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Determination of Felodipine in Bulk Drug and its Dosage Formulations using Bromophenol Blue and Bromothymol Blue as Reagents

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ABSTRACT

Two simple, rapid and inexpensive methods based on visible spectrophotometry have been developed for the determination of felodipine in pure form and in dosage forms with two acidic dyes [Bromophenol Blue (BPB) and Bromothymol Blue (BTB)] as the reagents. The proposed methods were based on the formation of ion-pair color complexes between the drug and the two acidic dyes in an acidic buffer. The ion-pair complexes formed, which has an absorption maximum at 420 and 424nm, and were quantitatively extracted into chloroform. All experimental variables for both the proposed methods were studied and optimized. Statistical analysis of the experimental results indicated that the proposed methods were precise and accurate. Excipients used as additives in pharmaceutical formulations did not interfere in the proposed procedures. The proposed procedures were successfully applied to the determination of the bulk drug and its pharmaceutical formulations.

Keywords: Spectrophotometry, Ion-pair color complex, Bromophenol Blue, Bromothymol Blue, pharmaceuticals

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INTRODUCTION

Felodipine , chemically, ethyl methyl-4(2,3-dichlorophenyl)-1,4-dihydro- 2, 6-dimethyl-3, 5-pyridine dicarboxylic acid-3-ethyl-5 methyl ester (Figure. 1), is a calcium antagonist widely used in the treatment of hypertension, heart failure and angina pectoris[1].A number of methods have been reported in the literature for the quantification of the drug in pharmaceutical dosage forms that include LC[2-5],GC[6] and three HPLC[7-9] methods for the assay of felodipine in dosage forms are found in the literature. Although a few visible spectrophotometric methods[10-12] for felodipine were found in the literature no methods using acidic dyes BPB and BTB as reagents has been reported. This present paper describes two new visible spectrophtometric methods for the determination of felodipine based on the complexation of the drug with BPB and BTB at pH-3.4 forming an ion-pair colored complexes, which were extracted into chloroform respectively. The proposed methods are more simple, rapid and sensitive than methods reported earlier (Table 1).

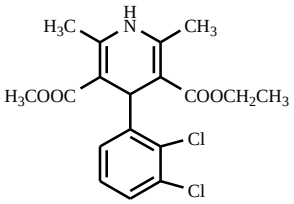

Figure.1, Structure of Felodipine

MATERIALS AND METHODS

Apparatus

All the absorbance measurements were carried out using a Systronics model 106 digital spectrophotometer (Systronics, India) with 1-cm quartz cells.

Materials and Reagents

Pharmaceutical grade CPH (Cipla India, Ltd., Mumbai, India) was used as working standard. All chemicals used were of analytical reagent grade and double distilled water was used throughout the investigation. A stock standard solution containing 1000µg.ml^{-1} of felodipine was prepared in water. Working standards of 100µg.ml^{-1} (for spectrophotometry) were prepared by appropriate dilution of the stock solution. Phthalate buffer, pH 3.4, was prepared by dissolving 2.04 g of potassium hydrogen phthalate in 100ml of water and the pH was adjusted by using 0.1 M hydrochloric acid. A 0.5% solution of Bromophenol Blue was prepared by dissolving 0.5 g of the reagent (RANBAXY Fine Chemicals Ltd., New Delhi, India) in 100 ml of water, and filtering it to remove the insoluble residue. Similarily a 0.2% solution of Bromophenol Blue was prepared by dissolving 0.2 g of the reagent (RANBAXY Fine Chemicals Ltd., New Delhi, India) in 100 ml of water, filtered and was used for the proposed procedures.

Preparation of sample solution:

Plendil tablets (felodipine ;5.0mg) was purchased from local pharmacy. Twenty tablets were weighed and ground into a fine powder. An amount of powder equivalent to 100 mg of felodipine was extracted with chloroform and filtered through aWhatman No. 42 filter paper. This filtrate was evaporated to dryness over a water bath; the residue was to 100ml with water in a volumetric flask. Suitable aliquot of this solution was of the diluted for its assay by the proposed spectrophotometric methods described respectively.

ANALYTICAL PROCEDURES

BPB:

Aliquots of the standard solution containing 5.0 to 25µg.ml^{-1} felodipine were transferred into a 100 ml separating funnel. Then, 5.0 ml of phthalate buffer of pH 3.4 and 2.0 ml of 0.5% BPB dye solution were added to the separating funnel. The total volume was adjusted to 15ml by the addition of water and the contents were mixed well. Then, 10.0 ml of chloroform were added and the contents were shaken vigorously for 2min. The two layers were allowed to separate, the chloroform layer and the absorbance was measured at 420nm against a reagent blank. A calibration graph was prepared by plotting the measured absorbance as a function of concentration or a regression equation was calculated. The concentration of the unknown was read from the calibration graph or deduced from the regression equation.

BTB:

Same procedure described above in BTB was used for the assay of felodipine solution of concentration (100µg/ml) using 0.2% BTB dye solution. Absorbance of this final extracted chloroform layer was measured at wavelength maxima 424nm against blank. A calibration curve was plotted between concentration of drug and measured absorbance.

RESULTS AND DISCUSSION

The proposed procedures are based on the reaction between felodipine and BPB and BTB dyes in aqueous solution in acidic medium to form an yellow ion-pair complexes that were extracted into chloroform and measured spectrophotometrically. The experimental conditions for the proposed methods were optimized and the methods validated. The formation of the ion-pair color complex is shown in the reaction scheme given below. Figure. 3&4 represents the absorption spectra of the felodipine-BPB and felodipine-BTB ion-pair complex in chloroform. The absorption maximum of the ion-pair in chloroform is at 420nm for BPB and 424nm for BTB against the absorbance of the reagent blank which is insignificant and these absorption maxima

was used for the examination of the conditions for the determination of felodipine.

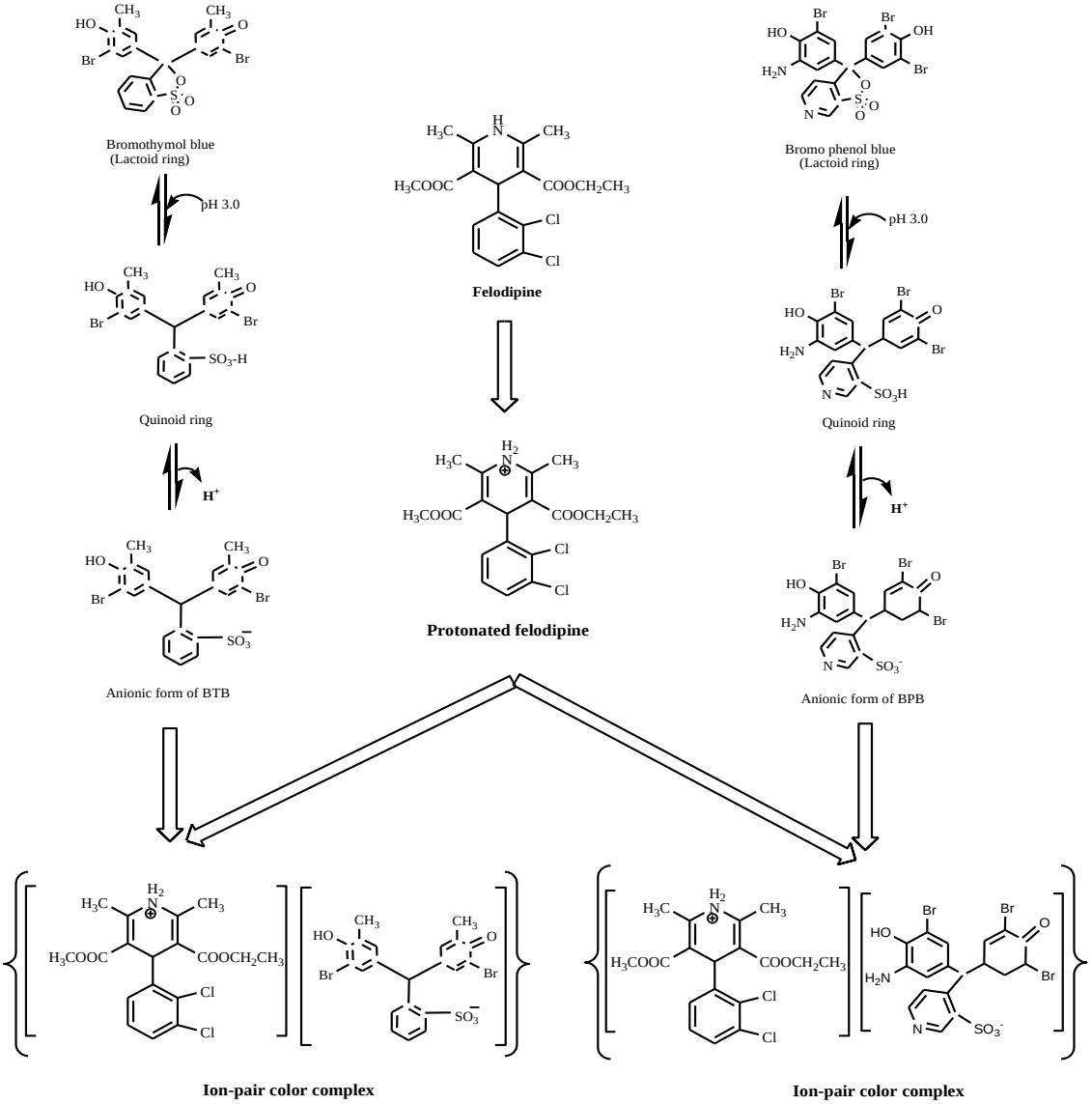

Figure.2, Reaction scheme of Felodipine with BTB and BPB

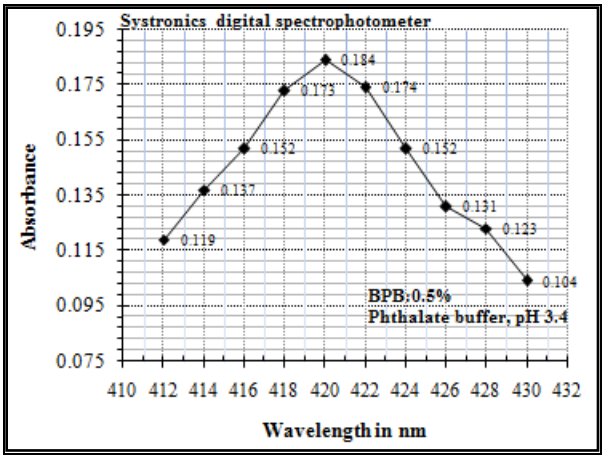

Figure.3, Absorption spectra of Felodipine with BPB

The Beer's law was obeyed in the range of 5.0-25 μg.ml^{-1}for BPB and BTB with the linear regression equations of Y420 = - 0.0022 + 0.01212 X for BPB and Y424 = - 0.0079 + 0.01566 X for BTB respectively , where Y is absorbance and X is concentration in μg.ml^{-1}.

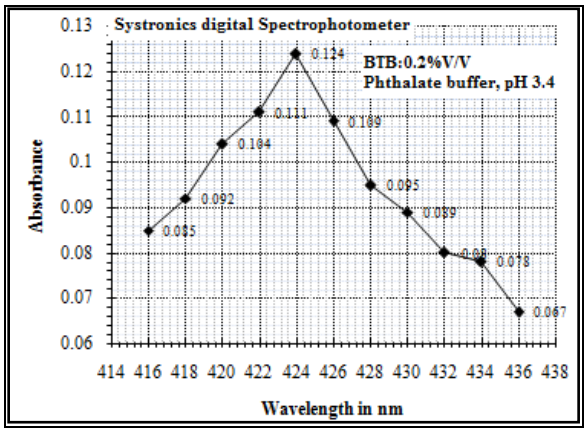

Figure.4, Absorption spectra of Felodipine with BTB

Table-1: Results of optical characteristics, precision and accuracy of the proposed methods for Felodipine assay

Parameter	BPB	BTB
λ_{max} (nm)	420	424
Beer's law limits (μg/ml)	5.0 –25.0	5.0 – 25.0
Molar absorptivity (1 mol^{-1}.cm^{-1})	6.532 x 10^4	2.896 x 10^4
Sandell's sensitivity (μg.cm^{-2}/0.001 absor. unit)	0.07854	0.04314
Optimum photometric range (μg/ml)	5.0 – 20.0	7.5 – 20.0
Regression equation (Y=a+bc) ;slope (b)	0.01212	0.01566
Standard deviation on slope (S_b)	4.41 x 10^{-5}	2.24 x 10^{-4}
Intercept (a)	2.20 x 10^{-3}	7.90 x 10^{-3}
Standard deviation on intercept (S_a)	7.65 x 10^{-5}	1.29 x 10^{-4}
Standard error on estimation (S_e)	1.21 x 10^{-3}	3.55 x 10^{-3}
Correlation coefficient (r)	0.9999	0.9996
Relative standard deviation (%)*	1.118	1.260
% Range of error (confidence limits)		
0.05 level	0.935	1.053
0.01 level	1.383	1.559

* Average of six determinations considered, ** Average of three determinations

Table- 2: Assay of Felodipine in Pharmaceutical formulations (PLENDIL)

Sample	Labelled amount (mg)	Amount obtained (mg) Proposed methods*		UV method	%Recovery of Proposed methods**	
		BPB	BTB		BPB	BTB
PLENDIL	5.0	4.86±0.011 F=1.190 t=1.20	4.85±0.07 F=2.938 t=1.64	4.94±0.12	99.19±0.72	99.09±0.63

*Average of six determinations,** Mean and standard deviation of six determinations

The regression co-efficient (r^2) was found to be 0.9999 and 0.9996 for felodipine-BPB and felodipine-BTB methods. The molar absorptivity and Sandell sensitivity were $6.532x10^4 L.mol^{-1}.cm^{-1}$, $0.07854\mu g.cm^{-2}$ for BPB and $2.896x10^4$ $L.mol^{-1}.cm^{-1}$ and $0.04314\mu g.cm^{-2}$ for BTB, respectively. The complex extracted into chloroform was stable up to 72 hours. The results of regression characteristics like standard deviation of slope (S_b), standard deviation of intercept (S_a), standard error of estimation (S_e), % range of error (0.05 and 0.01 confidence limits) and detection limit were calculated for both methods are summarized in Table. 1. The Accuracy and precision were found by analysis of six replicate samples containing three different amounts (within the linear ranges). The range, percent error and relative standard deviation obtained are given in Table.1, and reveal that the methods are reasonably accurate and precise. Statistical analysis of the results did not detect any significant difference in performance between the proposed method and reference method with respect to accuracy and precision as revealed by the Students t-value and variance ratio F-value. The results of assay are given in Table-2.

CONCLUSIONS

The proposed methods developed in the present paper for the assays of felodipine were simple, rapid are simple, accurate and precise. The sensitivity of the proposed spectrophotometric methods were significantly higher than that of all the spectrophotometric, potentiometric, GC and some HPLC methods proposed(reported methods in literature) earlier. Moreover the proposed methods for the assay of felodipine were easier and cheaper to carry out and do not require expensive or toxic chemicals, and are free from interference when compared with the HPLC separation methods and therefore the proposed methods can therefore be generally applicable to the for routine analysis of the felodipine in pure and dosage formulations.

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