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Research Article

Spectrophotometric estimation of naftopidil in bulk and dosage form

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ABSTRACT
A simple, sensitive, accurate, precise, reproducible and inexpensive UV Spectrophotometric method has been developed and subsequently validated for the determination of Naftopidil in bulk and its pharmaceutical formulation. Methanol was used as a solvent in the present investigation. The UV spectrum was scanned between 200 to 400 nm and 232 nm was selected as maximum wavelength for absorption. Beer's law was obeyed in the concentration range of 2-10 µg/ml with correlation coefficient r = 0.9994.The percent recoveries of naftopidil were found to be 99.75 to 100.293.The intra and inter day precision percent relative standard deviation values in the range of 0.41 to 0.86 and 0.33 to 0.74.The LOD and LOQ were found to be 0.089 µg/ml and 0.27197 µg/ml. The method has been successfully utilized to determine the naftopidil in tablets and can be extended for routine analysis in bulk drugs. Results of the analysis were validated as per ICH guidelines.
Key words: Naftopidil, UV Spectrophotometric method, Methanol,Validation

INTRODUCTION

Naftopidil, a phenopermine derivative (Fig.1) was first synthesized in 1970s and introduced into clinical trial as a new antihypertension agent. It is a selective α_1-adrenoreceptor antagonist, a calcium antagonist and a 5-HT_1A agonist[(1)].It is a renal urological drug that is utilized extensively for the treatment of arterial hypertension and benign prostatic hypertrophy(BPH)[(2)].

Literature survey revealed that some HPLC[(3-8)] and phosphorimetric methods[(9,10)] reported for the estimation of naftopidil. So far, no UV Spectrophotometric method has been reported for the determination in dosage form. The aim of the study was to develop simple, sensitive, accurate, precise, reproducible and in expensive UV Spectrophotometric method[(11)] for the estimation of naftopidil in bulk and dosage form.

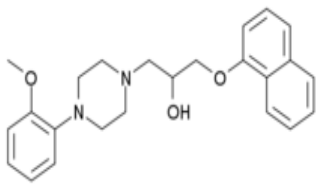

Fig.1 Structure of Naftopidil

MATERIALS AND METHODS

Instruments used: An Elico model SL 159 UV-Visible Single beam spectrophotometer with 1cm matched quartz cells were used for recording spectra and absorbance measurements. A schimadzu electronic analytical balance (AX-200) was used for weighing the sample. An ultrasonic 3.5L 100H (Pci) was used for sonicating the sample solution.

Reagents: Pure sample of naftopidil was supplied by Sun pharma, Baroda. All reagents used were of analytical grade and were obtained from Qualigens fine chemicals,Mumbai. Formulation was purchased from local market.

Preparation of standard stock solution:

10 mg of naftopidil was accurately weighed and transferred to 100 ml volumetric flask .20 ml of methanol was added and sonicated for 30 min. The volume was made up to the mark with methanol to give 100 ug/ml solution.

Preparation of standards for calibration curve:

To prepare calibration standards,0.2,0.4,0.6,0.8,1ml of working standard solutions were diluted to obtain drug concentrations of 2 ,4,6,8,10 µg/ml and linearity was studied. Linearity relationship was observed in the range 2 to 10 µg/ml against a reagent blank as reference at 232 nm. (Table 1)

Analysis of marketed formulations:

Tablet powder equivalent to 10 mg of naftopidil was weighed and transfer into 100ml volumetric flask .20 ml of methanol was added and sonicated for 30 min .The final volume was made up to the mark with methanol to give 100 µg/ml solution. From this stock solution, various dilutions of the sample solution were prepared and analysed. (Table 4)

Method validation

The optimized Spectrophotometric method was completely validated according to the procedures described in ICH guidelines Q2 (R1) for the validation of analytical methods (ICH, 2005) [(12)].

Accuracy

For the accuracy of proposed method, recovery studies were performed by standard addition method at three different levels (50%, 100% and 150% of final concentration).A known amount of pure drug was added to pre-analyzed tablet powder and the sample was then analyzed by proposed method. Results of recovery studies were found to be satisfactory and reported in table 3.

Precision

The precision of the method was determined by repeatability and intermediate precision (intra-day and inter-day).

Repeatability

The Repeatability of the proposed method was ascertained by actual determination of six replicates of fixed concentration of the drug within the Beer's range and finding out the absorbance by the proposed method. From this absorbance %RSD was calculated. (Table 2)

Intra-day precision

Intra–day precision was determined by analyzing three different concentration of drug (4 µg/ml, 6 µg/ml, 8 µg/ml) for three times in the same day. %RSD was calculated. (Table 2)

Inter-day precision

Inter-day precision was determined by analyzing three different concentration of drug (4 µg/ml, 6 µg/ml, 8 µg/ml) for three days in a week. %RSD was calculated. (Table 2)

Ruggedness

Ruggedness of the proposed method was determined by analysis of aliquots from slot in different laboratories using similar operational and environmental condition. The readings were shown in table 5.

Limit of detection and Limit of quantification:

Limit of detection (LOD) and Limit of Quantification (LOQ) were determined by using the formula based on the standard deviation of the response and the slope.LOD and LOQ were calculated by using equations, LOD=3.3 $\Delta x/s$ and LOQ=10 x Δ/s,where Δ=standard deviation, S= slope of the calibration curve.(Table 2)

RESULTS AND DISCUSSION

The present study describes a highly sensitive, economic, accurate, precise and reproducible method for the determination of naftopidil. The Beer's law was obeyed in the concentration range 2-10 µg/ml with correlation coefficient 0.9994.The linear regression equation was found Y=0.1131x – 0.0019.The percentage recovery values of pure drug from the analyzed formulation were in between 99.75% - 100.293%.The precision of the proposed method was checked in terms of the repeatability, inter-day and intra-day time periods and %RSD was found to be less than 2%.LOD and LOQ were found to be 0.089 µg/ml, 0.27197 µg/ml respectively. The assay values for marketed formulation were found to be within limit. Hence the results of the analysis were validated and recovery studies were carried out as per ICH guidelines. Therefore the newly developed method was successfully applied in tablet dosage form.

CONCLUSION

The proposed analytical method is rapid, accurate, precise and reproducible and hence can be used for the routine analysis of naftopidil in bulk, tablet dosage forms. High percentage recovery showed that the method was free from interference of excipients used in the formulation.The most striking features of the method is its simplicity and rapidity, not requiring tedious sample preparations such as extraction of solvents, heating, degassing which are many needed for HPLC procedure.

Values of LOD and LOQ showed that the proposed method was sensitive enough to analyze the drug in bulk as well as in its pharmaceutical formulation. All the above result indicates that, the method employed here is very simple, accurate, economic and rapid for routine analysis of the naftopidil.

Fig.2 UV spectra of Naftopidil in Methanol

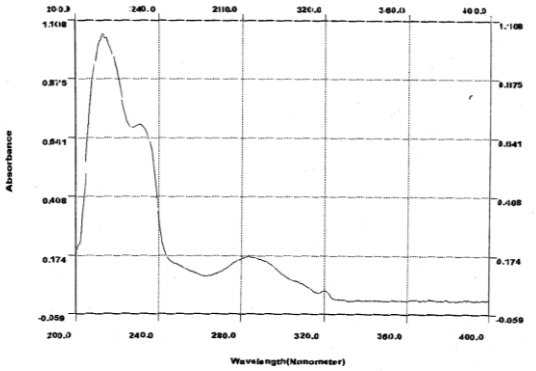

Table 1.Linearity data of naftopidil

Conc(µg/ml)	Absorbance
2	0.219
4	0.457
6	0.686
8	0.877
10	1.143

Fig.3 Calibration curve of Naftopidil.

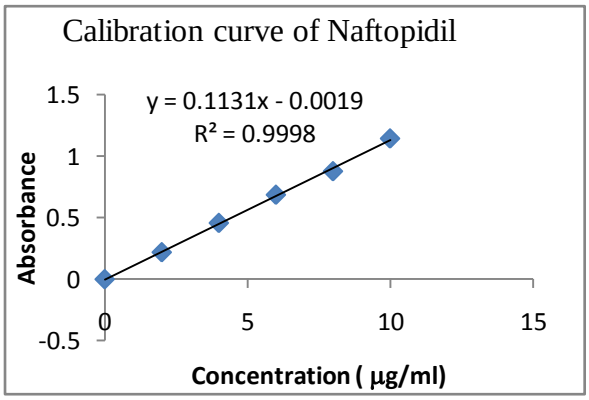

Table 2.Optical characteristics and validation parameters of the proposed method

Parameters	**Result**
Measured wavelength(λmax)	232 nm
Beers law limit(µg/ml)	2-10
Molar absorptivity(lit/mole/cm)	$4.4116x10^4$
Specific absorbance $A^{1\%}_{1cm}$	1124.01
Sandell's sensitivity (µg/cm^2/0.001 absorbance unit)	0.0088417
Regression equation (y=mx+c)	0.1131x-0.0019
Slope(b)	0.1131
Intercept(a)	-0.0019
Correlation coefficient(r)	0.9994
Validation parameters	
Repeatability (%RSD, n=6)	0.45
Inter-day precision(%RSD, n=6)	0.33-0.74
Intra-day precision(%RSD, n=6)	0.41-0.86
LOD(µg/ml)	0.08975
LOQ(µg/ml)	0.2719

Table 3.Results of % recovery data (accuracy) for tablet

Levels	Amount of drug (tablet)taken(µg/ml)	Amount of pure drug added(µg/ml)	Amount of drug recovered(µg/ml)	% Recovery
50%	2	1	2.9925	99.75
100%	2	4	6.0175	100.29
150%	2	7	9.0144	100.16
			Mean %recovery 100.06 SD 0.281	

Table 4.Analysis of marketed formulations

Formulation	Labeled Amount(mg)	Amount obtained(mg)	%Drug present	%RSD
Nafodil 75	75	74.95±0.3391	99.898	0.46

(* each value is average of six determinations ± standard deviation)

Table 5.Ruggedness data

Amount taken (mg/ml)	ELICO SL 159		SHIMADZU PHARMA SPEC 1700	
	Amount found (mg/ml)	%RSD	Amount found (mg/ml)	%RSD
6 6 6	5.95 5.92 5.93	0.26	5.97 5.96 5.99	0.26

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