Z. Rechtsmedizin 71, 270—273 (1973)


# Identification of a Dextropropoxyphene Metabolite by Gas Chromatography—Mass Spectrometry

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Received June 22, 1972

*Summary.* Gas chromatography in combination with high and low resolution mass spectrometry has been used for identification of metabolites of dextropropoxyphene isolated from liver extract.

*Zusammenfassung.* Für die Identifikation der Metaboliten von Dextropropoxyphen aus Leberextrakten wurde eine Kombination der Gaschromatographie mit der hoch und niedrig auflösenden Massenspektrometrie angewandt.

*Key words:* Dextropropoxyphene metabolite, identification.

## Introduction

Spectrophotometric as well as gas chromatographic methods have been used for quantitative determination of dextropropoxyphene in plasma and tissue [1—3]. Metabolites of dextropropoxyphene isolated from urine were identified by gas chromatography in combination with mass spectrometry [4]. The structure of one of these metabolites is shown in Fig. 2a. The authors mentioned the possibility that this compound was obtained as a result of an intramolecular acyl migration in N-desmethyl propoxyphene via a hydroxyintermediate, followed by dehydration, but the intermediate was not shown as a component on the chromatogram. It can be noted that no detectable amount of metabolites of dextropropoxyphene in blood have been identified. This paper will describe the gas chromatographic mass spectrometric studies of metabolites of dextropropoxyphene from liver extracts.

When using liver extracts from autopsy cases for determination by gas chromatography additional peaks besides dextropropoxyphene and its combination substance often appear on the chromatogram. A rather large number of such cases were analyzed in our laboratory, and it was of importance to also identify the small GC-peaks present and for this purpose a gas chromatograph-mass spectrometer was used.

## Method

All liver samples (10 g) were extracted with ethanol over a 24 hrs period followed by centrifugation, evaporation and removing of fat [5]. The remaining acid water-phase was extracted by chloroform and evaporated to 0.5 ml. 0.5 ul was injected (equivalent to 10 mg from liver) into the combined gas chromatograph-mass spectrometer LKB 9000. A 1% OV-17

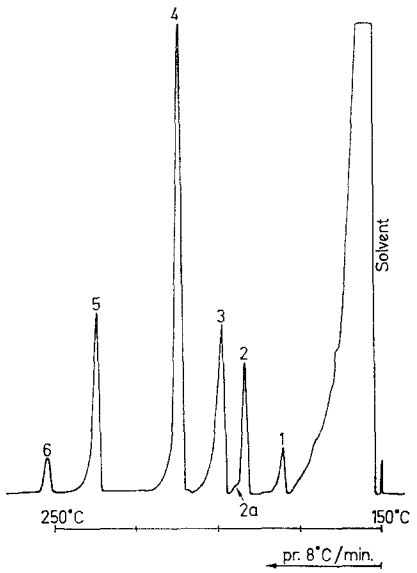


Fig. 1. Gas-chromatographic separation of liver extract. Identified components: peak 1. Salicylic acid. 2. Coffein. 2a. Biphenyl. 3. Fenazon. 4. Dextropropoxyphene. 5. Metabolite V and 6. Metabolite VI. A 2.5 m × 2 mm glas column packed with 1% OV-17 was used. The Helium carrier gas flow rate was 30 ml per minute

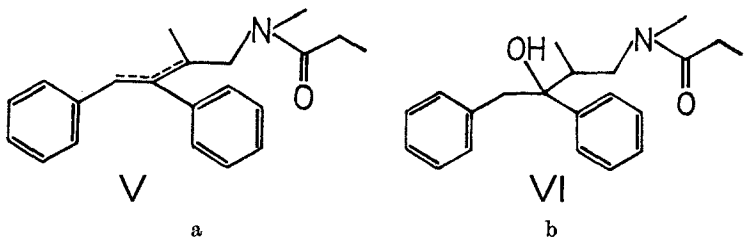


Fig. 2. a The structure of the component V isolated from urine [4]. b The supposed structure of compound VI isolated from liver

column was programmed from 100 to 250°C at a rate of 8°C/min, and the gas chromatogram with the separated components are shown in Fig. 1. All the spectra were recorded by a magnetic tape off line system and the tape was processed and evaluated by an IBM 1800 computer. The elemental composition of some fragments was obtained by a gas chromatograph combined with a double focusing mass spectrometer Atlas SMl [6].

## Results and Discussion

The components 5 and 6 shown in Fig. 1 are found to be dextropropoxyphene metabolites of which component 5 correspond to a compound separated from urine extract and identified by the GC-MS method [4]. Fig. 2 shows the structures of compound V and of the suggested compound VI. The mass spectrum of the

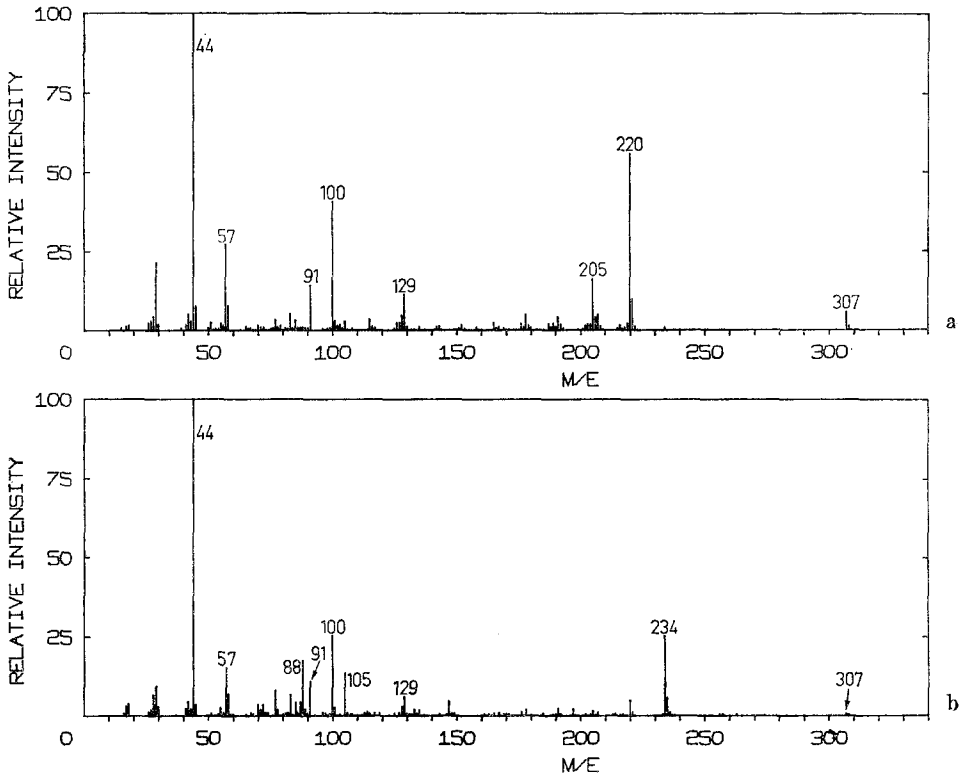


Fig. 3a and b. Mass spectra of (a) compound V, (b) compound VI

compound VI is closely related to the spectrum of compound V as is shown in Figs. 3b and a.

The most intense peak in the spectra of compound V and VI is m/e 44. Other characteristic peaks which are found in both spectra are m/e 57, 77, 91, 100, 129 and 220 but with differences in intensity. High resolution data from the two compounds show that the elemental composition of the ions m/e 105 and m/e 129 for compound V were $C_8H_9$ resp. $C_{10}H_9$ and for compound VI $C_7H_5O$, $C_7H_{15}NO$ respectively. The ion at m/e 100 has the same composition in both spectra. The cracking of the compound VI into fragments are shown in Fig. 4. The greatest differences between compound V and VI appear mainly at m/e 88 and m/e 234 with the suggested composition of $C_4H_{10}NO$ and $C_{14}H_{20}NO_2$. The expected molecular ion at M = 325 is absent but a small peak at m/e 307 indicates the loss of water (M-18). The postulated compound VI is the same as the known intermediate amide from the N-demethylated propoxyphene [7]. The choice of column is of great importance, because most of the drugs containing dextropropoxyphene also contain other drugs as is shown in the chromatogram Fig. 1, which includes three additional drugs which must be separated from dextropropoxyphene and its metabolites. The separation and identification of the unknown gas chromatographic peaks were thus necessary in creating a method for quantitative estimation of dextropropoxyphene including its metabolites.

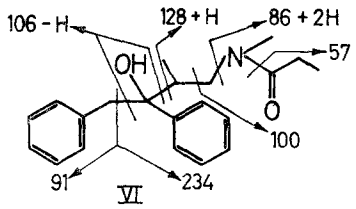


Fig. 4. Characteristic fragment of compound VI

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