

Retrospective Aspects of Cyclamate and Cyclohexylamine Studies in Japan

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Summary

Since the use of cyclamate was banned in the USA and Japan in 1969 on the basis of the findings in rats that cyclamate might increase the risk of bladder cancer in humans, more than thirty-seven years have passed. Here the author describes retrospectively toxicological and biochemical studies on cyclamate and its metabolite, cyclohexylamine (CHA) in our country as well as foreign countries.

In 1966 two Japanese pharmacists found for the first time the presence of CHA in the urine of man and dog after ingestion of cyclamate, although early studies indicated that cyclamate was excreted unchanged. As a result of studies carried out by staff at the National Institute of Hygienic Sciences (present National Institute of Health Sciences) in Japan for safety evaluation of cyclamate, some interesting facts have emerged, such as the discovery of new enzymes, sulphamatase and CHA oxidase from microorganisms in the animal intestine, and clarification of new metabolic routes of CHA in mammals using the stable isotopes Deuterium and oxygen-18. Toxicological data involving teratogenicity and carcinogenicity in animals suggest that cyclamate does seem very safe. Upon the evaluation of additional data and the reexamination of cyclamate carcinogenicity, most scientists concluded that cyclamate was not a carcinogen or a co-carcinogen. However, the use of cyclamate is not permitted by the FDA at present, though the real reason is unclear.