Department of Hygienic Chemistry
Division of Pharmaceutical Health Science & Environmental Toxicology
School of Pharmaceutical Sciences

Outline

Overconsumption of *Ginkgo biloba* seeds induces food poisoning. The main symptoms of *Ginkgo biloba* seed poisoning are tonic and/or clonic convulsion 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 B_6, resulting in vitamin B_6 deficiency and leading to diminished γ -aminobutyric acid (GABA) synthesis (Fig. 1, Kobayashi *et al.*, 2015). Since the food poisoning has occurred frequently in children under six years of age (Fig. 2, Kobayashi *et al.*, 2014), the mechanism of age-related sensitivity to MPN is being studied in our laboratory.

Faculty members

Professor : Naoya HAMAUE, Ph.D.
Associate professor : Daisuke KOBAYASHI, Ph.D.
Assistant professor : Toshiki YAMASHIRO, Ph.D.

Main research in progress

1) Epidemiological investigation of food poisoning by *Ginkgo biloba* seeds (Mei *et al.*, 2017, Kobayashi *et al.,* 2019)
2) Diagnostic assay of MPN and vitamin B_6 analogues in biological specimen (plasma, serum, cerebral spinal fluid or urine) of patient of food poisoning by *Ginkgo biloba* seeds (Sado *et al., 2019*, Azuma *et al.*, 2020)
3) Metabolisms of 4′-*O*-methylpyridoxine and their contribution of MPN toxicity
4) Vitamin metabolism in patient with Hypophosphatasia (Akiyama *et al.,* 2018)
5) Activation and inactivation mechanisms of vitamins (Shichinohe *et al.,* 2022)

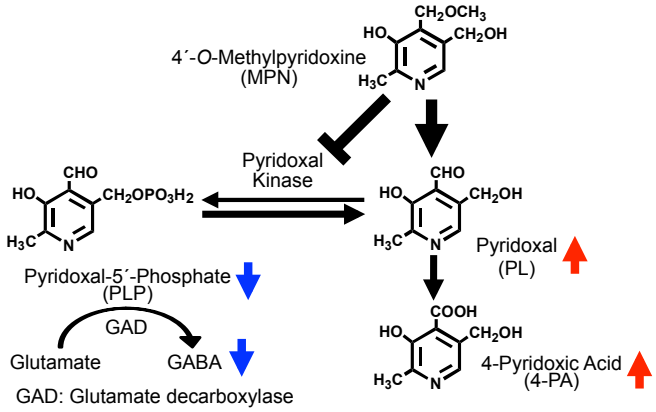

Fig. 1 Effects of 4′-*O*-methylpyridoxine on vitamin B_6 activation pathway and GABA synthesis.
(Kobayashi *et al.*, 2015)

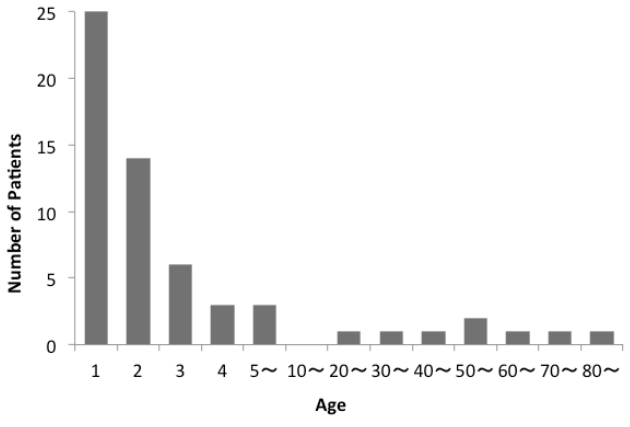

Fig. 2 Age-specific numbers of patients with food poisoning by *Ginkgo biloba* seeds in Japan.
(Kobayashi *et al.,* 2014)

Current publications

Kobayashi D, Yoshimura T, Johno A, Sasaki K & Wada K, Toxicity of 4′-*O*-methylpyridoxine -5′-glucoside in *Ginkgo biloba* seeds, *Food Chem*, **126**: 1198-1202(2011).

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Kobayashi D, Yoshimura T, Johno A, Ishikawa M, Sasaki K & Wada K, Decrease in pyridoxal-5′-phosphate concentration and increase in pyridoxal concentration in rat plasma by 4′-*O*-methylpyridoxine administration, *Nutr Res*, **35**: 637-642(2015).

Mei N, Guo X, Ren Z, Kobayashi D, Wada K & Guo L, Review of *Ginkgo biloba*-induced toxicity, from experimental studies to human case reports, *J Environ Sci Health C Environ Carcinog Ecotoxicol Rev*, **35**: 1-28 (2017).

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, Food Poisoning by *Ginkgo* Seeds through Vitamin B6 Depletion (Japanese), *Yakugaku Zasshi*, **139**: 1-6 (2019).

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).

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