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A validated RP-HPLC method for simultaneous estimation of Dexrabeprazole and Domperidone in pharmaceutical dosage form

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ABSTRACT

A validated reverse phase high performance liquid chromatography method has been developed for the simultaneous determination of Dexrabeprazole and Domperidone in combined dosage form. Chromatography was carried out on a C-18 column (4.6 mm × 250 mm, 5 µm) using Acetonitrile: 0.025 M potassium dihydrogen orthophosphate buffer (pH adjusted to 5.1 with triethylamine) in the ratio of 30:70 (v/v) as the mobile phase at a flow rate of 1.0 mL/min and eluents were monitored at 284 nm. The calibration curves were linear over the range of 10 - 50 µg/mL for Dexrabeprazole and 20 – 100 µg/mL for Domperidone. The average retention time of Dexrabeprazole and Domperidone was found to be 9.28 min and 6.66 min respectively. The results of the analysis have been validated statistically and by recovery studies.

Key words: Dexrabeprazole sodium, Domperidone, RP-HPLC, Validation.

INTRODUCTION

Chemically, Dexrabeprazole sodium (DEX) is R (+)-isomer of rabeprazole (2-[[[4-(3-methoxypropoxy)-3-methyl-2-pyridinyl]-methyl] sulfinyl] 1H-benzimidazole). It is a proton pump inhibitor that suppresses gastric acid secretion[1-2]. Domperidone (DOM) is 5-chloro-1-[1-[3-(2-oxo-2,3-dihydro-1H-benzimidazol-1-yl)propyl]-piperidin-4-yl]-1,3-dihydro-2H-benzimi -dazol-2-one. It is a dopamine receptor (D2) antagonist which is used as antiemetic drug and is official in British Pharmacopoeia[3]. Domperidone alone or in combination with other drugs is reported to be estimated by HPLC [4-6], Spectrophotometry[7-10] , HPTLC [11] , LC-MS [12] Whereas no analytical method is reported for analysis of dexrabeprazole.

The present work describes a method for determination of DEX and DOM in capsules using RP-HPLC. The method is simple and requires less time for routine analysis. The proposed method was optimized & validated as per ICH guidelines [13-14].

MATERIALS AND METHODS

Materials

Standard gift samples of DEX and DOM were provided by Emcure pharmaceuticals Ltd, Pune. Combined dose capsule formulation R-Pure D (10 mg of DEX and 30mg of DOM, Manufactured by Emcure), were purchased from local market. All chemicals and reagents used were of HPLC grade.

Instrumentation

Lachrom HPLC quaternary gradient system (Make: Merck-Hitachi) with L-7100 double reciprocating pump and L-7400 UV detector was used. Chromatographic data was acquired using Winchrome software. A reversed-phase Thermo C18 column (250 × 4.6 mm i.d., particle size 5 µm) was used for separation.

Chromatographic conditions

Thermo C18 column (4.6 mm i.d. × 250 mm) was used as stationary phase. Acetonitrile: 0.025 M potassium dihydrogen orthophosphate buffer (pH adjusted to 5.1 with triethylamine) in the ratio of 30:70 % v/v was used as mobile phase and was filtered before use through 0.45 µ membrane filter. A constant flow of 1.0 ml/min was maintained throughout the analysis. Detection was carried out using UV detector at 284 nm. To ascertain the suitability of the proposed chromatographic conditions, system suitability tests were carried out and the results are shown in Table 1. Chromatogram of standard solution containing DEX and DOM is shown in Fig. 1.

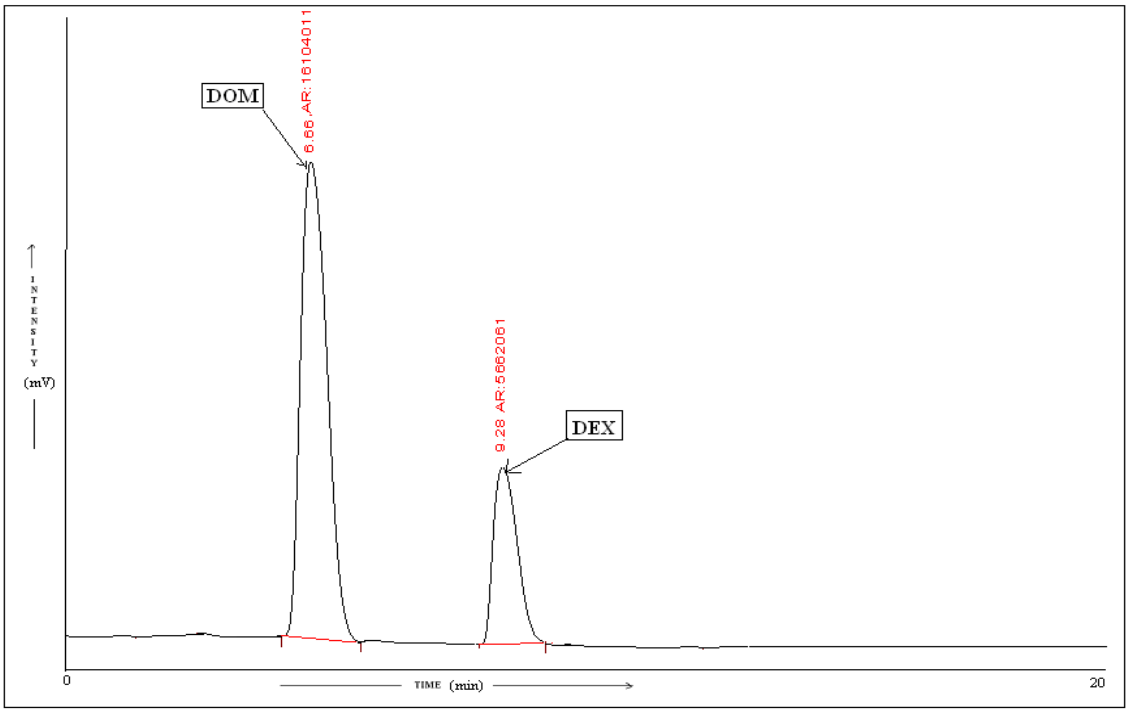
Table 1: System Suitability Parameters

System Suitability Parameter	Component	
	DEX	DOM
Retention times (RT in min)	9.28	6.66
Theoretical plates (N)	2468.83	2149.65
Tailing factor (AS)	0.98	1.1
Resolution (RS)	2.1432	

Preparation of standard calibration curves (Linearity)

Standard stock solution of DEX and DOM were prepared by transferring 10 mg of DEX and 20 mg DOM in 100ml volumetric flask. Sufficient amount of mobile phase was added, sonicated and remaining volume was made up to the mark with mobile phase. Aliquots of standard stock solution were appropriately diluted with mobile phase to obtain concentration range of 10-50 µg/ml for DEX and 20-100 µg/ml for DOM. The diluted standard solutions with varying concentration were injected (in triplicate) into the HPLC system separately and chromatographed under above mentioned chromatographic conditions. Chromatographic peaks were recorded at 284 nm using UV detector. The calibration curves of mean peak area versus concentration were plotted.

Figure 1: Typical Chromatogram of DEX and DOM



Analysis of Capsule formulation

For the estimation of drugs in the commercial formulations, twenty capsules were uncapped, weighed and average weight was calculated. The powder equivalent to 10 mg DEX and 30 mg of DOM was transferred to 100 ml volumetric flask; 50 ml portion of mobile phase was added and sonicated for 20 min. and then volume was made up to the mark with mobile phase. The resulting solution was mixed and filtered through Whatmann filter paper and filtrate was appropriately diluted to get approximate concentration of 16 µg/ml of DEX and 48 µg/ml of DOM. The diluted solutions were filtered through 0.20 µ filter. From the filtrate, 20 µl was injected in to the column and chromatographed under above mentioned chromatographic conditions. Each sample solution was injected and chromatographed in triplicate. Six such samples were prepared and analyzed. Content of DEX and DOM in capsule was calculated by comparing mean peak area of sample with that of the standard. Results of analysis of capsule formulation are shown in Table No. 2.

Table 2: Results of Analysis of Capsule Formulation

Component	Label claim * (mg/capsule)	Amount found * (mg/capsule)	Percent label claim*	S.D.	C.V.
DEX	10	9.96	99.58	0.6902	0.6872
DOM	30	30.13	100.43	0.5879	0.5904

**Average of six determinations, SD-Standard Deviation, CV- Coefficient of Variation.*

Method Validation

Accuracy

To ascertain the accuracy of the proposed method recovery studies were carried out by standard addition method, adding known amount of each drug to the preanalysed capsule powder, at three levels 80 %, 100 % and 120 % of the label claim. Recovery studies were carried out in triplicate at each level. The results of recovery studies were expressed as percent recovery and are shown in Table No. 3

Table 3: Result of recovery studies

Level of Recovery	Component	Amt. Taken (mg)	Amt. of pure drug added (mg)	% recovery* (mg)	S.D.	C.V.
80 %	DEX	10	8	99.15	0.4500	0.4539
	DOM	30	24	100.92	0.2219	0.2199
100 %	DEX	10	10	99.62	0.2987	0.2998
	DOM	30	30	100.41	0.1358	0.1352
120 %	DEX	10	12	99.36	0.2691	0.6150
	DOM	30	36	100.3	0.2683	0.6190

**Average of three determinations*

Precision

Intra-day precision was determined by analyzing the capsule samples at three different time intervals on the same day and for inter-day precision capsule samples were analyzed on three different days. Standard deviation for intra-day and inter-day assay precision was calculated. Results of precision studies are shown in Table No. 4.

Table 4: Result of Precision studies

Parameters	Component	% Estimation*	S.D.	C.V.
Intra-day	DEX	100.18	0.8886	0.8870
	DOM	99.82	1.1000	1.1020
Inter-day	DEX	99.96	0.6040	0.6042
	DOM	100.02	0.8768	0.8766

**Average of six determinations*

Limit of detection (LOD) and Limit of quantitation (LOQ)

LOD and LOQ for both the drugs were calculated by using the values of slopes and intercepts of the calibration curves.

Robustness

Robustness of the proposed method was ascertained by deliberately changing the chromatographic conditions such as change in flow rate of the mobile phase (± 0.1 mL/min), change in composition of the mobile phase (± 1 ml) and change in pH of the buffer solution used in mobile phase. Effect of change in chromatographic parameters on resolution and tailing factor of peak was studied.

RESULTS AND DISCUSSION

The proposed chromatographic system was found suitable for effective separation and quantitation of DEX (RT-9.28 min) and DOM (RT-6.66 min) with good resolution, peak shapes and minimal tailing. The peak areas of the drugs were reproducible as indicated by low coefficient of variance indicating the repeatability of the proposed method. Both the drugs were found to give linear detector response in the concentration range under study with correlation coefficient of 0.9963 and 0.9975 for DEX and DOM, respectively. The sample recoveries from the formulation were in good agreement with their respective label claim indicating that there is no interference from the capsule excipients. The method exhibited good selectivity and sensitivity. Percent recoveries for DEX and DOM were 99.38 % and 100.54 %, respectively indicating accuracy of the proposed method. %RSD for capsule analysis, recovery studies and intra-day & inter-day precision studies is less than 2. LOD and LOQ were found to be 0.1368 & 0.4144 for DEX and 0.3378 & 1.0237 for DOM, respectively. The results of robustness study also indicated that the method is robust and is unaffected by small deliberate variations in the method parameters.

CONCLUSION

The proposed method was validated as per ICH guidelines. The standard deviation and % RSD calculated for the proposed method is low, indicating high degree of precision of the method. The results of the recovery studies performed show the high degree of accuracy of the proposed method.

Hence, it can be concluded that the developed RP-HPLC method is accurate, precise and selective and can be employed successfully for the estimation of DEX and DOM in bulk and marketed formulation.

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