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UV Spectroscopic Method Development and Validation of Nimodipine in Bulk and Its Tablet Dosage Form

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ABSTRACT

A simple, specific, rapid, precise and accurate UV-spectrophotometric method have been developed and validated for determination of nimodipine in API and its formulation. Nimodipine showed the absorption maxima in at 230 nm and was linear for a range of 5 µg/ml-25 µg/ml with correlation coefficient of 0.997.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 deviation0.11% and inter precision with relative standard deviation is 0.22% which is less than 2. The percentage recovery at three different levels i.e. 80%, 100% and120%was found tobe91.66%, 98.33%and 101.25% respectively. The proposed method was validated for the parameter specificity, precision, linearity and ruggedness, accuracy and recovery. Hence proposed analytical method for estimation of nimodipine in API and its formulation by UVspectrophotometer in can be applied for the routine quality control analysis.

Key words: Nimodipine, UV-spectrophotometer, validation, calcium channel blocker.

I. 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.The IUPAC name is isopropyl-2-methoxyethyl-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridine dicarboxylate.Nimodipine having molecular formula with $C_{21}H_{26}N_2O_7$ and molecular weight is 418.44 g/mol.It is official in European/British Pharmacopoeia and United States Pharmacopoeia with assay method by potentiometrictitration[1,2].

Analysis is an important procedure in the formulation and development of any drug molecule. A suitable and validated method must be available for the analysis of drug in the bulk, in drug delivery systems, for dissolution studies as well as in-vivo studies.

Literaturesurveyrevealedthatfewanalyticalmethodsa reavailableincluding titrimetric, UV Spectrophotometerand HPLC.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 anomalousepically 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[3,4].

The current research work deals with the development of UV Spectrophotometric method and its validation as per International Conference on Harmonization (ICH) guidelines.

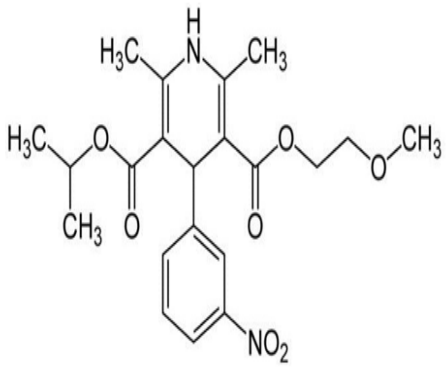

Figure 1: Structureof nimodipine

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II. MATERIALS AND METHODS

Instruments used

UV-Visible spectrophotometer with UV Win software, weighing balances and matching quartz cells with a 1 cm cell path length were utilized along with the mentioned equipment, which had automatic wavelength accuracy of 0.1 nm.

Chemicals and reagents

Pharmaceutical grade nimodipine(API) was procured as gift sample from Hetero Drugs Ltd., Hyderabad, Telangana, India. The marketed pharmaceutical dosage form of nimodipinetablets (Nimodip30 mg) was purchased from local pharmacy, Hyderabad, Telangana, India. All chemicals and reagents were of analytical grade.

Solvent selection

A number of trails were done to find out the ideal solvent for dissolving the drug. The solvents such as double distilled water, ethanol was tried based on the solubility of the drug.

Selection of detection wavelength

Appropriate volume 1 ml of standard stock solution of nimodipine was transferred into a 10 ml volumetric flask, diluted to a mark with ethanol to give concentration of 10 µg/ml. The resulting solution was scanned in the UV range (200-400 nm).

Preparation of stock solution[5,6]

A precisely weighed, 10 mg of nimodipine was transferred to 10 ml volumetric flask (clean and dry). Then few ml of ethanol was added and dissolved the drug by vigorous shaking. The volume was then made up to the mark with ethanol to obtain the stock solution of 1000 µg/ml.

Preparation of working standard solution

From stock solution 1 ml was pipetted out further diluted to 10 ml with ethanol to get the solution having the concentration of 100µg/ml.

Preparation of calibration curve

From the working standard solution, pipetted out 0.5ml, 1ml, 1.5 ml,2ml, and 2.5ml was diluted to 10 ml using ethanol to produce5,10,15,20 and 25µg/mlsolutionsrespectively. The absorbance of the solutions at the λ_{max} of 230 nm using ethanol as blank was measured. The calibration curve was plotted by taking concentration on X-axis and absorbance on Y-axis. The curve shows linearity in the concentration range of 5-25 µg/ml. The correlation co-efficient (r^2) was found to be 0.997.

Assay of pharmaceutical formulation

20 Tablets of nimodipine marketed formulations were weighed and powdered. A quantity of tablet powder equivalent to 50mg of nimodipine was transferred to 100 ml volumetric flaskand volume was made up to the mark with ethanol.The absorbance of the resulting solution was measured at 355 nm and the amount of nimodipine was computed from its calibrationplot.

Method development and validation[7-9]

These current validation characteristics describe the validation parameters stated by the International Conference on Harmonization (ICH) guidelines.

Linearity

The linearity of an analytical procedure is its ability to obtain test results, which are directly proportional to the concentration of analyte in the sample. Linearity can be assessed by performing single measurements at several analyte concentrations. A linearity correlation coefficient above 0.997 is acceptable for most methods, especially for major components in assay methods. The range of an analytical procedure is the interval between the upper and lower concentration of analyte in the sample.

Precision

The precision of an analytical procedure expresses the closeness of agreement between a series of measurements obtained from multiple sampling of the same homogenous sample under prescribed conditions. Precision was determined by intra-day and inter-day study. The repeatability of the method was evaluated by carrying out the assay 3 times on the same day and intermediate precision was evaluated by carrying out the assay on 3 consecutive days for the sample solution. The percent relative standard deviation (%RSD) was calculated.

Accuracy (Recovery studies)

The accuracy of analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted true value. Accuracy studies were performed at three different levels (80%, 100% and 120%) by standard addition method and the samples were analyzed in triplicate by the proposed method. Known amount of standard sitagliptin at 80%, 100% and 120% of

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predetermined sample was added to a pre-quantified tablet sample.

Ruggedness

Method ruggedness is defined as the reproducibility of results when the method is performed under actual use conditions. This includes different analysts, laboratories, columns, instruments, sources of reagents, chemicals, solvents and so on. Method ruggedness may not be known when a method is first developed, but insight is obtained during subsequent use of that method.

Robustness

The concept of robustness of an analytical procedure has been defined by the ICH as "a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters". The most important aspect of robustness is to develop methods that allow for expected variations in the separation parameters. For the determination of a method's robustness, parameters such as variation in detector wavelength are varied within a realistic range and the quantitative influence of the variables is determined. If the influence of the parameter is within a previously specified tolerance, the parameter is said to be within the method's robustness range. The absorbance was measured and assay was calculated for six times.

LOD and LOQ

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantified as an exact value. The quantitation limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy.

LOD = 3.3 × σ/S

LOQ = 10 × σ/S

Where, σ = Standard deviation of the response, and S = Slope of the calibration curve

III. RESULTS AND DISCUSSION

The object of the study was to develop analytical method for the estimation of nimodipine. Hence an attempt was made to develop new method on the basis of UV spectra.

The method discussed in the present work provides a simple, stable, rapid, accurate, precise,reliable, less expensive (Economical), timesavingand convenient method for the analysis of nimodipine using UVSpectrophotometry. λ_{max} selected for quantitation was 230 nm. In the developed analytical method, the linearity was observed 0.997 in the concentration rangeof 5 µg/ml-25 µg/ml.

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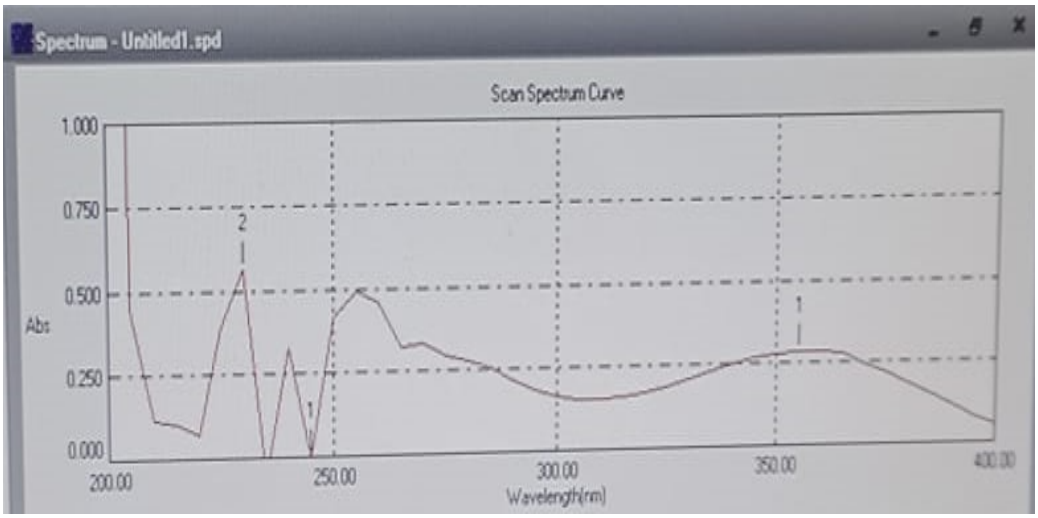

Figure 2: Absorption maxima of nimodipine

Table 1: Linearity of nimodipine

Concentration (µg/ml)	Absorbance
5	0.199
10	0.401
15	0.624
20	0.835
25	0.996

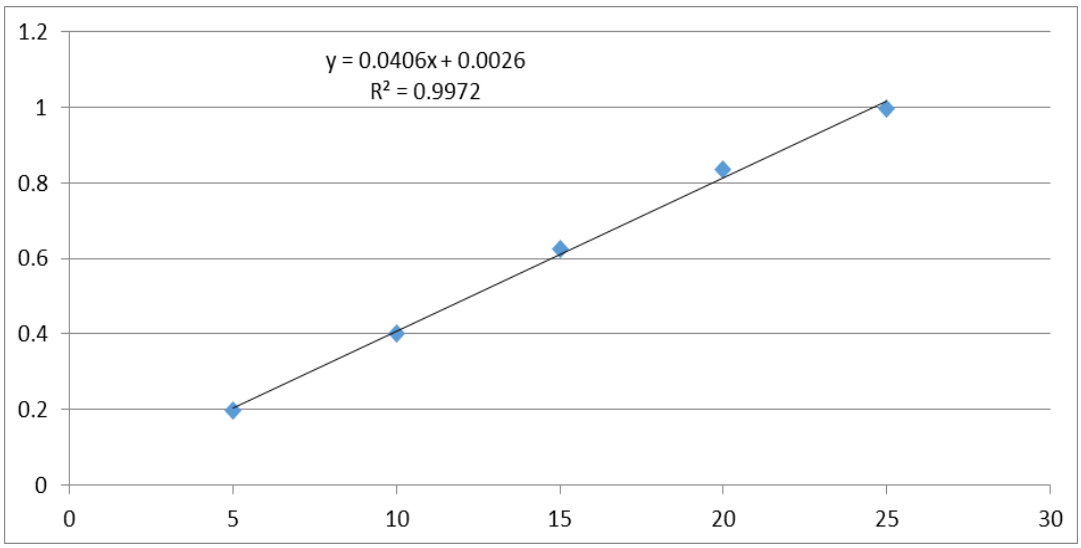

Figure 3: Linearity

Table 2: Precision

S. No.	Concentration (µg/ml)	Absorbance (intraday)	Absorbance (interday)
1	10	0.646	0.618

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2	10	0.642	0.62
3	10	0.643	0.619
4	10	0.642	0.62
5	10	0.644	0.621
6	10	0.645	0.62
Mean		**0.645**	**0.619**
Std. dev.		**0.00071**	**0.00141**
% RSD		**0.11**	**0.227**

Table 3: Results for accuracy

S. No.	Level of adding	Amount added (µg/ml)	Amount recovered(µg/ml)	Percentage recovery
1	80	1.2	1.10	91.66
2	100	1.5	1.47	98.33
3	120	1.8	1.82	101.25

Table 4: Results for robustness

S. No.	Wavelength	Absorbance
1.	227 nm	0.615
2.	230 nm	0.616
3.	233 nm	0.617

Table 5: Results for ruggedness study

S. No.	Analyst	%RSD
1	Analyst-1	0.924
2	Analyst-2	0.915

Table 6: Assay of tablets

Drug	Labelled amount	Mean	SD	% Assay	% RSD
Nimodipine	30mg	0.994	0.001414	99.66	0.142

Table 7:LOD and LOQ of nimodipine

LOD	0.0675µg/ml
LOQ	0.204µg/ml

Method precision for the nimodipine at concentrations level 10µg/ml was found in the rangeof 98.5%-100.5%. Accuracy of the proposed method was ascertained by recovery studies andthe results were expressed as percent recovery and were found in the range 91.66%-101.25%. Values of standard deviation and coefficient of variance was satisfactorily indicatingthe accuracy of both the methods. Intra-day and inter-day precision studies were carried outby 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.

IV. CONCLUSION

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 timesaving and less expensive (Economical). The analytical method can be employed for routine quality control estimation of nimodipine formulation drug pharmaceutical analysis.Thus, these can be used as alternatives for rapid and routine determination of bulk samples and tablets.

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Competing interest statement

No conflict of interests regarding publication of this paper.

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REFERENCES

[1]. Langley MS and Sorkin EM. Nimodipine: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in cerebrovascular disease. Drugs. 1989;37(5):669–699.

[2]. Nirmala B, Prakash MS, Nagarajan M and Asok Kumar K. Spectrophotometric determination of nimodipine and its formulations. Indian Drugs. 1999;36(10):661–662.

[3]. Tegeli VS, Gajeli GK, Chougule GK, Thorat YS, Shivsharan US, KumbharST.Significance of Impurity Profiling: A review. International Journal of Drug Formulation and Research. 2011; 2(4):174-195.

[4]. Chowdary KPR and Devala Rao G. A new spectrophotometric method for the determination of nimodipine. Indian Drugs. 1995;32(11):548–550.

[5]. Thaidala Sriveni, Vanamala Naveen, Vemula Sai Rupa, Aeruva Renuka, Sunil Porika, M Akiful Haque, Vasudha Bakshi, Narender Boggula. Development and Validation of Dolutegravir in Bulk and Formulation: An Anti-Retroviral Drug Using UV-Spectroscopy. International Journal of Pharmaceutical Quality Assurance. 2021; 12(1):57-60.

[6]. Belal F, Al-Majed AA, Julkhuf S and Khalil NY. Spectrofluorometric determination of nimodipine in dosage forms and human urine. Pharmazie. 2003;58(12):874–876.

[7]. Reddy MN, Murthy TK, Rao Kanna KV, Gopal Hara AV and Sankar DG. New spectrophotometric methods for the determination of nimodipine. Indian Drugs. 2001;38(3):140–142.

[8]. Madhuri Lode, Rama Rao Tadikonda, Kiran Rapolu, Narender Boggula. Development and Validation by UV Spectrophotometric Method for the Determination of Sitagliptin in Bulk and its Formulation. International Journal of Development Research. 2024; 14(1):64716-64719.

[9]. Kiran Rapolu, Raja Reddy Aleti, Rama Rao Tadikonda, Pravalika Patlolla, Narender Boggula. Method Development and Validation of Pregabalin in Bulk and Tablet Dosage Forms by UV Spectroscopy. International Journal of Advanced Chemistry Research. 2024; 6(1):53-57.