



REVIEW ARTICLE

Health Risk Assessment of Heavy Metals in Edible Mushrooms and their Effect on Anemia: A Review Study

Alireza Esmaeili^{1,2}, Shabnam Shamaei³, Ebrahim Molaee Aghae⁴, Zabih Nosrati Akhtar⁵, Seyede Fatemeh Hosseini⁶, Samira Shokri^{*4}

¹Non-Communicable Disease Research Center, Ilam University of Medical Sciences, Ilam, Iran

²Assistant Professor of Hematology and Oncology, School of Medicine, Ilam University of Medical Sciences, Ilam, Iran

³Department of Chemistry, Khorramabad Branch, Islamic Azad University, Khorramabad, Iran

⁴Department of Environmental Health, Food Safety Division, Faculty of Public Health, Tehran University of Medical Sciences, Tehran, Iran

⁵Master of Veterinary Parasitology, Boroujerd Branch, Islamic Azad University, Boroujerd, Iran

⁶Department of Biology Faculty of Basic University of Mazandaran, Babolsar, Iran

Received: 11 June 2021

Accepted: 2 September 2021

KEYWORDS

Mushroom;
Risk assessment;
Anemia;
Carcinogenic;
Toxic;
Heavy metal

ABSTRACT: Anemia patients are more susceptible to environmental contaminations such as heavy metals. The present study aimed at risk assessment of heavy metals in edible mushrooms and Anemia. The databases searched in those articles were Google Scholar, SID, Scopus, PubMed, Science Direct, and ISI. Related human health risks were calculated using the target hazard quotient (THQ). THQ ratio of Cd, Cu, Fe, Pb, Cr, Ni, and Mn were 3×10^{-3} , 2.31, 8.43×10^{-1} , 2.35, 2.92×10^{-1} , 6.6×10^{-2} and $1.96 \times 10^{-1} \text{ m m}^{-1}$ respectively. The highest non-carcinogenic diseases risk for adults were found in Pb (2.35 m m^{-1}) while the lowest value was observed in Cd ($3 \times 10^{-3} \text{ m m}^{-1}$). The risk of carcinogenicity of lead was at the level of acceptable (10^{-4} to 10^{-6} m m^{-1}). There is no concern about the non-carcinogenic risk of consuming heavy metals in edible mushrooms, in Iran except Cu and Pb. In some countries, adults and children can be exposed to non-cancerous foods by eating mushrooms. And can aggravate anemia in the consumer.

INTRODUCTION

Mushrooms' edibles are one of the most popular foods in the diet of many countries [1]. Edible mushrooms are in people's baskets and diets. Some edible mushrooms include champignon, Crimino, Portabello, Shiitake, Maitake, Oyster, Enoki, Beech, King Trumpet, Chanterelle, Hedgehog, Morel, Porcino, Wood Blewit, Reishi, Lion's Mane and Matsutake [2-4]. A very rich and

low-calorie food source and has 17.5% protein, 39.9% carbohydrates, 2.9% fat, 12.5% ash, and minerals (iron, zinc, selenium, and sodium) [2-4]. For this reason, households use edible mushrooms to a significant extent in the food basket. Studies showed mushrooms are useful in preventing diseases such as high cholesterol, diabetes, hypertension, cancer, and prostate. Due to its low level of

uric acid, it can be a good alternative for all types of meat [2, 5, and 6].

Epidemiological studies show that the amount of mushroom production in Iran in 2004 was about 15,000 tons, which much lower than western countries such as, United States, Japan, the Netherlands, the United Kingdom, and Italy that produced mushrooms 344,000, 336,000, 165,000, 118,000 and 102,000 tons per year, respectively [7]. Every year, about 30% of people in developed countries suffer from foodborne illness, and this rate is reported in developing countries around 2.2 million people annually [8].

Metals with critical concentrations into the food chain have detrimental metabolic and physiological effects on living organisms. Cadmium, lead, arsenic, mercury, copper, and zinc are the most dangerous metals [9]. Studies demonstrated that mushrooms have the property of accumulation of these metals and the concentration of heavy metals in mushrooms is higher than compared to other agricultural products including fruits and vegetables. This depends on the physiology of the fungus, the ecosystem, and their species [4]. Heavy metals cause adverse effects on the body [10]. Lead disrupts hemoglobin biosynthesis, causes anemia and high blood pressure [11]. People with anemia are vulnerable to environmental contaminants, including heavy metals. Anemia is one of the most common blood diseases in children and women [12]. Studies show that there is a significant relationship between anemia in pregnant women and the rate of heavy metal absorption [12-14]. Increasing the prevalence of anemia increases the risk of cancer [12]. In Iran, the rate of iron deficiency anemia is reported to be 11% [15]. World Health Organization (WHO) reports the standard limits of arsenic, lead, and copper in food by 0.5, 2, 40 mg/kg, respectively [16].

In the study of Cheraghi et al the concentration of arsenic, lead, and copper in all samples of edible mushrooms was higher than the standard [17]. The results of the study of Anbari et al. in Tehran showed that in 25% of the studied mushroom, Pb was higher than the standard limit of the European Union and the amount of cadmium was lower than the allowable limit [18]. Food safety is a fundamental

principle of public health. Therefore, high levels of toxic compounds in mushrooms may offset its beneficial health benefits from a mushroom meal [3].

The present study was conducted to investigate and evaluate the risk of heavy metals in edible mushrooms and the incidence of anemia. It is hoped that the results of this study will lead to the regulation of a proper and safe nutritional pattern of edible mushrooms in the family diet and increase the level of health in consumers of such foods.

MATERIALS AND METHODS

This study was conducted as a review article of articles published between 1980 and 2020. For this purpose, based on searches in Magiran, Google Scholar, SID, Scopus, PubMed, Science Direct, and ISI databases, articles were founded with the keywords including edible mushrooms, heavy metals, risk assessment, anemia, and carcinogenicity.

Non-carcinogenic diseases risk index

The formula provided by the US Environmental Protection Agency (USEPA) [19] was used to calculate the hazard of people being diagnosed with non-cancerous diseases.

$$EDI = (CF \times IR \times FI \times EF \times ED) / (BW \times AT)$$

EDI is the estimation of daily intake) $\mu\text{g kg}^{-1}\text{day}^{-1}$; CF, the concentration of heavy metals in different foods ($\mu\text{g kg}^{-1}$); IR; ingestion rate daily (g day^{-1}), FI; the amount of contaminant that is absorbed through food. This coefficient varies between 0.25 to 0.4. A coefficient of 0.4, which indicates the worst case, is usually used to calculate the risk. In this study, this coefficient was also considered 0.4. EF, exposure frequency (day year^{-1}); ED, exposure duration (years); BW, bodyweight (70 kg); AT; $(EF \times ED)$ average time exposure, RfD; Reference dose.

$$THQ = EDI (\mu\text{g kg}^{-1} \text{ day}^{-1}) / \text{RfD} (\mu\text{g kg day}^{-1})$$

When the non-cancer hazard index (HI) reaches one, it indicates a high hazard of non-cancerous diseases.

$$HI = THQ$$

Carcinogenic diseases risk index

The factor of additional risk evaluation for cancer incidence in life is an index for the carcinogenicity of the received toxin, and if it is calculated less than one million, it will indicate negligible conditions for the toxicity of the received toxin. However, the calculation of numbers higher than 1.10000 of this index shows that this risk cannot be ignored and should be examined more accurately and sensitively. The level of acceptable cancer risk is considered within the range of 10^{-4} to 10^{-6} .

$$\text{Excess Lifetime Cancer Risk} = \text{EDI} * \text{Slope Factor}$$

The Slope Factor Pb value was determined to be 8.5×10^{-3} $\text{mg}^{-1} \text{kg}^{-1} \text{day}$

RESULTS

Table 1 showed the average concentration and extent of heavy metal contamination in edible mushroom samples in various countries. In some studies, the average concentration of heavy metals is higher than the tolerable recommended by who. And have a high potential risk to the health of consumers. The Provisional Tolerable Daily Intake (PTDI) for lead and copper metals are 3.75 and 500 mg kg^{-1} body weight respectively [20].

The estimation of daily intake (EDI) of copper and lead metals were 85.344 and 8.28 $\mu\text{g kg}^{-1}\text{day}^{-1}$, respectively. The daily absorption rate of the element copper is lower than the daily tolerable absorption rate (PTDI) by WHO. Appraising the hazard potential of cancer was calculated within the range of 10^{-4} to 10^{-6} (Table 2).

Table 1. Prevalence of Heavy metals in edible mushroom samples from various countries.

Country	Year	Sample	Cd	Cr	Cu	Mn	Zn	Pb	As	Ni	Al	Fe	Hg	Unit	Method	Ref.
Iran	2012	18	0.0087	0.2469										m m ⁻¹	Atomic absorption spectrometry	[21]
Iran	2011	8	0.423±0.01					2.85±0.08						m m ⁻¹	Atomic absorption spectrometry	[18]
Iran	2013	60	0.32		48.868		24.072	3.152	89.742					m m ⁻¹	Atomic emission technique	[17]
Iran	2017	30					66.23±2.80		65.23±13.57					m m ⁻¹	ICP-OES	[22]
Iran	2016	24		51.23±0.66	24.37±6.175	5.025±0.34	59.88±22.025	2.06±0.45				27.295±10.26		m m ⁻¹	Atomic absorption spectrometry	[23]
Iran	2021	23	0.180±0.20	10.16±9.13	37.88±28.94	7.23±5.62	2394.01±183.74	3.150±2.70	0.5910±0.91	7.97±5.48		92.06±76.50	0.951±0.74	m m ⁻¹	(ICP-OES)	[24]
Iran	2021	6	2.470±2.12	11.53±3.07	31.93±13.16	22.08±20.14	1777.36±887.08	6.330±2.99	0.5910±0.91	18.19±7.27		618.70±583.41	0.651±0.09	m m ⁻¹	(ICP-OES)	
Turkey	2004	10	1.5±1	10.34±0.85	42.26±3.27	29.54±2.31	48.72±3.61	2.31±0.2		5.68±0.46		272.8±20.33		m m ⁻¹	Atomic absorption spectrometry	[5]

India	2014	3	0.0014 - 0.0019		5 - 9	1 - 5	0.06 - 0.09		0.074		241-276	0.062-0.087	m m ⁻¹	Atomic absorption spectrophotometer	[25]
Turkey	2020		0.88±0.10	12.03±0.55	10.35±1.42	168.08±2.9	83.36±1.01	17.19±0.69	2.09±0.07		576.12±4.08		m m ⁻¹	atomic absorption spectrophotometer	[26]
Turkey	2011	15	0.37 ±0.01 -5.28 ±0.21				75 ±3-213 ±8	9.15 ± 0.37	0.3±0.1		467 ±19 3,280 ±131		m m ⁻¹	IC P-OES	[3]
Greece	2009	10	0.822±0.02	2.445±0.03				0.37±0.06					m m ⁻¹	Atomic absorption spectrometry	[1]
Netherlands	1982	125	13.9±9.05		64.93±17.68		203.16±109	13.78±24.56					m m ⁻¹	Atomic absorption spectrometry	[27]
Turkey	2006	6	1.26±0.25	6.765±3.2	42.07±4.2	31.28±2.63	45.19±3.55	2.97±0.23	5.06±4.8		261.3±21.3		m m ⁻¹	Atomic absorption spectrometry	[28]
China	2008	14	0.177±0.008	21.73±1.71	11.61±1.08	42.13±2.97	63.42±4.83	3.02±0.19	1.9±0.11		155.02±11.9		m m ⁻¹	ICP-OES	[29]
Turkey	2008	14			39.27±3.39	70.62±7.86	109.60±9.2	1.77±0.15		22.97±1.95	602.14±51.5		m m ⁻¹	Atomic absorption spectrometry	[30]
Turkey	2011	12	5.63±0.012	3.80±0.03	42.25±2.49	32.16±0.35	98.5±0.35	1.75±0.108	1.93±0.058		496.58±5		m m ⁻¹	ICP-OES	[31]

India	2016	11	0.826±0.13		204.40±4.26	110.06±3.5	219.34±2.50	0.863±3.35		615.95±19.7	m m ⁻¹	ICP-OES Atomic absorption spectrometry	[32]	
Turkey's Black Sea region	2018	21	0.08-3.37	0.36-6.26	17.5-122	4.61-102	34.4-225	0.151.80		12.7-24.2	m m ⁻¹	ICP-MS	[33]	
Romania	2010	4	0.52-5.27	0.93-13.4	6.43-32.8	7.85-168	35.4-158	0.64-12.5		0.92-9.63	m m ⁻¹	FAAS	[34]	
Rudňany	2014	62	1.6	1.15	61.3	41.6	82.16	1.08		1.13	m m ⁻¹	Flame Spectropho tometry	[35]	
Turkey	2019	2	31.3±0.65	128±8.5	3.4±0.15	5.5±0.2	3.14±0.265	119.53	19.95±1.3	87±2	75.±9	m m ⁻¹	ICP - MS	[36]
Serbia	2015	4	0.97±0.01	6.212±0.06	46.8±0.42	17.935±0.07	71.93±0.4			3.49±0.03	m m ⁻¹	ICP OES	[37]	
Turkey	2011	34		8/58+1/08						53.96	m m ⁻¹	ICP OES	[38]	
Ethiopia	2019	4	2.12±0.03		8.40-34.33	4.22-6.63	40.25- 120.91	8.58±.58			m m ⁻¹	flame atomic absorption spectrometry	[39]	

Table 2. Indicated the risk assessment of heavy metal intake through edible mushroom consumption in Iran

Heavy metals	Concentration index mg kg ⁻¹	Daily value g day ⁻¹	RFD Mg kg ⁻¹ day ⁻¹	EDI µg kg ⁻¹ day ⁻¹	THQ	Cancer risk
Cd	0.680	0.42	1.0 × 10 ⁻³	1.632	3 × 10 ⁻³	
Cu	35.56	0.42	4.0 × 10 ⁻²	85.344	2.31	
Fe	246	0.42	7.0 × 10 ⁻¹	590.4	8.43 × 10 ⁻¹	
Pb	3.45	0.42	3.5 × 10 ⁻³	8.28	2.35	7.03 × 10 ⁻⁵
Cr	18.29	0.42	1.5	43.896	2.92 × 10 ⁻¹	
Ni	13.08	0.42	4.0 × 10 ⁻¹	26.592	6.6 × 10 ⁻²	
Mn	11.44	0.42	1.4 × 10 ⁻¹	27.456	1.96 × 10 ⁻¹	

DISCUSSION

Paying attention to the importance of the share of mushroom consumption in the household consumption basket and providing health of mushrooms have a significant impact on public health as well as on the indicators and variables of our country's economy. In recent years, some studies of food health and safety have examined the status of fungal contamination with heavy metals.

Glalipura studied the effects of lead toxicity on mouse blood cell changes and found that serum hemoglobin, hematocrit levels, MCH, and MCV decreased [40]. Gallagher reported in a study the presence of anemia in women increased the risk of cadmium concentrations in blood samples [41]. It has been indicated that the levels of Cd in mushrooms can be accumulated to high concentration ratios [27]. Due to the accumulation of metals, the consumption of infected mushrooms can exacerbate anemia in adults. Studies have shown that serum lead and cadmium levels have a significant relationship with anemia [40, 41]. The levels of cadmium, copper, and lead in serum were significantly higher in children with iron deficiency anemia (IDA) than those of controls ($p < 0.05$, $p < 0.05$, $p < 0.01$, respectively) [13]. Willows reported that infants with iron deficiency anemia had significantly higher mean blood lead concentrations

than infants without iron deficiency anemia [43]. One way to get heavy metals into the body is to eat edible mushrooms. The concentration of heavy metals in mushrooms is mainly influenced by ecosystem factors, soil, acidic substances, and the type of mushroom. This is because the exchange of materials takes place through the soil and is directly in the path of mineralization of the crop [17]. In addition, some factories produce organic fertilizer for composting from municipal waste, which can contain high amounts of organic matter [42]. Zubiri et al. reported the highest risk of carcinogenicity in adults and children in the Nigerian Delta because the delta region is the hub of petrochemical and industrial activities [42]. The results of the present study showed that the amount of nickel metal in edible mushrooms is lower than the limit recommended by the Iranian national standard. Also, the risk of non-cancerous disease is lower than the allowable limit.

It has been found that the highest mean concentration of Cr in both types of mushrooms (cultivated and wild) was lower than recommended level by Codex Alimentarius/Food and Agriculture Organization/World Health Organization (CODEX/FAO/WHO) [24].

While the corresponding values for Hg, As, Ni, Mn, Zn, and Pb were higher than related standard levels.

According to the risk assessment, there was no concern about the non-carcinogenic risk due to the consumption of heavy metals through the consumption of edible mushrooms, except lead for the consumer group. In the present study, the concentration of arsenic in edible mushrooms is at a moderate level. In the study of Shokrzadeh et al, the level of chromium concentration in all samples was higher than the codex standard "0.20 mg m⁻¹". The high level of chromium contamination in the mushroom can be due to the high amount of chromium in (compost) or water pollution [21]. The results of a study by Khodabakhshi et al. in Shahrekord indicated that some samples contain the heavy metal chromium, lead, iron with higher amounts than level tolerable. The cause of edible mushrooms contamination is due to excessive use of chemical fertilizers [23]. It has been shown that the As, Sn, and Al concentrations of mushroom samples 0.02 mg m⁻¹ for each element. It has been reported that the levels of Cd, Pb, Zn, and Mn conformed to the FAO/WHO (1976) standards [5]. It has been demonstrated that the results indicate that in general, heavy metal contents in all mushroom species were lower than the underlying soil substrates except for some mushroom species [5]. Edible *Melanoleuca* species have great nutritional value and health benefits and could be considered for further phytochemical and pharmacological studies [36]. Edible wild mushroom *Helvella leucopus* was found that the mushroom contains high levels of Pb and Mn. *H. leucopus* could be used as a natural agent in pharmacological designs due to its antioxidant activity [26]. Food contamination has been reported as environmental contamination and heavy metals [43, 44]. The use of medicinal plants and herbal antioxidants [45-56] is one of the solutions remove dirt or treatment of diseases.

CONCLUSIONS

Based on the results obtained from reviewing the texts in this review article, it was determined that there is no concern about the non-carcinogenic risk of consuming heavy metals in edible mushrooms, in Iran except Cu and Pb. In some countries, adults and children can be exposed to

non-cancerous foods by eating mushrooms. And can aggravate anemia in the consumer.

ACKNOWLEDGEMENTS

The authors appreciate the cooperation of Tehran University of Medical Sciences, Tehran, Iran

Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

REFERENCES

1. Ouzouni P.K., 2009. Nutritional value and metal content of wild edible mushrooms collected from West Macedonia and Epirus, Greece. *Food Chemistry*. 115(4), 1575-1580.
2. Firenzuoli F., L. Gori L., Lombardo G., 2008. The medicinal mushroom *Agaricus blazei murrill*: review of literature and pharmaco-toxicological problems. *Evidence-Based Complementary and Alternative Medicine*. 5(1), 3-15.
3. Kula I., 2011. Determination of mercury, cadmium, lead, zinc, selenium and iron by ICP-OES in mushroom samples from around thermal power plant in Muğla, Turkey. *Bulletin of Environmental Contamination and Toxicology*. 87(3), 276-281.
4. Mendil D., 2004. Determination of trace elements on some wild edible mushroom samples from Kastamonu, Turkey. *Food Chemistry*. 88(2), 281-285.
5. Isildak Ö., 2004. Analysis of heavy metals in some wild-grown edible mushrooms from the middle black sea region, Turkey. *Food Chemistry*. 86(4), 547-552.
6. Liu Y., Fukuwatari Y., Okumura K., Takeda K., Ishibashi K.I. Furukawa M., Ohno N., Mori Ming Gao K., Motoi M., 2008. Immunomodulating activity of *Agaricus brasiliensis* KA21 in mice and in human volunteers. *Evidence-Based Complementary and Alternative Medicine*. 5(2), 205-219.
7. Manzi P., 1999. Mushrooms as a source of functional ingredients. *Euro Food Chemistry* 10. In European Conference on: Functional foods, A new challenge for

- the food chemist, Budapest. 3.
8. Alloway B.J., 2012. Heavy metals in soils: trace metals and metalloids in soils and their bioavailability. Environmental Pollution book series. 22, 4.
 9. Tchounwou P.B., Yedjou C.G., Patlolla A.K., Sutton D.J., 2012. Heavy metal toxicity and the environment. Molecular, Clinical and Environmental Toxicology. 133-164.
 10. Singh A., Kumar R., Sharma R., Agrawal M., Marshall F.M., 2010. Health risk assessment of heavy metals via dietary intake of foodstuffs from the wastewater irrigated site of a dry tropical area of India. Food and Chemical Toxicology. 48(2), 611-619.
 11. Marx J., Hockberger R., Walls R., 2013. Rosen's Emergency Medicine-Concepts and Clinical Practice E-Book: 2-Volume Set. 2013: Elsevier Health Sciences. 8-11.
 12. Fesharakinia A., 2014. The prevalence of iron deficiency and its anemia in 1-5 years old children and their mothers in Birjand City. Journal of Fasa University of Medical Sciences. 3(4), 325- 329.
 13. Turgut S., 2007. Interaction between anemia and blood levels of iron, zinc, copper, cadmium and lead in children. The Indian Journal of Pediatrics. 74(9), 827-830.
 14. Neoh K., 2017. Estimating prevalence of functional iron deficiency anaemia in advanced cancer. Supportive Care in Cancer. 25(4), 1209-1214.
 15. Eslami M., 2013. Importance of pre-pregnancy counseling in Iran: results from the high risk pregnancy survey 2012. International Journal of Health Policy and Management. 1(3), 213-215.
 16. Joint F., W.E.C.o.F. Additives, and W.H., 1990. Organization, Evaluation of certain food additives and contaminants: thirty-fifth report of the Joint FAO. 1990: World Health Organization.
 17. Cheraghi M., Lorestani B., Mardokh Rohani N., 2013. Evaluation of heavy metal concentration in compost, soil cover and button mushroom in Kurdistan greenhouses. Food Hygiene. 2(4 (8)), 81-96.
 18. Anbari M., 2011. Investigation of lead and Cadmium contents of cultivated edible mushrooms consumed in Tehran, 2011. Technology. 30, 8, 85-91.
 19. USEPA (US Environmental Protection Agency). 1992. Guidelines for exposure assessment. Available at <http://www.epa.gov/ncea/pdfs/guidline.pdf>.
 20. Institute of Standards and Industrial Research of Iran. Food and feed-maximum limit of heavy metals. Standard No. 12968. Tehran: Institute of Standards and Industrial Research of Iran, 2010.
 21. Shokrzadeh M., 2014. The Levels of Lead, Cadmium and Chromium in Edible Mushrooms in Sari. Journal of Mazandaran University of Medical Sciences. 24 (117), 165-172.
 22. Ardakani S., Jahangard A., 2017. Toxicological assessment of inorganic arsenic and zinc content in button mushrooms. Journal of Advances in Environmental Health Research. 5(4), 246-251.
 23. Khudabakhshi A., Sedehi Shakeri K., 2016. Determination of some heavy metals in edible fungi in Shahrekord. Journal of Shahrekord University of Medical Sciences. 18(1), 3-9.
 24. Karami H., 2021. The Concentration and Probabilistic Health Risk of Potentially Toxic Elements (PTEs) in Edible Mushrooms (Wild and Cultivated) Samples Collected from Different Cities of Iran. Biological Trace Element Research. 199(1), 389-400.
 25. Kumari B., Atri N.S., 2014. Nutritional and nutraceutical potential of wild edible macroleptoid mushrooms of north India. International Journal of Pharmacy and Pharmaceutical Sciences. 6(2), 200-204.
 26. Sevindik M., Akata I., 2020. Antioxidant, oxidant potentials and element content of edible wild mushroom *Helvella leucopus*. Indian Journal of Natural Products and Resources (IJNPR)[Formerly Natural Product Radiance. 10(4), 266-271.
 27. Gast C., Jansen E., Bierling J., Haanstra L., 1988. Heavy metals in mushrooms and their relationship with soil characteristics. Chemosphere. 17(4)789-799.
 28. Isildak O., 2007. Bioaccumulation of heavy metals in some wild-grown edible mushrooms. Analytical Letters. 40(6), 1099-1116.
 29. Zhu F., 2011. Assessment of heavy metals in some

- wild edible mushrooms collected from Yunnan Province, China. *Environmental Monitoring and Assessment*. 179(1), 191-199.
30. Sesli E., Tuzen M., Soyak M., 2008. Evaluation of trace metal contents of some wild edible mushrooms from Black sea region, Turkey. *Journal of Hazardous Materials*. 160(2-3), 462- 467.
31. Sarikurkcu C., 2011. Metal concentration of wild edible mushrooms in Soguksu National Park in Turkey. *Food Chemistry*. 128(3), 731-734.
32. Lalotra P., 2016. Bioaccumulation of heavy metals in the sporocarps of some wild mushrooms. *Curr. Res. Environ. Appl Mycol J Fungal Biol*. 6, 159-165.
33. Türkmen M., Budur D., 2018. Heavy metal contaminations in edible wild mushroom species from Turkey's Black Sea region. *Food Chemistry*. 254, 256-259.
34. Radulescu C., 2010. Studies concerning heavy metals bioaccumulation of wild edible mushrooms from industrial area by using spectrometric techniques. *Bulletin of Environmental Contamination and Toxicology*. 84(5), 641-646.
35. Árvay J., Tomáš J., Hauptvogel M., Kopernická M., Kováčik A., Bajčan D., Massányi P., Contamination of wild-grown edible mushrooms by heavy metals in a former mercury-mining area. *Journal of Environmental Science and Health, Part B*. 49(11), 815- 827.
36. Bahadori M.B., Kcu C.S., Yalcin O.U., Cengiz M., Gungor H., 2019. Metal concentration, phenolics profiling, and antioxidant activity of two wild edible *Melanoleuca* mushrooms (*M. cognata* and *M. stridula*). *Microchemical Journal*. 150, 104172-104173.
37. Cvetkovic J.S., 2015. Elemental composition of wild edible mushrooms from Serbia. *Analytical Letters*. 48(13), 2107-2121.
38. Durkan N., 2011. Concentrations of trace elements aluminum, boron, cobalt and tin in various wild edible mushroom species from Buyuk Menderes River Basin of Turkey by ICP-OES. *Trace Elements and Electrolytes*. 28(4), 242.
39. Tsegay M.B., Asgedom A.G., Belay M.H., 2019. Content of major, minor and toxic elements of different edible mushrooms grown in Mekelle, Tigray, Northern Ethiopia. *Cogent Food & Agriculture*. 5(1), 13-19.
40. Gopalipour M.J., Roshandel D., Roshandel G.R., Ghafari S., Kalavi M., Kalavi K., 2007. Effect of lead intoxication and D-penicillamine treatment on hematological indices in rats. *International Journal of Morphology*. 25(4), 717-722.
41. Gallagher C.M., Chen J.J., Kovach J.S., 2011. The relationship between body iron stores and blood and urine cadmium concentrations in US never-smoking, non-pregnant women aged 20–49 years. *Environmental Research*, 111(5), 702-707.
42. Boudaghi H., Younesian M., Mahvi A.H., Mohammadi M.A., Dehghani M.H., Nazm ara Sh., 2011. Determination of arsenic, cadmium and lead in soil and groundwater and its relationship with chemical fertilizer in Ghaem shahr city (case study farm in Vahdat). *Journal of Mazandaran University of Medical Sciences*. 21(86), 21-29.
43. Manouchehri A.A., Pirhadi, M., Parsaei, P., Alikord, M., Safian Boldaji H., 2021. A review of aflatoxin M1 in milk and dairy products and new procedure for evaluating aflatoxin M1. *J Chem Health Risks*. [In press].
44. Pirhadi M., Shariatifar N., Bahmani M., Manouchehri A.A., 20121. Heavy metals in wheat grain and its impact on human health: A review. *J Chem Health Risks*. [In press].
45. Farzan B., Shahsavari S., Abbaszadeh S., Teimouri H., 2019. Phytotherapy for seizure: An overview of the most important indigenous Iranian medicinal plants with anticonvulsant properties. *Plant Science Today*. 6(4), 367-372.
46. Manouchehri A., Shakib P., Biglaryan F., Nazer M., Darvishi M., 2021. The most important medicinal plants affecting bee stings: A systematic review study. *Uludag Arıcılık Dergisi*. 21(1), 91-103.
47. Esmaeili A., Parsaei, P., Nazer, M.R., Bakhtiari R., Mirbehresi H., Safian Boldaji H., 20121. Phytotherapy in Burn Wound Healing: A Review of Native Iranian Medicinal Plants. *J Chem Health Risks*. [In press].
48. Alizadeh M., Safarzadeh, A., Bahmani, M., Beyranvand, F., Rafieian-Kopaei, M., Abbaszadeh, S., 2018. Brucellosis: Pathophysiology and new promising treatments with medicinal plants and natural antioxidants.

Asian Pacific J Trop Med. 11(11), 597-608.

49. Abbaszadeh S., Andevvari A.N., Koochpayeh A., Naghdi, N., Alizadeh, M., Beyranvand, F., Harsej, Z., 2018. Folklore medicinal plants used in liver disease: A review. *Int J Green Pharmacy*. 12(3), 463-472.

50. Sedighi M., Sewell R.D.E., Nazari A., Abbaszadeh S., Cheraghi M., Amini A., Heydari Z., Rafieian-Kopaei M., 2019. A review on the most important medicinal plants effective in cardiac ischemia-reperfusion injury. *Current Pharmaceutical Design*. 25(3), 352-358.

51. Nouri A., Heidarian E., Amini-Khoei H., Abbaszadeh S., Basati G., 2019. Quercetin through mitigation of inflammatory response and oxidative stress exerts protective effects in rat model of diclofenac-induced liver toxicity. *J Pharmacy Pharmacog Res*. 7(3), 200-212.

52. Abbasi N., Khalighi Z., Eftekhari Z., Bahmani M., 2020. Extraction and phytoanalysis of chemical compounds of *Eucalyptus globulus* leaf native to Dehloran, Ilam province, Iran by HS-SPME and GC-MS. *Advances in Animal and Veterinary Sciences*. 8(6), 647-652.

53. Eftekhari Z., 2020. Garlic: A brief overview of its interaction with chemical drugs. *Plant Biotechnol Persa*. 2(2), 31-32.

54. Aidy A., Karimi E., Ghaneialvar H., Mohammadpour S., Abbasi N., 2020. Protective effect of *Nectaroscordum tripedale* extract and its bioactive component tetramethylpyrazine against acetaminophen-induced hepatotoxicity in rats. *Advances in Traditional Medicine*. 20(3), 471-477.

55. Karimi E., Abbasi S., Abbasi N., 2019. Thymol polymeric nanoparticle synthesis and its effects on the toxicity of high glucose on OEC cells: Involvement of growth factors and integrin-linked kinase. *Drug Design, Development and Therapy*. 13, 2513-2532.

56. Abbasi N., Khosravi A., Aidy A., Shafiei M., 2016. Biphasic response to luteolin in MG-63 osteoblast-like cells under high glucose-induced oxidative stress. *Iranian Journal of Medical Sciences*. 41(2), 118-125.

