Risk assessing thermal breakdown and reaction products for E-cigarette flavours

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INTRODUCTION

Flavours are an important aspect of the e-cigarette sensory experience. However, the unknown behaviour of flavour compounds when used in this application, including the potential thermal degradation due to the formulation contact with the hot coil, highlights the need for robust stewardship. Our toxicological risk assessment approach to flavours considers both the flavour itself and the identification, measurement, and risk assessment of any potential thermal breakdown and/or reaction products. The initial flavour formulation is analysed and risk assessed, but here we focus on the risk assessment of potential flavour breakdown and reaction products.

Experimental Methods

Flavours were characterised under ambient, thermally stressed and in their diluted e-cigarette generated aerosol states, in order to understand potential degradation products on heating.

Thermal stressing involved placing 25g of the neat flavour concentrate into 20 ml headspace vials, heating to 30°C using the following temperature program: 40°C to 300°C at 100°C/min, hold for 5 minutes. After thermal stressing the vials were left to cool to room temperature before analysis.

Samples were analysed using Solid Phase Micro Extraction (SPME) Gas Chromatography (GC) linked to a Mass Spectrometer (MS) operated in scanning mode. Figures 1-3 are examples of SPME GC-MS data. Two different MS libraries (NIST and WILEY MS) were used to increase confidence in the peak assignations. Additionally, ‘standard’ liquid injection GC-MS was conducted on some samples to corroborate the SPME data, given the potential selectivity issues of SPME and improved semi quant nature of the analysis. The table presented contains a combination of data obtained by SPME and liquid injection.

Conclusions

Flavourings can result in significant thermal breakdown products in the aerosol from the e-cigarette under normal use conditions. Flavour selection should take account of this possibility.

The most important step of evaluation is to determine what is actually present in the aerosol that is normal use conditions. Flavour selection should take account of this possibility.

Different susceptibility to thermal breakdown

Figures 1 and 2 are examples of SPME-GC MS scans of two different experimental flavours at ambient temperature, versus when heated to 300°C in a closed system for 5 minutes. Flavour 1 was made up of aroma chemicals and did not show significant thermal breakdown. Flavour 2 contained only a single natural extract, which was an ill-defined mixture of substances. Subjecting flavour 2 to 300°C resulted in a wide variety of thermal breakdown products. It is very possible that the original flavour contained several compounds that were not GC-amenable, but that did result in GC-amenable thermal breakdown products.

The SPME-GC MS scan of the actual aerosol from an e-liquid using flavour 2, was less complex than that of the flavour heated to 300°C for 5 minutes, indicating less thermal breakdown (Figure 3). Most likely this is because the residence time of the compounds at the coil will have been much less than the 5 minutes used in the earlier experiment. However, comparing the aerosol scan (red trace in figure 3) with the ambient flavour (blue trace in figure 2), it is clear several thermal breakdown products are formed by this particular natural extract flavour under normal use conditions.

Table 1: Compound concentration in e-cigarette aerosol

<table>
<thead>
<tr>
<th>Compound</th>
<th>Estimated Exposure per Day from use of two devices (µg)</th>
<th>Oral Cramer Class TTC (µg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxycitric acid</td>
<td>16</td>
<td>1800</td>
</tr>
<tr>
<td>Glycerol</td>
<td>13</td>
<td>200</td>
</tr>
<tr>
<td>Benzoic acid-pyrogallic acid</td>
<td>374</td>
<td>NA</td>
</tr>
<tr>
<td>Tolyl aldehyde-pyrogallic acid</td>
<td>30</td>
<td>NA</td>
</tr>
<tr>
<td>Toluene</td>
<td>21</td>
<td>1800</td>
</tr>
<tr>
<td>Ethyl glycidol dimmer</td>
<td>8</td>
<td>90</td>
</tr>
<tr>
<td>Methylmercury</td>
<td>128</td>
<td>90</td>
</tr>
<tr>
<td>Cinamaldehyde-pyrogallic acid</td>
<td>47</td>
<td>NA</td>
</tr>
<tr>
<td>Heteropropyl pyrogallic acid</td>
<td>1101</td>
<td>NA</td>
</tr>
<tr>
<td>Ethyl vanillin pyrogallic acid</td>
<td>310</td>
<td>NA</td>
</tr>
<tr>
<td>Vanillin pyrogallic acid</td>
<td>477</td>
<td>NA</td>
</tr>
<tr>
<td>Cotinine</td>
<td>48</td>
<td>90</td>
</tr>
<tr>
<td>Hydroxybenzene ethanal</td>
<td>26</td>
<td>1800</td>
</tr>
<tr>
<td>(Hydroxyphenyl)-butanone pyrogallic</td>
<td>137</td>
<td>NA</td>
</tr>
</tbody>
</table>

Risk assessment considerations for example compound

Glycidol - IARC 2A but:
- Identity uncertain [how match factors]
- Over several scans, generally below detection limit
- Estimated exposure up to 13 µg/day. To contextualise, this is equivalent to air exposure where the glycidyl air concentration is orders of magnitude below occupational exposure limits.
- Overall burden from direct metabolising agents in e-cig aerosol insignificantly reduced versus cigarette smoke

Risk assessment for reaction products and thermal breakdown products

Figures 1 and 2 after 5 min

Note: Flavour 2 after 30 min (red trace overlaid)

Peaks identified via SPME or liquid injection GCMS, in the e-cigarette aerosol of an experimental flavoured formulation, that were not present in the ambient flavour.

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