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Review Article

Analytical Techniques for the Determination of Rilpivirine – A Review

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Abstract

Rilpivirine is an Anti-viral drug. Rilpivirine acts by inhibiting the replication of HIV – 1 by binding in a non – competitive manner directly to reverse transcriptase enzyme. In the present paper the authors have presented a review of various analytical methods published so far in the literature for the quantification of Rilpivirine in pharmaceutical preparations as well as biological samples.

Keywords: Rilpivirine; HIV; Anti-viral Drug

Introduction

Rilpivirine is chemically known as 4-[[4-[[4-[(E)-2-cyano-ethenyl]-2, 6-dimethylphenyl] amino]-2-pyrimidinyl] amino] benzonitrile, is a second-generation non-nucleoside reverse transcriptase inhibitor from antiviral drugs [1,2]. Rilpivirine (Figure 1) ($C_{22}H_{18}N_6$) (Mo. wt. 364.417 g/mol) is used to treat infection caused by human immuno deficiency virus (HIV). Rilpivirine acts by inhibiting the replication of HIV – 1 by binding in a non – competitive manner directly to reverse transcriptase enzyme. This leads to conformational changes and altered function of reverse transcriptase. Rilpivirine is associated with a low rate of transient serum aminotransferase elevations during therapy and has been implicated in rare cases of clinically apparent acute liver injury [3].

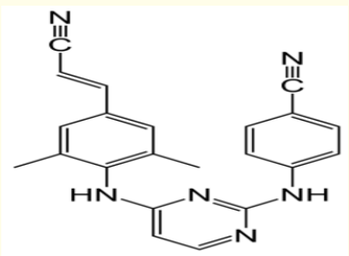

Figure 1: Structure of Rilpivirine.

Rilpivirine is available in India with brand name Edurant (Lable claim: 25 mg) (Chandra Bhagat Pharma Pvt. Ltd) as film coated tablets and Rilpivirine is also available in combination with Dolutegravir (Juluca), Emtricitabine/Tenofovir (Odefsey, Complera) etc. Baert et al developed a long-acting injectable formulation with nanoparticles of Rilpivirine (TMC278) for HIV treatment [4]. The present review article summarises the analytical techniques so far developed such as spectrophotometry [5-10] (Table 1), high performance liquid chromatography [11-15] (Table 2), liquid chromatography-mass spectrometric methods [16-19] (Table 3) for the determination of Rilpivirine and some of the analytical parameters were highlighted.

Reagent	Linearity (µg/ml)	λ_{max} (nm)	Comment	Ref
Bromo thymol blue	4 -20	425	Visible region	[5]
Bromo cresol green		415		
Methanol	2 - 8	282	UV region	[6]
Methanol: Water (8:2)	0.5 – 3.5	305	Multivariate technique	[7]
Methanol	6 - 16	306	First derivative method	[8]
0.01N HCl	0.5 – 7.5	280 275-285 264 237	Zero order, AUC First and Second derivative methods	[9]
DMF: Acetonitrile (10: 100) Acetonitrile (Diluent)	1-16	281.6	UV region	[10]

Table 1: Review of spectrophotometric methods for the determination of Rilpivirine.

Mobile phase (v/v)/Flow rate (ml/min)/ Detection wavelength (nm)	Column	Linearity (µg/ml)	Ref
Acetonitrile: Acetate buffer (pH 4.0) (65:35)/1/260	Develosil ODS HG-5 RP C18 (5 µm, 150 x 4.6 mm)	HPLC (0-25)	[11]
Acetonitrile: 25 mM potassium dihydrogen phosphate (50:50)/0.6/290	Gemini RP C18 (5 µm; 150 ×4.6 mm)	HPLC (0.025-2.0)	[12]
Acetonitrile: Phosphate buffer (pH 3.5) (60:40)/1/282	C8 (5 µm, 250 x 4.6 mm)	HPLC (10-50)	[13]
Acetonitrile: Potassium dihydrogen phosphate buffer (pH 2.8) with ortho phosphoric acid (40:60)/1/282	Develosil ODS HG-5 RP C18 (5 µm; 150 ×4.6 mm)	HPLC (0-30)	[14]
0.1% Ortho phosphoric acid: Acetonitrile (65:35)/1/205	Develosil ODS HG-5 RP C18 (5 µm; 150 ×4.6 mm)	HPLC (20-70)	[15]

Table 2: Review of HPLC methods for the determination of Rilpivirine.

Mobile phase (v/v)/Flow rate (ml/min)	Column	Linearity (ng/ml)	Ref
0.1 mM EDTA in acetic acid: Acetonitrile: Methanol (Gradient mode) 6,7-dimethyl-2,3-dipyridyl) quinoxaline (Internal standard)	Sunfire C18	LC-MS Human plasma (18-715)	[16]
Acetonitrile: Methanol: 0.1% Acetic acid in 5 mM Ammonium acetate (20:25:55)/0.6 Didanosine (Internal standard)	Discovery C18 (5 µm; 150 ×4.6 mm)	LC-MS/MS sprague dawley rat serum (2-1000)	[17]
Rilpivirine-d6 (Internal standard)	Gemini C18 (150 × 4.6 mm, 5 µm)	LC-MS/MS Human plasma (5-200)	[18]
Acetonitrile and 0.1% formic acid buffer (80:20)/0.5	C18	LC-MS Human plasma (51-200)	[19]

Table 3: Review of LC-MS methods for the determination of Rilpivirine.

Conclusions

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 Rilpivirine.

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