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Original Article

RAPID ANALYTICAL METHOD FOR ASSAY DETERMINATION FOR PROCHLORPERAZINE EDISYLATE DRUG SUBSTANCES BY ULTRA PERFORMANCE LIQUID CHROMATOGRAPHY

KISHORKUMAR L. MULE

Department of Chemistry, Shri Jagdish Prasad Jhabarmal Tibrewala University, Vidyanagari, Jhunjhunu 333001 Rajasthan, India
Email: kishormule@rediffmail.com

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ABSTRACT

Objective: To develop and validate new, simple and rapid assay method for Prochlorperazine edisylate drug substance by UPLC as per ICH guidelines.

Methods: Ultra performance liquid chromatographic method was developed, optimized and validated on Acquity UPLC by using Acquity BDH300 C4 (100 x 2.1 mm) 1.7µ column. 3.85g ammonium acetate in 1000 ml of water add 0.5 ml trifluoroacetic acid and 1 ml triethylamine (Mobile phase A): 0.5 ml trifluoroacetic acid in 1000 ml acetonitrile mobile phase (Mobile phase B) with gradient program. Detector wavelength 254 nm and column temperature 30 °C.

Results: Linearity study was carried out for prochlorperazine edisylate, linearity was calculated from 80 % level to 120% with respect to specification level. The correlation coefficient (r) = 0.999 was proved that the method is robust. The resolution between known impurities and Prochlorperazine edisylate found more than 2.5, it was evident from specificity test that Prochlorperazine edisylate peak are well separated from its related impurities, hence the method is specific. Prochlorperazine edisylate sample solution and mobile phase were found to be stable for at least 3 d.

Conclusion: A new, simple and rapid method has been developed and validated for assay determination of prochlorperazine edisylate in drug substance by Ultra Performance Liquid Chromatography (UPLC). The analytical method was developed and validated as per ICH guidelines. The developed method can be used for the fast assay determination of prochlorperazine edisylate drug substances in research laboratories and in the pharmaceutical industry.

Keywords: Prochlorperazine edisylate, UPLC, Assay, Reverse phase, Method validation, Solution stability

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INTRODUCTION

Prochlorperazine edisylate is widely used to treat nausea and vomiting caused by radiation therapy, cancer chemotherapy, surgery and other condition. It has also been used to relieve pain associated with migraine headaches. Prochlorperazine edisylate blocks postsynaptic dopamine receptors in cortical and limbic areas of the brain thereby preventing the excess of dopamine in the brain [1]. It is having chemical name, 2-Chloro-10-[3-(4-methyl-1-piperazinyl) propyl] phenothiazine 1, 2 ethane disulfonate (1:1) [1].

The chemical formula is $c_{20}h_{24}cln_3s$. $C_2H_6O_6S_2$, chemical structures show in (fig. 1), process-related impurities are prochlorperazine sulfoxide, dimer-I, dimer-II and perazine. 2-chlorophenothiazine is starting material of Prochlorperazine edisylate drug substances. In literature there are HPLC method of Simultaneous Quantitation ff Plasma Doxorubicin and Prochlorperazine content By High-Performance Liquid Chromatography [2], quantification of prochlorperazine maleate in human plasma by liquid chromatography–mass spectrometry: application to a bioequivalence study [3].

In the literature, there is no analytical method was reported for rapid assay of prochlorperazine edisylate drug substances using ultra-performance liquid chromatography (UPLC) technique. The UPLC is recent, advanced and rapid chromatographic technique.

This report describes a reverse-phase UPLC method for the assay test for prochlorperazine edisylate on by using Acquity BDH UPLC column C4 (100 x 2.1 mm) 1.7µ. The developed UPLC method was validated for assay determination of prochlorperazine edisylate in drug substance as per validation of analytical procedure guidelines

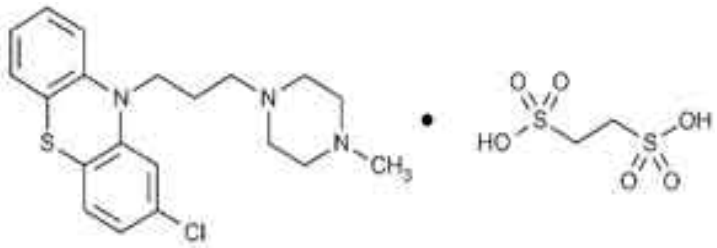

Fig. 1: Chemical structure for prochlorperazine edisylate

MATERIALS AND METHODS

Chromatographic method is developed and validated as per ICH guideline [5]. Method details are as follows,

Chemicals

Prochlorperazine edisylate sample, Prochlorperazine edisylate USP standard, sulphoxide impurity, perazine Impurity, 2-chloro-

phenothiazine, Dimer-I Impurity and Dimer-II Impurity were kindly gifted by Emcure Pharmaceuticals Ltd Pune, Maharashtra, India. Trifluoroacetic acid (AR grade) was purchased from merck, Triethylamine (AR grade) was purchased from merck, HPLC grade acetonitrile was purchased from merck, Ammonium acetate (AR grade) was purchased from merck and Millipore water is used for mobile phase preparation and diluents preparation.

Equipment

Waters UPLC having make Acquity system with PDA detector and inbuilt auto injector was used for method development and validation. Empower software was used for data acquisition and system suitability calculations.

Standard preparation

Weigh accurately about 75 mg of prochlorperazine edisylate USP standard in 50 ml volumetric flask dissolve in diluents and dilute up to the mark (stock solution), further pipette out 5 ml of stock solution and dilute 50 ml volumetric flask. (150 ppm standard).

Sample preparation

Weigh accurately about 75 mg of prochlorperazine edisylate USP sample in 50 ml volumetric flask dissolve in diluents and dilute up to the mark (stock solution), further pipette out 5 ml of stock solution and dilute 50 ml volumetric flask. (150 ppm standard).

Chromatographic conditions (method)

The chromatographic conditions were optimised by using Acquity BDH UPLC C4 (100 x 2.1 mm) 1.7µ column, the flow was set as 0.4 ml/min. The column oven temperature was maintained at 30 °C and the detection was carried out at the wavelength of 254 nm. The injection volume was 1µl.

Gradient program: Time–mobile phase A, 0.0-75, 1.00-50, 3.00-00, 6.00-00, 6.10-75, 8.00-75.

Mobile phase

Mobile phase preparation-A

3.85 gm ammonium acetate in 1000 ml of water. Add 0.5 ml trifluoroacetic acid and 1 ml triethylamine.

Mobile phase preparation-B

0.5 ml trifluoroacetic acid in 1000 ml acetonitrile

Diluent preparation

Acetonitrile and water (1:1)

RESULTS AND DISCUSSION

The analytical method was validated as per ICH guideline [5]. All the validation parameters like specificity, forced degradation, linearity and range, precision, solution stability, and robustness are studied.

Specificity

Specificity study was carried out to verify that there is no interference with analyte (prochlorperazine edisylate and all known impurities) peak is observed from the blank solution. All the impurities peaks are well separated from prochlorperazine edisylate and peak purity of prochlorperazine edisylate peak was found complying. Typical chromatogram of system suitability solution showed in (fig. 2). The results are tabulated in (table 1).

Table 1: Specificity data of prochlorperazine edisylate

Injection number	Peak area of prochlorperazine edisylate
1	1293136
2	1291813
3	1276581
4	1282901
5	1290159
6	1281740
Mean	1286055
SD	6610
(%) RSD	0.5

Forced degradation

As part of specificity study, product was subjected for degradation under different conditions like basic, acidic, oxidation, thermal, photolytic, aqueous degradation and humidity conditions. In degradation study, degradants found well separated from the peak of isosulfan blue. It is also found that all impurities are separated from prochlorperazine edisylate.

Linearity and range

Linearity was calculated from 80% to 120 % with respect to specification level for prochlorperazine edisylate. The range was selected from 80%, 90%, 100%, 110% and 120% of specification limit for prochlorperazine edisylate.

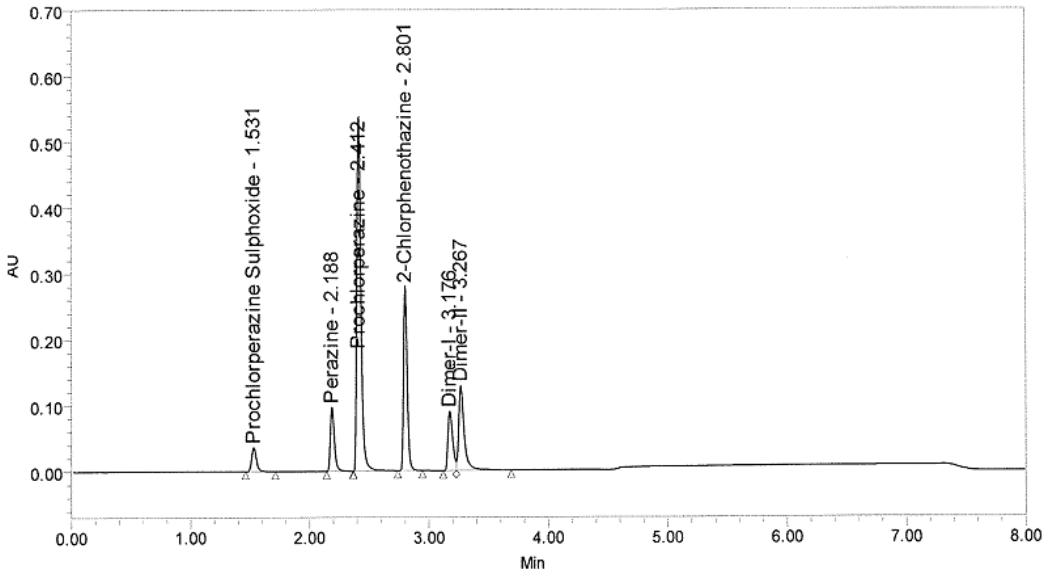

Fig. 2: Typical UPLC chromatogram with data of system suitability (spiked sample)

Table 2: Forced degradation study

Condition	Degradation achieved in %	Peak purity angle	Purity threshold
Acid degradation	0.684	0.055	0.264
Base degradation	0.649	0.058	0.262
Peroxide dégradation	13.596	0.071	0.286
Thermal degradation	0.614	0.047	0.261
Photolytic degradation	0.306	0.049	0.250
Aqueous degradation	0.250	0.049	0.264
Humidity degradation	0.371	0.051	0.261
Untreated (as is)	-	0.052	0.262

Table 3: Linearity of prochlorperazine edisylate

Linearity level	Concentration (ppm)	Area		Mean area
		Run-1	Run-2	
Level 1 (80%)	120.029	1036751	1028846	1032799
Level 2 (90%)	135.032	1142805	1142746	1142776
Level 3 (100%)	150.036	1289255	1281526	1285391
Level 4 (110%)	165.039	1405094	1409616	1407355
Level 5 (120%)	180.043	1541717	1525079	1533398
correlation coefficient (r)		0.999		

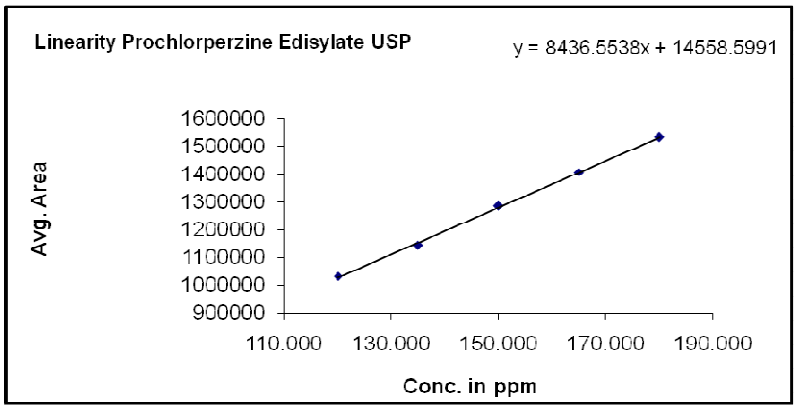

Fig. 3: Linearity of prochlorperazine edisylate system precision

Six replicate injections of standard solution were injected as per methodology. % RSD of area obtained from six replicate injections of standard solution was calculated. Results are tabulated in (table 4).

Method precision

Method precision was demonstrated by assay test of six replicate samples at specification level. Results are tabulated in (table 5).

Table 4: System precision

Injection number	Peak area for prochlorperazine edisylate standard
1	1276087
2	1283898
3	1268996
4	1272755
5	1276010
6	1278496
Mean	1276040
SD	5063
(%) RSD	0.4

Table 5: Method precision results

Injection No.	Area of prochlorperazine edisylate	% assay for six replicate test preparations
1	1293040	99.596
2	1282518	99.470
3	1277641	100.166
4	1278395	99.996
5	1290122	99.115
6	--	99.166
Mean	1284343	99.585
SD	6940	0.4280
(%) RSD	0.5	0.43

Intermediate precision

Intermediate precision of the analytical method was determined by using method precision parameters on different days, by different analysts, on different instrument and by different column lot number using the same sample used in method precision. Analysis was performed as per methodology, under same experimental condition by injecting six replicate sample preparations. %RSD of results was calculated. Overall % RSD of method precision and intermediate precision results was also calculated. The tabulated data shows that the Analyst–I have done the method precision and Analyst–II has done the intermediate precision. Results are tabulated in (table 5, table 6 and table 7).

Table 6: Intermediate precision results

Injection No.	Area of prochlorperazine edisylate	% assay for six replicate test preparations
1	1254805	100.248
2	1255464	100.074
3	1254858	99.956
4	1254446	100.073
5	1254581	99.680
6	---	99.889
Mean	1254831	99.987
SD	391	0.1940
(%) RSD	0.0	0.19

Table 7: Overall % RSD for method and intermediate precision

Overall RSD of method precision and intermediate precision results (n=12)		
Compound	Mean (%)	Overall RSD (%)
Prochlorperazine edisylate	99.786	0.38

Table 8: Solution stability data

Interval	Assay (%) on anhydrous basis	Cumulative RSD
Sample Preparation Fresh	99.762	-
Sample Preparation, 1 D Old	99.958	0.14%
Sample Preparation, 2 D Old	99.782	0.11%
Sample Preparation, 3 D Old	99.901	0.09%

Table 9: Robustness study

Robustness study	% RSD	Mean Assay
Column lot-I	0.04	100.181
Column lot-II	0.05	99.864
Flow+10%	0.04	100.101
Flow-10%	0.07	99.904
Column oven temp+5 °C	0.09	100.182
Column oven temp-5 °C	0.16	99.944

Solution stability

Solution stability was performed at the room temperature. Test sample was prepared at specification level and injected as fresh, 1 d, 2day and 3day intervals.

Robustness

Robustness of the method was verified by varying the instrumental conditions such as by changing flow rate ± 10% (flow= 0.385 ml/min and 0.315 ml/min) by changing column oven temperature ± 5 °C (temp.= 35 °C and 25 °C) by mobile phase concentration ± 2% (buffer 71+29 acetonitrile and buffer 75+25 acetonitrile) and by changing column lot number. The system suitability was evaluated in each condition and sample was analyzed in triplicate.

CONCLUSION

A new, simple and rapid method is developed and validated by UPLC technique as per ICH guideline. Linearity was obtained with correlation coefficient 0.999. In specificity study, the resolution of known impurity and principal peak found more than 2.5, hence the known impurity found well separated from principal peak. Forced degradation shows all degradants are well separated from principal peak and peak purity was within limit. The results for precision, robustness found comparable and well within the limit. The sample solution, standard solution and system suitability solution are stable up to 3 d.

In literature, there is no analytical method reported for assay determination of Prochlorperazine edisylate drug substances by UPLC. In this method all the known and degrading impurities are well separated within five minute run time, hence the analysis time required is very less as compared to other published methods. The developed method can be used for rapid assay of Prochlorperazine edisylate drug substances in research laboratories, in pharmaceutical industries.

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CONFLICT OF INTERESTS

Declare none

REFERENCES

1. Miller Ma, Levsky Me, Enslow W, Rosin A. Randomized evaluation of octreotide vs prochlorperazine for ed treatment of migraine headache. Am J Emergency Med 2009;27:160-4.

2. Mou C, Ganju N, Sridhar Ks, Krishan A. Simultaneous quantitation of plasma doxorubicin and prochlorperazine content by high-performance liquid chromatography. J Chromatogr B Biomed Sci Appl 1997;703:217-24.
3. Yan M, Zhu Yg, Li Hd, Chen Bm, Ma N. Quantification of prochlorperazine maleate in human plasma by liquid chromatography–mass spectrometry application to a bioequivalence study. J Chromatogr B 2009;877:3243-7.
4. Jadhav HP. Determination of r-isomer impurity of pantoprazole sodium in a bulk drug substance by normal phase chiral liquid chromatography method. Int J Pharm Pharm Sci 2015;l 7:45-8.
5. ICH Guidelines on Validation of Analytical Procedures, Definitions and Terminology. Federal Register Ifpma Switzerland 1995;60:11260-262.

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