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Development and Validation of Simple UV Spectrophotometric Method for the Estimation of Dextromethorphan Hydrobromide in Bulk and Marketed Dosage Formulations

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ABSTRACT

A simple, rapid and economic UV spectrophotometric method has been developed and validated using a solvent 0.1N HCl to determine Dextromethorphan hydrobromide content in bulk and two different pharmaceutical solid dosage formulations, lozenges and chewable tablets. At the pre-determined λmax of 278 nm, it was proved linear in the range of 5.0-30.0 µg/ml and exhibited good correlation coefficient (R^2=0.9993) and excellent mean recovery (101.37-100.76%) and (100.66-101.17%) for lozenges and chewable tablets respectively. This method was successfully applied to the determination of Dextromethorphan hydrobromide content in lozenges and chewable tablets and the results were in good agreement with the label claim. The method was validated as per ICH guidelines for linearity, precision, accuracy, specificity, LOD and LOQ. The obtained results proved that the method can be employed for the routine analysis of Dextromethorphan hydrobromide in bulks as well as in the pharmaceutical formulations.

Keywords: Dextromethorphan Hydrobromide, UV spectrophotometric method, validation.

INTRODUCTION

Dextromethorphan Hydrobromide (DXM) (3-methoxy-9a-methylmorphinan hydrobromide monohydrate) is methyl analog of Dextrorphan (Fig. 1). It shows high affinity binding to several regions of the brain, including the medullary cough center. [1-2] DXM is one of the widely used antitussives and is official in British Pharmacopeia (BP) [3], Indian Pharmacopeia (IP) [4], and United State Pharmacopeia/ National Formulary (USP/NF). [5]

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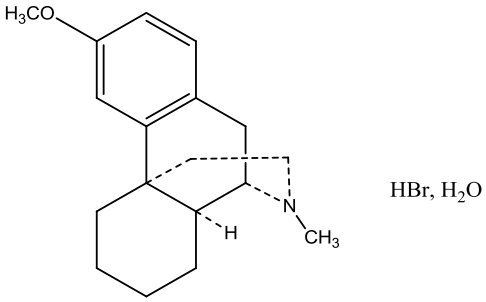

Fig. 1: Chemical Structure of Dextromethorphan Hydrobromide

DXM is available in various pharmaceutical dosage forms like syrup, tablet, spray, and lozenge.

Reported methods for estimation of DXM individually and in combination with other drugs from bulk and its formulation include high performance liquid chromatography (HPLC) [6], gas chromatography [7],

capillary electrophoresis [8], UV Spectrophotometry [9-10] and thin layer chromatography. [11]

In this study, efforts were made to develop a simple, easy and economic UV spectrophotometric method for the determination of DXM in raw material as well as in lozenges and chewable tablets. The developed method was optimized and validated as per the International Conference on Harmonization (ICH) [12] and demonstrated excellent specificity, linearity, precision and accuracy for DXM.

Table 1: Linearity study of DXM

Concentration (µg/ml)*	Absorbance	Correlation coefficient
5	0.046772	0.9993
10	0.072269	
15	0.095695	
20	0.121566	
25	0.144978	
30	0.166522	

*mean of 3 determinations

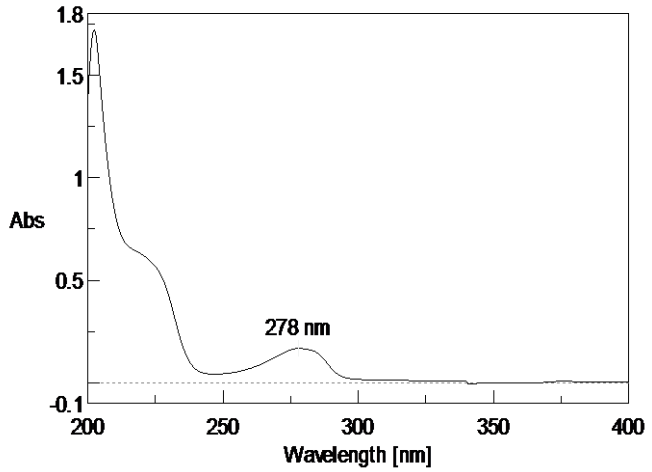

Fig. 2: UV spectrum of DXM at 278 nm

MATERIALS & METHODS

Instrumentation

A JASCO double beam UV-visible Spectrophotometer (Model V- 630) was used for all absorbance measurements with pair of 10 mm matched quartz cells.

Chemicals and materials

Sample of DXM was purchased from Sigma Aldrich Pvt. Ltd. Mumbai, India. All solvents used were of analytical grade obtained from SDFCL Private Limited, Mumbai. Lozenges (5 mg) and Chewable Tablets (10 mg) were purchased from local market.

Preparation of standard stock solution of DXM

10 mg of DXM was accurately weighted and transferred to 10 ml volumetric flask. It was dissolved in about 5 ml of 0.1N HCl and then volume was made up to the 10 ml mark with 0.1N HCl (1000µg/ml). 1 ml of the stock solution (1000µg/ml) was pipetted out and transferred into 10 ml volumetric flask and was diluted to 10 ml with 0.1N HCl solution to give concentration of 100µg/ml.

Determination of λ max and calibration curve

1 ml of standard stock solution (100µg/ml) was transferred into a 10 ml volumetric flask, diluted to a mark with 0.1N HCl to give concentration of 10µg/ml. The absorbance of resulting solution was scanned in the UV spectrometer in the range (200-400 nm) in 1cm cell against 0.1N HCl as blank and spectrum was recorded. In spectrum DXM showed absorbance maximum at 278 nm.

Determination of active ingredients in lozenge and tablet formulations

For lozenges

The proposed method was applied to analyze commercially available DXM lozenges. Twenty lozenges were weighted and average weight was found. The lozenges were triturated to a fine powder. Powder equivalent to 5 mg DXM was transferred to a 10 ml volumetric flask and dissolved in 0.1N HCl. By frequent shaking volume was made up to mark with 0.1N HCl. The solution was sonicated for 15 minutes and filtered through a 0.45µ syringe filter. The absorbance of sample solution was measured at selected wavelength. The amount of DXM was calculated from the calibration curve. This procedure was repeated for six times. Results are shown in Table 1.

For chewable tablets

The proposed method was applied to analyze commercially available DXM tablets. Twenty tablets were weighted and average weight was found. The tablets were triturated to a fine powder. An accurately weighted quantity of powder was transferred into 10 ml volumetric flask and added a minimum quantity of 0.1N HCl to dissolve the substance and the volume was made up to 10 ml with the 0.1N HCl. The solution was sonicated for 15 minutes and filtered through a 0.45µ syringe filter. The absorbance of sample solution was measured at selected wavelength. The content of DXM in sample solution of chewable tablet was calculated. This procedure was repeated for six times.

Validation of the method

The method was validated with respects to linearity, LOD (Limit of detection), LOQ (Limit of quantitation), precision, and accuracy.

Linearity

The linearity was determined by analyzing six independent levels of calibration curve in the range of 5-30µg/ml. Absorbance of each solution against 0.1N HCl was recorded at curve of absorbance vs. concentration was plotted and correlation co-efficient and regression line equation for DXM were determined.

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

The LOD and LOQ were estimated from the set of 3 calibration curves used to determine method linearity.

$$LOD = 3.3*\sigma/S \text{ and } LOQ = 10*\sigma/S$$

Where, σ = the standard deviation of y-intercepts of regression lines, S = the slope of the calibration curve.

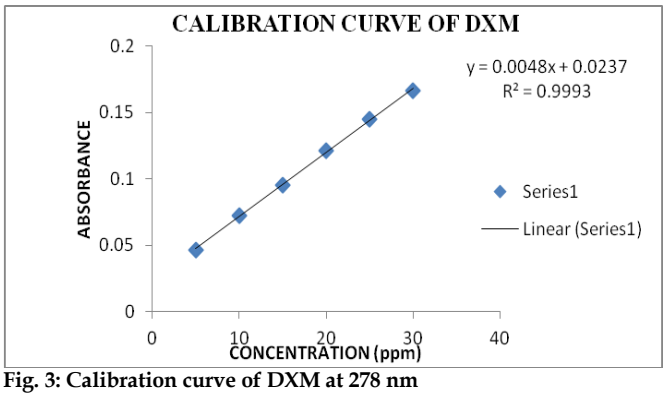

Fig. 3: Calibration curve of DXM at 278 nm

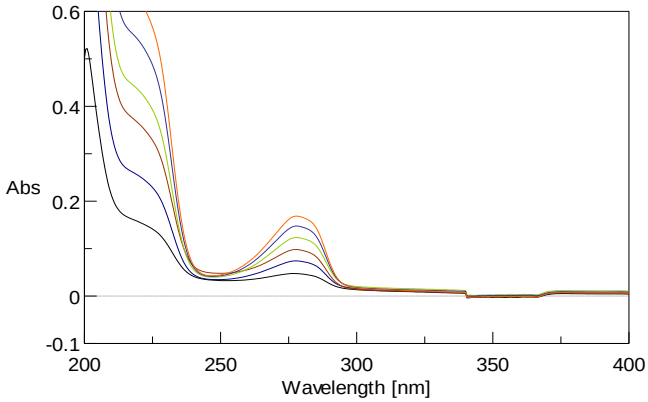

Fig. 4: An Overlain spectra of DXM (5-30µg/ml) at 278 nm

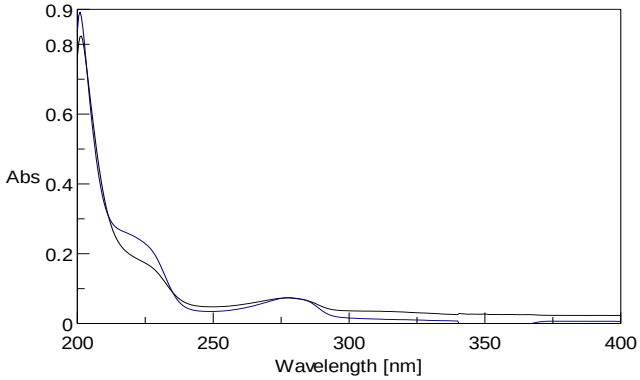

Fig. 5: An overlain spectrum of lozenges extract and standard of DXM

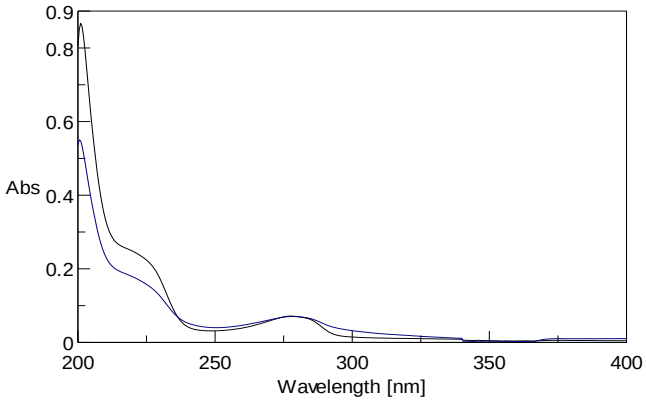

Fig. 6: An overlain spectrum of chewable tablet extract and standard of DXM

Precision

Precision of the method was demonstrated by repeatability, intraday and interday variation studies. For repeatability study six samples of same concentration, (20µg/ml), were taken and the absorbances were observed and the %RSD was calculated. The results are shown in (Table 5).

Intra-day precision was determined by analyzing DXM (5, 20, 30 µg/ml) at three different time points of the same day and inter-day precision was determined by analyzing the DXM (5, 20, 30 µg/ml) at three different time points on different days and %RSD was calculated.

Accuracy

Accuracy was determined by performing recovery studies by spiking different concentrations of pure drug in the pre-analyzed samples within the analytical concentration range of the proposed method at three different set at level of 80%, 100% and 120%. The amount of DXM was calculated at each level and % recoveries were calculated.

RESULTS AND DISCUSSION

Linearity

The linearity of DXM was found to be in the range of 10-30 µg/ml with correlation coefficient 0.9993. The result is shown in Table 1 and calibration curve is shown in Figure 3.

Specificity

When the spectra of standard DXM was overlaid with the spectra of sample (chewable tablet extract and lozenges extract)it was observed that the spectra of DXM was matching with the spectra of chewable tablet and lozenges extract as shown in Fig. 5 and 6. Thus the method was found to be specific.

Accuracy/recovery

The solutions were reanalyzed by the proposed method; results of recovery studies are reported in Table 2 and Table 3 which showed that the percent recovery of DXM in lozenges and chewable tablets was found to be in the range 100.66-101.17% and 100.37-100.76% with % RSD less than 2% respectively.

Precision

The % RSD values for interday and intraday precision were found to be less than 2% which indicate that the developed method is precise for the determination of DXM [Table 4].

Limit of Detection and Limit of Quantitation

The LOQ and LOD for DXM were found to be 1.30µg/ml and 3.93µg/ml, respectively.

Determination of DXM in bulk

The concentrations of the drug were calculated from linear regression equations. The % amount found was 99.99% [Table 5].

Application of the proposed method for pharmaceutical formulations

For chewable tablet formulation

The concentrations of the drug were calculated from the linear regression equation. The % amount found was between 99.6% [Table 6].

For lozenges formulation

The concentrations of the drug were calculated from the linear regression equation. The % amount found was 100.06% [Table 7].

Table 2: Results of Recovery studies for lozenges

S. No.	Level of recovery (%)	Amount of sample added	Amount of drug added (µg/ml)	Total	Amount of drug recovered (mg)*	% Recovery *	% RSD
1	80	10	8	18	18.21	101.18	0.140
2	100	10	10	20	20.14	100.94	0.543
3	120	10	12	22	22.36	100.66	0.258

*mean of 3 determinations, RSD- Relative Standard Deviation

Table 3: Results of Recovery studies for Chewable tablets

S. No.	Level of recovery (%)	Amount of sample added	Amount of standard added	Total	Amount of drug recovered (mg)*	% Recovery *	% RSD
1	80	10	8	18	18.06	100.37	00.17
2	100	10	10	20	20.15	100.76	0.15
3	120	10	12	22	22.08	100.45	1.15

*mean of 3 determinations, RSD- Relative Standard Deviation

Table 4: Precision studies

Concentration (µg/ml)	Observed conc. of DXM by proposed method (µg/ml)					
	Intraday			Interday		
	Mean(n=3)	S.D	%RSD	Mean(n=3)	S.D	%RSD
5	0.0458	0.000608	1.325	0.0457	0.000665	1.454
20	0.1274	0.000671	0.525	0.1212	0.000351	0.289
30	0.1664	0.001213	0.728	0.1560	0.001137	0.728

Table 5: Analysis of DXM in bulk

Concentration (µg/ml)	Amount found (µg)	Amount found (%)	SD	%RSD
10	9.999	99.998	0.0993	0.998

*mean of 6 determinations, RSD- Relative Standard Deviation

Table 6: Results of Analysis of chewable tablet formulation

Drug	Label Claim	Amount of drug estimated*(mg/tablet)	% Content	S.D	% R.S.D
DXM	10 mg	9.96	99.6	0.097	0.97

*mean of 6 determinations, RSD- Relative Standard Deviation

Table 7: Results of Analysis of lozenges formulation

Drug	Label Claim	Amount of drug estimated*(mg/tablet)	% Content	S.D	% R.S.D
DXM	5 mg	5.003	100.06	0.048	0.96

*mean of six determinations, RSD- Relative Standard Deviation

The UV-spectrophotometric method for the estimation of DXM in bulk and formulation (lozenge and tablet) was found to be accurate, precise and robust. The method was found to be linear over a convenient range, economical and utilised a solvent which can be easily prepared. It can be used in laboratories and also for the routine analysis of DXM in bulk preparation and in pharmaceutical dosage forms.

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