



Nederlandse Voedsel- en
Warenautoriteit
Ministerie van Economische Zaken



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: **pyridoxine**, an alcohol; **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)



Vitamin B6



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



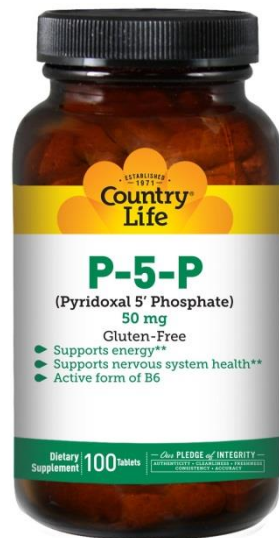
Advice

- 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)

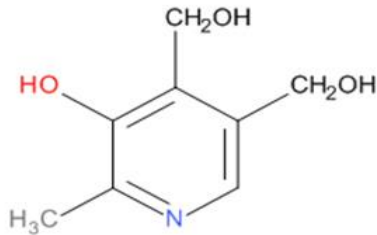


What is the alternative ?

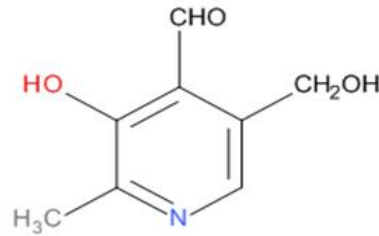
- Lowering dose of supplements
- Changing PN supplements to PLP or PL supplements?



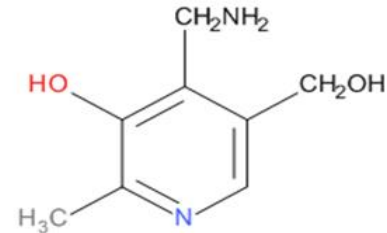
Vitamin B6



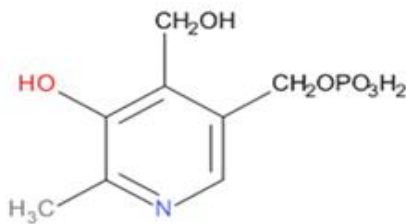
Pyridoxine (**PN**)



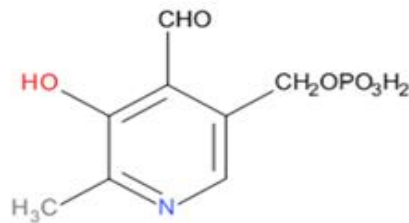
Pyridoxal (**PL**)



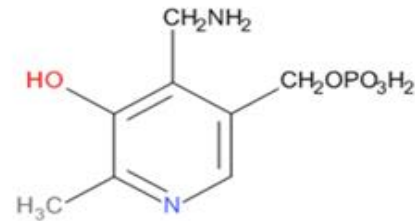
Pyridoxamine (**PM**)



Pyridoxine phosphate (**PNP**)



Pyridoxal phosphate (**PLP**)

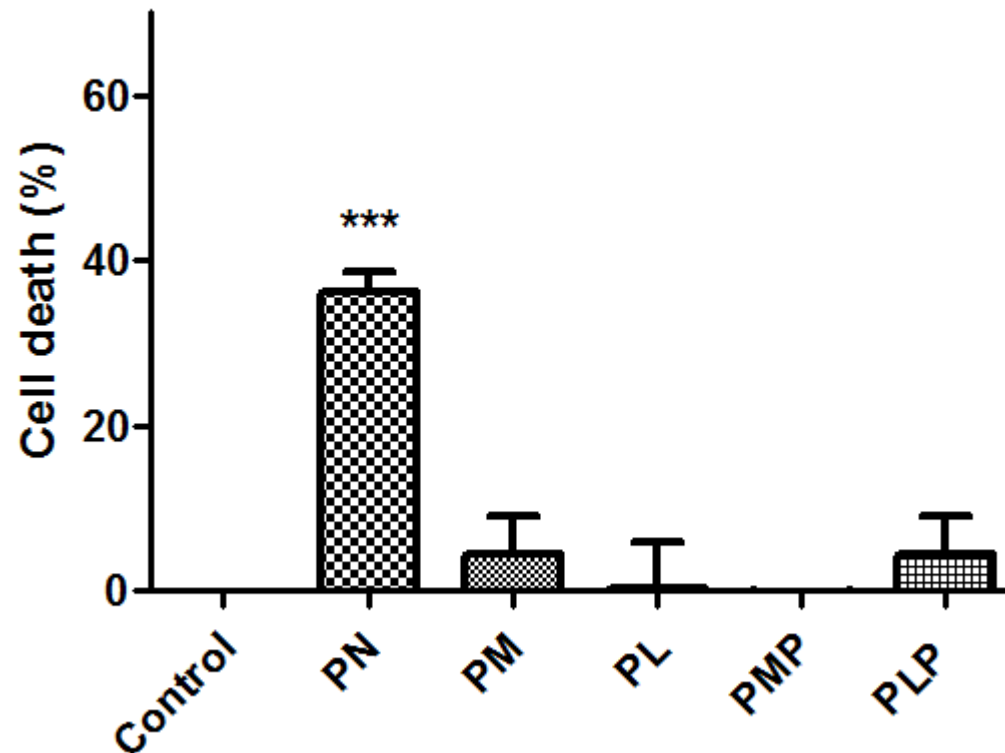


Pyridoxamine phosphate (**PMP**)

- RDA: 1,3-2,0 mg/day
 - UL: 25 mg/day
 - Deficiency leads to:
 - Demyelination of nerves
 - Peripheral neuropathy
- } Neuropathic pain



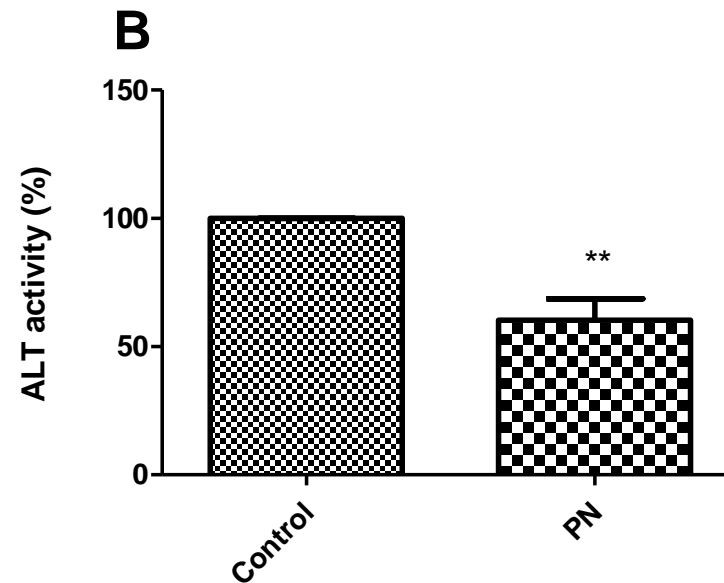
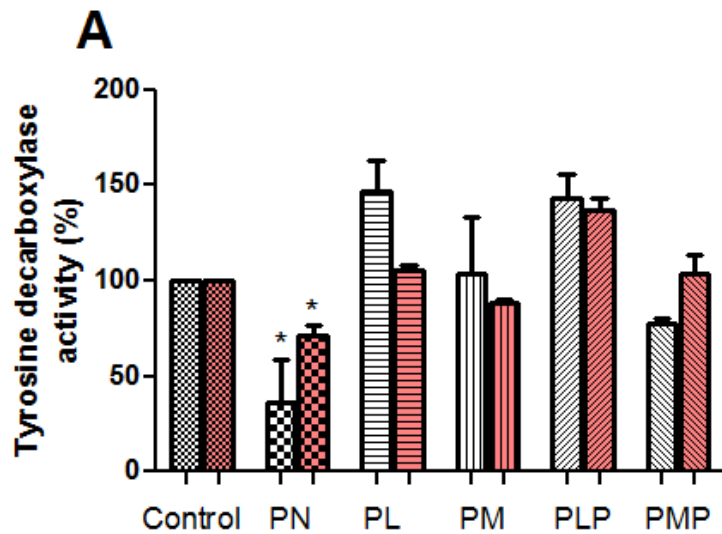
The effect of the vitamers on cell death of neuronal cells



Only PN significantly induces cell death at 5 μ M



PLP dependent enzymes



At 5 μ M PN significantly inhibited tyrosine decarboxylase and alanine transaminase



Conclusion

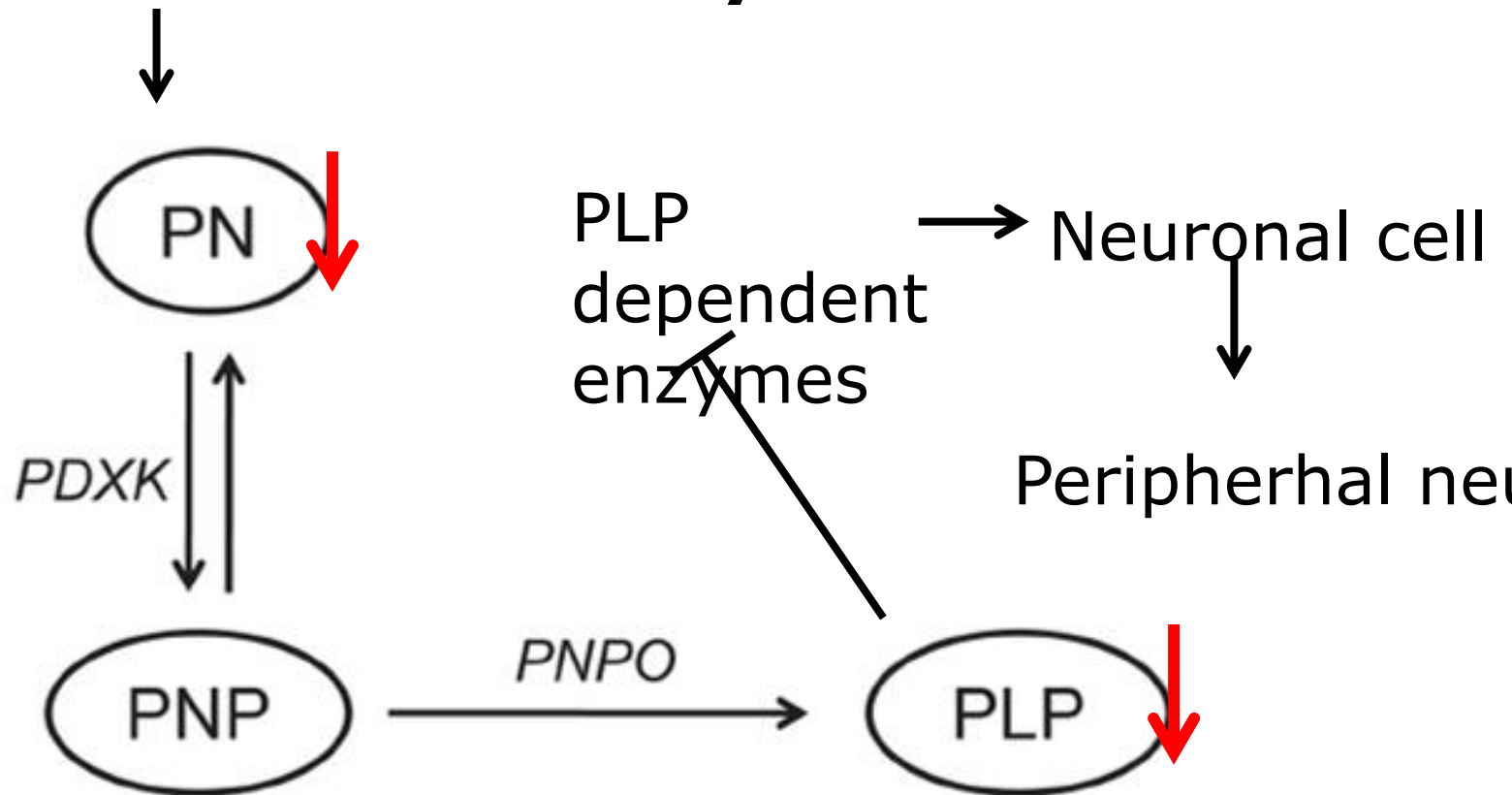
- These results indicate the neuropathy observed after taking a relatively high dose of vitamin B6 supplements might be due to the vitamer that is used in the supplements, namely PN.
- PN exerts a toxic effect, at concentrations where the other vitamers are not toxic.
- The activity of PLP-dependent 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





Vitamin B6 paradox

Vitamin B6 supplementation

