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Research Laboratories,
Takeda Chemical Industries, Ltd.,
Juso-nishino-cho,
Higashi-yodogawa-ku, Osaka.

Mikio Honjo (本庄美喜男)
Yoshiyasu Furukawa (古川 純康)
Hiroki Moriyama (森山 博規)
Kuniyoshi Tanaka (田中 邦喜)

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Metabolites of *p*-Dimethylaminoazobenzene in Rat Bile

Since the work of Stevenson and his co-workers¹⁾ on the metabolism of *p*-dimethylaminoazobenzene, a carcinogenic aminoazo dye, many reports have been published about it and the work was reviewed by Miller and Miller.²⁾ Some new metabolites of this dye were also found by Ishidate and Hashimoto³⁾ in this laboratory. Majority of the past work concerned with urinary metabolites and, since it has been observed that many conjugated and non-conjugated aminoazo dyes were excreted in a rat bile during liver perfusion technique originated by Ishidate and Nakajima,⁴⁾ examination using a whole animal to detect these metabolites in rats bile was carried out. A solution of 15 mg. of *p*-dimethylaminoazobenzene dissolved in 1 cc. of olive oil was injected into the stomach of a rat through a catheter. After 1 hour, the rat was anesthetized with Nembutal, and a polyethylene tube with external diameter of ca. 1 mm. was inserted into the bile duct by surgical operation. The bile was collected for the following 5 hours, spotted directly on Toyo Roshi filter paper No. 51, and subjected to chromatography with a solvent system of PrOH-BuOH-H₂O (2:3:5).

The paper chromatogram revealed more than eight kinds of aminoazo dyes and these were subjected to qualitative analyses; color reaction with 2*N* hydrochloric acid, Ehrlich reagent, or Gibbs reagent, hydrolysis of conjugated form with β -glucuronidase or diastase, separation by partition chromatography over silica gel, adsorption chromatography on alumina, or paper electrophoresis, and measurement of absorption spectra. By comparison with synthesized aminoazo dyes, the main metabolites in the bile were identified with the following seven kinds of dyes :

1) E. S. Stevenson, K. Dobriner, C.P. Rhoads : Cancer Research, 2, 160 (1942).

2) J. A. Miller, E. C. Miller : Advances in Cancer Research, 1, 366 (1953).

3) M. Ishidate, Y. Hashimoto : This Bulletin, 10, No. 2 (1962).

4) M. Ishidate, T. Nakajima : Represented at the Annual Meeting of the Pharmaceutical Society of Japan, July, 1961.

While the products formed by reductive cleavage of the azo bond were excreted mainly in the urine, the present result indicates that such compounds are hardly found in the bile and that metabolites retaining the azo bond are mainly excreted in the bile. The present result has also shown that a large quantity of the glucuronides of hydroxylated amino azo dyes are excreted in the bile although such compounds were not detected in the urine.³⁾

Details of this experiment will be reported in the near future.

Faculty of Pharmaceutical Sciences,
University of Tokyo,
Hongo, Tokyo.

Morizo Ishidate (石鎭 守三)
Zenzo Tamura (田村 善蔵)
Terumi Nakajima (中島 暉躬)
Keijiro Samejima (鮫島啓二郎)

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Eine verbesserte Überführung der Cinchona-Alkaloide der Chinolin-Reihe in diejenigen der Indol-Reihe

Ochiai und Ishikawa^{1~4)} haben die Cinchona-Alkaloide der Chinolin-Reihe in diejenigen der Cinchonamin-Reihe nach den unten in Formeln ausgedrückten Reaktionsstufen übergeführt.

Diese Methode hat jedoch in der Stufe der Oppenauer-Oxydation der Aminosäure (IV) einen grossen Nachteil für präparative Zwecke. Die Hydroxylgruppe in (IV), die auf der

1) Masayuki Ishikawa : Dieses Bulletin, 6, 67 (1958).

2) Idem : Ibid., 6, 71 (1958).

3) M. Ishikawa, E. Ochiai : Ibid., 6, 208 (1958).

4) M. Ishikawa, E. Ochiai, Y. Oka : Ibid., 7, 744 (1959).