Analysis of Antiarrythmic Drugs by HPLC

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Abstract

Quinidine, disopyramide, procainamide and its metabolite N-acetylprocainamide are common drugs used to treat cardiac arrythmias. Because of the relatively narrow therapeutic range of quinidine and the considerably varying pharmacokinetics between individual patients using disopyramide, it is important to monitor the required drug concentration by an exact and reliable method. The inter-individual variations in absorption, metabolism and excretion of procainamide correlate poorly between dose and therapeutic effect. Therefore, it is also important here to use an accurate method to determine the concentration in biological fluids. HPLC and immunoassays are techniques that fulfill these requirements.

The HPLC method presented here separates the four antiarrythmic drugs using gradient analysis on a reversed phase column and UV detection. To avoid decomposition of samples the autosampler temperature was set to 4 ºC.

A detector program was used because of the different absorbance maxima of the four compounds.

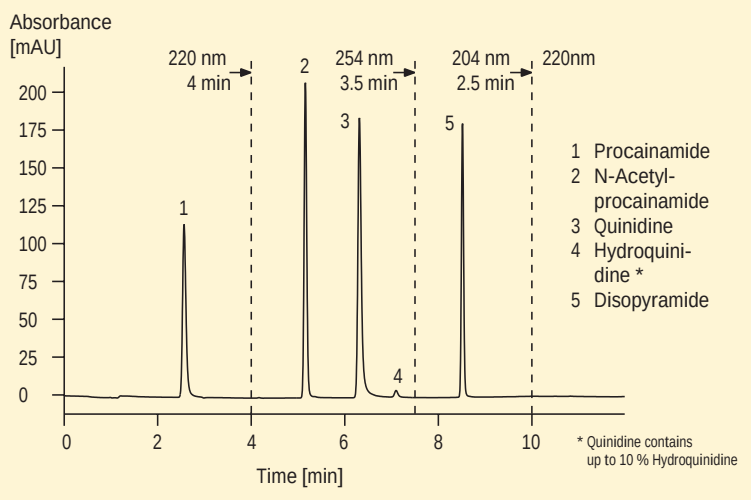

Figure 1
Analysis of four antiarrythmic drugs

Conditions

Column
4 x 125 mm Purospher RP-18 5 µm
Mobile phase
A = 0.05 M KH_2P0_4 in water
(pH = 2.5 with H_2S0_4); B = acetonitrile
Flow rate 1.0 ml/min
Gradient
0 % B to 10 % B in 5 min
10 % B to 40 % B in 5 min
Column wash
40 % B for 1 min
40 % B to 0 % B in 1 min
UV detector
variable wavelength detector
220 for 4 min, 254 for 3.5 min
204 nm for 2.5 min, 220 nm, standard cell
Column compartment temperature
60 °C
Stop time 12 min
Post time 5 min
Injection volume 5 µl

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The performance of the HPLC method is shown in the table below.

Compound	LOD for S/N=2 (mg/l)*	Precision of RT (RSD of 10 runs) (100 mg/l)*	Precision of Area (RSD of 10 runs) (100 mg/l)*
Quinidine	0.1	0.02	0.45
Procainamide	1.0	0.04	0.20
N-acetylprocainamide	0.1	0.05	0.27
Disopyramide	0.1	0.02	0.20

* Injection volume: 5 µl

The presented method shows an easy but reliable and precise analysis of the antiarrythmic drugs quinidine, disopyramide, procainamide and N-acetylprocainamide. The values for LOD, precision of RT and precision of area show the good performance of the analysis.

Equipment

Agilent 1100 Series

- Quaternary pump (includes vacuum degasser)
- Thermostatted autosampler
- Thermostatted column compartment
- Variable wavelength detector, standard flow cell, 10-mm path length, 13-µl cell volume

Alternative:

- Vacuum degasser
- Binary pump
- Diode-array detector, standard flow cell 10-mm path length, 13-µl cell volume
- Agilent ChemStation + 3D software

Columns

- Purospher RP-18, 5 µm, 4 x 125 mm (Agilent part number 79925PU-564)
- *Recommended:* Guard cartridges Purospher RP-18, 5 µm, 4 x 12.5 mm (Agilent part number 79925PU-504, 10/pk)

Note:
Since the method was specifically developed on the Agilent 1100 Series system you might not be able to reproduce this analysis on an older system or even on a new system with lower performance. To avoid sample decomposition it is necessary to use a cooled autosampler, for example, the Agilent 1100 Series thermostatted autosampler.

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