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Design and chemical evaluation of reduced machine-yield cigarettes

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ABSTRACT

Experimental cigarettes (ECs) were made by combining technological applications that individually reduce the machine measured yields of specific toxicants or groups of toxicants in mainstream smoke (MS). Two tobacco blends, featuring a tobacco substitute sheet or a tobacco blend treatment, were combined with filters containing an amine functionalised resin (CR20L) and/or a polymer-derived, high activity carbon adsorbent to generate three ECs with the potential for generating lower smoke toxicant yields than conventional cigarettes. MS yields of smoke constituents were determined under 4 different smoking machine conditions. Health Canada Intense (HCI) machine smoking conditions gave the highest MS yields for nicotine-free dry particulate matter and for most smoke constituents measured. Toxicant yields from the ECs were compared with those from two commercial comparator cigarettes, three scientific control cigarettes measured contemporaneously and with published data on 120 commercial cigarettes. The ECs were found to generate some of the lowest machine yields of toxicants from cigarettes for which published HCI smoke chemistry data are available; these comparisons therefore confirm that ECs with reduced MS machine toxicant yields compared to commercial cigarettes can be produced. The results encourage further work examining human exposure to toxicants from these cigarettes, including human biomarker studies.

1. Introduction

Tobacco smoke is a complex, dynamic, mixture of more than 5000 identified constituents (Rodgman and Perfetti, 2009) of which approximately 150 have been documented as toxicants (Fowles and Dybing, 2003; Green et al., 2007). The toxicants are present in the mainstream smoke (MS) inhaled by a smoker and are also released between puffs as constituents of sidestream smoke (SS).

In 2001 the Institute of Medicine (IOM) reported that, since smoking related diseases were dose-related, and because epidemiologic studies show reduction in the risk of smoking related diseases following cessation, it might be possible to reduce smoking related risks by developing potential reduced-exposure products (PREPs). These they defined as (1) products that result in the substantial reduction in exposure to one or more tobacco toxicants and (2), if a risk reduction claim is made, products that can reasonably be expected to reduce the risk of one or more specific diseases or other adverse health effects (Stratton et al., 2001). To date, no combustible cigarette product has been shown to meet the general requirements outlined by the IOM.

The IOM and other groups (Life Sciences Research Office (LSRO), 2007; World Health Organization (WHO), 2007) describe a number of stages of activity which are likely to be required for a combustible tobacco product to be recognised as a PREP; however, the detailed approach and stages required to provide relevant data have yet to be agreed amongst the scientific community. For example, some groups have proposed MS yield limits for specific smoke toxicants (Burns et al., 2008) and others have suggested that biomonitoring should play a role in this assessment (Hecht et al., 2010). Recently Hatsukami et al. (2012) described a sequence of activities designed to assess modified risk tobacco products, starting with pre-human studies involving constituent yield analysis (of the kind described in this paper) prior to pre-market human studies and post-market studies. The USA FDA is also currently considering approaches for the Scientific Evaluation of modified risk tobacco product (MRTP) applications (FDA, 2011).

Abbreviations: BT, blend treatment (tobacco); CA, cellulose acetate (filter); CR20L, amine-functionalised resin; dwb, dry weight basis; ECs, experimental cigarettes; HCI, Health Canada Intense (machine smoking conditions); IOM, the Institute of Medicine of the USA; ISO, International Organization for Standardization; LOQ, limit of quantification; LSRO, the Life Sciences Research Office; MS, mainstream smoke; NAB, N'-Nitrosoanabasine; NAT, N'-Nitrosoanatabine; NFDPM, nicotine-free dry particulate matter, sometimes called "tar"; NNK, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN, N'-Nitrosonornicotine; PAH, polycyclic aromatic hydrocarbon; PREP, potential reduced-exposure product; RTP, reduced toxicant prototype; RMYP, reduced machine-yield prototype; SS, sidestream smoke; TSNA, tobacco-specific nitrosamines; TSS, tobacco-substitute sheet; WHO, World Health Organization; wwb, wet weight basis.

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From a cigarette design and manufacturing viewpoint, we propose the following step-wise approach to exposure assessment with modified tobacco products.

The first stage in the design of a cigarette-based PREP would involve the development of technologies which reduce the yields of smoke toxicants. Experimental cigarettes (ECs) would be assembled using these technologies and then assessed for their toxicant yields using smoking machines; comparison to relevant control and reference products would indicate the effectiveness of the cigarette design in generating reduced yields of toxicants. Those ECs that are found to reduce smoking machine measured yields of smoke toxicants, in comparison to reference products, are termed "reduced machine-yield cigarettes".

A second stage of testing is necessary to establish the ability of a reduced machine-yield cigarette to reduce smokers' exposure to toxicants, under real-world use conditions. Those that successfully demonstrate reductions in smokers' exposure to toxicants are termed "reduced toxicant prototypes". A reduced toxicant prototype designation is insufficient to satisfy the IOM's definition of a PREP and further assessment would be required to demonstrate that these cigarettes can reasonably be expected to reduce the risk of one or more specific diseases or other adverse health effects.

Over many years there have been numerous attempts to develop cigarettes with reduced machine yields of toxicants. These have been reviewed in depth on a number of occasions (e.g. NCI, 1968; Wnyder and Hoffmann, 1979; Gori and Bock, 1980; Gori, 2000; Hoffmann et al., 2001; Proctor et al., 2003; Baker, 2006a,b; Rees and Connolly, 2008; O'Connor and Hurley, 2008).

Technological developments for reduction in yields of smoke toxicants have included modified agricultural and curing practices (O'Connor and Hurley, 2008), selective removal of tobacco constituents (Gori and Bock, 1980), the substitution of tobacco with alternative, diluent materials (Sittig, 1976), addition of chemical species to the tobacco blend (Hatsukami et al., 2004) and selective reduction of cigarette smoke toxicants through use of filter materials such as cellulose acetate (NCI, 1968), resins (Horsewell, 1975), and activated carbon (Kensler and Battista, 1963; Tokida et al., 1985; Norman, 1999; Rouquerol et al., 1999; Laugesen and Fowles, 2006; Rees et al., 2007; Polzin et al., 2008; Hearn et al., 2010; Branton et al., 2009; Branton and Bradley, 2010).

A number of these technological approaches have been employed in commercial or test marketed cigarettes such as ADVANCE (Breland et al., 2003,2006; Advance, 2001; Counts, 2002), OMNI (Hatsukami et al., 2004; Counts, 2002), and Marlboro UltraSmooth (Laugesen and Fowles, 2006; Rees et al., 2007).

Alternative approaches to conventional cigarettes have included devices that heat but do not burn tobacco, such as PREMIER (RJ Reynolds, 1988), ECLIPSE (Eclipse Expert Panel, 2000), ACCORD (Holzman, 1999; Patskin and Reininghaus, 2003) and HEATBAR (Rees and Connolly, 2008). Further descriptive details of these products were found at the website Tobaccoproducts.org (Tobaccoproducts, 2011).

However, despite the range of approaches described above, to date none of these attempts have led to a commercially successful PREP.

In recent papers, in an extension to previous published studies, we have described four different individual technological approaches to the reduction of toxicants in cigarette smoke, two of which modified the tobacco blend (McAdam et al., 2011; Liu et al., 2011), and two of which modified the cigarette filter (Branton et al., 2011a,b). The two tobacco blend technologies, a tobacco-substitute sheet material (TSS) and a tobacco blend treatment (BT), acted to reduce the generation of toxicants at source within the burning cigarette. The two filter technologies, an amine functionalised resin material (CR20L) and a high activity, polymer-derived, carbon adsorbent, acted to remove volatile species from the smoke stream after formation. The technologies described in those reports are summarised in Section 2.1 below.

This current paper describes the design of three ECs made using combinations of these blend and filter technologies. The goal of the current work was to assess whether the technologies could be combined into ECs which reduce machine yields of toxicants in comparison to commercial products, and have the potential to reduce exposure of smokers to toxicants as a consequence of human smoking. Four considerations shaped the approach taken in the development of these ECs: first, a lack of consensus in the scientific community over which toxicants in smoke are priorities for reduction; second, uncertainty over the extent of reductions necessary for a biologically substantial effect; third, a desire to avoid inadvertent and substantial increases in yields of any toxicants when changing cigarette design to make ECs; and fourth, the need to maintain consumer acceptability when reducing overall yields of smoke constituents – a principle recognised by Wnyder and Hoffmann (1979).

In terms of priorities for reduction, a major unresolved challenge in understanding the causes of smoking-related diseases is identification of the key smoke toxicants mechanistically involved. Without this detailed knowledge, modifications to cigarette design cannot precisely target the smoke constituents involved in driving disease processes. However, even if this knowledge were available, with few exceptions, it is unlikely that specific smoke constituents or chemical classes could be entirely eliminated from MS, and a more pragmatic approach is to develop cigarettes with substantially reduced overall smoke toxicant yields.

Testing the ECs under a variety of smoking machine conditions and analysing the yields of smoke constituents on a per cigarette basis and as a ratio per milligram of nicotine yield, permits comparisons with relevant commercial comparator cigarettes, and also to a wide range of products reported in the literature. The results presented in this work demonstrate that the development of combustible reduced machine-yield cigarettes is feasible. Further studies on these ECs to assess their ability to reduce exposure to toxicants in smokers have been conducted and will be reported separately.

2. Materials and methods

2.1. Design of experimental, control and comparator cigarettes

The approach taken was to develop ECs that gave reductions in a wide range of machine smoked yields of toxicants, without overall increases in MS emissions. This was considered the most appropriate strategy for the initial stages in combustible PREP development, bearing in mind the constraints discussed above. Consequently, the ECs described here were constructed from combinations of blend and filter technologies that were developed to reduce specific chemical classes of smoke toxicants or their precursors in tobacco (Table 1). For each EC individual tobacco grades with low tobacco-specific nitrosamine (TSNA) and metal contents were selected and blended to provide a low toxicant starting point for the design of experimental cigarettes.

The BT process was described in detail by Liu et al. (2011). Briefly, the tobacco blend is subjected to an aqueous extraction step and the extract is subsequently passed through two stages of filtration to remove polyphenols and proteins. The residual tobacco solids are treated with protease to remove insoluble proteins. After washing and enzyme deactivation, the tobacco solids and filtered aqueous extract are re-combined. The BT process results in reduced smoke yields of phenolics, aromatic amines, HCN, and a number of other nitrogenous smoke constituents; however, there are also increases in the yields of formaldehyde and isoprene (Liu et al., 2011).