

Determination of Bromhexine HCl, Dextromethorphan HBr, Chlorpheniramine Maleate in Sedosolvin Suspension

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A simple, fast and accurate high performance liquid chromatographic method has been developed for the determination of bromhexine HCl, dextromethorphan HBr, chlorpheniramine maleate in sedosolvin suspension. Sedosolvin suspension contains bromhexine HCl a mucolytic, dextromethorphan HBr a cough suppressant and chlorpheniramine maleate which is an antiallergic drug. Sedosolvin suspension is indicated for dry cough. The low values of standard deviation and coefficient of variation indicate high precision of the method. The average recovery was found to be within pharmacopoeial limits.

Key Words: High performance liquid-chromatography, Sedosolvin suspension, Bromhexine HCl, Dextromethorphan HBr, Chlorpheniramine maleate

INTRODUCTION

Sedosolvin suspension contains bromhexine HCl a mucolytic, dextromethorphan HBr a cough suppressant and chlorpheniramine maleate which is an antiallergic drug. Sedosolvin suspension is an expectorant and is indicated for dry cough. Sedosolvin has resultant effect in test masking involving dextromethorphan HBr and bromhexine HCl. This is possible by combining physico-chemical complexation through ion exchange phenomenon. The literature survey revealed that there is no HPLC method reported. The present work describes a simple, fast and an accurate HPLC method for the determination of bromhexine HCl, dextromethorphan HBr, chlorpheniramine maleate in sedosolvin suspension. The following is the typical chromatographic condition for HPLC determination of bromhexine HCl, dextromethorphan HBr, chlorpheniramine maleate in sedosolvin suspension.

EXPERIMENTAL

(1) Standard stock preparation: Accurately about 80 mg of bromhexine HCl standard (Purity 99.7%), 100 mg of dextromethorphan HBr standard (Purity 99.3%) and 20 mg of chlorpheniramine maleate standard (purity 100.1%) were weighed and transferred to a 100 mL volumetric flask. The drug was then dissolved in diluent to give standard stock solution of 800 ppm of bromhexine

HCl, 1000 ppm of dextromethorphan HBr and 200 ppm of chlorpheniramine maleate.

Standard preparation: Pipetted 10 mL of above standard stock solution to a 100 mL volumetric flask and diluted up to the mark with diluent to give standard solution of 80 ppm of bromhexine HCl, 100 ppm of dextromethorphan HBr and 20 ppm of chlorpheniramine maleate.

(2) **Sample preparation:** Pipetted 5.0 mL of sedosolvin suspension to 100 mL volumetric flask containing about 50 mL of diluent and sonicated for 15 min to dissolve. Cooled to room temperature and volume made up to the mark with diluent.

Chromatographic conditions:

- (1) Instrument: High performance liquid chromatograph (make: JASCO)
- (2) Column: Novapack C-18, 30 mm × 3.9 mm, 4 μ
- (3) Detector: photodiode array detector
- (4) Wavelength of detection: 265 nm
- (5) Injection volume: 20 μL
- (6) Flow rate: 1.0 mL/min
- (7) Run time: about 40 min.

Preparation of Diluent: 670 mL of water mixed with 330 mL of acetonitrile and added 10 mL of glacial acetic acid

Preparation of Mobile phase: 3.0 g of sodium octane sulfonate and 5.2 g potassium nitrate dissolved in 670 mL water; to this added 330 mL acetonitrile and 10 mL of glacial acetic acid and mixed. Filtered through 0.45 μ nylon membrane. Sonicated for 10 min.

The assay values for bromhexine HCl are calculated for formulations A, B & C using the following formula:

$$\frac{\text{Area } I_{\text{spl}}}{\text{Area } I_{\text{std}}} \times \frac{\text{Wt. } I_{\text{std}}}{100} \times \frac{10}{100} \times \frac{100}{5} \times \frac{5}{L_1} \times \text{Purity of Std 1}$$

where,

Area I_{spl} = peak area response of bromhexine HCl in chromatogram of sample preparation

Area I_{std} = peak area response of Bromhexine HCl in chromatogram of standard preparation

Wt I_{std} = weight of the standard bromhexine HCl in mg

L_1 = Label claim of bromhexine HCl (in mg)

Purity of Std 1 = % purity of bromhexine HCl standard on as is basis

The assay values for dextromethorphan HBr are calculated for formulation-A, B & C using following formula

$$\frac{\text{Area } 2_{\text{spl}}}{\text{Area } 2_{\text{std}}} \times \frac{\text{Wt. } 2_{\text{std}}}{100} \times \frac{10}{100} \times \frac{100}{5} \times \frac{5}{L_2} \times \text{Purity of Std 2}$$

where,

Area 2_{spl} = peak area response of for dextromethorphan HBr in chromatogram of sample preparation

Area 2_{std} = peak area response of for dextromethorphan HBr in chromatogram of standard preparation

Wt. 2_{std} = Weight of the standard dextromethorphan HBr in mg

L₂ = Label claim of dextromethorphan HBr (in mg)

Purity of Std 2 = % purity of dextromethorphan HBr standard on as is basis

The assay values for chlorpheniramine maleate are calculated for formulation-A, B & C using following formula

$$\frac{\text{Area } 3_{\text{spl}}}{\text{Area } 3_{\text{std}}} \times \frac{\text{Wt. } 3_{\text{std}}}{100} \times \frac{10}{100} \times \frac{100}{5} \times \frac{5}{L_3} \times \text{Purity of Std 3}$$

where,

Area 3_{spl} = peak area response of for chlorpheniramine maleate in chromatogram of sample preparation

Area 3_{std} = peak area response of for chlorpheniramine maleate in chromatogram of standard preparation

Wt. 3_{std} = weight of the standard chlorpheniramine maleate in mg

L₃ = Label claim of chlorpheniramine maleate (in mg)

Purity of Std 3 = % purity of chlorpheniramine maleate standard on as is basis

RESULTS AND DISCUSSION

To determine the precision of the proposed method seven samples were weighed and analyzed.

% label claimed, the corresponding values of standard deviation and coefficient of variation for bromhexine HCl, dextromethorphan HBr and chlorpheniramine maleate are given in Tables 1a, 1b and 1c respectively.

TABLE-1a

Formulation	(%) label claim	Standard deviation	Coefficient of variation
A	99.7	0.711	0.711
B	99.5	0.569	0.568
C	98.9	0.817	0.817

TABLE-1b

Formulation	(%) label claim	Standard deviation	Coefficient of variation
A	98.7	1.321	1.321
B	100.6	0.698	0.698
C	99.3	0.796	0.796

TABLE-1c

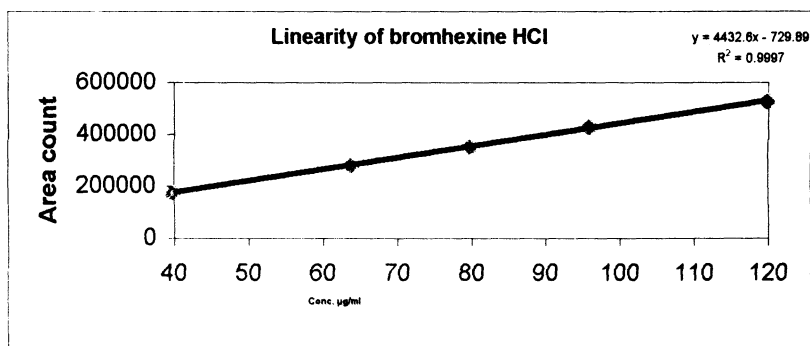
Formulation	% label claim	Standard deviation	Coefficient of variation
A	99.0	0.559	0.559
B	99.2	0.754	0.754
C	99.6	0.592	0.592

Linearity: Five linearity levels for bromhexine HCl were prepared by diluting standard stock solution as given below in Table-2a:

TABLE-2a

Linearity levels	Volume of std stock solution added in mL	Volume made up to in mL
50%	5	100
80%	8	100
100%	10	100
120%	12	100
150%	15	100

Linearity level for assay	
Conc. of bromhexine HCl (ppm)	Std. area
40	176439
64	282308
80	352862
96	428474
120	529321

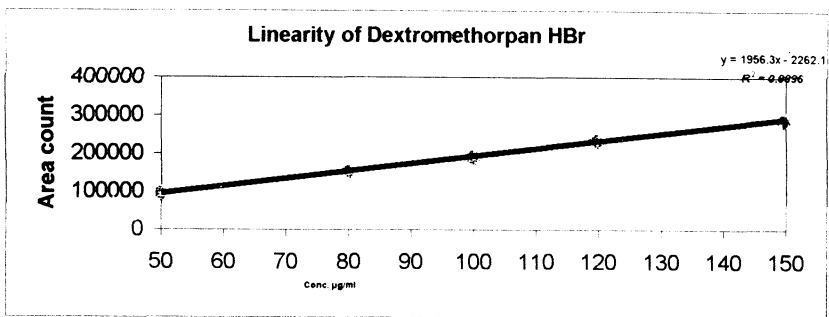


Five linearity levels for dextromethorphan. HBr were prepared by diluting standard stock solution as given below in Table-2b:

TABLE-2b

Linearity levels (%)	Volume of std stock solution added in mL	Volume made up to in mL
50	5	100
80	8	100
100	10	100
120	12	100
150	15	100

Linearity level for assay	
Conc. of dextromethorphan HBr (ppm)	Std. Area
50	95090
80	154777
100	192121
120	234862
150	289986

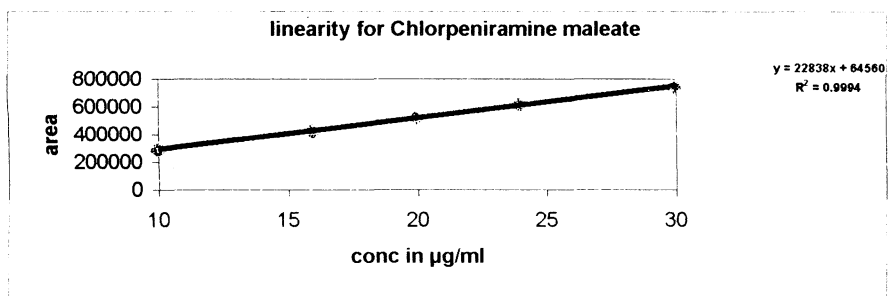


Five linearity levels for chlorpheniramine maleate were prepared by diluting standard stock solution as given below in Table-2c.

TABLE-2c

Linearity levels (%)	Volume of std stock solution added in mL	Volume made up to in mL
50	5	100
80	8	100
100	10	100
120	12	100
150	15	100

Linearity level for assay	
Conc. of chlorpheniramine maleate (ppm)	Std. Area
10	293052
16	426108
20	522630
24	619146
30	745682



Recovery: The tablet formulation contains various excipients. Recovery experiment was performed in order to check that there is no interference from excipients on assay value. The recovery was done by spiking the standard solution to the sample. The recovery was done at three different levels, *i.e.*, 10, 20 and 30% of the assay level. The recovery was performed as follows in Table-3.

To a 100 mL volumetric flask, 5 mL of sample stock solution, 45 mL of water and specified amount of std stock solution was added as given below and proceeded same as standard preparation.

Preparation of Standard Stock Solution: Pipetted 10 mL of above standard stock solution to 100 mL volumetric flask and diluted up to the mark with diluent to give standard solution of 80 ppm of bromhexine HCl, 100 ppm of dextromethorphan HBr and 20 ppm of chlorpheniramine maleate.

TABLE-3

Recovery levels	Volume of sample suspension added in mL	Volume of std stock solution added in mL	Volume made up to in mL
10	5	10	100
20	5	20	100
30	5	30	100

The recovery experiment was repeated seven times. The values of amount added and amount found are given in Table-4.

TABLE-4
AMOUNT FOUND IN THE RECOVERY EXPERIMENT

S. No.	Formulation	Amount found (mg per tablet)							Mean
		1	2	3	4	5	6	7	
1	Dextromethorphan HBr	109.88	109.61	110.97	109.02	110.14	110.89	109.35	109.98
2		120.49	119.20	120.68	120.03	120.98	121.11	121.19	120.53
3		129.78	130.24	131.22	130.56	129.64	130.54	128.89	130.12

S. No.	Formulation	Amount found (mg per tablet)							Mean
		1	2	3	4	5	6	7	
1	Bromhexine HCl	110.08	109.86	110.13	110.65	109.21	111.56	109.28	110.11
2		119.98	120.02	120.71	119.17	121.43	119.07	120.37	120.10
3		130.38	130.62	131.86	131.66	131.12	130.22	129.09	130.71

S. No.	Formulation	Amount found (mg per tablet)							Mean
		1	2	3	4	5	6	7	
1	Chlorpheniramine maleate	110.47	110.48	110.48	108.06	108.6	110.43	110.03	109.57
2		119.66	121.18	121.18	120.02	121.45	119.19	120.37	120.04
3		128.56	130.68	130.68	130.1	128.12	131.40	130.06	130.05

Discussion

The r^2 value was found 0.999 for dextromethorphan HBr, bromhexine HCl and chlorpheniramine maleate which shows that the response is linear from 50 to 150 ppm for dextromethorphan HBr, from 40 to 120 ppm for bromhexine HCl and from 10 to 30ppm for chlorpheniramine maleate. High percentage of recovery shows that the method is free from interference of excipients. The recovery values prove that the method is accurate and reproducible. The proposed method is simple, fast, accurate and precise; thus proposed method can be used for the routine quality control analysis of bromhexine HCl, dextromethorphan HBr and chlorpheniramine maleate in suspension form.

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REFERENCES

1. The Merck Index, 12th Edn., Merck & Co. Inc. Rahway, N.J., p. 1412.
2. Martindale, The Extra Pharmacopoeia, 31st Edn., Pharmaceutical Press, p. 1064 (1996).
3. J.W. Barnhar and E.N. Massad, Determination of Dextromethorphan in Serum by Gas Chromatography, **63**, 390 (1979).
4. W.C. Benitz and D.S. Tatro, The Pediatric Handbook, 2nd Year Book Medical Publishers, Inc., Chicago, IL (1988).
5. D.J. Vadodaria, P.M. Parikh and S.P. Mukherji, *Indian J. Pharm.*, **24**, 180 (1962).
6. B.K. Gupta, S. Gupta and J.J.V. DeSouza, *Indian J. Pharm.*, **33**, 38 (1971).

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