

Research article

Lead and cadmium blood levels and transfer to milk in cattle reared in a mining areaDoris Maritza Chirinos-Peinado^{*}, Jorge Isaac Castro-Bedriñana

School of Animal Husbandry, Universidad Nacional del Centro del Perú, Av. Mariscal Castilla N° 3909, El Tambo, Junín, Huancayo, Peru

ARTICLE INFO

Keywords:
 Food science
 Food safety
 Agriculture
 Food analysis
 Nutrition
 Zoology
 Environmental science
 Toxicology
 Public health
 Heavy metals
 Cow milk
 Smelting
 Codex alimentarius
 Maximum permissible limit

ABSTRACT

The presence of heavy metals in milk is a public health problem that negatively effects human health, especially infant health. This study evaluated the concentration levels of lead (Pb) and cadmium (Cd) in blood and its transfer to the milk of 20 cows in production in a rural community near the La Oroya Metallurgical Complex in Peru, which has emitted fine particulate matter for more than 90 years. Validated protocols were used for sample collection. The samples were analyzed by atomic absorption spectrophotometry. The results of the analysis indicated that the levels, in mg/kg, of Pb in blood and milk were 0.38 ± 0.041 and 0.58 ± 0.018 , respectively; Pb in milk was 54% higher than that in blood ($P < 0.01$). Cd levels, in mg/kg, in blood and milk were 0.016 ± 0.002 and 0.02 ± 0.007 , respectively; milk had 28% more Cd than did blood ($P < 0.05$). The results for Pb in milk were compared with the Codex Alimentarius standard (0.002 mg/kg); the mean concentration of Pb in milk was 29 times higher than the acceptable limit, and the mean concentration of Cd was 2 times higher than the acceptable limit of the Romanian standard (0.01 mg/kg). The result could be attributed to the impact of environmental pollution by mining waste. In Peru, there are no norms for maximum Pb and Cd values, and the establishment of maximum value norms for these metals in milk is suggested.

1. Introduction

Air pollution by fine particulate matter (PM) is a risk factor for morbidity and mortality around the world (Gakidou et al., 2017). PM emitted by the metallurgical industry, due to its strong adsorption capacity, can adsorb to, combine with and transport heavy metals and other toxic substances (Dergham et al., 2012). PM-bound heavy metals are mobilized by air and deposited in irrigation water and in agricultural/grazing soils, and the heavy metals are transferred to plants and other parts of the ecosystem, entering the trophic chain (Yilmaz et al., 2009; Alloway, 2013) and affecting animal and human health due to their high toxic potential (Lokeshwari and Chandrappa, 2006; Castro et al., 2013, 2016).

In the ecosystem, heavy metals can geoaccumulate, bioaccumulate or biomagnify (Lokeshwari and Chandrappa, 2006; Beltrán and Gómez, 2014). The bioaccumulation of Pb and Cd and their transfer to the food chain affects food safety and innocuousness (Nava-Ruiz and Méndez-Armenta, 2011; Tchounwou et al., 2012; Castro et al., 2013), and their consumption puts human health at risk (Nava-Ruiz and

Méndez-Armenta, 2011; CDC, 2012; Counter et al., 2012; Castro et al., 2016; Tepanosyan et al., 2017).

In Peru, mining-metallurgical activity generates 20% of all tax revenue and is located mainly in the Andean highlands and midlands (Delgado, 2016), where livestock farming is also conducted, thus exposing livestock to the impact of mining-metallurgical activity (Alvarez-Berrios et al., 2016). In communities near the La Oroya Metallurgical Complex, Andean livestock is produced and sustained in pastures exposed to contamination by heavy metals, especially Pb and Cd, which are dynamically transferred to milk (Skipin et al., 2016; González-Montaña, 2009), and thus, their quantification and impact on biological systems is important (Léopold et al., 2016).

The objective of this study was to evaluate the Pb and Cd concentrations in blood samples from cows raised at the Paccha-La Oroya Rural Community (PRC) and the transfer of Pb and Cd to milk. These data can provide scientific evidence of the suitability of milk produced under these conditions for human consumption.

* Corresponding author.

E-mail address: dchirinos@uncp.edu.pe (D.M. Chirinos-Peinado).

2. Materials and methods

2.1. Study site and period

This study was conducted in May 2018 in the barn of the PRC, 11°31'03" South latitude and 75°53'58" West longitude, encompassing an area of 323.7 km², at an altitude of 3742 m and with minimum and maximum temperatures of -3.1 and 18.2 °C, respectively. The PRC has natural pastures composed mainly of grasses of low nutritional value of the genera *Festuca*, *Piptochaetium*, *Bromus* and *Calamagrostis*, where cattle and sheep are raised.

The PRC is located 10.2 km from the largest metallurgical complex in Peru, where copper, zinc, silver, lead, indium, bismuth, gold, selenium, tellurium and antimony are mined and processed and where, for more than 90 years, smoke and PM-bound heavy metals have been emitted, contaminating ecosystems (Barrios-Napuri, 2008; Alvarez-Berrios et al., 2016). This fine PM, rich in Pb, Cd and other heavy metals, is deposited in the soil and in irrigation water and transferred to plants (Peláez-Peláez et al., 2016; Olayinka et al., 2017) that are the source of food for cattle raised in the High Andean Zone, close to the metallurgical complex.

The chemical analyses were performed at Baltic Control SAC, a laboratory accredited by the Accreditation Directorate of the National Institute of Quality (Instituto Nacional de Calidad – INACAL), Peru.

2.2. Population and biological samples

The population consisted of dairy cows from the PRC. The sample consisted of 20 lactating Criollo cows, aged 4–6 years (first or second lactation), accounting for 74% of the cows available at the PRC. Older animals were excluded. A total of 10 ml of blood was collected from the coccygeal vein into heparinized vacutainer tubes, following the procedure of Zambrano and Díaz (2014). Additionally, 500 ml of milk per cow was manually extracted during the morning milking and stored in labeled never-used polyethylene bottles previously washed with bidistilled water, following the protocol of Rodríguez et al. (2005). The samples were placed in styrofoam boxes at -4 °C and transported to the laboratory for analysis.

2.3. Chemical analysis

For the analysis of Pb and Cd in blood and milk, a flame atomic absorption spectrophotometer (NAMBEI AA320N) was used according to the reference standard (Latimer, 2016) and to the laboratory's internal methodology. For the digestion of the blood and milk samples, specific procedures were followed. For blood, 10 µl of the sample was digested with repeated additions of nitric acid (0.5% HNO₃) at a drying temperature, and subsequently, hydrogen peroxide (H₂O₂) attack was performed. Hot digestion was performed, the solution was filtered with Whatman No. 40 filter paper, and the volume was adjusted with bidistilled water.

For milk, 50 g of raw milk was placed in 100-ml porcelain crucibles for drying in an oven at 100 °C to constant weight and then placed in a muffle furnace at 450 °C for 16 h. The incinerated samples were cooled and bleached with 2 ml of 2N HNO₃ and dried on a thermostatic plate. The acid was evaporated, and the samples were reincinerated in a muffle furnace at 450 °C for 1 h. For ash recovery, 5 ml of 2N HNO₃ and 20 ml of 0.1N HNO₃ were used. The samples were filtered using Whatman No. 40 filter paper and stored in polypropylene tubes under refrigeration.

The wavelengths for the quantification of Pb and Cd were 283.3 nm and 228.8 nm, with detection limits of 0.045 and 0.002 mg/kg, respectively.

Standards of 1000 mg/kg were used to generate the calibration curves. The data from the standard solutions for Pb and Cd in the blood samples were 100 ± 0.01 and 100 ± 0.02 mg/kg, respectively, and those for the milk samples were 155 ± 0.04 and 150 ± 0.05 mg/kg, respectively. All standards were acquired from Sigma-Aldrich. The precision of the instrumental methods and analytical procedures was verified by running the samples in duplicate. The high and low range for the blank

(BK), duplicate sample (DS) and control standard (CS) were determined for every 15 samples. The concentrations of each element are expressed in mg/kg.

2.4. Statistical analysis

The results are expressed as the mean ± standard deviation (n = 20). To determine statistically significant differences in the concentration of Pb and Cd in blood and milk, samples were compared using the t test for paired samples. P < 0.05 was adopted as the significance level. Regression analysis was performed for Pb and Cd concentrations in blood and milk. All analyses were performed in SPSS v.23.

2.5. Bioethical aspects

The animals were treated responsibly and respectfully during the study. Blood sampling was performed by qualified and experienced staff, avoiding unnecessary injury and stress to the animals. The study was reviewed and approved by the Specialized Research Institute of the School of Zootechnics of the National University of the Center of Peru (Universidad Nacional del Centro del Perú) and was authorized by the PRC's Assembly.

3. Results

3.1. Pb concentration in the blood and milk of cows raised at the PRC

The mean concentration of Pb in the analyzed milk samples was significantly (p ≤ 0.01) higher than the levels determined in the blood (Table 1, Figure 1).

Pb in milk was 154% higher than that in blood, equivalent to a transfer factor (TF) of 1.54 ± 0.189. The correlation between the Pb content in blood and milk was -0.193 (p = 0.416), which indicated that the higher the concentration of Pb in the blood, the lower the concentration in the milk, which would be an indication that the mammary gland functions as a barrier to the transfer of Pb from blood to milk, which warrants further study.

3.2. Cd concentration in the blood and milk of cows raised at PRC

The mean Cd concentration in the milk samples was higher (p ≤ 0.05) than that in blood (Table 2, Figure 2).

The Cd in milk samples was 128% higher than that in blood, equivalent to a TF of 1.283 ± 0.553. The correlation between Cd concentration in blood and milk was -0.249 (p = 0.290), also indicating the probable barrier action of the mammary gland.

Figure 3 shows the box plot for the TFs of Cd and Pb from the blood to the milk of cattle raised near a metal smelting zone. A less variable distribution was observed for Pb than for Cd, for which the maximum and minimum values were more dispersed.

4. Discussion

This study was conducted because of the lack of scientific evidence on the concentrations of Pb and Cd in cow milk in areas close to metal smelting activities. It is therefore important for public health, and the results could serve as an indicator of the quality of milk for human consumption.

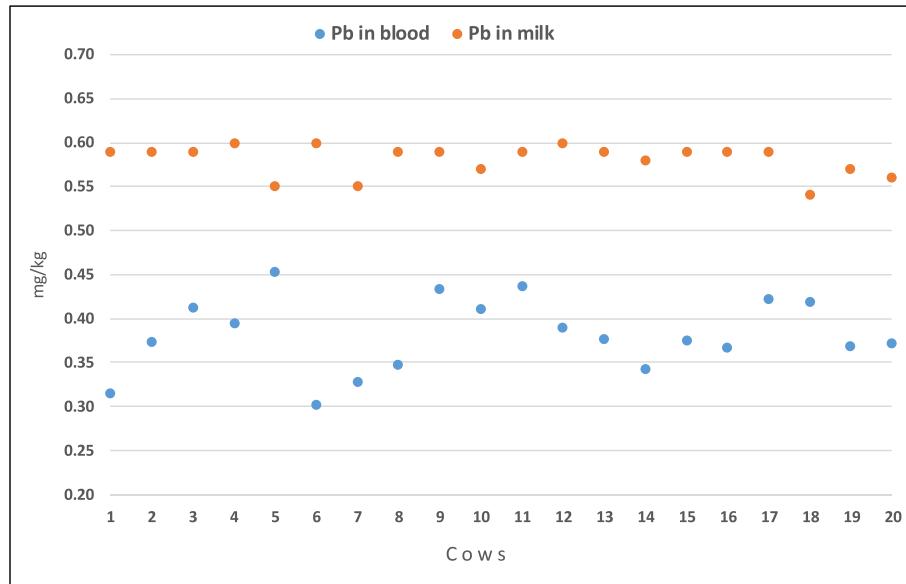
The reference values for mean Pb and Cd concentrations in the blood of cows in production are, respectively, 0.5 and 0.05 mg/kg (Codex Standard, 2010; CEE, 2006), and in the present study, these concentrations were 0.38 and 0.016 mg/kg. We found TFs of 1.53 and 1.25 for Pb and Cd, respectively.

Comparing the mean concentrations of Pb and Cd with the limits allowed for cow milk according to the international standards of the European Union (CEE, 2006), Romania (Banu et al., 1985), Codex

Table 1. Concentration of Pb in the blood and milk of lactating cows reared near a metal smelting zone (n = 20).

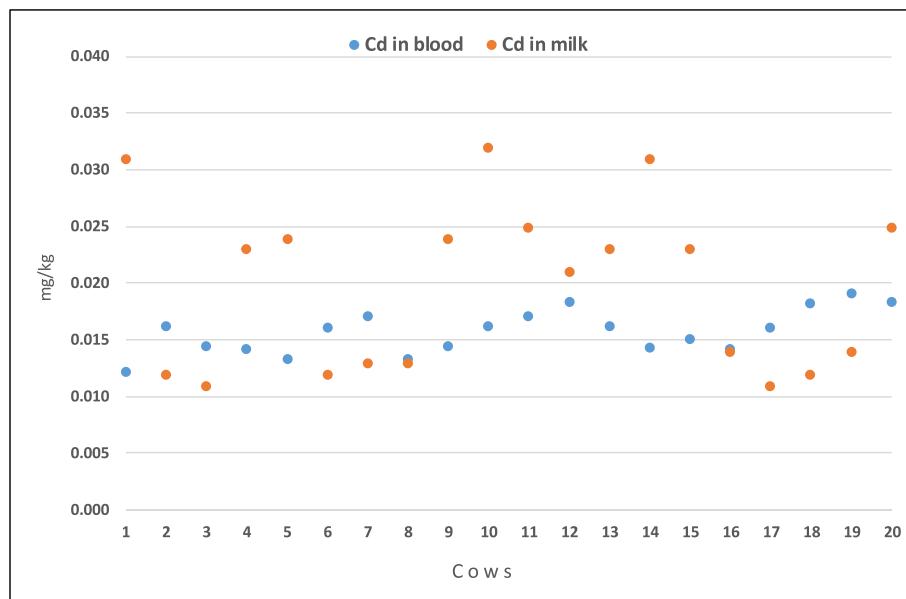
Variable	Mean	SD	CV (%)	Minimum	Maximum
Pb in blood, mg/kg	0.38b	0.041	0.20	0.302	0.453
Pb in milk, mg/kg	0.58a	0.018	0.00	0.540	0.600

^{a,b}Means followed by different letters differ significantly (p ≤ 0.01).

**Figure 1.** Scatter plot of Pb concentrations in blood and milk of lactating cows reared near a metal smelting zone (n = 20).**Table 2.** Cd content in blood and milk of cattle raised near a metal smelting zone (n = 20).

Variable	Mean	SD	CV (%)	Minimum	Maximum
Cd in blood, mg/kg	0.0157b	0.0019	0.00	0.0122	0.0191
Cd in milk, mg/kg	0.0197a	0.0073	0.00	0.0110	0.0320

^{a,b}Means followed by different letters differ significantly (p ≤ 0.01).

**Figure 2.** Scatter plot of Cd concentrations in blood and milk of cows raised near a metal smelting zone (n = 20).

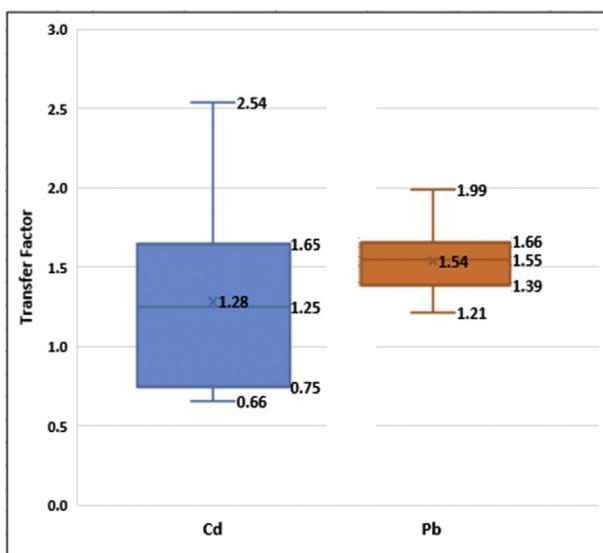


Figure 3. Box plot of Pb and Cd transfer factors from blood to milk in cows reared near a metal smelting zone ($n = 20$).

Alimentarius (FAO and OMS, 2015) and the Ecuadorian Technical Standard NTE INEN 9: 2012 (Pernia et al., 2015), it was observed that the mean concentration of Pb was 29 times higher than the value allowed for human consumption (0.02 mg/kg). For Cd, the Romanian norm (Banu et al., 1985) establishes a maximum value in milk of 0.01 mg/kg; the Cd level in milk produced at the PRC was thus 2 times higher than the allowed value. This situation puts consumers at risk, especially children.

The present results are similar to those from studies conducted in highly polluted areas in other countries, such as Mexico, Egypt, Italy and Pakistan (Licata et al., 2004; Rodríguez et al., 2005; Enb et al., 2009). In 5 dairy barns in the municipalities of General Zuazua and Marín in Mexico, the mean concentrations of Pb and Cd were reported to be 0.74 and 0.30 mg/kg (Rodríguez et al., 2005), values slightly higher than those found in the present study. In barns in the province of León, Mexico, a mean Pb concentration of 0.0043 mg/kg was reported, a much lower value than that recorded in our study, as it is a rural area far from industrial activity (González-Montaña, 2009).

Maximum concentrations of Pb in milk have been reported. In Ecuador, Egypt, Italy, Mexico and Pakistan, they were 7.77, 0.96, 1.32, 0.74 and 0.058 ppm, respectively; the maximum concentrations of Cd in milk reported in Ecuador, Egypt, Italy, Mexico, Pakistan and Romania were 0.46, 0.11, 0.02, 0.29, 0.06 and 0.01 ppm, respectively (Pernia et al., 2015). Gonzales-Montaña (2009) reported a maximum Pb content of 0.02 mg/kg fresh weight for raw cow milk.

In Peru, Chata (2015) conducted a study at Coata-Puno River basin and reported 0.21 mg/l of Pb, a value that exceeds the maximum limit established by the Codex Alimentarius and European Union. The Cd content was 0.0037 mg/l, a value that does not exceed the maximum limit of the Technical Norm of Romania. In the present study, the mean Pb and Cd values were determined to be 2.8 and 5.4 times higher than those recorded at Coata-Puno, which may be due to the high air, water and soil contamination by emissions from the La Oroya Metallurgical Complex, which has been in operation for more than 90 years and is located just 10.2 km away from the highland Andean community of Paccha.

Milk produced at the PRC, due to its high concentration of Pb and Cd, can cause health problems, especially in children (WHO, 2018). Pb bioaccumulates in different tissues, mainly bone (Castro et al., 2013), inhibits hemoglobin synthesis, causing anemia (Counter et al., 2012; Castro et al., 2016), increases blood pressure, damages renal tissue and alters the central nervous system (Nava-Ruiz and Méndez-Armenta, 2011), causing delayed mental development and decreased cognitive function

(Lassiter et al., 2015), aggressive behaviors and a tendency to violence (Needleman et al., 2002) and can cause stomach and lung cancer (Mushak, 2011).

Cd, due to its capacity for bioaccumulation and bioamplification in the food chain (Pernía et al., 2008), is associated with renal diseases, hypertension, anemia, osteoporosis, osteomalacia, diabetes, anosmia, chronic rhinitis and eosinophilia (Åkesson, 2012; Gallagher and Meliker, 2010; Schwartz et al., 2003; Henson and Chedrese, 2004). It is a carcinogen that causes leukemia and pancreatic, lung, breast and prostate cancer (Henson and Chedrese, 2004; McElroy et al., 2006; Julin et al., 2010).

Under the study conditions, the main source of Pb and Cd contamination is PM emitted by metal smelting, which reaches the water and grazing fields, mainly in the rainy season, and is transferred to pastures, then to the blood and milk of cows, binding with fat and proteins such as casein and whey proteins (Magariños, 2000; Alais, 2003). Cd in milk is transferred to the cream, rennet and milk curd. A concentration of Cd 3 times higher in the milk of sheep fed diets with Cd compared to those fed a Cd-free diet have been reported (Milhaud et al., 1998).

This study shows that Pb and Cd are easily transferred to milk, being a risk factor for health, especially in children. Daily consumption of 200 ml of this milk would provide 0.12 mg of Pb and 0.004 mg of Cd, which after 180 days would represent a cumulative intake of 216 and 0.72 mg of Pb and Cd, respectively. The problem is more concrete when considering that the mean per capita milk consumption in Peru is 87 kg/person/year (MINAGRI, 2018). Therefore, the consumption of milk produced at Paccha-La Oroya, containing 0.58 mg/kg of Pb, would result in an ingestion of Pb per capita of 50.46 mg.

5. Conclusion

All blood samples from the evaluated cows contained Pb and Cd; the concentration intervals for Pb and Cd ranged from 0.40 to 0.36 mg/kg and 0.017 and 0.015 mg/kg, respectively.

All evaluated milk samples contained Pb and Cd; the concentration intervals for Pb and Cd ranged from 0.59 and 0.57 mg/kg and 0.023 and 0.016 mg/kg, respectively, exceeding the limits allowed by international standards for raw cow milk.

The TFs of Pb and Cd from blood to milk were 1.53 and 1.25, respectively.

The milk produced at the PRC, due to its high level of contamination by Pb and Cd, is not suitable for human consumption. Pb and Cd can bioaccumulate, which represents a serious risk to public health.

Declarations

Author contribution statement

Doris M. C. Peinado: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Jorge I. C. Bedriñana: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Funding statement

This work was supported by Canon, Sobrecanon and Mining Royalties, and by the General Research Institute of the National University of Central Peru (No. 004-2017-VRI-UNCP).

Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

Acknowledgements

The authors thank the National University of the Center of Peru (Universidad Nacional del Centro del Perú). We thank the president of the Paccha-La Oroya Rural Community and the head of the communal barn for their support in the field phase and the professional staff responsible for blood and milk sampling, who agreed to sign the informed consent form and thus fulfilled ethical practices when conducting this study.

References

- Åkesson, A., 2012. Cadmium exposure in the environment: renal effects and the benchmark dose. *Encycl. Environ. Health* 465–473.
- Alais, C., 2003. Ciencia de la Leche: principios de técnica lechera, fourth ed. Editorial Reverté, S.A. Barcelona, p. 877.
- Alloway, B., 2013. Heavy Metals in Soils. Trace Metals and Metalloids in Soils and Their Bioavailability. Environmental Pollution. Springer Netherlands, USA.
- Alvarez-Berríos, N., Campos-Cerdeira, M., Hernández-Serna, A., Amanda Delgado, J.C., Román-Dañobeytia, F., 2016. Impacts of small-scale gold mining on birds and anurans near the Tambopata Natural Reserve, Peru, assessed using passive acoustic monitoring. *Trop. Conserv. Sci.* 9 (2), 832–851.
- Banu, C., Preda, N., Vasu, S., 1985. Food Products and Their Toxicity (In Romanian). Technical Publishing House, Bucharest, pp. 45–47.
- Barrios-Napuri, C., 2008. El desarrollo empresarial desde la perspectiva local. España: Red Académica Iberoamericana Local Global. Universidad de Málaga. Disponible en: <http://www.eumed.net/libros-gratis/2008b/403/index.htm>.
- Beltrán Pineda, M.E., y Gómez Rodríguez, A.M., 2014. Metales pesados (Cd, Cr y Hg): su impacto en el ambiente y posibles estrategias biotecnológicas para su remediación. *Revista I3+ 2* (2), 82–112.
- Chata, Q.A., 2015. Presencia de metales pesados (Hg, As, Pb y Cd) en agua y leche en la cuenca del río Coata-2015. Tesis Escuela de Nutrición Humana de la Universidad Nacional del Altiplano, Puno, Perú, p. 51pp.
- Castro, J., López de Romaña, D., Bedregal, P., López de Romaña, G., Chirinos, D., 2013. Lead and cadmium in maternal blood and placenta in pregnant women from a mining-smelting zone of Peru and transfer of these metals to their newborns. *J. Toxicol. Environ. Health Sci.* 5 (8), 156–165.
- Castro, J., Chirinos, D., Ríos, E., 2016. Lead content and placental weight and its association with gestational age, weight, length and hemoglobin in newborns of metallurgical region - Peru. *Rev. Toxicol.* 33 (2), 88–92.
- CDC (Centers for Disease Control and Prevention), 2012. Low Level Lead Exposure Harms Children: A Renewed Call of Primary Prevention. Report of the Advisory Committee on Childhood Lead Poisoning Prevention of the CDC, 1–54. Centers for Disease Control and Prevention. Disponible en: http://www.cdc.gov/nceh/lead/ACC_LPP/Final_Document_030712.pdf.
- Codex Estándar 193-1995, 2010. Norma General del Codex para los contaminantes y las toxinas presentes en los alimentos y piensos. Adoptada en 1995. [Revisada en 1997, 2006, 2008, 2009 y Enmendada el 2010:1-43]. Disponible en: www.fao.org/fileadmin/_user_upload/livestockgov/documents/CXS_193s.pdf.
- CEE (Comisión Económica Europea) Reglamento CE N°, 1881/2006, 2006. Contenido máximo de determinados contaminantes en los productos alimenticios. Diario Oficial de la Unión Europea, pp. 19–20. Disponible en: <https://www.boe.es/DOUE/2006/64/L00005-00024.pdf>.
- Counter, S.A., Buchanan, L.H., Ortega, F., 2012. Association of hemoglobin levels and brainstem auditory evoked responses in lead-exposed children. *Clin. Biochem.* 45 (15), 1197–1201.
- Delgado, M.V., 2016. El impacto de la minería en el Perú, bajo la exégesis del análisis económico del derecho, período del 2010 al 2015. Tesis Derecho. Universidad de Las Américas, p. Pp70.
- Dergham, M., Lepers, C., Verdin, A., Billet, S., Cazier, F., Courcot, D., Shirali, P., Garçon, G., 2012. Prooxidant and proinflammatory potency of air pollution particulate matter (PM2.5) produced in rural, urban, or industrial surroundings in human bronchial epithelial cells (BEAS-2B). *Chem. Res. Toxicol.* 25, 904–919.
- Enb, A., Donia, M., Abd-Rabou, N., Abou-Arab, A., El Senaity, M., 2009. Chemical composition of raw milk and heavy metals behavior during processing of milk products. *Global Vet.* 3 (3), 268–275.
- FAO & OMS, 2015. Norma general para los contaminantes y las toxinas presentes en los alimentos y piensos. CXS 193-1995. OMS, Roma. Enmienda 2015. Codex Alimentarius. http://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCX%252FB193-1995%252FCX%253A_193s.pdf.
- Gallagher, C.M., Meliker, J.R., 2010. Blood and urine cadmium, blood pressure, and hypertension: a systematic review and meta-analysis. *Environ. Health Perspect.* 118 (12), 1676–1684.
- Gakidou, E., Afshin, A., Abajobir, A.A., Abate, K.H., Abbafati, C., Abbas, K.M., et al., 2017. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 390 (10100), 1345–1422.
- González-Montaña, J.R., 2009. Metales pesados en carne y leche y certificación para la Unión Europea (UE). *Rev. Colombiana Ciencias Pecuarias* 22 (3), 305–310.
- Disponible en: <http://www.redalyc.org/pdf/2950/295023525006.pdf>.
- Henson, M.C., Chedrese, P.J., 2004. Endocrine disruption by cadmium, a common environmental toxicant with paradoxical effects on reproduction. *Exp. Biol. Med.* 229 (5), 383–392.
- Julin, B., Wolk, A., Johansson, J., Andersson, S., Andrén, O., Akesson, A., 2010. Dietary cadmium exposure and prostate cancer incidence: a population-based prospective cohort study. *Br J Cancer* 107 (5), 895–900.
- Latimer, G.W., 2016. In: AOAC Official Method 973.35 Lead in Evaporated Milk Atomic Absorption Spectrophotometric Method First Action 1973 Final Action 1974_AOAC, twentieth ed., Vol 1
- Lassiter, M.G., Owens, E.O., Patel, M.M., Kirrane, E., Madden, M., Richmond-Bryant, J., Dubois, J., 2015. Cross-species coherence in effects and modes of action in support of causality determinations in the U.S. Environmental protection agency's integrated science assessment for lead. *Toxicology* 330, 19–40.
- Leopold, E.N., Sabine, D.D., Philémon, Z.Z., Jung, M.C., 2016. Physical and metals impact of traditional gold mining on soils in Kombo-Laka area (meiganga, Cameroon). *Int. J. Geosci.* 7, 1102–1121.
- Licata, P., Trombetta, D., Cristani, M., Giofrè, F., Martino, Calò, M., Naccari, F., 2004. Levels of “toxic” and “essential” metals in samples of bovine milk from various dairy farms in Calabria, Italy. *Environ. Int.* 30 (1), 1–6.
- Lokeswari, H., Chandrappa, G.T., 2006. Impact of heavy metal contamination of Bellandur Lake on soil and cultivated vegetation. *Curr. Sci.* 91 (5), 622–627.
- Magarinos, H., 2000. Producción Higiénica de la Leche Cruda. Calzada Mateo, Guatemala: Producción y Servicios Incorporados S.A. Disponible en: www.innocua.net/web/download-795/leche-all.pdf.
- McElroy, J.A., Shafer, M.M., Trentham-Dietz, A., Hampton, J.M., Newcomb, P.A., 2006. Cadmium exposure and breast cancer risk. *J. Natl. Cancer Inst.* 98 (12), 869–873.
- MINAGRI. Ministerio de Agricultura y Riego, 2018. Producción nacional de leche alcanzará 2.7 millones de toneladas al año 2021. Disponible en: <http://minagri.gob.pe/portal/publicaciones-y-prensa/noticias-2018/21579-minagri-estima-que-prroducción-nacional-de-leche-alcanzará-2.7-millones-de-toneladas-al-ano-2021>.
- Milhaud, E., Vassal, L., Federspiel, B., Delacroix-Buchet, A., Mehennaoui, S., Charles, E., Enriquez, B., Kolf-Clauw, M., 1998. Devenir du cadmium du lait de brebis dans la crème et les caillés prévue ou lactique. *Le Lait INRA Ed.* 78 (6), 689–698.
- Mushak, P., 2011. Chapter 17 - carcinogenic and genotoxic effects of lead in human populations. *Trace Metals Other Contam. Environ.* 10, 635–670.
- Nava-Ruiz, C., Méndez-Armenta, M., 2011. Efectos neurotóxicos de metales pesados (cadmio, plomo, arsénico y talio). *Arch. Neurocienc (Mex)* 16 (3), 140–147.
- Needleman, H.L., McFarland, C., Ness, R.B., Fienberg, S.E., Tobin, M.J., 2002. Bone lead levels in adjudicated delinquents: a case control study. *Neurotoxicol. Teratol.* 24 (6), 711–717.
- Olayinka, O.O., Akande, O.O., Bamgbose, K., Adetunji, M.T., 2017. Physicochemical characteristics and heavy metal levels in soil samples obtained from selected anthropogenic sites in Abeokuta, Nigeria. *J. Appl. Sci. Environ. Manag.* 21 (5), 883–891.
- Peláez-Peláez, M.J., Bustamante, C.J., Gómez, L.E., 2016. Presencia de cadmio y plomo en suelos y su bioacumulación en tejidos vegetales en especies de Brachiaria en el magdalena medio colombiano. *Rev. Luna Azul* 43, 82–101.
- Pernía, B., Mero, M., Bravo, K., Ramírez, N., López, D., Muñoz, J., Egas, F., 2015. Detección de cadmio y plomo en leche de vaca comercializada en la ciudad de Guayaquil, Ecuador. *Rev. Cient. Nat. Ambien.* 8 (2), 81–86.
- Pernía, B., De Sousa, Reyes, R., Castrillo, M., 2008. Biomarcadores de contaminación por cadmio en las plantas. *Interciencia* 33 (2), 112–119.
- Rodríguez, F.H., Sánchez, A.E., Rodríguez, S.M., 2005. Metales Pesados en Leche Cruda de Bovino. *Rev. Salud Pública Nutr.* 6 (4), 137–141. Disponible en: <http://respyn.ua.nl.mx/index.php/respyn/article/view/155/137>.
- Schwartz, G., Il'Yasova, D., Ivanova, A., 2003. Urinary cadmium impaired fasting glucose, and diabetes in the NHANES III. *Diabetes Care* 26 (2), 468–470.
- Skipin, L., Gaevaya, E., Zaharova, E., Petukhova, V., Sidorova, K., 2016. Biogeochemistry of heavy metals in trophic chain in terms of the South of tumen region. *Proc. Eng.* 165, 860–868.
- Tchounwou, P.B., Yedjou, C.G., Patlolla, A.K., Sutton, D.J., 2012. Heavy metals toxicity and the environment. *EXS* 101, 133–164. Disponible en: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4144270/pdf/nihms414261.pdf>.
- Tepanosyan, G., Sahakyan, L., Belyaeva, O., Maghakyan, N., Saghatelian, A., 2017. Human health risk assessment and riskiest heavy metal origin identification in urban soils of Yerevan, Armenia. *Chemosphere* 184, 1230–1240.
- WHO, 2018. Intoxicación por plomo y salud. Organización Mundial de la Salud. Disponible en: <http://www.who.int/es/news-room/fact-sheets/detail/lead-poisoning-and-health>.
- Yilmaz, K., Akinci, I.E., Akinci, S., 2009. Effect of lead accumulation on growth and mineral composition of eggplant seedlings (*Solanum melongena*). *N. Z. J. Crop Hortic. Sci.* 37 (3), 189–199.
- Zambrano, J.L., Díaz, S., 2014. Guía para la correcta toma de sangre en bovinos a partir de la vena coccigea y de la vena yugular externa. Comité de Bioética de la Facultad de Medicina Veterinaria y Zootecnia, Universidad Nacional de Colombia. Disponible en: http://medicina veterinaria y zootecnia.bogota.unal.edu.co/fileadmin/FVMZ/Servicios/bioetica/Pro_autorizados/001_Guia_toma_sangre_bovinos.