National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

Safety aspects of food additives

Prof.Dr. Hans Verhagen
28 Sept 2015

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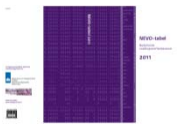
Ministry of Health, Welfare and Sport

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



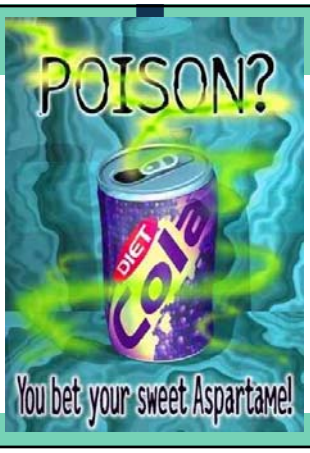
gekookte groenten	mg/100 g
Wortelen bospeen	0.2
Bloemkool	0.3
Snijbonen	0.5
Sperziebonen	0.8
Boerenkool	1.0
Doperwten	2.0
Spinazie	2.4
Snijbiet	4.0

'1870': 10* to high iron values published

(, wrong)

1929

Discovered only in 1937 : correct values



E Numbers, food additives and your health

No.	Description
E100	Safe ??
E101	Safe ??
E102	Dangerous
E103	Forbidden
E104	Suspicious
E105	Forbidden
E110	Dangerous
E111	Forbidden
E120	Dangerous
E121	Forbidden
E122	Suspicious
E123	Very Dangerous
E124	Dangerous
E125	Forbidden
E126	Forbidden
E127	Dangerous
E130	Forbidden
E131	Cancer

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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.

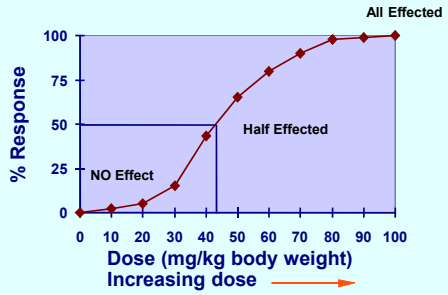
"All substances are poisons.
There is none which is not a poison.
The right dose differentiates a poison from a remedy."

Paracelsus (1493-1541)

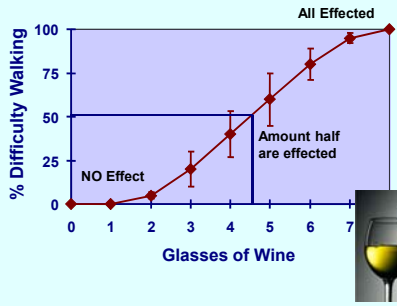
Table 2.1. Approximate Acute LD50s of Some Common Chemical Agents

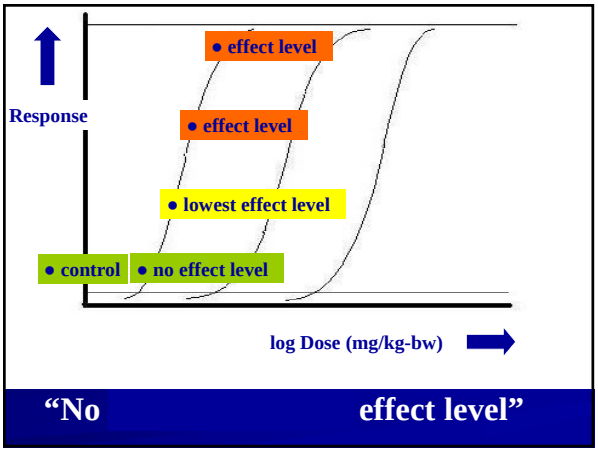
Agent	LD-50 (mg/kg)
Ethyl alcohol	10,000
Salt (sodium chloride)	4,000
Iron (Ferrous sulfate)	1,500
Morphine	900
Mothballs (paradichlorobenzene)	500
Aspirin	250
DDT	250
Cyanide	10
Nicotine	1
Tetrodotoxin (from fish)	0.01
Dioxin (TCDD)	0.001 (for some species)
Botulinum Toxin	0.00001

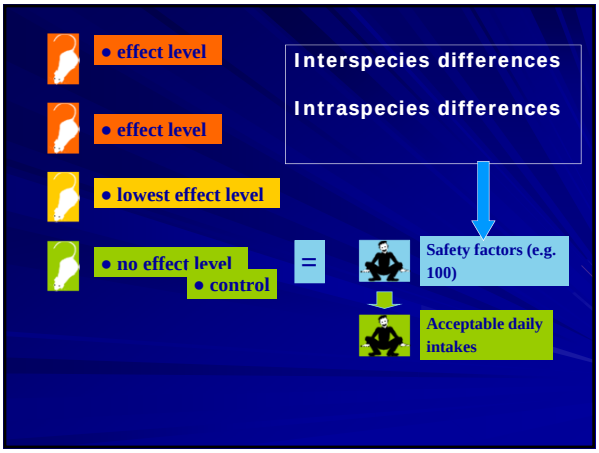
Dose Response Function



Glasses of Wine - Dose Response

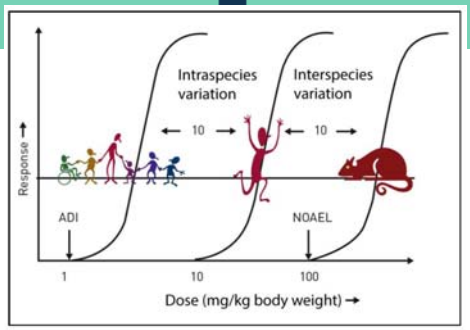






Acceptable daily intakes (ADI)=

"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)



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

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risk analysis paradigm

risk assessment paradigm

Hazard identification

Hazard characterisation

Exposure assessment

Risk characterisation

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E =

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).

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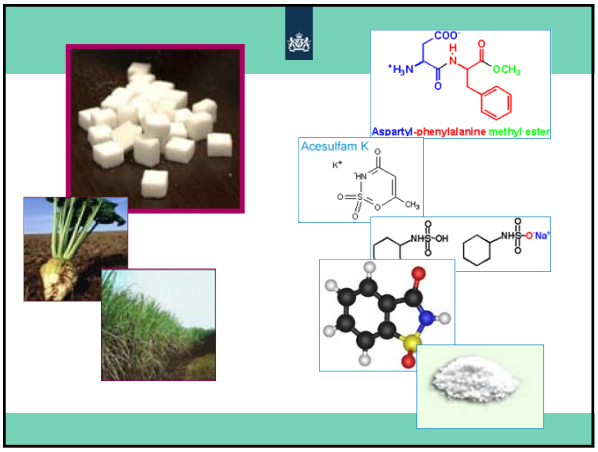
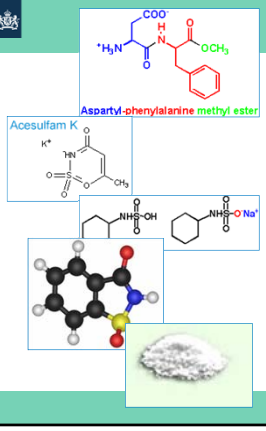


Aspartame

Acesulfam-K

Cyclamate

Saccharin



De volgende E-nummers zijn allemaal zoetstoffen:

- E420 (sorbitol)
- E421 (mannitol)
- E950 (acesulfaam-K)
- E951 (aspartaam)
- E952 (cyclamaat)
- E953 (isomalt)
- E954 (saccharine)
- E955 (sucralose)
- E957 (thaumatine)
- E959 (neohesperidine-DC)
- E960 (steviolglycosiden)
- E961 (neotaam)
- E962 (aspartaam-acesulfaamzout)
- E965 (maltitol)
- E966 (lactitol)
- E967 (xylitol)

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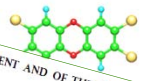
1990's

- BSE
- Dioxins

etc



REGULATION (EC) No 178/2002 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety

Brussels, 12 January 2000
COM (1999) 719 final

WHITE PAPER ON FOOD SAFETY

efsa
European Food Safety Authority

EFSA structure

efsa
European Food Safety Authority

Management Board + **Advisory Forum**

\+ \+

EFSA Staff **Scientific Committee and Panels**

= efsa European Food Safety Authority

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Risk assessment

efsa
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)

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EFSA's guiding principles

efsa
European Food Safety Authority

Core values

- Scientific excellence
- Independence
- Openness
- Transparency
- Responsiveness

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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)

ADI's of some sweeteners in EU

Sweetener	E number	ADI (mg/kg body weight)
Aspartame	E 951	40
Acesulfame K	E 950	9
Cyclamate	E 952	7
Saccharin	E 954	5
Sucralose	E 955	15
Steviol glycosides	E 960	4

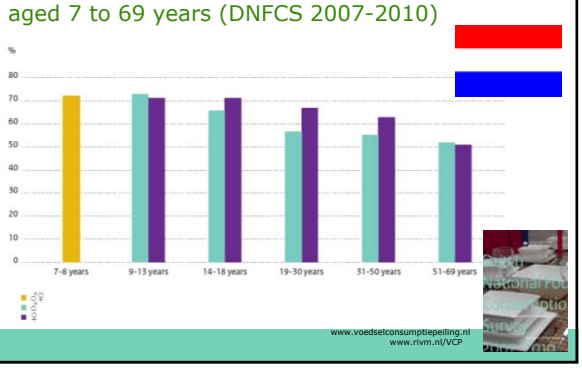
ADI versus liter frisdrank

(dagelijks, levenslang)

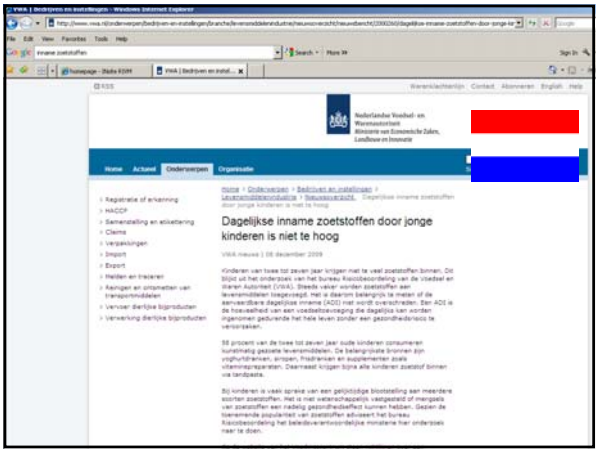
	Bw = 25 kg	BW = 65 kg
Aspartaam	1,67 L	4,33 L
Acesulfaam K	0,64 L	1,67 L
Cyclamaat	0,70 L	1,82 L
Sacharine	1,56 L	4,06 L
Sucralose	1,25 L	3,25 L
Steviol Glycosiden	1,25 L	3,25 L

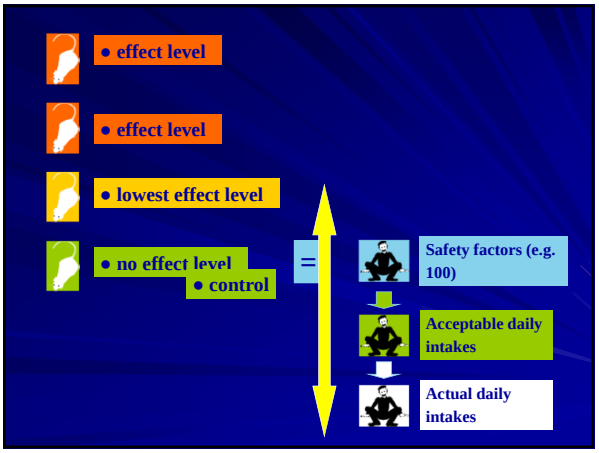
Berekend via: zoetstoffen.nl

Consumption of Artificially Sweetened foods aged 7 to 69 years (DNFCS 2007-2010)



www.voedselconsumptiepeiling.nl
www.rivm.nl/VCP





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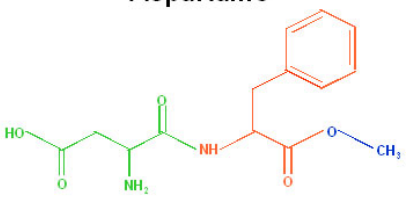
Aspartame



L-aspartyl-L-phenylalanine methyl ester

Aspartate Phenylalanine Methanol

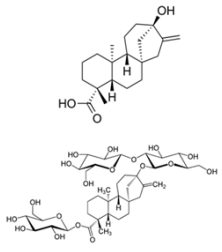
EFSA : **FAQ on aspartame**

What is aspartame?	low-calorie, intense sweetener which is approximately 200 times sweeter than sucrose
Has EFSA ever evaluated the safety of aspartame?	1984 SCF ….. EFSA 2006, 2009, 2011, and …2013
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 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…….

Steviol glycosides



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

EFSA : Steviol glycosides

- …. establishes an ADI for steviol glycosides, expressed as steviol equivalents, of 4 mg/kg bw/day based on application of a 100-fold uncertainty factor to the NOAEL in the 2-year carcinogenicity study in the rat of 2.5% stevioside in the diet.
- corresponding to approximately 388 mg steviol equivalents/kg bw/day
- ……. → 4 mg/kg bw/day

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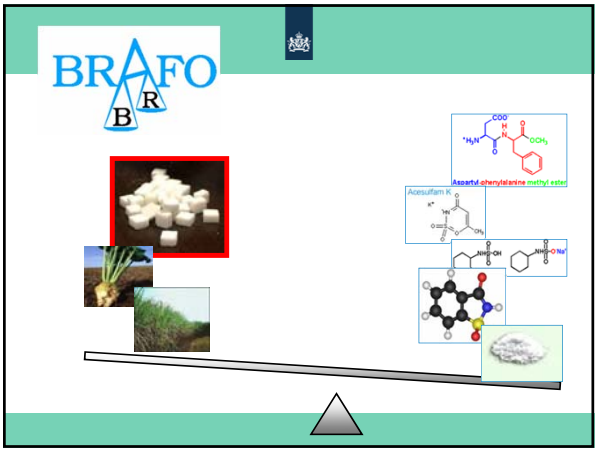
BRAFO



Low calorie sweeteners

ILSI

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

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Further work (outside BRAFO remit)

ILSI

- keep eye on intakes > ADI levels
- public perception of (non real) risks

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Further work (outside BRAFO remit)

ILSI

- 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*)

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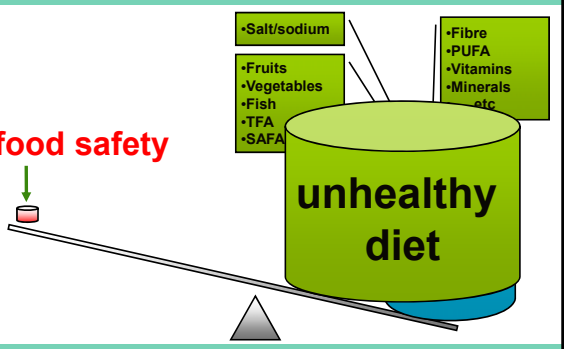
Ons voedsel is veilig

efsa
European Food Safety Authority

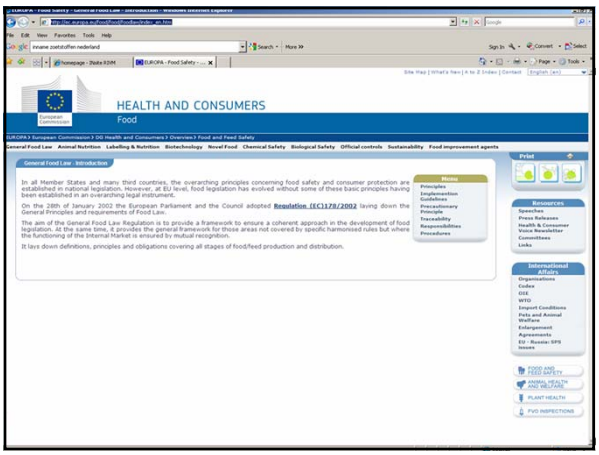
2004 2006



Evidence based nutrition

Evidence based policy decisions

Fact-free (policy) decisions ……..



Thank you - questions?

©ontact

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