INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Research Article

STABILITY STUDY OF RAMIPRIL TABLETS USING HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

Kalpana Patankar-Jain[1], Parag Gadkari[2] and Pushkar Pradhan[3*]

[1]Department of Chemistry, B.N.N. College, Bhiwandi, Maharashtra, India.
[2]Inventia Healthcare Pvt. Ltd., Thane, Maharashtra, India.
[3]Department of Chemistry, Ramnarain Ruia College, Mumbai, Maharashtra, India.

ABSTRACT

In the current method, a HPLC method is developed for analysis and stability study of Ramipril tablets using Waters Alliance instrument. The mobile phase used consist of Buffer : ACN in 50 : 50 ratio at 1 ml/min flow rate. Merck Lichrosphere C-18 column with dimensions 250 * 4 mm * 5 µ. The detection was carried out using a PDA detector at 210 nm. The total run time for the method was set at 9 min with retention time for the standard as 5.44 min. The stability study was carried out under bench top conditions, at 10° C and also using Filter paper validation. The standard was found to be stable for atleast 24 hours under all conditions.

INTRODUCTION

Ramipril, is an angiotensin-converting enzyme (ACE) inhibitor, used to treat high blood pressure (hypertension) and congestive heart failure. By inhibiting an enzyme, ACE inhibitors relax the muscles around small arteries (arterioles). The arterioles expand and allow blood to flow through more easily. This reduces blood pressure. Ramipril tablets are used to treat high blood pressure (hypertension), to reduce the risk or delay the worsening of kidney problems and for treatment when heart cannot pump enough blood to the rest of your body.

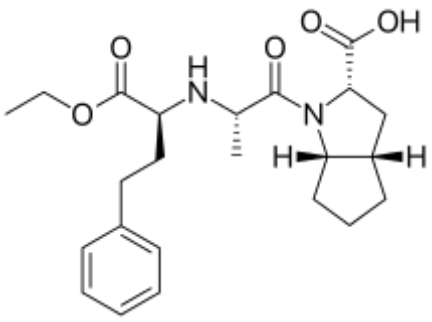

Fig. 1: Chemical Structure of Ramipril Compound

Clinical trials are understandably a critical and well-known part of the drug discovery, development and approval process, with results often featured. The testing process is necessary for the assessment of drug safety and efficacy. Stability testing assesses how the quality of a drug substance or drug product (including its packaging) varies with time under the influence of environmental factors, including temperature, humidity and light. The process determines whether any physical, chemical or microbiological changes affect the efficiency and integrity of the final product, thereby ensuring that a pharmaceutical product is safe and effective, irrespective of where in the world it will be supplied. Moreover, stability testing establishes the shelf life and recommended storage conditions of a finished pharmaceutical product and the retest periods for a drug substance.

MATERIALS AND METHODS

MATERIALS

Solid Perchlorate AR grade, HPLC grade water, Orthophosphoric acid (OPA) HPLC grade, Ramipril standard 99.48 %.

Chemical and Standard Solution Preparations

Standard Solution

50.05 mg of standard is diluted with Methanol to 50 mL in a standard flask. 5 mL of this solution is further diluted to 1000 mL with 0.1 M HCl. 5 mL of this solution is finally diluted to 10 mL using mobile phase.

Instrumentation and Chromatrographic Conditions

High Performance Liquid Chromatography instrument manufactured by Waters Alliance was used for the stability study. The separation was done using a Merck Lichrosphere C-18 column with dimensions 250 mm * 4.0 mm with 5 µ particle size. The mobile phase consists of CAN and buffer prepared by dissolving 4.0 g of solid sodium perchlorate in 600 mL of HPLC water and adjusted to pH 2.6 using OPA. The composition of mobile phase is Buffer : ACN in 50 : 50 ratio. The flow rate is adjusted to 1.00 mL/min. The total run time is of 9.0 min with retention time of standard at 5.44 min. The injection volume of solution is set to 20 µL. The detection is carried out using a PDA detector at 210 nm.

Stability Study

Stability of solution is checked at bench top level, at 10° C, under three filtration conditions and using centrifugation technique. The three filtration conditions used filtration using filter paper no. 1, filter paper no. 41 and by passing through 0.45 µ membrane. The readings for the above solutions were taken at an interval of 0 hr, 1 hr, 2 hr, 3 hr, 4 hr, 5 hr, 18 hr and 24 hr.

RESULTS AND DISCUSSIONS

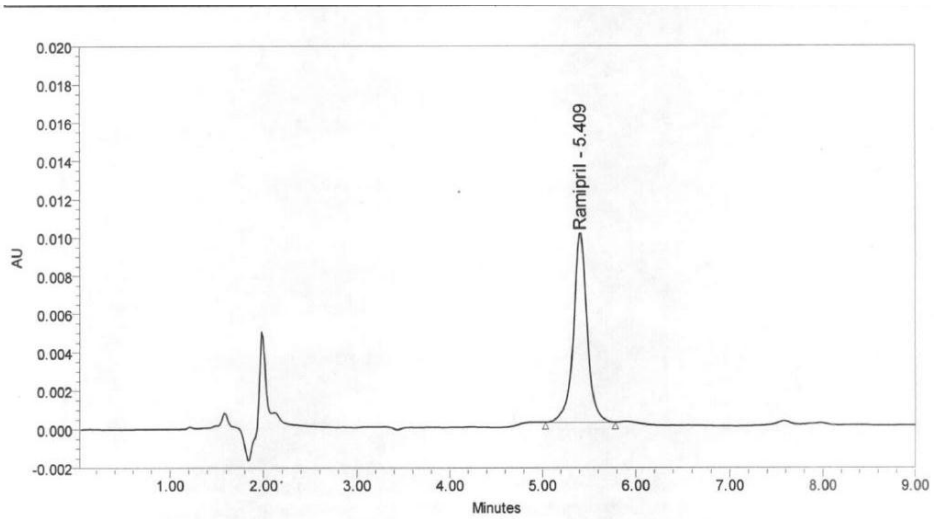

Fig. 2: Chromatogram for Ramipril Standard

The retention time for the standard was found to be 5.44 min. The areas obtained for standard under various conditions are tabulated below.

Table 1: Areas obtained for Bench Top studies

Sr No.	Time (Hours)	Area of Standard Ramipril			Average Area
1	0	100890	100497	100950	100779
2	1	101028	98447	100900	100125
3	2	101228	101613	101712	101518
4	3	102097	101213	101925	101745
5	4	102597	102157	101516	102090
6	5	102028	101770	102381	102060
7	18	101176	101218	101575	101323
8	24	103055	101612	101927	102198
				Average :	101480
				STDEV :	722
				% RSD :	0.71

Table 2: Areas obtained for Solutions stored under 10° C

Sr No.	Time (Hours)	Area of Standard Ramipril			Standard
1	0	100890	100497	100950	100779
2	1	100989	100921	101117	101009
3	2	101678	101693	101187	101519
4	3	102392	101855	102171	102139
5	4	101728	102110	102285	102041
6	5	103022	102972	102500	102831
7	18	101625	102418	102470	102171
8	24	102681	103104	102911	102899
				Average :	101924
				STDEV :	775
				% RSD :	0.76

Table 3: Areas obtained for Filter Paper Validation

	Area of Standard Ramipril							
Sr. No.	Without filteration (As Such)	Filtered through filter Paper No. 1	% Variation for filter Paper No. 1	Filtered through filter Paper No. 41	% Variation for filter Paper No.41	Filtered through 0.45u Membrane filter	% Variation for 0.45 µ Membrane filter	Centrifuge	% Variation for Centrifuge
1	100779	100530	0.25	102241	1.43	101386	0.60	102104	1.30
		101685	0.89	102580	1.76	102083	1.28	102282	1.47
		101812	1.01	102489	1.67	101443	0.65	101672	0.88
2		102389	1.57	102460	1.64	100925	0.14	102308	1.49
		101452	0.66	102337	1.52	101126	0.34	101535	0.74
		102134	1.33	102428	1.61	102564	1.74	102160	1.35
3		102147	1.34	102464	1.64	101498	0.71	102033	1.23
		101415	0.63	102783	1.95	101027	0.25	101642	0.85
		101955	1.15	101973	1.17	102635	1.81	101822	1.02
Average % Variation :		101724	0.98	102417	1.60	101632	0.84	101951	1.15

The RSD for all the stability studies was found to be below 2 % and hence it could be concluded that the standard is stable for at least 24 hours under ambient conditions.

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