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Research Article

HEALTH RISK ASSESSMENT OF HEAVY METALS IN GOAT'S MILK FOR ADULTS GROUP IN JIJEL PROVINCE (ALGERIA)

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ABSTRACT. The continuous urbanization and industrialization in many parts of the world and Algeria have led to high levels of heavy metal contamination in the soil, groundwater, and food chain products. Given the importance of milk and dairy products in the human diet, the aim of this study is to estimate the concentration of heavy metals (lead, cadmium, zinc, and copper) in goat's milk and to assess the potential health risks of those metals on adult consumers. To do so, goat milk was collected from three regions (El-Milia, Texenna, and Djimla) of Jijel, Algeria. Three samples were taken from each region and mixed to create a final sample that was pooled from each region. Then, Flame Atomic Absorption Spectrometry (FAAS) was used to determine the concentration of heavy metals. On the other hand, an online survey was carried out to estimate the daily intake of goat milk. The non-carcinogenic and carcinogenic health risk values were calculated. Our experiment demonstrated that the concentration of lead, cadmium, and copper significantly exceed the acceptable limit values; whereas, the zinc concentration was within the acceptable limit. The highest lead concentration was found in the El-milia region (0.42 mg/kg). The concentration gradient of average cadmium is as follows: C Djimla>C El-milia>C Texenna. They range from (0.0359±0.00247) mg/kg, (0.0155±0.00214) mg/kg, (0.00397±0.000742) mg /kg respectively, while the Texenna region has the highest copper concentration. Daily estimated intake (EDI) of all metals did not exceed the limit value. In addition, the target hazard quotient (THQ) of all metals and hazard index (HI) of the mixture of metals were both below the acceptable limit, representing no carcinogenic risk to the residents. Contrariwise, it was found that the carcinogenic risk (CR) for Cd was higher than the acceptable level (1×10^{6}), as was the cumulative carcinogenic risk for Cd and Pb. This study will be quite helpful for both inhabitants in taking protective measures and government officials in reducing heavy metal contamination.

Keywords: *Goat milk, heavy metals, non-cancer risk assessment, cancer risk assessment, Jijel province.*

INTRODUCTION

The global demand for milk is expected to increase by 35% by 2030, driven largely by growth demand in Africa, as well as Asia and Latin America [1]. Dairy production is increasing drastically in developing countries, making significant contributions to health, nutrition, environment, and livelihoods [2]. Milk and its derivatives are the main constituents of the daily diet, practically for all age groups (infants, school-age children, adults and old age), due to their richness of essential nutrients including proteins, calcium, magnesium, sodium, potassium, zinc, riboflavin, vitamin B12, and vitamin D that contribute to the development and maintenance of human life and health [3, 4, 5]. However, milk can also contribute to human disease in many ways, as a mammary gland excretion, it may contain numerous xenobiotic compounds and various environmental pollutants, including plant constituents, pesticides, disinfectants, drugs, and metals, which constitute a technological risk factor for dairy derivatives and consumer health [6]. Because of their toxicity and bioaccumulation, the presence of metals in food have become a major bugbear worldwide in recent decades. Milk products have been shown to accumulate heavy metals from diets and environment [7], which may pose a serious health threat to humans.

Heavy metals, including lead (Pb), cadmium (Cd), copper (Cu), and zinc (Zn), have been detected in milk products [8, 9, 10]. Firstly, although copper (Cu) and zinc (Zn) are considered as essential micronutrients to living beings, they can also have non-carcinogenic hazardous effects on human health when exposure levels are higher than the acceptable reference levels [11, 12]. Copper (Cu) plays a critical role in many biological processes including cellular respiration, free radical detoxification, neuropeptide processing, cell proliferation and angiogenesis [13, 14]. Excessively enhanced Cu levels, however, lead to cancer progression: proliferation, angiogenesis, and metastasis [15]. Zinc (Zn) is involved in numerous aspects of cellular metabolism; it is an essential component of more than 300 catalytic enzymes in our body. It plays a role in DNA and protein synthesis, cell division, immune function, and wound healing. It supports normal growth and development. A daily intake of Zn is required to maintain a steady state because the body has no specialized system to store it [16]. Zinc deficiency as well as excess result in severe disturbances in immune cell numbers and activities, which can result in increased susceptibility to infections and development of especially inflammatory diseases [17]. On the other hand, the metal of lead (Pb), and cadmium (Cd) is listed in the priority list of hazardous substances by the Agency for Toxic Substances and Disease Registry (ATSDR) [18,19]. Lead (Pb) is a potentially toxic element that accumulates in blood and bones, as well as in organs such as the liver, kidneys, brain and skin. Its negative health effects can be both acute and chronic. In humans, lead has been shown to affect the function of the nervous, reproductive, hepatic, endocrine, immune and gastrointestinal systems [20, 21]. Lead exposure has been associated with cancer in several countries [22, 23]. Cadmium (Cd) is produced primarily as a byproduct of Zn or Pb smelting. Cadmium toxicity has been demonstrated in several organs inducing tissue injury through creating oxidative stress [24, 26], epigenetic changes in DNA expression [27, 29], and inhibition or upregulation of transport pathways [30, 31, 32] particularly in the proximal S1 segment of the kidney tubule [33]. Other pathologic mechanisms include inhibition of heme synthesis [34], and impairment of mitochondrial function potentially inducing apoptosis [35]. The United States Environmental Protection Agency considered Cd to be a Class B1 carcinogen [36]. There is scant evidence linking Cd exposure to breast cancer [37, 38]. Prostate cancer is also correlated with Cd consumption [39] as is pancreatic cancer [40]. Other investigators have found a plausible association between Cd and lung cancer [41].

Therefore, it is essential to determine the residual metal concentrations in milk and assess the health risks related to them in order to ensure consumer safety. In Jijel province, a northeast town of Algeria, The intensive traffic jam and the industrial activities such as thermal power plant, Bellara steel complex, and the tannery may result in a high risk of heavy metals contamination [42, 43, 44]. Although, there have been a reduced number of studies about metal contamination in food in Algeria [45,46], but information regarding the heavy metal contents in milk and its products and the evaluation of their health risks still scarce. So, the major aims of this study were to determine the levels of four metals (Pb, Cd, Cu, and Zn) in raw goats milk from three tragted location in Jijel province, and to assess their potential health risks for adult population using target health quotients (THQ) and hazard index (HI). The results of this investigation provide insights into heavy metal accumulation in goat's milk and will serve as a basis for comparison with other regions and milk of other species. The findings of this investigation shed light on the presence of heavy metals in goat milk and will be used to compare it to milk from other areas and species.

MATERIALS AND METHODS

Presentation of study area

Jijel town is located in the North-East of Algeria; it occupies 2398 km^2; goat's milk was sampled from three different locations of Jijel. The first is El Milia, the largest city area of the region, located in northeast of Jijel province, it occupies 332 km^2, and encompasses 99.515 inhabitants [47]. Algerian Qatari Steel runs a steel complex with a total area of 523 hectares in the commune of El-Milia, in the industrial zone of Bellara (60 kilometers east of Jijel). This steel complex is situated in a privileged position between Jijel, Mila, Constantine, and Skikda. The second city is Texenna, 20 kilometers southeast of Jijel, with a total area of 125.79 km^2 and 19.985 inhabitants. The third one Djimla, located 45 km south-east of Jijel, it covers a total area of 65.28 km² and has a population of 22.140 according to DPAT censuses (2021) [47]. Between the municipalities of Texenna and Djimla, there is the Tabellout dam a gravity type dam about 70 km south of the Jijel wilaya (district), in Algeria. It was built between 2010 and 2018, with a height of 115 m, it is the fifth largest dam in Algeria with a capacity of 294 million m^3.

According to the Directorate of Agricultural Statistics and Information Systems (DSASI) of Jijel wilaya and according to the agricultural campaign of (2019/2020) the consumption of goat's milk in El Milia, Texenna and Djimla was estimated at 29.40×10^3, 15.00×10^3 and 12.50×10^3 l/year respectively [48]. The study was focused on adults population (20 to 70 years old).

Packaging of equipment and bottling

During all steps of the study, the instructions to avoid contamination were respected. Polyethylene bottles (250 ml) designed for sampling, as well as all the bottles used during the preparation of reagents and assays (vials, beakers, filtration set) were cleaned with detergent and rinsed with tap water. Subsequently, a nitric acid decontamination was carried out, this step consisted of soaking the bottles in a nitric acid solution (10 %) for 48 hours, combined with successive rinsing with distilled water [49]. Finally, the bottles were sterilized at 120°C over 12 h, and then, labled.

Sampling

Three samples of goat's milk were collected by breeders, at three different targeted areas in the Jijel province (El-Milia, Texenna, and Djmila). Over four days from April 11th to 14th, 2021.To avoid any contamination hygiene measures have been applied such as washing of the hands, and the udders of the animal before milking, and the elimination of the first jet of each milking. Then, the collected milk was stored immediately in polyethylene bottles previously decontaminated with nitric acid and transported in a cool box to the laboratory refrigerator before use. Three samples from each location were pooled to create a single representative pool for each region.

Heavy metals extraction

Goat's milk extracts were prepared according to the method of Shahbazi et al., (2016). 15 ml of goat's milk was mixed with 20 ml of HNO_3 (65 w/w %), and heated to dryness using a hotplate. Then, 5 ml of H_2SO_4 (95 w/w %) wad added and heated to dryness using a hotplate. After that, 5 ml of H_2O_2 (30 v/v %) was added and heated until the sample becomes colorless and dry (hotplate). Finally, residues were dissolved and completed to 5 ml using distilled water. Each extraction was performed in triplicate for each region (Fig.1). The extract obtained was then filtered, and the filtrates were stored in bottles closed in the refrigerator until the day of AAS assay [10].

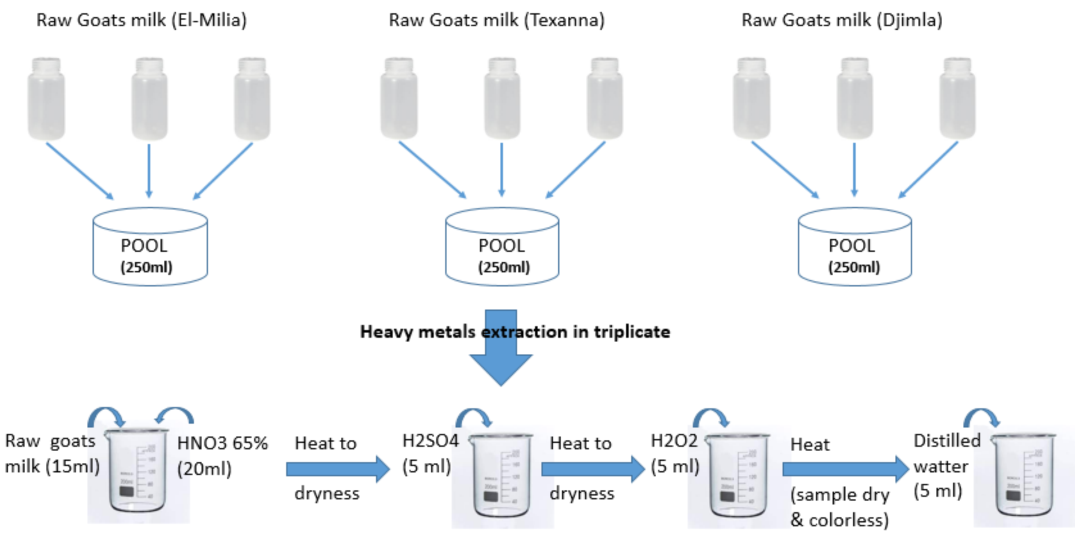

Fig. 1. *Heavy metals extraction [10].*

Analysis methods

The Goat's milk extracts were examined for the presence of heavy metals using the SAA- 6200 Atomic Absorption Spectrophotometer (*Shimadzu Corporation, KYOTO, JAPAN*). The limit of detection (concentration of an element that gives a signal equal to three standard deviations of the background noise) varied from 0.001 to 0.02 µl with an accuracy of 1 to 2 % on relative error. The samples were nebulised in an air/acetylene flame, which atomises the metal elements. The stock solutions of the reagents were prepared using ultrapure water, and all standard solutions were made daily by diluting the appropriate stock with the same procedure of extraction. Calibration solutions of the target metal ions were prepared from the standard stocks by serial dilution. The ranges of concentrations chosen corresponded to the concentrations most commonly encountered in milk samples. The specific method parameters are resumed in Table 1.

Table 1. *SAA measuring conditions.*

Parameters / Metals	Measurement wavelength	Lamp current	Slit width	Burner height	Fuel gas (C2H2) flow
Lead (Pb)	283.3 nm	10 mA	0.5 nm	7mm	0.8 l/min
Cadmium (Cd)	228.8 nm	8 mA	0.5 nm	7mm	0.8 l/min
Copper (Cu)	324.7 nm	6 mA	0.5 nm	7mm	1.8 l/min
Zinc (Zn)	213.9 nm	8 mA	0.5 nm	7mm	0.8 l/min

Health risk assessment

The non-carcinogenic health risks of a single metal via consumption of goat's milk were assessed based on the THQ, a ratio of determined doses for one pollutant to its reference dose (RfD), and can be calculated as the following equations (1) and (2):

$$THQ = \frac{EDI}{RFD}$$

Eqn. 1

$$EDI = \frac{Cmetal \times Wmilk}{BW}$$

Eqn. 2

EDI: the estimated daily intake of heavy metals (mg/kg/d)
RfD: the oral reference dose.
C_{metal}: the mean concentration of heavy metals in milk samples (mg/kg)
W_{milk}/BW: the intake of milk per kg body weight per day (kg/day·bw(kg)

The RfD values of Pb, Cd, Cu, and Zn are set to be 0.0036 [50], 0.001, 0.04, and 0.3, mg/kg/d [51]. The average adult body weight has been set at 70 kg according to the literature [52]. Whereas, the mean intake of milk was estimated from the online survey.

If the THQ is less than 1, the exposed population is unlikely to experience obvious adverse effects [53]. The severity of health risks caused by toxic compounds is enhanced with the increasing THQ value.

Exposure to two or more metals may result in additive and/or interactive effects. The health index, HI, was used to estimate the total no carcinogenic health risk caused by mixture of heavy metals [54]. HI can be estimated by equation (3):

$$HI = \sum THQ$$

Eqn. 3

If the calculated hazard index (HI) was less than 1, this confirms that consumption of goat's milk does not pose a formal non-carcinogenic risk to human health, and this risk increases with the value of HI.

The cancer risk CR for cadmium and lead was calculated based on the equation (4):

$$CR = EDI \times CFS0$$

Eqn. 4

CSF (Cancer Slope Factor): the carcinogenic slope factor for the oral route of the metals.

CSF Pb and Cd is estimated at 0.0085 and 15 mg /kg/day respectively [55]. According to the US EPA (2001) [52], cancer risk is considered acceptable for the range from 1×10^{-6} to 1×10^{-4}.

The cumulative risk of cancer (CR_c) in the present study was evaluated following exposure to the two carcinogenic heavy metals, Cd and Pb, as the sum of the individual risks of these two metals, according to the equation (5):

$$CRc = CRCd + CRPb$$

Eqn.5

CRCd: cancer risk for cadmium.
CRPb: cancer risk for lead.

Online survey

160 people took part in the conducted online survey during April 2022. Two types of questions were used online for voluntary respondents to collect information on the health risks associated with metals exposure in goat's milk:

- General question: 1) are you adult (>18 years, 2) what is your gendre,
- The daily (24h) quantity of milk consumed: 1) Do you consume goat's milk, 2) if yes, how much is consumed each day (one, two, three, or four 200 ml glasses of milk every day).

All of the questions were multiple choice, so you only had to select the right response for each.

Statistical analysis

The concentrations of heavy metals (Pb, Cd, Cu and Zn) were expressed in milligram per killogram of raw milk, and presented as the mean±SEM for each metal. A one-way analysis of variance (ANOVA) was performed to assess the differences in the metallic profile of milk between the three regions targeted by the study. The p-value<0.05 was considered to indicate a statistically significant difference between the regions being compared. Significantly different groups are processed by post hot analysis with the Tukey test.

The correlations were established using the Pearson correlation method to assess the dependence between the profiles of the four metals at the same time in the same region, and between the three selected regions.

Descriptive statistics were performed by Microsoft Excel 2016 spreadsheet, while hypothesis testing and factor analysis were performed by SigmaPlot software version 12.0, GraphPad Prism7 and SPSS Statistics 25.

RESULTS AND DISCUSSION

Concentrations of Metals in goat's milk

The contents of heavy metals (Pb and Cd), and trace elements (Cu and Zn) in all analyzed milk samples and their relevant threshold values of international standards were summarized in Table 2, One-way analysis of variance showed that the concentration of lead significantly exceed the threshold value in all regions, especially El-Milia (0.4250±0.0065* $^{\mathbf{a}}$ mg/kg**)** "P=0.012" with an average lead value of 0.381±0.0018 mg/kg. In the same way, Djimla (0.338±0.0223* mg/kg**)** "p=0.0001" has a cadmium concentration that is significantly higher than the limit value, followed by El-Milia (0.0155±0.0021* mg/kg**)** and Texenna (0.00397±0.0007* mg/kg). An average value of 0.01845±0.00026 mg/kg) was recorded for this toxic metal. Likewise, copper concentration exceeds the threshold value, in particular in the region of Texenna (0.0633± 0,0044^{*c} mg/kg) "p=0.003" with an average value of 0.0500±0.0001 mg/kg. While, the zinc concentration was within the acceptable limit and did not exceed the threshold value with an average value of 1.868±0.731 mg/kg.

Table 2. *Concentrations of heavy in goat's milk metals and threshold values (mg/kg).*

Region / Metals	El-Milia	Texenna	Djimla	Threshold value	References
Lead (Pb)	0.425 ± 0.0065^{*a}	0.382 ± 0.0026*	0.338 ± 0.0223*	**0.02**	[56]
Cadmium (Cd)	0.0155 ± 0.0021*	0.00397 ± 0.0007*	0.0359 ± 0.0025^{*b}	**0.0026**	[57] [58]
Copper (Cu)	0.0500± 0,0024*	0.0633± 0,0044^{*c}	0.0369± 0,0019*	**0.01**	IDF 1979 [59]
Zinc (Zn)	1.425 ± 0.1042*	2.712± 0.1148^{*d}	1.467± 0.1298*	**3.28**	IDF 1979 [59]

Mean±SEM. (*) p.0.5 a significant difference heavy metals concentration vs threshold limit, (a) p=0.012 a significant difference El-Milia vs Djimla, (b) p<0.0001 a significant difference Djimla vs El-Milia and Texenna, (c) p=0.03 a significant difference Texanna vs Djimla, (d) p=0.0003 a significant diffrence Texenna vs El-Milia and Djimla.

Correlation analysis

Pearson coefficient (R) was calculated to assess the plausible association between metals in the set of regions targeted in this work.

In El-Milia, lead was positively correlated with cadmium "R=0.542", and negatively correlated with copper and zinc "R=-0.865,-0.499" respectively; otherwise, copper and zinc are highly correlated "R=0.867". Strong correlations characterized the metals in Texenna, we have a positive correlation between lead and zinc "R=0.912", and a negative correlation between zinc and copper "R=-0.984". Moreover, in Djimla, we observed a high correlation between lead and zinc "R=1", and a negative correlation between copper and cadmium "R=-0.982".

Estimated Daily Intake of Metals and Their Respective Human Health Risks

Online survey results

The observed population (160 individuals) shows a relative female dominance with 51.25% (82) against 48.75% for men. It also shows a dominance of adult goat milk consumers with 85% (136) against a minority of 15% who report not drinking goat's milk. For the milk consumption rates, the majority of participants (53.7%) reported drinking one cup of milk, equivalent to 200 ml per day. Only 2.5% of adults take 4 cups and milk daily, compared to 38.75% of those who drink two cups daily and 5% of those who drink three cups. The outcomes were consistent with the rate of milk intake determined by DSASI [48].

Estimated daily intake (EDI)

Since the majority of metal concentrations exceeded the threshold values of standards, to assess if there was or not a risk for human health, the exposure of milk consumers to heavy metals and associated health risk is determined not only by metals concentrations in milk, but also by milk consumption rates which was estimated to 200 ml/day by the online survey. So it is necessary to carry out health risk assessments according to the daily intake of metals. The *EDI* values of heavy metals *via* the consumption of milk were calculated and shown on (Fig. 2). The results obtained show that the lead EDI for the three regions (average value of 0.00109±0.0001mg/kg BW/jour**)** are in below the FAO proposed limit value (0.0036 mg/kg/day). Similarly, cadmium EDI in the three study regions (average value of 3.6087×10^{-4} mg/kg body weight/day) does not exceed the standard EDI (Cd) < 0.0083 mg/kg body weight/day. In the same way, the EDI of copper (average value of 0.000143 mg/kg body weight/day) and zinc (average value of 0.00533 mg/kg/day) was below the limit value (0.04 and 0.3 mg/kg body weight/day respectively).

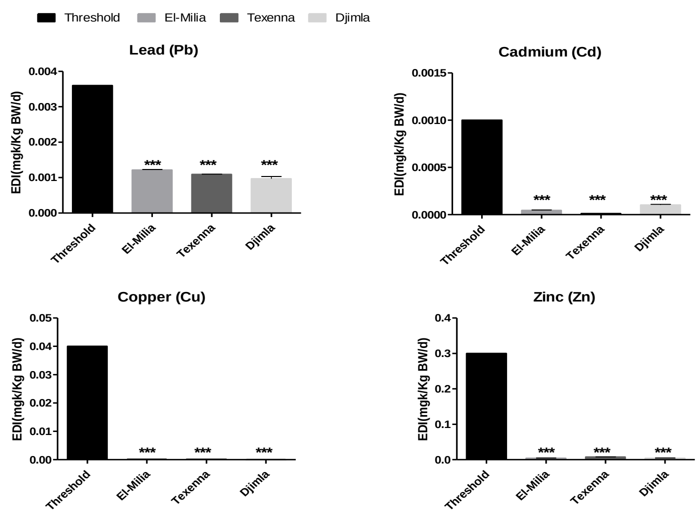

Fig. 2. *Estimated daily intake (EDI) of Cd, Pb, Cu and Zn through goat's milk consumption, in El-Milia, Texenna and Djimla. Espressed as Mean±SEM, (***): p<0.0001 vs threshold.*

The target hazard quotient (THQ)

According to the results of the calculation obtained from the THQ "Pb", it is found that the highest non-carcinogenic risk is observed at El-Milia (0.3467±0.005487) compared to both other regions (Texenna and Djimla) (0.3117±0.002028 and 0.2763±0.01819 respectively) (Fig. 3). The highest non-carcinogenic risk for "Cd" is in the Djimla area (0.1027±0.007094). A low non-carcinogenic risk that does not exceed the value indicated (THQ<1) of "Cu" was found. Texenna region showed the highest value compared to the other two regions. As with "Cu", "Zn" has a low non-carcinogenic risk and the highest in the Texenna region compared to the other two regions. For all the results, the THQ values of metals obtained do not exceed the limit value.

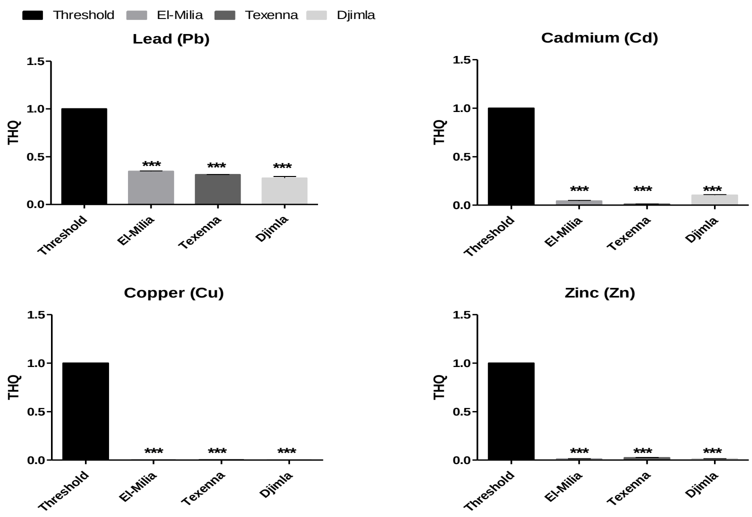

Fig. 3. *THQ values of metals for all groups due to milk consumption. Expressed as Mean±SEM. (***) p<0.0001 vs threshold.*

Hazard Index (HI)

The Hazard Index determines the potential non-carcinogenic risk induced by simultaneous exposure to a mixture of several metals, it results from the sum of all the THQ of the individual heavy metals analyzed. The assessed values of HI revealed significant differences between the three regions studied (p=0.0455). Furthermore, the region of El-Milia presents the highest estimated value of this risk (0.4043±0.0126) compared to other regions while all the values in the Table 3 do not show a non-carcinogenic risk for consumers.

Table3. *Metal hazard index results.*

Regions	Hazard Index Mean ± SEM	P-value
El-Milia	0.4043±0.0126	0.0455*
Texenna	0.3533 ± 0.0034	
Djimla	0.3957 ± 0.0156	

*The results are expressed as mean ± Standard Error of Mean (SEM). "*****": Significant differences between the three regions studied.*

Cancer risk (CR)

The results revealed the absence of carcinogenic risks associated with the ingestion of lead ($1.03\times10^{-5}\pm1.732\times10^{-7}$) for El-Milia, $9.27\times10^{-6}\pm6.35\times10^{-8}$ for Texenna and $8.22\times10^{-6}\pm5.427.10^{-7}$) for Djimla. However, the ingestion of cadmium is associated with a carcinogenic risk, especially in the region of Djimla (0.00154±0.0001041) (Fig. 4).

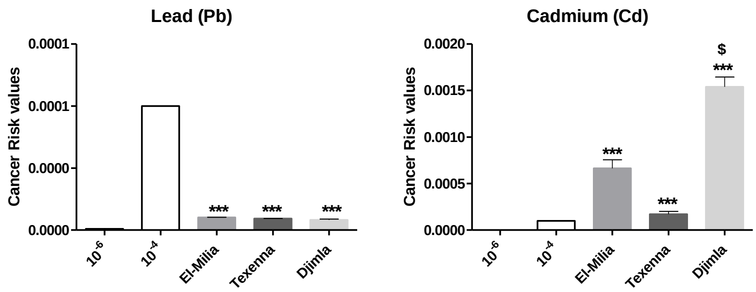

Fig. 4. *Cancer risk values of heavy metals for adults from milk consumption. Results are expressed as Mean ± SEM. (***) p<0.0001 vs threshold values (10-6-10-4), ($)p<0.001 vs El-Milia and Texenna.*

Cumulative cancer risk (CR_C)

Cumulative risk represents the result of exposure to multiple carcinogenic heavy metals, statistical analysis (ANOVA) revealed a significant difference between the three regions El-Milia ($0.0006747\pm9.19\times10^{-5}$), Texenna ($0.000179\pm3{,}188\times10^{-5}$) and Djimla (0.00155±0.0001041) ($p<0.001$) as shown in the (Fig. 5).

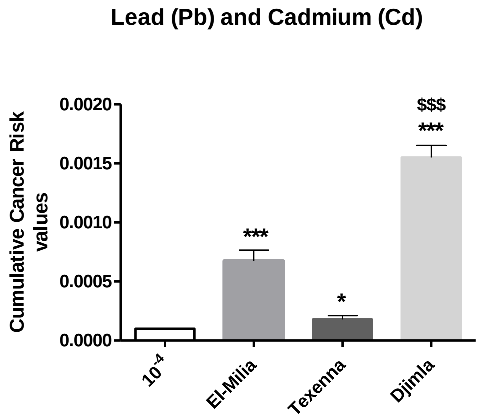

Fig. 5. *Cumulative cancer risk of lead and cadmium. Results are expressed as Mean±SEM. (***) p<0.001 vs threshold (10^{-4}), (*) p<0.05 vs threshold (10^{-4}) and ($$$) p<0.001 vs El-Milia and Texanna.*

During the period of April, 2021 metals (Pb-Cd-Cu and Zn) concentrations were measured in goat's milk from three different locations of Jijel province (Algeria). The mean concentrations of heavy metals in all areas followed the same pattern Zn>Pb>Cu>Cd. The mean concentrations of toxic metals lead and cadmium were significantly higher than the threshold values, this could underscore the release of toxic metals into the ambient air of Jijel province, concentrations of these metals may also be observed in the forage samples of the exposed area [60]. Lead is one of the most harmful heavy metals for humans; it can cause cancer, bleeding, and kidney disorders. Based on the recommendation of the WHO, the lead limit for milk is 0.02 mg/kg [56]. The average lead concentration of goat milk samples in our study (0.338-0.425) mg/kg was significantly higher than the WHO limit, these results are in accordance with those of El Sayed et al., (2011) with Pb values close to our results (0.327 mg/kg) [61]. However, our results showed that lead content in the goat milk samples was lower than that observed in Nigeria (0.168-1.394) mg/kg [62], and higher than the values reported in Egypt (0.044 mg/kg) [63], and Iran (0.141 mg/kg) [64]. The high concentration of Pb in milk observed in the present study could be explained by the pollution of the environment. Indeed, agricultural and industrial activities (particularly in El-Milia), and road transport are known anthropogenic sources for the increase lead's concentration in the environment. Regarding road transport, many countries banned the fuel by the 1980s, but it was only in July 2021 that Algeria became the last country to ban it; according to a study day conducted by Sonatrach on the media coverage of unleaded petrol, the global consumption of fuels containing lead in Algeria reached 2.71 million tons in 2017 [65]. At result, lead alkyl additives in gasoline are burned and emitted into the atmosphere and may be responsible for the high concentration of lead in certain vegetation, roadsides, soil, air, water and plants [66]. Likewise, cadmium (Cd) is one of the most toxic industrial and environmental pollutants due to its long half-life (15-30 years), which amplifies the deleterious effects on human health [67]. The maximum permissible level of Cd in dairy products has been reported to be 0.02 mg/kg of wet weight in Turkey, 1.0 mg/kg of wet weight in Malaysia, 0.05 mg /kg of wet weight in Egypt, and 0.01 μg/g of wet weight in FAO/WHO limits [68]. By comparing our data results with the FAO limit on Cd, which is the most meticulous legislator, the average Cd values in this study ranged from (0.00397 mg/kg) to (0.0359 mg/kg), with the Djimla region recording the highest alarming result (three times the allowed value). Our research consequently demonstrates very substantial toxicological risks to the population's health in this area when goat milk is consumed. The sources of this high concentration of Cd can be due to both natural sources (altered bedrock) and anthropogenic (road traffic, activities related to the Tabellout dam and local farming). Our results are in accordance with other studies where the level in milk exceeded the permissible limit [69,70]. However, our results are higher than SolaLarr anaga and Navarro-Blasco [71]; Bilandzic et al. [72]; Pilarezyk et al. [73] and Khan et al. [74] who reported Cd values 0.0004, 0.003, 0.004 and 0.002 mg/kg, respectively. Nevertheless, Cd concentrations in milk may increase to more severe levels, as is the case for the Cd concentration in raw cow milk samples from India which far exceeds those found in this study (12 mg/kg) [75]. On the other hand, trace elements such as Cu and Zn are referred to as microelements, and have been identified to be vital for normal growth. When the amount of intake exceeds the determined levels, they may produce toxic and harmful effects [15, 16, 17]. The daily tolerable amount for copper is 3 mg while its permissible limit in milk is 0.01 mg/kg [59]. The mean concentrations of copper in our study (0.03 -0.06) mg/kg were above the permissible limit, other studies reported higher level of copper than this study, Homayonibezi et al. [64] estimate copper content in Asaluyeh and Kaki to 0.146 mg/kg and 0.171 mg/kg, respectively. Meshref et al. [63]; Shahbazi et al. [68] and Bakircioglu et al. [76] estimated Cu content to 0.888 – 18.316 mg/kg; 0.427 mg/kg and 0.094 -29 mg/kg respectively [64 -10 -74]. On the other hand, Ahmad et al. [77] reported a lower level of copper 0.223×10^{-3} mg/kg. Concentrations of Zn were less than the normal level adopted by the IDF (1979) 3.28 mg/kg [58], the Japanese 4 mg/kg, Chinese 2.5–6.7 mg/kg and Brazilian Food Standard 5mg/kg [10]. This parameter is important because Zn has many functions in the body and deficiency of Zn leads to disruption in different physiological functions [17]. The differences in the metals contents between this study and previous reports could be due to several factors such as goat breed and local environment; production equipment, storage, and transport containers are also important supplies of heavy metal contamination.

Although the estimation of metals concentration is a crucial step, but it is insufficient to infer toxicity or non-toxicity of milk, because the exposure of milk consumers to heavy metals and associated health risk is determined not only by pollutant concentrations in milk products, but also by milk consumption rates. So, it is necessary to carry out health risk assessments according to the daily intake of metals (EDI), which is used to assess the non-carcinogenic health risk.

The mean EDI values of metals for each location group *via* the consumption of milk were calculated and represented in figure 2. As shown in figure 2, the largest contributor of studied elements to daily intake is Zn, the trends of EDI values for metals in milk were in the order of Zn>Pb>Cu>Cd respectively. In our study, (Pb, Cd, Cu and Zn) EDI values were estimated to approximately (0.00109057, 4.3714E-05, 0.000136 and 0.00458857) mg/kg Bw/d respectively. All did not exceed threshold values (0.0036, 0.001, 0.04 and 0.3) mg/kg Bw/d respectively [50,51].

As shown in figure 3, for all groups no THQ value over 1 was observed, which indicate that the consumption of goats milk in these regions do not represent a significant health risk [53], the higher values of THQ were noticed for Pb, implying that this metal could be of concern for adults in terms of non-carcinogenic risk. Our results differ from those of Yu et al, (2015) where the maximum values of THQ were reported for Cd [75]. Although risk assessment of metals *via* milk ingestion was found to be within safe limits (THQ<1); exposure to multiple heavy metals could result in cumulative effects. Therefore, a cumulative non-carcinogenic risk assessment was performed, HI values (sum of individual metal THQs) were calculated.

As shown in table 2, for average exposure, the data of HI for all groups were less than one (0.3533- 0.4043), which indicated that there was no potential health risk to adults by consumption of goat's milk [54]. Despite the safety based on HI values, in comparison to other studies that showed a lower HI values than those obtained in our study, around (0.085- 0.238) [76, 77, 78], the danger index obtained remains alarming.

The carcinogenic risk assessment is given in Figures 4 and 5, for one heavy metal, an ILCR less than 1×10^{-6} is considered as insignificant and the cancer risk can be neglected; while an ILCR above 1×10^{-4} is considered as harmful and the cancer risk is troublesome. For the total of all heavy metals through all exposure routes, the acceptable level is 1×10^{-5} [79]. Our data showed that CR values of Cd (1.93×10^{-4}-1.59×10^{-3}) exceed the limit values; also the cumulative cancer risk values (2.02×10^{-4}-1.60×10^{-3}) are higher than the threshold value for all regions. The results of this research demonstrate that there is a cancer risk through the ingestion of goat's milk.

CONCLUSION

The purpose of this study was to evaluate the levels of four specific metals (Pb, Cd, Cu, and Zn) in goats milk in three rural regions in Jijel wilaya (El-Milia, Texenna, and Djmila) as well as the risks associated with consuming this milk for human health.

In comparison to the IDF standard, EC, and Codex Alimentarius Commission, the assessment of heavy metals in goat's milk revealed high amounts of lead, cadmium, and copper (0.02, 0.0026, and 0.01 mg/kg), respectively, and low values in comparison to zinc (3.26 mg/kg).

The EDI of all metals did not exceed the limit value. In addition, the THQ of all metals and HI of the mixture of metals were both below the acceptable limit, representing no carcinogenic risk to the residents. Contrariwise, it was found that the carcinogenic risk (CR) for Cd was higher than the acceptable level (1×10^{6}), as was the cumulative carcinogenic risk for Cd and Pb.

In conclusion, people should pay more attention when consuming goat's milk in Jijel province since the level of lead and cadmium exceed the threshold value, and on the other side goat's milk is poor on essential's trace elements (Zn, Cu). In addition, data showed the high cancer risk associated with goat's milk consumption.

Therefore, in order to reduce the levels of exposure to these toxics for the general population and to protect it from the substantial toxicological dangers associated with this exposure, it is urgently necessary to put measures in place to combat the sources of contamination of this staple food.

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REFERENCES

[1] International Farm Comparison Network. (2018): Dairy Outlook 2030. Accessed May 28, 2020. https: / / ifcndairy .org/ wp -content/uploads/ 2018/ 06/ IFCN -Dairy -Outlook -2030 -Brochure .pdf.

[2] Grace, D., Wu, F., Havelaar, A.H. (2020): MILK Symposium review: Foodborne diseases from milk and milk products in developing countries-Review of causes and health and economic implications. Journal of Dairy Science 103(11):9715-9729.

[3] Fayet, F., Ridges, L.A., Wright, J.K., Petocz, P. (2013): Australian children who drink milk (plain or flavored) have higher milk and micronutrient intakes but similar body mass index to those who do not drink milk. Nutrition Research 33(2):95–102.

[4] Iannotti, L., Lesorogol, C. (2014): Animal milk sustains micronutrient nutrition and child anthropometry among pastoralists in Samburu, Kenya. American Journal of physical Anthropology 155(1):66-76.

[5] De Oliveira, T.M., Peres, J.A., Felsner, M.L., Justi, K.C. (2017): Direct determination of Pb in raw milk by graphite furnace atomic absorption spectrometry (GF AAS) with electrothermal atomization sampling from slurries. Food Chemistry 229:721–725.

[6] Licata, P., Trombetta, D., Critani, M., Giofre, F., Martino, D., Calo, M., Naccari, F. (2004): Levels of "toxic" and "essential" metals in samples of bovine milk from various dairy farms in Calabria, Italy. Environment International. 30 (1): 1.

[7] Soma, G., Gurdeep, S., Jha, V.N., Tripathi, R.M. (2011): Risk assessment due to ingestion of natural radionuclides and heavy metals in the milk samples: a case study from a proposed uranium mining area, Jharkhand. Environmental Monitoring and Assessment 175 (1-4): 157-66.

[8] Malhat, F., Hagag, M., Saber, A., Fayz, A.E. (2012): Contamination of cows milk by heavy metal in Egypt. Bulletin of Environmental Contamination and Toxicology 88(4): 611-613.

[9] Winiarska-Mieczan, A. (2014): Cadmium, lead, copper and zinc in breast milk in Poland. Biological Trace Element Research. 157(1):36-44.

[10] Shahbazi, Y., Ahmadi, F., Fakhari, F. (2016): Voltammetric determination of Pb, Cd, Zn, Cu and Se in milk and dairy products collected from Iran: An emphasis on permissible limits and risk assessment of exposure to heavy metals. Food Chemistry.192:1060-1067.

[11] Jarup, L. (2003): Hazards of heavy metal contamination. British Medical Bulletin 68:167-182.

[12] Cao, H.B., Zhang, H., Qiao, L., Chen, J.J. (2010): Exposure and risk assessment for aluminium and heavy metals in Puerhtea. Science of the Total Environment 408 (14): 2777-84.

[13] Gaetke, L.M., Chow-Johnson, H.S., Chow, C.K. (2014): Copper: Toxicological relevance and mechanisms. Archives of Toxicology 88(11):1929–1938.

[14] Balsano, C., Porcu, C., Sideri, S. (2018): Is copper a new target to counteract the progression of chronic diseases? Metalloids 10(12):1712–1722.

[15] Garber, K. (2015): Cancer's copper connections. Science 349(6244):129.

[16] Poudel, R.R., Bhusal, Y., Tharu, B., Kafle, N.K. (2017): Role of zinc in insulin regulation and diabetes. Journal of Social Health 5:83-7.

[17] Maywald, M., Wessels, I., Rink, L. (2017): Zinc Signals and Immunity. International Journal of Molecular Sciences 18(10):2222.

[18] Kafaei, R., Tahmasbi, R., Ravanipour, M., Vakilabadi, D.R., Ahmadi, M., Omrani, A., Ramavandi, B. (2017): Urinary arsenic, cadmium, manganese, nickel, and vanadium levels of schoolchildren in the vicinity of the industrialised area of Asaluyeh, Iran. Environmental Science and Pollution Research 24(30):23498–23507.

[19] Ahmad, I., Zaman, A., Samad, N., Ayaz, M., Rukh, S. (2017): Atomic absorption spectrophotometery detection of heavy metals in milk of camel, cattle, buffalo and goat from various areas of Khyber-Pakhtunkhwa (KPK). Journal of Analytical & Bioanalytical Techniques 8(367) :2.

[20] Krzywy, I., Krzywy, E., Pastuszak-Gabinowska, M., Brodkiewicz, A. (2010): Lead—Is there something to be afraid of? Annales Academiae Medicae Stetinensis 56: 118–128.

[21] Wani, A.L., Ara, A., Usmani, J.A. (2015): Lead toxicity: A review. Interdisciplinary Toxicology 8, 55-64.

[22] Ahn, J., Park, M.Y., Kang, M.Y., Shin, I.S., An, S., Kim, H.R. (2020): Occupational Lead Exposure and Brain Tumors: Systematic Review and Meta-Analysis. International Journal of Environmental Research and Public Health 17:3975.

[23] Steenland, K., Barry, V., Anttila, A., Sallmen, M., Mueller, W., Ritchie, P., McElvenny, M.D., Straif, K. (2019): Cancer incidence among workers with blood lead measurements in two countries. Occupational and Environmental Medicine 76: 603-610.

[24] Matović, V., Buha, A., Bulat, Z., Dukić-Ćosić, D. (2011): Cadmium toxicity revisited: focus on oxidative stress induction and interactions with zinc and magnesium. Archives of Industrial Hygiene and Toxicology 62(1):65-76.

[25] Patra, R.C., Rautray, A.K., Swarup, D. (2011): Oxidative stress in lead and cadmium toxicity and its amelioration. Veterinary Medicine International 457327.
[26] Cuypers, A., Plusquin, M., Remans, T., et al. (2010) : Cadmium stress : an oxidative challenge. Biometals 23(5) : 927-940.
[27] Wang, B., Li, Y., Shao, C., Tan, Y., Cai, L. (2012): Cadmium and its epigenetic effects. Current Medicinal Chemistry 19(16):2611-2620.
[28] Martinez-Zamudio, R., Ha, H.C. (2011): Environmental epigenetics in metal exposure. Epigenetics 6(7) : 820-827.
[29] Luparello, C., Sirchia, R., Longo, A. (2011): Cadmium as a transcriptional modulator in human cells. Critical Reviews in Toxicology 41(1):75-82.
[30] Thévenod, F. (2010): Catch me if you can! Novel aspects of cadmium transport in mammalian cells. Biometals 23(5) :857-875.
[31] Wan, L., Zhang, H. (2012): Cadmium toxicity: effects on cytoskeleton, vesicular trafficking and cell wall construction. Plant Signalling and behavior 7(3):345-348.
[32] Van Kerkhove, E., Pennemans, V., Swennen, Q. (2010): Cadmium and transport of ions and substances across cell membranes and epithelia. Biometals 23(5):823-855.
[33] Vesey, D.A. (2010): Transport pathways for cadmium in the intestine and kidney proximal tubule: focus on the interaction with essential metals. Toxicology Letters 198(1):13-19.
[34] Schauder, A., Avital, A., Malik, Z. (2010): Regulation and gene expression of heme synthesis under heavy metal exposure--review. Journal of Environmental Pathology, Toxicology, and Oncology 29(2):137-158.
[35] Cannino, G., Ferruggia, E., Luparello, C., Rinaldi, A.M. (2009): Cadmium and mitochondria. Mitochondrion 9(6):377-384.
[36] Zafarzadeh, A., Bonyadi, Z., Feyzi, K. (2020): Health risk assessment related to cadmium in dairy products in Gorgan, Iran. International Journal of Environmental Analytical Chemistry 1-9.
[37] Aquino, N.B., Sevigny, M.B., Sabangan, J., Louie, M.C. (2012): The role of cadmium and nickel in estrogen receptor signaling and breast cancer: metalloestrogens or not?. Journal of environmental science and health. Part C, Environmental carcinogenesis & ecotoxicology reviews 30(3):189-224.
[38] Filippini, T., Torres, D., Lopes, C., et al. (2020). Cadmium exposure and risk of breast cancer: A dose-response meta-analysis of cohort studies. Environment International 142:105879.
[39] Rapisarda, V., Miozzi, E., Loreto, C., et al. (2018) : Cadmium exposure and prostate cancer : insights, mechanisms and perspectives. Frontiers in Bioscience-Landmark (Ed) 23(9):1687-1700.
[40] Djordjevic, V.R., Wallace, D.R., Schweitzer, A., et al. (2019) : Environmental cadmium exposure and pancreatic cancer: Evidence from case control, animal and *in vitro* studies. Environment International 128:353-361.
[41] Chen, C., Xun, P., Nishijo, M., He, K. (2016): Cadmium exposure and risk of lung cancer: a meta-analysis of cohort and case-control studies among general and occupational populations. Journal of Exposure Science & Environmental Epidemiology 26(5):437-444.
[42] Querol, X., Viana, M., Alastuey, A., Amato, F., Moreno, T., Castillo, S. et al. (2007): Source origin of trace elements in PM from regional background, urban and industrial sites of Spain. Atmospheric Environment 41(34): 7219-7231.
[43] Leghouchi, E., Laib, E., Guerbet, M. (2009): Evaluation of chromium contamination in water, sediment and vegetation caused by the tannery of Jijel (Algeria): a case study. Environmental Monitoring and Assessment 153(1-4):111-117.
[44] Amodio, M., Andriani, E., Dambruoso, P.R., de Gennaro, G., Di Gilio, A., Intini, M., Palmisani, J., Tutino, M. (2013): A monitoring strategy to assess the fugitive emission from a steel plant. Atmospheric Environment 79: 455-461.

[45] Amrane, C., Bouhidel, K.E. (2019): Analysis and speciation of heavy metals in the water, sediments, and drinking water plant sludge of a deep and sulfate-rich Algerian reservoir. Environmental Monitoring and Assessment 191(2):73.

[46] Mehouel, F., Bouayad, L., Hammoudi, A.H., Ayadi, O., Regad, F. (2019): Evaluation of the heavy metals (mercury, lead, and cadmium) contamination of sardine (*Sardina pilchardus*) and swordfish (*Xiphias gladius*) fished in three Algerian coasts. Veterinary World 12(1):7-11.

[47] DPAT (Direction de programmation et de suivi de budget) Jijel. (2021).

[48] DSASI (Direction des statistiques agricoles et des systèmes d'information) Jijel. (2020).

[49] Quemerais, B., COSSA, D. (1997) : Procedures for sampling and analysis of mercury in natural water. Environment Canada-Quebec region, Environmental Conservation, St. Lawrence Centre, Scientific and Technical Report, ST-31E, pp. 34.

[50] J.E.C.F.A. (2003): (Summary and Conclusions of the 61st Meeting of the Joint FAO/WHO Expert Committee on Food Additives). JECFA/61/Sc Rome, Italy.

[51] US EPA (U.S. Environmental Protection Agency)(2014):Regional Screening Level (RSL) Summary Table May.

[52] U.S. EPA (U.S. Environmental Protection Agency) (2008): Child-specific exposure factors handbook. EPA/600/R-06/096F. Washington, DC: National Center 526 for Environmental Assessment Office of Research and Development.

[53] Basaran, B. (2022): Comparison of heavy metal levels and health risk assessment of different bread types marketed in Turkey, Journal of Food Composition and Analysis, 108:104443.

[54] US EPA (U.S. Environmental Protection Agency) (2022): Guidelines for the health risk assessment of chemical mixtures. Federal Register 51: 34014:1986.

[55] Basaran, B., Anlar, P., Oral, Z. F. Y., Polat, Z., & Kaban, G. (2022): Risk assessment of acrylamide and 5-hydroxymethyl-2-furfural (5-HMF) exposure from bread consumption: Turkey. Journal of Food Composition and Analysis, *107*: 104409.

[56] FAO/WHO (Food and Agriculture Organization/World Health Organization (2012): Joint FAO/WHO food standards program: Codex committee on contaminants in foods (Editorial amendments to the general standard for contaminants and toxins in food and feed), sixth session, Maastricht, Netherlands, CX/CF 12/6/11.

[57] Commission Codex Alimentarius (2014): FAO/WHO Joint Food Standards Programme, Codex Committee on Contaminants in Foods, Eighth Session The Hague, The Netherlands, (Prepared by Japan and the Netherlands).

[58] Codex Alimentarius Commission (1999): Discussion paper on maximum level for Pb in milk and secondary milk products. Joint FAO/WHO food standards programme, twenty-third session. The Rome, the Italy.

[59] IDF (IDF Standard (87-1979) : Determination of the Dispersibility and Wettability of Instant Dried Milk.

[60] Norouzirad, R., González-Montaña, J.R., Martínez-Pastor, F., Hosseini, H., Shahrouzian, A., Khabazkhoob, M., Malayeri, F.A., Bandani, H.M., Paknejad, M., Foroughi-nia, B. (2018): Lead and cadmium levels in raw bovine milk and dietary risk assessment in areas near petroleum extraction industries. Science of the Total Environment 635:308-314.

[61] El Sayed, E. M., Hamed, A.M., Badran, S.M., Mostafa, A. A. (2011): A survey of selected essential and heavy metals in milk from different regions of Egypt using ICP-AES. Food Additives & Contaminants: Part B 4(4):294- 298.

[62] Garba, S., Abdullahi, S., Abdullahi, M. (2018): Heavy Metal content of cow's milk from Maiduguri Metropolis and its environs, Borno state Nigeria. American journal of Engineering Research 7:63-73.

[63] Meshref, A.M., Moselhy, W.A., Hassan, N.E.H.Y. (2014): Heavy metals and trace elements levels in milk and milk products. Journal of Food Measurement and Characterization 8(4):381-388.

[64] Homayonibezi, N., Dobaradaran, S., Arfaeinia, H., et al. (2021): Toxic heavy metals and nutrient concentration in the milk of goat herds in two Iranian industrial and non-industrial zones. Environmental Science and Pollution Research 28(12) :14882-14892.

[65] Sellami, S., Zeghouan, O., Lassaad, M. et al. (2020) : Determination of lead concentrations in the soils of Setif City, Eastern Algeria. Arabian Journal of Geosciences 13: 929.

[66] Tunegova, M., Toman, R., Tancin, V. (2016) : Hevy metals environmental contaminants and their occurrence in different types of milk. Slovak Journal of Animal Science 49 (3):122-131.

[67] World Health Organization (WHO) (2005): Enhancing Participation in Codex Activities: An FAO/WHO Training Package. Food and Agriculture Organization, pp. 187.

[68] Shahbazi, Y., Ahmadi. F., Fakhari, F. (2016): Voltammetric determination of Pb, Cd, Zn, Cu and Se in milk and dairy products collected from Iran: An emphasis on permissible limits and risk assessment of exposure to heavy metals. Food Chemistry 192:1060-1067.

[69] Imam, M.M., Muhammad, Z., Zakari, Z. (2017): Determination of some heavy metals in milk of cow grazing at selected areas, of Kaduna Metropolis. Computer Science vs. Software Engineering 7: (7).

[70] Iqbal, H., Ishfaq, M., Abbas, M.N., Wahab, A., Qayum, M., Mehsud, S. (2016): Pathogenic bacteria and heavy metals toxicity assessments in evaluating unpasteurized raw milk quality through biochemical tests collected from dairy cows. Asian Pacific Journal of Tropical Disease 6(11):868-872.

[71] Sola-Larranaga, C., Navarro-Blasco, I. (2009)**:** Chemometric analysis of minerals and trace elements in raw cow milk from the community of Navarra, Spain. Food Chemistry 112: 189-196.

[72] Bilandzic, M., Dokic, M., Sedak, M., Solomun, B., Varenina, I., Knežević, Z., Benić, M. (2011): Trace element levels in raw milk from northern and southern regions of Croatia. Food Chemistry 127: 63-66.

[73] Pilarezyk, R., Wojcik, J., Czerniak, P., Sablik, P., Pilarezyk, B., Tomza-Marciniak, A. (2013): Concentrations of toxic heavy metals and trace elements in raw milk of Simmental and Holstein-Friesian cows from organic farm. Environmental Monitoring and Assessment 185:8383-8392.

[74] Khan, N., Jeong, I.S., Hwang, I.M., Kim, J.S., Choi, S.H., Nho, E.Y., Choi, J.Y., Park, K.S., Kim, K.S. (2014): Analysis of minor and trace elements in milk and yogurts by inductivel coupled plasma-mass spectrometry (ICP-MS). Food Chemistry147: 220-224.

[75] Raghu, V. (2015): Study of dung, urine, and milk of selected grazing animals as bioindicators in environmental geoscience a case study from Mangampeta barite mining area, Kadapa District, Andhra Pradesh, India. Environmental Monitoring and Assessment 187: 4080.

[76] Bakircioglu, D., Topraksever, N., Yurtsever, S., Kizildere, M., Kurtulus, Y.B. (2018): Investigation of macro, micro and toxic element concentrations of milk and fermented milks products by using an inductively coupled plasma optical emission spectrometer, to improve food safety in Turkey. Microchemical Journal 136:133-138.

[77] Ahmad, I., Zaman, A., Samad, N., Ayaz, M.M., Rukh, S., Akbar, A. (2017): Atomic Absorption Spectrophotometery Detection of Heavy Metals in Milk of Camel, Cattle, Buffalo and Goat from Various Areas of Khyber- Pakhtunkhwa (KPK), Pakistan. Journal of Analytical & Bioanalytical Techniques 8:367.

[78] Yu, M., Liu, Y., Achal, V., Fu, Q., Li, L. (2015) : Health Risk Assessment of Al and Heavy Metals in Milk Products for Different Age Groups in China. Polish Journal of Environmental Studies 24(6): 2707-2714.

[79] Giri, A., Bharti, V.K., Kalia, S., Kumar, B., Chaurasia, O.P. (2021): Health Risk Assessment of Heavy Metals Through Cow Milk Consumption in Trans-Himalayan High-Altitude Region. Biological Trace Element Research1 99(12):4572-4581.

[80] Castro Gonzalez, N.P., Moreno-Rojas, R., Calderón Sánchez, F., Moreno Ortega, A., Juarez Meneses, M. (2017): Assessment risk to children's health due to consumption of

cow's milk in polluted areas in Puebla and Tlaxcala, Mexico. Food Additives and Contaminants: Part B Surveillance 10(3):200-207.

[81] Miclean, M., Cadar, O., Levei, E.A., Roman, R., Ozunu, A., Levei, L. (2019): Metal (Pb, Cu, Cd, and Zn) Transfer along Food Chain and Health Risk Assessment through Raw Milk Consumption from Free-Range Cows. International Journal of Environmental Research and Public Health 16(21):4064.

[82] Mohammadi, A.A., Zarei, A., Majidi, S. et al. (2019): Carcinogenic and non-carcinogenic health risk assessment of heavy metals in drinking water of Khorramabad, Iran. MethodsX 6:1642-1651.