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THE DETERMINATION OF PRAZOSIN HYDROCHLORIDE IN PHARMACEUTICAL PREPARATIONS BY FLOW INJECTION ANALYSIS USING UV-DETECTION

UV DETEKTÖR KULLANILARAK FLOW İNJEKSİYON ANALİZ YÖNTEMİ İLE FARMASOTİK PREPARATLARDA PRAZOSİN HİDROKLORÜRÜN TAYİNİ

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A Flow Injection Analysis(FIA) of prazosin hydrochloride (PRZ) using UV detection is described. Methanolic HCl(0.2 mol.l^{-1}) was used as the solvent. A flow rate of 1 ml.min^{-1} was pumped and the active material was detected at 245 nm. The calibration equation was linear in the range of 1x10^{-6} - 5x10^{-6} mol.l^{-1}. Limit of detection(LOD) and limit of quantitation(LOQ) were calculated to be 1.3x10^{-7} and 3.2x10^{-7} mol.l^{-1}, respectively. The proposed method was applied to the determination of PRZ in pharmaceutical preparations. The results were compared with those obtained from UV-spectrophotometry.

Prazosin hıdroklorürün(PRZ), UV detektörü kullanılarak, Flow Injeksiyon Analizi(FIA) yöntemi ile tayini geliştirilmiştir. Solvent sistemi olarak metanolik HCl(0.2 mol.l^{-1}) kullanılmıştır. Aktif materyal 1 ml.dk^{-1} akış hızında pompalanmış ve 245 nm de detekte edilmiştir. Kalibrasyon denklemi için 1x10^{-6}-5x10^{-6} mol.l^{-1} derişim aralığında doğrusallık elde edilmiştir. Saptama (LOD) ve tayin sınırları (LOQ) sırasıyla, 1.3x10^{-7} ve 3.2x10^{-7} mol.l^{-1} olarak hesaplanmıştır. Yöntem PRZ içeren farmasötik preparatlara uygulanmış, sonuçlar UV-spektrofotometrik yöntem ile karşılaştırılmıştır.

Key words: *Determination; Prazosin hydrochloride; Flow injection analysis; Pharmaceutical application*

Anahtar kelimeler: *Tayin; Prazosin hidroklorür; Flow injeksiyon analiz yöntemi; Farmasotik uygulamalar*

Introduction

Prazosin hydrochloride, (PRZ) 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furoyl) piperazine hydrochloride, is an antihypertansive agent. It is a post-sympathetic selective α-1 adrenoreceptor antagonist(1). Its chemical structure is shown in fig.1.

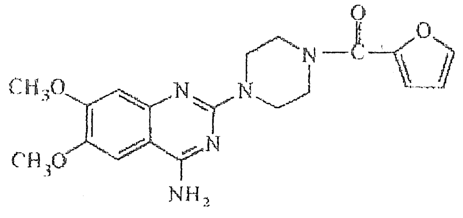

Fig.1. The chemical structure of PRZ.

The methods that have been reported for the determination of PRZ include; Spectrophotometry and fluorimetry(2), spectrophotometry(3,4), coulometry(5), thin-layer chromatography(6), potentiometry(7), differential pulse polarography(8) voltammetry (9, 10) and HPLC (11, 12).

Flow Injection Analysis(FIA) is a new methodology characterized by its versatility, ease of automation, high sampling frequency and minimum sample requirement. The FIA techniques have found wide applications recently due to reduction of the analysis time and reagents consumption compared with conventional manual procedures(13). On the other hand, their high sensitivity makes them suitable for the determination of low concentrations of pharmaceuticals in biological fluids when used as detectors in HPLC. They can also optimize the detection of analyte independently from the way process occurring in the chromatographic column(14). The aim of this study was the direct determination of

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PRZ by FIA method and its application to pharmaceutical preparations.

Material and methods

Apparatus and chemicals: The HPLC apparatus used was a Model LC 6A pump equipped with a 20μl manual loop injector, a Model SPD-A10 UV variable wavelength detector and a Model C-R7A integrator. Spectrophotometric studies were done using a Model UV-2401 PC (all Shimadzu). Standard PRZ (99.8%) and Minipress® tablets containing 5 mg active material were kindly supplied by Pfizer Ilaçları A.Ş. (Istanbul, Turkey). Other chemicals were of analytical grade from Merck.

Solutions: A stock solution of PRZ ($1x10^{-3}$ mol.l^{-1}) was prepared using methanolic HCl (0.2 mol.l^{-1}). The dilutions were made in the range of $1x10^{-6}$-$5x10^{-6}$ mol.l^{-1} with the same solvent. As a carrier phase an aqueous solution of MeOH (10% v/v) was used.

Analyses of the tablets: Ten Minipress® tablets were weighed and finely powdered in a mortar and the average weight of a tablet was calculated. A sample equivalent to one tablet was weighed, transferred to a 100 ml calibrated flask and 50 ml methanolic HCl (0.2 mol.l^{-1}) was added, magnetically stirred for 20 min and made up to volume with the same solvent. A sufficient amount of the solution was pipetted into a tube and centrifuged for 10 min. The supernatant was diluted to the predetermined values and injected into the sample loop by means of a syringe.

Results and discussion

A PRZ solution of $5x10^{-6}$ mol.l^{-1} and a solvent system consisting of methanolic HCl (0.2 mol.l^{-1}) were used to determine the parameters for the optimisation. The optimum concentration of MeOH, in view of peak morphology, was determined to be 10%. Since the flow rate of the carrier is an important parameter affecting the sensitivity of the method, it was gradually changed from 0.5 to 3 ml.min^{-1} and the best flow-rate was found to be 1 ml.min^{-1}. The absorbance of PRZ in methanolic HCl was measured at 245 nm. All experiments were performed at ambient temperature. When the base line was reached, another sample was injected. The signals of PRZ at concentrations ranging from $1x10^{-6}$ to 5x 10^{-6} mol.l^{-1} were obtained under the given conditions (Fig.2).

The relationship between area under the curve(AUC) and PRZ concentration was found to be: AUC=$8.25x10^{10}$C(mol.l^{-1}) + 41655.5 ; r=0.9998. The detection limit (LOD, S/N=3) and limit of quantitation (LOQ, S/N=10) were extrapolated to be $1.3x10^{-7}$ mol.l^{-1} with RSD=1.18% and $3.2x10^{-7}$ mol.l^{-1} with RSD=0.82% (n=8), respectively. The results indicated that this method was highly precise and reproducible.

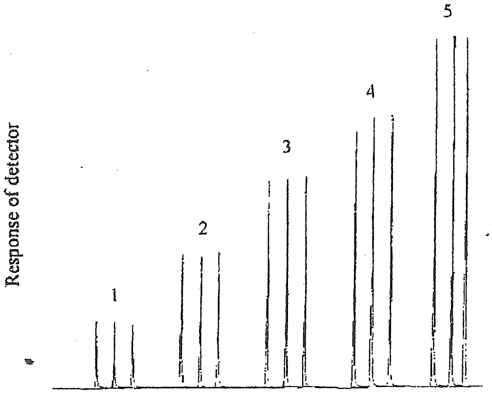

Fig.2. The signals in the $1x10^{-6}$-$5x10^{-6}$ mol.l^{-1} concentration range of PRZ.

Linearity and accuracy in the concentration range of $1x10^{-6}$ -$5x10^{-6}$ mol.l^{-1} were examined employing intra-day and inter-day (for eight days) studies for the determination of PRZ. The results for intra-day and inter-day experiments with a good correlation were obtained and evaluated statistically as demonstrated in table 1. These results indicate that the FIA method could be used for the analysis of PRZ.

Application to the pharmaceutical dosage forms: The proposed technique was applied to tablets containing 5 mg PRZ and no interferences were observed from the additives or excipients. The AUC values were used for calibration. UV-spectrophotometry was chosen as the comparison method. The absorbances of the same solutions used for FIA were as demonstrated in table 1 measured at 245 nm. The relationship between absorbance (A) and concentration of PRZ (C) was found to be: A=112264 C (mol.l^{-1}) + 0.017; r=0.9999.

The validity of the method was examined by applying to commercial tablets. All results of the assays were evaluated statistically as presented in table 2.

Table1. Linearity and accuracy of FIA method for PRZ.

Parameters	Intra-day precision (k=1; n=8)	Inter-day precision (k=4; n=32)
Slope±SD	$8.25 \times 10^{10} \pm 5579$	$8.22 \times 10^{10} \pm 5635$
Intercept	42368	44734
Correlation coefficient (r)	0.9997	0.9996
Slope±CL(p=0.005)	$8.25 \times 10^{10} \pm 5443$	$8.22 \times 10^{10} \pm 5708$

SD: Standard deviation CL: Confidence limit
k: Number of the set, n: Number of the sample

Table 2. The assay results of PRZ in tablets containing 5 mg PRZ.

Parameters	FIA	UV-spectrophotometry
Mean	4.8	4.9
n	8	8
%RSD	1.2	0.7
CL	±0.14	±0.11
F-test of insignificant	2.68	$F_{0.05}$=4.28(table)
t-test of insignificant	1.25	$t_{0.05}$=2.18(table)

High reproducibility and insignificant differences were observed between FIA and UV-spectrophotometry at the 95% probability level. As a conclusion, the method proposed is simple, accurate, precise, rapid and more practical, regarding the time of analysis, consumption of solvents and size of sample required for the routine analysis of PRZ.

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