Quantitative Determination of Terazosin HCl in Tablet Preparation by Fluorimetry

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Accepted 18 December 1997
Received 29 May 1997

A simple and sensitive fluorimetric procedure for the estimation of terazosin HCl in tablet preparation has been developed. The method consists of measurement of fluorescence for the drug samples extracted by methanolic 0.1N H_2 H_2SO_4. The samples showed an excitation at 246 nm and an emission at 382 nm. The linearity was found in the range of 25 - 150 ng/ml. The effect of change in ionic strength of aqueous sulfuric acid solutions on fluorescence intensity of drug sample was also studied.

TERAZOSIN HCl in the form of a tablet is widely used as an anti-hypertensive agent. There is no official method of analysis for the estimation of the drug from its tablet preparations. However, there are HPLC[1] and UV[2] methods available for assay of this drug from its marketed preparations. The literature reported states that terazosin degrades in aqueous acids and alkalis with exposure to temperature[1]. As an extension of our earlier studies on fluorescence measurements of drug substance for their estimation from commercial preparations,[3-6] in this study we report a fluorimetric determination of terazosin HCl from its commercial preparations and also the effect of varying strengths of aqueous sulfuric acid solutions on the fluorescence intensity of terazosin.

A JASCO FP-777 spectrofluorimeter with 1.0 cm cell was used. All reagents used were of analytical reagents. Stock solution of the pure drug was prepared by dissolving 6.25 mg of the drug in 25 ml of methanol in a volumetric flask. A 0.1 ml portion of this solution was transferred to a 25 ml volumetric flask and made up to volume with methanol. Further more, various dilutions were prepared by using the stock solution to obtain concentrations of 25-150 ng/ml in methanolic 0.1N H_2SO_4. The solutions were excited at 246 nm and the fluorescence intensity measurements were made at an emission wavelength of 382 nm.

Twenty tablets (each containing 1 mg of pure drug) were accurately weighed and made to a fine powder. The powder equivalent to 50 µg of pure drug was transferred into a 50 ml volumetric flask and made upto volume with methanol. The solution was filtered through Whatman filter paper No. 1. A 0.5 ml portion of the above filtrate was transferred into a 10 ml volumetric flask and made up to volume with methanolic 0.1N H_2SO_4 to obtain a concentration of 50 ng/ml. The sample solution was excited at 246 nm and the intensity was measured at 382 nm for quantitation of drug in the formulation.

Table 1: Results of Analysis of Commercial Tablets by Fluorimetry

Sample	Lable Claim (mg/tablet)	Amount taken (mg/tablet)	Amount found* (mg/tablet)	% Recovery	CV%
Brand A	1.0	1.0	0.9965	99.65	1.64
Brand A	1.0	1.0	0.9843	98.43	0.76

*Each value is an average of seven determinations

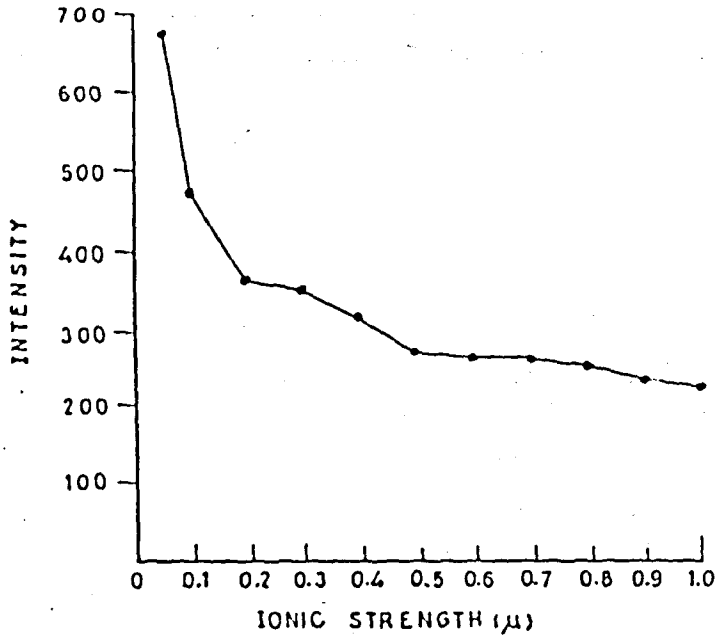

Fig. 1a : Effect of Ionic Strength of Acid Solution on a) Fluorescence Intensity, b) Emission wavelength of Terazosin HCl

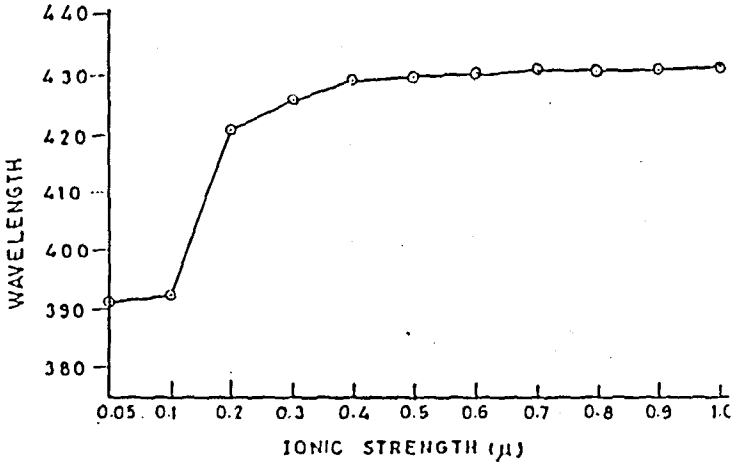

Fig.1 b

To determine the effect of varying ionic strength of aqueous acidic solutions on the fluorescence pattern of the drug, different ionic strength solutions ranging from 0.05N to 1.0N of H_2SO_4 were prepated with each containing 150 ng/ml of drug pipetted from stock solution. The solutions were then excited at 242 nm and their fluorescence intensitites were measured at the maximum emission wavelength.

Terazosin is highly fluorescent in aqueous sulfuric acid solution. The fluorescence intensity was found to be decreasing with an increase in ionic strength of sulfuric acid solution as shown in Fig. 1a. The fall being more at lower values of acid strength than at higher values and which makes it undesirable to do estimation at lower acid strength due to possible fluctuations in intensity values with a small change in acid strength. The emission wavelength was found to shift towards higher wavelength with a change in ionic strength of acid solution as shown in Fig. 1b. The above observations resulted in selecting methanolic 0.1N H_2SO_4 as suitable solvent medium for the quantification of drug from its solutions due to greater stability. The drug

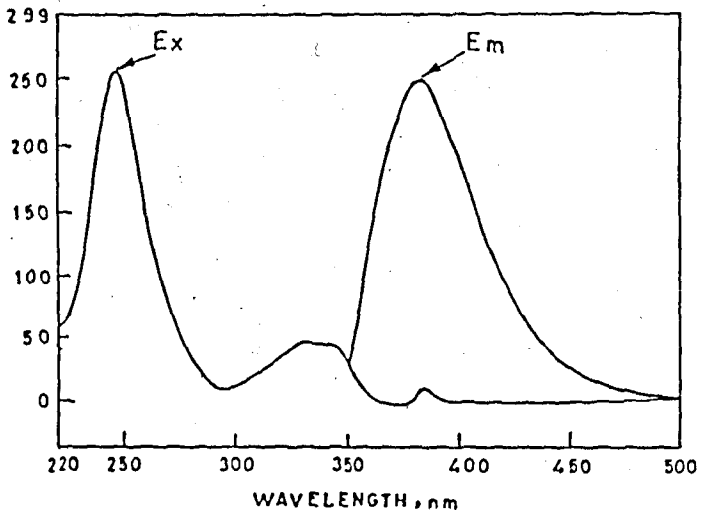

Fig. 2: Excitation (Ex) - Emission (Em) Spectra of 50 ng/ml of Terazosin HCl in Methanolic 0.1 N H_2SO_4

solutions prepared in methanolic 0.1 N H_2SO_4 showed an excitation at 246 nm and an emission at 382 nm (Fig. 2). Further, the drug solutions were found to be linear in the concentration ranges of 25-150 ng/ml. The intensity values of 50 ng/ml standard solution was considerable for the estimation of terazosin from sample mixtures. The

results of the estimation and recovery studies are given in Table 1.

Our results have demonstrated that the developed method is simple sensitive, reproducible and the excipients contained in the formulation do not offer any interference in the determination. Hence, this method can be used for the routine analysis of the drug preparations.

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Formulation and Evaluation of Polymeric Films of Indomethacin For Transdermal Administration

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Accepted 22 December 1997

Received 16 June 1997

Polymeric films of indomethacin were formulated employing ethyl cellulose and polyvinyl pyrrolidone as film formers and evaluated for transdermal administration. The *in vitro* percutaneous absorption of indomethacin through rat abdominal skin was dependent on film composition and initial drug loading dose. The films composed of EC:PVP:Drug (8:2:2 and 8:2:3) exhibited good anti-inflammatory activity over a period of 24 h. Significant ($p<0.01$) prevention of ulcerogenicity of indomethacin was observed by transdermal route compared to oral adminisration.

THE development of technology for the release of drugs at controlled rate to systemic circulation,using skin as port of entry, has become popular for various reasons[1]. The transdermal delivery of a drug to systemic circulation at a desired rate can be achieved by uniform distribution of drug throughout the polymer matrix[2]. The rate of drug release from these matrix diffusion-controlled transdermal drug delivery systems depends on the initial drug loading dose, solubility and diffusivity of drug in the polymer matrix. Further, the rate of drug release can be altered by changing the composition and dimensions of the polymer matrix[3]. The present investigation was carried out to study the influence of polyvinyl pyrrolidone (PVP) and initial drug loading dose on *in vitro* permeation of indomethacin through rat abdominal skin. Further, the promising films were evaluated for their antiinflammatory activity against carrageenan induced rat paw oedema model and ulcer index.

Ethyl cellulose (14cps, S.D Fine Chem), polyvinyl pyrrolidone (loba chemie), dibutyl phthalate (Ranbaxy Laboratories Ltd.) Chloroform (HPLC grade, Qualligens),Carrageenan (Sigma Co.,USA), Indomethacin (gift sample from M/s.Invinex Laboratories, Hyderabad).

The method of Munden *et al*[4] was adopted for the preparation of films. Dibutyl phthalate at a concentration of 30% w/w of dry polymers was used as plasticizer. The thickness of films was measured at five different places using a micrometer (MITOTOYO, Japan) and the mean