

CHROM. 13,197

## RAPID ISOTHERMAL GAS-LIQUID CHROMATOGRAPHIC DETERMINATION OF TRICYCLIC ANTIDEPRESSANTS IN SERUM WITH USE OF A NITROGEN-SELECTIVE DETECTOR

JAN ERIK BREDESEN\* and ODD FINN ELLINGSEN

*Division of Clinical Pharmacology and Toxicology, The Central Laboratory, Ullevål Hospital, Oslo (Norway)*

and

JAN KARLSEN

*Institute of Pharmacy, University of Oslo, Oslo (Norway)*

---

### SUMMARY

A rapid and simple gas-liquid chromatographic method suitable for routine use is described for quantitation of tricyclic antidepressants. The method can be used for quantitation of amitriptyline, nortriptyline, imipramine, desmethylimipramine, doxepine, desmethyldoxepine, clomipramine, desmethylclomipramine, trimipramine, desmethyltrimipramine and dibenzepine. The method involves one extraction with hexane-isopropyl alcohol, no derivative formation of the metabolites and chromatography using an OV-25 liquid phase which permits isothermal quantitation of the different drugs within 5–10 min. Standard curves for the different tricyclic antidepressants were linear over the concentration range tested (10–1500  $\mu\text{g/l}$ ) and the maximum coefficient of variation was 7.7%.

---

### INTRODUCTION

Tricyclic antidepressants are widely used in treatment of mental disorders and routine monitoring of plasma concentration should provide useful clinical information. Plasma concentrations in patients treated with tricyclic antidepressants may be as low as 10–20 ng/ml while the concentration after an overdose with tricyclic antidepressants can reach several milligrams per litre<sup>1</sup>. During the past decade numerous methods have been described for routine determination of plasma levels of tricyclic antidepressants<sup>2</sup>. Previously reported methods include spectrophotometry<sup>3</sup>, fluorimetry<sup>4</sup>, radioimmunoassay<sup>5</sup>, thin-layer chromatography (TLC)<sup>6</sup>, mass spectrometric procedure<sup>7</sup>, isotope-derivative dilution technique<sup>8</sup>, high-performance liquid chromatography (HPLC)<sup>9,10</sup> and gas-liquid chromatography (GLC) using electron-capture detection<sup>11</sup>, flame ionization detection<sup>12</sup> or nitrogen-selective detection<sup>13,14</sup>. Nevertheless, the routine determination of tricyclic antidepressants still remains difficult. The spectrophotometric, fluorimetric, radioimmunological and TLC procedures have too low sensitivity, are non-specific or time-consuming. The major disadvantage of the