ISSN- 2230-7346
Journal of Global Trends in Pharmaceutical Sciences

STABILITY INDICATING METHOD FOR THE DETERMINATION OF RELATED COMPOUNDS IN PERAMPANEL BY-HPLC

Dr. Subash sahoo*[1], Dr. S. Srinivasa Rao[2], S. Sindhuja[3]

[1,2,3] Pulla Reddy Institute of Pharmacy, Department of Pharmaceutical analysis, Domadugu, Gummadidala (M), Sangareddy district, Telangana, India.

*Corresponding author E-mail: sindhujasavasani@gmail.com

ARTICLE INFO

Key words:
Perampanel , stability indicating , ICH guidelines

Access this article online
Website:
https://www.jgtps.com
Quick Response Code:

ABSTRACT

A new RP-HPLC method has been developed and validated for the determination of Perampanel in its tablets using HPLC system equipped with prominence photodiode array detector on Luna Amine (250x4.6mm,5µm) maintained at room temperature. Mobile phase consisting of a mixture of Water: Acetonitrile 80:20 (v/v) was chosen with a flow rate of 0.8ml/min (UV detection at 220nm) on isocratic mode. Perampanel obeys Beer-Lambert's law over the concentration range 0.05–120 µg/ml with linear regression equation y=73084x+13800 (r^2=0.9999). Forced degradation studies were performed and the method was validated as per ICH guidelines.

INTRODUCTION

Perampanel is an antiepileptic drug used for the treatment of various neurological disorders caused by neuronal hyperexcitation. Chemically it is α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid receptor antagonist. It has been recently approved in the United States and the European Union for the adjunctive treatment of focal seizures and primary generalized tonic-clonic seizures associated with idiopathic generalized epilepsy. The antagonistic action results in the inhibition of neuronal excitation, repetitive neuronal firing, and the stabilization of hyper-excited neural membranes. It is extensively (> 90%) metabolized *via* cytochrome P450 CYP3A4/5.Perampanel was assayed in human plasma using LC-MS, HPLC and HPLC with fluorescence detection but no stability indicating method was available for the determination of Perampanel tablets.

In the present study the authors have proposed a simple validated stability indicating RP-HPLC method for the quantification of Parampanel in tablets. The method was validated as per ICH guidelines.

METHODOLOGY:

Typical chromatographic conditions:

HPLC : liquid chromatograph
Colum: Luna Amine (250x4.6mm,5µm)
Wavelength : 220nm
Flow rate: 0.8mL/minute
Temperature: 30°C
Injection volume: 10µL
Runtime: 60 minutes
Diluent: Water: Acetonitrile 80:20 (v/v)

S.No	Name of the compound	~RT(Minutes)	~RRT
1	PPP	12.80	0.44
2	BPP	23.20	0.80
3	PMP	28.82	1.00

Arrangement fitness

Established system suitability / system precision by inserting standard resolution for six times and calculated %RSD for peak area of all impurities.

S.No	Area counts PPP	Area counts BPP	Area counts PMP
1	45860	39411	49798
2	44408	38943	47825
3	44329	38592	47681
4	43517	37788	46560
5	42563	37121	45280
6	42428	36997	45689
Average	43851	38142	47139
St.dev.	1293.9	993.3	1657.0
%RSD	3.0	2.6	3.5

Observation:

The %RSD for PPP is 3.0, BPP is 2.6 and PMP is 3.5.

Specificity

Each known pollution arrangement and Perampanel standard arrangement was arranged Independently at target centralization of the test. An answer of all realized pollutions spiked with the Perampanel test (Mix arrangement) was likewise ready.This multitude of arrangements were broke down involving the PDA locator according to the HPLC technique.

Component	Retention time	
	Blend solution	**Individual solution**
PPP	12.10	12.14
BPP	22.75	22.76
PMP	28.37	28.35

Test Solution Stability

Perampanel test spiked with impurities was taken and analyzed for solution stability at about 12Hrs

Name of the Impurity	Preliminary (Fresh) results %	After 12 hrs Results %	Variation
PPP	0.11	0.11	0.00
BPP	0.09	0.09	0.00
MSUI	0.02	0.02	0.00
TI	0.25	0.24	0.01

Observation: Test arrangement was steady upto12Hrs at room temperature.

Limit of Quantitation (QL)

QL Fall outs:

S.No.	Name	Conc.(%)w.r.to.Test	S/Nratio
1	PPP	0.0002	12.92
2	BPP	0.0003	14.26
3	PMP	0.0002	13.60

Observation: **S/N percentage of each module was within the limit.**

LINEARITY

Linearity for PPP:

Near	Absorption in% (X axis)	Extent
1	0.0002	7955
2	0.0008	32350
3	0.0011	49304
4	0.0015	63716
5	0.0019	81248
6	0.0023	100492
Correlation coefficient		**0.9993**
Intercept		**-937**
% Y Seize		**-0.93**

Linearity for PMP:

Level	Absorption in % (X-axis)	Area
1	0.0002	21391
2	0.0005	39189
3	0.0008	51953
4	0.0010	67474
5	0.0013	84059
6	0.0016	106003
Correlation coefficient		**0.9946**
Capture		**8309**
%Y Intercept		**7.84**

Observation: Correlation coefficient an incentive for every part was in side limit.(Supplementary than 0.99)

ACCURACY: Exactness of the strategy stayed demonstrated by examination the % recuperation of every pollution in test Arrangement, spiked with every debasement at QL level, 100 percent level and 150% level.

% of Regaining	Accuracy		
	QL Level	100% Level	150% Level
PPP	107.4	99.6	99.7
BPP	85.1	101.3	100.7

Comment:

The % recuperation of all pollutants was inside the breaking point.

ROBUSTNESS

pH. Variety: Perampanel test Sharp with all above pollutants was taken and dissected at two unique pH settings

pH. Dissimilarity Outcomes:

Name of the Uncleanness	Preliminary pH3.0 results(%)	pH 2.8 Outcomes (%)	Distinction	pH 3.2 Content(%)	Variation
PPP	0.12	0.12	0.00	0.13	0.01
BPP	0.10	0.10	0.01	0.10	0.00
MSUI	0.02	0.02	0.00	0.02	0.00
TI	0.26	0.27	0.01	0.29	0.03.0

Observation:Initial results and pH variation results are comparable.

Temperature Variation: Perampanel test model Sharp with all above filths was engaged and analyzed at two unlike diseases (38°C and 42°C).

Appellation of the Adulteration	Initial 40°C results(%)	38°C Outcomes (%)	Variation	42°C results(%)	Variation
PPP	0.12	0.11	0.01	0.13	0.01
BPP	0.10	0.10	0.00	0.10	0.00
MSUI	0.02	0.02	0.00	0.02	0.00
TI	0.26	0.25	0.01	0.28	0.02

Observation: Preliminary results and disease distinction grades are comparable.

Rockiness(Transitional meticulousness)

Variation study of Ruggedness (Intermediate precision)

Distinction study	Process Care	In-between Precision
Instrument	Waters(AD/LC/130)	Waters(AD/LC/132)
Day to Day	19-08-2022	21-08-2022
Analyst	S. SindhujaReddy	J.Mounika

Ruggedness Results

Appellation of the Impurity	Preliminary results(%)	Intermediate Precision Results (%)	Disparity
PPP	0.12	0.12	0.00
BPP	0.10	0.10	0.00
MSUI	0.02	0.02	0.00
TI	0.26	0.26	0.00

Observation: The outcomes got from technique accuracy study and Middle Accuracy were equivalent. Degradation conditions and description of sample

Name of the sample	Period of exposure	Physical appearance
Sample	--	White powder
Updraft example	2 Periods	Silver precipitate
UV unprotected sample	26 minutes	Silver precipitate
Explanation in 1.0 N HCl at 80°C	2 Periods	Clear , No ransformation
Resolution in1.0 N NaOH at 80°C	2 Periods	Clear, No variation
Resolution at 80°C	2 Periods	Clear, No variation
Explanation in 10 % w/w tint at 80°C	2 Periods	Clear, No modification
Light uncovered explanation	2 Periods	Clear, No variation

Observation & Inference: No change is seen in the portrayal of the examples in any of the circumstances.

SUMMARY:

S.No	Parameter	Result	Acceptance Criteria
1	Arrangement fittingness Notional saucers Asymmetry Retaining time, %RSD	47139 1657.0 28.82 3.5	Not a lesser amount of than 2000 Not supplementary than 2
2	Specificity 1. Total prying 2. Control interference	Specific	Specific
3	Method precision (%RSD)	0.66	Not more than 2.0 %
4	Linearity parameter Capture Relationship coefficient(r^2)	50-150mcg/ml -937 0.9993	Not not as much of than 0.999
5	Accuracy % recapture	101	80-120%
6	Robustness Stream proportion dissimilarity Disease dissimilarity	All the arrangement fittingness restrictions are in doors the boundaries.	

Buffer preparation:

Broken up1.36gr of strong Potassium dihydrogen phosphate in1000mL of water. Changed pH to 7.0±0.05 with Potassium Hydroxide arrangement. Dissolvable B: Arranged a combination of water and Acetonitrile in the proportion of 20:80v/v.

Grounding of Mix explanation: Evaluate correctly each5.0 mg of PPD, PPP and BPP and of PMP reference standards into a 5 mL volumetric flask, liquefy and dilute to the bulk with diluent and mix.

Preparation of Reference stock solution: Readiness of Framework arrangement:

Weigh precisely around10.0mg of PMP reference standard into a 20mL volumetric jar, add 1.0mL of reference stock arrangement disintegrate and weaken to the volume with diluent and blend.

Planning of Reference arrangement:

Take 1.0mL reference stock arrangement into a 20mL volumetric carafe,disintegrate and weak to the volume with diluent and blend.

Planning of Test arrangement:

Weigh precisely around 10.0mg of test into a 10mL volumetric carafe, disintegrate and weaken to the volume with diluent and blend. The absolute retention times of impurities w.r.to Perampanel peak areas follows

CONCLUSION:

The method proposed for the determination of Perampanel tablets is simple, sensitive and economical. There is no interference of excipients. Perampanel highly resistant towards all stress degradation conditions and the method was validated.

REFERENCES:

1. Greenwood J, Valdes J. Perampanel, a review of clinical efficacy and safety in epilepsy. P. T. 41; 2016: 683-698.
2. Franco V, Crema F, Iudice A, et al. Novel treatment options for epilepsy: focus on Perampanel. Pharmacol Res. 70; 2013: 35-40.
3. Patsalos PN. The clinical pharmacology profile of the new antiepileptic drug Perampanel: a novel noncompetitive AMPA receptor antagonist. Epilepsia. 56; 2015:12-27.
4. Ugo de Grazia, Annachiara D' Urso, Federica Ranzato, Valentina De Riva, Giorgia Contarato, Giuseppe Billo, Francesco Perini, Elisabetta Galloni. A liquid chromatography-mass spectrometry assay for determination of Perampanel and concomitant antiepileptic drugs in the plasma of patients with epilepsy compared with a fluorescent HPLC assay. Therapeutic Drug Monitoring. 40(4); 2018: 477-485.
5. Mano Y, Takenaka O and Kusano K.High-performance liquid chromatography-tandem mass spectrometry method for the determination of Perampanel, a novel α- amino-3- hydroxy-5-methyl-4-isoxazolepropionic acid receptor antagonist in human plasma. J. Pharm. Biomed. Anal. 107; 2015: 56-62.
6. Franco, Valentina; Marchiselli, Roberto; Fattore, Cinzia; Tartara, Elena; De Sarro, Giovambattista; Russo, Emilio; Perucca, Emilio. Development and validation of an HPLC-UV assay for the therapeutic monitoring of the new antiepileptic drug Perampanel in human plasma. Therapeutic. Drug Monitoring. 38(6); 2016: 744-750.
7. Mano Y. An inter-laboratory cross-validation study for determination of Perampanel in human plasma by liquid chromatography assays. Biomedical Chromatography. 30(12); 2016: 2067-2069.
8. Susan Mohamed, Carmina Candela, Roberto Riva and Manuela Contin. Simple and rapid validated HPLC-fluorescence determination of Perampanel in the plasma of patients with epilepsy. Practical Laboratory Medicine. 10; 2018:15-20.
9. Mano Y, Takenaka O, Kusano K. HPLC with fluorescence detection assay of Perampanel, a novel AMPA receptor antagonist, in human plasma for clinical pharmacokinetic studies. Biomedical Chromatography. 29(10); 2015: 1589-1593.
10. ICH Stability Testing of New Drug Substances and Products Q1A (R2), International Conference on Harmonization, 2003.
11. ICH Validation of analytical procedures: Text and methodology Q2(R1), International Conference on Harmonization, 2005.