Invited Speaker

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Development of a novel hazard index of mainstream cigarette smoke and its application on risk evaluation of cigarette products.

A novel hazard index of mainstream cigarette smoke for risk evaluation of cigarette products was developed. 163 commercial cigarettes, including international and Chinese brands, American Blend and Virginia Blend cigarettes purchased in China were investigated. The yields of 29 toxic chemicals (4 TSNAs, 3 PAHs, 8 carbonyls, 7 phenolic compounds, HCN, NO, NOx, NH3, CO, NIC and Tar) in mainstream cigarette smoke were determined, and the toxicity of cigarette smoke was measured employing a bacterial mutagenicity assay (Ames Salmonella mutagenicity assay) with cigarette smoke condensate (CSC), the MTT cytotoxicity assay with CSC, the mouse in vivo micronucleus assay with CSC, and a mouse inhalation study.

In order to establish the functional relationships between smoke yields and smoke toxicity, the correlation between the yields of 29 toxic chemicals and four toxicity assay results were investigated. The key toxic chemicals were screened with uninformative variable elimination (UVE) and genetic algorithm. The results indicate that the contributions of seven toxic chemicals (CO, HCN, NNK, NH3, B[a]P, phenol and crotonaldehyde) to the toxicity of mainstream cigarette smoke were significant. The correlation models between seven key chemicals and four toxicity assay responses were developed by multiple linear regression analysis. The R square for Ames assay, MTT assay, in vivo micronucleus assay, and mouse inhalation study were 0.504, 0.595, 0.571, and 0.524, respectively. The relative errors of leave-one-out cross-validation for all models were less than 40%.

Based on the yields of seven toxic chemicals in mainstream cigarette smoke, a novel hazard index was developed to evaluate the risk of mainstream cigarette smoke; the calculation is as follows:

\[ H = \frac{Y_{CO}}{C_1} + \frac{Y_{HCN}}{C_2} + \frac{Y_{NNK}}{C_3} + \frac{Y_{NH_3}}{C_4} + \frac{Y_{B[a]P}}{C_5} + \frac{Y_{PHE}}{C_6} + \frac{Y_{CRO}}{C_7} \]

Y: yields of toxic chemicals in mainstream smoke
C1–C7: Constant

Applying this index, the hazard of mainstream cigarette smoke of the main cigarette products from the Chinese market was evaluated. The results indicate that the product ranking according to the hazard index is different from the ranking according to tar deliveries, so the hazard index may be a more reasonable way to evaluate the risk of cigarette products.

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**Evaluation of tobaccos grown under organic cultural practices.**

Organic plant cultivation appeals to cultural practices concerned with the respect of natural balances. It limits the use of inputs and excludes the use of chemical fertilizers, GMO and synthetic pesticides with, as a consequence, no PPP residues in the raw matter thus produced.

European consumers are asking for more and more organic agricultural products, creating new opportunities and markets. A niche market for organic tobacco appears to exist and may grow.

Prior experiments allowed us to select some efficient organic products against the main tobacco diseases.

In 2007, greenhouse trials were carried out to establish an organic float bed transplant production. An organic compost was used and among five fertilizers that were evaluated, one helps to produce transplants comparable to traditional ones.

Field trials were also set up with two varieties of Burley and two varieties of filler flue-cured tobacco. Organic cultivation was compared to traditional cultivation.

Castor-oil plant cake, feather flour and natural potassium sulfate were evaluated as fertilizers and a seaweed elicitor to control blue mould. After topping, rapeseed oil was used to inhibit sucker development.

The organic route for Burley tobacco is to be improved in 2008 so as to obtain better quality of cured raw matter and yields, especially by applying part of the organic fertilizers several weeks before planting so that it has time to release nitrogen. Mean yields of organic tobaccos were lower: from 700 to 1600 kg/ha less according to the variety.

On the other hand, the flue-cured organic route used was well adapted. Yields were greater than 4000 kg/ha and quality not significantly different from that of the same varieties cultivated according to a classic farming route.

Finally, other results concerning physical and chemical measurements on the raw tobaccos will also be discussed as well as smoke evaluation and cigarette sensory analysis.

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Developing risk assessment paradigms for tobacco smoke constituents.

The scientific literature detailing the identity of tobacco smoke constituents potentially responsible for the adverse health effects of cigarette smoking has grown significantly over the last 20 years. Increasingly there is a trend towards providing a quantitative risk estimate of the contribution of individual constituents.

In some assessments conducted, a component of the calculated potency figures includes a cigarette constituent yield figure as well as a disease potency factor, usually taken from a regulatory database that includes information from a single critical publication.

To provide a disease potency factor considered more representative of that from tobacco smoke exposure, for lung cancer, chronic obstructive pulmonary disease and cardiovascular disease, the literature has been reviewed and a range of papers for each compound and disease selected.

The margins of exposure (MOE) model developed by the European Food Safety Authority (EFSA) has been applied to smoke toxicants and data tabulated in relation to the EFSA critical MOE value of 10,000. When the MOE <10,000 the situation is considered a 'high priority for risk management actions' (Table1).

<table>
<thead>
<tr>
<th>Smoke Toxicant</th>
<th>MOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaldehyde</td>
<td>1300</td>
</tr>
<tr>
<td>Acrylonitrile</td>
<td>1230</td>
</tr>
<tr>
<td>Arsenic</td>
<td>2.0E+13</td>
</tr>
<tr>
<td>Benzo(a)pyrene</td>
<td>2270000</td>
</tr>
<tr>
<td>Benzene</td>
<td>11200</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>152</td>
</tr>
<tr>
<td>N-nitrosonornicotine</td>
<td>57</td>
</tr>
</tbody>
</table>

Under this EU base assessment procedure, tobacco smoke toxicants can be segregated to identify those compounds that would be considered a higher priority for risk management actions.

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