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Detection of Phentermine and Phentermine Derivatives as Metabolites of Oxethazine
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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.

![Chemical structures]

**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.

![Graph showing m/z values and peak intensities for β-hydroxyphentermine and β-hydroxymephentermine.]

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

Fig. 5: Spectra of β-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


2. Fa. Wyeth Pharma GMBH, Fachinformationen

3. Donike M., Untersuchung zum Nachweis, zur Pharmakokinetik und zum Metabolismus von Oxethacain, 1988, not published