AFRICA ENVIRONMENTAL REVIEW Journal

ISSN: 1727-8341

AER Journal Volume 3, Issue 1, pp. 43-50, 2018

RESEARCH ARTICLE

Available Online at *http://www.aer-journal.info*

Heavy Metal Content in Scalp Hair of People Living in Fluorspar Mining Belt in Elgeyo Marakwet County, Kenya

J. N. Kemboi Olero[1*], G. M. Simiyu[1], E. C. Kipkorir[2] and J. Wakhisi[3]

[1]*Department of Biology and Health School of Environmental Studies, University of Eldoret, P.O Box 1125-30100 Eldoret, Kenya*

[2]*School of Engineering, Moi University, P.O Box 3900-30100 Eldoret, Kenya*

[3]*Department of Biochemistry, School of Medicine, Moi University, P.O. Box 4606-30100 Eldoret, Kenya*

Abstract

Human hair is a stable matrix that presents many advantages as a bioindicator of exposure to contaminants. Levels of Arsenic, Cadmium, Chromium and Lead in scalp hair of people in Upper, Middle and Lower Kimwarer zones in Fluorspar mining belt were determined using the Atomic Absorption Spectrophotometer (AAS) for Cadmium, Chromium and Lead but for Arsenic, Vapour Generating Atomic, Absorption Spectrophotometer was used. The levels of the heavy metals were discussed basing on their concentrations in food crops and water consumed by the inhabitants within the mining belt. Results showed the highest level of the metals was Pb, with an average concentration of 2.83±0.50mg/kg, followed by Cr (2.81±0.62 mg/kg), As (2.73±0.50 mg/kg), and Cd (1.53±0.28 mg/kg), following a decreasing order of Pb > Cr > As > Cd. Arsenic and Lead concentration in Upper and Lower Kimwarer and in Middle and Lower Kimwarer results showed a significant difference in ($p<0.05$, $\alpha=0.05$). Cadmium and Chromium levels in all the sites had no significant difference $p=0.133$ and $p=0.290$ respectively. There was, however a significant correlation ($p<0.01$) between Pb concentration in milk and the Pb levels in scalp hair. This study provides information on levels of heavy metals in hair which implies their exposure occurred through ingestion of contaminated maize, beans, millet, water and milk in the study area. Given heavy metal levels in the scalp hair the people living within the mining belt could be at risk of adverse health risks from heavy metal exposure. Therefore, the results of this study can be used to analyze the internal heavy metal burden in the resident population of Kimwarer sub-catchment and can also serve as reference for further studies.

Key Words: Mining, Heavy Metals, Hair

INTRODUCTION

Globally, heavy metals have been found to be widely distributed in different environmental media that include soil, water, air and food crops (Haiyan and Stuanes, 2003; Granero and Domingo, 2002; Nadal *et al.*, 2005). These heavy metals enter the human body through several pathways such as inhalation of dust, dermal contact, and ingestion of contaminated food and water (Tchounwou *et al.*, 2004; Nikolaids *et al.*, 2012). Numerous investigations have established the link between heavy metal levels in soil-plant-food that pose a major risk to the health of the people exposed to those contaminants (Hough, *et al.*, 2004; Baastrup, *et al.*, 2008). The most dangerous and pernicious forms of pollution arise from the potential mobilization of a spectrum of toxic trace metals and metalloids in our environment. The heavy metals that are broadly distributed in the environment and originate from anthropogenic and natural sources are becoming major environmental pollutants as their concentration increases due to industrial waste and sewage discharge (Bystricka & Thomas, 2009) (Jan *et al*., 2015). The toxic effects of metals depend on the forms and routes of exposure, interruptions of intracellular homeostasis such as the damage to lipids, proteins, enzymes and DNA through the production of free radicals. Following exposure to heavy metals, their metabolism and subsequent excretion from the body depends on the presence of antioxidants associated with the quenching of free radicals by suspending the activity of enzymes (Manish *et al*., 2014; Jan *et al*., 2015).

Exposure to metals may result in adverse health effects, and national and international health agencies have methodologies to set health-based guidance values with the aim to protect the human population (Dorne, *et al.,* 2011). Heavy metal in hair was determined by the human bio-monitoring technique of measuring the concentration of natural and synthetic compounds in the tissues for information on environmental exposures and identifying potential health risks (Cutler, 2004; Alamdar, *et al*., 2016). For metal toxicity monitoring and environmental risk assessment, the identification of heavy metals from biological samples such as blood, urine or hair is useful for identifying exposure. The heavy metal levels in hair sample were assessed to establish the long-term exposure of the measured contaminant (Qu *et al*., 2012).

Arsenic is a widely occurring environmental contaminant. Bio-monitoring for As in hair has been used in many studies and is particularly useful in evaluating chronic exposures to Arsenic. Studies show that interpreting the health implications of As concentrations in biological samples is limited by the small number of studies that provide information on the correlation and dose-response relationship between bio-monitoring test results and adverse health effects (Yoshida *et al.,* 2004).

Bioavailability of ingested Cadmium has been confirmed in studies of persons with elevated dietary exposure (Schlekat *et al.,* 2000). Moreover, the findings have been strengthened by the substantial amounts of Cadmium accumulated in kidneys, eyes, and other tissues and organs of environmentally exposed individuals (Satarug *et al.,* 2009). Most persons are in an approximate Cadmium balance and tend to excrete Cadmium until approximately age 50, after which a negative balance ensues (Ryan *et al*., 1982; Bernard, 2008). The correlation of metal concentrations in hair with those in the critical organs was investigated by tracer studies using ^{51}Cr and ^{109}Cd in mice. Hair was found to be a poor indicator of Cadmium contamination, as the concentration of Cd in hair was not parallel to that in the critical organs of the experimental animal, the mouse

Different countries have put in place systems and agencies that have sets regulatory limits for the amounts of certain contaminants in water and food to protect public health. These include Environmental Protection Agency (EPA), Food Agricultural Organization (FAO) and Kenya Bureau Standards (KEBS) in Kenya. The law in Kenya provides that the set water quality standards should not place the health of the public customers at risk hence the need for compliance to these set provisions. The stringent environmental laws in industrialized countries, contamination levels of public concern are often too low to cause an increase in the incidence of disease that is large enough to be detected by epidemiological studies. Thus, the determination of biomarkers of exposure is a more appropriate method of assessment than to take the respective diseases as an endpoint (Yüksel *et al*., 2018). Hair samples have been widely used to assess human exposure to different contaminants because of its many advantages (Tatsy, 2015). Agusa *et al.,* (2005) had similar results on exposure to Arsenic through drinking contaminated groundwater.

MATERIALS AND METHODS

Ethical Consideration

A formal approval to carry out research (FAN: IREC 1649) was granted by Moi University, School of Medicine at the Institute of Research and Ethics Committee.

Study Area

The study was carried out in Fluorspar mining area in Kimwarer sub-catchment. The mining activities carried out by the company are excavation, transportation and processing of the mineral ore to obtain the Fluorspar which has been going on since 1970s. Kimwarer sub-catchment is located partly in two divisions of Soy and Metkei in Elgeyo Marakwet County. The sub-catchment was divided into three topographical zones that are the Highlands (Upper Kimwarer), the Escarpment (Middle Kimwarer) and Kerio Valley (Lower Kimwarer). The zones were selected on the basis of the distances or the proximity to the mining belt. Upper Kimwarer is the farthest zone, about 20-25 km on the windward direction while Middle Kimwarer is 10-15 Km from the mining site. The Elgeyo escarpment separates the Upper from Lower Kimwarer zone. The geographical locations of the three sampled zones are shown in Figure 1.

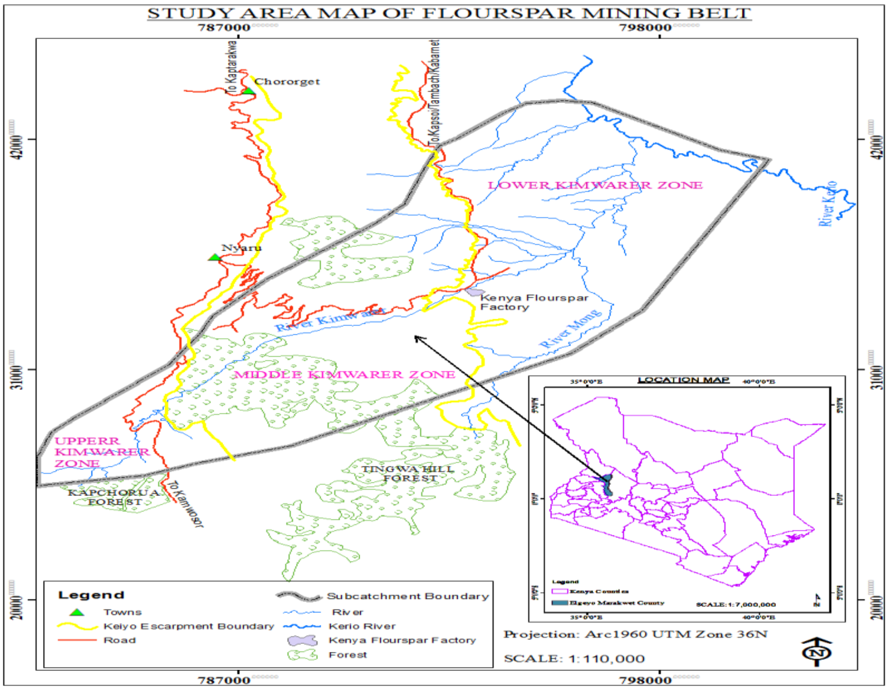

Figure 1. Map of Fluorspar Mining Belt 2018

Sampling, Transportation and Analysis

Hair samples (30 pieces) were obtained from the people at the barber salons. The scalp hair samples collected were for men above 18 years old. The hair samples were taken from the nape of the neck. A total of 30 scalp hair samples of approximately125 milligrams or one full teaspoon of scalp hair each were collected during the study period with 10 scalp hair samples from each zone; Upper, Middle and Lower Kimwarer. The scalp hair samples were put in envelopes after collecting sufficient weight of dry hair and stored in the laboratory awaiting analysis.

Samples of human hair weighing 20 mg were washed twice with a mixture of ethyl ether/Acetone and then de-ionised water and dried on a clean paper. Once dry the hair was cut into 2-4 cm lengths weighed 0.5 gm and put into a digestion block test tubes. 2ml of nitric acid and 1ml of H_2O_2 were added and heated at 160°C for 4hrs following (Gang liang *et al.*, 2017) procedure. The digest was transferred into a 25 ml volumetric flask and was filled to 25 ml mark by adding de-ionized water then analyzed using the Atomic Absorption Spectrophotometer (AAS Model Spectra 10/20) analysis for Cd, Cr and Pb. Arsenic was analyzed using Atomic Absorption Spectrophotometer coupled with Vapour generating component.

Quality Control

All the procedures were strictly followed in order to produce quality results. These included the use of high purity analytical grade acids in cleaning and preparation of samples. Calibration of the equipment was done after every batch of the analysis. The contamination of the analysis using AAS was checked using the analysis of blank samples. The readings obtained from the blanks were subtracted from all the concentrations obtained from the analyses.

RESULTS AND DISCUSSION

Concentration of Selected Heavy Metals in Human Hair

The study established that there were traces of As, Cd, Cr and Pb in the sampled human hair in Upper, Middle and Lower Kimwarer zones. The results showed a significant difference in Arsenic concentration Upper and Lower Kimwarer and also in Middle and Lower Kimwarer ($p>0.05$, t-test, $\alpha=0.05$). Cadmium and Chromium levels in all the sites had no significant difference with $p=0.133$ and $p=0.290$, respectively. Lead had a significant difference of $p<0.001$ between the Upper and the Lower and also with the Upper Kimwarer and Lower Kimwarer zones.

Table 1. Concentration of Arsenic, Cadmium, Chromium and Lead Metals in Human Hair

Zone	Statistic	As (mg/kg)	Cd (mg/kg)	Cr (mg/kg)	Pb (mg/kg)
Upper Kimwarer	Mean	0.04 ± 0.01^{a}	0.55 ± 0.21^{a}	1.25 ± 0.37	0.16 ± 0.07^{a}
	Minimum	0.01	0.01	0.04	0.001
	Maximum	0.07	2.08	3.65	0.59
Middle Kimwarer	Mean	0.18 ± 0.03^{a}	1.26 ± 0.33^{b}	2.07 ± 0.42	0.53 ± 0.30^{a}
	Minimum	0.07	0.02	0.23	0.01
	Max	0.30	2.54	4.97	0.30
Lower Kimwarer	Mean	2.73 ± 0.50^{b}	1.53 ± 0.28^{a}	2.81 ± 0.62	2.83 ± 0.50^{b}
	Minimum	0.02	0.03	0.03	0.02
	Maximum	9.22	4.66	12.93	9.22
P-value		<0.001	0.133	0.290	<0.001

Mean values followed by the same small letter within the same row do not differ significantly from one another (one-way ANOVA, SNK, $\alpha=0.05$).

The minimum and maximum concentrations of As in hair in the three zones were 0.01 mg/kg at Upper Kimwarer and 9.22 mg/kg respectively. The concentrations of Cd in human hair had a minimum 0.01mg/kg at Upper Kimwarer and maximum 4.66 mg/kg at Lower Kimwarer respectively. Chromium levels in human hair in the study area were 0.23 mg/kg in Upper Kimwarer and 12.93 mg/kg in Lower Kimwarer for minimum and maximum respectively. For Pb metal, the minimum and maximum concentrations in all zones were 0.001mg/kg and 9.22 mg/kg in Upper and Lower Kimwarer respectively. The lowest minimum concentration was Cr 0.04 mg/kg at the Upper Kimwarer while the highest maximum metal concentration was Cr 12.93 mg/kg in Lower Kimwarer zone. The lowest metal mean concentration was As 0.04±0.01mg/kg at the Upper Kimwarer while the highest metal mean concentration was Pb 2.83±0.50 mg/kg in Lower Kimwarer zone. The metal concentrations in the human hair were higher in the exposed zone (Middle and Lower Kimwarer) compared to the unexposed (Upper Kimwarer) zone.

The order of heavy metals in Upper Kimwarer was Cr>Cd>Pb>As, in Middle Kimwarer was Cr>Cd>Pb>As and Mean concentration was Pb>Cr>As>Cd in Lower Kimwarer. The descending order of the metal mean concentration in Lower Kimwarer was similar to order in Xiangtan inhabitants in China (Ni *et al.,* 2011). Considering the zones, all the metals starting with the zone with the highest was Lower Kimwarer>Middle>Upper Kimwarer, for Cadmium Lower. This indicates that the Lower Kimwarer which is located near the mines had the highest concentrations of all the heavy metals while the Upper zone which is the farthest from the mining site.

A study in Turkey showed a significant positive correlation between hair chromium concentrations and urinary chromium / creatinine ratios in workers working in a tannery indicating that urinary chromium excretion can be used as an indicator of chromium exposure (Saner *et al.,* 1984). This implies that the presence of the heavy metals in the hair could also indicate possibilities of people suffering from diseases that are associated with heavy metal toxicity.

An evaluation of the use of human hair for bio-monitoring the deficiency of essential and exposure to toxic elements indicated that there was a weak correlation (r=0.22, p<0.001) between Pb levels in hair and blood (Rodrigues *et al*., 2008). The findings also suggested that while the idea of measuring trace elements in hair is attractive, hair is not an appropriate biomarker for evaluating Pb exposure. Saad and Hassanie (2001) in a study on As level of hair samples of apparently healthy Egyptian found levels ranging from 0.04 to 1.04 mg As/kg hair of which about 55% of the analyzed hair samples were within the range of allowable values (0.08–0.25 mg As/kg hair). The study concluded that As levels in water at concentrations of 100 µg/liter or less seem not to produce an undue body burden.

Previous studies (Qu *et al*. 2012), showed that hair sample are useful assessment tool in characterizing long-term exposure of the measured contaminant though with some challenges. Interpreting the health implications of As concentrations in biological samples is limited by the small number of studies that provide information on the correlation and dose-response relationship between bio-monitoring test results and adverse health effects (Orloff, Mistry, and Metcalf, 2009). Hair also was found to be a poor indicator of Cd contamination, as the concentration of Cd in hair was not parallel to that in the critical organs of the experimental animal, the mouse (Matsubara and Machida, 1985).

The level of Arsenic in hair was above the minimal limit of As (0.02-0.5g/kg) in all the zones except in Upper Kimwarer which had an average of 0.04±0.01 g/kg. Chromium concentrations in hair were above maximum limit of Cr (0.03-1.88 g/kg) in Upper, Middle and Lower Kimwarer. Lead concentrations in Upper and Middle were below the upper limit of (0.03-1.4 g/kg) while Lower Kimwarer was (2.83±0.50 g/kg) hence above the recommended levels by India, Japan and England reference as stated by (Ngure *et al.,* 2017).

The study by (Olero *et al.* 2018) showed that Arsenic, Cadmium, Chromium and Lead were present in water, milk, maize, beans and millet in Upper, Middle and Lower Kimwarer zones. The presence of heavy metals in hair is an indication of exposure to heavy metals through multiple pathways that include inhalation, ingestion or dermal routes. The relationship of the concentrations of Arsenic in soil, water, food and hair is shown in Table 2.

Table 2. Pearson' Correlations between Intake and Hair Levels of Studied Population

	Heavy Metal Concentration in Hair (mg/kg)			
Media	**As**	**Cd**	**Cr**	**Pb**
Water	-0.006	0.078	-0.098	-0.053
Milk	0.070	0.216	-0.085	0.403**
Maize	0.083	-0.018	0.026	-0.024
Beans	0.009	-0.047	-0.233	-0.059
Millet	-0.265	-0.186	-0.137	-0.11

** Correlation is significant at the 0.01 level (2-tailed)
* Correlation is significant at the 0.05 level (2-tailed).

In Kimwarer sub-catchment concentration of Arsenic in hair had an insignificant positive correlation to Arsenic concentrations in milk r = 0.070, maize r = 0.083 and beans r = 0.009 and a negative insignificant correlation to Arsenic concentrations in water and millet r = 0.006 and r = 0.265 respectively. The concentration of Cd in hair had an insignificant negative correlation to maize, beans and millet p>0.05. The concentration of Cd in hair had an insignificant negative correlation to maize, beans and millet p>0.05. Chromium in hair had an insignificant positive correlation to maize and a negative insignificant correlation to water, milk and millet (p> 0.01) (2-tailed) Lead in hair had a significant positive correlation (p<0.05) to milk (r=0.403) and a negative insignificant correlation (p>0.05 to water, maize and beans.

In summary, the correlations showed a weak significant correlation (p=0.403) between Pb concentration in milk and the Pb levels in hair. This implies that the heavy metal content in hair do not correspond to the concentrations of the heavy metals in maize, beans, millet, milk and water ingested. Previous studies by (González-Muñoz et al., 2008) had similar results where the studied metals had insignificant correllation and the heavy metals in hairexcept for Cadmium which had a weak negative correlation.

CONCLUSION

1. The higher levels of Arsenic, Cadmium, Chromium and Lead in scalp hair of people living in Lower Kimwarer compared to those living in Upper Kimwarer shows that the heavy metal levels could be linked to mining activities.
2. There was a significant correlation (p<0.01) between Pb concentration in milk and the Pb levels in scalp hair.
3. The order of heavy metals in Upper and Middle Kimwarer had the same order in concentrations Cr>Cd>Pb>As while the Lower Kimwarer was Pb>Cr>As>Cd.
4. An analysis of the correlations between heavy metal consumed through ingestion and scalp hair concentrations indicated that hair levels cannot be considered as a suitable biological indicator of the exposure to toxic elements through the diet. However, further researches are needed to determine the importance of using hair as a marker of heavy metal consumption through diet.

REFERENCES

Agusa, T., Kunito, T., Iwata, H., Monirith, I., Tana, T. S. and Subramanian, A. (2005). Mercury contamination in human hair and fish from Cambodia: levels, specific accumulation and risk assessment. *Environmental Pollution, 134* (1), 79-86.

Alamdar, A., Eqani, S. A., Ali, S. W., Sohail, M., Bhowmik, A. K. and Cincinelli, A. (2016). Human Arsenic exposure via dust across the different ecological zones of Pakistan. *Ecotoxicology and environmental safety, 126*, 219-227.

Albering, V. L. (1999). Human health risk assessment: A case study involving heavy metal soil contamination after the flooding of the river Meuse during the winter of 1993–1994. *Environmental Health Perspective 107:37-43*, 107:37-43.

Baastrup, R., Sørensen, M., Balstrøm, T., Frederiksen, K., Larsen, C. L. and

Tjønneland, A. (2008). Arsenic in drinking-water and risk for cancer in Denmark. *Environmental Health Perspective*, 116: 231.

Bernard, A. (2008). Cadmium and its adverse effects on human health. *Indian Journal of Medical Research, 128* (4), 557.

Cutler, A. (2004). *Hair test interpretation: finding hidden toxicities.*

Dorne, J.-L. C., Kass, G. E., Bordajandi, L. R., Amzal, B., Bertelsen, U. and Castoldi, A. F. (2011). Human risk assessment of heavy metals: principles and applications. *Journal of Metal Ions Life Science., 8*, 27-60.

Granero, S. and Domingo, J. L. (2002). Levels of metals in soils of Alcalá de Henares, Spain: human health risks. *Environmental International Journal, 28* (3), 59-164.

Grusak, M. A. and DellaPenna, D. (1999). Improving the nutrient composition of plants to enhance human nutrition and health. *Annual review of plant biology,, 50* (1), 133-161.

Haiyan, W. and Stuanes, A. O. (2003). Heavy metal pollution in air-water-soil-plant system of Zhuzhou City, Hunan Province, China. . *China. Water Air Soil Pollution., 147* (1-4), 79-107.

Hough, R. L., Breward, N., Young, S. D., Crout, N. M., Tye, A. M. and Moir, A. M. (2004). Assessing potential risk of heavy metal exposure from consumption of home-produced vegetables by urban populations. *Environmental Health Perspective, 112* (2), 215.

Hussain, A. L. (2012). Concentration of some heavy metals in organically grown primitive, old and modern wheat genotypes: Implications for human health. . *Journal of Environmental Science and Health,* , Part B, 47 (7), 7.

Jan, A. T., Azam, M., Siddiqui, K., Ali, A., Choi, I. and Haq, Q. M. (2015). Heavy metals and human health: mechanistic insight into toxicity and counter defense system of antioxidants. *International journal of molecular sciences,, 16* (12), 29592-29630.

MacIntosh, D. L., Spengler, J. D., Ozkaynak, H., Tsai, L., and Ryan, P. B. (1996). Dietary exposures to selected metals and pesticides. *Environmental Health Perspective, 104* (2), 202.

Man YB, S. X. (2010). Health risk assessment of abandoned agricultural soils based on heavy metal contents in Hong Kong, the world's most populated city. . *Environmental international journal*, 36: 570–576.

Mari M, N. M. (2009). Exposure to heavy metals and PCDD/Fs by the population living in the vicinity of a hazardous waste landfill in Catalonia, Spain: Health risk assessment. *Environmental Iternational Journal*, 35: 1034– 1039.

Manisha J, Tenzin T, Narish A, Blessy B. M. and Krishnamurthy, N. B. (2014). Toxicity Mechanism and Health effects of some Heavy Metals. *Interdisciplinary Toxicology* , Vol 7 (2), 62-70.

Matsubara, J. and Machida, K. (1985). Significance of elemental analysis of hair as a means of detecting environmental pollution. *Environmental Research, 38* (2), 225-238.

Nadal, M., Bocio, A., Schuhmacher, M. and Domingo, J. (2005). Trends in the levels of metals in soils and vegetation samples collected near a hazardous waste incinerator. *Archiecture of Environmental Contamination Toxicology, 49* (3), 290–298.

Ni, S., Li, R., and Wang, A. (2011). Heavy metal content in scalp hair of the inhabitants near Dexing Copper Mine, Jiangxi Province, China. *Science China Earth Sciences, 54* (5), 780-788.

Nikolaidis, C., Orfanidis, M., Hauri, D., Mylanos, S. and Constantinidis, T. (2012). Public health risk assessment associated with heavy metals and arsenic exposure near an abandoned mine(Kirki,/Greece). *International Journal of Environmental Health Research* .

Orloff, K., Mistry, K. and Metcalf, S. (2009). Biomonitoring for environmental exposures to arsenic. *Journal of Toxicology and Environmental Health, Part B, 12* (7), 509-524.

Olero, N. K. J., Simiyu, M. G., Kipkorir, C. E. and Wakhisi, J. (2018). Cancer Risks Associated with Arsenic, Cadmium, Chromium and Lead in Flourspar Mining Belt Elgeyo Marakwet County, Kenya. Eldoret: University of Eldoret.

Qu, C. S., Ma, Z. W., Yang, J., Liu, Y., Bi, J. and Huang, L. (2012). Human exposure pathways of heavy metals in a lead-zinc mining area, Jiangsu Province, China. *PloS one, 7* (11), e46793.

Risher, J. F. (2002). Organic mercury compounds: human exposure and its relevance to public health. . *Toxicology and industrial health,*, 18 (3), 109-160.

Rodrigues, J. L., Batista, B. L., Nunes, J. A., Passos, C. J. and Barbosa Jr, F. (2008). Evaluation of the use of human hair for biomonitoring the deficiency of essential and exposure to toxic elements. *Science of the Total Environment, 405-1-3*, 370-376.

Rodríguez-Gil., H. R. (2018). Analysis of lipid peroxidation in animal and plant tissues as field-based biomarker in Mediterranean irrigated agroecosystems (Extremadura, Spain). *Journal of Environmental science and health, part B,*, Parrt B, 1-13.

Ryan, J. A., Pahren, H. R. and Lucas, J. B. (1982). Controlling cadmium in the human food chain: a review and rationale based on health effects. *Environmental Research, 28* (2), 251-302.

Saner, G., Yüzbasiyan, V. and Cigdem, S. (1984). Hair chromium concentration and chromium excretion in tannery worker. *Occupational and Environmental Medicine, 41* (2), 263-266.

Satarug, S., Garrett, S. H., Sens, M. A. and Sens, D. A. (2009). Cadmium, environmental exposure, and health outcomes. *Environmental Health Perspectives, 118* (2), 182-190.

Schlekat, C. E., Decho, A. W. and Chandler, G. T. (2000). Bioavailability of particle-associated silver, cadmium, and zinc to the estuarine amphipod Leptocheirus plumulosus through dietary ingestion. *Limnology and Oceanography, 45* (1), 11-21.

Tchounwou, P., Clement G. Y., Patlolla, A. K. and Dwayne J. S. P. C. (2012). Arsenic toxicity, mutagenesis, and carcinogenesis- a health risk assesment and management approach. *Mollecula and Cellular Biochemistry, 255(1-2),* , 47-55.

Yoshida, T., Yamauchi, H. and Sun, G. F. (2004). Chronic health effects in people exposed to arsenic via the drinking water: dose–response relationships in review. *Toxicology and Applied Pharmacology, 198* (3), 243-252.

Yüksel, B., Şen, N., Türksoy, V. A., Tutkun, E., and Söylemezoğlu, T. (2018). Effect of exposure time and smoking habit on arsenic levels in biological samples of metal workers in comparison with controls. *Marmara Pharmaceutical Journal, 22* (2).