Determining a safe intake of vitamin B6 from food supplements
Vitamin B6 supplementation

• Doses up to 250 mg
Question: what is a safe intake of vitamin B6 from supplements?

• Background: health complaints from consumers; RASFF alerts; media attention

• Vitamin B6 is the generic name for six compounds (vitamers) with vitamin B6 activity: \textit{pyridoxine}, an alcohol; \textit{pyridoxal}, an aldehyde; and pyridoxamine, which contains an amino group; and their respective 5’-phosphate esters
Question: what is a safe intake of vitamin B6 from supplements?

• Variety of functions in the body; involvement in more than 100 enzyme reactions (*mainly pyridoxal phosphate*)

• Water-soluble, vitamers have similar bioactivity (*because of metabolism*)

• Same toxicity? (*details can be shown*)
Approach

- Food consumption surveys: intake vitamin B6 from foods
- Literature review: safety and metabolism
- *In vitro* experiment (UM)

Maximum intake of vitamin B6 from supplements = **Upper Limit – intake from foods** (P95, corrected for lower bioavailability)
Results

• Vitamin B6 intake in NL for all age groups sufficient → no need to advise use of supplements (for healthy population)
Results

• EFSA’s UL = 25 mg/day for adults; intake from foods does not exceed UL

• UL based on studies with pyridoxine(-HCl)

• Long term use of high-dosed vitamin B6 supplements can lead to adverse health effects (sensory neuropathy, dermatological lesions, photosensitivity and gastrointestinal symptoms, such as nausea and heartburn)
Conclusions

- Safe intake adults by supplements: 21 mg/day (children: amount depending on body weight)
- Safe intake for all vitamers
Considerations

• EC: Directive 2002/46/EC indicates that max. daily amounts should be assessed

• Various countries regulate B6 supplements in different ways

• We presented a possible approach to assess max. amounts
Advice

• Minister: draft national legislation (max. amounts; warnings) until European law drafted and into force based on a :

• maximum of 21 mg intake by supplements (in line with Norway, Belgium)
What is the alternative?

- Lowering dose of supplements
- Changing PN supplements to PLP or PL supplements?
Vitamin B6

- RDA: 1,3-2,0 mg/day
- UL: 25 mg/day

- Deficiency leads to:
  - Demyelination of nerves
  - Peripheral neuropathy
  - Neuropathic pain
The effect of the vitamers on cell death of neuronal cells

Only PN significantly induces cell death at 5 µM
At 5 µM PN significantly inhibited tyrosine decarboxylase and alanine transaminase
Conclusion

• These results indicate the neuropathy observed after taking a relatively high dose of vitamin B6 supplements might be due to the vitamer that is used in the supplements, namely PN.

• PN exerts a toxic effect, at concentrations where the other vitamers are not toxic.

• The activity of PLP-dependent enzymes is inhibited by PN.

→ Paradox: Supplementation of high concentrations of the vitamer pyridoxine leads to decreased vitamin B6 function and symptoms of vitamin B6 deficiency
Vitamin B6 paradox

Vitamin B6 deficiency

\[ \text{PN} \]

\[ \text{PDXK} \]

\[ \text{PNP} \]

\[ \text{PNPO} \]

\[ \text{PLP} \]

PLP dependent enzymes

Neuronal cell death

Peripheral neuropathy
Vitamin B6 paradox

Vitamin B6 supplementation

PLP-dependent enzymes

Neuronal cell

Peripheral neuropathy