Review Article

Analytical Method Development and Validation for Estimation of Nifedipine in Drug and Dosage Form: A Review

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ABSTRACT

Nifedipine is a calcium channel blocker in the dihydropyridine subclass. It is primarily used as an antihypertensive and as an anti-anginal medication. FDA-approved indications include chronic stable angina, hypertension. It also has other off-label indications. This activity outlines the indications, mechanism of action, methods of administration, important adverse effects, contraindications, monitoring, and toxicity of nifedipine, so providers can direct patient therapy successfully in instances where nifedipine provides a benefit to patient care. During the depolarization phase of smooth muscle cells, there is an influx of calcium ions through voltage-gated channels. Nifedipine inhibits the entry of calcium ions by blocking these voltage-dependent L-type calcium channels in vascular smooth muscle and myocardial cells. Nifedipine thus has hypotensive and antianginal properties. Literature survey reveals Nifedipine that is determined by HPLC, GC, LC-MS, Electrochemical Methods, TLC, CE, UV -Visible Spectrophotometry. Most of these literatures show that majority of studies are conducted in concentration range between 5-30 µg/ml gives accurate correlation.

Keywords: nifedipine, potassium hydroxide, ammonium molybdate, pharmaceutical formulations, validation, spectrophotometry, HPLC, GC, LC-MS, TLC, CE.

INTRODUCTION

Development and validation of analytical method play an essential role in the discovery, development and manufacturing of pharmaceuticals. Every year, number of drugs entered into the market; hence it is mandatory to develop newer analytical methods for such drugs. After the development, it becomes necessary to validate the new analytical method. Method development is the process which proves that the analytical method is acceptable for use. Validation of analytical method gives information about various stages and parameters like accuracy, precision, linearity, Limit of Detection, Limit of Quantification, specificity, range and robustness. Validation should be done as per regulatory guidelines such as ICH guidelines. This article was prepared with an aim to review various analytical method development and validation of nifedipine[2].

Nifedipine is a calcium channel blocker. It works by affecting the movement of calcium into the cells of the heart and blood vessels. As a result, nifedipine relaxes blood vessels and increases the supply of blood and oxygen to the heart while reducing its workload. Nifedipine is used alone or together with other medicines to treat severe chest pain (angina) or high blood pressure (hypertension). High blood pressure adds to the workload of the heart and arteries[3].

The most frequently used separation techniques for nifedipine are by HPLC, GC, LC-MS, Electrochemical Methods, TLC, CE, UV -Visible Spectrophotometry.

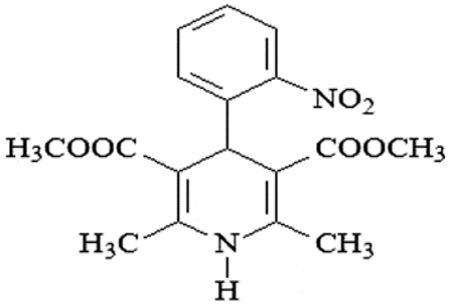

Figure 1: Scheme of Nifedipine

This study aims to develop a simple, precise, authentic, cost effective and validated analytical method for the estimation of Nifedipine in drug and dosage form. Analytical method development is very important in development and production of new drugs and formulations. The validation of analytical method is a regulatory requirement for submission of New Drug Application (NDA) and Abbreviated New drug Application (ANDA) as a part of U.S generic drug approval. Analytical method development and validation play a vital role in bio-availability, bioequivalence studies and the risk assessment/management.

ANALYTICAL METHODOLOGIES

- **PROF.DEEPAK BHOSLE** *et al* reported a new, simple, sensitive, precise and reproducible UV spectroscopic method was developed for the estimation of Nifedipine in bulk and formulation. The UV spectrum of Nifedipine in phosphate buffer ph7.4 showed λ max at 213nm. Beer's law is valid in the concentration range of 5-25µg/ml. This process was authenticated for linearity, accuracy, precision, ruggedness and robustness. The method has demonstrated excellent linearity over the

range of 5-25µg/ml with regression equation y = 0.025x + 0.014and regression correlation coefficient r = 0.996. Moreover, the method was found to be highly sensitive with LOD (5.64µg/ml) and LOQ (1.86µg/ml). Depending on results the given method can be successfully applied for assay of Nifedipine in Semisolid formulation[4].

- **THANGABALAN BOOVIZHIKANNAN** *et al* reported Nifedipine, sold under the brand name Adalat and Procardia, among others, is a calcium channel blocker medication used to manage angina, high blood pressure, Raynaud's phenomenon, and premature labor. The review presented here systematizes various analytical and bio-analytical methods developed for Nifedipine alone and in combination with other drugs. It represents a comprehensive data of UV-Visible spectroscopy, HPTLC, HPLC and LC-MS methods reported by various scientists on Nifedipine [5].

- **LILIYA LOGOYDA** *et al* reported that the aim was to develop a simple, rapid, less expensive, linear, precise, and accurate reverse phase high performance liquid chromatography method for determination of nifedipine in tablets. The chromatographic analysis of nifedipine was performed using liquid chromatograph Agilent 1290 Infinity II LC System. Selected conditions were isocratic elution with binary mobile phase consisting of solution methanol and 0.1% trifluoroacetic acid (55:45). Detection was carried out using spectrophotometric detector at 265 nm. The method was validated as per ICH guidelines. The retention time for nifedipine by proposed high performance liquid chromatography (HPLC) method is observed as 3.5 minutes. The correlation coefficients are 1.0000. The developed chromatographic method was found to be accurate with -99.8% and was found within the acceptance criteria (i.e. 98.0-102.0%) with acceptable % relative standard deviation of not more than 2% at each level The assay results of nifedipine in tablets by developed method are highly reproducible, reliable and are in good agreement with the label claim of the medicines (average 99.62 %). it should be noted that a new simple, rapid, linear, precise, accurate HPLC method was developed and validated for the determination of nifedipine in medicines in accordance with the ICH guidelines. These results show the method are accurate, precise, sensitive, economic, and rugged. The proposed HPLC method is rapider (retention time is 3.5 minutes). This method can be useful for the routine analysis of nifedipine in pharmaceutical dosage form[6] .

- **P.TULASAMMA** *et al* reported Two rapid, simple, sensitive and selective spectrophotometric methods have been developed for the quantitative estimation of nifedipine in pharmaceutical formulations and different human body fluids (serumandurine).The proposed methods are based on the reduction of the nitro group to amino group of the drug. The resulting amine was then subjected to proposed methods.Method A is based on the oxidation followed by coupling of nifedipine with 3-methyl2-benzothiazolinonehydrazone (MBTH) in presence of ferric chloride (FeCl3) to form green colored chromogenat 685nm.Method B is based on the formation of oxidative coupling reaction between the corresponding drug and brucine–NaIO4 to form violet colored chromogenat546nm.The procedures described were applied successfully to the determination of the compound in their dosage forms and body fluids. The results showed that the proposed procedures compared favourably with reference method are satisfactory sensitive, accurate and precise. The optical characteristics such as Beer's law limits, molar absorptivity, Sandell's sensitivity and various statistical data are reported. The results of the analysis for the two methods have been validated statistically and by recovery studies [7] .

- **SHELKE O. S** *et al* reported that simultaneous estimation and validation of developed method of Nifedipine (NIF) and Atenolol (ATN) in combined dosage form as well as in laboratory mixture is studied under this paper. Nifedipine and Atenolol are used in combined dosage form for Cardiovascular System Diseases. The compound was identified by taking the IR spectra. The method is applied for laboratory mixture and marketed tablet. The developed method was validated as per ICH guidelines using the parameter such as accuracy, linearity and range, ruggedness, limit of detection & quantification, robustness, and precision. Precision was analysed by taking Reading inter day and Intraday. Ruggedness was analysed by different analyst and robustness by changing the solvent composition[8].

- **NAFISUR RAHMAN** *et al* reported two simple, sensitive and economical spectrophotometric methods were developed for the de termination of nifedipine in pharmaceutical formulations. Method A is based on the reaction of the nitro group of the drug with potassium hydroxide in dimethyl sulphoxide (DMSO) medium to form a coloured product, which absorbs maximally at 430 nm. Method B uses oxidation of the drug with ammonium molybdate and subsequently reduced molybdenum blue is measured at 830 nm. Beer's law is obeyed in the concentration range of 5.0–50.0 and 2.5–45.0 µg ml–1 with methods A and B, respectively. Both methods have been successfully applied for the assay of the drug in pharmaceutical formulations. No interference was observed from common pharmaceutical adjuvants. The reliability and the performance of the proposed methods are established by point and interval hypothesis tests and through recovery studies[9].

- **S CHOIRI** *et al* reported that Nifedipine (NIF) is a photo-labile drug that easily degrades when it exposures a sunlight. This research aimed to develop of an analytical method using a high-performance liquid chromatography and implemented a quality by design

approach to obtain effective, efficient, and validated analytical methods of NIF and its degradants. A 22 full factorial design approach with a curvature as a center point was applied to optimize of the analytical condition of NIF and its degradants. Mobile phase composition (MPC) and flow rate (FR) as factors determined on the system suitability parameters. The selected condition was validated by cross-validation using a leave one out technique. Alteration of MPC affected on time retention significantly. Furthermore, an increase of FR reduced the tailing factor. In addition, the interaction of both factors affected on an increase of the theoretical plates and resolution of NIF and its degradants. The selected analytical condition of NIF and its degradants has been validated at range 1 – 16 g/mL that had good linearity, precision, accuration and efficient due to an analysis time within 10 min[10].

- **SOHAM SAMAJPATY** reported Nifedipine is chemically dimethyl 2,6- dimethyl-4-(2-nitrophenyl)-1,4-dihydropyridine 3,5-dicarboxylate, a dihydropyridine derivative used frequently as anti-hypertensive. It is a Ltype calcium channel blocker (CCB). Few analogical discrepancies were found between Nifedipine's clinical output report and chemical analysis of solubility. The ambition of this research is to conduct a re-check and proper quantification of partition co-efficient (logP) of Nifedipine and clarify the discrepancy and rectify if any mistake has been done in recent past. The method used is the "gold standard" shake-flask method followed by analysis through UV spectrophotmetry[11].

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