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Research Article

SPECTROPHOTOMETRIC DETERMINATION OF DEXRABEPRAZOLE SODIUM IN BULK & TABLET DOSAGE FORM BY FIRST ORDER DERIVATIVE SPECTROSCOPY AND AREA UNDER THE CURVE

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Abstract

Dexrabeprazole sodium (DEX), 2-{[4-(3-methoxy propoxy)-3-methylpyridin-2-yl]methyl sulfinyl}-1H-benzimidazole is a proton pump inhibitor. The drug is commercially available as tablets for oral administration. In the present work, two rapid, economical and accurate methods have been developed for the estimation of Dexrabeprazole sodium (DEX) in tablet dosage form. Method A is first order derivative spectroscopy where derivative amplitudes were calculated by considering one minima and one maxima of the curve. Method B is area under the curve in which wavelength range 278-303nm was selected. Linearity was observed in the concentration range 6-36 µg/ml for both the methods (r^2=0.9994 for method A and r^2=0.9991for method B). The % assay for the marketed formulation by first order derivative and area under the curve was found to be 99.75 % and 100.03% respectively. The method was validated with respect to linearity, precision and accuracy studies. Recovery studies for first order derivative spectroscopy and area under the curve was found to be in the range of 100.08%-102.08% and 98.25% - 100.75% respectively. Both the methods were found to be simple, precise and accurate and can be employed for routine quality control analysis of dexrabeprazole sodium in bulk as well as from its dosage form.

Keywords: Area under the curve, Dexrabeprazole sodium, First order derivative spectroscopy and UV spectrophotometery.

Introduction: Dexrabeprazole sodium (DEX) is chemically 2-{[4-(3-methoxy propoxy)-3-methylpyridin-2-yl]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]

Literature survey reveals one spectrophotometric method[2] and one RP-HPLC method[3] have been reported for DEX in combined dosage form. No analytical method is available for estimation of DEX in single dosage form. Therefore, in the present work an attempt has been made to estimate Dexrabeprazole sodium (DEX) in tablet dosage form by UV spectrophotometric methods which are simple, economical and rapid. The proposed methods were optimized and validated as per ICH guidelines

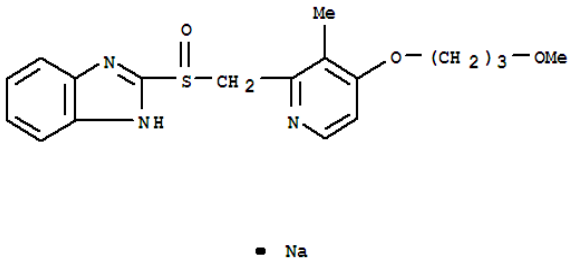

Fig 1: 2-{[4-(3-methoxy propoxy)-3-methylpyridin-2-yl]methyl sulfinyl}-1H-benzimidazole

Material and Methods:

Instrumentation: For the present study JASCO double beam UV/Visible spectrophotometer (Model V-630) was used with slit width fixed at 1.5nm ,equipped with spectra manager software (Version 1.5).A pair of 1-cm matched quartz cells were used to measure the absorbance of solution. The samples were weighed on electronic analytical balance (Contech Model CB-50).

Table: Instruments.

Name	Model	Manufacture
UV/Visible spectrophotometer	V-630	Jasco
Electronic analytical balance	CB-50	Contech

Materials: Gift sample of Dexrabeprazole sodium was provided by Emcure Pharmaceuticals Limited, Pune,

India. The pharmaceutical dosage form used in this study was Dexpure tablets (Emcure Pvt. Limited). Each enteric coated tablet contains 10mg Dexrabeprazole sodium.

Solvent: Methanol Spectroscopic grade (Thomas Baker), 0.1N NaOH.

Preparation of stock solutions: Standard stock solution of Dexrabeprazole sodium was prepared by dissolving 10 mg of DEX in methanol in 100ml volumetric flask. Final volume was made up to 100ml with methanol to get working standard solution containing 100µg/ml of DEX and further dilutions were made by using 0.1N NaOH.

Method:

First Order Derivative method [4] :

In this method, standard solution of DEX was scanned in the spectrum mode from 400 nm to 200 nm and the absorption spectra thus obtained were derivatized to first order. First order derivative spectra were selected for the analysis of drug. First order derivative spectra of drug [Fig. 1], showed λmaxima = 305 nm and λminima = 280 nm and amplitude difference was measured for the respective concentration of standard and was plotted against concentration and regression equation was calculated. The concentration range of 6-36 µg/ml for DEX was chosen for the derivative analysis [Fig. 2]. The equation obtained to determine concentrations of DEX is as follows.

C_{DEX} = dA/dλ – intercept (C)/slope (m) …[I]

Area Under the Curve method[5]:

For the selection of analytical wavelength standard solutions of DEX were prepared and series of dilutions of standard solutions of DEX were prepared by using 0.1N NaOH and were scanned from 400 to 200 nm [Fig. 3]. From the spectra of drug obtained after scanning of standard solution of DEX, area under the curve in the range of 278-303 nm was selected for the analysis. The calibration curve was plotted with concentration v/s area under the curve and regression equation was calculated.[Fig. 4].

Analysis of tablet formulation:

For the estimation of drug in the commercial formulations, twenty tablets each containing 10 mg of DEX were weighed and average weight was calculated. The tablets were crushed and powdered in glass mortar. For the

analysis of drugs, quantity of powder equivalent to 10 mg of DEX was transferred to 100 ml volumetric flasks and dissolved in sufficient quantity of methanol. It was sonicated for 40mins and volume was made up to obtain a stock solution of 10 μg/ml of DEX. This solution was then filtered through whatmann filter paper # 42. Further dilutions were made using 0.1N NaOH to get required concentration. In first order derivative method, amplitude difference was calculated by measuring difference between absorbance maxima at 305nm and minima at 280nm (i.e. $dA/d\lambda$) and in area under the curve, wavelength selection was done in the range of 278nm to 303nm. Results of tablet analysis are shown in Table No. 1. The assay procedure was repeated six times (n=6).

Validation:

The method was validated according to ICH guidelines to study linearity, accuracy and precision.[5]

Linearity:

The linearity of measurement was evaluated by analyzing different concentrations of the standard solution of DEX. For both the methods, the Beers law was obeyed in the concentration range 6-36 μg/ml. The correlation coefficient for method A was found to be 0.9994 and for method B was found to be 0.9991.

Accuracy (Recovery studies):

To ascertain the accuracy of proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% and 120%). Percent recovery for first order derivative spectroscopy and area under the curve was found to be in the range of 100.08% – 102.08% and 98.25% – 100.75% respectively [Table No.2 and 3].

Precision:

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

Limit of detection and limit of quantitation:

The LOD and LOQ were separately determined based on calibration curve. The slope and the y intercept of the linearity plot were determined. For each of the six replicate determinations the residual standard deviation

(σ) of the y intercepts of the regression line was computed. From these values LOD and LOQ were determined on the basis of response and slope of the regression equation. The results are given in table no.4.

LOD= 3.3σ/ slope

LOQ=10σ/slope

Results and Discussion:

Under experimental conditions described, linearity, accuracy studies and precision were performed. In both the methods linearity was observed in the concentration range of 6-36µg/ml and correlation coefficient for method A was found to be 0.9994 and for method B was found to be 0.9991. The results of commercial tablet formulation are presented in Table 1. Results of accuracy studies for first order derivative spectroscopy and area under the curve are presented in Table 3 and 4 respectively. S.D. and R.S.D. for six determinations of tablet sample, was found to be less than 2.0 indicating the precision of DEX. Hence, it can be concluded that the developed spectrophotometric methods are accurate, precise and can be employed successfully for the estimation of DEX in bulk and formulation.

Table No – 1: Result of marketed formulation analysis:

Method	Label claim	% Label Claim*(Mean±SD)	%RSD
First order Derivative method	**DEX 10mg**	**99.75 ± 0.0202**	**1.37**
Area under the curve	**DEX 10mg**	**100.03 ± 0.0964**	**1.48**

*Average of six determinations

Table No – 2: Results of recovery studies (First order derivative spectroscopy):

Level Recovery (%)	Drug	Conc. Of Drug in µg/ml		Method *		
		Drug taken	Std drug added	%recovery	SD	%RSD
80		**10**	**8**	**101.62**	**0.0098**	**1.28**
100	**DEX**	**10**	**10**	**100.08**	**0.0129**	**1.51**
120		**10**	**12**	**102.08**	**0.0125**	**1.32**

* Average of six determination

Table No – 3: Result of recovery studies (Area under the curve):

Level Recovery	Drug	Conc. Of Drug in µg/ml		Method *		
		Drug taken	Std drug added	%recovery	SD	%RSD
80	DEX	10	8	98.25	0.0621	1.59
100		10	10	99.60	0.0660	1.5
120		10	12	100.75	0.0664	1.35

*Average of six determinations

Table no. 4: LOD and LOQ of DEX and DOM.

Parameter	DEX
Limit of detection (µg)	2.16
Limit of quantitation (µg)	3.56

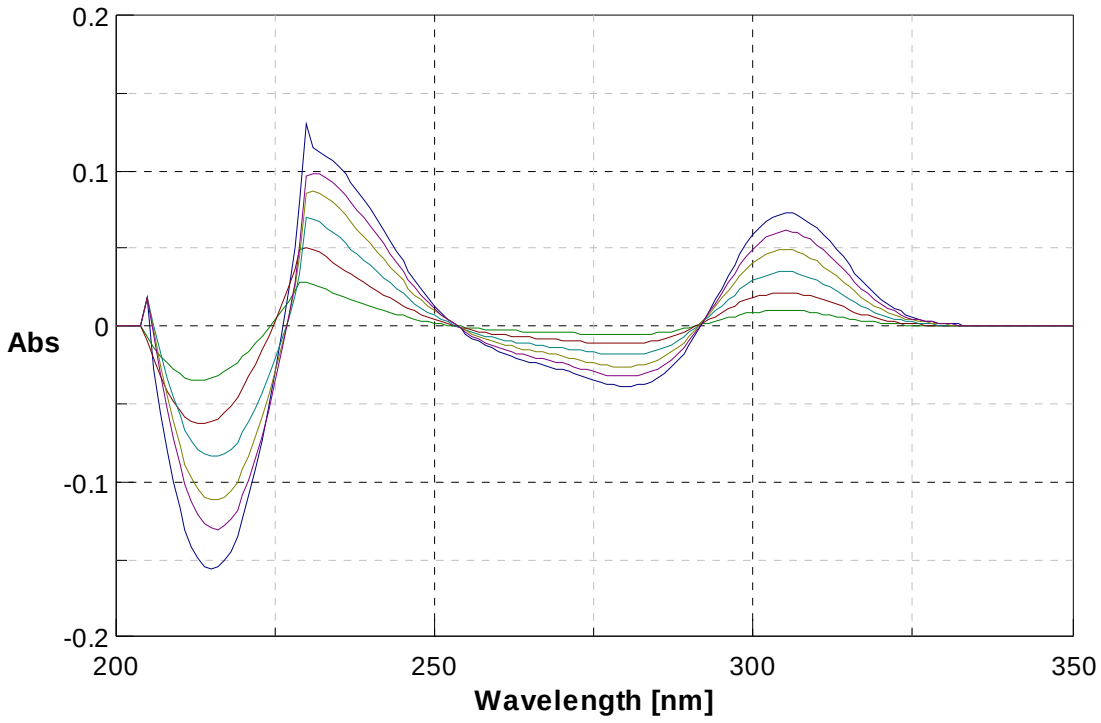

Fig 1: Overlay spectra of dex for first order derivative method.

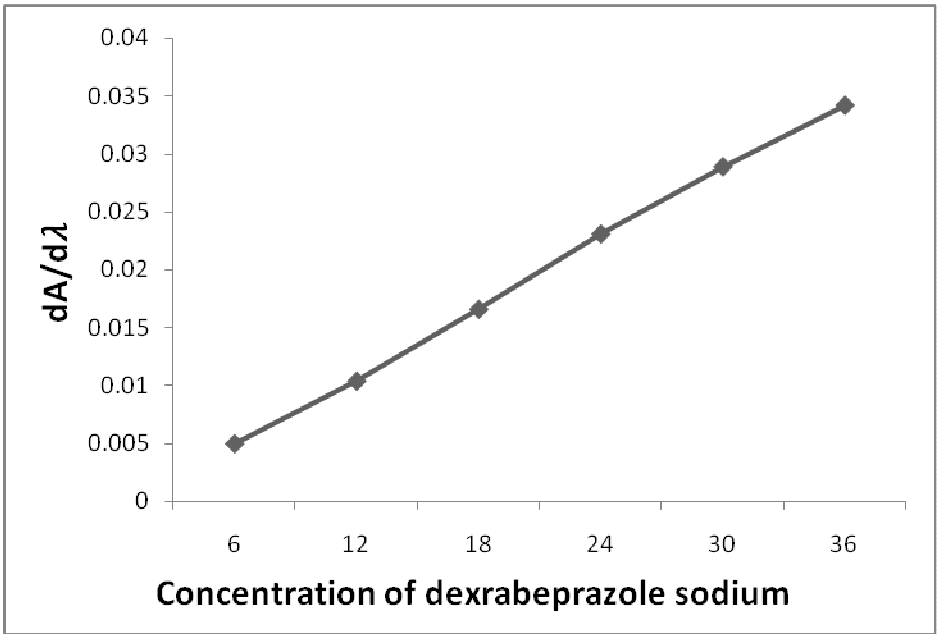

Fig 2: Calibration curve for dexrabeprazole sodium.

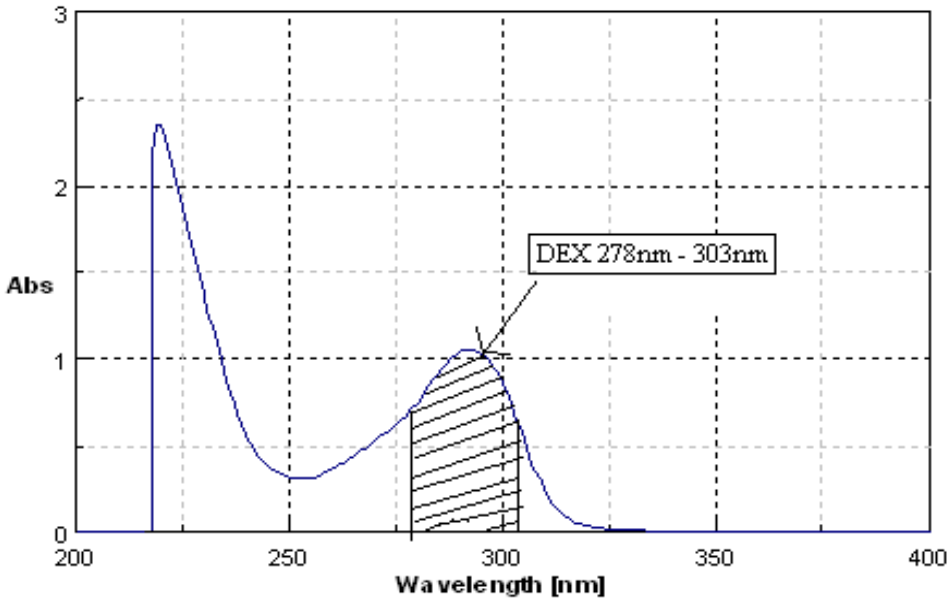

Fig 3: Overlain spectra of dex for auc.

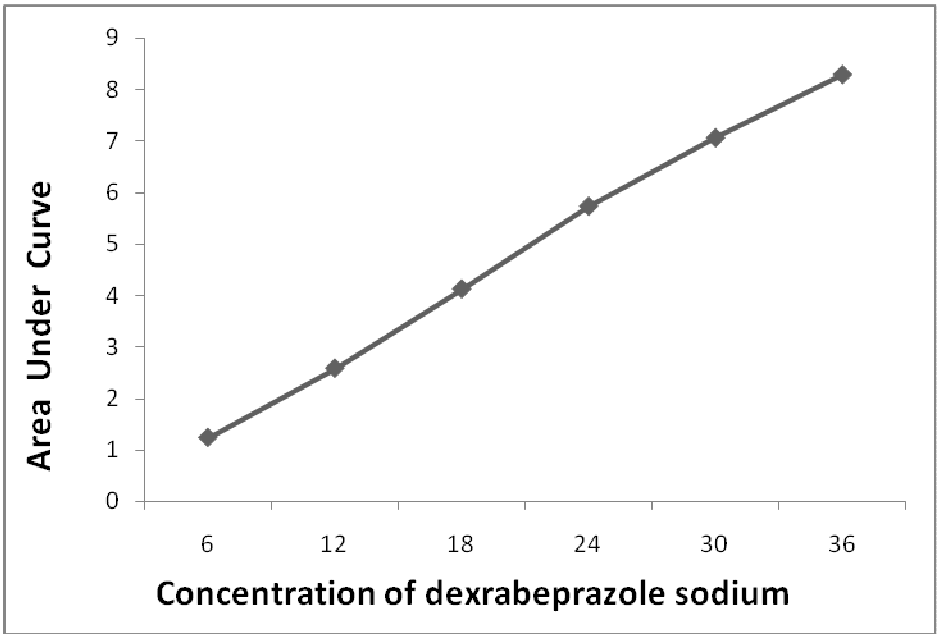

Fig.4: Calibration curve for dexrabeprazole sodium.

Conclusion:

The spectrophotometric methods were developed and validated as per ICH guidelines. The standard deviation and % RSD calculated for the proposed methods are within limits, indicating high degree of precision of the methods. The results of the recovery studies performed indicate the methods to be accurate. Hence, it can be concluded that the developed spectrophotometric methods are accurate, precise and can be employed successfully for the estimation of dexrabeprazole sodium in bulk and formulation.

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