



Extractive visible spectrophotometric determination of naftopidil in pharmaceutical preparations

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ABSTRACT

A simple, sensitive, rapid and accurate extractive visible spectrophotometric method has been developed for the determination of Naftopidil in pure and in pharmaceutical formulations. The method is based on the formation of orange red colored chloroform extractable ion-pair complex between the basic nitrogen of the drug and acidic dye Tropaeolin ooo (TPOOO) in the presence of 0.1M HCl with an absorption maximum of 502.0 nm. The conditions necessary for the assaying the drug are established. The calibration graph is linear over the concentration range of 4-24µg/ml. The proposed method is applied to commercial available tablets or capsules and the results are statistically compared with those obtained by the UV reference method and validated by recovery studies. The method offers the advantages of rapidity, simplicity and sensitivity and low cost and can be easily applied to resource poor settings without the need for expensive instrumentation and reagents.

Key words: ACE inhibitor, Beer's Law, Chloroform, Extraction Spectrophotometry, Tropaeolinooo



INTRODUCTION

Naftopidil is a phenyl piperazine derivative and alpha 1-adrenoceptor antagonist chemically it is 1-[4-(2-methoxyphenyl) piperazine-1-yl] -3-(1-naphthyloxy) propan-2-ol. It is used for the bladder outlet obstruction in patients with benign prostatic hyperplasia (BPH) and utilized extensively for the treatment of arterial

hypertension. Naftopidil has distinct characteristics because it has a three times greater affinity for the $\alpha 1D$ -adrenergic receptor subtype than for the $\alpha 1A$ subtype. Naftopidil is strongly suppressed cell proliferation of stromal cells, resulting in decreased tumorigenic soluble factor, suggesting that Naftopidil might be effective in preventing stromal support of tumor cells.

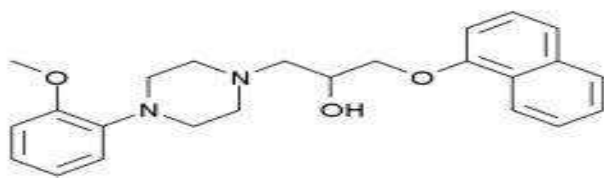


Fig. 1: Showing the chemical structure of NFPD

NFPD is official in USP and BP which describes HPLC and potentiometric titration method for its assay in tablets. Literature survey revealed that several analytical techniques which include HPLC, HPTLC, LC-MS, GC, Voltametry, Radioimmunoassay, Capillary electrophoresis, ion selective electrode potentiometry, atomic

absorption Spectrophotometry, Spectrofluorometry, visible spectrophotometric and UV have been reported for quantitative determination of NFPD in biological fluids and pharmaceutical formulations. The main purpose of the present study was to establish a relatively simple, sensitive, validated and inexpensive extractive visible spectrophotometric method for the determination of NFPD in pure form and in pharmaceutical preparations, since most of the previous methods involve critical reaction conditions or tedious sample preparations and less specificity. So the authors have made some attempts in this direction and succeeded in developing a method based on the reaction between the drug and acidic dye Tropaeolin ooo in the presence of 0.1M HCl. The method can be

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extended for the routine quality control analysis of pharmaceutical products containing NFPD. As the extraction spectrophotometric procedures are popular for their sensitivity and selectivity in the assay of drugs, the acid dye technique was therefore, utilized in the present work for the estimation of NFPD. The present paper describes simple and sensitive extraction visible spectrophotometric method for the determination of NFPD, based on its tendency to form chloroform extractable ion-association complex with acidic dye belonging to Azo (monoazo) category dye TP000 under experimental conditions by exploiting the basic nature of the drug molecule.

MATERIALS AND METHODS

A Systronics UV/Visible spectrophotometer model - 2203 with 10mm matched quartz cells was used for all spectral measurements. All the chemicals used were of analytical grade. Tropaeolin 000 (Fluka, 0.2%, $5.7 \times 10^{-3}M$ prepared by dissolving 200mg of Tropaeolin 000 in 100ml distilled).

Preparation of standard drug solution: The stock solution (1mg/ml) of drug was prepared by dissolving 100 mg of it in 100 ml of 25:75 (v/v) of acetonitrile: 0.1M HCl, followed by dilution to 100 ml with distilled water. The working standard solution of NFPD (100 μ g/ml) was obtained by appropriately diluting the standard stock solution with the same solvent.

Sample solution: About 20 tablets were pulverized and the powder equivalent to 100mg of NFPD was weighed, dispersed in 25ml of Isopropyl alcohol, sonicated for 30 minutes and filtered through Whatman filter paper No 41. The filtrate was evaporated to dryness and the residue was dissolved as under standard solution preparation.

Assay: Aliquots of standard NFPD solution (0.1-0.6ml), 4 – 24 μ g/ml, were placed in a series of 125 ml separating funnels. 5.0 ml of 0.1M HCl, and 2.0 ml of TPOOO were added successively. The total volume of aqueous phase in each separating funnel was adjusted to 15 ml with distilled water. Then 25ml of chloroform was added to each separating funnel and the contents were shaken for 2 min and allowed to separate. The organic layer was collected through cotton plug and the absorbance was measured immediately at 502 nm against a reagent blank. The colored species was stable for one hour. The amount of NFPD in the sample solution was obtained from the Beer's law plot.

RESULTS AND DISCUSSIONS

Optimum operating conditions used in the procedure were established adopting variation of one variable at a time (OVAT) method. The effect of various parameters such as time, volume and strength of TPOOO reagent, 0.1M HCl and solvent for final dilution of the colored species were studied. The water immiscible solvents tested for the extraction of colored complex into organic phase include chlorobenzene, dichloromethane, carbon tetra chloride, benzene, n - butanol or chloroform. Chloroform was preferred for its selective extraction of colored drug - dye complex into organic layer from the aqueous phase. The stoichiometric ratio of the drug to dye was determined by the slope ratio method and was found to be 1:1. The optical characteristics such as Beer's law limit, Sandell's sensitivity, molar absorptivity, percent relative standard deviation amount of the upper Beer's law limits), Regression characteristics like standard deviation of slope (Sb), standard deviation of intercept (Sa), standard error of estimation (Se) and % range of error (0.05 and 0.01 confidence limits) were calculated and are shown in Table - 1. Commercial formulations containing NFPD were successfully analyzed by the proposed method. The values obtained by the proposed and reference methods for formulations were compared statistically by the t - and f - test and found not to differ significantly. As an additional demonstration of accuracy, recovery experiments were performed by adding a fixed amount of the drug to the preanalyzed formulations at three different concentration levels (50%, 75% and 100%). These results are summarized in Table - 2., (calculated from the six measurements containing 3/4th of the amount of the upper Beer's law limits), Regression characteristics like standard deviation of slope (Sb), standard deviation of intercept (Sa), standard error of estimation (Se) and % range of error (0.05 and 0.01 confidence limits) were calculated and are shown in Table - 1.

CONCLUSION

The reagents utilized in the proposed method are normal cost, readily available and the procedure does not involve any critical reaction conditions or tedious sample preparation. The proposed extractive visible spectrophotometric method is validated and possesses reasonable precision, accuracy, simple, sensitive and can be used as alternative method to the reported ones for the routine determination of NFPD depending on the need and situation.

Table 1: Optical Characteristics, Precision And Accuracy Of Proposed Method

PARAMETER	VALUES
λ_{max} (nm)	502nm
Beer's law limit($\mu\text{g/ml}$)	4-24
Sandell's sensitivity ($\mu\text{g/cm}^2/0.001$ abs. unit)	0.0226
Molar absorptivity (Litre/mole/cm)	1.74×10^4
Correlation Coefficient	0.9903
Regression equation (Y)*	
Intercept (a)	0.2699
Slope(b)	1.2423
%RSD	0.2325
% Range of errors(95% Confidence limits)	
0.05 significance level	0.0799
0.01 significance level	0.1148

*Y = a+bx, where Y is the absorbance and x is the concentration of NFPD in $\mu\text{g/ml}$

Table 2: Analysis Of naptopidil By Proposed And Reference Method

MetMETHOD	*Formulations	Labeled Amount(mg)	Found by Proposed Methods ** Amount found \pm SD	t	f	%Recovery by Proposed Method
TPOTPOOO	Tablet - 1	50mg	49.867 \pm 0.0665	1.12	0.67	99.39%
	Tablet - 2	75mg	74.843 \pm 0.1176	0.32	0.54	99.63%

Average \pm Standard deviation of 2 determinations, the T and F values refer to comparison of proposed method with reference method. Theoretical values at 95% confidence limits T=2.23 and F=5.12.

**Fig. 2: Showing Absorption Spectra of NFPD TPOOO
TPOOO(0.2%)+ HCl(0.1M)**

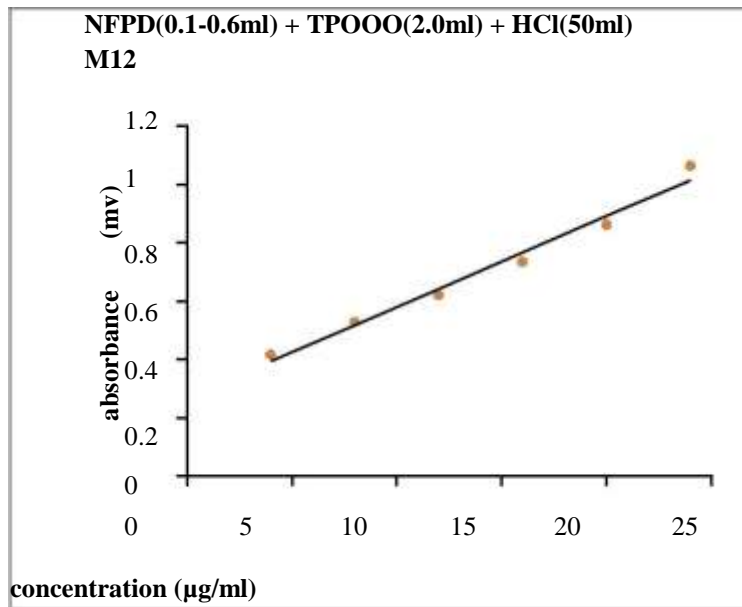
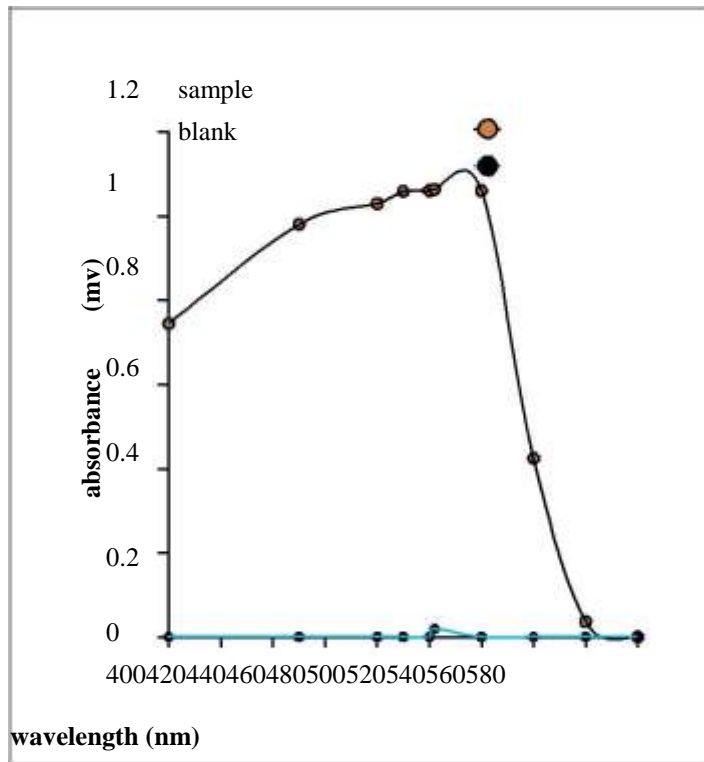


Fig. 3: Showing Calibration Graph of NFPD TPOOO

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