OTC Aerosol Spray Products – Particle Size Distribution

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Abstract

Background: Potential unintended inhalation of OTC spray/powder/aerosol drug products has placed importance on understanding characteristic particle size distributions in the sprayed products, which is crucial to determine lung deposition. There are little or no data on the toxicity of OTC spray ingredients inhaled into the lung. Because of this lack of data, FDA has previously attempted to limit lung exposure to spray ingredients by proposing limits on the size of particles dispensed from consumer containers such as finished spray sunscreens in the February 26, 2019 proposed rule, Sunscreen Drug Products for Over-the-Counter Human Use (84 FR 6204). FDA is interested in learning more about the particle size distributions of sprays emitted from consumer spray products.
Purpose: Herein, we developed a real-time assessment method for the aerosol particle size distributions, between 15 nm and 20 µm, of 12 OTC sunscreen spray products.
Methods: A cylindrical environmental chamber (11-1/2" ID, 2 ft long) was designed and built for the simultaneous sampling of sunscreen sprays into real-time particle sizing instruments, including but not limited to: Scanning mobility particle sizer spectrometer (SMPS) and Aerodynamic particle sizer spectrometer (APS). A case study was also conducted to evaluate the effect of rapid evaporation of the sunscreen spray droplets or some other testing condition on the measured particle size distribution.
Results: The aerosol sampling and testing system for inhalation exposure assessment on OTC sunscreen spray products has been developed. The measured particle number concentrations for the sunscreen spray aerosols are from 8×10^3 to 3×10^5/cm^3. Most of the particles are in the sub-micron range. The mass concentrations are from 2 to 131 mg/m^3. The mass fraction for particles smaller than 1 µm is from 0% to 8%, and smaller than 5 µm is from 58% to 80%. More studies are needed to investigate analytical methods for the impact of these and other factors on the sunscreen particle size distribution measurements.
Conclusion: A real-time method for measurement of size distributions of OTC sunscreen spray products was developed to potentially provide data to better inform the proposed particle size requirements for OTC consumer

Introduction

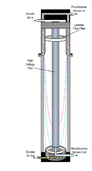
In 2019, our lab published a particle distribution study of sunscreen spray products using laser diffraction to support FDA regulation.[1] This study demonstrated that most of the spray (by volume) from sunscreen spray products consisted of large droplets, with mean diameters between 40 µm and 106 µm. However, the measurement range of the laser diffraction system was [0.5 µm, 175 µm]. New methods were needed to determine if smaller particles were present.
Scanning Mobility Particle Sizer (SMPS) is a useful on-line particle sizing tool for smaller particles between 2.5 nm and 1 µm (outside the range of laser diffraction) and can be extended up to 20 µm by combining an aerodynamic particle sizer (APS). Herein, particle size distribution (PSD) between 2.5 nm and 20 µm were evaluated for 12 spray sunscreens using this new method.
During method development, evaporation of the spray solvent during testing was shown to affect the particle size distribution results. We examined the effects that the experimental setup had on evaporation and the particle size distribution.

1. Liu, X, D Rua, A Wokovich, C Guo, D Keire, 2019, Particle Size Distribution Analysis of OTC Aerosol or Powder Drug Products With Potential for Inadvertent Inhalation Exposure to Consumers, J. Pharm. Sci., 108, 1506–1511.

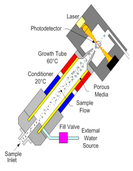
Materials and Methods

Materials: 12 different OTC sunscreen spray drug products were tested.

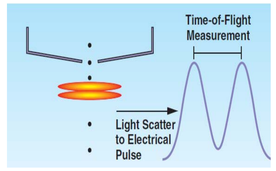
Real-time measurements principles
-Differential mobility analysis (DMA)
Inverse relationship between the electrical mobility and particle size
Separate aerosols based on electrical mobility
-Condensation particle counting (CPC)
Particles with condensed vapor grow in size and are optically counted
-High-resolution aerodynamic particle sizing (APS)
Time-of-flight technique measures aerodynamic diameter in real time



Differential mobility analyzer schematic



Water-based CPC flow schematic

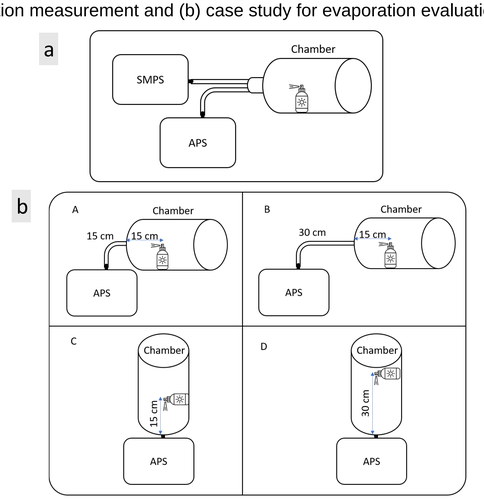


Aerodynamic particle sizer schematic

Experimental setup
A cylindrical environmental chamber (11-1/2" ID, 2 ft long) was designed and built for the simultaneous sampling of sunscreen sprays into real-time particle sizing instruments, including but not limited to: Scanning mobility particle sizer spectrometer (DMA+CPC) and Aerodynamic particle sizer spectrometer (APS) (Fig. 1a).

A case study was also conducted to evaluate how rapid evaporation of the sunscreen spray droplets in the testing setup (product 9) affected the measured particle-size distribution. Four experimental settings (A, B, C, and D) were tested (Figure 1b).

Figure 1. Experimental setups for (a) general sunscreen particle size distribution measurement and (b) case study for evaporation evaluation



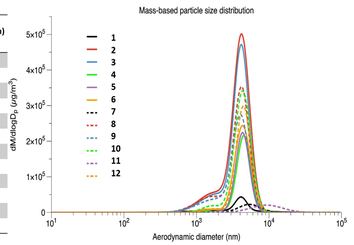
Results and Discussion

General sunscreen measurements
The aerosol sampling and testing system for inhalation exposure assessment on OTC sunscreen spray products has been developed.
•**Particle Number concentrations**: 8×10^3 to 3×10^5/cm^3
•**Mass concentrations**: between 2 to 131 mg/m^3
•**Number fractions**: 1.) 83% to 99% for particles < 1 µm 2.) Nearly 100% for particles < 5 µm
•**Mass fraction**: 1.) 0% to 8% for particles < 1 µm and 2.) 58% to 80% for particles < 5 µm.
The mass-based particle size distributions are shown in Fig.2.

Table 1. Summary of mass-based particle size distribution of the sunscreen spray products

Products	Fraction <1 µm	Fraction <5 µm	Total Conc. (mg/m^3)	Mass Median Diameter (µm)
1	0.08±0.01	0.76±0.11	13.0±3.0	4.0±0.1
2	0.03±0.00	0.75±0.01	131.0±9.0	4.0±0.0
3	0.04±0.00	0.78±0.02	99.0±21.0	4.0±0.1
4	0.01±0.00	0.67±0.01	43.0±21.0	4.4±0.0
5	0.01±0.00	0.72±0.02	63.0±8.0	4.3±0.0
6	0.01±0.00	0.68±0.02	98.0±47.0	4.3±0.1
7	0.00±0.00	0.65±0.15	6.0±2.0	4.6±0.3
8	0.04±0.00	0.77±0.00	111.0±10.0	4.0±0.0
9	0.04±0.00	0.80±0.02	116.0±3.0	3.9±0.1
10	0.01±0.00	0.67±0.10	66.0±2.0	4.3±0.1
11	0.01±0.00	0.58±0.06	2.0±0.0	4.8±0.3
12	0.01±0.00	0.60±0.03	50.0±16.0	4.6±0.1

Figure 2. Mass-based particle size distribution of the sunscreen spray products



Case study for evaporation test
The change of spray PSD over time was captured by APS. The concentration initially peaked, then decreased quickly afterwards, and kept stable for the rest of the sampling (Fig.3). PSD for each case is summarized in Table 2 and shown in Fig. 4.
- The total particle mass was reduced by 30% when the tubing length was increased from 15 cm (A) to 40 cm (B) in the horizontal chamber. Particle wall loss and evaporation may account for the reduction.
- When spray distance increases from 15 cm (C) to 30 cm (D) in the vertical chamber, median mass aerodynamic diameter (MMAD) increased from around 6 to 8 µm and the total number concentration decreased 33% while total mass reduced slightly. The extra travel distance for the particles in D provided more time for evaporation and particles larger than 20 µm (out of APS range) to shrink into the APS measuring range. Thus, the MMAD increased without noticeable change in total mass.
- The case of vertical chamber with no tubing (C) provides the highest number concentration and smallest MMAD among all configurations. These findings indicate that the tubing length, tubing bending, and spray distance all affect the particle size distributions.

Table 2. Particle size distribution summary (±SD).

Setting	A	B	C	D
CMD (nm)	896(11)	918(1)	873(2)	895(27)
Number Conc. (#/cm³)	55533(9613)	32867(5774)	92567(777)	62100(8960)
MMAD (nm)	7155(116)	7286(948)	5938(567)	8262(419)
Mass Conc. (mg/m³)	405(29)	276(22)	498(18)	476(31)
FPF<1 µm	0.014(0.0005)	0.014(0.0016)	0.024(0.0007)	0.016(0.0036)
FPF<5 µm	0.339(0.0074)	0.34(0.0386)	0.428(0.0232)	0.325(0.0057)

Figure 3. PSD over time for one of the sprays in configuration C: vertical chamber, no tubing, and spray at 15 cm.

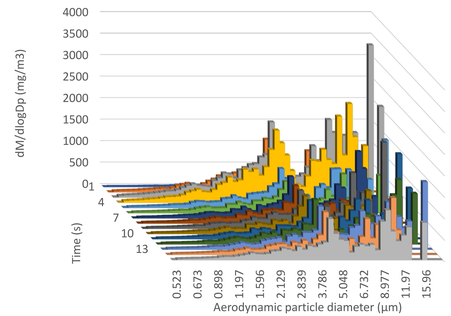
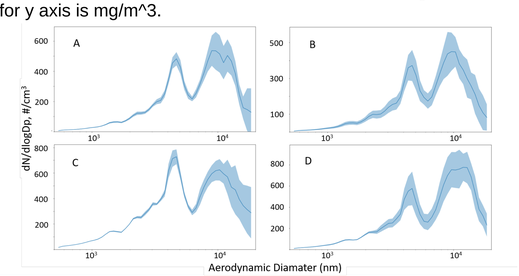


Figure 4. Mass-based particle size distribution for 4 configurations. The unit for y axis is mg/m^3.



Conclusion

An aerosol sampling and testing system for the measurement of particle size distributions of OTC sunscreen spray products has been developed with a range of 2.5 nm to 20 µm. The method has the potential to provide data to better inform the proposed particle size requirements for OTC consumer spray products.
In this study, particles between 2.5 nm to 20 µm were observed for all 12 sprays. Most of these particles (by particle count) were in the sub-micron range. However, these particles account for a small fraction of the total mass between 2.5 nm and 175 µm (i.e., including laser diffraction data). Moreover, evaporation during testing influenced the reported particle size distribution results. More studies are needed to investigate analytical methods that can determine the impact of evaporation, as well as other factors, on sunscreen particle size distribution measurements.
Case study of evaporation:
The chamber setup with the shortest path to the instrument (experimental setup C) provided the highest number concentration and smallest MMAD among all configurations. These findings indicate that the tubing length, tubing bending, and spray distance all affected the particle size distributions. Therefore, setup C was identified as the preferred setup to minimize evaporation.

Disclaimer

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