. Brussels, Belgium; European Commission. 2010.
21. OECD. The OECD Guideline for Testing of Chemical usage in Experiment. Organization of Economic Co-operation Development, Paris. 2010; 1-14.
22. Alarifi S, Aldahmash B, EL-Nagar D, Dkhil M. Effect of corn oil, flaxseed oil and black seed oil on lead acetate-induced hepatic tissue damage: A histological study. *J. med. Pl. Res.* 2012; 6: 4128-4134.
23. EL-Nager D and Aldahmash B. Effect of corn oil, flaxseed oil and black seed oil on testicular damage induced by lead acetate in albino mice: A histological study. *Pakistan J. Zool*. 2013; 45:1083-1089.
24. Jin Xu, Lian L, Chen Wu, Wang X, Wen Fu, Xu J. Lead induces oxidative stress, DNA damage and alteration of p53, Bax and Bcl-2 expressions in mice. *Food and Chemical Toxicology.* 2008; 46:5, 1488–94.
25. Sasidharan S, Chen Y, Saravanan D, Sundram KM, Yoga LL. Extraction, Isolation and Characterization of Bioactive Compounds from Plants' Extracts. *Afr J Tradit Complement Altern Med.* 2011; 8(1):1-10.
26. Schoenwolf GC, Bleyl SB, Brauer PR, Francis-west PH and Philipa H. Larsen's Human Embryology. New York; Endinburgh: Churchill Livingstone, Edition 5th, 2015; Chapter 16.
27. Ezugworie JO and Uchewa OO. Efficient use of traditional medicine to detoxify upper reproductive organs toxicity that may lead to infertility. *Int J Pharm Sci & Res.* 2019; 10(1): 347-55. *doi: 10.13040/IJPSR.0975-8232.10(1).347-55.*
28. Martin D, Glass TA, Bandeen-Roche K, Todd AC, Shi W, Schwartz BS. Association of blood lead and tibia lead with blood pressure and hypertension in a community sample of older adults. *Am J Epidemiol*. 2006; 163(5):467–478.
29. Prozialeck WC, Edwards JR, Nebert DW, Woods JM, Barchowsky A, Atchison WD. The vascular system as a target of metal toxicity. *Toxicol Sci*. 2008; 102(2):207–18.
30. Bagchi D, Preuss HG. Effects of acute and chronic oval exposure of lead on blood pressure and bone mineral density in rats. *J Inorg Biochem*. 2005; 99(5):1155–64.
31. Zeller I, Knoflach M, Seubert A, Kreutmayer SB, Stelzmüller ME, Wallnoefer E, et al. Lead contributes to arterial intimal hyperplasia through nuclear factor erythroid 2-related factor-mediated endothelial interleukin 8 synthesis and subsequent invasion of smooth muscle cells. *Arterioscler Thromb Vasc Biol*. 2010; 30(9):1733–1740.
32. Assi MA, Hezmee MNM, Haron AW, Sabri MY, Rajion MA. The detrimental effects of lead on human and animal health, *Veterinary World, 2016; 9*(6): 660-671.
33. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for lead. (Draft for Public Comment) Agency for Toxic Substances and Disease Registry, Public Health Service, United State Department of Health and Human Services, Atlanta, GA. 2005; p43-59.
34. Vaziri, N.D. and Sica, D.A. Lead-induced hypertension: Role of oxidative stress. *Curr. Hyper. Rep. J. 2004;* 6: 314-320.
35. Kilikdar, D., Mukherjee, D., Dutta, M., Ghosh, A.K., Rudra, S., Chandra, A.M. and Bandyopadhyay, D. Protective effect of aqueous garlic extract against lead-induced cardiac injury in rats. *J. Cell Tissue Res. 2013;* 13(3): 3817.
36. Baranowska-Bosiacka, I., Gutowska, I., Rybicka, M., Nowacki, P. and Chlubek, D. Neurotoxicity of lead. Hypothetical molecular mechanisms of synaptic function disorders. *Neurol. Neurochir. Pol. J. 2012;* 46(6): 569-578.
37. Carmignani M, Boscolo P, Poma A, Volpe AR . Kininergic system and arterial hypertension following chronic exposure to inorganic lead. *Immunopharmacology.* 1999; 44: 105–110.