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Detection of phentermine and phentermine derivatives as metabolites of oxethazaine

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INTRODUCTION

Oxethazaine (Tepilta®) is a local anaesthetic for application to a mucus membrane, which is especially used for therapy of the acute and chronic gastritis and duodenitis [2]. It is not on the IOC list of prohibited substances.

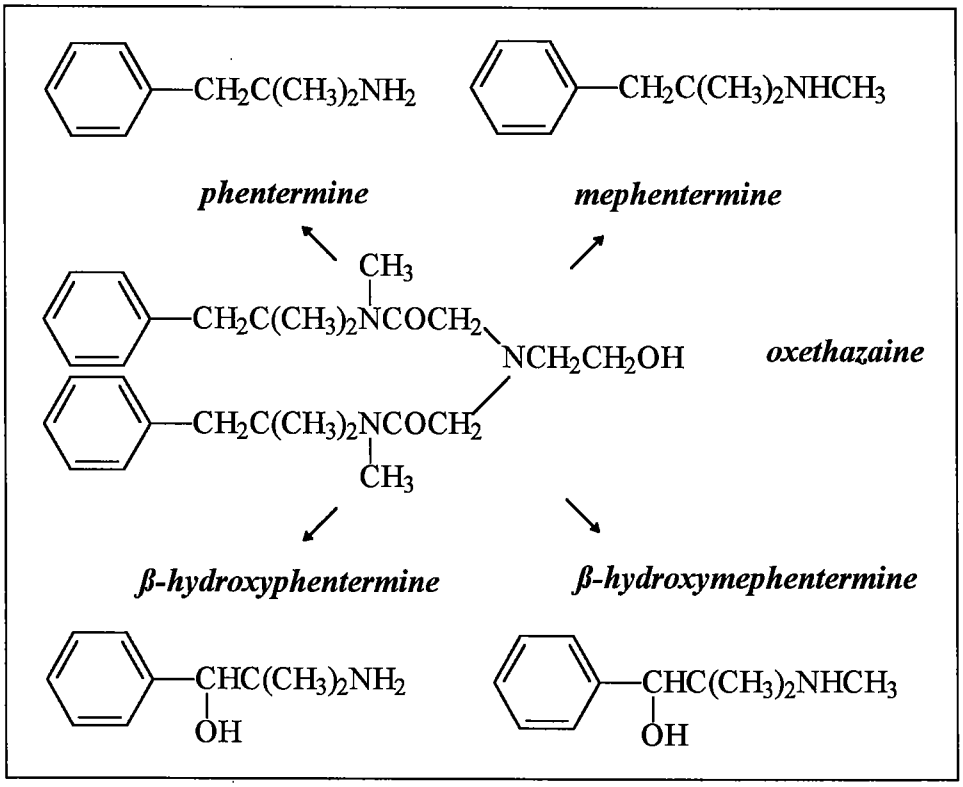

Fig.1: Metabolism of oxethazaine

EXPERIMENTAL

An excretion study with an oral application of therapeutical doses of oxethazaine was performed. Two volunteers took 4 doses of 10 mg oxethazaine during a period of 8 hours. The urine was prepared according to the standard procedure screening 1 [1].

GC/MS, GC/NPD PARAMETERS

A combined system GC/MSD and GC/NPD was applied.

GC/MSD, GC/NPD -System:	Hewlett Packard 5890/5973
Carrier gas:	Helium (1ml/min flow)
Split ratio:	1:10
Analytical column:	HP-5 MS fused silica capillary column, 0.25 mm i.D., 0.25 µm film thickness length MSD: 24m length NPD: 19m
Temperature program:	100°C, 22°C/min till 320°C, 1 min. constant

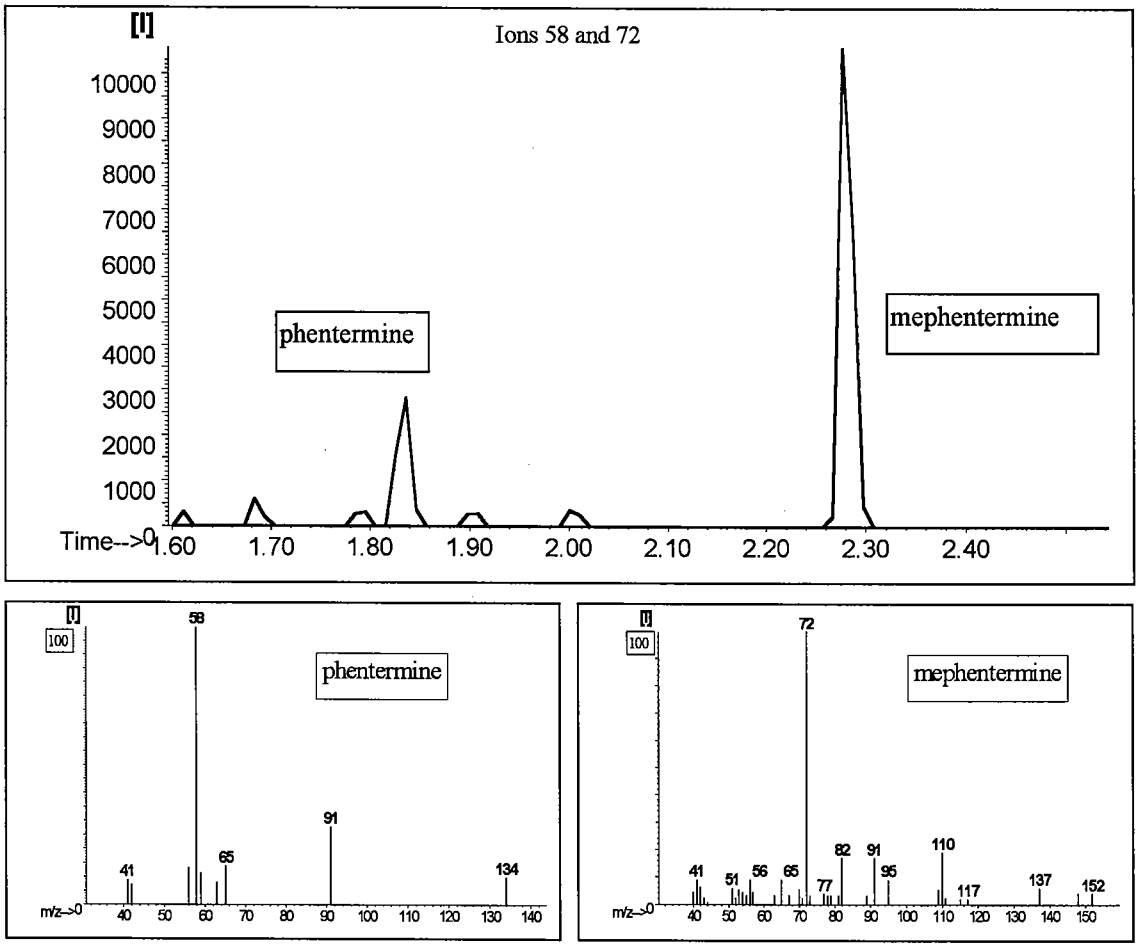

Fig. 2: GC/MSD-Chromatogram and spectra of phentermine and mephentermine; Scr.1 pH 14; 5 ml urine (2h after last application); extract concentrated in 200 µl solvent

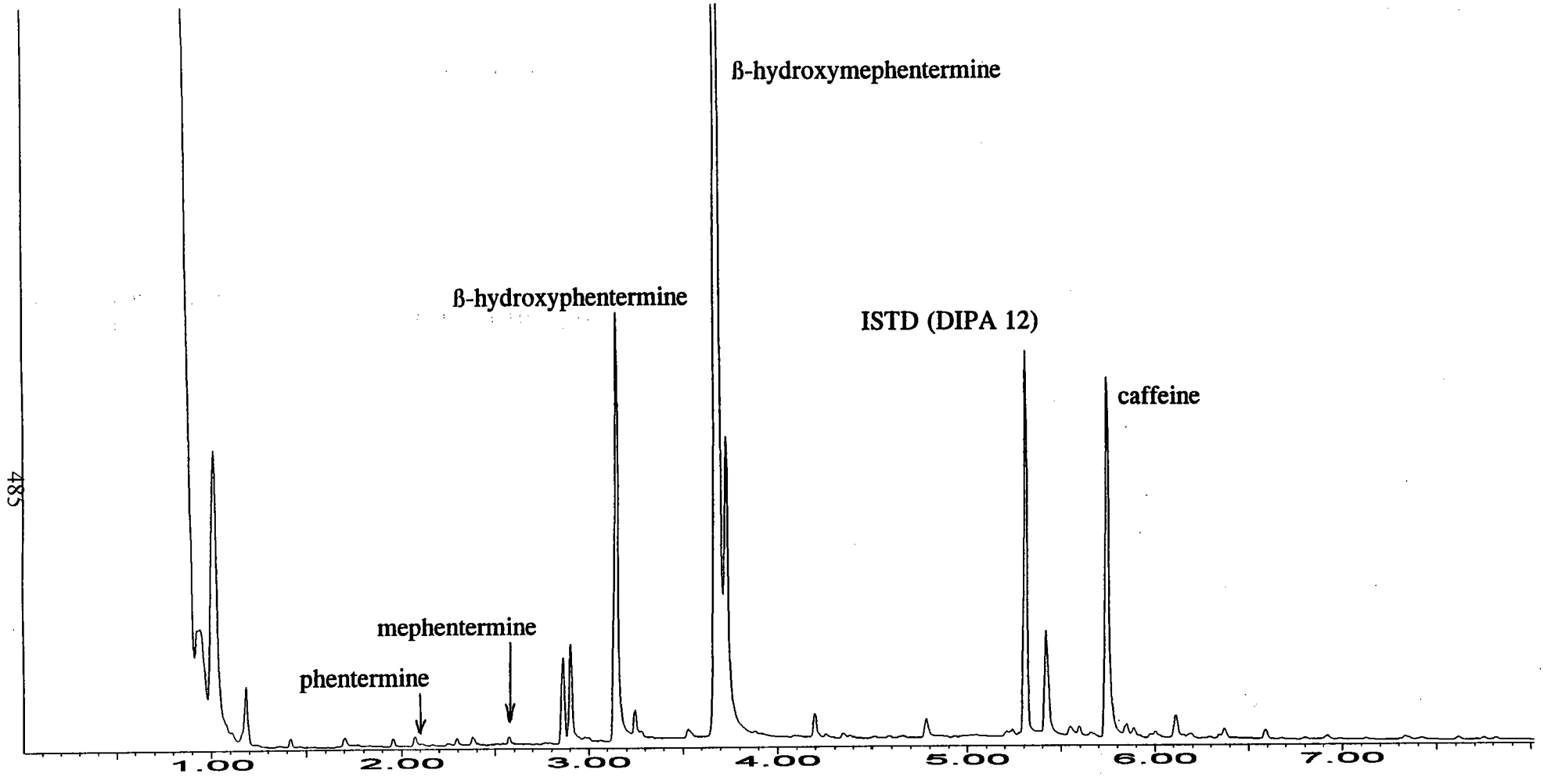

Fig. 3:

GC/NPD-chromatogram; Screening 1 pH 14;
5 ml urine (2h after last application) extracted with 2ml ether

RESULTS AND CONCLUSION

Figure 3 shows the Screening 1 NPD chromatogram of a urine two hours after the last application of oxethazaine. As shown in figure 2 and 3 traces of phentermine and mephentermine could be detected in the urine with concentrations up to 0.2 µg/ml. The drug could be identified in full scan mode which would lead to a positive case.
In contrast to a phentermine or mephentermine abuse, the excretion study showed also the main metabolites of oxethazaine β-hydroxyphentermine and β-hydroxymephentermine. Both metabolites could be detected in much higher concentrations (up to 15 µg/ml). SCAN-spectra are shown in figure 4 and 5.

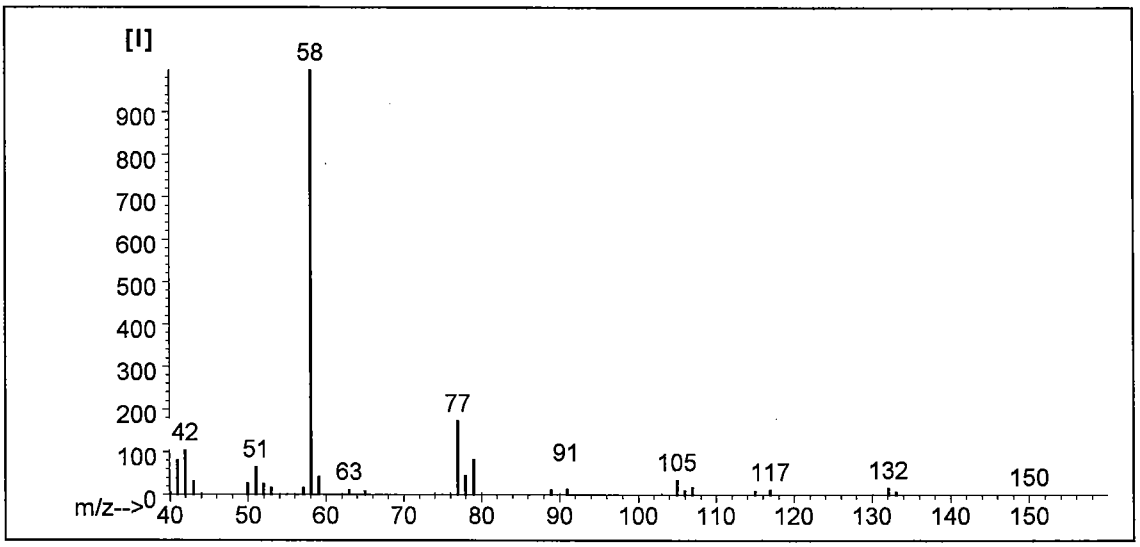

Fig. 4: Spectra of ß-hydroxyphentermine (M^+ 150)

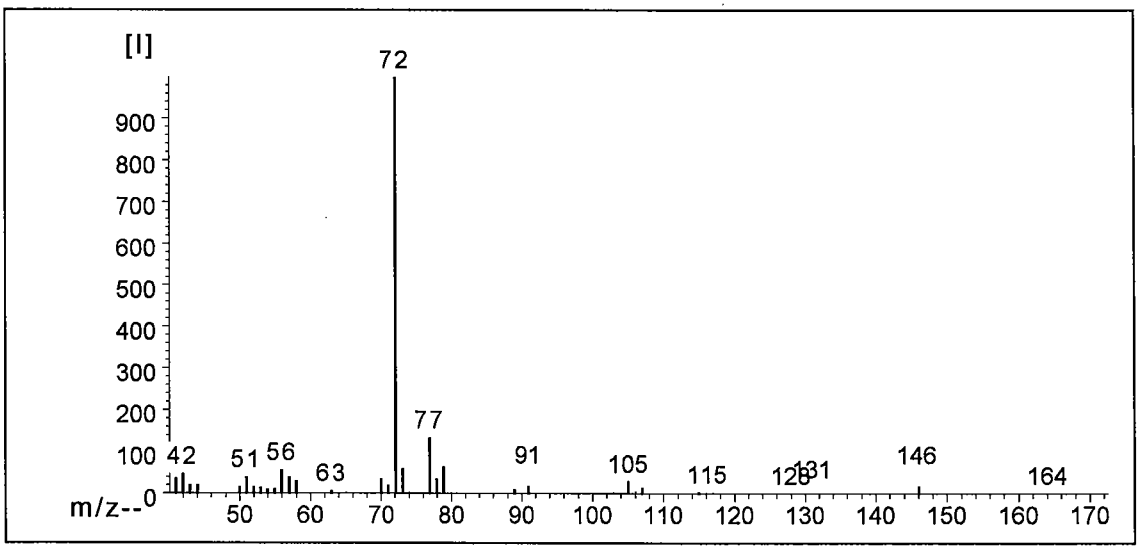

Fig. 5: Spectra of ß-hydroxymephentermine (M^+ 164)

In a positive case of phentermine or mephentermine, we recommend to look for the higher concentrated β-hydroxymetabolites as indication for an oxethazaine application. Nevertheless it has to be discussed, if the detection of phentermine or mephentermine after an oxethazaine application has to be treated as a positive case or not.

LITERATURE

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