Flow-Injection and Batch Spectrophotometric Methods for Determination of Metoclopramide .HCl in Pharmaceutical Formulations

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Abstract

Background: This study describes a batch and flow-injection spectrophotometric methods for the determination of Metoclopramide.HCI in aqueous solution and in pharmaceutical preparations.

The method is based on the reaction of Metoclopramide.HCI with ferric nitrate to produce Fe(II) ion which upon further reaction with potassium hexacyanoferrate in acidic medium forms a Prussian blue colored product that has a maximum absorption at 770 nm. The proposed method was successfully applied to determine Metoclopramide.HCI in the range of 0.2-6 $\mu g.ml^{-1}$ for the batch spectrophotometric method and 2-80 $\mu g.ml^{-1}$ for flow-injection (FI) spectrophotometric method with correlation coefficients of 0.9997 and 0.9999, deletion limits of 0.114 $\mu g.ml^{-1}$ and 0.700 $\mu g.ml^{-1}$, and relative standard deviations of 0.46% and 0.41% respectively. Both procedures were applied to analyze the assay of Metoclopramide.HCI in pharmaceutical preparation with recoveries of 99.46% and 99.85% respectively.

Objectives: The aim of this study is to investigate A simple accurate and sensitive FIA system to determine Metoclopramid.HCL in pharmaceutical preparations.

Keywords: Spectrophotometry , Metoclopramid.HCL.

الخلاصة

تمهيد: تصف هذه الدراسة طريقة طيفية طريقة الدفعات والحقن الجرياني لتقدير دواء الميتوكلوبرومايد. هيدروكلورايد في المحاليل المائية والمستحضرات الصيدلانية . تعتمد الطريقة على تفاعل الميتوكلوبرومايد . هيدروكلورايد مع نترات الحديد لتعطي Fe(II) الذي بدوره يتفاعل مع بوتاسيوم سداسي سيانيد الحديد في وسط حامضي ليعطي ناتج بروسيان الأزرق اللون الذي له امتصاص أعظم عند 770 نانوميتر. الطريقة المقترحة طبقت بنجاح لتقدير دواء الميتوكلوبرومايد . هيدروكلورايد ضمن المدى 0.2 – 6 مكغم . مل$^{-1}$ في طريقة الدفعات وبين 2 – 80 مكغم . مل$^{-1}$ في طريقة الحقن الجرياني مع معامل ارتباط مقداره 0.9997 و 0.9999 وحد كشف مقداره 0.114 مكغم . مل$^{-1}$ و 0.7 مكغم . مل$^{-1}$ وانحراف قياسي نسبي مقداره 0.46 % و 0.41% لطريقة الدفعات والحقن الجرياني على التوالي . كلا الطريقتين طبقت لتقدير دواء الميتوكلوبرومايد. هيدروكلورايد في المستحضرات الصيدلانية مع نسبة استرداد مقدارها 99.46 % و 99.85% على التوالي.

الأهداف : يهدف البحث الى اكتشاف طريقة طيفية حساسة و دقيقة ومضبوطة وسهلة لتقدير دواء الميتوكلوبرومايد. هيدروكلورايد في المستحضرا الصيدلانية.

مفاتيح الكلمات : طيفية . الميتوكلوبرومايد. هيدروكلورايد .

Introduction

Metoclopramide.HCI (4-Amino-5-chloro-N-[(2-diethylamino)ethyl]-2-methoxybenzamide hydrochloride[1,2]. Many methods have been developed to determine Metoclopramide.HCI in pharmaceutical preparations and other materials such as urine and blood. These include spectrophotometric[3], colorimetric[4], Schiff's base formation[5], chromatographic[6], indirect flameless atomic absorption spectrophotometry[7] and flow injection technique[8]. Flow injection technique became a popular method utilized in the field of

pharmaceutical analysis[9,10]. Such as catecholamine drugs[11,12] and methyldopa drug[13] . The present study describes new batch spectrophotometric and FIA-spectrophotometric methods for the determination of Metoclopramide.HCI in pharmaceutical preparations via reaction with ferric nitrate in the presence of potassium hexacyanoferrate forming Prussian blue colored product that has a maximum absorption at λ_{max} at 770 nm.

Apparatus

A Shimadzu 1650 PC UV-VIS double beam spectrophotometer was used for λ_{max} determination. Shimadzu 120 UV-VIS spectrophotometer equipped with a Cecil 50uL flow cell was used. A three-channel manifold (Fig.1) was employed for the FIA-spectrophotornetric determination of Metoclopramide.HCl. A peristaltic pump (Gilsason minipuls(2)) was used to transport the carrier solution equipped with flexible polyvinyl chloride tubes of 0.8 mm internal diameter. Injection valve (Rheodyne-USA) was employed to provide appropriate injection volumes of standard solutions and samples. Channel A in the Manifold was used to transport ferric nitrate solution, while channel B to transport potassium hexacyanoferrate solution which was served as oxidizing agent and channel C to transport the stream of alkaline oxalate solution. The sample introduced into carrier stream of ferric nitrate and it was mixed well in the reaction coil RC#1. The product was mixed with potassium hexacyanoferrate stream in the reaction coil RC#2. The stream of alkaline oxalate was combined with the result product after mixing coil RC#2 at point (y).

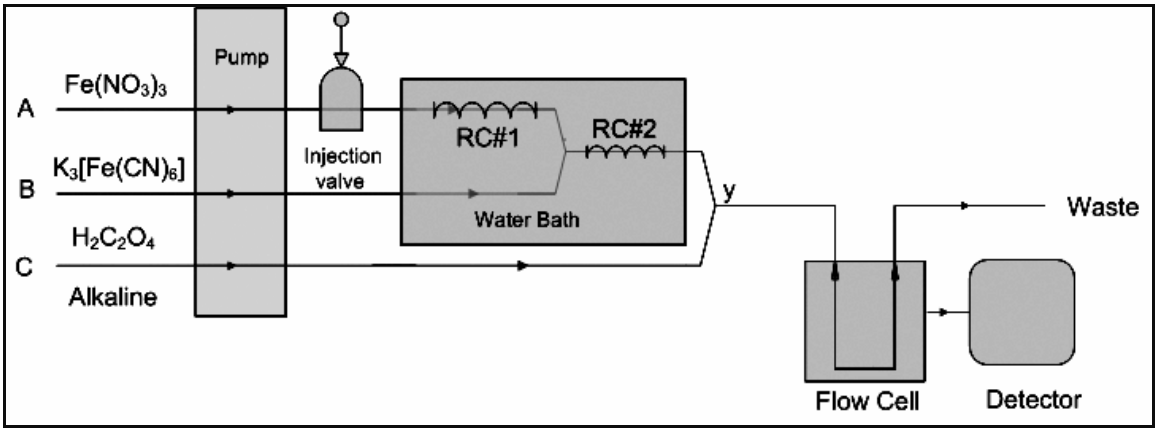

Fig l. Manifold employed for the FIA Spectrophotometric determination of Metoclopramide.HCl.

Reagents and Chemical Materials

All reagent and chemical materials used were of analytical reagent grade. Metoclopramide.HCI, $C_{14}H_{22}ClN_3O_2.HCl.H_2O$, M.wt. 354.3 g/mole, (SDI) Samarra-Iraq. Hydrous ferric nitrate, $Fe(NO_3)_3.9H_2O$, M.wt 404 g/mole, BDH. Potassium hexacyanoferrate, $K_3[Fe(CN)_6]$, M.wt 329 g/mole, BDH. Oxalic acid, $C_2H_2O_4$ M.wt 78 g/mole, Merk, Sodium hydroxide, NaOH M.wt. 40 g/mole, BDH and Sulfuric acid, M.wt 98 g/mole Puris Fluka.

Preparations of Solutions

Metoclopramide.HCl stock solution (1000 $\mu g.ml^{-1}$) was prepared by dissolving 0.1000 gm Metoclopramide.HCl in 100 ml of deionized water. Required concentrations were prepared by dilution of the corresponding stock solution with deionized water.

Hydrous ferric nitrate (0.1 M) stock solution was prepared by dissolving 4.0400gm of $Fe(NO_3)_3.9H_20$ in deionized water containing 1 ml of nitric acid and the

solution was made up to 100 ml with deionized water.

Potassium hexacyanoferrate, (0.1 M) stock solution was prepared by dissolving 3.2900 g of $K_3[Fe(CN)_6]$ in 100 ml of deionized water.

Pharmaceutical Preparations

Mecloden tablets, provided from (SDI) Samara-Iraq.

10 tablets were grinded well and a certain portion of the final powder was accurately weighted to give an equivalent to about 10 mg of Metoclopramide.HCl , that the powder was dissolved in deionized water. The prepared solution was transferred to 500 ml volumetric flask and made up to the mark with deionized water forming a solution of 100 $\mu g.ml^{-1}$. The solution filtered by using a Whatnan filter paper No. 42 to avoid any suspended particles. Required concentrations were prepared by dilution of the corresponding stock solution with deionized water.

Voperan syrup, provided from Razi Lab. Syria. Each 100 ml of the syrup contains l00 mg of Metoclopramide.HCl. A solution of the drug was prepared by diluting the syrup with deionized water to obtain solution with l00 $\mu g.ml^{-1}$.

Methods

General procedure for Batch method

Into a series of volumetric flasks of 25 ml, increasing volumes of Metoclopramide.HCl solution were transferred followed by the addition of 2.5 ml of $5x10^{-2}$ M ferric nitrate, 2.5 ml of $4.0x10^{-2}$ M of potassium hexacyanoferrate and 2.5 ml of 2 M sulfuric acid. The solutions were diluted to the mark with deionized water and the reaction mixtures were allowed to stand for 10 minutes in a water bath maintained at 45 ºC. The absorbances were measured at 770 nm against blank.

General procedure for FIA method

100µl sample is injected into a 1.5 $ml.min^{-1}$ stream of $1x10^{-2}$ M ferric nitrate solution in a 150 cm reaction coil submerge in a water bath at 45 ºC , and the stream allow to merge with another stream of $1x10^{-2}$ M potassium hexacyanoferrate solution in a 250 cm , at a PTFE T-piece. The reaction is carried out by passing the mixture maintaining the second coil at 45 ºC in a water bath, and the absorbance of blue product is measured at 770 nm.

Results and Discussion

Through out the preliminary investigations on the reaction of Metoclopramide.HCl with ferric nitrate and potassium hexacyanoferrate (III) in acidic medium, a Prussian blue colored product was formed. The color shows a maximum absorption at λ_{max} 770 nm as shown in Fig. (2).

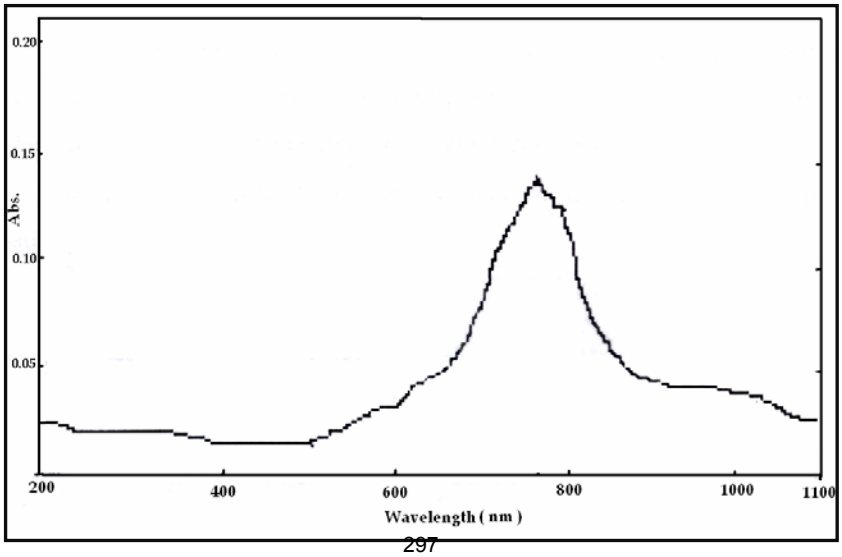

Fig 2. Absorption spectrum of Metoclopnimide.HCI treated as described under procedure.

It has been found that reaction temperature is a very essential parameter and it is greatly enhances the sensitivity of the reaction therefore, it was necessary to be optimized first. The reaction was carried out in a water bath set at a temperatures of 0, 27 and 45°C. High absorbances were obtained at 45°C in both batch and FI methods. The influences of various reaction variables on the formation of the colored product were tested to establish the most favorable conditions for the determination of Metoclopramide.HCl.

In the Batch method the effect of the amount of potassium hexacyanoferrate solution was tested for the concentration range of $1x10^{-3}$ to $6x10^{-3}$ M and it was found that best results were obtained with 4.0×10^{-3}M, also the effect of ferric nitrate solution from $0.5x10^{-3}$ to $7x10^{-3}$ was tested and the concentration with $5x10^{-3}$ gave the best result). The development of the color of Metoclopramide.HCl from a mixture containing 10µg.ml^{-1} in 0.20 M sulfuric acid.

On the other hand, FI procedure was carried out using the manifold illustrated in Fig 1. The absorbance intensity of the colored product at 770 nm has been improved by studying different FI parameters affecting the reaction mentioned previously. The effect of the concentration of the oxidizing agent and potassium hexacynoferrate for the range ($1x10^{-1}$ - $1x10^{-4}$ M) , total flow rate in the range of (1.2-9.6 ml.min^{-1}), lengths of the two reaction coils used in the manifold (both coils were submerged in a 45°C water bath) and finally the effect of injection different volumes using different lengths of sample loops 50, 100, 150. 200 and 250 cm were studied.

The results Fig 3. showed that a concentration of $1x10^{-2}$M of oxidizing agent gave the highest absorption signal .

A 4.5 ml.min^{-1} total flow rate of the carrier solution showed a remarkable increase in the measured signal when it was used with 100 cm and 250 cm lengths of the first and second reaction coils were used respectively Fig 4,5 .

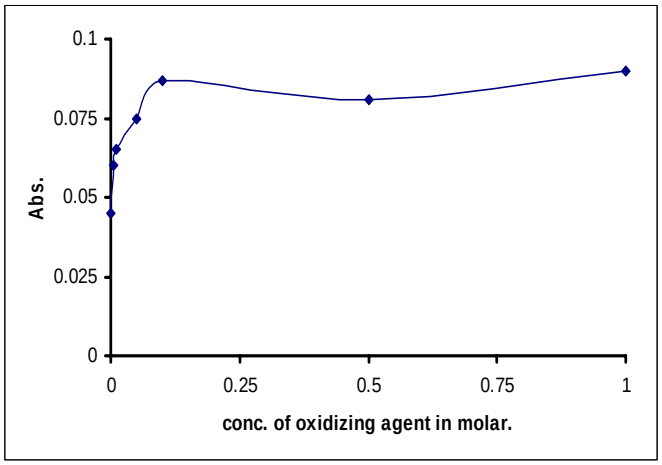

Fig 3. Effect of oxidizing agent.

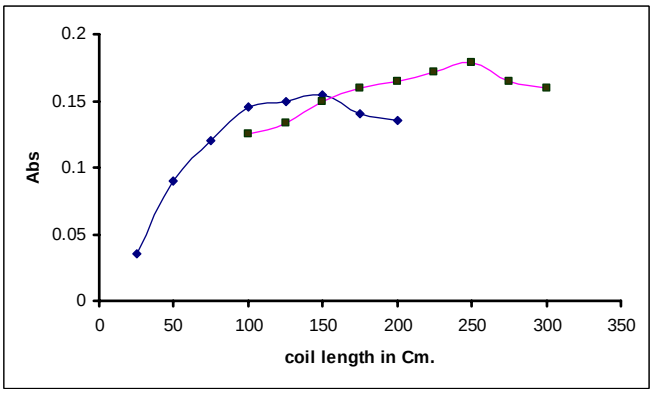

Fig 4. Effect of reaction coil length

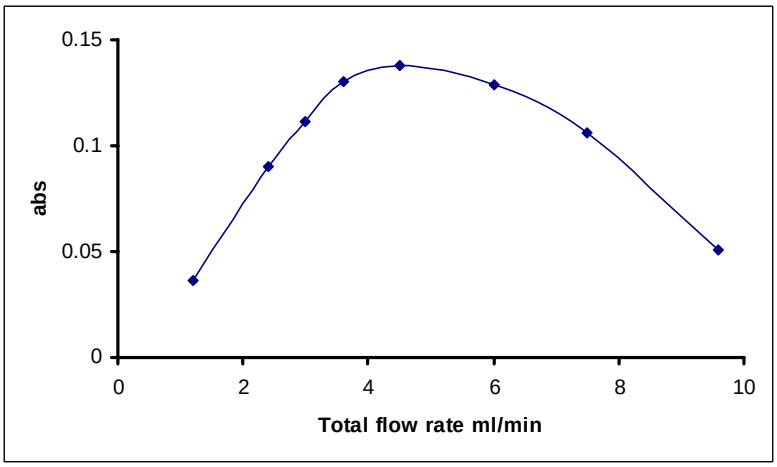

Fig 5. Effect of total flow-rate

While results showed in Fig 6. that injected sample volume of 50 µl provides the highest absorption and sensitivity.

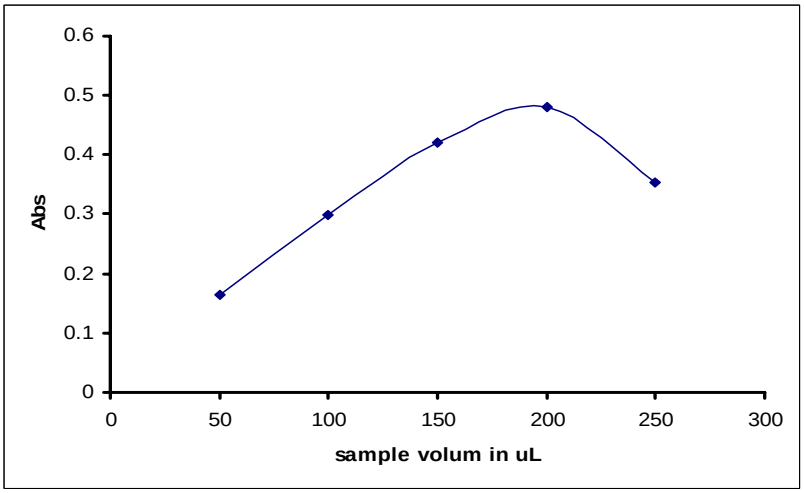

Fig 6. Effect of sample volume injected.

Figures 7 and 8 show the constructed of the calibration curves under the optimum conditions for Metoclopramide.HCI determined following both procedures mentioned previously. The analytical data are summarized in Table (1) .

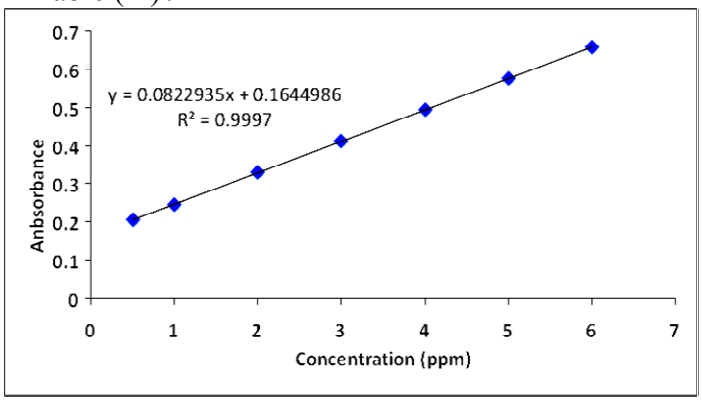

Fig 7. Typical calibration curve for Metoclopramide.HCI using Batch method

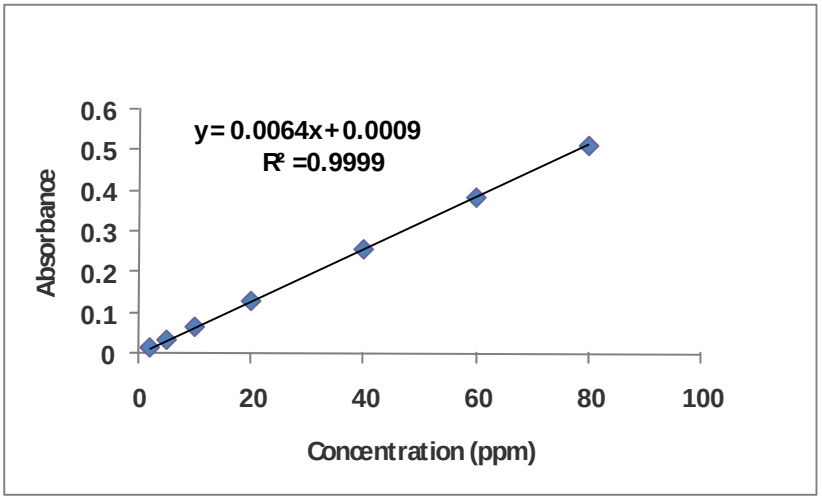

Fig 8. Typical calibration curve for Metoclopramide.HCl using FI-method.

Table 1. Analytical data for the determination of Metoclopramide.HCl using Batch and FI-spectrophotometric methods.

Analytical data	Batch method	FI method
Detection limit (D.L.)	0.114 µg.ml^{-1}	0.700 µg.ml^{-1}
Sensitivity	0.0823 abs. unit of µg.ml^{-1}	0.0064 abs. unit of µg.ml^{-1}
Correlation coefficient	0.9997	0.9999
Linear range	0.2-6.0 µg.ml^{-1}	2.0-80.0 µg.ml^{-1}
RSD %	0.46%	0.41%

Analytical Application

Application of the proposed methods for the assay of pharmaceutical tablets was investigated using two types of drugs containing Metoclopramide.HCl. Good precision and recovery were obtained according to the results obtained in Table (2).

Table 2. Application of the proposed methods for the determination of Metoclopramide.HCl

Sample	Batch method		FI method	
	Recovery %	RSD %	Recovery %	RSD %
Pure Metoclopramide.HCl	100.10	0.46	100.00	0.41
Mecloden	99.50	0.45	99.89	0.42
Voperan syrup	99.42	0.46	99.81	0.42

Conclusion

Batch and flow-injection spectrophotometric methods were developed for the determination of Metoclopramide.HCl in pharmaceutical Preparations. A simple accurate and sensitive F1A system was designed, constructed and used in conjunction with a spectrophotorneter detector. The proposed method can be carried out with no need for further steps such as solvent extraction step or pH control.

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