Heavy Metals Analysis of Selected Analgesic Syrups in Ibadan, Nigeria

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Author's contribution

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

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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.

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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 mammals 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 valiency 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.

Anaesthetic syrups are group of drugs such as Paracetamol and Ibuprofen that reduces pain without inducing unconsciousness. Paracetamol N-(4-hydroxyphenylaceticamide) is usually simply abbreviated as APAP, for N-acetyl Paraminophenol often more commonly known by its alternative name acetaminophen, it is widely used for management of pain and fever in a...
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 the 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>
<thead>
<tr>
<th>Metal</th>
<th>Target Organs</th>
<th>Primary Sources</th>
<th>Clinical effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic</td>
<td>Pulmonary Nervous System, Skin</td>
<td>Industrial Dusts, Medicinal Uses Of Polluted Water</td>
<td>Perforation of Nasal Septum, Respiratory Cancer, Peripheral Neuropathy: Dermatomes, Skin, Cancer</td>
</tr>
<tr>
<td>Cadmium</td>
<td>Renal, Pulmonary Skeletal</td>
<td>Industrial Fumes And Polluted Water And Food Dust And</td>
<td>Proteinuria, Glucosuria, Osteomalacia, Aminoaciduria, Emphysemia</td>
</tr>
<tr>
<td>Chromium</td>
<td>Pulmonary</td>
<td>Industrial Fumes And Polluted Food Dust And</td>
<td>Ulcer, Perforation of Nasal Septum, Respiratory Cancer</td>
</tr>
<tr>
<td>Manganese</td>
<td>Nervous System</td>
<td>Industrial Fumes Dust And</td>
<td>Central And Peripheral Neuropathies</td>
</tr>
</tbody>
</table>

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

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

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

<table>
<thead>
<tr>
<th>Code</th>
<th>Name of Sample</th>
<th>Ni (mg/l)</th>
<th>Cd (mg/l)</th>
<th>Cr (mg/l)</th>
<th>Zn (mg/l)</th>
<th>Pb (mg/l)</th>
<th>Hg (mg/l)</th>
<th>Ca (mg/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Panadol syrup</td>
<td>0.94</td>
<td>1.8</td>
<td>0.49</td>
<td>0.67</td>
<td>-0.1</td>
<td>0.91</td>
<td>ND</td>
</tr>
<tr>
<td>B</td>
<td>Bonabe syrup</td>
<td>0.49</td>
<td>1.1</td>
<td>0.04</td>
<td>0.04</td>
<td>-0.2</td>
<td>0.55</td>
<td>62.0</td>
</tr>
<tr>
<td>C</td>
<td>Paracetamol syrup</td>
<td>4.12</td>
<td>1.3</td>
<td>0.24</td>
<td>0.15</td>
<td>0.7</td>
<td>0.23</td>
<td>ND</td>
</tr>
<tr>
<td>D</td>
<td>Ibuprofen suspension</td>
<td>0.60</td>
<td>3.5</td>
<td>0.18</td>
<td>0.15</td>
<td>0.3</td>
<td>0.36</td>
<td>ND</td>
</tr>
<tr>
<td>E</td>
<td>Rexifen suspension</td>
<td>2.60</td>
<td>1.7</td>
<td>0.31</td>
<td>0.48</td>
<td>0.2</td>
<td>0.54</td>
<td>ND</td>
</tr>
</tbody>
</table>
Bonabe Syrup has the lowest concentration of nickel while the concentration of nickel in Paracetamol syrup is higher. Also, cadmium concentration is very high in Ibuprofen suspension and lowest in Bonababe syrup. Chromium concentrations is higher in Panadol syrup and lower in Bonababe syrup as well as zinc concentrations is higher in Panadol syrup and also lower in Bonababe syrup. Lead concentration is negative in Bonababe syrup and Panadol syrup which means lead is very harmful and the concentration of mercury is higher in Panadol syrup and lower in Paracetamol syrup. Calcium was not detected in Rexifen suspension, Panadol syrup, Ibuprofen suspension and Paracetamol. Lead and cadmium present in water or other syrups beyond acceptable limit can accumulate thereby progressing from cute to chronic intoxication with serious health issues. The concentrations of the studied metals were lower than the WHO standard limits. Hence the studied syrups are safe for human consumption.

Metals are important for drug interaction in the body [29] and thus has great influence in drug assimilation and adsorption accordingly. As seen in Table 3, The cumulative influence of Ni, Cd, Cr, Zn, Pb, Hg and Ca concentration shows that there is no health risk but consumption of these syrups over a period has detrimental impact to human health via bioaccumulation and increased biological toxicity in bodily organs and tissues leading to carcinogenic and non-carcinogenic illness. These includes blood disease, skeletal defect, respiratory effect, Alveolar congestion, gastrointestinal cramps and vomiting, neurological disorder and brain damage [30].

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 solution. Heavy metals have a deleterious effect on human beings, Lead Pb, being a serious cumulative body poison enters into the body system through air, water and food. Also, the pH values fall within the specifications for a product to be passed. Therefore, the selected analgesic syrups are very suitable for infant consumption.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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