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Lack of effect of menthol level and type on smokers' estimated mouth level exposures to tar and nicotine and perceived sensory characteristics of cigarette smoke

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ABSTRACT

Menthol can reduce sensory irritation and it has been hypothesised that this could result in smokers of mentholated cigarettes taking larger puffs and deeper post-puff inhalations thereby obtaining higher exposures to smoke constituents than smokers of non-mentholated cigarettes. The aim of our study was to use part-filter analysis methodology to assess the effects of cigarette menthol loading on regular and occasional smokers of mentholated cigarettes. We measured mouth level exposure to tar and nicotine and investigated the effects of mentholation on smokers' sensory perceptions such as cooling and irritation. Test cigarettes were produced containing no menthol and different loadings of synthetic and natural L-menthol at 1 and 4 mg ISO tar yields. A target of 100 smokers of menthol cigarettes and 100 smokers who predominantly smoked non-menthol cigarettes from both 1 and 4 mg ISO tar yield categories were recruited in Poland and Japan. Each subject was required to smoke the test cigarette types of their usual ISO tar yield. There were positive relationships between menthol loading and the perceived 'strength of menthol taste' and 'cooling' effect. However, we did not see marked menthol-induced reductions in perceived irritation or menthol-induced increases in mouth level exposure to tar and nicotine.

1. Introduction

L-Menthol, ([1*R*,2*S*,5*R*]-2-isopropyl-5-methyl-1-cyclohexanol) CAS number 2216-51-5 is the main form of menthol occurring in nature, particularly in the plant cornmint (*Mentha canadensis*) (Fig. 1). There are eight menthol isomers, each having different flavour characteristics but with L-menthol having the highest values of 'fresh' and 'cool' flavour characteristics. L-menthol can be produced synthetically and there are several methods of production using starting materials such as dementholized cornmint oil, (+)-citronellal and m-cresol depending on availability and price (Hopp and Lawrence, 2007).

Both natural and synthetic L-menthol are used in tobacco products and the choice of which tends to be due to availability and cost. Natural and synthetic L-menthol preparations have similar chemical properties, and there may be differences in sensory characteristics due to traces of other menthol isomers (Hopp and Lawrence, 2007).

Menthol can produce a number of sensory effects when applied topically to the skin and mucosal surfaces of the nose, mouth and throat. These include the sensation of cooling (Cliff and Green, 1994; Yosipovitch et al., 1996; Wasner et al., 2004; Dessirier et al., 2001) and sensory irritation (Cliff and Green, 1994; Dessirier et al., 2001). Wasner et al. (2004) hypothesised that the stimulation of cold receptors by menthol may partially attenuate a pain or irritant sensation mediated via C fibre nociceptors. This putative mode of action of menthol is often referred to as a counter-irritation effect. Recently, Willis et al. (2011) described the counter-irritation effects of menthol against the respiratory irritants acrolein, acetic acid and cyclohexanone, in mice.

It has also been demonstrated that menthol can either sensitise or desensitise nerve endings initiating irritation responses in sites such as the skin, mouth, nose and throat (Cliff and Green, 1994, 1996; Green and McAuliffe, 2000; Dessirier et al., 2001; Wise et al., 2011). In a study involving the application of nicotine and menthol solutions to human tongues, Dessirier et al. (2001) observed that menthol application produced a cross-desensitisation effect on nicotine induced sensory irritation.

Menthol is used as a flavouring agent in many brands of cigarettes. Cigarette smoke elicits a number of sensory responses including sensory irritation responses in the mouth and throat during the puffing and post-puff inhalation phases of smoking (Dixon and Baker, 2003). Because the topical application of menthol to the mucosal surfaces of the mouth and tongue can, in some circumstances, reduce the sensory irritation induced by topical

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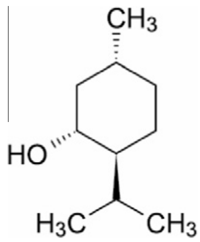

Fig. 1. The chemical structure of L-menthol.

applications of nicotine, a number of researchers have claimed that menthol in cigarette smoke may reduce the levels of sensory irritation in the mouth and throat induced by cigarette smoke (Ahijevych and Garrett, 2004; Ferris Wayne and Connolly, 2004; Kreslake et al., 2008a,b; Lawrence et al., 2011). It has also been hypothesised by these researchers that a menthol induced reduction in the sensory irritation produced by cigarette smoke could result in mentholated cigarette smokers taking larger puffs and deeper post-puff inhalations and hence obtain higher exposures to smoke constituents than smokers of non-mentholated cigarettes.

As the published studies on the sensory effects of menthol do not involve the assessment of menthol delivered in cigarette smoke to smokers, many of the inferences drawn from these studies may not apply to menthol in cigarette smoke. Thus, the two main aims of our study were:

1. To assess the effects of different levels of natural and synthetic menthol loadings to cigarettes on mouth level exposure (MLE) to tar and nicotine in both smokers of primarily mentholated cigarettes and smokers who occasionally use mentholated cigarettes, and;
2. To investigate the effects of cigarette mentholation on sensory attributes, such as the perceived levels of mouth and throat irritation and cooling, in these smoker groups.

Our technique for the estimation of MLEs relied on using the relationships between the smoke yields of tar and nicotine emerging from the mouth-end of a cigarette during puffing (mainstream smoke yields of tar and nicotine), and the amounts of tar and nicotine retained within the filter tips of the cigarettes. The method used in this study was based on the part-filter analysis technique described by St. Charles et al. (2009).

Our studies were conducted in Japan and Poland during June to August 2006. These two locations were chosen because they have relatively large market shares of mentholated cigarettes (19.4% in Japan, 12.8% in Poland in 2006) (Chris Sykes, personal communication) and there is a large difference between the two in typical levels of menthol concentrations in commercial mentholated cigarettes. Menthol concentrations for a selection of typical Japanese products in 2006 ranged from around 8.2 to 13.0 mg/cigarette for 1 mg ISO tar yield products and 4.8 to 6.3 mg/cigarette for 4–5 mg tar yield products (Peter Wan, personal communication). European cigarette products typically contain lower levels of menthol ranging between 4.5 and 5.3 mg for 1 mg ISO tar yield products and between 2.3 and 4.2 mg for 4 mg ISO tar yield products (Martin Blumenstock, personal communication).

2. Materials and methods

2.1. Test cigarettes

The test cigarettes were designed and manufactured to produce yields of 1 and 4 mg tar under ISO smoking conditions, with 83 mm cigarette length, 27 mm filter length and a 24.6 mm circumference. All of the samples were American blend style cigarettes and mentholated and non-mentholated cigarettes were made to the same physical and blend specifications within each tar yield category. Different specifications, however, were used for the two tar yield categories, with the main differences between the 1 and 4 mg tar yield products being the use of a higher efficiency filter, higher levels of filter ventilation, and a higher inclusion of dry ice expanded tobacco in the 1 mg products in order to lower the ISO tar yields from 4 to 1 mg.

For each country, five products were produced at each tar level. One product was not mentholated and the other four products differed in the type and level of applied menthol. Menthol (natural or synthetic L-menthol purity at least 99%, supplier Tien Yuan Chemical (PTE) Ltd.) was applied to the products by application to the foil packaging. Menthol was also applied directly to the paper surrounding the tobacco as it passed through the cigarette making machine to increase the menthol concentrations of two of the Japanese products (J1S 11.7 and J1N 11.6) from a target of 7 mg per cigarette to a target of 13 mg per cigarette. The products were then stored for three weeks to enable the menthol to migrate throughout the tobacco rods and filters of the cigarettes. Table 1 shows the target and measured menthol application levels together with the tar, nicotine and menthol yields of the products when smoked on a smoking machine under ISO standard conditions (ISO 10362-1, 1999; ISO 3308, 2000a; ISO 4387, 2000b; ISO 10315, 2000c; ISO/DIS 13110, 2011). The levels of menthol application were designed to reflect the high and low ends of the ranges of menthol used in commercial mentholated brands sold in Poland and Japan. Table 2 contains the key for the product codes that are used in Table 1 to identify each type of test cigarette.

2.2. Subjects

This study included four groups of smokers in each of the two markets. The groups were as follows:

Regular smokers of 1 mg tar yield menthol cigarettes;
Smokers of non-menthol 1 mg tar yield cigarettes who occasionally smoked 1 mg tar yield menthol cigarettes;
Regular smokers of 4 mg tar yield menthol cigarettes;
Smokers of non-menthol 4 mg tar yield cigarettes who occasionally smoked 4 mg tar yield menthol cigarettes.

Potential subjects were asked for details of their usual brand of cigarette smoked, and also to show a pack of their usual brand to the recruiters to enable confirmation of the brand identity. They were also asked to provide details of any additional brands smoked. This information enabled the recruiters to assign potential subjects to the correct groups for the study. The recruitment target was 100 subjects in each of the eight groups.

The subjects were aged between 21 and 65 years with a self-reported average consumption of at least ten cigarettes per day of their most popular 1 and 4 mg ISO tar product. The subjects were required to have been smoking their usual brand of cigarette for at least six months and female subjects were excluded if they reported themselves to be pregnant or lactating.

2.3. Study protocol

The recruitment and fieldwork in Japan and Poland was conducted by respective market research agencies (MRA), Field Planning Research (Japan) and Millard and Brown (Poland). All subjects who met with the recruiting criteria were briefed on the study protocol before giving their written informed consent to participate in the study. The subjects were visited at home by an