

Research Article



RP-HPLC Method for the Simultaneous Estimation of Metoclopramide Hydrochloride and Dexamethasone Sodium Phosphate

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ABSTRACT

A simple, precise and rapid Revers Phase High Performance Liquid Chromatography method was developed for simultaneous determination of metoclopramide hydrochloride and dexamethasone sodium phosphate in bulk and pharmaceutical dosage form. The chromatography was carried out on RP-C18 column (Chromosil, 250×4.6mm id, 5micron particle size) and SPD-M20 photo diode array detector by using isocratic mobile phase system consisting of methanol: water (20:80) at flow rate of 1ml/min. The quantification was carried out at 260 nm. Retention time of metoclopramide hydrochloride and dexamethasone sodium phosphate was 1.845min and 2.773min respectively. Calibration curve was plotted. Drugs show good correlation coefficient and linearity. The developed method was validated according to ICH guidelines, it was found to be accurate precise and selective method for the simultaneous determination of metoclopramide hydrochloride and dexamethasone sodium phosphate.

Keywords: Metoclopramide hydrochloride, dexamethasone sodium phosphate, RP-HPLC, simultaneous determination.

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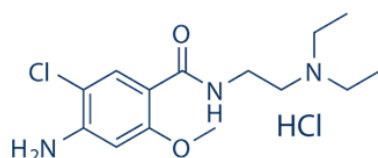
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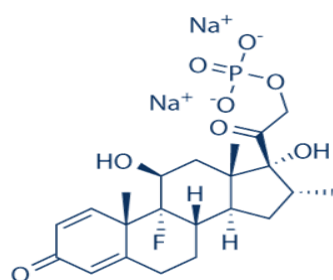
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INTRODUCTION

Metoclopramide hydrochloride is 4-amino-5-chloro-N-(2-diethylaminoethyl)-2-methoxy benzamide, is a dopamine receptor antagonist, mainly used as antiemetic. Dexamethasone sodium phosphate (Dexamethasone 21-phosphate disodium salt), is becoming increasingly used in antiemetics.



Metoclopramide Hydrochloride



Dexamethasone Sodium

In a pilot study a combination of metoclopramide and dexamethasone were administered to 29 patients receiving emetogenic chemotherapy. Result shows combination Metoclopramide and Dexamethasone therapy can effectively prevent emesis in 94% patients receiving potentially emetogenic chemotherapy, and can prevent nausea and emesis in 88% of untreated patients²⁶.

Here this graph is obtained by conducting a study on female patients having a age range between 21 to 64, undergoing myomectomy under spinal anesthesia. Post operative nausea and vomiting (PONV) is a generally revealed complexity following a medical procedure or anesthesia. Its frequency differs from the sort of medical procedure to the kind of sedative strategy utilized. The patients are divided to 3 categories, in which first category receives combination of Metoclopramide and Dexamethasone, category two receives Metoclopramide alone, and category three receives dexamethasone alone. Dexamethasone alone group had the highest incidence of late PONV, Metoclopramide alone group had an incidence of both early and late PONV. There was reduced incidence of both early and late PONV²⁷.

There is no a RP-HPLC method reported for the simultaneous determination of both the drug in their combined dosage form. The aim of this study was to develop simple, precise, and rapid reverse phase HPLC method for the simultaneous determination of metoclopramide hydrochloride and dexamethasone sodium phosphate in combined pharmaceutical dosage forms¹⁻².



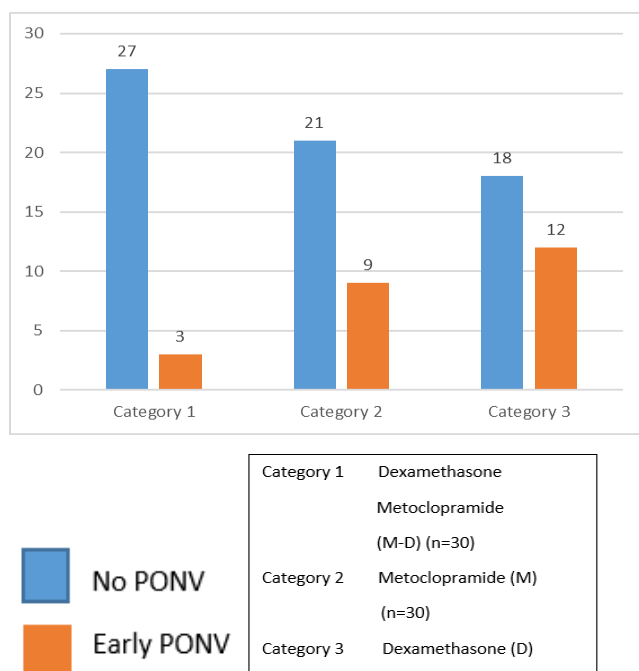


Figure 1: Incidence of early post-operative nausea and vomiting in each group

MATERIALS AND METHODS

Materials and standard

Metoclopramide hydrochloride and Dexamethasone sodium phosphate was obtained from YARROW CHEM PRODUCTS, MUMBAI. Water (HPLC GRADE) was purchased from Research lab fine chem industries, Mumbai, and methanol from Finar chemicals

Instrument

HPLC is carried out using a model of Shimadzu UFLC equipped with LC 20 AD pump, SPD-M 20 detector and RP-C18 column (chromosil, 250mm*4.6mm id, 5 micron particle size) was used. A Rheodyne injector with a 20 μ l loop used for injecting sample. Data processing performed using CLASS VP software²⁻³.

Electronic Balance of Tandem TJ series.

Preparation of Stock Solution

Take 100mg of Metoclopramide hydrochloride and 100 mg and Dexamethasone sodium phosphate in 100ml standard flask and make up to 10ml so that final concentration contain 1000 μ g/ml. From that 0.8, 1.0, 1.2, 1.4, 1.6ml Metoclopramide hydrochloride and 0.6, 0.75, 0.9, 1.05, 1.2ml Dexamethasone sodium phosphate were taken and up to 10ml to get further dilutions of 8, 10, 12, 14, 16 μ g/ml Metoclopramide and 6, 7.5, 9, 10.5, 12 μ g/ml Dexamethasone respectively.

Selection of Detection Wavelength

The standard solution of Metoclopramide and Dexamethasone were scanned over UV range 200-400nm. The wavelength for Metoclopramide and Dexamethasone were 273nm and 241nm respectively. The detection was carried out at 260nm.

Chromatographic Conditions

Methanol and HPLC Water in the ratio of 20:80. The mobile phase used was filtered through a 0.45 μ m membrane filter by vacuum filtration and degassed by ultra sonicator. Stationary phase was C18 column (250 \times 4.6mm) dimension at ambient temperature. Flow rate 1.0ml/min; detection wave length 260nm; injection volume 20 μ l. The retention time was found to be 1.8 and 2.7 for Metoclopramide and Dexamethasone respectively. The run time was for 5 minutes.

Preparation of Sample Solution

1ml of standard working solution of Metoclopramide and 0.75ml of standard working solution of Dexamethasone were pipetted out and transferred into 10ml standard flask. The volume made up with mobile phase to get final concentration of 10 μ g/ml of Metoclopramide and 7.5 μ g/ml of Dexamethasone. The test solution was injected and chromatogram was recorded, thus results calculated to determine amount of drug present in the laboratory sample.

Method Validation

1. Linearity

Linearity is the ability of the analytical method to the analyte in the sample. Linearity was demonstrated by analyzing five different concentration of active compound and each solution was injected to be confirmed. Peak areas were recorded, for all the peaks and calibration plot was constructed by plotting peak area v/s concentration of MET and DEX respectively.

2. Accuracy

Accuracy is the measure of exactness of the analytical method. It was performed by preparing solutions at varying levels 80%, 100%, 120% of test concentration using MET and DEX standard solution. Each solution was injected three times. The accuracy of the method was determined on three concentration level by recovery experiments. The recovery studies were carried out six times by standard addition method and the percentage recoveries with standard deviation were calculated.

3. Precision

It is the closeness or agreement between a series of data obtained from multiple sampling of an homogenous sample under prescribed conditions. Precision can be of three levels repeatability, reproducibility and intermediate. It should be performed in a homogenous sample. It can be expressed in terms of variance, standard deviation and coefficient of variance. To demonstrate agreement among results, a series of measurements are done with six replicate injections of the specific standard of MET and DEX at various interval on the same days were carried out.

4.Limit of detection (LOD)/ Limit of quantification (LOQ)

LOD of an analytical procedure is the lowest amount of an analyte that can be detected. LOQ of an analytical procedure is the lowest amount that can be quantified. LOD and LOQ of the developed method were determined by injecting progressively low concentrations of the standard solutions using the developed RP-HPLC method^{11, 12, 14}.

RESULTS AND DISCUSSION

To optimize an HPLC method parameters, several mobile phase compositions were tried. A satisfactory separation and good peak symmetry was observed with a mobile phase methanol: water (20:80) at a flow rate of 1.0ml?min to get better reproducibility. Quantification was carried out at 260nm based on peak area. Complete resolution of the peaks with clear baseline was obtained. The developed method was validated according to ICH guidelines

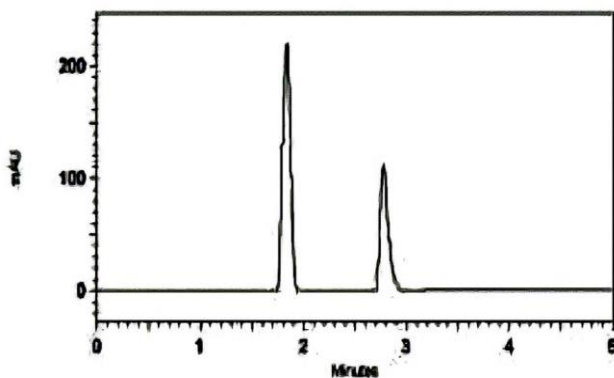


Figure 2: Chromatogram obtained in the ratio of 20:80 methanol: water

Method validation

1. Linearity

The linearity was checked against ICH guidelines. Linear correlation was obtained between peak area Vs. concentration of metoclopramide hydrochloride and dexamethasone sodium. Both drugs showed good linearity over a concentration range.

Metoclopramide hydrochloride

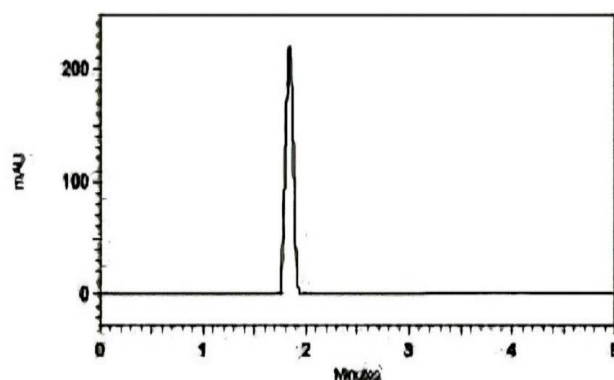


Figure 3: Chromatogram of Metoclopramide Hydrochlorid

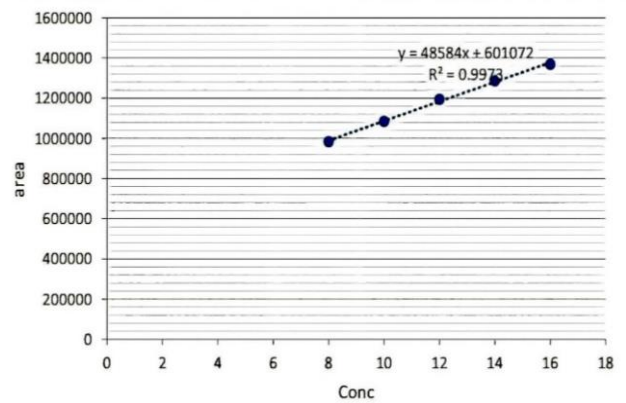


Figure 4: Calibration curve for MET.HCl

Table 1: Calibration data for MET.HCl

Sl.No	Concentration (µg/ml)	Area (Au)
1	8	9846238
2	10	1084756
3	12	1194875
4	14	1286548
5	16	1369582

Dexamethasone sodium phosphate

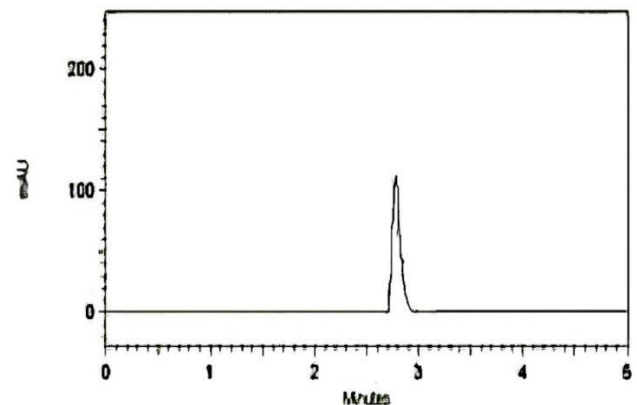


Figure 5: Chromatogram of Dexamethasone sodium

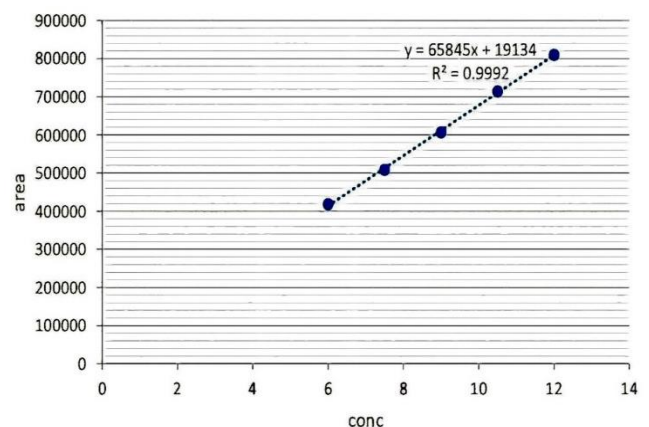


Figure 6: Calibration curve for dexamethasone sodium

Table 2: Calibration data of DEX

SL.NO	Concentration (µg/ml)	Area (Au)
1	6	418632
2	7.5	508963
3	9	606893
4	10.5	714536
5	12	8096584

3. Accuracy

Table 3: Determination of Accuracy

Drug	Accuracy Level (%)	Amount			% Recovery	Mean±SD	%RSD
		Actual (µg/ml)	Added (µg/ml)	Found (µg/ml)			
MET HCL	80	10	8	17.8	98.83	98.83±0.154	0.155
	100	10	10	19.8	99		
	120	10	12	21.7	98.63		
DEX	80	7.5	6	13.4	99.25	98.89±0.254	0.257
	100	7.5	7.5	14.8	98.66		
	120	7.5	9	16.3	98.78		

4. Precision

Table 4: Determination of Precision

SL.NO	Intra Day (n=3)		Inter Day (n=3)	
	MET	DEX	MET	DEX
1	1194875	606893	1194862	606853
2	1194875	606879	1194889	606882
3	1194894	606869	1194849	606899
Mean	1194875	606880.3	1194867	606878
SD	15.10	9.84	16.66	18.99
	0.001	0.001	0.001	0.003

System suitability parameters

Table 5: System suitability parameters

Parameters	MET±%RSD (n=3)	DEX±%RSD (n=3)
Retention Time	1.845±0.15	2.773±0.36
Tailing Factor	1.124±0.05	1.412±0.19
Theoretical Plates	411±0.15	1045±0.08

Result of percentage recovery of sample by the proposed method

Table 6: Result of percentage recovery of sample by the proposed method

RP-HPLC Method	MET (%recovery+SD)	DEX (%recovery+SD)
	98.5±0.32	98 ±0.51

2. Limit of Detection and Limit of Quantification

According to ICH guidelines there are several methods for the determination of LOD and LOQ in the present study the LOD and LOQ were calculated by equation. The LOD and LOQ of metoclopramide was found to be 219.47 and 665.06 µg/ml respectively. For Dexamethasone it is 133.20 and 403.65µg/ml.

SUMMARY AND CONCLUSION

A simple as well as precise analytical method were developed for the estimation of Metoclopramide hydrochloride and Dexamethasone in bulk formulation. The method was developed by using HPLC.

The developed high performance liquid chromatographic method is suitable for the analysis of drugs and here the calibration curve was plotted by using 8-16 µg/ml of MET.HCl and 6-12 µg/ml of DEX. The correlation coefficient was found to be 0.9973 for MET.HCl and 0.9992 for DEX.

In conclusion, using the developed analytical method, analysis of the selected drugs can be run fast with low cost and without prior extraction or losing accuracy.

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