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Stability-Indicating HPLC Method for Betaxolol HCl and Its Pharmaceutical Dosage Forms

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ABSTRACT

The present work describes a specific, stability-indicating high-performance liquid chromatographic method for determination of betaxolol HCl and its pharmaceutical dosage forms. Betaxolol HCl was chromatographed on a microbondapak C18 column utilizing a simple mixture of methanol:acetonitrile:0.1% diethylamine (pH 3.0 adjusted using orthophosphoric acid). It was detected at 222 nm. The method is accurate and precise with a percent relative standard deviation of 0.11 based on 6 readings. A number of inactive ingredients present in the dosage forms (eye drop, tablet, gel) did not interfere in the assay procedure. The recovery from synthetic mixtures was quantitative. The extraction procedure from the dosage forms is very simple. The drug appears to be very sensitive to acids (such as sulfuric acid) since 100% of the drug decomposed on boiling for 5 min.

INTRODUCTION

Betaxolol HCl USP, chemically: 1-{4-[2-(cyclopropylmethoxy)-ethyl] phenoxy}-3-isopropylaminopropan-2-ol hydrochloride, is a β-selective adrenergic blocking agent useful in the treatment of chronic open angle glaucoma and ocular hypertention. The purpose of this investidation was to develop a stability-indicating high-performance liquid chromatographic (HPLC) method for quantification of betaxolol in its dosage forms (1,2).

EXPERIMENTAL

Reagents and Materials

Betaxolol HCl was obtained from M\S Lusochimica, Italy. All the solvents used were of HPLC grade. Dis-

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tilled, deionised water, filtered through 0.45 micron membrane filter was used throughout the experiment.

Apparatus

The high-performance liquid chromatograph used (Perkin-Elmer series 4) was equipped with a model LC-4 series pump, LC-85 B variable wavelength spectrophotometric detector, and a rheodyne injector. The chromatographic peaks were integrated and recorded with a model LCI-100 laboratory computing integrator. The separations were performed on an C-18 (15 mm × 3.9 mm ID, particle size 5 μm) column of Perkin–Elmer, using methanol:acetonitrile:0.1% diethylamine (pH adjusted to 3.0 with orthophosphoric acid) as the mobile phase. The chromatography was performed at ambient temperature using a flow rate of 1.0 ml/min. The detector sensitivity was set at 1.0 a.u.f.s. and the eluents were monitered at 222 nm.

Standard and Sample Preparation

Betaxolol HCl stock solution of 1.0 mg/ml concentration was prepared. The stock was suitably diluted to obtain a final concentration of 10.0 μg/ml with mobile phase.

A stock solution of trimethoprim (the internal standard) was prepared by dissolving 10 mg of the powder in the mobile phase to make a 1.0-μg/ml solution.

A standard solution was prepared by mixing 1.0 ml of the stock solution of drug with 0.5 ml of the stock solution of the internal standard, and bringing to volume (10.0 ml) with mobile phase. The solutions of other concentrations were prepared as needed.

Extraction from Tablets

Five tablets (each containing 20 or 40 mg of the drug) were ground and mixed with 35 ml methanol, stirred occasionally for 5 min, then brought to volume (50.0 ml) with mobile phase. The mixture was filtered and 1.0 ml of the filtrate was mixed with 1.0 ml of internal standard stock solution and suitably diluted to obtain a final concentration of 10.0 μg/ml of the drug.

Extraction from Gels

Sufficient quantity (equivalent to 10.0 mg of the drug) of the gel was transferred to a 50.0-ml volumetric flask. To it 30.0 ml of the mobile phase was added, and the preparation was vortexed for 10 min. The volume was made up with mobile phase and stirred for 10 min. The preparation was filtered and suitably diluted as described above.

Assay Procedure

A 100-μl quantity of the assay solution was injected into the chromatograph using the conditions described. For comparison, an identical volume of the standard solution was injected after the sample eluted.

Decomposition of Betaxolol HCl

A 1.0 ml quantity of the stock solution of betaxolol (10 mg per 100 ml of water) was mixed with 5 ml of water, and either 1.0 ml of H_2SO_4 or 1.0 ml of 2.5 N HCl was added to it. The mixture was heated to boiling (20 min), cooled, and brought to volume (100 ml) with water. The mixtures were injected without the addition of an internal standard in order to detect new peaks (if any) in the chromatograms.

Recovery Studies

The efficacy of the procedure was evaluated by performing recovery studies. To accurately measured aliquots of the assay solution, known quantities of the pure drug solution, for three different levels, were added and reanalyzed by the method already described.

RESULTS AND DISCUSSION

The proposed method is simple, accurate, and reproducible. The results (Table 1) indicate that the developed method can be used to quantify betaxolol in pharmaceutical dosage forms. The method is accurate and precise, with a percent relative standard deviation of 0.11 based on 6 readings. Under the proposed conditions betaxolol showed a linear response over a range of 0.1 to 1.0 μg/

Table 1

Assay Results

Product	% Assay	% Recovery
Betaxolol eye drops	99.16	100.01
Tablets	98.30	100.15
Gels	98.65	99.89

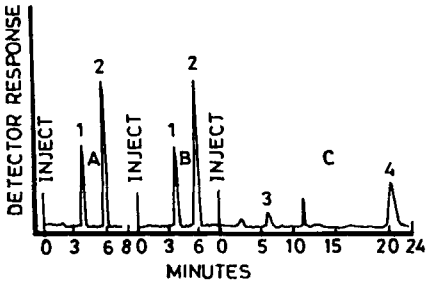

Figure 1. Sample chromatograms. Peaks 1–4 are from betaxolol, trimethoprim, and the products of decomposition, respectively. Chromatogram A is from a standard solution; B from tablets; and C from a solution decomposed using sulfuric acid. For chromatographic conditions; see text.

ml. The correlation factor r was 0.9999. The recovery from the synthetic mixtures was quantitative (Table 1) and there was no interference from the excipients present in the dosage forms.

The decomposition of the solution using sulfuric acid resulted in the formation of two new products [Fig. 1(C)]. The first peak (peak 3) eluted out between the drug and the internal standard. The second peak (peak 4) did not interfere in the assay procedure. In this solution, no betaxolol was left intact.

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