



INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND DEVELOPMENT (IJPRD)

Platform for Pharmaceutical Researches & Innovative Ideas
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RP-HPLC METHOD FOR THE SIMULTANEOUS DETERMINATION OF DROTAVERINE HYDROCHLORIDE AND PARACTAMOL IN TABLET DOSAGE FORM.

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ABSTRACT

A simple, specific, accurate and precise reverse phase high performance liquid chromatographic method was developed for the simultaneous estimation of drotaverine hydrochloride and paracetamol in tablet dosage form. A Grace-C18, 5 μ m column 250 mm \times 4.6 mm in isocratic mode, with mobile phase containing methanol buffer in proportion of (55:45v/v) pH 4.0 adjusted with orthophosphoric acid were used. The flow rate was 1 ml/min. The retention time of Paracetamol and drotaverine hydrochloride were 3.3 and 5.4 min respectively, and the resolution factor was 3.0. Linearity range for Paracetamol and drotaverine hydrochloride was 8-24 μ g/ml. The proposed method is accurate, precise, specific and rapid for simultaneous estimation of paracetamol and drotaverine hydrochloride in tablet dosage form.

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Key Words

paracetamol and Drotaverine
hydrochloride RP-HPLC

INTRODUCTION

Paracetamol chemically is N-(4-Hydroxyphenyl) acetamide. It has analgesic, anti-inflammatory and anti-pyretic properties. It works by blocking the action of a substance in the body called cyclooxygenase which is responsible for production of prostaglandins. Drotaverine hydrochloride (DRO) is 1-(3, 4-diethoxyphenyl) methylene-6, 7 diethoxy-1, 2, 3, 4-tetrahydroisoquinoline hydrochloride. It is an antispasmodic agent with smooth muscle relaxant properties. It exerts its action by inhibiting phosphodiesterase enzyme IV which is specific for smooth muscles. It particularly acts on spastic site correcting cyclic AMP and calcium imbalance thereby relieves the smooth muscle spasms. [1-3] the analytical techniques reported for the determination of PARA include high- performance liquid chromatography [4-10], thin-layer chromatography [10] and spectrophotometry [11-12] in Human plasma, Human serum, Human urine and formulation. Literature survey reveals that analytical methods including high- performance liquid chromatography [13-15], thin-layer chromatography [16] and new membrane selective electrodes [17] have been available for the determination of DRO in pharmaceuticals preparation and plasma. Analytical methods for estimation of PARA and DRO in combination are not found reported in literature. The present paper describes a precise, accurate, specific and sensitive RP-HPLC method for simultaneous estimation of DRO and PARA in tablet dosage forms.

MATERIALS AND METHOD

High performance liquid chromatography system consisted of Thermo separation Product quaternary Gradient System. Chromatographic analysis was performed on a 250 mm × 4.6 mm i.d. column packed with Grace -C18, 5 µm particle sizes. Reference standard of drotaverine hydrochloride and Paracetamol was obtained from Alkem Laboratories Ltd .Aurangabad. All the solvents used were of HPLC grade, obtained from E.Merck (India) Ltd., Nagpur. Tablets containing Paracetamol (500 mg) and drotaverine hydrochloride (80 mg) (FDC Pharma Ltd, Aurangabad.) were purchased from a local pharmacy store.

Preparation of mobile phase and standard stock solution

Mobile phase was prepared by mixing Methanol and buffer in proportion of 55: 45 v/v, pH 4.0 adjusted with orthophosphoric acid. The mobile phase was filtered through 0.45 micron membrane filter and degassed by ultrasonicated for 15 min. Standard stock solutions of PARA and DRO (200 µg/ml) were prepared separately by dissolving 10mg of drug in 50 ml of methanol.

Calibration curve

Aliquots of 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, and 1.2 ml from standard DRO and PARA stock solutions were transferred to different volumetric flasks of 10 ml capacity. The volume was adjusted to the mark with methanol give a solution containing 5, 10, 15, 20 and 25 µg/ml DRO and PARA respectively.

The mixed standard solution was chromatographed for 20 minutes using mobile phase at a flow rate of 1.0 ml/min. Plot the graph of peak area vs. concentration for both the drugs. Temperature of the column was kept at ambient, and the effluent was monitored at 240 nm. The retention time of DRO is 5.4 min and PARA is 3.3 min respectively with resolution factor of 2.1.

Analysis of marketed formulation

Twenty tablets were weighed and finely powdered. The powder equivalent to 80 mg DRO and 500 mg PARA was accurately weighed and transferred to volumetric flask of 50 ml capacity. 25 ml of methanol was transferred to volumetric flask and sonicated for 20 min. The flask was shaken and volume was made up to the mark with methanol. The above solution was filtered through Whatman filter paper grade 602h. 1 ml of aliquot was taken and transferred to volumetric flask of 10 ml capacity along with 3.4 ml DRO standard solution of 1000 µg/ml. Volume was made up to the mark with the methanol. Further 0.3 ml of this solution was transferred to volumetric flask of 10ml capacity. Volume was made up to the mark with methanol to give a solution containing 15µg/ml DRO and 15µg/ml PARA. This solution was used for the estimation of DRO and PARA the prepared sample solution was chromatographed for 20 minutes using mobile phase at a flow rate of 1.0 ml/min. From the peak area obtained

in the chromatogram, the amounts of both the drugs were calculated.

Table 1: System suitability parameter

Parameter	DRO (min)	PARA (min)
Retention time	5.4 ± 0.07	3.3 ± 0.05
Resolution	-	2.1
Theoretical plate (N)	2275.24	3055.34
Tailing factor	1.9	2.0

RESULTS AND DISCUSSION

Several mobile phase compositions were tried to resolve the peaks of DRO and PARA. The optimum mobile phase containing methanol: buffer (55:45 v/v), pH 4.0 adjusted with orthophosphoric acid was selected because it was found ideal to resolve the peaks of DRO (RT =5.4 min) and PARA (RT =3.3 min) Quantification was achieved

with UV detection at 240 nm based on peak area. A representative chromatogram is shown in [Figure – 1]. Retention time for DRO and PARA were 5.4 and 3.3 min. respectively, Theoretical plate for PARA and DRO was 3055.521 and 2275.247 respectively, while tailing factor for DRO and PARA was 1.9 and 2.0 respectively. Linear regression data showed a good linear relationship over a concentration range of 8-24 µg/ml for DRO and PARA. The correlation coefficients (r^2) were 0.999 and 0.999 for DRO and PARA respectively. Indicate that the method is sensitive. The intra-day and inter-day different analyst precisions were determined by analyzing standard solutions in the concentration range of 12-20 µg/ml for DRO and PARA and results are reported in terms relative standard deviation [Table – 2].The lower values of % RSD indicate that the method is precise. Repeatability was performed by injecting 20 µg/ml solution of DRO

Table 2: Validation parameters

Parameter	Drotaverine HCl	Paracetamol
Calibration range (µg/ml)	0.5-5 ml	0.5-5 ml
<u>Precision (% RSD)</u>		
Intra-day (n=3)	0.76	0.67
Inter-day (n=3)	0.42	0.65
<u>Different analyst</u>		
Analyst I	0.54	0.31
Analyst II	0.49	0.55

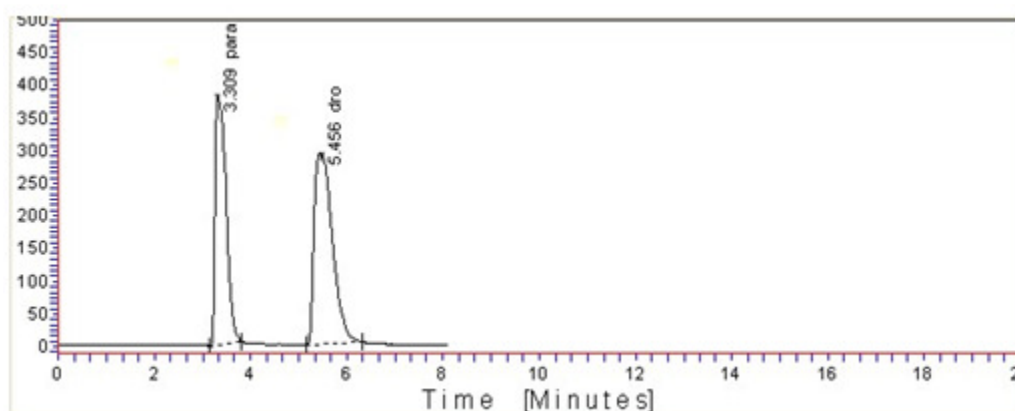


Figure 2:- Typical chromatogram of drotaverine hydrochloride and paracetamol

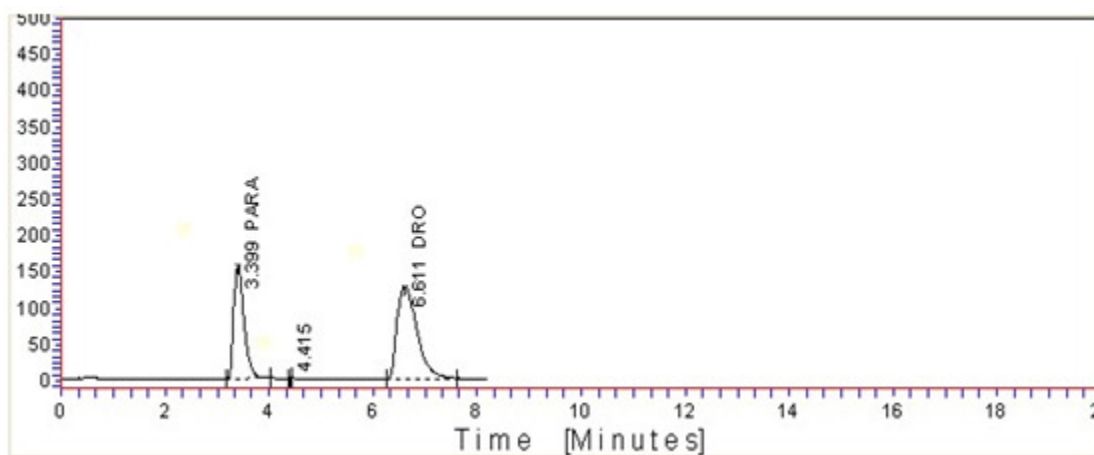


Figure 3: Chromatogram of tablet formulation of drotaverine hydrochloride and paracetamol

and PARA five times, and peak areas were measured. The % RSD was found to be 0.547 and 0.610 for DRO and PARA respectively. The accuracy of the method was evaluated by carrying out recovery studies. For that, known concentrations of standard solutions were added to pre-analysed sample solution, and the recovery was calculated. The recoveries of DRO and PARA were found to be in the range 99.49 % and 99.38 %, respectively which are satisfactory [Table – 3]. Amount of DRO was found to be 80.11 mg/tablet instead of 80 mg/tablet i.e.

more than label claim, while PARA was found to be 497.18 mg/tablet instead of 500 mg/tablet i.e. less than label claim,. Assay of the combination in tablet dosage form was found to be 100.13 % of DRO and 99.87 % of PARA. The results revealed that there was no interference of excipients. [Figure – 2] Same results were obtained with standard samples of DRO and PARA. [Figure-1] The proposed RP-HPLC method is accurate, precise, sensitive, selective and rapid for simultaneous estimation of DRO and PARA in combined tablet dosage form.

Table 3: Recovery data

Level	Amount added (mg)		Amount found (mg)*		% Recovered*		% RSD*	
	DRO	PARA	DRO	PARA	DRO	PARA	DRO	PARA
50%	20.5	20.5	40.50	250.51	99.50	99.21	0.31	0.35
100%	40	40	80.70	501.58	99.89	99.50	0.49	0.70
150%	60.5	60.5	120.65	751.27	100.50	100.2	0.80	0.99

Table 4: Result of analysis of formulation

Drug	Amount (mg/tablet)		% Label claim*	S. D.*
	Labelled	Found*		
DRO	80	80.11	100.13	1.08
PARA	500	497.18	99.87	1.24

* An average value \pm standard deviation of 6 determinations

ACKNOWLEDGEMENTS

The authors are thankful to Alkem Laboratories Ltd., Aurangabad for providing gift sample of drugs.

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