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Q-Absorbance and Multicomponent UV Spectrophotometric Methods for Simultaneous Estimation of Propranolol Hydrochloride and Flunarizine Dihydrochloride in Capsules

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ABSTRACT

Two simple UV-Spectrophotometric methods have been developed for simultaneous determination of Propranolol hydrochloride(PRH) and Flunarizine dihydrochloride(FNZ) in capsule dosage form. Methanol was used as solvent. In Method-I (Q-absorbance absorbance ratio) involves formation of Q-absorbance equation at two wavelengths i.e. 272.8 nm (iso-absorptive point) and 253 nm (λ max of FNZ). While, in Method-II (Multicomponent Mode of Analysis) involves the measurement of absorbance at two wavelengths i.e. 289 nm, λ max of PRH and 253 nm, λ max of FNZ. In both these methods PRH and FNZ followed linearity in the concentration range of 08 - 48 µg/ml for PRH and 03 – 18 µg/mL for FNZ at their respective λ max. Both these methods were found to be accurate, precise and rugged as indicated by low values of % RSD. Both these methods were also found to be rapid and economical can successfully be applied for the routine analysis of PRH and FNZ in bulk and combined capsule dosage form.

Keywords: Propranolol Hydrochloride, Flunarizine Dihydrochloride, Q-Absorbance ratio method, Multicomponent mode of analysis.

INTRODUCTION

Propranolol hydrochloride (PRH), 1-(isopropylamino)-3-(1-naphthyloxy)-2-propanol, is a non selective β blocker [1]. It is used in management of hypertension, angina pectoris, and cardiac arrhythmias [2].

Many analytical methods for determination of propranolol have been described such as HPLC [3], UV - spectrophotometric method [4] and HPTLC [5].

Flunarizine (FNZ), (*E*)-1-[Bis(4-fluorophenyl) methyl]-4-(3-phenyl-2-propenyl) piperazine[6], is difluorinated derivative of cinnarizine. FNZ has antihistamine, sedative and calcium channel blocking activity [2]. Several analytical methods have been reported such as GC [7], HPLC [8],

and UV - spectrophotometric method [9] in bulk, pharmaceutical dosage form and in biological fluids for determination of FNZ.

To our knowledge no method(s) have been reported for simultaneous estimation of both drugs in their combined dosage form. In present work, an endeavor has been made to estimate both drugs simultaneously by 'Q -absorbance ratio method' and 'Multicomponent mode of analysis'. Further, methods were validated for precision, accuracy and ruggedness as per USP guidelines [10].

MATERIALS AND METHODS

Chemicals

Propranolol hydrochloride and Flunarizine dihydrochloride supplied as a gift sample by Alkem Pharma Ltd, Mumbai. Methanol (A.R. Grade) was purchased from Merck Ltd., Worli, and Mumbai, India. Capsule (BETACAP PLUS 10) was purchased from local market, containing FNZ 10 mg and PRH 40 mg per capsule.

Instrumentation

A UV-Visible spectrophotometer (Shimadzu 2450 with UV Probe 2.21 software and Shimadzu-1601 for 'Q absorbance ratio method' and 'Multicomponent mode of analysis', respectively)

Selection of common solvent

Methanol of analytical reagent grade was selected as common solvent for developing spectral characteristics of drug. The choice of the solvent was made after evaluating the solubility in different solvents.

Preparation of Stock standard solutions

Stock standard solutions of PRH and FNZ were prepared separately by dissolving 10 mg in 100 mL methanol to obtain concentrations 100 µg/mL of each. From these stock solutions, working standard solutions having concentration 10 µg/mL of PRH and 10 µg/mL of FNZ were prepared by proper dilutions. They were scanned in the UV- region i.e. 400 – 200 nm. The overlain spectrum **(fig.1)** was obtained to determine the maximum absorbance (λ max) and iso-absorptive point.

Study of linearity curves

An appropriate volume of PRH and FNZ in the range of 0.8 - 4.8 mL and 0.3 – 1.8 mL were transferred into series of separate 10 mL volumetric flasks and volume was made up to mark with methanol to get concentrations in the range of 04 – 48 µg/mL and 03 – 18 µg/mL, respectively. The absorbance of these drugs was measured at 289 nm and 253 nm, respectively and calibration curves were plotted as concentrations *versus* absorbances.

Method – I (Q-Absorbance Ratio)

Q-Absorbance method uses the ratio of absorbance at two selected wavelengths, one at iso-absorptive point and other being the λ max of one of the two drugs. PRH and FNZ have λ max at 289 nm and 253 nm, respectively and iso-absorptive point 272.8 nm. The wavelengths selected for analysis were 253 nm and 272.8 nm, respectively. E (1%, 1cm) values of FNZ and PRH were determined at selected wavelengths.

The concentration of two drugs in mixture was calculated by using following equations:

$$C_{PRH} = \frac{Qm - Qy}{Qx - Qy} \times \frac{A}{ax1} \quad (1)$$

$$C_{FNZ} = \frac{Qm - Qx}{Qy - Qx} \times \frac{A}{ay1} \quad (2)$$

Where,

$$Qm = \frac{\text{Absorbance of sample at 253 nm}}{\text{Absorbance of sample at 272.8 nm}}$$

$$Qx = \frac{\text{E (1 \% 1cm) of PRH at 253 nm}}{\text{E (1 \% 1cm) of PRH at 272.8 nm}}$$

$$Qy = \frac{\text{E (1 \% 1cm) of FNZ at 253 nm}}{\text{E (1 \% 1cm) of FNZ at 272.8 nm}}$$

'A', is the absorbance of mixture at 272.8 nm and ax1 (162.66), ax2 (47) and ay1 (163), ay2 (633) are E (1%, 1 cm) of PRH and FNZ at 272.8 nm and 253 nm and Qm= A2/A1, Qy = ay2/ay1 and Qx = ax2/ax1.

Method – II (Multicomponent mode of analysis)

Six mixed standard solutions of PRH and FNZ in the ratio of 1:4 µg/mL were prepared in methanol. All the standard solutions were scanned over the range of 400 - 200 nm, in the multicomponent mode, using two sampling wavelength 289 nm (λ max of PRH) and 272.8 nm (λ max of FNZ). The data from these scans were used to determine the concentrations of two drugs in capsule sample solutions.

Analysis of Capsule Formulation

The content of twenty capsules were accurately weighed and crushed into fine powdered. A quantity of powder equivalent to 40 mg of PRH and 10 mg of FNZ was transferred to 100 mL volumetric flask containing 60 mL methanol, shaken manually for 20 min and the volume was made up to the mark and filtered through Whatmann filter paper (no.41). The solution was further diluted with methanol to give the concentration within Beer's Law range. Absorbance of this solution was measured at 253 nm and 272.8 nm and concentrations of these two drugs in the sample were calculated using equation (1) and equation (2) (Method I). The same sample solutions were subjected to analysis in the multicomponent mode of instrument (UV-Spectrophotometer 1601). The solution was scanned over the wavelength range of 400 - 200 nm and the concentration of each drug were determined by analysis of spectral information of the sample solution with reference to the mixed standards (Method II). The analysis procedure was repeated six times with capsule formulations. The results of analysis are reported in **Table- 1.**

RESULTS AND DISCUSSION

In methanol, PRH and FNZ obeyed linearity in the concentration range of 08 - 48 µg/mL, and 03 - 21 µg/mL, respectively at their respective λ max with correlation coefficient ($r^2 > 0.99$) in both the case. Marketed brand of capsule were analyzed. The amounts of PRH and FNZ determined by 'Method I' was found to be 100.49 and100.41, respectively; while, by 'Method II', it was found to be 100.82 and 101.08, respectively. In both these methods precision was studied as repeatability (% RSD < 2) and inter and intra-day variations (%RSD < 2) for both drugs. The accuracy of method was determined by calculating mean percentage recovery. It was determined at 80,100 and 120 % level. The ruggedness of the methods was studied by two different analysts using the same operational and environmental conditions. The % recovery, repeatability data, ruggedness data are presented in **Table-2.**

Table-1: Results of simultaneous estimation of marketed formulation (BETACAP PLUS 10) for Method I and II

Method	Drug	Label claim (mg/capsule)	% label amount	%RSD
I	PRH	40	100.49	0.442
	FNZ	10	100.41	0.454
II	PRH	40	100.82	0.845
	FNZ	10	101.08	0.697

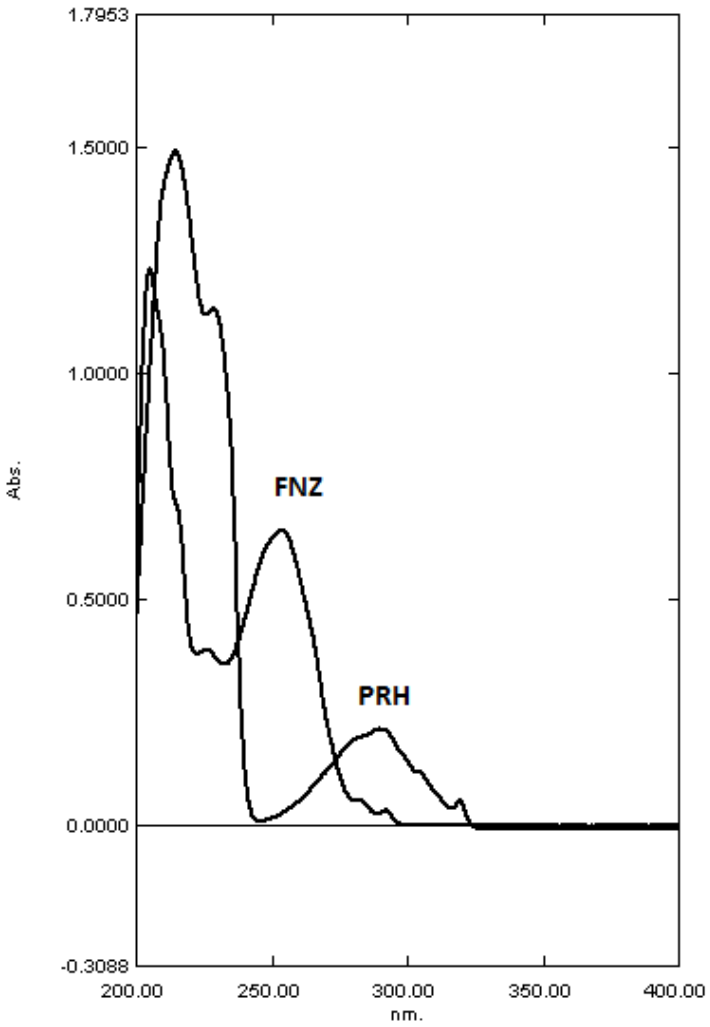

Fig. 1 Overlay spectra of PRH (10mg/mL) and FNZ (10mg/mL)

Table 2: Validation Parameters

Parameter	PRH		FNZ	
	Method I	**Method II**	**Method I**	**Method II**
Working Wavelengths	289	289	253	253
Linearity range (µg/mL)	04 - 48	04 – 48	03 - 18	03 - 18
Precision(%RSD)				
Inter-day [n = 3]	0.26 - 1.27	0.11 - 1.68	0.27 - 1.20	0.18 - 1.98
Intra-day [n = 3]	0.07 -0.64	0.09 - 0.64	0.06 - 0.70	0.13 - 0.87
Repeatability [n = 6]	0.43	0.63	0.49	0.79
Ruggedness [%RSD]				
Analyst I [n = 6]	0.68	0.75	0.68	0.93
Analyst II [n= 6]	0.71	0.85	0.70	0.53
% Recovery [n = 9]				
	100.08 -100.41	99.47 - 100.66	100.08 - 100.81	99.27 - 101.25
%RSD	0.35 - 0.88	0.92 - 1.35	0.31 - 0.84	0.96 - 1.48

CONCLUSION

Both developed methods are found to be accurate, precise and rugged. Further, the developed methods are economical and simple and can usually be used for estimation of both these drugs in their combined dosage form.

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