Heavy Metals Analysis of Selected Analgesic Syrups in Ibadan, Nigeria

F. O. Nnaneme¹*

¹Department of Pure and Industrial Chemistry, Nnamdi Azikiwe University, Awka, Nigeria.

Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

Article Information

DOI: 10.9734/AJACR/2021/v8i330191

Editor(s):

(1) Dr. Angélica Machi Lazarin, State University of Maringá, Brazil

Reviewers:

(1) Raju Mondal, Central Sericultural Germplasm Resources Center (CSGRC), India.

(2) Jane M. Hightower, USA.

Complete Peer review History: http://www.sdiarticle4.com/review-history/68099

Received 22 February 2021
Accepted 28 April 2021
Published 03 May 2021

ABSTRACT

Some heavy metals have bio-importance as trace elements but the biotoxic effects of many of them in human biochemistry are of great concern. Hence, there is a need for proper understanding of mechanism involved, such as the concentrations and oxidation states, which make them harmful. This study determined the physical parameters and the mean concentrations of some heavy metals (Ni, Cd, Cr, Zn, Pb, Hg, and Ca) in some analgesic syrups. The heavy metals presence in the syrups were estimated by Atomic Absorption Spectroscopy after digestion. All analyses were repeated three times for each sample and the mean concentration of the heavy metals taken. The physical parameters showed that the syrups are of red colour, which had a clear solution with sweet tastes. They also gave different pH and density range values. The level of nickel in the samples ranges from 0.49mg/l to 4.12mg/l, cadmium concentration ranges from 1.1mg/l to 3.5mg/l and chromium ranges from 0.04mg/l to 0.49mg/l. The concentration of zinc ranged from 0.04mg/l to 0.67mg/l, lead ranged from -0.1mg/l to 0.7mg/l and mercury concentration ranges from 0.23mg/l to 0.91mg/l. Calcium concentration was not detected in the four samples studied. The concentrations of the studied metals were lower than the W.H.O standard limits, hence the studied syrups are safe for human consumption.

Keywords: Heavy metals; analgesic syrup; toxic effect; human health.

*Corresponding author: Email: felixnna22@gmail.com;
1. INTRODUCTION

Human exposure to heavy metals is primary through food and water intake [1]. Heavy metals are largely used in commercial and industrial applications, due to this, exposure can occur from indirect and direct paths. These exposures maybe associated with such processes as smelting, electroplating, welding, oil spillage and many other product manufacturing processes. Heavy metals are ubiquitous and resistant to natural degradation. Even though their concentration may vary from one location to another, they occur naturally in the ecosystem [2]. Although excessive levels can be damaging to living organisms, iron, cobalt, copper, manganese and zinc are required by humans at acceptable levels [3]. While other heavy metals such as mercury, plutonium and lead are toxic heavy metals that have no known vital or beneficial effects on organisms and their accumulation over time in the bodies of animals can cause deleterious effects [3].

Heavy metals are generally referred to as those metals which possess a specific density of more than 5 g/cm³ and adversely affect the environment and living organisms [4]. These metals are quintessential to maintain various biochemical and physiological functions in living organisms when in very low concentrations, however they become noxious when they exceed certain threshold concentrations. Although it is acknowledged that heavy metals have many adverse health effects and last for a long period of time, heavy metal exposure continues and is increasing in many parts of the world. Heavy metals are significant environmental pollutants and their toxicity is a problem of increasing significance for ecological, evolutionary, nutritional and environmental reasons [5-6]. Various sources of heavy metals include soil erosion, natural weathering of the earth’s crust, mining, industrial effluents, urban runoff, sewage discharge, insect or disease control agents applied to crops, and many others [7]. In general, the toxicity of heavy metal ions to mammalian systems is due to chemical reactivity of the ions with cellular structural proteins, enzymes and membrane system. The target organs of specific metal toxicities are usually those organs that accumulate the highest concentrations of the metal in vivo. This is often dependent on the route of exposure and the chemical compound of the heavy metal i.e. its valiancy state, volatility, lipid solubility etc. The target organs and clinical manifestations of chronic exposures to the metal are given in Table 1. Besides the general toxicities of metals, we are today also concerned with the potential carcinogenicity of metal compounds. Certain metals such as chromium and nickel have been linked with cancers in exposed human populations.

Metals have been shown to cause acute as well as chronic poisoning in man and other experimental animals. Harmful effects of individual metals are presented briefly below.

Exposure to metals can be external (e.g. through pollution, occupation, cosmetics, and handling of metallic items) or internal (e.g. through foods, dental restorations, orthopedic implants, and vaccines). Cigarette smoke contains many metals, such as mercury, cadmium, lead, arsenic, and nickel, and increasing evidence is linking it to autoimmune disorders [8].

It has been known for decades that exposure to mercury through skin-lightening ointments will, in some individuals, lead to the development of serious side effects, such as kidney disease [9], as well as neurological complications such as peripheral polyneuropathy [9]. Nickel is the most common sensitizer, [10]. In Swedish patients with chronic fatigue syndrome (CFS), the frequency of nickel allergy was around 40%, as diagnosed by LTT-MELISA [11].

Aluminum is a ubiquitous metal, widely occurring in the environment and used in many everyday objects, foods, and pharmaceuticals. Aluminum is a well-known adjuvant in vaccines, despite its neurotoxic properties [12]. As described by [13] adjuvants can promote ASIA in susceptible patients. Allergy to aluminum is rare, but has been described. Delayed-type hypersensitivity to aluminum and itching nodules were found in children exposed to aluminum-containing vaccines [14,15] described a patient who developed CFS after multiple vaccinations with aluminum-containing vaccines. A muscle biopsy confirmed the presence of aluminum-containing macrophages; the aluminum content in the patient’s urine was also increased.

Analgic syrups are group of drugs such as Paracetamol and Ibuprofen that reduces pain without inducing unconsciousness. Paracetamol N-(4-hydroxyphenylacetamide) is usually simply abbreviated as APAP, for N-acetyl Paraceminol often more commonly known by its alternative name acetaminophen, it is widely used for management of pain and fever in a
variety of patients including children, [16]. Ibuprofen, a 2-propionic acid derivative discovered by the research arm of the British Boots Group in the 1960s, is a peripherally acting analgesic with a potent anti-inflammatory action that works through a reversible and balanced COX-1/COX-2 inhibition. Ibuprofen exists as a racemic mixture of both R (−) and S (+) enantiomers, and its anti-inflammatory, analgesic and anti-platelet effects (determined by cyclooxygenase inhibition) are related to the S (+) enantiomer. By contrast R (−) ibuprofen is less active as a prostaglandin (PG) synthesis inhibitor but has shown some pharmacological properties relevant to the anti-inflammatory actions of ibuprofen (28). However, 50-60% of the R (−) - form of ibuprofen is metabolically converted to the S (+) form in the intestinal tract and liver after oral absorption [17]. Some oral pharmaceutical drugs, if stored in a favorable environment, can serve as nutrients source for microorganisms. Humidity and high amount of sugar in the oral- liquid drugs -in particular can support the microbial growth. Oral liquid drug formulations such as aqueous solutions, suspensions, emulsions and syrups used in pediatrics are at a more risk of microbial contamination during use due to sweetening agents, reconstitution methods, unsuitable storage and handling defects. Microbial contaminations may ultimately contribute to secondary bacterial infections in pediatric patients [18].

Heavy metal analysis of some selected soft drinks in Nigeria was studied by [19]. It revealed that 60% of the selected beverages mostly taken by children and young adults in Nigeria have either/both lead and arsenic levels above the recommended limits while 10% of the samples have both lead and cadmium concentrations above the limits. All sampled beverages had acceptable zinc, copper and iron concentration when compared with WHO limits.

Nickel in terrestrial biota: comprehensive review on contamination, toxicity, tolerance and its remediation approaches was done by [20]. From the result, Ni concentration was estimated up to 26 g kg⁻¹ in terrestrial and 0.2 mg L⁻¹ in aquatic resources. In case of vegetables and fruits, mean Ni content has been reported in the range of 0.08 – 0.26 and 0.03 – 0.16 g kg⁻¹. Considering Ni toxicity and its potential health hazards, there is an urgent need to find out the suitable remedial approaches.

Determination of selected heavy metal concentrations in an oil palm plantation soil was carried out by [21]. From the study, the soil from the oil palm plantation does not indicate serious pollution problem. The concentration of heavy metals in soil was mainly from natural sources such as windblown dust and derivative of rock and soil. However, the application of chemical fertilizer in the oil palm soil will increase the level of heavy metal, unless it is controlled. Cu concentration in soil samples was dominant and perhaps related to the application of chemical fertilizer. The amount of chemical fertilizers that are applied to the oil palm should be controlled to avoid soil toxicity.

A review on lead toxicity: health Hazards, influence on food chain, and sustainable remediation approaches was done by [22]. From the review, the source, bioaccumulation, and health hazards of Pb are due to industrial and agricultural activities. Translocation of Pb from soil to a crop system is a complex and species dependent phenomenon. The human consumptive plant species have shown different bioaccumulation, tolerance, and toxicity levels for lead. Based on the tolerance mechanism, different concentrations of Pb accumulate in the food chain and cause different magnitudes of human health hazards. To minimize these Pb based health risks, different remediation options are available for reducing the concentration of heavy metals in soil and the food chain.

Assessment of Heavy Metal Pollution in a Gold Mining Site in Southwestern Nigeria was done by [23]. From the study, the concentration levels of heavy of metals (Zn, As, Cd, Pb, Ni, Cr, and Cu) in the soil and plants samples from Ijana mining site were generally low and found to be within the World Health Organization (WHO) permissible levels. This could probably be due to the fact that most mining operations in the site are low scale and artisanal in operation unlike other sites where mechanized mining techniques could predispose release of more pollutants and tailings.

Bio-remediation approaches for alleviation of cadmium contamination in natural resources was carried out by [24]. The study showed that Cadmium (Cd) is a harmful heavy metal that can cause potent environmental and health hazards. Bioremediation of cadmium is an eco-friendly and sustainable cost effective technology. Cd removal under the contrasting environment needs more attention for addressing ecological
security. Transgenic species are promising in bio-removal of Cd and the technology could be exploited for optimum cd bioremediation. Nanotechnology coupled bioremediation can substantially enhance Cd bioremediation efficiency.

The present study was to determine the level of zinc, nickel, chromium, mercury, lead, calcium and cadmium found in some brands of analgesic syrups marketed in Ibadan, Oyo state, Nigeria. The study also helped to know if the various syrups are within W.H.O. standard limits for human consumption.

2. MATERIALS AND METHODS

2.1 Samples Collection

Five samples of analgesic syrups of five companies having different manufacturing dates were collected from various retail pharmacies in Ibadan, Oyo state, Nigeria and labeled with the code A, B, C, D, and E. The sample syrups were stored at conditions similar to those of pharmaceutical shops. Absorption Spectrophotometer (AAS) was used to determine the heavy metal contents of these analgesic syrups.

2.2 Physical Analysis of Sample

The color was assessed in each sample by visual examination, whereas the taste was evaluated by using the appropriate, relevant sense organs. The pH value was measured once by a Metrohm pH meter instrument (Switzerland) model (827pH Lab). The density measured by density instrument (Mettler Toledo, Japan) model (DA-100M).

2.3 Preparation of Sample

2.3.1 Digestion of sample

Two ml (2ml) of each sample was weighed into a 250ml beaker, 10ml mixture of nitric acid and hydrochloric acid in a ratio of 1:3 was added. The solution was then heated on hot plate in a fume cupboard until a brown dense fume was observed. The solution was allowed to cool after which 10ml of 30% hydrogen peroxide solution was added. The solution was then filtered into a 100ml volumetric flask and made up to the mark with distilled water.

2.3.2 Analysis of heavy metals

The concentration of the heavy metals like Cadmium (Cd), Lead(Pb), Zinc (Zn), Mercury (Hg), Calcium (Ca), Nickel (Ni), Chromium (Cr) in digested syrups were analyzed using Smart spectrophotometer.

3. RESULTS AND DISCUSSION

3.1 Physical Parameters of the Sample

In this study, the results showed that the analgesic syrup samples appearance were light red with a sweet taste, and are in agreement with [25]. Liquid preparations for oral use may contain suitable excipients such as stabilizing, flavoring and sweetening agents and coloring matter, authorized by the competent authority [26]. From the results of Table 2, the pH value results were within the acceptable range according to [26] standards.

The density results in the analgesic syrup samples were 1.149–1.184 g/ml. The density of a substance is the ratio of its mass to its volume at 20°C.

pH shows the impact of physiochemical interaction of the syrup or suspension as it impacts taste, color and quality of drug interaction in babies [27]. Density in relation to water shows the presence of particles from manufacturing process thus influences quality of syrup or suspension respectively [28].

3.2 Concentration of Heavy Metals in the Sample

The concentrations of all the metals studied in the five analgesic syrups were presented as mean of three replicate values in Table 3. The concentration of nickel in the samples ranges from 0.49mg/l to 4.12mg/l, cadmium concentration ranges from 1.1mg/l to 3.5mg/l and chromium ranged from 0.04mg/l to 0.49mg/l. The concentration of zinc ranges from 0.04mg/l to 0.67mg/l, lead concentration ranges from -0.1mg/l to 0.7mg/l and mercury ranges from 0.23mg/l to 0.91mg/l. The level of calcium is 62.0mg/l in Bonababe syrup and not detected in other syrups.
Table 1. Clinical aspects of chronic toxicities

| Metal     | Target Organs         | Primary Sources             | Clinical effects                                 |
|-----------|-----------------------|------------------------------|-------------------------------------------------|
| Arsenic   | Pulmonary Nervous     | Industrial Dust, Medicinal Uses, Polluted Water | Perforation of Nasal Septum, Respiratory Cancer, Peripheral Neuropathy; Dermatomes, Skin, Cancer |
|           | System, Skin          |                              |                                                 |
| Cadmium   | Renal, Pulmonary      | Industrial Fumes And Polluted Water And Food | Proteinuria, Osteomalacia, Aminoaciduria, Emphysema |
| Chromium  | Pulmonary             | Industrial Fumes And Polluted Food | Ulcer, Perforation of Nasal Septum, Respiratory Cancer |
| Manganese | Nervous System        | Industrial Fumes And Polluted Food | Central And Peripheral Neuropathies               |

Table 2. Physical parameters of the different brands of the analgesic syrups

| Code | Name of Sample       | Colour | Description       | Taste  | pH       | Density (g/mL) |
|------|----------------------|--------|-------------------|--------|----------|----------------|
| A    | Panadol syrup        | Red    | Clear Solution    | Sweet  | 4.62 – 4.70 | 1.18 – 184     |
| B    | Bonabe syrup         | Red    | Clear Solution    | Sweet  | 5.61 – 5.67 | 1.15 – 1.16    |
| C    | Paracetamol syrup    | Red    | Clear Solution    | Sweet  | 4.44 – 4.48 | 1.15 – 1.16    |
| D    | Ibuprofen suspension | Red    | Clear Solution    | Sweet  | 5.81 – 5.88 | 1.15 – 1.15    |
| E    | Rexifen suspension   | Red    | Clear Solution    | Sweet  | 5.71 – 5.92 | 1.14 – 1.15    |

Table 3. The mean concentration of heavy metals in five different analgesic syrups

| Code | Name of Sample       | Ni (mg/l) | Cd (mg/l) | Cr (mg/l) | Zn (mg/l) | Pb (mg/l) | Hg (mg/l) | Ca (mg/l) |
|------|----------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| A    | Panadol syrup        | 0.94      | 1.8       | 0.49      | 0.67      | -0.1      | 0.91      | ND        |
| B    | Bonabe syrup         | 0.49      | 1.1       | 0.04      | 0.04      | -0.2      | 0.55      | 62.0      |
| C    | Paracetamol syrup    | 4.12      | 1.3       | 0.24      | 0.15      | 0.7       | 0.23      | ND        |
| D    | Ibuprofen suspension | 0.60      | 3.5       | 0.18      | 0.15      | 0.3       | 0.36      | ND        |
| E    | Rexifen suspension   | 2.60      | 1.7       | 0.31      | 0.48      | 0.2       | 0.54      | ND        |
4. CONCLUSION

The heavy metal level determined was based on the digested syrup samples. Levels of Nickel and Cadmium were observed to be highest for the samples, while the level of Lead appears to be lowest in the samples. Calcium was not detected in four (4) of the samples. The physical analysis done also showed that all the syrups are red in colour, having a sweet taste and are of clear consistency. Thus, the selected analgesic syrups are very suitable for infant consumption.

ACKNOWLEDGEMENTS

The Author is thankful to Prof. B.A. Omotara of Department of Community Medicine, University of Maiduguri Teaching Hospital for his knowledgeable contributions.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

1. Orisakwe OE, Oragwu CI, Maduabuchi JUM, Nzegwu CN and Nduka JKC. Heavy metals, occurrence and toxicity for food and water. Africa Journal of Environmental Science and Technology. 2009;3(1):042-049.

2. Donkin SG, Ohison DL, and Teaf CM. Properties and effects of metals, in: Principles of Toxicology, Environmental Science and Technology. 2nd Edition. 2000;325-326.

3. Lane TW, Saito MA, George GN, Pickering IJ and Prince RC. A cadmium enzyme from a marine diatom, Nature. 2005;435(7038):42.

4. Khlifi R, Hamza A. Head and neck cancer due to heavy metal exposure via tobacco smoking and professional exposure: A review. Toxicol Appl Pharmac. 2010; 248:71–88.

5. Jarup L. Hazards of heavy metal contamination. Br Med Bull. 2003;68 (1):167–182.

6. Jaishankar M, Mathew BB, Shah MS, Gowda KRS. Biosorption of few heavy metal ions using agricultural wastes. Journal of Environment Pollution and Human Health. 2014;2(1):1–6.

7. Nagajyoti PC, Lee KD, Sreekanth TVM. Heavy metals, occurrence and toxicity for plants: A review. Environ Chem Lett. 2010;8(3):199–216.

8. Arnson Y, Shoenfeld, Y, and Amital, H. Effects of tobacco smoke on immunity, inflammation and autoimmunity. J Autoimmun. 2010;34(3):J258–65.

9. Adawe A, Oberg C. Skin-lightening practices and mercury exposure in the Somali community. Minn Med. 2013;96 (7):48–9.

10. Thyssen JP, Menné T. Metal allergy – a review on exposures, penetration,
genetics, prevalence, and clinical implications. Chem Res Toxicol. 2010;23 (2):309–18.
11. Schmidt, M., Raghavan, B., Müller, V., et al. Crucial role for human Toll-like receptor 4 in the development of contact allergy to nickel. Nat Immunol. 2010;11(9):814–19.
12. Shaw, C.A. and Tomljenovic, L. Aluminum in the central nervous system (CNS): toxicity in humans and animals, vaccine adjuvants, and autoimmunity. Immunol Res. 2013;56(2–3):304–16.
13. Shoenfeld Y, Agmon-Levin N. “ASIA” – Autoimmune/inflammatory syndrome induced by adjuvants. J Autoimmun. 2011 36(1):4-8.
14. Bergfors E, Trollfors B, Inerot, A. Unexpectedly high incidence of persistent itching nodules and delayed type hypersensitivity to aluminum in children after the use of adsorbed vaccines from a single manufacturer. Vaccine. 2003;22: 64–9.
15. Exley C, Swarbrick K, Gherardi RK, Authier FJ. Medical A role for the body burden of Aln vaccine-associated macrophagic myofascitis and chronic fatigue syndrome. Med Hypotheses. 2009;72:135–9.
16. Morais S, Costa FG, Pereira ML. Heavy metals and human health, in Environmental health emerging issues and practice (Oosthuizen J ed). 2012;227–246, InTech.
17. Oluseun PE, Abiodun A, Oyelola T, Babatunde I, Ologundudu T. Paracetamol content in tablets and syrups of some common brands in Nigeria. An Inter J Sci Manag. 2012;1:1-3.
18. Ogbulie N, Ibe J, Nguma C. The microbial associates of unexpired and expired pediatric syrups. Nig J Microbiol. 2009;23:1817 1822.
19. Ogunlana OO, Ogunlana OE, Akinsanya AE, Ologbenla OO. Heavy metal analysis of selected soft drinks in Nigeria. Journal of Global Biosciences. 2015;4(2):1335–1338. ISSN: 2320-1355.
20. Amit K, Cabral-Pinto MMS, Ashish KC, Aftab AS, Gangavarapu S, Raju M, et al. Nickel in terrestrial biota: comprehensive review on contamination, toxicity, tolerance and its remediation approaches; 2020. Available:www.elsevier.com/locate/chemosphere.
21. Wan Noni Afida Ab Manan, FazrulRazmanSulaiman, Rubaiyah Alias and RusdinLaiman. Determination of selected heavy metal concentrations in an oil palm plantation soil. Journal of Physical Science. 2018;29(Supp. 3):63–70.
22. Amit K, Cabral-Pinto MMS, Ashish KC, Aftab AS, Gangavarapu S, Raju M, et al. Lead toxicity: health hazards, influence on food chain and sustainable remediation approaches. International Journal of Environmental Research and Public Health. 2020;17,2179.
23. Assessment of Heavy Metal Pollution in a Gold Mining Site in Southwestern Nigeria. Journal Scientific and Technical Research. 2019;5(8). ISSN: 2574-124.
24. Amit K, Gangavarapu S, Raju M, Cabral-Pinto MMS, Aftab AS, Dharmendra KJ, et al. Bio-remediation approaches for alleviation of cadmium contamination in natural resources; 2020. Available:www.elsevier.com/locate/chemosphere.
25. World Health Organization, Guidelines for drinking-water quality [electronic resource]: Incorporating 1st and 2nd addenda, Recommendations, Third editions. 2008;1. Available:http://www.who.int/water-sanitation-health/dwq/fulltext.pdf.
26. United States Pharmacopoeia (USP), 30-NF/25, Monograph: Paracetamol oral solution. Antimicrobial effectiveness testing, microbiological examination of non-sterile products, acceptance criteria for pharmaceutical preparations and substances for pharmaceutical use and spectrophotometry and light-scattering. The United States Pharmacopeial Convention: Rockville. 2007;30(25):172
27. Omokpia DO, Nduka JK, Omokpia PL and Omokpia ECO. Ionic composition of rainwater from different sampling surfaces across selected locations in Rivers State, Nigeria. World Sci News. 2020;150:132-147.
28. Nduka JK, Kelle HI and Ogoko EC. Hazards and risk assessment of heavy metals from consumption of locally manufactured painkiller drugs in Nigeria. Toxicol Reports. 2020;7:1066–1074.
29. Omokpia DO and Omokpia PL. Health and exposure risk assessment of heavy metals in rainwater samples from selected locations in Rivers state, Nigeria. Physical Sci. Reviews. 2020;1-14.
30. Ekeanyanwu RC, Njoku JO, Nwodu PU and Njokuobi AE. Analysis of some selected toxic heavy metals in some Branded Nigerian herbal product, Int. J. Appl. Pharm. Sci. Res. 2013;3(4):88–91. Available: https://doi.org/7324/japs.2013.3416.

© 2021 Nnaneme; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/68099