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Original Article

DEVELOPMENT OF HPTLC METHOD FOR DETERMINATION OF BROMPHENIRAMINE MALEATE AND PHENYLEPHRINE HYDROCHLORIDE TABLETS

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ABSTRACT

Objective: To develop a new, simple, precise and rapid HPTLC method for the simultaneous determination of brompheniramine maleate and phenylephrine hydrochloride in tablet dosage form.

Methods: The optimized chromatographic method was carried out on silica gel 60 F_{254} precoated TLC plates using a mixture of methanol: strong ammonia (100: 1.5, v/v) as mobile phase.

Results: Phenylephrine hydrochloride and brompheniramine maleate were resolved with Rf value of 0.32 and 0.43 respectively. Linearity was found to be in the range of 0.8-3.6 μg/spot for brompheniramine maleate and 2.0-9.0 μg/spot for phenylephrine hydrochloride. The mean percentage recoveries were 100.6 and 101.0 for brompheniramine maleate and phenylephrine hydrochloride with %RSD of 1.5 and 1.1 respectively.

Conclusion: A new, simple, precise and rapid HPTLC method was developed and validated for the determination of brompheniramine maleate and phenylephrine hydrochloride in tablet dosage form.

Keywords: HPTLC, Analytical method, Brompheniramine maleate, Phenylephrine hydrochloride, Tablets.

INTRODUCTION

Brompheniramine maleate (BPM) is an antihistaminic drug used to relieve symptoms of allergy, sneezing, itching, watery eyes and running nose. Phenylephrine hydrochloride (PEH) is a sympathomimetic drug mainly used to treat nasal decongestion. The chemical structures of BPM and PEH are shown in Figure 1. The combination of brompheniramine maleate and phenylephrine hydrochloride was frequently used as active ingredients in cold medications. The official methods are available for determination of each one in various dosage forms [1-2], however, no official method is available for simultaneous estimation of these two combination drugs. Literature survey reveals that several methods for determination of PEH alone or in combination with other drugs by UV spectroscopy [3-8], HPLC [9-12] and CE [13] have been reported. No method has been reported for the estimation of BPM and PEH in combined tablet dosage form. The present study illustrates development and validation of a simple, specific, accurate, and reproducible method for the simultaneous determination of BPM and PEH in combined tablet dosage form.

MATERIALS AND METHODS

Instrumentation

Analysis was performed on a Camag HPTLC system containing Camag Linomat 5, Camag TLC scanner 3 with winCATS software. Sonicator was used for this study. Silica gel 60 F_{254} TLC plates 20x20 cm with layer thickness 0.2cm (E. Merck) were used as stationary phase.

Chemicals

Brompheniramine maleate (99.74%) and phenylephrine hydrochloride (99.46%) working standard were gifted by Siam Bheasach Co., Ltd. Bangkok, Thailand. All chemicals were of analytical grade. The commercial fixed-dose combination tablets containing 4 mg of BPM and 10 mg of PEH were purchased from local pharmacy store.

Preparation of standard stock solutions

Standard stock solution of BPM and PEH was prepared by dissolving 20 mg of BPM and 50 mg of PEH in 10.0 ml volumetric flask with 7 ml ethanol. The standard solution was sonicated for 5 min and then adjusted to volume with ethanol.

Preparation of sample solutions

Twenty tablets were accurately weighed and ground to fine powder. The powder equivalent to 4 mg of BPM and 10 mg of PEH was accurately weighed and transferred to a 10.0 ml volumetric flask and dissolved in 7 ml of ethanol. The sample was sonicated for 5 min and adjusted to volume with ethanol. The solution was filtered through filter paper. The resulting solution was used for further analysis.

Chromatographic condition

The experiment was performed on silica gel 60F_{254} aluminum sheets (20x20 cm) as stationary phase, using mobile phase comprised of a mixture of methanol: strong ammonia (100:1.5, v/v). The solutions were applied on TLC plate using a Camag Linomat 5 automatic sample applicator. The developed TLC plate was air dried and then scanned between 220 to 350 nm. The detection wavelength was selected at 265 nm due to good absorbance of both components. The slit dimension of 4 x 0.45 mm and scanning speed of 50 mm/s were set with Camag TLC scanner 3 using winCATS software.

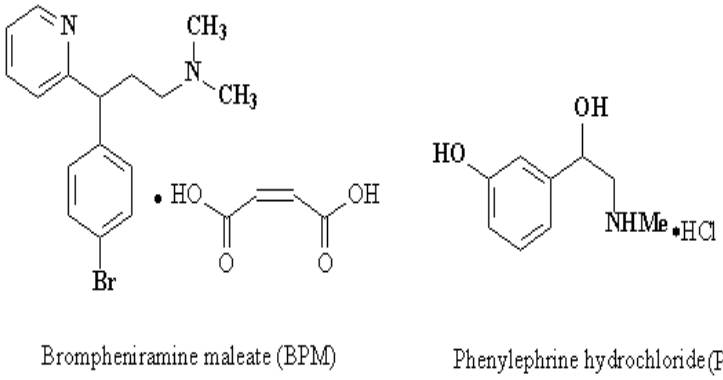
Method validation

After the development of HPTLC method for the simultaneous determination of BPM and PEH was established. Validation of the method was carried out with respect to specificity, linearity, accuracy, and precision.

RESULTS AND DISCUSSION

Optimization of mobile phase

Chromatographic separation studies were carried out on the working standard solution of BPM and PEH. Various mobile phase systems were tried for good separation of BPM and PEH. After several trials, a mixture of methanol: strong ammonia (100:1.5, v/v) was chosen as the mobile phase. With this mobile phase system, complete resolution of the peak with clear baseline separation was obtained at 265 nm (Fig. 2). The Rf values were 0.32 and 0.43 for PEH and BPM respectively.



Brompheniramine maleate (BPM) Phenylephrine hydrochloride (PEH)

Fig. 1: Chemical structures of brompheniramine maleate and phenylephrine hydrochloride

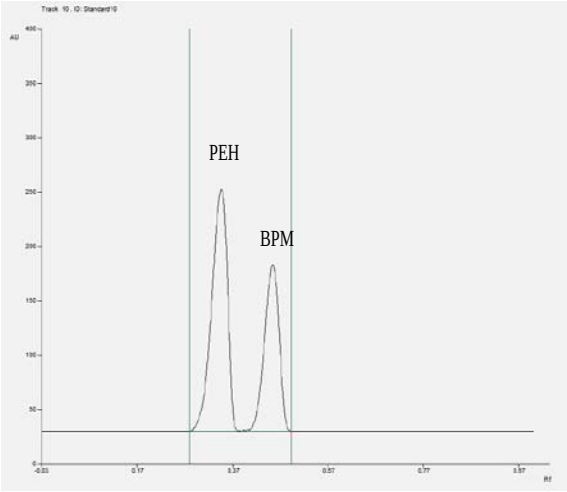


Fig. 2: Typical HPTLC Chromatogram of BPM and PEH

Specificity

The specificity of the method was ascertained by analyzing standard drugs and the sample. The spots for BPM and PEH in the samples were confirmed by comparing the Rf and chromatogram of the spots with that of the standards. It was observed that the excipients present in the formulation did not interfere with the peaks of BPM and PEH

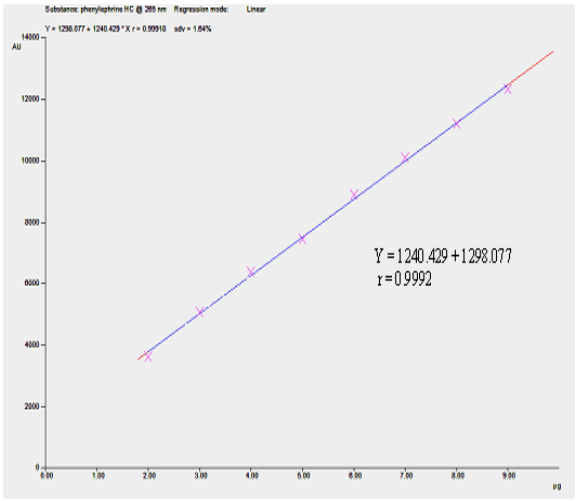


Fig. 3: Calibration curve of PEH at 265 nm by HPTLC method

Linearity

Calibration curves were plotted over the concentration range of 0.8-3.6 µg/spot and 2.0- 9.0 µg/spot for BPM and PEH, respectively. Accurately measured mixed standard solutions of BPM and PEH were applied to the TLC plate. The TLC plate was developed and analyzed as described under chromatographic separation. The calibration curve was prepared by plotting peak area versus concentration (µg/spot) corresponding to each spot. Figure 3 showed linearity between peak area and concentration of PEH with the linear equation of y = 1240.429 X + 1298.077. And the linear equation of BPM was found to be y = 2.036X + 314.62 as shown in Figure 4. Correlation coefficient (r) was 0.9992 and 0.9997 for PEH and BPM respectively.

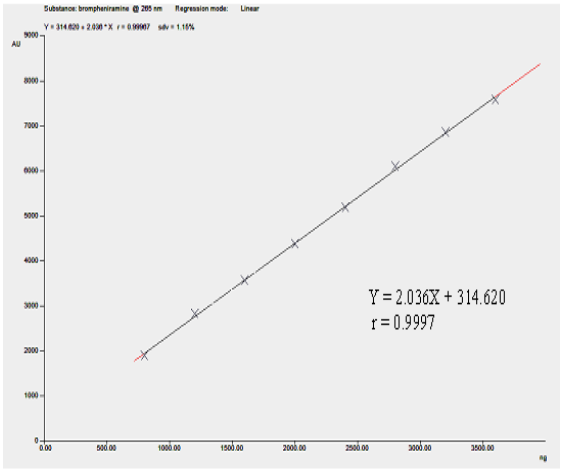


Fig. 4: Calibration curve of BPM at 265 nm by HPTLC method

Precision

The precision of the system was checked by repeatedly analyzing six independent standard solutions of BPM and PEH. The % RSD value for peak area obtained was calculated to determine any intraday variation as shown in Table 1. Interday precision was also assessed by analyzing these solutions on three different days as shown in Table 2. The low % RSD values of intraday (1.23 for BPM and 1.01 for PEH) and interday precision (1.15-1.34 for BPM and 1.22 - 1.33 for PEH) revealed that the proposed method was precise.

Accuracy

The accuracy of the method was determined by performing recovery studies at three different levels of standard additions. Accuracy was checked by adding 80, 100 and 120 % amount of BPM and PEH to pre-analyzed sample solution. The amount of BPM and PEH was

determined by applying the obtained values to the calibration curves. Results and statistical parameters were reported in Table 3. The percent average recoveries obtained were 100.6 (%RSD =1.5) and 101.0 (%RSD =1.1) for BPM and PEH, respectively, indicating that the proposed method was accurate. Hence this method was employed for determination of BPM and PEH in tablet dosage form.

Table 1: **Intraday precision of the HPTLC method**

S. No.	Intraday precision (area)	
	BPM	PEH
1	3040.24	4020.50
2	3072.20	4075.22
3	3067.96	3999.34
4	3030.10	4100.12
5	2996.36	4034.4
6	2980.12	4002.63
average	3031.16	4038.70
SD	37.25	40.76
%RSD	1.23	1.01

Table 2: Interday precision of the HPTLC method

S. No.	Day 1 (area)		Day 2 (area)		Day 3 (area)	
	BPM	PEH	BPM	PEH	BPM	PEH
1	3019.18	4027.21	3020.54	4020.21	3030.65	3998.65
2	3092.97	4120.75	3012.62	4110.54	3002.35	4109.76
3	2971.64	3979.66	2930.24	3989.69	2940.86	3996.64
4	3010.94	4104.36	3019.34	4101.21	3049.94	4091.11
5	3000.00	4034.40	2998.58	4025.25	3012.54	4005.98
6	3010.32	4022.63	3012.82	4019.93	3039.12	4050.56
average	3017.51	4048.17	2999.02	4044.47	3012.58	4042.12
SD	40.50	53.67	34.59	49.29	39.18	49.62
%RSD	1.34	1.33	1.15	1.22	1.30	1.23

Table 3: Recovery studies of BPM and PEH

Amount of drug added (%)	BPM			PEH		
	Amount added (µg/spot)	Amount found (µg/spot)	% recovery	Amount added (µg/spot)	Amount found (µg/spot)	% recovery
80	0.8	0.81	101.3	2.0	1.98	99.0
	0.8	0.82	102.5	2.0	1.99	99.5
	0.8	0.82	102.5	2.0	2.02	101.0
100	1.0	0.99	99.0	2.5	2.53	101.2
	1.0	1.01	101.0	2.5	2.56	102.4
	1.0	1.0	100.0	2.5	2.54	101.6
120	1.2	1.18	98.3	3.0	3.04	101.3
	1.2	1.19	99.2	3.0	3.05	101.7
	1.2	1.22	101.6	3.0	3.05	101.7
average			100.6			101.0
S.D.			1.5			1.1
%RSD			1.5			1.1

Table 4: Analysis of BPM and PEH tablets by proposed HPTLC method

S. No.	Amount of BPM (label claim=4mg)		Amount of PEH (label claim=10mg)	
	Found	% labeled amount	Found	% labeled amount
1	4.12	103	9.68	96.8
2	4.16	104	9.88	98.8
3	4.20	105	9.90	99.0
average	4.16	104	9.82	98.2
% RSD		1.0		1.24

Analysis of the tablet dosage form

Triplicate of sample solution from formulation was applied separately on TLC plate, developed and scanned as described in chromatographic separation. The amount of BPM and PEH present in the sample solution was determined by fitting area values of peak corresponding to BPM and PEH into the respective calibration curve. The drug content was found to be 104.0 % (%RSD=1.0) and 98.2 (%RSD=1.24) for BPM and PEH respectively as shown in Table 4. The low % RSD value indicated the method was suitable for analysis of these drugs in tablet dosage form.

CONCLUSION

The developed HPTLC method was simple, specific, accurate, precise, rapid and suitable for simultaneous determination of phenylephrine hydrochloride and brompheniramine maleate combined tablets. It can be used for the routine quality control

analysis of drugs in tablet dosage form with low cost without interference from any excipients.

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