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Analytical Method Development and Validation of Ketoconazole by UV Spectroscopy

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Abstract: *A UV spectroscopic method which is simple, accurate and rapid is developed for the determination of ketoconazole in pharmaceutical formulations as active substance in tablets. The absorption maxima of ketoconazole solutions in ethanol are recorded at 257 nm. The linearity for ketoconazole in ethanol with correlation coefficient values higher than 0.999 is found. The intra– and inter–day assay is within 2% relative standard deviation. The obtained results for tablets are in good agreement with their respective product, label claims. The developed method can be successfully applied for the purpose routine analysis of ketoconazole in pharmaceutical formulations. Ketoconazole is a drug used in the management and treatment of fungal infections. It is in the imidazole antifungal class of medications.*

Keywords: ketoconazal, UV Spectroscopy, Multicomponent Analysis

I. INTRODUCTION

UV-Visible spectrophotometry is one of the most frequently employed technique pharmaceutical Analysis. It involves measuring the amount of ultraviolet or visible radiation absorbed by a substance inAnalysis. It involves measuring the amount of ultraviolet or visible radiation absorbed by a substance inSolution. Instrument which measure the ratio, or function of ratio, of the intensity of two beams of light in the U.V-Visible region are called uv visible spectroscopy. Beer's law: It states that the intensity of beam of Parallel monochromatic radiation decreases exponentially with the number of absorbing molecules. In other Words, absorbance is proportional to the concentrationLambert'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 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=a b c

Where, A=absorbance or optical density A=absorptivity or extinction coefficientB=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 cWhen c is in gm/100 ml, then the constant is called A The principle of uv visible Spectroscopy is base on theabortion of ultraviolet light or visible light chemical compounds, which results In the production of districtspectra. spectroscopy is based on the interaction between light and meter energy Stat to another energy state .

1. Analytical Method :

A sample can be analyzed qualitatively, quantitatively, or structurally for one or more analyses using an analytical method that uses specific technology and specific, step-by-step instructions. Analytical techniques are typically divided into two categories: Instrumental and classical techniques. The classical approach is one in which the signal is inversely correlated with the analyses' absolute concentration. The term "instrumental method" refers to a technique where the signal is inversely proportional to the concentration of the analytic. The three primary categories of classical procedures are:

- Analyze separation
- Qualitative analysis
- Quantitative analysis

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Extraction, distillation, precipitation, and filtering are processes used toseparateanalyses. The boiling point, freezing point, colour, odor, density, reactivity, and refractive index are all examples of qualitative analysis. Gravimetric analysis and volumetric analysis are both types of quantitative analysis. Spectroscopic methods, electrochemical methods, chromatographic methods, and other techniques are the four primary categories into which instrumental methods can be broken down. Ultraviolet- visible spectroscopy, infrared spectroscopy, Raman spectroscopy, atomic absorption and emission spectroscopy, x-ray spectroscopy, and nuclear magnetic spectroscopy are examples of spectroscopic techniques. Potentiometric, coulometer, and voltammetry are examples of electrochemical approaches. Chromatographic techniques include column chromatography, paper chromatography, thin layer chromatography, high-performance liquid chromatography, gas chromatography, and contemporary techniques (LC-MS, GC-MS, LC-MS-MS, GC-MS-MS, LC-NMR, and GC-NMR). X-ray methods, radioactivity, mass spectrometry, optical methods (refract meter, optical rotation), thermal methods (thermogravimetry, differential thermal analysis, and differential scanning calorimetric), and radioactivity are further Techniques.

2. Introduction to Spectroscopy :

The study of electromagnetic radiation's interactions with matter is known as spectroscopy. Theseinteractions involve the matter absorbing and emitting radiation (energy). There are two forms of spectroscopy: emission spectroscopy and absorption spectroscopy. Absorption spectroscopy (UV, visible, infrared, nuclear magnetic resonance, microwave, and radio wave spectroscopy) is the study of electromagnetic energy absorbed by the sample and represented as spectra. Emission spectroscopy is the study of electromagnetic radiation emitted by the sample in the form of spectra (flame photometry and fluorimetry). The study of atomic and molecular structure can benefit from the use of spectroscopy, which is also used to analyze a variety of samples. The study of electromagnetic radiation's interactions with atoms and the changes in energy that result at the atomic level is known as atomic spectroscopy (e.g. atomic absorption spectroscopy and flame photometry). The study of electromagnetic radiation's interactions with molecules and energy changes that occur at the molecular level is known as molecular spectroscopy (e.g., ultraviolet and infrared spectroscopy)UV-VIS spectroscopy: It is based on the Beer-Lambert law, which states that the absorbance of a solution is directly proportional to the concentration of the absorbing species in the solution and path length. Ultraviolet (UV) spectroscopy is a physical method of optical spectroscopy that uses light in the visible, ultraviolet, and near- infrared ranges. Consequently, it can be used to calculate the concentration of the absorber in a solution for a specific path length. Since UV-VIS spectroscopy has been in widespread use for the past 37 years, it has evolved into the most crucial analytical tool in the modern laboratory. It is crucial to understand how quickly the absorbance varies with concentration.

3. Principle of UV :

When radiation induces an electronic transition in a molecule or ion's structure, the object will exhibit absorption in the visible or ultraviolet range. As a result, when a sample absorbs light in the ultraviolet or visible range, the molecules inside the sample experience a change in their electronic state. Electrons will be promoted from their ground state orbitals to higher energy orbitals, such as excited state orbitals or anti-bonding orbitals, by the energy provided by the light. Potentially, three types of ground state orbital may be involve

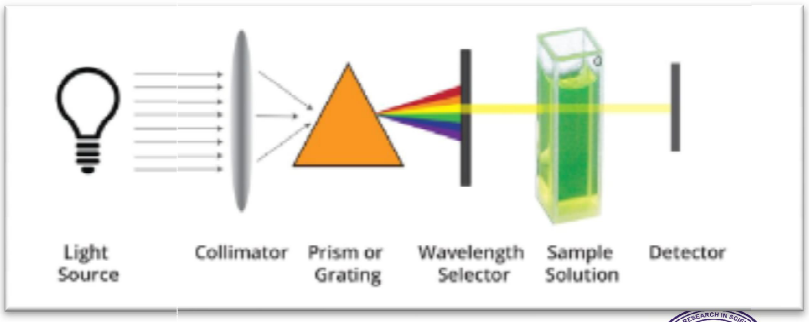

Figure 1. Instrumentation of UV Spectroscopy.

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Radiation sources: Most commonly used radiation sources are tungsten lamps, hydrogen discharge lamps, deuterium lamp, xenon discharge lamps and mercury arcs.
Wavelength selector: To distribute the light in accordance with the wavelength, a monochromator is utilized. An entrance slit, a dispersing component, and an exit slit make up the fundamental components of a monochromator.
Sample cell: Cells or cuvettes are sample containers used in UV-Visible spectroscopy to hold liquid samples. Quartz is used to make cuvettes.
Photo detector: The photocell, barrier layer cell, and photomultiplier tube are the detectors that are most frequently employed in UV spectrophotometers. Readout device: After being amplified appropriately, the detector's output is shown on a readout device. The Beer-Lambert law state

II. AIM AND OBJECTIVES:

Aim: To develop & validate analytical method of Ketoconazal by UV Spectroscopy.

Objective:

- To develop a simple, specific, accurate and precise method of UV spectroscopy for ketoconazal.
- To develop economical, robust and reproducible method.
- To develop analytical method for quantitation of ketoconazal by UV Spectroscopy.
- Validation of all developed analytical methods as per ICH guidelines.

III. MATERIAL & METHODS

Materials

- Chemical and reagents
- Instrumentation and chromatographic conditions.
- Preparation of standard stock solution.
- Analysis of ketoconazal.
- Validation parameter:
- Optimization of Procedure
- Linearity
- Range
- Precision
- Accuracy
- Quantitation limit

Chemicals & Reagents: Ethanol, distilled water, .
Instrument: UV Spectroscopy.
Preparation of stock solution:-The standard stock solution of ketoconazal by dissolving accurately wt. 10mg of drug in ethanol & volume was made up to 100 ml with ethanol to get conc. of 10ppm from the stock solution.
Determination of ג max:-An appropriate aliquot portion of ketoconazal (0.1 mL) were transferred to two separate 10 mL volumetric flask the volume was made up to the mark using 80% v/v ethanol to obtain (10 µg/mL). Drug solutions were scanned separately. between 200 nm to 400 nm.

Validation to Proposed method :

Analytical method validation is an essential requirement to perform the chemical evaluation. Method validation is a procedure of performing numerous assessments designed to verify that an analytical test system is suitable for its intended reason and is capable of providing beneficial & legitimate analytical data.
Steps in method validation:
Develop a validation protocol or operating procedure for the validation Define the application, purpose and scope of the method

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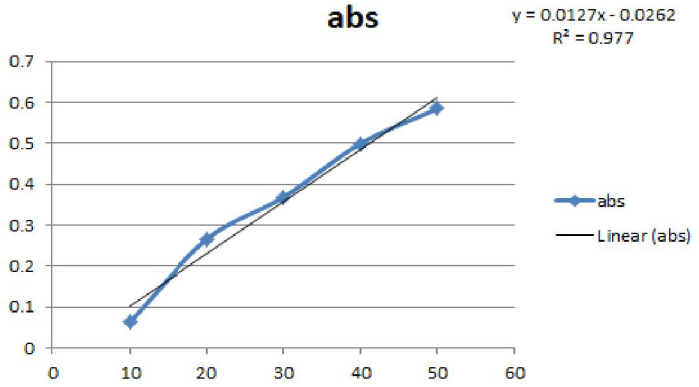
Define the performance parameters and acceptance criteria
Define validation experiments Verify relevant performance characteristics of equipment Qualify materials, e.g. standards and reagents
Perform pre-validation experiments Adjust method parameters or/and acceptance criteria if necessary.
Perform full internal (and external) validation experiments Develop SOPs (standard operating procedures) for executing the method in the routine Define criteria for revalidation.
Define type and frequency of system suitability tests and/or analytical quality control (AQC) checks for the routine Document validation experiments and results in the validation.

Linearity

The linearity of an analytical method is its ability to elicit test results that are directly (or by a well def.need mathematical transformation) proportional to the analytic concentration in samples within a given range.
Linearity usually expressed in terms of the variance around the slope of regression line calculated according to an established mathematical relationship from test results obtained by the analysis of samples with varying concentrations of analytic.



Precision :

The precision of an analytical method is the degree of agreement among individual test results when the method is applied repeatedly to multiple samplings of homogenous samples. This is usually expressed as the standard deviation or the relative standard deviation (coefficient of variation).Precision is a measure of the degree of reproducibility or of the repeatability of the analytical method under normal operating circumstances. According to ICH guidelines acceptance criteria for precision the % RSD should NMT 2%

Repeatability :

Repeatability involves analysis of replicates by the analyst using the same equipment and method and conducting the precision study over short period of time while reproducibility involves precision study at different occasions, different laboratories and different batch of reagent, different analysts and different equipment's**.**

Reproducibility :

Reproducibility means the precision of the procedure when it is carried out under different conditions-usually in different laboratories-on separate, putatively identical samples taken from the same homogenous materials.
Precision is a measure of the degree of reproducibility or of the repeatability of the analytical method under normal operating circumstances**.**

Limit of Detection :

The limit of detection (LOD) is usually defined as the lowest quantity orconcentration of a component that can be reliably detected with a given analyticalmethod. Intuitively, the LOD would be the lowest concentration obtained from themeasurementofasample(containingthecomponent)thatwewouldbeabletodiscriminate from the concentration obtained from the measurement of a blank sample(asample not containingthe component).
Limit of Quantitation :

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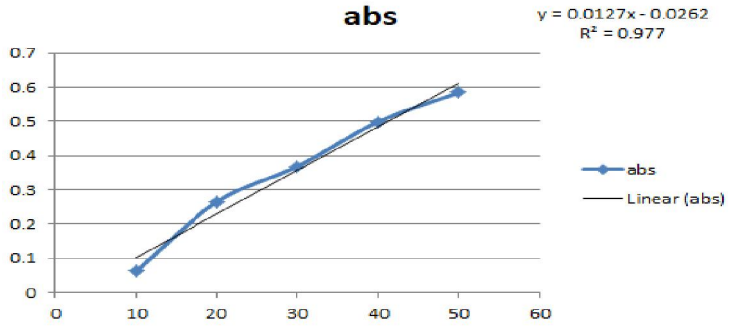
Limitofquantitationisthelowestconcentration(%,ppm)thatcanbedeterminedwith acceptable precision (RSD of~5%).

Robustness :

The evaluation of robustness should be considered during the development phase and depends on the type of procedure deliberate variations in method parameters. If measurements are susceptible to variation in analytical conditions, the analytical condition should be suitably controlled or a precautionary statement should be included in the procedure. In this presentworkabsorptionmaximawasdecreasedandincreasedby1nmandtheprocesswascarriedfor9 mg/mlstandard solution. The% RSD was calculated.

IV. RESULT AND DISCUSSION

The present study was carried out to develop a simple, sensitive, precise and accurate UV spectrophotometric method for the simultaneous estimation of Omeprazole in pharmaceutical dosage forms. *P exhibits at 301 nm and 287.2 nm



VI. SUMMARY AND CONCLUSION

The UV spectrophotometric method for the simultaneous determination of Omeprazole in marketed formulations was developed and validated as per ICH guidelines.

The satisfying recoveries, low correlation coiftent and assay results confirmed the suitability of proposed method for the routine quality control analysis for simultaneous determination of OMP in pharmaceutical formulations. The %RSD values for the proposed method reveals high degree of precision of method. The assay and validation results are satisfactory a therefore the developed method. Can used for routine analysis of formulations without interference from excipients.

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