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# Might limiting liquid nicotine concentration result in more toxic electronic cigarette aerosols?

**Soha Talih**[1,3], **Rola Salman**[1,3], **Rachel El-Hage**[2,3], **Ebrahim Karam**[2,3], **Nareg Karaoghlanian**[1,3], **Ahmad El-Hellani**[2,3], **Najat Saliba**[2,3], **Thomas Eissenberg**[3], **Alan Shihadeh**[1,3,*]

[1]Mechanical Engineering Department, Faculty of Engineering and Architecture, American University of Beirut, Bliss Street, P.O. Box 11-0236, Beirut, Lebanon

[2]Chemistry Department, Faculty of Arts and Sciences, American University of Beirut, Bliss Street, P.O. Box 11-0236, Beirut, Lebanon

[3]Center for the Study of Tobacco Products, Psychology Department, Virginia Commonwealth University, USA

## Abstract

Some jurisdictions have instituted limits on electronic cigarette (ECIG) liquid nicotine concentration, in an effort to control ECIG nicotine yield, and others are considering following suit. Because ECIG nicotine yield is proportional to the product of liquid nicotine concentration (mg/mL) and device power (watts, W) regulations that limit liquid nicotine concentration may drive users to adopt higher wattage devices in order to obtain a desired nicotine yield. In this study we investigated, under various hypothetical regulatory limits on ECIG liquid nicotine concentration, a scenario in which a user of a common ECIG device (SMOK TF-N2) seeks to obtain in 15 puffs the nicotine emissions equivalent to one combustible cigarette (i.e. 1.8 mg). We measured total aerosol and carbonyl compound (CCs) yields in 15 puffs as a function of power (15–80 W) while all else was held constant. The estimated nicotine concentration needed to achieve combustible cigarette-like nicotine yield at each power level was then computed based on the measured liquid consumption. We found that for a constant nicotine yield of 1.8mg, reducing the liquid nicotine concentration resulted in greater amount of liquid aerosolized ($p<.01$) and greater CC emissions ($p<.05$). Thus, if users seek a given nicotine yield, regulatory limits on nicotine concentration may have the unintended consequence of increasing exposure to aerosol and respiratory toxicants. This outcome demonstrates that attempting to control ECIG nicotine yield by regulating one factor at a time may have unintended health effects and highlights the need to consider multiple factors and outcomes simultaneously when designing regulations.

[*]Corresponding Author: Alan Shihadeh, Tel: + 961 1 344444, as20@aub.edu.lb, Address: Aerosol Research Laboratory, Department of Mechanical Engineering, American University of Beirut, PO Box 11-0236 Beirut, Lebanon.

CONTRIBUTORSHIP STATEMENT

conception: ST, TE, AS; acquisition and interpretation of data: ST, RS, RH, EK, NK, AH, NS, TE, AS; drafted the work: ST, AS; revised the work: ST, RS, RH, EK, NK, AH, NS, TE, AS.

## INTRODUCTION

As of May 2016, the EU limits ECIG nicotine concentration to ≤20mg/mL nicotine to allow "for a delivery of nicotine that is comparable to the permitted dose of nicotine derived from a standard cigarette…".[1] In the USA similar measures are under consideration.[2] However, these measures do not account for the unique capabilities of ECIGs; no other category of tobacco product offers users control over so many factors that determine nicotine emissions, such as electrical power and liquid composition. [3] Typically, early ECIG models were powered at 5W; however, today, ECIG devices can reach wattages as high as 250W, equivalent to five times that required to power a typical laptop. These wattages allow users to obtain a cloud-like nicotine-containing aerosol.[4]

Limiting liquid nicotine concentration while leaving device power unregulated might lead ECIG users to transition to higher-powered devices and inhale more aerosolized liquid to obtain cigarette-like nicotine delivery.[5] Indeed, recent data demonstrated that in the natural environment, low-nicotine concentration ECIG users utilized devices with relatively high wattage, which, in turn, led them to consume three times the amount of liquid for a similar total weekly nicotine consumption as users of high nicotine concentration liquids.[6] By consuming more liquid, the high-power group may also be exposed to greater amounts of respiratory toxicants such as carbonyl compounds (CCs), which are thermal degradation products of propylene glycol and glycerin, two major constituents of ECIG liquids. [4] In this study, we examine the amount of liquid aerosolized and CC yields when nicotine concentration is traded for power to maintain a given nicotine yield in a fixed number of puffs of a given volume and duration.

## METHODS

A SMOK®TF-N2 Air Core ECIG device (0.22Ω resistance heating element) was filled with PG (≥99.5%, CAS 57-55-6) and puffed using the AUB Aerosol Lab Vaping Instrument (ALVIN), which was programmed to draw four-second puffs at a flow rate of 1LPM, with a 10-sec interpuff interval. An external power supply was used to supply power to the coil head. The power was increased in small increments between the range 15–80W, corresponding to a thermal heat flux between 67 and 360W/mm$^2$ at the ECIG heating coil surface.[4] Three new coil heads from the same make and model were used, each covering the span of heat fluxes tested, resulting in three samples per condition. The entire aerosol flow was drawn through a 47 mm glass fiber filter trap (Pall Type A/E) followed by a DNPH-coated silica cartridge (3mL LpDNPH H Series Cartridges H10, Sigma Aldrich) to trap and derivatize CC species as described in Talih, Salman [4]. The number of puffs per session used to generate the aerosol differed according to the power input and was equal to 15puffs for powers below 50W, and to two puffs above 50W to avoid overloading the particulate trap. In separate measurements of coil temperature (not reported), we found that at powers of 50W and greater, the TF-N2 reaches a steady state temperature in a negligible time relative to the 4s puff duration, and therefore did not utilize "warm up puffs" for the two-puff bouts. We report the results on an equivalent 15-puff basis by extrapolating linearly to 15 puffs. A detailed description of the conditions is presented in Table S1. The SMOK TF-N2 incorporates two adjustable airflow slots; the bottom airflow slot was kept half-open, and the top slot was kept closed during sampling. The amount of liquid aerosolized was determined gravimetrically as the change in mass of the ECIG tank pre and post-sampling. CCs were quantified by extracting the DNPH cartridges in 90/10 (vol/vol) ethanol/acetonitrile and analyzing the prepared extract by HPLC-UV, as described in Al Rashidi, Shihadeh [7]. Species analyzed included formaldehyde, acetaldehyde, acetone, acrolein, propionaldehyde, benzaldehyde, valeraldehyde, glyoxal, and methyl glyoxal. Limits of quantification are provided in Talih, Salman [4].

Mass of liquid aerosolized was fitted to device power using a $2^{nd}$ order polynomial expression, while total CC yields were fitted to power using an exponential expression. The liquid used in this study did not contain nicotine; therefore, we computed the liquid nicotine concentration estimated to produce combustible cigarette-like nicotine yield (1.8mg/cigarette,[8]) for any given power, assuming that the nicotine mass concentration of the aerosol equals that of the parent liquid. This assumption holds for most practical circumstances.[9] It readily follows that the estimated nicotine concentration $C$ (mg/ml) required to meet a given nicotine yield $Y$ (mg) equals the yield multiplied by the liquid density $r$ (mg/ml), divided by the mass of liquid consumed $M$ (mg), : $C = (Y \times r) / M$.

## RESULTS

Liquid consumed and CC emissions increased significantly with power ($R^2$=0.99, $p$<.01; $R^2$=0.60, $p$<.05, respectively). The relationship between power, computed nicotine concentration required to produce a nicotine yield of 1.8 mg, and total CC emissions is graphed in Figure 1. The results are summarized in Supplementary Table S1.

## DISCUSSION

Increasing power was found to increase the mass of liquid consumed and total CC yields. Because the liquid content in the aerosol is proportional to that of the parent liquid,[9] a high nicotine/low power device can provide the same nicotine yield as a low nicotine/high power device pairing. However, the high power/low nicotine pairing results in greater CC yields.

The data shown in Figure 1 demonstrates how a user of a variable power ECIG can readily circumvent the intent of regulations designed to limit nicotine emissions by simply trading decrements in liquid nicotine concentration for increments in power. It also demonstrates how limiting nicotine concentration will drive up exposure to respiratory toxicants for any user that seeks a given nicotine yield. For example, device A in Figure 1 represents a 36mg/mL nicotine concentration, 15W power ECIG model that can produce in 15 puffs the nicotine yield of a combustible cigarette. However, device A is not accessible in areas where the EU limit on nicotine concentration is in effect. Users may opt instead for device B, which emits the same nicotine as device A, but does so using a 3mg/mL nicotine concentration liquid and 75W power. Compared to device A, device B exposes users to roughly 83 times the levels of CCs and 14 times the mass of liquid aerosolized for the same nicotine yield, making it a more hazardous product. In the ECIG market today, device A resembles small form factor pod-systems such as JUUL, [10] while B resembles larger high-powered sub-ohm devices. In summary, regulating one factor at a time – in this case nicotine concentration – is not only ineffective for meeting stated objectives, but may have the unintended consequence of increasing toxicant exposure.

A limitation of this study is that puff topography is assumed to be constant across power and nicotine concentration. While the main focus of this paper is the tradeoff between nicotine concentration and power, other compensatory behavior such as altering puff duration and volume may also increase users toxicant exposure. Previous reports found that, when given lower nicotine concentration liquids, users took longer,[11–13] larger,[12] and more frequent puffs,[11, 12] which resulted in more liquid consumed,[11] and higher levels of CCs.[14] Additionally, we note that the CC profile and total CCs, reported in this study represent 100/0 PG/VG liquid. Other PG/VG ratios may result in differing distributions of specific CC species and total CCs. However, while only PG was studied, the tradeoff illustrated in Figure 1 is intrinsic to the physics of ECIGs. That is, users facing regulatory limits on nicotine concentration can circumvent the intended effect of such restrictions by resorting to higher power devices, which will vaporize more liquid, likely involving higher toxicant emissions. Such compensatory behavior and associated increase in toxicant exposure led Wagener, Floyd [5], to recommend setting a lower instead of an upper limit on the liquid nicotine concentration.

As we have argued elsewhere,[3] this study illustrates the intrinsic risk of regulating one variable in isolation; holding all else constant, restrictions on nicotine concentration can be circumvented with greater power devices, resulting in greater amounts of liquid consumed and greater exposure to toxic carbonyl compounds. Similarly, a floor on nicotine concentration may drive the market towards lower power, smaller battery, and more concealable devices like JUUL that may particularly appeal to youth.[15] In conclusion, in order to minimize harm, regulating nicotine exposure requires addressing multiple relevant variables and outcomes in combination, rather than one at a time.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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The authors declare the following competing financial interest(s): Dr. Shihadeh and Dr. Eissenberg are paid consultants in litigation against the tobacco industry and are named on a patent application for a device that measures the puffing behavior of electronic cigarette users. Dr. Eissenberg is also a paid consultant in litigation against the electronic cigarette industry.

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**WHAT THIS PAPER ADDS**

- Combustible cigarette-like nicotine yields can be obtained by numerous combinations of electroniccigarette liquid concentration and device power
- If regulations limit nicotine concentration of electronic cigarette liquids, users may compensate by adopting higher power devices, and be exposed to greater emissions of toxic and carcinogenic carbonyl compounds.
- Regulating one factor at a time may have unintended health effects and highlights the need to consider multiple factors and outcomes simultaneously when designing regulations

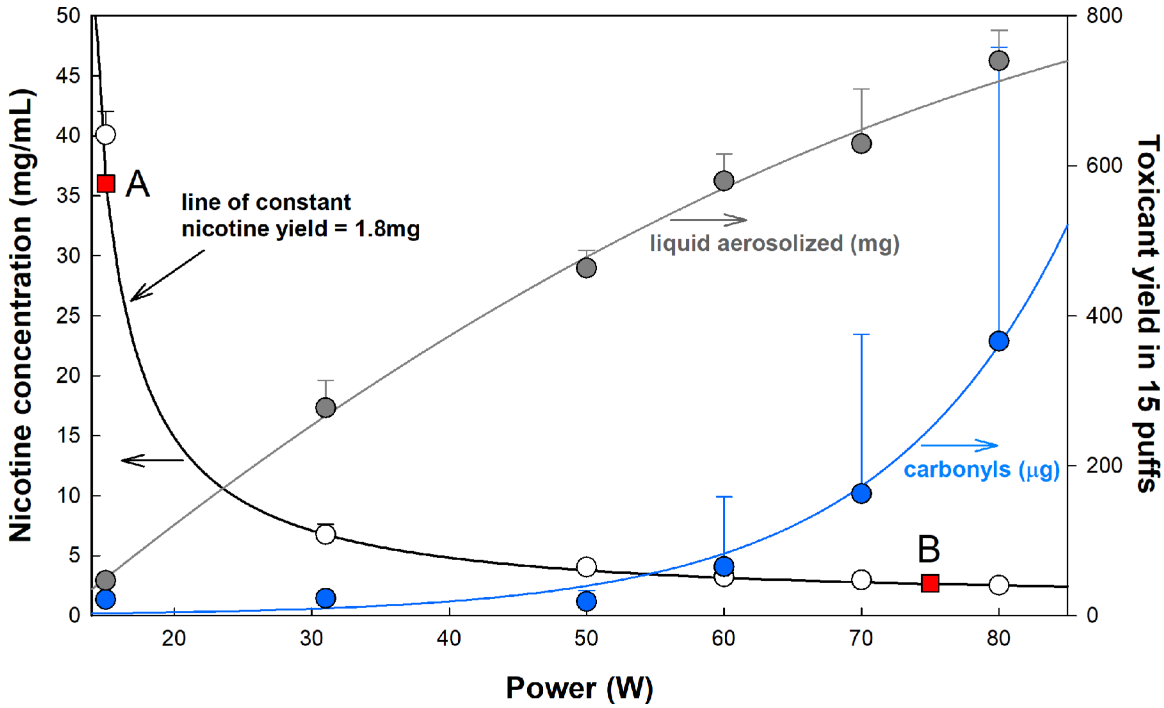


**Figure 1.**

Solid line indicates the power required to achieve 1.8 mg nicotine yield as a function of nicotine concentration for the TF-N2 SMOK device, illustrating the inherent tradeoff between the two variables. 1.8 mg corresponds to a combustible cigarette nicotine yield. The right vertical axis shows the total carbonyl emissions and liquid aerosolized as a function of power. For example if nicotine concentration was limited to 20 mg/ml, a power of approximately 18 W is required to produce a combustible cigarette like yield of 1.8 mg. This condition, in turn, would result in CC emissions of 4 ug and 90mg of liquid aerosolized. A and B represent low power/high nicotine and high power/low nicotine devices, respectively. Devices A and B illustrate how substituting nicotine (A) for power (B) results in more liquid being aerosolized and higher CC emissions.