Comparison of Aerosol Characteristics and Nicotine Delivery by Conventional Pharmaceutical Inhalation Devices and Electronic Nicotine Delivery Systems (ENDS)

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Summary

An understanding of the aerosol characteristics and delivery of nicotine is important in the continuous development of a class of products called electronic nicotine delivery systems (ENDS) that has the potential to reduce the harm associated with tobacco use, particularly cigarette smoking. We compared the physical characteristics (aerosol mass, particle size distribution) and nicotine delivery of aerosols from three nebulizers, a multi-dose propellant-free inhaler device (no nicotine) and two ENDS products – one generating aerosols thermally and one non-thermally. Aerosols from inhalation devices, which are also generated by non-thermal means, had lower mass deliveries compared to aerosols from ENDS products that generate aerosols thermally. Aerosols generated by inhalation devices also have larger particles which usually deposit in the upper airways mostly, and deliver a lower level of nicotine compared to aerosols from ENDS.

Introduction

Whilst evidence suggests that a class of tobacco products called electronic nicotine delivery systems (ENDS) are likely to be far less harmful than conventional cigarettes,[1] effort is on-going to continue to develop devices that would offer nicotine and sensory satisfaction comparable to that of cigarette smoking, but with reduced harm. Such devices may facilitate transition from cigarette smoking and contribute to tobacco harm reduction.

Pharmaceutical inhalation devices have been traditionally used with success in the delivery of drugs via the inhalation pathway. A comparison of aerosol characteristics (aerosol mass, particle size distribution) and nicotine delivery from these two classes of inhalation products may yield insights that inform the development of next generation ENDS.

Key Message

Conventional pharmaceutical inhalation devices deliver aerosols with supermicron particles (>1 µm) compared to the submicron particles from electronic nicotine delivery systems (ENDS). From formulations with the same concentration of nicotine, inhalation devices deliver less nicotine in the aerosols compared to ENDS.

Methods

Four pharmaceutical inhalation devices were compared to two ENDS products in terms of aerosol mass, nicotine delivery, and particle size. Detailed descriptions of the devices and formulations (aerosol precursors) being studied are shown in Table 1. Also described in Table 1 are the aerosol collection conditions.

Given the devices had very different aerosol generation mechanisms, a best attempt was made in adjusting the formulations to enable each device to deliver similar amount of aerosol so they could be meaningfully compared. For example, Inhalation Devices 2 and 3 would only work with aqueous nicotine solutions, Inhalation Device 1 would not work with formulations with high propylene glycol and glycerine content. Inhalation Device 4 was a closed system prefilled with a drug formulation not containing nicotine. The formulation in ENDS 2 product was close to that in ENDS 1 product, except that ENDS 2 would not work properly with any water in the formulation. The air flow rate and aerosol collection time for ENDS 1 followed a standard recommended method.[2] An initial trial of aerosol collection indicated that the air flow used to entrain the aerosol had to be modified for ENDS 2 and Inhalation Device 4 compared to that for the other devices, again, to achieve comparable aerosol and also to reduce aerosol loss during transit from the device to measurement instrument. Aerosol from five puffs was collected from all devices. To minimize variability in aerosol mass measurements the duration of each puff of some of the devices was extended to 10 s (Table 1).

Five puffs were collected using filter pad[2] for aerosol mass measurement per replicate. The Cambridge filter pad was then extracted with isopropanol using Carvol as internal standard to determine nicotine delivery. For particle size, Spraytec (Malvern Panalytical) was used to measure aerosols generated by the four inhalation devices. Fumex[3] (Fraunhofer Institute, Germany), which is based on light scattering and designed for characterizing ENDS, was used to measure ENDS 1 and ENDS 2.

Table 1. Devices, Formulations Studied and Aerosol Collection Conditions

Device	Description	Formulation (% total weight)	Air Flow Rate (LPM)	Aerosol Collection Time (s/puff)
ENDS 1	• Ciga-like E-vapor product • Non-refillable liquid cartridge • Thermal aerosol generator • Puff activated delivery • Battery operated	2.5% nicotine, 15% water, 49.5% glycerin, 33% propylene glycol	1.10	3
ENDS 2	• Refillable tank E-vapor product • Ultrasonic aerosol generator (2.4 MHz) • Button activated delivery • Battery operated	2.5% nicotine, 58.5% glycerin, 39% propylene glycol	0.66	10
Inhalation Device 1	• Jet nebulizer • Compressed air operated	2.5% nicotine in 48.75% glycerin, 48.75% water	1.10	10
Inhalation Device 2	• Vibrating mesh nebulizer • 180 kHz • Button activated delivery • Battery operated	2.5% nicotine in water	1.10	10
Inhalation Device 3	• Ultrasonic nebulizer • 2.4 MHz • Button activated delivery • Battery operated	2.5% nicotine in water	1.10	10
Inhalation Device 4	• Multi-dose propellant-free inhaler • Aerosol generated by colliding liquid jets • Non-refillable cartridge • Mechanical activation • No battery	Non-nicotine containing drug formulation	2.60	5

LPM, litres per minute

Results

Table 2 shows a summary of data collected. Due to the varying aerosol collection regimes used, the mass delivery and nicotine delivery of each of the devices were normalized to unit volume and time to facilitate comparison.

ENDS 1 and Inhalation Device 3 generated the highest normalized aerosol mass. The two ENDS products delivered higher normalized level of nicotine. The particle size, characterized by mass median diameter (MMD), is submicron for both ENDS products and supermicron (>1 µm) for all the pharmaceutical inhalation devices. The difference in particle size between these two classes of inhalation products exceeds what would be expected because of the use of the two optical devices.

Table 2. Measured Aerosol Properties from ENDS and Inhalation Devices (3 replicates, mean ±SD values shown)

Device	Aerosol Mass (mg/puff)	Normalized Mass Delivery (mg/cc/s)	Nicotine Delivery (µg/puff)	Normalized Nicotine Delivery (µg/cc/s)	Particle Size (MMD) (µm)
ENDS 1	3.0±0.1	0.0167	100±6	0.606	0.60±0.03
ENDS 2	3.6±0.9	0.0033	590±220	0.536	0.87±0.03
Inhalation Device 1	22.0±2.1	0.0014	627±48	0.041	2.40±0.05
Inhalation Device 2	13.4±1.5	0.0073	389±60	0.212	6.20±0.52
Inhalation Device 3	27.0±4.1	0.0147	749±84	0.408	4.95±0.14
Inhalation Device 4	10.0±1.7	0.0090	N/A	N/A	4.80±0.04

MMD, mass median diameter

References

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3. Dunkhorst W, Lipowicz P, Li W, Hux C, Wang Q, Koch W: In-situ characterization of e-cigarette aerosols by 90°-light scattering of polarized light, Aerosol Science and Technology, 2018; 52: pp 717-724.

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Discussion & Conclusion

Data from this study clearly illustrate some fundamental differences between aerosols from conventional pharmaceutical inhalation devices and from ENDS products.

Aerosols from inhalation devices, which are generated by non-thermal means, had lower normalized mass deliveries compared to aerosols from ENDS products that generate aerosols thermally, i.e. ENDS 1. Aerosols generated by inhalation devices have larger particles which usually deposit in the upper airways mostly, and deliver a lower level of nicotine compared to aerosols from ENDS.