Toxic and carcinogenic constituents in Camel Snus and other U.S. smokeless tobacco products

Irina Stepanov, PhD
Associate Professor
School of Public Health
University of Minnesota

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Outline

- New Product Watch Project
- Recent data on moist snuff
- Products marketed as snus
New Product Watch

Web-based national monitoring network
Monitors - State tobacco program staff and their community partners
Six regions; three locations per region
# Carcinogens in smokeless tobacco products

<table>
<thead>
<tr>
<th>Group</th>
<th>Constituents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco-specific $N$-nitrosamines</td>
<td>NNN, NNK</td>
</tr>
<tr>
<td>Volatile $N$-nitrosamines</td>
<td>NDMA, NPYR, NPIP, NMOR, NDELA</td>
</tr>
<tr>
<td>Nitrosamino acids</td>
<td>NSAR</td>
</tr>
<tr>
<td>Metals and metalloids</td>
<td>As, Be, Cd, Co, Cr VI, Pb, Ni, Po-210</td>
</tr>
<tr>
<td>Aldehydes</td>
<td>Formaldehyde, acetaldehyde</td>
</tr>
<tr>
<td>Inorganic salts</td>
<td>Nitrate, nitrite</td>
</tr>
<tr>
<td>Fermentation-related compounds</td>
<td>Ethyl carbamate</td>
</tr>
<tr>
<td>Mycotoxins</td>
<td>Aflatoxin, ochratoxin</td>
</tr>
<tr>
<td>Other plant material</td>
<td>Areca nut</td>
</tr>
</tbody>
</table>
Tobacco-specific \( N \)-nitrosamines (TSNA)

- Specific to tobacco exposure (formed from tobacco alkaloids)
- Systemic, organ-specific carcinogens
- Cancers of target organs are most strongly associated with tobacco use
- Classified by IARC as carcinogenic to humans (Group 1)

Product pH and unprotonated (free) nicotine

Source: Brunemann and Hoffmann, 1974.
Constituents and characteristics monitored in the New Product Watch

- Pouch size
- Moisture content,
- pH
- Nicotine
- Unprotonated nicotine
- NNN
- NNK
Selected data: focus on time trends

Pouch weight  Moisture content  pH

Stepanov Laboratory (manuscript in preparation)
Selected data: focus on time trends

Total nicotine, mg/dry wt

Free nicotine, mg/dry wt

Free nicotine, mg/portion

Stepanov Laboratory (manuscript in preparation)
Selected data: focus on time trends

NNN, µg/dry wt

NNK, µg/dry wt

NNN+NNK, µg/portion
Comparisons with the U.S. moist snuff data

Sum of NNN and NNK
Comparison of NNN data from recent analyses (per gram tobacco)

~1.6 ug/g dry weight NNN + ~0.5 ug/g dry weight NNK

Stepanov Laboratory (manuscript in preparation)
Other key constituents in recent analyses:
Total and free nicotine

Total nicotine

Free nicotine

Camel Snus

Camel Snus

Stepanov Laboratory (manuscript in preparation)
Other key constituents: Nornicotine and nitrite

Nornicotine

Nitrite

Camel Snus

Camel Snus

Stepanov Laboratory (manuscript in preparation)
Minor alkaloids and β-carbolines: potential contribution to addictiveness

- **Minor alkaloids:**
  - binding to nicotine receptors
  - enhancement of nicotine effects

- **β-Carbolines:**
  - MAO inhibitors
  - Plasma levels increase 10-fold in 5 minutes after smoking a cigarette
  - Measured in brain
Anatabine and anabasine data from recent analyses (per gram tobacco)

Anatabine, mg/g

Anabasine, mg/g

Camel Snus

Stepanov Laboratory (manuscript in preparation)
Harman and norharman data from recent analyses (per gram tobacco)

Harman, ng/g

Norharman, ng/g

Camel Snus

Marlboro Snus

Marlboro Snus
Particular importance of NNN in smokeless tobacco products

- Specific to tobacco
- Potent oral and esophageal carcinogen in laboratory animals
- Evidence for carcinogenicity in humans

J.-M. Yuan et al, Carcinogenesis 32(9): 1366-1371 (2011);
Reported relative risks associated with smokeless tobacco use in various countries

- Lee & Hamling, BMC Medicine, 7: 36, 2009
- IARC Vol 83, 2004

**Average NNN levels in moist snuff (our laboratory):**
- ~1.7 µg/g product in recent analyses
- ~2.5 µg/g product 10 years ago
## There is snus, Snus, and “snus”

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Content (2013)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrite (µg/g)</td>
<td>1.1 (1.0 - 1.1)</td>
</tr>
<tr>
<td>NNN + NNK (µg/g)</td>
<td>0.47 (0.46 - 0.48)</td>
</tr>
<tr>
<td>NDMA (ng/g)</td>
<td>&lt;0.6</td>
</tr>
<tr>
<td>B(a)P (ng/g)</td>
<td>&lt;0.6</td>
</tr>
<tr>
<td>Cadmium (µg/g)</td>
<td>0.28 (0.28 - 0.29)</td>
</tr>
</tbody>
</table>


### U.S. Snus

<table>
<thead>
<tr>
<th>Product</th>
<th>NNN</th>
<th>NNK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marlboro Snus</td>
<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Camel Snus</td>
<td>1.0</td>
<td>0.6</td>
</tr>
<tr>
<td>Skoal Snus</td>
<td>1.6</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Stepanov Laboratory (2015)

### Swedish snus

### Indian “snus”

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Stepanov et al. Tobacco Control 2014

Stepanov Laboratory (manuscript in preparation)
Summary

- Constituent profile of Camel Snus has been evolving since its first introduction to the market.

- Current levels of NNN in Camel Snus are comparable to the levels found in many popular moist snuff brands.

- The increase in NNN levels in Camel Snus occurred while NNN levels in some major moist snuff brands were declining.

- Available data on other constituents show comparable (minor alkaloids, nitrite, nitrate, harman, metals) or lower (norharman, PAH) levels between Camel Snus and moist snuff.

- Products marketed as snus vary substantially in their constituent profiles and other characteristics.
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