JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

RP-HPLC METHOD DEVELOPMENT AND VALIDATION OF LASMIDITAN IN BULK DRUG AND PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

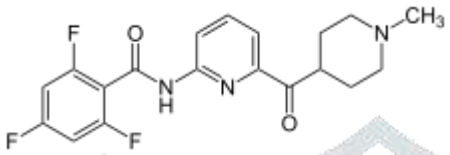
A simple specific and accurate RP-HPLC method has been developed and validated for the estimation of Lasmiditan in bulk drug and pharmaceutical dosage forms. The chromatographic conditions were viably created for the unit of Lasmiditan by using Inertial - ODS C18(250 x 4.6 mm,5µ), stream is 1.0 ml/min, convenient stage extent was Methanol: Water (80:20), recognizable proof wave length was 271nm. Acetonitrile was used in this experiment. The results of the tablet analysis were validated with respect to accuracy (recovery), linearity, limit of detection(LOD) and Limit of quantitation (LOQ) were found to be satisfactory.

Key words: Lasmiditan, RP-HPLC, Acetonitrile, Acuracy,linearity, limit of detection (LOD) and Limit of quantification(LOQ)

1. INTRODUCTION

Migraine is one of the most common neurological disease [(1)].Migraine presents with severe ,intermittent attacks of headache associated with nausea,vomiting,phonophobia and photophobia.It can be chronic ad disabling[(2)]. It is treated by non specific analgesics, like NSAIDS and specific drugs like triptans and ergot derivatives[(3)].The triptans have the risk of life threatening cardiovascular side effects because of their activation of 5 $_{HT1B}$receptor [(4,5)].

Lasmiditan is a newer oral 5-hydroxy tryptamine receptor agonist with high selectivity and affinity for 5-HT_{1F}receptor[6]without any serious adverse effects on cardiovascular system due to its low affinity for $5HT_{1B}$ receptors[6]. Lasmiditan is a centrally penetrating ,non vasoconstrictive drug which inhibits trigeminalvascularnociception[7].It is also called as COL-144 and LY 573144.Lasmiditan is approved for migraine with or without aura in adults by US Food and Drugs administration in 2019[8].Although there are many side effects, Lasmiditan is effective and safe for treatment of acute migraine[9].



Formula Chemical : $C_{19}H_{18}F_3N_3O_2$

Molecular Strength : 377.367g/mol

- **IUPAC :** 2,4,6-Trifluoro-*N*-[6-[(1-methyl-4-piperidinyl)carbonyl]-2-pyridinyl]benzamide

2.MATERIALS AND METHODS

Pure samples of Lasmiditan were obtained from Hetero drugs Pvt.Ltd. for the analytical development and validation of Lasmiditan. HPLC grade Orthrophosphric acid, Acetonitrile and Methanol were procured from Merck. High pure water prepared by using Qualigens. Necessary PPE (personal protective equipment) was used during the analysis. Destruction of solid samples and disposition of solvents was done.

2.1. Instruments

- HPLC –Waters Model NO.2690/5 series Compact System Consisting of Inertsil-C18 ODS column.
- Electronic balance (SARTORIOUS)
- Sonicator(FAST CLEAN)

2.2.Selection of wave length (λ max)

A solution of 100 µg/ml of Lasmiditan was prepared in Qualigens water. The resulting solutions were scanned individually on HPLC PDA detector from 200nm to 400 nm and also in UV-Visible spectrophotometer. The optimal response for both of them was obtained at 271 nm. Hence the complete method was processed at the wavelength of 271 nm.

2.3. Preparation of standard solution

100 mg of Lasmiditan was accurately weighed and transferred into a 100 ml clean dry volumetric flask and added methanol sonicated (30 minutes) to dissolve it completely and the volume was made up to the mark with the same solvent to give a concentration of 1000ppm (Stock solution). Further 4 ml of Lasmiditan was pipetted out from the above stock solution into a 10 ml volumetric flask and diluted up to the mark with diluent to give a concentration of 40ppm.

2.4. Preparation of sample solution

10ml of Lasmiditan was pipetted out from the above stock solution into a 100 ml clean dry volumetric flask and diluents was added it and was shaken by mechanical stirrer and sonicated for about 10 minutes by shaking at intervals of five minutes and was diluted up to the mark with diluent to give a concentration of 1000ppm and allowed to stand until the the residue settles before taking an aliquot for further dilution (stock solution). 4ml of upper clear solution was transferred to a 10 ml volumetric flask and diluted with diluents up to the mark to give the required concentration.

3.RESULTS AND DISCUSSION

3.1. Validation of the developed method:

From the system suitability studies it was observed that % RSD of retention time was found to be 2.650nm for Lasmiditan, % RSD of peak area was found to be 3058296.64for Lasmiditan.A graph of peak area versus concentration (on X-axis concentration and on Y-axis Peak area) was plotted and the correlation coefficient was calculated. From the Linearity data it was observed that the method was showing linearity in the concentration range of 40-50ppm for Lasmiditan.The standard solution was injected for six times and the area for all six injections was measured in HPLC. The % RSD for the area of six replicate injections was found to be within the specified limits. The % RSD of Lasmiditan for repeatability and precision was found to be150%. Assay was performed in triplicate for various concentrations of Lasmiditan and equivalent to 100, and 150 % of the standard amount was injected into the HPLC system The recoveries of pure drug from the analysed solution of formulation was 100.22% which shows that the method was accurate. The Chromatograms of Standard and sample are identical with nearly same Retention time. No interference due to Placebo and Sample at the retention time of analyse which shows that the method was specific. As the % RSD of retention time and asymmetry were within limits for variation in flow rate (• 0.1 ml). Hence the allowable flow rate should be within 0.1 ml to 1.2 ml/min.Method was optimized and the retention time was reported as 2.650nm .The Chromatograms were recorded as table no.1-3 and fig no.1-3 for standard, sample respectively.

Table 1:Chromatographic conditions that have been optimized:

Parameters	Method
Stationary phase (column)	Inertsil -ODS C_{18}(250 x 4.6 mm, 5 µ)
Mobile Phase	Methanol: Acetonitrile (80:20)
Flow rate (ml/min)	1.0 ml/min
Run time (minutes)	6 min
Column temperature (°C)	Ambient
Volume of injection loop (µl)	20
Detection wavelength (nm)	271nm
Drug RT (min)	2.650min

Table 2: Data of System Suitability

Injection	RT	Peak Area	USP Plate count	USP Tailing
1	2.651	3058296.64	10087	1.111
2	2.649	3058388.08	10095	1.112
3	2.650	3058422.84	10080	1.111
4	2.652	3058359.19	10060	1.113
5	2.649	3058555.05	10070	1.115
Mean	2.6502	3058404.36	10078.4	1.112
SD	0.001304	96.122247	-------	-------
% RSD	0.049198	0.0031428	-------	-------

TABLE-3: Data of Repeatability (Method precision)

	Injection	Peak Areas of Lasmiditan	%Assay
Concentration 40ppm	1	3058687.12	100.25
	2	3058458.26	100.24
	3	3058588.92	100.25
	4	3058622.48	100.25
	5	3058782.28	100.25
	6	3058654.15	100.25
Statistical **Analysis**	**Mean**	3058632.20	100.25
	SD	107.9303	0.00353
	% RSD	0.00352	0.00352

Variability (LINEARITY):

Table 4: Data of Linearity

Concentration (ppm)	Average Area	Statistical Analysis	
0	0	Slope	76034
20	1529106.51	y-Intercept	9579
30	2293659.45	Correlation Coefficient	0.999
40	3058213.02		
50	3822765.15		
60	4587318.61		
70	5305126.45		

Fig1:Normal Chromatogram-2 device appropriateness

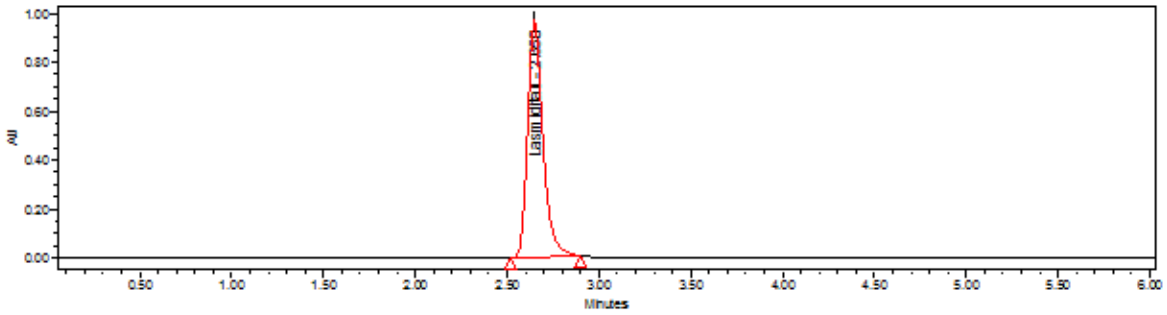


Fig 2: Standard chromatogram

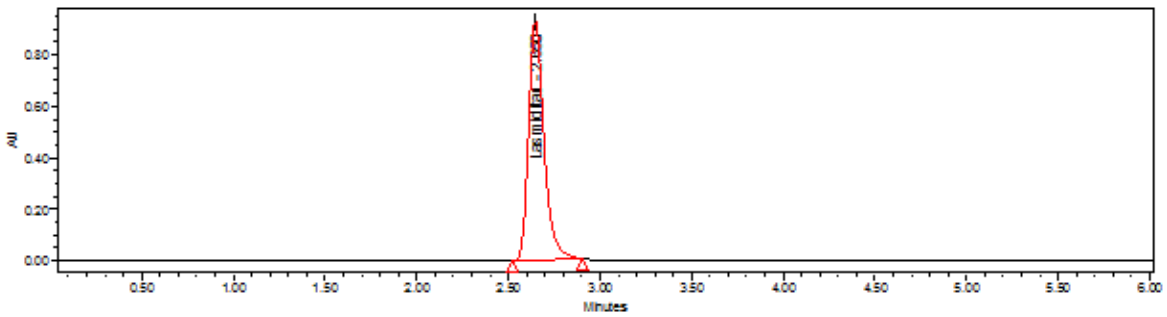
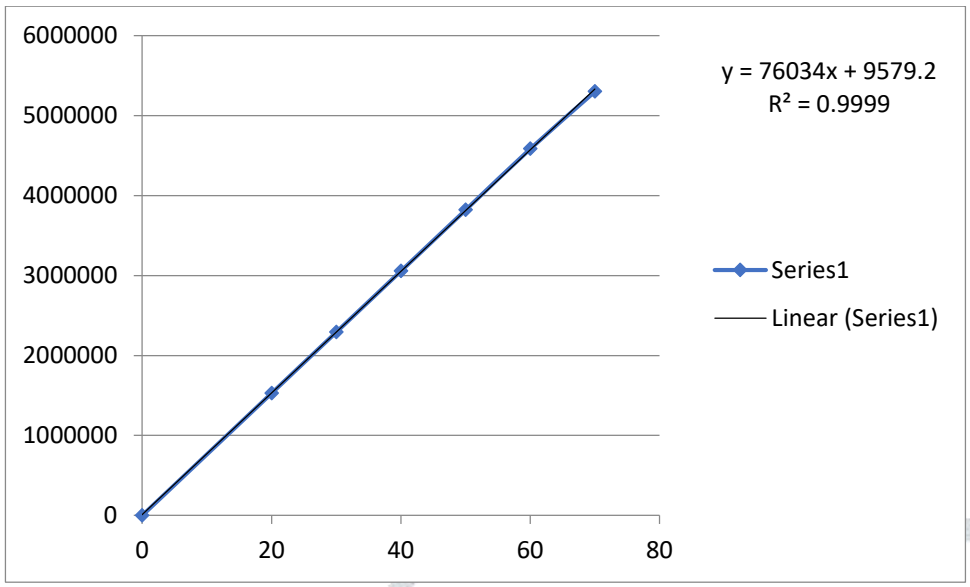


Fig3:linearity plot(concentration vs response**)**



4.CONCLUSION

Good agreement was seen in the assay results of pharmaceutical formulation by developed and validated method. The method was validated for parameters such as system suitability, linearity, precision, accuracy, specificity, ruggedness robustness, LOD and LOQ.The system suitability parameters were within limit, hence it was concluded that the system was suitable to perform the assay. Hence it can be concluded that the proposed method was a good approach for obtaining reliable results and found to be suitable for the routine analysis of Lamiditan in Bulk drug and pharmaceutical formulation.

5.ACKNOWLEDGMENT

The authors thank the Head, Department of chemistry,Osmania University, India for providing necessary facilities to carry out the present investigation

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