

Outline

Overconsumption of *Ginkgo biloba* seeds induces food poisoning. The main symptoms of *Ginkgo biloba* seed poisoning are tonic and/or clonic convulsions and vomiting. Our group demonstrated that 4'-*O*-methylpyridoxine (MPN) is responsible for food poisoning by *Ginkgo biloba* seeds (Wada *et al.*, 1985). Plasma MPN concentration in patients who suffered from the poisoning is analyzed by HPLC in our laboratory in response to the doctor's request. MPN inhibits enzymatic activation of vitamin B₆, resulting in vitamin B₆ deficiency and leading to diminished γ -aminobutyric acid (GABA) synthesis (Fig. 1, Kobayashi *et al.*, 2015, 2019, Sado *et al.*, 2019). Since the food poisoning has occurred frequently in children under six years of age, the mechanism of age-related sensitivity to MPN is being studied in our laboratory.

We recently revealed that extracellular hydrolysis of active vitamins by GPI-anchored proteins alkaline phosphatase (Akiyama *et al.*, 2018) and CD73 contributes to the uptake of vitamin B₂ and B₆ (Fig. 2, Shichinohe *et al.*, 2022).

Faculty members

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Main research in progress

- 1) Epidemiological investigation of food poisoning by *Ginkgo biloba* seeds
- 2) Diagnostic assay of MPN and vitamin B₆ analogues in biological specimen (plasma, serum, cerebral spinal fluid or urine) of patient of food poisoning by *Ginkgo biloba* seeds
- 3) Metabolisms of 4'-*O*-methylpyridoxine and their contribution of MPN toxicity
- 4) Vitamin metabolism in patient with Hypophosphatasia and Inherited GPI deficiency.
- 5) Activation and inactivation mechanisms of vitamins
- 6) Synthesis of vitamins and its derivatives

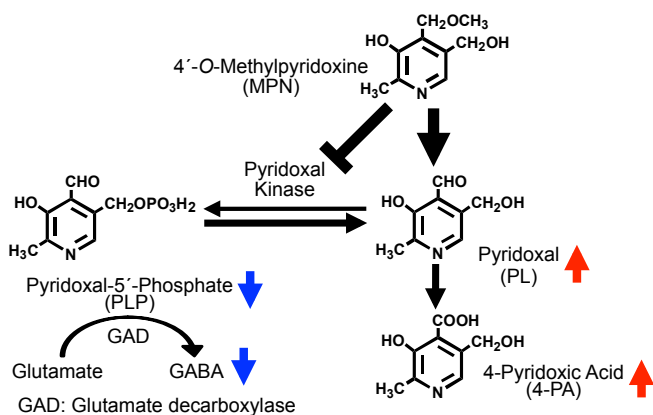


Fig. 1 Effects of 4'-*O*-methylpyridoxine on vitamin B₆ activation pathway and GABA synthesis.

(Kobayashi *et al.*, 2015, 2019, Sado *et al.*, 2019)

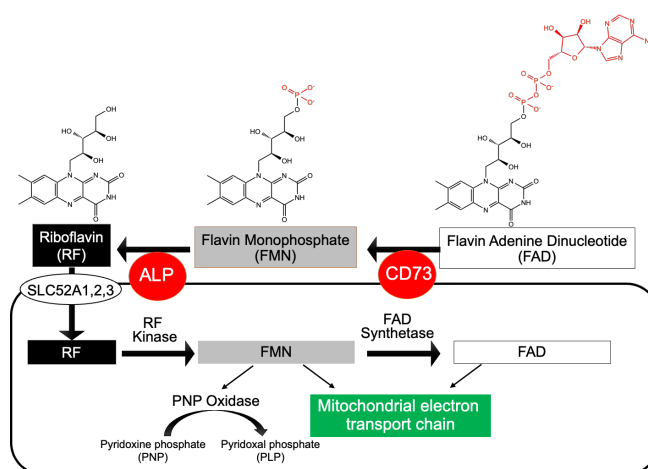


Fig. 2 Hydrolysis of FAD and FMN by CD73 and ALP for its uptake into cells, vitamin B₆ metabolism and mitochondria function

(Shichinohe *et al.*, 2022)

Current publications

- Sugitate K., Yamashiro T., Takahashi I., Yamada K., & Abe T., Oxytrofalcatin Puzzle: Total Synthesis and Structural Revision of Oxytrofalcatins B and C. *J. Org. Chem.*, **88**: 9920-9926(2023).
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- Shichinohe N., Kobayashi D., Izumi A., Hatanaka K., Fujita R., Kinoshita T., Inoue N., Hamaue N., Wada K. & Murakami Y., Sequential hydrolysis of FAD by ecto-5' nucleotidase CD73 and alkaline phosphatase is required for uptake of vitamin B2 into cells. *J. Biol. Chem.*, **298**: 102640(2022).
- Tsuchida S., Takahashi R., Yabe K., Hamaue N. & Aoki T., A simple method for preparing a diamino cellulose disk from a dialdehyde cellulose disk by reductive amination using 2-picoline-borane. *Cellulose*, **29**: 3025–3033(2022).
- Emoto M.C., Sato-Akaba H., Hamaue N., Kawanishi K., Koshino H., Shimohama S. & Fujii H.G. Early detection of redox imbalance in the APP^{swe}/PS1^{dE9} mouse model of Alzheimer's disease by in vivo electron paramagnetic resonance imaging. *Free Radic. Biol. Med.*, **172**: 9–18(2021).
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- Sado T., Nakata S., Tsuno T., Sato M., Misawa Y., Yamauchi S., Inaba Y., Kobayashi D. & Wada K., Concentrations of various forms of vitamin B6 in ginkgo seed poisoning. *Brain Dev.*, **41**: 292-295(2019).
- Kobayashi D., Food Poisoning by Ginkgo Seeds through Vitamin B6 Depletion (Japanese), *Yakugaku Zasshi*, **139**: 1-6 (2019).
- Akiyama T., Kubota T., Ozono K., Michigami T., Kobayashi D., Takeyari S., Sugiyama Y., Noda M., Harada D., Namba N., Suzuki A., Utoyama M., Kitanaka S., Uematsu M., Mitani Y., Matsunami K., Takishima S., Ogawa E. & Kobayashi K., Pyridoxal 5'-phosphate and related metabolites in hypophosphatasia: Effects of enzyme replacement therapy, *Mol. Genet. Metab.*, **125**: 174-180(2018).
- Kobayashi D., Tendo Y., Abe K., Tanda R., Ishikawa M. & Wada K., Ginkgo seed poisoning (Japanese), *Jpn. J. Pediatr. Med.*, **50**: 703-705 (2018).

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