Exposure assessment and risk characterization of metals intake through consumption of wine by population of winemakers in Bosnia and Herzegovina and Croatia

ELMA OMERAGIC – DINO RADOSEVIC – AMIR CAUSEVIC – ALEKSANDRA MARJANOVIC – JASMINA DJEDJIBEGOVIC – MIROSLAV SOBER

Summary

The primary focus of this study was to determine the amounts of arsenic, iron, lead, cadmium, nickel and copper in wines originating from Bosnia and Hercegovina and Croatia, and to estimate the toxicological risk associated with the consumption of wine regarding selected heavy metals. The metals content was determined in 57 wine samples. Analysis of the metals was performed by graphite furnace atomic absorption spectrometry. The wine consumption levels as well as body mass values were determined using questionnaires specially designed for the purposes of this study and conducted among winemakers ($n = 46$). The health risk was determined by the estimated daily intake, hazard index (*HI*) and cancer risk (*Rc*). To estimate the daily intake of selected metals through wine consumption, 36 different scenarios using a $4 \times 3 \times 3$ design were developed. For each of these scenarios, *HI* and *Rc* were calculated. The content of metals was below the maximum residue level set by the European Union and also by Bosnia and Herzegovina. Cd content was generally higher in wine samples originating from the Dalmatia region in Croatia. *HI* and *Rc* for certain scenarios of exposition showed possible health risks that were unacceptable.

Keywords

wine; heavy metal; atomic absorption spectrometry; health risk

Heavy metals represent natural constituents of soil, originating from natural and anthropogenic sources. The natural source of metals is the parent substrate from which metals are released by decomposition of rocks. Anthropogenic sources are fossil fuel combustion, industrial plants, ore extraction, motor vehicles, industrial and municipal waste landfills, fertilizers and atmospheric sediments [1].

Metals reach the wines in various ways, while their structure and concentration in the wines depend on four groups of factors. The first group includes the ability of the wine to absorb the various minerals from the soil on which the vineyard was founded. The second group is related to the conditions and modes of grape production, where air pollutants and pesticide application are often emphasized. The third group is related to the addition of various oenological substances, as needed, during wine production and to the realization of alcoholic fermentation. The fourth group includes the characteristics of the containers in which the wine is stored and the characteristics of the glass used as wine bottles. The latter group includes the subsequent contamination of the wine with metals by the equipment used to process the grapes into the wine [2].

Since the metals are very often present in food and the environment as contaminants or pollutants, the control of food and the assessment of the uptake of certain metals into the human body are important in terms of assessing and determining human exposure to the harmful effects of metals. Recommendations on the maximum levels

Elma Omeragic, Dino Radosevic, Aleksandra Marjanovic, Jasmina Djedjibegovic, Miroslav Sober, Department of Pharmaceutical Analysis, Faculty of Pharmacy, University of Sarajevo, Zmaja od Bosne 8, 71000 Sarajevo, Bosnia and Herzegovina.
Amir Causevic, Department for Chemical Analysis of Food and General Use Items, Institute for Public Health Federation of Bosnia and Heregovina, Marsala Tita 9, 71000 Sarajevo, Bosnia and Herzegovina.

Correspondence author:
Elma Omeragic, e-mail: elma.omeragic@ffsa.unsa.ba

of individual toxicants, their total acceptable daily intake (*ADI*) and provisional allowable weekly intake (*PTWI*) for adults in food are made by the World Health Organization (WHO) and the Food and Agriculture Organization (FAO). In addition, each country, in accordance with its studies and the recommendations of the WHO and FAO, adopts national rulebooks setting maximum levels for certain contaminants in food. The values determined in foodstuffs must be within the limits of the maximum levels prescribed by the Regulations.

ADI is used in most cases for nutrients, while tolerated daily intake (*TDI*) for contaminants or occasionally for additives (in the past). Due to some degree of uncertainty in the data for contaminants and some additives, the FAO/WHO Joint Expert Committee on Food Additives (JECFA) has proposed provisional maximum tolerable daily intake (*PMTDI*). In USA, Environmental Protection Agency (US EPA) has replaced *ADI* and *TDI* with the term reference dose (*RfD*). The term *RfD* was introduced to avoid the implication that exposure to a given chemical at a given dose (defined by *ADI* or *TDI* values) is completely safe or acceptable. According to US EPA, the reference dose is "an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime" [3]. For metals that are the focus of this study, oral *RfD* values are 0.0003 $mg\cdot kg^{-1}$, 0.0005 $mg\cdot kg^{-1}$, 0.037 $mg\cdot kg^{-1}$, 0.7 $mg\cdot kg^{-1}$, and 0.02 $mg\cdot kg^{-1}$ of body weight (BW) per day for arsenic, cadmium, copper, iron, and nickel, respectively. As lead is a non-threshold toxicant, US EPA has not developed *RfD* for it [4, 5].

The primary focus of this study was to determine the contents of As, Cd, Cu, Fe, Pb and Ni in wines originating from Bosnia and Hercegovina

Tab. 1. Wine samples.

Sort	Sample code	Species	Place	Region	Year of production
Registered wineries					
White	PER2017	Graševina	Kutjevo	Slavonia	2017
	PETJAK2018	Žilavka and following sort (Bena, Krkosija)	Međugorje	Hercegovina	2017
	RUK2017	Rukatac	Vrgorac	Dalmacia	2017
	Z2018	Zlatarica	Vrgorac	Dalmacia	2018
	R2018	Rukatac	Vrgorac	Dalmacia	2018
	ŽIL2017	Žilavka	Mostar	Hercegovina	2017
Red	PETJAK2802	Blatina and following sort (Alicant, Bouschet, Tnjak, Vranac)	Međugorje	Hercegovina	2016
	TRNJ2017	Trnjak, Syrah	Vrgorac	Dalmacia	2017
	BOV2015	Merlot, Syrah	Vrgorac	Dalmacia	2015
	CRLJ2018	Crljenak	Vrgorac	Dalmacia	2018
	TR2018	Trnjak	Vrgorac	Dalmacia	2018
Rose	ROS2017	Plavina	Vrgorac	Dalmacia	2017
Wineries producing wine for own use					
White	05121998	Žilavka	Počitelj	Hercegovina	2018
	IR1808	Kujundžuša	Slivno	Dalmacia	2018
	RK92018	Rukatac, Kujundžuša	Grabovac	Dalmacia	2018
	MARVUJ1	Trbljan, Žutina, Zlatarica	Vrgorac	Dalmacia	2018
	KUNA2018	Babić, Plavac, Vranac, Trbljan	Donje Sitno	Dalmacia	2018
	IGB2015	–	Imotski	Dalmacia	2018
	CUKI78	Kujundžuša, Mednica	Vrgorac	Dalmacia	2017
	DVMVM2018	Debit, Vezuljka, Big and Small Maraškin	Seget Donj	Dalmacia	2018
	CHAR2018	Chardonnay	Vrgorac	Dalmacia	2018
	VL2018	Žutuja	Kaštel Lukšić	Dalmacia	2018
	SKR2015	Pošip	Skradin	Dalmacia	2015
	MARAŠ2018	Maraština, Debit	Cista Velika	Dalmacia	2018
	ICP2018	Kujundžuša, Pošip	Zagvozd	Dalmacia	2018
	MAKB2018	Maraština, Zlatarica, Medne, Kuc, Bogdanuša	Vrgorac	Dalmacia	2017
	JUPO2	Maraština	Vrgorac	Dalmacia	2018

(BIH) and Croatia, to estimate the toxicological risk associated with the consumption of wine regarding selected heavy metals. The toxicological risk was determined by the estimated daily intake (*EDI*), hazard index (*HI*) and cancer risk (*Rc*).

MATERIALS AND METHODS

Reagents preparation

All chemicals used during the analytical procedure were of ultra-pure grade. Standards solutions for As, Cd, Cu, Fe, Ni and Pb (1 000 ± 4 mg·l^{-1}; Sigma-Aldrich, St. Louis, Missouri, USA) were used to construct calibration curves. Standard dilutions were prepared from a stock solution of 1 000 mg·l^{-1} by successive dilution for each metal. Aqueous solutions of reagents and standard solutions were prepared using ultra-pure water (18.2 µS·cm^{-1}; Arium 611, Sartorius Mechatronics, Goettingen, Germany). To prevent cross-contamination, all glassware and utensils used in the work were soaked in 10% HNO_3 (v/v) for 24 h, after which they were washed with ultra-pure water. Quartz vessels for microwave digestion were also cleaned, being firstly washed with detergent, thoroughly rinsed with ultra-pure water and then dried at 105 °C for 2 h. Thereafter, the so-called UV-test was made with a special program defined in the microwave oven Easycontrol software (Milestone, Sorisole, Italy). Quartz vessels that were heated after the UV-test were cleaned again.

Sample collection

A total of 57 wine samples were collected during May 2019. These comprised wine samples originating from registered wineries (n = 12) and wine samples from wineries without a marketing authorization, producing wine for own use (n = 45). Out of 57 wine samples, 21 samples were

Tab. 1. *continued*

Sort	Sample code	Species	Place	Region	Year of production
Red	150470	Vranac	Počitelj	Hercegovina	2018
	STIV2018	Vranac	Krstatice	Dalmacia	2018
	GUDI2018	Trnjak	Krstatice	Dalmacia	2018
	D2018	Plavka, Merlot, Syrah	Staševica	Dalmacia	2018
	ŠOLTA2018	Dobričić	Grohote, Šolta	Dalmacia	2018
	MAGMAT1009	Merlot, Plavka	Vrgorac	Dalmacia	2018
	IBM2018	Merlot	Vrgorac	Dalmacia	2018
	MAGPHARM1	Plavac, Babica	Kaštel Stari	Dalmacia	2017
	MARIHRV2	Babić, Plavac, Minčuša	Primorski Dolac	Dalmacia	2018
	PSŠ92018	Plavac, Syrah, Šarka	Grabovac	Dalmacia	2018
	MAGZDR12	Small Plavac, Crljenak	Kaštel Gomilica	Dalmacia	2018
	NJ92018	Plavac	Staševica	Dalmacia	2018
	NEBO1	Shyrah	Vrgorac	Dalmacia	2017
	IGC2014	–	Imotski	Dalmacia	2018
	JS2018	Plavac	Prapatnica	Dalmacia	2018
	RUSOLIN2018	Babić, Small Plavac, Crljenak	Solin	Dalmacia	2018
	ŽBC2018	Small Plavac	Pelješac	Dalmacia	2017
	PMVD2018	Plavka, Merlot, Vranac, Dobričić	Tugare	Dalmacia	2018
	PELJ2018	Small Plavac	Pelješac	Dalmacia	2018
	GPMSC2018	Glavinuša, Plavac, Maraština, Smederevka, Crljenak	Solin	Dalmacia	2018
	MOPV2018	Merlot, Omiški Plavac, Vranac	Zagvozd	Dalmacia	2018
	BC2018	Babić	Ljubitovica	Dalmacia	2018
	MKAT2018	Merlot, Syrah	Vrgorac	Dalmacia	2017
	JUPO1	Small Plavac, Babić	Vrgorac	Dalmacia	2018
	JUPO3	Vranac, Plavka, Big Plavac	Vrgorac	Dalmacia	2018
	JUPO4	Plavina, Babić, Zadarka, Lasin	Unešić	Dalmacia	2018
Rose	MPZS1	Plavina, Linčuša	Kaštel Gomilica	Dalmacia	2018
	ČIZMA2018	Kujundžuša	Zadvarje	Dalmacia	2017
	DONA2018	Debit, Plavac	Donje Sitno	Dalmacia	2017
	BŠCR2018	Babić, Šibenka	Ljubitovica	Dalmacia	2018

Fig. 1. Geographical location of sample collection.

white wine sorts, 31 samples red wine sorts and 5 samples were rose wine sorts (Tab. 1). Sample collection was done in Croatia (region Dalmatia and Slavonia) and Bosnia and Herzegovina (region Herzegovina) (Fig. 1). The wine samples in a volume of approximately 500 ml were collected in plastic (PVC) bottles, transported to the laboratory and stored at –4 °C until analysis, which was done in August 2019.

Sample preparation

Sample preparation was done by standard methods of microwave BAS EN 13805:2015 [6]. Briefly, approximately 1 ml of samples was microwave-digested in a Microwave Ethos D (Milestone, Sorisole, Italy) oven for 30 min in a closed quartz vessel with 3 ml of 68% nitric acid (≥0.68 g·ml^{-1}, p.a., Sigma-Aldrich) and 2 ml 35% hydrogen peroxide (≥0.35 g·ml^{-1}, p.a., Sigma-Aldrich). The microwave oven was programmed at 1500 W and 4500 kPa as maximum power and pressure limit (ramp time 15 min, hold time 15 min and cooling time 20 min). An appropriate blank (3 ml of 68% nitric acid and 2 ml of 35% hydrogen peroxide) was prepared in the same way. After mineralization, the quartz vessels were opened and the solutions were transferred to volumetric flasks, diluted to a known volume (50 ml) with ultrapure water and stored, until analysis for a maximum of 2 days.

Tab 2. Analytical method parameters.

Metal	Recovery [%]	*LOQ* [mg·kg^{-1}]	*LOD* [mg·kg^{-1}]
Cd	89.3	0.0798	0.0266
Cu	98.6	0.0014	0.0004
Pb	96.4	0.0011	0.0003
As	98.2	0.0021	0.0007
Ni	87.5	0.0019	0.0060
Fe	96.3	0.0016	0.0005

LOQ – limit of quantification, *LOD* – limit of detection.

Analysis of metals

Analysis of metals was performed in AA-7000F Dual Atomizer System (Shimadzu, Tokyo, Japan) atomic absorption spectrometer, equipped with self-reversal (SR) background correction, autosampler and graphite furnace. The argon flow was used to remove residues from the graphite tube during pyrolysis. Analysis of Fe, Cu, Pb and Cd was done using the standard method for determination of trace elements in foodstuffs BAS EN 14084:2003 [7], while the analysis of As and Ni was done using the internal methods (IM-OP-5.4-01-15-1-S and IM-OP-5.4-01-16-1-S) of the Department for Food Analysis and subjects for General Use of the Federal Institute of Public Health (Sarajevo, Bosnia and Herzegovina) [8, 9].

Samples of wines were analysed in triplicate. The blanks and calibration standards were analysed using the same methods. The content of heavy metals was expressed in milligrams per kilogram of sample.

Quality assurance

Recovery assays were carried out for the trueness study purpose. A white wine sample was spiked, before mineralization, at 3 levels of content, which covered measurement range, and analysed in 3 replicates. The elemental recovery for each sample (content level) was calculated, and the global recovery as an average recovery for each level of content were calculated. Laboratory reagent blank was carried out with each batch of samples. All the samples were analysed in triplicate and the metal content was presented as an average. The differences between triplicates were ≤5.1%. Analytical method parameters are shown in Tab. 2. Blanks did not contain detectable amounts of the measured metals.

Intake assessment

The wine consumption level was estimated using a questionnaire. A 12-items questionnaire, structured by the authors of the paper only for this research, was used (Tab. 3). All participants provided informed consent prior to the study. The link for the questionnaire was sent to the

Tab. 3. Questionnaire items.

Item	Type of question	Answer options for closed questions
National origin	Open	–
Current place of residence	Open	–
Current age (years)	Open	–
National origin	Open	–
Body height [cm]	Open	–
Current body weight [kg]	Open	–
Gender	Closed	Man; Female
Do you drink wine?	Closed	Yes; No
At which age you drank wine for the first time?	Open	–
How often you drink wine?	Closed	Once daily; Once weekly; Two-three times per week; Once monthly; Two-three times per month; Once in six months; Once in a year; I do not drink wine at all
Usually, how many glasses of wine you drink at an occasion (one glass = 2 dl)?	Open	–
Which sort of wine do you drink usually?	Closed	Red; White; Rose
Did you drink wine in the past month?	Closed	Yes; No

winemakers working in wineries from which wine samples had been collected, and the winemakers were called to complete the questionnaire. Eligible were adults, who were active in wine making. A total of 46 questionnaires were completed. At least one person who actively participated in wine production from each winery completed a questionnaire. All participants completed the questionnaire correctly. All participants met the predefined eligibility criteria.

Statistical analysis was performed using SPSS Statistics 21 Premium software (IBM, Armonk, New York, USA). It is important to emphasize that, for all calculations and comparatives, we assumed that 1 kg of wine is equal to 1 l of wine. The estimated daily intake (*EDI*) of each of the metals was calculated according to Eq. 1:

$$EDI = DI \cdot \frac{c}{BW} \tag{1}$$

where *EDI* is expressed in milligrams per kilogram of body weight (BW) per day, *DI* is daily consumption expressed in litres per day, *c* is content of metal expressed in milligrams per kilogram and BW is expressed in kilograms. Daily intake of wine and body weight were estimated from the previously mentioned questionnaires (Tab. 3.).

To estimate the daily intake of each of the metals through wine consumption, we developed 36 different scenarios using a $4 \times 3 \times 3$ design. Specifically, four content levels of certain contaminants were chosen: mean, maximal, 50th and 95th percentile; three wine consumption levels were included: 2.2 ml that represented 5th percentile, 57.14 ml that represented 50th percentile and 416.7 ml that represented 95th percentile. Finally, three body mass values were used: a body mass of 54.35 kg that represented 5th percentile, 75.5 kg that represented 50th percentile, and a body mass of 106.5 kg that represented 95th percentile of the group of 46 adult healthy winemakers from the questionnaire. For each of these scenarios, the hazard index (*HI*) was calculated based on Eq. 2 and Eq. 3.

$$HI = \frac{EDI}{RfD} \tag{2}$$

$$\Sigma HI = HI_{As} + HI_{Cd} + HI_{Cu} + HI_{Fe} + HI_{Ni} + HI_{Pb} \tag{3}$$

where *HI* is hazard index for single metal, *RfD* is reference oral dose expressed in milligrams per kilogram BW per day, and Σ*HI* is total hazard from multiple metals exposure.

Reference oral doses for As, Cd, Cu, Fe and Ni are 0.0003, 0.0005, 0.037, 0.7 and 0.02 $mg \cdot kg^{-1}$ BW per day, respectively [5]. Regarding lead, *HI* was calculated based on three provisional tolerable daily intakes (*PTDI)* values recommended by the European Food Safety Authority (EFSA) [10]: A – 6.3×10^{-4} $mg \cdot kg^{-1}$ per day (prevalence of chronic/renal kidney disease), B – 1.5×10^{-3} $mg \cdot kg^{-1}$ per day (systolic blood pressure) and C – 5.0×10^{-4} $mg \cdot kg^{-1}$ per day (developmental neurotoxicity of the central system).

Any *HI* value greater than value 1 indicates a potential health risk. If the *HI* value is less than 1, there is no obvious health risk. Although *HI* does not quantify the likelihood of adverse health effects, it does provide an indication of health risk.

For cancer risk (*Rc*) evaluation [11], values were calculated following Eq. 4.

$$R_c = \frac{EDI}{CPS_0} \quad (4)$$

where CPS_0 is cancer slope expressed in milligrams per kilograms BW per day; As cancer slope is 1.5 mg·kg^{-1} BW and Ni 1.7 mg·kg^{-1} BW per day according to US EPA. For Cd, Cu, Fe and Pb, cancer slope values are not available. For Cd, Cu and Fe, no studies on oral ingestion of these metals with quantitative output are available. Quantification of cancer risk of Pb is biased by many uncertainties, thus, the Carcinogen Assessment Group recommends that a numerical estimate not be used [5]. Thus, US EPA established acceptable guideline values of $Rc < 10^{-4}$ [11].

RESULTS AND DISCUSSION

Heavy metals content

Data on the content of heavy metals in wine samples are presented in Tab. 4. Metals content was in the following order Fe > Cu > Ni > Pb > Cd > As.

In the European Union (EU) [12] and BIH national regulation [13], maximum levels are established for Fe (20 mg·kg^{-1}, 15 mg·kg^{-1} and 10 mg·kg^{-1} for red, white and rose wine sorts, respectively), Cu (1.0 mg·kg^{-1}) and Pb (0.2 mg·kg^{-1}) in wines that are placed on the market. According to the national regulation of Croatia [14], the maximum levels for Pb, Cd, As, Cu and Ni are 0.3 mg·l^{-1}, 0.01 mg·l^{-1}, 0.2 mg·l^{-1}, 1.0 mg·l^{-1} and 0.1 mg·l^{-1}, respectively, and for Fe 10.0 mg·l^{-1}, 15.0 mg·l^{-1} and 20.0 mg·l^{-1} for red, white and rose wine sorts, respectively. The International Office for Vine and Wines (IOV) defined the limits of the metal concentrations in wines as 0.01 mg·l^{-1}, 0.15 mg·l^{-1}, 0.2 mg·l^{-1} and 1 mg·l^{-1} for Cd, Pb, As and Cu, respectively [15].

In this study, metals were determined at contents below the maximum levels set by the EU and BIH legislations [12, 13]. However, EU and BIH Regulatory Agency do not present any legislation for Cd, As and Ni in wines. The maximum acceptable limit for Cd according to the national regulation of Croatia and IOV is 0.01 mg·l^{-1} [14, 15] and in 25 % of the analysed samples in this study, concentrations of Cd were above 0.01 mg·l^{-1} (Tab. 4). All the samples with a concentration of Cd above 0.01 mg·l^{-1} originated in Dalmatia, Croatia. Two of those samples (12.5 %) were from registered wineries and 14 (87.5 %) were produced for own use (Tab. 1 and Tab. 5).

Cd concentrations higher than 0.01 mg·l^{-1} were previously found in wines from Hungary [16, 17] and Serbia [18, 19] (Tab. 6). High concentrations of Cd in Hungarian wines were explained to be

Tab. 4. Content of selected metals in the wine samples.

Metal	Wine sort	Content [mg·kg^{-1}]						
		P_{25}	P_{50}	P_{75}	P_{95}	Mean ± *SD*	Min.	Max.
Fe	Red	12.928	14.054	15.165	17.021	14.127 ± 1.693	10.990	17.030
	White	8.001	8.873	9.103	10.062	8.460 ± 0.949	6.220	10.120
	Rose	8.836	10.885	11.348	–	10.382 ± 1.525	8.100	12.320
Ni	All sorts	0.028	0.034	0.044	0.073	0.039 ± 0.016	0.013	0.080
Cu	All sorts	0.102	0.130	0.182	0.216	0.141 ± 0.046	0.068	0.271
As	All sorts	0.006	0.008	0.010	0.020	0.008 ± 0.004	0.003	0.021
Pb	All sorts	0.006	0.008	0.011	0.022	0.010 ± 0.006	0.003	0.032
Cd	All sorts	0.005	0.009	0.011	0.021	0.009 ± 0.005	0.002	0.027

P_{25} – 25th percentile, P_{50} – 50th percentile, P_{75} – 75th percentile, P_{95} – 95th percentile, *SD* – standard deviation.

Tab. 5. Content of metals.

Sort	Sample code	Content [mg·kg-1]					
		Fe	Ni	Cu	As	Pb	Cd
Registered wineries							
White	PER2017	8.4389	0.0321	0.0897	0.0072	0.0069	0.0048
	PETJAK2018	6.2198	0.0321	0.1198	0.0075	0.0052	0.0092
	RUK2017	8.9872	0.0301	0.1123	0.0105	0.0121	0.0092
	Z2018	9.3176	0.0400	0.0785	0.0083	0.0038	0.0021
	R2018	9.0001	0.0302	0.1120	0.0040	0.0060	0.0040
	ŽIL2017	9.5290	0.0402	0.0800	0.0046	0.0050	0.0097

Tab. 5. *continued*

Sort	Sample code	Content [mg·kg-1]					
		Fe	Ni	Cu	As	Pb	Cd
Red	PETJAK2802	13.5721	0.0422	0.1564	0.0047	0.0100	0.0090
	TRNJ2017	16.6329	0.0677	0.1980	0.0090	0.0062	0.0074
	BOV2015	15.0943	0.0632	0.1732	0.0103	0.0100	0.0112
	CRLJ2018	16.9908	0.0763	0.1512	0.0098	0.0104	0.0115
	TR2018	15.0663	0.0408	0.1984	0.0090	0.0065	0.0076
Rose	ROS2017	10.7665	0.0398	0.1109	0.0089	0.0093	0.0088
Wineries producing wine for own use							
White	05121998	8.8732	0.0445	0.0889	0.0088	0.0071	0.0050
	IR1808	9.0932	0.0342	0.1009	0.0052	0.0074	0.0095
	RK92018	8.1321	0.0432	0.1109	0.0098	0.0043	0.0180
	MARVUJ1	7.0075	0.0297	0.0967	0.0045	0.0034	0.0057
	KUNA2018	9.2100	0.0402	0.0980	0.0100	0.0089	0.0126
	IGB2015	7.1298	0.0234	0.1053	0.0089	0.0061	0.0087
	CUKI78	7.3411	0.0301	0.1211	0.0109	0.0076	0.0197
	DVMVM2018	8.0043	0.0246	0.1023	0.0065	0.0069	0.0050
	CHAR2018	9.1121	0.0432	0.1108	0.0089	0.0094	0.0100
	VL2018	8.1121	0.0270	0.1007	0.0075	0.0080	0.0060
	SKR2015	8.2101	0.0320	0.0921	0.0054	0.0048	0.0038
	MARAŠ2018	8.9067	0.0280	0.1003	0.0042	0.0050	0.0056
	ICP2018	10.1213	0.0432	0.0675	0.0053	0.0034	0.0028
	MAKB2018	8.9087	0.0560	0.0865	0.0078	0.0048	0.0094
	JUPO2	8.0142	0.0290	0.1213	0.0095	0.0087	0.0045
Red	150470	17.0121	0.0530	0.1809	0.0045	0.0078	0.0095
	STIV2018	14.0522	0.0200	0.1423	0.0045	0.0062	0.0110
	GUDI2018	15.0023	0.0310	0.1657	0.0065	0.0098	0.0182
	D2018	11.9422	0.0200	0.1422	0.0040	0.0210	0.0054
	ŠOLTA2018	14.0411	0.0386	0.2445	0.0034	0.0099	0.0112
	MAGMAT1009	11.0233	0.0219	0.1862	0.0056	0.0211	0.0093
	IBM2018	12.1241	0.0332	0.1063	0.0112	0.0052	0.0210
	MAGPHARM1	12.5234	0.0211	0.1409	0.0067	0.0122	0.0089
	MARIHRV2	12.0442	0.0522	0.1876	0.0210	0.0198	0.0265
	PSŠ92018	13.1322	0.0298	0.2008	0.0076	0.0113	0.0089
	MAGZDR12	14.0564	0.0232	0.2123	0.0080	0.0140	0.0067
	NJ92018	13.2198	0.0421	0.1532	0.0200	0.0164	0.0221
	NEBO1	11.5003	0.0250	0.1620	0.0080	0.0320	0.0132
	IGC2014	13.2131	0.0150	0.1300	0.0080	0.0135	0.0090
	JS2018	14.1120	0.0700	0.2120	0.0210	0.0100	0.0060
	RUSOLIN2018	10.9887	0.0210	0.1543	0.0067	0.0300	0.0113
	ŽBC2018	15.3218	0.0342	0.1895	0.0070	0.0054	0.0072
	PMVD2018	16.0087	0.0563	0.1872	0.0107	0.0132	0.0121
	PELJ2018	15.5121	0.0503	0.1832	0.0079	0.0084	0.0045
	GPMSC2018	17.0312	0.0301	0.2709	0.0056	0.0089	0.0023
	MOPV2018	14.6231	0.0543	0.1340	0.0056	0.0076	0.0029
	BC2018	15.1121	0.0280	0.1541	0.0067	0.0092	0.0050
	MKAT2018	14.7854	0.0803	0.1809	0.0073	0.0062	0.0094
	JUPO1	12.0889	0.0132	0.1214	0.0078	0.0121	0.0089
	JUPO3	13.0633	0.0655	0.2000	0.0187	0.0098	0.0043
	JUPO4	13.9453	0.0730	0.2100	0.0109	0.0045	0.0022
Rose	MPZS1	12.3210	0.0310	0.1002	0.0063	0.0101	0.0095
	ČIZMA2018	8.0954	0.0231	0.1009	0.0099	0.0056	0.0109
	DONA2018	9.0823	0.0342	0.1089	0.0121	0.0109	0.0210
	BŠCR2018	11.0043	0.0433	0.1052	0.0054	0.0082	0.0100

Tab. 6. Selected literature data on toxic metals in wine along with toxic metals in this study.

Wine samples				As	Cd	Cu	Fe	Ni	Pb	Ref.
CC	Sort	*n*	Method							
Experimental results				Content [mg·kg^{-1}]						
BA HR	White	21	FAAS	0.003–0.021	0.002–0.027	0.068–0.271	6.220–10.120	0.013–0.08	0.003–0.032	
	Red	31					10.990–17.030			
	Rose	5					8.100–12.320			
Literature				Concentration [mg·l^{-1}]						
HR	White	–	EDXRF	ND	–	0.006	0.061	0.006	0.030	1
BA	White, red	24	FAAS	–	–	ND–2.874	–	ND–0.489	ND–0.189	2
HU	Red, white	35	GFAAS	< *LOD*	0.000–0.002 (0.001)	0.002–0.640 (0.148)	–	–	0.006–0.090 (0.032)	16
HU	Red, white	183	–	0.010–0.100	0.010–1.000	0.200–50.000	–	0.020–0.200	–	17
RS	Red, white	8	FAAS	–	0.009–0.018 (0.012)	0.090–2.300 (0.580)	1.930–10.700 (4.550)	–	0.100–0.230 (0.140)	18
RS	–	20	FAAS	–	–	0.070–0.570	2.930–36.200	–	–	19
BR	White	7	DPASV	–	0.002–0.005	0.001–0.010	–	–	0.005–0.018	20
TR	White	6	AAS	–	0.003	0.131	1.700	0.134	–	21
	Red	37		–	< *LOD*	0.157	0.700	0.573	–	

CC – country codes (BA – Bosnia and Herzegovina, HR – Croatia, BR – Brazil, TR – Turkey, RS – Serbia, HU – Hungary).
Methods: AAS – atomic absorption spectroscopy, FAAS – flame atomic absorption spectroscopy, GFAAS – graphite furnace atomic absorption spectrometry, DPASV – differential pulse anodic stripping voltammetry, EDXRF – energy-dispersive X-ray fluorescence.
n – number of samples, (–) – data not available, ND – not detected, *LOD* – limit of detection. Values in brackets represent mean.

due to contamination from containers and to contamination during the winemaking process [16]. In the case of wines from Serbia, Ražić et al. [22] indicated that traffic exhaust gases are the most relevant source of Cd, while Suturović and Marjanović [19] assumed that the increased Cd concentration was due to the raw material contamination or irregularities in the technological process of the wine production. Further investigation is needed to detect the possible source of higher Cd content in our study. However, our results are in good agreement with other published data (Tab. 6).

Wine consumption level

The age of the individuals who took part in a survey was in a range of 19–64 years (mean ± standard deviation, 36.9 ± 15.5). This study found that this population starts to drink wine very young, in the age of 16.8 ± 5.5 years (mean ± standard deviation). According to our data, the involved population of winemakers consumed 57.1 ml of wine per day (Tab. 7). Consumption data were further analysed according to wine type, with adults having a higher consumption of red (71.4 ml per day) than white wine (50.0 ml per day). The quantity of wine consumed in our study was lower than in USA, where adult wine drinkers (aged > 21 years) consumed a median of 195 g of wine per day with a higher consumption of white wine (205.8 g per day) than red wine (180 g per day) [23].

Risk assesment

The estimated daily intake by wine consumption of each of the metals did not exceed the refer-

Tab. 7. Wine consumption by winemakers.

	P_5	P_{50}	P_{75}	P_{95}	Mean ± *SD*	Min.	Max.
Body weight [kg]							
	54.4	75.5	90.0	106.5	77.2 ± 14.8	54.0	116.0
Wine consumption level [mg·l^{-1}]							
White wine	0.5	50.0	200.0	400.0	117.1 ± 127.9	0.5	416.7
Red wine	2.2	71.4	200.0	416.7	171.8 ± 253.7	2.2	1000.0
All sorts of wine	2.2	57.1	200.0	416.7	137.8 ± 185.9	0.5	1000.0

P_5 – 5th percentile, P_{50} – 50th percentile, P_{75} – 75th percentile, P_{95} – 95th percentile, *SD* – standard deviation.

Tab. 8. Estimated daily intake of metals through wine consumption by winemakers.

Consumption	5th percentile of consumption				50th percentile of consumption				95th percentile of consumption			
Metal content	Mean	P_{50}	Max.	P_{95}	Mean	P_{50}	Max.	P_{95}	Mean	P_{50}	Max.	P_{95}
5th percentile of body weight												
Cd	0.0001	0.0001	0.0004	0.0003	0.0073	0.0071	0.0209	0.0166	0.0586	0.0568	0.1672	0.1332
Pb	0.0002	0.0001	0.0005	0.0004	0.0076	0.0066	0.0252	0.0173	0.0606	0.0530	0.2019	0.1387
As	0.0001	0.0001	0.0003	0.0003	0.0066	0.0062	0.0166	0.0159	0.0526	0.0492	0.1325	0.1268
Cu	0.0023	0.0021	0.0044	0.0035	0.1114	0.1025	0.2136	0.1700	0.8910	0.8201	1.7089	1.3596
Ni	0.0006	0.0006	0.0013	0.0012	0.0304	0.0270	0.0633	0.0578	0.2431	0.2157	0.5066	0.4626
Fe	0.1881	0.1929	0.2751	0.2745	9.1833	9.4175	13.4307	13.4005	73.4607	75.3345	107.4373	107.1958
50th percentile of body weight												
Cd	0.0001	0.0001	0.0003	0.0002	0.0053	0.0051	0.0209	0.0120	0.0422	0.0409	0.1203	0.0959
Pb	0.0001	0.0001	0.0004	0.0003	0.0055	0.0048	0.0182	0.0125	0.0436	0.0381	0.1453	0.0999
As	0.0001	0.0001	0.0002	0.0002	0.0047	0.0044	0.0119	0.0114	0.0379	0.0354	0.0954	0.0913
Cu	0.0016	0.0015	0.0032	0.0025	0.0802	0.0738	0.1538	0.1223	0.6414	0.5903	1.2302	0.9787
Ni	0.0004	0.0004	0.0009	0.0009	0.0219	0.0194	0.0456	0.0416	0.1750	0.1553	0.3647	0.3330
Fe	0.1354	0.1389	0.1981	0.1976	6.6107	6.7794	9.6683	9.6466	52.8820	54.2309	77.3406	0.3330
95th percentile of body weight												
Cd	0.0001	0.0001	0.0002	0.0002	0.0037	0.0036	0.0107	0.0085	0.0299	0.0290	0.0854	0.0680
Pb	0.0001	0.0001	0.0003	0.0002	0.0039	0.0034	0.0129	0.0089	0.0309	0.0271	0.1031	0.0708
As	0.0001	0.0001	0.0002	0.0002	0.0034	0.0031	0.0085	0.0081	0.0269	0.0251	0.0676	0.0647
Cu	0.0012	0.0011	0.0022	0.0018	0.0569	0.0523	0.1091	0.0868	0.4549	0.4187	1.2302	0.6941
Ni	0.0003	0.0003	0.0007	0.0006	0.0155	0.0138	0.0323	0.0295	0.1241	0.1102	0.2586	0.2362
Fe	0.0960	0.0985	0.1405	0.1402	4.6887	4.8083	6.8573	6.8419	37.5067	38.4634	54.8541	54.7308

Estimated daily intake is expressed in milligrams per kilogram of body weight per day.
P_{50} – 50th percentile of metal content, P_{95} – 95th percentile of metal content.

Tab 9. Hazard index values for 36 exposure scenarios.

Consumption	5th percentile of consumption				50th percentile of consumption				95th percentile of consumption			
Metal content	Mean	P_{50}	Max.	P_{95}	Mean	P_{50}	Max.	P_{95}	Mean	P_{50}	Max.	P_{95}
5th percentile of body weight												
Cd	0.0003	0.0003	0.0009	0.0007	0.0146	0.0142	0.0418	0.0333	0.1171/	0.1135	0.3343	0.2663
Pb (A)	0.0002	0.0002	0.0008	0.0006	0.0120	0.0105	0.0401	0.0275	0.0962	0.0841	0.3204	0.2202
Pb (B)	0.0001	0.0001	0.0003	0.0002	0.0050	0.0044	0.0168	0.0116	0.0404	0.0353	0.1346	0.0925
Pb (C)	0.0003	0.0003	0.0010	0.0007	0.0151	0.0132	0.0505	0.0347	0.1212	0.1060	0.4037	0.2774
As	0.0004	0.0004	0.0011	0.0011	0.0219	0.0205	0.0552	0.0528	0.1755	0.1640	0.4416	0.4227
Cu	0.0001	0.0001	0.0001	0.0001	0.0030	0.0028	0.0058	0.0046	0.0241	0.0222	0.0462	0.0367
Ni	0.0000	0.0000	0.0001	0.0001	0.0015	0.0013	0.0032	0.0029	0.0122	0.0108	0.0253	0.0231
Fe	0.0003	0.0003	0.0004	0.0004	0.0131	0.0135	0.0192	0.0191	0.1049	0.1076	0.1535	0.1531
$\sum HI_A$	0.0014	0.0013	0.0034	0.0029	0.0662	0.0628	0.1652	0.1403	0.5299	0.5022	1.3213	1.1222
$\sum HI_B$	0.0012	0.0012	0.0029	0.0025	0.0593	0.0567	0.1419	0.1243	0.4742	0.4535	1.1355	0.9945
$\sum HI_C$	0.0014	0.0013	0.0036	0.0030	0.0694	0.0655	0.1756	0.1474	0.5550	0.5241	1.4046	1.1794
50th percentile of body weight												
Cd	0.0011	0.0010	0.0006	0.0005	0.0105	0.0102	0.0418	0.0240	0.0843	0.0817	0.2407	0.1917
Pb (A)	0.0002	0.0002	0.0006	0.0004	0.0087	0.0076	0.0288	0.0198	0.0692	0.0605	0.2307	0.1585
Pb (B)	0.0002	0.0002	0.0002	0.0002	0.0036	0.0032	0.0121	0.0083	0.0291	0.0254	0.0969	0.0666
Pb (C)	0.0002	0.0002	0.0007	0.0005	0.0109	0.0095	0.0363	0.0250	0.0872	0.0763	0.2906	0.1997
As	0.0001	0.0001	0.0008	0.0008	0.0158	0.0148	0.0397	0.0380	0.1263	0.1181	0.3179	0.3043
Cu	0.0002	0.0002	0.0001	0.0001	0.0022	0.0020	0.0042	0.0033	0.0173	0.0160	0.0332	0.0265
Ni	0.0003	0.0003	0.0000	0.0000	0.0011	0.0010	0.0023	0.0021	0.0088	0.0078	0.0182	0.0166
Fe	0.0000	0.0000	0.0003	0.0003	0.0094	0.0097	0.0138	0.0138	0.0755	0.0775	0.1105	0.1102
$\sum HI$ (A)	0.0000	0.0000	0.0024	0.0021	0.0477	0.0452	0.1306	0.1010	0.3815	0.3616	0.9512	0.8078
$\sum HI$ (B)	0.0002	0.0002	0.0021	0.0018	0.0427	0.0408	0.1139	0.0895	0.3413	0.3264	0.8174	0.7159
$\sum HI$ (C)	0.0010	0.0009	0.0026	0.0022	0.0499	0.0472	0.1381	0.1061	0.3995	0.3773	1.0112	0.8490
95th percentile of body weight												
Cd	0.0002	0.0001	0.0004	0.0003	0.0075	0.0072	0.0213	0.0170	0.0598	0.0580	0.1707	0.1360
Pb (A)	0.0001	0.0001	0.0004	0.0003	0.0061	0.0054	0.0205	0.0141	0.0491	0.0429	0.1636	0.1124
Pb (B)	0.0001	0.0000	0.0002	0.0003	0.0026	0.0023	0.0086	0.0059	0.0206	0.0429	0.0687	0.0472
Pb (C)	0.0001	0.0001	0.0003	0.0002	0.0039	0.0034	0.0129	0.0089	0.0309	0.0271	0.1031	0.0708

Tab. 9. *continued*

Consumption	5th percentile of consumption				50th percentile of consumption				95th percentile of consumption			
Metal content	Mean	P_{50}	Max.	P_{95}	Mean	P_{50}	Max.	P_{95}	Mean	P_{50}	Max.	P_{95}
As	0.0002	0.0002	0.0006	0.0006	0.0112	0.0105	0.0282	0.0270	0.0896	0.0837	0.2255	0.2158
Cu	0.0000	0.0000	0.0001	0.0000	0.0014	0.0013	0.0027	0.0022	0.0114	0.0105	0.0308	0.0174
Ni	0.0000	0.0000	0.0000	0.0000	0.0008	0.0007	0.0016	0.0015	0.0062	0.0055	0.0129	0.0118
Fe	0.0001	0.0001	0.0002	0.0002	0.0067	0.0069	0.0098	0.0098	0.0536	0.0549	0.0784	0.0782
$\sum HI$ (A)	0.0007	0.0007	0.0017	0.0015	0.0337	0.0320	0.0841	0.0714	0.2697	0.2556	0.6818	0.5715
$\sum HI$ (B)	0.0006	0.0006	0.0015	0.0013	0.0301	0.0288	0.0723	0.0633	0.2412	0.2307	0.5869	0.5063
$\sum HI$ (C)	0.0007	0.0006	0.0018	0.0015	0.0353	0.0333	0.0894	0.0751	0.28242	0.2667	0.7243	0.6008

P_{50} – 50th percentile of metal content, P_{95} – 95th percentile of metal content.
A – hazard index calculated using provisional tolerable daily intake (*PTDI*) 6.3×10^{-4} mg·kg^{-1} per day, B – hazard index calculated using *PTDI* 1.5×10^{-3} mg·kg^{-1} per day, C – hazard index calculated using *PTDI* 5.0×10^{-4} mg·kg^{-1}, $\sum HI$ – total hazard from the multiple metals exposures.

Tab. 10. Cancer risk values for 36 scenarios.

Consumption	5th percentile of consumption				50th percentile of consumption				95th percentile of consumption			
Metal content	Mean	P_{50}	Max.	P_{95}	Mean	P_{50}	Max.	P_{95}	Mean	P_{50}	Max.	P_{95}
5th percentile of body weight												
As	2.25×10^{-7}	2.10×10^{-7}	5.67×10^{-7}	5.42×10^{-7}	5.67×10^{-7}	5.42×10^{-7}	1.47×10^{-5}	1.41×10^{-5}	4.26×10^{-5}	3.99×10^{-5}	1.07×10^{-4}	1.03×10^{-4}
Ni	9.18×10^{-7}	8.14×10^{-7}	1.91×10^{-7}	1.75×10^{-6}	2.38×10^{-5}	2.12×10^{-5}	4.97×10^{-5}	4.53×10^{-5}	1.74×10^{-4}	1.54×10^{-4}	3.62×10^{-4}	3.31×10^{-4}
50th percentile of body weight												
As	1.62×10^{-7}	1.52×10^{-7}	4.08×10^{-7}	3.90×10^{-7}	4.21×10^{-6}	3.94×10^{-6}	1.06×10^{-5}	1.01×10^{-5}	3.07×10^{-5}	2.87×10^{-5}	7.73×10^{-5}	7.40×10^{-5}
Ni	6.61×10^{-7}	5.86×10^{-7}	1.38×10^{-6}	1.26×10^{-6}	1.72×10^{-5}	1.52×10^{-5}	3.57×10^{-5}	3.26×10^{-5}	1.25×10^{-4}	1.11×10^{-4}	2.61×10^{-4}	2.38×10^{-4}
95th percentile of body weight												
As	1.15×10^{-7}	1.07×10^{-7}	2.89×10^{-7}	2.77×10^{-7}	2.99×10^{-6}	2.79×10^{-6}	7.51×10^{-6}	7.19×10^{-6}	2.18×10^{-5}	2.04×10^{-5}	5.48×10^{-5}	5.25×10^{-5}
Ni	4.69×10^{-7}	4.16×10^{-7}	9.76×10^{-7}	8.91×10^{-7}	1.22×10^{-5}	1.08×10^{-5}	2.54×10^{-5}	2.32×10^{-5}	8.87×10^{-5}	7.88×10^{-5}	1.85×10^{-4}	1.69×10^{-4}

P_{50} – 50th percentile of metal content, P_{95} – 95th percentile of metal content.

ence oral dose for metals [5] or the recommended tolerable daily intake for lead [10] in any of the scenarios observed (Tab. 8).

According to the *HI* values for each metal, there was no health risk in any of the exposure scenarios observed. However, according to Σ*HI* values that were greater than 1, there was a health risk in the scenario where individuals weighing 75.5 kg or less (50 % of the population analysed in our study) consumed 416.7 ml (or more) wines (5% of the population analysed in our study), with a median value of the metal content, or a content of selected heavy metals, corresponding to the content of 50 % of the samples in our study (50th percentile of content; Tab. 9).

Santos et al. [24] assessed the risk to health due to wine consumption by the general adult population, analysing metals (As, Hg, Cd, Ni and Pb) in 25 most commonly consumed wines in Portugal. To calculate target hazard quotients (*THQ*) values, data on average daily wine consumption (19.29 ml daily during life), body weight (women 63.5 kg and men 75.9 kg) were obtained from literature [24] and data on the 25th, 50th, 75th percentiles, minimum and maximum values for the metal concentration determined in the analysed wine samples were used. According to the results of that study, the established *THQ* values were lower than 1 but close to 1 for both genders, which indicated that there is no reason for special concern regarding the public health safety regarding metals in wine. In the study, Ni had the highest contribution to the total value of *THQ* [24]. Our findings also showed that the total hazard for multiple metal exposures in the case of 50th percentile of body weight (75.5 kg) and 50th percentile of wine consumption (57.1 ml) are very low (0.0408–0.1061) and, for this exposure scenario, there is no special health risk.

A study conducted in South-East Australia [25] included analysis of red wine, stout and apple juice purchased from stores for the concentration of Pb, Zn, Cu, Ni, Mn, Cr and V. For the purpose of consumer health risk assessment, *THQ* was calculated using data on the average daily consumption for all three beverages of 11.75 ml, body weight 83.11 kg and 69.81 kg for men and women, and the mean values of the determined concentrations of metals. The *THQ* values for individual elements in red wine were dominated by V (> 100) with high values for Mn (> 10), Cu (> 5), Zn (> 2.8) and Ni (> 1). The combined *THQ* values in the case of red wine exceeded 125. Vanadium contributed by over 80 % and Mn by 10 % to the total *THQ* for red wine [25]. According to our results, the *HI* values for individual metals were in the order As > Cd > Pb > Fe > Cu > Ni. The highest contribution to the total value of Σ*HI* was by As (contribution range 23.5–42.5 %) and Cd (contribution range 22.5–38.4 %).

The values for cancer risk obtained in our study indicated that the analysed wines were safe for consumption but, in certain circumstances, there may be a potential of adverse effects due to exposure to Ni and/or As by wine consumption. According to our results, there is a risk of carcinogenic effects of As and/or Ni when individuals weighing 54.4 kg (or less) consume 416.7 ml (or more) wine in which Ni and/or As correspond to the maximum content of these elements determined in our study (0.021 $mg\cdot l^{-1}$ and 0.008 $mg\cdot l^{-1}$ for As and Ni, respectively), that is the content of 5 % of the analysed wine samples (95th percentile for As was 0.020 $mg\cdot l^{-1}$ and for Ni was 0.073 $mg\cdot l^{-1}$). The risk of carcinogenic effects of Ni existed additionally when an individual weighing 75.5 kg (or less) consumed 416.7 ml (or more) wine in which the Ni content corresponded to the mean content of this element determined in our study (0.039 $mg\cdot l^{-1}$). This is the content that had 5 % of the wine samples analysed in our study (95th percentile for Ni was 0.073 $mg\cdot l^{-1}$; Tab. 10).

CONCLUSIONS

The metals Fe, Cd, Cu, As, Pb and Ni were detected in all analysed wine samples, with the highest contents recorded for Fe. The contents of the metals were below the maximum residue level set by EU and by Bosnia and Herzegovina [12, 13]. Cd content was generally high in wine samples originating from the Dalmatia region in Croatia. Calculated values for hazard index and cancer risk for certain scenarios of exposition showed possible health risks that were unacceptable.

REFERENCES

1. Orescanin, V. – Katunar, A. – Kutle, A. – Valkovic, V.: Heavy metals in soil, grape, and wine. Journal of Trace and Microprobe Techniques, *21*, 2003, pp. 171–180. DOI: 10.1081/TMA-120017912.
2. Blešic, M. – Drmac, M. – Batinic, K. – Spaho, N. – Smajic Murtic, M. – Zele, M.: Levels of selected metals in wines from different Herzegovinian viticultural localities. Croatian Journal of Food Science and Technology, *9*, 2017, pp. 1–10. DOI: 10.17508/CJFST.2017.9.1.01.
3. Nordberg, G. F. – Fowler, B. A.: Dose-response for essential metals and the evaluation of mixed exposures. In: Nordberg, G. F. – Fowler, B. A.: Risk assessment for human metal exposures. Amsterdam :

Academic Press, 2018, pp. 167–197. ISBN: 978-0-12-804227.
4. Khan, S. – Cao, Q. – Zheng, Y. M. – Huang, Y. Z. – Zhu, Y. G.: Health risks of heavy metals in contaminated soils and food crops irrigated with wastewater in Beijing, China. Environmental Pollution, *152*, 2008, pp. 686–692. DOI: 10.1016/j.envpol.2007.06.056.
5. IRIS Assesments. In: Integrated Risk Information System [online]. Washington, D. C. : United Stated Environmental Protection Agency, 2011 [cit. 24 February 2021]. <https://iris.epa.gov/AtoZ/?list_type=alpha>
6. BAS EN 13805:2015. Foodstuffs – Determination of trace elements – Pressure digestion. Sarajevo : Institute for Standardization of Bosnia and Herzegovina-ISBIH, 2015.
7. BAS EN 14084:2005. Foodstuffs – Determination of trace elements – Determination of lead, cadmium, zinc, copper and iron by atomic absorption spectrometry (AAS) after microwave digestion. Sarajevo : Institute for Standardization of Bosnia and Herzegovina-ISBIH, 2005.
8. Internal method IM-OP-5.4-01-15-1-S. Foodstuffs – Determination of trace elements – Determination of arsenic by atomic absorption spectrometry AAS.) Sarajevo : Institute for Public Health Federation of Bosnia and Heregovina, 2018.
9. Internal method IM-OP-5.4-01-16-1-S. Foodstuffs – Determination of trace elements – Determination of nickel by atomic absorption spectrometry AAS.) Sarajevo : Institute for Public Health Federation of Bosnia and Heregovina, 2018.
10. Alexander, J. – Benford, D. – Boobis, A. – Ceccatelli, S. – Cravedi, J. P. – Doerge, D. – Dogliotti, E. – Edler, L. – Farmer, P. – Filipič, M. – Fink-Gremmels, J. – Fürst, P. – Guérin, T. – Knutsen, H. – Machala, M. – Mutti, A. – Schlatter, J. – Rolaf, L.: Scientific opinion on lead in food. EFSA Journal, *8*, 2010, article 1570. DOI: 10.2903/j.efsa.2010.1570.
11. Guidance for assessing chemical contaminant data for use in fish advisories. Volume 2: Risk assessment and fish consumption limits. In: EPA – United States Environmental Protection Agency [online]. Washington, D. C. : United States Environmental Protection Agency, 2000 [cit. 11 March 2021]. <https://www.epa.gov/sites/production/files/2018-11/documents/guidance-assess-chemical-contaminant-vol2-third-edition.pdf>
12. Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs. Official Journal of European Communities, *L364*, 2006, pp. 5–24. ISSN: 1725-2555. <http://data.europa.eu/eli/reg/2006/1881/2020-07-01>
13. Pravilnik o maksimalno dozvoljenim količinama za određene kontaminante. (Regulation on maximum levels for certain contaminants in foodstuffs.) Službeni Glasnik Bosne i Hercegovine, *84*, 2018, pp. 16–18. ISSN: 1512-7486. In Bosnian.
14. Pravilnik o proizvodnji vina. (Rulebook of wine production.) Narodne novine – Službeni list Republike Hrvatske, *2*, 2005, pp. 17–27. ISSN: 0027-7932. <ELI: /eli/sluzbeni/2005/2/17> In Croatian.
15. International code of oenological practices. Paris : International Organisation of Vine and Wine, 2021. ISBN: 978-2-85038-030-3. <https://www.oiv.int/public/medias/7713/en-oiv-code-2021.pdf>
16. Ajtony, Z., – Szoboszlai, N. – Suskó, E. K. – Mazei, P. – György, K. – Bencsc, L.: Direct sample introduction of wines in graphite furnace atomic absorption spectrometry for the simultaneous determination of arsenic, cadmium, copper and lead content. Talanta, *76*, 2008, pp. 627–634. DOI: 10.1016/j.talanta.2008.04.014.
17. Murányi, Z. – Kovács, Z.: Statistical evaluation of aroma and metal content in Tokay wines. Microchemical Journal, *67*, 2000, pp. 91–96. DOI: 10.1016/S0026-265X(00)00103-X.
18. Kostic, D. – Mitic, S. – Miletic, G. – Despotovic, S. – Zarubica, A.: The concentrations of Fe, Cu and Zn in selected wines from South-East Serbia, Journal of the Serbian Chemical Society, *12*, 2010, pp. 1701–1709. DOI: 10.2298/JSC100104133K.
19. Suturovic, Z. J. – Marjanovic, N. J.: Determination of zinc, cadmium, lead and copper in wines by potentiometric stripping analysis. Food/Nahrung, *42*, 1998, pp. 36–38. DOI: 10.1002/(SICI)1521-3803(199802)42:01<36::AID-FOOD36>3.0.CO;2-K.
20. Maciel, J. V. – Souza, M. M. – Silva, O. L. – Dias, D.: Direct determination of Zn, Cd, Pb and Cu in wine by differential pulse anodic stripping voltammetry. Beverages, *5*, 2019, article 6. DOI: 10.3390/beverages5010006.
21. Alkis, M. – Öz, S. – Atakol, A. – Yilmaz, N. – Ertan Anli, R. – Atakol, O.: Investigation of heavy metal concentrations in some Turkish wines. Journal of Food Composition and Analysis, *33*, 2014, pp. 105–110. DOI: 10.1016/j.jfca.2013.11.006.
22. Ražic, S. – Čokeša, D. – Sremac, S.: Multivariate data visualization methods based on elemental analysis of wines by atomic absorption spectrometry. Journal of the Serbian Chemical Society, *72*, 2007, pp. 1487–1492. DOI: 10.2298/JSC0712487R.
23. Towle, K. M. – Garnick, L. C. – Monnot, A. D.: A human health risk assessment of lead (Pb) ingestion among adult wine consumers. International Journal of Food Contamination, *4*, 2017, article 7. DOI: 10.1186/s40550-017-0052-z.
24. Santos, S. – Lapa, N. – Alves, A. – Morais, J. – Mendes, B.: Analytical methods and validation for determining trace metals in red wines. Journal of Environmental Science and Health, Part B: Pesticides, Food Contaminants and Agricultural Wastes, *48*, 2013, pp. 364–375. DOI: 10.1080/03601234.2013.742374.
25. Hague, T. – Petroczi, A.– Andrews, P. – Barker, J. – Naughton, P. D.: Determination of metal ion content of beverages and estimation of target hazard quotients: a comparative study. Chemistry Central Journal, *2*, 2008, article 13. DOI: 10.1186/1752-153X-2-13.

Received 20 November 2020; 1st revised 12 March 2021; accepted 13 April 2021; published online 23 May 2021.