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

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 B₆, resulting in vitamin B₆ 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.

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
- 5) Activation and inactivation mechanisms of vitamins

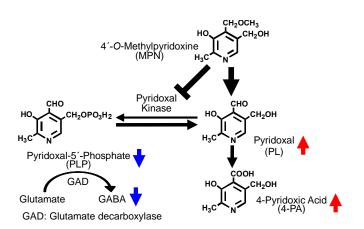


Fig. 1 Effects of 4'-O-methylpyridoxine on vitamin B₆ activation pathway and GABA synthesis.

(Kobayashi *et al.*, 2015)

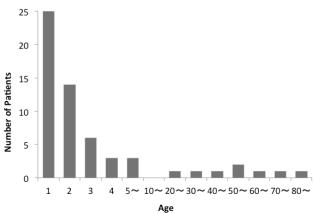


Fig. 2 Age-specific numbers of patients with food poisoning by *Ginkgo biloba* seeds in Japan. (Kobayashi *et al.*, 2014)

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).
- Wada K, Ginkgo biloba seeds (Japanese), Japanese Journal of Pediatrics, 65: 1403-1407(2012).
- Kobayashi D, Aoki Y, Yoshimura T, Ishikawa M, Wada K, Food poisoning by *Ginkgo biloba* seeds (Japanese), *Nihon Rinsho Shinryouikibetsushoukougun*, **30**: 728-731(2014).
- 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).
- Azuma F, Nokura K, Kako T, Kobayashi D, Yoshimura T, Wada K., An Adult Case of Generalized Convulsions Caused by the Ingestion of Ginkgo biloba Seeds with Alcohol. Intern Med, **59**: 1555-1558(2020).

Contact e-mail address

kobadai@hoku-iryo-u.ac.jp