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Research Article

Simultaneous Spectrophotometric Estimation Of Dexrabeprazole And Domperidone In Capsule Dosage Form

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ABSTRACT

Three UV spectrophotometric methods for the simultaneous determination of dexrabeprazole (DEXRAB), and domperidone (DOM), in capsules were developed in the present work. Method I is simultaneous equation method, wavelength selected are 258.5 nm (λ_{max} for dexrabeprazole) and 286.5 nm (λ_{max} for domperidone). Method II involves multicomponent mode of analysis, wavelength selected are 258.5 nm (λ_{max} for dexrabeprazole) and 286.5 nm (λ_{max} for domperidone). Method III is area under curve method, wavelength range selected are 263.5-253.5 nm for dexrabeprazole and 291.5-281.5 nm for domperidone respectively. All the methods were found linear between 5-35 µg/ml for dexrabeprazole and 10-70 µg/ml for domperidone. The accuracy and precision of the methods were determined and validated stastically which showed no significant difference between the results obtained by the three methods. The proposed methods are highly sensitive, precise and accurate and therefore can be used for its intended purpose.

KEY WORDS: Dexrabeprazole, domperidone, simultaneous equation method, multicomponent mode of analysis, area under curve method .

INTRODUCTION

Chemically, Dexrabeprazole sodium (DEXRAB) 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 by specific inhibition of the gastric H+ K+ ATPase enzyme system at the secretory surface of the gastric parietal cell.[1,2]. Chemically, 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-benzimidazol-2-one. It is a dopamine receptor (D2) antagonist which is used as antiemetic drug and is official in British Pharmacopeia .It increases spontaneous gastric activity and antagonizes dopamine inhibition of gastric emptying[3] .

Domperidone alone or in combination with other drugs is reported to be estimated by HPLC [4-11] , LC [12] , Spectrophotometry [13-16] , HPTLC [17] , LC-MS [18] Whereas no analytical method is reported for analysis of dexrabeprazole.

Since no spectrophotometric methods are reported for the simultaneous estimation of dexrabeprazole & domperidone in combination therefore, in the present work, a successful attempt has been made to estimate both these drugs simultaneously by three simple UV-spectrophotometric methods (Simultaneous equation method, Multicomponent mode of analysis [19], Area under curve method [20].The proposed methods were optimized & validated as per ICH guidelines [21].

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MATERIAL AND METHODS

Instrument: A double-beam Shimadzu UV- Visible spectrophotometer, 1700 Pharmaspec, with spectral bandwidth of 2 nm, wavelength accuracy ± 0.5 nm and a pair of 1-cm matched quartz cells was used to measure absorbance of solution.

Material: Standard gift samples of dexrabeprazole and domperidone were provided by Emcure pharmaceuticals Ltd, Pune. Combined dose capsule formulation containing dexrabeprazole and domperidone (R-Pure D, 10 mg of dexrabeprazole and 30mg of domperidone, Manufactured by Emcure), were purchased from local market.

Solvent used: Methanolic HCL (0.1 N) was used as solvent.

Preparation of stock solution: Accurately weighed quantity of dexrabeprazole (5 mg) and domperidone (5 mg) were transferred to two separate 50.0 ml volumetric flask. Then diluted to the mark with the methanolic HCL (Stock solution 100 µg/ml).

Method I: Simultaneous equation method.

For the selection of analytical wavelength, solutions of dexrabeprazole (10µg/ml) and domperidone (30 µg/ml) were prepared separately by appropriate dilution of standard stock solution (100 µg/ml) with methanolic HCL (0.1N) and scanned in the spectrum mode from 400 nm to 200 nm. Dexrabeprazole has λ_{max} of 258.5 nm

Table No – 1: Result of marketed formulation analysis.

Method	Drug	Label Claim (mg/capsule)	Amount of drug estimated (mg/ capsule)	% of label claim estimated ± S.D*
I	DEXRAB	10	10.04	100.15 ± 0.34
	DOM	30	30.12	100.36 ± 0.35
II	DEXRAB	10	10.05	100.53 ± 0.66
	DOM	30	30.26	100.85 ± 0.77
III	DEXRAB	10	10.03	100.27 ± 0.18
	DOM	30	29.96	99.87 ± 0.38

* Mean of six estimation. DEXRAB= Dexrabeprazole, DOM= Domperidone.

and domperidone has λ_{max} of 286.5 nm. Standard solutions were prepared having concentrations 5-35 µg/ml for dexrabeprazole and 10-70 µg/ml for domperidone. The absorbances of these standard solutions were measured at selected wavelength and calibration curves were plotted. Two simultaneous equations (in two variables C_1 and C_2) were formed using absorptivity coefficient values.

$$A_1=(0.03666)C_1+(0.00294)C_2 \quad \ldots(1)$$

$$A_2=(0.02249)C_1+(0.03512)C_2 \quad \ldots(2)$$

Where C_1 and C_2 are the concentrations of dexrabeprazole and domperidone measured in µg/ml, in sample solutions. A_1 and A_2 are the absorbances of mixture at selected wavelengths i.e., 258.5 nm and 286.5 nm.

By applying the Cramer's rule to equation 1 and 2, the concentration C_{DEXRAB} and C_{DOM}, can be obtained as follows,

$$C_{DEXRAB} = \frac{A_2\,(0.00294) - A_1\,(0.03512)}{-\ 0.0012213} \quad \ldots (3)$$

$$C_{DOM} = \frac{A_1\,(0.02249) - A_2\,(0.03666)}{-0.0012213} \quad \ldots(4)$$

Method II: Multicomponent mode of analysis.

In this method, six mixed standard solutions with concentration of dexrabeprazole and domperidone in the ratio of 10:30 µg/ml were prepared in methanolic HCL (0.1N). All the standard solutions were scanned over the range of 400-200 nm, in the multicomponent mode, using two working wavelength 258.5 nm (λ_{max} of dexrabeprazole) and 286.5nm (λ_{max} of domperidone). The data from these scans was used to determine the concentrations of two drugs in capsule sample solutions.

Method III: Area under curve method.

From the overlain spectra of both drugs, area under the curve in the range of 263.5-253.5 nm (for dexrabeprazole) and 291.5-281.5 nm (for domperidone) were selected for the analysis (Fig.1). The calibration curves for dexrabeprazole and domperidone were plotted in the concentration range of 5-35 µg/ml and 10-70 µg/ml, respectively. The 'X' values for both the drugs were determined at the selected AUC range. The 'X' value is the ratio of area under the curve at selected wavelength ranges with the concentration of component in g/lit. These 'X' values were the mean of six determinations. A set of two simultaneous equations obtained by using mean 'X' values are given below.

$$A_1= (0.3575)\ C_1 + (0.03249)\ C_2 (\text{at } \lambda_{263.5\text{-}253.5}\text{nm}) \ldots(5)$$

$$A_2= (0.2263)\ C_1 + (0.3265)\ C_2\ (\text{at } \lambda_{291.5\text{-}281.5}\text{ nm}) \ldots (6)$$

Where A1 and A_2 were area under curve of sample at the wavelength range 263.5-253.5 nm and 291.5-281.5 nm, respectively. 0.3575 and 0.2263 were 'X 'values of dexrabeprazole at wavelength range 263.5-253.5 nm and 291.5-281.5 nm respectively. Similarly 0.03249and 0.3265 were 'X 'values of domperidone at wavelength range 263.5-253.5 nm and 291.5-281.5 nm, respectively. The concentration of dexrabeprazole and domperidone in sample was determined by using the equations (5) and (6).

Assay of capsule formulation by method I, II & III.

For the estimation of drugs in the commercial formulations, twenty capsules were weighed and average weight was calculated. The powder equivalent to 5 mg dexrabeprazole and 15 mg of domperidone was transferred to 50.0 ml volumetric flask containing 30 ml of methanolic HCL (0.1N) and sonicated for 20 min. The volume was then made up to the mark with methanolic HCL (0.1N). The resulting solution was appropriately diluted to get approximate concentration of 10 µg/ml of dexrabeprazole and 30 µg/ml of domperidone. In method I, the concentration of both dexrabeprazole and domperidone were determined by measuring absorbances of sample solutions at 258.5 nm (λ_{max} of dexrabeprazole) and 286.5nm (λ_{max} of domperidone) using equations (3) and (4). For method II, the same capsule sample solutions were subjected to analysis in the multicomponent mode of instrument, the concentration of both dexrabeprazole and domperidone determined by analysis of spectral data of the sample solution with reference to the mixed standards at 258.5 nm (λ_{max} of dexrabeprazole) and 286.5 nm (λ_{max} of domperidone). For method III, the concentration of both dexrabeprazole and domperidone were determined by measuring area under curve in the range of 263.5-253.5 nm (for dexrabeprazole) and 291.5-281.5 nm (for domperidone) and values were substituted in equations (5) and (6) to obtain concentration of both the drugs. Results of tablet analysis are shown in Table No.1

Validation

The proposed methods were validated as per ICH guidelines.

Accuracy

Table 2: Result of recovery studies

Level of recovery	Drug	Amt. of drug taken µg/ml	Amt. of Std. Drug Added µg/ml	Method I		Method II		Method III	
				Recovery (%)*	± S.D*	Recovery (%)*	± S.D*	Recovery (%)*	± S.D*
80	DEXRAB	10	8	100.50	0.055	100.78	0.241	99.78	0.092
	DOM	30	24	100.44	0.035	100.33	0.360	100.09	0.026
100	DEXRAB	10	10	100.35	0.087	100.35	0.409	100.13	0.095
	DOM	30	30	100.20	0.214	100.18	0.137	99.88	0.006
120	DEXRAB	10	12	100.23	0.381	100.2	0.295	100.12	0.029
	DOM	30	36	100.29	0.131	100.01	0.227	100.37	0.02

* Mean of three estimation. DEXRAB= Dexrabeprazole, DOM= Domperidone.

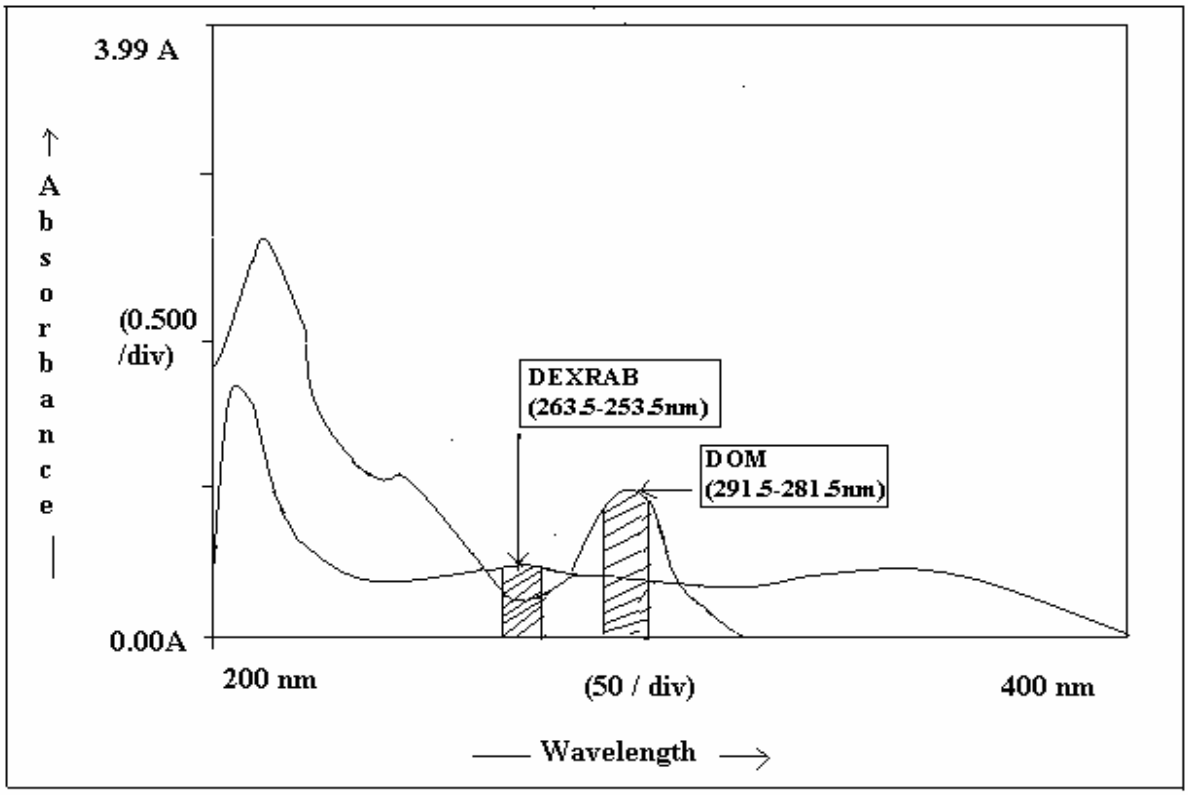

Fig.1: Overlain spectra of Dexrabeprazole and Domperidone

To ascertain the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% &120%). The results of recovery studies were satisfactory and are presented in Table No.2.

Linearity

The linearity of measurement was evaluated by analyzing different concentration of the standard solution of dexrabeprazole and domperidone. For all three methods, the Beer- Lambert's concentration range was found to be 5-35 µg/ml and 10-70 µg/ml for dexrabeprazole and domperidone respectively.

Precision

The reproducibility of the proposed methods were determined by performing capsule assay at different time intervals on same day (Intra-day assay precision) and on three different days (Inter-day assay precision).

CONCLUSION

All The three methods were validated as per ICH guidelines. The standard deviation and % RSD calculated for the proposed methods are low, indicating high degree of precision of the methods. The results of the recovery studies performed show the high degree of accuracy of the proposed methods.

Hence, it can be concluded that the developed spectrophotometric methods are accurate, precise and selective and can be employed successfully for the estimation of dexrabeprazole and domperidone in marketed formulation.

RESULT AND DISCUSSION

For all the methods linearity was observed in the concentration range of 5-35 µg/ml and 10-70µg/ml for dexrabeprazole and domperidone, respectively. Commercial formulations containing dexrabeprazole and domperidone were analyzed by the proposed methods. Six replicate analysis of formulation were carried out and the mean assay values were found in the range of 99.87 to 100.85 % shown in table no.1 .The proposed methods were validated as per the ICH guidelines. The accuracy of the proposed method was determined by

recovery studies. Pure dexrabeprazole and domperidone was added to the preanalysed capsule powder at three levels viz 80, 100, 120 %. Three replicate analyses were carried out at each level. The mean percent recovery was found in the range of 99.78 to 100.37 % for all the methods shown in table no.2. Precision is calculated as interday and intraday variations for both the drugs. Percent relative standard deviations for estimation of dexrabeprazole and domperidone under intraday and interday variations were found to be less than 1.

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