Addictive Behaviors 73 (2017) 137–143

Contents lists available at ScienceDirect

Addictive Behaviors

journal homepage: www.elsevier.com/locate/addictbeh

E-cigarette liquids: Constancy of content across batches and accuracy of labeling

Jean-François Etter[a,*], Aurélie Bugey[b]

[a] Institute of Global Health, Faculty of Medicine, University of Geneva, Switzerland
[b] Service of Consumer and Veterinary Affairs, Canton of Geneva, Switzerland

ARTICLE INFO

Keywords:
Electronic cigarette
Electronic nicotine delivery systems
E-cigarette
E-liquid
Quality control

ABSTRACT

Aims: To assess whether bottles of refill liquids for e-cigarettes were filled true to label, whether their content was constant across two production batches, and whether they contained impurities.

Methods: In 2013, we purchased on the Internet 18 models from 11 brands of e-liquids. We purchased a second sample of the same models 4 months later. We analyzed their content in nicotine, anabasine, propylene glycol, glycerol, ethylene glycol and diethylene glycol, and tested their pH.

Results: The median difference between the nicotine value on the labels and the nicotine content in the bottles was 0.3 mg/mL (range − 5.4 to + 3.5 mg/mL, i.e. − 8% to + 30%). For 82% of the samples, the actual nicotine content was within 10% of the value on the labels. All models contained glycerol (median 407 mg/mL), and all but three models contained propylene glycol (median 650 mg/mL). For all samples, levels of anabasine, ethylene glycol and diethylene glycol were below our limits of detection. The pH of all the e-liquids was alkaline (median pH = 9.1; range 8.1 to 9.9). The measured content of two batches of the same model varied by a median of 0% across batches for propylene glycol, 1% for glycerol, 0% for pH, and 0.5% for nicotine (range − 15% to + 21%; 5th and 95th percentiles: − 15% and + 10%).

Conclusions: The nicotine content of these e-liquids matched the labels on the bottles, and was relatively constant across production batches. The content of propylene glycol and glycerol was also stable across batches, as was the pH.

1. Introduction

E-cigarettes are now used by millions of persons, and 16% of daily smokers and 18% of recent quitters in the United States report currently using these products (Brown & West, 2015; Delnevo, Giovenco, Steinberg, et al., 2016; Hajek, Etter, Benowitz, Eissenberg, & McRobbie, 2014). Regular users of e-cigarettes ("vapers") generally use refillable models (Krishnan-Sarin, Morean, Camenga, Cavallo, & Kong, 2015; Yingst et al., 2015), which comprise a battery-powered atomizer that produces vapor for inhalation from refillable tanks (Etter, Bullen, Flouris, Laugesen, & Eissenberg, 2011). Refill liquids (e-liquids) usually contain propylene glycol or glycerol (or a mix of both), flavors, nicotine, water and ethanol (Etter, Zather, & Svensson, 2013; Peace et al., 2016). Some reports suggest that some refill liquids (e-liquids) for e-cigarettes may not be filled true to label (Cameron et al., 2014; Davis, Dang, Kim, & Talbot, 2015; Goniewicz, Gupta, Lee, et al., 2015; Peace et al., 2016) (Cheng, 2014; Goniewicz, Kuma, Gawron, Knysak, & Kosmider, 2013), or may contain toxic substances and impurities (Cheng, 2014; Goniewicz, Knysak, Gawron, et al., 2014a; Hajek et al., 2014; Trehy, Ye, Hadwiger, et al., 2011; Uchiyama, Inaba, & Kunugita, 2010; Williams, Villarreal, Bozhilov, Lin, & Talbot, 2013), although other reports showed that most e-liquid bottles are filled true to labels and contain few impurities or toxic elements (Etter et al., 2013; Varlet, Farsalinos, Augsburger, Thomas, & Etter, 2015), and that the quality of e-liquids is compliant with norms (Etter et al., 2013). Several toxicants were also found in e-cigarette aerosols (Goniewicz et al., 2014a; Herrington & Myers, 2015; Williams et al., 2013), although usually at levels lower than in cigarette smoke (Farsalinos & Polosa, 2014). High doses of nicotine can be toxic (Mayer, 2014), and it is therefore important that labels on e-liquid bottles be accurate and that e-liquid content be constant.

One concern is the lack of mandatory manufacturing standards for e-cigarettes and e-liquids. Associations of manufacturers and distributors have published guidelines and manufacturing standards, but these guidelines and standards are not mandatory (e.g. AFNOR in France, AEMSA in the U.S.) (AEMSA, 2013; AFNOR, 2016). The U.S. and E.U. regulations require declaration of the content of the refill liquids, but do not enforce manufacturing standards (EU, 2014; Pirschel, 2016). There

* Corresponding author at: Institute of Global Health, University of Geneva, Campus Biotech, 9 chemin des Mines, CH-1202 Genève, Switzerland.
E-mail address: Jean-Francois.Etter@unige.ch (J.-F. Etter).

http://dx.doi.org/10.1016/j.addbeh.2017.05.012
Received 5 December 2016; Received in revised form 4 May 2017; Accepted 8 May 2017
Available online 10 May 2017
0306-4603/

are many manufacturers and retailers globally, and products are not always manufactured along standards imposed on food, flavors, and cosmetics, let alone medications. In particular, there is no guarantee that the composition of e-liquids is constant across successive production batches.

There is little published information on the constancy of e-liquid content across successive production batches, but the only two available reports on the variability of content across batches show similar results (Davis et al., 2015) (Goniewicz, Hajek, & McRobbie, 2014b) Goniewicz et al. found that the difference in nicotine content between two different batches of the same models (N = 6 duplicates) ranged from 1% to 31% (median 15%) (Goniewicz et al., 2014b). Davis et al. found that, across two different batches of the same e-liquid models (N = 23 duplicates), the color of the liquids varied across duplicates for some samples, and that the nicotine concentrations varied by 16% (median) across two batches of the same model (quartiles 9% and 26%, range 0% to 57%) (Davis et al., 2015). To our knowledge, there is no published report of the constancy of levels of propylene glycol, glycerol and pH across different production batches of e-liquids.

Thus, the objectives of this study were to check whether bottles of e-liquids were filled true to label, whether they contained impurities, whether their composition (nicotine, propylene glycol, glycerol, pH) was constant across two different production batches, and if there were variations across batches, whether these variations were comparable to variations observed in previous reports (Davis et al., 2015; Goniewicz et al., 2014b).

2. Methods

Previous online surveys of vapers enabled us to identify the most frequently used brands of e-liquids used in the U.S., the U.K., France, and Switzerland (Etter, 2010; Etter & Bullen, 2011a; Etter & Eissenberg, 2015; Etter et al., 2013). Where possible, we selected these frequently used brands, and we selected other brands for their accessibility (e.g. from websites that sent products to Switzerland). We purchased two samples of each model of e-liquid on the same websites, four months apart, in February and June 2013, and checked whether the two samples actually proceeded from different production batches, identified either by batch number or production date or validity date. Nicotine-containing e-liquids cannot be sold in Switzerland, but small quantities can be imported for personal use (OFSP, 2009), which explains why we purchased the liquids online rather than in vape shops. The distributors were not aware that the products would be used for research purposes. We checked whether the same products were still available online in April 2017.

Upon receipt in Geneva (Switzerland), the bottles were kept at room temperature and protected from the light until they were sent for analysis to the official food control authority in Geneva (Service Cantonal de la Consommation et des Affaires Vétérinaires). The liquids were kept at room temperature by this laboratory from reception of the products until the analyses, which were performed in 2013. We analyzed the liquids for their content in nicotine, anabasine, propylene glycol, glycerol, ethylene glycol and diethylene glycol. We also tested the apparent pH of the liquids. Anabasine is an alkaloid found in tobacco, it is considered an impurity in e-liquids and nicotine medications. Nicotine of pharmaceutical grade, in accordance with the European Pharmacopoeia, may as a raw material contain no more than 0.3% of anabasine (EDQM, 2012). For finished medicinal products, other limits can be justified with rationale and supportive data (i.e., stability data, relationship to the daily dose) (ICH, 2006). Ethylene glycol and diethylene glycol are toxic impurities of propylene glycol and should not be present in e-liquids.

2.1. Chemical analyses

The e-liquids were diluted with methanol and analyzed with a gas chromatographer coupled to a mass spectrometer equipped with an automatic split/splitless injector, a flame ionization detector, and a longitudinally modulated cryogenic system. Nicotine, anabasine, ethylene glycol, diethylene glycol and glycerol were identified and quantified in selected ion monitoring mode after electron impact ionization at 70 eV. Because of the high amount of propylene glycol in the samples, this compound was diverted to a flame ionization detector via a switching valve to be quantified. For reference, standard stock solutions were provided by Sigma-Aldrich (Buchs, Switzerland) and working solutions were prepared by dilution with methanol. The limits of detection were 0.01 mg/mL for nicotine, ethylene glycol and diethylene glycol, and 0.1 mg/mL for anabasine, propylene glycol and glycerol. The limits of quantification were 0.1 mg/mL for nicotine, ethylene glycol and diethylene glycol, and 1 mg/mL for anabasine, propylene glycol and glycerol. For all compounds, the uncertainty level was 20%.

Given the organic composition of the e-liquids, only the apparent pH value can be obtained by dilution of the sample with deionized water using a pH meter (Metrohm, Zofingen, Switzerland), as described by Stepanov and Fujioka (Stepanov & Fujioka, 2015)

2.2. Accuracy of the labels

We compared the nicotine concentrations in the liquids to the nicotine concentrations declared on the labels on the bottles. We also assessed whether the labels indicated that the products contained propylene glycol (PG), glycerol (i.e. vegetable glycerin, VG), or both, and in this case whether the proportions of PG and VG were indicated.

3. Results

3.1. Data collection

The first series of samples was purchased in February 2013 and the second series (same models and brands, on the same websites) in June 2013. For both series, we received by mail 18 different models of e-liquids from 11 different brands (Table 1). For each model, we identified samples from different production batches either by the batch number or by the production date or the validity date printed on the bottle or on the cardboard box that contained the bottle. For 5 models from 3 brands (*E-cig.com*, *Ecigexpress* and *Kyozen*), the samples had no indication of batch number or date. Thus, the analysis of stability across different batches was conducted only in the 13 models from 8 brands for which there were clear indications that the samples were from different production batches, identified either by date or by batch number. All the other analyses were conducted in all the 18 samples.

3.2. Nicotine

3.2.1. Labels

The median nicotine content indicated on the bottles' labels was 18 mg/mL (range 16–48 mg/mL; 25th and 75th percentiles 18 and 24 mg/mL). One sample (Kyozen) had no indication of nicotine content on the bottle or on the packaging (Table 2).

3.2.2. Content

All samples contained nicotine. The median nicotine concentration measured in the liquids was 19.6 mg/mL (range 15.5 to 52.0 mg/mL, 25th and 75th percentiles 17.1 and 24.7 mg/mL). For the 17 samples with nicotine indication on the labels, the median difference between the nicotine content indicated on the labels and the measured nicotine content was 0.3 mg/mL (= 1.9%); range − 5.4 to + 3.5 mg/mL (− 7.8% to + 30%); 25th and 75th percentiles − 2.1 and + 0.4 mg/mL (− 1% and + 7%). For 82% of the samples, the actual nicotine content was within 10% of the value on the labels. The correlation coefficient between label and actual content was r = 0.98, 95.6% of