

Original article

Extent of some heavy metals in cough syrups abused in Sokoto, Nigeria

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Background: Cough syrup abuse is an emerging public health trend in our society that shall be tackled because it exposes the drug abusers to harmful chemicals and manifestation of harmful biological effects. Determination of the possible embedded constituents in drugs such as heavy metals will guide stakeholders and the public for taking right measures in curtailing the trend.

Objective: The purpose of this study was to assess the levels of heavy metals (Zn, Cu, Fe, Cr, Cd, Pb, Ni and Mn) in commonly used cough syrups in Sokoto, Nigeria.

Methods: A survey using atomic absorption spectroscopy was employed for the study and the descriptive statistics were performed.

Results: Levels of essential heavy metals in abused cough syrup drugs showed that the manganese concentrations ranged from 0.60 ± 0.03 to 1.10 ± 0.40 (ppm), copper ranged from 0.13 ± 0.07 - 0.30 ± 0.02 (ppm), zinc ranged from 0.60 ± 0.01 to 1.16 ± 0.12 (ppm), and iron ranged from 0.10 ± 0.2 to 3.0 ± 0.05 (ppm). Levels of non-essential heavy metals in abused cough syrup drugs show that the chromium levels ranged from 0.81 ± 0.01 to 3.05 ± 0.07 (ppm), lead levels ranged from 0.29 ± 0.01 to 0.43 ± 0.01 (ppm), nickel extent ranged from 0.68 ± 0.07 to 1.19 ± 0.41 (ppm), and cadmium levels ranged from 0.10 ± 0.01 to 0.71 ± 0.01 (ppm).

Conclusion: There were significant levels of the determined heavy metals in cough syrups commonly abused in Sokoto, Nigeria. Consequently, toxicity may occur among the users. Governments need to screen heavy metals in all the drugs and put up measures that strictly allowed access to these drugs only on medical basis.

Keywords: Cadmium, copper, cough syrup, heavy metals, iron, lead, substance abuse.

Heavy metals are defined based on certain terms, one of them is their specific gravity of at least five times bigger than water. Among this group of heavy metals there are the famous metals such as iron, copper, nickel, lead, chromium, zinc, and cadmium. Heavy metals like other metals are under ideal conditions present in the environment embedded in deposits or compounds of various nature. However, anthropogenic activities have succeeded in expunging these metals and made them in contact with air, water,

soils, plants, animals, and other mediums that affect man in one way or the other. ^(1,2) Albeit, there are more than fifty heavy metals, some of them have been found to play an important role in the human biological system at very low concentrations. For instance, iron, copper, and zinc in the biological system provided the optimum concentrations. Therefore, a slight elevation in the optimum levels of these essential heavy metals could lead to consequent effects that can be detrimental to the human or plant body. ^(1,2) Other heavy metals have no known biological roles, like in the case of lead, chromium, cadmium etc; in turn have tendency to accumulate and trigger toxicity in the biological system even at very little concentration. ⁽³⁾ Lead causes cardiovascular disease, hypertension, neurological and behavior defects, poor reproductive health, renal problem, and the likes. Nickel causes

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dermatitis, reduced sperm, and encephalopathy. Cadmium is implicated in many cases of cardiovascular disease, impaired growth, learning defect, osteomalacia, cancer, and weak bone. ^(1,2)

Heavy metals find their way into many products that come in contact with humans or plants. Parable, in medicinal or pharmaceutical products, heavy metals are involved advertently as additives, color enhancers, catalysts and other intentional ways. In the same streak, heavy metals are involved in medicines or drugs as impurities through the manufacturing processes, storage, transport etc. or as components of containers (such as plastics) that carry the drugs. People who engage in substance/ drug abuse have tendency to come in contact with heavy metals that are present in the said drug materials and faced the consequential effects therein. ^(1,4)

Cough syrups are groups of medicines meant to suppress or cure cold symptoms or cough. Since most of them act by suppressing the nervous system and are metabolized by the liver, there are consequent effects of abusing these types of drugs as reported by several studies. Effects of abuse due to the drugs can be hallucination, paranoia, delusions, hypertension, ataxia, confusion, tachycardia, and in prolonged abuse DNA fragmentation of the liver and consequent dysfunction. ^(5,6) The availability of the drugs as over-the-counter substances readily encourages tendency for abuse and chronic use that is associated with detrimental health effects that could be due to heavy metals or other components of the drugs. ^(7,8) Certainly, nowadays the pattern of drug or substance abuse is becoming a thing of concern and an increasing trend. Many sorts of things are used as drugs/ substances of abuse and across different age brackets. This is a great concern to public health. A study on heavy metals determination in herbal medicines from India found mercury, lead, arsenic, and cadmium in different herbal preparations. ⁽⁹⁾ Another study of Indian traditional medicine preparations reiterated that the preparations contain toxic metals such as mercury, arsenic, and lead; a condition that threatens public health. ⁽¹⁰⁾ In Pakistan, an investigation of heavy metals in herbal stuffs lead to the determination of zinc, copper, manganese, and iron metals below toxic. ⁽¹¹⁾ In a similar work on over-the-counter children's drugs in Uganda (Africa) found cadmium and lead at excess levels. Therewith, manganese was detected at low levels. ⁽¹²⁾ An assessment of beverages conducted in Nigeria concluded that, the consumption of beverages

that contain arsenic, lead, chromium, mercury, and cadmium is unsafe to health. ⁽¹³⁾ Pertaining tobacco, another substance of abuse in Nigeria, it was revealed that Sokoto tobacco contains zinc, cobalt, chromium, nickel, and lead that can pose harm to human consumers. ⁽¹⁴⁾ Unfortunately, another study of Nigeria-made cough syrups used to treat children shows that there are excess nickel, and chromium levels in the examined syrups, and therefore can threaten public health. ⁽¹⁵⁾ These aforementioned studies had highlighted the possibility of pollution in drugs of abuse around the parts of the world. However, there is scarce information about quantification of heavy metals in cough syrups.

Presently, both in the developed and developing worlds. In Nigeria (Sokoto state included) there is a great challenge of increasing use of the cough syrup drugs for psychoactive use, and there is little information reported especially about the possible harmful, constituents of the drugs such as the heavy metals. ^(16,17) Therefore, it is pertinent to pay much attention on monitoring of levels of some heavy metals in some common cough syrups in Sokoto, Nigeria. The objective of this work was to assess the levels of heavy metals (Mn, Cu, Zn, Fe, Cd, Pb, Cr, and Ni) in commonly used cough syrup in Sokoto, Nigeria.

Materials and methods

Study location

The study was carried out in Sokoto state, Nigeria. Sokoto State is located in the North West Zone of Nigeria between longitude 11° 30' - 13° 50' and latitude 4° - 6°. It borders Niger Republic to the north and Benin Republic to the northwest, Kebbi State to south and Zamfara State to the east. It has a land mass area of about 32,000 sq km, and consists of 23 local government areas and 244 political wards. The population is predominantly rural, Muslim and consists almost entirely of Hausa/Fulani ethnic groups. ^(18,19)

Elemental analysis

After buying the drugs from shops in Sokoto city, heavy metal elements were determined according to standard methods described in Umar AI, *et al.* ⁽⁴⁾ Fifty ml of each sample was transferred into a beaker and 5 ml of concentrated HNO₃ was added into each beaker. The samples were heated on a hot plate until the solution appears pale yellow colored indicating the digestion was completed. After which solution allowed to cool and transferred to a 50 ml volumetric flask

and distilled water was added to the mark and transferred into a sample bottle for atomic absorption spectroscopy. ⁽¹⁴⁾ In Atomic Absorption Analysis, the absorption of light uses an instrument called Atomic Absorption Spectrophotometer (AAS). In this process, flame system is generally employed to dissociate element from their chemical bonds. The atoms absorb light at characteristic wavelength of chemical bonds. The atoms absorb light at characteristic wavelength when present in their ground state. A mixture of air and acetylene produce a flame which is of a sufficient high temperature to ensure the presence of free atoms of most elements. The use of nitrous oxide in place of air result in a higher temperature and this is necessary for the estimation of certain elements. The narrow spectral line of the sample necessitates the use of light source as well as high resolution monochromator. This help to prevent interference from adjacent spectral lines of other species on the sample matrix. AAS in conjugation with flame atomizer was used to determine specific metals (Mn, Cu, Zn, Fe, Cd, Pb, Cr, and Ni) in a liquid sample, the availability of a spectrometer equipped with a lamp facilitates the measurement of multiple metals in a sample. ⁽¹⁴⁾ After the digestion has been completed, the AAS machine was used to determine the concentrations of Mn, Cu, Zn, Fe, Cd, Pb, Cr, and Ni in the sample. ⁽¹³⁾

Statistical analysis

Data were expressed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) with post hoc analyses was used to compare data among multiple groups. *P* < 0.05 was considered as statistical significance. Statistical analysis was performed using the Statistical Package for Social Sciences Software program (SPSS) (version 22, Chicago, Il).

Results

In Table 1, the extent of essential heavy metals in some commonly abused cough syrup drugs in Sokoto, Nigeria was shown. The manganese concentrations ranges from 0.60 ± 0.03 to 1.10 ± 0.40 (ppm), copper range from 0.13 ± 0.07 - 0.30 ± 0.02 (ppm), zinc ranges from 0.60 ± 0.01 to 1.16 ± 0.12 (ppm), and iron ranges from 0.10 ± 0.02 to 3.0 ± 0.05 (ppm). From this finding, it has denoted that the cough syrup taken by many of our youth in form of abuse contains significant amount (*P* < 0.05) of heavy metals that more especially under chronic intake can lead to harms to their body. Manganese element (0.60 ± 0.03 - 1.10 ± 0.40 ppm) is an essential element required by human; therewith, adversity and deficiency can be due to excess, and low manganese respectively. The high intake of manganese can cause neurological problems. ^(20,21) In this study the levels of the element are in most of the types of drugs higher than the 3.5 - 7.0 mg per day recommended in drinking water to be consumed by adult. ⁽²¹⁾ Only two types of drugs had lower value. And all the results of manganese were higher than the levels determined in cough syrups taken by children as prescribed medications. ⁽²²⁾ Copper element has a vital role in metabolism in humans and relations. In this study, the levels of copper (0.13 ± 0.07 - 0.30 ± 0.02 ppm) (Table 1) was lower than the recommended amount for daily intake and lower than the concentrations of copper from tobacco and cigarette revealed by a Ghana study. ⁽²¹⁾

Zinc is needed for activities of many enzymes in the body for homeostatic functions, such as in protein synthesis, energy production, as well as regulation of growth. ⁽²²⁾ Zinc (0.60 ± 0.01 to 1.16 ± 0.12 ppm) (Table 1) in this study is similar to levels determined in tobacco leaves in an Ethiopian study. ⁽²²⁾

Table 1. Concentrations of essential heavy metals found in commonly abused cough syrups in Sokoto, Nigeria.

| Type of cough syrup | Manganese (Mn) | Copper (Cu) | Zinc (Zn) | Iron (Fe) |
|---------------------|----------------|-------------|-------------|-------------|
| Type A | 1.10 ± 0.18 | 0.13 ± 0.07 | 0.60 ± 0.01 | 0.10 ± 0.02 |
| Type B | 0.90 ± 0.02 | 0.18 ± 0.02 | 0.62 ± 0.01 | 3.0 ± 0.05 |
| Type C | 1.01 ± 0.01 | 0.30 ± 0.02 | 0.80 ± 0.07 | 0.20 ± 0.00 |
| Type D | 0.60 ± 0.03 | 0.19 ± 0.04 | 1.15 ± 0.11 | 0.15 ± 0.00 |
| Type E | 1.10 ± 0.40 | 0.26 ± 0.02 | 1.16 ± 0.12 | 2.25 ± 0.01 |

Values are expressed as mean ± standard deviation

Table 2. Extent of some non-essential heavy metals found in commonly abused cough syrups in Sokoto, Nigeria.

| Type of drug | Chromium (Cr) | Lead (Pb) | Nickel (Ni) | Cadmium (Cd) |
|--------------|---------------|-------------|-------------|--------------|
| Type A | 0.83 ± 0.04 | 0.31 ± 0.01 | 0.92 ± 0.02 | 0.71 ± 0.07 |
| Type B | 0.81 ± 0.01 | 0.43 ± 0.01 | 0.71 ± 0.01 | 0.14 ± 0.01 |
| Type C | 3.05 ± 0.07 | 0.19 ± 0.01 | 0.68 ± 0.01 | 0.14 ± 0.01 |
| Type D | 0.89 ± 0.01 | 0.29 ± 0.01 | 1.19 ± 0.41 | 0.16 ± 0.01 |
| Type E | 0.91 ± 0.01 | 0.28 ± 0.01 | 0.79 ± 0.01 | 0.14 ± 0.01 |

Values are expressed as mean ± standard deviation

Iron is vital in the transport of oxygen in the blood shuttle across the parts of the body, slight reduction in iron can spur anemia and chronic lack of iron stirs heart failure. The levels (0.10 ± 0.20 to 3.00 ± 0.05 ppm) (Table 1) in this study are higher than the World Health Organization/Food and Agriculture Organization of the United Nations tolerable daily intake (0.05 mg/kg/day) pointing a possible concern regarding this particular element; however, a study from Saudia Arabia of levels of heavy metals in cigarette brands has related higher amounts of Fe in cigarette than the levels reported by this study (0.10 ± 0.2 to 3.0 ± 0.05 ppm).⁽²³⁾

Levels of non-essential heavy metals in abused cough syrup drugs were shown in Table 2. The chromium levels range from 0.81 ± 0.01 to 3.05 ± 0.07 (ppm), lead levels ranges from 0.19 ± 0.01 to 0.43 ± 0.01 (ppm), nickel extent ranges from 0.70 ± 0.01 to 1.20 ± 0.40 (ppm), and cadmium levels range from 0.10 ± 0.01 to 0.71 ± 0.01 (ppm). This result has denoted that there exists significant level ($P < 0.05$) of heavy metals in the cough syrup taken by abusers in the state for non-medical use, and the effects observed in them might be linked to the concentrations of the metals involved. The Cr, Cd, Pb, Ni, are virtually not needed by human biological system at whatever amount; therefore, their presence in whatsoever is taken in by human body may present some harms. Chromium (0.81 ± 0.01 to 3.05 ± 0.07 ppm) (Table 2) in this study was in disagreement with the study that shows no chromium level was detected in various cough syrups (such as Broncholyte, Septrin syrup, Coflin, Emzolyln) taken by children.⁽²²⁾ Likewise, the nickel (0.68 ± 0.01 to 1.19 ± 0.41 ppm) levels are higher than a study of cough syrup prescribed to children in the country as shown by a study conducted on foreign and domestic drugs.⁽²²⁾ The levels of lead (0.19 ± 0.01 to 0.43 ± 0.01 ppm) are of concern, because no safe lead level is known. And the finding is showing lead concentrations that are higher than the permitted daily dose ($5\mu\text{g/day}$) in drugs as enshrined

by Food and Drug administration of the United States of America. Therewith, the consequences are bound to happened and could be more pronounced in children and youngsters taking the drugs especially without medical prescription.⁽²⁴⁾ The found cadmium (0.14 ± 0.01 to 0.71 ± 0.01 ppm) in this study was higher than the levels found in other used drugs in a study from Dubai.⁽¹⁾

Discussion

Sokoto state is from the northwestern region of the country that experiences a threatening trend of substance abuse. More specifically, there is a rising number of people especially among the youths/ adolescent and in turn leading to several consequences on the society, and many individuals in the state.^(25 - 29) Among the harmful type of drug/ substance abuse in the state is the issue of cough syrup. This type of drug abuse that involves use of cough syrups as psychoactive substance is causing a lot of biological effects especially among the youths. However, it is safe to regard the effects of cough syrup as an after-effects of the constituent compounds in the drug that are either added deliberately or inadvertently.⁽⁴⁾ It is indeed right to say that; the heavy metals could be among the sources of biological effects seen in people that are cough syrup abusers. This is possible because the heavy metals have been found in the cough syrups analyzed in this study, and the heavy metals are famous in causing toxicity in humans and other biological systems. It can be discerned from this study that, actually all the types/ brands of drugs analyzed in this study contain both the essential and non-essential heavy metals therein. It is noteworthy, that the cough syrups have great tendency of stirring abuse or dependency in their users; therefore, even the essential heavy metals found in this study can cause toxicity during chronic use or large acute intake.^(1, 24, 29) Likewise, the non-essential heavy metals determined in this study can potentially lead to toxicity during minute intake of the syrups or

chronic intake. Therefore, there is need for more effective measures to strictly and truthfully restrict the accessibility of cough syrups in the society to avoid damages to individuals and society at large; the rampant availability of the drugs has invariably encouraged drug abuse.⁽³⁰⁾ Moreover, it was evidently pointed that, there is less concern on the parts of the agencies about the heavy metals contents of drugs; it is indeed needed for all the authorities concern to force the producers of drugs to screen their products for levels of heavy metals to safeguard public health among the abusers and lawful (prescribed) users.^(1, 31)

Conclusion

Substance/drug abuse is a prevalent thing of concern in many parts of the world, including Nigeria. Therewith, the abuse of cough syrup is becoming a thorn in the flesh of many Nigerian youths. Thus, it is important to determine the levels of heavy metals in cough syrup. The levels of essential and nonessential heavy metals (Mn, Cu, Zn, Fe, Cd, Pb, Cr, and Ni) in common cough syrup have been abused in the state. Mostly, these metals are in levels that are beyond the set concentrations approved by constituted authorities. Heavy metals shall not be found in drugs, however, due to impurities (pollutions) or deliberate addition they are found in cough syrups abused in Sokoto state. The essential heavy metals posed great health effects to the drug users and the non-essential heavy metals alike. It can be said that, these metals are found in drugs because of the inability of constituted authorities to screen them. Additionally, the rampant and cheap cost of the drugs have made it very available for people especially youths for abuse and in turn exposing the consumers to possibility of heavy metals toxicity. Government should take measures to screen heavy metals in these drugs, and enforce banning on improper sell of drugs in the state.

Conflicts of interest statement

Each of the authors has completed an ICMJE disclosure form. None of the authors declare any potential or actual relationship, activity, or interest related to the content of this article.

Data sharing statement

The present review is based on the references cited. Further details, opinions, and interpretation are available from the corresponding authors on reasonable request.

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