Safety aspects of food additives
Prof. Dr. Hans Verhagen
28 Sept 2015

1. Introduction
2. A very short course in toxicology
3. Food additives in EU
4. Low calorie sweeteners
5. EFSA
6. (Acceptable) daily intakes
7. Examples: stevia and aspartame
8. Benefit-risk assessment
9. Conclusions

Mythes in de voeding: spinazie en ijzer

<table>
<thead>
<tr>
<th>gekookte groenten</th>
<th>mg/100 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wortelen bospeen</td>
<td>0.2</td>
</tr>
<tr>
<td>Bloemkool</td>
<td>0.3</td>
</tr>
<tr>
<td>Snijbonen</td>
<td>0.5</td>
</tr>
<tr>
<td>Sperziebonen</td>
<td>0.8</td>
</tr>
<tr>
<td>Boerenkool</td>
<td>1.0</td>
</tr>
<tr>
<td>Doperwten</td>
<td>2.0</td>
</tr>
<tr>
<td>Spinazie</td>
<td>2.4</td>
</tr>
<tr>
<td>Snijbiet</td>
<td>4.0</td>
</tr>
</tbody>
</table>

‘1870’: 10* to high iron values published
(, wrong)

1929

Discovered only in 1937: correct values
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Water intoxication

- A potentially life-threatening condition caused by drinking too much water

- Clinical manifestations are abdominal cramps, nausea, vomiting, lethargy, and dizziness.

- An increase in the volume of free water in the body, resulting in dilutional hyponatremia, which may result in seizures, coma, and death.

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“All substances are poisons. There is none which is not a poison. The right dose differentiates a poison from a remedy.”

Paracelsus (1493-1541)
Table 2.1. Approximate Acute LD50s of Some Common Chemical Agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>LD-50 (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethyl alcohol</td>
<td>10.00</td>
</tr>
<tr>
<td>Salt (sodium chloride)</td>
<td>42.00</td>
</tr>
<tr>
<td>Iron (Ferric sulfate)</td>
<td>1.50</td>
</tr>
<tr>
<td>Morphine</td>
<td>9.00</td>
</tr>
<tr>
<td>Methylnitrosourea (paradichlorobenzene)</td>
<td>500</td>
</tr>
<tr>
<td>Aspirin</td>
<td>250</td>
</tr>
<tr>
<td>EDTA</td>
<td>50</td>
</tr>
<tr>
<td>Cyanide</td>
<td>10</td>
</tr>
<tr>
<td>Nicotine</td>
<td>1</td>
</tr>
<tr>
<td>Tetradotatin (from fish)</td>
<td>0.01</td>
</tr>
<tr>
<td>Dioxin (TCDD)</td>
<td>0.001</td>
</tr>
<tr>
<td>Botulism Toxin</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Dose Response Function

Glasses of Wine - Dose Response

Acceptable daily intakes (ADI) =

“No observed adverse effect level” (WHO, 1962)
Safety factors: interspecies diff's and intraspecies diff's, e.g. 10 * 10 = 100

Hazard versus Risk

A Hazard ≠ a Risk until there is exposure

risk analysis paradigm

risk assessment paradigm

risk analysis paradigm

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E = European

E100–E199 (colours)
E 200–E299 (preservatives)
E300–E399 (antioxidants, acidity regulators)
E400–E499 (thickeners, stabilizers, emulsifiers)
E500–E599 (acidity regulators, anti-caking agents)
E600–E699 (flavour enhancers)
E700–E799 (antibiotics)
E900–E999 (miscellaneous)
E1000–E1999 (additional chemicals)

E-numbers
- Food additives that have been assessed for use within the European Union
- Safety assessment and approval are the responsibility of the European Food Safety Authority.
- Numbering scheme follows International Numbering System (INS) as determined by the Codex Alimentarius
- In casual language = artificial food additives, but also natural ingredients have an E number such as vitamin C (E300) or lycopene (E160d).

Safety Aspects of Low Calorie Sweeteners

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Aspartame
Acesulfam-K
Cyclamate
Saccharin

De volgende E-nummers zijn allemaal zoetstoffen:
- E420 (sorbitol)
- E421 (mannitol)
- E950 (acesulfam-K)
- E951 (aspartaam)
- E952 (cyclamaat)
- E953 (saccharine)
- E954 (isomalt)
- E955 (sucralose)
- E957 (thaumatin)
- E959 (neohesperidine-DC)
- E960 (steviolglycosiden)
- E961 (neotaam)
- E962 (aspartaam-acesulfamzout)
- E965 (maltitol)
- E966 (lactitol)
- E967 (xylitol)
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1990’s
• BSE
• Dioxins
• etc

EFSA structure

Management Board + Advisory Forum + EFSA Staff = European Food Safety Authority

Scientific Panels
• Animal health and welfare (AHAW)
• Food additives and nutrient sources (ANS)
• Biological hazards (BIOHAZ)
• Food contact materials, enzymes, flavourings (CEF)
• Contaminants (CONTAM)
• Feed additives (FEEDAP)
• Genetically modified organisms (GMO)
• Nutrition (NDA)
• Plant health (PLH)
• Plant protection products (PPR)

EFSA’s guiding principles

Core values
• Scientific excellence
• Independence
• Openness
• Transparency
• Responsiveness

Risk assessment
Acceptable daily intakes (ADI)=

"the daily intake of a chemical, which during an entire lifetime appears to be without appreciable risk on the basis of all known facts at that time" (WHO, 1962)

<table>
<thead>
<tr>
<th>Sweetener</th>
<th>E number</th>
<th>ADI (mg/kg body weight)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspartame</td>
<td>E 951</td>
<td>40</td>
</tr>
<tr>
<td>Acesulfame K</td>
<td>E 950</td>
<td>9</td>
</tr>
<tr>
<td>Cyclamate</td>
<td>E 952</td>
<td>7</td>
</tr>
<tr>
<td>Saccharin</td>
<td>E 954</td>
<td>5</td>
</tr>
<tr>
<td>Sucralose</td>
<td>E 955</td>
<td>15</td>
</tr>
<tr>
<td>Steviol glycosides</td>
<td>E 960</td>
<td>4</td>
</tr>
</tbody>
</table>

ADI versus liter frisdrank (dagelijks, levenslang)

<table>
<thead>
<tr>
<th></th>
<th>BW = 25 kg</th>
<th>BW = 65 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspartaan</td>
<td>1,67 L</td>
<td>4,33 L</td>
</tr>
<tr>
<td>Acesulfame K</td>
<td>0,64 L</td>
<td>1,67 L</td>
</tr>
<tr>
<td>Cyclamaat</td>
<td>0,70 L</td>
<td>1,82 L</td>
</tr>
<tr>
<td>Sacharain</td>
<td>1,56 L</td>
<td>4,06 L</td>
</tr>
<tr>
<td>Sucralose</td>
<td>1,25 L</td>
<td>3,25 L</td>
</tr>
<tr>
<td>Steviol Glycosides</td>
<td>1,25 L</td>
<td>3,25 L</td>
</tr>
</tbody>
</table>

Consumption of Artificially Sweetened foods aged 7 to 69 years (DNFCS 2007-2010)
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EFSA: FAQ on aspartame

**What is aspartame?**
Low-calorie, intense sweetener which is approximately 200 times sweeter than sucrose

**Has EFSA ever evaluated the safety of aspartame?**

**So if aspartame is safe, why is EFSA doing a full re-evaluation now?**
By 2020, EFSA must re-evaluate all food additives which were authorised in the EU prior to 20 January 2009. May 2011, EC asked EFSA to re-prioritise the full re-evaluation of the safety of aspartame to 2012

EFSA: FAQ on aspartame

**Why have questions been raised about aspartame in the past?**
The safety of aspartame has sparked interest and controversy. The scientific evidence is sufficient to confirm that aspartame is safe for human consumption.

**When will EFSA’s new safety review be finished?**
10 Dec 2013

**How does EFSA guarantee the independence of its scientific advice?**
EFSA is constantly vigilant to potential conflicts of interest whilst recognising that the top scientific experts in Europe can only gain their expertise by being active in their fields.
EFSA: Steviol glycosides

- Steviosides: SCF .... 1999: "... "the substance is not acceptable as a sweetener on the presently available data"
- *Stevia rebaudiana* Bertoni plants and leaves: SCF ...1998 "...".... information submitted was insufficient"
- Steviol glycosides: EFSA 2010: positive opinion, EC 2011 permission
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Low calorie sweeteners

Benefits
- Reduced energy intake
- Reduced body weight/weight balance
- Reduced caries

Risks
- None (only perception; E-numbers)
- ADIs established

Non-effects
- CVD
- Cancer
- Diabetes / metabolic syndrome
- Gout

Further work (outside BRAFO remit)

- Keep eye on intakes > ADI levels
- Public perception of (non real) risks

Further work (outside BRAFO remit)

- Keep eye on intakes > ADI levels
- Public perception of (non real) risks
- Calculate potential health benefits
  - - 542 kJ/day
  - - 357 kJ/day
  - - 1.7 BMI
  - - 1.3 BMI
(young adults, many assumptions, Hendriksen et al. 2010)

Conclusions
Ons voedsel is veilig

Evidence based nutrition
Evidence based policy decisions
Fact-free (policy) decisions ........
Thank you - questions?