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Full Length Research Paper

The concentration of toxic metals in teas: A global systematic review, meta-analysis and probabilistic health risk assessment

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Background: The tea next to water is the heavily consumed beverage among the world's population. In current investigation was evaluated the concentration of different metals in teas consumptions through meta-analysis. **Methods:** The related studies regarding to the concentration of toxic metals in teas were collected from international major databases. A random effect model was used for meta-analysis concentration of Cd, Pb and As in tea among defined subgroups. **Results:** The mean concentration of toxic metals in the teas was Pb (0.55 mg/kg) > Cd (0.13 mg/kg) > As (0.07 mg/kg), respectively. The highest concentration of metals in green and black tea was related to Pb and As, respectively. **Conclusion:** Due to the high concentration of metals in different tea samples in many of countries and the health risk for consumers it is need to performing of control plans by governments and farmers for decrease concentration of toxic metals in tea.

Keyword: Toxic metals, Tea, Concentration, Systematic review, Meta-analysis

INTRODUCTION

The tea next to water is the heavily consumed beverage among the world population, which is prepared from leave of *Camellia sinensis* plant and cultivates in certain areas of China, Japan, and India (Antoine Jet et al., 2017). According to processes of fermentation, teas categorize to the three popular types (green, oolong, and black). Nearly 75-80 % of total tea consumption is related to black tea (Al-Othman et al., 2012). Economic and social impotent of tea

is obvious from the fact that about 18 to 20 billion cups of tea are consumed daily in the world (Fernández-Cáceres et al., 2001). Tea has complex matrix and is rich of antioxidant compounds such as flavonoids, polyphenols that are benefit to human health. Antioxidant compounds available in tea act as a scavenger of reactive free radicals and can reduce risk of heart diseases like stroke, heart attack and various types of cancer like oral, pancreatic and prostate in human (Karak and Bhagat 2010). In addition to antioxidant properties, this high consumption drinking has macro elements such as sodium, potassium, phosphorus, and manganese, which activates numerous enzymes in the

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human body (Shen and Chen 2008). However, tea might be contaminated with heavy metals and posed a serious threat to human (Nkansah et al., 2016). It is observed of many studies that more than 90% of human exposure to metals is associated with the consumption of contaminated food (Shen and Chen 2008; de Oliveira et al., 2018; Zhu et al., 2013; Zhang et al., 2018). Recently, remarkable increase in industrial development, agricultural activities, urbanization and mining in different parts of the world led to increase in amount of metals like lead (Pb), cadmium (Cd) and arsenic (As) in different samples of foods (Heshmati et al., 2020). It is worthy to note that, addition to, type and specie of metals, intensity, frequency, duration, and routes of exposure, half-life, biodegradable property, cumulative nature of metals, and also kind of body tissue like fat and done of human are of effective parameters in toxicity of metals (Khaneghah et al., 2019). The different amounts of metals in various foods related to factories such as climatic conditions, geographical location, handling, storage, and processing (Popović et al., 2017; Zhelev et al., 2019; Sofuoglu and Kavcar 2008). As mentioned of previous investigations, the toxicity effects reported due to chronic exposure to metals are the carcinogenicity, genotoxicity, mutagenicity, neurotoxicity, endocrine disorders, and teratogenicity. Exposure with various amounts of pb could lead to decrease in cognitive function, IQ deficits in young children and change in blood pressure level in the adults (Mason et al., 2014). On the other hand, due to the structure similarity of Pb to calcium (Ca), Pb accumulates in the bone and causes calcium deficiency in the body (Brown and Margolis 2012). Current studies have showed Cd in addition disease (Itai-Itai) can lead to cancer of prostate, lung, and bladder in human (Abbasi et al., 2009; Ensafi et al., 2006). Chronic exposure to As may lead to cancer of kidney, lung, and skin lesions (Gomez et al., 2007). Since the one of the most concerns in terms of food safety is the contamination of food products by metals that attend to have attracted attention from many researchers around the world (Gomes et al., 2019), and also, due to the lack of a global meta-analysis regarding the toxic metals in tea, the current investigation for first was conducted in order to estimate the concentration of different metals (Pb, Cd, and As) in tea consumptions among different countries through a systematic review and meta-analytic approach.

MATERIAL AND METHODS

Search Strategy:

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Fig 1) (Liberati et al., 2009). A comprehensive literature searches was done of the following international electronic bibliographic

databases including: Scopus, Web of Science, PubMed and Embase from inception to Feb 01, 2020. In addition to identify additional relevant studies, hand searches were also performed. Key search terms included terminology for Scopus: ((ti/ab ("metals") OR ti/ab ("heavy metals"))) OR ti/ab ("metal(oid)s") AND ((ti/ab ("tea") ((ti/ab ("green") OR ((ti/ab ("black") OR ((ti/ab ("plant"); Medline: Search((((("Metals"[Mesh]) OR (((heavy metals [Ti/Ab]) OR metals [Ti/Ab]) OR metal(oid)s [Tit_Abs]))) AND ((((((Plant [Ti/Ab]) OR tea[Ti/Ab]) green [Ti/Ab]) black[Ti/Ab]); Embase: ('metals':abt OR 'heavy metals':abt OR 'metal(oid)s':abt) AND 'tea':abt OR plants'. Also, the reference lists of collected articles were investigated to attain additional articles based on similar studies performed.

Extraction of data and inclusion / exclusion criteria

The inclusion criteria in this study were including: (1) full-text published in the English language; (2) cross-sectional study; (3) reporting of mean and/or range concentration of toxic metals in black and green tea. In this regard, books, workshops, reviews, clinical trial researches, experimental studies were excluded (Salahinejad and Aflaki 2010; Piskin et al., 2013; Özden and Özden 2018). The collected data of each study were including the year of study; country; type of teas; sample size; average; standard deviation and range of toxic metals concentration. Aiming to unify units, all unit of concentration of toxic metals including µg/kg, ppb and ng/g were changed to mg/kg-dry-weight.

Quality Assessment and Statistical analysis

Two independent authors (FM and SK) reviewed the retrieved studies. The kappa statistics (95%) was used to identify the inter-authors reliability. The third author (MA) was considered as arbiter to resolve any disagreements. The Q-test and I^2 test were performed to assess between-study heterogeneity and considered significant if I^2 index > 50%. A random effect model was used for meta-analysis concentration of Cd, Pb and As in tea among defined subgroups (tea type and continent). Data were analyzed by the Stata software, version 14 (Stata Corp, College Station, TX, USA) at a significance level of 0.05.

Risk assessment

The non-carcinogenic risk because of ingestion of metals via consumption of teas was considered by the following equation

$$EDI = C \times IR \times EF \times ED / BW \times ATn \quad (1)$$

Based on mentioned equation, C is mean concentration of metals in teas (mg/kg); IR, ingestion rate of teas (kg/n-day); EF, exposure frequency (350 days/year); ED, exposure duration (children=6 years and adults=30 years); BW, Body weight (children=15 kg and adults=70 kg); ATn

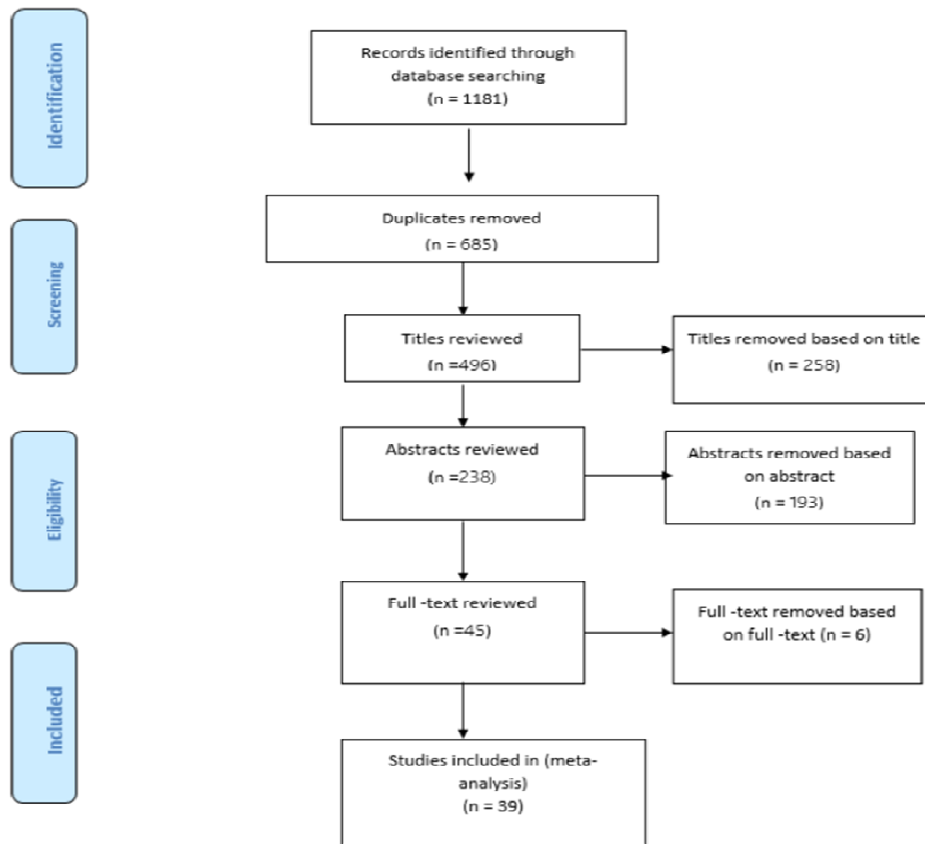


Figure 1: Selection process evidence searches and inclusion

(EF×ED), average time exposure (children= 2190 days and adults=10,950 days). The average world ingestion rate of tea is 750 g/n d, (Helgilibrary 2011).

Target hazard quotient (THQ) due to intake metals in teas was estimated by the following equation (Rezaee et al., 2012):

$$THQ = EDI / RfD \quad (2)$$

In this equation, EDI estimated daily intake; RfD, oral reference dose. Rfd of Pb, Cd, As, was 0.003, 0.001, 0.003mg/kg/day, respective (Antoine et al., 2017).

$$TTHQ = \sum_{i=1}^n THQi \quad \text{Equation (4)}$$

TTHQ show the sum of the each THQfor whole metal analyzed in tea samples (Antoine et al., 2017). If TTHQ was lower than 1, health hazard was considered acceptable for health human (Qin et al., 2015).

Uncertainty analysis

In order to raise precise of risk assessment via considering uncertainties, Monte Carlo simulated (MCS) method was utilized. MCS is a precise method for considering parameters affecting uncertainties and provides accurate health risk. To conduct this method, the Oracle Crystal Ball software (version 11.1.2.4.600) was used. In this method, the parameters like the concentration of metals (C), ingestion rate (IR) and body weight (BW) were considered

as lognormal distribution (Qin et al., 2015; Zhu et al., 2019), the number of repetitions was at 10,000 and percentile 95% of THQ, TTHQ, and ILCR was considered cut point of human health risk (Qu et al., 2012).

RESULTS

Retrieve studies process and characteristics of studies

To conduct systematic review process by searching, 1,181 papers were retrieved from Web of Science (n=187), Scopus (n=607), Embase (n=93) and PubMed (n=294) databases publications from 1 Jan 1973 to 1 Sep 2019. In the first step, 685 articles were excluded via Endnote software (EndNote X7.7.1; Bld 10036) because of repetition. Based on the title of retrieved articles, 496 papers were considered suitable for study and 258 articles were excluded. Based on abstract, 238 articles were reviewed, and then 193 articles were excluded. The Full text of 45 articles were reviewed, and finally, 39 papers were included (2, 6-9, 12, 14, 22, 32-61) (Fig. 1). The study characteristics and results are displayed in Tables 1-3S (Supplementary). In regard of Cd, included studies were

Table 1 S. Main characteristic included in our study for pb metal

| Author | Year | Type of tea | Country | N of sample | Mean | SD | Range | Method | LOD |
|---------------------|------|-------------|--------------|-------------|-------|------|--------------|----------|-------|
| Al-Othman et al., | 2012 | Black | Saudi Arabia | 10 | 5.9 | 2.41 | BDL-8.7 | (FAAS) | NM |
| Zhang et al., | 2018 | Black | China | 10 | .93 | .19 | 0.56- 1.26 | ICP-AES | 0.2 |
| Srogi et al., | 2006 | Black | Italy | 7 | 9 | 4 | 0.10-27.32 | FAAS | NM |
| Milani et al., | 2016 | Black | Brazil | 9 | .16 | .02 | 0.13-0.20 | ICP-MS | 0.013 |
| Lv, H. P et al., | 2013 | Black | China | 56 | 2.32 | .73 | 0.66–4.66 | ICP-AES | NM |
| Salahinejad et al., | 2010 | Black | Iran | 11 | 1.41 | .706 | 0.92- 2.92 | ICP-AES | 0.04 |
| Shokrzadeh et al., | 2005 | Black | Iran | 10 | 6.09 | 2.01 | 4.78- 5.99 | AAS | NM |
| Zhu et al., | 2013 | Black | China | 80 | .62 | .21 | 0.380–0.867 | ICP-MS | 0.01 |
| Karimi et al., | 2008 | Black | Iran | 10 | 2.31 | .29 | 2.08 - 2.59 | AAS | NM |
| Narin et al., | 2004 | Black | China | 14 | .17 | .07 | 0.08- 0.27 | FAAS | 0.1 |
| Nasri et al., | 2017 | Black | Iran | 7 | .13 | .4 | 0.04 - 10.12 | AAS | NM |
| Rubio et al., | 2012 | Black | Spain | 36 | .65 | .71 | NM | ICPS | NM |
| Zhang et al., | 2011 | Black | China | 20 | .32 | .16 | 0.13 -0.49 | AAS | NM |
| Sofuoglu et al., | 2008 | Black | Turkey | 50 | .017 | .013 | 0.003- 0.065 | ICP-AES | NM |
| Seth et al., | 1973 | Black | Indian | 10 | .007 | .002 | 0.002-0.012 | AAS | NM |
| Árvay, J. et al., | 2015 | Black | Slovakia | 10 | 1.387 | .54 | NM | GF-AAS | NM |
| Prki? et al., | 2017 | Black | Croatia | 11 | .103 | .054 | 0.053 – 0.25 | FAAS | 0.07 |
| Yousefi et al., | 2017 | Black | Iran | 32 | .19 | .12 | 0.01 – 0.45 | ICP-OES. | NM |
| Nkansah et al., | 2016 | Black | Ghana | 15 | .16 | .6 | 0.10- 0.40 | AAS | 0.01 |
| Prki et al., | 2018 | Black | Croatia | 19 | .925 | .231 | 0.561- 1.28 | AAS | 0,08 |
| Hosseni et al., | 3013 | Black | Iran | 20 | .368 | .184 | 0.016-0.108 | GFAAS | 0.15 |
| Oliveira et al., | 2018 | Black | US | 16 | .64 | .11 | 0.26- 1.90 | ICP-MS | NM |
| Ozdwn et al., | 2015 | Black | Turkey | 15 | 4.6 | 2.1 | 3.22-5.98 | ICP-OES | 0.1 |
| Jin et al., | 2005 | Black | China | 20 | 2.21 | 1.04 | 0.11- 4.55 | GFAAS | NM |
| Rubio et al., | 2012 | Black | Spain | 36 | .22 | .13 | NM | ICPS | NM |
| Rashid et al., | 2016 | Black | Bangladesh. | 10 | .089 | .004 | 0.03- 0.13 | GF?AAS | 0.052 |
| Ashraf et al., | 2008 | Black | Saudi Arabia | 17 | 1.7 | .81 | 0.3 -2.2 | ICP-AES | NM |
| Jin et al., | 2005 | Black | China | 17 | 2.2 | 1.5 | 0.59- 4.49 | AAS | NM |
| Shaltout et al., | 2016 | Black | Saudi Arabia | 7 | .35 | .15 | 0.23 - 0.53 | ICP-MS | 0.48 |
| Tokaliolu et al, | 2012 | Black | Turkey | 30 | 1.5 | .55 | 0.02 - 3.01 | ICP-MS | NM |
| Zhang et al., | 2017 | Black | China | 30 | .82 | .74 | NM | AAS | 0.54 |
| Kalianin et al., | 2013 | Black | Serbia | 24 | .75 | .375 | 0.73-0.77 | GFAAS | NM |
| Cao et al., | 2010 | Black | Yunnan | 36 | .47 | .61 | 0.01–2.4 | ICP-AES | 0.22 |
| Ghuniem et al., | 2019 | Black | Egypt | 35 | 0 | 0 | NM | ICP-OES | NM |
| Naghipour et al., | 2016 | Black | Iran | 54 | 2 | .9 | 0.5-3.5 | ICP-AES | NM |
| Zazouli et al. | 2010 | Black | Iran | 10 | 11.42 | 2.28 | 8.38- 15.48 | AAS | NM |
| Nejatolahi et al., | 2014 | Black | Iran | 60 | .44 | .14 | 0.28-0.56 | AAS | NM |
| Oliveira et al., | 2018 | Green | US | 14 | .76 | .12 | 0.36- 1.70 | ICP-MS | NM |
| Baronet e al., | 2016 | Green | Italy | 16 | .55 | .35 | 0.10-1.08 | AAS | 0.1 |
| Árvay, J. et al., | 2015 | Green | Slovakia | 14 | .875 | .59 | NM | GF-AAS | NM |
| Milani et al., | 2016 | Green | Brazil | 9 | .2 | .12 | 0.05- 0.37 | ICP-MS | 0.005 |
| Othman et al., | 2011 | Green | Saudi Arabia | 20 | 3.28 | 1.2 | 0.23 – 6.3 | ICP-MS | 0.3 |
| Podwika et al., | 2018 | Green | Poland | 27 | .049 | .03 | 0.006-0.15 | AAS | NM |
| Baronet e al., | 2016 | Green | Italy | 14 | .47 | .07 | 0.30-0.57 | AAS | 0.1 |
| Popovi? et al., | 2018 | Green | Serbia | 9 | .21 | .08 | NM | FAAS | 0.48 |

Table 1S. Continue

| | | | | | | | | | |
|-------------------------|------|-------|--------|-----|------|-----|--------------|---------|-------|
| Ghuniem et al., | 2019 | Green | Egypt | 35 | 1.23 | .5 | NM | ICP-OES | NM |
| Li et al., | 2015 | Green | China | 26 | .92 | .42 | 0.12–2.24 | ICP-AES | NM |
| Peri-Gruji et al., | 2009 | Green | Serbia | 12 | 2.9 | 1.4 | 1.4- -4.4 | FAAS | 0.1 |
| Brzezicha-Cirocka et al | 2016 | Green | Poland | 41 | .45 | .38 | 0.09–1.38 | AAS | 0.004 |
| Tsushida et al., | 1997 | Green | Japan | 139 | .49 | .23 | 0. 11- 1. 93 | AAS | NM |

Table 2S. Main characteristic included in our study for Cd metal

| Author | Year | Type of tea | Country | N of sample | Mean | SD | Range | Method | LOD |
|-------------------------|------|-------------|--------------|-------------|-------|-------|--------------|----------|-------|
| Tsushida et al., | 1997 | Black | Japan | 139 | .04 | .002 | 0.013-0.098 | AAS | NM |
| Narin et al., | 2004 | Black | China | 14 | .02 | .04 | 0.01-0.03 | FAAS | 0.06 |
| Shokrzadeh et al., | 2005 | Black | Iran | 10 | .6 | .23 | 0.09- 1.09 | AAS | NM |
| Srogi et al., | 2006 | Black | Italy | 7 | .27 | .12 | 0.06-0.49 | FAAS | NM |
| Ashraf et al., | 2008 | Black | Saudi Arabia | 17 | 1.1 | .51 | 0.3 -2.2 | ICP-AES | NM |
| Sofuoglu et al., | 2008 | Black | Turkey | 50 | .0002 | .0002 | 0.002-0.079 | ICP-AES | NM |
| Yaylali-Abanuz Et al., | 2009 | Black | Turkey | 10 | .06 | .02 | 0.02 - 0.12 | AAS | 0.01 |
| Yaylali-Abanuz Et al., | 2009 | Black | Turkey | 10 | .74 | .27 | 0.27 - 1.86 | AAS | 0.002 |
| Cao et al., | 2010 | Black | China | 36 | .02 | .0002 | 0.01–0.03 | ICP-AES | 0.011 |
| Zazouli et al. | 2010 | Black | Iran | 10 | .67 | .51 | 0.13 - 1.92 | AAS | NM |
| Salahinejad et al., | 2010 | Black | Iran | 11 | .66 | .33 | Nd-0.78 | ICP-AES | 0.003 |
| Al-Othman et al., | 2012 | Black | Saudi Arabia | 10 | .15 | .08 | BDL-0.7 | (FAAS) | NM |
| Prkic et al., | 2013 | Black | Croatia | 7 | .21 | .13 | 0.02- 0.38 | ETAAS | NM |
| Lv, H. P et al., | 2013 | Black | China | 56 | .06 | .02 | 0.023–0.13 | ICP-AES | NM |
| Hossenli et al., | 2013 | Black | Iran | 20 | .03 | .01 | 0.005- 0.069 | GFAAS | 0.18 |
| Zhu et al., | 2013 | Black | China | 80 | .02 | .01 | 0.010–0.032 | FAAS | 0.005 |
| Árvay, J. et al., | 2015 | Green | Slovakia | 14 | .16 | .08 | NM | GF-AAS | NM |
| Árvay, J. et al., | 2015 | Black | Slovakia | 10 | .4 | .07 | NM | GF-AAS | NM |
| Ozdwn et al., | 2015 | Black | Turkey | 15 | .39 | .19 | 0.32-0.47 | ICP-OES | 0.1 |
| Li et al., | 2015 | Green | China | 26 | .06 | .02 | 0.025–0.11 | ICPMS | NM |
| Orisakwe et al., | 2015 | Black | Nigeria | 20 | .1 | .05 | 0.01-0.25 | AAS | 0.01 |
| Baronet e al., | 2016 | Green | Italy | 16 | .04 | .03 | 0.01-0.08 | AAS | 0.1 |
| Shaltout et al., | 2016 | Black | Saudi Arabia | 7 | .03 | .02 | 0.01 - 0.05 | ICP-MS | 0.48 |
| Rashid et al., | 2016 | Black | Bangladesh | 10 | .27 | .003 | 0.05- 1.14 | GF-AAS | 0.026 |
| Milani et al., | 2016 | Black | Brazil | 9 | .01 | .03 | 0.010-0.02 | ICP-MS | 0.001 |
| Naghipour et al., | 2016 | Black | Iran | 54 | .33 | .16 | 0.07-0.6 | ICP-AES | NM |
| Brzezicha-Cirocka et al | 2016 | Green | Poland | 41 | .01 | .004 | 0.003–0.01 | AAS | 0.003 |
| Nkansah et al., | 2016 | Black | Ghana | 15 | .36 | .18 | 0.10- 1.50 | AAS | 0.007 |
| Baronet e al., | 2016 | Green | Italy | 14 | .03 | .01 | 0.01-0.05 | AAS | 0.1 |
| Milani et al., | 2016 | Green | Brazil | 9 | .01 | .0001 | 0.004-0.01 | ICP-MS | 0.001 |
| Prkic et al., | 2017 | Black | Croatia | 11 | .02 | .02 | 0.011-0.131 | FAAS | 0.08 |
| Zhang et al., | 2017 | Black | China | 30 | .05 | .03 | NM | AAS | 1.1 |
| Nasri et al., | 2017 | Black | Iran | 7 | .06 | .02 | 0.01 - 0.12 | AAS | NM |
| Yousefi et al., | 2017 | Black | Iran | 32 | .19 | .12 | 0.01 – 0.45 | ICP-OES. | NM |
| Oliveira et al., | 2018 | Green | US | 14 | .04 | .01 | 0.01-0.04 | ICP-MS | NM |

Table 2S. Continue

| | | | | | | | | | |
|------------------|------|-------|---------|----|-----|-----|--------------|---------|------|
| Zhang et al., | 2018 | Black | China | 10 | .06 | .01 | 0.04 - 0.08 | ICP-AES | 0.02 |
| Oliveira et al., | 2018 | Black | US | 16 | .05 | .01 | 0.01-0.19 | ICP-MS | NM |
| Popovic et al., | 2018 | Green | Serbia | 9 | .34 | .02 | NM | FAAS | 0.11 |
| Prkic et al., | 2018 | Black | Croatia | 19 | .53 | .22 | 0.082- 0.805 | AAS | 0.07 |
| Ghuniem et al., | 2019 | Green | Egypt | 35 | .09 | .03 | NM | ICP-OES | NM |
| Ghuniem et al., | 2019 | Black | Egypt | 35 | 0.4 | 0.2 | NM | ICP-OES | NM |

Table 3S. Main characteristic included in our study for As metal

| Author | Year | Type of tea | Country | N of sample | Mean | SD | Range | Method | LOD |
|--------------------|------|-------------|--------------|-------------|------|-----|-------------|---------|-------|
| Shaltout et al., | 2016 | Black | Saudi Arabia | 7 | .12 | .04 | 0.07- 0.19 | ICP-MS | 3.07 |
| Nasri et al., | 2017 | Black | Iran | 7 | .16 | .8 | 0.04 - 0.28 | AAS | NM |
| Karimi et al., | 2008 | Black | Iran | 10 | .09 | .02 | 0.08 - 0.12 | AAS | NM |
| Zhang et al., | 2017 | Black | China | 30 | .15 | .1 | NM | AAS | 1.46 |
| Zhu et al., | 2013 | Black | China | 80 | .06 | .02 | 0.009–0.124 | ICP-MS | 0.036 |
| Lv, H. P et al., | 2013 | Black | China | 56 | .15 | .03 | 0.07–0.25 | ICP-AES | NM |
| Popovi et al., | 2018 | Green | Serbia | 9 | .21 | .08 | NM | FAAS | 0.48 |
| Popovi et al., | 2018 | Green | Serbia | 9 | .04 | .01 | NM | FAAS | 0.45 |
| Milani et al., | 2016 | Black | Brazil | 9 | .02 | .01 | 0.018-0.04 | ICP-MS | 0.013 |
| Oliveira et al., | 2018 | Black | Us | 16 | .22 | .02 | 0.05-0.36 | ICP-MS | NM |
| Rashid et al., | 2016 | Black | Bangladesh | 10 | 1.21 | 0 | 0.19- 2.06 | GF-AAS | 0.046 |
| Nkansah et al., | 2016 | Black | Ghana | 15 | 1.66 | .83 | 1.40- 2.00 | AAS | 0.004 |
| Naghypour et al., | 2016 | Black | Iran | 54 | .07 | .03 | 0.03-0.1 | ICP-AES | NM |
| Zhang et al., | 2018 | Black | China | 10 | .29 | .06 | 0.18- 0.453 | ICP-AES | 0.05 |
| Cao et al., | 2010 | Black | China | 36 | .17 | .06 | 0.08–0.36 | ICP-AES | 0.038 |
| Sofuoglu et al., | 2008 | Black | Turkey | 50 | 0 | .07 | 0.016-0.053 | ICP-AES | NM |
| Barman et al., | 2019 | Black | India | 497 | .11 | .05 | 0.01 - 0.37 | AAS | 0.005 |
| Nejatolahi et al., | 2014 | Black | Iran | 60 | .21 | .08 | 0.17-0.29 | AAS | NM |
| Ashraf et al., | 2008 | Black | Saudi Arabia | 17 | 1.1 | .52 | 0.3 -2.2 | ICP-AES | NM |
| Milani et al., | 2016 | Green | Brazil | 9 | .04 | .01 | 0.029-0.06 | ICP-MS | 0.005 |
| Oliveira et al., | 2018 | Green | Us | 14 | .18 | .07 | 0.01- 0.70 | ICP-MS | NM |

published between 1997 and 2019, the sample size of included articles varied from 7 to 139 with a total of 956 samples. For Pb, included studies were published between 1973 and 2019, the sample size of included articles varied from 7 to 139 with a total of 1240 samples and for As, included studies were published between 2008 and 2018. The sample size of included articles varied from 7 to 497 with a total of 1005 samples. Rank order of countries according to the number of studies were: Iran(51.28%)~China (51.28%) >Saudi Arabia (23.07%) >Turkey(20.47%) >Brazil (15.38%)~Us(15.38%) >Serbia (12.82%)> Egypt (10.25%)~Italy(10.25%)~Slovakia (10.25%)> Bangladesh(7.69%)~Croatia(7.69%)~Ghana(7.69%)~ Poland(7.69%)>India(5.12%)~Spain(5.12%) >Nigeria (2.56%)~Yunnan (2.56%)(Tables 1-3S).

The concentration of toxic metals in teas based on teas types and continents

The results of Cochran's Q test and I^2 statistics suggested a significant heterogeneity among the included studies for Cd ($Q=3205.92$, $df=40$, $p<0.001$ and $I^2=100\%$), Pb ($Q=11373.46$, $df=48$, $p<0.001$ and $I^2=99.6\%$) and As ($Q=2585.79$, $df=19$, $p<0.001$ and $I^2=99.3\%$). In order to reduce the heterogeneity, we performed subgroup analysis based on teas types and continents (Tables 1, 2). The concentration of Pb was higher in green tea and according to continents, the highest and lowest concentration was belonging to African countries and American countries, respectively (0.703 mg/kg vs. 0.44 mg/kg). Accordingly, the concentration of Cd in black tea was 0.09 mg/kg (0.082 mg/kg, 0.098 mg/kg) and in green tea was 0.08 mg/kg

Table 1. Meta-analysis of concentration of toxic metal (mg/kg) based on kind of tea.

| Toxic metals | WHO regions | Number study | ES | Lower | Upper | Weight (%) | Statistic | df | P value | I ² (%) |
|--------------|-------------|--------------|-------|-------|-------|------------|-----------|----|---------|--------------------|
| Pd | black | 33 | 0.54 | 0.51 | 0.58 | 69.99 | 90008.7 | 35 | <0.001 | 99.6 |
| | green | 13 | 0.779 | 0.587 | 0.971 | 30.01 | 1771.37 | 12 | <0.001 | 99.3 |
| Cd | black | 32 | 0.09 | 0.082 | 0.098 | 68.14 | 3202.05 | 31 | <0.001 | 100 |
| | green | 9 | 0.08 | 0.065 | 0.096 | 36.86 | 3108.34 | 8 | <0.001 | 99.7 |
| AS | black | 16 | 0.149 | 0.116 | 0.182 | 77.61 | 2147.21 | 15 | <0.001 | 99.3 |
| | green | 4 | 0.101 | 0.067 | 0.134 | 22.39 | 94.42 | 3 | <0.001 | 96.8 |

Table 2. Meta-analysis of concentration of toxic metal (PTEs) (mg/kg) in teas based on WHO regions

| Toxic metals | WHO regions | Number study | ES | Lower | Upper | Weight (%) | Statistic | df | P value | I ² (%) |
|--------------|-------------|--------------|-------|-------|-------|------------|-----------|----|---------|--------------------|
| Pd | Asia | 26 | 0.661 | 0.613 | 0.708 | 48.59 | 8018.07 | 25 | <0.001 | 99.7 |
| | Europe | 17 | 0.558 | 0.472 | 0.644 | 35.25 | 1705.86 | 16 | <0.001 | 99.1 |
| | Africa | 2 | 0.703 | 0 | 1.75 | 2.73 | 36.76 | 1 | <0.001 | 97.3 |
| | America | 4 | 0.44 | 0.114 | 0.766 | 13.43 | 594.87 | 3 | <0.001 | 99.5 |
| Cd | Asia | 19 | 0.103 | 0.085 | 0.12 | 48.79 | 833356.5 | 18 | <0.001 | 100 |
| | Europe | 14 | 0.131 | 0.114 | 0.149 | 29.27 | 3779.41 | 13 | <0.001 | 99.7 |
| | Africa | 4 | 0.224 | 0.137 | 0.311 | 6.86 | 113.93 | 3 | <0.001 | 97.4 |
| | America | 4 | 0.028 | 0.003 | 0.063 | 15.09 | 381.88 | 3 | <0.001 | 99.2 |
| AS | Asia | 13 | 0.159 | 0.129 | 0.188 | 59.79 | 930.15 | 12 | <0.001 | 98.7 |
| | Europe | 3 | 0.075 | 0.014 | 0.136 | 16.8 | 56.69 | 2 | <0.001 | 96.5 |
| | Africa | 0 | - | - | - | - | - | - | - | - |
| | America | 4 | 0.114 | 0.023 | 0.206 | 23.41 | 1237.05 | 3 | <0.001 | 99.8 |

(0.065 mg/kg, 0.096 mg/kg). The highest concentration of Cd in tea was in African countries and lowest in American countries (0.224 mg/kg vs. 0.028 mg/kg). In regard of As, black teas had higher concentration (0.149 mg/kg vs. 0.101 mg/kg) and teas in Asian countries had highest concentration (0.159 mg/kg). As seen of results, the concentration of toxic metals in tea was greatly diverse between different countries. Discrepancy observed could be related to the numerous factors like physicochemical characteristics of heavy metals, condition during plant growth (PH, humidity of soil, water), altitude of sea level, speed of rainfall, different bioavailability of metals (Shi et al., 2008; Yongsheng et al., 2011; Chaoua et al., 2019), and characteristics of soil used for cultivation tea. Generally, It is obvious that chemical properties of soil including pH (Li et al., 2013), level of carbon (Lei et al., 2013), amount of nitrogen (Oh et al., 2008), potassium sulfur (Kamau et al., 2008), and phosphate fertilizers have effect role in metals uptake via tea plants (Ananthacumaraswamy et al., 2003); Yaylali-Abanuz and Tuysuzin their studies indicated that there was a significant

negative relation between soil pH and uptake of metals by tea plants (Yaylali-Abanuz and Tuysuz 2009). As mentioned in previous studies, high concentration of metals in teas may be effective by environmental pollution level during plant growth. For sample, Sharafi et al., 2019 in their studies indicated, crops cultivate near factories, mines, and highways had high amounts of metals (Sharafi et al., 2019). As a result, the metals pattern in tea shows the geography conditions of different countries and the natural environments in which tea plants are grown.

Processing of tea production

Meta-analysis regarding to concentration of toxic metal (mg/kg) based on kind of tea was presented in Table 1. The ranking of metals concentration in black and green tea was Pb > As > Cd, respectively. The highest contamination in black tea was related to As metal whereas in green tea was related to Pb metal. These differences in concentration of metals may be dependent on processing of tea production (Heshmati et al., 2020; Mehri et al., 2019). It is

Table 3. Uncertainty analysis for TTHQ of metals in children and adult due to consumption of tea in various countries

| Country | Adults | | | | Children | | | |
|--------------|----------------|-------|-------|-------|----------------|-------|--------|-------|
| | Percentile 95% | | | | Percentile 95% | | | |
| | AS | Cd | Pb | TTHQ | AS | Cd | Pb | TTHQ |
| Bangladesh | 0.045 | 0.037 | - | 0.066 | 0.212 | 0.172 | - | 0.307 |
| Brazil | 0.002 | 0.002 | 0.082 | 0.068 | 0.007 | 0.008 | 0.382 | 0.314 |
| China | 0.006 | 0.009 | 0.740 | 0.440 | 0.030 | 0.041 | 3.458 | 2.057 |
| Croatia | - | 0.072 | 0.285 | 0.259 | - | 0.337 | 1.325 | 1.207 |
| Egypt | 0.101 | 0.057 | 0.521 | 0.495 | 0.466 | 0.264 | 2.443 | 2.312 |
| Ghana | 0.006 | 0.076 | 0.235 | 0.100 | 0.030 | 0.359 | 1.095 | 0.468 |
| Indian | - | - | 0.004 | 0.003 | - | - | 0.019 | 0.012 |
| Iran | 0.007 | 0.075 | 1.095 | 0.651 | 0.033 | 0.351 | 5.113 | 3.036 |
| Italy | - | 0.013 | 2.458 | 0.766 | - | 0.062 | 11.422 | 3.595 |
| Japan | - | 0.005 | 0.221 | 0.181 | - | 0.023 | 1.030 | 0.844 |
| Nigeria | - | 0.021 | - | 0.011 | - | 0.100 | - | 0.050 |
| Poland | - | 0.002 | 0.172 | 0.119 | - | 0.009 | 0.804 | 0.556 |
| Saudi Arabia | 0.048 | 0.141 | 2.319 | 1.111 | 0.224 | 0.661 | 10.900 | 5.186 |
| Serbia | 0.007 | 0.046 | 0.865 | 0.479 | 0.033 | 0.216 | 4.051 | 2.235 |
| Slovakia | - | 0.045 | 0.639 | 0.422 | - | 0.207 | 2.990 | 1.970 |
| Spain | - | - | 0.346 | 0.158 | - | - | 1.614 | 0.737 |
| Turkey | 0.001 | 0.043 | 0.980 | 0.454 | 0.006 | 0.203 | 4.535 | 2.121 |
| US | 0.009 | 0.007 | 0.314 | 0.262 | 0.043 | 0.034 | 1.466 | 1.226 |
| Yunnan | 0.009 | 0.008 | 0.555 | 0.176 | 0.041 | 0.036 | 2.560 | 0.817 |

quite clear that content of metal varies among teas and an assortment of synergistic factors can be involved in these diversities. Besides to age and content of leaves of tea that used in packaging process, degree of maturing, storage and also the ways of fermentation have basic role in contamination sources of tea. As mentioned in previous studies, green tea is produced by young leaves, vapor of water, dry and fry without fermentation, in contrast to black tea, which it is produced by older leaves, dry via air along with fermentation (Szymczycha-Madeja et al., 2012; Mosleh et al., 2014; Matsuura et al., 2001). Also, In addition contamination sources during the production of tea, agricultural activities, use of fungicides and fertilizers in process of cultivation, handling and storage of tea can be the most important parameters in the presence of metals in tea plants (Falahi and Hedaiati 2013).

Health risk assessment

The non-carcinogenic risk assessment of toxic metals by consumption of the black and green teas in different countries was indicated in Table 3. The results showed that accounted TTHQ amounts for adult groups in all investigated countries, except Saudi Arabia country, were lower than 1 which indicated no acceptable health risk for

tea consumers. TTHQ amounts accounted for children groups in countries like Saudi Arabia > Italy > Iran > Egypt > Serbia > Turkey > China > Slovakia > US > Croatia respectively were higher than 1 while in other countries was lower than 1. Therefore, consumers are at the considerable non-carcinogenic health risk in countries with risk higher than one. TTHQ level in children was higher in comparison with adult that may be due to lower BW, which can make children to be at higher hazard risk. This finding was similar to previous studies (77-79). It is worth noting different amount of TTHQ among countries can be related to pattern and rate of consumption, consumption frequency, concentration of toxic metal and body weight (Barone et al., 2016; Atamaleki et al., 2019).

CONCLUSIONS

This study was first systematic review and meta-analysis regarding the concentration of the toxic metals in teas according to types of teas and continents in the world. On-carcinogenic health risk in regarding to the adults and children was assessed. The results of 39 papers showed that the ranking of metals concentration in black and green was Pb > As > Cd. The highest contamination in black tea

was related to Asmetal whereas in green tea the highest level of contamination was related to Pbmetal. According to continents, the higher and lower concentration of toxic metals was related to Pb in Africa and Cd in America. Some parameters such as physicochemical characteristics of heavy metals, agricultural activities, status during plant growth (Ph. and humidity of soil, water), and also handling, storage, and processing practices play critical roles among these diversities. The health risk assessment indicated risk pattern was different in various countries and TTHQ level in children was higher in comparison with adult, hence, performing of control plans should be considered by governments as well as farmer for decrease concentration of toxic metals in black and green tea.

Conflict interest

All authors express that they have any conflict of interest.

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