A comparative study on mercury, arsenic and cadmium in herbal fairness cream products in local market

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Abstract
This study determines Mercury, Arsenic and Cadmium levels in selected herbal fairness cream brands in Sri Lankan market demonstrating the risk on dermal application. Brand quality is assessed by analyzing heavy metals levels in samples from 06 consecutive batches. Hg and Cd concentrations were determined by The GF-AAS method and HG-AAS was used to determine As concentration. Results indicated Hg contamination in its' highest with Brand C ($1.9880 \pm 7.71\mu g$ $g^{-1} \times 10^3$), secondly for Brand B ($6.130\pm 1.01\mu g$ $g^{-1} \times 10^3$) followed by Brand A (38.16 ± 16.41 μg $g^{-1} \times 10^3$). Mean mercury values of above three brands exceeded USA-FDA permissible limits ($1\mu g$ g-1/wet weight). ANOVA, Tukey's test ($p<0.05$) statistically concluded that mean Hg concentration of samples are significantly different batch-wise. Mean Cd level of brand A was recorded 3.954 ± 0.7807 μg $g^{-1} \times 10^3$, as the highest value. The values ranging from 0.01806-$0.09922\mu g$ $g^{-1}\times10^3$, 0.1880-2.954 μg $g^{-1}\times10^3$, 0.08245-$0.$ μg $g^{-1}\times10^3$were identified for brand B, C and D respectively. Arsenic levels in all brands found below the maximum permissible limit of 3 ppm. Inconsistencies of batches were observed for every brand regarding every metal, indicating inferior quality. Hence frequent analysis of heavy metal levels in herbal fairness creams is proven necessary.

Keywords: Heavy-metal contamination, Herbal Farness cream, Mercury, Cadmium, Arsenic

1. Introduction
Today, there is a high demand for cosmetics containing herbal ingredients. Major driving force behind this is the popular belief stating natural products are healthier [1]. In South Asian skin care market, face whitening products are dominating [2] due to the consideration of pale skin as an ideal beauty standard in South Asia [3, 4]. Hence there is a high demand for skin whiteners and the key consumers are young women [5-7].

Despite most advertisements mention that herbal fairness creams have no added chemicals, all commercially manufactured herbal cosmetic products have chemical bases which give them texture, consistency and preserving ability [1]. Hence it could introduce impurities during manufacturing, or as byproducts from breaking down of intermediate ingredients. Use of metallic containers or other manufacturing utensils might release metal ions during manufacturing processes of cosmetics. Furthermore, if cosmetics have plant derived ingredients, from plants which are grown in seriously polluted soil [8] or water can be contaminated with heavy metals. [9, 10]. Most importantly, some heavy metals such as Mercury have been added intentionally to fairness creams, due to its ability to prevent melanogenesis as a potential melanotoxin [11].

The maximum allowable level of Hg in cosmetic products for human consumption specified by the United States of Drug Administration is 1 mg kg-1 wet weight [4]. According to Health Canada, they mention some heavy metals in cosmetics are unavoidable due to its ubiquitous nature. According to Health Canada MPL for mercury is 3 ppm [12, 13].

In Sri Lanka specification for raw materials and adjuncts are given under SLS 457: part 2. Raw materials other than dyes, pigments and colour additives generally not recognized as safe. Mercury and its compounds are listed under "GNRAS" list. This list indicates, "Ingredients which are generally not recognized as safe". Compounds in this list are not tolerable in any amount or tolerate under some limitations.

Mercury in skin whitening creams can enter the human body through skin absorption. Intestine and kidney are mainly affected by the chronic exposure of inorganic Mercury. Corrosive effects would be prominent in intestinal tissues while failures might occur in nephrons [14, 15]. Even more, Hg disrupts the immune functions along with intracellular activities as microtubule formation, and might restrain enzyme systems. This promotes shifting the balance of intracellular calcium and membrane potentials, which directly effects in constraining protein and DNA synthesis [1, 16, 17].

Cadmium [18] and Arsenic [19] can be introduced to cosmetics with colour additives or with other raw materials [20, 21]. As an example, D & C RED 6 which is used as coloring agent and Aluminium starch octenylsuccinate functioning as anticaking agent found to possess these heavy metals. Hence in this study we focus on achieving the objectives namely, Determination of Mercury, Arsenic and Cadmium levels in selected brands of herbal fairness cream in Sri Lankan market to assess the risk upon application of those herbal fairness cream brands, and to assess the quality of brands considering the levels of consistency among consecutive batches of a given brand [22-24].

2. Materials and Methods
2.1 Apparatus
2.1.1 Graphite furnace atomic absorption spectroscopy
Thermo Scientific iCE 3000 series graphite furnace AAS was used to take absorbance measurements regarding Mercury and Cadmium levels. SOLAAR software was used to control spectrometer parameters including programed temperature, time, ramp rate, gas type and gas flow.

2.1.2 Hydride generation atomic absorption spectroscopy
The iCE mode 3000 series with VP100 Thermo Scientific model HGAAS was used for Arsenic determination. Arsenic discharging lamp was used as the radiation source.

2.1.3 Microwave digestion system
Analytik Jena, Top wave® microwave digestion system was used to digest the samples. Teflon vessels of 100 ml volume, allowing maximum 100 bar of pressure were used.

2.2 Reagents preparation
2.2.1 Glass-ware used
Pipettes, 50 ml volumetric flasks, beakers

2.2.2 Analytical balance
Highly accurate and precise analytical balance (Precisa XT 220A model) was used to measure the masses.

2.2.3 Chemicals and reagents used
1. 0.5% w/v sodium hydroxide.
2. 1% w/v sodium borohydride solution stabilized with 0.5% v/v sodium hydroxide
3. Concentrated nitric acid (HNO_3) reagent grade.
4. 30% hydrogen peroxide (H_2O_2) reagent grade.
5. Commercially available AAS grade Hg stock solution (1000 ppm)
6. Commercially available AAS grade Cd stock solution.
7. Commercially available AAS grade As stock solution.

2.3 Sample collection for the analysis
Five brands of herbal fairness cream samples were selected according to customers' preferences. These brands were purchased in local markets from Nugegoda, Sri Lanka. Six consecutive batches from each brand were taken which manufactured within the same duration of time, ranging for 12 months. Two bottles from each batch which had same batch number were purchased for the analysis.

2.4 Digestion of samples
Duplicated samples of different brands were weighed accurately in range 0.2000 g to 0.2500 g was placed in Teflon vessels. Then 2.00 ml of H_2O_2 and 8.00 ml of HNO_3 were added in to the vessel. Mixtures were shaken carefully and waited for 10 minutes before the vessel closed. The vessels were capped and placed in microwave oven and optimized digestion program was employed (Table 1). Upon completion of microwave step, vessels were removed from microwave. Then, the Vessels were kept for cooling under a fume hood and the screw caps of vessels were unscrewed, allowing gasses to escape slowly. The digested samples were appropriately diluted with purified water.

Table 1: Digestion program used in microwave digestion system.

Temperature/ ^{0}C	Pressure / bar	Time / min	Power/ W
190	60	20	99
180	60	05	99
150	60	05	99
100	60	05	99
50	60	05	99

2.5 Graphite furnace atomic absorption spectrometric procedure
Total amount of cadmium and mercury were obtained, using Thermo Scientific iCE 3000 series GF-AAS instrument. Hg analysis was done by Mercury hollow cathode lamp at wave length 253.7 nm and for Cd analysis; Cadmium hollow cathode lamp at wave length 228.8 was used. Background effect was corrected using deuterium background correction [25-27]. Argon gas was used as purge gas to volatilize matrix material while providing chemically inert environment. GF-AAS instrument was calibrated for Hg and Cd in the linear range. Working standards were prepared by automatic dilution of master standards. Calibration curves were ranged from 5 µg/L to 15 µg/L and 5 µg/L to 30 µg/L for cadmium. Calibration curves for Hg ranged from 10 µg/L-50 µg/L, 25 µg/L-75 µg/L and 250 µg/L to 1000 µg/L. Samples were then analyzed and their absorbance values were recorded. Using calibration curves, heavy metal levels in samples were obtained directly from instrument by comparing the absorbance of samples to calibration curve. Recovery test was done at same time in order to ensure the reliability of the method [28, 29].

Table 2: Temperature program for the determination of cadmium content in herbal fairness cream samples by GF-AAS.

Step	Temperature (^{0}C)	Ramp (^{0}C/sec)	Hold time (sec)	Internal flow (L/min)
1	100	10	300	0.2
2	800	150	20.0	0.2
3	1000	0	3.0	Off
4	2500	0	3.0	0.2

Table 3: Temperature program for the determination of mercury content in herbal fairness cream samples by GF-AAS.

Step	Temperature (^{0}C)	Ramp (^{0}C/sec)	Hold time (sec)	Internal flow (L/min)
1	100	10	300	0.2
2	200	150	20.0	0.2
3	750	0	3.0	Off
4	2500	0	3.0	0.2

2.6 Hydride generation atomic absorption spectroscopy
In hydride generation technique, instrument was changed to vapor mode. Operating parameters chosen in this experiment is given in table 4. [30].

Table 4: Operating parameters of arsenic determination in HGAAS.

Parameter	Value
Wave length	193.7 nm
Band pass	0.5 nm
Measurement time	4.0 sec
Gas	Argon
Gas flow rate	25 ml/min
Vapor mode	Electrical heating

In this study 1.0% sodium borohydride was used as reducing agent which was stabilized with 0.5% m/V of sodium hydroxide. Then 50% hydrochloric solution was aspirated to reaction vessel by capillary force generated in the automatically rotating wheel. At the same time sample and the reducing agent also aspirated in to the reaction vessel. Volatile hydrides of Arsenic which produced in the reaction vessel was passed into optical cell where it decomposed in to it's elemental form. Generated elemental Arsenic was excited by the radiation of arsenic hollow cathode lamp at 193.7 nm. Concentrations of all samples were measured using calibration curve. When calibrating the instrument, external calibration method was used. The calibration curve was ranged from 20 µg/L to 50 µg/L. Recovery test was done at same time in order to ensure method reliability.

2.7 Calculation of Mercury, Arsenic and Cadmium levels
The concentration values for herbal fairness cream samples were calculated in mg/kg using sample weight.

$$\text{Heavy metal concentration (mg/kg)} = \frac{\text{Concentration of sample (ppb)} \times \text{Dilution Factor}}{\text{Sample weight (g)} \times 1000}$$

2.8 Statistical data analysis
Heavy metal concentrations obtained from final calculation for batches and brands were presented as mean with standard deviation. Minitab one way ANOVA Tukey's test and Wilcoxon signed rank test were done for statistical analysis.

3. Results and Discussion
3.1 Mercury level in herbal fairness cream products
The GF-AAS technique was used to determine the Hg concentrations in samples [31]. Instrumental calibration was done, based on absorbance measured for different levels of Hg standard prepared at time of analysis. According to the calibration plots obtained, total Hg concentrations of duplicated samples were obtained in ppb and converted to ppm values.

3.1.1 Comparison of mean mercury concentration among brands
Mercury concentrations for each batch and brand are represented as mean±standard deviation and results obtained are summarized below in tables 5 to 9.

3.1.2 Comparison of mean mercury concentration in different batches of a brand
Mercury concentrations of six batches with different manufacturing dates were analyzed for all brands. This comparison was done in order to determine the different mercury levels among the batches, thus highlighting the idea about changeability of product with manufacturing date.

Ultimately this will provide an overall picture about the quality of the product. If the samples had underwent good manufacturing and analytical practices, there should be a good consistency of products along with low contamination levels of heavy metals.

3.1.2.1 Variation of mercury concentration within brand A

Table 5: Mean mercury concentrations for brand A

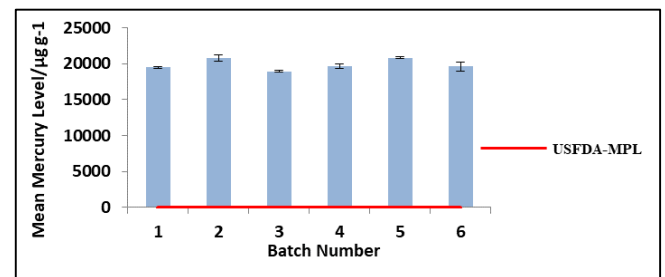| Brand	Batch number	Mean Hg level for batch/ µg g^{-1}
Product A	A1	72.7±1.31
	A2	31.2±0.247
	A3	34.7±0.268
	A4	31.7±0.622
	A5	25.0±1.46
	A6	31.2±1.63
	Mean Level for brand A	38.1±16.4

The resultant data is presented in Figure 1.

Fig 1: Variation of mean mercury concentrations in different batches of brand A.

3.1.2.2 Variation of mean mercury concentrations within brand B

Table 6: Mean mercury concentrations for brand B

Brand	Batch number	Mean Hg level for batch/ µg g^{-1} ×10^{3}
Product B	B1	5.57±0.171
	B2	8.21±0.632
	B3	5.93±0.0961
	B4	5.74±0.432
	B5	5.83±0.0254
	B6	5.48±0.0459
	Mean Level for brand B	6.13±1.01

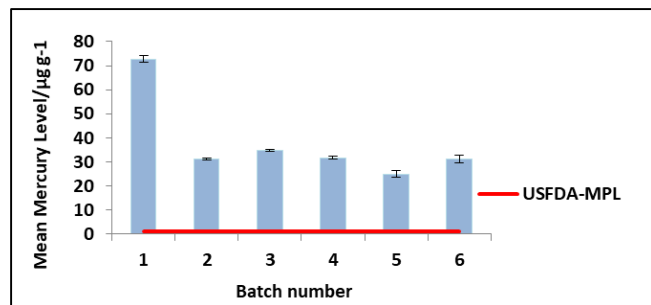The resultant data is presented in figure 2.
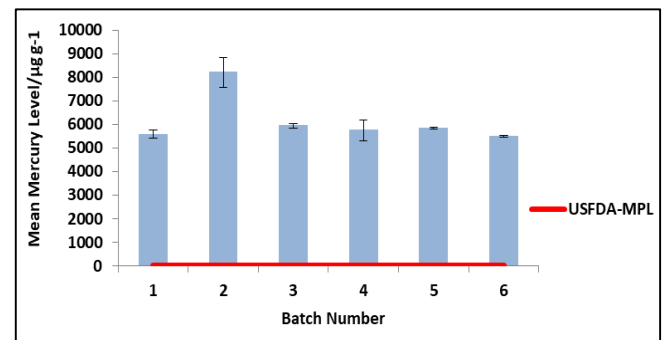
Fig 2: Variation of mean mercury concentrations in different batches of brand B.

3.1.2.3 Variation of mean mercury concentrations within brand C

Mean mercury levels in every batch in brand C were observed more than 19,000 $\mu g\ g^{-1}$. Hence mean Hg level is exceptionally higher than MPL. This is clearly seen in the figure 3.

Table 7: Mean mercury concentrations for brand C

| Brand	Batch number	Mean Hg level for batch/ $\mu g\ g^{-1} \times 10^3$
Product C	C1	1.94±0.0153
	C2	2.08±0.0426
	C3	1.89±0.0104
	C4	1.96±0.0363
	C5	2.08±0.0076
	C6	1.95±0.0608
	Mean Hg Level for brand C	1.98±0.0771

Fig 3: Variation of mean mercury concentrations in different batches of brand C.

3.1.2.4 Variation of mean mercury concentrations within brand D

Table 8: Mean mercury concentrations for brand D

Brand	Batch number	Mean Hg level for batch/ $\mu g\ g^{-1} \times 10^3$
Product D	D1	0.102±0.002
	D2	ND
	D3	0.121±0.0134
	D4	0.134±0.001
	D5	0.143±0.0029
	D6	0.0003
	Mean Hg Level of brand D	0.0837±0.0632

Figure 4 below represents the mean Hg values obtained for different batches of brand D.
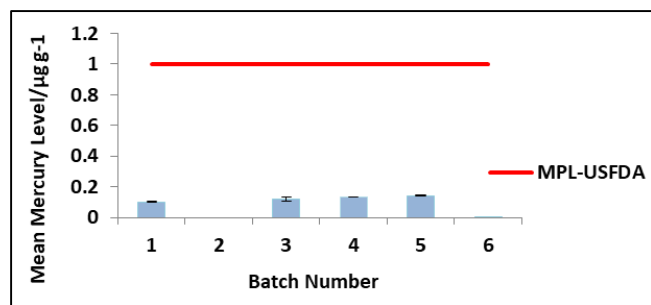
Fig 4: Variation of mean mercury concentrations in different batches of brand D.

3.1.2.5 Variation of mean mercury concentrations within brand E

Mean mercury level observed for every batch in brand E are gained below the MPL. Figure 5 represents this.

Table 9: Mean mercury concentrations for brand E

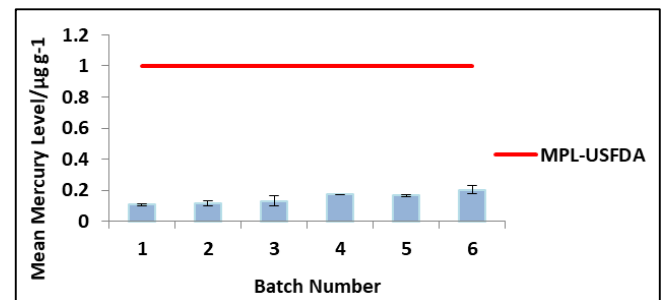| Brand	Batch number	Mean Hg level for batch/ $\mu g\ g^{-1} \times 10^3$
Product E	E1	0.107±0.0075
	E2	0.1156±0.0186
	E3	0.131±0.0338
	E4	0.172±0.0007
	E5	0.166±0.00466
	E6	0.201±0.0258
	Mean Hg Level for brand E	0.149±0.0378

Fig 5: Variation of mean mercury concentrations in different batches of brand E

According to the results obtained, mean Hg level of three brands exceeded the United State Food and Drug Administration maximum permissible limit ($1\mu g\ g^{-1}$). These were in the ascending order of brand A< brand B< brand C. Highest mercury concentration was observed with brand C. Its mean mercury concentration is (19,880 $\mu g\ g^{-1}$) more than 19,000 times larger than permissible level. This is shown in figure 1 and brand B contained mean mercury level 6,130 $\mu g\ g^{-1}$

3.2. Cadmium levels in herbal fairness cream products

According to the results obtained, mean Cd level of brand A exceeds the maximum permissible limit for Canada (3 $\mu g\ g^{-1}$). Mean Cd levels for other brands did not exceed the MPL and for brand E, Cd was not detected. This is shown in figure 6.

3.2.1.1 Variation of cadmium concentrations within brand A

The resultant data for each batch is presented in Table 10, as below.

Table 10: Mean cadmium concentrations for brand A

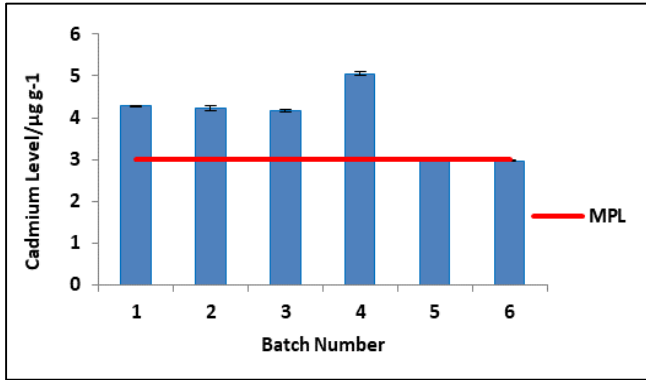| Brand	Batch number	Mean Cd level for batches/$\mu g\ g^{-1} \times 10^3$
Brand A	A1	4.27±0.0042
	A2	4.22±0.0608
	A3	4.17±0.0361
	A4	5.05±0.0361
	A5	2.97±0.0042
	A6	2.96±0.0078
	Mean Cd Level for brand A	3.95±0.780

Fig 6: Variation of mean cadmium concentrations in different batches of brand A.

According to figure 9, it is obvious that there is a batchwise variation of mean Cd levels. First four batches show very high concentration of Cd with exceptional value for batch number 4 and for subsequent batches, Cd concentrations decline slightly. Statistical analysis (ANOVA, Tukey's test $p < 0.05$) also concluded that mean Cd concentration of samples of brand A are significantly different from batch to batch. Thereby it can be implicated that the products are in inferior quality due to its inconsistency in manufacturing process.

3.2.1.2 Variation of cadmium concentrations within brand B

Table 11: Mean cadmium concentrations for brand B

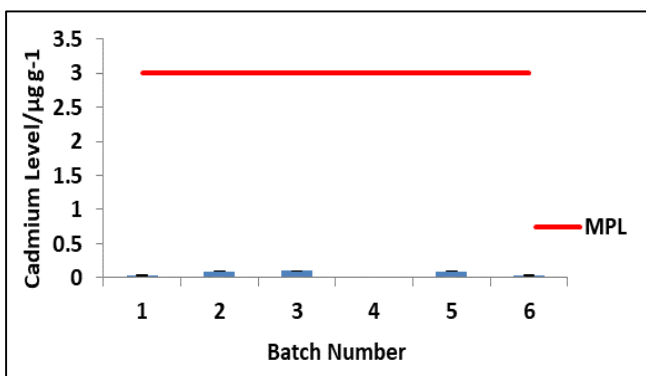| Brand	Batch number	Mean Cd level for batches/µg g^{-1}×10^3
Brand B	B1	0.0333±0.008
	B2	0.0962±0.0084
	B3	0.0983±0.0045
	B4	ND
	B5	0.0930±0.0021
	B6	0.0309±0.0029
	Mean Cd Level for brand B	0.0586±0.0405

Fig 7: Variation of mean cadmium concentrations in different batches of brand B.

Cadmium was not detected for batch number 4 and the other batches contained less amount of Cd. All mean Cd levels were far below the Maximum Permissible Levels (MPL). Batch to batch variation of mean Cd levels observed even though these contained less Cd concentrations. Statistical analysis was performed (ANOVA Tukey's test $p < 0.05$).

Results proved the inconsistency of mean Cd level in brand B.

3.2.1.3 Variation of cadmium concentrations within brand C

Table 12: Mean cadmium concentrations for brand C

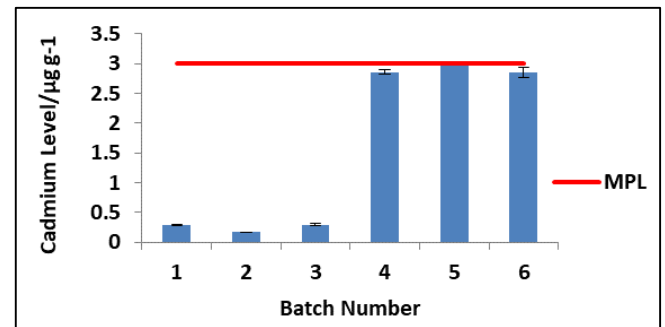| Brand	Batch number	Mean Cd level for batches/µg g^{-1}×10^3
Brand C	C1	0.288±0.0076
	C2	0.166±0.0001
	C3	0.292±0.0146
	C4	2.85±0.0396
	C5	2.97±0.0001
	C6	2.85±0.0778
	Mean Cd Level for brand C	1.57±0.138

Fig 8: Variation of mean cadmium concentrations in different batches of brand C

Mean Cd concentration in batch number 4, 5 and 6 have almost reached the MPL. This indicates the inferior quality of product C. Evenmore, there is a considerable inconsistency of mean Cd levels among the batches.

3.2.1.4 Variation of cadmium concentrations within brand D

Table 13: Mean cadmium concentrations for brand D

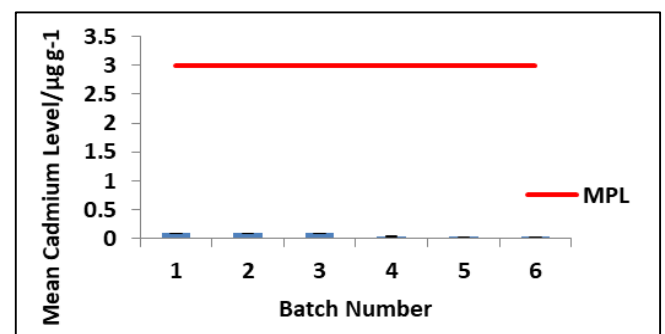| Brand	Batch number	Mean Cd level for batches/µg g^{-1}×10^3
Brand D	D1	0.0866±0.0042
	D2	0.0921±0.0010
	D3	0.0897±0.0039
	D4	0.0304±0.0047
	D5	0.0310±0.0010
	D6	0.0299±0.0005
	Mean Cd Level for brand D	0.0599±0.0296

Fig 9: Variation of mean cadmium concentrations in different batches of brand D.

Variation of mean Cd levels observed among batch numbers even though these contained lesser levels of detectable Cd concentration. According to the results obtained, mean Cd level of brand A exceeds the maximum permissible limit for Canada (3 μg g^{-1}). [32] Mean Cd levels for other brands did not exceed the maximum permissible limits. For brand E, Cadmium contamination was not detected.

3.3. Comparison of mean Arsenic concentrations among brands
3.3.1.1. Variation of Arsenic concentration with in brand A

Table 14: Mean Arsenic concentrations for brand A.

Brand	Batch number	As level for batch/μg g^{-1} ×10^3
Brand A	A1	ND
	A2	0.0724±0.0020
	A3	0.0716±0.0028
	A4	0.107±0.0067
	A5	0.104±0.0069
	A6	0.105±0.0016
	Mean Level of brand	0.0768±0.03935

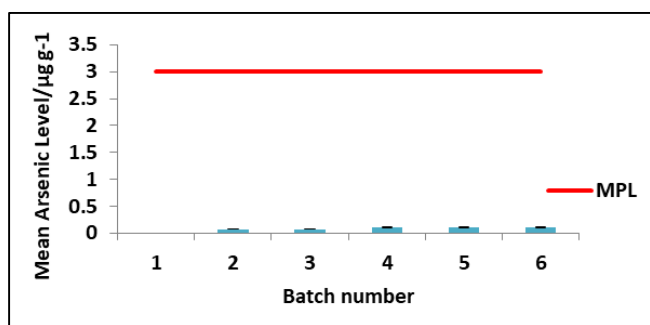Figure 10 represents the mean As values obtained for different batches of brand A.

Fig 10: Variation of mean arsenic concentrations in different batches of brand A.

For batch number 1, As was not detected and for the other batches minor concentrations of As were discovered.

3.3.1.2 Variation of Arsenic concentrations with in brand B

Mean As level observed for every batch in brand B is observed below the maximum permissible limit.

Table 15: Mean Arsenic concentrations for brand B

Brand	Batch number	As level for batch/μg g^{-1} ×10^3
Brand B	B1	0.549±0.0204
	B2	1.09±0.0148
	B3	1.09±0.0113
	B4	1.25±0.0177
	B5	1.25±0.0014
	B6	ND
	Mean Level of brand	0.871±0.0476

There was a slight variation of mean arsenic concentrations batchwise. As further investigation statistical analysis was performed (ANOVA Tukey's test p<0.05), and the results proved the inconsistencies of mean As levels in brand B.

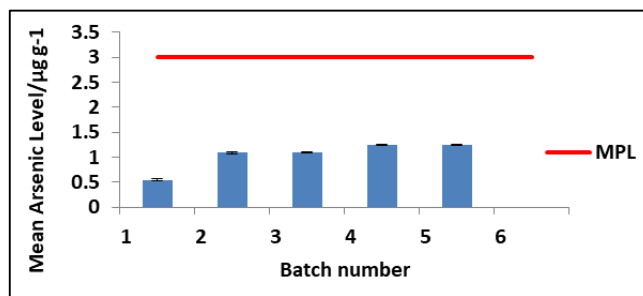Fig 11: Variation of mean arsenic concentrations in different batches of brand B

3.3.1.3 Variation of Arsenic concentrations with in brand D

Table 16: The mean as values obtained for different batches of brand D

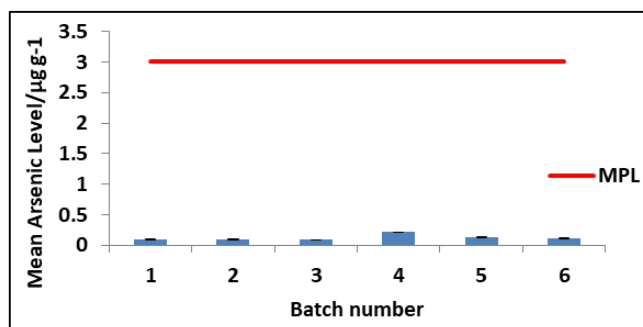| Brand	Batch number	As level for batch/μg g^{-1} ×10^3
Brand D	D1	0.0965±0.0021
	D2	0.0960±0.0039
	D3	0.0934±0.0008
	D4	0.219±0.0005
	D5	0.121±0.0089
	D6	0.113±0.0069
	Mean Level of brand	0.123±0.0005

Fig 12: Variation of mean arsenic concentrations in different batches of brand D.

Mean As level observed for every batch in brand D is observed below the MPL. There were slight variations in As level among different batches. A significant difference of As level was seen among brands.

Likewise, statistical analysis performed (ANOVA Tukey's test p<0.05-APPENDIX II) have indicated that there are significant differences of As levels in herbal fairness cream brands.

As the mean arsenic levels for all brands do not exceed the MPL for Canada, the impact to human health is minimal. This is proven using the Wilcoxon signed rank test. (Following null and alternative hypotheses were used. H_0:M(median)≥3ppm versus H_1:M (median) ≤ 3ppm). Since p<0.05, null hypothesis was rejected). Results confirmed that the available As levels are non toxic to human health. In this section only brands A, B and D were taken to comparison as Arsenic was not detected in brand E and C under the performed tests.

3.4. Rationalization of obtained results
Results obtained for 5 brands of herbal fairness cream samples analyzed, indicated that products are contaminated with Hg in different degrees. Product C contained highest

amount (1.988 ± 771 µg g^{-1} $\times 10^3$), secondly for product B (6.130 ± 10.13 µg g^{-1} $\times 10^3$) and followed by product A (38.16 ± 16.41 µg g^{-1} $\times 10^3$). By considering the obtained values, it is obvious that there is an alarming situation regarding the Hg toxicity when using these brands. Brand C contained a mean mercury level more than 1,000 times larger than maximum permissible limit and product B more than 5,000 times. This creates a fatal risk of mercury poisoning over prolonged dermal application.

In this study, brand A was identified with relatively high value of Cd (mean value 3.954 ± 0.7807 µg g^{-1} $\times 10^3$). As Cd is absorbed through skin in moderately low rate, this value might seems not toxic [24]. Arsenic levels found for all brands were below the maximum permissible limit for Canada, seemingly to be non-toxic.

3.5 General discussion
3.5.1 Microwave digestion
Determination of heavy metals with spectroscopic technique requires digestion of samples. In this study microwave digestion is used. In this method, Speed and decomposition efficiency is higher and also decomposition procedures are relatively rapid. Also, it requires a small quantity of sample and offer a good reproducibility. Here, contamination during digestion process and loss of analyte due to volatilization are minimized. In this study, concentrated HNO_3 and H_2O_2 was used in microwave digestion to digest cosmetics. Digestion method was optimized by changing the time of digestion and temperature followed by recovery test.

3.5.2 Recovery test
Microwave digestion technique was employed for the conversion of sample matrix, in to a solution form for the elemental analysis. However, analyzed samples had complex matrices with combination of organic and inorganic materials. The accuracy of the technique was confirmed from the recovery percentages for spiked recovery test.

Table 17: Recovery test results

Metal	Concentration of sample /ppb	Added concentration/ppb	Recovery %
Hg	0.7210	20.00	96.19
	0.7203	20.00	95.66
As	1.9005	20.00	91.42
	1.9135	20.00	91.51
Cd	0.4605	20.00	98.89
	0.4332	20.00	98.48

According to results obtained more than 90% of all the metals were recovered. Hence the techniques used in this study can be considered well fitting for the purpose.

4. Conclusions
In the study, all products analyzed contained mercury. Also, there were significant differences of Hg levels between brands. Three brands contained extremely high amounts of Hg, thus violating the laws imposed on maximum permissible limits. Cadmium was found in four brands and one brand exceeded the maximum permissible limits. Another three brands were found with Arsenic contamination, yet below than maximum permissible limit.

Moreover, inconsistencies of batches were observed for every brand and for every metal, specifying the inferior qualities of brands. Hence mandatory testing programs to analyze herbal fairness cream products against heavy metal ion contamination should be conducted.

7. Conflicts of Interest
The authors declare no conflict of interest.

8. References
1. Antignac E, et al. Safety of botanical ingredients in personal care products/cosmetics. Food and Chemical Toxicology, 2011; 49(2):324-341 https://doi.org/10.1016/j.fct.2010.11.022.
2. Chauhan GS, A Tiwari. Unfair Promotion of Whitening Creams: Is Beauty No More Skin Deep? Media Watch. 2019; 10(2):365-373. http://doi.org/10.15655/mw/2019/v10i2/49635
3. Pollock S, et al. The dark side of skin lightening: An international collaboration and review of a public health issue affecting dermatology. International Journal of Women's Dermatology, 2020. https://doi.org/10.1016/j.ijwd.2020.09.006
4. Pramanik S. M Kumar, A Qureshi. Mercury in skin-care products in India and consumer exposure risks. Regulatory Toxicology and Pharmacology. 2021; 121:104870. https://doi.org/10.1016/j.ijwd.2020.09.006
5. Ladizinski B, N Mistry, RV Kundu. Widespread use of toxic skin lightening compounds: medical and psychosocial aspects. Dermatologic Clinics, 2011; 29(1):111-123. https://doi.org/10.1016/j.det.2010.08.010.
6. Mohiuddin AK. Heavy metals in cosmetics: the notorious daredevils and burning health issues. American Journal of Biomedical Science and Research. 2019; 4:332-337. http://doi.org/10.34297/AJBSR.2019.04.000829
7. Abdalla AA, MS Ahmed. Facts, Traditions, and Complications of Skin Whitening Products among Female Students in Sudan: A Cross-Sectional Study. Global Journal of Health Science. 2020; 12(3):103-103. https://doi.org/10.5539/gjhs.v12n3p103
8. Panda BP, et al. Habitat heterogeneity and seasonal variations influencing avian community structure in wetlands. Journal of Asia-Pacific Biodiversity. 2021. 14(1):23-32. https://doi.org/10.33263/BRIAC102.085090
9. Gupta SK, et al. Risk of metal contamination in agriculture crops by reuse of wastewater: an ecological and human health risk perspective, in Water conservation, recycling and reuse: issues and challenges, 2019, 55-79. https://doi.org/10.1007/978-981-13-3179-4_3
10. Ezzat H, et al. DFT: B3LYP/LANL2DZ study for the removal of Fe, Ni, Cu, As, Cd and Pb with Chitosan. Biointerface Res. Appl. Chem. 2020; 10:7002-7010. https://doi.org/10.33263/BRIAC106.70027010.
11. Jones K, et al. Aqueous composition comprising active ingredients for the de-pigmentation of the skin, 2000.

Google Patents.

12. Syversen T, P Kaur. The toxicology of mercury and its compounds. Journal of Trace Elements in Medicine and Biology. 2012: 26(4):215-226. https://doi.org/10.1016/j.jtemb.2012.02.004

13. Michalek IM, *et al*. A systematic review of global legal regulations on the permissible level of heavy metals in cosmetics with particular emphasis on skin lightening products. Environmental research. 2019; 170:187-193. https://doi.org/10.1016/j.envres.2018.12.029

14. Podgórska A, *et al*. Natural and conventional cosmetics—mercury exposure assessment. Molecules, 2021; 26(13):4088. https://doi.org/10.3390/molecules26134088

15. Yawei S, *et al*. Epidemiology, clinical presentation, treatment, and follow-up of chronic mercury poisoning in China: a retrospective analysis. BMC Pharmacology and Toxicology. 2021. 22(1):1-9. https://doi.org/10.1186/s40360-021-00493-y

16. Abbas HH, *et al*. Mercury Exposure and Health Problems of the Students Using Skin-Lightening Cosmetic Products in Makassar, South Sulawesi, Indonesia. Cosmetics. 2020. 7(3):58. https://doi.org/10.3390/cosmetics7030058.

17. Mesko MF, *et al*. Toxic and potentially toxic elements determination in cosmetics used for make-up: A critical review. Analytica chimica acta. 2020; 1098:1-26. https://doi.org/10.1016/j.aca.2019.11.046

18. Fatima N, *et al*. Toxicity of cadmium (Cd) on microalgal growth,(IC50 value) and its exertions in biofuel production. Biointerface Research in Applied Chemistry. 2020. 10(4):5828-5833. https://doi.org/10.33263/BRIAC104.828833

19. Eneh OC. Toxic effects of selected trace elements contained in make-ups on female university students in Nigeria. Environmental Monitoring and Assessment. 2021; 193(7):1-10. https://doi.org/10.1007/s10661-021-09161-4

20. Parashram PA. Determination of heavy metals (arsenic, cadmium and lead) from different body lotions, 2017. https://doi.org/10.20959/wjpr201712-9780

21. Jose A, JG Ray. Toxic content of certain commercially available fairness creams in Indian market. Cogent Medicine. 2018; 5(1):1433104. https://doi.org/10.1080/2331205X.2018.1433104

22. Mohiuddin AK. Cosmetics' safety: gray areas with darker inside. Current Educational Research. 2019; 2(01). https://doi.org/10.36346/SARJPS.2019.v01i02.002

23. Khan NH, *et al*. Personal-Care Cosmetic Practices in Pakistan: Current Perspectives and Management. Clinical, Cosmetic and Investigational Dermatology. 2021; 14:9. https://doi.org/10.2147%2FCCID.S270667

24. Alam M, *et al*. Assessment of some heavy metals in selected cosmetics commonly used in Bangladesh and human health risk. Journal of Analytical Science and Technology. 2019; 10(1):1-8. https://doi.org/10.1186/s40543-018-0162-0

25. Butcher DJ. Recent highlights in graphite furnace atomic absorption spectrometry. Applied Spectroscopy Reviews. 2017; 52(9):755-773. https://doi.org/10.1080/05704928.2017.1303504

26. Valasques GS, *et al*. Multivariate optimization for the determination of cadmium and lead in crude palm oil by graphite furnace atomic absorption spectrometry after extraction induced by emulsion breaking. Microchemical Journal. 2020; 153:104401. https://doi.org/10.1016/j.microc.2019.104401

27. Saadatzadeh A, *et al*. Determination of heavy metals (lead, cadmium, arsenic, and mercury) in authorized and unauthorized cosmetics. Cutaneous and ocular toxicology. 2019; 38(3):207-211. https://doi.org/10.1080/15569527.2019.1590389

28. Peregrino CP, *et al*. Mercury levels in locally manufactured Mexican skin-lightening creams. International Journal of Environmental Research and Public Health. 2011; 8(6):2516-2523. https://doi.org/10.3390/ijerph8062516

29. Perelonia KBS, *et al*. Validation of an analytical method for the determination of cadmium, lead and mercury in fish and fishery resources by graphite furnace and Cold Vapor Atomic Absorption Spectrometry. Food Control. 2021; 130:108363. https://doi.org/10.1016/j.foodcont.2021.108363.

30. Chakraborty K, S Chaudhary. Estimation the Presence of Heavy Metals and Trace Elements in Indian Herbal Cosmetics by Atomic Absorption Spectrophotometer. Asian Journal of Pharmaceutical Research and Development. 2019; 7(5):59-64. https://doi.org/10.22270/ajprd.v7i5.556

31. Shelar M, V Gawade, S Bhujbal. A Review on Heavy Metal Contamination in Herbals. Journal of Pharmaceutical Research International, 2021, 7-16. https://doi.org/10.9734/jpri/2021/v33i29A31561

32. Akpe M, R Anozie, F Inezi. Heavy Metals Concentrations in Five Brands of Lip Gloss and Mascara Cosmetics Sold and Used in Calabar, Cross River State, Nigeria. Journal of Applied Sciences and Environmental Management. 2020; 24(7):1223-1227. https://doi.org/10.4314/jasem.v24i7.15.