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Short Communication

DETERMINATION OF NAPROXEN IN TABLETS BY USING FIRST DERIVATIVE POTENTIOMETRY

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Abstract

In this article the potentiometric determination of naproxen sodium is described. A solvent system consisting of aqueous solution of 20% ethanol (v/v) at an ionic strength of 0.1 adding sodium chloride was found to be suitable for the determination of naproxen. Same solvent system was employed for titrant of 0.1 N HCl and to titrate the active material. Validation processes as repeatability (precision) (n=6) were computed. It was found to be 0.70 for RSD % and 0.3 for ±CL (p=0.05). The analysis of 275 and 550 mg naproxen sodium tablets were carried out in the filtered and unfiltered tablet solutions for three consecutive days considering intra and inter-days. Precision values were in the range of 0.16-0.33 for unfiltered and 0.10-0.29 for filtered solutions and the amount of the tablets was found to be in the range of (103.0-108.7%) for unfiltered and (102.9-107.7%) for filtered solutions. The method proposed here is precise simple and rather cheap. Therefore, it is suggested for the routine analysis of naproxen sodium tablets.

Key words: *Naproxen sodium, Determination, Potentiometry, First derivative potentiometry.*

Naproksen'in Tabletlerde Birinci Türev Potansiyometri ile Miktar Tayini

Bu çalışmada, naproksen sodyumun potansiyometrik tayini tanıtılmaktadır. Naproksenin tayini için en iyi çözücü sistemi, sodyum klorür ilavesiyle 0,1 iyonik şiddete ayarlı % 20 etanol (h/h) olarak bulundu. Aktif maddenin titrasyonunda ve 0,1 N HCl için de benzer çözücü sistemi kullanıldı. Validasyon işlemleri tekrarlanabilirlik (kesinlik) (n=6) olarak hesaplandı. % RSD için 0,70 ve CL (p=0,05) için 0,3 olarak hesaplandı. Naproksen sodyumun 275 ve 550 mg'lık tabletlerinin analizi, tablet çözeltilerinin süzülerek ve süzülmeden ardışık üç gün, güniçi ve günlerarası bakımından yapıldı. Kesinlik değerleri, süzülmemiş tablet çözeltileri için 0,16-0,33, süzülmüş tablet çözeltileri için 0,10-0,29 ve tabletlerin miktarı süzülmemişler için (%103,0-108,7), süzülmüşler için (%102,9-107,7) olarak bulundu. Önerilen bu metot tekrarlanabilir, basit ve oldukça ucuzdur. Bu nedenlerle, bu yöntem naproksen sodyum tabletlerinin rutin analizleri için önerilmektedir.

Anahtar Kelimeler: *Naproksen sodyum, Tayin, Potansiyometri, Birinci türev potansiyometri.*

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Introduction

Naproxen sodium (NAPS) is a non-steroidal anti-inflammatory drug (NSAI) which is used for the treatment of severe pain and inflammation. It acts by reducing the levels of prostaglandins, chemicals that are responsible for pain, fever and inflammation. Naproxen blocks the enzyme that makes prostaglandins (cyclooxygenase), resulting in lower concentrations of prostaglandins. (1, 2).

Several analytical methods have been published for the determination of NAPS in pharmaceutical preparations and biological fluids. These methods included first derivative non-linear variable-angle synchronous fluorescence spectroscopy (3), CE with electro spray mass spectrometry (4), HPLC (5, 6), and capillary isotachophoresis (7, 8) flow-injection analysis (FIA) (9) and FIA by using complex formation of NAPS (10, 11).

There have been no reports concerning the determination of NAPS in tablets using electro analytical technique. Thus, the aim of this study is to develop a simple, rapid and cheap potentiometric method for the determination of NAPS in pharmaceutical tablets.

Experimental

Apparatus

Titrations were conducted by a Model of DL50 Mettler-Toledo automatic titrator (Schwerzanbach, Switzerland) cabled to a glass pH electrode. It was calibrated adjusting the pH to those of buffers at pH 4.01 and 7.00.

Chemicals

Standard NAPS and its commercial tablet Apranax® labeled 275 mg and 550 mg were kindly supplied from Abdi İbrahim İlaçları A. Ş. (İstanbul, Turkey). All other chemicals were of analytical grade and provided from Merck (Darmstadt, GmbH, Germany). Double distilled water and ethanol were prepared in our laboratory by distil-ling them in all glass apparatus.

Procedures

Preparation of standard solution of HCl

Stock solution of HCl was prepared by pipeting the necessary volume of concentrated HCl and necessary amount of ethanol in different percentage and sodium chloride to adjust the ionic strength to 0.1 and then the volume was made up to 1L. The titrant of HCl was standardized against to primer standard of sodium carbonate.

The ratios of ethanol in the aqueous solutions were varied in the range of 5-30 percent and they were separately prepared to examine the effect of solvent strength.

Titration procedure

Appropriate amounts of NAPS accurately weighed and transferred to a 50-mL cell of the titrator. Then, the volume was made up to 50 mL with double distilled water after addition of necessary amount of EtOH, sodium chloride. That solution was titrated using standardized HCl.

Analysis of tablets

For the quantification of NAPS in tablets, ten tablets were accurately weighed. The average weight of a tablet was calculated and they were powdered and finely mixed in a mortar. A sufficient amount of tablet powder equivalent to the weight of one tablet was accurately weighed and transferred to a 500-mL volumetric flask. After addition of 50 mL of 1 M NaCl, 100 mL of EtOH, the volume made up to 500 mL with double distilled water and the solution was vigorously shaken. This solution was titrated with the standard solution of HCl at constant ionic strength (I=0.1) in the medium of 20 % EtOH-water (v/v).

Results and Discussion

Certain electrolyte systems were tried to find out for the titration medium in which NAPS could be completely dissolved and not to be affected from compositions elements. Ethanol was preferred as solvent because of its low cost. The variations of ethanol in double distilled water were tested in the range of 5-30 % (v/v), to investigate the optimum conditions as curve morphology. Besides, the ionic strength of the electrolyte was adjusted to 0.1 by adding NaCl to avoid from the collosion of the molecules during the titration.

Well-defined potentiometric curve was obtained when the titration was conducted in the solvent system containing 20 % ethanol (v/v). Thus, using that solvent system carried out rest of the study. First derivative potentiometric curve was used to precisely establish the end-point of titration. It is obviously known that the volume corresponds to the end-point of the titration is obtained via first derivation of the potentiometric curve. Starting point of view, the determination of NAPS was made by employing the volume of titrant, which is integrated by the automatic titrator.

Titration curve of the potentiometric and its first derivative form of NAPS in the solvent system containing 20 % of ethanol are demonstrated in Figure 1.

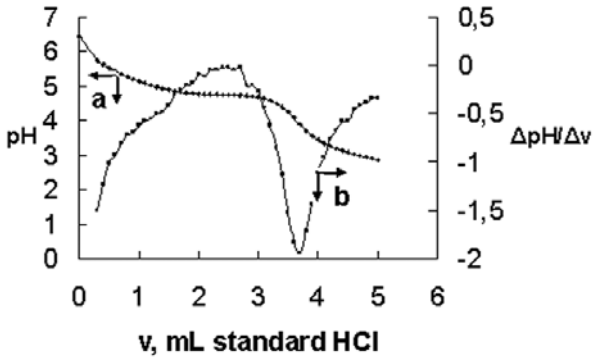

Figure 1. Titration curves of NAPS by titrating standard HCl in the solvent system of 20 % ethanol (v/v) aqueous solution having I= 0.1 ionic strength a) potentiometric titration curve b) first derivative curve of the potentiometric titration curve.

The precision test (repeatability) of the method was examined by titrating the same amount of NAPS with standard HCl in the optimum conditions. To perform the test, a stock solution (420 mg/100 mL) was prepared and six titrations were made by pipeting definite volume solution. The results of the assays were calculated using common procedures and they were evaluated statistically. The results and the statistical data, which are calculated from titrations of NAPS, are given in Table 1.

TABLE 1. Precision test (repeatability) of the method.

Statistical elements	values
Mean, mg (n=6)	41.6
SD	0.29
RSD (%)	0.70
±CL (p=0.05)	0.3

The low values of standard deviation, relative standard deviation and confidence limits in the 95% probability level indicate that the method is highly precision (repeatable) and reliable, in the mentioned conditions.

The analysis of 275 and 550-mg NAPS tablets were achieved obeying the pharmaceutical rules as stated in USP XXIV (12). Although, it is explained that the tablet solutions have to be filtered, we have analyzed the tablet solutions as filtered and unfiltered form. Besides, the analyses were performed three consequent days, actually in the same conditions. Table 2 demonstrates that the results of 275 and 550-mg NAPS tablets in the filtered and unfiltered conditions which were achieved three independent days.

TABLE 2. The results of the NAPS tablets labeled 275 and 550 mg in filtered and unfiltered solutions.

	275-mg tablet						550-mg tablet					
	Unfiltered (n=4 each)			Filtered (n=4 each)			Unfiltered (n=4 each)			Filtered (n=4 each)		
days	first	second	third	first	second	third	first	second	third	first	second	third
Mean mg	296.7	283.1	283.6	296.2	283.0	281.4	598.1	573.3	573.3	568.4	573.2	573.2
(%)	(108.0)	(103.0)	(103.1)	(107.7)	(102.9)	(102.3)	(108.7)	(104.2)	(104.2)	(103.3)	(104.2)	(104.2)
SD	0.85	0.93	0.57	0.43	0.77	0.54	1.97	0.93	0.93	1.63	0.56	0.56
RSD %	0.29	0.33	0.20	0.14	0.27	0.19	0.33	0.16	0.16	0.29	0.10	0.10
±CL (p=0.05)	1.4	1.5	0.9	0.7	1.2	0.9	3.1	1.5	1.5	2.6	0.9	0.9

USP XXIV (12) accepts the results in the range of 90-110 percent of a declared amount in NAPS tablets. As is seen in the Table 2, the mean results as percent provide the pharmacopoeia suggestions. Thus, they are completely in agreement for the official or pharmaceutical principals. In conclusion, the repeatability of the tablet solutions are seemed to be low both filtered and unfiltered solutions. The analysis of a tablet was realized within ten minutes, that is, very reasonable duration for routine laboratory analysis.

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