

A Review on Analytical Techniques for the Quantification of Dolutegravir - An Integrase Strand Transfer Inhibitor

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Abstract

Dolutegravir is a novel integrase strand transfer inhibitor active against human immunodeficiency virus. Dolutegravir is an integrase strand transfer inhibitor which preferentially blocks the strand transfer step of integration of the viral genome into the host cell's DNA mediated by the viral integrase enzyme. The authors have reviewed the analytical methods developed for the estimation of Dolutegravir in pharmaceutical dosage forms and in biological samples in the present paper.

Keywords: Dolutegravir; Integrase Strand Transfer Inhibitor; DNA

Introduction

Dolutegravir is chemically (4R,12aS)-N-(2,4-difluorobenzyl)-7-hydroxy-4-methyl-6,8-dioxo-3,4,6,8,12,12a-hexahydro-2H-pyrido[1',2':4,5]pyrazino[2,1-b][1,3]oxazine-9-carboxamide (C₂₀H₁₈F₂N₃NaO₅). Dolutegravir is an integrase strand transfer inhibitor [1]. Dolutegravir sodium is a white to light yellow powder and is slightly soluble in water and methanol and is rapidly absorbed after oral administration and it was approved by FDA. Dolutegravir is active against HIV type 1 and also has some *in vitro* activity against HIV type 2 [2].

Dolutegravir blocks the strand transfer step of the integration of the viral genome into the host cell and prevents HIV from replicating and lowers the amount of HIV in the blood. Dolutegravir will not cure or prevent HIV infection or AIDS, however, it helps keep HIV from reproducing and appears to slow down the destruction of the immune system.

Dolutegravir is available as tablets with brand name Instra (Labelled claim 50 mg) from Avalon Pharma Pvt Ltd (India). Dolutegravir is also available in combination with Rilpivirine (Juluca) (Labelled claim: Dolutegravir: 50 mg and Rilpivirine: 25 mg) as film coated tablets; Lamivudine (Dovato) (Labelled claim: Dolutegravir: 50 mg and Lamivudine: 300 mg); Lamivudine and Tenofovir Disoproxil Fumarate (Viiro) (Labelled claim: Dolutegravir: 50 mg, Lamivudine: 300 mg and Tenofovir Disoproxil Fumarate: 300 mg).

gravir: 50 mg, Lamivudine: 300 mg and Tenofovir Disoproxil Fumarate: 300 mg).

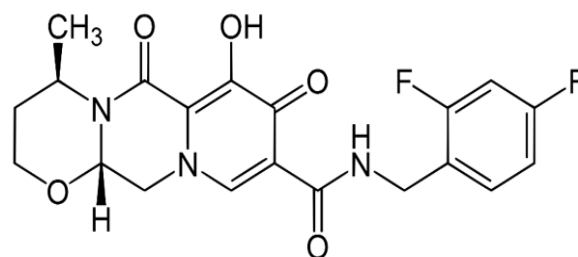


Figure 1: Structure of Dolutegravir.

The authors have summarised the analytical methods so far developed in the literature for the determination of Dolutegravir in the present review article. The methods include are spectrophotometry [4-7], HPLC [8,9], HPTLC [10] (Table 1) for the pharmaceutical formulations. Liquid chromatographic methods were also developed for the separation of optical isomers of Dolutegravir [11,12] and for the estimation of Dolutegravir in human plasma using HPLC [13], UPLC [14] and LC-MS/MS [15].

Reagent	Linearity ($\mu\text{g}/\text{ml}$)	λ_{max} (nm)	Comment	Ref
Spectrophotometric methods				
Water	5 - 40	259.8	-	3
Ferric chloride and 1,10-Phenanthroline reagent	40 - 140	520	Orange red complex	4
0.8 M aq. Urea	2.5 - 20	258 248 - 268 256	λ_{ma} AUC First derivative	5
Water	2 - 18	259	-	6
Water	5 - 40	259.8	-	7
Liquid chromatographic methods				
0.1% Aq. Trifluoro acetic acid: Methanol	0.076 - 1.5	240	HPLC (Gradient mode)	8
Dipotassium hydrogen orthophosphate: Methanol (70:30),	50 - 150	260	HPLC	9
Acetonitrile: water (pH 7.5) (80:20) Methanol: Chloroform: Formic acid (8: 2: 0.5)	5 - 35 200 - 900 ng/ spot	260 265	HPLC HPTLC	10
Acetonitrile: water: ortho phosphoric acid	0.161-2.276 (Enantiomer) 0.195-2.180 (Diastereomer)	258	Chiral HPLC Stability indicating	11
Phosphate buffer (pH 2.0): Solvent mixture (63: 37) Solvent mixture: tert-butyl methyl ether: Acetonitrile (10:35)			Chiral HPLC	12
20 mM Sodium acetate buffer (pH 4.0): Methanol (30: 70)	0.102- 7.004	254	HPLC Human plasma	13
50 mM Formic acid and 50 mM Ammonium acetate: Acetonitrile	0.25-10	258	UPLC Plasma Gradient mode	14
Acetonitrile: 0.1% Formic acid	0.005-10	-	LC-MS/MS Human plasma	15

Table 1: Review of analytical methods for the determination of Dolutegravir.

Conclusion

The present review article helps the readers to do research in a new field apart from the presenting existing analytical techniques for the anti-viral drug Dolutegravir.

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