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A New Spectrophotometric Method for the Determination of Nitrendipine

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A simple and sensitive spectrophotometric method for the determination of nitrendipine is described. The method is based on the reaction of reduced nitrendipine with 3-methyl-2-benzo-thiazolinone hydrazone hydrochloride (MBTH) in the presence of ferric chloride to form a green colored chromogen with an absorption maximum of 670 nm. The color obeyed Beer's law in the concentration range of 2-10 µg/ml.

Nitrendipine[1,2] chemically ethyl 1,4-dihydro-5-(acetoxy carbonyl)-2,6-dimethyl-4-(3-nitrophenyl)-3-pyridine carboxylate, is a relatively new antianginal drug. It is not yet official in any pharmacopoeia. A survey of the literature revealed that HPLC[3-6] and few spectrophotometric methods[7-8] are reported earlier for the determination of nitrendipine in biological fluids and in dosage forms. Huning and Fritsch[9] had described the oxidative coupling of MBTH with aromatic amines in the presence of an oxidant under acidic conditions. Sawicki *et al.*[10] investigated the reaction of MBTH with a number of amines and found that the reagent MBTH reacts readily with most aromatic amines resulting in the formation of an intensely colored azodye cation. The presence of primary aromatic amino group in the reduced nitrendipine enable the use of MBTH-Fe (III) reagent to form a green colored chromogen.

An ELICO model SL-150 UV-VIS spectrophotometer with 1 cm matched quartz cells was used for all absorbance measurements. All the chemicals used were of AnalaR grade. An aqueous solution of MBTH (0.2% w/v) and solution of ferric chloride (0.7% w/v) in 0.5 N hydrochloric acid were prepared. Nitrendipine was obtained as gift sample from a local industry.

Nitrendipine (20 mg), 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, the solution was filtered through cotton wool, and the residue was washed with 3x10 ml portions of methanol and the total volume was brought to 100 ml with distilled water. Working standard solutions were obtained by appropriate dilution of the standard solution.

In a series of 10 ml volumetric flasks, aliquots of reduced nitrendipine solutions (1.0-5.0 ml, 20 µg/ml) were placed. A 1.5 ml portion of MBTH solution was added to each flask and kept aside for 2 min at room temperature. Then 2.0 ml of ferric chloride solution was added, kept for 10 min and diluted to the mark with distilled water. The absorbances were measured at 670 nm against a reagent blank.

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TABLE 1 - ANALYSIS OF NITRENDIPINE FORMULATIONS

Formulation	Label Claim (mg/Tablet)	Amount found		% Recovery
		Proposed method (mg)	Reported method[7] (mg)	
Tablet-1	20	19.97	19.98	101.00
Tablet-2	20	19.89	19.99	99.00

Two brands of commercial tablets containing nitrendipine were analysed by the proposed method. In each case, twenty tablets were weighed and powdered. Tablet powder equivalent to 20 mg of nitrendipine was taken in a flask, 20 ml of methanol was added and mixed to dissolve the drug. To each flask, 5 g of zinc dust and 4 ml of concentrated hydrochloric acid were added, mixed and set aside for 1 h. Further analysis was carried out by using the above procedure. The amount of nitrendipine was computed from its reduced product's calibration graph.

Recovery experiments were performed by adding a known amount of the drug to the previously analysed pharmaceutical formulations and also to various excipients used in formulations. The results are given in Table-1.

The colored solution exhibited λmax at 670 nm. The color obeyed Beer's law in the concentration range of 2-10 µg/ml. The regression line was found to be $Y=3.6 \times 10^{-3} + 4.5 \times 10^{-3} X$, where X is the concentration of reduced nitrendipine in µg/ml of dilution and Y is the absorbance at 670 nm. Sandell's sensitivity (µg/Cm^2/0.001 abs. unit) and molar absorptivity (lit.$mole^{-1}$. cm^{-1}) were found to be 0.022 and 1.65×10^4 respectively. When the stock solution containing 80 µg of drug was assayed repeatedly (n=5) the per cent RSD and percent range of error (0.05 significance level) were found to be 1.22 and 1.02 respectively. When tablets containing nitrendipine 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 method (Table -1). The excipients usually present in the dosage forms did not interfere in this method.

The reaction of MBTH with reduced nitrendipine in the presence of ferric ions proceeds via oxidative coupling which is similar to reported[11,12] earlier for aromatic amines. Under the reaction conductions, MBTH loses two electrons and one proton forming the electrophilic intermediate, which is the active coupling species. The intermediate attacks the position para to $-NH_2$ in reduced nitrendipine resulting in the formation of a green colored azodye cation.

These results indicate that the proposed method is sensitive, accurate, precise and reproducible and can be used for the routine determination of nitrendipine in bulk and in dosage forms.

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