Sensitive Spectrophotometric Methods for the Determination of Nicardipine in Pharamaceuticals Using Bromothymol Blue and Methyl

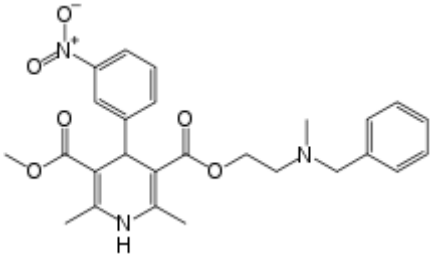
Y. Suneetha[1], N. V. S. Naidu[2]

Department of Chemistry, S. V. University, Tirupati-517 501, India

Abstract: ***Simple, sensitive and rapid spectrophotometric methods are developed for the determination of Nicardipine in pharmaceutical formulations. Method A is based on the extractive spectrophotometry and the final color developed is due to ion association complex formation with Bromothymol blue (BTB) at P^H 3.7 resulting in the formation of a yellow color solution that exhibited maximum absorption at wavelength 380nm. Method B is based on the yellow color developed which is due to ion association complex between methyl orange (MO) at P^H 3.7 and nicardipine that exhibited maximum absorption at a wave length of 430nm. Both ion association complexes are extracted into chloroform and Beer's law is obeyed over the concentration ranges 1.0-10.0 µgml^{-1} and 2.0-10.0 µgml^{-1} for methods A and B respectively. Both the methods have been successfully applied for the assay of the drug in pharmaceutical formulations. There is No interference was observed from common pharmaceutical adjuvants. The reliability and the performance of the proposed methods are established by point and interval hypothesis tests and through recovery studies.***

Keywords: Nicardipine, Bromothymol blue (BTB), Methylorange(MO), Spectrophotometer, Bulk drugs and tablet formulations

1. Introduction



Nicardipine2-[benzyl(methyl)amino]ethylmethyl2,6-dimethyl-4-(3-nitrophenyl) 1,4dihydropyridine-3,5-dicarboxylate is a medication used to treat high blood pressure and calcium-channel blocking agent used for the treatment of vascular disorders such as chronic stable angina, hypertension, and Raynaud's phenomenon. It is available in oral and intravenous formulations. Literature survey reveals that different analytical methods are used including Derivative Spectrophotometry[1], MS[2-4], GC[5], HPLC[6-8] and Polarography[9]. Extractive spectrophotometric procedures are popular for their sensitivity in the assay of drugs and, therefore, ion-pair extractive spectrophotometry has received considerable attention for the quantitative determination of many pharmaceutical compounds. Though few methods mentioned above have been reported in the literature, there are no simple spectrophotometric methods. This methods described here are simple and sensitive and has been used for the routine quality control analysis of pharmaceutical formulations containing Nicardipine involve an ion association complex formation with acidic dyes Bromothymol Blue (BTB) which is extractable into chloroform, which absorbs at 380nm (method A) and Methyl orange (MO) resulting in the formation of a yellow color solution that exhibited absorption at 430 nm (Method B).

2. Experimental

2.1 Instrumentation

Spectral and absorbance measurements were made with Shimadzu UV/Visible double beam spectrophotometer (model 2450)

2.2 Reagents

All the reagents used were of analytical reagent grade. The solutions were freshly prepared and for Method-A Bromothymol blue (BTB) (0.2%) for Method B Methyl orange (MO) (0.1%) were freshly prepared.

2.3 Procedure

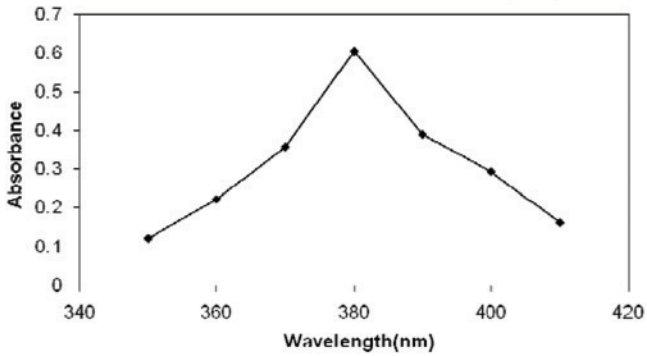
Standard Stock solution:
A standard stock solution containing 1mg/ml was prepared by dissolving accurately, 100mg of Nicardipine in 100ml methanol. From this a working standard solution containing 100µg/ml was prepared for both A and B methods dilution with methanol.

2.4 Method A

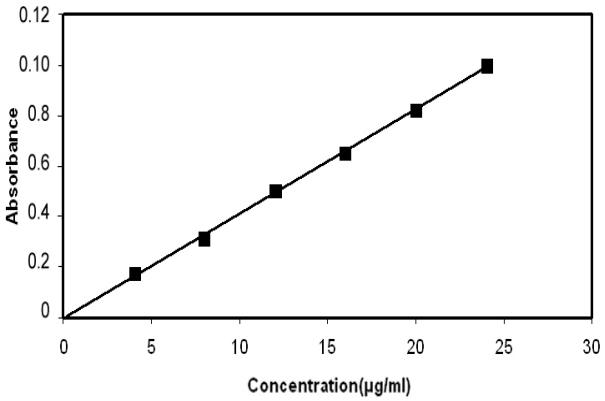
Aliquots of standard and reduced Nicardipine (1ml=100µg/ml) solutions ranging from 0.1-0.5ml of 100µwere transferred into a series of 50ml separating funnels To that 2ml of BTB (0.2%) was added and then total volume of the aqueous phase was made up to10ml with distilled water. about 10ml of chloroform was added to each funnel and the contents were shaken for 2minits the two phases were allowed to separate and the absorbance of chloroform layer was measured 380nm against the corresponding reagent blank. The amount of Nicardipine present in the sample solution was computed from its calibration curve.

2.5 Method B

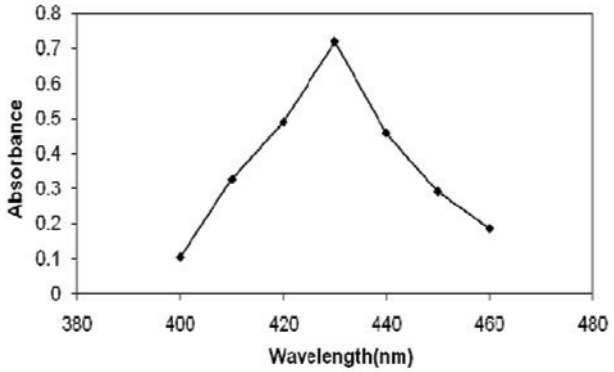
The standard and reduced Nicardipine (1ml=100µg/ml) solutions from 0.5-2.5ml were taken into a series of 50ml separating funnels and 2ml of MO (0.1%) was added. Remaining volume of water required to make it 10ml was added. 10ml chloroform was added to each funnel and the contents were shaken for 2min. The two phases were allowed to separate and the absorbance of the chloroform layer was measured at 430nm using corresponding reagent blank, and the calibration curve was drawn.



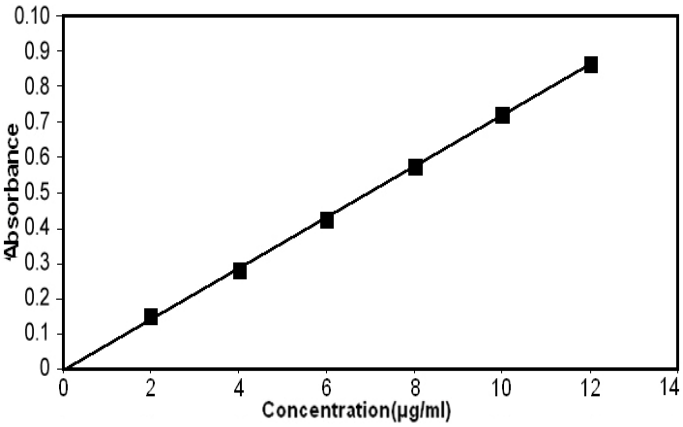
Absorption spectrum of NCD with BTB/$CHCl_3$ system



Beer's law plot of NCD with BTB/$CHCl_3$ system



Absorption spectrum of NCD with MO/$CHCl_3$ system



Beer's law plot of NCD with MO/$CHCl_3$ system

2.6 Preparation of Sample Solutions

Tablets containing Nicardipine were successfully analysed by the proposed methods. 20 mg of the drug was dissolved in 20ml methanol. After the tablets were dissolved completely the solution was treated with 10ml 5N HCl and 4g of Zinc dust. The solution was allowed to undergo reduction by allowing to standing for one hour. After one hour the solution was slowly filtered and residue was washed with about 15ml of water 3 to 4 times. The solution finally made up to 100ml with water in volumetric flask. The solution was progressively diluted and analysed as given under the assay procedure for blank samples.

3. Result and Discussion

Anionic dyes like BTB, MO form ion-association complexes with the positively charged drugs. The drug and dye stoichiometric ratio as calculated by the continuous variation and mole- ratio method was found to be 1:1 both with BTB and MO. The drug dye complex, with two positively charged ions, behaves as a single unit held together by an electrostatic force of attraction.

3.1 Optimization of variables

Optimum conditions necessary for rapid and quantitative formation of colored ion-pair complexes with maximum stability and sensitivity were established preliminary experiments. Chloroform was preferred as better solvent for these methods for its selective and quantitative extraction. Optimum conditions were fixed by varying one parameter at a time while keeping other parameters constant and observing its effect on the absorbance at 380nm for BTB and 430nm for MO. The optical characteristics such as molar absorptivity, Beer'.s law range, Sandell.s sensitivity is presented in TABLE 1.The regression analysis using the method of least squares was made for the slope (a), intercept (b) and correlation coefficient (r) obtained from different concentrations and the results are summarized in Table 1. The relative standard deviations and percent range of error (0.05 and 0.01) l confidence limits are calculated for the eight measurements each.

Table 1: Optical Characteristics, precision and accuracy of the proposed methods for Nicardipine

Parameter	*Method-A*	*Method-B*
λmax (nm)	380	430
Beer's law Limits (µg/ml)	4-20	2-10
Molar absorptivity(1 mole^{-1} cm^{-1})	6 x 10^3	6.87 x 10^3
Sandell's sensitivity (µg/cm^2/0.001 absorbance unit)	0.0125	0.01433
Slope (b)	0.0132	0.0442
Intercept(a)	0.018	0.0026
Correlation coefficient(r)	0.9832	0.04472
Standard deviation	2.7281	0.1692
%Relative standard deviation	0.90	0.77
%Range of Error (Confidence limits)		
0.05 level	±0.463	±0.743
0.01 level	±1.13	±0.952

From these values it is indicated that method A is more sensitive than method B.

3.2 Assay procedures

Aliquots of standard Nicardipine ranging from0.1-0.5ml were transferred into a series of 50ml separating funnels. To that 2ml of BTB (0.2%) and Methylorange (0.2%) was added and the total volume of the aqueous phase was made up to 10 ml with distilled water. 10 ml of chloroform was added in three initial amounts to each funnel and the contents were shaken for two minutes . The two phases were allowed to separate and the absorbance of the chloroform layer was measured at 380 nm and 430nmagainst the reagent blank. Satisfactory results were obtained for drug analysis in pharmaceutical formulations and the results were reproducible with low R.S.D.values. The average percent recoveries obtained were quantitative, indicating good accuracy of these methods. The results of analysis of the commercial tablets and the recovery studies of drug suggested that there is no interfere for many excipients (such as Strarch, Lactose, Titaniumdioxide, and Magnesium stearate) which are presented in TABLE-2

Table 2: Assay and recovery of NCD in dosage forms

S.NO.	Pharmaceutical Formulation	Labelled amount (mg)	proposed method			Found by reference method ±S.D	% recovery by proposed methods ±S.D
			Amount found (mg)	t (Value)	F (Value)		
1	Cardene	10	9.97±0.015	0.617	2.169	9.94±0.016	100.2±0.64
	Cardene	10	9.93±0.012	0.075	2.540	9.96±0.091	99.41±0.79
	Cardene	10	9.96±0.095	0.617	2.169	9.99±0.019	100.1±0.85
2	Cardene	10	9.91±0.009	0.183	2.474	9.94±0.018	100.9±0.61
	Cardene	10	10.04±0.082	0.262	2.175	10.01±0.090	9.82±0.94
	Cardene	10	10.01±0.008	0.391	2.638	10.04±0.017	99.92±1.04

4. Conclusions

The proposed methods are simple and sensitive and reproducible for the determination of Nicardipine in any pharmaceutical preparations and did not suffer any interference due to common excepients of tablets like talk starch and magnesium sterate, lactose etc.

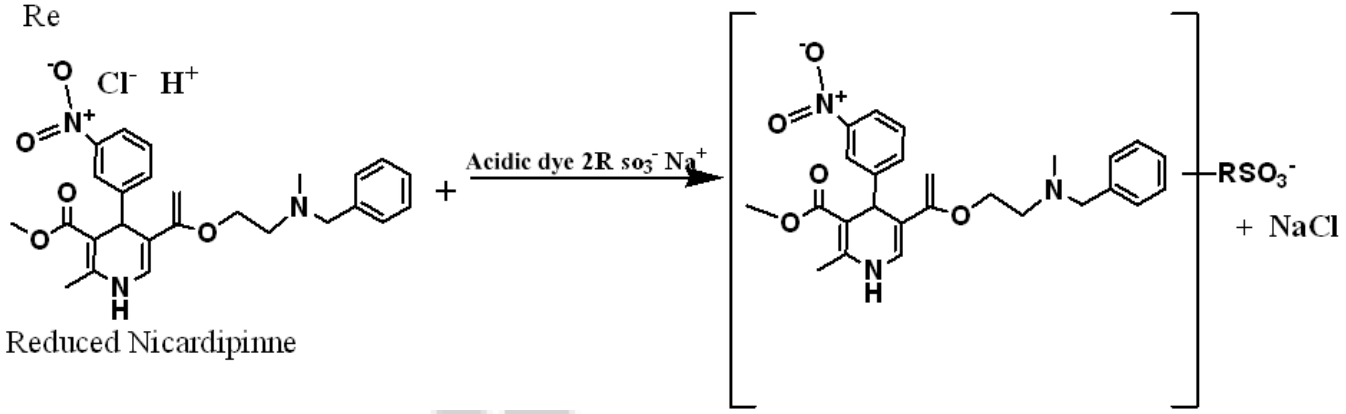
5. Acknowledgements

The authors are thankful to the Head of the Department of Chemistry, S.V. University, and Tirupati for providing the necessary facilities to complete this work.

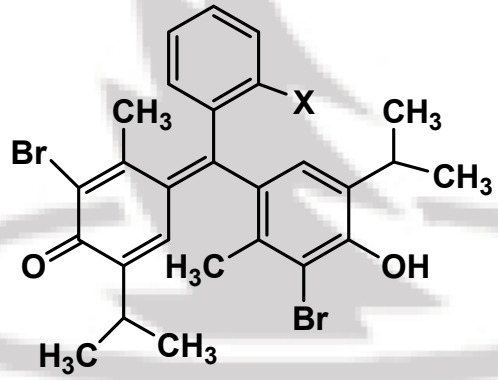
Reference

[1] Y.S.Estaharty Analytical chemistry Dept of faculty of Pharmacy. Journal of Pharmaceutical and Biomedical Analysis volume 33, issue 4, 24 November 2003 pages 699-709.
[2] R.Bakhtiar, F.L.S.Tse, volume 14, issue 13, pages 1128-1135, 15 july 2000.
[3] AL-Ghannam S.M., AL-Olyan A.M. Chemical Industry and Chemical Engineering Quarterly 2009 volume 15, Issue 2 , pages 69-76.
[4] WU Hua ZHANG Lau-tong, YUAN Zhi-Fang Liuwei-na. CNKI: SUN: YWFX.0, 2006-06-025.
[5] Sheikha M. AI-Ghannam and Abeer M, AL.Olyan central European Journal of Chemistry volume 6, Number 2, 222-228 pages.
[6] Valentina Marinkovic, Danica Agbaba, Katarina Karljikovic Rajic , Jozef Comor and Dobrila Zivanov-stakic , ll Farmaco volume 55, Issue 2, Febrauary 2000 pages 128-133. Polarography
[7] J.A Squella, Y.Borges, C.Celedon, Peredo L.T NuneJ-Veragara Electro Analysis Journal 9 April 2005.
[8] Qing Chem Meng , Albert T, Cheung , DMitric Guvakov , Stuart J.weiss , Josephs , Savino, lvan S.Salgo and Brayn E.Marshall. Journal of Chromatography: Biomedical Applications Volume 718, Issue 1, 23 October 1998, pages 121-127.
[9] Sheikha M, AL-Ghannam, Abeer M. AL-Olyan orbital 2009, 1 (1), 64-74.

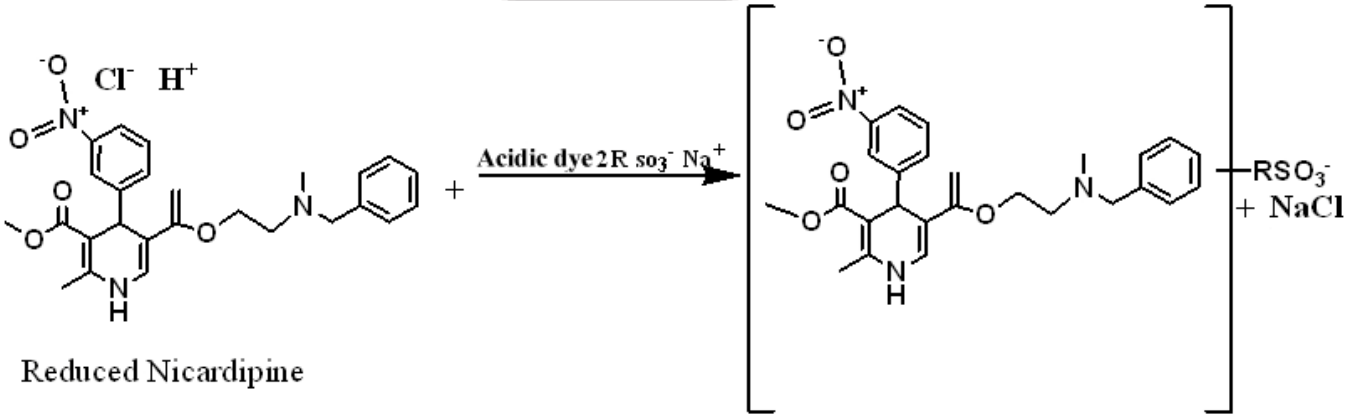
Re



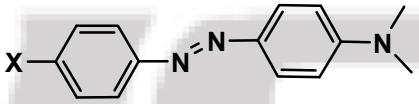
Reduced Nicardipinne

Where R =  and X = SO_3^-Na

Scheme: Reaction of NCD with BTB



Reduced Nicardipine

Where R =  and X = SO_3^-Na

Scheme: Reaction ofNCD with Methyl ORange