Research Article

Simultaneous Estimation of Metoclopramide Hydrochloride and Dexamethasone Sodium Phosphate Using Vierodt's 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. Assistant Professor, Dept. of Pharmaceutical Analysis, KTN College of Pharmacy, Chalavara, Ottapalam, Palakkad, Kerala, India.

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

Received: 05-12-2024; **Revised:** 28-02-2025; **Accepted:** 10-03-2025; **Published online:** 20-03-2025.

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 metoclopramide hydrochloride and dexamethasone sodium phosphate 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 isobestic point was 260 nm. The UV method is developed by using 8-16µg/ml metoclopramide hydrochloride and 6-12µg/ml dexamethasone sodium phosphate. In simultaneous equation method correlation coefficient of metoclopramide hydrochloride was 0.9994. Dexamethasone sodium phosphate shows correlation coefficient of 0.9962. Developed methods are validated as per ICH guidelines.

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.

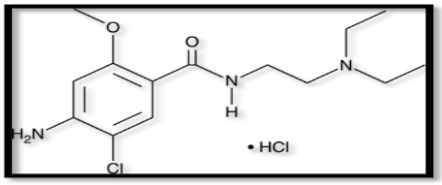

Figure 1: Chemical structure of Metoclopramide hydrochloride

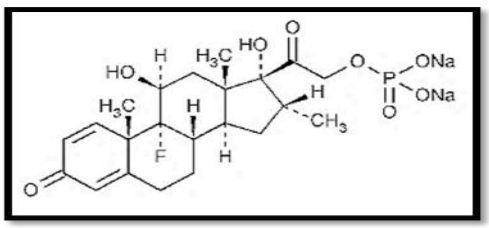

Figure 2: Chemical structure of Dexamethasone Sodium Phosphate

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

In a pilot study a combination of metoclopramide and dexamethasone were administered to 29 patients receiving emetogenic chemotherapy. Results 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]

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]

Simultaneous Equation Method

If a sample contains two absorbing drugs (x and y) each of which absorbs at the λmax of the other, it may be possible to determine both the drugs by the technique of simultaneous equation (Vierordt's method) provided that certain criteria apply. Absorbance was measure at the maximum wavelength of the drugs and apply to simultaneous equation.[6]

The absorbance of the mixture is the sum of the individual absorbance of x and y. Simultaneous equation need algebraic skills. They are called simultaneous because they are solved at the same time. This is a simple, precise, accurate, reproducible and efficient method.

Let CX and CY the concentration of x and y respectively in the diluted samples.

A1 = ax1 b Cx + Ay1 b Cy ..... (1)

A2 = ax2 b Cx + Ay2 b Cy ..... (2)

Where , A1 and A2 = absorbance of the diluted samples at λ1 and λ2 respectively.

ax1 and ax2 = absorptivities of x at λ1 and λ2 respectively

ay1 and ay2 = absorptivities of y at λ1 andλ2

Cx and Cy = concentration of x and y respectively in the diluted samples.

Rearrange equation (2)

cX = A2aY1 – A1aY2/ aX2aY1 – aX1aY2

cY = A1aX2 – A2aX1/aX2aY1 – aX1aY2

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.)

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

Both MET and DEX were dissolved separately in water, and appropriate dilutions were prepared by taking aliquots from the stock solution .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 (100mg) and DEX (100 mg) were transferred to a separate 100 ml volumetric flask. Water is used to dissolve the drugs, and the volume was made up to the mark with water to get the solution having a concentration of 1000µg/ml. And the solution is used as the first stock, from that further dilutions carried out.

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 8-16 µg/ml of metoclopramide hydrochloride and 6-12µg/ml of dexamethasone sodium phosphate. The absorbance of all the solutions were calculated by scanning from 200-400 nm, against water as the blank.

Methodology

The working standard solutions of MET and DEX were scanned in UV from the range of 200-400 nm. Where metoclopramide shows 273nm and dexamethasone sodium phosphate shows 241.60 nm as the wavelength having maximum absorbance. And this wavelengths are selected for the quantitative estimation of metoclopramide and dexamethasone. A set of two simultaneous equations were framed using absorptivity coefficient at selected wavelengths, from the overlain spectra of drugs, Based on the equations, the concentration of the two components in the mixture were calculated.

Analysis of drugs in synthetic admixture

25mg of synthetic mixture was prepared as by using 12mg MET and 9mg DEX and excipients like 2mg lactose, 1mg methyl paraben and 1mg propylene glycol were added to the mix. Sample was prepared by a weight equivalent to 12mg MET and 9mg 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: Absorbance of each solutions were noted down at their respective wavelengths (273,241.60)

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 were 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

In this method the dilute solutions of MET and DEX were scanned from 200-400 nm. Two wavelengths 273 nm and 241.60 nm are selected for Metoclopramide hydrochloride and Dexamethasone respectively. Here 273 nm is the absorbance maxima of MET (fig 3) and 241.60 nm is the λ_{max} of DEX (fig 4).

A set of two simultaneous equations were framed using absorptivity coefficient at selected wavelengths. Overlay spectrum was obtained for two drugs (fig 5). The concentrations of two drugs in the mixture were calculated using equations. The concentration of the two drugs in sample mixture (fig 6) are also calculated as shown in Table 1.

Linearity

Different dilutions of concentration 8,10,12,14,16 µg/ml of metoclopramide and 6, 7.5, 9, 10.5, 12µg/ml of dexamethasone were used to record the absorbance of each solutions at their respective wavelengths (273,241.60) the calibration curve was recorded.

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

Precision(Repeatability)

Here the % 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 guidelines there are several methods for the determination of LOD and LOQ. In the present study the LOD and LOQ were calculated by equation.

LOD and LOQ were calculated by equation. The LOD and LOQ of MET was found to be 0.2860 &0.8668 respectively. For DEX it is 0.5508&1.6693 µg/ml.

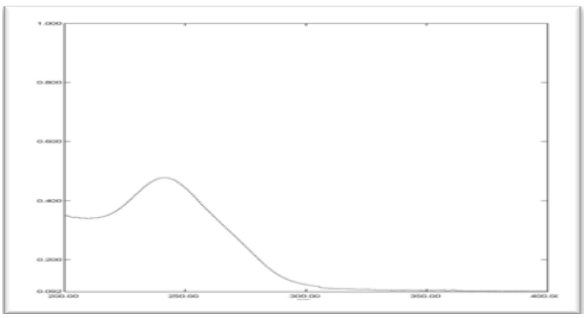

Figure 3: Zero order absorption spectra of MET.Hcl at 273nm

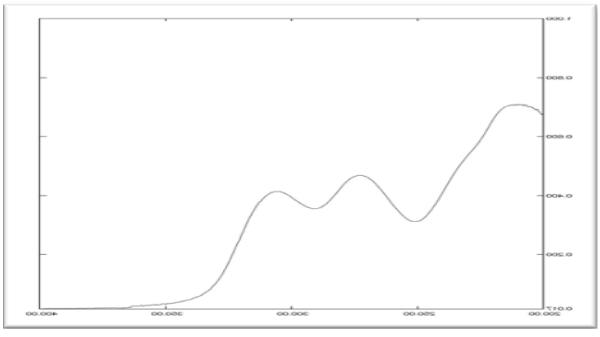

Figure 4: Zero order absorption spectra of DEX at 241.60nm

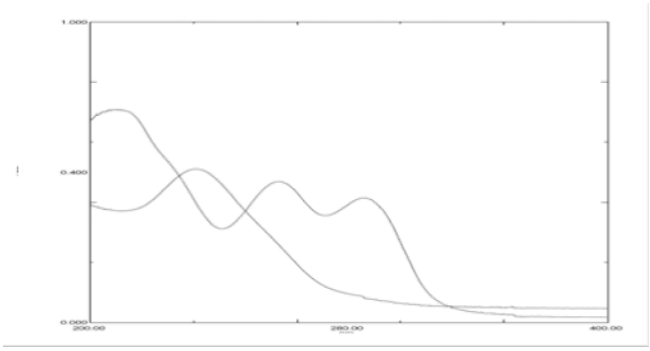

Figure 5: Overlay spectrum

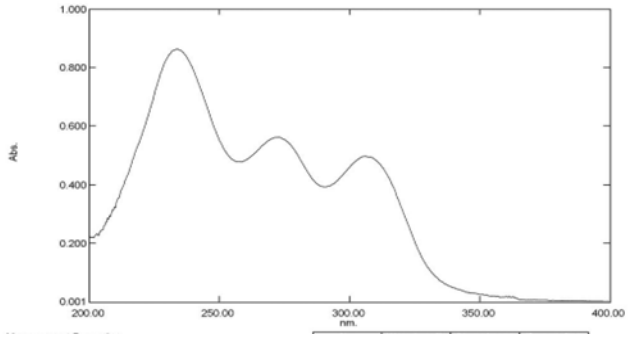

Figure 6: Zero order absorption spectra of sample

Table 1: Assay of Drugs in Synthetic mixture

Admixture	Drug	Sample Solution Concentration (µg/ml)	Amount Found	Drug Content (%) ± SD
1	MET.Hcl	12	11.874	99.1%±0.08
	DEX	9	8.988	98.5%±0.12

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

Parameter	Metoclopramide hydrochloride	Dexamethasone Sodium
Absorption maximum	273 nm	241.60 nm
Linearity range (µg/ml)	8-16	6-12
Correlation coefficient	0.9994	0.9962
Regression equation	Y=0.04845x-0.01380	Y=0.08087x+0.03200
slope	0.04845	0.08087
Y intercept	0.01380	0.03200
RSD	0.00364	0.01177

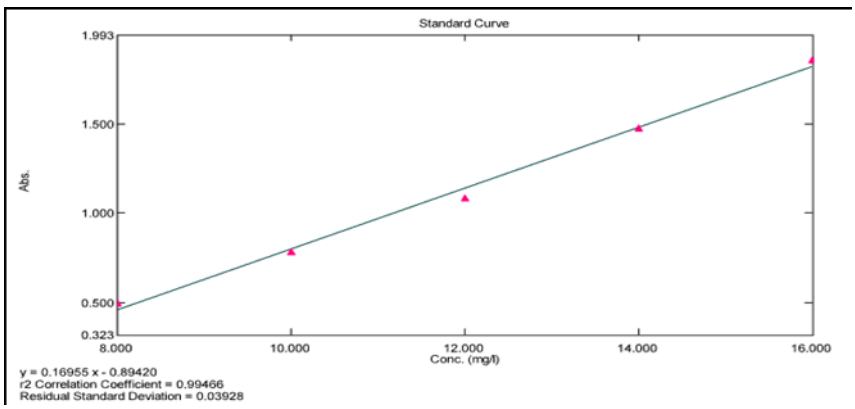

Figure 7: Calibration curve of MET

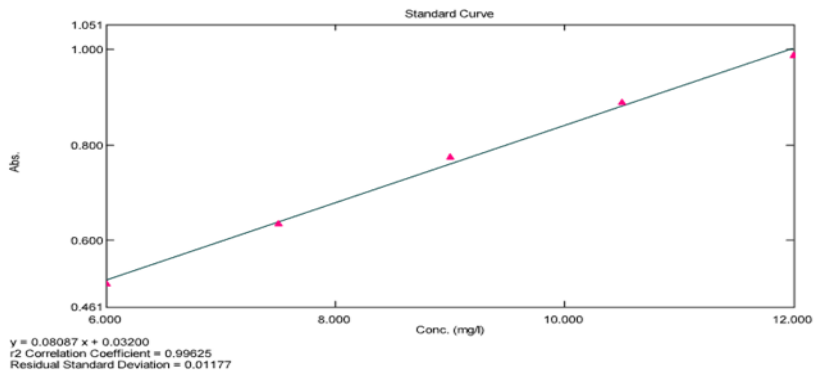

Figure 8: Calibration curve of DEX

Table 3: Accuracy

Drug	Accuracy Level (%)	Amount			% Recovery	Mean ± SD	% RSD
		Actual (µg/)	Added (µg/)	Found (µg/)			
MET. Hcl	80%	10	8	17.9	99.44	99.01± 0.384	0.391
	100%	10	10	19.7	98.5		
	120%	10	12	21.8	99.09		
DEX	80%	7.5	6	13.4	99.25	98.87± 0.274	0.277
	100%	7.5	7.5	14.8	98.6		
	120%	7.5	9	16.3	98.78		

Table 4: Repeatability

Concentration MET:DEX (10&7.5) n=6	Absorbance	
	Metoclopramide Hydrochloride (273nm)	Dexamethasone Sodium (241.60nm)
1	0.469	0.635
2	0.467	0.637
3	0.465	0.638
4	0.465	0.632
5	0.47	0.633
6	0.466	0.638
MEAN	0.467	0.635
SD	0.0018	0.0023
RSD (%)	0.396	0.371

Table 5: Reproducibility (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. Simultaneous equation 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 0.9994 for MET.HCl and 0.9962 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.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

1. Nusieba A Mohammed Ibrahim, Yahya Saber E Mansour, Ali A M Sulieman. Antiemetic medications: Agents, current research, and future directions International Journal of Research in Pharmacy and Pharmaceutical Sciences 2019;4:07-14.
2. Amit Kumar, Anoop Kumar. Antiemetics: A Review. IJPSR 2013;4(1):113-123.
3. S B Strum, J E McDermed, B R Streng, and N M McDermott, J Clin Oncol ''Combination Metaclopramide and Dexamethasone; an effective antiemetic regimen in outpatients receiving non-cisplatin chemotherapy''. Journal of American society of clinical oncology 1984;2(9): 1057-63.
4. K U Tobi, C O Imarengiaye, FE Amadasun ''Effects of dexamethasone and metoclopramide on early and late post operative nausea and vomiting in women undergoing myomectomy under spinal anaesthesia'' Nigerian Journal of clinical practice 2014; 17(4):449-55.
5. A.Thangamani, A.Anton Smith and B.Vedhapriya. Development Of Analytical Method for Metoclopromide Using UV-Spectrophotometry. IJPCBS 2014;4(3):551-555.3.
6. B.Vedhapriya. Development Of Analytical Method For Metoclopromide Using UV-Spectrophotometry. IJPCBS 2014;4(3):551-555.3.
7. Skoog, Douglas A, Holler F.James, Crouch, Stanley R. Principles of instrumental analysis(6th edition). Belmont, CA: Thomson brooks/cole p 169173.
8. Jasmine chaudhary, Akash Jain, Vipin Saini. Simultaneous estimation of multi-component formulations by UV-Visible spectroscopy; An overview. International research journal of pharmacy 2011;2(12):81-83.
9. Vinay Wamorkar, Manjunath S.Y., M. Mohan Varma. Development And Validation of Uv Spectroscopic Method for Determination of Metoclopramide Hydrochloride In Bulk And Tablet Formulation. International Journal of Pharmacy and Pharmaceutical Sciences 2011;3(3):0975-1491.
10. G.N. Renuka Devi, V.Prathyusha, K. Shanthakumari, S. A. Rahaman. Development And Validation Of Uv-Spectrophotometric Method For The Estimation Of Dexamethasone Sodium Phosphate In Bulk And Pharmaceutical Dosage Form. Indo American Journal Of Pharmaceutical Research 2013;2231-6876.
11. Jasmine chaudhary, Akash Jain, Vipin Saini. Simultaneous estimation of multi-component formulations by UV-Visible spectroscopy; An overview. International research journal of pharmacy 2011;2(12):81-83.
12. Rossana Barcellos Friedrich, Aline Ravanello, Luiz Carlos Cichota, Clarice Madalena Bueno Rolim e Ruy Carlos Ruver Beck. Validation of A Simple and Rapid UV Spectrophotometric Method for Dexamethasone Assay in Tablets. Quim. Nova 2009;32(4):1052-1054.