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TAMSULOSINE IN BULK AND PHARMACEUTICAL FORMULATION: A VALIDATED RP-HPLC METHOD BY QUALITY BY DESIGN

HIRE GJ[1*], BHANGALE C[2] AND KHADSE A[3]

1: Department of Quality Assurance, PRE'S College of Pharmacy (for women) Chincholi, Nashik, 422102, India

2: Department of Pharmaceutical chemistry, PRE'S College of Pharmacy (for women) Chincholi, Nashik, 422102, India

3: Department of Pharmaceutical chemistry, PRE'S College of Pharmacy (for women) Chincholi, Nashik422102, India

***Corresponding Author: Dr. Hire Gauri Jeevan: E Mail: gaurihire34@gmail.com**

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ABSTRACT

There have been several reports of spectrophotometric and HPLC techniques for determining the amount of tamsulosine in medications and dosage formulations. Therefore, a novel, sensitive, appropriate, and reliable reversed-phase high-performance liquid chromatography method was created and verified in this study to measure tamsulosine in tablet and bulk medication formulations and quality by design is to cross check the calculated results with the help of DOE software. Using an Openlab EZchrome software-equipped UV detector and a Kromasil C18, 250 mm X 4.6 mm, 5 µm column, methanol and water (75:25% v/v) were employed as the mobile phase in the RP-HPLC procedure. The flow rate of the column was 1.0 ml/min. To detect, 224 nm was used. The technique produced an appropriate retention period for tamsulosine or 3.60 minutes. The validity of the analysis results in the following areas was confirmed: robustness; limit of detection; limit of quantification; filter study; stability of the solution; specificity; linearity; accuracy; precision (repeatability and intermediate precision); and more. The assay of tamsulosine in tablet and bulk medication formulations was straight forward and accurate. The technique is less time-consuming and requires frequent reagents for analysis; it can be used in the industry to analyze marketed tamsulosine products and bulk drugs.

Keywords: RP-HPLC, Tamsulosine, Validation, QbD, Box-Behnken design, DOE

INTRODUCTION

The study of analytical chemistry is often referred to as a discipline of chemistry which is concerned with the qualitative and quantitative evaluation of a matter's composition. Tragically, this explanation downplays the distinct viewpoint that analytical chemists provide to the field of chemistry research. Instead of doing a routine analysis on a routine sample, which is more appropriately referred to as chemical analysis the craft of analytical chemistry consists of refining already established procedures, expanding their relevancy to new sample types, and creating new techniques for measuring chemical phenomena **[1]**. Instrumental analysis dominates modern analytical chemistry. Currently, there are numerous distinct kinds of instruments available that it can appear more like a perplexing collection of acronyms than a cohesive subject of study. A lot of analytical chemists concentrate on just one kind of instrument. Researchers usually concentrate on either novel applications and findings or innovative techniques for analysis. The identification of a blood molecule that raises the risk of cancer is one discovery that an analytical chemist could be involved in. A controllable laser could be used in an attempt to create a novel technique in order to boost the spectrometric method's sensitivity and specificity. To allow data to be compared over extended periods, many methods are intentionally maintained static once they are designed. This is especially true for applications related to forensics, the environment, and industrial quality assurance (QA). Analytical chemistry is becoming more and more significant in the pharmaceutical sector, where it is utilized not just for quality assurance but also for the identification of novel drug candidates and in clinical settings where it is crucial to comprehend how medicine interacts with a patient **[2]**. There are some types of analytical methods used to carried out the validation and to take trials for different samples; they are as follows:- Spectrophotometry , colorimetry, UV-visible spectroscopy , Chromatography and Electrophoresis and, Commonly used methods are, High-Performance Liquid Chromatography (HPLC) , High-Performance Thin Layer Chromatography (HPTLC), Gas Chromatography (GC) , Gas Chromatography-Mass Spectroscopy (GC-MS), Liquid chromatography-Mass spectroscopy (LC-MS) **[3, 4]**.

EXPERIMENTAL PROCEDURE

MATERIALS

1. SELECTION OF ANALYTICAL WAVELENGTH

1.1 Selection of solvent

Methanol was selected as the solvent for dissolving Tamsulosine hydrochloride.

1.2 Preparation of standard solutions for UV scan to determine Absorption maxima wavelength

In order to prepare stock solution, weighed accurately 20 mg Tamsulosine HCl and transferred into 20 ml volumetric flask, added 14 ml of methanol and sonicated to dissolve the standard completely and diluted up to the mark with methanol (100 PPM).

Further diluted 0.2 ml to 20 ml with methanol (10 PPM)

1.3 Selection of analytical wavelength

Methanol as a blank and Tamsulosine hydrochloride standard solution having concentration 10 PPM were scanned from 400 nm to 200 nm. Absorption maxima were determined for drug. 224 nm wavelength used for further analysis.

2. METHOD DEVELOPMENT BY RP – HPLC

We will develop a method until we get good chromatography

An acceptance criterion for good chromatography is as follows:

Retention time: Optimum R.T., Asymmetry (Tailing factor): 0.8 to 2.0, Theoretical plates: NLT 2000

2.1 Preparation of standard solution for Chromatographic development:

Tamsulosin hydrochloride Standard stock solution was prepared by dissolving 20 mg Tamsulosin hydrochloride into a 20 mL clean and dried volumetric flask, added about 14 mL of methanol to dissolve it completely and made volume up to the mark with methanol (1000 PPM).

Further diluted 1 mL to 10 mL with mobile phase of each trial and injected in respective trial. (100 PPM)

2.2 Selection of analytical wavelength for HPLC method development: Analytical wavelength for the examination was selected from the wavelength of maximum absorption from the spectrophotometric analysis and it was 224 nm**.**

2.3 Optimization of Developed RP-HPLC Method with Design Space and Control Strategy determination by optimization study [5–7]

All the computations for the current optimization study and statistical analysis were performed using Design Expert® software (Design Expert version 7.0.0; State-Ease Inc., Minneapolis, MN, USA).

2.4 Application of design of experiments for method optimization:

2.5 Design of experiments (DOE-1): Thus, 3^3 randomized response surface designs with a Box-Behnken design were used with 17 trial runs to study the impact of three factors on the three key response variables. In this design 3 factors were evaluated, each at 3 levels and experimental trials were performed at all 3 possible combinations. The mobile phase composition (X1), flow rate (X2) and column oven temperature (X3) were selected as independent variables and retention time (RT) and asymmetry were

selected as dependent variables. The resulting data were fitted into Design Expert 7.0.0. software and analysed statistically using analysis of variance (ANOVA). The data were also subjected to response surface methodology to determine the influence of mobile phase composition, flow rate and column oven temperature on dependent variables. The probable trial runs using 3^3 Box Behnken designs are as shown in following table.

3 center points per block considered for designing the DOE trials under Box behnken model.

2.6 Preparation of standard solutions to inject in DOE runs:

In order to prepare stock solution, weighed accurately 10 mg Tamsulosine hydrochloride and transferred into 20 ml volumetric flask, added 14 ml of methanol and sonicated to dissolve the standard completely and diluted up to the mark with methanol.

Further diluted 0.8 mL to 20 mL with mobile phase. (20 PPM)

3. PREPARATION OF SYSTEM SUITABILITY TEST (TAMSULOSINE HYDROCHLORIDE STANDARD SOLUTION)

Weighed accurately 10 mg of Tamsulosin hydrochloride and transferred to 25 mL volumetric flask. Added 20 ml of methanol and sonicated to dissolve it completely, made the volume up to the mark with methanol. Pipette out 1 ml from standard stock solution and transferred into 20 ml volumetric flask and made volume up to the mark with mobile phase. chromatograms were recorded.

System suitability is a Pharmacopeial requirement and is used to verify, whether the chromatographic system is adequate for analysis to be done. The tests were performed by collecting data from five replicate injection of standard drug solution and the results are recorded.

Acceptance criteria

1. RSD should not be more than 2.0 % for five replicate injections of standard.
2. USP Tailing Factor/ Asymmetry Factor is not more than 2.0.
3. The column efficiency as determined for Plate Count should be more than 2000.

4. ANALYSIS OF MARKETED TEST SAMPLE

Marketed test sample Having Name Veltam 0.4 mg tablets are selected for analysis and for doing validation.

Average weight of test sample (Veltam 0.4 mg):

Weighed the 20 tablets at a time and calculated average weight of tablet by following formula:

Average weight (mg) = Weight of 20 tablets (mg) / 20

Sample preparation of Marketed test sample:

Weighed 20 tablets transferred in mortar pestle and crushed to fine powder. Mixed the contents with butter paper uniformly. Weighed the powder material equivalent to 1 mg of Tamsulosine hydrochloride (298.5 mg) and transferred to clean and dried 25 mL of volumetric flask. Added 20 mL of Metahnol, sonicated for 15 minutes with intermittent shaking. After 15 minutes allowed the solution to cool at room temperature and made volume up to the mark with Methanol. Filtered the solution through suitable 0.45 µ syringe filter discarding 3-5 mL of initial filtrate. Further diluted 5.0 ml of filtered stock solution to 10 ml with mobile phase. (20 mcg of Tamsulosine hydrochloride), injected the resultant solution and chromatograms were recorded and results are recorded.

5. VALIDATION OF RP-HPLC METHOD [8–10]

The developed method for estimation of Tamsulosine hydrochloride was validated as per ICH guidelines for following parameters.

1. Filter study
2. Stability
3. Specificity
4. Linearity and range
5. Limit of detection (LOD) and limit of quantitation (LOQ)
6. Accuracy (% recovery)
7. Precision
8. Robustness

RESULTS AND DISCUSSION

1. PRELIMINARY CHARACTERIZATION AND IDENTIFICATION OF DRUG

1.1. Colour, odour and appearance

Colour, odour and appearance of Drug

Tamsulosine hydrochloride- White, odourless and Amorphous powder

1.2. Solubility study

Solubility study of Tamsulosine hydrochloride

Water- Drug was not found soluble in water.

Methanol- Methanol used as a diluent for preparing stock solution.

1.2.1. Selection of solvent

Methanol was selected as the solvent for dissolving Tamsulosine hydrochloride.

1.2.2. Selection of analytical wavelength

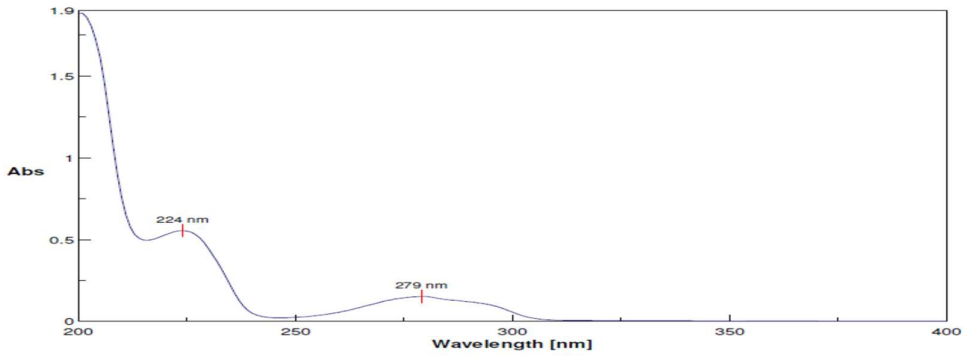


Figure 1: UV spectrum of Tamsulosine hydrochloride (10 PPM)

Observation: The Blank and standard solutions 100 ppm was scanned from 400 nm to 200 nm. Tamsulosine hydrochloride showed absorption maxima at 224 nm.

Conclusion: 224 nm considered as an analytical wavelength for further determination.

1.3 METHOD DEVELOPMENT BY RP – HPLC [8, 11, 12]

1.3.1 HPLC METHOD DEVELOPMENT

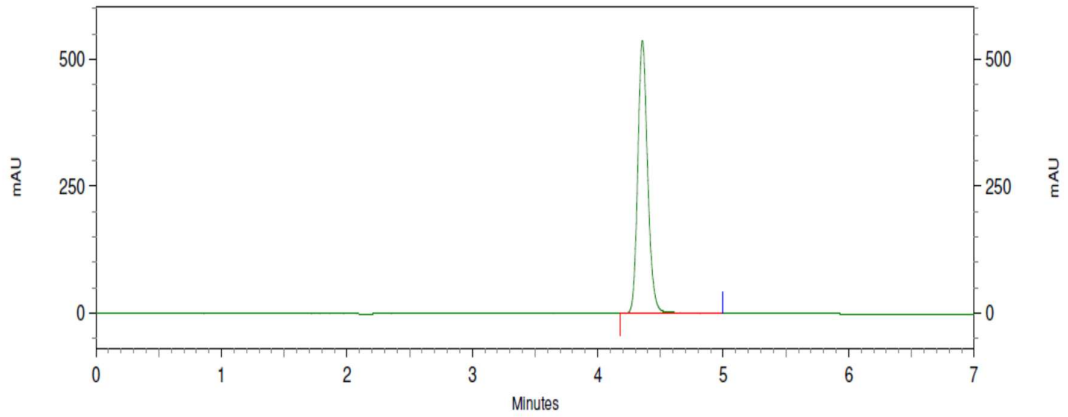


Figure 2

Observation: Tamsulosine hydrochloride eluted at 4.36 minutes with acceptable chromatography. (Asymmetry = 1.16 and theoretical plates 14992)

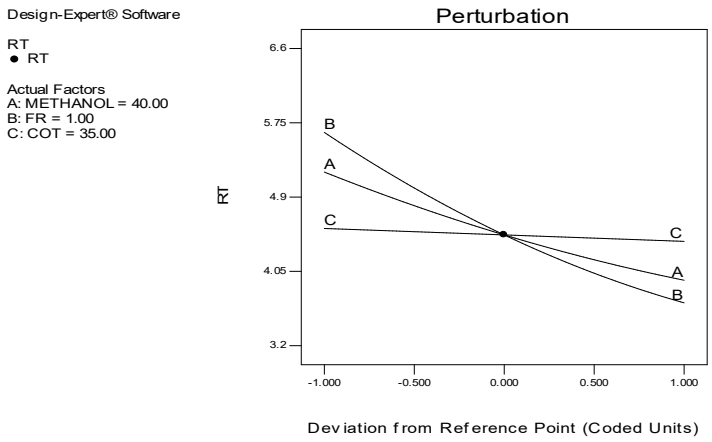
Conclusion: From the observations of trials first to seven, it was concluded that chromatographic conditions in trial seven gives better peak, good retention time and tailing factor therefore chromatographic conditions in trial seven was used for further optimization by DOE software.

Developed Chromatographic Condition

Parameter	Description
Mode	Isocratic
Column Name	Phenomenex C18, 250 mm X 4.6 mm i.d., 5µm
Detector	UV Detector
Injection Volume	20 µl
Wavelength	224nm
Column Oven temp	35ºC
Mobile Phase	Methanol: 0.05% OPA in water (40:60)% v/v
Flow Rate	1.0 ml/min

RESULT AND DISCUSSION

The layout of the Actual Design of DOE



Effect of All 3 factors on R.T

Runs	Factor1	Factor 2	Factor3	Response 1	Response 2
	A: % Methanol	B: Flow rate	C: COT (°C)	Retention time (RT)	Asymmetry
6	35	1.2	35	4.28	1.13

Selection of Optimized method:

Trial no. 6 selected as a optimized chromatography, as it has Optimum R.T. and theoretical plates.

Summary of effect of independent variable on dependent variables:

Sr. No.	Independent variables	Retention time	Asymmetry
1	% methanol ratio in mobile phase	Inversely proportional (As methanol increases, R.T. decreases)	Directly proportional (As Methanol increases, Asymmetry increases)
2	Flow rate	Inversely proportional (As Flow rate increases, R.T. decreases)	Inversely proportional (As Flow rate increases, asymmetry decreases)
3	Column oven temperature	Inversely proportional (As COT increases, R.T. decreases)	COT do not have impact on Asymmetry (Found insignificant factor in ANOVAs test)

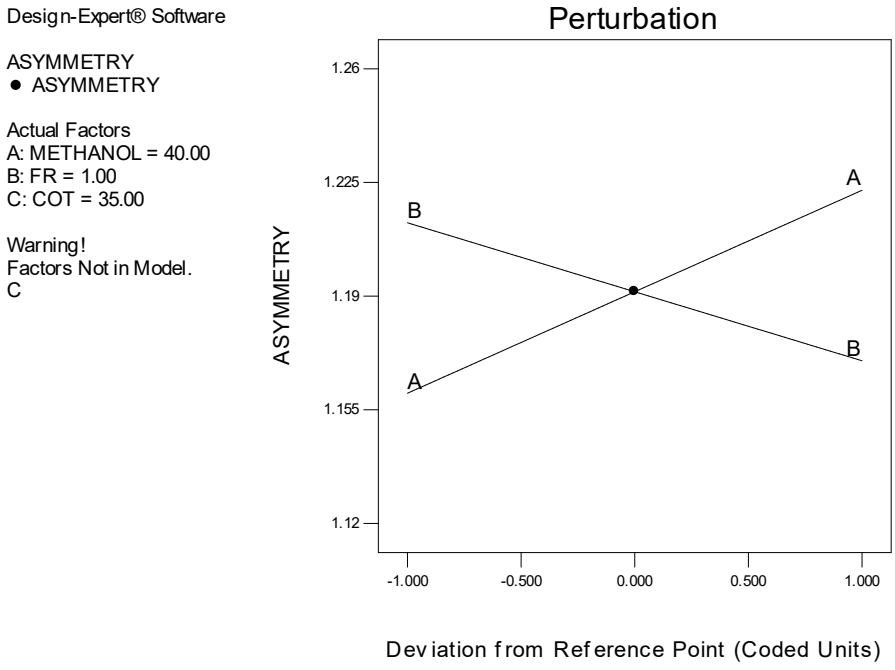
Final Equation in Terms of coded Factors for R.T. of DOE: [13]

RT	=
4.4669	
-0.6188	* A
-0.9750	* B
-0.0738	* C
0.1375	* A * B
0.1004	* A^2
0.1979	* B^2

The equation in terms of coded factors can be used to make predictions about the response for given levels of each factor.

Final Equation in Terms of Coded Factors of Asymmetry:

ASYMMETRY	=
1.1913	
0.0313	*** A**
-0.0213	*** B**



Effect of A & B on Asymmetry (Perturbation plot)

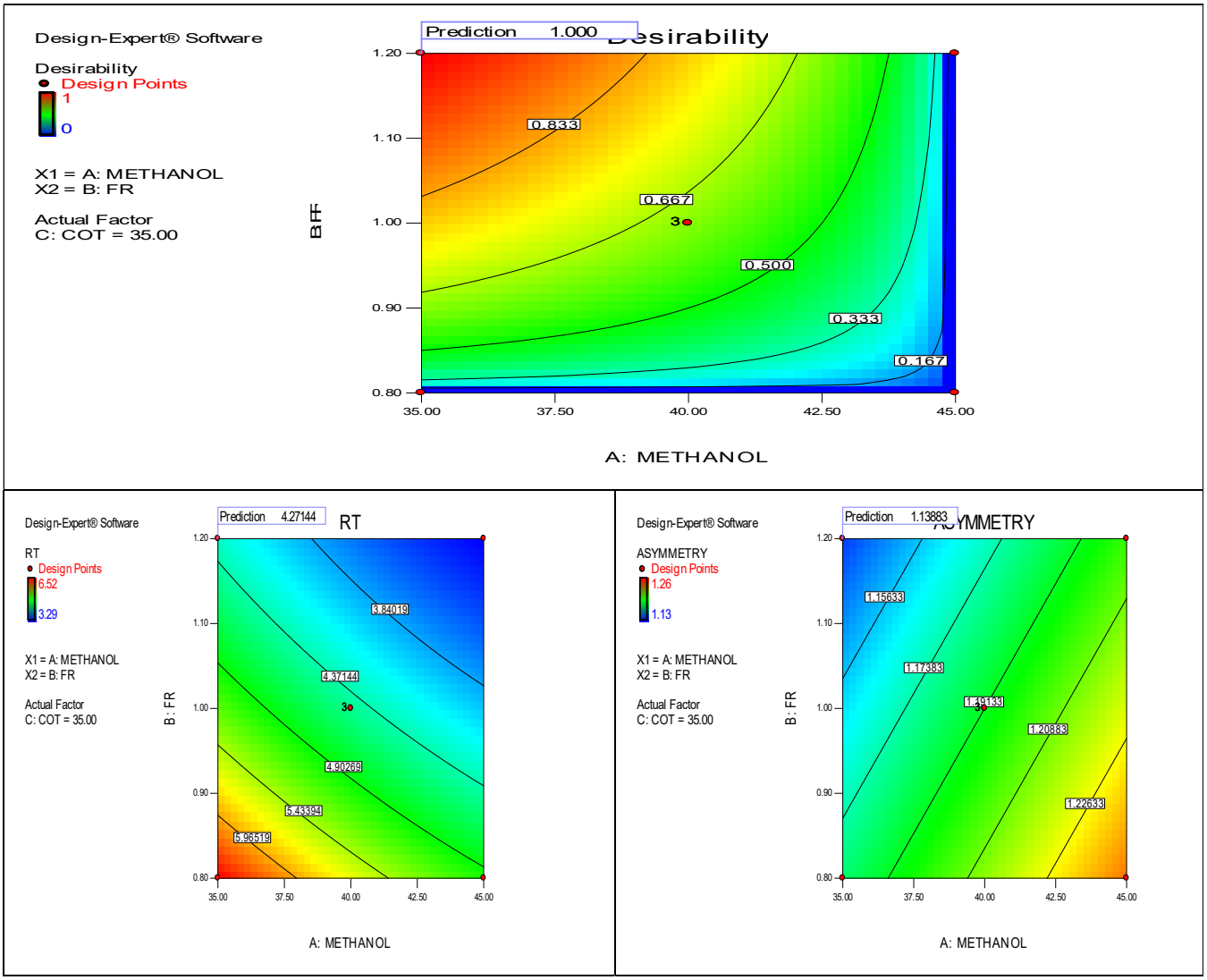
Conclusion:

Percent of Methanol in mobile phase has effect on Asymmetry, as Percent of Methanol increases asymmetry increases.

Flow rate of mobile phase also has impact on asymmetry, as Flow rate of mobile phase increases, asymmetry decreases.

COT does not have impact on asymmetry, as it's found as insignificant factor in ANOVA test

Design space [5–7, 14]



System suitability test

Results for System Suitability Test of Tamsulosine HCl

Data interpretation: It was observed from the data tabulated above; the method complies with system suitability parameters. Hence, it can be concluded that the chromatographic method is adequate for intended analysis.

Sr No.	Standard solution	Area	Asymmetry	Theoretical plates
1	Standard_1	8455420	1.13	15535
2	Standard_2	8456961	1.13	15540
3	Standard_3	8453967	1.13	15521
4	Standard_4	8450153	1.12	15519
5	Standard_5	8455867	1.12	15537
Mean		8454474	1.13	15530
STD Dev		2643.323		
% RSD		0.03		

Analysis of Marketed Test samples (Assay)

a) Veltam 0.4 mg Tablet:

Weight of 20 tablets = 2.3880 gm

Average weight of tablet = 2.3880 / 20 = 0.1194 gm = 119.4 mg

Assay results of Veltam 0.4 mg Tablet:

Sample	Area	% Assay	Mean Assay
Sample 1	8312682	98.29	98.57
Sample 2	8352413	98.86	

Data interpretation:

From the above results, it can be concluded that the assay result is within the limit for selected marketed test sample and sample can be used for validation.

CONCLUSION

The creation and verification of analytical methods are crucial to pharmaceutical discovery, advancement, and production. Each year, several medications reach the market; hence, developing more advanced analysis techniques for these drugs is imperative. Validating the new analytical approach is now required following development. The procedure that establishes the suitability of an analytical method for application is known as method development. The process of validating an analytical method provides details on several phases and factors, including specificity, range, robustness, limit of detection, quantification, accuracy, precision, and linearity. Regulations like the ICH rules should be followed when performing validation. The purpose of the study is to assess the development of analytical methods and validate them. In this case, the software analysis in the analytical field was done using the QBD approach, which aids in developing high-quality product processes in the analytical development field and helps ensure that results are accurate to the intended value.

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