IJPSR (2021), Volume 12, Issue 9 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 19 September 2020; received in revised form, 27 February 2021; accepted, 23 May 2021; published 01 September 2021

DEVELOPMENT AND VALIDATION OF A NEW ISOCRATIC RP-HPLC METHOD FOR SIMULTANEOUS ESTIMATION OF DEXTROMETHORPHAN HYDROBROMIDE, PHENYLEPHRINE HYDROCHLORIDE AND TRIPROLIDINE HYDROCHLORIDE IN THEIR COMBINED LIQUID DOSAGE FORM

Vivek Kumar Pandey, Gulzar Alam * and Jai Narayan Mishra

Kailash Institute of Pharmacy & Management, GIDA, Gorakhpur - 273209, Uttar Pradesh, India.

Keywords:

Phenylephrine hydrochloride, Triprolidine hydrochloride, Dextromethorphan hydrobromide, ICH guidelines, RP-HPLC, Mehtod validation

Correspondence to Author:
Dr. Gulzar Alam

Kailash Institute of Pharmacy & Management, GIDA, Gorakhpur - 273209, Uttar Pradesh, India.

E-mail: gulzar_alam@rediffmail.com

ABSTRACT: A new isocratic HPLC method based on reverse phase separation has been developed for simultaneous estimation of Dextromethorphan hydrobromide (DMP), Triprolidine hydrochloride (TPN), and Phenylephrine hydrochloride (PHE) in their mixed liquid dosage form. The chromatographic separation was accomplished on Agilent TC-C18 (250 x 4.6 mm, 5× m) column with a flow rate of 1 ml/min, UV detection (271 nm). Mobile phase consisting of 5 g DOSS, methanol, tetrahydrofuran, and water in the ratio of (70:10:20) pH 4.0 adjusted by acetic acid. The method was found to be selective for PHE, TPN, and DMP with retention time 4.7 min, 5.9 min, and 6.9 min, respectively. The linearity was established over the concentration range of 160-240 mcg/ml, 40-60 mcg/ml and 320-480 mcg/ml for PHE, TPN and DMP, respectively. Limit of detection and Limit of quantification for PHE was found to be 37.87 µg/ml, and 114.77 µg/ml, respectively, for TPN was found to be 10.19 µg/ml and 30.89 µg/ml, respectively and for DMP was found to be 57.50µg/ml and 174.26 µg/ml, respectively. The developed method was further validated in compliance with ICH guidelines. The statistical result showed that the method was precise, accurate, reproducible, and specific for the analysis of PHE, TPN, and DMP.

INTRODUCTION: Dextromethorphan Hydrobromide (DMP), Triprolidine (TPN) and Phenylephrine Hydrochloride (PHE) in combined liquid dosage form, has gained increasing acceptance in temporarily reliving symptoms due to common cold, hay fever (allergic rhinitis) and other respiratory allergies. Dextromethorphan chemically (+)-3-methoxy-17-methyl-(9α,13α,14α)-morphinan is an NMDA (N-methyl-D-aspartic acid) antagonist, non-competitive channel blocker, which is one of the most widely used antitussive[1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.12(9).4920-26

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.12(9).4920-26

Triprolidine hydrochloride, chemically [(E)-2-[3-(l-pyrrolidinyl)-l-p-tolylpropenyl] pyridine monohydrochloride] is a histamine H1-receptor antagonist [2-3]. Phenylephrine hydrochloride, chemically 3 - (1 – hydroxyl - 2- methyl amino-ethyl) phenol is indicated for general cold-related distress or short-term stuffy nose caused by allergic rhinitis.

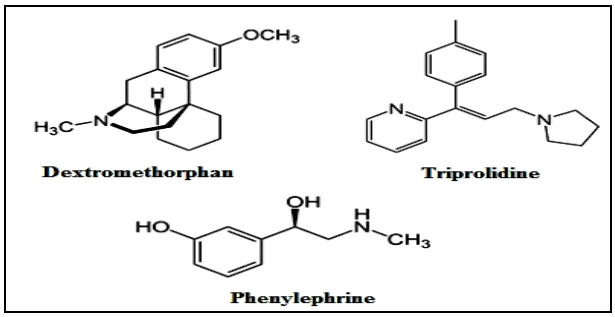

FIG. 1: CHEMICAL STRUCTURE OF DEXTROMETHORPHAN, TRIPROLIDINE AND PHENYLEPHRINE

As a vasoconstrictor, Phenylephrine has both indirect and direct sympathomimetic activity **Fig. 1** [4-5]. A detailed investigation revealed that analytical methods exist for estimating specified drugs with other combinatorial by RP-HPLC [6-16].

There were few RP-HPLC methods for the estimation of DMP, PHE, and TPN simultaneously, for specified combination in solid dosage form 17 and for combined liquid dosage form [18].

The objective of the present approach was to develop and validate a reversed-phase high-performance chromatographic technique for simultaneous estimation of PHE, TPN and DMP in their combined liquid dosage form. The developed method was later validated in terms of accuracy, inter-day and intra-day precision, specificity, linearity, LOD and LOQ values.

MATERIALS AND METHODS:

Chemicals and Reagents: Pharmaceutical grade Dextromethorphan Hydrobromide, Triprolidine Hydrochloride, and Phenylephrine Hydrochloride were provided as gift samples by Apple International Pharmaceuticals Pvt. Ltd. Nepal. HPLC grade water (Thermo Fischer Scientific), Tetrahydrofuran (Thermo Fischer Scientific), HPLC Methanol (Thermo Fischer Scientific).

Instrument: Chromatography was performed on Shimadzu HPLC L201055, equipped with a UV detector. For Intermediate Precision Shimadzu HPLC L204350 equipped with UV detector, by using Agilent TC-C18 (250 x 4.6 mm, 5μm) column.

Chromatographic Condition: For method development, a reverse phase C18 column (250 x 4.6 mm, 5 μm), a mobile phase consisting of 5 g DOSS, Methanol, Tetrahydrofuran and Water in the ratio of (70:10:20 % v/v/v) pH 4.0 adjusted by Acetic acid, the flow rate of 1.0 ml/min at a wavelength of 271 nm (UV detection).

Preparation of Standard Solution:

Dextromethorphan HBr Stock Solution: Fifty milligrams of Dextromethorphan HBr raw material was weighed and transferred to a 25 ml volumetric flask and then dissolved with solvent mixture sonicating for 10 min in sonicator. The volume was then made up to 25 ml with the same solvent.

Phenylephrine HCl Stock Solution: Twenty-five milligram of Phenylephrine HCL raw material was weighed and transferred to a 25 ml volumetric flask and then dissolved with solvent mixture sonicating for 10 min in a sonicator. The volume was then made up to 25 ml with the same solvent.

Triprolidine HCl Stock Solution: Twenty-five milligram of Triprolidine raw material was weighed and transferred to a 100 ml volumetric flask and then dissolved with solvent mixture sonicating for 10 min in a sonicator. The volume was then made up to 100 ml with the same solvent

Mixed Standard Solution: Five milliliters of Dextromethorphan stock solution, five milliliters of Phenylephrine stock solution, and five milliliters of Triprolidine stock solution was pipetted in 25 ml volumetric flask and volume made up to 25 ml with the solvent mixture to obtain PHE (200 μg/ml), TPN (50 μg/ml) and DMP (400 μg/ml).

Sample Solution: 11.972 grams of syrup was weighed in 50 ml volumetric flask and then dissolved with solvent mixture sonicating for 10 minutes in a sonicator. The volume was then made up to 50 ml with the same solvent.

Method Validation: The developed method was subjected to validation under various criteria such as linearity and range, precision, accuracy and robustness in accordance with the international conference of harmonization Guidelines [19].

Linearity: Suitable aliquots of PHE, DMP, and TPN working standard solutions were taken in different 10 ml volumetric flask and diluted up to the mark with mobile phase to obtain a final concentration of 160, 180, 200, 220, and 240 μg/ml of PHE, 40, 45, 50, 55 and 60 μg/ml of TPN and 320, 360, 400, 440 and 480 μg/ml of DMP respectively. The calibration curve was constructed by drawing the mean peak area versus concentrations, and regression equations for all three drugs were calculated.

Precision: The repeatability (Intraday) study was performed by estimating the response of PHE, TPN, and DMP at three different concentrations (160, 200 and 240 μg/ml), (40, 50 and 60 μg/ml) and (320, 400 and 480 μg/ml), three replicates each respectively. Intermediate precision, *i.e.*, inter-day

and equipment change studies for PHE, TPN and DMP, were calculated by assaying the sample solution on different days and on different equipment, and the result were reported in terms of relative standard deviation.

Accuracy: The accuracy of the developed method was determined by calculating recoveries of PHE, TPN, and DMP by standard additions method. Known amounts of PHE (60, 100 and 140 µg/ml), TPN (15, 25 and 35 µg/ml) and DMP (120, 200, and 280 µg/ml) were added to a pre-selected sample solution and by measuring the peak areas amounts of PHE, TPN and DMP were estimated. Recovery (%) and RSD (%) were calculated for each contraction.

Limit of Detection (LOD) and Limit of Quantitation (LOQ): The LOD and LOQ of PHE, TPN, and DMP were calculated by using the following equation as per ICH guidelines.

$$LOD = 3.3\times \sigma / S$$

$$LOQ=10\times\sigma/S$$

Where σ is the standard deviation of y-intercepts of regression line and S is the slope of calibration curve.

Robustness: The robustness of this method was investigated by purposefully changing experimental conditions such as flow rate and pH. The study was carried out by changing 0.2 units in pH and 0.2 ml/min of flow rate.

System Suitability: During method development and validation, system suitability is essential-function.5 repeated injections were studied for the analysis of PHE, TPN and DMP in reference to their retention time, tailing factor, theoretical plates and asymmetry factor.

RESULTS AND DISCUSSION:

Selection of Mobile Phase: Numerous Mobile Phase compositions were attempted to figure out the peak of PHE, TPN, and DMP. The ultimate mobile phase containing Doss (5.5 g); Methanol, THF and water (70: 20: 10) adjusted pH 4.0 by using Acetic acid, since it was able to resolve peaks of PHE (4.66 ± 0.03), TPN (5.82 ± 0.04) and DMP (6.80 ± 0.05) with resolution factor of 5.33 and 4.17. For quantification λ was set to 271 nm.

Specificity and Selectivity: By using the mobile phase as a solvent, a mixture of PHE, TPN, and DMP (200, 50, and 400 µg/ml) was prepared and introduced in the column and retention time was inspected. While comparing the results with the blank, it was found that there is no interference at the retention time. The method was found specific and precise. An illustrative chromatogram of PHE, TPN and DMP standard and sample is demo-nstrated in **Fig. 2** and **3.**

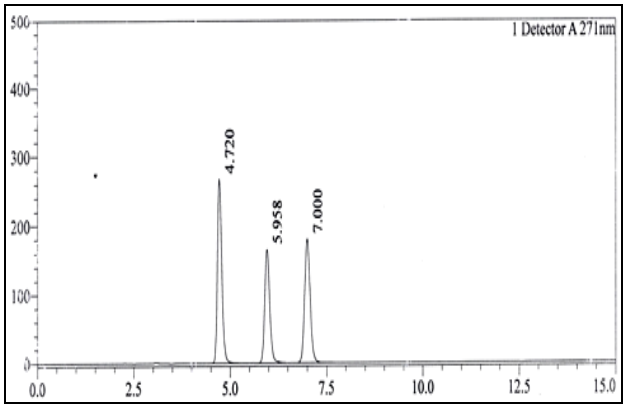

FIG. 2: CHROMATOGRAM OF STANDARD PHE, TPN AND DMP

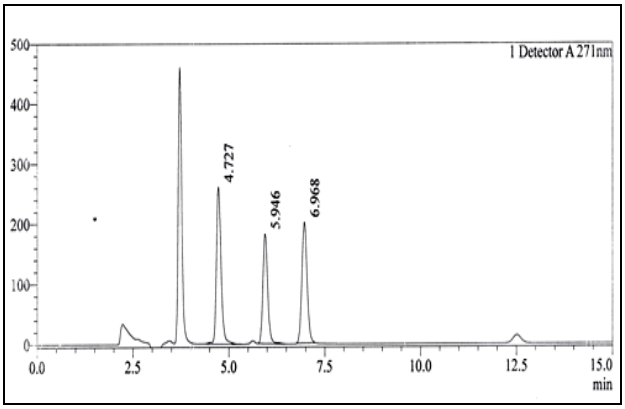

FIG. 3: CHROMATOGRAM OF TEST PHE, TPN AND DMP

Linearity: With a focus on linearity range of developed HPLC method peak areas versus concentrations were plotted. An excellent linear relationship (r^2 = 0.998), (r^2 = 0.997) and (r^2 = 0.998) were witnessed for PHE, TPN and DMP respectively. The harmonious relation eq. was y = 10594x + 17103 for PHE, y = 30642x – 32669 for TPN and y = 4386.7x + 66901 for DMP. The data are expressed in the Table.1 calibration curves are drawn in **Fig. 4, 5** and **6.**

TABLE 1: REGRESSION DATA OF CALIBRATION CURVE OF PHE, TPN AND DMP

Sample	Range (mcg/ml)	Regression Coefficient (r^2)	Slope	Intercept
PHE	160-240	0.998	10594	17103
TPN	40 – 60	0.997	30642	32669
DMP	320 – 480	0.998	43867	66901

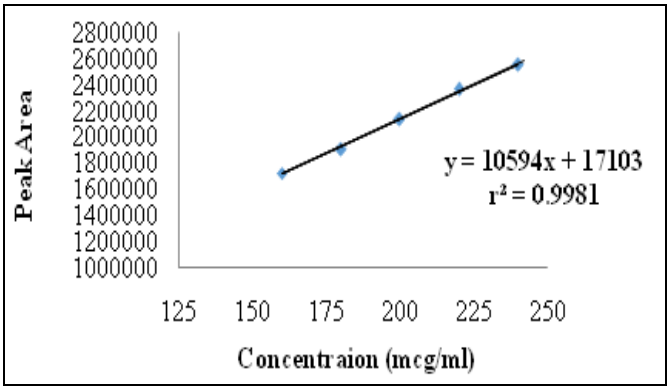

FIG. 4: CALIBRATION CURVE OF PHE

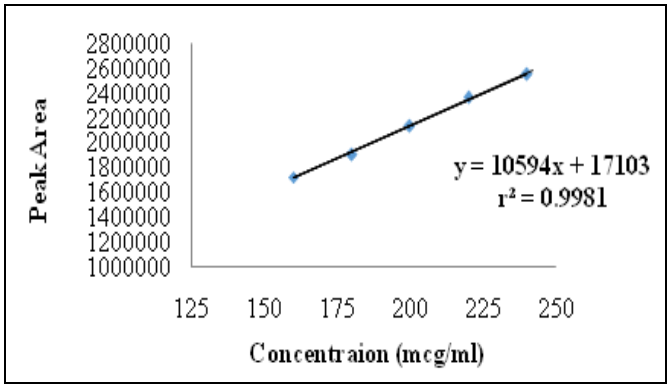

FIG. 5: CALIBRATION CURVE OF TPN

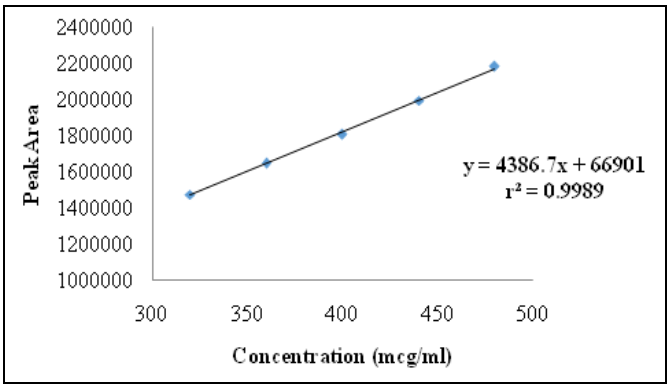

FIG. 6: CALIBRATION CURVE OF DMP

Accuracy: For the proposed method, accuracy was evaluated by calculating % recoveries of PHE, TPN and DMP by pattern of standard additions (in terms of target assay concentration).A sound recoveries were achieved between the necessary criteria (98.0-102.0 %) as illustrated in **Table. 2, 3,** and **4.**

TABLE 2: ACCURACY DATA OF PHE

Conc [%]	Std Conc [mcg/ml]	Sample Conc [mcg/ml]	Amt of Std Recovered	[%] Recovery	Mean Recovery [%]	SD	% RSD
80	60	100	59.552	99.25			
80	60	100	60.036	100.06	99.65	0.40	0.40
80	60	100	59.800	99.66			
100	100	100	100.012	100.01			
100	100	100	99.096	99.09	99.61	0.47	0.47
100	100	100	99.744	99.74			
120	140	100	138.824	99.16			
120	140	100	139.132	99.38	99.07	0.35	0.36
120	140	100	138.164	98.68			

TABLE 3: ACCURACY DATA OF TPN

Conc [%]	Std Conc [mcg/ml]	Sample Conc [mcg/ml]	Amt of Std Recovered	[%] Recovery	Mean Recovery [%]	SD	%RSD
80	15	25	15.280	101.86			
80	15	25	15.256	100.70	101.20	0.59	0.58
80	15	25	15.160	101.06			
100	25	25	24.652	98.60			

100	25	25	24.828	99.31	98.87	0.38	0.38
100	25	25	24.680	98.72			
120	35	25	34.652	99.00			
120	35	25	34.640	98.97	98.94	0.07	0.07
120	35	25	34.600	98.86			

TABLE 4: ACCURACY DATA OF DMP

Conc [%]	Std Conc [mcg/ml]	Sample Conc [mcg/ml]	Amt of Std Recovered	[%] Recovery	Mean Recovery [%]	SD	%RSD
80	120	200	119.276	99.39			
80	120	200	117.720	98.10	98.90	0.70	0.71
80	120	200	119.080	99.23			
100	200	200	199.332	99.66			
100	200	200	199.044	99.52	99.49	0.18	0.18
100	200	200	198.596	99.29			
120	280	200	277.524	99.11			
120	280	200	277.212	99.00	99.07	0.06	0.06
120	280	200	277.488	99.10			

Precision: Precision was determined in terms of repeatability (intra-day precision) and intermediate precision (inter-day precision). For repeatability, an assay of three concentrations (80%, 100%, and 120%), three replicates each were performed in a single day. Intermediate precision (different day & equipment change) was performed at 100% concentration by evaluating assay of the freshly prepared test solution and the same solution after 24 h and also in different equipment. The % RSD of PHE, TPN, and DMP was found to be less than 2.0 in all the determinations **Table 5** and **6.**

TABLE 5: INTRA DAY PRECISION (REPEATABILITY) OF THE PROPOSED METHOD

Drug	Conc [%]	Wt of Std[mg]	Wt of Spl [mg]	Mean Area of Spl	Assay [%]	Average± SD
PHE	80	25	9.577	850160	99.87	
	100	25	11.972	1062022	99.81	99.71 ± 0.18
	120	25	14.366	1269982	99.46	
TPN	80	25	9.577	625409	100.58	
	100	25	11.972	772905	99.44	99.80± 0.55
	120	25	14.366	926970	99.38	
DMP	80	25	9.577	747453	99.58	
	100	25	11.972	935759	99.74	99.59 ± 0.11
	120	25	14.366	1119671	99.46	

TABLE 6: INTER DAY PRECISION OF THE PROPOSED METHOD

Drug	Variables	Mean Area of Std	Mean Area of Spl	Assay [%]	% RSD
PHE	Day 1	2124526	2151188	100.68	0.23
	Day 2	2113934	2157038	100.60	0.28
	Equipment 1	2124526	2151188	100.68	0.23
	Equipment 2	1094541	1082609	100.23	0.11
TPN	Day 1	1503539	1521430	100.43	0.17
	Day 2	1503559	1523375	100.56	0.16
	Equipment 1	747421	1521430	100.43	0.17
	Equipment 2	747192	747421	100.21	0.78
DMP	Day 1	1801474	1827747	100.52	0.29
	Day 2	1804835	1823715	100.11	0.19
	Equipment 1	1801474	1827747	100.52	0.29
	Equipment 2	908288	913099	100.13	0.17

System Suitability: In order to verify that the system is functioning properly during a test, system suitability parameters need to be checked. Five replicates of the optimized standard were injected and method performance data comprising column efficiency (N), resolutions separating nearest peaks (Rs) and asymmetry factor (As) were put on the list in **Table 7**. All the parameters were in accordance with the fundamentally prescribed ones.

TABLE 7: RESULT OF SYSTEM SUITABILITY TEST

Sample	Retention time (min)	Tailing Factor (A_s)	Theoretical plates (N)	Resolution (R_s)
PHE	4.721	1.251	7599	--
TPN	5.957	1.171	9496	5.371
DMP	6.998	1.105	10847	4.06

Limits of Detection and quantification (LOD and LOQ): LODs and LOQs were identified using the ICH method based on the calibration curve to assess that the validated concentration ranges of the analytical sample were above their LOQ values 19. The LOD and LOQ values for PHE (37.87 µg/ml and 114.77µg/ml), TPN (10.19µg/ml and 30.89µg/ml) and DMP (57.50µg/ml and 174.26µg/ml)

Robustness: The optimized HPLC factors were revised slightly to investigate the robustness of the method. Robustness was studied using Plackett-Burmann design, keeping pH and flow rate as two variables (pH 3.8, flow rate 0.8), (pH 3.8, flow rate 1.2), (pH 4.2, flow rate 0.8) and (pH 4.2, flow rate 1.2). At higher flow rates, analytes do not have enough time to interact with the stationary phase as compared to lower flow rates. Therefore, analytes elute faster, and retention times are shorter. The theoretical plate number is directly proportional to the retention time. Therefore, as the flow rate increases, the number of theoretical plates decreases.

The method was observed to be robust to peak parameters, as the number of Theoretical Plates exceeded 2000, the Tailing Factor was less than two and the resolution was greater than 2 in all conditions.

TABLE 8: RESULT OF ROBUSTNESS

Drug	Parameter		RT[a]	Area	TF[b]	TP[c]
	pH	Flow rate				
PHE	3.8	0.8	7.001	2683220	1.253	9341
	3.8	1.2	4.704	1809672	1.218	7288
	4.2	0.8	6.820	2714165	1.265	8960
	4.2	1.2	4.569	1805486	1.222	7175
TPN	3.8	0.8	9.766	1858741	1.114	11329
	3.8	1.2	6.535	1264750	1.110	8881
	4.2	0.8	9.189	1891075	1.123	11128
	4.2	1.2	6.133	1257903	1.113	8832
DMP	3.8	0.8	11.941	2333518	1.111	12708
	3.8	1.2	7.963	1573508	1.109	9979
	4.2	0.8	11.322	2311346	1.111	12623
	4.2	1.2	7.519	1558556	1.107	9989

[a]Retention time; btailing factor; [c]theoretical plate

CONCLUSION: A credible and instantaneous liquid chromatography method for simultaneous estimation of PHE, TPN, and DMP in liquid dosage form has been developed and validated. The chromatographic run time of 15 minutes enables analysis of stacks of samples in a short time. The experimental design was applied for rational robustness study and presentation of its suitability for the desired objective. The results suggest that the method is linear, sensitive, precise, accurate, and robust in response to the mixture under examination. The optimized and validated HPLC procedure was found to be simple, responsive, precise, and accurate. Subsequently, it can be used for routine analysis of PHE, TPN and DMP in the liquid dosage form.

ACKNOWLEDGEMENT: The author would like to thank the Director (Dr. J. N. Mishra) and Dr. Gulzar Alam, Kailash Institute of Pharmacy & Management, Gorakhpur, (UP), India, and Apple International Pharmaceuticals Pvt. Ltd, Nepal, for providing gift sample Dextromethorphan, Phenylephrine, and Triprolidine.

CONFLICTS OF INTEREST: The authors declare no conflicts of interest.

REFERENCES:

1. Dextromethorphan Pre-Review Report. World Health Organization 2012; 1-26.
2. Deal D, Chandrasurin P, Shockcor J, Minick D, Findlay J and McNulty M: Disposition and metabolism of

triprolidine in mice. Drug metabolism and disposition. The Biological Fate of Chemicals 1992; 20(6): 920-27.
3. Aman T, Ahmad A, Aslam M and Kashmiri MA: Spectrophotometric determination of triprolidine hydrochloride by m-dinitrobenzene in pharmaceutical preparations. Analytical Letters 2002; 35(4): 733-46.
4. Trommer H, Raith K and Neubert RHH: Investigating the degradation of the sympathomimetic drug phenylephrine by electrospray ionisation-mass spectrometry. Journal of Pharmaceutical and Biomedical Analysis 2010; 52(2): 203-09.
5. Gelotte CK and Zimmerman BA: Pharmacokinetics, Safety, and Cardiovascular Tolerability of Phenylephrine HCl 10, 20 and 30 mg after a Single Oral Administration in Healthy Volunteers. Springer Open Choice 2015; 35(9): 547-58.
6. Palur K, Archakam SC and Koganti B: Chemometric Assisted UV Spectrophotometric and RP-HPLC methods for simultaneous determination of Paracetamol, Diphenhydramine, Caffeine and Phenylephrine in Tablet Dosage Form. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2020; 243: 118801.
7. Kirkpatrick D, Fain M, Yang J, Santos L and Anthony C: UHPLC Assay and Impurity Methods for Diphenhydramine and Phenylephrine Hydrochloride Oral Solution. Separation Science Plus 2019; 1-8.
8. Reid I and Kariem E: Development and validation of a hplc method for the simultaneous determination of Pseudoephedrine, Dextromethorphan and Triprolidine in their combined cough and cold syrups. Journal of Advances in Chemistry 2017; 13(11): 6011-17.
9. Rao PM, Santosh T and Babu DKR: Development, validation & stress degradation studies of triprolidine by reverse phase-high performance liquid chromatographgy (rp-hplc). International Journal of Pharmaceutics & Drug Analysis 2016; 4(2): 72-78.
10. Alam Md I, Siddiqui A ur-Rahim, Khanam N and Kamaruddin SJ: A Multivariate Quantification of Box-Behnken Design Assisted Method Development and Validation of Dextromethorphan Hydrobromide and Desloratadine Simultaneously by Reverse-Phase HPLC in in-House Syrup Formulation. Journal of Separation Science 2020; 43(18): 3597-06.
11. Mostafa NM, Elsayed, GM, Hassan, NY and El Mously, DA: Development and Validation of Eco-Friendly Liquid Chromatographic and Spectrophotometric Methods for Simultaneous Determination of Coformulated Drugs: Phenylephrine Hydrochloride and Prednisolone Acetate. Journal of AOAC International 2019; 100(6): 1761-70.
12. Chakraborty D, Chakraborty R, Kundu S and Kumar R: Development and validation of a new HPLC-UV method for simultaneous estimation of Cetirizine Hydrochloride and Phenylephrine Hydrochloride in tablet formulation. International Journal of Pharmaceutical Sciences and Research 2019; 10(7): 3349-53.
13. Abdelhamid AG, El-Kafrawy DS, Abdel-Khalek MM and Belal TS: Analytical investigation of Ternary mixture of Phenylephrine Hydrochloride, Dimetindene Maleate and Benzalkonium Chloride Using Validated Stability Indicating HPLC-DAD Method. Drug Developm and Industrial Pharmacy 2020; 4 (8): 1278-88.
14. Purnima K, Madhusudan Y and Channabasavaraj KP: Development and validation of analytical methods for simultaneous estimation of Dextromethorphan and Quinidine by RP-HPLC and UV-spectrometry. International Journal of Pharmaceutical Sciences and Research 2017; 8(3): 1301-13.
15. Nezhadali A, Shapouri MR, Amoli-Diva M, Hooshangi AH and Khodayari F: Method development for simultaneous determination of active ingredients in cough and cold pharmaceuticals by high performance liquid chromatography. Heliyon 2019; 5(12): 02871-2871.
16. Dongala T, Katari N, Palakurthi A and Jonnalagadda S: Development and Validation of a Generic RP-HPLC PDA method for the simultaneous separation and quantification of Active Ingredients in Cold and Cough Medicines. Biomedical Chromatography 2019; 33: 1-10.
17. Venisetty RK and Kumar SK: RP-HPLC method development and validation for simultaneous estimation of dextromethorphan, phenylephrine and triprolidine in bulk and its application in the evaluation of marketed tablet dosage forms. International Journal of Advanced Biomedical & Pharmaceutical Research 2014; 3(1): 14-18.
18. Baghel U, Sharma H, Chouhan A, Sharma A, Siddiqui M and Singh D: Gradient RP-HPLC Method development for simultaneous estimation of Dextromethorphan hydrobromide, Phenylephrine hydrochloride, and Triprolidine hydrochloride in Liquid Dosage Form. Research Journal of Pharmacy and Technology 2020; 13: 583-88.
19. ICH Harmonised Tripartite Guidelines. Validation of Analytical Procedures: Text and Methodology Q2 (R1). Published Online 2005.

How to cite this article:
Pandey VK, Alam G and Mishra JN: Development and validation of a new isocratic RP-HPLC method for simultaneous estimation of dextromethorphan hydrobromide, phenylephrine hydrochloride and triprolidine hydrochloride in their combined liquid dosage form. Int J Pharm Sci & Res 2021; 12(9): 4920-26. doi: 10.13040/IJPSR.0975-8232.12(9).4920-26.