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Flow injection analysis of amlodipine using UV-detection

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Amlodipine, (**1**) [*R,S*-2-[(2-aminoetyoxy)methyl]-4-(2-chlorophenyl)-3-ethoxy-carbonyl-5-methoxycarbonyl-6-methyl-1,4-dipydropyridine] is a potent dihydropyridine calcium channel bloker [1]. A limited number of methods have been reported for the determination of **1** including HPLC [2–6], spectrophotometry [7], micellar electrokinetic chromatography [8–9], and capillary electrophoresis [10].

The aim of this study was the direct determination of **1** by flow injection analysis (FIA) without colourizing the solutions and its application to pharmaceutical preparations. To determine the parameters for the optimization a **1** solution (3.5×10^{-6} mol/l) was used. The solvent system consisted of methanol and bidistilled water. It was found that the optimum concentration of methanol, in view of peak morphology, was 20% (v/v). The best flow-rate was found to be 1 ml/min. The final concentration of buffer in the test solutions was 0.1 mol/l. When the base line was reached, another sample was injected. The peak areas versus pH ranged from 1.01 to 11.02 and there were no appreciable differences at pH values from 5.95 to 7.99. Therefore 0.1 M phosphate buffer (pH = 7.12) was chosen as working media. The signals of the **1** at concentrations ranging from 1.17×10^{-6} to 5.87×10^{-6} mol/l were obtained under the conditions given above.

The relationship between the area under curve (AUC) and **1** concentration was found to be $AUC = 7.3 \times 10^9$ C (mol/l) + 30525.0; r = 0.9999. The detection limit (S/N = 3) was 1.4×10^{-7} mol/l with RSD 1.24% (n = 8).

Linearity and accuracy in the concentration range of $1.17 \times 10^{-6} - 5.87 \times 10^{-6}$ mol/l were examined employing intra-day and inter-day (for eight days) studies. Very accurate results were obtained for intra-day and inter-day experiments with a good correlation. These results indicate that the FIA method could be used for the analysis of **1**.

The validity of method was examined by applying it to tablets. All results of the assays were evaluated statistically and are presented in the Table.

High reproducibility and insignificant differences between FIA and UV-spectrophotometry were observed at the 95% probability level. As a conclusion, the method proposed in this study is accurate, precise and rapid. Therefore it can be suggested for the routine analysis of **1**.

Table: Assay results of 1 in tablets*

	FIA	UV-Spectrophotometry
Mean	4.99	4.92
n	8	8
RSD%	1.2	0.7
CL	±0.14	±0.11
F-test of insignificant	2.68	$F_{0.05} = 4.28$
t-test of insignificant	1.25	$t_{0.05} = 2.18$

*Each tablet contains 5 mg of **1**

Experimental

1. Apparatus and chemicals

The HPLC apparatus was a Model LC 6A pump equipped with a 20 µl manual loop injector, a Model SPD-A10 UV variable wavelength detector and a Model C-R7A integrator (all Shimadzu, Japan). Spectrophotometric studies were done using a Model UV-2401 PC (Shimadzu, Japan). A Model WTW Multiline P4 Universal pH-meter cabled Sen-Tix 92T pH electrode (Germany) was employed for measuring and adjusting the pH of the solution. Standard **1** (99.97%) and Norvasc® tablets containing 5 mg active material were kindly supplied from Pfizer Ilaçlar A.S. (Istanbul, Turkey). Standard **1** was used without further purification. Other chemicals were of analytical grade of Merck (Germany).

2. Procedures

2.1. Solutions

A stock solution of **1** (1×10^{-3} mol/l) was prepared using bidistilled water and the dilutions were made in the range of $1.17 \times 10^{-6} - 5.87 \times 10^{-6}$ mol/l. As a mobile phase an aqueous solutions of MeOH (10%, v/v) was used. The buffer solutions were prepared using 1 mol/l K_2HPO_4 (pH 7.12–11.02) and their pH values were adjusted using 2 mol/l HCl or 2 mol/l KOH.

2.2. Application to tablets

Ten tablets were weighed and finely powdered in a mortar. The average weight of a tablet was calculated. A sample equivalent to one tablet was weighed and transferred to a 100 ml calibrated flask, 1 ml phosphate buffer (1 mol/l, pH 7.12) was added, magnetically stirred for 20 min and made up to volume with bidistilled water. A sufficient amount of the solution was pipetted in a tube and it was centrifuged for 10 min. The supernatant was diluted to the predetermined values and injected in to sample loop by means of a syringe. The absorbances was monitored at 240 nm. The areas under curve values were used for calibration.

UV-Spectrophotometry was chosen as a comparison method. The absorbances of the same solutions were measured at 240 nm using quartz cells. The relationship between absorbance (A) and concentration of **1** (C) was found to be A = 16691.5 C (mol/l) + 0.041; r = 0.9995.

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