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Short Communication

Chromium and Cobalt levels in Commonly used Paediatric Syrups in Nigeria

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Abstract

Studies on the human exposure to elemental impurities like chromium and cobalt in pharmaceutical products in the African environment are scarce and limited. In this study we determined the concentrations of these elemental impurities in twenty-eight different brands of paediatric syrups, purchased randomly from patent medicine retail outlets in Port Harcourt, Rivers State, Nigeria. The aim of this study is to compare the antimony, tin and mercury levels in these paediatric syrups with the recommended limits United States Pharmacopea USP. Twenty eight different paediatric syrups were randomly sampled and purchased using the market basket protocol from pharmacy shops in Port Harcourt city, Rivers State, Nigeria in December 2010. Syrups were ashed before digestion using conc. aqua regia, HCl: HNO_3 (3:1) and chromium and cobalt were analysed using Unicam Atomic Absorption Spectrophotometer (AAS) Model 929. The range of heavy metal content in these paediatric syrups were 0.66µg/g – 2.04µg/g and 0.62µg/g – 2.02µg/g for chromium and cobalt respectively. The mean of chromium and cobalt in these paediatric syrups were 1.571±0.069 and 1.015±0.0083 respectively. The estimation of chromium and cobalt as a result of the consumption of paediatric syrups on an average daily basis were 29.35µg/g and 29.9µg/g respectively. Chromium and cobalt content in paediatric syrups did not constitute a significant source of heavy metal exposure to the children.

Keywords: Chromium, cobalt, paediatric syrups, metal contaminants, public health, Nigeria

Introduction

Impurities in pharmaceuticals are the unwanted chemicals that remain with the active pharmaceutical ingredients, or develop during formulation. Inorganic impurities such as heavy metals may be derived from the manufacturing processes used for bulk drugs and the sources are, water used and the reactors where acid hydrolysis takes place. Metal catalysts and reagents used in the synthesis of pharmaceutical products can potentially result in trace levels of metals in the final product that can be toxic to human life [1]. The safety profile and efficacy of these heavy metal contaminated pharmaceutical products may be compromised[1]. Chromium usage as a catalyst in the synthesis of chlorinated aromatic compounds[2] is well established and hence can contribute as a source of non-occupational chromium exposure. Regulatory agencies monitoring the quality of these pharmaceutical products have recommended allowable limits for heavy metal impurities in active pharmaceutical ingredients and finished pharmaceutical formulations[1].

Chromium in the trivalent form, studies have shown may be a nutritional supplement for humans and also may play a vital role in the metabolism of glucose[3] and the deficiency of cchromium leads to derangement in the metabolism of glucose and lipids and may be associated with maturity-onset diabetes, cardiovascular diseases, and nervous system disorders[4]. The daily requirement of chromium is not defined[5] but sources of non occupational exposure to trivalent chromium in humans is from diet and drinking water. Chromium in the hexavalent form has been shown to be carcinogenic, induce mutations, chromosomal aberrations and DNA damage in the form of single strand breaks[5].

The impact of inorganic contaminants from consumables such as beverages, dairy products, paediatric syrups on the health of children is one of the major health concerns today. This becomes more important when considering certain age groups like the unborn in the womb through the first five years of life because according to reports, about 70 – 80% of chemical contaminants accumulate in the body during this period of life [6]. This kind of health risk requires that their effects be further investigated. Consumption of syrups by children is a fact that can't be ruled out. It is worthy of note that about 99% of children receive medications which of course are mostly syrups before even going to the hospital to consult the doctor[7]. Only recently biomonitoring of heavy metals in children aged 2 – 6 years in Nigeria revealed the presence of many heavy metals including cobalt[8,9]. In a bid to determine the likely sources of these elemental contaminants, this study has as its aim, the investigation of the levels of cobalt and chromium in paediatric syrups sold as over – the – counter (OTC) drugs in pharmacies and patent medicine stores in Nigeria and to compare these levels with the recommended allowable limits by United States Pharmacopoeia USP. Previous studies have not considered chromium and cobalt in paediatric syrups from Nigeria. Also, in Nigeria there is insufficient scientific data to guide the formulation of necessary legislation that can appropriately check heavy metal exposure to humans.

Material and Methods

Using the market basket protocol twenty-eight paediatric syrups were purchased from patent medicine stores and pharmaceutical shops in Port Harcourt, the Rivers State capital in Nigeria, were used for the study. The samples were ashed and digested in teflon lab ware that had been cleaned in a high-efficiency particulate air (HEPA) filtered (class 100), trace-metal-clean laboratory to minimize contamination. This protocol involved sequential cleaning of the lab ware in a series of baths in solutions (1 week each) and rinses (five per solution) in a three-step order, namely a detergent solution and deionized water rinses, then 6-NHCl (reagent grade) solution and ultrapure water rinses, finally 7.5 N HNO_3 (trace metal grade) solution and ultra pure water rinses. The lab ware was then air dried in a polypropylene laminar air flow-exhausting hood. Dry ashing method was used by adding 30 ml of each sample into a conical flask and heated on a hot plate at 200°C, for 45min, then in a furnace at 500°C until the volume was drastically reduced to near dryness. Digestion was done by addition of 10 ml conc. aqua regia (HCl:HNO_3, 3:1), it was then heated to dryness. 20 ml deionized water was added, stirred and filtered. The filtrate was made up in standard volumetric flask and chromium and cobalt were assayed with atomic absorption spectrophotometry 205A.

Appropriate quality procedures and precautions were carried out to assure the reliability of the results. Reagents used to calibrate the instrumentation were of analytical grades. A spike-and-recovery analysis was performed to assess the accuracy of the analytical techniques used. Post-analysed samples were spiked and homogenized with varying amounts of the standard solutions of the different metals. The spiked samples were then processed for the analysis by the dry ashing method.

The true intake using the arithmetic mean according to Parkhurst method[10] was calculated by multiplying contaminant level i.e., heavy metal level by amount/ volume of syrup. In all the estimated or calculated levels of antimony, tin and mercury in the syrups, 5 mL was assumed to be the average volume for all the syrups.

Results and Discussion

The levels of heavy metals chromium and cobalt of commonly used paediatric syrups in Nigeria is shown in table 1. The range of heavy metal content in these paediatric syrups were 0.66µg/g – 2.04µg/g and 0.62µg/g – 2.02µg/g for chromium and cobalt respectively. The mean of chromium and cobalt in these paediatric syrups were 1.571±0.069 and 1.015±0.0083µg/g respectively.

The highest levels of chromium was seen in Clavatin suspension (2.04 µg/g) and Furoxtil suspension (1.94µg/g) whereas lowest levels were found in Piriton syrup and Benylin cough syrup of 0.66 and 0.97 µg/g respectively both manufactured in Nigeria. The highest level of cobalt was recorded in Arenus Plus (2.02 µg/g) and Benylin cough syrup (2.02 µg/g), while the lowest levels of cobalt were recorded in Rophegan (0.62 µg/g). None of the pediatric syrups exceeded the United States Pharmacopoeia limits.

The ingestion of chromium and cobalt from a combination of three paediatric syrups most commonly used (an average daily basis) for treatment of malaria (ie maximal doses stated in the leaflet for treatment of malaria paediatric syrups) are shown in table 2 below. The estimated or calculated amounts of chromiun and cobalt in the three most likely administered syrups in children with malaria (which is endemic in Nigeria) for instance were 29.35µg/mL and 29.9µg/mL respectively.

The aim of this study was to determine the levels and estimated daily intakes of chromium and cobalt in commonly used paediatric syrups in Nigeria. In this study the range of heavy metal content in commonly used paediatric syrups in Nigeria were 0.66µg/g – 2.04µg/g and 0.62µg/g – 2.02µg/g for chromium and cobalt respectively. The mean of chromium and cobalt in these paediatric syrups were 1.571±0.069 and 1.015±0.0083 µg/g respectively. None of the paediatric syrups used in this study violated the United States Pharmacopoeia oral limit for chromium and cobalt[11].

Previous studies on heavy metal levels in paediatric Syrups done in Nigeria demonstrate the presence of lead (60%) and cadmium (98%) of the samples investigated in Nigeria[12]. In this study using the arithmetic mean method we estimated the daily intake of chromium and cobalt to be 29.35µg/g and 29.9µg/g respectively. The heavy metal content of these paediatric syrups were below the oral permitted daily exposure limits for chromium and cobalt of 150µg/day and 1,000µg/day respectively set up by the United States Pharmacopoeia[10].

From this study, we suggest that the ingestion of these syrups does not constitute a significant route of heavy metal exposure to the children. We recommend a broader study of more paediatric syrups using inductively coupled plasma mass spectrometry to further confirm the low risk of exposure of these metals..

References

1. Roy J., Pharmaceutical Impurities- A Mini-Review, *AAPS Pharm Sci Tech*., **3(2), (2002)**

2. Oberg T. and Bergstrom J., Chromium as a potential catalyst in the thermal formation of chlorinated aromatic compounds, Organohalogen compounds 66 **(2004)**

3. Mertz W., Chromium and its relation to carbohydrate metabolism, *Med. Clin. North. Am*., **60,** 739-744 **(1976)**

4. Anderson R.A., Recent advances in the clinical and biochemical effects of chromium deficiency, *Prog Clin Biol Res* **380,** 221-234 **(1993)**

5. International agency for Research on Cancer (IARC), IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans, some metals and metallic compounds, Lyon, France: World Health Organization, *IARC,* **(1990)**

6. Goldman L.R., Children-unique and vulnerable, Environmental risks facing children and recommendations for response *Environ., Health Perspect.,* **103,** 13-18 **(1995)**

7. Orisakwe O.E., Akah P.A. and Orish C.N., Prevalence of parental administration of drugs to children before coming to the hospital, *Trop. Doc.*, **24,** 182-183 **(1994)**

8. Nriagu J., Afeiche M., Linder A., Arowolo T., Ana G., Sridhar M.K.C., Obi E., Orisakwe O.E. and Adesina A., Lead poisoning associated with malaria in children of urban areas of Nigeria, *Int. J. Env. Hyg.,* **211,** 591-605 **(2008)**

9. Nriagu J., Nigerian children biomonitoring project (Unpublished data)

10. Parkhurst D.F., Arithmetic versus geometric means for environmental concentration data, *Environ. Sci. Technol.* **32,** 92A-98A (**1998)**

11. http://www.usp.org/pdf/EN/hotto pics/2009-04- 22 Metal Impurities Tox Chart.pdf **(2009)**

12. Orisakwe O.E. and Nduka J.K., Lead and cadmium levels of commonly administered pediatric syrups in Nigeria, A Public health concern, *Science of the Total Environment* **407,** 5993–5996 (**2009**)

Table 1
Chromium and cobalt levels (µg/g) in paediatric syrups

S/No	Drug Name	Manufacturer	Batch No.	Date of Production	Expiry Date	NAFDAC NO.	Heavy Metal (µg/g)	
							Chromium	Cobalt
1	REFUCIL	REALS	W038	03-Oct	03/13	04-4702	1.34	0.89
2	CAMOQUIN	PFIZER	950	03-Oct	03/12		1.78	0.71
3	SINUFED	SKG	210	11-Oct	11/12		1.74	1.04
4	ZITHROMAX	PFIZER	96427702	11-Sep	11/11	04-1387	1.89	1.06
5	ZOLAT	EMZOR	L1194N	10-Sep	12/11		1.66	0.72
6	AMPICLOX	BEECHAM	190849	11-Sep	11/12	04-3376	1.83	1.24
7	ROPHEGAN	M&B	1Z385	04-Sep	03/12	04-0290	0.98	0.62
8	PARACETAMOL	SKG	10003	11-Oct	11/13	04-2633	1.66	0.92
9	LIXYPED	M&B	1Z248	03-Sep	02/12	04-0320	1.83	0.77
10	COLIPAN	NGC	U130	07-Aug	07/11	04-4044	1.67	1.94
11	EM-VIT-C	EMZOR	L313P	03-Oct	03/13	04-0262	1.21	1.47
12	BENYLIN	NGC	H436	08-Oct	08/13	04-0887	0.97	2.02
13	ARENAX PLUS	SWIPHA	ARX1003	01-Oct	12/12	A4-3822	1.86	2.02
14	PIRITON	EVANS MED PLC	4022	09-Oct	08/13	04-0437	0.66	1.34
15	EMCILLIN	EMZOR	2970M	07-Aug	07/11	04-0396	1.51	0.64
16	FANSIDAR	SWIPHA	LS210040	03-Oct	03/12	04-0155	1.86	0.76
17	NORAVITE	SKG	1004	06-Oct	06/12	04-2111	1.54	0.74
18	VENTOLIN	GLAXOWELLCOME	083527A	10-Aug	10/10	04-0250	1.27	0.62
19	FUROXETIL	M&B	068F1	10-Sep	09/11	04-7820	1.94	0.64
20	CLAVATIN	SKG	9161128	09-Sep	08/11	04-4467	2.04	1.12
21	REPROFEN	REALS	RW118	06-Oct	05/13	04-7474	1.42	0.69
22	EMGYL	EMZOR	L962N	09-Sep	09/12	04-1452	1.12	0.65
23	EM-B-PLEX	EMZOR	L522P	05-Oct	05/13	04-0287	0.99	0.68
24	IPCAMOX	IPCA	AXR9002Z	06-Sep	05/12	04-5638	1.86	1.37
25	RHINATHIOL	SANOFI AVENTIS	90071	03-Sep	03/12	04	1.85	0.67
26	VANCLOX	EVANS MED PLC	6703025	07-Oct	06/13	A4-0219	1.89	1.41
27	HALFAN	SMITHKLINE BEECHAM	A005	10-Sep	10/12	04-2181	1.77	1.03
28	LOXAPRIM	M&B	1Z342	04-Sep	03/12	04-4135	1.86	0.64
% (number) of products violating the United States Pharmacopoeia (USP)							**USP Oral Limit (15ppm) 0% (0)**	**USP Oral Limit (100ppm) 0% (0)**

Chromium (Range: 0.66 – 2.04; Mean Value = 1.571±0.069 (n=28) and cobalt (Range: 0.62-2.02; Mean Value = 1.015±0.0083 (n=28).

Table-2
Estimated intake of chromium and cobalt in paediatric syrups

True metal intake	Calculation	Total intake of metal
Chromium	5mL x 2.04 + 5mL x 1.94 + 5mL x 1.89	29.35µg/g
Cobalt	5mL x 2.02 + 5mL x 2.02 + 5mL x 1.94	29.90µg/g

(i.e., assumed syrup volume multiplied by heavy metal contaminant level for each of the three products: the volume of the syrup was assumed to be 5 mL each).