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RP-HPLC method for the simultaneous determination of metoclopramide hydrochloride and paracetamol in tablet dosage form

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Abstract

A simple precise and rapid reversed phase High Performance Liquid Chromatography method was developed for simultaneous determination of metoclopramide hydrochloride and paracetamol from pharmaceutical dosage form. The method was carried out on a HiQsil C8, (4.6×250mm) column with a mobile phase consisting of acetonitrile: acetate buffer (pH 6.78) (50:50v/v) at a flow rate of 1ml/min. Detection was carried out at 308 nm. The retention time of paracetamol and metoclopramide hydrochloride was 3.2 and 5.5 min respectively. The developed method was found to be accurate, precise and selective for simultaneous determination of Metoclopramide hydrochloride and paracetamol in tablets.

Keywords: Metoclopramide hydrochloride, paracetamol, RP-HPLC, simultaneous determination

Introduction

Paracetamol is N-(4-hydroxy phenyl) acetamide used as antipyretic and analgesic.Metoclopramide hydrochloride is 4-amino-5-chloro-N-(2-diethylaminoethyl)-2-methoxy benzamide. It is dopamine receptor antagonist, mainly used as antiemetic2-6. Literature survey reveals that many instrumental methods are reported for the determination of paracetamol alone or in their combined dosage form. A simultaneous spectrophotometric estimation of paracetamol and metoclopramide hydrochloride is available in solid dosage form7. There is no RP-HPLC method reported for the simultaneous determination of both the drugs in their combined dosage form8, 9. The aim of this study was to develop simple, precise and rapid reverse phase HPLC method for simultaneous determination of Metoclopramide hydrochloride and paracetamol in combined tablet dosage form. This method was simple, rapid and provides accurate and precise results.

Metoclopramide hydrochloride and paracetamol were received as gift samples from Medioral pharmaceuticals Limited, Satara. HPLC grade solvents were purchased from Merck Laboratories, India.

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Material and methods

Apparatus:

HPLC was carried out using a model (Jasco PU 980 plus) equipped with an UV visible detector (Jasco UV 975 plus). Column used was HiQsil C8 (4.6×250mm).Manual injector was used. Loop was of 20 µl capacity.

HPLC conditions:

A mixture of acetonitrile: acetate buffer (pH adjusted to 6.7 using Glacial acetic acid) (50:50 v/v) was used as mobile phase at a flow rate 1 ml/min. detection was carried out at 308 nm. The mobile phase was filtered through 0.45 µm membrane filter and degassed. The separation was carried out at room temperature, 25±10C.

Preparation of standard solutions:

The stock solution of Metoclopramide hydrochloride and paracetamol each of 100 µg/ml and 1000 µg/ml respectively in mobilephase were prepared and used. The working standards of Metoclopramide hydrochloride and paracetamol were prepared by dilution of standard.

Analysis of formulation:

Twenty tablets, each containing 5 mg of metoclopramide hydrochloride and 500 mg of paracetamol were weighed and finely powdered. A quantity of powder equivalent to 2.5 mg of metoclopramide hydrochloride and 250 mg of paracetamol was weighed accurately and transferred to a 50 ml volumetric flask and volume was made up with the mobile phase and it was filtered using 0.45 µm membrane filter. From the above prepared solution 1ml is taken and diluted to 10 ml with mobile phase. The 20 µl of the solution is injected into the column and chromatogram was recorded.

Result and discussion

Chromatograms of mixed standard solution with contained paracetamol and Metoclopramide hydrochloride were recorded and shown in fig 1. The retention time of paracetamol and metoclopramide hydrochloride was 3.2 and 5.5 min respectively. The method was validated in terms of linearity, accuracy, intraday precision, interday precision, and reproducibility.

Linearity: Calibration curves were obtained by plotting peak area verses concentration, paracetamol and metoclopramide hydrochloride shows linearity in the range of 200-1000 µg/ml and 10-50 µg/ml with correlation coefficient values at 0.9999 and 0.9996 respectively. The linear regression equations are Y=48702.4X+15285.94 for Metoclopramide hydrochloride and Y=987.45X+6175.5 for paracetamol.

Accuracy: The accuracy of the method was evaluated by carrying out recovery study. Known concentrations of standard solution were added to the pre-analyzed sample solution. Recovery studies were carried out on metoclopramide hydrochloride by preparation of standard and sample stock solution of 50 µg/ml and 500 µg/ml respectively. Further dilutions were made and the contents of metoclopramide hydrochloride were determined by proposed method by recording the chromatograms. The concentration of Metoclopramide hydrochloride added and percentage found after recovery study, are shown in Table 1.

Precision: The intra-day precision was determined by analyzing standard solution in the linearity range of calibration curve in triplicate on the same day, while interday precision was determined by analyzing corresponding standard solution daily for a period of one week. The %RSD or CV was observed at less than 2. Besides all system suitability parameter that was checked are listed in Table 2.

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Fig 1: Chromatogram of standard solution

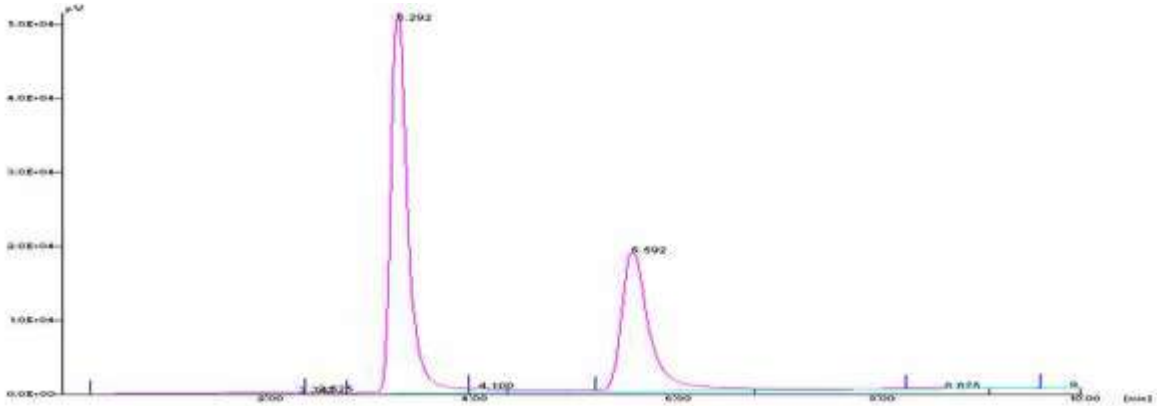

Fig 1: Chromatogram of samplesolution

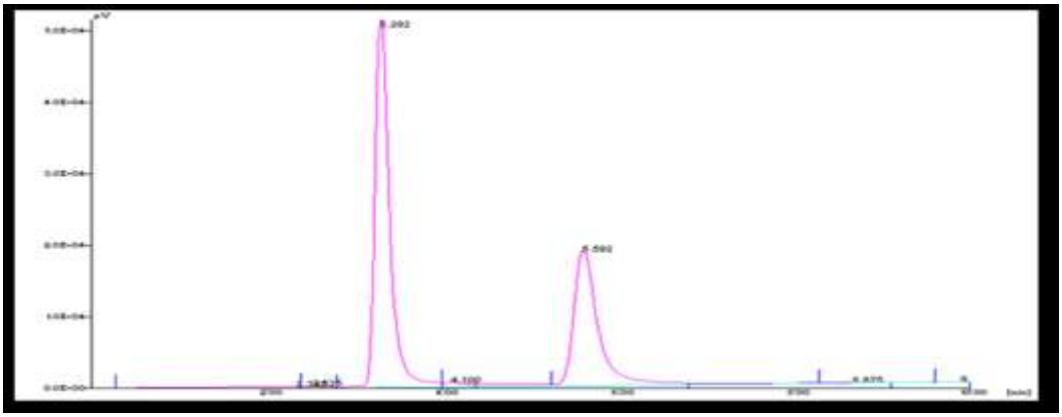

Table No.1: Analysis of Test formulation

Drug	Label Claim [Mg]	Amount Found [Mg]	Amount Found [%]
Paracetamol	500	497.04	99.41
	500	497.00	99.40
	500	497.17	99.43
	500	496.92	99.38
	500	497.07	99.41
	500	494.43	98.89
	Mean ± S.D	496.60 ± 1.07	99.32 ± 0.21
	% R.S.D.	0.22	0.22

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Drug	Label Claim [Mg]	Amount Found [Mg]	Amount Found [%]
Metoclopramide hydrochloride	5	4.927	99.16
	5	4.86	99.83
	5	4.94	99.16
	5	4.979	99.11
	5	4.874	99.23
	5	4.976	98.16
	Mean ± S.D	198.55 ± 0.55	99.27 ± 0.28
	% R.S.D.	0.28	0.28

Table No.2: Recovery study

Drug	Amount Added [%]	Amount Added [µg/ml]	Amount Recovery± S.D. [µg/ml, n=3]	Amount Recovery [%]	% R.S.D.
Paracetamol	80	400.4	397.03 ± 0.96	99.16	0.24
	100	501.9	496.91 ± 1.26	99.01	0.25
	120	601.2	602.24 ± 0.93	100.17	0.15
Metoclopramide hydrochloride	80	4.0	3.93 ± 0.45	98.82	0.17
	100	5.0	4.95 ± 0.98	99.19	0.80
	120	6.0	5.95 ± 0.76	99.20	0.82

Table No. 3: Intra Day Precision For Paracetamol

Concentration [µg/ml]	Trial I	Trial II	Trial III	Mean Peak Area ± S.D.	% RSD
200	239438.055	236372.3822	234413.23	236741.222±2532.63	1.06
400	447723.212	446322.121	447243.973	447096.423±712.099	0.15
600	697944.000	696877.34	697344.143	697388.493±836.96	0.12

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Table No. 4: Intra Day Precision for Metoclopramide hydrochloride

Concentration [µg/ml]	Trial I	Trial II	Trial III	Mean Peak Area ± S.D.	% RSD
40	2162168.8674	2160262.372	2204839.6452	2175756.96±1218.068	0.17
60	3059155.75	3032442.478	3130002.6705	3073866.96±50146.3962	1.6
80	3957470.44	4012903.268	4003214.16	3991195.97±29606.2046	0.7

Table No.5 :System Suitability Parameters

System Suitability Parameters	Paracetamol	Metoclopramide hydrochloride
Retention Time (Rt)	3.2	5.5
Resolution (Rs)	2.095	4.439
Theoretical Plates (T.P.)	2702.79	2808.39
Tailing Factor (T.F.)	1.07	0.89

Conclusion

The standard deviation is low, and low percent RSD as required by ICH guideline, indicate high degree of precision of the method. The results of the recovery study performed at three levels (80, 100 and 120 %) of the test concentration showed the high degree of accuracy of the proposed method; hence this method is simple, rapid, precise and accurate and can be employed for the routine estimation of metoclopramide hydrochloride and paracetamol in bulk and tablet dosage form.

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