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Analysis and Quantification of Alkyl (C12-22) Trimethyl Ammonium Chloride Content in Cosmetics: Regulatory Compliance Gap Analysis

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Abstract: Background: Exceeding the recommended Alkyl (C12-22) trimethyl ammonium bromide and chloride levels in cosmetics and personal care products is a serious health threat. Objectives: To quantify and investigate Cetrimonium chloride and Behentrimonium chloride in cosmetics and personal care products in the UAE market to gauge whether or not they adhered to requirements for safety and health. Methods: A total of 164 cosmetics products were collected and analyzed in this study. The gas chromatography–mass spectrometry (GC–MS) method was developed and validated for the determination of Cetrimonium chloride and Behentrimonium chloride surfactants in cosmetics products. With each product, Cetrimonium chloride and Behentrimonium chloride (%) were calculated. To test cross-group differences in Cetrimonium chloride and Behentrimonium chloride (%), Kruskal–Wallis test was applied. Results: Of the 125 tested cosmetics and personal care products, five (4%) exceeded the recommended Cetrimonium chloride level in rinse-off hair products (2.5%), 10 (8%) exceeded the recommended Cetrimonium chloride level in leave-on hair products (1%), and 24 (61.5%) exceeded the recommended Cetrimonium chloride level used as a preservative in cosmetics products. Moreover, of the 125 tested cosmetics and personal care products, 21 (53.8%) exceeded the recommended Behentrimonium chloride level used as preservatives in cosmetics products. Conclusions: Although several structures for cosmetics quality and control across the globe are fairly comprehensive and intricate, there is a need to make them more rigorous to apply compliance with GMP and ensure regulatory control. Doing so would help enhance the inspection and regulation of cosmetics containing Behentrimonium chloride/Cetrimonium chloride preservatives. Furthermore, there is a dire need to establish a unified cosmetovigilance worldwide.

Keywords: Cetrimonium chloride; Behentrimonium chloride; cosmetics; skin sensitivity; leave-on; rinse-off

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1. Introduction

As our body's biggest surface, skin is involuntarily exposed to both abiotic [1,2] and biotic elements [3,4] because it engages with extraneous environments, whereas voluntary exposure is attributed to the use of cosmetics and personal products. Because the majority of these products are applied and used in a myriad of ways every day, it is assumed that the products boost our appearance and personal hygiene because they are purported to be

safe for use/consumption. Considering the frequency of skin contact as well as the mucosa, it is paramount to ensure that the products do not comprise hazardous substances. In fact, each ingredient utilized in cosmetics products should comply with regulatory norms [5]. In addition, it is important to consider these products' long-term side effects [6,7]. At the same time, other substances could cause many side effects like allergies and dermatitis [8].

Considering the United Arab Emirates' (UAE's), regulations, cosmetics products must not cause any harm to consumers' health and safety under foreseeable or normal scenarios. To that end, the role of manufacturers in ensuring the safety of these products becomes paramount, as they are the ones responsible for a product's launch. However, in this context, safety is not confined to preventing the use of banned chemical substances; it also entails appropriate stability and purity on microbiological levels. Because it is imperative to guarantee this, producers tend to depend on preservatives, typically synthetic compounds such as Alkyl (C12-22) trimethyl ammonium bromide and chloride, for example, Behentrimonium chloride and Cetrimonium chloride. Due to the extensive use of Cetrimonium chloride, people are expected to gain exposure to such compounds for a prolonged period.

Cetrimonium chloride has anti-frizz, detangling, and anti-static attributes. In cosmetics products, the ingredient's chemical structure enables its use in formulating hair care products like colors and hair dyes. Cetrimonium chloride also helps clean the skin by curtailing microorganisms' growth as well as by mixing water with dirt and oil to allow for rinsing. It bears a strong resemblance to Behentrimonium chloride, a conditioning ingredient. The difference lies only in carbon atoms, as, due to its intrinsic lightness, it makes slight alterations in how the conditioner feels after application to the hair.

State regulations strongly control Cetrimonium chloride's concentration in cosmetics personal care and cosmetics products. The Cosmetics Regulation (EC) No 1223/2009 suggests that the concentration of substances identified by the denominations of alkyl (C12-22) trimethyl ammonium bromide and chloride as preservatives is 0.1%. The recommended Cetrimonium chloride level in rinse-off hair products is 2.5%, while the recommended levels are 1% in leave-on hair products and 0.5% in leave-on face products. Moreover, the recommended Behentrimonium chloride level in rinse-off hair products is 5%, while the recommended levels are 3% in rinse-off hair products and 3% in leave-on face products [9]. Similarly, the UAE cosmetics technical regulations are adopted from EU regulations and apply the same concentrations limit in cosmetics and personal care products [10].

However, despite the regulations, many instances of tainted cosmetics products have been found in the UAE. As a case in point, a study on the UAE's personal care/cosmetics products revealed that 13% of the products tested contained higher than recommended levels of formaldehyde, and not even a single product was labeled formaldehyde or formaldehyde-free [11].

Research shows that 5% of the 100 products (personal care and cosmetics) tested in the UAE were infested by aerobic mesophilic bacteria, while 13% of products contained mold or yeast [12]. Another study assessing the safety of cosmetics products in Dubai revealed that six of the 102 hand sanitizers (alcohol-based) contained unlisted/undeclared methanol, with other samples comprising below 60% alcohol, although their labels suggested that they contained 70% alcohol content [13–15].

This study quantifies and investigates Cetrimonium chloride and Behentrimonium chloride in the cosmetics and personal care products in the UAE market to gauge whether or not they adhere to requirements for safety and health. Its findings will help ensure compliance with existing regulations and enhance the inspection and regulation of cosmetics containing Behentrimonium chloride/Cetrimonium chloride preservatives.

2. Methods and Materials

2.1. Sample Collection

This study searched local business directors to identify the outlets that sell personal care/cosmetics products and contain information about each healthcare and pharmacy/parapharma retailer in the UAE. After 2183 such retailers were identified, a sample framework

was created using an Excel spreadsheet. It contained all of the pertinent information, such as business names, emails, phone numbers, and addresses. Then, a study sample was created by adopting basic selection (random-sample) based on business ID numbers, and stratification was implemented based on location/type. The criterion for selecting products was that their label must consist of Behentrimonium chloride or Cetrimonium chloride. Across all locations, a package of all personal care/cosmetics products was randomly selected regardless of their place of manufacturing. Then, a reference number (code) was assigned to each item to facilitate tracking and prevent duplication. For each sample, the details were noted in the following manner: brand name, product name, category of item, manufacturer's country, dosage form, subcategory, size/volume, bar code, batch number, recommended dosage, and shop location. If identical products were seen for more than one outlet (that is, manufacturer/name/barcode/volume/size/formulation), the first product to be selected underwent testing and the rest were returned. If different firms shared a common product name or were found in several formats, they were deemed separate. In addition, in that case, both products underwent testing. All the chosen products were dispatched to a laboratory where they were assessed on the day of collection.

2.2. Measurement of Cetrimonium Chloride and Behentrimonium Chloride Content (Procedure Summary)

A gas chromatography–mass spectrometry (GC–MS) method is developed and validated for the determination of Cetrimonium chloride and Behentrimonium chloride surfactants in hair products. Sodium Dibutylnaphthalenesulfonate is used as an internal standard. The limit of quantitation (LOQ) is 0.5 ng/mL with a signal-to-noise ratio greater than 5. The calibration curve is linear from 0.5 to 250 ng/mL with an R^2 greater than 0.99. The coefficients of variation for within-and between-assay imprecision, including LOQ, are $\leq$ 15% and $\leq$ 8%, respectively. The percentage of inaccuracy for within- and between-assay, including LOQ, are $\leq$ 9% and $\leq$ 5%, respectively. The percentage determinations of Cetrimonium chloride and Behentrimonium chloride are greater than 84% and 82%, respectively.

2.3. Apparatus

Solvent delivery was achieved using a Shimadzu GCMS-QP2010 SE set at 1 mL/min. Sample injection was carried out using a Shimadzu AOC 30 series autoinjector. A Shimadzu column oven containing 5%-phenyl-95%-dimethylpolysiloxane was used. Detection was by MS-QP2010 SE. All PE SCIEX software was supplied by Shimadzu. The NM20ZA high-purity nitrogen and air generators were supplied by Shimadzu.

2.4. Chromatographic System

A Shimadzu column oven containing 5%-phenyl-95%-dimethylpolysiloxane was used. The mobile phase 99.99% used which was generated by a nitrogen generator. The flow rate was fixed at 1 mL/min. The GCMS-QP2010 SE is a single quadrupole gas chromatograph–mass spectrometer. The sample injection volume was 10 µL for MS. Nitrogen was used as the collision gas. Lab solution software was used to control the GC–MS, record the output from the detector, perform integration of peak areas, and calculate the concentrations of Cetrimonium chloride and Behentrimonium chloride. Dibutylnaphthalenesulfonate was used as an IS. All calculations were based on peak-area ratios of Cetrimonium chloride, Behentrimonium chloride, and IS. The precursor ions for Cetrimonium chloride, Behentrimonium chloride, and Dibutylnaphthalenesulfonate were m/z 348.96, 334.98, and 385.98, respectively, while after collisional dissociation, the product ions were 92.77, 95.66, and 152.86, respectively. The retention times for Cetrimonium chloride, Behentrimonium chloride, and Dibutylnaphthalenesulfonate during the assay were 6.2, 5.7, and 4.5 min.

2.5. Assay Procedure

Stock solution A of Cetrimonium chloride and Behentrimonium chloride was prepared in methanol. All the sub stock solutions were stored frozen at approximately −20 °C. All the

calibrators and quality control (QC) sample concentrations were prepared by appropriate dilution of the sub stock dilution. The contents were mixed for a minimum of 5 min by the shaker and then centrifuged at 3000–3500 rpm for 5 min. The top layer was then transferred into an autosampler vial. A 10-µL volume was injected into GCMS.

2.6. Selection of Operating Protonated Ions

The chemical structure and protonated ions of Cetrimonium chloride, Behentrimonium chloride, and Dibutylnaphthalenesulfonate used in this study related to their mass. The fragment ions at m/z 92.77 for Cetrimonium chloride, m/z 95.66 for Behentrimonium chloride, and 152.86 Dibutylnaphthalenesulfonate were selected for the assay.

2.7. Specificity

No significant interfering peaks were found in the retention times of Cetrimonium chloride and Behentrimonium chloride. The signal-to-noise ratios for both drugs were greater than 5 shows the chromatogram obtained from blank methanol.

2.8. Calibration Curve

The calibration curve covered the range from 0.5 to 250 ng/mL of Cetrimonium chloride and Behentrimonium chloride with seven calibrators. All of the results were calculated using a $1/\times 2$ weighted quadratic regression. The peak-area ratio, regression coefficient, and parameters of the calibration line were calculated from the peak area data by the analyst program. The regression coefficient for all the calibration curves was greater than 0.99. Mean results obtained from five curves are summarized.

2.9. Ethical Consideration

The Institutional Review Board of An-Najah National University approved this study. Reference number: lnt.R. March.2021/10.

2.10. Statistical Analysis

SPSS version 24 obtained from Chicago, IL (USA) was used to carry out data analysis. In this analysis, a summary of qualitative variables was provided using percentages and frequencies. With each product, Cetrimonium chloride and Behentrimonium chloride (%) were calculated. To test cross-group differences in Cetrimonium chloride and Behentrimonium chloride (%), Kruskal–Wallis test was applied. p-values < 0.05 were chosen as the statistically significant boundary.

3. Results

3.1. Sample Characteristics

Table 1 displays the sample baseline characteristics of the cosmetics and personal care products. A total of 164 cosmetics products were collected and analyzed in this study. Of this total, 97% (n = 159) were hair and scalp products while 3% (n = 5) were face and neck preparations. Among the analyzed samples, 125 (76.2%) were rinse-off cosmetics and 39 (23.8%) were leave-on cosmetics. The product countries of origin were as follows: 16 (9.8%) United States, 10 (6.1%) United Arab Emirates, 7 (4.3%) Turkey, 7 (4.3%) Israel, 7 (4.3%) India, 62 (37.8%) European Union, 6 (3.7%) China, 5 (3%) Canada, 40 (4.4%) Brazil, and 4 (2.4%) Australia.

Table 1. Number and percentages of sample baseline characteristics (n = 164).

Characteristics	Groups	Frequency	Percentage
Cosmetic category	Hair and scalp products	159	97%
	Face and neck preparations	5	3%
Cosmetic application	Rinse-off	125	76.2%
	Leave-on	39	23.8%
Country of origin	United States	16	9.8%
	United Arab Emirates	10	6.1%
	Turkey	7	4.3%
	Israel	7	4.3%
	India	7	4.3%
	EU	62	37.8%
	China	6	3.7%
	Canada	5	3%
	Brazil	40	24.4%
	Australia	4	2.4%

3.2. Assessment of Cetrimonium Chloride and Behentrimonium Chloride Content of Cosmetics and Personal Care Products

The estimated average of Cetrimonium chloride content in rinse-off products was 0.793 (95% CI [0.63–0.95]). The estimated average of Cetrimonium chloride content in leave-on products was 0.789 (95% CI [0.51–1.1]). Of the 125 tested cosmetics and personal care products, 5 (4%) exceeded the recommended Cetrimonium chloride level in rinse-off hair products (2.5%), 10 (8%) exceeded the recommended Cetrimonium chloride level in leave-on hair products (1%), and 24 (61.5%) exceeded the recommended Cetrimonium chloride level used as a preservative in cosmetics products. Overall, 39 (23.8%) did not comply with the recommended Cetrimonium chloride levels in cosmetics and personal products (Table 2).

The results of the Cetrimonium chloride content stratified by sample characteristics of each sample are provided in Table 3.

The estimated average of Behentrimonium chloride in rinse-off products was 1.154 (95% CI [0.91–1.4]). The estimated average of Behentrimonium chloride in leave-on products was 0.361 (95% CI [0.16–0.56]). Of the 125 tested cosmetics and personal care products, 21 (53.8%) exceeded the recommended Behentrimonium chloride level used as preservatives in cosmetics products (Table 4).

Table 2. Estimates of Cetrimonium chloride content from cosmetics and personal care products and Maximum Allowable Limit (n = 164).

Parameters	Maximum Allowable Limit	Products Exceeding Maximum Limit		Estimates of Concentration (%)			
				Rinse-off Products (n = 125)		Leave-on Products (n = 39)	
		n	%	Mean ± SD	Median	Mean ± SD	Median
Cetrimonium chloride	2.5% a (n = 125)	5	4%	0.793 ± 0.92	0.630	0.789 ± 0.85	0.746
	1% b (n = 125)	10	8%				
	0.5% c (n = 125)	0	0				
	0.1% d (n = 39)	24	61.5%				

Maximum allowable limits according to the EU and UAE cosmetics technical regulations. a: Rinse-off hair products. b: Leave-on hair products. c: Leave-on face products. d: For use as a preservative.

Table 3. List of analyzed cosmetics and personal care products exceeding the maximum allowable limit of Cetrimonium chloride.

Category	Product Description	Product Application	Cetrimonium Chloride (%)	Function	Country of Origin	Reason
Hair and scalp products	Anti frizz for hair	leave on	1.3	emulsifying	Brazil	B
Hair and scalp products	Professional hold & color	leave on	1.5	conditioning agent	India	B
Hair and scalp products	Professional hold & color	leave on	1.5	conditioning agent	India	B
Hair and scalp products	Professional hold & color	leave on	1.5	conditioning agent	India	B
Hair and scalp products	Professional care repair max masque	Rinse off	3	conditioning agent	India	A
Hair and scalp products	Protein straightening with argan oil	leave on	2.5	surfactants	EU	B
Hair and scalp products	Smoothing protein	Rinse off	4	surfactants	Brazil	A
Hair and scalp products	Hair conditioner	Rinse off	1.4	preservative	EU	D
Hair and scalp products	Hair balancing conditioner	Rinse off	0.9	preservative	EU	D
Hair and scalp products	Hair replenishing mask	Rinse off	0.9	preservative	EU	D
Hair and scalp products	Frizz off conditioner	Rinse off	0.9	preservative	EU	D
Hair and scalp products	Hair growth activation conditioner	Rinse off	0.75	preservative	EU	D
Hair and scalp products	Bleach blondes toning conditioner	Rinse off	0.9	preservative	EU	D
Hair and scalp products	Conditioning masque	Rinse off	0.3	preservative	India	D
Hair and scalp products	Scalp revitalizing shampoo	Rinse off	0.5	preservative	India	D
Hair and scalp products	Reconstructor nano	Rinse off	0.62	preservative	Brazil	D
Hair and scalp products	Reconstructor nano	Rinse off	0.62	preservative	Brazil	D
Hair and scalp products	Activation treatment	Rinse off	0.9	preservative	EU	D
Hair and scalp products	Hair conditioner	Rinse off	5	Antistatic	Turkey	A
Hair and scalp products	Hair conditioner	Rinse off	3	conditioning agent	Brazil	A
Hair and scalp products	Hair oil	leave on	2	emulsifying	Brazil	B
Hair and scalp products	Hair mask	Rinse off	0.305	preservative	EU	D
Hair and scalp products	Masque capillaire	Rinse off	0.1387	preservative	EU	D
Hair and scalp products	Hair mask	leave on	3	conditioning agent	Brazil	B
Hair and scalp products	Hair botox reconstructive	Rinse off	1.5	preservative	Brazil	D
Hair and scalp products	Keratin conditioner	Rinse off	0.8	preservative	Brazil	D
Hair and scalp products	Keratin shampoo	Rinse off	0.2	preservative	Australia	D

Table 3. *Cont.*

Category	Product Description	Product Application	Cetrimonium Chloride (%)	Function	Country of Origin	Reason
Hair and scalp products	Keratin treatment	leave on	2	conditioning agent	United Arab Emirates	B
Hair and scalp products	Hair cream	leave on	0.15	preservative	EU	D
Hair and scalp products	Hair balm	Rinse off	0.63	preservative	EU	D
Hair and scalp products	Hair	Rinse off	0.63	preservative	EU	D
Hair and scalp products	Hair conditioner	Rinse off	3.75	conditioning agent	United Arab Emirates	A
Hair and scalp products	Hair cream	leave on	2.4	surfactants	Brazil	B
Hair and scalp products	Arganoil nourishing treatment	Rinse off	0.9	preservative	EU	D
Hair and scalp products	Açai oil conditioner	leave on	2.5	conditioning agent	United Arab Emirates	B
Hair and scalp products	Hair botox reconstructive mask	Rinse off	1.5	preservative	Brazil	D
Hair and scalp products	Keratin conditioner	Rinse off	0.8	preservative	Brazil	D
Hair and scalp products	Hair conditioner	Rinse off	0.6546	preservative	EU	D
Hair and scalp products	Hair conditioner	Rinse off	1.1755	preservative	EU	D

A: exceeding the limit of 2.5% in rinse-off hair products. B: Exceeding the limit of 1% in Leave-on hair products. C: exceeding the limit of 0.5% in Leave-on face products. D: exceeding the limit of 0.1% for use as a preservative.

Table 4. Estimates of Behentrimonium chloride content from cosmetics and personal care products and Maximum Allowable Limit (n = 164).

Parameters	Maximum Allowable Limit	Products Exceeding Maximum Limit		Estimates of Concentration (%)			
				Rinse-off Products		Leave-on Products	
		n	%	Mean ± SD	Median	Mean ± SD	Median
Behentrimonium chloride	5% a (n = 125)	0	0	1.154 ± 1.4	0.70	0.361 ± 0.63	0.252
	3% b (n = 125)	0	0				
	3% c (n = 125)	0	0				
	0.1% d (n = 39)	21	53.8%				

Maximum allowable limits according to the EU and UAE cosmetics technical regulations. a: Rinse-off hair products. b: Leave-on hair products. c: Leave-on face products. d: For use as a preservative.

The results of the Behentrimonium chloride content stratified by sample characteristics of each sample are provided in Table 5. Supplementary Materials shows the chromatograms for some analyzed cosmetics and personal care products (Supplementary Figure S1).

Table 5. List of analyzed cosmetics and personal care products exceeding the maximum allowable limit of Behentrimonium chloride used as a preservative.

Category	Product Description	Application	Behentrimonium Chloride (%)	Function	Country of Origin
Hair and scalp products	Hair balancing conditioner	Rinse off	0.428	preservative	EU
Hair and scalp products	Hair replenishing mask	Rinse off	1.4	preservative	EU
Hair and scalp products	Hair growth activation conditioner	Rinse off	1.4	preservative	EU
Hair and scalp products	Deep conditioning masque	Rinse off	1	preservative	India
Hair and scalp products	Reconstructor nano	Rinse off	0.78	preservative	Brazil
Hair and scalp products	Reconstructor nano	Rinse off	0.78	preservative	Brazil
Hair and scalp products	Grow longer activation treatment	Rinse off	0.2	preservative	EU
Hair and scalp products	Hair masque	Rinse off	2.5	preservative	EU
Hair and scalp products	Masque capillaire	Rinse off	2.5	preservative	EU
Hair and scalp products	Hair botox reconstructive	Rinse off	1.5	preservative	Brazil
Hair and scalp products	Keratin conditioner	Rinse off	0.495	preservative	Brazil
Hair and scalp products	Intensive repair mask	Rinse off	1.2	preservative	EU
Hair and scalp products	Hair balm	Rinse off	0.7	preservative	EU
Hair and scalp products	Hair balm	Rinse off	0.7	preservative	EU
Hair and scalp products	Hair mask	Rinse off	2.5	preservative	EU
Hair and scalp products	Hair mask 1000ml	Rinse off	0.7	preservative	EU
Hair and scalp products	Hair botox reconstructive mask	Rinse off	1.5	preservative	Brazil
Hair and scalp products	Keratin conditioner	Rinse off	0.495	preservative	Brazil
Hair and scalp products	Hair conditioner	Rinse off	1.3597	preservative	EU
Hair and scalp products	Hair conditioner	Rinse off	2.5173	preservative	EU
Hair and scalp products	Arganoil nourishing conditioner	Rinse off	3.825	preservative	EU

3.3. Comparison of Cetrimonium Chloride and Behentrimonium Chloride Content According to Country of Origin

The distribution of Cetrimonium chloride and Behentrimonium chloride content according to country of origin is presented in Table 6. The table also provides the comparison analysis along with *p*-values. These *p*-values were provided from the results of the Kruskal–Wallis test. There was a statistically significant difference in Cetrimonium chloride concentration according to country of origin ($p < 0.001$).

Post hoc analysis showed that significantly increased concentrations of Cetrimonium chloride were observed in products made in the United Arab Emirates ($p = 0.009$), Israel ($p = 0.026$), India ($p = 0.008$), and Brazil ($p = 0.001$) compared to products made in the United States.

Moreover, a statistically significant difference was found in concentrations of Behentrimonium chloride and country of origin ($p = 0.002$). In post hoc analysis, lower concentrations of Behentrimonium chloride were observed in products manufactured in Turkey ($p = 0.012$) and Brazil ($p = 0.001$) in comparison to products manufactured in the United States.

Table 6. Comparison of Cetrimonium chloride and Behentrimonium chloride content according to country of origin.

Country	Cetrimonium Chloride (%)			Behentrimonium Chloride (%)		
	Mean	**±SD**	***p*-Value**	**Mean**	**±SD**	***p*-Value**
United States	0.15	±0.29	<0.001	2.17	±1.1	0.002
United Arab Emirates	1.37	±1.22		0.780	±1.6	
Turkey	1.003	±1.84		0.142	±0.38	
Israel	1.40	±0.65		0.80	±1.5	
India	1.53	±0.96		0.71	±1.5	
EU	0.523	±0.64		1.16	±1.3	
China	0.37	±0.42		0.33	±0.82	
Canada	0.207	±0.44		1	±1.37	
Brazil	1.21	±0.87		0.54	±0.89	
Australia	0.603	±0.32		0.87	±1.7	

Notes: *p*-values obtained from the Kruskal–Wallis test.

4. Discussion

Behentrimonium chloride and Cetrimonium chloride are known to be very effective hair conditioners with detangling, anti-frizz, and anti-static features. As per the technical regulations of the UAE cosmetics market, the concentrations of these agents in personal care/cosmetics products are strictly regulated. As far as we know, this is the first study to quantify and examine the Behentrimonium chloride and Cetrimonium chloride content in the UAE's cosmetics and personal care product market to gauge the extent to which they adhere to the safety and health norms of the nation. As per this research, among all products, 61.5% were found to not adhere to the proposed levels of Cetrimonium chloride. In its entirety, this typically denotes grave health hazards linked to the utilization of cosmetics products. Similarly, 53.8% of these products were found to exceed the permitted levels of Behentrimonium chloride and were utilized as preservatives across personal care and cosmetics products.

Quality assurance-related problems may have led to this non-compliance. Variations with regard to quality are attributed mainly to a failure on the part of the manufacturer to adhere to good manufacturing practices (GMP) or their tendency to engage in unethical practices. For this reason, the technical problems undermining the tests' accuracy must be duly addressed. Manufacturers must ensure that there is no compromise as far as specifications are concerned and that tests are conducted appropriately to determine the reliability of the preservatives' content. They must also outsource certification/testing to an adequately proficient laboratory.

Alarmingly, this study finds that these non-compliant cosmetics products include dyes, preservatives, and fragrances—the most salient elements that cosmetics are known to contain and that can cause hypersensitivity [16,17]. Moreover, the continuous exposure to and everyday use of a broad array of these products containing all sorts of chemicals obtained from myriad sources may lead to the "cocktail effect" because of different substances' synergistic interaction along with the "additive effect," as the same ingredient is commonly found in several products. At the same time, it is necessary to devote more attention to leave-on products because they remain in contact with the skin for a longer period. Therefore, hazardous substances are likely to play a key role in damaging the health of humans [18,19].

To make matters worse, the use of these products on inflamed/irritated skin exacerbates the side effect-related risks. In such cases, the dangers of infection increase significantly when the subject makes use of a cosmetic that exceeds the preservatives' recommended levels [14,15].

It is interesting to note that cosmetics products manufactured in the UAE, India, Brazil, and Israel contain higher Cetrimonium chloride levels in comparison to those manufactured in the United States. By contrast, lower Behentrimonium chloride levels have been found in products made in Brazil and Turkey, as compared to those made in

the United States. This indicates the lack of a worldwide consensus on regulatory controls applicable to cosmetics products and stresses the need to establish a balanced framework of regulation whereby authorities can safeguard the consumption safety of cosmetics for humans and ensure that all claims of reliability and accuracy are not misleading.

The health hazards associated with these cosmetics products are snowballing into a major public health concern, as, over the past nine years, around 12% of users belonging to the general population have already witnessed adverse side effects following the use of at least one personal care and cosmetics product [20,21]. The growing body of literature on this issue reveals that the number of cases in which exposure to cosmetics leads to allergic reactions is growing in several nations [16,22]. Thyssen et al. conducted a study among Denmark's citizens and showed that 33.6% of men and 56.7% of women have witnessed a side effect on at least one occasion during their lifetimes [23]. Nearly 10% of all people are known to suffer from allergy-induced irritation, general side effects, or hypersensitivity [16]. Wojciechowska et al. suggest that approximately 15% of people who use cosmetics experience side effects [24]. These findings agree with those of the study which suggests that cosmetics cause dermatitis in 8–15% of all cases [16,25].

Thus, it is amply clear that the use of cosmetics exposes most people across the world to a variety of possibly hazardous substances. Although the quantum of exposure might be negligible, and the side effects are often not properly understood, prolonged exposure to these chemicals may have deleterious effects on people's wellbeing and health. Although the existing legislation considers these risks and subjects these substances to a threshold concentration, the risk of a "cocktail effect" caused by the use of a combination of products throughout the day cannot be denied. Moreover, it is possible to find the same ingredient in more than one product derived from more than one source ("additive effect"), thus overcoming the established safety threshold. This underscores the importance of enhancing the legislative approach, as many unsafe chemicals are still not prohibited from being sold in the market. Furthermore, there is a dire need to establish a unified cosmetovigilance worldwide. Such an all-encompassing strategy of public health can go a long way toward genuinely deriving information about cosmetics product safety and substances and prevent the risks linked to their usage, which can pose a threat to public health [26].

5. Conclusions

Although several structures for cosmetics' quality and control across the globe are fairly comprehensive and intricate, there is a need to make them more rigorous to apply compliance with GMP and ensure regulatory control. Doing so would help enhance the inspection and regulation of cosmetics containing Behentrimonium chloride/Cetrimonium chloride preservatives.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/cosmetics8040103/s1, Figure S1. Chromatograms for some analyzed cosmetics and personal care products.

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