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Assessment of concentration and toxicological (Cancer) risk of lead, cadmium and chromium in tobacco products commonly available in Bangladesh

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ABSTRACT

This study aimed to assess the concentrations of heavy metal ('lead (Pb)''cadmium (Cd)', and 'chromium (Cr)') in various brands of four types of tobacco products (zarda, gul, cigarettes, and bidi) as well as calculate toxicological risk as a lifetime cancer risk for Pb, Cd, and Cr. In smokeless tobacco products, the metal concentration ranged from 0.99 to 10.02 µg/g for Pb, 1.05–3.53 µg/g for Cd, and 1.23–7.29 µg/g for Cr, respectively. Metal concentrations in the smoke-based tobacco products ranged from 0.98 to 3.07 µg/g for Pb, 0.91–3.46 µg/g for Cd, 1.08–6.75 µg/g for Cr, respectively. When assuming a 100% transfer of these metals, the calculated lifetime cancer risk was found 'unacceptable' in 33 out of 35 tobacco samples which exceeded the U.S. Environmental Protection Agency (USEPA) benchmark of an 'acceptable' cancer risk range of 10E-4 to 10E-6. Our study demonstrated higher levels of Pb, Cd, and Cr in various tobacco products of Bangladesh compared to GOTHIATEK standard. This study shows the need for the development of industry standards and regulation for tobacco products to reduce the levels of heavy metals.

1. Introduction

Tobacco was inaugurated in Bangladesh in the middle of the 1900's century, and its usage has increased over the last four decades [1]. According to International tobacco control (ITC) report [2], there are 41.1 million people using tobacco in Bangladesh, of which 20.9 million people are consuming tobacco either through cigarettes or bidis or both. A World Health Organization (WHO) [3] study on the impacts of tobacco-related illnesses in Bangladesh reported that eight tobacco-related illnesses could be found among 2.9 million cases and about 1.2 million could be due to tobacco usage. The approximate number of deaths caused by tobacco is 57,000 on an average per year [2], and this number will rise soon. Another study assessed that cigarette smoking is responsible for around 25.0% and 7.6% of deaths in males and females, respectively in Bangladesh [4].

Nearly 4000 chemicals of tobacco were classified into different groups according to their health hazard index [5]. The International Agency for Research on Cancer (IARC) has designated cadmium (Cd) and chromium (Cr) (VI) as group 1 carcinogenic to humans. Additionally, lead (Pb) is an IARC group 2 A probable human carcinogen [6]. The users of tobacco take in substantial levels of heavy metals in their body via inhalation, although these chemical elements are present in low amounts but exhibit high toxicity [7,8]. Bioaccumulation of metals also occurs in people due to chronic exposure to tobacco smoke via inhalation, also known as passive smoking [9–12]. Lead and cadmium concentrations were described to be significantly higher in four out of five lobes, while the concentrations of chromium have been found to be significantly higher in all five lobes of smokers' lungs than in nonsmokers' [13]. Cadmium, one of the many chemicals present in tobacco smoke is a "strong carcinogen" [14]. It is a non-essential, potentially toxic metal, which gets accumulated in tobacco plants and is transferred to tobacco smoke affecting humans via inhalation [15]. As per the WHO report [16], cadmium inhaled via tobacco smoking is 10–20% of the total Cd present. Lead is a toxic metal and can affect the brain and bone causing changes in mineral density as well as fetal growth and brain development [17,18]. World Health Organization [19] estimated that smokers inhaled 2–6% of Pb from cigarettes. Only a very few reports are available on Cr concentrations in

Abbreviation: USEPA, U.S. Environmental Protection Agency; ITC, international tobacco control; WHO, World Health Organization; IARC, International Agency for Research on Cancer; CEPA, California Environmental Protection Agency

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marketed cigarettes. However, chromium was detected in cigarette smoke and ash [20], this metal may lead to hemorrhage, respiratory impairment and liver lesions in humans [21].

Several studies have been conducted on environmental impacts of tobacco production in Bangladesh at the local level to address social and health problems. This study is the first to quantify the presence of Pb, Cd, and Cr in both smokeless (zarda, gul) and smoking tobacco (cigarettes, bidi) that are commonly available in Bangladeshi market. We aimed to relate the concentration of heavy metals to the potential cancer risks and to create better awareness of tobacco related health/safety issues.

2. Materials & method

2.1. Sample collection and preparation

A total number of 35 different brands of smokeless and smoke-based tobacco products including zarda, gul, cigarettes, and bidi were collected from various shops of Dhaka, Chuadanga and Khulna districts based on market popularity and price range. The market was surveyed via personal communication about the popularity of brands and their price. The tobacco samples were collected and immediately transferred into zipping locked transparent polypropylene bags to maintain moisture content and quality. Tobacco from the cigarettes and bidi was first separated from the filter as well as cover paper, dried in the dry heat oven (Nuve FN 400) at 105° temperature for 24 h and grounded to make it powder-like using mortar and pestle. A mixture of ternary acid was prepared from HNO_3 (68%–72%), H_2SO_4 (95%–97%), and $HClO_4$ (69%–72%) with a volume ratio of 5:1:2 following the method [22]. Typically, 1 g of each sample product was first pre-digested by using 30 ml of freshly prepared ternary mixture acid leaving them overnight, followed by digestion on hot sand bath for 2–3 hours at 150 °C until a white precipitate was obtained. Samples were analyzed in triplicate and results were reported as means ± standard deviation based on these replicate measurements. Triplication was done to maintain the accuracy and minimize the experimental error. The final volume of digested samples was adjusted to 50 ml and analyzed for selected heavy metals, viz., Pb, Cd, and Cr by Atomic Absorption Spectroscopy (Varian AA240).

2.2. Assessment of potential toxicity

Separate cancer potency factors were applied for both ingestion and inhalation processes to calculate the risk of the smokeless and smoke based tobacco consumption on a long-term basis. Potential Toxicity of smokeless tobacco products was determined by using the equation described by [23] and [24] as follows:

Lifetime Cancer Risk = ADE lifetime × CPF

Where, ADE lifetime = lifetime average daily exposure (mg/kg body-weight/day) and CPF = cancer potency factor ((mg/kg body-weight/day)$^{-1}$).

ADE lifetime = ADE × no. of years of consumption/average lifetime.

ADE was calculated assuming the daily consumption of 10 gm of tobacco by an individual with a body weight of 57.7 kg for 30 years out of an average lifespan of 70 years. The CPF values of Pb: 0.0085 ((mg/kg body-weight/day)$^{-1}$), Cd: 15 ((mg/kg body-weight/day)$^{-1}$), and Cr (VI): 0.42 ((mg/kg body-weight/day)$^{-1}$) were obtained as described by California Environmental Protection Agency (CEPA), [25].

The above equation was also used for the exposure to metal from smoke-based tobacco products. The following equation was further used only when estimated risk value exceeded 0.01, as per the guidance of U.S. Environmental Protection Agency (USEPA) [26]:

Cancer Risk = 1– Exp. (-CDI x SF)

Where, cancer risk = a unitless probability of individual developing cancer, Exp. = the exponential, CDI = exposure to the metal (mg/10 g of tobacco/57.7 kg body weight) × 30 Years of Exposure/70 Year Lifespan = Chronic Daily Intake averaged over 70 Years (mg/kg-day) and SF = Slope factor = Cancer Potency Factor ((mg/kg/day)$^{-1}$). The method of calculation for smokeless tobacco products is similar to the smoke based products. Different cancer potency values for inhalation were used, namely 0.042 ((mg/kg body-weight/day)$^{-1}$) for Pb and 510 ((mg/kg body-weight/day)$^{-1}$) for Cr (VI) [25].

The method of estimating potential toxicity assumes that 100% of the toxicant is potentially bio-available in ideal conditions and can fully contribute to the overall risk of the product [14,27]. We have assumed 100% transfer of Cr as no established literature was available. However, we have also considered a reduced potential risk of 6% based on the bioavailability of the carcinogens [24,28] in smokeless tobacco, 6% of Pb [19] and 20% of the total Cd [16] in smoke based tobacco. In this study, 57.7 kg body weight was considered as the body weight of an Asian adult [29], and daily tobacco consumption data was collected from the report on Global adult tobacco survey by WHO [30].

2.3. Statistical Analysis

Data were presented as the means ± standard deviation of the mean (SD). The correlation test was done by using Microsoft Excel (version 2013) and the graphical representations of heavy metal concentrations in different tobacco products were created by using gg_plot2 packages of R (version 3.4.2).

3. Results

The mean concentrations for Pb, Cd, and Cr for the 35 samples obtained from four different types of tobacco products are presented in Table 1. A large number of brands were chosen for each tobacco product category. The low standard deviation (SD) values for the analysis of various samples of each brand are indicative of good data quality.

The concentration of Pb in different zarda products ranged from 0.99 ± 0.04 μg/g to 10.02 ± 0.03 μg/g with a similar concentration observed in gul products for Pb (1.16 ± 0.0 μg/g to 1.74 ± 0.07 μg/g). Cadmium concentration ranged from 1.08 ± 0.03 μg/g to 3.53 ± 0.08 μg/g and 1.05 ± 0.03 μg/g to 3.06 ± 0.17 μg/g in zarda and gul products. However, Cr concentration varied widely from 1.23 ± 0.20 μg/g to 7.29 ± 0.03 μg/g and 1.71 ± 0.15 μg/g to 6.01 ± 0.13 μg/g for zarda and gul products, respectively.

For smoke based tobacco products, concentration of Pb, Cd, and Cr in bidi was found about 0.98 ± 0.03 μg/g to 3.07 ± 0.02 μg/g, 1.00 ± 0.05 μg/g to 2.14 ± 0.16 μg/g, and 1.77 ± 0.15 μg/g to 2.58 ± 0.12 μg/g, respectively. In cigarettes, the concentration of Pb, Cd, and Cr was found about 1.07 ± 0.09 μg/g to 2.54 ± 0.06 μg/g, 0.91 ± 0.01 μg/g to 3.46 ± 0.02 μg/g and 1.08 ± 0.13 μg/g to 6.75 ± 0.06 μg/g, respectively.

The toxicological risk calculated as a cancer risk for Pb, Cd, and Cr at a transfer rate of 6%, 20%, and 100% are presented in Tables 2 and 3 for smokeless and smoke-based tobacco products along with overall cancer risk. Cancer risks for tobacco products were compared here with the limit value of 10E-4 to 10E-6 prescribed by USEPA. The gul product exceeded the limit of 10E-4 to 10E-6 at 6% and 100% transfer, while many of the zarda products also exceeded the prescribed limit. The risk of individual metal for smokeless tobacco products ranges from 1.02E-06 to 9.94E-07 for Pb, 1.09E-01 to 3.93E-03 for Cd and 1.00E-04 to 9.96E-05 for Cr when 100% transfer is considered. In case of smoke-based tobacco products, risks of individual metals range from 4.84E-03 to 9.57E-06 for Pb, 1.02E-3 to 1.86E-03 for Cd as well as 1.43E-01 to 9.32E-02 for Cr for 100% transfer. The total value of these three metals exceeded the acceptable range of cancer risk for both cigarette and bidi.

Table 1
Concentration of Pb, Cd, and Cr in Smokeless and Smoke-based Tobacco Products.

Smokeless tobacco		Pb (μg/g) ± SD	Cd (μg/g) ± SD	Cr (μg/g) ± SD
Zarda	SLT-1	10.02 ± 0.03	1.08 ± 0.03	1.34 ± 0.15
	SLT-2	7.39 ± 0.11	2.05 ± 0.09	1.23 ± 0.20
	SLT-3	1.30 ± 0.03	1.37 ± 0.02	3.19 ± 0.18
	SLT-4	2.16 ± 0.14	3.21 ± 0.20	5.20 ± 0.25
	SLT-5	0.99 ± 0.04	2.49 ± 0.03	1.85 ± 0.07
	SLT-6	2.33 ± 0.16	1.22 ± 0.06	2.66 ± 0.10
	SLT-7	1.54 ± 0.06	2.78 ± 0.07	3.22 ± 0.12
	SLT-8	2.78 ± 0.06	2.49 ± 0.16	1.30 ± 0.12
	SLT-9	3.29 ± 0.21	1.29 ± 0.11	2.14 ± 0.13
	SLT-10	2.85 ± 0.07	1.39 ± 0.01	3.73 ± 0.10
	SLT-11	1.08 ± 0.08	1.08 ± 0.00	1.75 ± 0.11
	SLT-12	1.13 ± 0.03	3.12 ± 0.15	7.29 ± 0.03
	SLT-13	2.02 ± 0.12	1.23 ± 0.21	1.80 ± 0.09
	SLT-14	1.65 ± 0.14	3.53 ± 0.08	1.58 ± 0.07
	SLT-15	2.67 ± 0.11	1.40 ± 0.01	1.36 ± 0.02
Gul	SLT-16	1.74 ± 0.07	3.06 ± 0.17	4.35 ± 0.07
	SLT-17	1.16 ± 0.00	1.57 ± 0.05	6.01 ± 0.13
	SLT-18	1.54 ± 0.06	1.68 ± 0.12	1.71 ± 0.15
	SLT-19	1.57 ± 0.13	1.92 ± 0.03	5.73 ± 0.22
	SLT-20	1.61 ± 0.15	1.05 ± 0.03	3.55 ± 0.09
Smoke-based tobacco		**Pb (μg/g) ± SD**	**Cd (μg/g) ± SD**	**Cr (μg/g) ± SD**
Cigarette	SBT-1	1.07 ± 0.09	1.39 ± 0.01	1.25 ± 0.05
	SBT-2	1.47 ± 0.03	1.06 ± 0.10	4.07 ± 0.01
	SBT-3	2.11 ± 0.11	0.94 ± 0.03	1.25 ± 0.05
	SBT-4	1.76 ± 0.11	0.91 ± 0.01	1.80 ± 0.11
	SBT-5	1.22 ± 0.15	1.20 ± 0.17	1.40 ± 0.11
	SBT-6	2.09 ± 0.16	3.46 ± 0.02	1.35 ± 0.06
	SBT-7	2.05 ± 0.06	2.70 ± 0.06	6.75 ± 0.06
	SBT-8	2.54 ± 0.06	2.06 ± 0.06	3.19 ± 0.18
	SBT-9	1.22 ± 0.11	2.97 ± 0.03	1.08 ± 0.13
	SBT-10	1.56 ± 0.05	2.60 ± 0.17	1.37 ± 0.05
	SBT-11	2.35 ± 0.03	2.77 ± 0.12	1.33 ± 0.08
Bidi	SBT-12	1.55 ± 0.09	1.00 ± 0.05	2.08 ± 0.11
	SBT-13	3.07 ± 0.02	1.27 ± 0.12	2.32 ± 0.14
	SBT-14	1.77 ± 0.01	2.14 ± 0.16	2.58 ± 0.12
	SBT-15	0.98 ± 0.03	1.88 ± 0.03	1.77 ± 0.15

An effort was made to elucidate a trend of metal concentrations in relation to the price of the products as shown in Fig.1. We categorized the products from low to high price by one packet of product on the X-axis and total metal concentration (μg/g) on the Y-axis. We hypothesized that higher priced products would have lower concentrations of heavy metals, i.e. less harmful compared to lower priced products. There was a small positive correlation between total concentration and price of metals in smokeless tobacco products (Fig. 1a) although not significant, rejecting this hypothesis. A small negative correlation was found between product price and the total concentration of heavy metals in smoke-based tobacco products (Fig. 1b), but again this was not significant, hence also rejecting this hypothesis statistically.

4. Discussion

The presence of heavy metals in tobacco products is well established all over the world and also the individual metal concentrations estimated in various countries. The WHO Southeast Asian Region of 11-member states is the hub of smokeless tobacco users [31]. The use of different smokeless tobacco products is historical for centuries and especially popular in Bangladesh, India, Myanmar, and Nepal. The smokeless tobacco products are used by 19.7% of the population in Bangladesh [32]. A global tobacco survey by WHO for adult population showed that in Bangladesh the prevalence of current smoking of manufactured cigarettes and bidis were 14.2% and 11.2%, respectively [30].

Considering the prevalence and the market use of tobacco products in Bangladesh, the present investigation was designed to measure the concentration of heavy metals (Pb, Cd, and Cr) and estimate cancer risks in these products. The mean concentrations of each metal along with minimum and maximum concentration in different tobacco products are presented in Fig. 2, and here further compared with published data from other countries to give an overview on the concentration of heavy metals in tobacco products in different countries. The mean concentration of Pb (Fig. 2) in zarda and gul was 2.8 μg/g and 1.52 μg/g. The high concentration in zarda might be due to the processing and mixing of extra ingredients [28,33]. The mean concentration of Pb (Fig. 2) in bidi and cigarettes was found 1.84 μg/g, and 1.77 μg/g and a similar concentration of Pb was also found in India [33,34]. The mean concentration of Cd (Fig. 2) was found at 2.01 μg/g and 1.57 μg/g in cigarettes and bidi. The similar concentration of Cd in cigarettes and bidi was found in Turkey [35], Nigeria [36] and India [33]. A

Table 2
Estimated Cancer risk of Smokeless Tobacco Products.

Smokeless tobacco		Pb Cancer Risk Upon 100% Transfer	Pb Cancer Risk Upon 6% Transfer	Cd Cancer Risk Upon 100% Transfer	Cd Cancer Risk Upon 6% Transfer	Cr Cancer Risk Upon 100% Transfer	Over all Cancer Risk Upon 100% Transfer	Over all Cancer Risk upon reduced Transfer
Zarda	SLT-1	6.33E-06	3.80E-07	1.21E-03	7.25E-05	4.17E-05	1.26E-03	1.15E-04
	SLT-2	4.67E-06	2.80E-07	2.28E-03	1.37E-04	3.84E-05	2.33E-03	1.76E-04
	SLT-3	8.18E-07	4.91E-08	1.53E-03	9.19E-05	9.96E-05	9.96E-05	1.92E-04
	SLT-4	1.37E-06	8.20E-08	3.58E-03	2.15E-04	1.62E-04	3.74E-03	3.77E-04
	SLT-5	6.28E-07	3.77E-08	2.78E-03	1.67E-04	5.79E-05	2.83E-03	2.24E-04
	SLT-6	1.47E-06	8.84E-08	1.36E-03	8.18E-05	8.29E-05	1.45E-03	1.65E-04
	SLT-7	9.70E-07	5.82E-08	3.10E-03	1.86E-04	1.00E-04	3.20E-03	2.86E-04
	SLT-8	1.75E-06	1.05E-07	8.79E-02	5.27E-03	4.05E-05	8.80E-02	5.32E-03
	SLT-9	2.08E-06	1.25E-07	5.39E-02	3.23E-03	6.68E-05	5.40E-02	3.30E-03
	SLT-10	1.80E-06	1.08E-07	1.09E-01	6.52E-03	1.16E-04	1.09E-01	6.63E-03
	SLT-11	6.79E-07	4.07E-08	1.21E-03	7.25E-05	5.47E-05	1.26E-03	1.27E-04
	SLT-12	7.13E-07	4.28E-08	1.10E-01	6.61E-03	2.27E-04	1.10E-01	6.84E-03
	SLT-13	1.28E-06	7.65E-08	6.16E-02	3.69E-03	5.60E-05	6.16E-02	3.75E-03
	SLT-14	1.04E-06	6.24E-08	3.93E-03	2.36E-04	4.93E-05	3.98E-03	2.85E-04
	SLT-15	1.68E-06	1.01E-07	1.56E-03	9.38E-05	4.23E-05	4.40E-05	1.36E-04
Gul	SLT-16	1.10E-06	6.60E-08	1.36E-01	8.17E-03	1.36E-04	1.36E-01	8.31E-03
	SLT-17	7.34E-07	4.40E-08	7.87E-02	4.72E-03	1.87E-04	7.89E-02	4.91E-03
	SLT-18	9.70E-07	5.82E-08	4.21E-02	2.53E-03	5.33E-05	4.22E-02	3.59E-03
	SLT-19	9.94E-07	5.96E-08	6.07E-02	3.64E-03	1.79E-04	6.08E-02	2.58E-03
	SLT-20	1.02E-06	6.09E-08	5.83E-02	3.50E-03	8.92E-05	5.84E-02	3.82E-03

Table 3
Estimated Cancer risk of Smoke Based Tobacco Products.

Smoke based tobacco		Pb Cancer Risk Upon 100% Transfer	Pb Cancer Risk Upon 6% Transfer	Cd Cancer Risk Upon 100% Transfer	Cd Cancer Risk Upon 20% Transfer	Cr Cancer Risk Upon 100% Transfer	Over all Cancer Risk Upon 100% Transfer	Over all Cancer Risk Reduced Transfer
Cigarette	SBT-1	3.34E-06	2.01E-07	1.55E-03	3.11E-04	4.62E-02	4.78E-02	4.65E-02
	SBT-2	4.57E-06	2.74E-07	1.18E-03	2.36E-04	1.43E-01	1.44E-01	1.43E-01
	SBT-3	6.58E-06	3.95E-07	1.04E-03	2.09E-04	4.63E-02	4.73E-02	4.65E-02
	SBT-4	4.68E-06	2.81E-07	1.02E-03	2.03E-04	6.60E-02	6.70E-02	6.62E-02
	SBT-5	3.82E-06	2.29E-07	1.34E-03	2.67E-04	5.15E-02	5.28E-02	5.18E-02
	SBT-6	6.51E-06	3.91E-07	3.86E-03	7.72E-04	5.00E-02	5.39E-02	5.08E-02
	SBT-7	6.41E-06	3.84E-07	3.00E-03	6.01E-04	2.26E-01	2.29E-01	2.27E-01
	SBT-8	3.80E-06	2.28E-07	3.31E-03	6.62E-04	1.41E-02	1.74E-02	1.48E-02
	SBT-9	7.91E-06	4.75E-07	2.30E-03	4.60E-04	1.14E-01	1.16E-01	1.14E-01
	SBT-10	4.85E-04	2.91E-05	2.90E-03	5.80E-04	1.66E-02	2.00E-02	1.72E-02
	SBT-11	7.32E-03	4.39E-04	3.08E-03	6.16E-04	4.92E-02	5.96E-02	5.03E-02
Bidi	SBT-12	4.84E-03	2.91E-04	1.12E-03	2.23E-04	7.58E-02	8.18E-02	7.63E-02
	SBT-13	9.57E-06	5.74E-07	1.41E-03	2.83E-04	8.41E-02	8.55E-02	8.44E-02
	SBT-14	5.53E-06	3.32E-07	2.38E-03	4.76E-04	9.32E-02	9.56E-02	9.37E-02
	SBT-15	3.06E-06	1.83E-07	2.09E-03	4.19E-04	6.49E-02	6.70E-02	6.53E-02

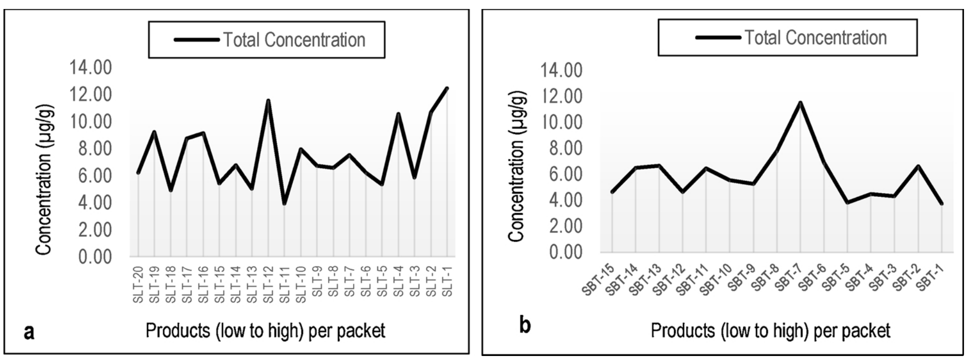

Fig. 1. Relation between the concentration of heavy metal (μg/g) and price of smokeless (a) and smoke-based (b) tobacco products.

considerable amount of Cd was found in gul (1.86 μg/g) and zarda (1.98 μg/g). The similar conentration of Cd was found in Oman [37], Pakistan [28], and in India [33]. Chromium concentration was high in every tobacco product and is supported by the literature [28,33,35–37].

When considering the GOTHIATEK® standard prescribed by Swedish Match Industries [38] the limit for Pb, Cd, and Cr in smokeless tobacco as 1.00 mg/kg, 0.5 mg/kg and 1.5 mg/kg; none of the smokeless or smoke based products in the present study meet this standard.

The USEPA guideline principles for the estimation of potential cancer risks were applied for risk assessment of smokeless and smoke-based products. Risk values for 10 g smokeless tobacco consumption indicated 2.5310E-6, 2.8310E-3 for Pb and Cd [24], while a risk value of 1.00E-08, 5.00E-06 for Pb and Cd was each found for 1 pack-year regular cigarette [27] and 7.68E–09, 2.16E–05, 3.15E–05 for Pb, Cd, and Cr (VI), respectively for a single cigarette exposure per day were also reported [14]. In the present study, Cd, and Cr, as well as the overall cancer risk exceeds the USEPA limit value of 10E-4 to 10E-6 for all smoke-based tobacco products. Total lifetime cancer risk calculated for Pb, Cd, and Cr for all smoke-based tobacco products ranges between 2.29E-01 and 9.56E-02. The overall cancer risk is about 7.90E-02 (on an average), which is 100–10000 times higher than the acceptable minimum range (10E-4 to 10E-6) indicating high cancer risk for the tobacco consumers in Bangladesh.

The true bioavailability of various metals in tobacco is most likely underestimated or overestimated here due to possible variations in bioavailability of different chemicals, increase in usage and chronic

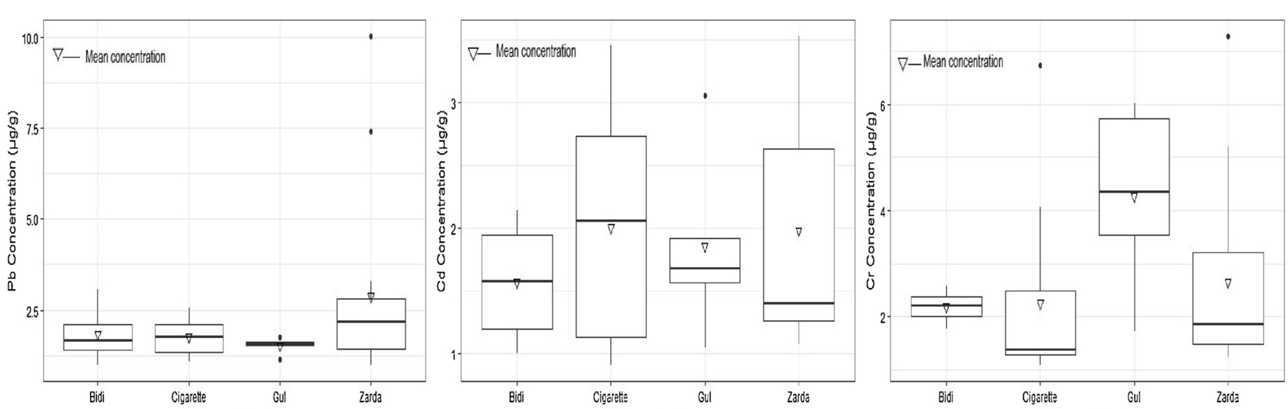

Fig. 2. Concentration of Pb, Cd, and Cr in four types of tobacco products.

exposure intensity [24]. It is important to note that these different products are processed differently from the raw tobacco leaves and priced accordingly.

Tobacco plants are prone to accumulate heavy metals in their leaves [39]. The accumulated contamination differs from country to country depending on production and processing procedures. The surrounding environment of plants, soil and animals interact complexly and accumulate heavy metals in the tobacco leaves during the process [40]. The concentration of metals in industry produced fertilizers and pesticides used for tobacco cultivation are the primary contributors to pollution of agricultural soil and plants [41]. The metal content is enhanced by tobacco processing [42–44] and eventually, the heavy metals enter the human body via inhalation and consumption [45–47].

This study has been intended to give an exemplary scenario on tobacco products available in Bangladesh. However, it was not possible to cover the whole market. The authors recognize the limitations of actual cancer risk assessment of Cr in studied products. The estimation was based on 100% bioavailability of Cr since no literature information involving human studies on the bioavailability of Cr from tobacco was available. Also, the assessed risk can be underestimated or oversimplified based on the consumer's practice, bodyweight, lifetime, availability and exposure to the metals.

5. Conclusion

The results of this study provide an overview of heavy metals in both smoke-based and smokeless tobacco products in Bangladesh. We demonstrated that all smoke-based and a majority of the smokeless tobacco products exhibited a high concentration of heavy metals (Pb, Cd, and Cr). It was assessed that the total calculated cancer risks of 33 out of 35 tobacco samples exceed the acceptable limit value of 10E-4 to 10E-6. These tobacco products carry an 'unacceptable' risk for cancer; therefore, require regulatory actions such as proper policy implementation to control tobacco cultivation and product processing. It is further suggested that close integration of basic research involving the tobacco crop production levels such as fertilizer use, pesticide quality regulation, and application methods be pursued, and efforts are made to reduce heavy metal concentrations. We suggest a further elaborate study to be conducted on the various other toxic metals present in the Bangladeshi tobacco products to understand the overall toxicity of the tobacco products better.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.toxrep.2018.08.019.

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