IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 3, November 2026
Impact Factor: 8.2

A Review : A Comprehensive Overview of UV Spectrophotometric Analysis of Diphenhydramine Hydrochloride

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Abstract : *The International Council for Harmonization (ICH) requirements for linearity, accuracy, precision, and specificity were followed in the validation of the created technique. Over the concentration range of 10–100 µg/mL, Beer–Lambert's law was followed. The calibration curve revealed a linear equation with a correlation coefficient of y = 0.016x + 0.018. To estimate the amount of diphenhydramine hydrochloride in soft gelatine capsule dosage forms, a straightforward, precise, economical, and repeatable UV spectrophotometric approach was created. It was discovered that 258 nm was the maximum absorption wavelength (λmax). 98.97 ± 0.2989% of the diphenhydramine hydrochloride was recovered from the capsule dose form. The International Council for Harmonization (ICH) requirements for linearity, accuracy, precision, and specificity were followed in the validation of the created technique. Over the concentration range of 10–100 µg/mL, Beer–Lambert's law was followed. The calibration curve revealed a linear equation with a correlation coefficient of y = 0.016x + 0.018. To estimate the amount of diphenhydramine hydrochloride in soft gelatin capsule dosage forms, a straightforward, precise, economical, and repeatable UV spectrophotometric approach was created. It was discovered that 258 nm was the maximum absorption wavelength (λmax). 98.97 ± 0.2989% of the diphenhydramine hydrochloride was recovered from the capsule dose form. The International Council for Harmonization (ICH) requirements for linearity, accuracy, precision, and specificity were followed in the validation of the created technique. Over the concentration range of 10–100 µg/mL, Beer–Lambert's law was followed. The calibration curve revealed a linear equation with a correlation coefficient of y = 0.016x + 0.018. To estimate the amount of diphenhydramine hydrochloride in soft gelatin capsule dosage forms, a straightforward, precise, economical, and repeatable UV spectrophotometric approach was created. It was discovered that 258 nm was the maximum absorption wavelength (λmax). 98.97 ± 0.2989% of the diphenhydramine hydrochloride was recovered from the capsule dose form. The International Council for Harmonization (ICH) requirements for linearity, accuracy, precision, and specificity were followed in the validation of the created technique. Over the concentration range of 10–100 µg/mL, Beer–Lambert's law was followed. The calibration curve revealed a linear equation with a correlation coefficient of y = 0.016x + 0.018.*

Keywords: Diphenhydramine Hydrochloride, Spectrophotometry, Validation, Method Development

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www.ijarsct.co.in
DOI: 10.48175/IJARSCT-40889

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I. INTRODUCTION

Diphenhydramine Hydrochloride (DPH) is 2- (diphenyl methoxy) -N, N-dimethyl ethanamine hydrochloride, a first-generation antihistamine. In addition to its sedative and hypnotic properties, it is frequently used to treat allergy problems. It is a component of some over-the counter sleep aids because of these qualities. Additionally, the medication has antiemetic properties, which help control nausea and vomiting. Diphenhydramine hydrochloride can be quantitatively determined using a variety of analytical methods, such as high-performance liquid chromatography, chemiluminescence analysis, and capillary gas chromatography. For routine drug analysis in pharmaceutical formulations, however, creating a simple, dependable, affordable, and repeatable analytical process is still crucial [1].

The literature has also documented the use of High-Performance Liquid Chromatography (HPLC) techniques and Fourier Transform Raman (FT-Raman) spectroscopy for the examination of liquid formulations. The identification and quantification of chemical compounds found in a variety of samples depend heavily on analytical chemistry. Instrumental analytical techniques have grown in significance in pharmaceutical analysis due to technological advancements [2, 3].

To create trustworthy analytical techniques for the estimate of pharmaceutical substances, many analytical chemists make use of tools like UV-visible spectrophotometers. These techniques can be used to determine quality assurance criteria and assess medication content in regular quality control labs. Diphenhydramine hydrochloride and naphazoline can be determined simultaneously using a second-derivative UV spectrophotometric technique, as reported by Santon G. et al [4].

Drug Profile

Drug Name: Diphenhydramine Hydrochloride

IUPAC Name: 2(Diphenyl methoxy)-NN-dimethyl ethanamine hydrochloride

Molecular Formula: $C_{17}H_{21}NO.HCl$ pKa: Approximately 9.0

Solubility: Freely soluble in water, alcohol and chloroform, Sparingly soluble in acetone.

Structure of Diphenhydramine HCl [5, 6].

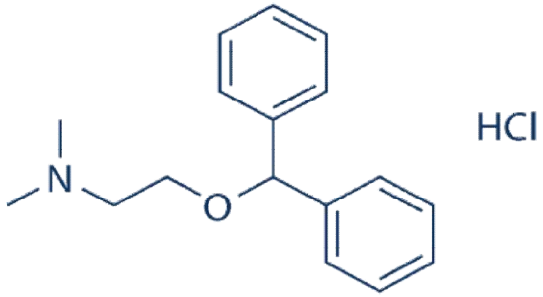


Figure.1.The Chemical Framework of Diphenhydramine hydrochloride [7].

Materials and Methods

Supplies and Substances

RPG Life Sciences Limited supplied the pure drug sample while Maharshi Laboratories Pvt. Ltd. supplied the pure sample of diphenhydramine hydrochloride (DPH). Without any additional purification, both samples served as reference standards. Drug solutions were prepared using distilled water as the solvent [8].

Equipment

A Shimadzu UV-1700 double-beam UV-visible spectrophotometer linked to a PC running Shimadzu UV Probe 2.34 software was used for spectrophotometric measurements. Using 1 cm quartz cells, the absorbance spectra of the produced solutions were recorded spanning the 200–400 nm wavelength range [9].

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Getting Ready -Individual 100 mL volumetric flasks were filled with precisely weighed amounts of 100 mg of DPH. To create stock solutions with concentrations of 1000 µg/mL, each medication was dissolved in distilled water and diluted to the appropriate level.
After that, 10 mL of working stock solutions containing 100 µg/mL were created [10].

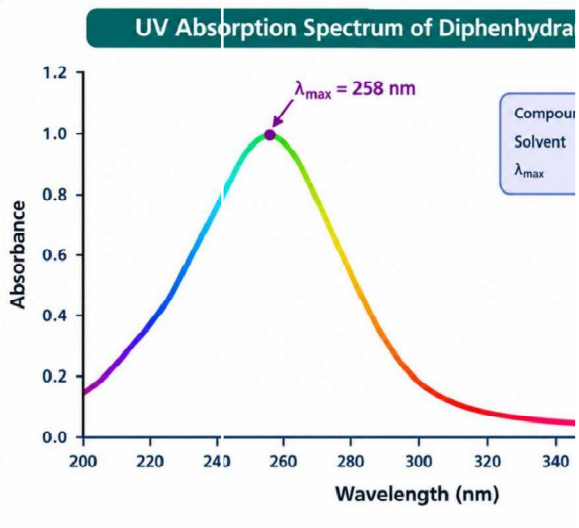
Standard Stock Solution Preparation
Individual 100 mL volumetric flasks were filled with precisely weighed amounts of 100 mg of DPH. To create stock solutions with concentrations of 1000 µg/mL, each medication was dissolved in distilled water and diluted to the appropriate level.
After that, 10 mL of each primary stock solution were transferred into individual 100 mL volumetric flasks, and the remaining volume was filled with distilled water to create working stock solutions of 100 µg/ ml [11].

Choosing a Solvent for Dual-Wavelength and First-Order Derivative Techniques
Because both medications were soluble in distilled water, it was used as the solvent for the simultaneous spectrophotometric measurement of DPH and First-order derivative and dual wavelength spectrophotometric techniques were used to evaluate the solvent's eligibility for analysis based on the superimposed absorption spectra of the two medications [12].

Wavelength Selection and Calibration Curve Preparation
First-Order Derivative Spectrophotometric Approach
The wavelength range of 200–400 nm was used to scan the standard solutions and diphenhydramine hydrochloride (DPH). A wavelength interval ($\Delta\lambda$) of 4 nm and a scaling factor of 10 were used to transform the recorded zero-order absorption spectra (D_0) into first order derivative spectra (D^1) [13].
To create its calibration curve, the derivative absorbance at 247.4 nm, which is the DPH zero crossing point, was measured for various concentrations and plotted against concentration.
Over the concentration range of 15–35 µg/mL, both medications showed good linearity [14].

Regarding the Dual-Wavelength Approach
Zero-order spectra of DPH standard solutions were produced by recording their absorption spectra throughout a wavelength range of 200–400 nm. The two medications were then simultaneously estimated using the dual-wavelength spectrophotometric technique [15].
The absorbance difference between 267.8 and 272.4 nm was measured in order to estimate DPH showed equal absorbance at these wavelengths, meaning that there was no [16].

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Absorbance difference. The absorbance difference at 247.6 nm and 249.6 nm, when DPH exhibited similar absorbance at both wavelengths, was also calculated for estimate.

Plotting the corresponding absorbance differences against the drug doses allowed for the construction of calibration curves. A linear concentration range of 15–35 µg/mL was demonstrated by both DPH [17].

Range and Linearity

DPH concentrations 15 µg/mL were used to assess linearity. Absorbance was determined at

266 nm for DPH and 247.4 nm for Absorbance differences were measured using the dual wavelength technique at 267.8–. Regression equations and correlation coefficients were calculated, and calibration curves were shown [18].

Consistency

Six replicate solutions of diphenhydramine hydrochloride (DPH) at a concentration of 25 µg/mL were prepared and analysed in order to evaluate repeatability. The first-order derivative and dual-wavelength spectrophotometric techniques were used to estimate absorbance. Calculations were made for the standard deviation (SD) and relative standard deviation (%RSD) [19].

Precision within and between days -DPH solutions with concentrations of 15, 25, and 35 µg/mL were used to assess intraday and intraday precision. For intraday precision, measurements were made three times in one day. The findings had an acceptability limit of no more than 2% and were presented as percentage relative standard deviation (%RSD) [20].

Precision (Recovery Study)

Three degrees of recovery tests were used to assess the accuracy of diphenhydramine hydrochloride (DPH): 80%, 100%, and 120%. The percentage recovery was computed after each level was examined in triplicate [21].

Limits of Quantification (LOQ) and Detection (LOD)

The mean slope from six calibration curves and the standard deviation of the calibration curve intercepts were used to calculate LOD and LOQ [22].

Formulas

LOD = 3.3 × SD/Slope

LOQ = 10 × SD / Slope

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Particularity

By adding known amounts of excipient stock solution to pre-analysed sample solutions containing DPH at a concentration of 15 µg/mL, the specificity of the suggested approach was evaluated. Three different amounts of excipients were added: 75%, 100%, and 125%. The suggested method was used to analyse the final solutions, and the specificity of the method was assessed by calculating the mean % recovery [23].

The accuracy of the suggested analytical approach was demonstrated by the 98.97% recovery of Diphenhydramine Hydrochloride (DPH) from the pre-analysed samples. The method is appropriate for regular pharmaceutical analysis, as evidenced by the high accuracy and precision attained in the assessment of DPH in capsule formulations [24].

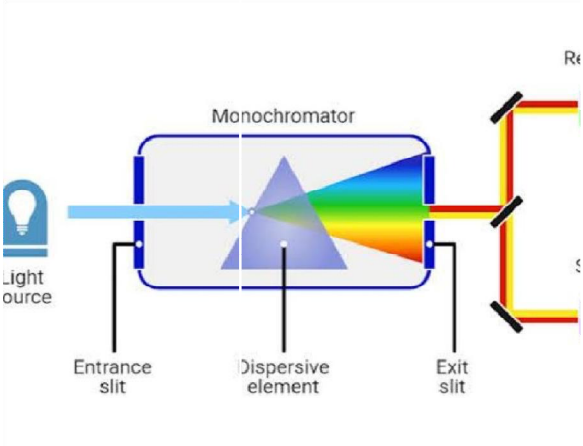
Table no: 1

Validation parameter	**Result**
Calibration curve	20-120/ml
Intraday Precision	0.86
Inter day Precision	0.48
Ruggedness	0.85
Recovery	99.4-100.3%
Robustness	0.65-1.37%
Limit of detection	0.04/ml
Limit of Qualification	0.15 ml
Change of percentage	0.15/ml

Standard addition method was used to assess the accuracy of the suggested analytical procedure. Diphenhydramine Hydrochloride (DPH) solutions of 60 and 70 µg/mL in 0.1 N HCl were prepared in order to evaluate precision. To ascertain intra-day and inter-day variability, the produced solutions were examined. While inter-day precision was examined over several days, intra-day precision was evaluated by doing analyses inside the same day. The percentage relative standard deviation (%RSD) was used to express the precision results. The corresponding results table displays the accuracy and precision data that were collected from the analysis.

To assess DPH's vulnerability to deterioration, its stability in a 0.1 N HCl solution was examined at various temperatures. According to the findings, DPH was constant at 50°C for up to 60 minutes. Nevertheless, non-reproducible absorbance values were found at temperatures of 60°C and higher, indicating decreased stability [25].

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Advantages of UV-Visible Spectroscopy:

• High Sensitivity: UV-Vis spectroscopy can detect low concentrations of substances, often in the micro molar or Nano molar range. This makes it useful for identifying trace compounds in complex mixtures.

• Simplicity and Speed: The technique is easy to perform and requires minimal sample preparation. Measurements can be completed quickly, making it suitable for analysing a large number of samples.

• -Wide Range of Applications: UV-Vis spectroscopy is used to analyse various substances, including organic and inorganic compounds, biological macromolecules, and Spectroscopy [26].

Disadvantages

• Limited to UV-Vis Active Compounds: Only substances that absorb ultraviolet or visible light can be analysed. Non-absorbing compounds cannot be detected directly.

• Solvent Interference: Some solvents absorb light in the UV-Visible region, which may interfere with measurements and reduce accuracy.

• Sensitivity to Environmental Conditions: Changes in temperature, pH, and ionic strength can affect absorbance and cause variations in results.

• Need for Calibration: Regular calibration is required to ensure accurate results. Improper calibration may lead to errors.

• Limited Structural Information: UV-Visible spectroscopy mainly provides information about electronic transitions and offers limited details about molecular structure.

•Path Length Limitations: At high concentrations, absorbance may become too high for accurate measurements, making dilution necessary.

• Deviation from Beer-Lambert Law: At high concentrations, deviations from Beer Lambert law may occur, leading to inaccurate concentration measurements.

• Overlapping Absorption Peaks: In complex mixtures, overlapping peaks can make it difficult to identify and analyse individual components.

• High Cost of Advanced Equipment: Basic UV-Visible spectrophotometers are relatively affordable, but advanced instruments and their maintenance can be expensive [28].

ANALYTICAL METHOD VALIDATION:

Analytical methods are essential for the development of new drugs, formulation and reformulation studies, stability testing, and quality control. These methods should be simple, precise, accurate, cost-effective, and easy to use.

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Method validation must be carried out during method development and routine use. Analytical method validation is the process of evaluating and confirming that an analytical method is suitable for its intended purpose [29].

ELEMENTS OF VALIDATION

1. Design Qualification (DQ)

Design Qualification ensures that the design of the equipment meets Good Manufacturing Practice (GMP) requirements. The design should fulfil all necessary GMP objectives. Mechanical drawings and design specifications provided by the equipment manufacturer must be reviewed carefully [30].

2. Installation Qualification (IQ)

Installation Qualification is an important process performed for newly installed or modified equipment, systems, and facilities. It verifies that the equipment has been installed correctly.

The following points should be included:

Inspection of the installation of instruments, infrastructure, utilities, and equipment.

Collection of the manufacturer's operating manuals, maintenance instructions, and calibration requirements.

Verification of construction materials, maintenance resources, and spare parts.

3. Operational Qualification (OQ)

Operational Qualification is performed after Installation Qualification (IQ). It involves testing the equipment, systems, and instruments to ensure that they operate correctly within their specified limits. This stage establishes and verifies the minimum and maximum operating ranges based on knowledge of the process and equipment [30].

Future prospective

UV–Visible spectrophotometry offers promising opportunities for the future assessment of diphenhydramine hydrochloride in pharmaceutical products. Further investigations may improve the precision, sensitivity, and dependability of the analytical procedure. The method can be optimized to determine drug content in tablets, capsules, syrups, and other appropriate dosage forms. Future research may emphasize the development of rapid, economical, and ecofriendly analytical techniques. The use of derivative spectrophotometry and mathematical approaches may help minimize interference from other formulation components. Additionally, the technique may be explored for routine quality assessment, drug stability evaluation, and monitoring during pharmaceutical production. Such improvements may contribute to reliable and efficient drug analysis in pharmaceutical laboratories.

II. CONCLUSION

The analytical method development and validation of Diphenhydramine Hydrochloride is an important process for ensuring the quality, safety, and efficacy of the drug. A suitable analytical method was developed to identify and quantify Diphenhydramine Hydrochloride accurately and precisely. The developed method was evaluated for various validation parameters, including accuracy, precision, linearity, specificity, robustness, and the limit of detection and limit of quantification, wherever applicable.

The validation results help establish the reliability, reproducibility, and suitability of the method for routine pharmaceutical analysis. A properly developed and validated analytical method can be used for the estimation of Diphenhydramine Hydrochloride in bulk drug and pharmaceutical dosage forms.

In conclusion, analytical method development and validation provide a reliable approach for quality control and ensure that Diphenhydramine Hydrochloride meets the required pharmaceutical standards. The developed method can be considered suitable for routine analysis when the experimental results comply with the applicable validation acceptance criteria.

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