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Development and Validation of RP-HPLC Method for the Determination of Dexrabeprazole Sodium

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Abstract

A rapid and simple liquid chromatographic method was developed for the quantitative determination of dexrabeprazole sodium in the tablet dosage form. The reverse-phase chromatographic analysis was carried out by using a C-18 column. The acetonitrile-phosphate buffer mixture was used as the mobile phase. The obtained retention time was 4.33∓0.02 min. by using 50:50 (v:v) acetonitrile:phosphate buffer(pH 7) and 1.0 mL/min. flow rate. Quantification of the analyte was based on measuring the peaks areas at 272 nm. The analytical performance of the developed RP-HPLC method was validated with respect to accuracy, precision, linearity, stability, and robustness. The obtained linearity range was 77-143 mg/L and the correlation coefficient was 0.9989. The obtained LOD and LOQ values were 0.010 mg/L and 0.034 mg/L, respectively.

Keywords: Dexrabeprazole, RP-HPLC, validation

1. INTRODUCTION

Dexrabeprazole sodium (DEX) is R (+)-isomer of rabeprazole. Rabeprazole has been used in the treatment of gastroesophageal reflux disease by suppressing gastric acid secretion. It acts as a proton pump inhibitor of the H^+/K^+ ATPase enzyme [1,2]. Several methods were described for the analyses of the racemic mixture of rabeprazole in pharmaceutical formulations and plasma samples. HPLC techniques are the best methods due to their rapid, low cost, and selective properties. These techniques are very useful for the simultaneous determination of pharmaceutically active compounds and ingredients in drugs, biological fluids and tissues [3]. Kim et al. [4] used a chiral column. The stationary phase of the chiral column was modified with cellulose. A mixture of ethanol, hexane, and ethylenediamine solutions was used as a mobile phase. The developed HPLC method assayed rabeprazole enantiomers determination in commercial tablets. The reported LOQ value was and 0.03 µg/mL and the LOD value was 0.01 µg/mL. Similarly, Miura et al. [5] investigated quantitative enantiomers of rabeprazole and their metabolites determination in human plasma. A chiral column was used. The mobile phase consisted of acetonitrile and $NaClO_4$. The achieved LOQ was 5 ng/mL. Su et al. [6] proposed an SFC-MS method to determine

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enantiomers of rabeprazole in dog plasma. They used using a supercritical fluid compatible chiral column. The used mobile phase consists of CO_2 and methanol. The obtained linearity was in the range of 1–1000 ng/mL. Also, some studies are available using the drugs' name as dexrabeprazole. Shedpure et al. [7] developed a first-order derivative spectroscopic method to determine domperidone maleate and dexrabeprazole sodium in capsule and bulk forms. The reported LOQ and LOD values were 1.28 µg and 0.75 µg, respectively. Khadangale et al. [8] determined impurities in dexrabeprazole sodium with an RP-UPLC. A C18 column was used as a stationary phase. The developed method was based on a gradient program. A mixture of phosphate buffer and acetonitrile was used as the first mobile phase. The second mobile phase contained acetonitrile and methanol. The reported LOD was 0.0075 ppm and LOQ was 0.023 ppm for the determination of dexrabeprazole sodium. Chitlange et al. [9] investigated simultaneous determination of domperidone and dexrabeprazole in the pharmaceutical dosage form. They used RP-HPLC method with a C-18 column as a stationary phase. The used mobile phase was a mixture of potassium dihydrogen orthophosphate buffer and acetonitrile.

In this study, dexrabeprazole sodium was determined in single dosage tablet form by the RP-HPLC method. A C18 column was used in the method. The developed RP-HPLC method was optimized and validated with accuracy, precision, linearity, and robustness according to the International Conference on Harmonization (ICH) guidelines [10].

2. MATERIALS AND METHODS

The stock solution (100 mg/L) of DEX was prepared in 50 mL acetonitrile. The serial concentrations of the calibration standard solutions (77 - 143 mg/L) were prepared from the stock solution by dilution. A calibration graph was obtained by using peak areas of the DEX. The commercial pharmaceutical analysis was performed in drug tablets containing 10 mg DEX. 20 tablet forms of the drug were taken, then weighed and powdered. The sample solutions were prepared by weighting two tablets amount and dissolving them in acetonitrile. The obtained solutions were filtered with 0.45 µm membrane filter. The final solutions were diluted to concentration of 100 mg/L DEX.

A Shimadzu UV 2401PC UV-VIS spectrophotometer with a 1 nm slit width was used for the absorption measurements. Chromatography was performed with an HPLC system (Shimadzu, Japan) equipped with an automated sample injector, a pump, and a UV–Vis DAD detector. The used stationary phase was a reverse-phase C18 column (250 mm × 4.6 mm × 5 µm, GL Sciences) and the temperature of the column oven was fixed 25 °C. The isocratic mode was used with 1.0 mL/min flow rate and the sample injection volume was 10 µL. A mixture of acetonitrile and phosphate buffer (pH 7) (50:50 v/v) was used as the mobile phase that was freshly prepared and filtered with a 0.45 µm membrane filter. Data treatments, regressions and statistical analysis were performed using EXCEL software.

3. RESULTS AND DISCUSSION

3.1. Optimization of experimental conditions

The UV–Vis absorption of DEX was measured between 200 and 800 nm region to find maximum absorption wavelength. The maximum absorption band was observed at 272 nm. The optimum experimental conditions of RP-HPLC were determined by examining flow rate, mobile phase composition, detector wavelength, and sample injection volume. The tested mobile phase compositions were 50:50 (v/v), 70:30 (v/v), 80:20 (v/v) of acetonitrile:phosphate buffer(pH 7) and the flow rates were ranging from 0.8 to 1.5. The peak of DEX was obtained in a short time with high intensity in 50:50 (v/v) acetonitrile:phosphate buffer as the mobile phase (Figure 1) at 1.0 mL/min flow rate. The found retention time was 4.2 min. at these conditions. The system suitability parameters (retention time, RT; theoretical plate, N and tailing, T) were calculated by six replicate injections of 10 µL standard solution. The found RT, N, and T values were 4.323, 5532, and 1.169, respectively. The calibration curve was obtained by plotting peak

areas versus concentrations of DEX solutions (Figure 2). The used DEX concentrations were range from 77 to 143 mg/L. The calibration equation and statistical parameters are summarized in Table 1.

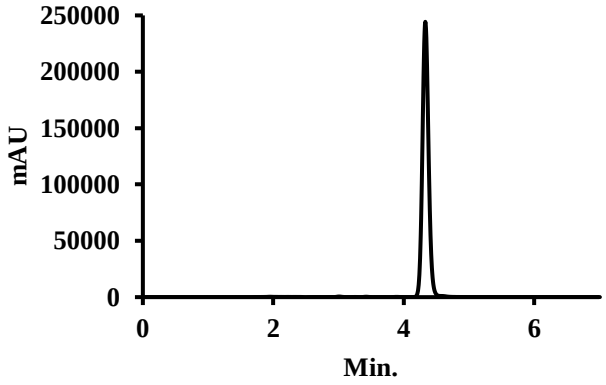

Figure 1 HPLC chromatogram of DEX (100 mg/L) at 272 nm

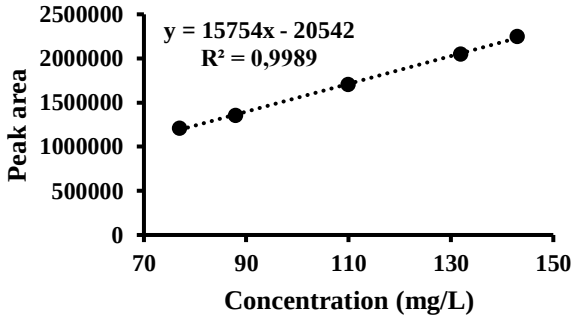

Figure 2 Calibration curve of DEX at 272 nm

Table 1 Statistical results of calibration curve

Method	RP-HPLC
λ (nm)	272
Regression equation	y=15753602.55x-20541.75
r	0.9989
SE(m)	303.70
SE(n)	34264.44
SE(r)	17034.23

r = Regression coefficient; SE(r) = Standard error of linear regression; SE(m) = Standard error of slope; SE(n) = Standard error of intercept.

3.2. Method validation

Linearity, precision, accuracy, solution stability, and robustness parameters were tested for the validation of the proposed method. The obtained linearity of the method was in the range of 77-143 mg/L. The calculated LOD and LOQ values were 0.010 mg/L and 0.034 mg/L, respectively. The method precision was performed with six replicates of 100 mg/L standard solution DEX. The intra-day and inter-day assays were carried out. The calculated standard deviations and relative standard deviations are shown in Table 2. Accuracy studies were carried out using standard solutions of 88 mg/L, 110 mg/L, and 132 mg/L DEX concentrations. The calculated recoveries and relative standard deviations are shown in Table 3. The standard solution (100 mg/L DEX) stability tests were carried out at room temperature (25 °C) for 24 hours and +4 °C for 30 days. No significant peak was observed in the chromatogram kept at room temperature (Figure 3a). Therefore, it can be stated that the standard solution of DEX could remain stable for 24 hours at room temperature. However, the degradation occurred in the other solution, which was kept at +4 °C after 30 days. New peaks were observed in the chromatogram (Figure 3b). The robustness of the proposed method was investigated by changing chromatographic conditions such as mobile phase compositions, column oven temperature, and flow rate. The mobile phase composition was changed from 50:50 (ACN : phosphate buffer, v:v) to 44:56 (v:v) and 36:64 (v:v). The column oven temperature was adjusted to 20.5, 22.5, and 25 °C and the flow rate was set to 0.9 mL/min., 1.0 mL/min. and 1.1 mL/min. The obtained retention times under the examined conditions are shown in Table 4.

Table 2 Results of intra-day and inter-day assays

Concentration (mg/L)	**Intra-day (mg/L)**	**Inter-day (mg/L)**
100	99	99
100	100	99
100	100	99
100	100	99
100	99	100
100	100	99
Mean	99.67	99.17
SD	0.471	0.373
RSD	0.473	0.376

SD = Standard deviation; RSD = Relative standard deviation

Table 3 Recoveries of DEX

Added mg/L	**Found mg/L**	**% Recovery**
0.088	0.090	102.27
0.088	0.089	101.14
0.088	0.089	101.14
0.110	0.111	100.91
0.110	0.109	99.09
0.110	0.111	100.91

0.132	0.131	99.24
0.132	0.132	100.00
0.132	0.134	101.52
	Mean:	100.69
	SD	1.05
	RSD	1.04

SD = Standard deviation; RSD = Relative standard deviation

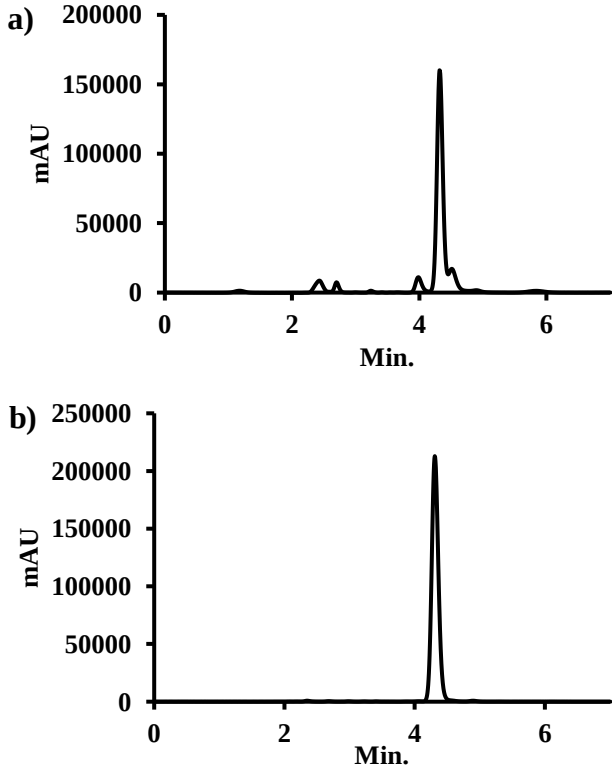

Figure 3 HPLC chromatograms of solution kept in room temperature for 1 day (a), in +4 °C for 30 days (b)

Table 4 The retention times at different chromatographic conditions

Mobile phase (ACN:buffer) v:v	Flow rate mL/min	Temperature °C	RT min
50:50	1.0	25.0	4.33
44:56	1.0	25.0	4.34
36:64	1.0	25.0	4.21
50:50	0.9	25.0	4.36
50:50	1.1	25.0	4.12
50:50	1.0	20.5	4.31
50:50	1.0	22.5	4.32
		Mean	4.28
		SD	0.08
		RSD	1.88

SD = Standard deviation; RSD = Relative standard deviation

3.3. Analyses of Pharmaceutical Tablet Samples

The optimized HPLC method was evaluated in the commercial tablets' assay to determine DEX in drug form. Six replicate determinations were carried out. The obtained results (Table 5) were in good agreement with the label claims. The recovery percentages were range from 90% to 100%.

Table 5 Analysis results of DEX in pharmaceutical tablets

Claimed value mg	Found mg
10	9.951
	10.042
	10.048
	9.971
	10.049
	9.939
Mean	10.000
SD	0.047
RSD	0.473

SD = Standard deviation; RSD = Relative standard deviation

4. CONCLUSIONS

A simple and rapid RP-HPLC procedure was developed for DEX determination in synthetic solution and commercial tablet form. The proposed chromatographic method was validated with respect to linearity, robustness, precision, and accuracy as per ICH guidelines. The calibration curve was obtained in 77–143 mg/L with a correlation coefficient of 0.9989. The calculated LOD and LOQ values were 0.010 mg/L and 0.034 mg/L, respectively. The calculated RSDs of all examined parameters were less than 2.00%. The optimized method was also successfully applied to the tablet form.

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The Declaration of Conflict of Interest/ Common Interest

No conflict of interest or common interest has been declared by the authors.

Authors' Contribution

The first author contributed 40%, the second author 40%, the third author 20%.

The Declaration of Ethics Committee Approval

This study does not require ethics committee permission or any special permission.

The Declaration of Research and Publication Ethics

The authors of the paper declare that they comply with the scientific, ethical and quotation rules of SAUJS in all processes of the paper and that they do not make any falsification on the data collected. In addition, they declare that Sakarya University Journal of Science and its editorial board have no responsibility for any ethical violations that may be encountered and that this study has not been evaluated in any academic publication environment other than Sakarya University Journal of Science.

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