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Research Article

APPLICATION OF EXTRACTIVE SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF FLUCLOXACILLIN AND TRANDOLAPRIL USING BROMOCRESOL GREEN

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ABSTRACT

Objective: The aim was to develop rapid, simple, sensitive, and accurate visible spectrophotometric methods for the determination of flucloxacillin and trandolapril.

Materials and Methods: These methods are based on the formation of ion-pair complex of the flucloxacillin, with bromocresol green in acidic medium. The colored products are extracted with chloroform and measured spectrophotometrically at 433 nm and 430 nm for flucloxacillin and trandolapril, respectively.

Results: Beer's law was obeyed in the concentration range of 0.5-2.5 mg/ml and 1-5 mg/ml with molar absorptivity of 2.46×10^2 L/mol/cm and 4.52×10^2 L/mol/cm and relative standard deviation of 0.28% and 0.32% for flucloxacillin and trandolapril, respectively.

Conclusion: These methods have been successfully applied for the assay of drug in pharmaceutical formulations individually. No interference was observed from common pharmaceutical adjuvants by adopting the proposed method.

Keywords: Flucloxacillin, Trandolapril, Extractive spectrophotometry, Bromocresol green.

INTRODUCTION

Flucloxacillin [1], chemically (6R)-6-(3-[2-chloro-6-fluorophenyl]-5-methylisoxazole-4-carboxamido) penicillanic acid and it is an isoxazolyl penicillin used primarily for the treatment of infections due to staphylococci resistant to benzyl penicillin. Like other β-lactam antibiotics, flucloxacillin acts by inhibiting the synthesis of bacterial cell walls. It inhibits the cross-linkage between the linear peptidoglycan polymer chains that makeup a major component of the cell wall of gram positive bacteria. The therapeutic importance of this drug has prompted the development of many methods for its assay. This drug is official in BP and European Pharmacopoeia. From the literature review, it was found that spectrophotometric [2-8] and high-performance liquid chromatography (HPLC) [9-11] methods have been developed for the determination of flucloxacillin.

Trandolapril [12], chemically is (3aR,7aS)-1-[N-1(S)-(ethoxycarbonyl)-3-phenylpropyl]-(S)-alanyl] octahydro-1H-indole-2(S)-carboxylic acid, is an angiotensin converting enzyme inhibitor widely used as an efficient orally active anti-hypertensive drug. It is especially recommended for the treatment of arterial hypertension in patients after myocardial infarction with dysfunction of the left heart ventricle. The drug has been determined by a variety of analytical techniques such as HPLC [13-17] and high-performance thin layer chromatography [18,19].

In this communication, two new-extractive spectrophotometric methods for the determination of flucloxacillin and trandolapril have been discussed. The methods are based on the formation of chloroform-extractable ion-pair complexes with bromocresol green (BCG).

MATERIALS AND METHODS

Apparatus

An SL 164 Elico Double beam ultra violet-visible spectrophotometer was used to measure the absorbance. An Elico-L1 610 pH meter was used for pH measurements.

Reagents and standards

A 1 mg/ml solution of flucloxacillin/trandolapril were prepared by dissolving 100 mg of flucloxacillin/trandolapril in methanol and diluted to 100 ml with the same diluent.

The 0.04 w/v%, solution of BCG was prepared by dissolving 0.1 g of BCG with 2.9 ml of 0.05 N NaOH and 5 ml of alcohol (90%) and add sufficient alcohol (20%) to produce 250 ml as per I.P. Buffer (pH 4) was prepared by taking 25 ml of 0.2 M potassium hydrogen phthalate, 0.05 ml of 0.2 M HCl in 100 ml volumetric flask and diluting the volume with doubly distilled water.

Procedure for the calibration curve

Into a series of 50 ml separating funnel appropriate volume of 1.0 mg/ml solution of flucloxacillin (0.5-2.5 ml) was placed followed by 1 ml of BCG and 1.5 ml of buffer and 1 mg/ml solution of trandolapril (1-5 ml) was placed followed by 2.5 ml buffer and 1.5 ml BCG and mixed well. Then, 5 ml of chloroform was added to each funnel. The contents were shaken for 2 minutes and allowed to separate the two layers. The absorbance of the organic layer was measured at 433 nm for flucloxacillin and 430 nm for trandolapril against a reagent blank prepared similarly in each case. The calibration curve was constructed in each case by considering the absorbance measured at five concentration levels of both flucloxacillin and trandolapril separately. The amount of drug was computed either from the calibration curve or from the regression equation. The colored complexes were stable for about 2 hrs.

Procedure for the assay of drug in dosage forms

Twenty tablets of commercial samples of flucloxacillin and trandolapril were accurately weighed and powdered. An amount of tablet powder equivalent to 50 mg of flucloxacillin and trandolapril were weighed separately and made up to 50 ml with methanol. The solutions were filtered and subjected to recommended procedure for the determination.

RESULTS AND DISCUSSION

Flucloxacillin and trandolapril were protonated in acidic medium that forms ion-pair complexes with BCG and were quantitatively extracted with chloroform. The absorption spectra were shown in Fig. 1, which revealed that the ion-pair complexes of flucloxacillin and trandolapril with BCG absorbed maximally at 433 nm and 430 nm, respectively. The reagent blanks prepared under similar conditions showed no absorption.

Optimization of the reaction conditions

The optimum conditions for quantitative estimation of the drug were established via a number of preliminary experiments.

Effect of dye concentration and order of addition

The order of addition of the reagent and buffer was optimized by several trials and found that drug, reagent and followed by buffer was the suitable order of addition. The effect of dye concentration on the intensity of the color developed at the selected wavelength and constant flucloxacillin/trandolapril concentrations were critically examined using different milliliters of reagent (0.045 w/v). The results (Fig. 1) indicated that the maximum absorbance for flucloxacillin was found with 1 ml of reagent and 1.5 ml for trandolapril, beyond, which absorbance become constant. Therefore, 1 ml of dye stuff for flucloxacillin and 1.5 ml dye stuff for trandolapril were used for ion-pair formation throughout the experiment (Fig. 2).

Choice of organic solvent

A number of organic solvents such as chloroform, carbon tetrachloride, dichloromethane, benzene and toluene were examined for extraction of the ion-pair complex in order to provide an applicable extraction procedure. Chloroform was preferred for its selective extraction of ion-pair complex from the aqueous solution. Shaking time of 0.5-4.0 minutes provided a constant absorbance and hence, 2 minutes was used as an optimum shaking time throughout the experiment. The ion-pair complexes were quantitatively recovered in one extraction only and were also stable for 2 hr.

Effect of excipients

A systematic study of the effect of excipients was performed, following the proposed procedures for a 10 ml sample system, by adding a known amount of excipients to the fixed flucloxacillin/trandolapril concentration (2.0 mg/ml). The results revealed that no significant interference was observed from the excipients, commonly present in pharmaceutical formulations. However, the drug content from the powdered tablets was extracted into chloroform, which completely eliminates the common excipients found in drug formulations.

Analytical data

Calibration graphs were constructed, by measuring the absorbance at seven concentration levels, which showed a linear response of absorbance in relation to concentration of flucloxacillin and trandolapril over the range of 0.5-2.5 and 1.0-5.0 mg/ml respectively. Regression analysis of calibration graphs indicated a linear relationship with negligible intercepts. Table 1 summarizes the analytical parameters, molar absorptivity and the results of statistical analysis of the experimental data. Regression equations computed from calibration graphs along with a standard deviation of the slope (S_b) and intercept (S_a), confidence interval of the slope (tS_b) and intercept (tS_a) on the ordinate. The detection limits were found to be 0.769 and 0.92 mg/ml for flucloxacillin and trandolapril, respectively. The small value of the variance, further, suggested least scatter of experimental data points around the line of regression.

The repeatability of the proposed procedures was checked by performing ten replicate determinations of flucloxacillin/trandolapril at concentration levels of 1.5-2.5 mg and 2.5-5.0 mg respectively. The percent relative standard deviation (%RSD) and recovery was found to vary over the range of 0.28-0.34% and 99.8-100.8%, respectively.

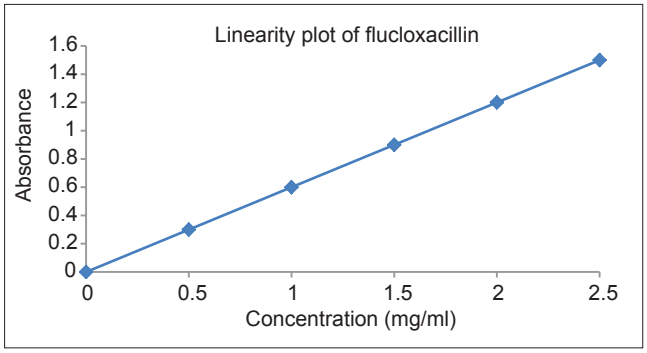

Fig. 1: Beer's law plot of flucloxacillin

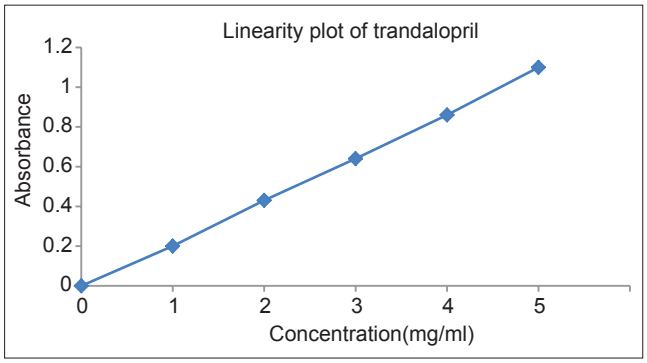

Fig. 2: Linearity plot of trandalopril

Table 1: Analytical characteristics of the proposed methods

Parameters	Flucloxacillin	Trandolapril
λ_{Max} (nm)	433	430
Beer's law limits (mg/ml)	0.5-2.5	1-5
Molar absorptivity (1/mol/cm)	2.46×10^2	4.52×10^2
Linear regression equation		
Intercept (a)	0.0332	−0.1276
Slope (b)	0.566	0.244
Correlation coefficient (r)	0.9996	0.9995
Variance (So^2)	0.207	0.77
Detection limit (µg/ml)	0.769	0.92
RSD (%)	0.283	0.32
Recovery (%)	99.89	99.94

RSD: Relative standard deviation

The accuracy of proposed methods was demonstrated by recovery experiments, which were carried out by adding a fixed amount of pure drug to the pre-analyzed dosage forms. The analytical results obtained were summarized in Table 1. The percentage of RSD (0.2-0.52%) could be considered satisfactory.

CONCLUSION

The proposed methods are sensitive with good linearity and molar absorptivities. No interference from common excipients was encountered for both drugs. Thus, the proposed methods are simple, sensitive, accurate, precise, economical, and suitable for routine analysis of flucloxacillin/trandolapril in tablets.

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