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REVIEW ON THE METHOD DEVELOPMENT OF MEBEVERINE HCL BY SPECTROSCOPY.

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ABSTRACT: A simple, precise, and accurate UV spectrophotometric method was developed and validated for the stability testing of Mebeverine Hydrochloride (HCl) in pharmaceutical formulations. The method involved the selection of an appropriate wavelength at 220 nm, where Mebeverine HCl exhibited maximum absorbance in a distilled water. The method was validated for parameters such as linearity, accuracy, precision. Linearity was observed in the concentration range of 2–20 µg/mL, with a correlation coefficient (R^2) greater than 0.999. The method demonstrated good intra-day and inter-day precision with %RSD values less than 2%. Recovery studies confirmed the accuracy of the method with recoveries ranging from 98% to 102%. Forced degradation studies under various stress conditions (acidic, alkali, oxidative and thermal) confirmed the stability-indicating nature of the method. The proposed UV spectrophotometric method offers a rapid, cost-effective, and reliable analytical tool for the routine quality control and stability assessment of Mebeverine HCl in bulk and pharmaceutical dosage forms.

KEYWORDS: UV visible Spectrophotometer, Mebeverine hydrochloride, Forced degradation

INTRODUCTION:

Spectroscopic Methods: It is the branch of science dealing with the study of interaction between Electromagnetic radiation and matter. It is a most powerful tool available for the study of atomic and molecular structures and is used in the analyses of wide range of samples. Optical spectroscopy includes the region on electromagnetic spectrum between 100 A and 400 jun. The regions of electromagnetic spectrum are

Region	Wavelength
Far (or vacuum) ultraviolet	10-200 nm
Near ultraviolet	200-400 nm
Visible	400-750 nm
Near infrared	0.75-2.2 µm
Mid infrared	2.5-50 µm
Far infrared	50-1000 µm

Table no.1: Region of electromagnetic spectrum

Ultraviolet-Visible Spectrophotometry: UV-Visible Spectrophotometry is one of the most frequently Employed technique in pharmaceutical analysis. It Involves measuring the amount of ultraviolet or visible radiation absorbed by a substance in solution.Instrument which measure the ratio, or function of ratio, of the intensity of two beams of light in the UV visible region are called Ultraviolet-Visible Spectrophotometers.

Figure No 1: UV Spectrophotometer

In qualitative analysis, organic compounds can be Identified by use of spectrophotometer, if any Recorded data is available, and quantitative Spectrophotometric analysis is used to ascertain the of molecular species absorbing the radiation. Spectrophotometric technique is simple, rapid, moderately specific and applicable to small quantities of compounds. The fundamental law that governs the quantitative spectrophotometric analysis is the Beer - Lambert law

Beer's law:

It states that the intensity of a beam of Parallel monochromatic radiation decreases Exponentially with the number of absorbing molecules. In other words, absorbance is proportional to the Concentration.

Lambert's law:

It states that the intensity of a beam of Parallel monochromatic radiation decreases Exponentially as it passes through a medium of Homogeneous thickness. A combination of these two Laws yields the Beer-Lambert law.

Beer-Lambert law:

When beam of light is passed Through a transparent cell containing a solution of an Absorbing substance, reduction of the intensity of light May occur. Mathematically, Beer-Lambert law is expressed as; A = abc

Where, A absorbance or optical density; a Absorptivity or extinction coefficient; b path length of Radiation through sample (cm): c = concentration of Solute in solution. Both b and a are constant so a is directly proportional to the concentration c

Quantification of medicinal substance using spectrophotometer may carried out by preparing solution in transparent solvent and measuring it's absorbance at suitable wavelength. The wavelength normally selected is wavelength of maximum absorption (max), where small error in setting the wavelength scale have little effect on measured absorbance.

Introduction Of Mebeverine HCL :

Mebeverine hydrochloride (Figure 1) is a white crystalline powder having a molecular formula C25H35NO5HCl, molecular weight 466 and melting point 105-107ºC. It is freely freely soluble in water and ethanol (96%), while practically insoluble in diethyl ether [1]. IUPAC name of Mebeverine hydrochloride is 3,4-Dimethoxybenzoic acid 4-[ethyl[2-(4-methoxy phenyl)-1-methylethyl]amino]-butylester. It is a direct antispasmodic acting mainly on the smooth muscles of the gastrointestinal tract and particularly effective against the colonic spasm [2]. Mebeverine hydrochloride is widely used as a relaxant agent for the treatment of gastrointestinal spasmodic disorders such as irritable bowel syndrome [3].

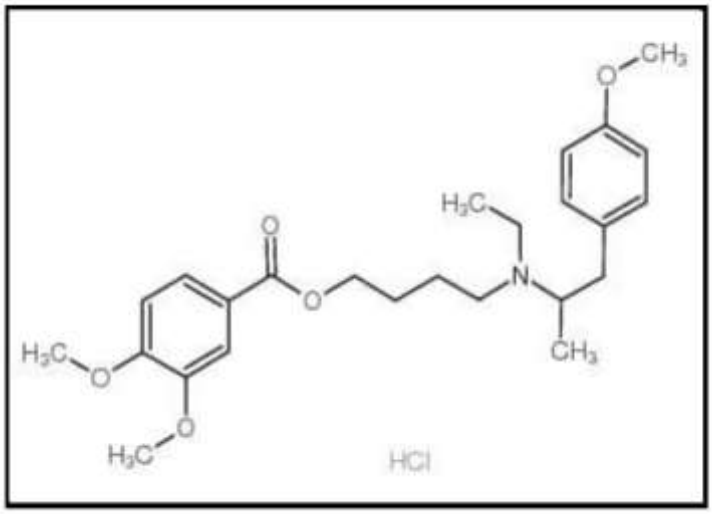


Figure1.Structure of Mebeverine HCL.

Method development for Mebeverine typically involves optimizing techniques for its extraction, identification, and quantification in various dosage forms, such as tablets, capsules, or oral solutions. High-performance liquid chromatography (HPLC), UV-Visible spectrophotometry, and gas chromatography (GC) are among the most commonly employed methods in the analysis of Mebeverine. A detailed literature survey reveals that there exists literature concerning analytical method development and validation for Mebeverine [1,3,6-7]. Hence we have explored in developing a new, accurate, precise and linear UV spectrophotometric method for the quantitative estimation of Mebeverine.

UV spectrophotometric method used for forced degradation studies:

Spectrophotometric method was used due to less equipment cost and economical maintenance advantages. By the help of this technique, the UV absorbance spectra are measured at 200-380 nm. In accordance with the International

Conference on Harmonization guideline, the force degradation state of active pharmaceutical substance includes acidic, basic and photolytic conditions.Acid/base stress testing is done to estimate the forced breakdown of a medicinal

component. This test involves the degradation of a pharmacological substanceover time through exposure to an acidic or basic media and the main degradationproducts. Labile carbonyl functional groups, such as amides (lactams), esters(lactones), aryl amines, imides, imines alcohols, and carbamates, undergocid/base hydrolysis. The method is used to identify an increase in thedegradation product and the resulting loss of pharmaceutical activity. Forceddeterioration is a component that can show whether the chosen technique is agood representation of stability. The objective of this study was to analyze forceddegradation Studies by treating paracetamol drug and paracetamol tablet underhydrolytic (acidic and basic), photolytic and thermal stress conditions, by usingspectrophotometer, as defined under International Conference on Harmonization guideline QIA (R2).

It is typically preferred over other methods due to the advantage of affordable maintenance and lower equipment costs. We have already conducted these degrading investigations, which Are beneficial for the field of pharmacy. It is typically preferred over other methods due to the advantage of affordable maintenance and lower equipment costs we have already conducted thesedegrading investigations, which are beneficial for the field of pharmacy.Acid/base stress tests, humidity, and temperature, as well as UV deterioration, are fundamental factors in drug degradation investigations.

Using acidic and alkaline solutions, the medication was forcedly degraded.Interaction between the basic (monomer) degradation product and the fundamental state. Alcohol, carbamates, amides (lactam), aryl amine esters(lactones), imines, and imides are some of the carbonyl functional groups thatcause the degradation of medicinal products. Hydrolysis of acid/base issubsequently performed.Forced degradation of drug substance in thermal/humidity environment wasperformed by exposing the drug product over long time which results in forcefuldegradation of drug substance to its primary components. By this process, testing

MATERIALS AND METHODS:

Materials Instruments

A double beam UV-visible spectrophotometer (Shimadzu, model 1900I) having two matched quartz cells with 1 cm light path and loaded with UV probe software was used for recording of spectra and measuring absorbance. An electronic analytical weighing balance, digital pH meter and a sonicator were used in this study.

Chemical & Reagents

Analytically pure sample of Mebeverine HCL was obtained as gift sample, 0.1N HCL used as solvent, Distilled water, Marketed formulation (Colospa 135mg).

Methods

Selection of suitable detection wavelength

By using UV spectrophotometer in the range of 200-400nm the scanning of the solution of Mebeverine hydrochloride (active drug) was carried out. It was examined that Mebeverine hydrochloride demonstrated maximum absorbance at 221 nm which was selected as the detection wavelength for the drug.

Preparation of standard solution of Mebeverine HCL

20mg of drug (Mebeverine hydrochloride) was dissolved in 0.1N HCL to prepare the standard stock solution and finally adjusted the volume with same solvent in 100 ml of volumetric flask to acquire a solution of 200µg/ml of Mebeverine.

Preparation of working sample solution for Mebeverine HCL

From the 200µg/ml of standard solution pipette out 10 ml and adjusted the final volume with same solvent in 100 ml of volumetric flask to acquire a working sample solution of 20µg/ml of Mebeverine.

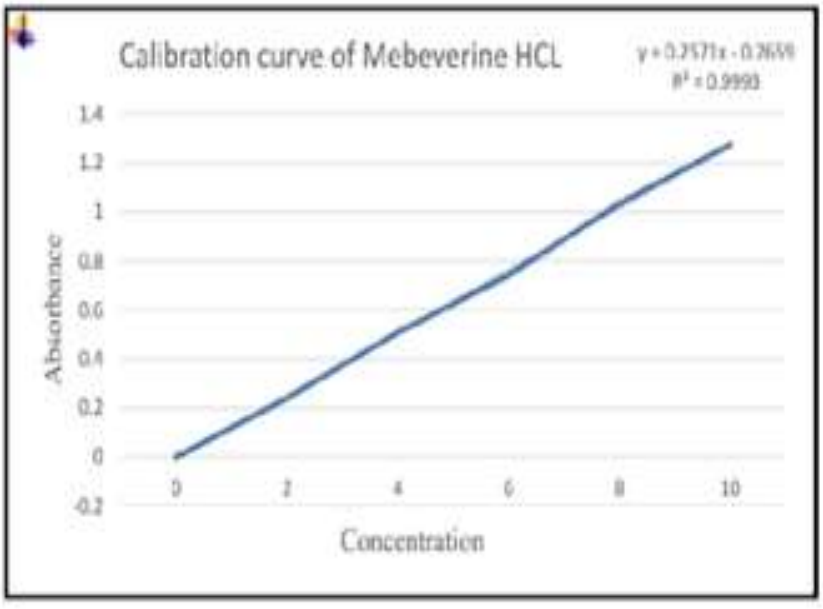
Preparation of stock & working solution for Mebeverine HCL

20 tablets were weighed and the average weight was determined. 20 tablets were grinded in a mortar and pestle and the average weight was transferred to a 100 ml volumetric flask containing 100ml diluent and then stirred for 10 minutes, to get sample stock solution of 200µg/ml. 10 ml of the above stock solution was pipetted out and made up to 100 ml to get working sample solution equivalent to a concentration of working standard of 20µg/ml.

Preparation Standard Calibration Curve:

Linearity

The precise volume of the standard stock solution of Mebeverine HCL was taken in 5 separate volumetric flask(10ml) and dilute the aliquots of the stock solution with 0.1N HCL to obtain the concentration of 2,4,6,8 and 10µg/ml. Calibration curve is plotted as absorbance vs concentration to calculate the regression coefficient for Mebeverine HCL. The regression coefficient is found to be 0.9993.



Graph no 1: Calibration curve of Mebeverine HCL

Method Validation

The method validated for the drug (Mebeverine HCL) are as follows:

1. Precision

2. Accuracy

3. LOD

4. LOQ

1. Precision

Precision of proposed analytical method was carried out for the 20µg/ml concentration for working solution and marketed formulation. Measure the absorbance, then after 1hours again measure absorbance and intraday using solvent as a blank. The result is express in the term of %RSD.

2. Accuracy

Accuracy of the method was assessed by using standard addition technique. The standard addition procedure was done by addition of 80%, 100%, and 120% of Mebeverine HCL standard in the sample. The percentage recovery was within the range of 99-100 % which shows the reliability of developed method. The results are tabulated in Table 6 .

Advantages and Disadvantages of Spectroscopy

Advantages

Cost-Effectiveness: The method is generally inexpensive compared to other analytical techniques like High-Performance Liquid Chromatography (HPLC).

Simplicity and Speed: The procedure is simple to perform, rapid, and does not require complex instrumentation or extensive sample preparation.

Routine Analysis: It is well-suited for routine quality control (QC) analysis in the pharmaceutical industry due to its ease of use and quick results.

Accuracy and Reproducibility: When validated correctly, spectroscopic methods can be highly accurate, precise, and reproducible, with low relative standard deviation (RSD) values.

Disadvantages

Specificity Limitations: UV spectroscopy might not be specific enough for complex formulations containing multiple active ingredients or potential impurities that absorb at similar wavelengths, requiring additional steps or different techniques (like derivative spectroscopy) to resolve interference.

Interference Issues: Excipients or degradation products in a formulation could potentially interfere with the absorbance reading of Mebeverine HCl, which needs careful method development and validation to mitigate.

Sensitivity: While sensitive in general, other methods like HPLC may offer lower limits of detection and quantification in specific complex matrices.

Sample State: This method is typically used for dissolved samples (solutions), so it is primarily used for quantitative analysis of the finished product or raw material, not usually for in-process monitoring of solid forms (though other forms of spectroscopy like FTIR can be used for solid characterization).

Degradation study of Mebeverine HCL API and formulation by UV Spectroscopy:

Stability testing is a critical aspect of pharmaceutical development and quality control, ensuring that a drug product maintains its identity, strength, quality, and purity throughout its shelf life. UV (Ultraviolet) spectroscopy is a widely used analytical technique in stability studies due to its simplicity, rapidity, sensitivity, and cost-effectiveness.

1.Thermal degradation

2.Oxidation degradation

3.Alkali degradation

4.Acid degradation

1. Thermal degradation:

Thermal degradation is a stability study method used to determine the effect of heat on a drug substance. In this procedure, a standard stock solution of the drug is prepared and subjected to elevated temperatures using a water bath or a hot air oven. The temperatures typically used are 40°C, 60°C, and 80°C, and the solution is exposed to these conditions for a defined time period

ranging from 1 to 4 hours. This controlled heating process helps to identify any degradation products formed as a result of thermal stress, which can then be analyzed to assess the stability and shelf-life of the drug under thermal conditions.

2. Oxidation degradation:

Oxidation degradation is a method used to assess the stability of a drug substance in the presence of oxidative stress. In this procedure, a standard stock solution of the drug is mixed with 3% hydrogen peroxide solution in a 1:9 ratio (1 ml of stock solution with 9 ml of hydrogen peroxide). The mixture is then allowed to stand at room temperature for 30 to 60 minutes to enable oxidation. For accelerated results, the solution can be heated at a temperature range of 40°C to 60°C, promoting faster oxidative degradation. This study helps identify the drug's sensitivity to oxidation and the potential formation of degradants.

3. Alkali degradation:

Alkali degradation is performed to assess the stability of a drug compound under basic conditions. In this procedure, a known concentration of the standard stock

solution of the test compound is prepared using a suitable solvent such as water or methanol. An aliquot of this stock solution is then treated with a basic solution, typically 0.1 N sodium hydroxide (NaOH). The mixture is heated at 60–70°C for 30 minutes to 2 hours, depending on the requirement, to promote degradation. After heating, the solution is cooled to room temperature. If needed, the sample is neutralized using hydrochloric acid (HCl) to bring the pH close to neutral (pH 6–7), preventing any interference during spectral analysis. The resulting solution is analyzed using a UV spectrophotometer, and the absorbance spectrum (200–400 nm range) of the degraded sample is compared with that of the standard solution to detect changes due to alkaline degradation.

4.Acid degradation:

Acid degradation is performed to evaluate the stability of a drug under acidic conditions. First, a stock solution of the test compound is prepared using a suitable solvent such as water or methanol. For acid degradation, an aliquot of this stock solution is treated with 0.1N or 1N hydrochloric acid (HCl). The mixture is then heated at a temperature of 60–70°C for 30 minutes to 2 hours, depending on the requirement. After heating, the solution is cooled to room temperature. If needed, the solution is neutralized using sodium hydroxide (NaOH) to avoid interference during UV analysis. The pH is adjusted close **to neutral (between 6 and 7). The** sample may be diluted and analyzed using a UV spectrophotometer in the 200–400 nm range, and the obtained spectra are compared with that of the standard solution to detect any degradation.

CONCLUSION:

The developed method exhibited linearity in the range.The precision for Mebeverine hydrochloride is exemplified by relative standard deviation of 1.72% and 100% respectively. Percentage Mean recovery for Mebeverine hydrochloride was found to be in the range of 98 -102, during accuracy studies. It is concluded that the developed UV spectrophotometric method is accurate, precise, linear, rugged and robust and therefore the method can be used for the routine analysis of Mebeverine hydrochloride.

The forced degradation study of Mebeverine HCl under various stress conditions—oxidation, thermal degradation, alkali, and acidic environments—demonstrates its stability profile and degradation behavior. The drug exhibited significant degradation under oxidative and alkaline conditions, indicating susceptibility to oxidative and alkaline stress, whereas thermal and acidic conditions resulted in comparatively minimal degradation. The study's parameters establish a comprehensive stability profile, essential for developing robust analytical methods and ensuring drug quality, safety, and efficacy throughout its shelf life.

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