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POLAROGRAPHIC DETERMINATION OF LORNOXICAM IN PHARMACEUTICAL FORMULATIONS

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Abstract : A simple, precise, fast and low-cost differential pulse polarographic (DPP) method for determination of lornoxicam in pharmaceutical formulations has been proposed. The results have been compared with those of high performance liquid chromatography (HPLC) method. Mean values and standard deviations calculated by ten determinations were 8.10 ± 0.12 mg for DPP and six determinations were 8.02 ± 0.08 mg for the HPLC method. The statistical evaluations indicated that there was no significant difference between the mean values and precessions of the two methods at 95% confidence level (t=2.64, F=2.25).

Keywords: *Lornoxicam, Anti-Inflammatory, Polarography.*

FARMASÖTİK FORMÜLLERDEKİ LORNOKSİKAMIN POLAROGRAFİK TAYİNİ

Özet : Bu çalışmada farmasötik formüllerde bulunan lornoksikamı tayin etmek için basit, duyarlı, hızlı ve ucuz bir yöntem önerilmiştir. Bu yöntemle elde edilen sonuçlar yüksek performanslı sıvı kromatografisi (HPLC) yöntemi ile elde edilenlerle karşılaştırılmıştır. Tabletlerdeki lornoksikam miktarı için ortalama değerler ve standart sapmalar diferansiyel puls polarografik (DPP) yöntem için on tayinle 8.10 ± 0.12 mg, HPLC için altı tayinle 8.02 ± 0.08 mg olarak hesaplanmıştır. İstatistiksel değerlendirme, % 95 güvenirlik düzeyinde bu iki yöntem arasında ortalama değerler ve duyarlık bakımından önemli bir fark olmadığını göstermiştir (t=2.64, F=2.25).

Anahtar Kelimeler: *Lornoksikam, Antienflamatuar, Polarografi.*

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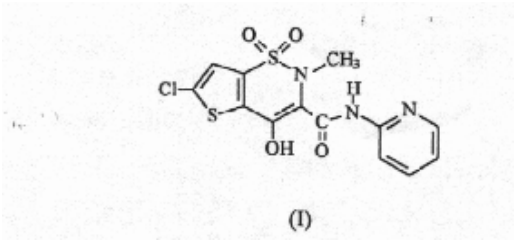
1. INTRODUCTION

Lornoxicam (rINN, G-chloro-4-hydroxy-2-methyl-N-2-pyridyl-2H-thienol [2, 3]- 1, 2-thiazine-3-carboxomide-1, 1-dioxide) is a non-steroidal anti-inflammatory drug (NSAID) [1]. Lornoxicam is a compound in the same chemical class as piroxicam, meloxicam and tenoxicam, with potent anti-inflammatory, antipyretic and analgesic activity [2-6]. Lornoxicam is non selective with a tolerability profile similar to diclofenac but superior to indometacin [7]. All NSAIDs treat inflammation in a way similar to the mechanism of aspirin, the most well-known and oldest member of the class.

In this paper, we present a differential pulse polarographic (DPP) method for the assay of lornoxicam in tablets and compare the results with those obtained by HPLC method.



(I)

$C_{13}H_{19}ClN_3O_4S_2$ (lornoxicam)

The best solvent for lornoxicam (**I**) to DPP measurements is ethanol. Several solvents were also tried to dissolve tablets as in our previous paper about DPP determination of some drugs [8–12].

DPP method involves the extraction of **I** from tablets with ethanol, filtration, appropriate dilution and recording the DP polarograms between 0.070 and - 0.700 V. E_{peak} was observed at - 0.030 V (Ag/AgCl, 3N KCl). A calibration graph was plotted between i_{peak} and **I** concentrations.

The mobile phase for HPLC method contained methanol, acetonitrile and aqueous solution of diammonium hydrogenphosphate. Prepared samples were injected in to the column and retention time of I was found as 1.87 min. The linear calibration range was found as 1-30 $\mu g\ mL^{-1}$.

2. EXPERIMENTAL

2.1. Materials

Pharmaceutical grade **I** was supplied from Abdi Ibrahim Drug Industry Company (Istanbul, Turkey). Commercial tablets were purchased from the market. Nitrogen gas was used for deoxygenation.

2.2. Apparatus

A polarographic analyzer (METROHM 746 Trace Analyzer) together with a capillary dropping mercury electrode and Lenseis LY 1600 model recorder was used. A platinum wire was used as the counter electrode. Chromatographic measurements were made by using Perkin Elmer 200 Series with UV detector. C_{18} column was used as an analytical column and analytes were detected at 364 nm using a UV detector. A Hanna Instruments pH 211 Microprocessor Model pH meter was employed for adjusting the pH of the solutions. Sartorius CP2245 Model delivery scale was used in weights. Pure water was obtained with Millipore Elix 5 Model machine. All measurements were done at room temperature.

2.3. Solutions

Stock solution of lornoxicam was prepared by accurate weighing to give a concentration of 100 $\mu g.mL^{-1}$ in ethanol. Standard solutions were prepared daily by appropriate dilution of the stock solutions over the range of desired concentrations with the ethanol.

Phosphate buffer was prepared by mixing solutions (equal volume) of $6.7x10^{-2}$ M $Na_2HPO_4.2H_2O$ and $6.7x10^{-2}$ M KH_2PO_4 appropriately to 5.3 the desired pH. Adjusting of pH was made with 1 M HCl and 0.1MNaOH.

Mobil phase consisted of an aqueous solution of ammonium monohydrogen phosphate, $(NH_4)_2HPO_4$ (50 mM), methanol and acetonitrile in the ratio of (3:6:1, V/V) was pumped at the rate 1.6 $ml.min^{-1}$.

All the reagents used were analytical-reagent grade (Merck, KGaA, Darmstadt, Germany). Only $(NH_4)_2HPO_4$ was obtained from Riedel-de Haën. Ultra pure H_2O was used.

2.4. Polarographic Procedure

Ten tablets were weighed and powdered. An accurately weighed portion of **I** was transferred into 50-60 mL of C_2H_5OH. After shaking for 30 min. the mixture was diluted to the volume with same solvent and filtered through a dry filter paper. A 0.1 mL portion of this solution was added to the polarographic cell containing 50 mL supporting electrolyte. DP polarogram of the solution was recorded between 0.070 and -0.700 V after deaeration with N_2 for 200 seconds. Then stock solutions of lornoxicam in ethanol were added twice (0.1 mL). Nitrogen was passed through the solution for 50 seconds. Polarograms of these solutions were recorded. The peak potential of lornoxicam was –31.0 mV (Figure 1).

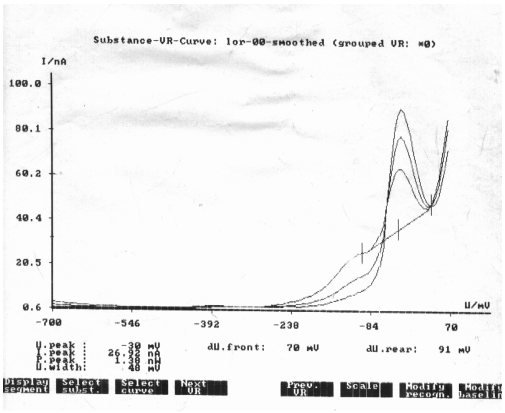


Figure 1. The effect of concentration on the peak current of lornoxicam by using DPP (supporting electrolyte is phosphate buffer pH 5.3) for two standard adding samples.

2.5. Chromatographic procedure (comparison method)

Lornoxicam sample was separated on a C_{18} column (ODS Hypersil 5µm, 250x4.6 mm ID; Bischoff Analysentechnik und Geräte, Leonber, Germany) with an aqueous solution of ammonium monohydrogenphosphate (50 $mmol\ L^{-1}$), methanol and acetonitrile in the ratio of (3:6:1, V/V) was pumped at the rate 1.6 mL/min. Detection was realized at 364 nm by using UV detector. The retention time of **I** was 1.87 min (Figure 2).

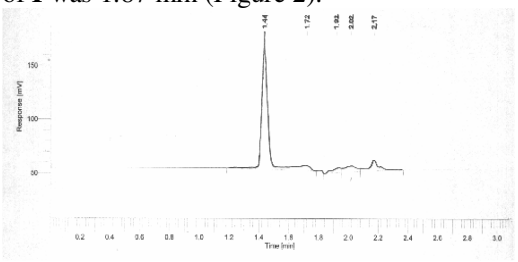


Figure 2. HPLC graph of lornoxicam.

3. RESULTS AND DISCUSSION

Commercially available tablets containing 8 mg of **I** were analyzed by developed DPP method and HPLC method for comparison.

The quantitative evaluation is based on dependence of peak current on lornoxicam concentration using standard adding technique. As shown Fig. 1, peak currents increased linearly with increasing amounts of lornoxicam.

The effect of lornoxicam concentration on the peak current was determined. A calibration graph of peak current versus lornoxicam concentration was found linear over the range 0.1-25.0 $\mu g.mL^{-1}$. Linear regression equation of this graph was calculated as

$I_{peak} = 0.667 + 6.800\ C$

(r=0.9994)

The limit of quantification (LOQ) was 0.1 $\mu g.mL^{-1}$ for lornoxicam. The relative standard deviation at % 1.4 was 14 $ng.mL^{-1}$ (n=10).

The effect of lornoxicam concentration on the peak high of chromatogram was determined. A calibration graph of peak high versus lornoxicam concentration was found linear over the range 1.0-30.0 $\mu g.mL^{-1}$.

The regression equation of this graph was calculated as

$h_{peak} = 1806.978 + 20767.624\ C$

(r=0.9998)

The results for lornoxicam containing commercial tablets analysed by two techniques and calculated t-value of Student's t-test. The calculated t-values did not exceed the tabulated values in the test, indicating, there was no significant difference between the methods.

Mean values and standard deviations calculated by ten determinations were 8.10 ± 0.12 mg for DPP and six determinations were 8.02 ± 0.08 mg for the HPLC method.

The statistical evaluations indicated that there was no significant difference between the mean values and precessions of the two methods at 95% confidence level (t=2.64, F=2.25).

The proposed differential pulse polarographic procedure can be used successfully to determine **I** in tablet dosage form. It compares reasonably with HPLC method and can be a good alternative for the analytical determination of **I.** Because it is simple, fast and low cost, and has sufficient precision, accuracy and sensitivity.

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