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A CRITICAL REVIEW ON DARUNAVIR: ANALYTICAL PROFILE AND RECENT ADVANCEMENTS

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ABSTRACT

Darunavir, also known as TMC114 in pharmaceutical terminology, is a second-generation protease inhibitor used to treat human immunodeficiency virus. Synthetic non-peptide protease inhibitor Darunavir has demonstrated remarkable potency against wild-type HIV and is a key component of highly active antiretroviral therapy (HAART), which is regarded as a major advancement in HIV therapy. Various analytical methods have been established for the determination of Darunavir in the pharmaceutical dosage form and bulk form. For Darunavir, methods for impurity profiling and human plasma stability are also discussed. These analytical techniques can be applied to the qualitative and quantitative determination of Darunavir as well as to the related degradants in bulk formulations and biological fluids. The paper that follows reviews analytical techniques, one of which is the estimation of antiretroviral medications.

Keywords: Darunavir, Antiretroviral drug, Analytical methods.

1. INTRODUCTION

Darunavir (Fig. 1) is an antiviral medication that inhibits the HIV protease in adults and children six years of age and up [1]. On June 23, 2006, the Food and Drug Administration gave it its approval. DRV, a second-generation protease inhibitor, is developed to overcome the concerns with early protease inhibitors (PIs) such as significant side effects and drug toxicities, requiring an elevated therapeutic dose, being expensive to produce, and displaying a troubling risk to drug-resistant mutations. To treat HIV, DRV is taken in addition to ritonavir and additional drugs. It functions by delaying the body's HIV infection. Infected cells containing HIV-1 encoded Gag-Pol poly proteins are specifically inhibited by DRV from cleaving, which stops the virus from maturing into mature particles [2]. DRV has been designed to establish strong contacts with the protease enzyme found in a variety of HIV strains. It inhibits HIV protease, an enzyme required for HIV replication. The immune system's vital CD4 (T) cells are destroyed by HIV infection. The immune system aids in the defense against infection. Lowering HIV levels and raising CD4 (T) cell counts may strengthen your immune system, lowering the chance of infection or mortality that might result from a weakened immune system. For the treatment of human immunodeficiency virus infection, darunavir is prescribed in combination with ritonavir and other antiretroviral medications [3].

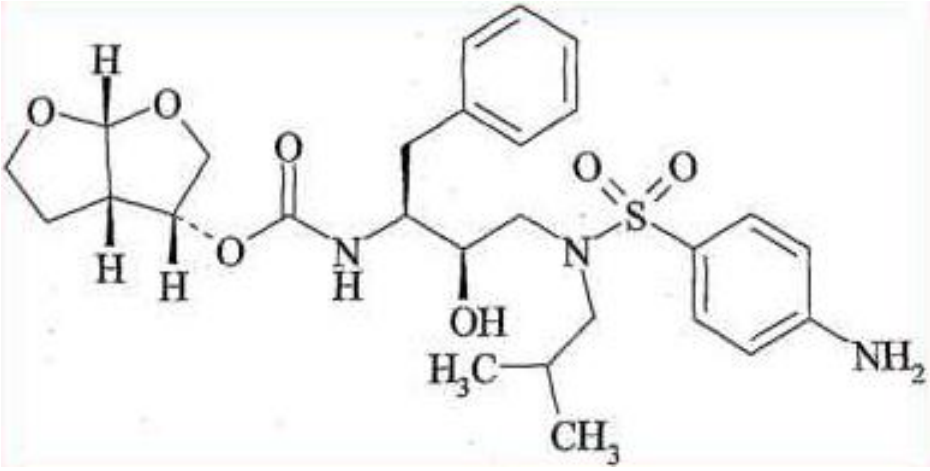

Figure-1: Structure of Darunavir

Chemical name: Chemically it is [(3aS,4R,6aR)-2,3,3a,4,5,6a hexahydrofuro[2,3-b]furan-4- yl]N-[(2S,3R)-4-[(4-aminophenyl)sulfonyl-(2-methylpropyl)amino]-3-hydroxy-1-phenylbutan-2yl]carbamate.

Chemical formula: $C_{27}H_{37}N_3O_7S$

Molecular weight: 593.73 g/mol

Category: Protease inhibitor.

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Table 1: Analytical methods described in the literature for the determination of Darunavir by spectrophotometric analysis

Title	Method	Wavelength	Description	Reference
Development and validation of UV-visible Spectrophotometric method for estimation of ritonavir in bulk and formulation	UV-Visible Spectrophotometric	255nm	The method was found to be robust and rugged in nature and was successfully used for the estimation of Ritonavir.	4
A new robust analytical method development, validation, and stress degradation studies for estimating ritonavir by UV-Spectroscopy and HPLC method	UV-Visible Spectrophotometric	273nm	(Method-A): Employed UV-spectroscopic method (Method-B): Employed HPLC method	5
Development and Validation of an Innovative Stability Indicating Method Using UV-Spectroscopy Techniques for Ritonavir in Bulk Drug and Pharmaceutical Dosage Form	UV-Spectroscopy	271nm for zero order 258nm for the first order 260-281nm for the area under the curve	(Method-A): Zero-order Spectrophotometric method (Method-B): First-order Spectrophotometric method (Method-c): Area under the curve Spectrophotometric method	6
Simultaneous Method Development, Validation, and Stress Studies of Darunavir and Ritonavir in Bulk and Combined Dosage Form Using UV Spectroscopy	UV Spectroscopy	240nm	The parameters linearity, precision, accuracy, limit of detection, and limit of quantitation were studied according to the International Conference on Harmonization guidelines. Forced degradation studies were conducted under various conditions.	7
Development and Validation of Infrared Spectroscopy Method for the Determination of Darunavir in Tablets	Infrared Spectroscopy	Data were analyzed at 1757-1671 cm^{-1}.	The parameters linearity, precision, accuracy, limit of detection, and limit of quantitation were studied according to the International Conference on Harmonization guidelines.	8

Reported HPLC methods of Darunavir

Title	Method	Mobile phase	Stationary phase	Wavelength	Reference
Determination of Darunavir and Cobicistat Simultaneously Using Stability Indicating RP-HPLC Method	RP-HPLC	0.1MNaH2PO4&methanol(70:30v/v)	C18(150*4.6 mm,5µm particle size)	260nm	9

Development and Validation of Stability Indicating HPLC Method for Estimation of Darunavir	HPLC	0.1% Acetic acid in water: ACN (63:37v/v)	C18,50*3mm,3.5 µm(X-Terra MS,Waters)	267nm	10
Analytical method development and validation of Darunavir- An antiretroviral agent by RP-HPLC method	RP-HPLC	CAN: Buffer pH 4.0(40:60 v/v)	ACE C18,3um(150*4.6mm)	265nm	11
Method Development and Validation For Estimation of Darunavir in Tablet Dosage Form	RP-HPLC	Potassium dihydrogen phosphate buffer, methanol in ratio(60:40)	ACE C18,(150*4.6mm) 3um or equivalent	265nm	12
Development and Validation of a new UPLC method for the simultaneous estimation of darunavir, dolutegravir, and ritonavir in combined tablet dosage form	UPLC	55% Phosphate buffer & 45% acetonitrile	BHE C18(50*2.1mm,1.7)	225nm	13
Stability indicating RP-HPLC method for simultaneous estimation of ritonavir and darunavir in bulk and its synthetic mixture	RP-HPLC	Phosphate buffer (pH 3.5): (ACN & methanol 5:1)(30:70)	Intersil ODS C18 column(150mm*4.6mm,5µm)	220nm	14
Development and validation of the RP-HPLC method for the simultaneous estimation of darunavir and cobicistat in combined tablet dosage form	RP-HPLC	(30:70v/v) 0.1%TEA: methanol	Intersil ODS C18 column(150mm*4.6mm,5µm)	242nm	15
RP-HPLC Method Development And Method Validation of Lopinavir and Ritonavir in Pharmaceutical Dosage Form	RP-HPLC	Acetonitrile: methanol &buffer of potassium dihydrogen phosphate	X-bridge C18(250mm*4.6mm i.d.,3.5µm)	220nm	16
Analytical method development and validation for the Simultaneous	RP-HPLC	0.01N KH2Po4:ACN (45:55%v/v)	C18 column(4.6*15mm,5µm)	290nm	17

estimation of Darunavir and Ritonavir by RP-HPLC method					
Development and Validation of New Analytical Method for The Simultaneous Estimation of Darunavir And Ritonavir in Pharmaceutical Dosage Form	RP-HPLC	Phosphate buffer(0.05M) pH 4.6:ACN(30:70% v/v)	XterraC18 5µm(4.6*250mm)	255nm	18
The Estimation of Darunavir in Tablet dosage form by RP-HPLC	RP-HPLC	0.02M dipotassium hydrogen orthophosphate +0.02M potassium dihydrogen orthophosphate in water and ACN in a ratio of 40:60v/v	Intersil OSD-3V C-18 ,250*4.6mm,5µm	265nm	19

2. CONCLUSION

This review concluded that various spectroscopic and chromatographic approaches are available for a single component as well as for a combination of protease inhibitors, such as Darunavir. It was found that most chromatographic techniques used a mobile phase that included phosphate buffer, methanol, and acetonitrile in order to increase resolution. It was noted that the most popular Darunavir and Ritonavir combination. The flow rate and a good retention time are monitored for the chromatographic technique. Therefore, all of the procedures are found to be straightforward, precise, accurate, economical, and repeatable. The majority of the methods used were UV absorbance detection and RP-HPLC since they offered the best possible sensitivity, repeatability, analysis time, and dependability. The current study concentrates on the cleaning technique validation for the estimate of Darunavir residue in the production area because the literature review indicates that there is no published work on the cleaning validation of Darunavir.

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