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DEVELOPMENT AND VALIDATION OF ANALYTICAL METHOD FOR ESTIMATION OF NIMODIPINE CONTENT BY UV-SPECTROSCOPIC METHOD

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ABSTRACT

A Simple, specific, rapid, precise and accurate UV Spectrophotometric method have been developed and Validated for determination of Nimodipine formulation drug. Nimodipine showed the absorption maxima in at 239.0 nm and was linear for a range of 5 µg/ml–25 µg/ml with correlation coefficient of 0.9996. The validation of the above proposed method was done by carrying out precision and accuracy studies. The analytical method showed good Intra precision (Repeatability) with relative standard deviation 0.522% and Inter precision with relative standard deviation is 0.355% which is less than 2. The percentage recovery at three different levels i.e. 50%, 100% and 150% was found to be 49.9%, 99.1% and 149.6% respectively. The proposed method was validated for the parameter Specificity, Precision, Linearity and range, Ruggedness, Accuracy and recovery. Hence proposed analytical method for estimation of Nimodipine formulation drug by UV spectrophotometer in pharmaceutical can be applied for the routine quality control analysis.

KEYWORDS: Validation, Nimodipine, UV Spectrophotometer.

INTRODUCTION

Nimodipine is cardio selective calcium channel blocker, an Anti-hypertensive drug being used for cerebrospinal haemorrhgae. Nimodipine is well known for its significant action on cerebral blood vessels and its potential cytoprotective effects by reducing calcium influx into nerve.[1] The IUPAC name is 3, 5-Pyridinedicarboxylic acid, 1, 4-dihydro-2, 6-dimethyl-4-(3-nitrophenyl)-, 2-Methoxyethyl 1-Methylether ester. Nimodipine having molecular formula

$C_{21}H_{26}N_2O_7$ and Molecular weight 418.44 g/mol. It is official in European/British pharmacopoeia[2] and United States pharmacopoeia[3] with Assay method by Potentiometric titration. Literature survey revealed that few analytical methods are available including Titrimetric[4], UV Spectrophotometry[5-8] and HPLC.[9-17]

In the present work, a simple, accurate and sensitive method for determining Nimodipine content in drug substance pure form was introduced. No simple and rapid work has been reported for the estimation of Nimodipine formulation drug. All these reported methods either took a long time for analysis or employ mobile phases with pH adjustment of Buffer solutions for sample preparation, which is tedious and anomalous[4-17], especially for routine testing of quality control samples of assay content study. Hence it was felt necessary to build up a simple, rapid, economical and precise Spectrophotometric method for the direct estimation of Nimodipine formulation drug.

The current research work deals with the development of UV Spectrophotometric method and its validation as per International Conference on Harmonization (ICH) guideline.[18-20] The developed method was found to be simple, specific, stable, rapid, accurate, precise, reliable, less expensive and time saving by UV Spectrophotometric method[5-8] for the estimation of Nimodipine content in drug substance.

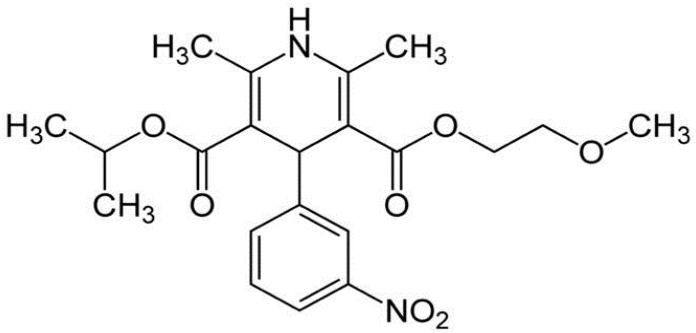

Figure 1: Chemical structure of Nimodipine.

MATERIALS AND METHODS

Instrumentation and Materials

U.V. visible double beam spectrophotometers SL 210 Elico with Spectra treat software having path length 1cm U.V. matched quartz cells were used. Nimodipine Sample and Standard gifted from Omicron Pharmaceuticals, Surat Gujarat. All chemicals, solvents and reagents i.e. Acetic acid, Ethanol, Water and Methanol used, were analytical grade and purchased from Merck Ltd, India, S.D. Fine Chem Ltd/Qualigens.

Method Development

Preparation of Diluent Solution

Transferred about 600 ml of water to the 1000 ml volumetric flask, then slowly added about 2.0 mL of Acetic acid with constant stirring and, mixed well, then with constant stirring slowly added Methanol up to mark to make volume 1000 ml. used this solution as diluent.

Preparation of Standard Solution

Weighed accurately about 120 mg of Nimodipine and transferred to 200 ml amber volumetric flask. Dissolved in 10 ml ethanol, then added diluent with intermittent shaking and made up the volume up to 200 ml, further transferred 2 ml of solution to 100 ml amber volumetric flask. Made volume up to mark to get a concentration of 12µg/ml.

Selection of wavelength for analysis of Nimodipine

The standard solution having concentration 12µg/ml was scanned at 200 nm to 400 nm with diluents as the blank to detect maximum wavelength (Figure-2).

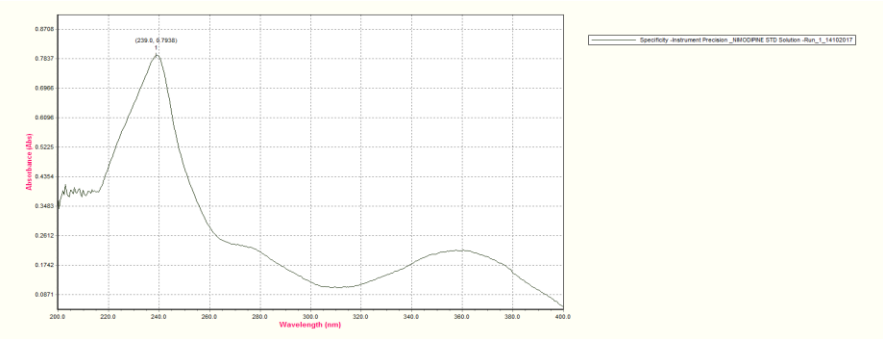

Figure 2: Estimation of Maxima of Nimodipine.

From the above (Figure-2) spectra of Nimodipine wavelength maxima identified for quantification were 239.0 nm (λmax).

Validation of proposed Analytical Method

The proposed method was validated according to International Conference on Harmonization (ICH) guidelines for validation of analytical procedures [22-24]. Analysis of variance was used to ensure the validity and performance effectiveness of the proposed analytical methods.

Specificity

Specificity is the ability to assess unequivocally the analyte in the presence of components which may be expected to be present. Typically these might include impurities, degradants,

matrix, etc. Specificity was done by scanning of diluent solution and Standard solution of Nimodipine having concentrations 12 µg/ml in Spectrophotometric range from 200 nm to 400 nm to check specific absorption maxima at predefined wavelength i.e. 239.0 nm and solution stability study performed to evaluate the solution stability at different time interval up to 26 hrs.

Instrument Precision

Instrument precision was performed to check the suitability of the developed analytical method with respect to ability of instrument consistency to provide the precise wavelength maxim when scanned the Standard solution of Nimodipine having concentrations 12 µg/ml in the UV range from 200 nm to 400 nm. To check specific absorption maxima at predefined wavelength 239.0 nm with reproducible absorption detection. Six separated standard preparations were scanned / analyzed according to the proposed method of analysis. The % RSD due to Nimodipine concentration for the six standards was found 0.350%. The % RSD due to Nimodipine concentration for the instrument precision meets the requirements. Results are tabulated in the Table 1.

Table 1 Instrument Precision.

Sr. No.	Standard number	Absorbance@239.0 nm	% RSD
1	Standard Preparation -1	0.7938	0.350% Limit < 2%
2	Standard Preparation -2	0.7953	
3	Standard Preparation -3	0.7968	
4	Standard Preparation -4	0.8001	
5	Standard Preparation -5	0.7954	
6	Standard Preparation -6	0.7919	
Average Absorbance		→ 0.7956	

Linearity and Range

The linearity of an assay method is its ability to elicit test results, which are directly proportional to the concentrations of drug in samples in a given range. Linearity justifies the use of single-point calibrations. The correlation coefficient of the Regression line for was found that 0.9996.

Five levels of five different concentrations Standard solution of Nimodipine having concentrations 5 µg/ml, 10 µg/ml, 15 µg/ml, 20 µg/ml and 25 µg/ml, in the range relative to the working concentrations, were prepared and read according to the method of analysis. A linear regression curve was constructed, the correlation coefficient (R2) and assessment value

calculated. The correlation coefficient (R2) for Nimodipine obtained is 0.9996. The plot is a straight line and the results are tabulated in the Table 2 and Curve is shown in the Figure 3.

Table 2 Linearity and Range.

Sr.No.	Standard Concentration (µg/ml)	Absorbance @ 239.0 nm	Correlation coefficient
1	5	0.2370	0.9996 Limit ≥0.999
2	10	0.6108	
3	15	0.9727	
4	20	1.3338	
5	25	1.6521	

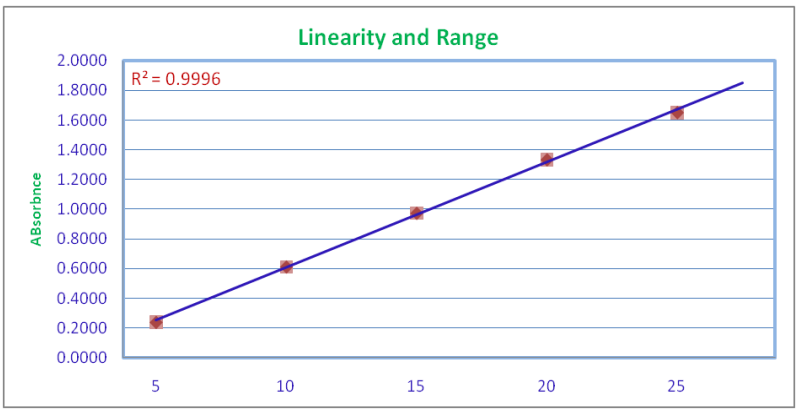

Figure 3: Linearity and Range of Nimodipine.

Analytical Method Precision

The precision of an analytical procedure expresses the degree of agreement among individual test results when the method is applied to multiple sampling of a homogenous sample.

Procedure for analysis of Sample

Weighed accurately about 120 mg of Nimodipine and transferred to 200 ml amber volumetric flask. Dissolved in 10ml ethanol, then added diluent and made up the volume to 200 ml, further transferred 2 ml of solution to 100 ml amber volumetric flask. Made volume up to mark to get a concentration 12 µg/ml.

Intra Precision (Repeatability)

This parameter determines the repeatability of Nimodipine assay results under the same operating conditions over a short period of time. The % RSD due to Nimodipine concentration for the six samples was found to be 0.522%. Six separated sample preparations were analyzed according to the proposed method of analysis. The % RSD due to Nimodipine concentration for the assay meets the requirements. Results are tabulated in the Table 3.

Table 3 Intra Precision (Repeatability) Results.

Sr. No.	Sample number	Nimodipine % Assay content	% RSD of Six Assay content
1	Sample Preparation -1	99.9	0.522% Limit < 2%
2	Sample Preparation -2	98.5	
3	Sample Preparation -3	99.0	
4	Sample Preparation -4	99.1	
5	Sample Preparation -5	99.5	
6	Sample Preparation -6	99.7	
Average % Assay		99.3	

Inter Precision (Repeatability*)*

This parameter determines the Intermediate repeatability of Nimodipine assay results under the same operating conditions test performed on a different day, using different makes of reagents and solvents. The %RSD due to Nimodipine concentration for the six samples was found to be 0.355%. Six separated sample preparations were analyzed according to the proposed method of analysis. The % RSD due to Nimodipine concentration for the assay meets the requirements. Results are tabulated in the Table 4.

Table 4 Inter Precision (Repeatability) Results.

Sr. No.	Sample number	Nimodipine % Assay Content	% RSD of Six Assay content
1	Sample Preparation -1	100.5	0.355% Limit<2%
2	Sample Preparation -2	99.6	
3	Sample Preparation -3	100.2	
4	Sample Preparation -4	100.3	
5	Sample Preparation -5	99.9	
6	Sample Preparation -6	99.7	
Average % Assay		100.0	

Ruggedness

Ruggedness of the method was determined by carrying out the analysis on different days, different makes of reagents and solvents. The respective test assay results of Nimodipine having concentration as 12µg/ml was illustrious. The result is expressed as shown in table-3, 4. The developed method for estimation of Nimodipine was found to be rugged as Shown in table 5.

Table 5 Ruggedness.

Sr. No.	Precision	% RSD of Assay (Six Preparation)	Limit For Ruggedness
1	Intra Precision	0.522	NMT 2%
2	Inter Precision	0.355	
% RSD of Overall 12 Assay content		0.576	

ACCURACY

This parameter determines the accuracy of the assay results under the same operating conditions test.

A Nimodipine sample was constituted analyzed for the accuracy with known quantity of samples of Nimodipine at 50%, 100%, 150% concentration levels and assayed as per the method stated under analytical Methods respectively. Three determinations were performed under each concentration levels respectively. Results are shown in Tables 6, 7, 8. The % RSD due to recovery of Nimodipine at 50%, 100%, 150% concentration levels was found to be 49.9%, 99.1% and 149.6% respectively. Nine sample preparations were analyzed according to the proposed method of analysis. The %RSD due to Nimodipine concentration for the assay meets the requirement and accuracy of recovery is within 98.0% to 102%. Results are tabulated in the Table 6, 7, 8.

Table 6 Accuracy and Recovery Results @ 50 % Concentration level.

Sr. No.	Accuracy @ 50% level	Recovery of Nimodipine % Assay content	% Recovery 98.0% to 102%	% RSD
1	Sample Preparation -1	49.5	99.8	0.923% Limit< 2%
2	Sample Preparation -2	49.8		
3	Sample Preparation -3	50.4		
Average % Assay		49.9		

Table 7 Accuracy and Recovery Results @ 100 % Concentration level.

Sr. No.	Accuracy @ 100% level	Recovery of Nimodipine % Assay content	% Recovery 98.0% to 102%	% RSD
1	Sample Preparation -1	99.7	**99.1**	0.748% Limit < 2%
2	Sample Preparation -2	98.3		
3	Sample Preparation -3	99.3		
Average % Assay		99.1		

Table 8 Accuracy and Recovery Results @ 150 % Concentration level.

Sr. No.	Accuracy @ 150% level	Recovery of Nimodipine % Assay content	% Recovery 98.0% to 102.0%	% RSD
1	Sample Preparation -1	151.1	**99.7**	1.023% Limit < 2%
2	Sample Preparation -2	148.0		
3	Sample Preparation -3	149.7		
Average % Assay		149.6		

Solution Stability

Solution stability of the Nimodipine solution was performed up to 26 hrs with different time interval and found the solution is stable showing cumulative % RSD of different time interval is 0.530 which is less than the 2. Hence the Nimodipine solution is found stable up to 26 hrs at room temperature and recommended 24 hrs solution stability.

RESULTS AND DISCUSSION

The method discussed in the present work provides a simple, stable, rapid, accurate, precise, reliable, less expensive (Economical), time *saving* and convenient method for the analysis of Nimodipine using U.V. Spectrophotometry. λ max selected for quantitation was 239.0 nm. In the developed analytical method, the linearity was observed 0.9996 in the concentration range of 5 µg/ml -25 µg/ml.

Method precision for the Nimodipine at concentrations level 12µg/ml was found in the range of 98.5%-100.5%. Accuracy of the proposed method was ascertained by recovery studies and the results were expressed as percent recovery and were found in the Range of 98.3%-100.7%.Values of standard deviation and coefficient of variance was satisfactorily indicating the accuracy of both the methods. Intra-day and Inter-day precision studies were carried out by analyzing the sample of Nimodipine different time interval on the same day and on different days respectively. Standard deviation and coefficient of variance for Intra-day and Inter-day precision studies was found to be less than 2 indicating precision of the proposed method.

Based on the outcome of analytical method development and analytical validation study test results, it was found that, the proposed analytical method for estimation of Nimodipine by UV Spectrophotometry is Accurate, Precise, Reproducible, Stable, Simple, Rapid Time saving and less expensive (Economical). The analytical method can be employed for routine quality control estimation of Nimodipine formulation drug in pharmaceutical analysis.

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