Potential Consumer Exposure to Respirable Particles and TiO$_2$
Due to the Use of Eyebrow Powders

Hyeon-Ju Oh, Ph.D.\textsuperscript{1}, Taewon T. Han, Ph.D.\textsuperscript{1}, Gediminas Mainelis, Ph.D.\textsuperscript{1}
\textsuperscript{1}Department of Environmental Sciences, Rutgers, The State University of New Jersey, 14 College Farm Road, New Brunswick, NJ 08901, USA

Abstract

Background—Cosmetic powders contain numerous components, including titanium dioxide (TiO$_2$), which is classified as possibly carcinogenic to humans (Group 2B). However, little is known about potential inhalation exposures to particles that are released during cosmetic powder applications.

Methods—We realistically simulated the application of five different eyebrow powders using a mannequin and then determined concentrations of total suspended particles (TSP), PM$_{10}$, and PM$_4$ fractions of particles that would be inhaled during powder application. We determined the size and shape of particles in the original powders and released particles, as well as their TiO$_2$ concentrations and Ti content of individual particles.

Results—The application of eyebrow powders resulted in the release and inhalation of airborne particles at concentrations ranging from 21.2 to 277.3 μg/m$^3$, depending on the particle fraction and the powder. The concentrations of TiO$_2$ in PM$_4$ and PM$_{10}$ samples reached 2.7 μg/m$^3$ and 9.3 μg/m$^3$, respectively. The concentration of TiO$_2$ in airborne particle fractions was proportional to the presence of TiO$_2$ in the bulk powder.

Conclusion—The application of eyebrow powders results in user exposures to respirable PM$_4$ and PM$_{10}$ particles, including those containing TiO$_2$. This information should be of interest to stakeholders concerned about inhalation exposure to TiO$_2$.

Keywords

eyebrow powders; respirable particles; inhalation exposure; titanium dioxide; PM$_4$; PM$_{10}$

INTRODUCTION

Various commercial cosmetics are widely used by consumers of different ages\textsuperscript{1–4} to improve their skin quality and appearance as well as to emphasize or deemphasize certain physical features\textsuperscript{5–7}. The global market for cosmetics is expected to reach $430$ billion by
The continuing development and expansion of commercial cosmetics have led to the incorporation of a long list of ingredients that users might come in contact with, either through dermal contact or inhalation. Thus, there is concern regarding potential health effects due to exposures to various ingredients in commercial cosmetics, especially those that have been shown to cause cytotoxicity, genotoxicity, and photo-genotoxicity in animal and in vitro studies.

The use of cosmetics powders typically results not only in dermal contact but also in particle release and potential inhalation exposure, including inhalation of respirable particles that are small enough to penetrate deep into the gas-exchange regions of the lung. However, inhalation exposure to specific powder ingredients and potential health effects have been minimally explored. TiO$_2$ is among the most frequently used powder ingredients, including as a component in loose and pressed powders as well as in eyebrow and eyeshadow products. TiO$_2$ offers high stability, photocatalysis, a high refractive index, and non-reactivity with other product ingredients throughout the product shelf life.

Also, advances in nanotechnology have led to the increased use of nanosized TiO$_2$ particles, especially particles of 60–120 nm in diameter, in sunscreens, due to their ability to block UV radiation effectively. Besides, nanosized TiO$_2$ particles are added to many commercial cosmetics to give them a white color and provide color adjustment.

However, TiO$_2$ particles are poorly soluble and known to induce pulmonary toxicity and lung cancer in a rat model. Other adverse health effects caused by exposure to TiO$_2$ have also been observed, including rhinitis, tracheitis, and pneumonia, as well as acute and chronic inflammation in a rat model. Ultrafine TiO$_2$ particles were shown to be more readily inhalable and cytotoxic compared with the same airborne mass concentration of fine TiO$_2$ particles.

The International Agency for Research on Cancer (IARC) stated that “there is sufficient evidence in experimental animals for the carcinogenicity of titanium dioxide” and that “titanium dioxide is possibly carcinogenic to humans (Group 2B)”.

The Safe Drinking Water and Toxic Enforcement Act, also known as California’s Proposition 65, effective September 2, 2011, added TiO$_2$ (airborne/unbounded particles of respirable size) to the list of chemicals known to the State of California to cause cancer, birth defects, or other reproductive harm. All these issues raise concerns regarding consumer exposures to TiO$_2$ particles, including due to the use of commercial cosmetics and the resulting negative health effects. At the same time, relatively little is known about the extent of exposures, including inhalation exposures, to TiO$_2$ when using commercial cosmetics in general or in specific product categories.

This study aims to fill this knowledge gap by investigating inhalation exposures to respirable particles, including determining exposures to TiO$_2$ in each particle fraction and analyzing the presence of TiO$_2$ within individual particles that were inhaled due to the application of different eyebrow powders. The application of powders was standardized through the use of a mannequin, and inhalation exposures were characterized in terms of inhaled total and respirable particle mass concentration and TiO$_2$ concentration. We also related the physicochemical properties of bulk powders with the properties of aerosolized and inhaled...
particles. To the best of our knowledge, this is the first investigation and characterization of inhalation exposures to respirable particles, and TiO₂ within such particles, due to the use of eyebrow powders. We expect that the results of this study will contribute to a better understanding of consumer exposures to particulate matter when using commercial cosmetics, especially for exposures to TiO₂ particles. The results should also be helpful to manufacturers, consumer advocate groups, and regulators concerned about inhalation exposures to TiO₂.

Materials and methods

Tested eyebrow powders

Five different eyebrow powders were selected based on the highest number of user comments on Amazon.com at the start of the study. The eyebrow powders and their ingredients, as provided by the manufacturers, are listed in Table S1. Three of the powders listed TiO₂ on their labels, while two others did not. Therefore, the powders were grouped into Group Tx and Group NTx, where T and NT indicate the presence or absence of TiO₂ on the label, respectively, and x is the powder number in the group. We tested all powders in the same chemical state as received, without any pretreatment or any other type of modification. A small eyeshadow brush (Wet n Wild, Los Angeles, CA) was used to apply powders to eyebrows, and a new brush was used for each application.

Experimental setup to measure and analyze “inhaled” particles

The experimental setup shown in Fig. 1 was used to determine potential inhalation exposures. In order to realistically simulate powder application and inhalation, the powders were applied to the eyebrows of a mannequin (Kanomax USA, Andover, NJ). The released particles were “inhaled” and then sampled through stainless sampling inlets installed in the mannequin’s nostrils. The mannequin used in this study features hard plastic. In order to minimize particle losses due to electrostatic effects, the stainless-steel sampling tubes extended to the back of the mannequin’s head and were then connected to the sampling/measuring instruments via conductive sampling lines and a flow splitter (TSI Inc., Shoreview, MN). In addition, we cleaned each nostril, sampling lines, the filter holders, and the cyclone with a sterile alcohol pad every application.

Three airborne fractions of released and “inhaled” particles were sampled onto filters: all particles without size preselection (total suspended particles, TSP); PM₁₀ particles (a 50% cutoff at 10 μm); and PM₄ particles (a 50% cutoff at 4 μm), which are respirable particles as defined by the Occupational Safety and Health Administration. The same particle fractions were measured by a direct-reading optical particle counter (Grimm OPC, model 1.108; Grimm Technologies Inc., Douglasville, GA), which detects airborne particles in 15 size channels, ranging from 0.3 to 20 μm, and then calculates their number and mass distribution.

We measured different inhaled particle fractions, including PM₁₀ and PM₄, for several reasons. First, the particle size fraction determines where the inhaled particles will be deposited in the respiratory system, and the deposition site is a major factor in determining...
the health effects of the particles. A preponderance of the PM$_{10}$ mass will be deposited in the upper respiratory tract, while the preponderance of the PM$_4$ particle mass will be deposited in the sensitive alveolar region, where it is capable of causing serious adverse health effects.

Second, effective September 2, 2011, TiO$_2$ was listed in California Proposition 65, which requires the State of California to publish a list of chemicals known to cause cancer, birth defects, or other reproductive harm. Specifically, the listing is for “titanium dioxide (airborne, unbound particles of respirable size),” and Prop. 65 indicates that “the listing does not cover titanium dioxide when it remains bound within a product matrix.” However, the Act does not specifically mention or define what is meant by “respirable size.” A document by the International Agency for Research on Cancer (IARC) states that “Respirable fraction is that fraction of an aerosol with an aerodynamic diameter suitable for penetration into the alveoli/gas exchange region of the lung (typically <10 μm).” On the other hand, the Occupational Safety and Health Administration (OSHA) has a specific definition for respirable particles in occupational settings, that is, particles with a 50% cutoff at 4 μm, also known as PM$_4$ particles. By measuring both PM$_{10}$ and PM$_4$ fractions and the TiO$_2$ presence in those fractions, we provide information about the exposures to airborne particles and TiO$_2$ satisfying both of the abovementioned definitions of respirable particles.

**Application procedures for eyebrow powders**

All eyebrow powders were applied to the mannequin’s right eyebrow in a way that simulated the actual product usage: the vertical distance between the powder container and the mannequin’s nostrils was approximately 12”, while the hand’s range of horizontal motion was ~8” (Fig. 1). During powder application, the brush was lightly dipped into the container to pick up the product via a light back-and-forth sweeping motion for 10 seconds, the powder was applied to the mannequin’s right eyebrow for 15 seconds, and the procedure was then repeated several times for a total duration of 5 minutes (loading of the brush plus the application time). Next, the brow was thoroughly wiped using a sterile alcohol prep pad (Thermo Fisher Scientific, Waltham, MA), allowed to dry for 2 min, and the powder applied several times for a total of 35 minutes. For comparison, an average eyeshadow application time is 3 minutes, and the average number of eyeshadow applications per day is 1.2.

Taking the application time of eyeshadows as a guide, we recognize that these application times are longer than the typical eyebrow powder application time in the real world; however, this extended application time was needed to ensure that the particle mass collected on filters was above the limit of detection and could be determined reliably. For the same reason, to collect enough PM$_4$ or PM$_{10}$ mass, the powders were applied to the right mannequin’s eyebrow only, and both PM$_4$ and PM$_{10}$ mass was collected on a filter connected to the right side nostril (Fig. 1). Since the sampling line to capture to TSP was connected to the left nostril and the powders were applied to the right eyebrow, TSP concentration might have been underestimated. However, this experimental arrangement still allowed us to measure differences in TSP concentration as a function of powder type because all powders were applied the same way.
**Measurement sequence**

A series of experiments were performed to quantify inhaled particle mass using Grimm OPC-based and filter-based measurement, their chemical composition using ICP-MS, and morphology using SEM/EDX analysis. For each of these analyses, the experimental setup remained the same; however, different cyclone filters had to be used, and there was also a difference in application time to collect sufficient particle mass for analysis. Therefore, experiments for each type of analysis was repeated, and the sequence of experiments is shown in Fig. 2.

For each product and analysis type, experiments were repeated three times. Before each measurement, the particle background concentration was measured with both a Grimm OPC for 5–10 min and a cyclone with filters, and the background data were subtracted from the Grimm OPC and filter-based data determined during powder application. Between powder applications, the tubing and connectors were purged with clean air. The room temperature and humidity were recorded before and during the application of the powders.

**Collection of PM mass fractions**

Due to experimental complexities that would have resulted in measuring PM$_{4}$ and PM$_{10}$ fractions simultaneously, these particle fractions were sampled in separate experiments, while the powders were applied using an identical protocol. When measuring PM$_{4}$ (Fig. 1a), a GK 2.69 Cyclone (Mesa Labs, Inc., Butler, NJ), loaded with a 37-mm PTFE filter (pore size 2.0 μm, SKC Inc., Eighty Four, PA) with a polymethyl pentene support ring and operated at a flowrate $Q_{PM4} = 4.2$ L/min, and a Grimm OPC operated at $Q_{GRIMM} = 1.2$ L/min were connected to the mannequin’s right nostril via a flow-splitter (TSI Inc.). To have equal airflow through both nostrils, a 25-mm filter holder (Delrin, SKC Inc.) loaded with a 2.0-μm pore size PTFE filter (SKC Inc.) and operated at $Q_{T1} = 5.4$ L/min was connected to the left nostril. The resulting total “inhalation” flow rate of 10.8 L/min (5.4 L/min per nostril) corresponds to the average human inhalation rate while sitting and performing a light activity.$^{56, 57}$

When measuring the PM$_{10}$ fraction, the GK 2.69 Cyclone was operated at $Q_{PM10} = 1.6$ L/min, and an additional filter sampler operating at $Q_{T2} = 2.6$ L/min was added to maintain the total flow rate of 5.4 L/min through the right nostril (Fig. 1b). As for PM$_{4}$ measurements, a filter operated at $Q_{T1} = 5.4$ L/min was connected to the left nostril. In both cases (Fig. 1a, b), the filter connected to the left nostril was used to determine the TSP. The flowrates through all samplers were calibrated and monitored by using mass flowmeters (TSI Inc.).

We estimated particle losses in the sampling lines due to settling using equations $8-51$, $8-52$, and $8-53^{58}$ on penetration efficiency in an inclined tube under the laminar flow condition provided in Baron and Willeke.$^{58}$ The penetration efficiencies for 4 and 10 μm particles that were captured by cyclones were 99.5 % and 92.7 %, respectively. For 20 μm particles, the penetration efficiency was 91.5%. Thus, for PM$_{4}$ and PM$_{10}$ particles (considered respirable in this study), the deposition losses were below 8%, and we considered them acceptable. The same fractional losses were experienced by all powders.
Analysis of TiO$_2$ mass concentration in bulk and collected powders

The TiO$_2$ mass concentration and a mass fraction (%) in all bulk powders and in airborne TSP, PM$_{10}$, and PM$_4$ fractions were determined using inductively coupled plasma mass spectrometry (ICP-MS, NEXION 300x-DT, PerkinElmer Inc., Shelton, CT) by an accredited analytical laboratory (RJ Lee Group, Monroeville, PA). The laboratory is certified and approved by multiple organizations, including by International Standard ISO/IEC 17025:2017 and uses rigorous QA/QC procedures, including internal and external standards, calibration blanks, quality control samples, and other accepted metrics.

The bulk powders were analyzed as purchased. When collecting airborne fractions for ICP-MS analysis, 37-mm MCE filters (0.8-μm pore size, SKC Inc.) were used in the experimental setup (Fig. 2), and powder application experiments were performed for 60 min using the procedures described above. Bulk powder samples, filter samples, and quality control (QC) samples were digested by placing them in 50-mL metal-free centrifuge tubes, to which 5 mL of 1:1 hydrofluoric acid:nitric acid was added, and incubated for 1 hour in a heating block. The samples were then removed from the heating block, allowed to cool, and their final volume increased to 20 mL by adding double-deionized water. The samples were then analyzed using ICP-MS. The Ti concentrations determined were then converted to TiO$_2$ concentrations based on the molecular weight difference between Ti and TiO$_2$. The Ti concentration range in the QC samples was between 5.37 μg/L and 49.79 μg/L Ti.

Analysis of morphology and chemical composition of individual particles

The size, shape, degree of agglomeration, and elemental composition of individual particles in the five products tested were examined in the bulk powders and also in the TSP, PM$_{10}$, and PM$_4$ fractions using a field emission scanning electron microscope (FESEM, Zeiss Sigma, Germany). For bulk products, a powder sample was placed on the carbon tab of sample mounts and then dispersed across the tab using an air duster. To analyze particles in the three airborne particle fractions (TSP, PM$_{10}$, and PM$_4$) using FESEM, the powder-application procedure was repeated for 35 min, as described above (Fig. 2), a nucleopore-type membrane filter (Isopore™, MilliporeSigma, St. Louis, MO) was used: 25-mm filter (1-μm pore size) for TSP and 37-mm filter (0.8-μm pore size) for the PM$_{10}$ and PM$_4$ fractions. A sample to fit the carbon tab was cut from each filter with the collected particles, and particle size was estimated from the resulting micrographs and the automatically added scale marks. The elemental composition of the individual particles within the collected particle fractions and the bulk powders, with a focus on the presence of Ti, was analyzed using a scanning electron microscope (SEM) with energy-dispersive X-ray spectroscopy (Aztec EDX, Oxford Instruments plc, Abingdon, UK). At least three microscope views from each sample (15 samples total) and several particles within each view were examined. Due to the limited number of particles in each view and the labor-intensive nature of this analysis, the number of particles examined was limited (Table S2).

Quality control

The quality of experiments was controlled by following written standard operating procedures. Real-time instruments were zero-checked before experiments. All flowrates were checked before and after the experiments. When weighing filters for mass, we followed
established protocols, including the use of control weights and control filters (e.g., filters that remain in the weighing room all the time). Appropriate blanks were used in all analyses. Analysis of filters for TiO$_2$ was performed by an accredited laboratory.

**Statistical analysis**

The mass concentrations were analyzed as a function of tested powders (i.e., T1, T2, T3, NT1, and NT2) and measurement type (i.e., optical or gravimetric) using a two-way ANOVA. For significant effects, all multiple pairwise comparisons were performed using the Holm–Sidak method with Sigmaplot 2011 (version 12.3, Systat Software Inc., San Jose, CA). Data normality was assessed across all replicates using the Shapiro–Wilk test, and, if needed, a nonparametric Mann–Whitney rank-sum test was used to determine significantly different pairs. The latter comparison was performed for all product pairs measured with the same method and also to compare measurement methods for each product.

**Results**

**Real-time inhaled aerosol mass concentrations and their number and mass distribution**

An example of real-time TSP and PM$_4$ aerosol mass concentrations that would be inhaled during eyebrow powder application, as measured by the Grimm OPC, is presented in Fig. 3. The average TSP concentrations ranged from 80.4 μg/m$^3$ to 184.1 μg/m$^3$, and the average PM$_4$ concentrations ranged from 16.1 μg/m$^3$ to 30.7 μg/m$^3$. There are numerous concentration spikes during powder application, with TSP concentrations as high as 1000 μg/m$^3$ and PM$_4$ concentrations as high as 200 μg/m$^3$. The spikes likely correspond to the initial contact of the powder-laden brush with the eyebrow. For all real-time data and average concentrations, the background particle concentration was subtracted.

The number and mass concentration distributions of all released and inhaled powders that were measured with a Grimm OPC using the setup in Fig. 1a are shown in Fig. S1. For comparison, the released particle concentrations when a clean brush was used are also presented. In this case, the released particle concentrations were orders of magnitude lower than during powder application. These results are discussed in the Supplemental Materials.

**Inhaled particle mass fractions collected on filters and measured using a Grimm OPC**

The average mass concentration of different PM size fractions that would be inhaled during powder applications is presented in Fig. 4, while the statistically significant pairwise comparisons are presented in Table 1. The main findings are as follows.

**a. PM$_4$ fractions of the released and inhaled powders (setup in Fig. 1a)**—The average PM$_4$ concentrations during a 35-min powder application based on Grimm OPC measurements ranged from 22.21 ± 1.88 μg/m$^3$ (powder T1) to 46.79 ± 17.36 μg/m$^3$ (powder T3), whereas filter-based PM$_4$ concentrations ranged from 21.17 ± 2.62 μg/m$^3$ (powder T1) to 53.67 ± 36.02 μg/m$^3$ (powder T3). A statistically significant difference between the Grimm OPC-based and filter-sampled PM$_4$ fractions was not observed (p > 0.05), likely due to large inter-sample variability and a relatively small sample number. Among powders, the only statistically significant difference in mass concentration was
observed between T1 and NT1 powders based on Grimm OPC and filter measurements of PM$_4$ concentrations ($p=0.00162$ for Grimm OPC-based and $p=0.016$ for filter-based measurements, Table 1).

b. **PM$_{10}$ fractions of the released and inhaled powders (setup in Fig. 1b)**—The average PM$_{10}$ concentrations based on Grimm OPC measurements ranged from 56.04 ± 40.65 µg/m$^3$ (powder NT2) to 206.35 ± 58.29 µg/m$^3$ (powder T3), whereas filter-based PM$_{10}$ concentrations ranged from 43.65 ± 20.90 µg/m$^3$ (powder T1) to 136.90 ± 5.95 µg/m$^3$ (powder T3).

For both OPC-based and filter-based measurements, the highest PM$_{10}$ concentrations were released by powders T2 and T3. The PM$_{10}$ concentrations released by T1, NT1, and NT2 powders were lower compared with T2 and T3. Statistically significant differences among PM$_{10}$ concentrations were observed based on OPC-based measurements, and the statistically different product pairs are listed in Table 1. The measurements of PM$_{10}$ concentrations by Grimm OPC and filter yielded similar PM$_{10}$ concentrations, except for the T3 powder, in which the difference between the two methods was statistically significant ($p=0.047$).

It should be noted that for all investigated particle fractions, there was only one measurement (e.g., T3 powder in the PM$_{10}$ fraction), where a statistically significant difference between OPC-based and filter-based measurements was observed. The relationship between scattering intensity and PM mass concentration depends on environmental conditions and particle properties, such as relative humidity (RH), particle chemical composition, refractive index, size distribution, and density$^{59-61}$, and, thus, differences between OPC-based and filter-based measurements should be expected. In our case, the stochastic nature of particle release from the eyebrow powders resulted in a relatively high variability among the samples, which likely masked any difference between the concentrations obtained by the two methods.

c. **TSP fractions of released and inhaled powders (setups in Fig. 1a, b)**—The average TSP concentrations based on Grimm OPC measurements ranged from 109.56 ± 36.06 µg/m$^3$ (powder T1) to 324.08 ± 117.34 µg/m$^3$ (powder T3), whereas filter-based TSP concentrations ranged from 99.94 ± 42.85 µg/m$^3$ (powder T1) to 262.28 ± 91.94 µg/m$^3$ (powder T2). There were no statistical differences between Grimm OPC-measured and filter-sampled TSP fractions for any product ($p>0.05$). Any differences in TSP concentration released by the products were observed only for Grimm OPC-based measurements: between T1 and T2 ($p=0.044$), between T1 and T3 ($p=0.001$), and between T3 and NT1 powders ($p=0.042$).

**Characterization of original powders and airborne particle fractions**

a. **Visual examination of particles using SEM**—Size, shape, and agglomeration of particles in bulk powders and in airborne particle fractions were examined using SEM, and representative micrographs are shown in Fig. 5a (bulk powders and TSP) and 5b (PM$_4$ and PM$_{10}$).
Micrographs of bulk eyebrow powders (Fig. 5a, left column) show the presence of large particles, agglomerates, and aggregates with particle sizes in at least one dimension reaching ~10 μm or more (NT2). Powders T1, T3, and NT1 contained spherical or spheroid structures with diameters of approximately 4-5 μm; they also had plate-shaped particles in which one dimension was much smaller (1-2 μm) than the other two dimensions. Products T2 and NT2 contained mostly plate-shaped particles. It is important to note that both the spheroids and plate-shaped particles in all products were complex agglomerates, in which micron and submicron particles were attached to the dominant large particles described above. Some of the attached particles were spheroids (products T1 and T3), while others were small plates attached to larger plate-shaped particles (products T2 and NT2).

Images of the TSP fraction (the right side of Fig. 5a) show aggregates much larger than 2 μm and mostly plate-shaped particles onto which much smaller particles are attached, as well as individual particles. All images, except this particular micrograph of the NT1 powder, show the presence of individual particles that are much smaller than the 2-μm scale marker, and some particles seem to be just a fraction of 1 μm, especially in the T3 and NT2 samples.

Particles captured in the PM\textsubscript{10} samples (Fig. 5b, left panel) have a similar appearance to those in TSP micrographs. The PM\textsubscript{4} sample from the T1 powder (right panel, Fig. 5b) even shows the presence of a chain-like agglomerate, with individual particles in the nanosize range and the agglomerate itself having dimensions of approximately 1.0 μm—similar to the pore size of the filter. In addition to showing the presence of submicron particles in the particular micrographs included in Figs. 5a and 5b, we provide further evidence of such particles in additional micrographs presented in Fig. S2.

\textbf{b. Sample analysis using ICP-MS and EDX—}Fig. 6a presents the mass-based concentration of TiO\textsubscript{2} (left y-axis) and the mass fraction of TiO\textsubscript{2} in the sample (weight of TiO\textsubscript{2}/sample weight [%], right y-axis) in the bulk powders as well as in the collected PM\textsubscript{4} and PM\textsubscript{10} particle fractions, that is, the “inhaled” particles, as determined by ICP-MS analysis.

TiO\textsubscript{2} was detected in all bulk powders, but the TiO\textsubscript{2} mass fraction (expressed as % of sample mass) varied substantially depending on the product. The TiO\textsubscript{2} mass fractions in T1, T3, and NT2 powders were 2.94 ± 0.29%, 7.44 ± 0.47%, and 8.34 ± 0.19%, respectively. T2 and NT1 had only trace amounts of TiO\textsubscript{2}: 0.07% and 0.03%, respectively. The highest TiO\textsubscript{2} mass fraction was detected in the NT2 powder, which, interestingly enough, was not labeled as containing TiO\textsubscript{2}. The other product not labeled as containing TiO\textsubscript{2}, powder NT1, had only a trace (0.03%) of TiO\textsubscript{2}. On the other hand, T2, which was labeled as containing TiO\textsubscript{2}, also had only a trace of TiO\textsubscript{2} at 0.07%.

The TiO\textsubscript{2} mass fraction in PM\textsubscript{4} samples ranged from 1.28 ± 0.34% (powder T1) to 8.94 ± 3.07% (powder NT2), whereas in PM\textsubscript{10} samples the TiO\textsubscript{2} mass fraction ranged from 1.75 ± 0.48% (powder T1) to 4.31 ± 2.77% (powder NT2). The TiO\textsubscript{2} mass fraction in PM\textsubscript{4} and PM\textsubscript{10} samples of T3 and NT1 was below the limit of detection (LOD), as per the analytical laboratory.
The average TiO$_2$ mass concentration in filter-based PM$_4$ samples ranged from 0.34 ± 0.06 μg/m$^3$ (powder T1) to 2.66 ± 1.03 μg/m$^3$ (powder T3), whereas for the PM$_{10}$ fraction the average TiO$_2$ mass concentration ranged from 2.04 ± 0.71 μg/m$^3$ (powder T1) to 9.31 ± 4.09 μg/m$^3$ (powder NT2). The TiO$_2$ concentration in the airborne samples of T3 and NT1 was below the LOD, and this finding was consistent with the low TiO$_2$ mass fraction in bulk powders of these products, which was 0.07% and 0.03% in T3 and NT1, respectively, as mentioned above.

On the other hand, the results calculated based on Grimm OPC measurement showed higher values than those obtained from filter-based measurement. The TiO$_2$ mass fraction in PM$_4$ obtained by Grimm OPC-based analysis ranged from 1.52 ± 0.31% (powder T1) to 5.10 ± 3.15% (powder NT2), whereas TiO$_2$ in PM$_{10}$ were from 2.49 ± 1.57% (powder T1) to 9.74 ± 5.07% (powder NT2).

The relationship between the presence of TiO$_2$ in bulk powders and in airborne particles released from those powders is further explored in Fig. 6b and Fig. 6c, in which TiO$_2$ mass fraction (%) and mass-based concentration (μg/m$^3$) in airborne samples are presented as a function of TiO$_2$ mass fraction (%) in the bulk powders, respectively. The data show that both the airborne TiO$_2$ mass concentration (μg/m$^3$) and TiO$_2$ fraction (TiO$_2$ mass / sample mass [%]) in the PM$_4$ and PM$_{10}$ fractions of the inhaled powders increase with the increasing presence of TiO$_2$ in the bulk powders.

We also analyzed individual particles in the bulk powders and in airborne PM$_4$ and PM$_{10}$ samples for the presence of Ti using EDX. The results in Fig. 7a and Fig. 7b show linear correlations between the Ti mass fraction in the collected PM$_4$ and PM$_{10}$ particles, respectively, and the Ti fraction in particles from the bulk powders. The fraction of Ti in the bulk powders ranged from 0.82 ± 0.90% (powder NT1) to 7.60 ± 2.62% (powder T3). In PM$_4$ particles, the Ti fraction ranged from undetected (powder NT1, indicated as 0% in Fig. 7a) to 5.20 ± 5.51% (powder T3), whereas in the PM$_{10}$ samples (Fig. 7b), the Ti fraction ranged from 0.40 ± 0.65% (powder NT1) to 6.03 ± 0.64% (powder T3).

**Discussion**

This study shows that the application of eyebrow powders results in exposure to airborne particles released from the powders, including exposure to TSP, PM$_4$, and PM$_{10}$ particles. The instantaneous exposure to TSP reached several hundred μg/m$^3$, while transient TSP concentration peaks exceeded 1000 μg/m$^3$. The mass concentration of inhaled PM$_4$ ranged from approximately 22.21 to 46.79 μg/m$^3$. Thus, the application of eyebrow powders adds to an individual’s daily burden of exposure to particulate matter, including respirable particles. The released aerosol concentrations of different size fractions depended on a particular product, and there were significant differences among product pairs (Table 1). These significant differences were mostly detected using Grimm OPC data and not filter data, likely due to large filter inter-sample variability and a relatively small sample number.

The actual amount of inhaled and eventually deposited particles will depend on an individual’s breathing rate and breathing pattern, lung anatomy, and, of course, powder

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application mode and duration. For example, using the data in Figs. 4 and 6, as well as equations provided by Hansen et al. 62 and Nazarenko et al. 57, we can estimate inhaled dose, ID (μg/kg B_w), of PM_4 and PM_10 mass and TiO_2 in those particle fractions:

\[ ID = C_{inh} \times Q_{inh} \times T_{contact} / B_w, \]  

(1)

Where B_w is body weight; C_{inh}, mass concentration of particulate matter or TiO_2 in inhaled air (μg/m^3), Q_{inh} inhalation flow rate for given gender/activity scenario (L/min); T_{contact} duration of contact per application (min); B_w, body weight. Table 2 presents the inhaled dose for a female with a body weight of 60 kg and the breathing rate of 10.8 L/min, which is a typical breathing rate for a female under sedentary conditions, for one minute of eyebrow powder application. These estimates are presented for the three products where TiO_2 was measured in the airborne phase and are based on both Grimm OPC data and filter measurement data.

It should be noted that even after the eyebrow powder has been applied, some powder aerosol would linger in the air resulting in additional inhalation exposure if the user remained in the same room, e.g., while applying other products. The actual inhaled amount would depend on the room layout, ventilation rate, and other factors.

To the best of our knowledge, no prior studies have addressed exposure to inhalable particles due to the use of eyebrow powders, nor investigated the chemical composition, specifically the presence of TiO_2, in various aerosol mass fractions of such powders when they are inhaled. Therefore, it not possible to directly compare exposure data from our study with other studies. However, comparisons could be drawn with studies analyzing household products that could be aerosolized and inhaled, such as other cosmetic products or surface treatment sprays 63.

Chen et al. (2010) 64 analyzed aerosols generated from bathroom cleaner/sanitizer that contained TiO_2 and was dispensed as a propellant spray using realistic spraying conditions of 2.5 minutes. Results indicated that while initial aerosol droplets were large with a count median diameter of 22 μm during spraying, the final aerosol contained primarily solid titanium dioxide particles with a diameter of 75 nm; the TiO_2 aerosol had a mass concentration as high as 3.4 mg/m^3 for the worst-case scenario. This concentration is higher than we observed in our study; however, the product type and its application mode between their study and our study are different.

Park et al. (2017) 65 evaluated the spatial-temporal dispersion of airborne nanomaterials during the use of consumer spray products and estimated consumer inhalation exposures using both experimental data and exposure factors. Eight spray products, including five propellant (household cleaner and deodorizer for air conditioners) and three pump types (deodorizer for air conditioners), were used, and the estimated nanoparticle concentrations were 51.1–181.9 μg/m^3 for propellant sprays that included Ag nanoparticles and 3.2–7.4 μg/m^3 for pump sprays that included TiO_2. These concentrations are in a general agreement with PM_4 mass concentrations measured in our study.
Recent studies have highlighted the importance of simulated “real-world” exposure assessments in order to understand aerosolized cosmetics-induced aerosol exposure and its potential impact on the human body. Using a mannequin, Nazarenko et al. (2012) quantified the potential nanoparticle exposures from the use of six cosmetic powders. They found that inhalation exposures to PM$_{2.5}$-PM$_1$ exceeded 100 ng/kg B$_w$ per application for several products. While our-calculated inhalation exposures are lower (Table 2), nonetheless, they add to the total body burden and potential adverse health effects, especially when specific elements, such as TiO$_2$, are considered.

Pearce et al. (2019) developed a fully automated aerosol generation system to examine aerosol properties of four aerosolized nano-enabled cosmetics using real-time monitoring and found that over a 20-minute spray duration, the total aerosol mass concentration within a glove box chamber reached several mg/m$^3$. Our experiments were performed in a large and ventilated room, and yet instantaneous concentrations of TSP reached as high as 1 mg/m$^3$.

One of the goals of the study was to investigate the presence of TiO$_2$ in respirable particles, both in PM$_4$ and PM$_{10}$ aerosol fractions. First, TiO$_2$ was detected at varying abundances in all bulk powders. Second, TiO$_2$ was measured in the PM$_4$ and PM$_{10}$ aerosols released by the T1, T3, and NT2 powders; TiO$_2$ concentrations were below the LOD in the PM$_4$ and PM$_{10}$ aerosols released by the T2 and NT1 powders (Fig. 6a). The results presented in Fig. 6 show that a higher TiO$_2$ fraction in the bulk powder leads to a higher TiO$_2$ concentration in the respirable PM$_4$ and PM$_{10}$ particles released from those powders.

A similar trend—that a higher Ti fraction in the bulk powders leads to a higher Ti fraction in the PM$_{10}$ and PM$_4$ aerosols—was observed when individual particles were examined using EDX (Fig. 7). The linear regression equations were $y = 0.59x - 0.51$ for PM$_4$ and $y = 0.70x - 0.02$ for PM$_{10}$, and the coefficients of determination ($R^2$) were 0.84 and 0.95 for PM$_4$ and PM$_{10}$, respectively. Similarly, Pearce et al. (2019) found that micron-sized particles decorated with nanoparticles found in original liquid cosmetic products were also present in the majority of aerosol particles $< 2 \mu$m released from the product. Also, the shapes of particles in the aerosol were similar to those in the original powder.

We recognize that the analysis of individual particles using EDX to determine the Ti fraction is a semi-quantitative measure, due to the randomness of the particle distribution in a sample and the limited number of particles that were examined. However, we observed a weak positive yet statistically significant (p<0.05 for the slope coefficient) correlation between the TiO$_2$ mass fraction in samples analyzed by ICP-MS and the Ti mass fraction in individual particles analyzed using EDX (Fig. S3), with a correlation coefficient $r = 0.19$. Thus, individual particle analysis using EDX adds another potential tool to relate the presence of Ti in bulk powders to the presence of TiO$_2$ in the released respirable particles.

The data presented in Figs. 5, 6, and 7 suggest that the analysis of cosmetics powders for the presence of TiO$_2$ using ICP-MS, EDX, or other techniques might serve as a screening tool to identify commercial cosmetics that are likely to release respirable particles containing TiO$_2$ during use. At the same time, for a wider application of methods such as FESEM-EDX as a screening tool for exposure assessment, especially the analysis of individual particles,
standardized methods of analysis should be developed, such as filter types used, the number of view fields or particles examined, as well as common sample preparation procedures.

Given the concerns over the potential health risks of inhaled TiO\textsubscript{2}, such as those expressed in California Proposition 65, powder screenings could be the first step in identifying powders that result in user exposures to TiO\textsubscript{2} and other ingredients of concern. If the analysis of powder products does not detect the presence of ingredients of concern beyond trace levels, it is unlikely that the resulting aerosols would contain a substantial concentration of that element, as illustrated by products T2 and NT1. However, one should keep in mind that an inability to detect a particular element does not exclude its presence and potentially harmful effects.

On the other hand, the presence of ingredients of concern in the bulk powders indicates likely instantaneous exposures to airborne particles containing that ingredient, as suggested by products T1, T3, and NT2. Such screening information would be informative to manufacturers, consumers, and consumer advocates concerned about exposures to TiO\textsubscript{2} and other ingredients of concern. While product labels are useful, they are not always accurate regarding the presence of particular components, as shown by products T2 and NT2. We made similar observations in our study examining cosmetics powders and sprays for the presence of nanoparticles\textsuperscript{67}.

The exposure to particles released during eyebrow powder application was investigated using a mannequin. The mannequin used in this study is made of plastic and silicone, and its surface properties might affect the retention of the applied powder, thus affecting particle release and potential inhalation of released particles. On the other hand, even if there are differences between the manikin’s surface and the actual human skin in terms of particle adhesion, this difference would apply to all powders, and relative differences between powders should remain valid. Such differences, however, would affect the estimates of instantaneous and long-term exposures. As more studies begin to use “real-world” exposure assessment scenarios through the use of mannequins\textsuperscript{66}, an ability of a mannequin’ surface to mimic human skin in terms of particle adhesion and release should be addressed in future studies.

In order to collect sufficient particle mass for weighing and chemical analysis, the powders were applied longer than a typical real-life powder application time. However, since our results were obtained in terms of PM\textsubscript{4} and PM\textsubscript{10} mass concentration and TiO\textsubscript{2} mass concentration in these respirable particle fractions, future exposure and health studies could use these data together with refined estimates of eyebrow powder application times and consumers’ breathing patterns to estimate the inhaled amounts of PM and TiO\textsubscript{2}.

**CONCLUSIONS**

This study found that the application of eyebrow powders can result in the release and inhalation of airborne particles at concentrations as high as \(\sim 280 \mu g/m^3\), \(\sim 200 \mu g/m^3\), and \(\sim 50 \mu g/m^3\) in TSP, PM\textsubscript{10}, and PM\textsubscript{4} aerosol fractions, respectively. TiO\textsubscript{2} was detected in all bulk powders, regardless of whether it was indicated on the product label. More importantly,
the abundance of TiO$_2$ in the bulk powders correlated with the abundance of TiO$_2$ in particles released and inhaled during powder application, including in respirable PM$_{10}$ and PM$_4$ aerosols. Thus, ICP-MS, EDX, or other techniques could be used as screening tools to determine the likelihood of encountering TiO$_2$ in airborne samples, including in respirable fractions.

Our study suggests that realistic exposure simulation and quantification, as well as morphological and chemical characterization of airborne particle fractions released due to the use of consumer products, could be part of a toolbox for assessing exposure risks. The experimental approach presented here could also be useful for the development and refinement of guidelines and safety regulations, such as California’s Prop 65, that are concerned with consumer exposures to TiO$_2$ or other specific powder components and potential health risks.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Experimental setup to realistically simulate human exposure to particles released during eyebrow application and collect total suspended particle (TSP), PM$_4$, and PM$_{10}$ fractions that would be inhaled during powder application. Each powder product was applied to the right eyebrow only. A Grimm 1.108 optical particle counter (OPC, Grimm Technologies Inc., Douglasville, GA) was used to measure the size distribution of inhaled aerosols. A cyclone (GK 2.69, Mesa Labs, Inc.) with a filter operated at 4.2 L/min and 1.6 L/min was used to collect the PM$_4$ and PM$_{10}$ fractions, respectively. TSP were collected on a filter at 5.4 L/min. The captured particles were analyzed for mass, presence of TiO$_2$, and presence of Ti in individual particles of the PM$_{10}$ and PM$_4$. The powder application experiments were repeated with different filter types suitable for selected analysis, as described in text. Three measurement repeats were performed for each eyebrow powder and for each analysis method.
Figure 2.
The schematic of the measurement protocol to quantify inhaled particles using OPC-based and filter-based measurement, the chemical composition using ICP-MS and the morphology using SEM/EDX analysis.
Figure 3.
Real-time inhaled TSP and PM$_4$ aerosol concentrations, as measured with a Grimm OPC as a function of eyebrow powders (i.e., T1, T2, T3, NT1, and NT2). The data for inhaled aerosol mass concentrations, both TSP and PM$_4$, represent averages of three repeats.
Figure 4.
Mass concentrations of PM$_{4}$, PM$_{10}$, and TSP aerosol fractions that would be inhaled during eyebrow powder application, as measured using a Grimm 1.108 OPC and filter-based gravimetric analysis for five eyebrow powders. The data are based on averages of three repeats, and error bars indicate one standard deviation.
| Bulk eyebrow powder | TSP |
|---------------------|-----|
| T1                  |     |
| T2                  |     |
| T3                  |     |
| NT1                 |     |
| NT2                 |     |

**Figure 5a.**
Scanning electron micrographs of bulk eyebrow powders and airborne samples of total suspended particles (TSP). All five bulk powders were prepared for analysis by loosely dispersing them on carbon tabs, while the TSP fractions were collected on membrane filters (Isopore™, MilliporeSigma, St. Louis, MO) during powder application, as shown in Figure 1.
|     | PM$_{10}$ | PM$_4$ |
|-----|-----------|-------|
| T1  | ![Image](image1.jpg) | ![Image](image2.jpg) |
| T2  | ![Image](image3.jpg) | ![Image](image4.jpg) |
| T3  | ![Image](image5.jpg) | ![Image](image6.jpg) |
| NT1 | ![Image](image7.jpg) | ![Image](image8.jpg) |
| NT2 | ![Image](image9.jpg) | ![Image](image10.jpg) |

**Figure 5b.**
Scanning electron micrographs of eyebrow powders in airborne PM$_{10}$ and PM$_4$ samples. PM$_{10}$ and PM$_4$ samples were collected on membrane filters (Isopore™, MilliporeSigma, St. Louis, MO) during eyebrow powder application using the experimental setup shown in Fig. 1.
Figure 6.
TiO$_2$ mass concentration ($\mu$g/m$^3$) and mass fraction (w/w, %) in the bulk powders and in PM$_{10}$ and PM$_4$ airborne samples: (a) observed TiO$_2$ concentration and mass fraction, (b) TiO$_2$ mass fraction (w/w [%]) in PM$_{10}$ and PM$_4$ samples as a function of TiO$_2$ mass fraction in bulk powder, and (c) TiO$_2$ mass concentration ($\mu$g/m$^3$) in PM$_{10}$ and PM$_4$ samples as a function of TiO$_2$ mass fraction in bulk powders. The TiO$_2$ mass concentration was determined by inductively coupled plasma mass spectrometry (ICP-MS). TiO$_2$ was measured in bulk powders T2 and NT1, but TiO$_2$ mass concentration and mass fraction were below the limit of detection ( LOD) in PM$_4$ and PM$_{10}$ samples; thus, to aid in data analysis and presentation, TiO$_2$ mass concentration and mass fraction values of T2 and NT1 in PM$_4$ and PM$_{10}$ samples are equated to LOD.
Figure 7.
Ti mass fraction in individual particles of the PM$_4$ and PM$_{10}$ samples as a function of Ti mass fraction in individual particles in bulk powders: a) PM$_4$ fraction and b) PM$_{10}$ fraction. The individual particles were analyzed using EDX.
Table 1.
Pairwise comparisons of particle mass concentrations released by different eyebrow powder pairs. Only pairs with statistically significant differences (p < 0.05) are shown.

| Variable | Particle fraction | Measurement method | Product (Mean concentration ± standard deviation, μg/m³) | Product (Mean concentration ± standard deviation, μg/m³) | P-value |
|----------|------------------|--------------------|----------------------------------------------------------|----------------------------------------------------------|---------|
| Product  | PM$_{4}$         | OPC-based          | T1 (22.21 ± 1.88)                                       | NT1 (33.95 ± 1.95)                                       | 0.00162 |
|          |                  | Filter-based       | T1 (21.17 ± 2.62)                                       | NT1 (32.06 ± 5.20)                                       | 0.016   |
| PM$_{10}$| OPC-based        | T2 (185.10 ± 78.36)| T2 (185.10 ± 78.36)                                     | T1 (65.57 ± 36.33)                                      | 0.011   |
|          | OPC-based        | T2 (185.10 ± 78.36)| NT1 (74.02 ± 21.69)                                     | T1 (65.57 ± 36.33)                                      | 0.015   |
|          | OPC-based        | T2 (185.10 ± 78.36)| NT2 (56.04 ± 40.65)                                     | T1 (65.57 ± 36.33)                                      | 0.011   |
|          | OPC-based        | T3 (206.35 ± 58.29)| T3 (206.35 ± 58.29)                                     | NT1 (74.02 ± 21.69)                                     | 0.005   |
|          | OPC-based        | T3 (206.35 ± 58.29)| NT2 (56.04 ± 40.65)                                     | T1 (65.57 ± 36.33)                                      | 0.004   |
|          | TSP              | OPC-based          | T1 (109.56 ± 36.06)                                     | T2 (252.51 ± 102.15)                                    | 0.044   |
|          |                  | OPC-based          | T1 (109.56 ± 36.06)                                     | T3 (324.08 ± 117.34)                                    | 0.001   |
|          |                  | OPC-based          | T3 (324.08 ± 117.34)                                     | NT1 (182.52 ± 60.63)                                    | 0.042   |
Inhalation exposure doses of PM$_4$ and PM$_{10}$ fractions and TiO$_2$ in those fractions per one minute of eyebrow powder application. Based on the Grimm 1,109 OPC measurement and filter measurement data. The data are based on a 60 kg body weight and a breathing rate of 10.8 L/min. The data represent the averages and standard deviations from three repeats.

|        | PM$_4$ (ng/kg B$_w$) | PM$_{10}$ (ng/kg B$_w$) |
|--------|----------------------|-------------------------|
|        | Entire PM$_4$ (Ave ± Stdev) | TiO$_2$ (Ave ± Stdev) | Entire PM$_{10}$ (Ave ± Stdev) | TiO$_2$ (Ave ± Stdev) |
|        | OPC-based | Filter-based | OPC-based | Filter-based | OPC-based | Filter-based | OPC-based | Filter-based |
| T1     | 4.76 ± 1.17 | 5.10 ± 2.20 | 0.06 ± 0.01 | 0.07 ± 0.03 | 22.74 ± 5.97 | 20.63 ± 2.27 | 0.40 ± 0.10 | 0.36 ± 0.04 |
| T3     | 8.99 ± 3.97 | 6.11 ± 1.13 | 0.69 ± 0.30 | 0.47 ± 0.09 | 53.68 ± 24.94 | 42.19 ± 15.56 | 1.18 ± 0.55 | 0.92 ± 0.34 |
| NT2    | 6.31 ± 1.82 | 3.33 ± 0.86 | 0.56 ± 0.16 | 0.30 ± 0.08 | 42.98 ± 18.66 | 42.25 ± 7.91 | 1.85 ± 0.80 | 1.82 ± 0.34 |