International Journal of Public Health, Pharmacy and Pharmacology, 9 (2), 10-18, 2024
Print ISSN: (Print) ISSN 2516-0400
Online ISSN: (Online) ISSN 2516-0419
Website: https://www.eajournals.org/
Publication of the European Centre for Research Training and Development -UK

Kidney-Induced Injury from Native Herbal Drugs: A Case Study of Certain Herbs Used in the Management of Infertility in Calabar, Nigeria

Victor Odey Ogar[1], Yemiode Bernard Itam[2]
[1]Department of Biochemistry, Faculty of Physical Science, University of Cross River State, P.M.B 1123, Calabar, Nigeria
[2]Department of Biochemistry, University of Calabar, Calabar, Cross River State, Nigeria.

doi: https://doi.org/10.37745/ijphpp.15/vol9n21018 Published March 25, 2024

Citation: Ogar V.O.and Itam Y.B. (2024) Kidney-induced Injury from Native Herbal Drugs: A Case Study of Certain Herbs Used in The Management of Infertility in Calabar, Nigeria, International Journal of Public Health, Pharmacy and Pharmacology, 9 (2), 10-18

ABSTRACT: *Infertility is a global concern among married couples. Severally treatment approaches have been used over the years to proffer solution. This research aims at investigating the kidney–induced injury from native herbal drugs-case study of certain herbs used in the management of infertility in Calabar. A total of 18 Wistar rats weighing 150 - 250 grams were separated into 3 groups of 6 rats each and 2 groups were administered with 200 mg/kg each of ethanol and n-hexane combined extracts for 7 days. Results showed that ethanol and n-hexane extracts groups significantly affected the renal tissues of the experimental animals. While in control group, a section of the kidney showed normal findings of glomeruli and renal tubules. The ethanol extract group showed swollen glomeruli with deeply stained mesangial cells while the n-hexane extract group showed the glomeruli had a hypocellular mesangium causing a peri-arteriolar mesangial haemorrhage. Ethanol extract group and n-hexane extract group showed injury to the renal tissues on histology.*

KEYWORDS: Kidney injury, Herbal extracts, Infertility.

INTRODUCTION

In recent years, the medical community has increasingly recognized the potentials of natural medicines to cause harm to various organs including the kidney [1]. Although some plants may have medicinal values, sometimes the medicinal preparation inflicts side effect [2]. Cell injury results from certain herbal products associated with complications which range from physical violence to subtle cellular abnormalities such as mutation, reduced or impaired enzyme activity and cell injury. Generally, cell injury can arise from various pathologies such as hypoxia, ischemia, chemical agents and drugs, physical agents; trauma, heat and infections, immunological reactions, genetic defects, Hemoglobin S in SS disease, inborn errors of metabolism, and nutritional defects

[3,4,5]. Renal cell injury can be due to dehydration-induced concentration or extensive exposure to crystal-forming substances resulting in crystallization of solutes in renal tubules [6]. These deposited crystals then contribute to kidney injury by inducing direct and indirect cytotoxicity as well as by setting up an auto-amplification loop of necro-inflammation [7,8,9]. Several case reports in Europe, Asia, China and Nigeria indicate increasing incidence of herbal medicine-induced nephrotoxicity [10,11]. Kidney-induced injury from the use of herbal remedies is about 30-33% of all cases of acute kidney failure in Africa [2,12,14]. Infertility may be a complication of other diseases such as cardiovascular disease, cancer and metabolic dysfunction [15,20] . Although various researches have been carried on infertility, the safety of these herbal remedies is still doubtful even though effectiveness of some have been validated through research and clinical studies [21].

MATERIALS AND METHODS

Collection of plant material

Fresh leaves of *Ipomea alba* (ufuk ikot), *Emilia sonchifolia* (awak mmong), *Hygrophylia polysperma* (mmeme), *Eremomastax polysperma* (edem ididout), *Dissotis rotundifolia* Triana (eyen ndang), *Eremomastax speciose* (ikpo ikong ukebe), *Piper umbellatum* (mweweb), as well as seeds of *Piper guinenses* (mfri etinkeni), were obtained from Gabu market in Yala Local Government Area of Cross River State, Nigeria. The plant was authenticated by a Botanist in the Department of Botany, University of Calabar. The leaves were air dried at room temperature, in Biochemistry Laboratory, Department of biochemistry, University of Calabar. After which the leaves were pulverized with an electric blender into powder forms, weighed and extracted according to the method described in Extraction Technologies for Medicinal and Aromatic Plant page 23-24 using 200ml of ethanol and n-hexane respectively.

The pulverized plant samples, 100g each were placed in No1 Whiteman filter paper, folded and placed in chamber of the Soxhlet apparatus and extracted with 200ml of ethanol or n-hexane extraction solvent heated in a flask. The extracts were subsequently concentrated to about 10 percent of their original volumes, using a rotary evaporator at <400C and dried to a semi solid form in a water bath.

Preparation of plant extract

Equal weights (0.2 g) of all the ethanol extracts were measured into a mortar and dissolved with 4 ml mixture of Dimethyl sulfoxide (DMSO) water (0.2:3.8 v/v) using a pestle until a homogenized phase were obtained. Similarly, n-hexane extracts were prepared with 4 ml mixture of DMSO-water (0.2:3.8 v/v).

Experimental animals

Eighteen (18) Wistar rats of both sexes, weighing between 150 - 250g were obtained from the animal house of the department of Biochemistry, University of Calabar, Nigeria. The animals were allowed to acclimatize for 7 days in ventilated cages under 12 hours' light/dark cycle. The animals

were fed rat chow and allowed free access to water *ad libitum* throughout the period of the experiment. The rats were randomly grouped into 3 experimental groups of six (6) rats each. Group 2 rats were administered with a calculated doses of 200 mg/kg body weight combined plant extracts of ethanol. Group 3 rats were administered with a calculated doses of 200 mg/kg body weight combined plant extracts of n-hexane. While Group 1 the control group were similarly given water. All treatment lasted for seven days.

Collection of blood samples for biochemical analysis

At the end of 7 days, the rats were anaesthetized using ketamine, dissected and blood samples were collected through cardiac puncture using a 5ml syringe and needle into properly labeled sample bottles. The blood samples were allowed to stand for 10 minutes and centrifuged at 3500 rpm for 15 minutes and serum obtained transferred into new labeled sample bottles, for the determination of aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase according to the method described by Randox®.[33]

Statistical analysis

Data obtained from this study were analyzed by using SPSS (2.1), and mean compared presented as mean ± standard error of mean (Mean ± SEM).

RESULTS AND DISCUSSION

The ethanol and n-hexane groups significantly affected the renal tissues of the experimental animals. In control group, a section of the kidney showed normal findings of glomeruli and renal tubules. Ethanol extract group showed swollen glomeruli with deeply stained mesangial cells. N-hexane extract group showed the glomeruli had a hypocellular mesangium causing a peri-arteriolar mesangial haemorrhage. Ethanol and n-hexane extract groups and showed injury to the renal tissues on histology.

Histological changes

Histopathological determination of the integrity of the kidney showed microscopic images of kidney (x100) of control group (see plate 1). For this group, a section of the kidney showed normal histology of the renal tissues.

For the ethanol extract, microscopic image of kidney (x100) of experimental animals treated with 1.0 ml ethanol extract, showed the kidney with swollen glomeruli, reduced bowman space and a cellular mesangial matrix. The mesangial cells were deeply stained and there was peri-arteriolar haemorrhages. The interstitium was scanty and contained congested blood vessels. The renal tubules were closely packed and lined by swollen cells. These findings were suggestive of glomeruli injury (see plate 2).

For the n-hexane extract, microscopic image of kidney at higher magnification (x400) for experimental animals treated with 1.0ml n-hexane extract, showed kidney cells with glomeruli and

renal tubules. The glomeruli had a hypocellular mesangium with prominent bowman space. There was periarteriolar mesangial haemorrhages and the intervening interstitium was scanty with congested blood vessels. (See plate 3).

In recent times, herbal treatment for various diseases has taken a frontier in our environment. Because most herbal supplements are without regulation, the risk of abuse is a common occurrence with attendant ill effects. organ damage is one major manifestation of unregulated herbal treatment. Herbal drugs have been gaining grounds globally especially in resource –poor countries. Researches show that about 80% of the world population are involved in taking herbal based drugs for various health challenges. Many of the medicinal plants have their side effects [22]. Aristolochic acid is the most implicated substance associated with renal damage following herbal drugs ingestion [22]. This study focuses attention on the effect of various herbal plants on the renal tissues. It is known to cause nephritis, renal tubular defects and some renal malignancies [23, 24] .In this study, histological findings of the renal tissues following the administration of the plant extract showed various degrees of kidney injury which were more pronounced at higher magnification. This agrees with the findings of some other researchers [22, 25]. Adejumo et al reported a case of acute kidney injury following the use of herbal vaginal pessary in a 22 year old female client [26]. Potential toxicities of herbal drugs are unknown to many people. Herbal drugs are known to cause up to 11 to 38% of acute kidney injury in hospital setting [27, 28, and 29]. Other authors concluded that in Africa, acute renal failure arising from the use of herbal remedies account for 30-35% of all cases of acute kidney failure in Africa [30,31] Herbal drugs are associated with high mortality and morbity and these are common findings in our environment [32,34]. Renal tubules are involved in active transport and urinary concentration, and therefore the localized concentration of these toxins is high, leading to direct injury to tubular cells.

CONCLUSION

We conclude that though many herbal extracts are of medicinal value, however, caution should be taken if given for a long time, as this may result in acute injury of renal tissues. A thorough assessment of the kidney should be done before, during and prolonged therapy with herbal formulations and drugs.

Conflict of interest
None declared by the authors.

REFERENCES

1. Jhav C.K. Nephropathy associated with animal, plant and chemical toxins in the tropies. *Semm Nephrol*.2013; 23:49-65.

2. Shiv D.L,Kamlesh L. Plant used by the Bhat community for regulating fertility. *Journal of Ecological Botany* 1980; 34 (3)273-245.

3. Kadric S., Arije A, Salako B.L. Traditional herbal Preparation and acute renal failure in Southwest Nigeria. *Tropical Doctor* 1999; 29(4):244-2461.

4. Robbins and Cotran (editors.). *Intl J Pathologic Basis of Disease* [9th Edition].
5. Margaret A. Miller, James F. Zachary in Pathologic Basic of Vertinary disease [6th Edition] 2017.
6. Cynthia D. K, Thomas J. F., Micheal W.D. "Naturalhigh magnetic field laboratory.The Florida State University, Tallahassee Florida 32310.
7. Terlinsky A, Grochowski J, Geolyke K L, Strauch BS. Hefter L; Monohydrate calcium oxalate crystallauria in ethylene glycol poisoning. *N Engl J Med* 1980; 302:922.
8. Mulay SR, Linkrmann A, Anders HJ: Necro-inflammation in kidney disease. *J Am Sci Nephrol* 2016; 27:27-39.
9. Mulay SR, Kumar SV, Lech M, Desai J, Anders HJ. How kidney cell death induces renal necro inflammation "*Semin Nephrol* 2016; 36:162-173.
10. Mulay SR, Holderied A, Kumar SV, Anders HJ. Targeting inflammation in acute kidney injury. *Semin Nephrol* 2016; 36:17-30.
11. Ogar VO, Itam YB, Akataobi US, Ukam EE, Ogar EA. Effect of Ethanol and N-Hexane Combined Extracts of Selected Plants on Liver Enzymes in Normal Albino Rats. Trop J Phytochem Pharm. Sci. 2023; 2(4):114-116. http://www.doi.org/10.26538.

12. Luyckx VA, Ballatone R., Claeys M. "Herbal remedy associated acute renal failure secondary to cape aloes. *American Journal of Kidney Disease* .2002; 39.
13. Chijoke, A A, Olarewaju T.D, Adekoya O.S. Prevalence of acute renal failure due to exogenous nephrotoxin in Illorin". *Tropical Journal of Nephrology*.2007 ;(2) 43-48.
14. Bennett W. M and Porter B. A. Nephrotoxic acute renal failure due to common drugs "*The American Journal of* Physiology.2007 ;(2):44-48.
15. Zegers H, Schild F, Adamson GD, De Mouzon JO,Shihara R,Mansour K.N, Sullivan E, Vandeerpoel S. International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the WHO revised glossary of ART Technology, 2009 *Fertil Steril.* 2009; 92(5):1520-1524.
16. Mascarenhas MN, Cheung H, Mathers CD, Gretchen A. S. Measuring Infertility in populations: Constructing a standard definition for use with demographic and reproductive health surveys. *Popul Health Metr.* 2012; 10(1):17.
17. Speroff L., Fritz M A. Intl Clinical Gynecologic Endocrinology and Infertility. Philadelphia, PA: Lippincott Williams & Wilkins: 2005.
18. Solomon CG, Frank B, Andrea D, Janet E. R.,Edwards M.J, Walter C. W, Frank S, Joann E. M. Menstrual cycle irregularity and risk for future cardiovascular disease. *J Clin Endocrinol Metab* 2002; 87(5) 2013-2017.
19. Gertrud S. B, Robert H., Rosemary W, Deborah L. Race/ethnicity and other risk factors for gestational diabetes. *Am J Epidemol* 1992; 135(9): 965-995.

20. Louise A B, Michael L. B, Rodrigue l, Leo B. T, Rolland J. B, Georage D. W, Linda L,Robert N.H. Reproductive, menstrual, and medical risk factors for endometrial cancer: results from a case control study. *Am J Obstet Gynecol*. 1992; 167(5):1317-1325.

21. Halim S, Z, Abdullah N.R, Afzan A. I, Abdul Rashid B.A, Jantan Z.I. Study of acute toxicity of leaf extract *J. Med plants Res* 2011;5:1867-1872.

22. Maurya N.K. Nephrotoxic effect of Herbal medicine and supplements: Research and Reviews. *Journal of Toxicology* 2019:28 – 35.

23. Pitt JI, Miller JD. Concise history of mycotoxin Research. *J Agr. Food Chem*. 2016 65(33): 7021-7033.

24. Maharaj SVM.Limitation and Plausibility of the Pliocene Lignite Hypothesis in explaining the etiology of Balkan Endemic Nephropathy. *Int J Occup Environ Health* 2014; 20(1): 77-91.

25. Kholia S, Herreru SM, Cedriono M. Human liver stem cell-chemical extracellular vesicles present. Aristolochic acid-induced kidney fibrosis.*Front Immunol* 2018; 19(9):1639.

26. Adejumo OA, Akinbodewa AA, Ogunleye A. Agori of Abolerin OS. A case report of acute kidney injury following the use of herbal vaginal pessary. *Afr J Med Health Sci.* 2017; 16:66-67.

27. Kaderi S, Oguwesi A, Osinfade K, Akinkugbe OO. The cause and course of acute tubular necrosis in Nigeria. *Afri J. Med Sci.* 1992; 21:91-6.

28. Otieno CS, McLigeyo SO, Luta M. Acute renal failure following herbal remedies. *East Afri Med J* 1991; 68: 99-3-8.

29. Okunola OO, Ayodele OE, Adekanle AD. Acute kidney injury requiring hemodialysis in the tropics. *Saudi J Kidney Dis Transpl* 2012; 23(13):15-9.

30. Kadiri S. Arije A, Salako BL. Traditional herbal preparations and acute renal failure in South West Nigeria. *Tropical Doctor* 1999; 29(4): 244-246.

31. Chijioke A, Aderibizbe A, Olarewajia T. O, Adekoya Prevalence of acute renal failure due to exogenous nephrotoxin in Illorin. *Tropical Journal of Nephrology* 2007; 2:43-48.

32. Akpan EE, Erikpo UE. Acute Renal failure- induced by Chinese herbal medications in Nigeria. *Case Reports in Medicine* 2015. Article in 150204:3.

33. Reitman S, Frankel S, Amer J. A colorimetric method for the determination of serum glutamic oxaloacetic and glutamic pyruvate transaminases. Am J Clin. Pathol. 1957; 28(1): 56-63.

34. Odey VO and Igbang JO. Potential effect of dietary supplement on the histology of the liver and kidney of streptozotocin-induced diabetic wistar rats using *vernonia calvoana* (bitter leaf) and *solanum gilo* (scarlet eggplant) leaves. *J of contemporary research (jocres)* 2023; 2(2): 2814-2241.

International Journal of Public Health, Pharmacy and Pharmacology, 9 (2), 10-18, 2024
Print ISSN: (Print) ISSN 2516-0400
Online ISSN: (Online) ISSN 2516-0419
Website: https://www.eajournals.org/
Publication of the European Centre for Research Training and Development -UK

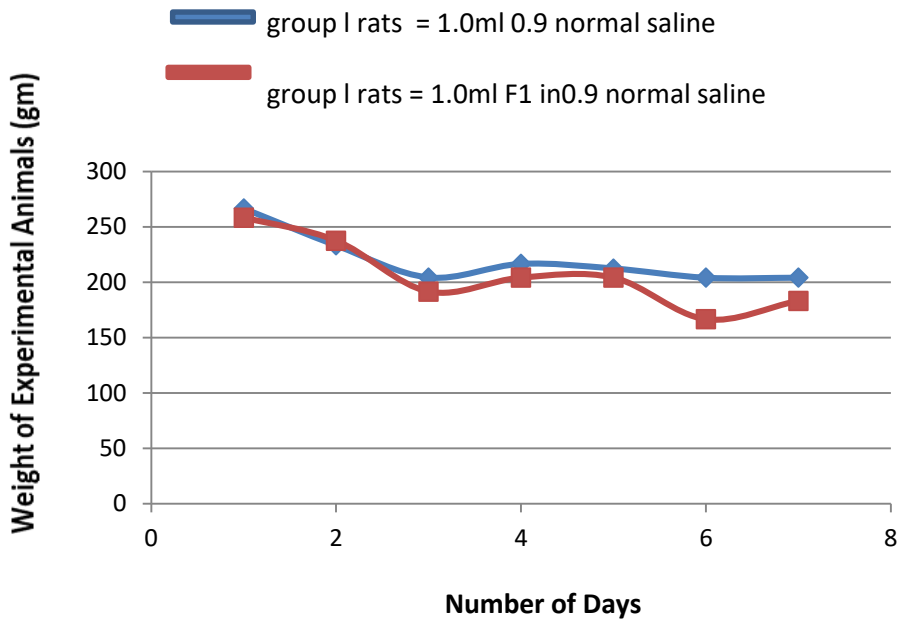

Figure 1: Effect of 200 mg/kg body weight ethanol extract on the body weight of experimental animals after a treatment period of 7 days.

International Journal of Public Health, Pharmacy and Pharmacology, 9 (2), 10-18, 2024
Print ISSN: (Print) ISSN 2516-0400
Online ISSN: (Online) ISSN 2516-0419
Website: https://www.eajournals.org/
Publication of the European Centre for Research Training and Development -UK

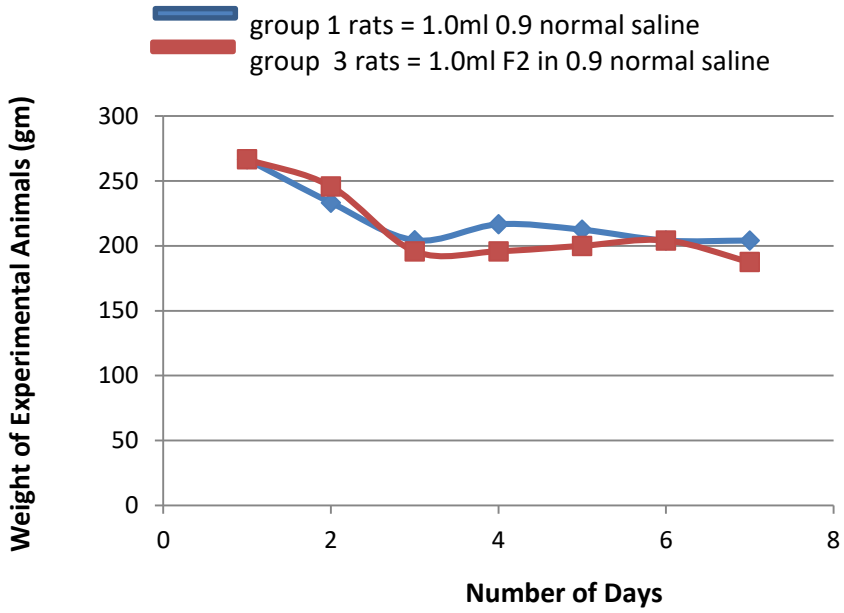

Figure 2: Effect of 200 mg/kg body weight n-hexane extract on the body weight of experimental animals after a treatment period of 7 days

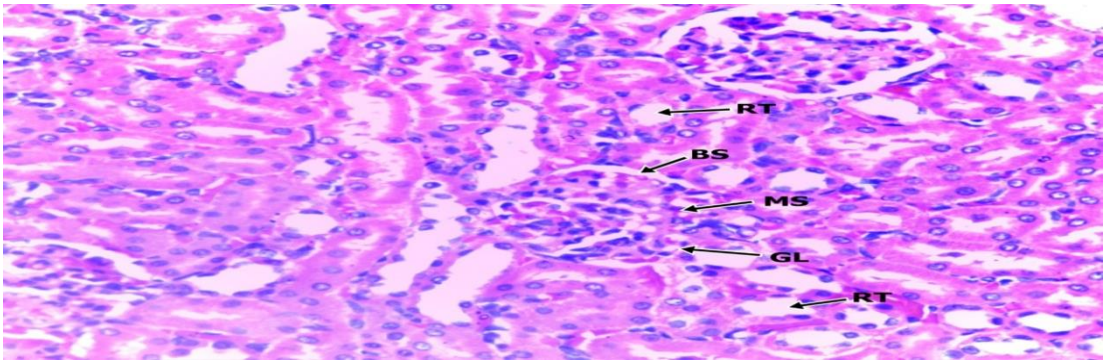

Plate 1: Microscopic image of kidney (x400) of experimental animals of normal control.

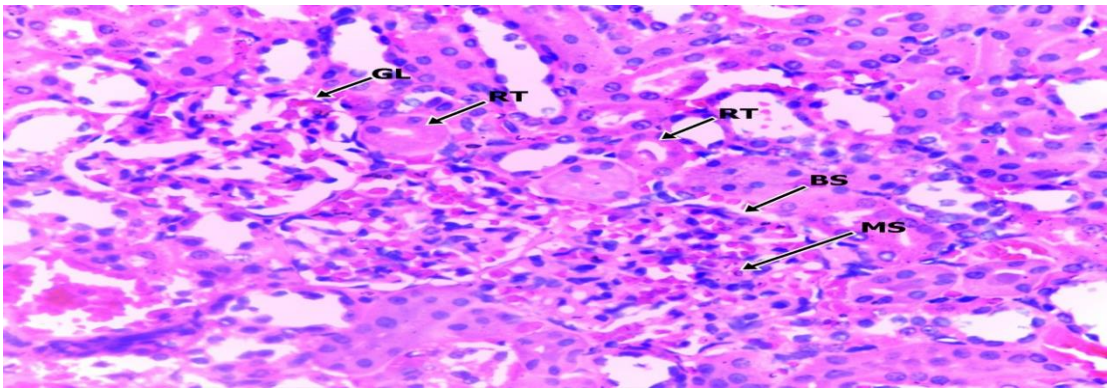

Plate 2: Microscopic image of kidney (x400) of experimental animals treated with 200 mg/body weight ethanol extract.

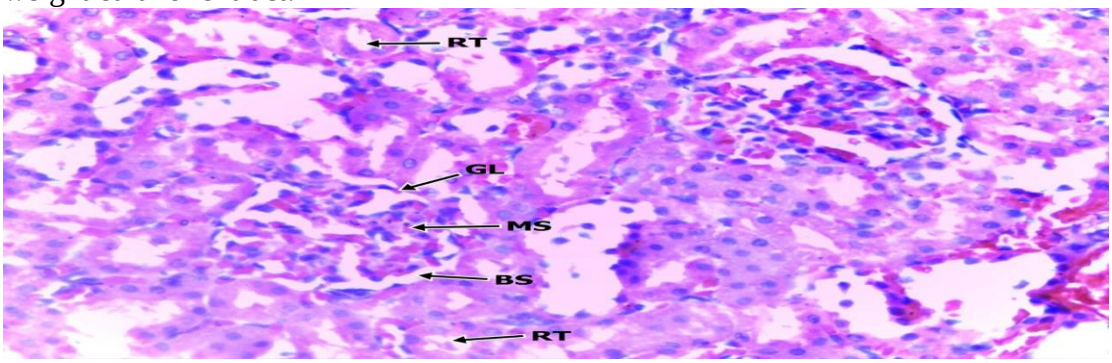

Plate 3: Microscopic image of kidney (x400) of experimental animals treated with 200 mg/body weight n-hexane.