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Research Article

A VALIDATED UV SPECTROPHOTOMETRIC METHOD FOR THE SIMULTANEOUS ESTIMATION OF DEXTROMETHORPHAN HYDROBROMIDE AND CHLORPHENIRAMINE MALEATE IN SYRUP FORMULATION

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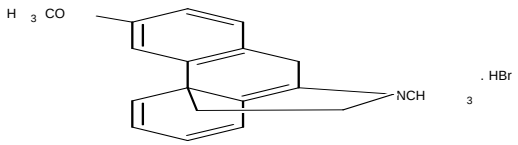
Abstract:

A novel, simple, sensitive and specific spectrophotometric method has been developed for the simultaneous estimation of Dextromethorphan hydrobromide and Chlorpheniramine Maleate in combined liquid dosage form,(i.e., syrup). This method involves solving derivative spectroscopic method. Dextromethorphan hydrobromide has absorbance maxima at 289.2nm and Chlorpheniramine maleate has absorbance maxima at 262.6nm in methanol. The proposed method was validated in terms of Linearity, Accuracy, Specificity, Precision, Ruggedness, Beer's Law was obeyed in the concentration range of 10-70 µg/ml for both the drugs. The regression coefficient r^2 = 0.999 for both drugs.

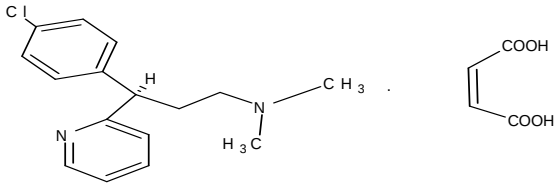
Key words: Dextromethorphan hydrobromide, Chlorpheniramine Maleate, Derivative spectroscopic method.

Introduction

Dextromethorphan hydrobromide (DXM) is antitussive (cough suppressant) drug used for the pain relief and in psychological conditions. It acts on cough centre to elevate the threshold for coughing [1]. Chemically, it is morphinan, 3-methoxy-17-meth (9, 13, 14)-, hydrobromide.



Chlorpheniramine maleate (CPM) is an antihistamine drug that is widely used in pharmaceutical preparations for symptomatic relief of common cold and allergic diseases [2]. Chemically, it is 3-(4- chlorophenyl)-N, N-dimethyl-3-pyridin-2-ylpropan-1-amine.



The structures of both the drugs are shown in figure (1). In the literature, several UV and HPLC methods have been reported for the estimation of DXM and CPM individually and in combination with other drugs. Literature survey revealed that different methods have been reported for the determination of DXM in bulk drug and in dosage forms in combination with other drugs. Spectrophotometry [3], RP-HPLC [4], electrophoresis [5], liquid chromatography [6], methods have been reported for the estimation of dextromethorphan hydrobromide in pharmaceutical formulations. For CPM in bulk drug and in dosage forms in combination with other drugs. Spectrophotometry [7] and RP-HPLC [8] methods have been reported for the estimation of chlorpheniramine maleate in pharmaceutical formulations. A variety of methods in the literature for the determination of some of the compounds but none describe the determination of these two compounds.

However, no UV method has been developed for the simultaneous determination of DXM and CPM in combined liquid dosage form. The present study describes a precise, accurate, specific and sensitive UV method for the simultaneous estimation of DXM and CPM in syrup formulation.

Experimental and Results

Chemicals

Pure drugs of Dextromethorphan hydrobromide and Chlorpheniramine maleate were procured as gift samples from Lupin Pharmaceuticals Ltd. (Aurangabad, India) and Zim Laboratories Ltd.

(Nagpur, India) respectively. Sodium hydroxide and Methanol AR grade. The liquid formulation of Dextromethorphan hydrobromide and Chlorpheniramine maleate were purchased from the local pharmacy.

Instruments:

Shimadzu UV 1800 double beam UV-visible spectrophotometer was used along with 1.0 cm path length matched pair of quartz cell for spectrophotometric method. Digital Balance: Shimadzu AUY-220. Sonicator: PCI Services and Innovative. Digital Hot Air Oven (8388), Meta-Lab Scientific industry. Calibrated glasswares were used for the study.

Preparation of standard solution

Accurately weighed 25.0 mg of DXM and 25.0 mg of CPM were dissolved in 5.0 ml of methanol and basified with 20.0 ml of 0.1N NaOH in a separating funnel. The solutions were extracted with three successions of 10.0 ml of chloroform each. The organic layers were separated and evaporated to dryness. The residues were extracted with 25.0 ml of methanol (stock solution 1 mg/ml). The 1.0 ml of stock solution was diluted with 10.0 ml of methanol (working standard solution 100µg/ml). Finally 1.0 ml of working solution was diluted with 10.0 ml of methanol (10 µg/ml) each.

Preparation of sample solution

Accurately weighed 5.0mL (4.18gm) of sample solution was basified with 25.0mL of 0.1N NaOH and extracted with three successions 10.mL of chloroform each in a separating funnel. The organic layer was evaporated to dryness and aqueous layer was discarded. The dried residue was diluted with 50.0mL of methanol. Finally 1.0 mL of the solution was diluted with 10.0 mL of methanol.

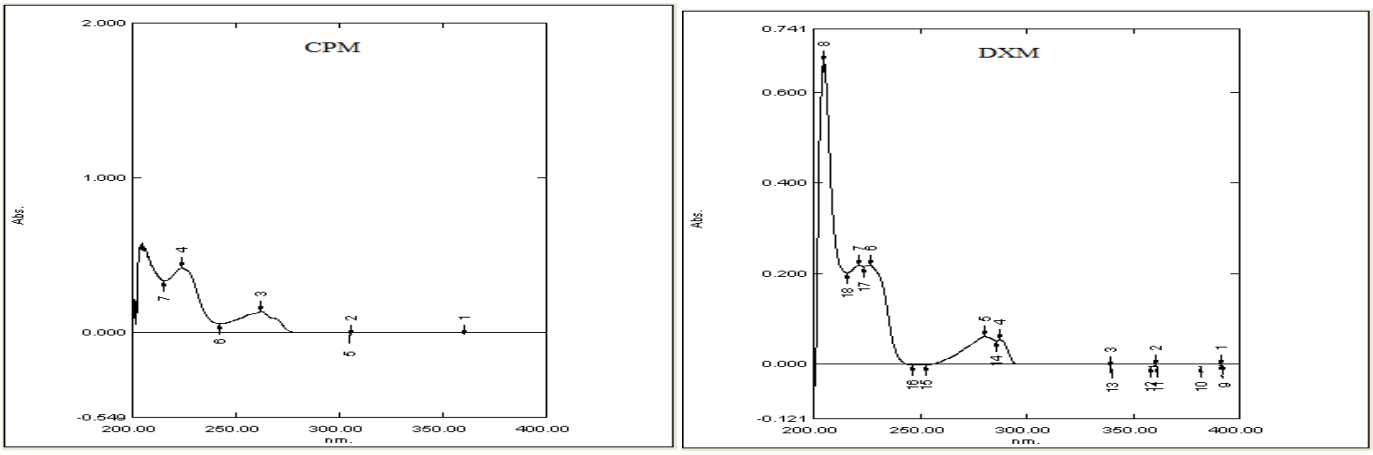


Figure no. 1: Spectra for a) DXM and b) CPM in methanol (10µg/ml).

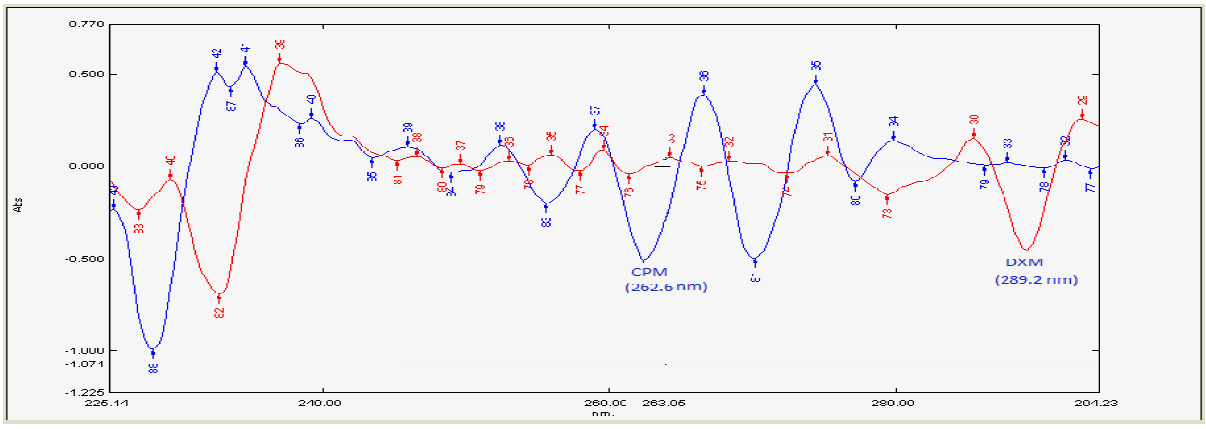


Figure no.2: Overlain 2nd derivative spectrum of DXM and CPM (N=2).

1. Study of Beer's law

The stock standards solution of DXM and CPM were diluted with methanol to get a series of concentrations from 10-70 µg/ml. Similarly stock standard solutions were appropriately mixed and diluted to get a series of concentrations ranging from 10-70 µg/ml of each drug. Absorbance of each of the solutions was measured at 289.2nm and 262.6 nm. The graphs plotted as concentration *vs* absorbance.

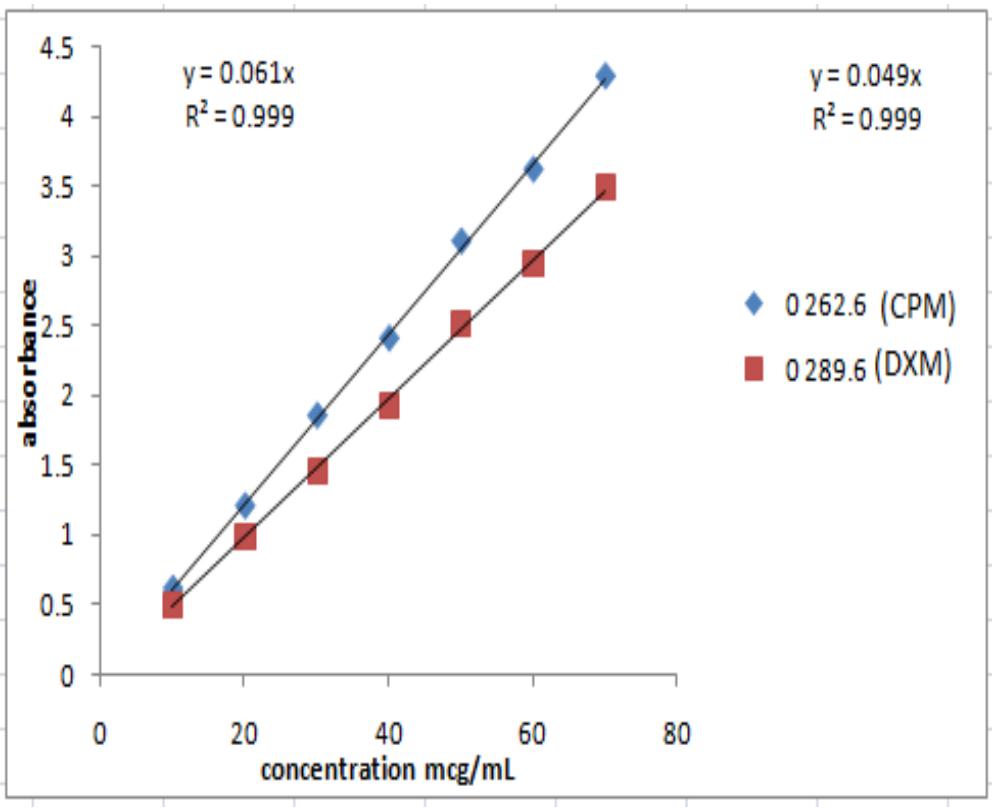


Figure no. 1: linearity for DXM and CPM

As the results were found to be within the acceptance limits, the proposed method was found to be linear at the concentrations of 10-70 µg/ml for DXM and CPM.

2. Estimation of DXM and CPM in standard laboratory mixture:

Accurately measured aliquot portions of stock standard solutions of DXM and CPM were mixed and diluted appropriately to get the concentrations in the ratio of 50:0, 40:10, , 30:20, 25:25, 20:30, 40:10 and 0:50, for DXM and CPM respectively in the mixture. The absorbance of each of the resulting solution was measured at 289.2 nm and 262.6 nm in 1.0 cm cell using methanol as blank.

Table No. 2: Results of estimation in standard laboratory mixture.

Sr.no.	Drug taken mcg/mL		Absorbance		% estimated	
	DXM	CPM	DXM	CPM	DXM	CPM
1	50.0	0.0	3.007	0.033	98.3	0.0
2	40.0	10.0	1.919	0.598	99.53	97.8
3	30.0	20.0	1.281	1.154	100.3	100.8
4	25.0	25.0	1.591	1.107	101.8	101.1
5	20.0	30.0	0.950	1.848	102.1	99.56
6	10.0	40.0	0.488	2.424	98.0	100.6
7	0.0	50.0	0.023	3.103	0.0	99.79
Mean					99.83	99.94
±SD					±1.95	±1.205
%RSD					1.953	1.205

The percentage of the drug estimated for different mix concentrations for both the drug were observed to be very close to 100%

3. Estimation of formulation

Accurately weighed 5.0mL (4.18gm) of sample solution was basified with 25.0mL of 0.1N NaOH and extracted with three successions 10.mL of chloroform each in a separating funnel. The organic layer was evaporated to dryness and

aqueous layer was discarded. The residue was diluted with 50.0mL of methanol. Finally 1.0 mL of the solution was diluted with 10.0 mL of methanol.

Table No. 3: Results of estimation DXM and CPM in syrup formulation.

Wt. of syrup/5ml (mg)	Absorbance		Amt. of drug estimated(mg)		% label claim	
	DXM	CPM	DXM	CPM	DXM	CPM
4180.2	0.877	0.369	10.03	3.915	100.3	98.0
4200.7	0.872	0.382	9.97	4.053	99.53	101.08
4210.6	0.879	0.380	10.05	4.031	101.0	100.6
4170.6	0.874	0.385	10.0	4.084	100.0	101.6
4220.1	0.869	0.380	9.94	4.031	99.18	100.5
Mean					100.02	100.3
± SD					±0.70	±1.38
% RSD					0.703	1.37

The proposed method applied for estimation of DXM and CPM in marketed formulations have yielded good and reliable results. The recovery data was also found to be very satisfactory.

Validation of the proposed method

1. Accuracy

The accuracy of an analytical method is expressed as percent recovery of a standard drug added in fixed quantity of prenalysed syrup sample. An accurately weighed five quantities of syrup equivalent to 5 mg of DXM and 2 mg of CPM were transferred to different 50 ml volumetric flasks. To each flask standard DXM and CPM were added. The solution in each flask was extracted in the same manner, as described in (Extraction chart of standard solution). The extracted residue was dissolved in adequate quantity of methanol and volume of each flask was adjusted to 50.0 ml with methanol. The solutions were further diluted appropriately with methanol to obtain concentrations in the range of 70 to 130 % of label claim.

Table No.4: Results of recovery studies.

Wt. of syrup (mg)/ 5mL	Wt. of pure drug added (mg)		Absorbance		Amt. of drug recovered (mg)		% drug recovered	
	DXM	CPM	DXM	CPM	DXM	CPM	DXM	CPM
4180.2	2.0	0.8	0.609	0.265	1.96	0.811	98.83	101.3
4200.7	3.5	1.4	0.742	0.323	3.48	1.42	99.70	101.0
4210.6	5.0	2.0	0.871	0.379	4.96	2.021	99.3	101.0
4170.6	6.5	2.6	0.1005	0.429	6.49	2.551	99.96	98.7
4220.1	7.0	3.2	1.136	0.487	6.85	3.167	98.0	98.96
Mean ± SD. % RSD							99.15 ±0.77 0.782	100.9 ±1.254 1.243

Accuracy was ascertained by carrying out recovery studies on marketed formulations with standard addition method over the range of 70 to 130 % of labeled claim. The recoveries of both the drugs were observed to be very close to 100 % representing the accuracy of the method and also showed that excipients have no interference in the estimation.

2. Specificity

Six quantities of syrup were weighed, each representing the amount equivalent to 20 mg DXM (also equivalent to 8 mg CPM). The solution in each flask was extracted in the same manner, as described in the extraction chart of standard solution. The extracted material was dissolved in adequate quantity of methanol and was transferred to 50.0 mL volumetric flask. 1.0mL of solution was diluted in adequate quantity of methanol and volume of each flask was adjusted to 10.0 ml with methanol. All these solutions were stored for 24 hrs under following different conditions.

1. Normal
2. 1.0 mL of 0.1N NaOH at 50^0C
3. 1.0 mL of 0.1N HCl at 50^0C
4. 1.0 mL of 0.1N 3% H_2O_2 at 50^0C
5. At 60 ^{0}C (Thermal)
6. In Sunlight

Table No.5: Results of specificity studies.

Sr. no.	Sample	% label claim	
		DXM	CPM
1	Normal	100.3	101.3
2	Acid	99.4	100.5
3	Alkali	100.3	100.7
4	Oxide	100.7	101.0
5	Heat	99.7	100.5
6	Sunlight	99.5	100.8

The results showed no significant differences were found to be close to normal samples, which indicated that there is either no degradation or otherwise the proposed method is incapable of detecting it.

3. Ruggedness

The study of ruggedness was carried out by means of different analysts are used to evaluate the intermediate precision (also known as Ruggedness) of the method.

Table no.6: Results for Ruggedness.

Sr. no.	**Analyst**	**%labell claim**	
		DXM	**CPM**
1	**Analyst-1**	**98.98**	**100.16**
2	**Analyst-2**	**99.21**	**98.10**
3	**Analyst-3**	**100.8**	**98.89**
Mean ±SD %RSD		**99.6±0.99 0.993**	**99.05±1.03 1.039**

Ruggedness of the proposed method was ascertained by getting the sample analysed from three different analysts. The results of estimation by proposed method by different analysts were respectively. This indicated that the ruggedness of the method in the hands of different expert analysts.

Conclusion

- A novel UV and RP-HPLC method has been developed for the simultaneous estimation of DXM and CPM in marketed formulations.
- The good % recovery in liquid forms suggests that the excipients present in the dosage forms have no interference in the determination.
- The proposed method can be used for routine analysis of DXM and CPM in combined liquid dosage form.
- It can be also used in the quality control in bulk manufacturing.

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