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Assessment of novel tobacco heating product THP1.0. Part 3: Comprehensive chemical characterisation of harmful and potentially harmful aerosol emissions

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A B S T R A C T

For a tobacco heating product (THP), which heats rather than burns tobacco, the emissions of toxicants in the aerosol were compared with those in cigarette smoke under a machine-puffing regimen of puff volume 55 ml, puff duration 2 s and puff interval 30 s. The list of toxicants included those proposed by Health Canada, the World Health Organization Study Group on Tobacco Product Regulation (TobReg), the US Food and Drug Administration and possible thermal breakdown products. In comparison to the University of Kentucky 3R4F reference cigarette the toxicant levels in the THP1.0 emissions were significantly reduced across all chemical classes. For the nine toxicants proposed by TobReg for mandated reduction in cigarette emissions, the mean reductions in THP1.0 aerosol were 90.6–99.9% per consumable with an overall average reduction of 97.1%. For the abbreviated list of harmful and potentially harmful constituents of smoke specified by the US Food and Drug Administration Tobacco Products Scientific Advisory Committee for reporting in cigarette smoke (excluding nicotine), reductions in the aerosol of THP1.0 were 84.6–99.9% per consumable with an overall average reduction of 97.5%.

1. Introduction

Cigarette smoking is one of the leading preventable causes of human morbidity and mortality, causing diseases such as cardiovascular disorders, chronic obstructive pulmonary disease and lung cancer (US DHHS, 2014). For more than 50 years, scientists have worked to establish smoking-related disease mechanisms and their sources in cigarette smoke, with efforts focusing on a number of toxic chemicals in cigarette smoke (Baker, 2006; Hoffmann and Hoffmann 1998; Liu et al., 2011). Most smoking-related diseases are not caused by nicotine (Benowitz, 2010) but by toxicants present in the inhaled smoke (Farsalinos and Le Houezec, 2015). When a cigarette is lit, the tobacco burns to form smoke containing more than 6500 compounds (Rodgman and Perfetti, 2013), of which about 150 are established toxicants (Fowles and Dybing, 2003). Notably, the US Surgeon General has stated that "burden of death and disease from tobacco use in the United States is overwhelmingly caused by cigarettes and other combusted tobacco products" (US DHHS, 2014).

In 1998, Hoffmann and Hoffmann (1998) published a list of compounds present in tobacco smoke that were known to have biological activity. This list of "Hoffmann analytes", which was based on a substantial body of work in the 1970s and 1980s, provided the first benchmark of toxicants that should be monitored in tobacco and tobacco smoke. Since then, various scientific bodies have acknowledged the presence of more than 100 harmful and potentially harmful constituents (HPHCs), including Group 1 and 2A carcinogens, in tobacco and cigarette smoke (Burns et al., 2008; FDA, 2012a; IARC, 2004; WHO, 2007) and regulatory authorities have begun to mandate the reporting of specific toxicants in smoke emissions from cigarettes (ANVISA, 2007; FDA, 2012b; Health Canada, 1999a,b; Taiwan DOH, 2012). Furthermore, the World Health Organization (WHO) Study Group on Tobacco Product Regulation has proposed mandatory lowering of the emission levels from cigarettes of nine specific toxicants: CO, formaldehyde, acetaldehyde, acrolein, 1,3-butadiene, benzene, benzo[a]pyrene, *N*-nitrosonornicotine (NNN), and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) (Burns et al., 2008).

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Over recent years, an increasing array of tobacco or nicotine next-generation products (NGPs) has become available. They include tobacco heating products (THPs), which heat but do not burn tobacco, and vapour products (e.g., electronic cigarettes [e-cigarettes]), which are likely to present reduced risk in comparison to conventional cigarettes (McNeill et al., 2015; RCP, 2016). Evidence to support this view includes the relatively simple composition of aerosols produced (Marco and Grimalt, 2015) compared with that of cigarette smoke (Rodgman and Perfetti, 2013).

While the use of NGPs, particularly vapour products, has been gradually increasing (European Commission, 2015; Schoenborn and Grindi, 2015; West et al., 2015), their regulation has been slow to develop. In the European Union, e-cigarettes were brought under the revised EU Tobacco Products Directive only in May 2016 (European Commission, 2016); similarly, they have been subject to tobacco laws in the USA since 2016 (FDA, 2016a), with draft regulations proposed for new Premarket Tobacco Product Applications, including the recommended analysis of 29 toxicants specific to these products (FDA, 2016b).

Initial studies to document the classes and levels of toxicants in e-cigarettes (Flora et al., 2016; Lauterbach et al., 2012; Lauterbach and Laugesen, 2012; Margham et al., 2016; Sleiman et al., 2016; Tayyarah and Long, 2014) showed that nearly all toxicants measured were present at much lower levels on a per-puff basis in e-cigarette aerosols than in smoke from a reference cigarette. However, there is no agreed list of toxicants and/or standard methods for analytical testing of constituents in the aerosols generated by NGPs, making cross-product and inter-study comparisons difficult. We previously addressed this issue by conducting a comprehensive analysis of the chemical composition of a commercial vapour product to compare the emissions of all known vapour product and tobacco cigarette priority compounds with those from a conventional cigarette by accredited analytical techniques (Margham et al., 2016). The resulting data set addressed an important gap by reporting the emission levels of 142 chemicals and eight collated measures, covering the widest practicable range of HPHCs in cigarette smoke and constituents of concern in vapour products (Margham et al., 2016).

In this series of publications, a comprehensive assessment approach is applied to evaluate the toxicant reduction potential of the THP1.0 product. As described in the first paper of this series (Eaton et al., 2017), a tobacco consumable rod is heated to temperatures that are sufficient to vaporise volatile compounds, including nicotine, into an inhalable aerosol but not high enough to burn the tobacco. This approach results in levels of combustion-related toxicants that are significantly lower in the generated aerosol than in cigarette smoke (Forster et al., 2015; Gonzalez-Suarez et al., 2016; Schorp et al., 2012; Smith et al., 2016; Zenzen et al., 2012).

Several ways to deliver an aerosol by heating tobacco have been described in patents and in the peer-reviewed literature. Studies of first-generation electrically heated cigarettes (EHCs) indicated that approximately two-thirds of priority compounds were reduced by at least 50% and many were reduced by more than 90%, compared with conventional cigarette smoke; however, formaldehyde yields were increased (Stabbert et al., 2003). Second-generation EHCs included ammonium magnesium phosphate in the cigarette paper to reduce the yield of formaldehyde (Moennikes et al., 2008).

Later characterisation of an EHC smoking system (EHCSS) demonstrated that the mainstream aerosol was distinctly different from that of mainstream smoke (MSS) from a conventional cigarette (Zenzen et al., 2012; Schorp et al., 2012). With very few exceptions, a substantial reduction was observed in the toxicological activity of the EHCSS aerosol relative to that of conventional cigarette smoke when smoked with comparable puffing intensities or at comparable nicotine yields. Recent studies of an updated version of the EHCSS, known as a tobacco heating system (THS), have also shown that the formation of HPHCs is greatly reduced compared with formation during cigarette smoking (Smith et al., 2016; Schaller et al., 2016).

Such studies have led to the commercial launch of THPs in some countries, including Eclipse (R. J. Reynolds, Winston Salem, NC, USA), Ploom TECH (Ploom™, San Francisco, CA, USA), iQOS™ (Philip Morris International, Neuchâtel, Switzerland) and glo™ (THP1.0, British American Tobacco, London, UK). Each of these THPs uses a different heating method characterised by the configuration of the heater relative to whether it is inside or outside the tobacco bed or rod, the temperature profile of the heater (heating rate, maximum temperature and duration) and the physical form and chemical composition of the tobacco material. Thus, it is necessary to understand how the tobacco material influences the aerosol chemistry under different heating conditions. For THP1.0, a multi-step thermophysical and thermochemical characterisation was conducted which confirmed that the aerosol is produced by evaporation and distillation and not by combustion (Eaton et al., 2017).

Cigarette smoke is mainly produced by distillation, pyrolysis and combustion reactions when the tobacco is burnt (Baker, 1987). In a previous study, a model system was used to investigate aerosol emissions from tobacco at different temperatures (Forster et al., 2015). The heating chamber heated samples of blended tobacco to between 100 °C and 200 °C, enabling a systematic investigation of the effect of temperature on selected vapour-phase compounds using the International Organization for Standardization (ISO) machine-smoking protocol. NNN and NNK were quantifiable when the tobacco was heated above 140 °C and 160 °C, respectively, whereas crotonaldehyde and formaldehyde were quantifiable at 180 °C and 200 °C, respectively. The concentrations of seven priority compounds in the aerosol (nicotine, CO, acetaldehyde, crotonaldehyde, formaldehyde, NNN and NNK) showed an increasing trend with temperature. The results demonstrated the practical utility of the model system to study low-temperature toxicant formation and emission from heated tobacco, and showed that, between 100 °C and 200 °C, nicotine and some priority compounds are released from the tobacco as a result of evaporative transfer or initial thermal decomposition (Forster et al., 2015).

To apply this understanding to a commercial product that is designed to heat tobacco with a controlled temperature profile and to provide acceptable sensory performance to the consumer, a comprehensive list of substances was measured in the aerosol emissions from THP1.0. Complemented by the other studies in this series, which include *in vitro* biological assessment of the aerosol emissions (Jaunky et al., 2017; Taylor et al., 2017; Thorne et al., 2017), we intend to provide a comprehensive baseline data package for THP1.0.

2. Experimental

2.1. Test products

The THP1.0 design and its main thermophysical functions have been described in detail (Proctor, 2017; Eaton et al., 2017). The emissions from THP1.0 were compared with those from the University of Kentucky 3R4F Reference Cigarette (University of Kentucky Center for Tobacco Reference Products, Lexington, KY, USA). Additional data were generated from the analysis of the more recently produced University of Kentucky 1R6F reference cigarette and a commercially available THS for quality assurance purposes. For the present study, non-mentholated and mentholated THP1.0 variants were used: THP1.0(T), comprising glo™ heating devices