Fluorochemicals used in food packaging inhibit male sex hormone synthesis

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Fluorochemicals used in food packaging inhibit male sex hormone synthesis


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Background & Aim

Polyfluorinated phosphate surfactants (PAPS) are widely used in food contact materials (FCMs) of paper and board and have recently been detected in 57% of investigated materials. Human exposure occurs as PAPS have been measured in blood; however knowledge is lacking on the toxicology of PAPS. Metabolic products of PAPS, fluorotelomer alcohol (FTOH) and perfluorocarboxylic acids (PFCAs) have shown potential to interfere with the endocrine system and thus the aim of this study was to elucidate the effects of six fluorochemicals on sex hormone synthesis and androgen receptor (AR) activation in vitro. Four PAPS and two metabolites, perfluorooctanoic acid (PFOA) and 8:2 fluorotelomer alcohol (8:2 FTOH) were tested.

Results

Hormone profiles, including eight steroid hormones, generally showed that 8:2 diPAPS and 8:2 FTOH led to decreases in testosterone, dehydroepiandrosterone, and androstenedione in the H295R steroidogenesis assay. Decreases were observed for progesterone and 17-OH-progesterone as well. None of the compounds showed effects in the AR reporter gene assay.

<table>
<thead>
<tr>
<th>Compound</th>
<th>LOEC (µM)</th>
<th>Emax (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:2 diPAPS</td>
<td>n.s.</td>
<td>26 ± 10</td>
</tr>
<tr>
<td>8:2 monoPAPS</td>
<td>3.1</td>
<td>22 ± 16</td>
</tr>
<tr>
<td>8:2 FTOH</td>
<td>12.5</td>
<td>60 ± 14</td>
</tr>
<tr>
<td>10:2 diPAPS</td>
<td>3.1</td>
<td>42 ± 10</td>
</tr>
<tr>
<td>8:2 triPAPS</td>
<td>n.s.</td>
<td>45 ± 18</td>
</tr>
<tr>
<td>8:2 hexaPAPS</td>
<td>12.5</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Concentration-effect relationships for steroidogenesis in the H295R cell line are shown as LOEC (lowest observable effect concentration) and Emax (maximum effective concentration). The Emax values are given as a percentage change of the control value. LOEC values were determined from the concentration-effect data. The hormone profiles include CYP19 (17β-estradiol), AOR (progesterone), androgen (testosterone) as well as cortisol and estrone.

Materials and Methods

Materials and methods are described in detail in the paper Fluorochemicals used in food packaging inhibit male sex hormone synthesis. The tested compounds include 8:2 diPAPS, 8:2 monoPAPS, 10:2 diPAPS, 8:2 heptaPAPS, and 8:2 triPAPS. H295R cells were cultured for 48 h with exposure concentrations ranging from 1.6 - 50.0 µM. After 48 h exposure the supernatant was sampled for hormone analysis and cell viability was tested. Hormones were extracted from cell supernatants by SPE and were measured both by time-resolved fluoroimmunoassays and HPLC-MS/MS. Effects on gene expression were assessed by qRT-PCR, mRNA isolation and conversion to cDNA were performed with TaqMan® Fast Cells-to-CT Kit. All cDNA were analyzed on a PCR system using TaqMan® Gene Expression Assays. Androgen receptor reporter gene assay. The assay was performed as previously described by Vinggaard et al. (2011). All reagents were generous gifts from Dr. Albert Brinkmann (Emmanuel University, Rotterdam). Test chemicals were added leading to final exposure concentrations ranging from 0.2 – 80.0 µM on agonist, antagonist and toxicity plates.

Conclusion

Overall, the results demonstrate that of the tested endpoints interference with steroidogenesis is the main target of the test compounds. Specifically, fluorochemicals used in food packaging and their metabolites can affect steroidogenesis through decreased Bzrp mRNA levels for 8:2 monoPAPS and 8:2 FTOH indicating interference with cholesterol transport to the inner mitochondria.

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