Research Article

# Simultaneous Estimation of Metoclopramide Hydrochloride and Dexamethasone Sodium Phosphate Using Area Under Curve Method

**Dr. Prasanth.S.S[1], Preethi .P.R[2]***

1. Professor & HOD, Dept. of Pharmaceutical Analysis, Al Shifa College of Pharmacy, Kizhattoor, Malappuram, Kerala, India.
2. Dept. of Pharmaceutical Analysis, Al Shifa College of Pharmacy, Kizhattoor, Malappuram, Kerala, India.

***Corresponding author's E-mail:** preethipr555@gmail.com

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**ABSTRACT**

The objective of the study is to develop simple, precise, authentic and cost-effective analytical method for the estimation of antiemetic drugs according to ICH guidelines. The working standard solutions of MET and DEX were scanned in UV from the range of 200-400 nm where the λmax or the absorption maximum of metoclopramide hydrochloride and dexamethasone sodium phosphate was 273 nm and 241.60 are respectively. The wavelength range selected for metoclopramide was 292-320 (λ1-λ2) nm and for dexamethasone sodium it was 219-256 (λ3-λ4) nm. Developed methods are validated as per ICH guidelines. The UV method was developed by using 8-16µg/ml of MET.HCl and 6-12µg/ml DEX. Area under curve method was developed. The correlation coefficient was found to be 0.9946 for MET.HCl and 0.9985 for DEX.

**Keywords:** Metoclopramide hydrochloride, dexamethasone sodium phosphate, validation, λmax.

## INTRODUCTION

Nausea is a sensation of discomfort in the stomach with an involuntary urge to vomit. Emesis, or vomiting is a physiological response to the presence of irritating and harmful substances in the gut or bloodstream.[1]

Metoclopramide (fig 1) is a dopamine antagonist used to treat nausea and vomiting that may be associated with diabetic gastroparesis in addition to gastroesophageal reflux disease. Metoclopramide increases gastric emptying by decreasing lower esophageal sphincter (LES) pressure. It also exerts effects on the area postrema of the brain, preventing and relieving the symptoms of nausea and vomiting. In addition, this drug increases gastrointestinal motility without increasing biliary, gastric, or pancreatic secretions.

Dexamethasone Sodium Phosphate (fig 2) is a corticosteroids which will inhibit phospholipase A2 thus preventing the generation of inflammatory mediators.[2]

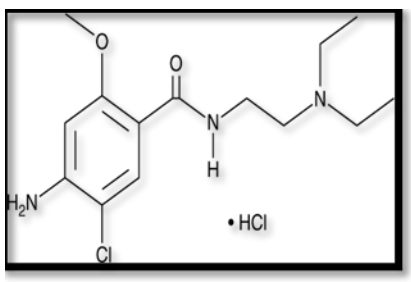


**Figure 1:** Chemical structure of Metoclopramide hydrochloride

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 patients[3]

A study conducted on female patients having an 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 PONV for the patients received combination[4].

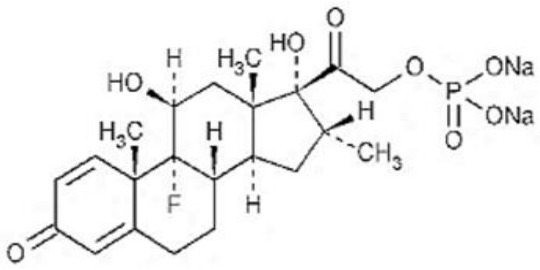


**Figure 2:** Chemical structure of Dexamethasone Sodium Phosphate

There is no UV 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, method for the simultaneous determination of

metoclopramide hydrochloride and dexamethasone sodium phosphate.

UV spectrophotometric techniques are mainly used for multicomponent analysis thus minimizing the task of separating interferents and allowing the determination of an increasing number of analytes, consequently reducing analysis time and cost.[5]

UV-Visible spectroscopy is based on the measurement of intensity of absorption of near UV and visible light by a sample and wavelength, In July 1941. Arnold Beckman introduced DU UV-Visible spectrophotometer. The absorption or reflectance in the visible region based on the colour of chemicals. In this region atoms and molecules undergo electronic transition[6].

**Area Under Curve (AUC) Method:**

This method uses two wavelength ranges. From the overlain spectra (fig 3) of both drugs the area under curve is selected at both the analytical wavelength ranges. The analysis was performed using "cramer's rule" and "matrix method".

Consider a binary mixture consisting of two components M and N. From the two spectra the following information are obtained:

The total area under the curve of a mixture at a particular wavelength range is equal to the sum of area under the curve of the individual components at the same wavelength range .[7]

1.$AUC^{M}_{\lambda 1-\lambda 2}$: Area under curve for component M at the wavelength range λ1λ2.

2.$AUC^{M}_{\lambda 3-\lambda 4}$: Area under curve for component M at the wavelength range λ3λ4.

3.$AUC^{N}_{\lambda 1-\lambda 2}$: Area under curve for component N at the wavelength range λ1λ2.

4.$AUC^{N}_{\lambda 3-\lambda 4}$: Area under curve for component N at the wavelength range λ3λ4.

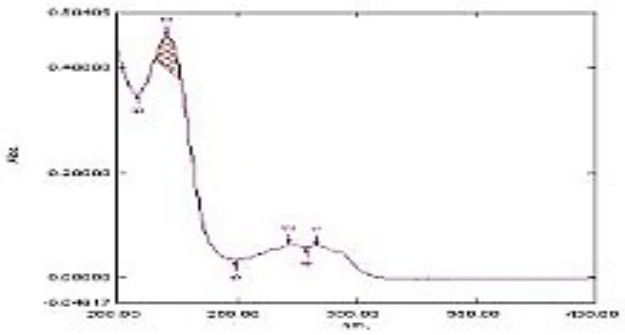

**Figure 3:** Area under curve

**Experimental Apparatus*:***

1 Electronic Balance Tandem TJ series

2 UV Spectrophotometer Shimadzu, UV1700, Pharmaspec, Japan (attached to a computer software UV probe 2.0, with a spectral width of 2 nm, wavelength accuracy of 0.5 nm and pair of 1 cm matched quartz cells.)

## MATERIALS AND METHODS

**Reagents and Materials:**

1. Metoclopramide Hydrochloride, Yarrow Chem Products, Mumbai
2. Dexamethasone Sodium Phosphate, Yarrow Chem Products, Mumbai

**Experimental Procedure:**

***Selection of wavelength range for estimation***

Suitable dilutions of metoclopramide hydrochloride and dexamethasone sodium phosphate were prepared by diluting with water. The drug solutions were scanned from 200-400 nm and from that wavelength ranges are selected for estimation of drugs.

***Preparation of standard stock solutions (1000µg/ml)***

An accurately weighed quantity of MET (100 mg) and DEX (100 mg) were transferred to a separate 100 ml volumetric flask. Water is used as the dissolving agent for drugs, Then the volume was made up to the mark with water to get the solution having a concentration of 1000µg/ml.

***Preparation of working standard solutions***

From the above prepared stock solutions of metoclopramide hydrochloride and dexamethasone sodium phosphate 1 ml were transferred separately to 10 ml volumetric flask to obtain working standard solutions having a concentration of 100 µg/ml.

***Preparation of calibration curve***

From the above working standard solutions of both MET (0.8, 1.0, 1.2, 1.4, 1.6 ml) and DEX (0.6, 0.75, 0.9, 1.05, 1.2 ml) aliquots were transferred separately in a series of 10 ml volumetric flask. The volume was adjusted to the mark with water. To get a concentration range of 8-16µg/ml of metoclopramide hydrochloride and 6-12µg/ml of dexamethasone sodium phosphate. The area of all the solutions were calculated by scanning from 200-400 nm.

**Methodology**

The working standard solutions of MET and DEX were scanned in UV from the range of 200-400 nm where for metoclopramide 292-320 ($\lambda_1$-$\lambda_2$)nm was selected and for dexamethasone sodium 219-256 ($\lambda_3$-$\lambda_4$) nm was the wavelength range. And these areas are selected for the quantitative estimation of metoclopramide and dexamethasone. Area was integrated between these ranges for both drugs which showed linear response with increasing concentration hence the same wavelength range were used for estimation of synthetic mixture.

**Analysis of drugs in synthetic admixture**

20mg of synthetic mixture was prepared by using 10mg MET and 7.5mg DEX and excipients like lactose 1mg, methyl paraben 1mg and propylene glycol 0.5mg were added to the mix. Sample was prepared by a weight equivalent to 10mg MET and 7.5mg DEX, dissolved in water, then sonicated for 30 minutes then the volume was made up to 100 ml with water. Then filtered through what Mann filter paper. For analysing the drugs above solution was appropriately diluted. Sample solutions were prepared in triplicate and analyzed according to above mentioned procedure.

**Method Validation**

***Linearity and range***

Different dilutions of concentration 8, 10,12,14,16µg/ml of MET and 6,7.5,9,10.5,12µg/ml of DEX were prepared. The calibration curve was plotted and interpreted in terms of correlation coefficient and equation of line.

Method: Area of each solution were noted down at their respective range (292-320 nm& 219-256nm)

***Accuracy (% Recovery)***

Accuracy can be reported in terms of % recovery. The percentage spiking levels are 80,100 and 120%, About 10µg of Metoclopramide hydrochloride and 7.5µg of dexamethasone sodium was used for the study.

***Method precision***

*Repeatability*

The precision of the instrument was checked by repeated scanning and measuring the absorbance of solution of (*n* = 6) MET (10µg/ml) and DEX (7.5µg/ml) without changing the parameters of developed methods.

*Reproducibility*

The intraday and interday precision was determined by analyzing the corresponding responses 3 times on the same day and on 3 different days over a period of 1 week for 3 different concentrations of standard solutions of MET (10, 12, 14µg/ml). and DEX (7.5, 9, 10.5µg/ml). Relative standard deviation (% RSD) was used to report the results.

***Limit of detection and Limit of quantification (LOD & LOQ)***

The LOD and LOQ were calculated by the equation method.

$LOD = 3.3 \times \sigma/S$

$LOQ = 10 \times \sigma/S$

Where, σ = the standard deviation of the response

S = slope of the calibration curve

## RESULTS AND DISCUSSION

Selection of the wavelength region to construct AUC method has a great effect on the analytical parameters such as slope, intercept and correlation coefficient. Different wavelength regions were selected 292-320nm for metoclopramide (fig 4) and 219-256nm for dexamethasone (fig 5). Area under curve of metoclopramide in the concentration range of 8-16µg/ml was calculated. For dexamethasone AUC of the absorption spectra in the concentration range of 6-12µg/ml was calculated. Area under curve of the sample was obtained (fig 6) and the concentration of the two drugs in sample mixture are also calculated as shown in table 1.

**Method validation**

***Linearity***

Different dilutions of concentration 8,10,12,14, 16µg/ml of metoclopramide and 6, 7.5, 9, 10.5, 12µg/ml of dexamethasone were prepared. Area of each solution were noted down at their respective range (292-320 nm& 219-256nm). The calibration curve (fig 7 and fig 8) was plotted and interpreted in terms of correlation coefficient and equation of line (Table 2).

***Accuracy***

Here the recovery results indicate the accuracy of the proposed method. The accuracy was calculated by recovery studies in various levels (Table 3).

***Precision (Repeatability)***

Here the percentage (%) RSD is less than 2 indicates the method is repeatable (Table 4).

***Reproducibility (Intermediate Precision)***

Here the percentage (%) RSD was found to be below 2% indicates the reproducibility of the developed analytical method (Table 5).

***Limit of detection and limit of quantification***

According to ICH guideline 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 MET was found to be 0.8816 & 2.6717 µg/ml. For DEX it is 0.3526 &1.0685 µg/ml.

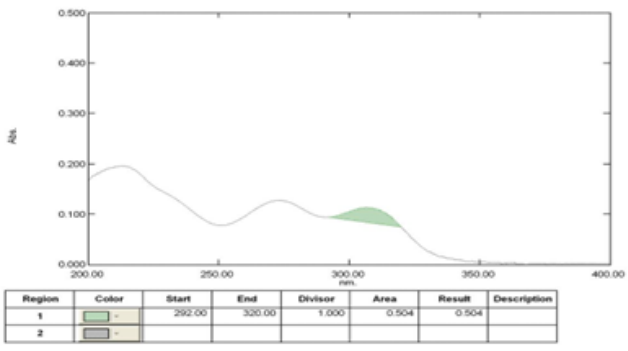


**Figure 4:** Area under curve of metoclopramide hydrochloride (292-320 nm)

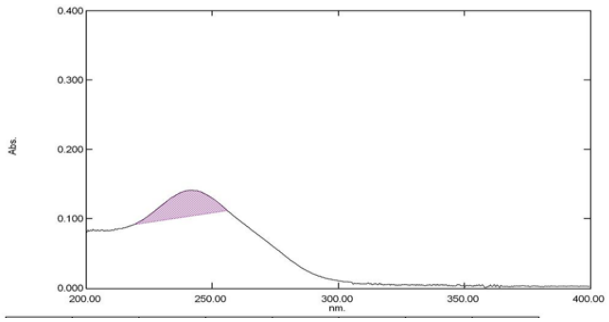


**Figure 5:** Area Under Curve of dexamethasone (219-256nm)

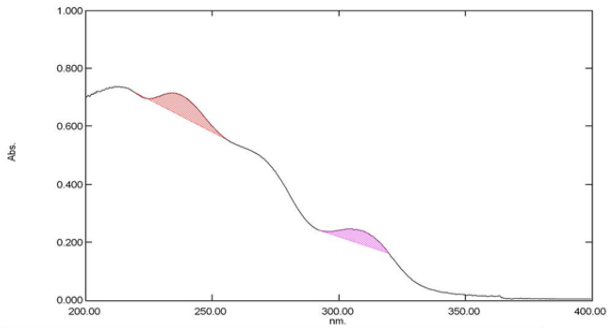


**Figure 6:** Area Under Curve of Sample

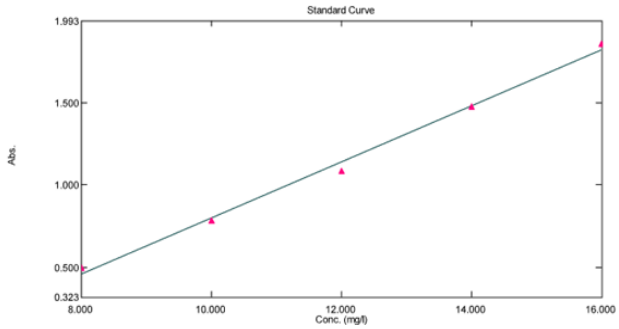


**Figure 7:** Calibration Curve of MET

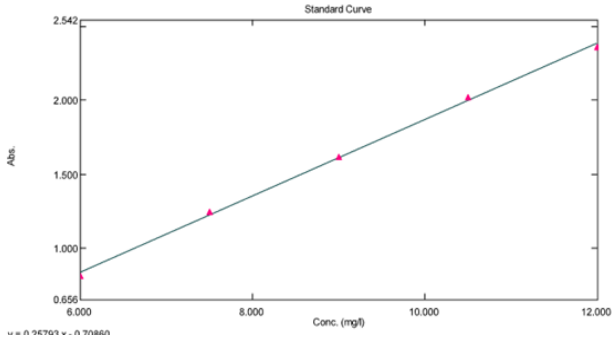


**Figure 8:** Calibration Curve Of DEX

**Table 1:** Assay of Drugs in Synthetic Mixture

| Admixture | Drug | Sample Solution Concentration (µg/Ml) | Amount Found | Drug Content (%)± Sd |
|---|---|---|---|---|
| 1 | MET. HCl | 10 | 9.662 | 96.62 ± 0.067 |
| | DEX | 7.5 | 7.35 | 98 ± 0.058 |

**Table 2:** Regression analysis data and summary of validation parameters from the calibration plot.

| Parameter | Metoclopramide Hydrochloride | Dexamethasone Sodium |
|---|---|---|
| Area | 292-320nm | 219-256 nm |
| Absorption maximum | 273 nm | 241.60 nm |
| Linearity | | |
| range(µg/ml) | 8-16µg/ml | 6-12µg/ml |
| Correlation coefficient | 0.99466 | 0.99848 |
| Regression equation | Y= 0.16955x-0.89420 | Y= 0.25793x-0.70860 |
| slope | 0.16955 | 0.25793 |
| Y intercept | 0.89420 | 0.70860 |

**Table 3:** Accuracy data for Metoclopramide and Dexamethasone

| Drug | Accuracy Level (%) | Amount | | | % Recovery | Mean ± SD | % RSD |
|---|---|---|---|---|---|---|---|
| | | Actual (µg/ ml) | Added (µg/ ml) | Found (µg/ ml) | | | |
| MET.HCl | 80% | 10 | 8 | 17.8 | 98.88 | 99.12+0.268 | 0.270 |
| | 100% | 10 | 10 | 19.8 | 99 | | |
| | 120% | 10 | 12 | 21.9 | 99.5 | | |
| DEX | 80% | 7.5 | 6 | 13.3 | 98.5 | 99.07+0.406 | 0.409 |
| | 100% | 7.5 | 7.5 | 14.9 | 99.33 | | |
| | 120% | 7.5 | 9 | 16.4 | 99.39 | | |

**Table 4:** Precision studies for Metoclopramide and Dexamethasone (Repeatability)

| Concentration MET:DEX (10&7.5) n=6 | Area | |
|---|---|---|
| | Metoclopramide Hydrochloride (292 -320nm) | Dexamethasone Sodium (219-256nm) |
| 1 | 0.785 | 1.249 |
| 2 | 0.787 | 1.247 |
| 3 | 0.789 | 1.245 |
| 4 | 0.784 | 1.251 |
| 5 | 0.785 | 1.249 |
| 6 | 0.787 | 1.247 |
| MEAN | 0.786 | 1.248 |
| SD | 0.0016 | 0.0019 |
| RSD (%) | 0.213 | 0.153 |

**Table 5:** Reproducibility for Metoclopramide and Dexamethasone (Intermediate Precision)

| Drugs n=3 | Concentration (µg/ml) | Intraday Absorbance found | | Interday Absorbance found | |
|---|---|---|---|---|---|
| | | Mean±SD | % RSD | Mean±SD | % RSD |
| MET.HCl | 10 | 0.467±0.001 | 0.396 | 0.468±0.003 | 0.780 |
| | 12 | 0.574±0.001 | 0.297 | 0.575±0.002 | 0.464 |
| | 14 | 0.665±0.001 | 0.256 | 0.665±0.002 | 0.324 |
| DEX | 7.5 | 0.635±0.002 | 0.371 | 0.636±0.003 | 0.613 |
| | 9 | 0.774±0.001 | 0.188 | 0.774±0.002 | 0.384 |
| | 10.5 | 0.893±0.001 | 0.220 | 0.894±0.002 | 0.298 |

## CONCLUSION

A simple as well as precise analytical method was developed for the estimation of metoclopramide hydrochloride and dexamethasone sodium phosphate in synthetic mixture. Area under curve method was developed, Beer's–Lamberts law was followed in concentration range of 8-16µg/ml for MET.HCl and 6-12µg/ml for DEX. The correlation coefficient was found to be 0.99466 for MET.HCl and 0.9985 for DEX. Using this developed analytical method, analysis of the selected drugs can be run fast with low cost and without prior extraction or losing accuracy. Hence the proposed method can be used for routine analysis of drug samples.

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