A Market Basket Survey of Horticultural Fruits for Arsenic and Trace Metal Contamination in Southeast Nigeria and Potential Health Risk Implications

Chigozie Damian Ezeonyejiaku,* 1 Maximilian Obinna Obiakor 2

1 Department of Zoology, Nnamdi Azikiwe University, PMB 5025, Awka, Anambra State, Nigeria
2 School of Environmental and Rural Science, University of New England, Armidale, NSW 2351, Australia

*These authors contributed equally to this work.

Introduction

Food systems in developing countries are not always as organized as in developed countries due to problems associated with a burgeoning population, rapid urbanization, and shortfall of resources needed to handle food processing. In addition, environmental dispersion of contaminants from uncoordinated industrialization and waste management systems further compromise food quality and safety, and raise the probability of dietary risk exposure among consumers. In addition to the fecal and microbial food contamination often related to poor hygiene and sanitation, risks of metal and metalloid (generally referred herein as metals except as otherwise indicated) ingestion through food consumption and associated health implications have received increased attention. Trace metals posing significant health risks (e.g., mercury (Hg), copper (Cu), lead (Pb), and Zinc (Zn)) have been detected in developing countries such as Nigeria, Egypt, Iran, and Bangladesh at substantial concentrations in food crops such as fruits, vegetables and cereals, and have prompted a debate on the efficacy of food quality assurance and safety assessment measures. Although metal contaminants may originate from discrete sources including soil, fertilizers, and atmospheric particulates, accumulation in plants

Background. Elevated arsenic and trace metal contamination of the terrestrial food chain represents one of the most significant environmental risk exposures for human populations in developing countries. Metalloid and metal contamination in horticultural crop produce such as fruit is a public health concern in Nigeria. Local fruits are cheap sources of vitamins and minerals for the resident population and pose an important dietary threat of metal(lloid) toxicity through consumption.

Objectives. Market basket investigation of five locally grown (guava, pineapple, orange, and pawpaw) and imported (apple) fruits was conducted to measure the total concentrations of arsenic (As), mercury (Hg), copper (Cu), and lead (Pb) present in these fruits from southeastern Nigeria (Awka, Anambra).

Methods. Fruits were analyzed for As and the three metals using atomic absorption spectrophotometry. Moisture content of fruits was determined and used to transform metal concentrations in dry weight to wet weight and compared to Codex food grade standards and assorted (sub)tropical fruits, edible and inedible peels.

Results. The mean ± standard deviation of elemental concentrations in dry weight ranged from 20.0±0.71–96.84±0.00 µg g⁻¹ for As, 0.02±0.02 – 0.89±0.33 µg g⁻¹ for Hg, 0.11±0.01 – 0.18±0.40 µg g⁻¹ for Cu, and <0.001 – 0.03±0.05 µg g⁻¹ for Pb. The As concentrations (wet weight) in fruits were ~32–166 orders of magnitude higher than Codex Alimentarius Commission (Codex) maximum As food grade levels. Guava and apple methyl Hg concentrations were ~6–~1 orders of magnitude higher than Codex maximum levels, while the content of Cu and Pb in fruits were within acceptable standard limits.

Conclusions. The significant concentrations of As and Hg in the examined fruits indicate a potential public health threat. Efforts are needed to initiate and sustain continued monitoring of trace elements in fruits and food sold to consumers due to variation in contaminating sources to ensure food safety. Although a great deal of information exists on Hg toxicity, research on metalloids such as As remains limited in Nigeria and no reliable guidelines exist. Further research is recommended to determine the ecotoxicity of As in Nigeria.

Competing Interests. The authors declare no competing financial interests.

Keywords. As, Cu, Hg, Pb, food safety, dietary toxicity, public health

Received February 20, 2017. Accepted July 7, 2017.

J Health Pollution 15: 40–50 (2017)
may depend on the species, soil characteristics, metal properties, and environmental conditions. Beyond dietetic metal exposure, air and water are significant random pathways of exposure reported in many case studies. The several mutually reinforcing physical and chemical properties of metals nevertheless enhance ease of bioaccumulation and biomagnification in food webs.

The growing concern of entrance and transference of metals into terrestrial food webs stems from the potential for adverse effects on the health status of both humans and animals continuously exposed to such harmful contaminants via food consumption. A number of studies have been conducted on trace metals linked to the incidence of gastrointestinal cancer, and cancer of the pancreas, urinary bladder or prostate. It is therefore crucial to determine the concentrations of metals present in food as a practical step for effective risk assessment.

While trace metals (often regarded as heavy metals) have been studied extensively and reliable guidelines developed in many jurisdictions, information on metalloid ecotoxicity is relatively limited and not fully understood. One of the few environmentally and biologically important metalloids, arsenic (As) has been widely studied due to its public health implications and identified multiple pathways of human exposure. The carcinogenicity of As in humans is well known. Inorganic As is a class one human carcinogen whose chronic ingestion may cause cancers of the bladder, kidney, liver, lung, prostate and skin. Environmental pollution resulting from industrial activities such as mining and smelting and production processes can increase the dispersion of As and contamination of agronomic crops through water and atmospheric deposition. Farm irrigation using As-contaminated groundwater has been shown to elevate As concentrations in rice grains. Food standards have not been widely developed for As in many countries, although efficient screening exercises and risk communication strategies are in place in most developed countries to safeguard consumers from As exposure. No such safeguards are in place in many developing African countries.

In Nigeria, there are poor food quality controls and existing mechanisms are not very effective at protecting consumers. Deleterious effects of food contaminants have been underreported in the country as a result of inadequate risk assessment, communication and resource deficits. Contamination of metals in commonly consumed horticultural fruits and effects on human health have not been previously investigated. In this study, we investigated As and trace metals (Hg, Cu, and Pb) contamination in orange (Citrus sinensis), pawpaw (Carica papaya), guava (Psidium guajava), apple (Malus domestica), and pineapple (Ananas comosus) commonly supplied in the Awka region where there has been a history of metal smelting activities. This market basket survey aimed to collate elemental concentration data and compare to internationally acceptable standards for use in preliminary exposure assessments for the local population.

Abbreviations

| Abbreviation | Description |
|--------------|-------------|
| Codex | Codex Alimentarius Commission |
| CRM | Certified reference materials |
| dw | Dry weight |
| ww | Wet weight |

Methods

Location Description and Sample Collection

Samples of locally supplied fruits were collected from the largest market in Awka South, which serves the entire Local Government Area and surrounding towns of Awka North. Awka South is in Anambra State of southeastern Nigeria. It is located within ~6.642° N and ~7.067° E (Figure 1) and experiences two distinct seasons brought about by two predominant winds that rule the area: the southwestern monsoon winds from the Atlantic Ocean and the northeastern dry winds from across the Sahara Desert. Seven months of heavy tropical rains (April–October) are followed by 5 months of dryness (November–March). Awka South is generally hot and humid with a temperature range of 27–28°C from July through December but rising to 35°C between February and April. It has an estimated population of over 400,000 inhabitants based on 2017 population projection. The region is comprised of Awka city (capital of Anambra State), Amawbia, Ezinato, Nibo, Nise, Umuawulu, Isiagu, Okpuno, and Mbaukwu. Awka city is the location of many commercial and social facilities and has a history of indigenous technology and crafts, including wood processing, metal smelting and blacksmithing. The uncoordinated waste management systems that characterize agriculture, wood processing and industrial
metal activities in the area have led
to increased environmental pollution
through indiscriminate disposal
and dumping of tailings. Although
there has been a gross decline of
these metal processing activities due
to rapid technological development,
unregulated artisanal production
still exists. The city is also one
of the most important industrial,
economic, cultural, political, and
commercial centres in southeast
Nigeria. It continues to undergo
heavy urbanization and infrastructure
development. The industrial facilities
in Awka South are scattered at the city
centre and surrounding suburbs.

Local fruits were purchased from a
wide variety of retailers at the market
(known as Eke Awka), including
fruits sold openly on market tables
and shelves. All fruits were locally
supplied except for apples, which are
largely imported in Nigeria from South
Africa. Ten samples were purchased
for each of the market basket survey
fruit (orange, pawpaw, guava, apple,
and pineapple). It was not determined
if use of adulterants had any effects
on apples imported into the country;
thus, such effects were deemed to be
negligible during preparation and
analysis.

Sample Preparation
Fruit samples were taken to a
laboratory in an air-tight container
to prevent further atmospheric
deposition that might interfere with
elemental analysis. Samples were
neither washed nor peeled prior to
preparation. The intent was to reflect
dietary exposures and common
consumer food handling strategies,
where fruits are purchased from an
open market and consumed without
washing. Samples were finely diced
in a food processor, which was
thoroughly cleaned with 10% extra
and rinsed in distilled water after
processing each sample. Ground
samples were then frozen until further
processing.

Analytical Determination of Arsenic,
Mercury, Copper, and Lead in Fruit
Samples
All samples were analyzed for total
As, Hg, Cu, and Pb using established
methods with modification. Analytical
grade reagents were used throughout
the metal determination with purity in
the range of 98–99.99%. Samples were
oven dried at 55°C. Approximately 0.5 g
each of the dried fruits was accurately
weighed out into 50 ml polyethylene
centrifuge tubes; 5 ml of concentrated
nitric acid was added to each sample
and then left overnight. We digested
the samples in a pre-programmed microwave
digestion system at a changing
temperature and time: 5 minutes ramp
to 60°C and then held at 60°C for 10
minutes (400 W); 5 minutes ramp
to 75°C and then held at 75°C for 10
minutes (400 W); and 5 minutes ramp
to 100°C and then held at 110°C for 30 minutes (400 W). All microwave digestions were carried out in triplicate with a reagent blank. After cooling, digested samples were diluted to 50 ml and total As, Hg, Cu, and Pb analysis was performed by atomic absorption spectrophotometry at a commercial laboratory.

Quality Control
Each analytical batch of ten runs was accompanied by an acid blank, and three certified reference materials (CRM): apple leaves, (National Institute of Standards and Technology (NIST) Standard Reference Material 1515); pine needles, (NIST Standard Reference Material 1575a); and rice flour, (NIST Standard Reference Material 1568a) to monitor for instrument accuracy and method extraction efficiency. Mixed element internal standards including all examined metals were measured as part of the analytical quality control. Thus, a total of 25 independent digests including reagent blanks and CRMs were analyzed. Mean recoveries were in an acceptable range (75–98.5%) compared to the CRM theoretical or certified values for the elements. All glassware used in the analyses were cleaned with a detergent-free solution, soaked in acid (10% hydrochloric acid) and then rinsed with metal-free distilled water. Metal concentrations were reported in µg/g dry weight at instrumental detection limit of 0.001 µg/g.

Moisture Content Determination
We determined the percentage (%) moisture contents of all the fruits examined to enable transformation of metals concentrations from dry weight (dw) to wet weight (ww) basis, and facilitate the comparison of our data with those of Codex Alimentarius Commission (Codex) guideline values (As = 0.50 µg/ g ww, Hg = 0.10 µg/ g ww, Cu = 2.00 µg/ g ww, and Pb = 0.10 µg/ g ww). Approximately 10 g of each fruit was weighed into aluminum foil, and dried for 48 hours in a 105°C oven. At the end of the drying period, samples were reweighed and % moisture content was calculated using Equation 1.

\[ M = \left( W_w - W_d \right) / W_w \times 100 \]

where \( M \) = moisture content (%) of fruit
\( W_w \) = wet weight of fruit sample
\( W_d \) = weight of the fruit sample after 48 hours drying

Statistical Analysis
Data generated from the study were subjected to analysis using IBM SPSS Statistics computer software program (version 22, SPSS Inc., Chicago, IL, USA) and Microsoft Excel (version 2016) at an alpha error of 0.05 and 95% confidence interval. The normality of data distribution was objectively evaluated by the Shapiro-Wilk test, and homogeneity of variance by Levene's test. We compared the concentrations of the metals in fruits using the Kruskal-Wallis method, a nonparametric analysis of variance test based on rank transformation, with Bonferroni correction and Monte Carlo approximation for unbiased estimate of the exact P value (based on 100,000 random tables from the reference set using a starting seed of 2,000,000). Metal concentration values less than the maximum detection level were replaced with 0 prior to analysis.

Results
The percentage moisture contents of all fruit samples examined were guava, 80.8%; apple, 84%; pineapple, 87%; orange, 87%; and paw paw, 85.5%. The data values were
subsequently used to transform metal concentrations from dry weights to wet weights (Figures 2–5). The mean, minimum, and maximum total As, Hg, Cu and Pb concentrations (dw) for the independent fruit samples collected from Awka market are presented in Table 1, while the corresponding comparisons of the metal concentrations (ww) with Codex guideline levels on a wet weight basis are shown in Figures 2–5. The results show that As concentration was highest in pawpaw (96.84±0.00 µg/g dw) followed by pineapple (56.84±0.71 µg/g dw), while the least concentration was measured in orange (43.68±0.00 µg/g dw) (Table 1). Comparatively, in wet weight, the level of As was significantly higher (P < 0.05) than the Codex maximum level for As in fruits (Figure 2).

The Codex provides a guideline level for methyl Hg of 0.10 µg/g ww. Based on the supposition that methyl mercury is ~83% of total mercury, as presented in Table 1, the concentration of methyl Hg in our samples was calculated in wet weight and compared with the Codex guideline level, and guava and apple methyl Hg concentrations were ~6 and ~1 orders of magnitude higher than the Codex maximum guideline level, respectively (Figure 3). The amounts of Cu and Pb in the sampled fruits were within the Codex standards (Figures 4 and 5). Apple, pineapple, orange, and pawpaw had Pb concentrations of <0.001 µg/g.

Discussion

The present study investigated concentrations of As, Hg, Cu, and Pb in commonly consumed horticultural fruits to assess food quality and make recommendations based on an explicit understanding of human health risks. Metal contamination of edible fruits poses a potential health risk to both humans and animals. Awka South was
selected for the current survey because of the open market system in the area, and because physical structural changes are rapidly taking place within its urban ecology, such as continuous road and building construction. These activities are, in many cases, not rigorously planned. Dust pollution and fog are common weather events that characterize the region, and markets are indiscriminately located along roads. Thus, monitoring of food contamination by metals and hazardous substances is necessary for the assessment and reduction of dietary exposures.5,7,19,23,46,51

The examined fruits had significantly higher total As concentrations (~32–166×) than the Codex maximum food grade level (0.5 µg/g ww). While fruit Cu and Pb concentrations were below the Codex standards, we found that Hg in guava and apple were 6.1 and 1.3 times higher than safe levels for consumption (0.1 µg/g ww), respectively.55 Fruits are capable of accumulating metals in their internal tissues, which are often species-specific and regulated by factors such as ecological setting and soil type.56-59 In some cases, surface contamination of fruits with hazardous substances are enabled by poor handling and processing.6

Our observation of relatively high As and Hg concentrations compared to Codex standards is particularly striking, and appears to indicate similar sources of contamination of these fruits. We postulate that surface/atmospheric deposition of soil and dust might be the primary mechanism of contamination.20,60 Awka has a high population density (~1283.2 inhabitants/km² as of the 2006 census) and it is near the metropolitan area of Onitssha which has a much higher population density (2017 projected population of 1,318,660 at +9.03%/year) and industrial activities.50 There is scanty vegetation cover in Awka, which is subject to wind erosion and consequent agricultural contamination.2-5,24,25,61 Despite poor handling of fruits at the market where they are sold, wood processing is also a common activity within the vicinity and could contribute to discrete As environmental load and the resultant high concentrations measured in fruits. Arsenate is used in wood preservation and it is converted to more toxic arsenite by incineration of wood waste.62 With the indiscriminate waste disposal system in Awka, airborne pollutants may deposit on unprotected food displayed for sale. Previous studies have demonstrated that direct atmospheric deposition of As was the dominant pathway of contamination in leafy vegetables grown proximal to a wood preservation factory.62 Arsenic is a
well known toxic element to humans with high levels of exposure. About 30%–95% of As is readily absorbed by humans when ingested, and children are more susceptible than adults to toxicity due to the lack of hepatic detoxification enzymes.

Mercury is one of the most toxic elements among the studied trace metals and exposure to high levels could permanently damage the brain, kidneys and developing fetus. Concentrations of total Hg reported in fruit samples are expected to be mostly composed of methyl Hg. The effects of public health exposure to methyl mercury are critical. Epidemiological studies on daily oral ingestion of methyl Hg concentrations as low as 0.86 µg/g/day from fish alone in expectant mothers have been correlated with neurophysiological disorders in their children by 7 years of age. The highest Hg concentration in both dry weight and wet weight was found in guava and the lowest found in orange. Although atmospheric and surface deposition is speculated to be a primary vehicle of metal mobilization, we cannot rule out the possibility that these metals were also present in the fruit samples as a result of direct uptake from soil, which has been previously reported. Furthermore, we did not wash or peel the fruit samples prior to analysis, which may have raised the observed metal concentrations levels, as processing prior to analytical determination appears to reduce metal concentrations in some studies.

The lower concentrations of Cu and Pb compared to the Codex guidelines indicates that fruits sold at the market may not have been contaminated with these metals at the time of sampling. There is lack of information on food trace metal contents in Awka and as this is the first market basket survey of fruits in this area, comparative analysis is difficult. However, the Hg concentrations measured in our work were higher than values (0.022–0.03 µg/g dw) reported in fruits collected from a Saudi Arabian market, but the fruit Cu and Pb concentrations (3.57–7.30 µg/g dw, and 2.62–6.70 µg/g dw, respectively) were ~33 and ~34× the highest Cu and Pb concentrations measured in our work, respectively. Market basket survey of some trace metals in fruits has been previously conducted in Owerri town, an area 117–121 km from Awka South, where a maximum Pb concentration of 4.33 µg/g dw was reported. The Pb level was ~21 orders of magnitude higher than the average Pb measured in our work. Interestingly, our present data on Cu and Pb concentrations in dry weight were ~11× and ~2× the maximum concentrations (0.02 and 0.13 µg/g, respectively) measured in fruits purchased from markets in the most densely populated and industrially active Nigerian city of Lagos. The observed difference in total trace metal concentrations between the published studies indicates variation in metal contaminations in response to spatial characteristics and other factors such as pollutant mobilization, deposition and or contamination rates. Although Cu is an essential element needed for biological mechanisms in both humans and animals, the measured concentrations of Pb in the examined fruits are of concern due to possible bioaccumulation and dietary toxicity. The International Agency for Research on Cancer has classified inorganic Pb compounds as probably carcinogenic to humans (Group 2A). Lead toxicity has numerous negative human health effects. For example, exposure to Pb in pre- and postnatal development periods causes delayed or reduced neurological and sexual development. Children are more susceptible than adults to the effects of Pb toxicity.

Conclusions

The present study shows that the concentrations of common metalloids and trace metals in fruits is varied and highlights the potential impact of anthropogenic activities on metal mobility, deposition, and food contamination. The elevated As and Hg concentrations measured in the fruits indicate potential dietary exposure to metals, and may be of great public health concern. Although Pb concentrations were lower than Codex standards, there is a need to investigate whether these low exposures may contribute to risks of adverse health effects given recent studies indicating health effects at relatively low concentrations. This is a pilot-based screening; larger-scale monitoring is necessary to assess fruits not included in the current survey and correlate contamination levels with metal concentrations in farm soil and atmospheric dust. Food intake assessment methods based on a more comprehensive determination of food types and consumption patterns of the local population need to be implemented and individual consumption data generated to facilitate the risk assessments of metals. Although the present investigation did not examine the effects of adulterants on imported apples, the screening system should be expanded to monitor and control their use on fruits, as there is evidence of adverse health effects associated with adulterants in the food industry. Further studies are needed to continue to improve the database on food metal contents for comparative studies. Moreover, an analytical approach for As and Hg speciation in fruits is necessary for effective food safety assessment. The development of a more robust risk communication framework is needed for better information on specific dietary exposures and food contamination.
Ezeonyejiaku, Obiakor

References

1. The importance of food quality and safety for developing countries [Internet]. Committee on World Food Security; 25th Session; 1999 May 31 – June 3; Rome, Rome: Food and Agriculture Organisation; 1999 Apr [cited 2016 Dec 11]. 13 p. Available from: http://ftp.fao.org/unfao/bodies/cfs/cfs25/X1845e.doc

2. Ezeonyejiaku CD, Obiakor MO. Metal enrichment in water and fish in a semi-urban Nigerian lake, and their associated risks. Afr J Aquat Sci [Internet]. 2016 [cited 2017 Jul 12];41(1):41-9. Available from: http://www.tandfonline.com/doi/abs/10.2989/16085914.2015.1136803 Subscription required to view.

3. Obiakor MO, Okonkwo JC, Ezeonyejiaku CD. Trace element contamination in tropical endemic fish: factorial effect interactions and in situ quantitative risk assessment. J Environ Occup Sci [Internet]. 2015 Jan-Mar [cited 2017 Jul 12];4(1):10-21. Available from: http://www.ejmanager.com/fulltextpdf.php?mno=173680

4. Obiakor MO, Okonkwo JC, Ezeonyejiaku CD, Ezenwul CO. Physicochemical and heavy metal distribution in freshwater column: season- location interaction effects and public health risk. J Life Sci Biomed [Internet]. 2013 [cited 2017 Jul 12];3(4):308-17. Available from: http://jlsb.science-line.com/attachments/article/23/f%20life%20sci%20biomed.%202013/4/20130317-%202013.pdf

5. Obiakor MO, Okonkwo JC, Ezeonyejiaku CD, Okonkwo CN. Polycyclic aromatic hydrocarbons (pahs) in freshwater media: factorial effects and human dietary exposure risk assessment. Resour Environ [Internet]. 2014 [cited 2017 Jul 12];4(6):247-59. Available from: http://article.sapub.org/10.5923%23.e.20140406.01.html

6. Food safety: what you should know [Internet]. Geneva, Switzerland: World Health Organization; 2015 Apr 7 [cited 2017 Jan 10]. [about 25 screens]. Available from: http://www.searo.who.int/entity/world_health_day/2015/whd-what-you-should-know/

7. Andras P, Turisovs I, Krnac J, Dirner V, Volekov-Lalinska B, Buccheri G, Jelen S. Hazards of heavy metal contamination at the Libe?ovac Cu- Deposit (Slovakia). Procedia Environ Sci [Internet]. 2012 [cited 2017 Jul 12];14:3-21. Available from: http://www.sciencedirect.com/science/article/pii/S187802961204720

8. Hayes RB. The carcinogenicity of metals in humans. Cancer Causes Control [Internet]. 1997 May [cited 2017 Jul 12];8(3):371-85. Available from: http://link.springer.com/article/10.1023%2FA%3A1018457305212 Subscription required to view.

9. Jarup L. Hazards of heavy metal contamination. Brit Med Bull [Internet]. 2003 [cited 2017 Jul 12];68(1):167-82. Available from: https://academic.oup.com/bmb/article/68/1/167/421303/Hazards-of-heavy-metal-contamination?searchresult=1

10. Khan S, Cao Q, Zheng YM, Huang YZ, Zhu YG. Health risks of heavy metals in contaminated soils and food crops irrigated with wastewater in Beijing, China. Environ Pollut [Internet]. 2008 Apr [cited 2017 Jul 12];152(3):686-92. Available from: http://www.sciencedirect.com/science/article/pii/S0269749010003351 Subscription required to view.

11. Wuana RA, Okieimen FE. Heavy metals in contaminated soils: a review of sources, chemistry, risks and best available strategies for remediation. ISRN Ecol [Internet]. 2011 [cited 2017 Jul 12];2011:1-20. Available from: https://www.hindawi.com/journals/ismn/2011/026467/

12. Shibata T, Meng C, Unmoren J, West H. Risk assessment of arsenic in rice cereal and other dietary sources for infants and toddlers in the U.S. Int J Environ Res Public Health [Internet]. 2016 Apr [cited 2017 Jul 12];13(4):361. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4847023/

13. Nriagu JO. Global metal pollution: poisoning the biosphere? Environ Sci Policy Sustain Dev [Internet]. 1990 [cited 2017 Jul 12];32(7):7-33. Available from: http://www.tandfonline.com/doi/abs/10.1080/00139157.1990.9929037 Subscription required to view.

14. Nriagu JO, Pacyna JM. Quantitative assessment of worldwide contamination of air, water and soils by trace metals. Nat [Internet]. 1988 May 12 [cited 2017 Jul 12];333:134-9. Available from: http://www.nature.com/nature/journal/v333/n6169/abs/333134a0.html Subscription required to view.

15. Ali MH, Al-Qahtani KM, Ali AL. Assessment of some heavy metals in vegetables, cereals and fruits in Saudi Arabian markets. Egypt J Aquat Res [Internet]. 2012 [cited 2017 Jul 12];38(1):31-7. Available from: http://www.sciencedirect.com/science/article/pii/S1687428512000839

16. Dolan LC, Matulka RA, Burdock GA. Naturally occurring food toxins. Toxins [Internet]. 2010 [cited 2017 Jul 13];2(9):2289-332. Available from: http://www.mdpi.com/2072-6651/2/9/2289

17. Shaheen N, Irfan NM, Khan IN, Islam S, Islam MS, Ahmed MK. Presence of heavy metals in fruits and vegetables: health risk implications in Bangladesh. Chemosphere [Internet]. 2016 Jun [cited 2017 Jul 13];152:431-8. Available from: http://www.sciencedirect.com/science/article/pii/S0045653516302120 Subscription required to view.

18. Taghipour H, Mosaferi M. Heavy metals in the vegetables collected from production sites. Health Promot Perspect [Internet]. 2013 [cited 2017 Jul 13];3(2):185-93. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3963666/

19. Yusuf AA, Arowolo TA, Bambose O. Cadmium, copper and nickel levels in vegetables from industrial and residential areas of Lagos City, Nigeria. Food Chem Toxicol [Internet]. 2003 Mar [cited 2017 Jul 13];41(3):375-8. Available from: http://www.sciencedirect.com/science/article/pii/S0268937002003535 Subscription required to view.

20. Norton G, Deacon C, Mestrot A, Feldmann J, Jenkins P, Baskaran C, Meharg AA. Arsenic speciation and localization in horticultural produce grown in a historically impacted mining region. Environ Sci Technol [Internet]. 2013 [cited 2017 Jul 13];47(12):6164-72. Available from: http://pubs.acs.org/doi/abs/10.1021/es400720r Subscription required to view.

21. Voutsa D, Grimanis A, Samara C. Trace elements in vegetables grown in an industrial area in relation to soil and air particulate matter. Environ Sci Pollut Res [Internet]. 2016 [cited 2017 Jul 13];23(3):325-35. Available from: http://www.sciencedirect.com/science/article/pii/S0269749116000887 Subscription required to view.

22. Kiende JI, Kawaka F, Orinda G, Okemo P. Assessment of heavy metal concentrations in urban grown vegetables in Thika Town, Kenya. Afr J Food Sci [Internet]. 2012 Feb [cited 2017 Jul 13];6(3):41-6. Available from: http://ir-library.ku.ac.ke/handle/12345678/5819

23. Zahir E, Naqvi II, Uddin SM. Market basket survey of selected metals in fruits from Karachi City (Pakistan). J Basic Appl Sci [Internet]. 2009 [cited 2017 Jul 13];5(2):47-52. Available from: https://www.researchgate.net/profile/Erum_Zahir/publication/228355837_Market_Basket_Survey_...
South China, in wild and mariculture food chains in Daya Bay, England, USA. Metal bioaccumulation by estuarine food webs in New Maine.

Sturup S, Jackson BP 27. pone.0089305 [cited 2017 Jul 13];9(2):e89305. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4186552/

38. Hughes MF, Beck BD, Chen Y, Lewis AS, Thomas DJ. Arsenic exposure and toxicology: a historical perspective. In: Nriagu JO, editor. Arsenic in the Environment. Basel, Switzerland: Springer Basel; 2012 [cited 2017 Jul 13]. p. 133-64. Available from: http://link.springer.com/book/10.1007%2F978-3-7643-8340-4_6.

39. Kapaj S, Peterson H, Liber K, Bhattacharya P. Human health effects from chronic arsenic poisoning—a review. J Environ Sci Health A Tox Hazard Subst Environ Eng [Internet]. 2006 [cited 2017 Jul 12];41(10):2399-428. Available from: http://www.tandfonline.com/doi/full/10.1080/10934520600873571 Subscription required to view.

40. Arsenic toxicity: what are the physiologic effects of arsenic exposure? Atlanta, Georgia: Agency for Toxic Substances and Disease Registry; 2009 Oct 1 [updated 2011 Oct 1; cited 2016 Mar 23]. p. 42-59. Available from: https://www.atsdr.cdc.gov/csem/arsenic/docs/arsenic.pdf

41. Some drinking-water disinfectants and contaminants, including arsenic [Internet]. International Agency for Research on Cancer Working Group on the Evaluation of Carcinogenic Risks to Humans; 2002 Oct 15-22; Lyon, France. Geneva, Switzerland: World Health Organization; 2004 [cited 2017 Jul 13]. 526 p. (vol. 84) Available from: http://monographs.iarc.fr/ENG/Monographs/vol84/index.php

42. Liu CP, Lao CL, Gao Y, Li BF, Lin LW, Wuu CA, Li XD. Arsenic contamination and potential health risk implications at an abandoned tungsten mine, southern China. Environ Pollut [Internet]. 2010 Mar [cited 2017 Jul 13];158(3):820-6. Available from: http://www.sciencedirect.com/science/article/pii/ S0269749109004813 Subscription required to view.

43. Munoz O, Diaz OP, Leyton I, Nunez N, Devesa V, Suner MA, Velez C, Montoro R. Vegetables collected in the cultivated Andean area of northern Chile: total and inorganic arsenic contents in raw vegetables. J Agric Food Chem [Internet]. 2002 [cited 2017 Jul 13];50(3):642-7. Available from: http://pubs.acs.org/doi/abs/10.1021/jf011027k Subscription required to view.

44. Sljekovec Z, van Elteren JT, Glass H-J, Jeran Z, Jasimovic R. Speciation analysis to unravel the soil-to-plant transfer in highly arsenic-contaminated areas in Cornwall (UK). Int J Environ Anal Chem [Internet]. 2010 [cited 2017 Jul 13];90(10):784-96. Available from: http://www.tandfonline.com/doi/abs/10.1080/03063109002977542 Subscription required to view.

45. Williams PN, Islam MR, Adomako EE, Raab A, Hossain SA, Zhu YG, Feldmann J, Meharg AA. Increase in rice grain arsenic for regions of Bangladesh irrigating paddies with elevated arsenic in groundwaters. Environ Sci Technol [Internet]. 2006 [cited 2017 Jul 13];40(16):4903-8. D Available

46. Li YS, Song K-H, Chung J-Y. Health effects of chronic arsenic exposure. J Prev Med Public Health [Internet]. 2014 Sep [cited 2017 Jul 13];47(5):245-52. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4186552/

47. Hong Y-S, Hong Y-S, Song K-H, Chung J-Y. Health effects of chronic arsenic exposure. J Prev Med Public Health [Internet]. 2014 Sep [cited 2017 Jul 13];47(5):245-52. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4186552/

48. Hughes MF, Beck BD, Chen Y, Lewis AS, Thomas DJ. Arsenic exposure and toxicology: a historical perspective. In: Nriagu JO, editor. Arsenic in the Environment. New York: Wiley-Interscience; 2002. Available from: http://onlinelibrary.wiley.com/doi/10.1002/0471579297.html Subscription required to view.

49. Kapaj S, Peterson H, Liber K, Bhattacharya P. Human health effects from chronic arsenic poisoning—a review. J Environ Sci Health A Tox Hazard Subst Environ Eng [Internet]. 2006 [cited 2017 Jul 12];41(10):2399-428. Available from: http://www.tandfonline.com/doi/full/10.1080/10934520600873571 Subscription required to view.

50. Arsenic toxicity: what are the physiologic effects of arsenic exposure? Atlanta, Georgia: Agency for Toxic Substances and Disease Registry; 2009 Oct 1 [updated 2011 Oct 1; cited 2016 Mar 23]. p. 42-59. Available from: https://www.atsdr.cdc.gov/csem/arsenic/docs/arsenic.pdf

51. Some drinking-water disinfectants and contaminants, including arsenic [Internet]. International Agency for Research on Cancer Working Group on the Evaluation of Carcinogenic Risks to Humans; 2002 Oct 15-22; Lyon, France. Geneva, Switzerland: World Health Organization; 2004 [cited 2017 Jul 13]. 526 p. (vol. 84) Available from: http://monographs.iarc.fr/ENG/Monographs/vol84/index.php

52. Liu CP, Lao CL, Gao Y, Li BF, Lin LW, Wuu CA, Li XD. Arsenic contamination and potential health risk implications at an abandoned tungsten mine, southern China. Environ Pollut [Internet]. 2010 Mar [cited 2017 Jul 13];158(3):820-6. Available from: http://www.sciencedirect.com/science/article/pii/ S0269749109004813 Subscription required to view.

53. Munoz O, Diaz OP, Leyton I, Nunez N, Devesa V, Suner MA, Velez C, Montoro R. Vegetables collected in the cultivated Andean area of northern Chile: total and inorganic arsenic contents in raw vegetables. J Agric Food Chem [Internet]. 2002 [cited 2017 Jul 13];50(3):642-7. Available from: http://pubs.acs.org/doi/abs/10.1021/jf011027k Subscription required to view.

54. Sljekovec Z, van Elteren JT, Glass H-J, Jeran Z, Jasimovic R. Speciation analysis to unravel the soil-to-plant transfer in highly arsenic-contaminated areas in Cornwall (UK). Int J Environ Anal Chem [Internet]. 2010 [cited 2017 Jul 13];90(10):784-96. Available from: http://www.tandfonline.com/doi/abs/10.1080/03063109002977542 Subscription required to view.

55. Williams PN, Islam MR, Adomako EE, Raab A, Hossain SA, Zhu YG, Feldmann J, Meharg AA. Increase in rice grain arsenic for regions of Bangladesh irrigating paddies with elevated arsenic in groundwaters. Environ Sci Technol [Internet]. 2006 [cited 2017 Jul 13];40(16):4903-8. D Available
71. Orisakwe OE, Nduka JK, Amadi CN, Dike DO, Bede O. Heavy metals health risk assessment for population via consumption of food crops and fruits in Owerri, South Eastern, Nigeria. *Chem Central J* [Internet]. 2012 [cited 2017 Jul 13];6(77):1-7. Available from: http://ccj.springeropen.com/articles/10.1186/1752-153X-6-77

72. Sobukola OP, Adeniran OM, Odedairo AA, Kajihausa OE. Heavy metal levels of some fruits and leafy vegetables from selected markets in Lagos, Nigeria. *Afr J Food Sci* [Internet]. 2010 Jun [cited 2017 Jul 13];4(2):389-93. Available from: http://www.academicjournals.org/article/article1380725945_Sobukola%20et%20al.pdf

73. Bost M, Houdart S, Oberli M, Kalonji E, Huneau J-F, Margaritis I. Dietary copper and human health: current evidence and unresolved issues. *J Trace Elements Med Biol* [Internet]. 2016 May [cited 2017 Jul 13];35:107-15. Available from: http://www.sciencedirect.com/science/article/pii/S0946672X16300207

74. Inorganic and organic lead compounds [Internet]. International Agency for Research on Cancer Working Group on the Evaluation of Carcinogenic Risks to Humans; 2004 Feb 10-17; Lyon, France. Geneva, Switzerland: World Health Organization; 2006 [cited 2016 May 19]. 529 p. (vol. 87) Available from: http://monographs.iarc.fr/ENG/Monographs/vol87/mono87.pdf

75. Toxicological profile for lead [Internet]. Atlanta, GA: Agency for Toxic Substances and Disease Registry; 2007 Aug [updated 2005 Sep; cited 2016 Jan 21]. 582 p. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp13.pdf

76. Jarup L. Hazards of heavy metal contamination. *Br Med Bull* [Internet]. 2003 [cited 2017 Jul 13];68(1):167-82. Available from: http://dx.doi.org/10.1093/bmbldg/032

77. Majed N, Reali III, Akter M, Azam HM. Food adulteration and bio-magnification of environmental contaminants: a comprehensive risk framework for Bangladesh. *Front Environ Sci* [Internet]. 2016 May 18 [cited 2017 Jul 13];4(34):1-21. Available from: http://journal.frontiersin.org/article/10.3389/fenvs.2016.00034