Development of a method for the estimation of mouth level exposure to nicotine from electronic cigarettes

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1. Introduction & Objective

Mouth-level exposure (MLE) assessments are valuable in helping to interpret, as well as potentially predict, the results from clinical investigations, such as biomarkers of exposure studies and pharmacokinetic studies (e.g., calculation of relative bioavailability) in tobacco products.

A method to estimate nicotine MLE from conventional cigarettes (CCs) has been established as the part-filter method (PFM)[1] which analyzes nicotine in a section of the filter. However, the PFM cannot be applied to electronic cigarettes (E-cigs) to estimate nicotine MLE because most E-cigs do not have filters.

We previously found a positive correlation between the nicotine yield from a tobacco vapor product (TVP) and weight loss (WL) from its whole product under various vaping conditions[2] (Fig. 1). The correlation between the nicotine yield from E-cigs and WL from its whole product has been reported in several studies[3,4], but was only observed under limited vaping condition (i.e., CRM81).

We assessed whether WL could be used to estimate nicotine MLE from E-cigs under various vaping conditions.

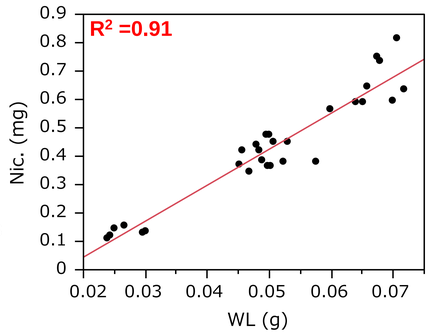
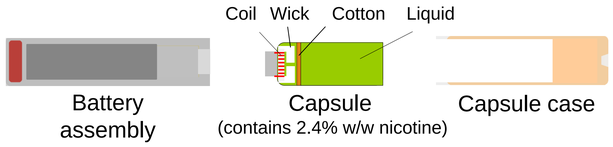


Fig 1. Single regression analysis in TVP

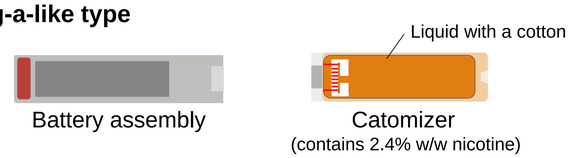
2. Materials & Methods

2.1 Products

◆ **Closed tank type**



◆ **Cig-a-like type**



2.2 WL measurement

◆ **Measurement conditions**

Temperature : 22 (±2) ℃
Humidity : 60 (±5) %

◆ **Instrument**

Mettler-Toledo AE200 (readability: 0.0001 g)

Fig 2. Weight measurement

◆ **Procedures**

1. Measured weight of whole product before vaping.
2. Vaped the product.
3. Measured weight of whole product after vaping.

Time interval from vaping until weight measurement : Within 5 min.

◆ **WL calculation**

$$WL = Weight_{(measured\ before\ vaping)} - Weight_{(measured\ after\ vaping)}$$

2.3 Aerosol Generation

✓Because MLE should be estimated under human vaping conditions, we selected machine-smoking regimes based on actual human puff topography[5,6] within the measurable range of the smoking machine (LM4E, Borgwaldt).

✓To assess the influence of puff profile on the correlations, we selected two puff profiles (square-shaped and bell-shaped) under several vaping regimes.

◆ **Vaping regimes**

Puff count : 10 puffs（Closed tank），20 puffs（Cig-a-like）
N : 3 times
Inter puff interval: 30 sec
Puff profile : square-shaped, bell-shaped

Puff volume & Puff duration	35 mL	55 mL	100 mL	140 mL
1 sec.	○	○		
1.5 sec.	○	○		
2 sec.	○	○		
3 sec.	○	○	○	○
5 sec.		○	○	○
8 sec.			○	○

○ : only square-shaped ○ : square-shaped and bell-shaped

2.4 Sampling and Chemical Analysis

Nicotine captured on a Cambridge filter pad was analyzed referring the general methodology listed in ISO 10315:2013 and ISO 4387:2000.

3. Results

3.1 Correlations between nicotine yield and WL

Single regression analysis of the square-shaped puff profile found positive correlations between nicotine yield and WL in the two types of E-cigs under various vaping regimes.

Closed-tank type : Nicotine (mg) = −0.028 + 17.819·WL (g), R^2>0.97.
Cig-a-like type : Nicotine = −0.125 + 18.151·WL, R^2>0.93.

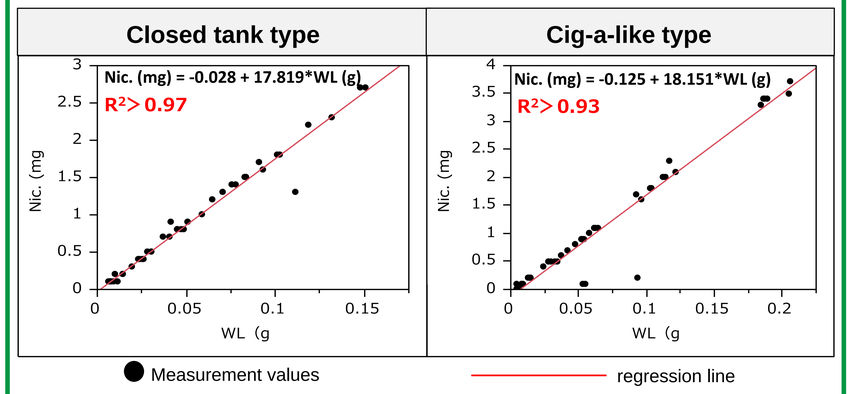


Fig. 3. Single regression analysis (square-shaped puff profile)

3.2 Influence of puff profile on correlation

Nicotine yields and WLs measured under the bell-shaped puff profile lay within the 95% confidence intervals for regression lines obtained under the square-shaped puff profile.

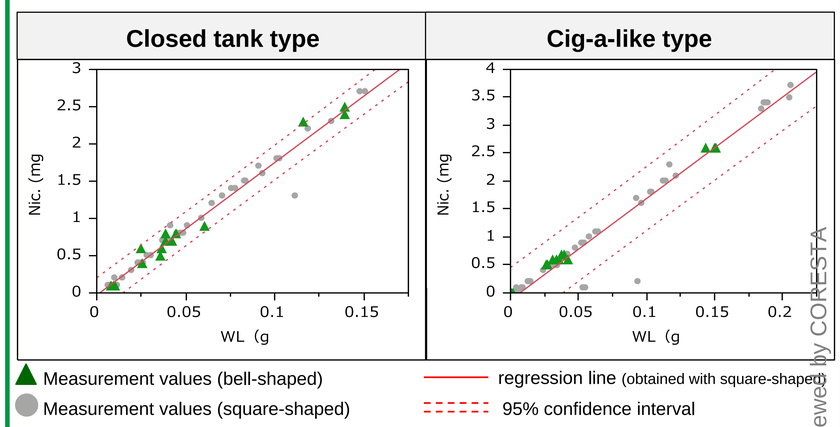


Fig. 4. Measurement values (bell-shaped puff profile)

References

*1 CORESTA Recommended Methods No.80, January 2016.
*2 Suzuki, T. *et al.* CORESTA Congress.2016;ST38.
*3 Yan, X. S. *et al.* Regulatory Toxicology and Pharmacology.2015 ;71:24–34.
*4 Tayyarah, R *et al*. CORESTA EVAP Technical Report, March 2017.
*5 Rachel, Z. *et al*. PLoS One 10(2): e0117222.
*6 Robinson, R. J. *et al*. PLoS One. 2015; 10(6): e0129296.
*7 Shepperd, C. J. *et al*. Contributions to Tobacco Research. 2006;22:176–184.

4. Conclusions

- As a result of machine smoking under various vaping regimes with square-shaped puff profile, the relation between the nicotine yield and WL from E-cigs showed a high linear relationship. The correlations between nicotine yield and WL from E-cigs were comparable to that of the PFM in CC (R^2>0.97)[7] and to that of WL from TVP (R^2>0.91)[2].
- As shown in “3.2 Influence of puff profile on correlation”, it is suggested that the correlations between nicotine yield and WL from E-cigs are not easily influenced by the difference in puff profile (i.e., square-shaped or bell-shaped).
- In conclusion, these results from this study support the hypothesis that WL can be used to estimate nicotine MLE from different types of E-cig, irrespective of puff profile.