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DEVELOPMENT A NEW RP-UPLC METHOD FOR THE DETERMINATION OF RABEPRAZOLE SODIUM IN PHARMACEUTICAL FORMULATION AND APPLICATION IN DISSOLUTION STUDIES

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ABSTRACT

Pharmaceutical analysis, in general, refers to the techniques required to ascertain the identification, strength, quality, and purity of such goods. However, it would be appropriate to expand the scope of this definition to include the study of intermediates and raw materials used in the production of medications for potential reasons. Both the pharmaceutical industry and the chemical industry that creates pharmaceutical raw materials must do this kind of analytical chemistry. Thousands of different organic compounds are used as raw materials in the synthesis of modern pharmaceuticals as well as as intermediates throughout research, development, and synthesis. As a result, in addition to having particular expertise in the evaluation of pharmaceutical products, the pharmaceutical analyst needs to have a solid understanding of fundamental organic analysis. The development and validation of analytical methods is crucial to the research, creation, and production of pharmaceuticals. It is essential to be aware of the product's quality and quantity. Researchers are currently focusing more on analytical techniques to create an innovative, economical, acceptable, and precise approach for estimating various pharmaceuticals and natural materials in their customary dose forms. Every year, more medications are being released onto the market. A drug's introduction to the market and the date of its inclusion in pharmacopoeias frequently occur at different times. This is brought on by potential risks associated with long-term and widespread use of these medications, reports of novel toxicities (leading to their removal from the market), the emergence of patient resistance, and the launch of superior medications by rival companies. Standards and analytical techniques for certain medications may not be included in the pharmacopoeias under these circumstances. Therefore, it becomes vital to create newer testing techniques for such natural items and different medications.

KEY WORDS: Development, Determination, Rabeprazole Sodium, Pharmaceutical, Formulation, Innovative, Economical, Acceptable.

INTRODUCTION

Like omeprazole, rabeprazole sodium is a proton pump inhibitor with similar effects and applications. It is administered orally in the form of enteric-coated rabeprazole pills, usually first thing in the morning. The typical dose is 20 mg once daily for 4 to 8 weeks for the treatment of severe ulcerative gastro- oesophageal reflux disease. In the USA, an additional 8-week course is allowed to treat erosive oeophagitis. Rabeprazole is 2-[(4)3-methoxy-propoxy-3-methyl-2-pyridinyl sulphinyl] sulphinyl in terms of chemistry.

HPLC, thin layer chromatography, UV spectrophotometry, and voltammetry are some of the methods that have been reported for the determination, While several techniques have also been published for the quantitative study of rabeprazole in combination with other medications, the determination of enantiomers and metabolites of rabeprazole using HPLC.

PURPOSE OF THE STUDY

The purpose of the current study is to compare the outcomes of HPLC and to create a straightforward ultra performance liquid chromatography (UPLC) method for the determination of rabeprazole sodium in tablets. An developing method of liquid chromatography called UPLC allows run times and solvent consumption to be significantly reduced. To the best of our knowledge, rabeprazole in pharmaceutical formulations has not yet been determined using a UPLC approach.

RESEACH METHODOLOGY

We were given standard rabeprazole sodium by Metro Labs Ltd. (Baddi, India). Pepraz®, 10 mg, East West Pharma, India) tablets containing rabeprazole sodium were acquired from a nearby pharmacy. Acetonitrile of the HPLC grade was bought from Merck (Mumbai, India). Using the Millipore Milli-Q water purification technology, high purity water was produced (Billerica, MA, USA). Other reagents were all of the analytical variety.

INSTRUMENTATION

The HPLC equipment used for all method development and validation was a Waters Corporation, Milford, USA, 2695 binary pump plus auto sampler, 2996 photo diode array, and 2487 UV detector. On a Waters Acquity UPLC system (Waters Corporation, Milford, USA) outfitted with a binary solvent manager, an auto sampler, and a column manager made up of a column oven and a TUV detector, the UPLC analysis was carried out. The Labindia 2000 dissolution apparatus (A six-tablet dissolution unit [Labindia, Mumbai, India]) was employed for the dissolving studies.

STANDARDIZATION OF WORK

A suitable quantity of rabeprazole sodium was dissolved in a 10 mM potassium hydroxide solution to create a stock solution with a concentration of 1.0 mg/mL. Serial dilution was used to get a workable solution of 10 g/mL from this stock solution.

TESTING SOLUTION PREPARATION FROM TABLETS

The weight and powder of twenty pills were done. A 100 mL volumetric flask was filled with a powder equivalent to 50 mg of rabeprazole sodium, which was then extracted for 10 minutes with a 10 mM potassium hydroxide solution. The solution was appropriately diluted to 10 g/mL and then passed through a millipore nylon filter paper with a 0.45 m pore size.

PREPARATION OF DISSOLUTION SAMPLES

The dissolution test was conducted using equipment 2 and paddles in accordance with the United States Pharmacopoeia USP (711) guidelines. The reaming dissolving conditions were followed in accordance with US FDA standards, and the paddle speed was 100 rpm. The media's temperature was held constant during dissolution at 37 0.5 °C. The US FDA advises a dissolution test in 700 mL of 0.1 N HCl for 2 hours for delayed-release rabeprazole sodium tablets (Samples were collected for the estimation of rabeprazole sodium). Thereafter, 300 mL of 0.6 M Tris-HCl buffer (pH 8.0) was added to the medium, and the dissolution test was continued for 45 min (Samples were collected for the estimation of rabeprazole sodium). 10 mL samples were taken automatically at regular intervals throughout the test period. A 0.45 m Millipore nylon filter was used right away to filter the samples. Before gathering the samples for analysis, the first 2 mL sample was thrown out.

RESULT AND DISCUSSION

CHROMATOGRAPHIC METHOD OPTIMIZATION

The developed method's primary objective was to separate and quantify rabeprazole using an isocratic mobile phase and a UPLC device. The UPLC technique was created to shorten the method's run time and use less solvent for standard analyses such assay, dissolution, and content uniformity during quality control. At 280 nm, rabeprazole could be detected adequately. Chromatographic separation was obtained on a Waters symmetrical C18 column during the initial trial utilising HPLC (150 x 4.6 mm, 5 micron). Because rabeprazole is an acid-labile substance, a mobile phase with a basic pH was chosen to prevent any degradation. The ratio of 10 mM potassium dihydrogen phosphate buffer to acetonitrile in the mobile phase was optimised to be 65:35 (v/v) with a flow rate of 1.0 mL/min and an injection volume of 20 L (pH 7.4, corrected with potassium hydroxide solution).

The fundamental chromatographic parameters of the HPLC method, including column, solvents, and UV detection, were followed when designing the UPLC method. To ensure the column's extended life, the stability at the higher pH was taken into account when choosing the UPLC column. The FDA suggests using pH 8.0 media for dissolving solution tests with rabeprazole sodium. The present study's optimum mobile phase pH is also on the basic side. The lifespan of the majority of commercial C18 columns is shortened because they are not stable at high pH over the long term. At a pH of 8.0, it was discovered that the Waters Acquity BEH C18 (50 mm x 2.1 mm, 1.7 micron) column was more suited and stable. The injection volume was decreased from 20 to 5 L, and the peak was clear and satisfactory. Additionally, the flow rate decreased from 1.0 to 0.4 mL/min.

Table-1: Optimized UPLC chromatographic conditions

Buffer	10 mM potassium dihydrogen phosphate buffer, pH adjusted to 7.4 with potassium hydroxide solution
Mobile phase	Mixure of buffer and acetonitrile (65:35, v/v)
Diluent	10 mM potassium hydroxide solution
Column	Waters Acquity BEH C_{18}, 50 mm x 2.1 mm, 1.7 micron

Column oven temperature	Ambient
Detection wavelength	280 nm
Injection volume	5 µL
Flow rate	0.4 mL/min

When these operating parameters were used with the devised method, rabeprazole showed a good peak that eluted at roughly 1.49 minutes, giving it a total run time of 2 minutes. The compares the elution duration, sensitivity, and other chromatographic properties of HPLC and UPLC following the injection of a reference solution. According to the findings, rabeprazole's elution time in UPLC was slashed by nearly nine times when compared to HPLC. The theoretical plates acquired for UPLC are almost 8 times higher than those for HPLC. This demonstrates that UPLC has a higher separation efficiency than HPLC.

Table: 2- Comparative operating parameters of HPLC and developedUPLC methods

System	Flow rate (mL/min)	Injection volume (µL)	USP tailing	USP platescount	Elution time(min)
UPLC	0.4	5	1.2	44790	1.49
HPLC	1.0	20	1.5	4700	12.72

METHOD VALIDATION

According to ICH and FDA criteria, the developed HPLC method's precision, ruggedness, linearity, specificity, selectivity, robustness, LOD, LOQ, and accuracy were all validated.

SYSTEM SUITABILITY

For the system appropriateness check, a standard solution was employed. USP theoretical plate count (30000), USP tailing factor (2.0), and percent RSD for five replicate injections (should be 2.0) were used to analyse the system appropriateness.

Table: 3 - System suitability results

Injection	RT (min)	Peak area	USP tailing	USP theoreticalplates
1	1.492	7019896	1.21	44222
2	1.491	7102321	1.19	45151
3	1.487	7082325	1.20	45132
4	1.493	7095331	1.19	44125
5	1.472	7152345	1.22	45321
Average	1.487	7090444	1.20	44790
% RSD	0.58	0.67	1.08	1.27

The results of the proposed UPLC method's system suitability testing are presented in Table 4.3. The results demonstrate that the optimised UPLC technique satisfies these parameters within the permitted ranges in terms of USP tailing factor, USP theoretical plates, and% RSD.

PRECISION

By performing six independent assays of test samples against a recognised reference standard, the precision of the procedure was assessed, and the assay's percent relative standard deviation (RSD) was computed. In the same lab, various analysts, columns (Different lot of Waters Acquity BEH C18 [50 x 2.1 mm, 1.7 micron]), and equipment (Different UPLC system of Waters Acquity) were used to assess the method's intermediate precision. The rabeprazole sodium assay's percent RSDs during the method precision and the intermediate precision were, respectively, 1.3 and 1.1, confirming the method's high precision.

Table-4: Precision results

Injection	Method precisionAssay (%)	Intermediate precisionAssay (%)
1	99.1	98.1
2	98.0	98.5
3	98.3	99.1
4	98.1	100.8
5	101.1	100.5
6	100.3	99.3
Average	99.2	99.4
% RSD	1.3	1.1

LINEARITY

From LOQ to 300% of analyte concentration, 10 concentration levels of test solutions were made from stock solution (0.03, 0.5, 1.0, 5.0, 7.5, 10.0, 12.5, 15.0, 20.0, and 30.0 g/mL). Least squares linear regression technique was used to handle the peak area versus concentration data. Over the calibration ranges examined, i.e., 0.03 g/mL to 30 g/mL, the method's calibration plot was found to be linear, and the correlation coefficient found was > 0.999. This showed a strong link between the analyte concentrations and peak regions. YRabeprazole sodium = 705304x - 23709 (r2 = 0.9999) is the regression equation.

ACCURACY

At six different concentration levels (between 10% and 150%), namely 1.0, 3.0, 5.0, 7.5, 10.0, and 15.0 g/mL, the assay method's accuracy was assessed in triplicate. Recoveries were calculated as a percentage. The method's high degree of accuracy was demonstrated by the range of rabeprazole sodium percent recovery (98.0% to 101.5%) and the RSD values being within 1.3%.

Table :5- Recovery data

Amount added		% Recovery(n = 3)	% RSD(n = 3)
Level (%)	Concentration(in µg/mL)		

10	1.0	99.3	0.5
30	3.0	100.9	1.1
50	5.0	98.0	0.8
75	7.5	99.5	1.3
100	10.0	101.5	0.9
150	150	99.2	1.2

ROBUSTNESS

Experimental settings were purposefully changed, and system suitability characteristics were tested, in order to assess the robustness of the developed method. The mobile phase was flowing at a rate of 0.4 mL/min. In order to evaluate the impact of flow rate, it was increased from 0.35 mL/min to 0.45 mL/min by 0.05 units. The UV detection wavelength (280 nm) was modified by 3 nm, and the amount of acetonitrile in the mobile phase (35%) was altered by 3.5%. In order to evaluate the impact of pH fluctuation in the mobile phase, pH was changed between 7.2 and 7.6 by a factor of 0.2. Changes to the method's chromatographic parameters, such as theoretical plates, the tailing factor, and the percent RSD, were assessed. The assay values were between 98% and 101% in all of the purposefully different chromatographic settings, and no appreciable changes in the chromatographic parameters were found. This demonstrates how reliable the method that was created is.

Table 6 Robustness results

Variations	**USP tailing factor**	**USP theoretical plates**	**% RSD**	**% Assay**
Flow rate				
0.40 mL/min (original)	44790	1.20	0.67	99.1
0.35 mL/ min	46188	1.17	1.10	98.1
0.45 mL/min	42881	1.21	0.90	101.0
pH				
7.4 (original)	44790	1.20	0.67	99.1
7.2	43112	1.22	1.20	98.0

7.6	45121	1.19	1.25	98.5
Organic composition				
Acetonitrile 35 %, v/v) (original)	44790	1.20	0.67	99.1
Acetonitrile (31.5 %, v/v)	42111	1.25	0.90	100.5
Acetonitrile (38.5 %, v/v)	43121	1.21	1.10	98.9
Wavelength				
280 nm (Original)	44790	1.20	0.67	99.1
277 nm	44790	1.20	0.67	99.1
283 nm	44790	1.20	0.67	99.1

CONCLUSION

The mean recovery of six replicates using the devised method to analyse a commercial brand of the formulation of rabeprazole sodium tablets was 99.69% with a 0.52 RSD. The % recovery value shows that the excipients in the dose form are not interfering.

The mean release in acid (pH 1.2) and alkaline (pH 8.0 buffer) solutions was 2.8% (for an average of 6 tablets) and 97.2% (for an average of 6 tablets), respectively, when the devised approach was applied to withdrawn rabeprazole sodium tablet dissolving samples. The assay and dissolution test analyses were completed in less than 45 minutes, demonstrating the speed of the UPLC technology for analysis.

The new, isocratic RP-UPLC approach was found to be quick, straightforward, linear, accurate, precise, and robust. More than what was possible with traditional HPLC, the new approach is capable of providing faster elution and maintaining good separation. For regular examination in the pharmaceutical sectors, the short retention time of 1.49 min makes it possible to analyse a lot of samples quickly and affordably. The rabeprazole sodium tablet's dissolution investigation was successfully completed using the suggested methodology. It is appropriate for the quick and precise quality monitoring of sodium rabeprazole tablet formulations.

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