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Method Development and Validation of UV-Spectrophotometric Method for Quantitative Estimation of Nimodipine in Pharmaceutical Dosage Form

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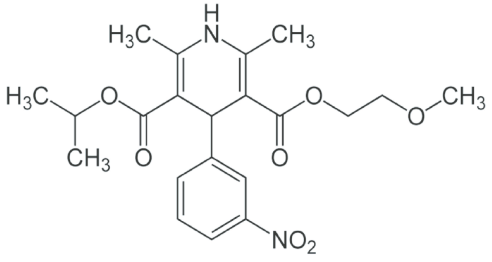
ABSTRACT

The aim of present work is to develop and validate simple, sensitive, economical and accurate Spectrophotometric method has been developed for determination of Nimodipine in pure form and in pharmaceutical formulations. Nimodipine in dimethyl sulphoxide shows maximum absorbance at 238.50 nm. The drug obeyed Beer's law in the concentration range of 15µg/ml in methanol. The proposed methods were successfully applied for the determination of drug in commercial tablet preparations. The results of the analysis have been validated statistically and by recovery studies.

Keywords: Analysis, Nimodipine, Method validation, Ultraviolet spectroscopy.

INTRODUCTION

Nimodipine is a second generation calcium channel blocker used in the treatment of cerebral vasospasm after subarachnoid hemorrhage. Nimodipine is not widely used and has not been implicated in causing clinically apparent acute liver injury [1]. Nimodipine (nye moe' di preen) belongs to the dihydropyridine class of calcium channel blockers (similar to amlopidine and felodipine) and is used to treat cerebral vasospasm after subarachnoid hemorrhage [2]. Like other calcium channel blockers, nimodipine acts by inhibition of the influx of calcium ions into smooth muscle cells during depolarization which results in vasodilation. Nimodipine has high lipid solubility and was developed specifically to treat cerebral vasospasm [3]. Clinical trials have suggested that nimodipine reduces infarct size and complications after subarachnoid hemorrhage. Nimodipine was approved for use in the United States in 1988 but is not widely used, largely because of its restricted indications [4]. Nimodipine is available in generic forms and under the commercial name Nimotop as capsules of 30 mg. The recommend dose in adults is 60 mg every 4 hours for 21 days starting as soon as possible or within 96 hours of the diagnosis of subarachnoid hemorrhage. Like most calcium channel blockers, nimodipine is generally well tolerated and side effects are largely due to its vasodilating activities and can include headache, dizziness, flushing, fatigue, nausea, diarrhea, peripheral edema, palpitations and rash [5].



Structure of Nimodipine

Nimodipine is practically insoluble in water, freely soluble in ethyl acetate, and sparingly soluble in absolute alcohol. During the depolarization of smooth muscle cells of blood vessels, there is an influx of calcium ions. The primary function of nimodipine is to block voltage-gated L-type calcium channels in their inactive conformation, avoiding this influx to prevent vasoconstriction [15]. Nimodipine preferentially acts on cerebral blood vessels as it is lipophilic and can cross the blood-brain barrier. Proposed mechanisms also include decreased angiographic vasospasm, increased fibrinolytic activity, and enhanced neuroprotection [6].

Literature survey reveals that several analytical methods have been reported for the estimation of Nimodipine by HPLC method. Apart from above no other work in the literature reported about the UV Spectrophotometric method for the analysis of Nimodipine in pharmaceutical formulations. Thus there is need to develop simple and economical method for routine analysis of Nimodipine. The objective of present study was to develop and validate simple, accurate, precise, robust and economical method for estimation of Nimodipine in bulk and pharmaceutical formulations as per ICH Guidelines [7].

MATERIALS AND METHODS

Materials

Nimodipine is procured from Dr. Reddy's laborataries, Hyderabad**;** all the chemicals used were of analytical grade and HPLC grade procured from Qualigens, India Ltd. The chemicals used for the study: Methanol (HPLC grade), Acetonitrile (HPLC grade), Water (HPLC grade), Methanol (Analytical grade) and DMSO (Analytical grade)

Methods

System precision/System Suitability

System suitability testing is an integral part of many analytical procedures. System suitability test parameters depend on the type of procedure being validated. System precision is determined by measuring the absorbance of standard solution containing 100% working concentration for six times and calculates the % RSD. The % RSD should be less than 2.0%. The relative standard deviation of six replicate measurement of standard solution was found to be 0.740% (limit NMT 2.0%), which indicates that the system is precise to analyze the sample [8].

Method Precision

Method precision was established by analyzing six separate samples at 100% of the working concentration. Percent of result was calculated against claimed label [9]. The % RSD of assay result of six separate samples from a single batch was found to be 0.291% (limit NMT 2.0%) which indicates that the method is precise to analyze the tablet

(Table-2).

Accuracy

Accuracy was established by analyzing nine sample solutions of Nimodipine at 80%, 100% and 120% of the working concentration (Three replicates for each concentration) into a placebo mixture and by calculating the percent recovery of active ingredient from the placebo solution. The percent recovery at each level should be within 97.0% to 103.0%. A linear curve was prepared by plotting amount added Vs amount recovered correlation co-efficient. The percent recovery was calculated for nine determinations and found to be within limit. A graphical representation between amount added Vs amount recovered also shows linearity [10]. Thus it has been concluded that the method is accurate to analyze the Tablet **(Table-2)**.

Specificity Identification

The UV absorption spectrum of the sample preparation for assay is concordant with the reference spectrum of standard sample from assay preparation [11].

Placebo Interference

Placebo solution was prepared in the same manner as standard and sample preparation. No interference of placebo was found [12].

Linearity

Five different standard solutions were prepared covering a concentration of 80% to 120% of the working concentration of Nimodipine and all absorbance were recorded. A linear curve was prepared by plotting actual concentration (µg/ml or ppm) Vs absorbance and correlation co-efficient was calculated. The results obtained correlate with the concentrations resulting in the following calibration curve [13]. The correlation co-efficient found 0.9915, which is within the limit (limit: NLT 0.990). Thus the graph confirms the linearity of the method in the range of 80% to 120% **(Table-4)**.

Robustness

Robustness of this method was determined by analyzing the Nimodipine Tablet in different equipment in different

day and by different analyst [14]. From the above-mentioned data it observed that the method is robust enough to analyze Nimodipine Tablet **(Table-5).**

RECOVERY STUDIES

In order to ensure the accuracy of the proposed method, recovery studies were carried out. To 50 % of the pre-analyzed sample solution, a definite concentration of 6.4, 8 and 9.6 µg/ mL standard solution of Nimodipine and 3.2, 4 and 4.8 µg/ mL. The absorbance of resulting solutions was measured at their corresponding wavelengths and the percentage recovery was calculated [15].

Limit of Detection and Limit of Quantification

The linearity studies were carried out for six times. The limit of detection and limit of quantification were calculated by using the average of slope and standard [16].

RESULT AND DISCUSSION

The analytical method development and validation for the drug Nimodipine was done, which shows the best elution of the peak. The specificity test studies shows that the analyte chromatographic peak is not attributable to more than one component.

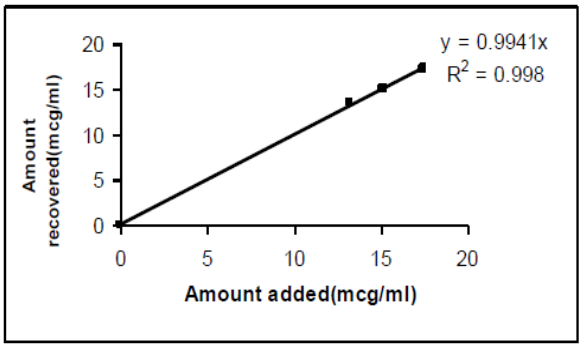


Figure 1: Graphical representation of Accuracy

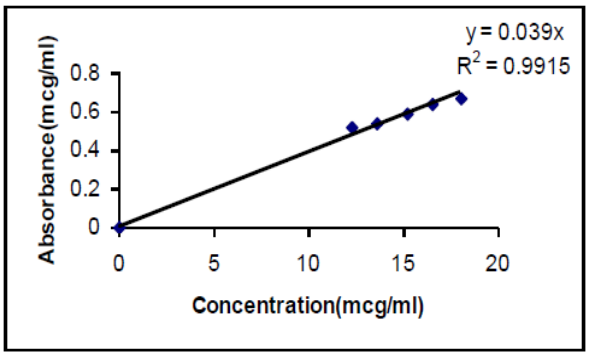


Figure 2: Graphical representation of Linearity

Table 1:Data for System Precision Test

Sample concentration (µg/ml)	No. of Measurements	Absorbance	Relative Standard Deviation
	01	0.609	
	02	0.606	
15.15(µg/ml)	03	0.602	0.642%
	04	0.610	
	05	0.614	
	06	0.609	

Table 2: Data for Method Precision Test

Sample No.	Sample Weight	Assay (mg)%	Label Claim	Relative Standard Deviation
01	485.78	2.77	105.75	
02	484.70	2.75	105.34	
03	484.68	2.76	105.73	
04	485.58	2.76	106.11	0.267%
05	485.77	2.75	105.35	
06	485.88	2.75	105.32	

Table 3: Data for Accuracy Test

Concentration level	Sample No.	Amount added (µg/ml)	Amount recovered (µg/ml)	% Recovery
	1	13.12	13.42	102.287
80%	2	13.13	13.4	102.056
	3	13.2	13.51	102.348
	1	15.2	14.96	98.4211
100%	2	15.22	14.9	97.8975
	3	15.06	15	99.6016
	1	17.26	17.28	100.116
120%	2	17.03	17.04	100.059
	3	17.13	17.12	99.9416

Table 4: Data for Linearity Test

Percent Concentration	Concentration (µg/ml/ppm)	Absorbance	Correlation Co-efficient
80	12.55	0.516	
90	13.78	0.524	0.945631
100	15.24	0.556	
110	16.38	0.658	
120	18.09	0.684	

Table 5: Data for Robustness Test

SI No.	Variable Parameters	Assay results
1	Analyst-1	102.51
	Analyst-2	100.26
2	Equipment-1 (UV Spectrophotometer Model-UV-1700)	100.97
	Equipment-2 (UV-Spectrophotometer Model-UV-1601PC)	100.95
3	Day-1	100.63
	Day-2	101.21

CONCLUSION

A new, simple, specific, sensitive, rapid and economical procedure has been developed for determination of Nimodipine in its dosage form. The objective of this validation of an analytical procedure is to demonstrate that the drug Nimodipine is suitable for its intended purpose. The analytical method development recommends the quality, purity and specificity of the drug Nimodipine tablet form during the manufacturing process and hence the standard of the drug may not vary, which produce the desirable therapeutic effect. The method is based on the ultraviolet absorbance maxima of the above drug at 238.50 nm. The drug obeyed Beer's law in the concentration range of 15µg/ml in methanol. The proposed methods were successfully applied for the determination of drug in commercial tablet preparations. The results of the analysis have been validated statistically and by recovery studies.

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