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Research Article

SIMULTANEOUS ESTIMATION OF DROTAVERINE HYDROCHLORIDE AND PARACETAMOL IN BULK AND TABLET DOSAGE FORM BY RP-HPLC METHOD

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ABSTRACT

A simple, rapid, reproducible, accurate and precise Reverse Phase HPLC method was developed for the quantitative simultaneous estimation of Drotaverine hydrochloride and Paracetamol in combined tablet dosage form. Drotaverine hydrochloride is an analog of papaver and is used mainly as an antispasmodic, smooth muscle relaxant. Paracetamol has analgesic and antipyretic activity. The chromatographic separation of both drugs was achieved with 250 x 4.6 mm, i.d 5 m C-18 column using Methanol: water pH adjusted to 4.0 with O- Phosphoric acid. (60:40 v/v) at the flow rate of 1ml/min. The measurements were made at 243.0 nm using UV detector. The linearity range was found to be 5-80 g/ml for Drotaverine hydrochloride and 5-70 g/ml for Paracetamol. The coefficient of correlation for Drotaverine hydrochloride and Paracetamol was found to be 0.9994 and 0.9990 respectively. The retention time for Drotaverine hydrochloride and Paracetamol were 4.562 min and 8.146 min, respectively. The tailing factor for Drotaverine hydrochloride and Paracetamol was found to be 1.12 and 1.18 respectively. The percent recoveries obtained for Drotaverine hydrochloride and Paracetamol were found to be 99.85 and 99.92 respectively. The relative standard deviation for intraday and interday precision in tablet was always less than 2%. The method was validated for linearity, range, precision, accuracy, specificity, selectivity, intermediate precision, ruggedness, robustness, stability and suitability.

Keywords: Drotaverine hydrochloride (DT); Paracetamol (PC); Method Validation; ICH guideline and RP-HPLC method.

INTRODUCTION

Drotaverine hydrochloride (DT) and Paracetamol (PC) are available in tablet dosage form in the ratio of 2:12.5. Chemically, Drotaverine hydrochloride is 1- [(3, 4-Diethoxy phenyl) methylene]-6, 7- diethoxy- 1, 2, 3, 4- tetrahydroisoquinoline[1]. It is an analog of papaver and is used mainly as an antispasmodic, smooth muscle relaxant[2]. DT is official in Martindale, The Extra Pharmacopoeia[2]. Paracetamol is 4- hydroxy acetanilide[1] has analgesic and antipyretic activity[1, 2]. PC is official in Martindale, The Extra Pharmacopoeia[2], I. P[3]., B. P[4]., and U. S. P[5]. Literature survey reveals that UV spectrophotometry[6,7], HPLC[8-10] methods are reported for determination of DT, HPLC with combinations of other drugs[11-13] and UV spectrophotometry[3,4], HPLC[3,5] methods are reported for determination of PC from its pharmaceutical formulations. Hence an attempt has been made to develop simple, sensitive, rapid, reproducible, accurate, precise and economical RP-HPLC method for the simultaneous estimation of DT and PC in bulk and tablet dosage forms.

MATERIAL AND METHODS

Instrument:

HPLC Agilent 1120 series containing degasser, binary gradient pump and UV detector is used.

Chemicals and reagents:

Standard gift samples of Drotaverine hydrochloride and Paracetamol were procured from Vishnu Chemicals Ltd., Hyderabad and Emcure Pharma Ltd., Pune respectively. Methanol (HPLC grade) was obtained from Qualigen Laboratories Pvt. Ltd., Mumbai.

Chromatographic conditions:

The chromatographic system used was an Agilent 1120 series, which comprised a degasser, binary gradient pump and UV detector. The system was controlled through Ezchrome software using Chromasil C18 (4.6 x 250 mm, 5 m; Advanced Chromatography Systems, Johns Island, SC) column maintained at 30°C temperature and a mobile phase flow rate of 1.0 ml/min. The mobile phase was composed of Methanol: water pH adjusted to 4.0 with O- Phosphoric acid. (60:40 v/v). The mobile phase was kept in ultrasonicator for 30 min. and filtered through a 0.45- m nylon membrane filter. Measurements were made with injection volume 20 L and UV detection at 243.0 nm.

Standard stock solutions:

The stock solution (100 g/ml) of DT and PC were prepared separately by dissolving accurately about 10 mg of each drug in 100 ml methanol HPLC grade in 100 ml volumetric flask.

Calibration curve:

Appropriate aliquots of standard stock solutions of DT and PC were diluted with mobile phase to obtain concentrations in the range of 5, 10, 20, 30, 40, 50, 60, 70 and 80 g/ml of DT and 5, 10, 20, 30, 40, 50, 60 and 70 g/ml of PC respectively. The linearity of DT and PC was found to be in the concentration ranges of 5-80 g/ml and 5-70 g/ml, respectively (Table 1), at their respective maximas. The coefficients of correlation were found to be 0.9994 for DT and 0.9990 for PC (Table 1). The mixed standard solution containing 8 g/ml of DT and 50 g/ml of PC was prepared from standard stock solution and injected into HPLC system (Fig. 1).

Analysis of tablet formulation:

Twenty tablets (Drotapar) each containing 80 mg of Drotaverine hydrochloride and 500 mg of Paracetamol were weighed and crushed in glass mortar to obtain fine powder. The powder sample equivalent to 8 mg of DT and 50 mg of PC was transferred into a 100 ml volumetric flask and dissolved in 50 ml methanol HPLC grade. The flask was kept in an ultrasonic bath for 20 min. The volume was adjusted to 100 ml with methanol HPLC grade. The solution was filtered through 0.2 nylon membrane filter. From this stock solution, 1 ml solution was pipetted out and transferred to 10 ml volumetric flask and made volume up to the mark with mobile phase to get the concentration 8 g/ml of DT and 50 g/ml of PC. The solution was injected into HPLC system (Fig.2). The results of the assay of tablet formulation and its statistical validation data is given in Table 2.

Table 1: System Suitability Parameters

Parameter	DT	PC
Linearity range* (µg/ml)	5-80	5-70
Correlation coefficient*	0.9994	0.9990
Slope*	12046	13318
Limit of detection (µg/ml)	0.026	0.034
Limit of quantitation (µg/ml)	0.080	0.095
Retention time* (min)	4.562	8.146
Resolution factor*	-	8.70
Tailing factor*	1.12	1.18
Theoretical plates*	8745	9543

*Average of six readings
DT and PC denotes Drotaverine hydrochloride and Paracetamol respectively.

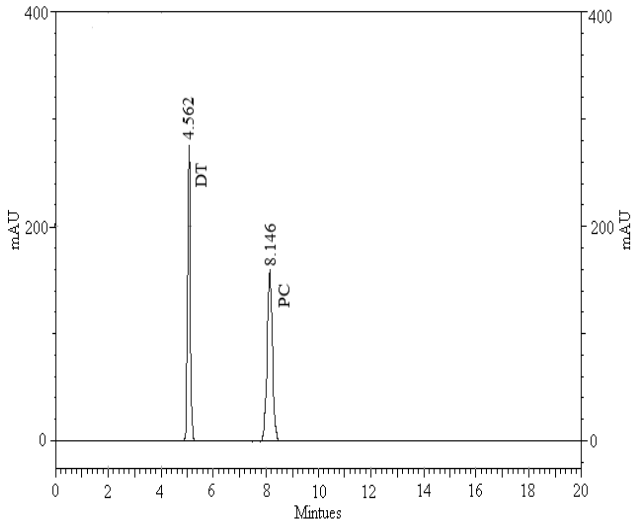

Fig. 1: Chromatogram of DT and PC in standard mixture

RESULTS AND DISCUSSION:

DT and PC were well- Advanced resolved using mobile phase composition of Methanol: water pH adjusted to 4.0 with O- Phosphoric acid (60:40 v/v) at flow rate of 1

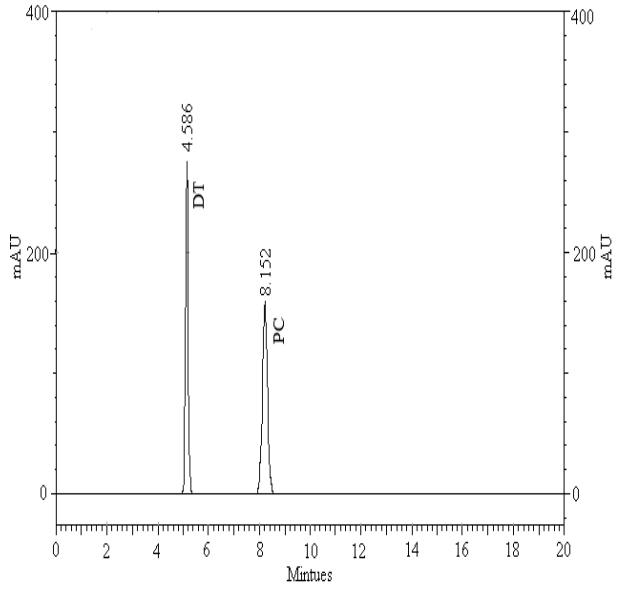

Fig. 2: Chromatogram of DT and PC in Tablet Formulation

ml/min, UV detection wavelength 243.0 nm and injection volume 20 l. The HPLC system was found to best for analysis. The retention time for Drotaverine hydrochloride and Paracetamol were found to be 4.562 min and 8.146 min, respectively. The resolution between two peaks was found to be 8.70.

Method Validation[14-15]:

Specificity: The specificity of the method is used to evaluate the homogeneity of drug peak.

Linearity: Linearity for DT and PC was selected at 5-80 g/ml and 5-70 g/ml. The correlation coefficients were selected at 0.9994 and 0.9990 for DT and PC, respectively. The results are shown Table 1.

Precision (repeatability): The precision of the method was studied by determining the concentrations of each drug in the tablets six times. The results of the precision study indicate that the method is reliable (%RSD < 2).

Accuracy: Accuracy of the method was studied by recovery experiments. The recovery was performed at three levels, 80 %, 100 %, and 120 % of the label claim of the tablet (80 mg of DT and 500 mg of PC). The results are shown in Table 3.

Robustness: The robustness of a method is the ability of method to remain unaffected by small changes in parameters like mobile phase composition, flow rate, pH of mobile phase and temperature etc.

Determination of limits of quantification and detection: The LODs for DT and PC were 0.026 g/ml and 0.034 g/ml, respectively, and the LOQs were 0.080 g/ml and 0.095 g/ml, respectively.

CONCLUSION

The reversed phase-HPLC method developed for analysis of binary mixture of DT and PC in their pharmaceutical

Table 2: Analysis of tablet formulation

Tablet sample	*Label claim (mg/tablet)*	*Amount found (mg/tablet)*	*% Label claim found**	*± Standard deviation*	*Standard error*
DT	*80*	*79.91*	*99.88*	*0.2472*	*0.3625*
PC	*500*	*499.60*	*99.92*	*0.3528*	*0.5623*

Table 3: Accuracy

Drug	Level of % recovery	% Mean*	Standard deviation	% RSD	Standard error
DT	80	100.16	0.1213	0.1207	0.0495
PC	80	99.94	0.2317	0.2310	0.0946
DT	100	99.87	0.1497	0.1489	0.0611
PC	100	99.91	0.4527	0.4520	0.1848
DT	120	99.78	0.3240	0.3234	0.1323
PC	120	99.89	0.1432	0.1428	0.0584

*Average of six readings

preparations is rapid, accurate, precise, and reproducible and with short run time. The method was fully validated showing satisfactory data for all the method validation parameters tested. A simple, rapid, reproducible, accurate and precise reverse phase HPLC method was developed for the quantitative simultaneous estimation of Drotaverine hydrochloride and Paracetamol in combined tablet dosage form. The developed method can be conveniently used by quality control department to determine the assay of pharmaceutical preparations.

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