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(RESEARCH ARTICLE)

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Estimation of terbinafine HCL by spectophotometric analysis with Tpooo, Nb12br and WFB

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Abstract

One simple and sensitive procedure (simple spectrophotometric method) for the assay of drug Terbinafine HCl in pure form and formulations. This method involves the formation of ion-association complex between TRB and the TPOOO, NB12BR and WFB. In order to establish the optimum conditions necessary for rapid and quantitative formation of coloured product with maximum stability and sensitivity, the author performed experiments by measuring the absorbance at λmax 480nm,420nm and580nm of respective series of solutions, varying one and fixing the other parameters in each case such as type, volume and concentration of acid, organic solvent used for extraction, ratio of organic phase to aqueous phase during extraction, shaking time and temperature. The variable parameters were optimized. The results were statistically validated.

Keywords: Terbinafine hydrochloride; Spectrophotometer; TPOOO; NB12BR; WFB

1 Introduction

Terbinafine hydrochloride is 1-Naphthalene methanamine, N-[(2E) 6,6 dimethyl

- 2-heptene-4ynyl]-N-methyl. Or (E) - 6, 6 – Dimethylhept –2en –4-ynl (methyl)
    - (1-naphthylmethyl) amine hydrochloride. Or (E) –N-(6, 6-dimethyl-2-heptene-4-ynyl)-N-methyl -1-naphthalene methanamine hydrochloride. It is official in, USP1, Merck index2, Martindale's extra pharmacopoeia3, Remington4, PDR5. Existing analytical methods are reveal that little attention paid in developing the spectrophotometric methods for its determination.

In the visible spectrophotometry (colourometry), both the oxidant and analyte being used are present at very low concentrations and the reaction rate is 1/1000 to 1/100000th of the rate, at the concentration commonly used. This magnifying of the time scale confers some selectivity to oxidants and makes it possible to oxidize certain compounds specifically in the presence of other more stable compounds. Useful differences in reaction rate, however will exist only between compounds in different structural classes (basic moiety, functional groups present or both differ), but not between the compounds in the same classes. Selectivity can also be attained by using different oxidants and by varying the experimental conditions, but the suitability of an oxidant depends upon the associating ingredients. The mentioned oxidants are selective as they react only with certain functional groups under controlled experimental conditions.

Existing analytical methods are revealing that little attention paid in developing the visible spectrophotometric methods for its determination. The present paper describes the determination of the drug namely terbinafine HCl by reaction with the reagent TPOOO, alizarin NB12BR and WFB by exploiting its structural features of tertiary amine.

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2 Experimental method

2.1 Instrumentation

All spectral and absorbance measurements were made on a Systronics 106 model visible spectrophotometer with 1 cm matched glass cells or Milton Roy spectronic 1201 UV-visible spectrophotometer with 1 cm matched quartz cells.

All pH measurements were made on a Systronics 335 model digital pH meter or an Elico LI 120 digital pH meter.

2.2 Standard solution of terbinafine hydrochloride method M_1

One mg ml^{-1} stock solution of TRB HCl was prepared by dissolving 100 mg of TRB initially in 5 ml of 0.1 N HCl followed by dilution to 100 ml with distilled water .

2.3 Pharmaceutical formulations

Sample Stock Solution: A quantity of tablet powder or cream equivalent to 100 mg of TRB HCl was treated with 4×20 ml portions of chloroform and the chloroform extract was transferred to 100 ml volumetric flask and made upto 100 ml with chloroform to obtain 1 $mg.ml^{-1}$ stock solution.

Fifty millilitres of the above stock solution (1 $mg.ml^{-1}$) was taken and chloroform portion was evaporated to dryness and the residue was tranferred to a 50 ml volumetric flask by dissolving it in 5 ml of 0.1 N HCl and diluted to the mark with distilled water.

3 Recommended Procedures

3.1 Method$_1$ TPOOO for TBR

Into a series of 100ml separating funnels containing aliquots of drug (TRB: 0.5-3.0 ml, 25 $\mu g.ml^{-1}$; solution, 6.0ml of 0.1M HCl and 2.0ml of (5.709×10^{-3}M) TPOOO solutions were added. The total volume of aqueous phase in each separating funnel was adjusted to 15.0ml with distilled water. To each separating funnel, 10.0ml of chloroform was added and the contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of separated chloroform layer was measured at 480 nm. Against a similarly prepared reagent blank. The amount of drug was calculated from the calibrated curve (Figs.1).

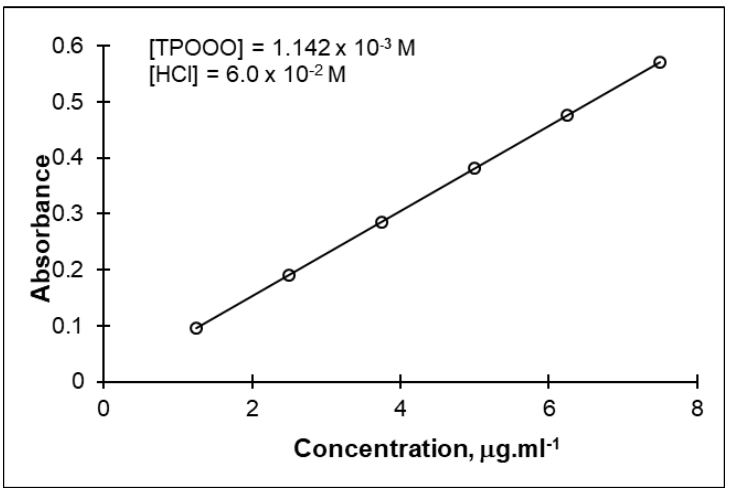

Figure 1 Beer's law plot of TRB-TPOOO (M1)

3.2 Method M_2(NB12BR) for TRB

Aliquots of standard drug solution (TRB: 0.5-3.0ml; 20 $\mu g.ml^{-1}$) were transferred into a series of 100ml separating funnels. To each one, 5.0ml of pH 1.5 buffer solution and 1ml of (5.17×10^{-3}M) of NB12BR solutions were added and the total volume of the aqueous phase was adjusted to 15ml with distilled water and 10ml of chloroform was added. The contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of the organic layer was

measured at 620 nm. Against a similarly prepared reagent blank. The amount of the drug was calculated from calibration curve (Fig.2.)

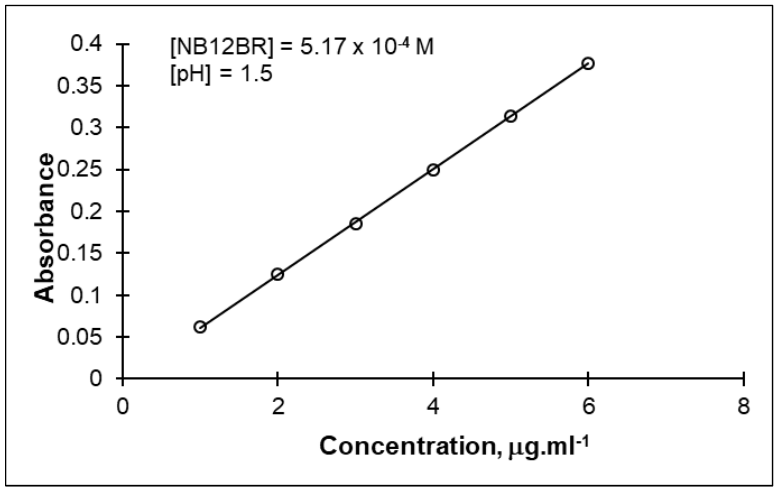

Figure 2 Beer's law plot of TRB-NB 12BR (M2)

3.3 Method M_3 (WFB) for TRB

Into a series of 100ml separating funnels containing aliquots of standard drug (TRB: 0.5-3.0 ml, 10 μg.ml^{-1}; solution 6.0 ml of buffer solution (pH 1.5) and 2.0 ml of (3.26×10^{-3}M) WFBBL solutions were added successively. The total volume of aqueous phase in each separating funnel was adjusted to 15.0ml with distilled water. To each separating funnel 10.0ml of chloroform was added and the contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of separated chloroform layer was measured at 580nm against a reagent blank prepared under similar conditions. The amount of the drug was deduced from the calibration graph (Fig 3.)

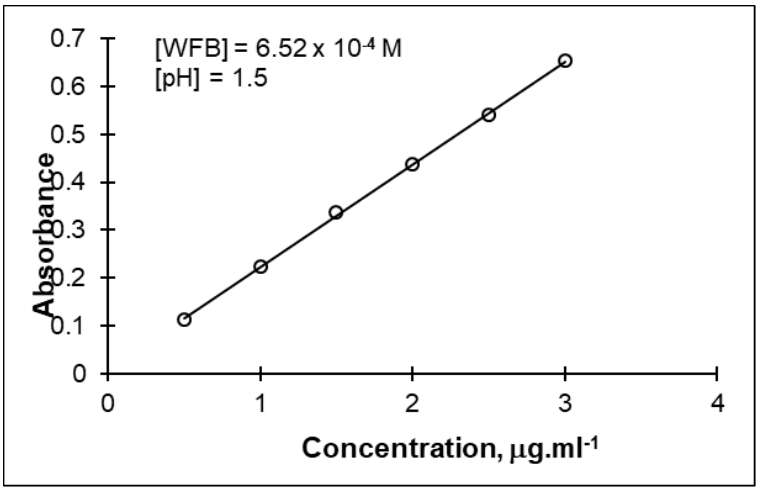

Figure 3 Beer's law plot of TRB-WFB (M3)

4 Results and discussion

Ion association complex extraction has been applied to the estimation of numerous compounds possessing basic moieties (secondary or tertiary aliphatic amino groups) by using an acid dye as a reagent and a chlorinated solvent as an extractant. The structure of the species formed may depend upon the experimental conditions (Concentration of the components, pH of the aqueous phase). The color can be altered or intensified upon acidification or reextracted into a buffer. The presence of hydrophilic substituents such as -OH or -COOH often prevents extraction of the complex into organic phase. The selectivity of the reaction may increase by using appropriate organic solvent as an extractant, which then depends upon parameters such as the polarities of the amine and of the dye. Several acidic dyes belonging to

different chemical classes have been used for the assay of basic drugs[1-4]. According to the same principle, basic dyes[5] can be used for the assay of acidic drugs.

4.1 Methods M_1 – M_3

Preliminary investigations were carried out using three acidic dyes (TPOOO[5], NB12BR[6] and WFBBL[7]) by extraction spectrophotometric technique for the assay of TRB drug . the basic drug have responded with three acidic dyes. The sensitivity and selectivity of the ion-association complex formation method depends upon the structural features of drug and dye. The involved basic moiety portions in drug is ⌐ (tertiary amine, TRB) . The ion-association complex formation products of preferred methods (based on λ_{max} andε_{max} values).

4.2 Spectral Characteristics of the proposed methods

4.2.1 Ion Association Complex Formation

Method M_1 for TRB, $M_2$for TRB, and $M_3$for TRB.

It was found that each dye is extractable from the aqueous phase into organic phase only in the presence of drugs (TRB) under experimental conditions. The drug- dye complexes were separately prepared for each dye in solution as under recommended procedures given in as above and then extracted into chloroform. After separation of chloroform and aqueous layers, the chloroform layer was collected in each case and scanned in the wavelength region 400-700nm against a reagent blank and the results are shown graphically in Figs. 4,5 and 6. The λ_{max} values were found to be 480nm for M_1, 620nm for M_2 and 580nm for M_3. The λ_{max} value of each dye in aqueous phase was almost the same as the complex in organic phase.

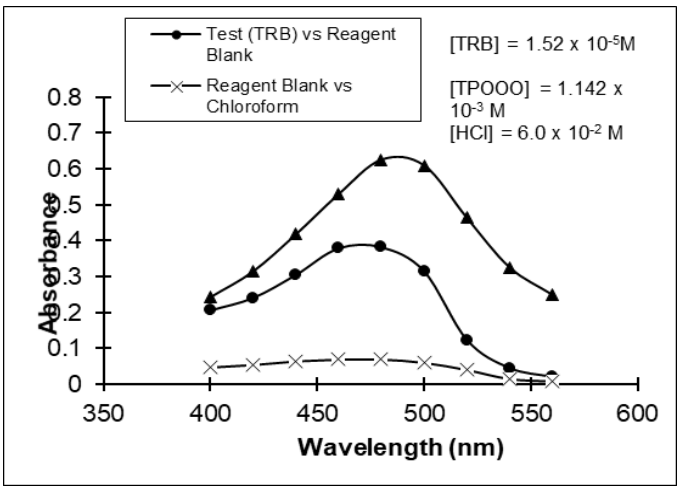

Figure 4 Absorption spectrum of TRB-TPOOO (M1)

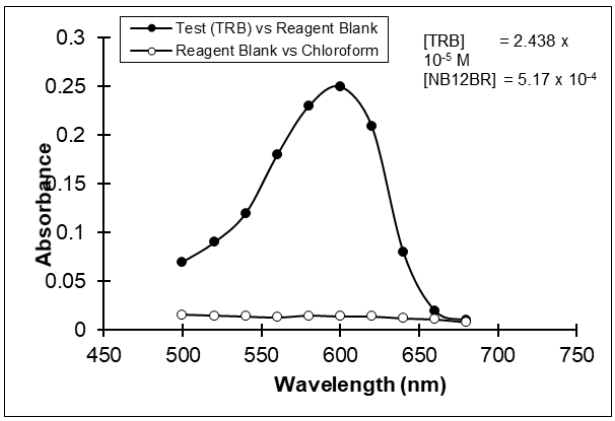

Figure 5 Absorption spectrum of TRB-NB12BR (M2)

The regression analysis using the method of least squares was made for the slope (b), standard deviation on slope (S_b), intercept (a), standard deviation on intercept (S_a), standard error of estimation (S_e) and correlation coefficient (r) obtained from different concentrations of each drug and the results are also summarized in Table 1 and 2.

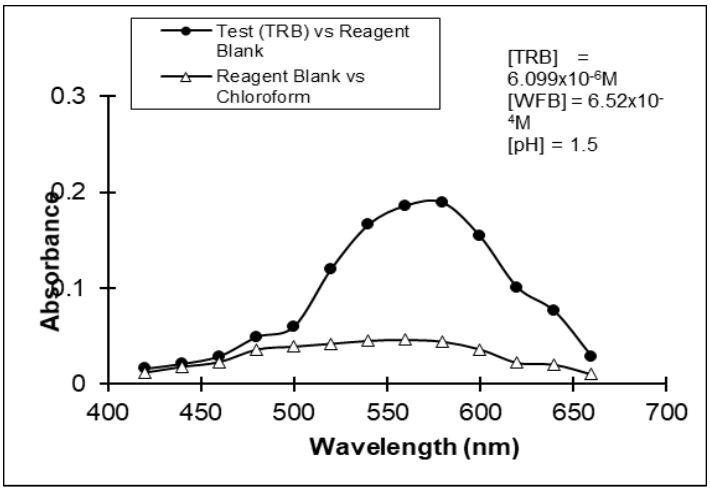

Figure 6 Absorption spectrum of TBR- WFBBL (M3)

Table 1 Optical and Regression Characteristics, PRECISION and Accuracy of the proposed methods For TRB

Parameter	**M1 TPOOO**	**M2 NB 12BR**	**M3WFB**
λ_{max} (nm)	480	620	580
Beer's Law Limits (μg.m1^{-1})	0.625-7.5	1-6	0.5-3.0
Detection limit (μg.m1^{-1})	2.675×10^{-2}	4.1×10^{-2}	1.799×10^{-2}
Molar absorptivity (mole^{-1}cm^{-1})	2.505×10^{4}	4.0592×10^{4}	3.6728×10^{4}
Sandell's sensitivity (μg.cm-2 / 0.01 absorbance unit)	1.30×10^{-2}	1.59×10^{-2}	4.621×10^{-3}
Regression equation (y=a+bc)			
Slope (b)	7.616×10^{-2}	6.302×10^{-2}	2.149×10^{-1}
Standard deviation on slope (S_b)	1.395×10^{-4}	2.249×10^{-3}	6.620×10^{-4}
Intercept (a)	1.333×10^{-4}	-1.6×10^{-3}	8.133×10^{-3}
Standard deviation in intercepts (S_a)	6.7909×10^{-4}	8.68×10^{-4}	1.289×10^{-3}
Standard error of estimation (S_e)	7.296×10^{-4}	9.327×10^{-2}	1.3847×10^{-3}
Correlation coefficient (r)	0.9999	0.9999	0.9998
Relative standard deviation (%)*	0.3181	0.4673	0.4376
% rang of error (confidence limits)*			
0.05 level	0.3339	0.4905	0.2477
0.01 level	0.5237	0.7693	0.3885
% Error in bulk samples**	0.3664	0.280	0.2283

*Average of six determinations considered; ** Average of three determi

Table 2 Assay of TBR in Pharmaceutical Formulations

	Labelled	Amount found by proposed methods **			Reference	% Recovery by proposed methods***		
Formulations*	amount	M_1	M_2	M_3	method	M_1	M_2	M_3
	(mg)	TPOOO	NB12BR	WFB		TPOOO	NB12BR	WFB
Tablets	125	124.19 ± 0.45	124.10 ± 1.02	123.88 ± 1.11	124.36 ± 0.72	99.35 ± 0.36	99.28 ± 0.82	99.10 ± 0.890
		F = 2.50	F = 2.01	F = 2.36				
		t = 0.70	t = 1.57	t = 0.552				
Tablets	250	249.2 ± 1.51	248.70 ± 1.366	248.63 ± 0.775	249.52 ± 0.82	99.64 ± 0.60	99.48 ± 0.53	99.45 ± 0.310
		F = 3.43	F = 2.69	F = 1.118				
		t = 0.34	t = 0.999	t = 1.049				
Cream	10	9.98 ± 0.03	9.97 ± 0.02	9.97 ± 0.622	9.99 ± 0.016	99.82 ± 0.30	99.71 ± 0.27	99.75 ± 0.227
		F = 3.39	F = 2.72	F = 1.19				
		t = 0.99	t = 0.78	t = 1.042				
Tablets	250	247.73 ± 2.59	245.3 ± 4.70	247.64 ± 2.47	247.86 ± 3.09	99.09 ± 1.03	98.14 ± 1.88	99.05 ± 1.096
		F = 1.41	F = 2.31	F = 1.27				
		t = 0.34	t = 0.42	t = 0.144				

* Formulations from four different pharmaceutical companies; ** Average ± standard deviation on six determinations, the t- and F – test values refer to comparison of the proposed method with the reference method; Theoretical values at 95% confidence limit, F= 5.05, t = 2.57; *** Recovery of 10 mg added to the pre-analyzed pharmaceutical formulations (average of three determinations)

5 Conclusion

An important step in the validation process of spectrophotometric method is the fixation of appropriate system suitability parameters to ensure successful analysis. They defined as a range of acceptance values for a series of key parameters such as precisition, accuracy, linearity of detector response and recovery as deemed appropriate for the scope of analysis.

The validity of the proposed methods for the determination of a fore mentioned drugs were established from the precision (calculating percent relative standard deviation, percent range of error at confidence limits with P=0.05 and 0.01 level from six determinations) and accuracy (percent error in pure samples, comparison of results obtained with proposed and reported methods in the case of pharmaceutical preparations and recovery experiments) studies. The sensitivity of each method was ascertained through molar extinction coefficient, sandell's sensitivity, optimum photometric range beer's law limits. The regression analysis using the method of least squares was made for the slope (b), standard deviation (S_b), intercept (a), standard deviation on intercept (S_a), standard error of estimation (Se) and correlation coefficient (r) obtained from different concentrations. The data obtained in the determination of each drug with different reagents are summarized in this section. The selectivity (or specificity) of each proposed method was ascertained through interference studies with other active and inactive ingredients usually present in pharmaceutical preparations.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

No conflict arises.

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