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Simultaneous Estimation of Flunarizinedihydrochloride and Propranolol hydrochloride in Bulk Drug and Capsule

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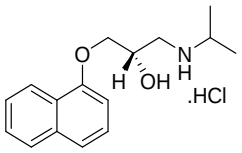
Abstract: The present study deals with UV spectrophotometric method development & validation for simultaneous estimation of Flunarizinedihydrochloride&Propranolol hydrochloride in bulk drug &capsule dosage form by simultaneous equation (Method I)and Q-analysis/absorption ratio method(Method II).The wavelengths selected for the Method I are 253nm and 289nm λmax of Flunarizine and Propranolol respectively&forMethod II wavelengths selected are262.2 nm (isobestic point at which both the drugs exhibit equal absorbance) and 289 nm (λ_{max} of Propranolol hydrochloride). The linearity of Flunarizinedihydrochloride&Propranolol hydrochloride was found to be in the range of 1-23 µg/ml &4-48 µg/ml respectively. The % recovery of Flunarizinedihydrochloride&Propranolol hydrochloride was found out to be 98.49 – 101.06 % (Method I) and 99.82 – 100.86% (Method II).The proposed method was validated as per ICH guidelines.
Keywords: Flunarizinedihydrochloride, Propranolol hydrochloride, Simultaneous equation method, Q-Analysis method.

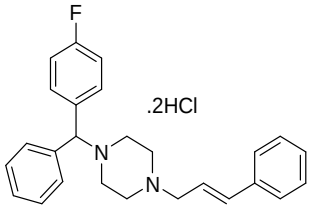
Introduction

Flunarizinedihydrochloride [30484-77-6] [FLU] chemically is (E)-1-[Bis(4-fluorophenyl)methyl]-4-(3-phenyl-2-propenyl) piperazine dihydrochloride. It is a calcium channel blocker which reduces arterial and arteriolar smooth muscle spasm by reducing intracellularCa^{2+} overload due to brain hypoxia. It is used in migraine prophylaxis and also as antihistaminic & sedative. Propranolol hydrochloride [525-66-6] [PRO] chemically is (2RS)-1-[(1-methylethyl) amino]-3-(1-naphthalenyloxy)-2-propanol hydrochloride. Propranolol Hydrochloride is a non-selective beta blocker, that is, it blocks the action of epinephrine on both β1- and β2-adrenergic receptors.It isused for the treatment of angina pectoris, cardiac arrhythmia, hypertension, anxiety attacks, migraine prophylaxis and glaucoma.So FLU and PRO these drugs are used in combination for migraine prophylaxis[1, 2]. Literature survey revels that various analytical methods as like UV[3-4], HPLC[5-10], HPTLC[11] and GC[12] are reported for the individual drug and in combination with others and one paper on UV using methanol as solventfor simultaneous estimation of FLU and PRO[13].Therefore, in the present work a successful attempt has been made to estimate both these drugs simultaneously by simple UV spectrophotometric methods using methanol & water. The present paper describes a simple, accurate,precise and economic method for

simultaneous estimation of FLU and PRO in bulk drug and sustained release capsule dosage form FLU &PRO are official in B.P.[14] and I.P.[15]respectively.



Propranolol hydrochloride



Flunarizine dihydrochloride

Objective

The present research work deals with the simultaneous determination using simultaneous equation method and Q-analysis method.

Experimental Method

Solubility Studies

PRO is freely soluble in water but FLUsparingly soluble in water (on sonication for 5 min freely soluble), while both are freely soluble in methanol. Hence for simultaneous determination methanol &water was selected as solvent system.

Instrumentation

The instrument used was Shimadzu double beam UV/Vis spectrophotometer model V- 1800. (UV Probe 2.32 software).Weighing was done on electronic single pan weighing balance (Make:Shimadzu Model: AX 200).

Materials

Flunarizinedihydrochloride (FLU) drug sample was gifted by FDC India Ltd. Jogeshwari (Mumbai, India) and Propranolol hydrochloride (PRO) drug sample was gifted by Shreepati Pharmaceuticals Pvt. Ltd. Indore (M.P., India), and were used without any further purification. Methanol (A.R. Grade) was purchased from LOBA Chem. Capsule (BETACAP PLUS 10) was purchased from local market, containing Flunarizine dihydrochloride 10 mg and Propranolol hydrochloride 40 mg per capsule.

Preparation of Standard Stock Solutions

Standard stock solutions of FLU and PRO were prepared separately by dissolving 10 mg of each drug in 10ml of methanol to get standard stock solution of 1000 µg/ml respectivelyand 1 ml was pipette out and further volume was made up to 10 ml with distilled water to obtain concentration of 100 µg/ml. Further dilutions were made in distilled water from stock solution to get concentrations of1-23 µg/ml of FLU & 4-48 µg/ml of PRO.

Experimental Method

Method I

Simultaneous Equation Method

FLU &PRO dilutions were prepared from 100ug/ml stock solution to get concentrations of 1-23 µg/ml &4-48 µg/ml respectively. The solutions were scanned at each wavelength i.e. 253nm and 289nm λmax of FLU and λmax of PRO. The calibration curve was plotted. The concentration FLU and PRO was calculated using following equations:

$$Cx = A_2\, ay_1 - A_1\, ay_2 / ax_2\, ay_1 - ax_1 ay_2 \quad \text{.....(i)}$$

$$Cy = A_1\, ax_2 - A_2 ax_1 / ax_2\, ay_1 - ax_1 ay_2 \text{.....(ii)}$$

Where, Cx andCy are concentration in µg/ml of FLUand PRO, A_1 and A_2 are absorbance of sample at 253nm and 289nm, respectively. ax_1 is theabsorptivity of FLU at 253nm, ax_2 is the absorptivity of FLU at 289nm, ay_1 is the absorptivity of PRO at 253 nm, ay_2 is the absorptivity ofPRO at 289nm.

Method II

Q-Analysis Method or Absorption Ratio:

In this method absorbances are measured at two wavelengths. One being 262.2nm wavelength of iso-absorptive point obtained by overlay spectra of FLU and PRO (Fig.1) and 289nm the λmax of PRO. Then absorbance of both drugs was recorded on selected wavelengths. Concentrations of FLU&PRO were calculated by using following equations.

$$C_{Flu} = Q_m - Q_y / Q_x - Q_y \times A_1 / ax_1 \text{.....(iii)}$$

$$C_{Pro} = Q_m - Q_x / Q_y - Q_x \times A_1 / ay_1 \text{.....(iv)}$$

Where, Qm is ratio of absorbances A_1 and A_2 of sample solution at $_1$ and λ_2 (isobestic point wavelength and λmax of PRO)Qx is ratio of absorptivitiesax_1 and ax_2 of standard solution at λ_1 and λ_2. Qy is ratio of absorptivitiesay_1 and ay_2 standard solution at λ_1 and λ_2. C_{Flu} and C_{Pro} are concentrations of FLU&PRO.

Procedure for the Analysis of Capsule Formulation

Ten capsules containing label claim of 10 mg of FLU and 40 mg of PRO were weighed and content finely powdered. Equivalent weight of the powderedcapsule was accurately weighed, transferred into a 100 ml flask, dissolved in

methanol to get concentration of 100ug/ml and this solution was sonicated for about 30 minutes then volume was made up to 10 ml and filtered to separate any insoluble matter.The clear solution obtained was diluted to get appropriate concentration with distilled water. The concentrations of two drugs in the mixture were calculated using above equations (i & ii) for Method I and (iii &iv) for Method II.

Validation of UV Method.

Validation of the UV method was done with respect to following parameters[16].

1) Linearity and Range

The standard solutions of both FLU &PRO were scanned in the range of 400-200 nm against solvent distilled waterand absorbance was measured at λmax of 253nm and 289nm respectively.

The stock solution was diluted with distilled water to reach a concentration range 1-23 µg/ml for FLU and 4-48 µg/ml for PRO. The absorbance was plotted against the corresponding concentrations to obtain the calibration graphs.

2) Accuracy

Recovery studies was carried out by applying the method to drug sample to which known amount of FLU and PRO corresponding to 80, 100, 120% of label claim has been added (standard addition method).

3) Precision

The standard solutions of drug sample were prepared and analyzed.The tablet assay was performed to determine reproducibility and repeatability. The percentage relative standard deviation (RSD %) was found to be within limits.

Table 1: The Method Was Validated As Per ICH Guidelines

Parameters	**Method I**		**Method II**	
	FLU (253nm)	PRO (289nm)	Isobestic point (262.2nm)	PRO (289nm)
Linearity range(µg/ml)	1-23 µg/ml	4-48 µg/ml	1-23 µg/ml	4-48 µg/ml
Correlation coefficient (r^2)	0.999	0.999	0.999	0.999
Interday	0.95	0.47	0.93	0.45
Intraday	0.93	0.45	0.91	0.42
Slope	0.0416	0.0196	0.0426	0.0199
Intercept	0.0066	0.0106	0.0059	0.0101

Table 2: Result Of Recovery Studies

Level of Recovery % of Label claim	Drug	Amt of Drug Added µg/ml	Amt of drug std added µg/ml	Method I			Method II		
				% Recovery	S.D. ±	%RSD	% Recovery	S.D. ±	% RSD
80	FLU	5	3	99.70%	0.3172	0.31	99.83	0.4346	0.43
80	PRO	20	16	98.49%	0.1150	0.11	100.16	0.1513	0.15
100	FLU	5	5	99.4%	0.2645	0.26	100.86	1.0010	0.99
100	PRO	20	20	99.19%	0.4003	0.40	99.82	1.1994	1.20
120	FLU	5	7	101.06%	0.4618	0.45	99.83	0.3728	0.37
120	PRO	20	24	99.65%	0.2218	0.22	98.88	0.1069	0.10

*n= 9 determinants S.D.-Standard Deviation %RSD – Percent relative standard deviation

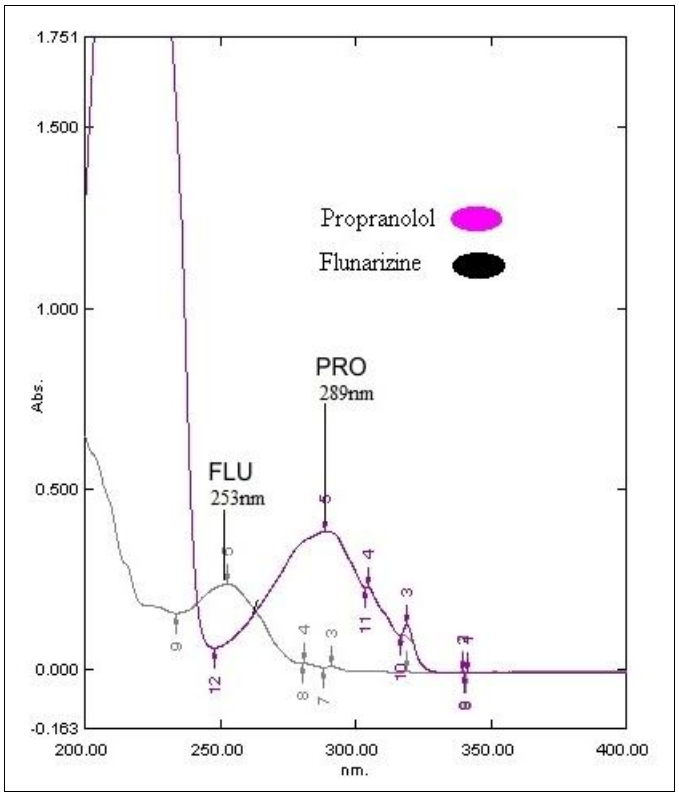


Fig.1. Overlay spectra of FLU and PRO for simultaneous estimation method.

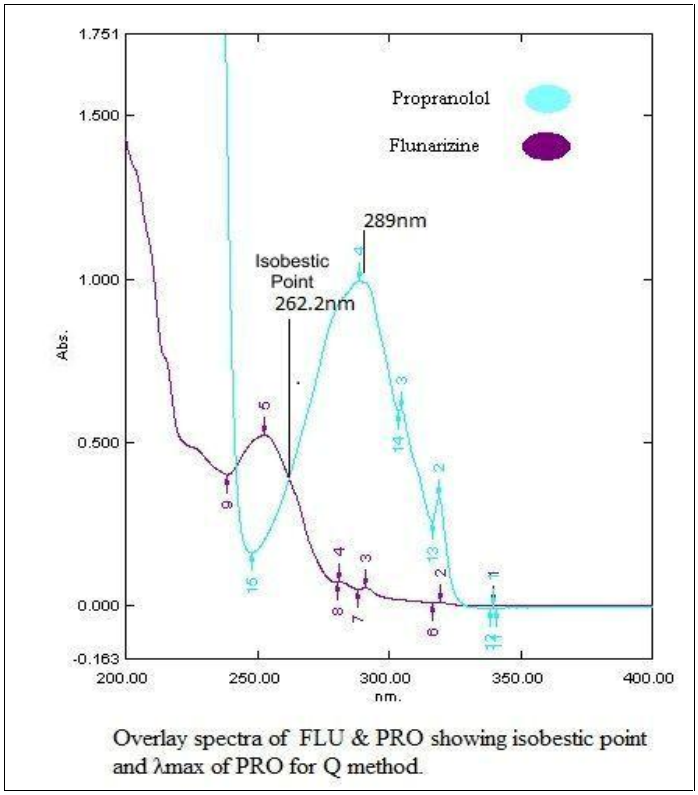


Fig. 2: Overlay spectra of FLU & PRO showing Isobestic Point & max of Pro for Q method

Results &Discussion

The present work provides an accurate, rapid, sensitive, economic method for the simultaneous analysis of FLU &PRO in bulk and capsule formulation. Linear relationships between drug concentrations were obtained over the range of at 1-23&4-48 µg/ml for FLU and PRO respectively. The correlation coefficient, slope and intercept obtained for each drug is as shown in Table1. The proposed method was also successfully applied to a pharmaceutical formulation. The % assay was found to be 99.81 for FLU and 99.28 for PRO by Method I and 99.69% for FLU and 99.13% for PRO by Method II. No interference was observed from the pharmaceutical adjuvants. Recovery studies results are tabulated in Table 2.For FLU percent recovery ranged from 99.4% - 101.06% andPROpercent recovery ranged from 98.49% - 99.65% for Method I, while 99.83-100.86% recovery of FLU and 99.82-100.16 % recovery of PRO by Method II. Hence, the proposed methods were evaluated statistically and were validated in terms of linearity, precision and accuracy.

Conclusion

The result demonstrates that simultaneous equation method and Q-Analysis method employed enables quantitation of mixture of FLU and PRO with good accuracy and precision in bulk drug and pharmaceutical formulation. Thus, it can be easily and conveniently adopted for routine quality control analysis.

Acknowledgement

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