II.3.3 Tricyclic and tetracyclic antidepressants

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Introduction

Many of antidepressants exert their effects by inhibiting the reuptake of norepinephrine and serotonin and by accelerating the release of them at synaptic terminals of neurons in the brain. As characteristic structures of such drugs showing antidepressive effects, many of them have tricyclic or tetracyclic nuclei; this is the reason why they are called “tricyclic antidepressants or tetracyclic antidepressants”.

There are many cases of suicides using the antidepressants; their massive intake sometimes causes death. About 10 kinds of tricyclic and tetracyclic antidepressants are now being used in Japan (Figure 3.1); among them, amitriptyline is best distributed [1, 2]. Recently, the use of tetracyclic antidepressants is increasing, because of their mild side effects and their high effectiveness with their small doses; the increase of their use is causing the increase of their poisoning cases. Although carbamazepine does not belong to the antidepressant group, its structure is very similar to those of tricyclic antidepressants; therefore, the drug is also included in this chapter.

GC/MS analysis

Reagents and their preparation

- Amitriptyline, carbamazepine, clomipramine, desipramine, imipramine, maprotiline, mianserin, nortriptyline and trimipramine can be purchased from Sigma (St. Louis, MO, USA); pure powder of the following drugs was donated by each manufacturer: amoxapine by Takeda Chem. Ind. Ltd., Osaka, Japan; dosulepin by Kaken Pharmaceutical Co., Ltd., Tokyo, Japan; lofepramine by Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan; and setipitiline by Mochida Pharmaceutical Co., Ltd., Tokyo, Japan.
- A 20-g aliquot of sodium carbonate is dissolved in distilled water to prepare 100 mL solution (20 %, w/v).
- A 9.85-mL volume of hexane is mixed well with 0.15 mL isoamyl alcohol to prepare an extraction solvent.
- A 1-mg aliquot of promethazine (Sigma) is dissolved in 10 mL acetonitrile to prepare internal standard solution (0.1 mg/mL).
Structures of tricyclic and tetracyclic antidepressants and carbamazepine.

**GC conditions**

GC column: an HP-5MS fused silica capillary column (30 m × 0.25 mm i. d., film thickness 0.25 µm, Agilent Technologies, Palo Alto, CA, USA).

GC/MS conditions; instrument: an HP 5890 Series II gas chromatograph (Agilent Technologies) connected with a mass spectrometer (HP-5971A MSD, Agilent Technologies); column (oven) temperature: 170 °C (1 min) → 5 °C/min → 280 °C (4 min); injection temperature: 250 °C; detection temperature: 280 °C; carrier gas: He (100 kPa); mass scan range: *m/z* 50–500.