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Estimation of Brexpiprazole in Bulk by using UV-Spectroscopy Method.

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ABSTRACT
UV – Visible Spectroscopic determination was carried out at absorption maxima of 215nm using methanol as a solvent. The linearities were in the range of 0.5-7.51µg/ml for UV-Visible Spectroscopic method.The value of limit of detection[LOD] and limit of quantification[LOQ] was found to be0.07 µg/mL and 0.22 µg/mLrespectivlyMethanol was used as a solvent throughout the work. The present method was found to be simple and linear which can be used for routine quality control analysis for spectrophotometric estimation of Brexpiprazole in bulk.

KEYWORDS
Brexpiprazole, limit of detection , limit of quantification , Antipsychotic, λmax

I. INTRODUCTION

Brexpiprazole is an Antipsychotic drug. It also works by changing the action of Chemicals in the brain. It is a dopamine D2 receptor partial agonist and has been described as a "Serotonin Dopamine Activity Modulator" (SDAM).

Partial agonists have both blocking properties and stimulating properties at the receptor they bind to. The ratio of blocking activity to stimulating activity determines a portion of its clinical effects. BREX has more blocking and less stimulating activity than its Predecessor, aripiprazole, which may decrease its risk for agitation and restlessness. The drug received FDA approved on July 10, 2015 for treatment of Schizophrenia and adjunctive treatment of depression. It has partial agonistic activity at serotonegic 5-HT1A and at dopaminergic D2 receptors,antagonistic activities at serotonergic 5-HT2A, and antagonist activity at noradrenergic α1/2 receptors

Literature survey revealed that Brexpiprazole was determined by UV-visible spectroscopy and HPLC [4-7]. In the current work, the authors have proposed a simple, specific, valid androbust RP-HPLC method for the estimation of Brexpiprazole in pharmaceutical active substance form.

Chemistry:

Brexpiprazole is chemically designated as 7-{4-[4-(1-benzothiophen-4-yl) piperazin-1-yl]butoxy}-1,2-dihydroquinolin-2-One. Its molecular formula is C25H27N3O2S, and its molecular weight is 433.57. Brexpiprazole is a white-to-off white powder. It is Freely soluble in methanol and practically insoluble in water.Brexpiprazole is store in cool and dry place. The melting point of Brexpiprazole is in between 272℃-274℃.

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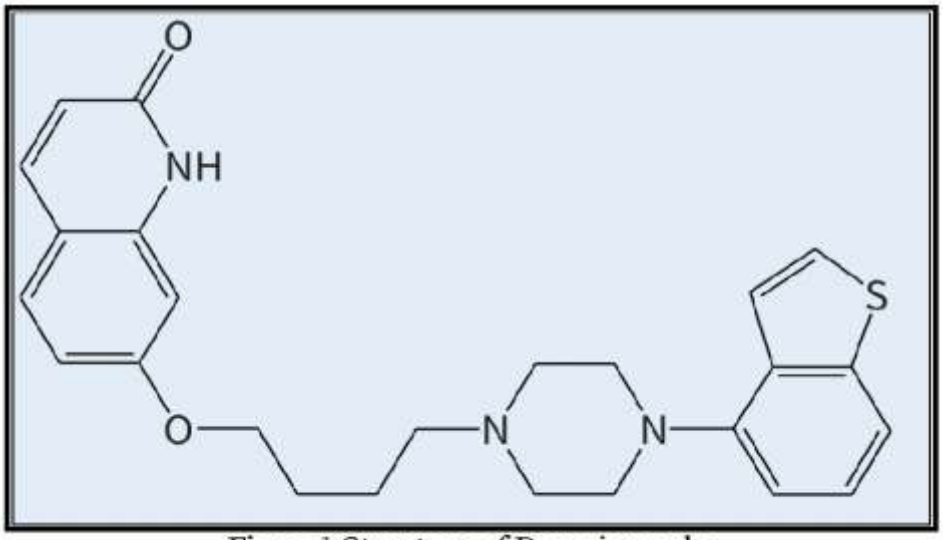

Fig.no.1 Structure of Brexpiprazole.

II. MATERIALS AND METHODS:

A]Apparatus

Spectrophotometer: All the absorption spectra and derivative Spectra were recorded on UV-visible double beam spectrophotometer (UV-550 ,Jasco Corp., Japan) with 1cm quartz cell.

Analytical balance: All the drugs and chemicals were weighed on Azcet High Precision Balance (Model –CY 224C).

B]Materials and reagents: Methanol was used throughout UV –Visible spectroscopic method development and validation.Pharmaceutically pure sample of Brexpiprazole were obtained as gift sample from Alkem Laboratories Ltd.All chemicals and reagent were of analytical grade

LOD and LOQ

The limits of detection (LOD) and quantification (LOQ) are defined as **the lowest concentration of the analyte that can be reliably detected and quantified**, respectively. The LOD and LOQ of analytical methods may refer to absolute and relative values, depending on the type of methodology and attribute

1) Priliminary test of Drug:

[a] Colour, odour and appearance:

Brexpiprazoleis evaluated for various preliminary parameters like colour, odour and appearance and confirmed that they complied with official standards and are shown in the table.

Table 1 .Colour, odor and appearance of Drug

Parameters	Observation
Colour	Off-White
Odor	Odorless
Appearance	Amorphous powder

[b]Melting point determination:

The melting point for Brexpiprazole is determined by an open capillary method and compared with standard literature values given in table .

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Table 2 . Melting Point (ºC) of Brexpiprazole

Sr.No.	Observed MP (ºC)	Std. M.P(ºC)
1	271-273	272-274
2	273-275	
3	271-272	

[c]Determination of Solubility

The solubility was determined in solvents under consideration i.e. methanol, water, acetonitrile, ethanol, DMF, DMSO etc. are given in results**.**

Table 3. Solubility study of Brexpiprazole

Sr. No.	Name of Solvent	Solubility
1	Water	Insoluble
2	Methanol	Slightly soluble
3	Acetonitrile	Slightly soluble
4	Phosphate buffer	Soluble
5	0.1 N HCl	Insoluble
6	Ethanol	Soluble
7	DMF	Soluble
8	DMSO	Soluble

2) To identify the λmaxof Brexpiprazole:

The standard solution was scanned between 200-400 nm. The wavelength of maximum absorption was determined for drugs. Brexpiprazole showed maximum absorbance at 216 nm. It is shown in Figure No.1.1. Therefore 216 nm considered as an analytical wavelength for further determination.

3) Method validation :

Linearity was studied by analyzing five standard solutions covering the range of 0.5-7.5 µg/ml of Brexpiprazole. From the primary stock solution 0.5ml,2.5ml,5.0ml,6.2ml,7.5ml of solution pipette into 10 ml volumetric flasks individually and made up to the mark with methanol to give a concentrations of 0.51µg/mL , 2.53µg/mL ,5.05µg/mL ,6.26µg/mL and 7.58 µg/mL of Brexpiprazole .

III. RESULTS AND DISCUSSION

The proposed UV- Spectroscopic, Area under Curve method for determination of Brexpiprazole show maximum absorbance at 215.00nm (λmax). The result of UV-Spectroscopic analysis has been showed in table. Indicates that the representative calibration curve of the Brexpiprazolewhere plotted at 215.00nm. A linear relationship was obtained for Amiloride in concentration range of 0.5-7.5 µg/ml. linear regression of absorbance gave the equation forBrexpiprazole . For bulk, y=910505.163x+-22876.12733. --- Equation 1 Correlation Coefficient (R^2=0.99997)

Calibration curve with concentration verses peak areas was plotted by injecting the above prepared solutions and the obtained data were subjected to regression analysis using the least squares method.

Table 4 . Linearity

Level	Conc.(ug/ml)	Area	%RSD
10%	0 .51	446980	0.363

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50%	2.53	2264762	0.331
100%	5.05	4554584	0.147
125%	6.26	5707982	0.478
150%	7.58	6866853	0.111

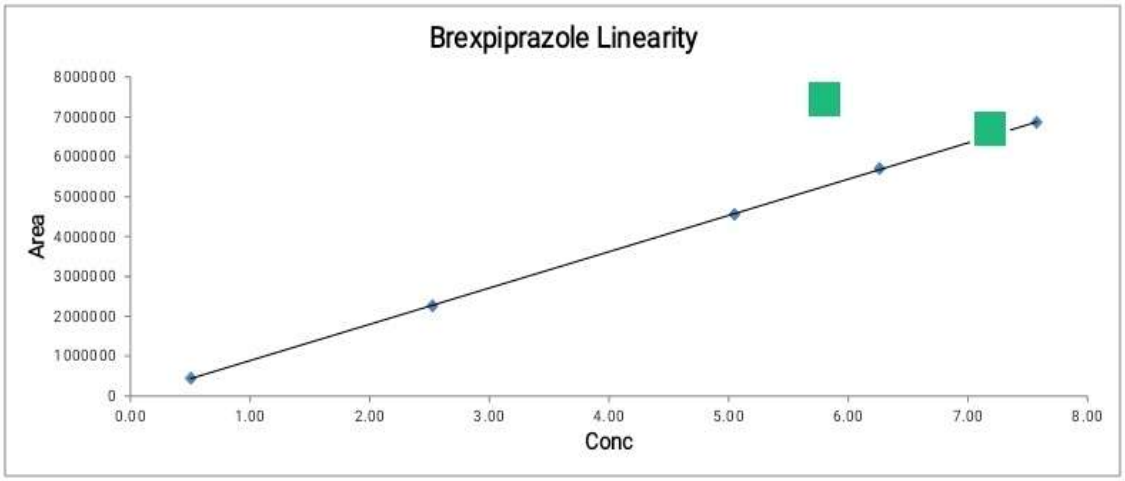

Fig. no.2 . Linearity (calibration) curve of Brexpiprazole

Table 5. Data for calibration curve of Brexpiprazole

Parameters	**Result**
Detection Wavelength	216 nm
Beer's law limit	5.05-75.75 µg/mL
Slope	910505.163
Intercept	-22876.12733
Correlation coefficient (R^2)	0.99997

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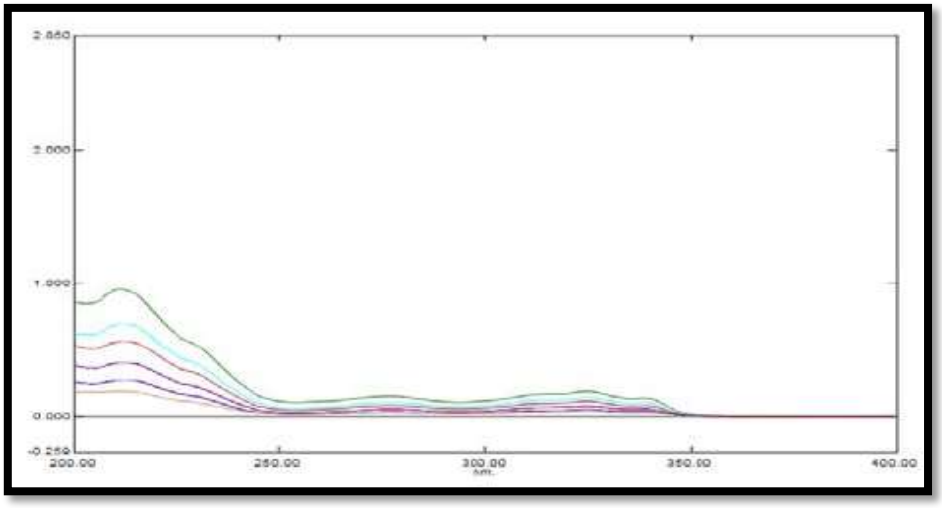

Fig. 3. Overlay spectra of BREX in Methanol (0.5-7.5µg/ml)

D) DETECTION:

(1) Limit of Detection:

It may be calculated based on the standard deviation (SD) of the response and slope of the curve(S).

LOD= 3.3 (SD)/S

Where, **SD**= Standard deviation= 19784.35213
S= Slope = 910505.163
LOD = 3.3 x19784.35213 /910505.163=0.07 µg/mL
The LOD of Brexpiprazole was found to be 0.07µg/mL

(2) Limit of Quantitation:

It may be calculated based on the standard deviation (SD) of the response and slope of the curve(S).

LOQ= 10 (SD)/S

Where, SD= Standarddeviation=19784.35213
S= Slope= 910505.163
LOQ = 10 x19784.35213 /910505.163= 0.22µg/mL
The LOQ of Brexpiprazole was found to be 0.22µg/mL

Table6 . Analytical data for LOD and LOQ

X(Conc.) µg/mL	Y(area)
5.05	10051.02
25.25	-11385.40
50.5	-20590.94
62.60	29274.80
75.7	-7347.47

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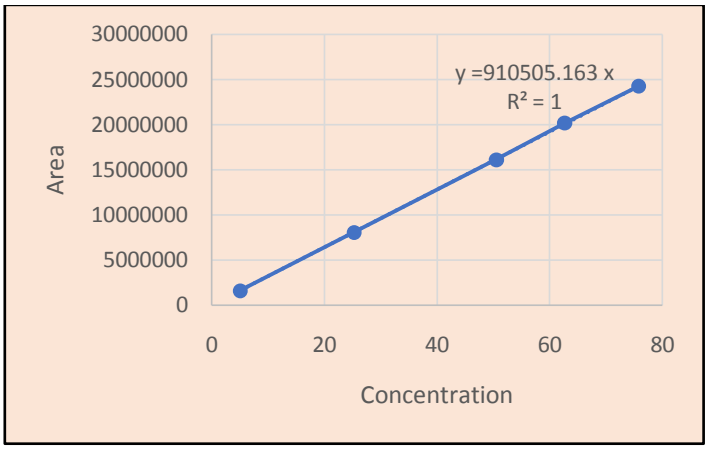

Fig.4 : Calibration curve of Brexpiprazole for LOD and LOQ

IV. CONCLUSION

The simple and economic UV spectrophotometric method has been developed for determination of Brexpiprazole.Also determine by LOD and LOQ The results of UV-Spectrophotometric method were found to be accurate, precise and sensitive. Because of cost-effective and minimal maintenance, the present UV-Spectrophotometric method can be preferred at small scale industries and successfully applied.

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