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Nicotine Emissions from Electronic Cigarettes: Individual and Interactive Effects of Propylene Glycol to Vegetable Glycerin Composition and Device Power Output

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Abstract

Introduction: The power output of e-cigarettes varies considerably, as does the composition of liquids used with these products. Most e-cigarette liquids contain two primary solvents: propylene glycol (PG) and vegetable glycerin (VG). The primary aim of this study was to examine the extent to which PG and VG composition and device power interact with each other to influence e-cigarette nicotine emissions.

Methods: Aerosols were generated using a 2nd generation e-cigarette and an automatic smoking machine. Nicotine was measured in aerosols, via gas chromatography, produced from three solutions containing pure PG, pure VG, or a mixture of both solvents (50:50) across three different power settings (4.3, 6.7, and 9.6 W).

Results: At the lowest power setting, nicotine yield increased significantly as more PG was added to the solution. However, as device power was increased, differences in nicotine yield across

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Conflict of Interest

MLG received research funding from *Pfizer* and served as an advisory board member to Johnson and Johnson, manufacturers of stop smoking medications. AS accepted personal fees from the eSmoking Institute in Poznan, Poland, and non-financial support from Chic Group LTD, a manufacturer of electronic cigarettes in Poland, outside of the submitted work. AS also works in the Institute of Occupational Medicine and Environmental Health. LK works as an expert for the Polish National Committee for Standardization and for the European Committee for standardization of requirements and test methods for e-liquids and emissions. LK was also an employee of the Institute of Occupational Medicine and Environmental Health. One of the institute's objectives is outsourcing for the industrial sector, including manufacturers of e-cigarettes. However, this has no influence on studies design. LK is supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Number P50DA036105 and the Center for Tobacco Products of the U.S. Food and Drug Administration. The content is solely the responsibility of the authors and does not necessarily represent the views of the NIH or the FDA. Other authors declare no conflict of interest.

liquids became less pronounced. At the highest power setting (9.6 W), nicotine yields did not differ across the three liquids examined.

Conclusions: The present study demonstrated that the extent to which e-cigarette liquid PG and VG composition influences nicotine emissions is dependent on device power. Thus, device power may influence e-cigarette nicotine emissions to a greater degree relative to solvent concentrations.

Keywords

electronic cigarettes; vapor; nicotine; wattage; propylene glycol; vegetable glycerin

1 Introduction

Electronic cigarettes (e-cigarettes) are a class of products that use an electrical heating element to aerosolize an often nicotine-containing liquid for user inhalation (Breland et al., 2017; Kosmider et al., 2012). The individual and public health effects of e-cigarettes remain unclear, as much is to be discerned regarding their effectiveness in facilitating switching from tobacco cigarettes, the consequences of their use by nicotine-naïve adolescents, and their long-term health effects. Gaining a further understanding of nicotine emissions of e-cigarettes may assist in answering these questions, as nicotine is the dependence-producing substance primarily responsible for producing the reinforcing effects which promote the continued use of other tobacco products. However, the nicotine present in the aerosols produced from e-cigarettes (also referred to as nicotine yield) is heavily influenced by design features and liquid ingredients of these products, both of which vary substantially (Farsalinos et al., 2016).

Electrical power output varies widely across e-cigarettes. Some e-cigarettes such as so-called “cigalikes” are relatively low powered (<5W) and unmodifiable while other e-cigarettes, sometimes referred to as “third generation,” afford users the ability to alter the power of the device based on their preference (Breland et al., 2017). Importantly, manipulating the overall power of an e-cigarette can profoundly influence nicotine emissions from these products. For example, increasing the voltage of the battery or decreasing the resistance of the heating element can each result in greater electrical power flowing through the heating element resulting in higher temperatures and greater yields of nicotine (Talih et al., 2017, 2015; Wagener et al., 2017).

The ingredients found in e-cigarette liquids including the concentration of nicotine (Talih et al., 2017, 2015) and the proportions of the principle solvents propylene glycol (PG) and vegetable glycerin (VG) can also affect nicotine emissions from these products (Talih et al., 2017). For instance, increasing the concentration of nicotine in e-cigarette liquids results in higher yields of nicotine in the resulting aerosol (Talih et al., 2017, 2015). In addition, nicotine yield can differ based on the proportions of PG to VG found in the e-cigarette liquid. One recent study determined that when holding all relevant device, liquid, and puff topography factors constant, increasing the amount of PG in an e-cigarette solution results in a corresponding increase in the nicotine yield of aerosols produced from e-cigarettes of low wattages (e.g., 4.3 W; Baassiri et al., 2017). This finding is likely the result of VG having a higher boiling point than PG (287°C, 187°C, respectively) resulting in more energy being

required to aerosolize VG-based liquids relative to PG-based liquids (Baassiri et al., 2017). However, additional research is necessary to determine the extent to which PG/VG composition influence nicotine yield at higher wattages given the proliferation of e-cigarettes allowing users to increase the power of their device to wattages far exceeding early generation e-cigarettes (Rudy et al., 2017; Wagener et al., 2017). Because PG and VG differ in their vapor pressure values (an index of a liquids' evaporation rate), the volatility of these two solvents likely will differ based on the internal temperature of the device. Given that the internal temperature of an e-cigarette increases as the overall power of the device increases, the extent to which PG/VG composition influence nicotine yield at wattage settings greater than 4.3 is unclear.

The present study extends previous work (Baassiri et al., 2017; Talih et al., 2015) by examining the extent to which e-cigarette liquid PG and VG content and device power collectively influence nicotine yield. By systematically manipulating both liquid PG and VG composition and device power, the present study is the first to examine the individual influence of each respective factor while also exploring whether interactive effects exist between these two important variables.

2 Methods

2.1 Materials

The eGo-3 Twist e-cigarette (Volish, Ltd, Poland) paired with the 2.4 Ohm Crystal 2 Clearomizer was used to generate all aerosols examined in this study. Three different voltage settings were used in the present study (3.2, 4.0, and 4.8V), corresponding to 4.3, 6.7, and 9.6 W. Voltages were verified using a voltmeter and determined to be within 0.1 V of the intended setting. Prior to each use, all batteries were fully charged for 24 hours and were replaced when they indicated a decrease in charging level from 100%–50% (white diode color) to 50%–10% (light blue diode color).

All liquids were purchased from Evaper (<http://evaper.pl>). One liquid contained 100% PG, one contained 50% PG and 50% VG, and the last contained 100% VG in accordance to the label information. Each liquid contained 18 mg/mL of nicotine and tobacco flavoring. Nicotine content measured in the e-liquids varied from the labelled nicotine concentrations by less than 5%.

Procedure

Aerosols were generated using a smoking machine (Technical University of Lodz, Poland) designed specifically for e-cigarettes as described elsewhere (Goniewicz et al., 2013). Three liquids with different PG/VG concentrations and three power settings were used resulting in nine different liquid/device power combinations being examined (see Table 1). Puff topography parameters used to produce all e-cigarette aerosols were: 15 total puffs with 2 second puff durations, 17 second interpuff-intervals, and 50 mL puff volumes (Goniewicz et al., 2013; Kosmider et al., 2015). These puffing parameters were used to generate aerosols 30 separate times for each of the nine liquid PG/VG proportions/power combinations. Prior to examining each liquid/power combination, the e-cigarette tank was filled with 1 mL of

liquid; this procedure was repeated after the 10th and 20th trial for each of the nine conditions. Nicotine yields were investigated using gas chromatography methods described elsewhere (Goniewicz et al., 2013).

2.3 Data Analysis

Data were analyzed using Statistica 10.0 software. The 30 trials performed for each liquid/power combination were averaged to produce nine mean nicotine yield values which are presented throughout as absolute values in μg . Differences between the mean nicotine yields of all liquid/power combinations were examined using a factorial ANOVA and Scheffe's method was used for post-hoc testing ($p < .05$).

3 Results

3.1 Influence of E-cigarette Liquid PG/VG compositions.

Liquid PG/VG composition significantly influenced nicotine yields at the 4.3 and 6.7 W setting (Figure 1). At each of these two lower power settings, the highest nicotine yields were observed with the 100% PG liquid while the lowest were observed with the 100% VG liquid. At the 4.3 W setting, nicotine yield increased significantly as more PG was added to the solution. However, as the device power was increased, differences in nicotine yield across liquids became less pronounced. At the 6.7 W setting, nicotine yield observed with the 100% PG liquid was significantly higher relative to the 100% VG and 50PG:50VG liquids but no differences were detected between the 100% VG and 50PG:50VG liquids. At the highest power setting (9.6 W) no differences in nicotine yield were observed across the three PG/VG compositions (Figure 1).

3.2 Influence of Device Power

For each of the three liquids examined, nicotine yield increased as the power of the device increased. However, the observed increases in nicotine yield did not occur at the same rate for each liquid PG/VG composition examined. For the 100% VG liquid, nicotine yield increased in a more pronounced manner as device power was increased relative to the increases observed with the other liquids. When the 100% VG liquid was used, the mean $[\mu\text{g}/\text{puff}] \pm \text{SD}$ nicotine yield released from one puff increased nearly three-fold from the lowest (30.5 ± 5.9) to the highest power setting (87.4 ± 19.3). Conversely nicotine yield increased more moderately from the lowest (56.7 ± 10.3) to highest power setting (85.9 ± 29.1) when the 100% PG liquid was used (Table 1).

4 Discussion

The purpose of the present study was to examine the individual and interactive effects of e-cigarette liquid PG:/VG composition and device power on nicotine emissions, as these two e-cigarette features vary substantially across this broad product category. Findings were consistent with previous reports demonstrating that e-cigarette liquid PG/VG composition (Baassiri et al., 2017) and device power (Talih et al., 2017, 2015) can each individually influence nicotine yield when all relevant device, liquid, and puff topography factors are held constant. Furthermore, the present study expanded on previous reports by

demonstrating that these two e-cigarette device and liquid characteristics can also interact with one another to alter the amount of nicotine released from these products. These findings and their implications are discussed in further detail below.

Liquid PG/VG composition significantly influenced nicotine yield in the present study, most drastically at the lowest power setting (i.e., 4.3 W). At this low power setting, nicotine yields detected in the aerosols examined increased as the concentration of PG increased. This finding is consistent with another study using a device of the same power setting that also examined the influence of liquid PG/VG composition on nicotine yields under comparable conditions (Baassiri et al., 2017). Also consistent with previous research (Talih et al., 2017, 2015), increasing e-cigarette power output in the present study resulted in corresponding increases in nicotine yields for each of the liquids examined. However, the present study is the first to demonstrate that device power and PG/VG composition do not influence nicotine emissions in isolation but instead can interact with one another and should be assessed simultaneously. For example, PG/VG composition had a less pronounced influence on nicotine yields as device power was increased and indeed at the highest power setting, no effect of PG and VG content on nicotine emissions was observed. These results may suggest that PG/VG composition can significantly influence nicotine delivery for users of low-powered devices such as “cigalikes” while having little to no influence on nicotine delivery for users of higher wattage “third generation” devices. Alternatively, the lower power output of “cigalike” devices may result in ineffective nicotine delivery across all liquids (Vansickel et al., 2010). Further, given that PG-based liquids produce smaller particles relative to VG-based liquids (Baassiri et al., 2017) and smaller particles generally deposit more effectively in the lungs (Heyder, 2004; Zhang et al., 2013), PG/VG composition may still influence nicotine delivery in e-cigarette users at wattages examined in the present study. Ultimately, future clinical laboratory research is needed in which the influence of e-cigarette liquid PG and VG concentrations on nicotine delivery is explored across multiple devices of varying wattages. Further examinations using even higher device power settings, and thus higher temperatures, may be warranted given the increased popularity of devices with far greater wattages than those used in the present study (Rudy et al., 2017; Wagener et al., 2017).

The differing rate of change in volatility in response to temperature increases may provide an explanation for PG/VG composition having less of an influence on nicotine yield as device wattage was increased. That is, PG has a lower threshold for evaporation, and thus is more volatile, relative to VG at normal temperatures. Temperature increases, such as those induced by increasing the power output of an e-cigarette, can cause solvents such as PG and VG to increase exponentially in their volatility. Importantly, substances such as VG that are ordinarily less volatile can increase to a greater extent in their evaporation rate in response to temperature increases relative to substances such as PG that are already volatile at relatively low temperatures. Thus, high temperatures, such as those produced with the highest power output in the present study, may result in comparable volatility rates for PG and VG and consequently comparable nicotine yields for e-cigarette liquids of all PG/VG compositions. Thus higher nicotine yields may be connected with higher aerosol yield vaporization (Korzun et al., 2018; Kosmider et al., 2016).

Taken together, findings from the present study highlight the need for future regulations attempting to control e-cigarette nicotine emissions to consider multiple device, liquid, and puff topography factors simultaneously that have proven to influence nicotine yield and/or delivery from these products. Attempts to regulate any one particular factor would likely prove to be ineffective, as a user could modify another aspect of their device or liquid in order to circumvent the regulation. For example, one regulation implemented by the European Union in 2014 attempted to limit e-cigarette nicotine delivery to levels comparable to a tobacco cigarette by prohibiting the sale of e-cigarette liquids with nicotine concentrations over 20 mg/ml. However, because other influential device, liquid, or user factors were not also regulated, users who are forced by this regulation to lower their liquid nicotine concentration could simply use a liquid with a higher PG content, increase the intensity of their puffs, or increase the power of their device to increase their nicotine delivery to levels they are accustomed to. The extent to which other e-cigarette device/liquid features individually and collectively influence emissions of nicotine and other toxicants needs further exploration in order to facilitate proper regulations of these products.

There were several limitations to the present study. First, the puff topography parameters used in the present study to generate the aerosols examined were less intensive relative to puffing behaviors recorded in human participants in other studies. For example the puff duration (2 s) and puff volume (50 mL) values used in the present study are lower than puff durations (e.g., ~4–5.5 s;(Farsalinos et al., 2013; Hiler et al., 2017; Spindle et al., 2016)) and puff volumes (~125 – 200 mL;(Hiler et al., 2017; Spindle et al., 2016)) measured for some e-cigarette users. Thus, the puffing parameters used in the present study may have underestimated e-cigarette users' nicotine exposure. Second, because the present study only examined nicotine in e-cigarette aerosols, the extent to which PG/VG composition will influence nicotine delivery in actual e-cigarette users remains unclear. Other factors such as inhalation depth, particle size, and user puff topography likely will also influence nicotine delivery. Thus e-cigarette liquid solvent content may not influence nicotine delivery and nicotine yield in the same manner. Future research in which the influence of e-cigarette liquid PG/VG composition on nicotine delivery is examined while other relevant device and liquid factors are held constant is important to discern whether the effects observed in the present study are clinically relevant.

In conclusion, the present study is the first to demonstrate that e-cigarette liquid PG/VG composition can influence nicotine emissions differentially according to the power of the device being used. Thus, in addition to the nicotine content present in e-cigarette liquids, physicochemical factors including temperature and liquid volatility play an important role in influencing nicotine emissions from these products. Future regulations attempting to control toxicant emissions of e-cigarettes such as nicotine will need to account for multiple device, liquid, and puff topography factors in order to be effective.

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Figure 1. Nicotine yields released with 15 puffs (puffs duration: 2 s; interpuff-intervals: 17 s; puffs volume: 50 mL). Comparison between solvents types.

The bars depict the mean concentration of nicotine and whiskers represent means $\pm$ 0.95 confidence interval of the mean. * - statistical significance was found: between VG and VG/PG; ** - statistical significance was found: between VG and PG; *** - between VG/PG and PG. VG - glycerin solvent liquid; VG/PG - liquid contains glycerin and propylene glycol; PG- propylene glycol solvent liquid. Limit of quantitation: 0.05 μ g/mL.

Table 1.

Wattage influence on nicotine release.

Liquid type*	Wattage [W]	Mean dose of nicotine generated by one puff [µg/puff]±SD	Relative dose of nicotine to dose generated for 4.3 W [%] for each liquid	Scheffe's test value**
VG	4.3	30.5±5.9	100%	a<0.01
VG	6.7	46.4±12.8	152%	b<0.01
VG	9.6	87.4±19.3	283%	c<0.01
VG/PG	4.3	39.3±9.6	100%	a>0.05
VG/PG	6.7	48.4±8.5	124%	b<0.01
VG/PG	9.6	80.8±26.2	205%	c<0.01
PG	4.3	56.7±10.3	100%	a>0.05
PG	6.7	69.3±15.4	121%	b<0.01
PG	9.6	85.9±29.1	152%	c<0.01

Note:

* VG - glycerin solvent liquid; VG/PG - liquid contains glycerin and propylene glycol; PG- propylene glycol solvent liquid.

** a, b and c represents p values for Scheffe test: a-between 4.3 [W] and 6.7 [W]; b-between 6.7 [W] and 9.6 [W]; c-between 4.3 [W] and 9.6 [W].
Limit of quantitation: 0.05 µg/mL.