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UV-VISIBLE SPECTROPHOTOMETRIC METHOD DEVELOPMENT AND VALIDATION OF BREXPIPRAZOLE IN BULK DRUG

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Abstract

A novel, safe and sensitive method of spectrophotometric estimation in UV region has been developed for the assay of Brexpiprazole in its bulk form. Brexpiprazole was tested using this method, which was developed and validated using acetonitrile, water, and methanol as diluents. that does not demonstrate any interference with spectrophotometric estimates. All of the analysis's parameters were selected in accordance with ICH [Q2 (R1)] guidelines, and they were all statistically validated using neat , RSD, and %RSD.

Index Terms: **Method validation, Method development, International Conference on Harmonisation (ICH), UV SPECTROSCOPY.**

Introducrion

Spectroscopy 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 structure/s and is used in the analyses of wide range of samples. Optical spectroscopy includes the region on electromagnetic spectrum between 100 Å and 400 µm. The regions of electromagnetic spectrum are 1, 2:

Ultraviolet-Visible Spectrophotometry: Undoubtedly one of the most popular techniques in pharmaceutical analysis is UV-visible spectrophotometry.This includes determining how much UV or visible light radiation a compound in solution can absorb. 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 Ultraviolet-Visible Spectrophotometers. In qualitative analysis, organic compounds can be identified by use of spectrophotometer, The number of molecules absorbing the radiation is estimated using quantitative spectrophotometric analysis, if any data are available. .The spectrophotometric approach works with small

amounts of substances and is quick, easy, fairly specific, and accurate. The Beer-Lambert law is the basic tenet of quantitative spectrophotometric analysis.[3]

Beer's law: According to this, a parallel monochromatic radiation beam's energy reduces exponentially when more absorbing molecules are present. In other words, the ratio with both absorbance and concentration.

Lambert's law: He states that when passing through a uniformly thick medium, the intensity of a parallel monochromatic radiation beam diminishes exponentially. The Beer-Lambert law results from the union of these two laws.

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.2

Mathematically, Beer-Lambert law is expressed as; **A = a b c**

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.

BREXPIPRAZOLE

Brexpiprazole is a serotonergic -noradrenegic-dopaminergic acting compound. It is a small molecule with molecular formula $C_{25}H_{27}N_3O_2S$, molecular weight 433.57 g/mol and chemically known as 7-{4-[4-(1-Benzothiophen-4-yl)piperazin-1-yl]butoxy} quinoline-2(iH)-one Brexpiprazole is non-hygroscopic, with whiteto off White crystal powder having an 183°C (decomposition) melting point [1].This medication does not dissolve in water because it is a weak molecule with a pKa of 7.8 . Brexpiprazole (Figure 1) is used in treatment of schizophrenia and adjunctive treatment of Major Depressive Disorder (MDD) [2].It has partial agonistic activity at dopaminergic D2 and serotonergic 5-HT1A receptors as well as partial antagonistic activity at serotonergic 5-HT2A and noradrenergic 1/2 receptors [2

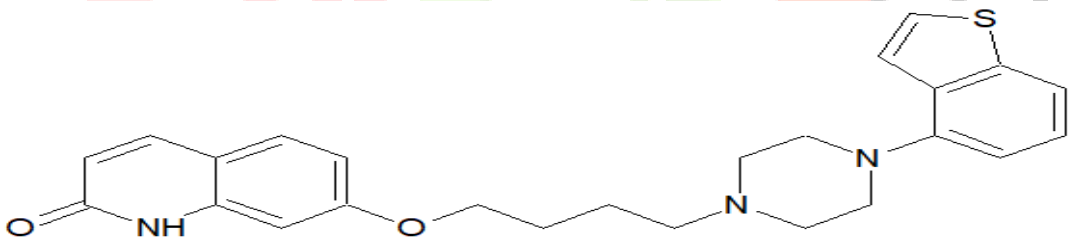

Fig no 1 structure of brexpiprazole

Validation

Accuracy

Accuracy is defined as the nearness of a measured value to the true or accepted value. Practically accuracy indicates the deviation between the mean value found and the true value. Applying the procedure to samples to which known concentrations of the examined substance were added yields the response.To make sure there are no interferences, they should be compared to both standard and empty solutions for analysis.The accuracy is then determined using the test results as input and expressed as a percentage of the analyte extracted from the analysis' output.By assessing known increased quantities of the analysed drug, it is frequently stated as recovery.[6]

Precision

It describes how closely measurements obtained from multiple sampling of the same homogenous sample under the specified conditions agree (the degree of scatter).A measure of precision is the reproducibility of the entire analytical process.[7]Repeatability and intermediate precision make up its two parts. The fluctuation that a single analyst encounters on a single instrument is known as repeatability. It does not differentiate between the change brought on by the instrument or system by itself and the method employed to prepare the sample. By examining numerous replicates of a composite sample for analysis using an analytical method, reproducibility is carried out during validation. Restoration costs are calculated. Intermediate precision is the variation within a laboratory such as different days, with different instruments, and by different analysts. [8- 9] The relative standard deviation is then used to express the precision.

Linearity

Linearity is the ability of analytical procedure to obtain a response that is directly proportional to the concentration (amount) of analyte in the sample.If the procedure is linear, the analyte concentration in the sample falls within a range that may be readily transformed mathematically into a relationship that is directly proportionate to the test.The confidence limit on the slope of the regression line is generally used to express linearity.[10]

Ruggedness:

This includes different analysts, laboratories, columns, instruments, sources of reagents, chemicals, solvents.The degree of correlation between test findings analysed from the same samples under varied standard test conditions shows the analytical method's dependability.The ruggedness of the method was studied by changing the experimental condition such as,Changing to another column of similar type andDifferent operations in the same laboratory.[11]

LOD and LOQ

The smallest concentration of an analyte that could be measured but never calculated ina sample is known as the LOD.LOD is defined as a concentration at a given signal-to-noise ratio, often 3:1.The least amount of an analyte found in a specimen that is determinable using respectable precision and accuracy there within the parameters of the method's circumstances is known as LOQ. For LOQ, ICH has recommended a signal-to-noise ratio of 10:1. The SD of the response and slope of the calibration curve(s) at values matching the LOD can also be used to calculate LOD and LOQ, as illustrated in the formulas below. [12,13]

- LOD = 3.3δ/S
- LOQ = 10δ/S.

The aim and scope of the proposed work are as under:

1. To develop suitable spectrophotometric method for assay of brexpiprazole .
2.Perform the validation for the method.

EXPERIMENTAL work :

Material method

1.Diluent Preparation: Methanol :AcN: Phosphate buffer (50:35:15) all PH maintain at 2 used as a diluents.

2.Preparation of standard stock solution

20 mg drug dissolve in already prepared 20 ml of Methanol :AcN:Phosphate buffer(50:35:15) all ph maintain at 2 then volume make up to 100 ml.from that 2.5 ml taken and diluted up to 50ml

3.Selection of wavelength of analysis

Appropriate volume 1ml of standard stock solution of brexpiprazol was transfer into a 10 ml volumetric flask diluted with Methanol :AcN:Phosphate buffer(50:35:15) all PH maintain at 2.

To give concentration of µg/ml.resulting solution was scanned in the uv range (200-400).in spectrum brexpiprazole shows lambda max at 216 nm

4.Validation of the method

Linearity

Transfer 1-5 ml from stock solution of brexpiprazole into series of 10 ml volumetric flask then the volume make up uto the mark with Methanol :AcN:Phosphate buffer(50:35:15) to get concentrations ,1,2,3,4and 5 µg/ml respectively.the solution where scanned on a spectrophotometer in uv range 200-400 nm

Accuracy

A standard stock solution was added to the pre-analyzed sample solution at various levels, such as 50%, 100%, and 150%. The solution was then reanalyzed using the suggested procedure.

Precision

Variations between and between days were examined for the precision of the approach.By examining the 3 g/ml solution of brexpiprazole three times on the same day, intraday precision was ascertained. By examining the 3 g/ml of brexpiprazole solution daily for three days during a week, interday precision was confirmed.

Ruggedness:

By analysing aliquots from homogenous slots by two analyzers under the identical operational and environmental settings, the robustness of the proposed approach is assessed for a 3g/ml concentration of brexpiprazole.

LOD and LOQ:

The LOD and LOQ were separately determined which is based on calibration curve. The S.D. of y intercept of regression line may be used as S.D.

LOD = 3.3 x σ/s

LOQ = 10xσ/s Where,

σ= Standard deviation of y Regression intercept lines

S = Slope of calibration curve.

Result

A) Analysis wavelength selection of Brexpiprazole solution was scanned in the uv range (200-400).in spectrum brexpiprazole shows lambda max at 216 nm

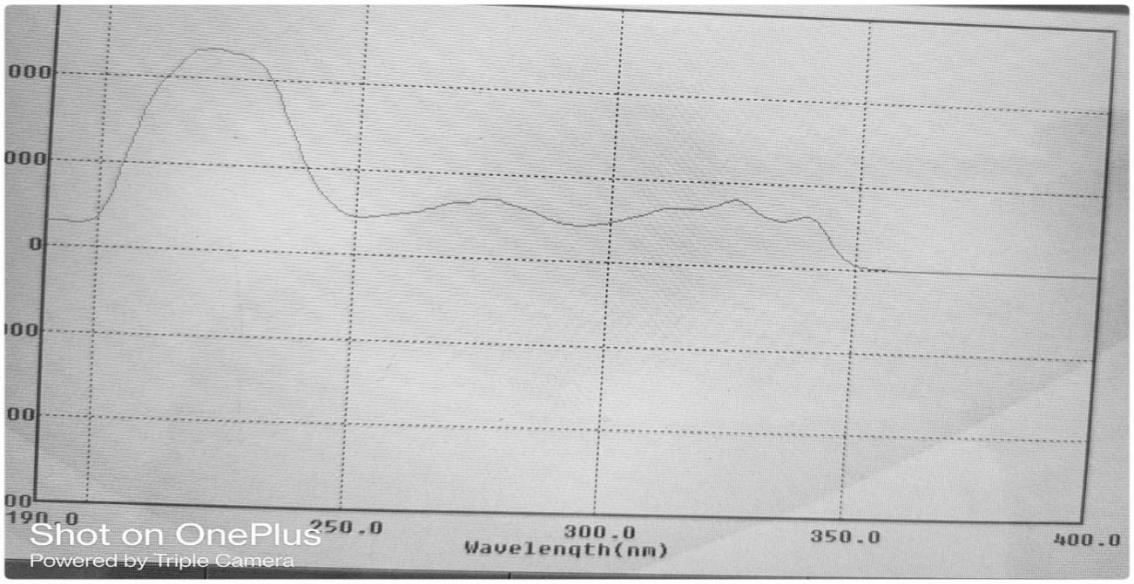

Fig no 2.UV spectra of brexpiprazole

C) Linearity : concentrations ,1,2,3,4and 5 µg/ml solution of brexpiprazole where scanned on a spectrophotometer in uv range 200-400 nm . give following results

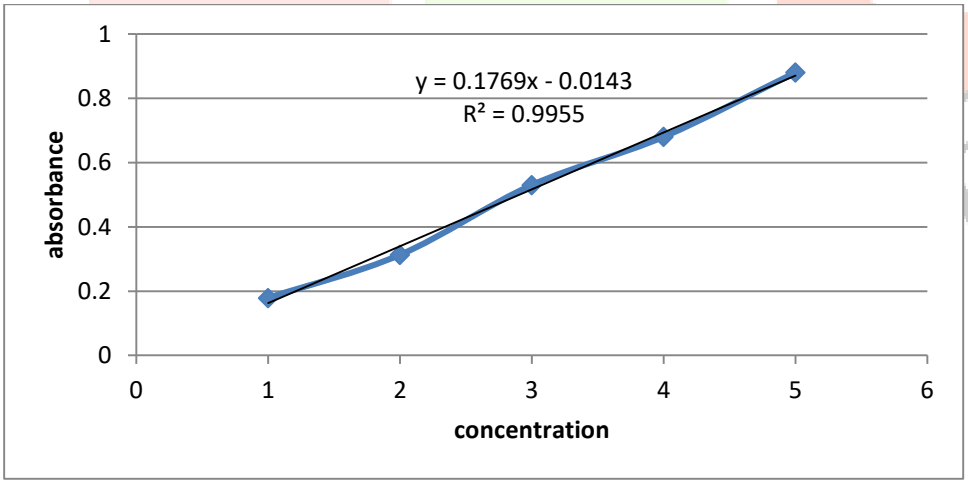

fig no 3. calibration curve for brexpiprazole

Table no 1 absorbance and concentration

concentration	absorbance
1	0.179
2	0.313
3	0.53
4	0.68
5	0.88

Table no 2.Calibration curve parameter

Sr no	parameter	VALUE
1	slope	0.1769
2	Intercept	0.0143
3	Regression coefficent	0.9955
4	range	1-5

B) Accuracy

Concentration level 50, 100, 150 analyze using proposed method and % RSD were calculated

Table no 3 accuracy study

%recovery level	%recovery	SD	%RSD
50	98.87	0.001	0.09442
100	99.19	0.001	0.320
150	99.81	0.0005	0.5617

D) Precision

3 µg/ml concentration solution analyze three different time in same day and also analyze three different day give following result .

Table no 4 precision study

CONCENTRATION	INTRADAY PRECISION		INTERDAY PRESCISION	
	SD	%RSD	SD	%RSD
3	0.007638	1.4118	0.01040	1.9217

E) Ruggedness

Two different analyst analyze the same concentration solution to give following results

Table no 5 ruggedness study

	absorbance	SD	%RSDS
Analyst 1	0.538	0.007638	1.4118
Analyst 2	0.59	0.00512	0.6515

F) LOD and LOQ:

LOD was found to - 0.052 µg/ml
LOQ is found to be - 0.15 µg/ml. which indicates adequate sensitivity method.

Conclusion

The present analytical method was validated as per ICH Q2(R1) guideline and it meets to specific acceptance criteria. The analytical approach was determined to be specific, precise, linear, accurate, robust, and having stability suggesting features. The current analytical technique can be applied to the desired outcome

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