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AN ANTIVITAMIN B₆, 4'-METHOXYPYRIDOXINE,
FROM THE SEED OF GINKGO BILOBA L.

Keiji Wada, Seikou Ishigaki, Kaori Ueda, Masakatsu Sakata,
and Masanobu Haga*

Faculty of Pharmaceutical Sciences, Higashi Nippon Gakuen University,
Ishikari-Tobetsu, Hokkaido 061-02, Japan

An antivitamin B₆, 4'-methoxypyridoxine (1) was isolated from the seed of Ginkgo biloba L. (Ginkgoaceae).¹⁾ The albumen of the seed of G. biloba L., which is called "Gin-nan or Ginkyo", is used as a crude drug in China and as food in Japan. However, in Japan, there have been about 70 reports of "Gin-nan sitotoxism."

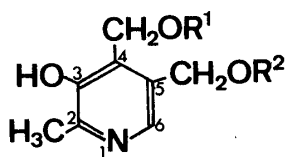
In this paper, we report that the substance responsible for this sitotoxism is 4'-methoxypyridoxine (1), which is known to have anti-vitamin B₆ activities. This compound (1) is reported for the first time from natural products.

KEYWORDS — Ginkgo biloba L.; Ginkgoaceae; antivitamin B₆;
4'-methoxypyridoxine; Gin-nan sitotoxism; convulsive agent;
acute toxicity; guinea pig

"Gin-nan" is the seed of Ginkgo biloba L. (maidenhair tree, Ginkgoaceae), and its albumen is used as a crude drug in China and as food in Japan. "Gin-nan sitotoxism" (cardinal symptom: convulsions) has sometimes occurred during food shortages in Japan (1930-1960). Mainly infants contracted this sitotoxism (lethality: about 27%). Several investigations have been undertaken to elucidate the cause of the sitotoxism,^{2,3)} but the cause of it remained unknown. This paper describes our finding that 4'-methoxypyridoxine (1), antivitamin B₆, isolated from G. biloba is the substance that causes "Gin-nan sitotoxism."

The albumen of Ginkgo seeds was dried at 40°C for 7 days and then ground. The powder was treated as reported before.²⁾ The outline of the procedure is shown in Chart 1. The toxicity was evaluated by orally administered acute toxicity tests using guinea pigs (250-400 g) of either sex. Test samples were dissolved or suspended in water in appropriate concentrations. Signs of toxicity were paralysis of legs, opisthotonus, tonic convulsions, and auditory hyperalgesia. These symptoms occurred within 30-40 minutes after administration of the toxic fractions.

The isolation procedure afforded compound (1) [ca. 0.01% yield, dry weight], which induced the characteristic convulsions in guinea pigs at an oral dose of 11 mg/kg.



4'-methoxyypyridoxine (1): $R^1=CH_3$, $R^2=H$

pyridoxine (vitamin B₆): $R^1=R^2=H$

4'-Methoxyypyridoxine is known to have antivitamin B₆ activities and to be a synthetic potent convulsive agent in a variety of animals and in man.⁷⁾ However, pyridoxine (vitamin B₆) prevents the convulsions, or promptly stops them.⁸⁾ Therefore, pyridoxine may prevent the symptoms of "Gin-nan sitotoxism," because these symptoms are derived from the effect of vitamin B₆ deficiency induced with compound (1). The lack of vitamin B₆ during food shortage times also may be one of the causes of "Gin-nan sitotoxism." Compound (1) (i.e. 4'-methoxyypyridoxine) was found for the first time from natural products.

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