Lead Relative Bioavailability in Lip Products and Their Potential Health Risk to Women

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Supported Information

ABSTRACT: Recent studies have investigated lead (Pb) concentrations in lip products but little is known about its oral bioavailability. In this study, 75 lipsticks and 18 lip glosses were assessed for Pb concentration, while 15 samples were assessed for Pb relative bioavailability (RBA, relative to Pb acetate absorption) using a mouse femur assay. Lead concentrations were 0.2−10 185 mg kg$^{-1}$, with 21 samples exceeding the Chinese limit of 40 mg kg$^{-1}$. Samples with orange and pink colors and/or low cost contained higher Pb concentrations. For samples with Pb > 7500 mg kg$^{-1}$, Pb was present due to the addition of lead chromate (PbCrO$_4$) as a colorant, which was confirmed by X-ray absorption near-edge structure analysis. Lead-RBA in 15 samples (87−10 185 mg kg$^{-1}$) ranged from 23% to 95%, being significantly higher in moderate Pb (56−95%; 87−300 mg kg$^{-1}$) than high Pb samples (23−48%; >300 mg kg$^{-1}$). The calculation of Pb intake based on Pb-RBA showed that lip product ingestion contributed 5.4−68% of the aggregate Pb exposure for women depending on Pb concentration. The high Pb concentration in some lip products together with their moderate Pb-RBA suggests that lip product ingestion is a potential health concern to women.

INTRODUCTION

Lead (Pb) exposure is a common environmental hazard to humans and is of great concern worldwide. Exposure to Pb causes loss of appetite, and anemia and sometimes leads to permanent brain damage or even death.$^{1,2}$ Pregnant women and young children are particularly vulnerable to Pb exposure. It has been demonstrated that women’s blood Pb levels (BLLs) rise during pregnancy and lactation due to increased bone turnover, which releases stored skeletal Pb.$^{3}$ Gulson et al.$^{4}$ reported a 20% increase in BLLs during pregnancy in women with BLLs at 3 μg dL$^{-1}$. In addition to being remobilized during pregnancy, maternal skeletal Pb may be transported across the placenta and enter fetal circulation.$^{5}$ Increased fetal Pb exposure has been linked with elevated incidences of low birth weight, miscarriages, and even fetal death.$^{6,7}$ The risks of maternal Pb exposure to fetal health warrants study of Pb exposure for women of childbearing age.

Lead exposure is complicated as it occurs from both dietary and nondietary pathways.$^{8}$ Food is the primary ingestion source of Pb exposure for the general population.$^{9}$ However, exposure from nondietary sources such as incidental ingestion of Pb-containing products may constitute a significant source. An important nondietary Pb exposure pathway for women is mouthing or ingestion of lip products such as lipsticks and lip glosses.$^{10,11}$ Since different pigments have been used to produce specific colors in paints, it is likely that Pb may be added to lip products.$^{12}$ Although a small amount of lip product is applied each time (~10 mg), the number of daily applications may vary depending on the type of lip product and the habit of users. According to Loretz et al.$^{13}$ the average number of applications among 311 women from the USA who regularly use lipsticks was 2.4; however, this may vary significantly (up to 20) with individual circumstances. It has been estimated that a woman may ingest ∼1.8 kg of lipstick inadvertently over a lifetime,$^{14}$ which represents a significant Pb exposure pathway depending on Pb concentration in lip products as well as oral Pb bioavailability (e.g., Pb fraction absorbed across gastrointestinal barrier following ingestion).

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In recent years, Pb contamination in lip products has gained increasing attention. In 2007, Campaign for Safe Cosmetics measured Pb concentrations in 33 brands of lipsticks manufactured in the USA, with Pb being detected in 61% of products with the highest concentration of 0.7 mg kg\(^{-1}\). On the basis of microwave-assisted digestion, Hepp et al. reported Pb concentrations of 0.1–3.1 mg kg\(^{-1}\) in 20 lipsticks from the USA. A subsequent extensive survey of 400 lipsticks completely dissolved lip products due to the high wax and grease contents. Therefore, exposure assessment based on total Pb absorbed into the bloodstream due to bioavailability conservative approach, conceivably, not all Pb in lip products is ingested. Reliable estimates of Pb exposure and health risks associated with oral ingestion of lip products depend on the quantification of Pb bioavailability using in vivo assays.

Therefore, the objective of this study was to (1) examine total metal concentrations including Pb in 93 lip products, (2) determine Pb relative bioavailability (RBA), relative to absorption of Pb acetate) in lip products using a mouse femur assay, and (3) assess the potential health risks of Pb in lip products to women based on Pb-RBA. Accurate assessment of Pb-RBA is an important step to understand the potential health risks of Pb in lip products to women via oral ingestion.

### MATERIALS AND METHODS

#### Sample Collection and Preparation

A total of 93 lip products, including 75 lipsticks and 18 lip glosses, were purchased from retail stores or via the Internet in China. Lip products included popular brands and colors (orange, pink, brown, red, purple, green, and white), varying in price (0.7–29 USD). Detailed information about lip products is provided in Table S1. Samples were stored at 4 °C until analyzed. The total concentrations of 7 metals (Co, Cd, As, Ni, Cr, Zn, and Pb) in lip products were determined using inductively coupled plasma mass spectrometry (ICP-MS, NexION300X, PerkinElmer, USA) following digestion of lip products (0.1 g) with repeated additions of concentrated HNO\(_3\) and H\(_2\)O\(_2\) based on USEPA Method 3050B. Although the HNO\(_3\)/H\(_2\)O\(_2\) method could not completely dissolve lip products due to the high wax and grease content, preliminary work suggested that Pb concentrations in lipsticks and lip glosses determined following the HNO\(_3\)/H\(_2\)O\(_2\) digestion protocol were in good agreement with data derived using a microwave-assisted HNO\(_3\)/HF method (Figure S1). Moreover, the HNO\(_3\)/H\(_2\)O\(_2\) digestion method has been widely used for lipstick analysis.

To better understand the source of Pb in lip products, typical raw materials that are commonly used to produce lip products including wax (n = 5), grease (n = 5), and pigments (n = 22) were purchased from the Internet and analyzed for Pb concentrations using ICP-MS following digestion with HNO\(_3\) and H\(_2\)O\(_2\). Waxes included beeswax, carnauba wax, cera alba, cera flava, and osmanthus wax; greases included castor oil, jojoba oil, coconut oil, palm oil, and olive oil while pigments having orange, red, pink, purple, and brown colors were purchased.

#### Assessment of Pb Relative Bioavailability

In this study, an in vivo mouse assay, utilizing Pb accumulation in femur as the biomarker of Pb exposure was used to measure Pb-RBA in lip products. Fifteen lip products with Pb concentrations ranging from 1 to 165 mg kg\(^{-1}\) were assessed for Pb-RBA using female Balb/c mice with body weights of 18–20 g. Following acclimation for 1 week under standard animal housing conditions (12 h light/dark cycle, 25 °C, and 50% humidity) with free access to Milli-Q water and a rodent basal diet, mice were fasted overnight, weighed, and randomly transferred to individual polyethylene cages prior to exposure.

Lead acetate and lip products were supplied to mice in amended diets. Initially, mouse basal feed was freeze-dried, ground to a powder, and then homogenized using a food processor. Lead acetate solution was thoroughly mixed with mouse feed to achieve three Pb concentrations (5, 50, and 80 mg Pb kg\(^{-1}\) dw). Lip products (~1 g) were thoroughly mixed with mouse feed powder at a ratio of 1:100 by grinding with a mortar and pestle. Milli-Q water was then added to the mixture of feed-lip product, which was made into a paste by kneading. The amended-feed was evenly divided into 21 portions after which it was pelleted and freeze-dried. A preliminary study that randomly selected pellets from a given amended-feed sample showed a relative standard deviation of <5% in Pb concentration, indicating thorough mixing of Pb acetate or lip products with the feed.

For Pb exposure, amended-feed (~5 g dw) was supplied to individually caged mice at 9:00 am every day. For each lip product and Pb acetate dose level, 5 separately caged mice were used as a group. At the end of a 7 d exposure period, remaining feed was removed from cages and weighed with food consumption calculated as the difference between food supplied and remaining. During the course of the experiment, mice had access to Milli-Q water ad libitum. The 7 d exposure period was selected as it was previously demonstrated that Pb accumulation in animals reaches a near steady state within 7–10 d.\(^{26}\)
At the end of the exposure, mice were fasted overnight and then sacrificed to collect femur samples by dissecting the hind limbs from the trunk of the body and through the knee joint. This end point has been used as a biomarker of Pb exposure in animals.26 Femur samples were immediately steamed to facilitate the removal of muscle and connective tissue from the bone. After removal of tissue, the bone was freeze-dried and then analyzed for Pb concentration using ICP-MS following digestion using concentrated HNO3 and H2O2 (USEPA Method 3050B). Following zero correction, a linear dose response curve (DRC) of Pb concentration in femur was established for Pb acetate exposed mice (Figure S2). Lead-RBA in lip products was calculated as the ratio of dose normalized Pb concentration in femur after lip product exposure to the slope of the corresponding DRC for Pb acetate (eq 1).

\[
Pb \text{ relative bioavailability (\%)} = \frac{\text{femur Pb after lip product exposure}}{\text{Pb dose level via lip product} \times \text{slope of DRC}_{\text{lead acetate}}} \times 100
\]  

(1)

**Spectroscopic Assessment of Lip Products.** To identify sources of Pb in lip products, two samples (#92 and #93) with the highest Pb concentration (7781 and 10 185 mg kg\(^{-1}\), respectively) were analyzed by X-ray absorption near-edge structure (XANES) spectroscopy at the Pb LIII-edge. XAS data were collected at the Materials Research Collaborative Access Team beamline 10-ID, Sector 10, at the Advanced Photon Source of the Argonne National Laboratory, United States. Detailed spectroscopic analysis is provided in the Supporting Information.

**Human Health Risk Assessment.** Assuming an ingestion rate (IR) of 24 mg d\(^{-1}\) for a young Asian woman with body weight (BW) of 50 kg,\(^{10}\) daily Pb intake (DI\(_{\text{total}}\) and DI\(_{\text{bioavailable}}\)) \(\mu g \text{ Pb kg}^{-1} \text{ bw d}^{-1}\) via lip product ingestion was calculated on the basis of total Pb concentration (\(C, \text{mg kg}^{-1}\)) and measured Pb-RBA (%) for the 15 lip products that were subjected to bioavailability assays as follows (eqs 2 and 3):

\[
DI_{\text{total}} = \frac{C \times IR}{BW}
\]  

(2)

\[
DI_{\text{bioavailable}} = \frac{C \times IR \times RBA}{BW}
\]  

(3)

The calculated daily Pb intake values were compared to the provisional tolerable daily intake (PTDI) of 3.5 \(\mu g \text{ kg}^{-1} \text{ bw d}^{-1}\) to assess the potential risks of lipstick ingestion by women.27 In addition, the contribution of lip product ingestion to aggregate Pb intake (considering Pb intake through dietary, ingestion of soil and dust, and inhalation of air) was assessed to quantify lip product ingestion to overall Pb exposure. Calculation of Pb exposure from dietary, soil, and air pathways is provided in the Supporting Information.

**QA/QC and Data Processing.** During digestion of the lip products using the USEPA 3050B, a cosmetics cream standard reference material (SRM) GBW09305 from the Chinese National Standard Reference Center was included. Although the matrix of the SRM was not lipstick or lip gloss, its similarity in composition with lip products made it suitable as a SRM for QA/QC. The accuracy of the HNO\(_3\)/H\(_2\)O\(_2\) digestion method was confirmed by an average Pb recovery of 34.2 \(\pm 0.4 \text{ mg kg}^{-1}\) \((n = 3)\) from GBW09305 (37.2 mg kg\(^{-1}\)). During measurement of Pb concentrations in digests of lip products and mouse femurs using ICP-MS, spiked and check samples (1–10 \(\mu g \text{ Pb L}^{-1}\)) were included every 20 samples. The spike and check recoveries \((n = 30)\) were 101 \(\pm 6.5\%\) and 99 \(\pm 8.3\%\) respectively.

Lead concentration and Pb-RBA results were expressed as the mean and standard deviation of 3 replicates. All graphs were performed using SigmaPlot (version 12.5, Systat Software Inc., San Jose, CA, USA). One-way ANOVA was used to determine the significant differences in concentration of different metals in lip products, Pb concentration in different raw materials, and Pb-RBA between different lip products using SAS (version 9.1.3 for Windows).

**RESULTS AND DISCUSSION**

**Pb Concentrations and Sources in Lip Products.** Due to daily exposure via ingestion, Pb in lip products has been receiving increasing attention. To determine whether lip products on the market in China are a source of Pb exposure, 93 lip product samples, varying in color and price, were purchased from retail stores or via the Internet. These samples were divided into two types, e.g., lipsticks \((n = 75)\) and lip glosses \((n = 18)\). Lead was detected in all samples, ranging from 0.2 to 10 185 mg kg\(^{-1}\), averaging 497 mg kg\(^{-1}\) (Figure 1). All lip products tested in this study exceeded the US FDA acceptable limit of 0.1 mg Pb kg\(^{-1}\) in candy, which is likely to be consumed frequently by children.19 Twenty-one out of the 93 samples (23\%) contained Pb concentrations exceeding the FDA and Chinese limits of 20 and 40 mg Pb kg\(^{-1}\), respectively, in color additives for cosmetics.18,28 Nine products had Pb concentrations >1000 mg kg\(^{-1}\), with the highest being 10 185 mg kg\(^{-1}\). Compared to those of other metals in the lip products (Co, Cd, As, Ni, and Cr), Pb concentrations were significantly higher (Figure S3), suggesting Pb in lip products is of potential health concern.

Type, color, and price are important factors influencing Pb concentration in lip products. With respect to type, 11 out of 75 lipstick samples (15\%) contained Pb > 40 mg kg\(^{-1}\) compared to 10 out of 18 (56\%) lip gloss samples (Figure 2A). On the basis of color, orange and pink products contained higher Pb concentrations than brown, red, and purple products (Figure 2B). Five out of 10 orange products (50\%) contained >1000 mg kg\(^{-1}\) while 13 out of 37 pink products (35\%) contained Pb > 40 mg kg\(^{-1}\). On the other hand, only 1 out of 10 brown (10\%) and 2 out of 26 red products (8\%) had Pb >

![Figure 1](image-url)
40 mg kg\(^{-1}\), while Pb concentrations in 6 purple products were below the FDA limit of 20 mg kg\(^{-1}\) (Figure 2B). In addition to lip product type and color, Pb concentration in lip products tended to decrease with increasing price (Figure 2C). All lip products with Pb >40 mg kg\(^{-1}\) were <5 USD, while Pb concentrations in samples costing >5 USD were below 20 mg Pb kg\(^{-1}\).

Previous studies have assessed Pb concentrations in lip products from Europe and US, showing significantly lower Pb concentrations than this study. Piccinini et al.\(^{26}\) reported Pb concentrations of 0.1–3.8 mg kg\(^{-1}\) for 223 lip products from 15 European countries, but showing higher Pb concentration in lipsticks (average 0.8 mg kg\(^{-1}\)) than in lip glosses (0.4 mg kg\(^{-1}\)). Similarly, more expensive lipsticks had lower Pb concentrations. Hepp\(^{17}\) reported the average Pb concentration in 400 lipsticks on the USA market was 1.1 mg kg\(^{-1}\). However, high Pb concentrations (2028–3760 mg kg\(^{-1}\)) were observed in 3 brands of lipstick sold in Saudi markets.\(^{18}\) Similarly, a high Pb concentration (1154 mg kg\(^{-1}\)) was observed for one lipstick in Iran.\(^{20}\) However, lip products from the USA, Italy, and France did not show Pb concentrations above the FDA limit of 20 mg kg\(^{-1}\). Pb preferentially accumulates in bone compared to other organs/tissue during long-term exposure.\(^{32}\) Preliminary studies demonstrated that Pb accumulation in mouse femur following Pb acetate exposure was linearly dose dependent (Figure S2), confirming our speculation that Pb chromate was added to lip products.

Pb Relative Bioavailability in Lip Products. Reliable assessment of Pb exposure to women depends not only on total Pb concentration but also on Pb bioavailability in lip products. To date, reports of Pb-RBA in lip products are lacking, although one study showed an increase in blood Pb concentration following oral daily gavage of a lipstick sample (19 mg kg\(^{-1}\) Pb) to rats for 12 weeks.\(^{20}\) To accurately quantify Pb exposure following ingestion of lip products, a mouse bioassay was conducted to determine Pb-RBA in 15 lip products (8 lip glosses and 7 lipsticks) with Pb concentrations ranging from 87 to 10 185 mg kg\(^{-1}\) Pb. Low Pb lip products (<40 mg kg\(^{-1}\)) were not selected as it was difficult to accurately quantify Pb accumulation in mice at these concentrations. Mouse femur was used as the biomarker of Pb exposure, since Pb preferentially accumulates in bone compared to other organs/tissue during long-term exposure.\(^{32}\) Preliminary studies demonstrated that Pb accumulation in mouse femur following Pb acetate exposure was linearly dose dependent (Figure S2), confirming the suitability of using Pb-femur accumulation following 7 d exposure to measure Pb-RBA in lip products.

In this study, lip products with Pb concentrations of <40 mg kg\(^{-1}\) Pb (Chinese limits) were considered as having low Pb levels, whereas 40–300 mg kg\(^{-1}\) Pb was moderate and >300 mg kg\(^{-1}\) was high. On the basis of femur as the biomarker of Pb exposure, Pb-RBA varied greatly from 23 ± 2.5 (#82) to 95 ± 9.8% (#73), averaging 45% (Figure 5). Lead-RBA (56–95%) was significantly higher for products #73–77 having moderate Pb concentration (87–299 mg kg\(^{-1}\)) compared to 23–48% for products #78–93 having high Pb concentrations (325–10 185 mg kg\(^{-1}\)). For the two lip products (#73 and #75) with the lowest Pb concentrations (87 and 124 mg kg\(^{-1}\)) among the 15 samples, Pb-RBA was the highest (95 ± 9.8% and 70 ± 6.9%),

**Figure 2.** Variation in Pb concentration with lip product type (A), color (B), and price (C). Boxes represent the 25th to 75th percentiles while solid and dashed lines in boxes denote the median and mean values, respectively. Error bars represent the 5th and 95th percentiles, and x signs represent the 1st and 99th percentiles, respectively.

**Figure 3.** Lead concentrations in raw materials of lip products including pigments, grease, and wax (A) and variation in Pb concentration with different pigment colors (B).
While significantly lower Pb-RBA values (34 ± 0.1% and 31 ± 7.1%) were observed for products #92 and #93 with the highest Pb concentrations (7781 and 10 185 mg kg⁻¹). Excluding the significantly higher Pb-RBA for moderate-Pb lip products (#73−77), Pb-RBA showed little variation with Pb concentration and there was no significant difference (p > 0.05) between lip gloss and lipstick, averaging ~40% (Figure 5).

The significantly higher Pb-RBA values for moderate-Pb lip products compared to high-Pb products may be due to the addition of different Pb minerals to moderate-Pb lip products, which are more bioavailable than PbCrO₄. Although XANES analysis was not undertaken for lip products #73 and #75, their molar ratios of Pb to Cr (0.72−0.76) were <1 (Figure S4B), suggesting that Pb in the moderate-Pb samples was not present as PbCrO₄. Other Pb minerals, such as oxides or carbonate, with higher Pb solubility in gastrointestinal fluid compared to PbCrO₄ (67−73% vs. 9%) were presumably used in these two products, thereby leading to higher Pb-RBA. For future studies, analysis of Pb speciation in moderate-Pb samples

![Figure 4](image)

**Figure 4.** Normalized XANES spectra (a) and corresponding derivatives (b) for two lip product samples #92 and #93 with Pb concentration of 7781 and 10 185 mg kg⁻¹ and Pb chromate (PbCrO₄).

![Figure 5](image)

**Figure 5.** Lead relative bioavailability in 15 lip products (8 lip gloss and 7 lipstick samples) determined using mouse femur as a biomarker after 7 d of lip product exposure via diet. For samples #73−93, total Pb concentration increased from 87 to 10 185 mg kg⁻¹. Bars represent the mean and standard deviation of three replicates.

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<th>bioavailable Pb (mg kg⁻¹)</th>
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<th>contribution of lip product ingestion to aggregate Pb exposure (%)</th>
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Table 1. Estimated Daily Pb Intake Values for Women with Body Weight of 50 kg and Lip Product Ingestion Rate of 24 mg d⁻¹ Based on Total Pb and Bioavailable Pb in 15 Lip Products

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**Table 1. Estimated Daily Pb Intake Values for Women with Body Weight of 50 kg and Lip Product Ingestion Rate of 24 mg d⁻¹ Based on Total Pb and Bioavailable Pb in 15 Lip Products**

- Bioavailable Pb was the product of total Pb concentration and Pb relative bioavailability.
- Based on total Pb concentration in the lip products.
- Based on bioavailable Pb concentration in the lip products.
- Based on total Pb in both lip product and other exposure pathways, which is described in Table S3. **Bold values indicate the estimated daily Pb intake exceeding the PTDI of 3.5 μg kg⁻¹ bw d⁻¹.**
should be undertaken to explain the variability in Pb-RBA among lip products.

Implications for Refining Risk Assessment for Women Using Lip Products. When assessing Pb exposure via the ingestion of lip products, previous studies rarely considered Pb bioavailability. In this study, we found that extremely high Pb concentrations in some lip products (e.g., 10.185 mg kg\(^{-1}\)) were due to the addition of PbCrO\(_4\) as a colorant (Figure 4). The high Pb concentrations together with moderate Pb-RBA (~40%, Figure 5) make lip products an important Pb exposure source for women using these products for adornment purposes.

To quantify the contribution of Pb intake via lip products to aggregate Pb exposure, we calculated daily Pb intake for women through oral ingestion of lip products based on total and bioavailable Pb values. Only the 15 lip products that measured Pb-RBA were included in the analysis. On the basis of total Pb concentration, daily Pb intake via the 15 lip products ranged from 0.04 to 4.9 μg kg\(^{-1}\) bw d\(^{-1}\) for a woman with body weight of 50 kg and lip product ingestion rate of 24 mg d\(^{-1}\) (Table 1).

Oral ingestion of the three lip products with Pb concentrations >7000 mg kg\(^{-1}\) led to daily Pb intake close to or exceeding the provisional tolerable daily Pb intake (PTDI) value of 3.5 μg kg\(^{-1}\) bw d\(^{-1}\). However, with the inclusion of Pb-RBA, daily Pb intake values were significantly reduced to 0.04–1.5 μg kg\(^{-1}\) bw d\(^{-1}\), with all values below the PTDI value. However, for a high rate of lip product ingestion (above the 95th percentile; 87 mg d\(^{-1}\)), ingestion of some lip products (e.g., #93) may lead to Pb intake (5.31 μg kg\(^{-1}\) bw d\(^{-1}\)) exceeding the PTDI value even when Pb-RBA was incorporated into calculations. This Pb exposure scenario may potentially occur considering that some women may be required to wear lipstick or lip gloss as a condition of employment resulting in a higher number of applications per day compared to the general public.

Ingestion of lip products is not the only Pb exposure pathway for women. Lead may enter human body through inhalation of air particulates, oral ingestion of soil and dust, and consumption of water and food (e.g., rice, vegetables, and meat). Therefore, it is necessary to assess the relative contribution of lip product ingestion to aggregate Pb exposure. Tables S2 and S3 show the calculation of Pb intake through these pathways, with the assumption that Pb concentrations in these media were equivalent to Pb guideline values based on Chinese environmental and food standards. Ingestion or inhalation rates for these media were adopted from Li et al. and Chen et al., while Pb bioavailability was set as 50%, 10%, 10%, and 50% for inhalation, food consumption, drinking water, and soil ingestion.

On the basis of total Pb in lip products and other media, oral ingestion of lip product #73 (87 mg Pb kg\(^{-1}\)) contributed little (1.0%) to overall Pb exposure, whereas 56% of aggregate Pb exposure came from sample #93 (10.185 mg Pb kg\(^{-1}\)) when ingested (Table 1). When taking Pb bioavailability into consideration for Pb exposure via lip product and other pathways, Pb contribution from lip products increased compared to calculations based solely on total Pb concentration due to higher Pb bioavailability in lip products than the default values for other Pb sources. Approximately 5% of aggregate Pb intake resulted from the ingestion of lip product #73, while the contribution of lip product Pb to overall Pb exposure reached 68% when lip product #93 (10.185 mg Pb kg\(^{-1}\)) was used. In general, oral ingestion of lip products with Pb concentrations >1800 mg kg\(^{-1}\) may lead to a contribution of >30% to aggregate Pb exposure, while ingestion of samples with Pb < 500 mg kg\(^{-1}\) contributed <10%.

In addition, the health risk of Pb exposure to lip products for women of childbearing age is of particular concern, as researchers have shown that Pb previously accumulated in the mother’s bones from past Pb exposure may be released into the bloodstream during pregnancy. Released Pb may pass through the placenta or be present in mother’s milk, thereby impacting the fetus or infant’s developments. It was recently reported that the Pb maternal to fetal transfer ratio may be as high as 0.85. Therefore, excessive Pb intake via lip products for pregnant women or women prior to conception may subject the fetus and infant to elevated Pb exposure. Assuming that a female uses lip products containing an average Pb concentration of 497 mg kg\(^{-1}\) (the average value of samples tested in this study) and Pb-RBA of 40% from the age of 12 (with an average daily ingestion of 24 mg) and is pregnant at the age of 25, a total of 22.6 mg of Pb will be absorbed from lip products prior to pregnancy. The accumulated Pb via lip product ingestion represents a source for remobilization, which has the potential to impact the fetus or infant’s developments.

Moreover, using XANES analysis, PbCrO\(_4\) was identified as the dominant Pb specie in lip products with high Pb concentrations. Hexavalent Cr (Cr\(^{VI}\)) is a well-recognized carcinogen. Presumably, when PbCrO\(_4\) in lip products was solubilized in the gastrointestinal tract, Cr\(^{VI}\) may be available for absorption into the systemic circulation, posing an additional health risk. In this study, although Cr bioavailability was not determined, total Cr concentration in the 93 lip products ranged from 0.5 to 2736 mg kg\(^{-1}\) (Figure S4A). On the basis of total concentration, daily Cr intake via lip products ranged from 0.01 to 65.7 μg d\(^{-1}\) for a woman with a lip product ingestion rate of 24 mg d\(^{-1}\). Ingestion of lip products containing Cr >1000 mg kg\(^{-1}\) would cause daily Cr intake exceeding the recommended daily Cr intake of 25 μg d\(^{-1}\) for women. Since Cr bioavailability in lip products was not performed, calculated daily intake values may represent a worst-case scenario. However, Cr intake and bioavailability assessment from the use of lip products may warrant further investigation.

ASSOCIATED CONTENT

Supporting Information
The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.6b01425.

Descriptions of types, colors, and prices of the 93 lip products and estimated daily Pb intake through all exposure routes for adults (Tables S1–S3); comparison of Pb concentrations determined using HNO\(_3\)/H\(_2\)O\(_2\) and the microwave-assisted HNO\(_3\)/HF methods, linear dose response of Pb accumulation in mouse femur following Pb acetate exposure, concentration of other metals in the lip products, and molar ratio of Pb to Cr in lip products (Figures S1–S4). (PDF)

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Notes
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REFERENCES


