Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2012, 4(6):3154-3157

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Application of RP-RRLC methods for estimation of paliperidone in tablet dosage forms

Khemchand Dadare*, N. C. Khatri and Mayank Pant

Department of Chemistry, Faculty of Engineering & Technology, Jodhpur National University, Jodhpur-Rajasthan, India

---

ABSTRACT

An approach for Simultaneous estimation of Paliperidone in formulation in presence of its degradation products. The method has shown adequate separation for Paliperidone from their associated main impurities and their degradation products. Separation was achieved on a Zorbax SB C-18, 50 mm x 4.6 mm, 1.8 µm (Agilent) column at 50°C temperature by using a mobile phase A consisting Buffer (pH 4.0) – Acetonitrile (95:5 v/v) [Buffer: 0.05M Na_2HPO_4 anhydrous and Ortho phosphoric acid] and Mobile phase B at a flow rate of 1.4 ml/min, and UV detection at 238 nm. In the present study, comprehensive stress testing of Paliperidone was carried out according to ICH guideline Q1A (R2). The specificity of the method was determined by assessing interference from the placebo and by stress testing of the drug (forced degradation). Drug was subjected to Acid hydrolysis, Alkali hydrolysis, Oxidation, Dry heat and Photolysis to apply stress conditions. There were no other coeluting, interfering peaks from excipients, impurities, or degradation products due to variable stress conditions, and the method is specific for determination of Paliperidone in the presence of degradation products. The method was validated in terms of linearity, precision, accuracy, specificity, robustness and solution stability. The linearity of the proposed method was investigated in the range of 30-90 µg/ml (r^2 = 0.9995) for Paliperidone. Degradation products produced as a result of stress studies did not interfere in the estimation of Paliperidone and the assay can thus be considered stability-indicating.

Keyword: HPLC, Paliperidone, Estimation, Tablets.

INTRODUCTION

Schizophrenia is a serious mental illness that affects how a person thinks, feels, and behaves. The person finds it difficult to tell the difference between real and imagined experiences, to think logically, to express feelings, or to behave appropriately. Schizophrenia literally means "a split mind," and this may be where the misconception of split personality took root.

Paliperidone (sold as INVEGA) is an Atypical Antipsychotic developed by Janseen Pharmaceutical. Invega is an extended release formulation of Paliperidone that uses the OROS extended release system to allow for once-daily dosing. Chemically, Paliperidone is primary active metabolite of the older atypical antipsychotic risperidone (Paliperidone is 9-hydroxyrisperidone, i.e. risperidone with an extra hydroxyl group). It is indicated for the acute and maintenance treatment of Schizophrenia.

EXPERIMENTAL SECTION

Materials

1) Paliperidone: - Working standard grade or Paliperidone Active Pharmaceutical Ingredient (API) was supplied by Mission Vivacare Research Centre (Indore, India), and its claimed purity was 99.51%.
2) Paliperidone Extended Release Tablet (label claim 6 mg) and placebo was manufactured and supplied Mission Vivacare Research Centre (Indore, India).
3) Oxo and N-oxide the major degradation products of Paliperidone were obtained from Mission Vivacare Research Centre (Indore, India). and their claimed purity was 61.0 and 99.42 %.

Impurity Oxo and N-Oxide are known impurities of drug substance.

Reagents and Chemicals

1) Di-sodium hydrogen phosphate anhydrous - AR grade, Merck, India.
2) Ortho-Phosphoric Acid: - AR grade, Merck, India.
3) Acetonitrile: -HPLC grade, Rankem, India.
4) Methanol: - HPLC grade, Rankem, India.
5) Tetrahydrofuran: - (HPCL grade), Spectrochem, India.
6) Milli-Q water: - It was purified by Millipore Corporation's system.
7) Hydrochloric acid: - Reagent Grade, Merck, India.
8) Sodium hydroxide: - Reagent Grade, Merck, India.
9) Hydrogen Peroxide (30%):- Reagent Grade, Merck, India.

Instruments, Apparatus and equipment

1) Rapid Resolution Liquid chromatography system (RRLC): Agilent 1200 Series,
2) Chromatographic software:– Chemstation 32
3) A double beam UV-visible spectrophotometer having two matched cells with 1cm light path: - UV- 2450, Shimadzu, Japan.
4) Analytical Balance: - AD 265S, Mettler Toledo, Schwerzenland.
5) pH Meter: - Labindia, India.
6) Sonicator: - 5510, Branson Ultrasonics Corporation, Danbury, CT, USA.
7) Hot air oven: - Labline, India.
8) Photo stability chamber: - SVI equipments, Germany

Chromatographic system

Degradation studies were carried out on a system consisted of 1200 series RRLC (Agilent Technologies, Japan) comprising of an on-line degasser (G1322A), binary pump (G1312A), auto injector (G1367C), column oven (G1310B), DAD detector (G1315C) and Chem Station (software) revised B.03.01.

Standard preparation:

Weigh and transfer about 30 mg of Paliperidone reference standard to a 50 mL volumetric flask. Add about 25 mL of solvent mixture, sonicate to dissolve, make up the volume with solvent mixture. Further take 5 ml of this solution and make up the volume 50 ml with solvent mixture (60 ppm)

Sample preparation

Weigh accurately 20 tablet and crush the tablet transfer the powder equivalent to 30mg into 50 mL volumetric flask add about 25 mL of solvent mixture , sonicate at 25°C for about 40 min with intermittent shaking, make up to volume with solvent mixture . Filter through 0.22µ nylon filter, first discard about 3 mL of the filtrate Further dilute 5mL of the solution to 50mL with solvent mixture. (60 ppm)

Buffer Preparation

Dissolve 0.05 M Di-Sodium Hydrogen Phosphate Anhydrous Buffer in 1000ml in water, adjust pH to 4.0 ± 0.5 with dilute Ortho phosphoric acid. Filter through 0.22µ Nylon Filter.

Mobile phase A

Use filtered Buffer through 0.22µ Nylon filter and Acetonitrile in the ratio of 95:5, sonicate to degass.

Mobile phase B

Use filtered Methanol through 0.22µ Nylon Filter and sonicate to degass.

Solvent Mixture
Use Methanol: (THF), in the ratio of 80:20.

Blank Solution: Use solvent mixture as blank.

Optimized RRLC Parameters:

Instrument	: Rapid Resolution Liquid Chromatography with UV detection.
Column	: Zorbax SB C-18, 50 mm x 4.6 mm, 1.8 µm
Flow Rate	: 1.4 mL/min
Injection volume	: 2 µL
Column temperature	: 50°C
Sample cooler Temperature	: Ambient
Detection	: 238 nm
Mobile Phase-A	: Buffer: Acetonitrile (95:5)
Mobile Phase-B	: Methanol
Solvent mixture	: Methanol: Tetrahydrofuran (THF), 80:20
Blank prep.	: Solvent mixture
Run time	: 16 minutes (Gradient)

Gradient Program
:

Time (Min)	%M.P. -A	%M.P. -B
0.01	85	15
1.40	85	15
2.40	75	25
12.0	30	70
14.0	85	15
16.0	85	15

System Suitability Test
Inject Blank preparation in single injection, standard preparation in five replicate, record the chromatogram and calculate the system suitability parameters as given below:

Theoretical plate for Paliperdone peak in five replicate standard injections : NLT 2500
% RSD for five replicate standard injections : NMT 2.0
Tailling Factor for Paliperdone peak in five replicate standard injections : NMT 2.0
If system suitability passes then inject sample preparation in duplicate.

RESULTS AND DISCUSSION

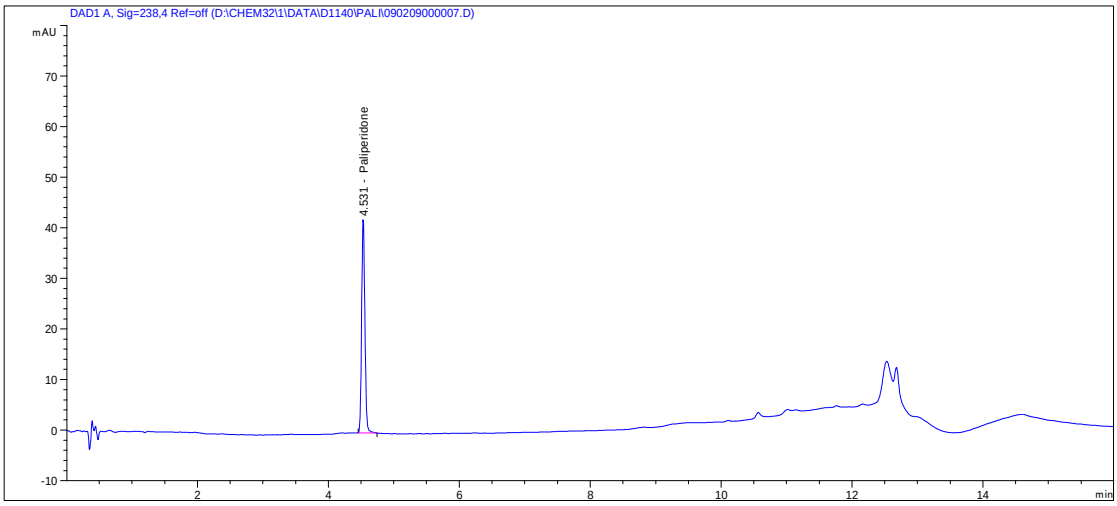

Figure 1: RRLC Chromatogram of standard preparation with RT-4.53 min

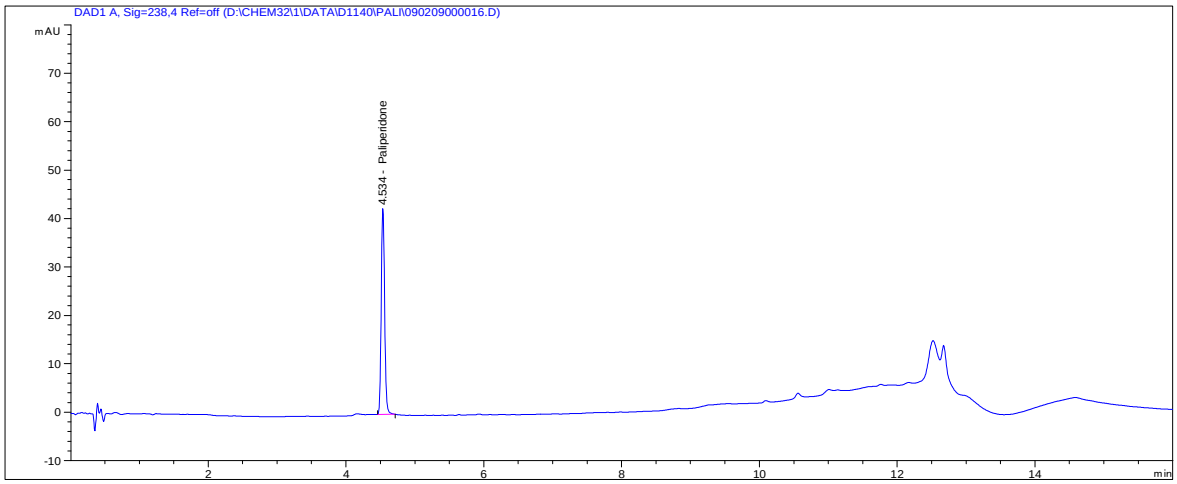

Figure 2: RRLC Chromatogram of Tablet preparation with RT-4.53 min

Table 1 : Mean values of system suitability parameters

Sr. No.	Parameters	Paliperidone
1.	Peak area	143.958
2.	No. of theoretical plates	38529
3.	Retention time (min)	4.531
4.	Asymmetry/USP Tailing	1.09
5.	% RSD	1.18

Table 2: Response (Peak Area) and Assay of Sample Preparation

Sample Preparation No.	Sample		
	Area	Mean Area	Assay (%)
1.	144.989	145.681	100.9
2.	146.374		

REFERENCES

[1] H. P. Rang, M. M. Dale, J. M. Ritter, P. K. Moore, Pharmacology, 6th edition , **2003**, 545-556.
[2] Goodman and Gilman, "The pharmaceutical basis of therapeutics" 11th edition , **2006**, edited by brunton, L. L. Lazo, J. S. Parker, K. L., 461-470.
[3] K.D. Tripathi, "Essential of medical pharmacology", 5th edition, Medical Publishers (P) LTD, **2003**, 352.
[4] www.ehealthmd.com/library/schizophrenia/sch_whatis.html
[5] B. M. Remmerie, L. L. Spips, R. de Rries, J de. Jong.; *Journal of chromatography*. B **2003**, 783(2): 461-472.
[6] K. Titier, S. Bouchet, F, Pehourcq, N. Moore, M. Moliard.; *Journal of chromatography*. B **2003**, 788(1, 5): 179-185.
[7] Silverstein, R.M., Webster, F.X., Spectroscopic identification of organic compounds, Sixth edition, John Wiley & Sons Ltd. Publication, 71-143.