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A novel hybrid tobacco product that delivers a tobacco flavour note with vapour aerosol (Part 1): Product operation and preliminary aerosol chemistry assessment

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ABSTRACT

Vapour products have demonstrated potential to be a lower-risk alternative to cigarettes. The present study describes a novel hybrid tobacco product that combines a warm aerosol stream generated by an electronic vaporisation mechanism with tobacco top flavour from cut tobacco. During operation, the aerosol stream released from the vapour cartomiser is passed through a bed of blended cut tobacco by the puffing flow, elevating the tobacco temperature and eluting volatile tobacco flavour components. A preliminary but comprehensive analysis of the aerosol composition of the hybrid tobacco product found that emissions were dominated by the control vapour formulation. In non-targeted chemical screening, no detectable difference in GC scans was observed between the hybrid tobacco product and the control vapour product. However, a sensorially elevated tobacco flavour was confirmed by a consumer sensory panel ($P < 0.05$). In a targeted analysis of 113 compounds, either identified by regulatory bodies as potential toxicants in cigarette smoke or formed from electronic vapour products, only 26 were quantified. The novel action of tobacco heating and liquid aerosolisation produced classes and levels of toxicants that were similar to those of the control vapour product, but much lower than those of a Kentucky 3R4F reference cigarette. For nine toxicants mandated by the WHO Study Group on Tobacco Product Regulation for reduction in cigarette emissions, the levels were 91%–99% lower per puff in the hybrid tobacco product aerosol than in 3R4F smoke. Overall, the novel hybrid tobacco product provides a sensorially enhanced tobacco flavour, but maintains a toxicant profile similar to its parent vapour product with relatively low levels of known cigarette smoke toxicants.

1. Introduction

The use of electronic nicotine delivery systems (ENDS) and e-cigarettes in particular has been steadily increasing in many countries (European Commission, 2015; Schoenborn and Grindi, 2015; West et al., 2015) since the first device was patented a decade ago (Lik, 2006). A systematic review found that, between 2009 and 2011, ENDS awareness increased from 16% to 58%, while use increased from 1% to 6% (Pepper and Brewer, 2013). More recent statistics mainly from North America, the European Union (EU) and Republic of Korea also indicate that ENDS use doubled between 2008 and 2012 (Grana et al., 2014).

Alongside this increasing use, the number of brands and flavours is expanding: an internet search of English-language websites by Zhu et al. in January 2014 identified 466 commercial brands of e-cigarettes with 7764 unique flavours—a substantial increase from the 288 brands available in 2012 (Zhu et al., 2014). ENDS are also evolving from products that look like conventional tobacco products (e.g. cigarettes, cigars and pipes) to those that resemble everyday items such as pens, USB memory sticks, and larger cylindrical or rectangular devices (WHO, 2014), hence "vaping or vapour products" may be a more appropriate name for the category rather than e-cigarettes.

So what are the risks of using e-cigarettes? ENDS, of which e-cigarettes are the most common, deliver an aerosol obtained by heating a solution or "e-liquid" that users inhale (WHO, 2014). The Royal College of Physicians (RCP) has reported that the health hazards from long-term inhalation of vapour from the e-cigarettes

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available today are unlikely to exceed 5% of the harm from smoking tobacco (RCP, 2016), while Public Health England similarly reports that "best estimates show e-cigarettes are 95% less harmful to your health than normal cigarettes" (McNeill et al., 2015). Scientific support for this position comes from the relatively simple composition of e-cigarette aerosols (Marco and Grimalt, 2015) in comparison to cigarette smoke with its thousands of constituents (Rodgman and Perfetti, 2013). Whereas nicotine is the main ingredient leading to tobacco smoking addiction (Benowitz, 2010), most of the toxicity arising from tobacco smoking stems from the burning process (Farsalinos and Le Houezec, 2015). Nevertheless, long-term inhalation toxicology on aerosol agents (propylene glycol and glycerol) are yet to be confirmed and require further investigation (Jensen et al., 2015).

The main constituents of the e-liquid by volume, in addition to nicotine when nicotine is present, are propylene glycol (PG), with or without vegetable glycerol (VG) and flavouring agents (WHO, 2014). However, impurities and flavour degradation products can be found in both liquids and aerosol emissions. In addition to known tobacco toxicants, e-cigarettes have been documented to contain potential toxicants such as glyoxal, methylglyoxal (Uchiyama et al., 2013), diacetyl and acetyl propionyl (Allen et al., 2015; Farsalinos et al., 2015), acetoin (Allen et al., 2015), copper (Lerner et al., 2015) and zinc (Williams et al., 2013). These are either possible thermal decomposition products of principal aerosol ingredients (e.g. glycerol), or derive from added flavour ingredients (e.g. diacetyl) or from contacting metal components of the device (e.g. copper). With the continued expansion of e-cigarette designs and e-liquid ranges, there is an increasing need to assess potential long-term toxicological effects of inhaling flavour ingredients used in e-cigarettes (Farsalinos and Polosa 2014). This has been reflected by findings from recent in vitro studies on the effects of nicotine, bulk aerosol agents and flavouring chemicals used, especially complex or plant extracts (Bahla et al., 2012; Behar et al., 2014; Cervellati et al., 2014; Lerner et al., 2015). Studies using human lung epithelium airway cells and other laboratory toxicological assays (Scheffler et al., 2015; Moses et al., 2017) have shown that aerosol produced from e-cigarettes can induce gene-expression changes in bronchial airway epithelium in vitro. These changes are generally less pronounced than the effects of cigarette smoke exposure and were more pronounced in e-cigarette aerosol containing nicotine than those without.

Studies are beginning to document the classes and levels of toxicants in e-cigarettes and other types of vapour product, with more extensive analyses reported by Flora et al. (2016), Sleiman et al. (2016), Tayyarah and Long (2014), Lauterbach et al., (2012), Lauterbach and Laugesen (2012), and Margham et al. (2016). The levels of nearly all toxicants that have been measured are much lower on a per-puff basis in e-cigarettes than in cigarette smoke. Relative to tobacco smoking, where several regulatory bodies have compiled lists of potential toxicants in cigarette smoke (Burns et al., 2008; FDA, 2012a; Health Canada, 1999) and the FDA and WHO's TobReg have mandated the monitoring and reporting of selected toxicants (Burns et al., 2008; FDA 2012a), the regulation of e-cigarettes is lagging behind. In the EU, e-cigarettes were brought under the revised EU Tobacco Products Directive in May 2016 (Ash, 2016). Similarly, the FDA only recently deemed e-cigarettes subject to tobacco laws (FDA, 2016b) and introduced draft regulations for new Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems (FDA, 2016a), including the recommended analysis of toxicants specific to e-cigarettes.

Within these draft guidelines, the FDA has recommended the 29 following constituents for analysis in e-liquids and aerosols for new ENDS for Premarket Tobacco Product Applications: acetaldehyde, acetyl propionyl (or 2,3-pentanedione), acrolein, acrylonitrile, 4-aminobiphenyl, 1-aminonaphthalene, 2-aminonaphthalene, ammonia, anabasine, benzene, benzo[a]pyrene, 1,3-butadiene, cadmium, chromium, crotonaldehyde, diacetyl, diethylene glycol, ethylene glycol, formaldehyde, glycerol, isoprene, lead, menthol, nickel, nicotine (including total nicotine and unprotonated nicotine), 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone) (NNK), *N*-nitrosonornicotine (NNN), propylene glycol, and toluene (FDA, 2016a). Notably, there is no agreed standard method for analytical testing of these constituents or other known tobacco smoke constituents in e-liquids or the aerosol compositions that they generate in order to enable comparison across products, although a recent study has attempted to address this (Margham et al., 2016).

For some regulators, e-cigarettes are often cited as a gateway to future tobacco use, but self-reported surveys show that most e-cigarettes are used by current or ex-smokers. Across the EU, for example, 4% of current smokers now use e-cigarettes or similar devices, as compared with 3% of ex-smokers and 0% of those who have never smoked (Eurobarometer, 2015). In the United States, current cigarette smokers and former smokers who quit smoking within the past year were more likely to use e-cigarettes than those who had never smoked (Schoenborn and Grindi, 2015). In England, current use of e-cigarettes by never smokers remains rare, and current use of e-cigarettes has been reported to be similar to the use of licensed nicotine products (West et al., 2015). A systematic review in 2013 also found that most ENDS users were current or former smokers, often engaging in dual use of ENDS and other tobacco (Pepper and Brewer, 2013). The available evidence indicates that e-cigarettes are being used mainly as alternatives to smoked tobacco (RCP, 2016). Most recently, a report by Public Health England found no evidence that e-cigarettes are undermining the long-term decline in cigarette smoking among both adults and youths (11–18 years) (McNeill et al., 2015). In addition, a systematic review found evidence, albeit with wide confidence intervals, that e-cigarettes helped smokers to stop smoking long term as compared with placebo e-cigarettes in two small trials, but no difference in effect between e-cigarettes and nicotine patches in another trial (McRobbie et al., 2014). In short, emerging evidences and analyses on e-cigarettes' potential to be an effective tobacco harm reduction product will continue to attract debates (Farsalinos and Le Houezec, 2015; RCP, 2016; McNeill et al., 2015; Kalkhoran and Glantz, 2016), and youths experimentation of e-cigarettes still require active monitoring as the vapour product design and e-liquids continue to evolve.

For e-cigarettes to help smokers to quit smoking, they have to meet the sensory and pharmacokinetic needs of the users. One common consumer complaint on current commercial e-cigarettes, as found in some online e-cigarette user blogs, is that they taste "synthetic" and lacking a tobacco note or richness of tobacco note. Several ways to deliver a controlled aerosol by heating tobacco have been described in patents and a number of tobacco-heating products (THPs), such as Revo, Ploom and iQOS, are commercially available in markets around the world. These THPs use different heating methods and have markedly different heating temperature profiles, and can deliver a different tobacco sensorial experience as compared with an e-cigarette. In this study, we report a novel mechanism of combining the aerosol generated from an electronic vapour product with the natural flavour tobacco note released from heating a segment of tobacco. We describe the characteristics of this product and also present aerosol chemistry data for analytes identified as smoke toxicants by different studies and regulatory bodies. The aerosol from the new product is compared with a control product without the tobacco insertion and also a reference cigarette.