Spectrophotometric Method for the Determination of Nimodipine in Pharmaceutical Dosage Forms

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A simple and sensitive spectrophotometric method has been developed for the determination of nimodipine in bulk and pharmaceutical dosage forms.The method is based on diazotisation of reduced nimodipine with nitrous acid followed by its coupling with β-naphthol in alkaline medium to form an orange red colored chromogen with an absorption maximum of 555 nm. Good agreement with Beer's law was found in the range of reduced nimodipine concentration of 0-10 μg/ml. The optimum reaction conditions and other analytical parameters are evaluated.The proposed method has been successfully applied to the analysis of the bulk drugs and their dosage forms. No interference was observed from talc, starch, dextrose and magnesium stearate in the proposed method. Statistical comparison of the results with those of reported method showed good agreement and indicated no significant difference in precision.This method does not require any extraction or heating.

Nimodipine is chemically 1,4-dihydro-2,6 dimethyl-4-(3-nitrophenyl)-3,5-pyridine dicarboxylic acid-2- methoxy ethyl-1 methyl ethyl ester[1,2]. It is a relatively new antianginal drug. It is not yet official in any pharmacopoeia. Survey of literature revealed that nimodipine is estimated in pharmaceuticals and biological fluids by GC[3], HPLC[4-6], HPTLC[7], polarography[8], and spectrophotometry[9-13]. In the present work, a simple and sensitive spectrophotometric method was developed for the determination of nimodipine after converting it to its reduced form by zinc dust and hydrochloric acid. The presence of primary aromatic amino group in reduced nimodipine enable the use of diazo coupling reaction with alkaline β-naphthol.

An ELICO-VIS spectrophotometer model SL-150 with 1 cm matched quartz cells was used for all absorbance measurements. All the chemicals used were of Analar grade. Nimodipine was obtained as a gift sample from a local pharmaceutical company and used with out further purification. Aqueous solution of hydrochloric acid (1 N), sodium nitrite (0.1% w/v), ammonium sulphamate (0.5% w/v) and alkaline solution of β-naphthol (0.1% w/v) in aqueous solution of sodium hydroxide (4% w/v).

About 100 mg of nimodipine was accurately weighed and dissolved in 20 ml of methanol and treated with 5 g of zinc dust and 4 ml of concentrated hydrochloric acid.

After keeping for 1 h at room temperature (25±2°), the solution was filtered through cotton wool and the residue was washed with 3x10 ml portions of methanol and diluted to 100 ml with distilled water. The final concentration of nimodipine was brought to 100 μg/ml with distilled water. Into a series of 10 ml volumetric flasks 0.2 to 1.0 ml of reduced nimodipine solution (100 μg/ml) was pipetted separately and to each flask 1 ml of 1 N hydrochloric acid and 1 ml of 0.1% w/v sodium nitrite solution were added and allowed to stand for ten min at 0-5°. One milliliter of ammonium sulphamate solution was added, mixed and allowed to stand for 2 min. To this solution, 0.5 ml of alkaline β-naphthol solution was added and mixed well. The final volume was made up to 10 ml with distilled water. The absorbance of the orange red color developed was measured at 555 nm against the reagent blank.

Twenty tablets of nimodipine were accurately weighed and powdered. Tablet powder equivalent to 100 mg of

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nimodipire was dissolved in 20 ml of methanol and treated with 5 g of zinc dust and 4 ml of concentrated hydrochloric acid and this solution was treated as described above.

Mixtures containing nimodipine and common excipients such as lactose, talc, methyl cellulose, magnesium stearate and starch were prepared. A portion of the mixture equivalent to 100 mg of nimodipine was weighed accurately and dissolved in 20 ml of methanol and this solution was treated as described above.

The effect of different concentrations and volumes of reagents (hydrochloric acid, sodium nitrite, β-naphthol, sodium hydroxide) were studied at 555 nm for a fixed concentration of nimodipine (4 μg/ml).

To ensure the accuracy and reproducibility of the results obtained, 5 mg of nimodipine reference standard was added to previously analysed tablet powder extracted and the solution so obtained was treated as described above. Absorbance or the β-naphthol complex with reduced nimodipine (4 μg/ml) was measured at 555 nm at intervals of 5 min up to 60 min to investigate the stability of the coloured complex.

Nimodipine undergoes diazotisation reaction after the reduction of the nitro group of nimodipine. The orange red colored species formed in the proposed method is due to the coupling of nimodipine diazonium salt with alkaline β-naphthol solution. The absorption spectrum of the orange red colored species showed absorption maximum at 555 nm (fig.1), hence all the measurements were made at 555 nm. The reagent blank has no absorbance at this wavelength. The orange red color has been found to be stable for 45 min after which the intensity of color decreases gradually. The color obeyed Beer's law in the concentration range of 0-10 μg/ml. The other optical characteristics are given in Table 1.

Temperature of the reaction, quantity, concentration and addition of various reagents were optimized after several experiments. The optimum quantity and concentration of hydrochloric acid, sodium nitrite, β-naphthol were found to be 1 ml, 1 ml, 0.5 ml and 1N, 0.1% w/v, 0.1% w/v in 4% w/v aqueous sodium hydroxide respectively. Replacement of β-naphthol in hydrochloric acid was also tried, but color did not develop. The optimum temperature was found to be 25±2° for reduction and 0-5° for diazonium reaction.

The results of the estimation of nimodipine in synthetic mixtures containing nimodipine and excipients

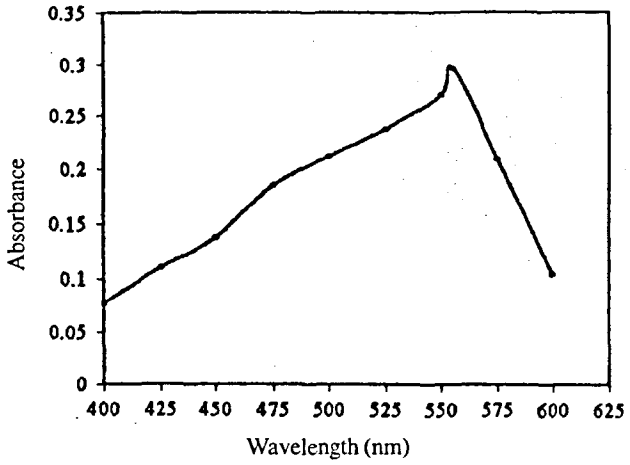

Fig.1: Absorption spectrum of dye
Concentration of reduced nimodipine is 4μg/ml

are indicative of non-interference of excipients in the drug. The accuracy of the method was checked by recovery, reproducibility studies and comparison with reported method.

Recovery studies were carried out using the procedure of standard addition and the results of which are given in Table 2. The reproducibility of the method was studied using different concentration of nimodipine and between different aliquots of the same concentration. The results were reproducible with a % coefficient variation of 0.7694.

TABLE 1 : OPTICAL CHARACTERISTICS, PRECISION AND ACCURACY DATA

λMax	555 nm
Beer's law limit	0-10 μg/ml
Molar absorptivity (L/mol/cm)	7.74×10^2
Sandell's sensitivity (μg/cm²/0.001 A.U)	0.0135
Slope	0.0814
Intercept	-0.0212
Regression equation	Y= - 0.0212 + 0.0814(x)
Correlation coefficient	0.9984
Relative standard deviation (%)	0.821

Where x is the concentration of reduced nimodipine in μg/ml of dilution and y is the absorbance at 555 nm.

TABLE 2: ESTIMATION OF NIMODIPINE IN PHARMACEUTICAL PREPARATIONS

Sample	Labeled amount (mg/tablet)	Amount found by *		Recovery studies*		% Recovery
		Proposed method (mg)	Reported method (mg)	Amount added (mg)	Amount found (mg)	
Tablet 1	30	29.92	29.39	5	5.05	101.00
Tablet 2	30	30.10	30.12	5	4.98	99.60
Tablet 3	30	29.90	29.95	5	5.02	100.40
Tablet 4	30	29.95	29.94	5	4.95	99.00

Tablets 1 and 2 are commercial and tablets 3 and 4 are prepared in the laboratory. *Average of five determinations.

When pharmaceutical preparations (tablets) containing nimodipine were analysed, the results obtained by the proposed method are in good agreement with the labeled amounts and are comparable with the results of a reported method[12]. The results are summarized in Table 2. The proposed method is simple, accurate and precise. It can be used for the routine analysis of nimodipine in bulk and in pharmaceutical formulations.

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