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Comparison of XRF, TXRF, and ICP-MS Methods for Determination of Mercury in Face Creams

Gordon A. Vrdoljak[a], Peter T. Palmer[b,*], Richard Jacobs[c], Bahman Moezzi[a], Alanna Viegas[a]

[a]*State of California Department of Public Health, Food and Drug Laboratory Branch, Richmond, CA*
[b]*Department of Chemistry & Biochemistry, San Francisco State University, San Francisco, CA*
[c]*Currently retired, formerly with Division of Field Science, Food and Drug Administration, Alameda, CA*

Abstract

Regulatory, media, and watchdog groups have identified numerous face cream products containing percent levels of mercury that far exceed the 1 ppm FDA regulatory limit. Mercury is added to these products to provide skin bleaching properties, and this poses a serious health risk to consumers. This study compares XRF, TXRF, and the more widely accepted ICP-MS methods for determination of mercury in face cream products. To identify contaminated products in a field setting, XRF is the preferred method, as it involves direct analysis of the sample, analysis times of a minute or less, and detection limits down to single ppm levels. XRF analysis gave quantitative results that compared well to those from ICP-MS for homogeneous products, but gave more variable results for products containing small crystals or chunks of inorganic mercury salts. More accurate results for these products requires preparation of a representative sample, microwave digestion, and TXRF or ICP-MS analysis. Given the continued production and distribution of mercury-containing face cream products, it is recommended that portable XRF be used to screen for such products or for accurate quantification of mercury in homogeneous products, and TXRF be used to determine the mercury content of more heterogeneous products.

Keywords: mercury, face creams, XRF, TXRF, ICP-MS

Abbreviations: AAS, atomic absorption spectrophotometry; CV-AAS, cold vapor atomic absorption spectrophotometry; FDA, Food and Drug Administration; ICP-AES, inductively coupled plasma – atomic emission spectrometry; ICP-MS, inductively coupled plasma mass spectrometry; ppm, part-per-million; TXRF, total reflectance X-ray fluorescence spectrometry; XRF; X-ray fluorescence

1. Introduction

Skin bleaching agents or lighteners are used in many parts of the world and often include mercury (Hg) as an active ingredient [15]. Consumers using these products can be exposed to Hg through dermal contact and inhalation of volatile forms of Hg. Given the high levels of Hg in these products, they represent a serious health risk, as Hg can permanently damage the brain, kidneys, and a developing fetus [1]. The use of Hg in commercial cosmetic products was banned by the European Union in 1976 and by the U.S. Food and Drug Administration (FDA) in 1990. FDA regulations require that if Hg is present, it must be at concentrations of less than 1 ppm (equivalent to 1 microgram of Hg per gram of sample) in cosmetics [19]. An exception to this is eye area cosmetics, where the use of Hg is allowed as a preservative at up to 65 ppm [19]. Excessive levels of Hg in face cream products that make drug claims such as "bleaching skin" can be interpreted as an unapproved drug and/or an adulterated product.

Outbreaks of health problems from Hg-containing face creams persist. These products are sold in Asia, Mexico, and the Middle East, and can be readily purchased over the internet [6, 10, 13, 18]. Several investigations by various regulatory, media, and watchdog groups identified numerous face cream products Hg levels greater than one percent (equivalent to 0.01 gram of Hg per gram of sample). In a 2010 study reported in the Chicago Tribune [8, 9], 50 different imported face cream products were sent to a certified lab for analysis. The majority of samples contained non-detectable levels of Hg, but five were found to contain Hg levels ranging from 0.6-3.0 percent. A 2010 study on people with elevated blood Hg levels in California and Virginia identified several face cream products as the likely cause, with Hg levels ranging from 2-6 percent, as determined by Inductively Coupled Plasma – Mass Spectrometry (ICP-MS) [5]. A 2011 study by a consumer watchdog group in the Philippines found detectable levels of Hg in 11 differ-

*Corresponding author: Pete Palmer, Email: palmer@sfsu.edu, Phone: 408-859-4628

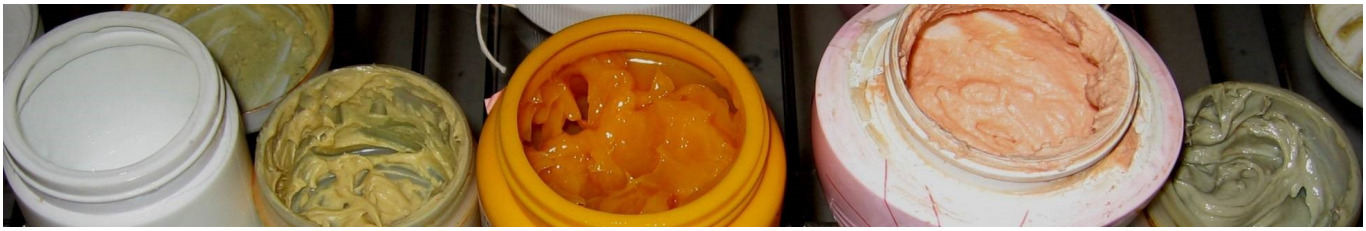

Figure 1: Photograph of some of the Hg-containing face cream products analyzed in this study

ent face cream products, but did not indicate how the analyses were performed [7]. In a 2011 study on Mexican face creams, Hg was found in six of the 16 products tested at levels ranging from 0.09-3.6 percent using Cold Vapor Atomic Absorption Spectrophotometry (CV-AAS) [18]. A group of investigators analyzed 676 different Cambodian skin whitening creams and found 16 percent contained Hg levels greater than 20 ppm, with good correlation between results from both X-Ray Fluorescence Spectrometry (XRF) and Inductively Coupled Plasma – Atomic Emission Spectrometry (ICP-AES) [14]. A report from China indicated that XRF was used to test heavy metal content of 477 whitening and freckle reducing products and found that 23 percent of these products contained Hg levels over 1 ppm Hg [20]. The frequency of occurrence and Hg levels shown in these studies clearly demonstrate that this is a significant public health problem in many different countries, including the U.S.

As indicated above, a variety of analytical methods can be used to determine total Hg in face cream products, including Atomic Absorption Spectrophotometry (AAS), CV-AAS, ICP-AES, and ICP-MS. All of these methods involve significant and time-consuming sample preparation, specifically acid digestion, filtration, and dilution. ICP-MS is often the method of choice for trace elemental analysis, with detection limits that are orders of magnitude lower than necessary for this application. Portable XRF analyzers are ideal to screen for contaminated products, given lower equipment cost, minimal sample preparation requirements, and fast analysis times [16, 17]. A relatively new method, Total Reflection X-Ray Fluorescence Spectroscopy (TXRF), has also been used for determination of Hg [3] and provides significantly lower detection limits compared to XRF. The purpose of this study was to develop, evaluate, and compare ICP-MS, XRF, and TXRF methods for accurate quantitation of Hg in face creams.

2. Materials and Methods

2.1. Samples

The products analyzed in this study were a subset of face creams collected during routine surveillance by the Food and Drug Laboratory Branch of the Department of Public Health in the State of California. Most of these products were manufactured outside the U.S. Many had high Hg content, with some containing percent levels. Appropriate safety precautions are highly recommended for anyone working with or handling these products. Gloves should be used to minimize dermal contact. Moreover, these products should be handled in a fume hood to minimize inhalation exposure, as some contain mercuric chloride ($HgCl_2$). This substance, formerly known as "corrosive sublimate", is volatile and highly toxic. This creates a quandary when using portable XRF to screen for these products in a field setting. While these products can be analyzed through the packaging, the XRF signal is attenuated by the container and packaging materials and gives erroneously low results. More accurate quantification can be achieved by opening the container and turning it upside down over the XRF analyzer window (protected with Mylar film), or better yet, by placing the sample into an XRF sample cup. The latter two approaches should only be used if a fume hood is available to ensure minimal exposure.

A photograph of some of the face cream samples is provided in Figure 1. Upon closer visual inspection, a few contained visible chunks of what appeared to be Hg-based salts added to these products. This presents a challenge in obtaining a representative sample and achieving high precision in the analyses, as discussed below. Given the limited amount of each product, inadequate amounts of the original 16 samples analyzed via ICP-MS were available for subsequent analysis via XRF and TXRF.

2.2. ICP-MS Method

To prepare samples for ICP-MS, ~0.5 g of sample was mixed with 5 mL of concentrated nitric acid and 1 mL of 30 percent hydrogen peroxide. The sample solution was digested in an Anton Parr microwave digester for 20 minutes at 180° C. Samples were diluted in 2 percent nitric acid, some by a factor as large as 1,000,000, to bring Hg levels within the ICP-MS calibration range of 0-5 ppb. The samples were analyzed using an Agilent 7500CE ICP-MS that was tuned for total Hg analysis according to the manufacturer's instructions. It should be noted that HCl should be used to stabilize low levels of Hg in aqueous solutions, but this precaution was not taken in these analyses because the standards and samples were analyzed on the same day to minimize potential losses of Hg. A calibration curve was used to compute concentrations in the sample extracts. This information was used along with dilution factors and sample masses to compute sample concentrations.

2.3. XRF Methods

Three different XRF methods, each using a different sample preparation procedure, were developed and evaluated. In the first, samples were analyzed "as is". XRF response was calibrated using standards ranging from ~100 to 100,000 ppm

(10 percent) Hg prepared by diluting known masses of mercuric sulfide (HgS) into a Hg-free face cream matrix and performing serial dilutions. In the second method, samples were diluted into a Carbomer 940 matrix, which served as an emulsion to suspend particulate matter in the samples. This matrix was prepared by suspending 8 g of powdered Carbomer 940 in 300 mL of deionized water, mixing several times, and neutralizing the hydrated Carbomer to pH 5.5-7.0 by adding 16 mL of 25 percent sodium hydroxide. Standards in the range of 20 to 80,000 ppm (8 percent) were prepared by adding known masses of mercuric sulfide into the Carbomer 940 matrix and performing serial dilutions. Samples and standards were loaded into bags, heat sealed, and mixed using a Stomacher 80 micro-biomaster (paddle-type) blender prior to analysis. In the third method, samples were diluted into a 1 percent sodium dodecyl sulfate (SDS) aqueous matrix to facilitate solvation of the face cream. Standards in the range of 100 to 1000 ppm were prepared by diluting known volumes of a 10,000 ppm Hg standard into a 1 percent SDS aqueous matrix.

In all three XRF methods, samples and standards were placed into single open-ended XRF sample cup, sealed with 3.5-micron Mylar film and a retaining ring, and analyzed using an Olympus Innov-X Delta premium model handheld XRF operated from a PC with associated software to control the instrument and acquire spectra. It is highly recommended to place (and replace as necessary) a piece of Mylar film over the XRF analyzer window to prevent inadvertent contamination of the instrument. XRF spectra were acquired using 1 minute "live" times in soil beam 2 mode (30 kV excitation). Quantitative results were computed from a calibration curve plotting the Hg L_α peak intensity as a function of concentration. This information was used along with dilution factors and sample masses to compute sample concentrations.

2.4. TXRF Methods

Three different TXRF methods, each based on the use of different sample preparation procedures, were developed and used to analyze the face cream products. Chromium (Cr) was used as the internal standard for all samples and was not detected in the initial screening of these products. In the first method, 0.2 g of face cream was mixed with 0.25 mL of 0.2 M ethylene diamine tetraacetic acid (EDTA) and 10 μL of 1000 ppm Cr internal standard for two minutes using an IKA T10 disperser. In the second method, ~0.2 g of face cream was mixed with 1 mL of 1 percent Triton X-100, 0.2 mL of 0.2 M EDTA, and 10 μL of 1000 ppm Cr internal standard and mixed for 1-2 minutes using a standard lab vortexer to suspend particulate matter in the samples. In the third method, samples were prepared using the same microwave digestion procedure used prior to ICP-MS analysis. The samples were diluted by a factor of 200 with 2 percent nitric acid. Approximately 1 g of diluted sample was then mixed with 0.5 mL Triton X-100, 0.2 mL 0.2 M EDTA, and 10 μL of 1000 ppm Cr.

In all three TXRF methods, 7 μL of sample was placed onto a quartz disc, dried on a hotplate, and analyzed using a Bruker S2 Picofox TXRF instrument. Acquisition times of 5-10 minutes were used for all samples. Hg was quantified using a Cr internal standard and a standard sensitivity curve that correlates the relative fluorescence intensities of different elements. This sensitivity curve was used to determine the concentrations of the target element(s) in the diluted samples [2], and the information was used along with dilution factors and sample masses to compute Hg concentrations in the original samples.

Quantification via TXRF is a "standardless" quantification, which is significantly different from most atomic spectrometry calibration techniques, and merits further discussion. Quantification of an element is based on the known concentration of an internal standard added to each sample and the known, factory-based sensitivity factors for each element calibrated for the detector. The relationship between the characteristic emission intensity of an element and its concentration is linear when the sample size is small, which is true for TXRF methods where the samples are prepared as thin films or layers. It should be noted that the use of TXRF in this manner, using an internal standard and "standardless" quantification, has been published in peer-reviewed literature and in methods promulgated by the International Standards Organization (ISO) [4, 11, 12]. In a separate study (data not shown), this method was compared to a second one based on a multipoint calibration with known levels of Hg, and gave similar results.

3. Results

3.1. ICP-MS Results

Results from ICP-MS analysis are presented in Table 1. Each result is an average of two replicates rounded to two significant figures. For the purposes of this study, these concentrations are interpreted as the "true" values for comparison to those from XRF and TXRF. It should be noted that ICP-MS methods are not necessarily more accurate and can be prone to determinate errors, including a non-representative sample, incomplete digestion, and propagation of uncertainty from sequential dilutions (dilution factors up to 1,000,000) of the samples. The limit of detection (LOD) for Hg using this method was in the low part-per-trillion range for sample extracts and ~10 parts-per-billion (ppb) in the sample (incorporating the sample masses digested and the volumes used for the initial dilution).

3.2. XRF Results

XRF should be the method of choice for rapid screening of ppm and higher levels of Hg in these products given its ability to analyze samples "as is" with analysis times in the order of a minute. XRF spectra of two of face cream products are provided in Figure 2. The presence of Hg is definitively established by the observation of two peaks at reference line energies of 9.99 (L_α) and 11.82 keV (L_β) with a relative intensity ratio (L_α:L_β) of ~1:1. Hg levels in F10C00766 are so high that additional Hg peaks are observed at 2.20 (M_α) and 13.83 (L_γ) keV. Both spectra show a broad hump in the range of ~12-34 keV which represents Bremsstrahlung (backscattered radiation from the X-ray tube source).

Accurate quantification via XRF requires preparation of a homogeneous sample and calibration of instrument response

Table 1: ICP-MS results for Hg in face creams

Sample ID	Average Hg Concentration	Relative Standard Deviation
F10C00693	5.6%	7%
F10C00694	2.5 ppm	12%
F10C00763	3.8%	2%
F10C00764	3.1%	3%
F10C00765	4.0%	6%
F10C00772	2.8%	7%
F10C00773	2.5%	23%
F10C00774	2.0%	6%
F10C00775	2.7%	2%
F10C00776	5.7%	8%
F10C01311	1.6%	1%
F10C01312	1.6%	2%
F10C01313	0.80 ppm	26%
F10C01314	0.50 ppm	15%
F11C00559	2.1%	17%
F11C00560	3.0%	4%

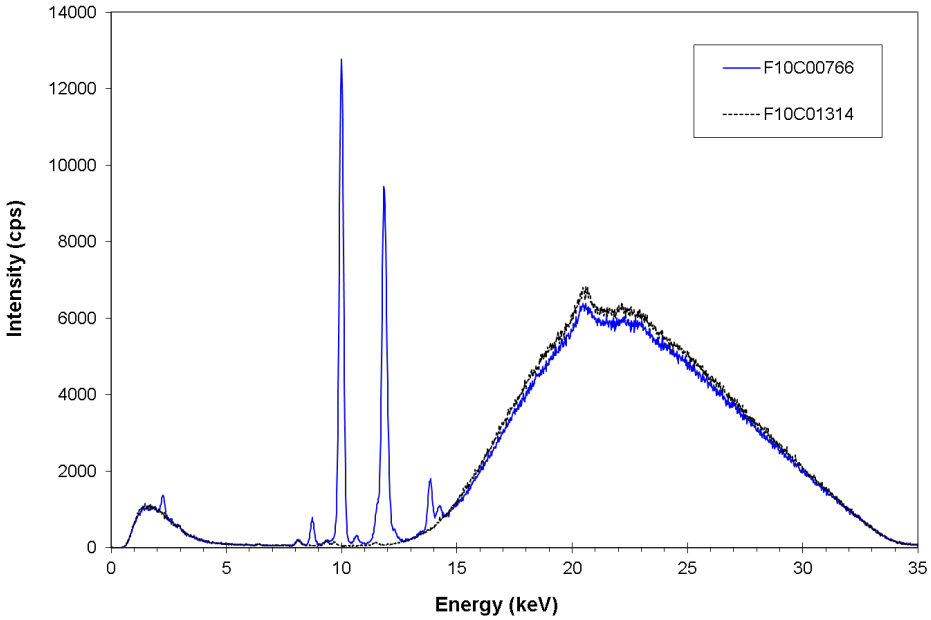

Figure 2: XRF spectra of two face cream products. The spectrum for F10C00766 shows two intense peaks at 9.99 (L_α) and11.82 (L_β) keV at an intensity ratio of 1:1, which definitively establishes the presence of Hg in this sample. The spectrum for F10C01314 does not show these peaks and non-detectable levels of Hg were found in this sample.

using appropriate and ideally matrix-matched standards. While most face cream products appeared to be fairly homogeneous, some contained visible flakes or chunks of Hg salts. It is difficult to prepare a representative sample by simple mixing of these products and hence their XRF results may be compromised. Note that none of three XRF methods involved the use of digestion to generate a more homogeneous subsample for analysis, as this obviates two of the key advantages of XRF (minimal sample preparation and fast analysis times).

The first XRF method was the simplest and fastest means

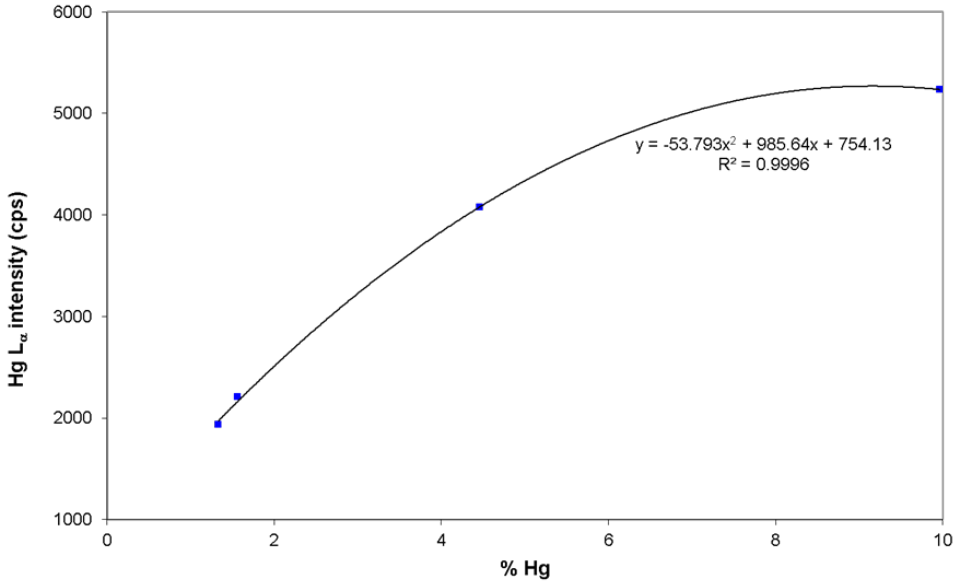

Figure 3: Calibration curve plotting Hg L_α intensity as a function of concentration for a series of standards prepared by gravimetric dilution of mercuric sulfide into a Hg-free face cream matrix

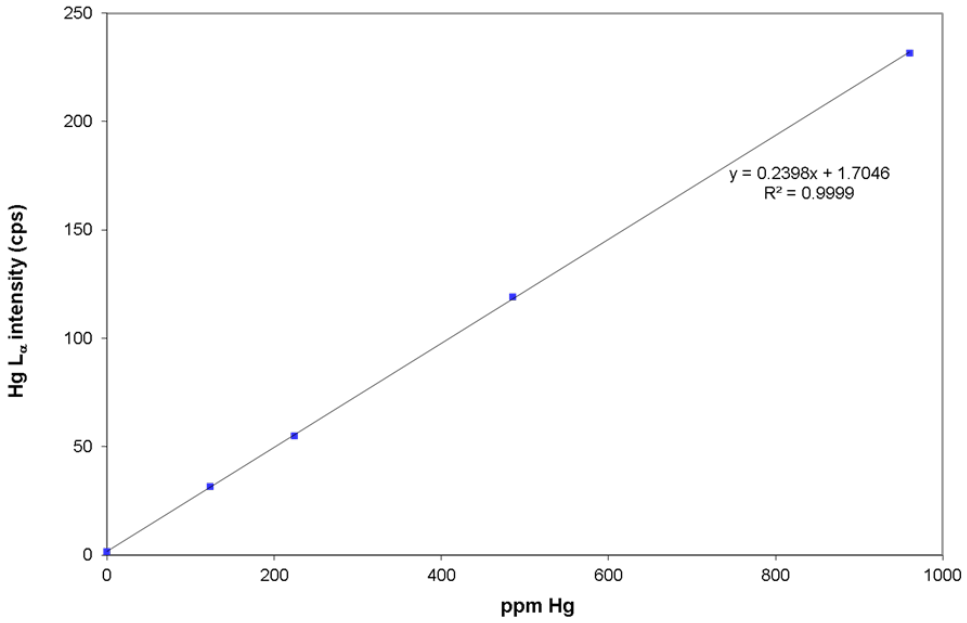

Figure 4: Calibration curve plotting Hg L_α intensity as a function of concentration for a series of standards prepared by serial gravimetric dilution of mercuric sulfide into a Hg-free face cream matrix

for determination of Hg. Calibration curves for this method are shown in Figures 3 and 4, spanning concentrations at percent and ppm levels, respectively. Figure 3 shows a nonlinear response due to self-absorption of fluorescence when Hg concentrations exceed 1 percent. Figure 4 shows a very linear response, which demonstrates the viability of the method used to prepare homogenous standards in the ppm range. The vendor of this portable XRF analyzer specifies an LOD of ~5 ppm for Hg.

These calibration curves were used to determine Hg in a subset of the original set of face cream samples shown in Table 1, as inadequate quantities of each sample remained for XRF analysis. Table 2 provides a comparison of XRF and ICP-MS results. The calibration curve shown in Figure 4 was used to quantify Hg at levels below 1000 ppm (samples F10C00694 and F10C01314), and the calibration curve shown in Figure 3 used to quantify Hg at levels above 1 percent (all other samples). Agreement between the two methods was fair, with percent errors greater than 20 percent attributed to lack of sample homogeneity (some face cream samples contained visible flakes of

Table 2: Comparison of results from determination of Hg in nine face cream samples via XRF and ICP-MS methods

Sample ID	XRF Results	ICP-MS Results	% difference vs. ICP-MS
F10C00694	ND	2.5 ppm	-
F10C00763	3.5%	3.8%	-8%
F10C00764	3.2%	3.1%	3%
F10C00765	3.3%	4.0%	-18%
F10C00766	3.7%	4.7%	-21%
F10C00773	1.7%	2.5%	-32%
F10C00774	1.2%	2.0%	-40%
F10C01314	ND	0.5 ppm	-
F11C00559	1.7%	2.1%	-19%

what appeared to be Hg salts added to these products), the difficulties in preparing standards for XRF analysis that represent the varying matrices of face cream products, and two samples whose levels were below the XRF LOD.

The second XRF method, which involved suspension of face cream in an emulsion, gave calibration curves similar to those shown in Figures 3 and 4. However, this method was not applied to the same samples because inadequate quantities were available. This method may be superior to the first method, since samples can be diluted into the linear region of the calibration curve for more accurate quantification. Moreover, diluting the samples into Carbomer should reduce matrix effects caused by differences in the composition of the samples and standards. The third XRF method involving suspension of face cream in a surfactant provided a calibration curve similar to that shown in Figure 4. This method gave XRF results with concentrations that were up to two times higher than those from ICP-MS. This large bias can be attributed to the presence of small flakes of Hg minerals in the diluted samples, which settled to the bottom of the XRF sample cup and enhanced response. Obviously, this method is inappropriate for preparing non-homogeneous face cream products containing solid Hg salts.

3.3. TXRF Results

As with XRF and ICP-MS, accurate quantification via TXRF requires preparation of a homogeneous sample for analysis. But with TXRF, preparation of a representative sample is even more critical, given that the amount of sample extract deposited onto a quartz disc for analysis is on the order of a few μL. Once the samples are prepared, quantification was accomplished using the sensitivity curves and an internal standard as described in the methods section. The LOD for Hg via this method was in the low ppb range for sample extracts and ~400 ppm in the sample (incorporating the 0.5 g sample mass, 100 mL digestion volume, 200-fold dilution as described in the methods section).

The first TXRF method, direct analysis, involved the least amount of sample preparation but gave poor reproducibility due to the heterogeneity of the samples as well as to the relatively small amount of sample (10 μg) used. The second method, involving suspension in a surfactant, gave better reproducibility. The third method, involving microwave digestion of the sample, gave the best reproducibility. This is illustrated in Table 3, which shows TXRF results from replicate analyses of a subset of the original set of face cream samples via this method, as inadequate quantities of each sample were available.

4. Discussion

The face creams sampled in this study had very different compositions, ranging from uniformly colored homogeneous creams to suspensions of multicolored solids, liquids, and oils. As noted earlier, this poses a significant challenge for method development, which requires preparation of a homogeneous sample for analysis.

Direct analysis via XRF (XRF method one) provides the simplest, cheapest, and fastest means for screening for the presence of Hg in these products [16, 17]. Samples can be analyzed "as is" with results available in a minute or less. Visual evaluation of the XRF spectrum can definitively establish the presence of Hg through observation of two peaks at the reference line energies of 9.99 (L_α) and 11.82 keV (L_β) with a relative intensity ratio of ~1:1 (L_α:L_β). Used in this manner, XRF can be used to screen 60 or more samples per hour and rapidly identify contaminated products. This method has an LOD in the order of 5 ppm, which is just above the 1 ppm regulatory limit. While this method is still undergoing validation for wider use in regulatory settings, these results indicate that XRF can give fairly accurate quantification of Hg in homogeneous samples (see Table 2). However, these same methods may not give accurate and reproducible results for non-homogenous face cream samples or for face creams that have matrices that are significantly different from that of the standards.

Microwave digestion followed by TXRF (TXRF method three) represents a less expensive and better alternative to ICP-MS for accurate quantification of Hg in these samples and provided the best reproducibility (see Table 3). Although both methods involve microwave digestion, the dilution factors involved in TXRF are smaller and the lower limits of detection

Table 3: Comparison of results from determination of Hg in face cream samples via TXRF method 3 and ICP-MS

Sample ID	TXRF Results	ICP-MS Results	% difference vs. ICP-MS
F10C00693	4.1%	5.6%	-31%
F10C00693 rep	4.4%	5.6%	-24%
F10C00694	ND	2.8 ppm	-
F10C00763	4.0%	3.8%	5%
F10C00764	3.9%	3.1%	23%
F10C00765	4.2%	4.0%	5%
F10C00774	2.2%	2.0%	10%
F10C00775	3.2%	2.7%	17%
F10C01311	2.0%	1.5%	29%
F10C01312	2.0%	1.6%	22%
F10C01314	ND	0.5 ppm	-
F11C00559	2.2%	2.1%	5%
F11C00560	3.3%	3.0%	10%

on the ICP-MS instrument are not necessary, particularly for samples containing percent levels of Hg. This TXRF method gives LODs on the order of 400 ppm in the priginal samples as described in the methods section. TXRF results compare quite well with those from ICP-MS for most of the samples but some show significant differences (F10C00693, F10C00764, F10C01311, F10C01312), most likely due to the heterogeneous nature of these particular samples. TXRF results also require care in the preparation of a homogenous subsample for analysis, especially given the fact that only a very small (7 μL) aliquot is placed on a quartz disc for analysis. TXRF offers significant advantages for quantification, since the analysis of a thin film on a quartz disc reduces matrix effects and enables "standardless" quantification based on a factory calibration and the use of an internal standard.

Although ICP-MS is often the method of choice for trace elemental analysis in many regulatory labs, it should not be considered as the method of choice for this application for a number of reasons. The method is time consuming with respect to sample preparation and analysis, involves expensive equipment, and requires significant operator expertise. Complete digestion of the sample is critical to ensure that all forms of Hg in the sample are dissolved (nitric acid alone will not completely dissolve HgS), and Hg can be readily volatilized through the production of excessive heat after adding acid(s) to the sample. Low levels of Hg can adhere onto surfaces, and hence the addition of hydrochloric acid is needed to stabilize low levels of Hg. Dilution factors as large as 1,000,000 are needed to dilute Hg from percent levels into the low ppb calibration range of the ICP-MS standards. These large dilution factors contribute to poor precision and accuracy. Moreover, inadvertent analysis of samples containing percent of Hg via ICP-MS may contaminate trace level analysis equipment (i.e., digestion vessels, autosampler tubing, and the ICP-MS instrument), leading to down time and costly replacement and cleaning. It should be noted that even ICP-MS results may not be adequately representative of these samples given their heterogeneity. The data shown in Tables 2 and 4 suggest that the low ppm levels of Hg via ICP-MS for samples F10C00694 and F10C01314 are incorrect compared to XRF and TXRF results, which show non-detectable levels of Hg in these samples. These low levels of Hg from ICP-MS may be due to cross contamination or carryover.

5. Conclusions

Despite the attention that numerous consumer advocacy groups, regulatory agencies, and publications have brought to this problem [5, 6, 7, 8, 9, 10, 13, 18], Hg-containing face creams continue to be distributed and sold around the world, including the U.S. Clearly, the development of new methods such as the one proposed here are needed to facilitate rapid identification of contaminated products and determine their elemental composition [16].

While most laboratories rely on the more common atomic spectrometry and ICP-MS methods for this application, both XRF and TXRF represent viable alternatives, as shown in this study. For screening purposes, portable XRF should be the method of choice, as it can detect Hg levels down to 1-10 ppm levels in a measurement that requires minimal sample preparation and analysis times on the order of one minute. Use of a new method typically requires validation prior to use in a regulatory setting. However, in the "bigger picture" one should consider whether an XRF analysis of a nonhomogeneous face cream product that shows 1 percent Hg and a relative uncertainty of 20 percent or more is adequate evidence to demonstrate that these levels are 10,000 times higher than the 1 ppm FDA regulatory limit, and whether this is enough information

to initiate a regulatory response such as detention and/or an import alert.

If accurate quantification of Hg in face cream products is required as part of the data quality objectives, TXRF is a faster and less expensive alternative to ICP-MS. Although both of these methods require preparation and digestion of a homogenous subsample for analysis, ICP-MS is more complex and expensive, requires dilution of sample extracts on the order of one million, and risks the possibility of inadvertent contamination of equipment commonly used for trace and ultra-trace level analysis.

The results of this study show that XRF and TXRF methods give comparable results to ICP-MS and can be used for both screening and accurate quantitative analysis of Hg in face cream products. In the future, it is hoped that these methods will see more widespread use to monitor face cream products and that regulatory agencies will use them to target those products, remove them from commerce, and protect the public health.

6. Declaration of Conflicting Interest

The authors declare that there is no conflict of interest.

7. Disclaimer

The views expressed here are those of the authors and should not be construed to represent the views or policies of the FDA. Any reference to a specific commercial product, manufacturer, or otherwise is for the information and convenience of the public and does not constitute an endorsement, recommendation, of favoring by the FDA.

8. Article Information

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