Acrylamide in Food Products—What is the risk?

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Acrylamide-What is it?

- **Chemistry/Structure**
  - $C_3H_5NO$
  - $MW = 71$

- Polymerizes to form a gel

Fig 1: The polymerisation of ethene in to poly(ethene)
Uses of Acrylamide

- **Acrylamide**
  - Binding, thickening or flocculating agent in grout, cement, sewage, waste water treatment, pesticide formulations, cosmetics, sugar manufacturing and soil erosion prevention

- **Polyacrylamide**
  - Ore processing, food packaging, plastic products, contact lens, soil conditioners and molecular biology/food chemistry laboratories
Acrylamide: Why a concern?

- Known toxicant and animal carcinogen
  - Polyacrylamide is nontoxic
  - In industrial exposure, found in bloodstream

- Acrylamide-hemoglobin (Hb) adduct found in individuals with no known exposure to acrylamide

- Hypothesized a Food Source...
First report in Foods

Swedish Press Release- April 2002

• Reported significant levels of acrylamide in a broad range of commercial foods subjected to extensive heat processing
  • Detection in baked and fried, but not boiled foods
  • Protein-rich foods (5 - 50 ppb) vs. Carbohydrate-rich foods (50 - 4000 ppb)

• Published Report followed (August, 2002)
International Concerns

- FAO/WHO Expert Consultation/Seminar
  - Geneva, Switzerland, June 2002
  - Tanzania, March 2003
- Acrylamide in Food Workshop: JIFSAN
  - Chicago, Oct. 2002
- FDA Public Meeting/Advisory Committee
  - Sept. and Dec. 2002; Feb. 2003
- EU Meetings/Workshop
  - July and October 2002; March 2003
- Numerous research/survey studies
  - Methodology
  - Mechanism of formation
  - Toxicology
Proposition 65

- Proposition 65, the **Safe Drinking Water and Toxic Enforcement Act or 1986**, was enacted as a ballot initiative in November 1986.

- Authors intended to protect California citizens and the State's drinking water sources from chemicals known to cause **cancer**, **birth defects or other reproductive harm**, and to inform citizens about exposures to such chemicals.

- Proposition 65 requires the Governor to publish, at least annually, **a list of chemicals known to the state to cause cancer or reproductive toxicity**.
>200 chemicals classed as carcinogens

No significant risk level (NSRL) for carcinogens and maximum allowable daily levels (MADL) for reproductive toxicity

**NSRL** = Daily intake level calculated to cause one excess case of cancer in exposed population of 100,000, assuming lifetime (70 years) exposure at the level in question.
• Acrylamide always on the list and NSRL for acrylamide originally set at 0.2 ug/day but proposed in 2005 to go to 1.0 ug/day in 2005
  • “Unintended Consequences
  • At current estimated consumption, would exceed either level from natural foods

• Warnings proposed on some foods or in restaurants or grocery stores where certain foods are sold
How does it get in our food?

• Natural process in cooking of foods
  • Maillard Reaction (Nonenzymatic Browning)

• Complex set of reactions that occurs when proteins/amino acids & carbohydrates are heated

\[
\text{H}_2\text{N}-\text{C}-(\text{CH}_2)_{n}\text{CH}-(\text{C}=\text{O})\text{OH} \xrightarrow{\Delta} \text{Flavor compounds} \\
\text{glucose} \quad \text{Brown color}
\]

• Produces desirable flavor and color compounds in many foods
How does it get in our food?

Maillard Reaction (Nonenzymatic Browning)
Mechanism of Acrylamide Formation

1. Asparagine

2. Reducing Sugars

3. Heat

\[ \text{glucose} \xrightarrow{\Delta} \text{Acrylamide} \]

0.1% reaction efficiency
Asparagine in Foods

• Potatoes, almonds, cocoa, wheat grain, and rice
  • Relatively high amounts of asparagine
  • When processed through heating show relatively high amounts of acrylamide.

• Asparagus, broccoli, green beans, and cauliflower
  • High quantities of asparagine
  • Not prepared or processed at the high temperatures and thus low acrylamide reported

Friedman (2003)
Why Potatoes?

- Relatively high content of asparagine
  potatoes, fresh 2,500-3,500 mg/kg
  potatoes, dry 580-3,300 mg/kg

- Relatively high content of reducing sugars

- Heated above 120º C

Influence of Temperature

Acrylamide Concentrations in Commercial French-fried Potatoes subjected to Oven-heating

Ways to Minimize in Potatoes

- **Removal/modification of reactants**
  - **Variety**
    - Lower reducing sugars and asparagine
  - **Storage**
    - Store above 8-10º C

- **Processing**
  - **Blanch**
    - 60% reduction
  - **Change processing temperature**
  - **Add competitive compounds**

- **Removal after formation**
## Acrylamide Levels in Food (FDA)

<table>
<thead>
<tr>
<th>Food Category</th>
<th>Acrylamide Levels (μg/kg or ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bread Products</td>
<td>&lt;10-130</td>
</tr>
<tr>
<td>Bread Products (toasted)</td>
<td>216-364</td>
</tr>
<tr>
<td>Crackers/Biscuits</td>
<td>26-620</td>
</tr>
<tr>
<td>Cookies</td>
<td>36-432</td>
</tr>
<tr>
<td>Breakfast Cereals</td>
<td>11-1057</td>
</tr>
<tr>
<td>French Fries</td>
<td>117-1325</td>
</tr>
<tr>
<td>Potato Chips</td>
<td>117-2762</td>
</tr>
<tr>
<td>Tortilla Chips</td>
<td>11-220</td>
</tr>
<tr>
<td>Popcorn</td>
<td>157-181</td>
</tr>
<tr>
<td>Coffee (ground)</td>
<td>37-374</td>
</tr>
<tr>
<td>Coffee (brewed)</td>
<td>5-11</td>
</tr>
<tr>
<td>Cocoa</td>
<td>ND-909</td>
</tr>
<tr>
<td>Nuts</td>
<td>ND-457</td>
</tr>
<tr>
<td>Peanut Butter</td>
<td>64-125</td>
</tr>
<tr>
<td>Frozen Vegetables</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Canned Fruits/Vegetables</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Mashed Potatoes</td>
<td>ND</td>
</tr>
<tr>
<td>Infant Formula</td>
<td>ND</td>
</tr>
</tbody>
</table>

ND = Not Detected

[http://www.cfsan.fda.gov/~dms/acrydino.html](http://www.cfsan.fda.gov/~dms/acrydino.html)
<table>
<thead>
<tr>
<th>Food</th>
<th>AA Conc (µg/kg)</th>
<th>Portion Size (g)*</th>
<th>AA (µg) Portion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast Cereal</td>
<td>131.0</td>
<td>55</td>
<td>7.3</td>
</tr>
<tr>
<td>Brewed Coffee</td>
<td>8.5</td>
<td>240</td>
<td>3.2</td>
</tr>
<tr>
<td>Postum</td>
<td>93</td>
<td>240</td>
<td>22.3</td>
</tr>
<tr>
<td>French Fries (RF)</td>
<td>333.7</td>
<td>70</td>
<td>23.3</td>
</tr>
<tr>
<td>French Fries (OB)</td>
<td>697.8</td>
<td>70</td>
<td>48.8</td>
</tr>
<tr>
<td>Potato Chips</td>
<td>545.9</td>
<td>30</td>
<td>16.4</td>
</tr>
<tr>
<td>Canned Black Olives</td>
<td>550</td>
<td>15</td>
<td>8.2</td>
</tr>
<tr>
<td>Prune Juice</td>
<td>174</td>
<td>140</td>
<td>24.4</td>
</tr>
</tbody>
</table>

* Portion Sizes From 21 CFR 101.12, Table 2
Level in Food Products

- Great variation in amounts
- Sampling, analysis and processing variability
- Low (ppb) quantities of acrylamide in food products
  - Need effective extraction and enrichment procedures
  - Need sensitive methods for detection
  - Quality of the results decreases for samples at or near the limit of quantification (30-50 ppb)

*Parts per billion* (‘ppb’) denotes one particle per 999,999,999 other particles. (one second per 32 years)
Level in Food Products

- Standard & recommended method of FDA
  - Liquid chromatography/tandem mass spectrometry (LC-MS/MS)
  - NEPA and FDA trying to develop reliable & standardized method
Estimated Exposure from Food

• Calculated Acrylamide Intake
  • FAO/WHO: 0.3 - 0.8 $\mu$g/kg body weight/day
  • FDA: 0.37 $\mu$g/kg body weight per day (mean)

• No one food accounts for the majority of the mean population intake
  • Foods with lower levels/high consumptions contribute significantly to estimated intake

• Foods known to contain acrylamide contribute significantly to nutrient intake
Estimated Exposure from Food

- **US Consumption**
  - Potato products-35%
  - Breads-25%
  - Breakfast Cereals-10%
  - Coffee-7%

- **Sweden**
  - Coffee-44%

The level of acrylamide in a cup of coffee depends on how strong it is and the level of roasting.
<table>
<thead>
<tr>
<th>Food</th>
<th>Mean AA intake (µg/kgbw-day)</th>
<th>Cumulative Percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>French Fries (RF)</td>
<td>0.058</td>
<td>0.13</td>
</tr>
<tr>
<td>French Fries (OB)</td>
<td>0.051</td>
<td>0.25</td>
</tr>
<tr>
<td>Breakfast Cereal</td>
<td>0.043</td>
<td>0.35</td>
</tr>
<tr>
<td>Potato Chips</td>
<td>0.041</td>
<td>0.45</td>
</tr>
<tr>
<td>Cookies</td>
<td>0.036</td>
<td>0.53</td>
</tr>
<tr>
<td>Brewed Coffee</td>
<td>0.029</td>
<td>0.60</td>
</tr>
<tr>
<td>Toast</td>
<td>0.023</td>
<td>0.66</td>
</tr>
<tr>
<td>Pies and Cakes</td>
<td>0.020</td>
<td>0.70</td>
</tr>
<tr>
<td>Soft Bread</td>
<td>0.019</td>
<td>0.75</td>
</tr>
<tr>
<td>Chile con Carne</td>
<td>0.015</td>
<td>0.78</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Food</th>
<th>Mean AA intake (µg/kgbw-day)</th>
<th>Cumulative Percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corn Snacks</td>
<td>0.011</td>
<td>0.81</td>
</tr>
<tr>
<td>Crackers</td>
<td>0.011</td>
<td>0.83</td>
</tr>
<tr>
<td>Pizza</td>
<td>0.007</td>
<td>0.85</td>
</tr>
<tr>
<td>Pretzels</td>
<td>0.007</td>
<td>0.87</td>
</tr>
<tr>
<td>Popcorn</td>
<td>0.007</td>
<td>0.88</td>
</tr>
<tr>
<td>Canned Black Olives</td>
<td>0.005</td>
<td>0.89</td>
</tr>
<tr>
<td>Peanut Butter</td>
<td>0.004</td>
<td>0.90</td>
</tr>
<tr>
<td>Bagels</td>
<td>0.004</td>
<td>0.91</td>
</tr>
<tr>
<td>Soup Mix</td>
<td>0.003</td>
<td>0.92</td>
</tr>
<tr>
<td>Breaded Chicken</td>
<td>0.003</td>
<td>0.93</td>
</tr>
<tr>
<td>Food Item</td>
<td>Average Daily Intake (µg/day)</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>-------------------------------</td>
<td></td>
</tr>
<tr>
<td>Breads (all types)</td>
<td>31 ppb</td>
<td></td>
</tr>
<tr>
<td>Cereals, Ready to eat</td>
<td>86 ppb</td>
<td></td>
</tr>
<tr>
<td>Chile con carne</td>
<td>130 ppb</td>
<td></td>
</tr>
<tr>
<td>Coffee (Brewed)</td>
<td>7 ppb</td>
<td></td>
</tr>
<tr>
<td>Cookies (All types)</td>
<td>188 ppb</td>
<td></td>
</tr>
<tr>
<td>Graham crackers</td>
<td>459 ppb</td>
<td></td>
</tr>
<tr>
<td>Chocolate chip cookies</td>
<td>130 ppb</td>
<td></td>
</tr>
<tr>
<td>French Fries</td>
<td>413 ppb</td>
<td></td>
</tr>
<tr>
<td>Potato Chips</td>
<td>466 ppb</td>
<td></td>
</tr>
<tr>
<td>Toast</td>
<td>213 ppb</td>
<td></td>
</tr>
</tbody>
</table>
Frequency of Consumption needed to exceed 1 µg/day

Wheatena®…………………..Once every 30 days
French Fries……………….Once every 26 days
Canned Sweet potatoes…..Once every 26 days
Prune Juice…………………..Once every 16 days
Postum®……………………Once every 14 days
Potato Chips…………………Once every 14 days
Cookies/Toast………………Once every 7 days
Popcorn…………………….Once every 4 days
Coffee………………………..Once every 3 days
What about the risks? (Exon, 2005)

- **Neurotoxic in animals**
  - Repeated daily exposure at levels of 0.5-50 mg /kg/day result in hind limb foot splay, ataxia, and skeletal muscle weakness (cats, rats, mice, guinea pigs, rabbits and monkeys)

- No evidence of effect at dietary levels but study needed on low level chronic exposures to determine cumulative effects
What about the risks? (Exon, 2005)

- Neurotoxic in humans
  - Observed in construction workers using a water-proofing sealing gel containing acrylamide
  - Tingling and numbness of the hands and feet, weak legs and loss of toe reflexes, all of which were reversible.
  - Longer exposures led to cerebellar dysfunction, excessive tiredness, ataxia (reversible)
What about the risks? (Exon, 2005)

- **Reproductive toxicity in animals**
  - Short and long term effects
  - Not seen in humans
  - Diet level not expected to induce any reproductive toxicity but studies on long-term low doses needed.

- **Cancer in rats**
  - Animals exposed to high concentrations in the drinking water for prolonged periods develop multiple tumors at multiple sites in both genders
What about the risks? (Exon, 2005)

- **Cancer in Humans**
  - No evidence from occupational or dietary exposures
  - All epidemiologic studies negative
    - Dietary intake of acrylamide not associated with colorectal cancers in women (61,467 in Sweden)
    - No association with risk of breast cancer in women (43,404 in Sweden)
    - Some studies may lack the necessary statistical power
What about the risks? (Exon, 2005)

- Most groups agree that more research is needed on the health effects
  - More studies on metabolism, storage, excretion and metabolic fate of ARC and its metabolites
  - Implications of neurotoxicity, reproductive toxicity and carcinogenesis represent serious health concerns but not proven
- Must better understand long-term, low level exposure
• **NSRL** for acrylamide originally set at 0.2 ug/day but proposed in 2005 to go to 1.0 ug/day in 2005
  • At current estimated consumption, exceed either level
• **Warnings** proposed on some foods or in restaurants or grocery stores where certain foods are sold
• Proposed exclusion of **breads and cereals**
• Proposed exclusion of foods where natural process of **cooking** results in acrylamide formation
Proposition 65

• In August 2005, state of California sued nine food manufacturers over their reluctance to issue warnings that some popular snacks could contain acrylamide. (McDonald's, Burger King and KFC included)

• Attorney general Bill Lockyer argues that Proposition 65 requires companies to warn consumers about products containing chemicals known to cause cancer or birth defects.
What is the future?

Assess, prevent and/or reduce the risk of acrylamide in food to the greatest extent possible. (FDA)

• More research needed
  • Rapid/inexpensive screening methods
  • Dietary exposure & significance
  • Toxicology/Assessment of Human Risk
  • Mechanisms of formation and means to minimize/reduce in food products

• Communication to general public on significance
What is the future?

• Risks versus Benefits
  • Risks
    • Unknown risk from long term consumption of acrylamide
    • Significant variation in levels in foods
    • 40% of foods in the diet contain acrylamide so not easy to limit and many are needed for a balanced diet
    • Warnings could create fear of food & create consumer misunderstandings
  
• Benefits of foods with acrylamide
  • Cooking is important to food acceptability (browning/flavor) and to food safety
  • Many of foods important to balanced diet
Keeping it in Perspective!

Do the risks outweigh the Benefits?