Communications to the Editor

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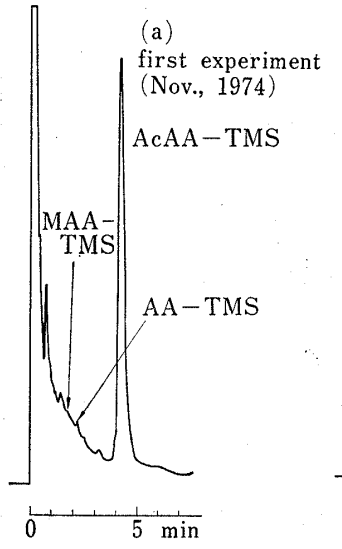
Excretion of 4-Formylaminoantipyrine as a New Metabolite of Aminopyrine in Experimental Animals

As an extention of the studies on metabolism and excretion of aminopyrine, 4-formylaminoantipyrine which has been already reported as a new metabolite in man's urine was detected also in the urine of rabbits, guinea pigs and rats by gas chromatography (GC) and gas chromatography-mass spectrometry (GC-MS).

It has been already reported that a new metabolite of aminopyrine (AM), *i.e.* 4-formylaminoantipyrine (FAA), was found first in man urine following oral administration of AM.[1,2] Thereafter, we have examined whether FAA might be excreted in the urine of experimental animals or not. As a result, the detection of FAA was also successful in rabbits, guinea pigs and rats. These results are reported briefly in this communication.

The first experiment was performed with three rabbits in November, 1974. The rabbits had not taken any drug at least for three months prior to the study. As the purpose of this experiment was to examine the excretion of FAA qualitatively, AM solution (50 mg/kg in 10 ml of water) was administered orally to the rabbits in the morning after 24 hr's fasting to collect their urine at 0—24 hr. The metabolites in urine were analysed by gas chromatography (GC) and gas chromatography-mass spectrometry (GC-MS) with the same extraction procedure and analytical condition as described in the previous paper.[1,2] In this first experiment, 4-aminoantipyrine (AA), 4-methylaminoantipyrine (MAA) and 4-acetylaminoantipyrine (AcAA) were found as main metabolites, while any amount of FAA could not be detected as shown in Fig. 1a. But three months later, when the second experiment was performed



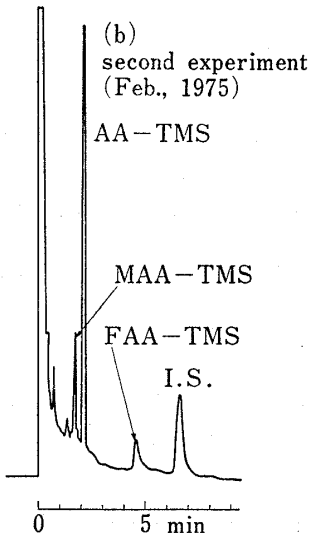
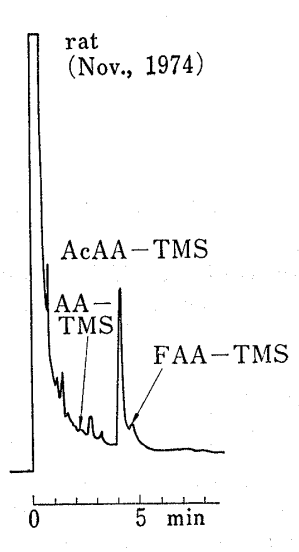


Fig. 1. Gas Chromatogram of TMS Derivatives of Rabbit Urine Extract after Oral Administration of Aminopyrine as Aqueous Solution

conditions : 1.5% OV—17 on Shimalite W (80—100 mesh), 3mm×1m, glass column. column temp : 220° injection port temp : 250° N_2 : 20ml/min, HFID instrument : GC-4BM-PF



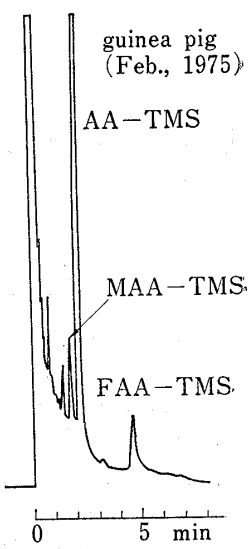


Fig. 2. Gas Chromatogram of TMS Derivatives of Rat and Guinea Pig Urine Extracts after Oral Administration of Aminopyrine as Aqueous Solutions

GC conditions were the same as those shown in Fig. 1.

1) S. Iguchi, T. Goromaru, and A. Noda, *Chem. Pharm. Bull.* (Tokyo), **23**, 932 (1975).
2) T. Goromaru, A. Noda, K. Matsuyama, and S. Iguchi, *Chem. Pharm. Bull.* (Tokyo), submitting for publication.

with the same rabbits which had been kept with a certain feed (Oriental RC 4) in the cages in a room without air conditioning and did not take any drug after the first experiment. The experimental condition was the same as the first time. As the result, it happened on a very interesting phenomenon that they began to excrete an appreciable amount of FAA but, the amount of AcAA was little detected in this case as shown in Fig. 1b. The amounts of metabolites in 0—24 hr's urine of a representative rabbit were as follows: AA 27.6 mg (13.8%), MAA 4.2 mg (2.1%) and FAA 11.0 mg (5.5%). These values are all converted ones into AM quantity and percentage in parentheses shows the ratio to the dose. At the present stage, it is considered that the changes of season or temperature might be the most important factor of these metabolic variation. The real reason why the rabbits showed such the remarkable variation in their metabolic behavior of AM despite of the constant feeding is worth examining from now.

As for the other experimental animals, it was also recognized this time that three guinea pigs and three rats also excreted FAA in their urine under the similar experimental condition (Fig. 2). Especially, the case with guinea pigs is noticeable, because they excreted FAA as a predominant metabolite from the initial administration similarly in the second experiment with rabbits. All experimental animals have been excreting FAA up to now.

These interesting new findings are very useful for our research and encouraging us in advancing the study on the mechanism of FAA formation and the variation of metabolism of AM both in men and experimental animals. The details of this study will be reported in the nearest future.

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Weitere Inhaltsstoffe aus *Pteris oshimensis* HIERON[1)]

Aus den oberirdischen Teilen von *Pteris oshimensis* HIERON wurden zwei weitere Pterosinglykoside isoliert und als Pterosin Q-3-β-L-Arabinopyranosid und Pterosin C-3-β-L-Arabinopyranosid identifiziert.

Aus den oberirdischen Teile von *Pteris oshimensis* HIERON. haben wir vor einiger Zeit[2)] neben dem Pterosin N ein neues Glied der Pterosin C-Reihe, Pterosin Q und sein 3-β-D-Glukosid isoliert, deren Strukturen ermittelt wurden.

In dieser Mitteilung berichten wir über die Isolierung und Strukturaufklarung von zwei weiteren neuen Pterosin-Glykoside.

Die Methanol-Extrakte der oberirdischen Teile wurden in 50% Methanol suspendiert und mit Äther ausgeschüttelt. Die wässerige Methanol-Phase wurde grob an Kieselgel säulenchromatographiert und die vereinigten dünnschichtschromatographisch analogen Fraktionen durch mehrfache präparative Dünnschichtschromatographie aufgetrennt.

1) Chemische und chemotaxonomische Untersuchungen der Gattung *Pteris* und der verwandten Gattungen (*Pteridaceae*) IX. Mitteil., VIII. Mitteil.: T. Murakami, N. Tanaka, T. Tezuka, und C.-M. Chen, *Chem. Pharm. Bull.* (Tokyo), **23**, 1634 (1975).
2) T. Murakami, N. Tanaka, K. Tanaka, und C.-M. Chen, *Chem. Pharm. Bull.* (Tokyo), **22**, 2758 (1974).