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ANALYSIS OF SOME NEUROLEPTICS BY GASCHROMATOGRAPHY/MASS SPECTROMETRY (GC/MS)

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Introduction

Neuroleptics are used mainly to calm slaughter animals during shipping. The application of animal drugs has to be applied long enough before slaughtering that residues may hardly be left. The major part of animal drugs is cleared out within the first 24 hours. Five to eight days after application normally animal drugs are not detectable. Arneth (1995) published a paper for the detection of some neuroleptics and carbazole in pig kidneys. This publication is based on a paper of van Ginkel et al. (1989). According to Arneth the neuroleptics and carbazole have been separated by HPLC using an Altima RP18 column (250 x 4,6 mm, 5 μm) and detected by UV absorption (diode array detector 1000S, Applied Biosystems) connected with a fluorescent detector (Model F 1000, Merck-Hitachi, Darmstadt). This procedure was very sensitive. The recovery of spiked pig kidneys with neuroleptics was better than 70 % with 15 μg/kg and for carbazole with 5 μg/kg added. The following neuroleptics have been analysed: azaperone, azaperole, acetylpromazine, carbazole, chlor- and propionylpromazine. These extracts have been analysed by GC/MS using total ion chromatograms and single ion monitoring (Finnigan "Magnum"): ionisation mode: CI with methane as ionisation gas.

Materials and Methods

The investigations of the above mentioned neuroleptics have been carried out with 10 g of pig kidneys. The kidneys have been homogenized within a 20 % alkaline solution of sodium hydroxide at 90^{o}C, in which the kidney sample is totally saponified. This solution is extracted and cleaned up according to Arneth (1995).

The separation of the neuroleptics was done on a DB35 column (0,25 mm iD, 0,25 μm DB35 layer), temperature program 80^{o}C 4 min isotherm, 15^{o}C temperature/min rate up to 300^{o}C on a gas chromatograph Varian connected with Finnigan Magnum.

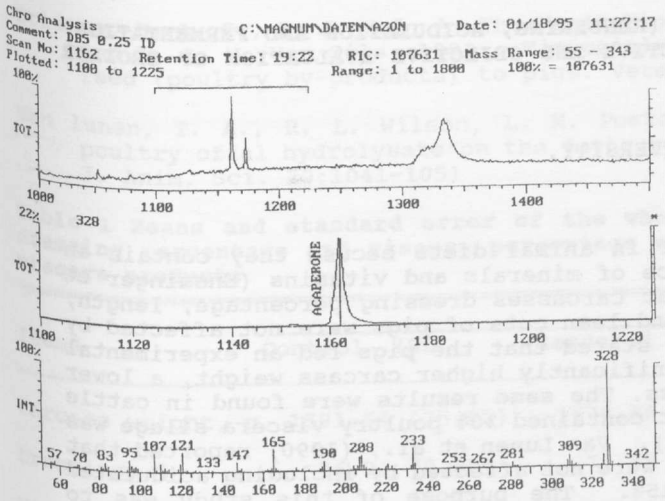
Results and discussion

Figure 1 shows a chromatogram of azaperone (upper part) and acetylpromazine (lower part) derived from standards. First run: total ion chromatogram, second run: single ion chromatogram (mass 328, 327).In the third run the mass fragmentograms are shown. Figure 2 shows a chromatogram of the same compounds in opposite order from kidneys of pigs, which received an injection with these compounds. The detections limits for the compounds are about 10 pg, thus we may find residues of those animal drugs during the first 5 days after the application of the drugs.

As one may learn from the total ion chromatograms of figure 2 that the kidney extracts are rather clean. The animal drugs are well separated without an interfereance of other compounds. This is a main reason that we get a high sensivity and especially single ion chromatograms which allow very acurate quantitative determination.

The application of GC/MS in the analysis of animal drugs is of special advantage for compounds which are of unknown origin. From the fragment spectra we may obtain some information of the unknown compound. It should be possible using literature spectra to receive further informations on these unknown compounds. With these informations we may detect drugs, which should have a similar or an identical composition.

When scientists find a method to analyze and determine forbidden drugs which are on the market, normally the producers are well prepared to substitute these drugs by a new generation of drugs. So our intention is to look for an extraction method, which allows to separate a wide spectrum of compounds with a pharmaceutical efficacy. If the extracts are clean enough for GC/MS - as they are in the extracts with Arneth's method - it should be possible to detect most compounds by GC/MS which normally are not detected in kidneys. Only these samples have to be analysed for drug residues.



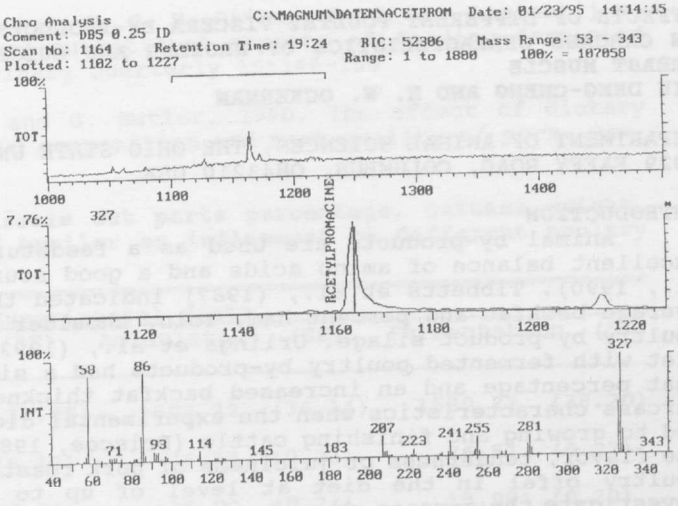
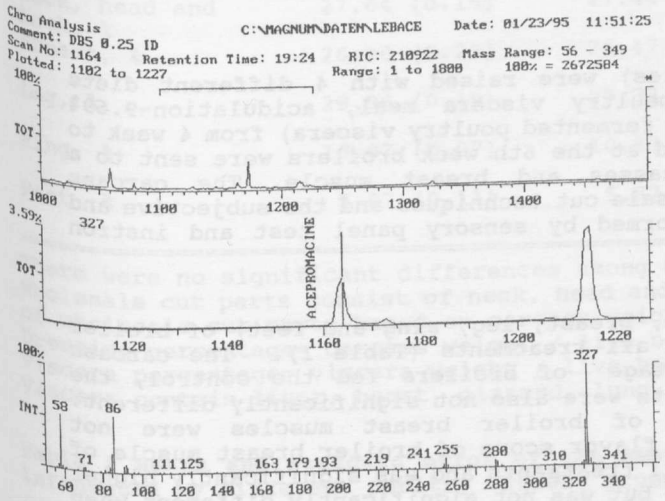


Fig. 1



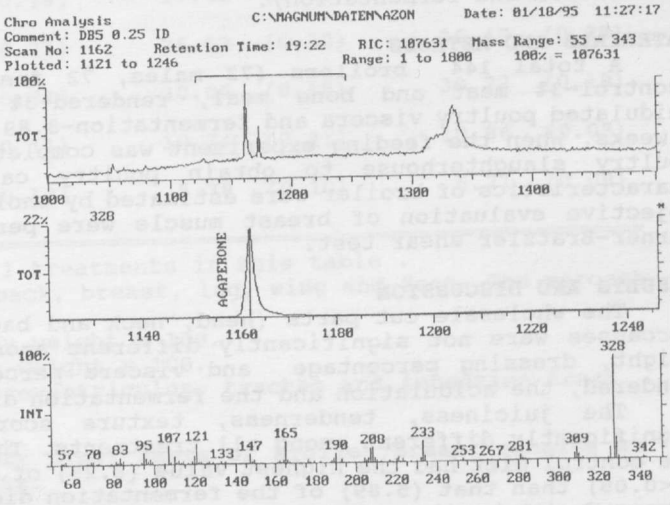


Fig. 2

Literature

ARNETH, W (1995): Analytik einiger Neuroleptika sowie von Carazolol in Schweinenieren. Z. Lebensm.Unters.Forsch. (in print)

VAN GINKEL, L., P. SCHWILLENS, M. OLLING (1989): Liquid chromatographic method with on-line spectrum identification and off-line thin layer chromatographic confirmation for the detection of tranquillizers and carazolol in pig kidneys. Anal. Chim. Acta, **225**, 137.