BICTEGRAVIR SODIUM ESTIMATION USING UV SPECTOPHOTOMETRIC METHOD IN PHARMACEUTICAL DOSAGE FORM

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Abstract

An effective, simple, accurate, precise UV Spectrophotometric method for estimation of Bictegravir sodium in bulk and tablet dosage form was developed. The method was developed using methanol as solvent and the λ max was found to be 230 nm. Linearity range for Bictegravir sodium was obtained as 2.5-15 µg/mL. The correlation coefficient value obtained was 0.9991. LOD and LOQ was obtained as 0.34 and 1.05 µg/mL.. According to ICH guidelines parameters such as Linearity, accuracy, precision, Limit quantification and Limit detection were validated.

Keywords:Bictegravir sodium, UV Spectrophotometry.

1. Introduction

Bictegravir is a recently approved investigational drug that has been used in trials studying the treatment of HIV-1 and HIV-2 infection. It has been approved for HIV-1 monotherapy combined with 2 other antiretrovirals in a single tablet. IUPAC name of bictagravir is 4-amino-1-[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]-1,2-dihydropyrimidin-2-one with molecular weight of average 229.256. It is in the form of powder in solid state. It has the melting point of 160-162^{0}C and its pK values are 14.29 (Acidic), -0.16 (Basic). It is an HIV-1 integrase strand transfer inhibitor (INSTI). This single dose medication inhibits the strand transfer of viral DNA into the human genome, preventing HIV-1 virus replication and propagation. In vitro, bictegravir has shown powerful antiviral activity against HIV-2 and various subtypes of HIV-1. It has shown synergistic effects when combined with other ARVs, including tenofovir alafenamide (TAF), emtricitabine (FTC), and darunavir (DRV).Marketed formulationsareTaffic, biktarvy dose is50mg. Bictegravir is rapidly absorbed within the body. Tmax is 2.0-4.0h. In a 10-day dose-ranging study, monotherapy (5 mg to 100 mg) once daily in adults who were not previously treated with bictegravir, the median

half-life of BIC ranged from 15.9 h - 20.9 h. BIC is mainly eliminated through UGT1A1 glucuronidation and CYP3A4 oxidation, equally 2. About 1% of the bictegravir dose is excreted in the urine, unchanged.Half-life is around 1.3h.

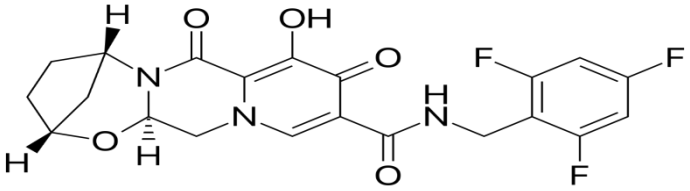

Fig.1: Structure of Bictegravir

2. Experimental procedure

Materials:

Bictegravir sodium, methanol, SLS, DMF, Chloroform, Acetonitrile.

Instruments:

Analytical Balance SHIMADZU ATX224R, Ultra sonicator Sonica®2200MH, UV Visible spectrophotometer, Spectro fluorophotometer SHIMADZU.

Methoddevelopment

UV visible spectroscopic method:

Selection of Solvent and *Wavelength Selection:*

Methanol was brought into consideration for further research due to its increased solubility and repeatable readings of maximum absorbance. The spectrum of uv wavelength which scans 200 to 400 nm was used to test the absorbance of the 10 gm/mL. Serial dilutions up to *10*ppmBictegravir solution were made with methanol. A 230 nm lamda maximum was found.

Preparation of Bictegravir Standard and Sample Solution Preparation:

Standard Solution:100 microgram per ml was prepared by serial dilutions of 100 mg per 100 ml.

Preparation regarding Test solution:10 tablets were weighed to determine their average weight and powered it. Exactly weigh about powder equivalent to 10 mg of Bictegravir sodium, into a volumetric flask of 100 mL. After adding 60 mL of methanol, shake well to dissolve it.To dilute to the proper amount, use methanol. Add 1 milliliter of this mixture to a volumetric flask. equipped with 10 ml capacity, dilution to the mark, and mixing. Over the solution to be filtered, place a 0.45 m nylon membrane filter.

Validation of method:

Specificity:

The specificity is determined by logging the UV spectrum for the blank, the Bictegravir standard, and the sample preparations from 200 nm to 400 nm.

Linearity:

Standard stock solutions were further diluted with buffer to produce 2.5 µg/mL and 15 µg/mL solutions.

Preparation of Bictegravir Standard Solution: Fill a volumetric flask with a 100 mL capacity with 100 mg of sodium Bictegravir sodium that has been weighed. 100mL of methanol must be added and then sonicate it to dissolve. To dilute within desired level, use diluent (methanol). In 100 millilitres volumetric flask, put 10mL of the above mixture, dissolve it to the proper amount, and then makeup to the mark.

Accuracy:

The recommended strategy is assessed by recovery tests at three distinct levels: 50 %, 100 %, and 150 %. Following each dilution, the absorbance of the pre-analyzed sample solution was measured. The sample solution was diluted three times with a specific amount of the standard drug solution..

Test solution preparation:10 tablets are weighed to determine their average weight and powered it. Exactly weigh about powder equivalent to 5 mg of Bictegravir sodium, into a volumetric flask of 100 milliliter. After adding 60 milliliter methanol, shake well to dissolve it.To dilute to the proper amount, use methanol. Add 1 milliliter of this mixture to a volumetric flask. equipped with 10 ml capacity, dilution to the mark, and mixing. Over the solution to be filtered, place a 0.45 m nylon membrane filter.

50 % spiked solution preparation:10 ml volumetric flask is used to transfer 0.5 milliliterof test stock solution., 1 milliliter fromEvery standard stock solution, along with the required dosage of methanol to create 80 % spiked solution.

100 % Spiked Solution Preparation: 10 milliliter volumetric flask containing 1 milliliter of each standardStock remedy, 1ml of diluent, and 1.0 ml of sample stock mixture.

150 % Spiked Solution Preparation: In order to make up the difference with diluent, 1milliliter of each common stock remedy is pipetted into a volumetric flask measuring 10 ml together with 1.5 milliliter of the sample stock solution.

Precision:

Intra-day precision:

Standard solution of 10 µg/ml. was infused five times in one day, the absorbances of each of these solutions were independently tested and recorded.

Inter-day precision:

Standard solution of 10 µg/ml infused five times in one day. The absorbances of these solutions were individually measured thrice in three days and recorded.

Robustness:

Although there were small, deliberate modifications made to the procedure, such as changing the wavelengths, the results were unaltered and were within the ICH Guideline range.

Wavelength Change (± 2 nm): (230 nm for Experimental Conditions Under Normal Conditions)

Samples were injected in duplicate while robustness conditions like Wavelength minus (228 nm) and Wavelength plus (232 nm) were maintained. The system appropriateness criteria were not considerably impacted.

Ruggedness: Bictegravir sodium test solutions for different labs were created using various analytical techniques. Different analysts examined these test solutions using various UV-Visible spectrophotometers. 12 test solutions were used, and percent RSD of the results was computed.

Limit of detection (LOD) and limit of quantitation (LOQ):

Limits of detection and quantitation, or LOD and LOQ, were established by the equations.

$LOD = 3.3 (\sigma / S)$

$LOQ = 10 (\sigma / S)$,

Where,

σ is blank's standard deviation, and S is calibration plot's slope.

Assay: Assay was performed with Bictegravir sodium formulation**.**Bictegravir's % Assay was determined by using the formula given below (label claim: 30mg).

Average Weight of Tablet: 75 mg

3. Results and discussions

UV Visible spectrophotometry:

Solubility Testing:

Table1: solubility Testing

Drug	observed
PH buffer	Slightly soluble
0.1N HCL	Slightly soluble
Water	Sparingly soluble
Methanol	Soluble

Wavelength Selection: The λ max was found to be 230nm.

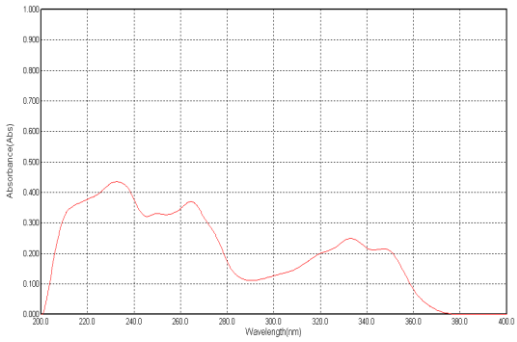

Fig.5: Wavelength absorption

Method Validation:

1. **Specificity / Selectivity:**

Table 2: Selectivity Results

S. No.	Absorbance of Bictegravir in 230 nm
1	0.434
2	0.432
3	0.430
4	0.431
5	0.436
Mean	0.433
SD (±)	0.002
(%) RSD	0.46

Linearity: Linearity was performed and the concentrations were taken from 2.5 to 15 ppm.

Table 3: Results of Linearity

Sample	Sample	Absorbance	Correlation
Conc (%)	Conc (ppm)		
25	2.5	0.293	
50	5	0.336	Coefficient
75	7.5	0.389	0.9991
100	10	0.433	
125	12.5	0.477	
150	15	0.531	

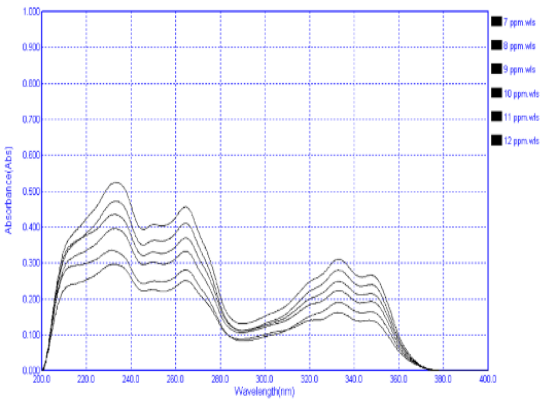

Fig.6: Linearity overlay spectrum

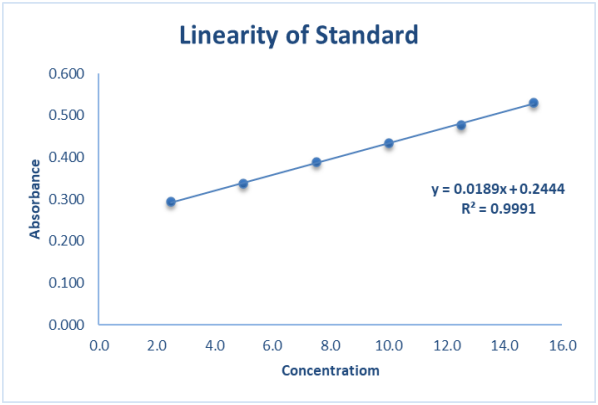

Fig.7: Linearity standard

2. Precision:

Table 4: intraday precision

s.no	Absorbance
1	0.438
2	0.435
3	0.437
4	0.436
5	0.435
Mean	0.436
Standard Deviation	0.001
% RSD	**0.22**

Intraday:

Table 5: Intraday precison

S.no	Absorbance
1	0.431
2	0.436
3	0.433
4	0.437
5	0.429
Mean	0.433
Standard Deviation	0.003
% RSD	**0.69**

3. Accuracy: Accuracy method was performed with three spiked levels, i.e., 50, 100 and 150 %.

Table 6: Accuracy

Spiked level	Conc of the sample	Conc of std	Total conc	% recovery	% RSD
50 %	5	2.5	7.5	99.97	0.21
100 %	5	5	10	99.59	
150 %	5	7.5	12.5	99.61	

2. Robustness:

Wavelength Change (± 2 nm):

Table 7: Robustness wavelength

Sr. No.	Absorbance of Bictegravir	
Standard	**228 nm**	**232 nm**
1	0.432	0.435
2	0.434	0.431
Mean	0.43	0.433
SD (±)	0.001	0.002
(%) RSD	**0.23**	**0.46**

Table 8: Wavelength Results

Wavelength	228 nm	232 nm
Sample	**% Assay**	
Test solution	99.34	99.57
Avg % drug release (precision)	100.49	100.49
Mean	99.91	100.03
SD (±)	0.81	0.65
(%) RSD	**0.81**	**0.64**

3. Ruggedness:

Different Analysts

Table 9: Ruggedness

Sr. No.	Absorbance of Bictegravir in 230 nm	
	Analyst -1	**Analyst-2**
1	0.432	0.432
2	0.435	0.435
3	0.431	0.431
4	0.436	0.436
5	0.430	0.430
Mean	0.432	0.433
SD (±)	0.002	0.002
(%) RSD	**0.46**	**0.46**

Table 10: Ruggedness

Sr. No.	Absorbance of Bictegravir at 230	
	Lab -I	**Lab-II**
1	0.436	0.432
2	0.433	0.435
3	0.434	0.431
4	0.438	0.436
5	0.434	0.430
Mean	0.435	0.432
SD (±)	0.002	0.002
(%) RSD	**0.45**	**0.46**

7. LOD and LOQ:

Table 11: LOD, LOQ

LOD Value	0.34
LOQ Value	1.05

8. Assay:

Table 12: Assay

Name of Drug	Label claim (mg)	% Assay
Bictegravir sodium	30	99.94

UV spectrophotometer:

Table 13: parameters of bictegravir

S.NO	PARAMETERS	RESULT
1.	Absorption maximum(nm)	230nm
2.	Linearity range(µg/ml)	5-15µg/ml
3.	Standard regression equation	y=0.0189x+0.2444
4.	Slope	M=0.0189
5.	Intercept	0.2444
6.	Correlation coefficient (r)	0.9991
7.	Selectivity	0.6
8.	Accuracy(%recovery)	99.72%
9.	Method Precision (intra-day) %RSD Intermediate precision(Inter-day) %RSD	99.92% 99.94%
10.	Assay(%mean assay)	99.94%
11.	Specificity	Specific
12.	Robustness(wavelength plus) (wavelength minus)	0.65 0.82

4. Conclusion

An effective, simple, accurate, precise UV Spectrophotometric and Spectrofluorometric method for estimation of Bictegravir sodium in tablet and bulk dosage forms. The method was developed using methanol as solvent and the λmax was found to be 230nm. The method is established according to ICH guidelines and definition. The method's linearity, precision, accuracy, specificity, robustness, and ruggedness were all confirmed. Linearity range for Bictegravir sodium was obtained as 2.5-15 µg/ml. The calibration plot for the method was constructed. Accuracy was investigated by analysing marketed formulation and percentage recovery was found to be within the limits. LOD and LOQ values obtained were 0.09 µg/ml and 0.29 µg/ml for Bictegravir sodium. % Assay was determined and it was found to be 99.94%.

Based on the above results, we came to the conclusion that the analytical methods are clear, exact, and concise and economical in contrast to the chromatography method. The suggested method, based on the UV Spectrophotometer method, is easy to use, and effective. It does not call for complicated equipments or chemicals.

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