

Spectrophotometric Method for the Determination of Nimodipine in Pharmaceutical Dosage Forms

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A simple and sensitive spectrophotometric method for the determination of nimodipine in bulk and pharmaceutical dosage forms is described. The method is based on diazotisation of reduced nimodipine with nitrous acid followed by its coupling with α -naphthylamine to form a pink colored chromogen with an absorption maximum of 550 nm. The color obeyed Beer's law in the concentration range of 2-12 μ g/ml.

Nimodipine^{1,2} is chemically 1,4-dihydro-3,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridine dicarboxylic acid 2-methoxyethyl-1-methylethylester. It is relatively a new antianginal drug. It is not yet official in any pharmacopoeia. Survey of literature reveals that nimodipine is estimated in pharmaceuticals and in biological fluids by spectrophotometry³⁻⁶, GC⁷, HPLC⁸⁻¹¹, HPTLC¹¹ and polarography¹². 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 diazocoupling reaction with α -naphthylamine. Spectrophotometric parameters are established for standardization of the method including statistical analysis of the data. This method has been successfully extended for the analysis of nimodipine in the pharmaceutical preparations.

An ELICO UV-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. Aqueous solutions of hydrochloric acid (5 N), sodium nitrite (0.1% w/v), ammonium sulphamate

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TABLE 1 : ESTIMATION OF NIMODIPINE IN PHARMACEUTICAL PREPARATIONS

| Sample | Labelled Amount (mg/tablet) | Amount found by | | Recovery Studies | | |
|----------|-----------------------------|----------------------|-----------------------------------|-------------------|-------------------|------------|
| | | Proposed method (mg) | Reported method ⁴ (mg) | Amount added (mg) | Amount found (mg) | % Recovery |
| Tablet 1 | 30 | 29.82 | 29.39 | 5 | 5.025 | 100.50 |
| Tablet 2 | 30 | 30.02 | 30.01 | 5 | 4.91 | 98.27 |
| Tablet 3 | 30 | 29.92 | 29.98 | 5 | 5.05 | 101.05 |
| Tablet 4 | 30 | 29.85 | 29.94 | 5 | 4.96 | 99.29 |

Tablet 1 and 2 are commercial and tablets 3 and 4 are prepared in the laboratory.

(0.5% w/v) and solution of α -naphthylamine (1mg/ml) in absolute ethanol were prepared. Nimodipine was obtained as gift sample from a local industry.

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 conc. hydrochloric acid. After keeping for 1 h at room temperature ($25 \pm 2^\circ$), the solution was filtered through cotton wool and the residue was washed with 3×10 ml portions of methanol and diluted to 100 ml with distilled water. The final concentration of reduced nimodipine was brought to 100 μ g/ml with distilled water.

Twenty tablets of nimodipine were accurately weighed and powdered. Tablet powder equivalent to 100 mg of nimodipine was dissolved in 20 ml of methanol and treated with 5 g of zinc dust and 4 ml of concentrated hydrochloric acid and the solution was prepared and analysed as given above.

Into a series of 10 ml volumetric flasks 0.2 to 1.2 ml of reduced nimodipine solution (100 μ g/ml) was pipetted separately and to each flask 1 ml of hydrochloric acid and 1 ml of sodium nitrite solution were added and allowed to stand for five minutes. One millilitre of ammonium sulphamate solution was added, mixed and allowed to stand for 2 minutes. To this solution 1 ml of α -naphthylamine solution was added and mixed well. The final volume was made upto 10 ml with distilled water. The pink color developed was measured at 550 nm against the reagent blank. The amount of nimodipine present in the sample solution was computed from calibration curve.

Recovery experiments were performed by adding a known amount of the drug to previously analysed phar-

maceutical formulations. The results are given in Table 1.

The colored solution exhibited λ_{max} at 550 nm. The color obeyed Beer's law in the concentration range of 2-12 μ g/ml. The regression line was found to be $Y = 5.0 \times 10^{-3} + 3.6 \times 10^{-3} X$, where X is the concentration of reduced nimodipine in micrograms per ml of dilution and Y is the absorbance at 550 nm. Sandell's sensitivity (μ g/cm²/0.001 absorbance unit) and molar absorptivity ($l \cdot mole^{-1} \cdot cm^{-1}$) were found to be 0.019 and 2.118×10^4 respectively.

When the stock solution containing 100 μ g of reduced nimodipine was assayed repeatedly (n=6), the % RSD and % range of error (0.05 and 0.01 level confidence limits) were found to be 1.362, 1.139 and 1.685 respectively. When pharmaceutical preparations (tablets) containing nimodipine were analysed the results obtained by the proposed method are in good agreement with the labelled amounts and are comparable with the results of a reported method⁴. The results are summarised in Table 1. The pink colored species formed in the proposed method is due to the coupling of diazonium salt (formed from reduced nimodipine and nitrous acid) with α -naphthylamine¹³. The proposed method is simple, accurate and precise. It can be used for the routine quality control analysis of nimodipine in bulk and in pharmaceutical formulations.

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