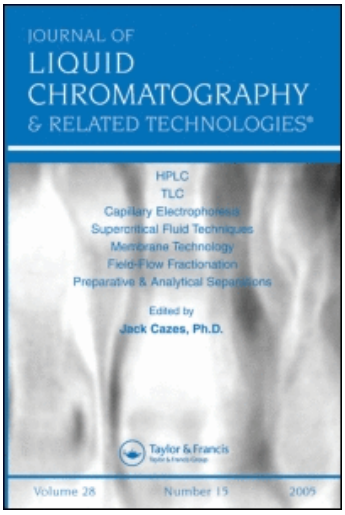

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Rapid Determination of Naproxen Sodium in Pharmaceutical Formulations by Flow Injection Analysis (FIA) Using UV-Detection

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ABSTRACT

A flow injection analysis (FIA) of Naproxen sodium (NAPS) using UV detection is described in this study. The best solvent system used as a carrier solution was found to be an aqueous solution of EtOH (10% v/v). A flow-rate of 1.2 mL min^{-1} was used and Naproxen was detected at 230 nm. Repeatability was examined using 8×10^{-6} M NAPS solution and relative standard deviation (RSD) values were found to be about 2.2

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for intra-day and inter-day studies. The calibration equation was the linear range of 4×10^{-6} to 1.18×10^{-5} M. Limit of detection (LOD) and limit of quantification (LOQ) were calculated as 5.8×10^{-7} (S/N = 3.3) and 1.7×10^{-6} M (S/N = 10), respectively. The proposed method was applied for the determination of NAPS in pharmaceutical tablet formulation, containing 275 mg active material. The proposed method is reliable, precise, accurate, and rather cost effective, and can be applied for uniformity tests in NAPS tablets.

Key Words: Naproxen; Flow-injection analysis; Pharmaceutical analysis.

INTRODUCTION

Naproxen sodium (NAPS), the sodium salt of (S)-6-methoxy-α-methyl-2-naphtalenacetic acid (Fig. 1) is a non-steroidal anti inflammatory drug, which is used in the treatment of severe pain and inflammation. The effect of NAPS is due to the inhibition of cyclooxygenase which is involved in the arachidonic acid conversion pathway, resulting in a decrease of prostaglandin synthesis.[1,2]

Several methods have been published for the determination of NAPS in pharmaceutical preparations and biological fluids. These methods include first derivative, non-linear, variable-angle synchronous fluorescence spectroscopy,[3] HPLC,[4,5] CE with electrospray mass spectrometry,[6] and capillary isotachophoresis.[7,8] Some studies using flow injection analysis (FIA) have been reported for the complex formation but they do not reflect any quantification processes of NAPS.[9,10] USP XXIV[11] describes an HPLC method for the determination of NAPS, as well.

There have been no reports concerning flow injection analysis of NAPS in tablets using UV detection. This paper describes the development of a rapid and simple method for the analysis of NAPS, using the FIA technique, detecting the signals by UV-spectroscopy. The optimization processes for this technique were investigated and the method was validated and applied for the analysis of pharmaceutical tablets of NAPS.

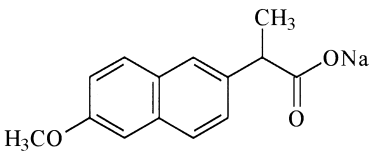

Figure 1. The chemical structure of NAPS.

EXPERIMENTAL

Apparatus

A HPLC consists of a model LC 6A pump and a model SPD-A10 UV of variable wavelength detector, and a model C-R7A integrator (Shimadzu, Japan). Standard solutions and samples were injected to a Rheodyne model with 20-μL loop injection port (Cotati, CA, USA). Carrier solvent was always filtered from a glass filter and degassed by a model of B-220 ultrasonic bath (Branson, CA, USA).

Chemicals

Standard NAPS was supplied by Ali Raif Ilaç Sanayi ve Ticaret A. S. (Istanbul, Turkey), the purity of which was checked spectrophotometrically. Aprowell® (Ali Raif Ilaç A.S, Istanbul, Turkey) having 275 mg NAPS were purchased from a local drug store. Other chemicals were of analytical grade and were provided by (Merck Co. Darmstad, Germany).

Procedures

Solutions

The stock solution of NAPS (1×10^{-3} M) was prepared in distilled water containing 10% EtOH. During the optimization and validation studies, solutions of 8×10^{-6} M NAPS, in the range of 4×10^{-6}–1.18×10^{-5} M were used, respectively.

Carrier Solvent

A carrier solvent was an aqueous solution of EtOH (10% v/v). It was prepared using 10% ethanol and double distilled water; the solvent was degassed by a sonicator.

Flow-Injection Analysis

Flow-injection analysis was performed in a supporting solution consisting of 10% ethanol. The signals were detected at 230 nm where monochromatic light is absorbed to the maximum. Standard and sample solutions were

injected into a 20-μL fixed volume of loop. The variation of flow-rate was examined in a wide range of 0.1–2.5 mL min^{-1}.

Recovery of Naproxen Sodium from Tablets

Ten Aprowell tablets (each containing 275 mg NAPS) 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 100 mL calibrated flask, 10 mL ethanol was added, sonicated for 15 min, and made up to volume with distilled water. Then the solution was centrifuged at 3000 rpm for 15 min, the supernatant was diluted with 10% ethanol, and then it was injected.

RESULTS AND DISCUSSION

The appropriate carrier solvent system, which is suitable to dissolve both naproxen and sodium salt of naproxen in their pharmaceutical tablets, is 10% ethanol solution. This solvent did not cause any precipitation of NAPS using this solvent system during the experiments.

For the optimization of the instrumental conditions, initially, spectrophotometric behavior was examined using 8×10^{-6} M NAPS. It was recorded in the range of 200–300 nm and a sharp peak appeared at 230.4 nm where molar absorptivity is 7398.

The effect of flow-rate on the area was investigated in the range of 0.1–2.0 mL min^{-1} at 230.4 nm. Although, all the flow-rates are equivalently usable, a flow rate of 1.2 mL min^{-1} was used for the rest of the experiments because it was practical and gave an appropriate peak with consecutive injections.

The signals, which have 8×10^{-6} concentration of NAPS consecutively recorded in the optimum conditions are shown in Fig. 2.

Repeatability

After investigation of optimum conditions, certain experiments were conducted for the examination of validity of the method.

Three sets, each having 8 fixed concentrations (8×10^{-6} M NAPS), were injected on the same day for three (3) consecutive days. The output of the results were evaluated as mean (x), standard deviation (SD), relative standard deviation (RSD), and confidence limits (CL) at the 95% probability level. The

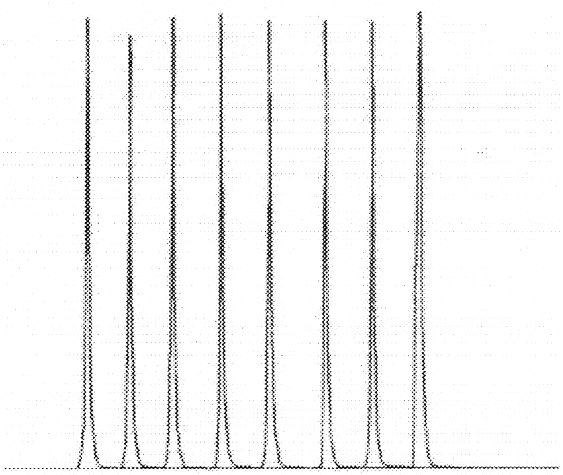

Figure 2. Consecutive injections of 8×10^{-6} M NAPS, in the optimum conditions, pumping through 1.2 mL min^{-1} flow-rate and detecting at 230.4 nm.

results are demonstrated in Table 1. It was observed that very good repeatability values were obtained.

Linearity

Linearity of the method was investigated as intra-day and inter-day examinations. Three sets of calibration dilutions (4×10^{-6}–1.18×10^{-5} M) were prepared and they were injected on consecutive days. These results are given in Table 2.

Table 1. The intra-day and inter-day repeatability of 8×10^{-6} M NAPS as area in the optimum analytical and instrumental conditions.

	Intra-day precision ($k = 3$; $n = 8$ for each)			Inter-day precision pooled ($n = 24$)
	First-day	Second-day	Third-day	
Mean (area)	311,477	307,290	313,105	310,624
SD	6,047	6,706	6,892	6,748
RSD	1.9	2.2	2.2	2.2
CL ($p = 0.05$)	4,190	4,647	4,776	2,699

Table 2. Results of linearity studies in the concentration of 4×10^{-6}–1.18×10^{-5} M NAPS.

	Inter-day ($n = 5$)			Intra-day ($n = 15$) whole-days
	First-day	Second-day	Third-day	
Slope, a	3.822×10^{10}	3.925×10^{10}	3.766×10^{10}	3.842×10^{10}
Intercept, b	5,687	−3,808	7,086	2,725
Correlation coefficient, r	0.9996	0.9996	0.9999	0.9999
SD of regression equation, $\pm S_r$	6,608	5,115	2,153	10,750
SD of the slope, S_e	1.054×10^{9}	1.154×10^{9}	4.857×10^{8}	1.190×10^{9}
CL ($p = 0.05$)	$\pm 1.00 \times 10^{9}$	$\pm 1.36 \times 10^{9}$	$\pm 5.71 \times 10^{8}$	$\pm 5.8725 \times 10^{8}$

Using the multiplication of standard deviation of signals during the repeatability experiments, limit of detection (LOD) S/N = 3.3 and limit of quantification (LOQ) S/N = 10 were 5.8×10^{-7} and 1.7×10^{-6} M, respectively.

Intermediate Precision

Synthetic mixtures were prepared by the addition of 50%, 100%, and 150% of the declared amount (275 mg NAPS per tablet), to a mixture of tablet excipients such as starch, magnesium stereate, microcrystalline cellulose, dicalcium phosphate, and lactose. These synthetic mixtures were analyzed in a similar method as the pharmaceutical tablets. The active compound was recovered and injected into the instrument and a related signal was obtained. The results are given in Table 3.

Table 3. Intermediate precision of synthetic matrix of NAPS prepared at the level of 50, 100, and 150% of a 275-mg tablet ($n = 6$ for each group).

	50% Recovery	100% Recovery	150% Recovery
Mean	97.7	98.9	99.9
SD	2	2	2
RSD	2.1	2.2	1.6
CL ($p = 0.05$)	1.65	1.75	1.26

Table 4. Result of uniformity test in NAPS tablets.

	% NAPS ($n = 6$)
Mean	107
SD	2.11
RSD	1.97
CL ($p = 0.05$)	1.69

It was observed that the recovery values is as high as 100%. Besides, RSD values are about two, which indicated the tablet excipients do not affect the analytical results.

Application of the Method to Naproxen Sodium Tablets

Tablet solutions were prepared as described in the experimental. These solutions were injected and the analysis was carried out in the optimum condition. The results were evaluated statistically and are presented in Table 4.

The monograph for the NAPS tablet in the USP XXIV[11] allows 10% deviation from declared amount of a tablet. Thus, the results obtained by the proposed method are in agreement with the official requirements. Furthermore, the RSD is about 2.2%, which is reasonable in such types of method development.

In conclusion, the proposed method is reliable, precise, accurate, and fast, which makes it suitable for routine analysis of NAPS tablet formulations.

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