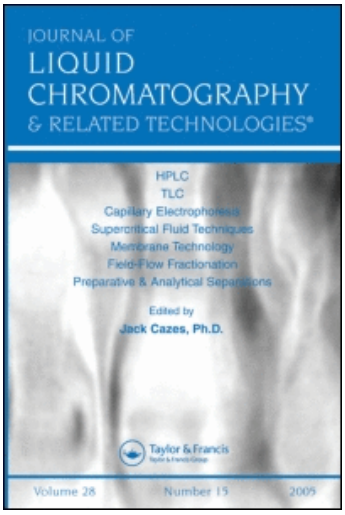

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Determination of Flurbiprofen in Dosage form and in Biological Fluids by High Performance Liquid Chromatography

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DETERMINATION OF FLURBIPROFEN IN DOSAGE FORM AND IN BIOLOGICAL FLUIDS BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

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ABSTRACT

A high performance liquid chromatograpy method is described for the determination of flurbiprofen in both dosage form and in biological fluids (urine and plasma) using fluorescence detection. The method for dosage forms involves grinding of a 100 mg tablet, suspension in methanol, filtration and adjusting to the appropriate concentration and 10 ul is injected onto the column. In the case of biological fluids a series of standard solutions were prepared in 0.1N sodium hydroxide and a known amount was added to 1 ml of serum or urine which was then acidified, extracted with ethylacetate, evaporated and the residue was then dissolved in a known volume of the mobile phase. Complete separation of the drug was achieved in about 6.5 minutes under the used conditions.

INTRODUCTION

Flurbiprofen a 2-(2-fluro-4-biphenylyl) propionic acid is a very strong non-steroidal anti-inflammatory, analgesic and antipyrectic drug (1-4). It was reported that this drug is one of the most potent inhibitors of platlet aggregation currently available. Previous methods of analysis involve gas chromatography (5,6) liquid chromatography (1,7 and 8). The present study reports a simple method for the analysis in both dosage forms and in biological fluids using HPLC.

EXPERIMENTAL

Apparatus

The analysis was carried out using Waters Associates system (Milford, Mass, U.S.A.) which consists of model 6000A solvent delivery system model 420 C with solvent programmer model 660, and 420 E fluorescence detector. The signal output was displayed on Philipps PM 8251 single-pen recorder.

Chromatographic System

A 3.9 ID x 30 cm commercially available stainless steel u-Bondapack phenyl column (Waters Associates) was used. The mobile phase was acetonitrile (filtered through HF Millipore membrane), water (filtered through 0.45 Mm Millipore membrane) 35:65. Each solvent was degassed for 15 minutes by filtration under vacuum. Solvent mixing was carried out using a solvent programmer. The flow rate was 1.5 ml/min. Column back pressure was 1500 PSI and detector gain was 128.

Reagents

Methanol and actonitrile were chromatographic grade obtained from Merck (61 Damstadt, Germany). An authentic sample of Flurbiprofen

(labelled purity 99.3%) was obtained from the Boots Company (Nottingham, England). The standard solution of flurbiprofen was prepared in methanol.

Standard Curve

A fresh solution of flurbiprofen was prepared by dissolving 20 mg in 100 ml methanol, from this stock solution. A series of dilutions were made ranging from 0.5 ug/ml to 20 ug/ml. 15 ul of each of these solutions were injected onto the column in triplicate. The peak height was measured and plotted versus the corresponding concentration injected. The results are shown in Figure 1.

Flurbiprofen in Tablets

Twenty tablets of 100 mg content were accurately weighed and the average weight per tablet was calculated. The tablets were then ground and an accurate weight equivalent to 20 mg of flurbiprofen was taken. The powder was transferred quantitatively into 100 ml volumetric flask with the aid of methanol. The suspension was shaken for 5 minutes and the volume was then adjusted to the mark with methanol. The suspension was filtered through an FH millipore membrane. From the filtrate a series of dilutions were made to cover concentrations ranging from 0.5 - 20 ug/ml. From each solution of this series 15 ul was injected onto the column in triplicate. The average peak height was calculated for each sample and the drug concentration was calculated from Figure 1.

Flurbiprofen in Plasma

A standard curve in plasma was constructed by adding various amounts of stock solution of the drug in 0.1N sodium hydroxide to 1 ml of plasma (collected from a healthy adult male) to give final concentrations of

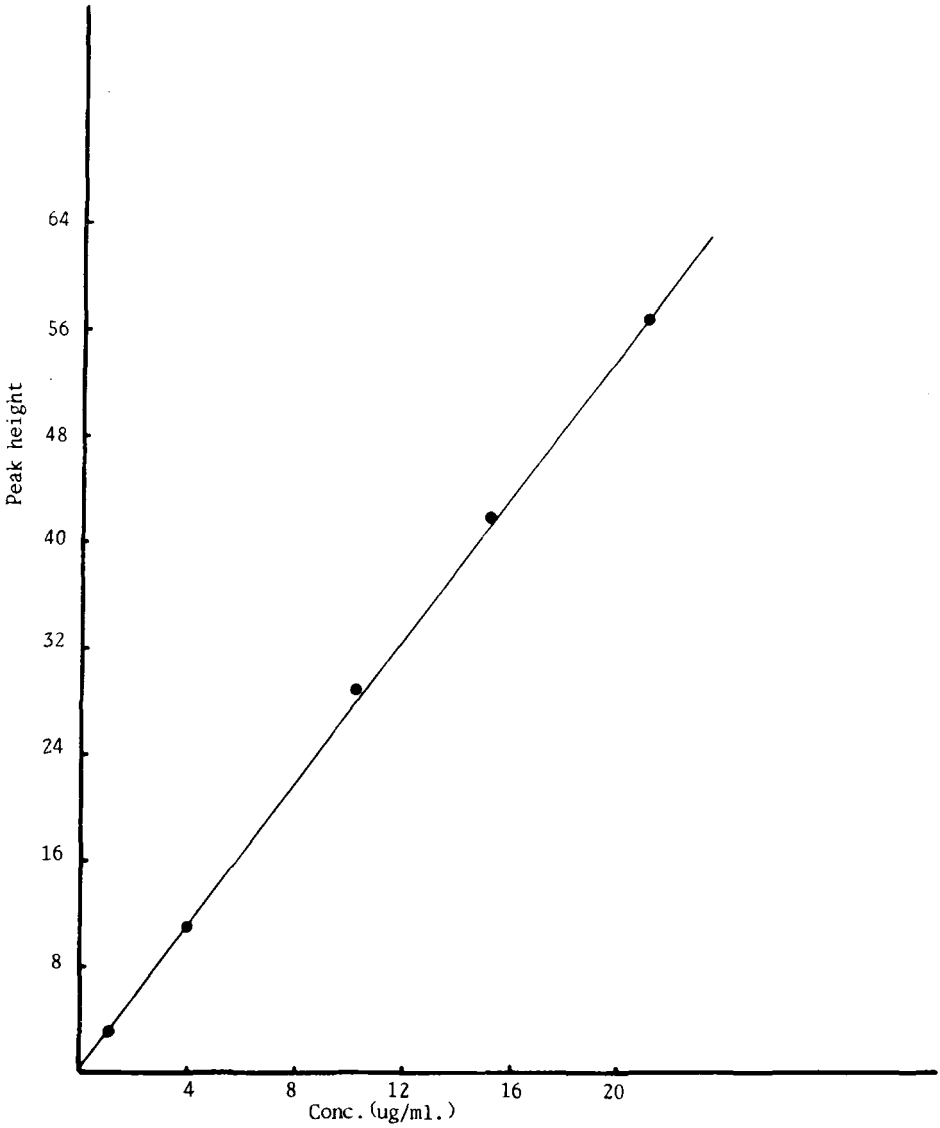

Fig. 1: Standard curve of flurbiprofen when the peak height was plotted versus the concentrated injected.

the drug ranging from 0.5 to 20 ug/ml. The drug was then extracted by adding 1 ml of 1N hydrochloric acid. The drug was then extracted with one portion of 20 ml ethyl acetate, 18 ml of the organic solvent was removed and was evaporated at 60°C under vacuum. The residue was dissolved in 1 ml of the mobile phase and 15 ul of the resulted solution was injected onto the column in triplicate. The results are shown in Figure 2.

Flurbiprofen in Urine

Urine samples were collected from an apparently healthy adult male. In each run, various amounts of the stock solution of flurbiprofen in 0.1N sodium hydroxide were added to 2 ml of urine to give final concentrations ranging from 0 - 20 ug/ml. Extraction of the drug from the urine was performed by acidifying the urine with 1N HCl and each sample was then extracted with two 10 ml portions of ethyl acetate. The combined extracts were then centrifugated for 10 minutes at 2500 r.p.m. 18 ml of ethyl acetate layer was transferred and evaporated at 60°C under vacuum. The residue was dissolved in 0.5 ml of the mobile phase and 25 ul of this solution was injected onto the column in triplicate. The results are shown in Figure 3.

RESULTS AND DISCUSSION

A simple method for the analysis of flurbiprofen in tablets and in biological fluids was developed (plasma and urine) using HPLC and fluorescence detection (excitation 254 nm, emission 337 nm). Typical chromatograms using this method are shown in figures 4,5 and 6. The results when peak height was plotted versus concentration injected from tablets, plasma and urine are shown in figures 1,2 and 3 respectively. The retention time for the drug was 6.5 minutes. The method is sensitive

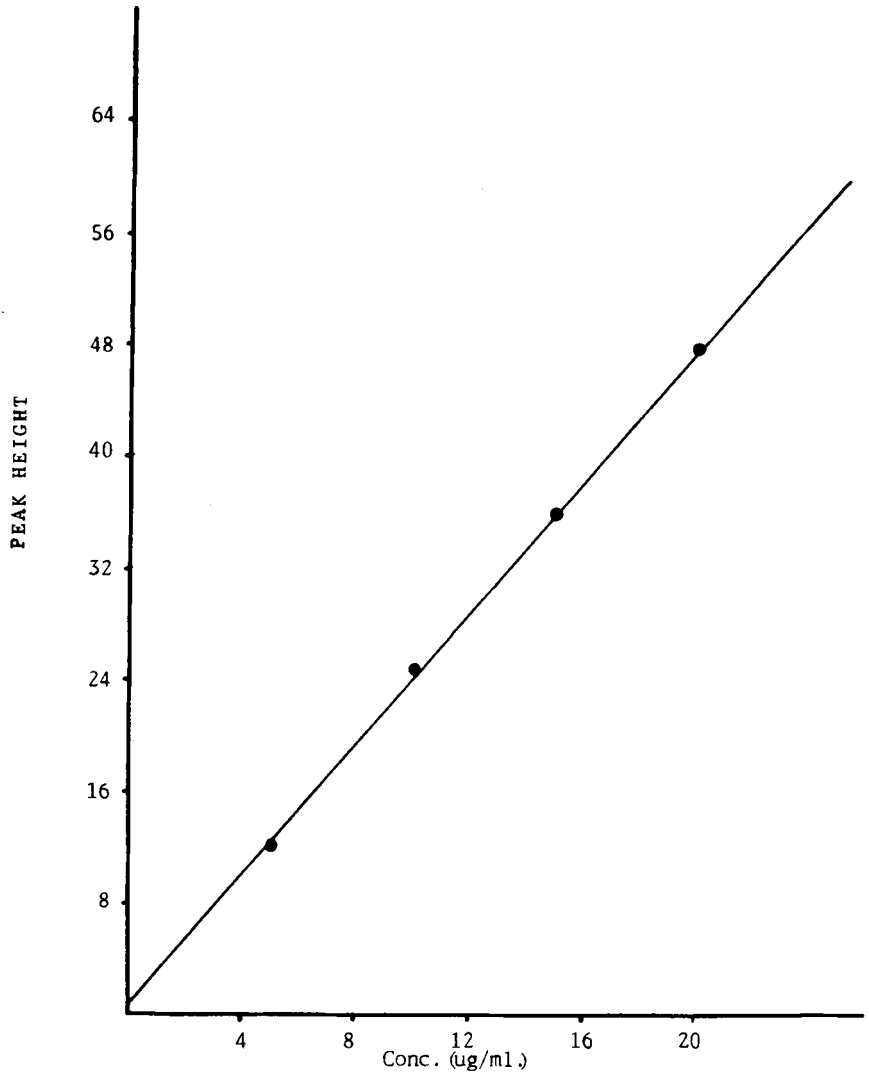

Fig. 2: Standard curve of flurbiprofen extracted from plasma.

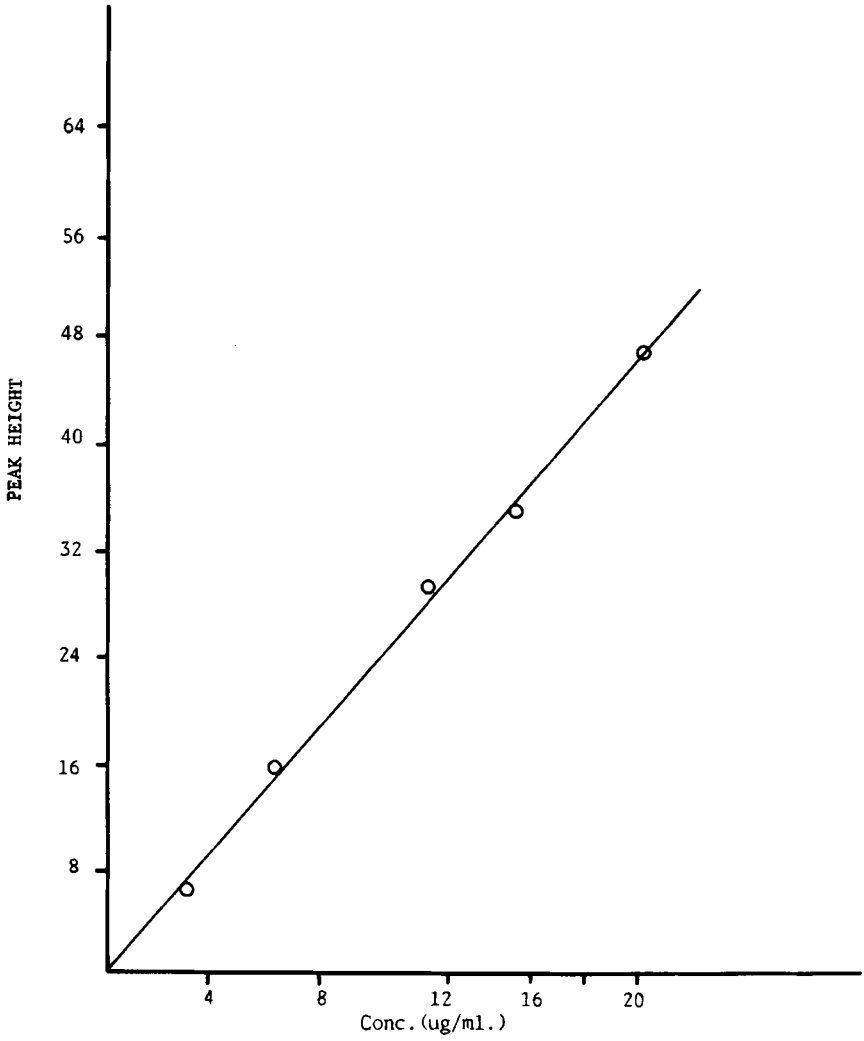

Fig. 3: Standard curve of flurbiprofen extracted from urine.

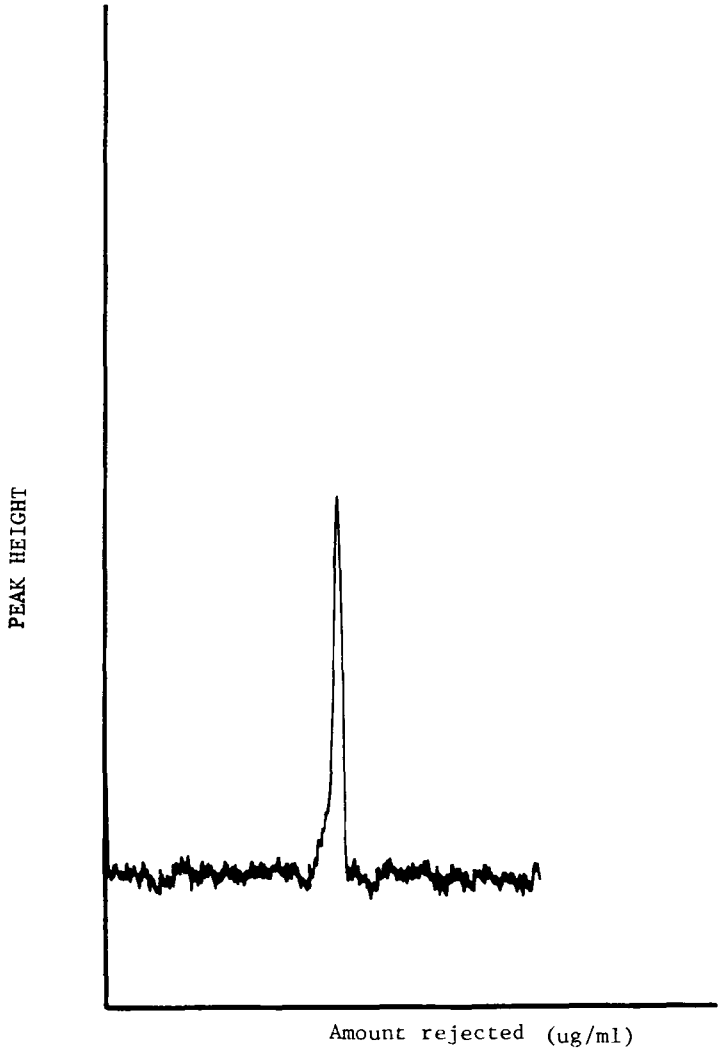

Fig. 4: Typical chromatogram when 15 ul of flurbiprofen standard solution was injected.

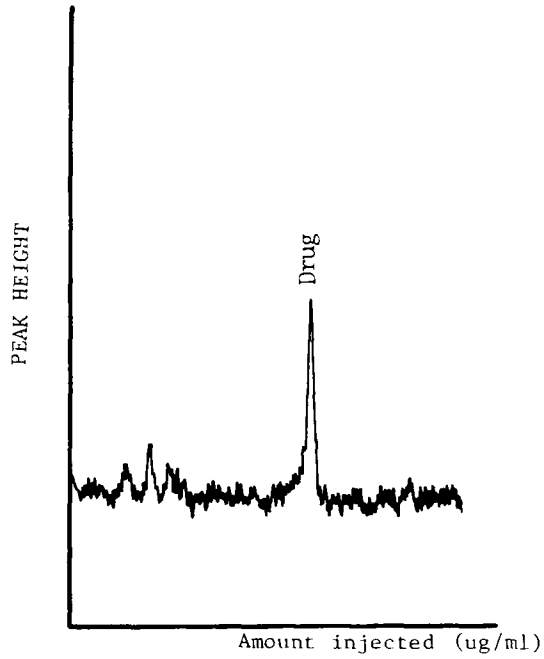

Fig. 5: Typical chromatogram when Flurbiprofen extracted from plasma was injected on HPLC.

and concentrations as low as 0.25 ug/ml (S/N 2; peak height ratio of smallest amount injected to base line noise) could be detected which is adequate for bioavailability studies. The peak heights were linearly correlated to the drug concentration for the standard curves in tablets, plasma and urine with correlation coefficients of 0.987, 0.991 and 0.969 respectively. Interference from other constituents of plasma and urine was minimal and recovery of drug from plasma and urine was 95 - 98%. Sensitivity of this method could be increased by dissolving the residue after evaporating ethyl acetate in 250 ul or even 100 ul of the mobile phase and injecting 50 ul of the constituted solution onto the column.

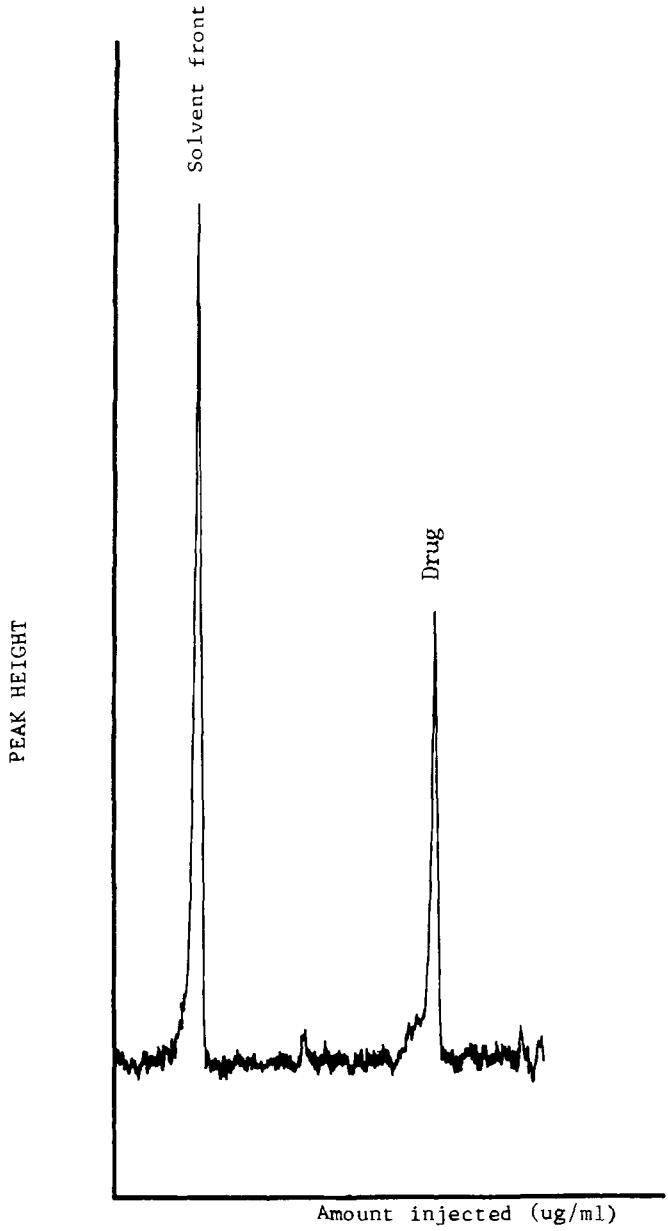

Fig. 6: Typical chromatogram when the flurbiprofen extracted from urine was injected.

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