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EXTRACTIVE SPECTROPHOTOMETRIC DETERMINATION OF NISOLDIPINE BY ION-PAIR COMPLEX FORMATION

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ABSTRACT

Nisoldipine, a 1-4-dihydropyridine drug is determined by the development of simple and sensitive Extractive Spectrophotometric method. In the present study an ion-pair complex of amino derivative of the Nisoldipine with Bromocresol Green Solution in acidic medium is formed with subsequent extraction of the ion-pair complex in Chloroform. Maximum absorption was seen at the wavelength of 418 nm that obeys the Beer's law in the concentration range of 5-25 µg/ml.All the variables were cautiously studied and optimised. International Conference of Harmonization guidelines were strictly followed for the validation of analytical performance of the method. Drugs in commercial tablets were determined by applying the suggested method. Results also compared statistically with the reference method.

Keywords: Nisodipine, Bromocresol green, Ion-Pair complex, validation

INTRODUCTION

Nisoldipine is a dihydropyridine-based calcium channel blocker. Nisoldipine is, (±) 3-isobutyl-5-methyl-1,4-dihydro-2,6-dimethyl-4- (2-nitrophenyl) pyridine-3,5-dicarboxylate. It comes under second generation of Dihydropyridine calcium antagonist which has a selective arteriolar vasodilatation but shows negligible effects on the other vessels and myocardium **[1, 2].** It is sold as brand name Sularin the United States.

Nisoldipine exist physically as yellow crystalline substance, practically insoluble in water but soluble in methanol. Nisoldipine selectively relaxes the muscles of small arteries causing the arteries to dilate but has little or no effect on muscles of veins or the heart. It is used to treat high blood pressure. In the market Nisoldipine is

available as extended release tablets. **Figure 1** shows the structural of Nisoldipine.

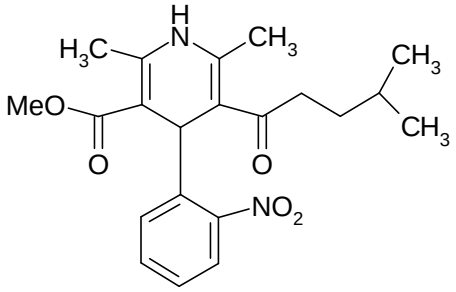
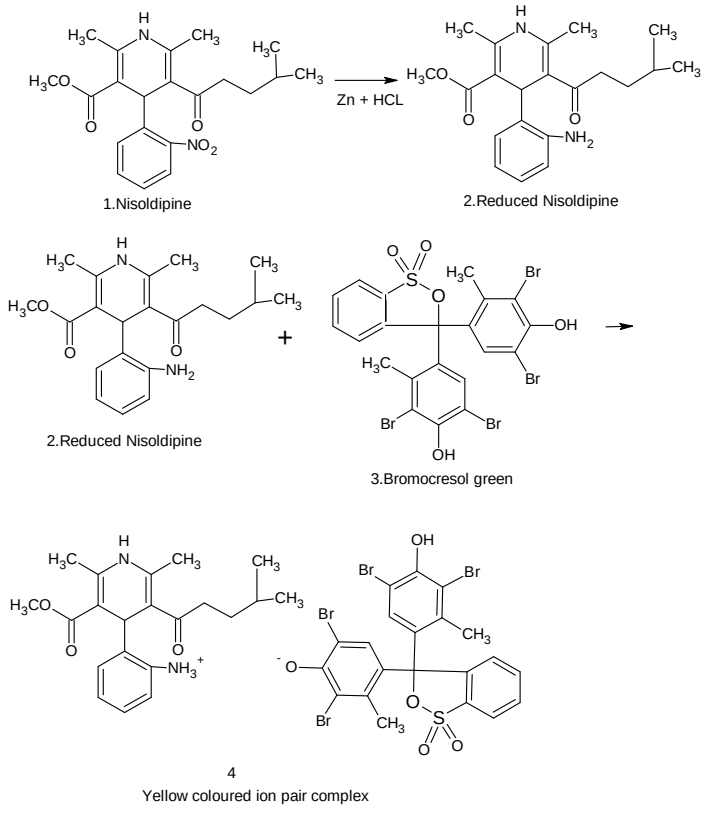


Figure 1

Few analytical methods have been developed for its determination of nisoldipine in human plasma by voltammetry **[3-6],** polarography **[7]** and HPLC and UV **[8-12].**Its pharmacokinetic properties and determination of impurities are reported by various techniques including UV **[13],** Polarography and HPLC **[14, 15].**

The present study revealed extractive visible spectrophotometric estimation which has not reported so far. The method was established to be simple, rapid, sensitive and precise. This method is based on the formation of an ion-pair complex [Scheme 1] of amino derivative of the Nisoldipine (2) with BCG (3) in acidic medium and the subsequent extraction of the ion-pair complex in chloroform. The yellow colored ion-pair complex (4) showed maximum absorption at the wavelength of 418 nm that obeys the Beer's law in the concentration rangeof 5-25 µg/ml.



Scheme 1

MATERIALS & METHODS

A Shimadzu UV/VIS Spectrophotometer (model 1700) with 1 cm., and matched quartz cells was used for all spectral measurements. All chemicals used were of A.R. grade procured from Sigma-Aldrich. Nisoldipine was gifted by ExelaPharmsci. Pvt. Ltd (Bangalore, India) and First Horizon Pharmaceutical Corporation (Alpharetta, USA).

Reagents

- Methanol
- Double distilled water
- Zinc dust
- Hydrochloric acid (4 M)
- BromocresolGreen solution
- Chloroform
- Phthalate Buffer of pH 3.5
- Anhydrous sodium sulphate

Preparation of standard and sample solutions

100 mg of nisoldipine (pure) was accurately weighed and dissolved in 30 ml. methanol. The methanolic solution of nisoldipine was treated with 10 ml. of 4N hydrochloric acid and 1.2 g of zinc dust was added in portions while shaking. After standing 1 hour at room temperature, the solution was filtered through cotton wool. The residue was washed with 10 ml portions of methanol three times and a total volume of the filtrate was made up to 100 ml with methanol (1mg/ml). The final concentration of reduced nisoldipine was brought to 100µg/ml with methanol. In case of formulation, commercially available tablets (sular) weretaken for the proposed analysis. Ten tablets of nisoldipine each containing 40 mg were accurately weighed and powdered. Tablet powder equivalent to 100 mg. of nisoldipine was taken for the study and solution of the sample prepared by above method.

Methods

Into a series of 125 ml. separating funnels, aliquots of standard drug solution 0.5-2.5 ml (1 ml = 100 µg) were pipetted out. To each separating funnel 5 ml of acid phthalate buffer of pH 3.5 solution was added, followed by 5 ml of bromocresol green solution. The yellow coloured ion-pair complex was then extracted with chloroform and dried over anhydrous sodium sulphate. The solution was diluted to 10 ml with chloroform and absorbance was measured at 418 nm against reagent blank. The colored chromogen was stable for more than 5 h. The amount of Nisoldipine present in the sample was computed from calibration curve.

RESULTS & DISCUSSION

Nisoldipine (1) contains nitro group, which is reduced to amino derivative (2) by zinc dust and Hydrochloric acid. In the present study the reduced Nisoldipine possessing primary aromatic amino group is protonated

in acidic medium, which forms ion-pair complex with bromocresol green. The ion – associated complex is quantitatively extracted with chloroform. The absorption spectra show that the ion-pair complex shows maximum absorption at 418 nm. The reagent blank prepared under similar conditions showed no absorption. The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and Sandell's sensitivity are presented in **Table 1.** The regression analysis using the method of least squares was made for the determination of slope (b), intercept (a) and correlation (r) obtained from different concentrations and results are summarized in Table1. The percent relative standard deviation and percent range of error (0.05 and 0.01 level of confidence limits) calculated from the eight measurements, 3/4thof the amount of upper Beer's law limits in each method are summarized in **Table 2**. The results showed that the methods have reasonable precision. The results obtained with the visible spectrophotometric methods are compared with the results obtained with UV spectrophotometric method.

The results obtained with proposed methods confirm the suitability of these methods for pharmaceutical dosage forms. The other active ingredients and additives usually present in the pharmaceutical dosage forms did not interfere with the estimation when some commercial dosage forms were analyzed by these methods. The accuracy of the methodis confirmed by the recovery studies by adding known amount of the pure drug to the formulation already analyzed by this method and the analytical data presented in **Tables 2**.

Table 1: Optical Characteristics and Precision

	BCG	**UV Method**
λ_{max} (nm)	**410**	**236**
Beer's law limits (μg /ml)	**5-25**	**3-18**
Molar absorptivity (L mol^{-1} cm^{-1})	**1.057x10^3**	**2.026x10^3**
Sandell's sensitivity (μg/cm^2 – 0.001 absorbance unit)	**0.0352**	**0.0196**
Regression equation (Y*) **Slope (b)** **Intercept (a)** **Correlation coefficient(r)**	 **0.0268** **0.005** **0.9998**	 **0.0529** **0.0055** **0.9998**
% RSD	**0.5070**	**0.3071**
Range of errors** **Confidence limits with 0.05 level** **Confidence limits with 0.01 level**	**0.00230** **0.00341**	**0.00160** **0.00237**

***Y= bC + a where C is the concentration of nisoldipne in μg/ml and Y is the absorbance at the respective λ_{max}., ** For eight measurements**

Table 2: Evaluation of Nisoldipine in Pharmaceutical Preparations

Sample (Tablet)	Labelled Amount (mg)	Amount obtained* (mg)		Percentage Recovery**
		Proposed method	Reference method	
		BCG	UV	BCG
T_1	40	39.91±0.07	39.95±0.03	99.9 ±0.04

*Average of five determinations, ** Mean and Standard deviation of eight determinations
(100 mg of nisoldipine was added and recovered)

CONCLUSION

In the above method, the optimum concentration for the estimation of Nisoldipine was established by varying one parameter at a time and keeping the other fixed and observing the effect of product on the absorbance of the colored species and incorporated in the procedures. After establishing the optimum concentration for the drug, the reagent concentration was varied. The above ranges of drug and reagent concentrations were chosen because the colored species formed gave better absorbance and obeyed Beer's law satisfactorily.

The other active ingredients and excipients like starch and colors like titanium dioxide, lake indigo carmine present in the dosage forms did not interfere, when added in the above concentration range to the drug and estimated by proposed method.

The methods reported here are found to be simple, sensitive, accurate, precise, and economical and can be used in the determination of nisoldipinein pharmaceutical dosage forms in a routine manner.

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