Simultaneous Spectrophotometric Estimation Of Dexrabeprazole And Domperidone In Capsule Dosage Form


Padmashri Dr.D.Y. Patil Institute of Pharmaceutical sciences and Research
Sant Tukaram Nagar, Pimpri, Pune-411018, Maharashtra, India.

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-benimidazole). 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].

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 from 400 nm to 200 nm. Dexrabeprazole has λ_{max} of 258.5 nm.
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 (λmax of dexrabeprazole) and 286.5 nm (λmax of domperidone). For method II, the same capsule sample solutions were subjected to analysis in the multicomponent mode of instrument, the concentrations of both dexrabeprazole and domperidone were 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, twenties 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 (λmax of dexrabeprazole) and 286.5 nm (λmax of domperidone). 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 were determined by using the equations (5) and (6).

**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 (λmax of dexrabeprazole) and 286.5 nm (λmax 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.

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

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

Where \( A_1 \) 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 0.03249 and 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).

**Validation**

The proposed methods were validated as per ICH guidelines.

**Accuracy**
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

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**Table 2: Result of recovery studies**

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

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

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![Fig.1: Overlain spectra of Dexrabeprazole and Domperidone](image)

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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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REFERENCES