# Using of Oxidative - Coupling Reaction in Spectrophotometric Determination of Metoclopramide Hydrochloride in Pharmaceutical Preparations

Rabee M. A. Yassin, Nabeel S. Othman *

Chemistry Department, College of Science ,University of Mosul , Mosul ,Iraq

*Corresponding author, E-mail: nsn20002004@uomosul.edu.iq

**Doi:10.29072/basjs.20220215**

**ARTICLE INFO**

**Keywords**

2,5-dihydroxybenzoic acid ,metoclopramide hydrochloride; oxidati coupling ; potassium periodate, pectrophotometric.

**ABSTRACT**

A simple, sensitive, and rapid spectrophotometric method has been developed for the determination of metoclopramide hydrochloride (METH). The method includes the oxidative coupling reaction of metoclopramide with 2,5-dihydroxybenzoic acid using potassium periodate as an oxidizing agent in an aqueous medium and at pH of 4.5 to give a water-soluble colored product. The highest absorbance occurs at a wavelength of 500 nm. The linear range of Beer's law was within the concentration range of 5-75 µg/ml of (METH) and the value of the molar absorptivity 2.196 $x10^3$ $l.mol^{-1}.cm^{-1}$ and Sandell's index value was equal to 0.0449 µg/ $cm^2$. The relative standard deviation value was ≤ 2.98, while the LOD and LOQ values were 0.059 $\mu g.ml^{-1}$ and 0.198 $\mu g.ml^{-1}$ respectively. The proposed method was successfully applied in the spectrophotometric estimation of metoclopramide preparations in the form of tablets and injections with acceptable recovery.

**Received 11 Mar 2022; Received in revised form 28 Jun 2022; Accepted 29 July 2022,Published 31 Aug 2022**

## 1. Introduction

Metoclopramide (METH) is 4-Amino-5-chloro-N-[2-(diethylamino)ethyl]-2-ethoxybenzamide mono hydrochloride monohydrate with molecular formula ($C_{14}H_{22}ClN_3O_2.HCl.H_2O$) and molecular weight =354.3g/mol (Fig.1). A white or almost white , crystalline powder, almost odorless and has a high solubility in water, freely soluble in ethanol and practically insoluble in ether and should be kept in a well -closed container ,protected from light [1].

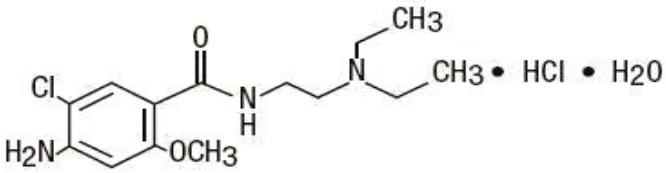



Figure 1: Chemical structure of METH.

Metoclopramide has dual activity as a $D_2$ receptor antagonist and a 5-$HT_4$ agonist, decreasing the effect of dopamine and thereby stimulating the restoration of fluid and electrolyte balance [2]. METH acts as an antiemetic in the therapy of postoperative nausea and emesis as common side effects after anesthesia in surgeries and to extend gastro intestinally. The drug used to be used for the control of sickness due to radiation therapy and chemotherapy. Also, it is used to for relative positive belly and esophagus problems such as diabetic gastroparesis and gastro esophageal reflux disorder[3,4]. Metoclopramide is bound to plasma protein. It is freely distributed in body and passes the blood-brain barrier. Half-life is 4 to 6 hours. It is mainly excreted in the urine [5].

There are many different techniques that have been used for the determination of metoclopramide by various methods, including spectrophotometric methods[6,15], HPLC [16-21], potentiometric [22], Densitometric and UPLC methods[23], fluorometric [24], Flow Injection Chemiluminescence Technique [25], voltammetric [26], electrochemiluminescence [27],Capillary electrophoresis [28],LC-MS/MS [29], Atomic Absorbance [30] and molar refraction and polarizability method [31]. The main aim of the current work is to suggest an accurate and sensitive visible spectrophotometric method for the assay of METH as pure and in dosage form via oxidative -coupling reaction with 2,5-dihydroxybenzoic acid in presence of potassium periodate.

## 2. Experimental

### 2.1 Instruments

Spectrophotometer with a double-beam( Jasco V-630 UV- Visible) was used on all measurements with 1 cm thick glass cells, and pH of solutions measured by using BP3001 professional pH meter.

### 2.2 Reagents

#### 2.2.1 Standard METH solution (500 µg/ml)

A 500 µg/ml solution of METH was prepare via dissolving 0.0500g of pure METH [(supplied by the General Company for Pharmaceuticals and Medical Appliances Samarra - Iraq (SDI)] in distilled water in 100 ml volumetric flask.

#### 2.2.2 2,5-Dihydroxy benzoic acid solution 2,5-DHBA (0.1%)

Dissolve 0.1000 g of 2,5-DHBA in a small amount of distilled water and then complete the volume with the same solvent using a volumetric flask of 100 ml and keep it in an opaque and airtight bottle and it daily prepared.

#### 2.2.3 Potassium periodate solution (0.01M)

It is prepared by dissolving 0.2300 g of $KIO_4$ in distilled water and the volume was completed with distilled water to the mark of a 100 ml volumetric flask.

#### 2.2.4 Formulation solutions

#### 2.2.4.1 Dosage solution(Tablet, 500 µg/ml)

Ten tablets (from the pharmaceutical preparation Metoclopramide / Ajanta /India /10 mg metoclopramide/tablet) were weighted and crushed, then a weight equivalent to 0.0500 g of pure metoclopramide was dissolved in warm distilled water with shaking, finally filter to 100 ml volumetric flask and complete the volume to the mark with distilled water.

#### 2.2.4.2 Injection solution (500 µg / ml)

The equivalent of 50 mg was taken from the injection (Emoject/ Turkey, each 2 ml contain 10 mg and then the volume was completed to100-ml in calibrate flask with distilled water.

### 2.3. Procedure and calibration curve

An increasing volumes from 0.1 - 1.5 ml METH solution (500 µg/ml) were added to a set of 10 ml volumetric flask to cover a concentration of 5 to 75 µg/ml , followed by the addition of 1.0 ml of $KIO_4$ (0.01 M) and 2 ml of the organic reagent 2,5-DHBA, waiting a period of 30 minutes, then diluting it with distilled water to the mark and reading the absorbance of the coloured product formed against the blank solution at the wavelength of 500 nm. The standard curve was obtained by plotting the relationship between absorbance and concentration of METH. Fig. 2, shows that there is a linear relationship between the METH concentration and the absorbance of the coloured product up to the concentration limit of 75 µg/ml, and a negative deviation occurs for Beer's law over 75 µg/ml and the value of the molar absorptivity 2.16 $x10^3$ $l.mol^{-1}.cm^{-1}$ and Sandell's index value 0.0449 $\mu g/cm^2$, LOD and LOQ values were 0.059 $\mu g.ml^{-1}$ and 0.198 $\mu g.ml^{-1}$ respectively.

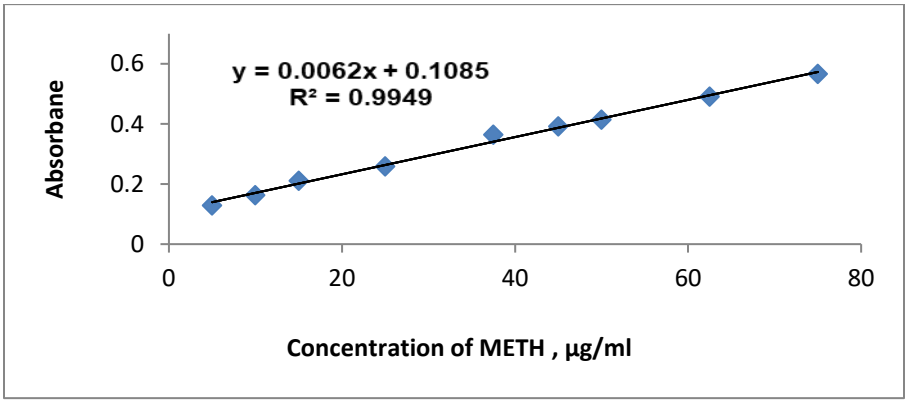



Figure 2: Calibration graph for assaying METH via the suggested method.

## 3. Results and discussion

The effect of all parameters and the components of the present reaction(oxidative-coupling) that affect the intensity of the coloured complex using 500 µg METH/ml in a final volume of 10 ml was studied separately and the optimal results followed.

### 3.1 The optimal conditions

The optimal conditions have been construct by studding the following parameters affected the formation of coloured product:

#### 3.1.1 Selection the type of oxidizing agent

Several oxidizing agents with a concentration of 1 x $10^{-2}$ M were used and the effect of each oxidizing agent on the absorbance of the coloured complex was studied for the purpose of choosing

the best oxidizing agent. 1 ml of the oxidizing agent (0.01 M) was added to a 10 ml volumetric flask containing 1 ml of METH (at a concentration of 500 µg/ml) followed by the addition of 1 ml of the organic reagent 2,5-DHBA (0.1%), wait for 15 minutes, and then dilute it with distilled water to the mark. The absorption spectrum of the resulting coloured product was scanned from 200 - 800 nm, and the results illustrated in Table 1. The results in Table (1) indicate that the highest absorbance of the coloured product was obtained by using potassium periodate as an oxidizing agent and it gave the highest value of color contrast ( $\Delta\lambda = \Delta\lambda_{max}$(Sample) - $\Delta\lambda_{max}$(Blank) ) , therefore it was adopted in subsequent experiments.

Table 1: Effect of the oxidizing agent on absorbance.

| Oxidizing agent ($1x10^{-2}$M) | Absorbance | $\lambda_{max}$ (nm) | $\Delta\lambda$ (nm) |
|---|---|---|---|
| Potassium hexacyanoferrate(III) | 0.168 | 495 | 55 |
| Potassium periodate | 0.320 | 498 | 177 |
| N-Chlorosuccinimide | 0.082 | 499 | 45 |
| N-Bromosuccinimide | No colour contrast | | |

### 3.1.2. Selection the optimal amount of oxidizing agent

An increasing volumes of 0.5 to 1.5 ml of $KIO_4$ were added to a set of 10 ml volumetric flasks containing a various amount of METH (25-100 µg/ml), then 1 ml of 2.5-DHBA reagent solution was added and waiting for 15 minutes, then dilution with distilled water and reading the absorbance of the coloured product at wavelength 498 nm (Table 2). The results in Table 2 indicated that 1 ml of the oxidizing agent is the optimum volume, which gave the highest absorbance of the coloured product and highest value of $R^2$, therefore it was chosen in the subsequent experiments.

Table 2: The optimal amount of the oxidizing agent.

| $KIO_4$ ml , (0.01M) | Absorbance /µg METH . $ml^{-1}$ | | | | $R^2$ |
|---|---|---|---|---|---|
| | 25 | 50 | 75 | 100 | |
| 0.5 | 0.090 | 0.208 | 0.296 | 0.334 | 0.9540 |
| 1.0 | 0.216 | 0.322 | 0.376 | 0.449 | .0.9818 |
| 1.5 | 0.187 | 0.310 | 0.365 | 0.436 | 0.9690 |

### 3.1.3 Effect of coupling agent amount

The effect of the amount of 2,5-DHBA as coupling agent on the intensity of the coloured product was studied. We observed from the results (Table 3) that 2 ml of 0.1 % reagent (2,5-DHBA) is the appropriate amount, which gave the highest intensity of the coloured complex and the highest value of $R^2$(the determination coefficient).

Table 3: Effect of reagent amount.

| 2,5-DHBA (ml of 0.1%) | Absorbance /µg METH $ml^{-1}$ | | | | $R^2$ |
|---|---|---|---|---|---|
| | 25 | 50 | 75 | 100 | |
| 0.5 | 0.154 | 0.201 | 0.288 | 0.344 | 0.9875 |
| 1.0 | 0.211 | 0.318 | 0.378 | 0.444 | 0.9809 |
| 1.5 | 0.255 | 0.339 | 0.476 | 0.567 | 0.9895 |
| 2.0 | 0.249 | 0.351 | 0.501 | 0.611 | 0.9947 |
| 2.5 | 0.167 | 0.275 | 0.351 | 0.482 | 0.9930 |

### 3.1.4. Effect of sodium hydroxide

It was observed that adding different amounts 0-1 - 1.0 ml of NaOH (1M) has a negative effect on the intensity of the colourd product , because the base completely removes the color contrast and

the colour becomes close to both the solution of the drug compound and the blank solution, and therefore the addition of the base was not recommended in subsequent experiments.

### 3.1.5. Effect of hydrochloric acid

The effect of acid on the absorbance of the resulting coloured solution was studied by adding different amounts (0.5 - 1.0) ml of dilute HCl (1 M) to the components of the oxidation reaction by $KIO_4$ (Table 4). The results in Table 4 show that hydrochloric acid(1M) has an effect on the oxidation of the drug compound under study, but in turn leads to a hypochromic shift, and on the other hand the absorbance of the blank solution at the same wavelength of complex is increased. The value of $\Delta \lambda_{max}$ ranged from 177 to 65 nm, and therefore it was excluded from the study.

Table 4: The effect of acid on some spectrophotometric variables.

| HCl ml,(1.M ) | Abs | $\lambda_{max}$ (nm) | pH | B vs. DW* | | $\Delta \lambda_{max}$ (nm) |
|---|---|---|---|---|---|---|
| | | | | Abs. | $\lambda_{max}$ (nm) | |
| Without | 0.357 | 500 | 5.01 | 0.078 | 323 | 177 |
| 0.5 | 0.418 | 471 | 2.05 | 0.673 | 409 | 62 |
| 0.75 | 0.414 | 473 | 1.84 | 0.638 | 409 | 64 |
| 1.0 | 0.406 | 473 | 1.63 | 0.653 | 408 | 65 |

* B= Blank , DW= Distilled water.

### 3.1.6. The best order of addition

Various order of addition of components have been studied .The sequence I, which gives the highest absorbance intensity for the coloured product has been recommended, otherwise a decrease in the absorbance intensity will occur (Table 5).

Table 5: Addition sequence effect.

| Order number | Reaction components | Absorbance |
|---|---|---|
| I | S + OX + R | **0.**360 |
| II | S + R + OX | 0.322 |
| III | R + OX + S | 0.320 |

S=METH , OX=$KIO_4$ , R=2,5-DHBA

### 3.1.7 The effect of oxidation time

The oxidation time required to complete the reaction was studied by performing the same previous steps in the suggested method, and then the reaction solutions were left at different time intervals before dilution with distilled water. It turned out that 30 minutes was sufficient to complete the oxidative coupling process (Table 6).

Table 6: Effect of oxidation time on the absorbance of coloured product.

| Time/min | 0 | 10 | 20 | 30 | 40 | 50 | 60 |
|---|---|---|---|---|---|---|---|
| Absorbance | 0.343 | 0.352 | 0.364 | 0.416 | 0.415 | 0.414 | 0.394 |

### 3.1.8.The effect of temperature

The effect of temperature on the intensity of absorbance of the coloured product formed over time was studied according to the optimal method of procedure. The results indicated that increasing or decreasing temperature has a negative effect on the intensity of coloured product and the room temperature (25 ± 2 ˚C**)** is the optimum temperature for the reaction, so it was adopted in subsequent experiments (Table 7) according to highest intensity and the good coloured product stability.

Table 7: Temperature effect on absorbance of product .

| Temp ˚C | Absorbance /minute standing | | | |
|---|---|---|---|---|
| | 30 | 40 | 50 | 60 |
| 5 | 0.351 | 0.341 | 0.334 | 0.331 |
| *RT | 0.415 | 0.418 | 0.416 | 0.401 |
| 40 | 0.390 | 0.400 | 0.401 | 0.401 |
| 50 | 0.362 | 0.372 | 0.383 | 0.405 |

*RT = 25 ± 2 ˚C

### 3.1.9 Effect of time on the stability

The results obtained (Table 8), indicated that the absorbance of the coloured product solution of METH proceeded according to the suggested method is stable for a period of time approximately 55 minutes, which is a sufficient period to perform many measurements.

Table 8: Effect of time on the stability of product absorbance.

| Time (min) | Absorbance of µg /ml METH | |
|---|---|---|
| | 25 | 50 |
| 0 | 0.259 | 0.415 |
| 5 | 0.258 | 0.416 |
| 10 | 0.258 | 0.415 |
| 15 | 0.258 | 0.414 |
| 20 | 0.256 | 0.414 |
| 25 | 0.255 | 0.413 |
| 30 | 0.254 | 0.413 |
| 35 | 0.254 | 0.415 |
| 40 | 0.253 | 0.415 |
| 45 | 0.252 | 0.412 |
| 50 | 0.252 | 0.410 |
| 55 | 0.250 | 0.401 |
| 60 | 0.246 | 0.396 |

### 3.1.10 Effect of the solvent used for dilution

Different solvents were used in the final dilution to know their effect on the absorption spectrum of the coloured product. It was observed that the highest absorbance was observed via using the methanol solvent and it gave a small difference in the absorbance (compared to the absorbance of water) while other solvents gave less absorbance, and therefore water was kept as a solvent used in subsequent experiments for its cheapness, availability and more safety (Fig.3) and (Table 9).

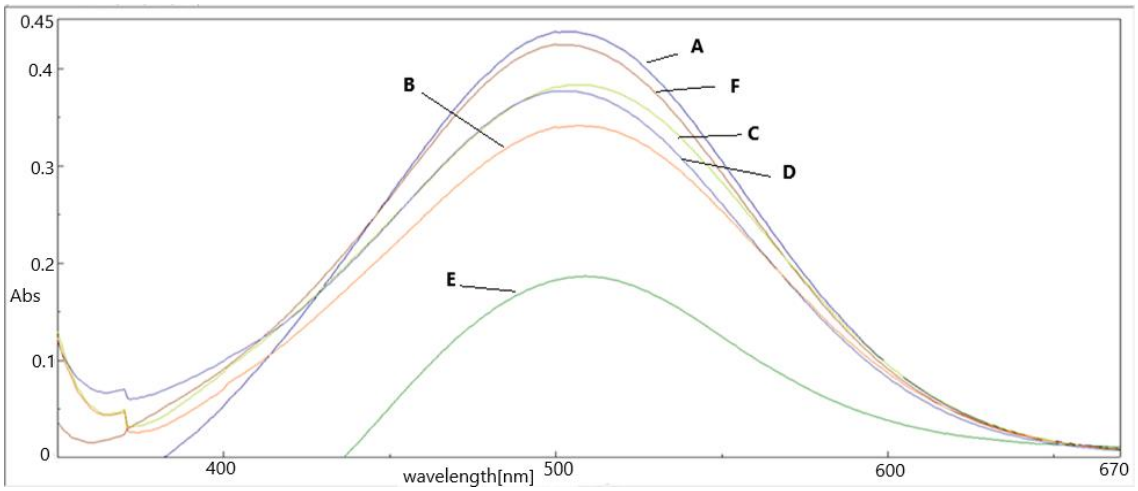



Figure 3: The absorption spectrums of the formed product using various solvents on dilution.

Table 9: The effect of the solvents on the absorbance of the coloured product.

| Solvent | | Abs. | $\lambda_{max}$ (nm) | ε (x10 $^{-4}$) |
|---|---|---|---|---|
| A | Methanol | 0.423 | 500 | 0.299 |
| B | Ethanol | 0.340 | 508 | 0.240 |
| C | 1-Propanol | 0.382 | 507 | 0.270 |
| D | Acetone | 0.376 | 500 | 0.266 |
| E | Acetic acid | 0.185 | 509 | 0.131 |
| F | Water | 0.417 | 500 | 0.295 |

### 3.2 The final absorbance spectrum

1.0 ml of 0.01 M $KIO_4$ oxidizing agent solution was added to a 10 ml volumetric flask containing 1 ml of METH at a concentration of 500 µg/ml, followed by the addition of 2 ml of reagent 2,5-DHBA, waiting for a period of 30 minutes at room temperature , then the volume was diluted to the mark with distilled water, then a spectrum scan from 200 to 800 nm was done. Figure (4) shows that the highest absorbance of the coloured product is at the wavelength of 500 nm.

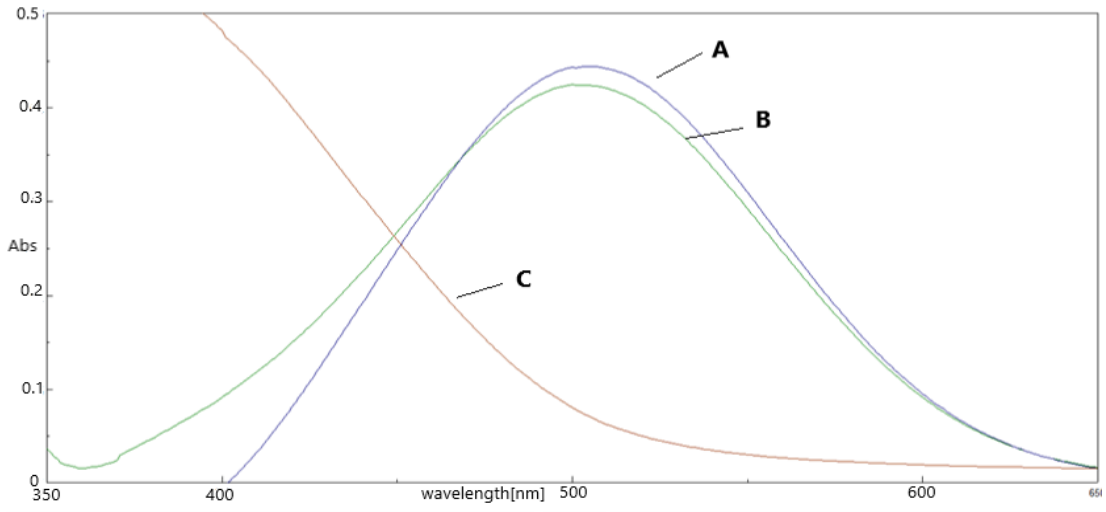



Figure 4: Absorption spectrums of A: 50 µg/ml of METH treated according to the recommended procedure versus distilled water, B: 50 µg/ml of METH treated according to the recommended procedure versus blank solution, C : Blank solution versus distilled water.

### 3.3. The nature of the coloured product

The continuous variation method and mole ratio method were applied in order to know the molar interaction ratios between METH and the used organic reagent 2,5-DHBA in the presence of the oxidizing agent $KIO_4$. Figure.5 shows that the coloured product has a 1:1 METH to 2,5-DHBA reagent at 500 nm.

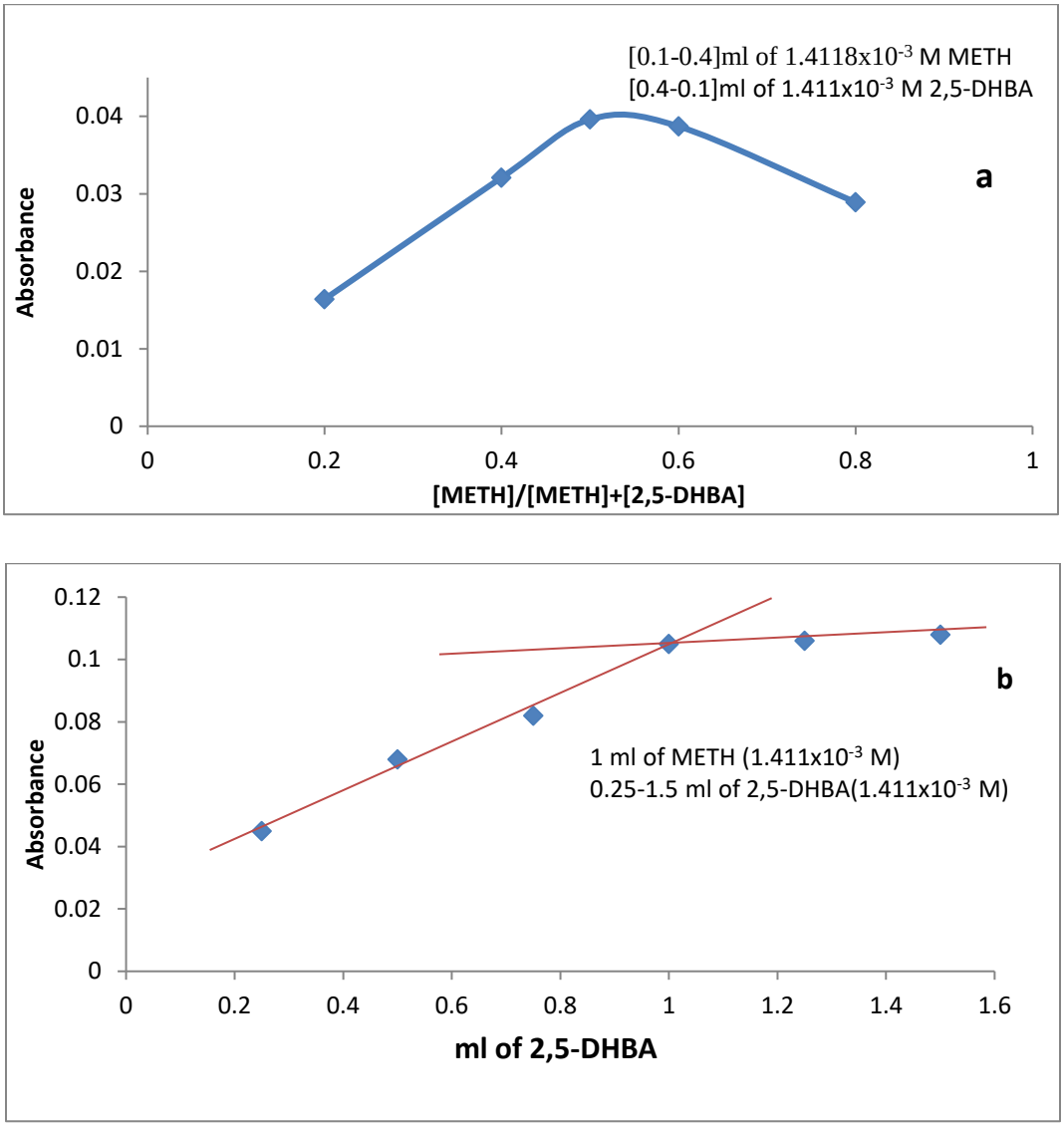



Figure 5: The Job method curve (a) and the mole ratio curve (b) for a reaction of METH with 2.5-DHBA.

The reaction mechanism of the proposed method can be written[32] as shown in Figure 6:

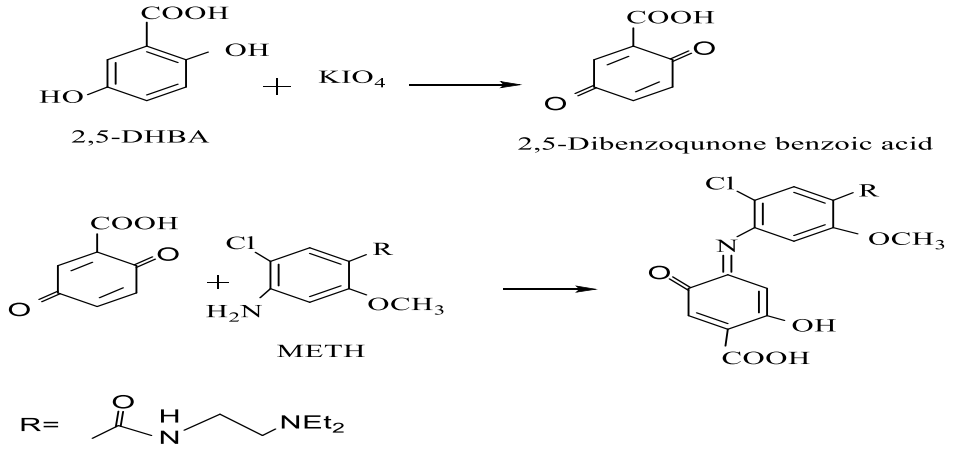



Figure 6: Suggested mechanism for the reaction of METH with 2,5-DHBA.

### 3.4 Application of the method

To find out the validity of the proposed method, the METH was estimated in its formulations ( tablets and injections) by applying the procedure of proposed method, a good recovery, accuracy and precision were obtained with satisfactory analytical results (Table10).

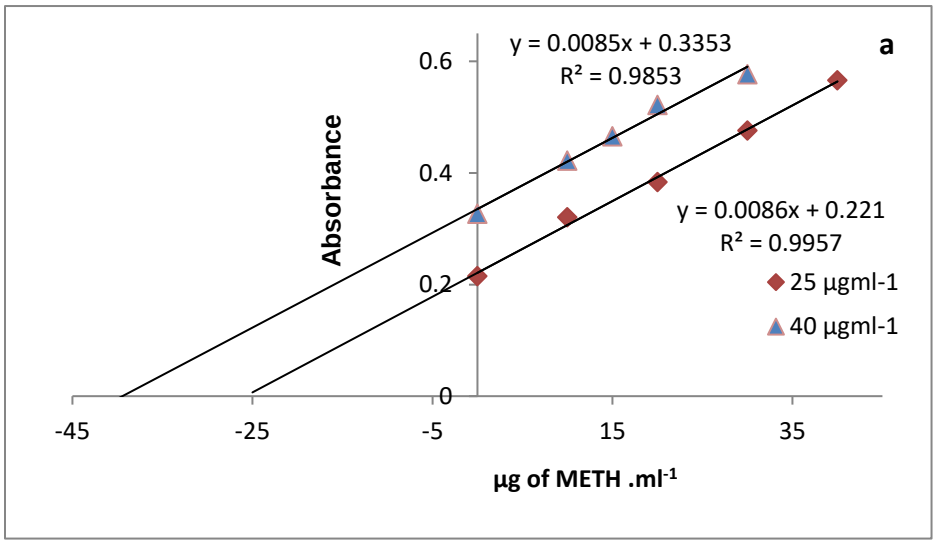
Table 10: Results of the estimation of METH in formulations.

| Drug content | METH amount taken µg/ml | METH amount measured µg/ml | Recovery* % | RE% | RSD* % | Drug content measured (mg) |
|---|---|---|---|---|---|---|
| Metoclopramide 10 mg/tablet Ajanta/India | 15 | 14.35 | 95.7 | -4.3 | 1.81 | 9.57 |
| | 30 | 28.95 | 96.5 | -3.5 | 1.52 | 9.65 |
| | 45 | 46.39 | 103.1 | 3.1 | 2.98 | 10.31 |
| Metoram 10 mg/2ml injection | 15 | 14.68 | 97.9 | -21 | 0.89 | 9.79 |
| | 30 | 30.84 | 102.8 | 2.8 | 1.02 | 10.28 |
| | 45 | 45.85 | 101.9 | 1.9 | 1.66 | 10.19 |

* Average for 4 determinations.

### 3.5 Standard addition method

In order to prove that the method is free from interference, the standard addition method was applied in the estimation of METH in its formulations (tablets and injections), by taking 25 and 40 µg/ml of METH solution. The results are cited in Figure 7 and Table 11 indicated the success of the proposed method in estimating METH, according to the permissible values from an analytical point of view for each of the % recovery and % RSD.



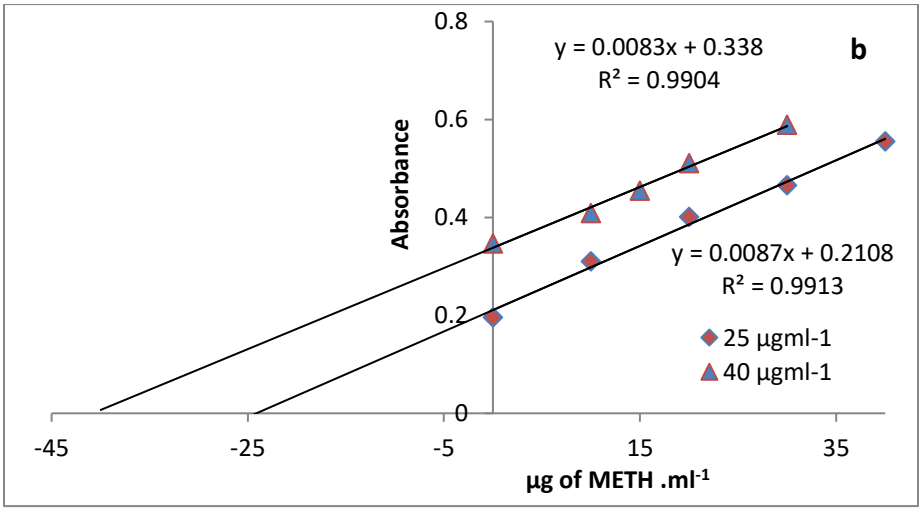




Figure 7: Standard addition curve for METH estimation: a- tablets, b- injection.

Table 11: Standard addition method for assaying METH.

| Drug content | METH amount (µg/ml) | Recovery* % | RE % | RSD* % | Drug content measured (mg) |
|---|---|---|---|---|---|
| Metoclopramide 10mg/tablet | 25 | 102.79 | 2.79 | 2.01 | 10.27 |
| | 40 | 98.61 | -1.39 | 1.68 | 9.86 |
| Metoram 10 mg/2ml | 25 | 96.91 | -3.09 | 1.08 | 9.69 |
| | 40 | 101.80 | 1.80 | 1.87 | 10.18 |

* Average of three determinations.

### 3.6. Comparing of the proposed method parameters with other methods.

The comparison was made for some analytical variables of the proposed method with the same of other spectrophotometric methods(see Table 12).

Table 12 : Comparing some of the analytical variables of the proposed method with the same of another method.

| Analytical parameters | Present method | Literature method[32] |
|---|---|---|
| Reagent | 2,5-Dihydroxybenzoic acid | Promethazine |
| Type of reaction | Oxidative coupling | Oxidative-coupling |
| max ( nm )λ | 500 | 596 |
| Linearity, µg $ml^{-1}$ | 5-75 | 3-30 |
| Media | Aqueous | Aqueous |
| Molar absorptivity $l.mol^{-1}.cm^{-1}$)( | $x10^3$2.196 | 1.10 x $10^4$ |
| Dye's color | Orange | Blue |
| Sandell's Index(µg/$cm^2$) | 4490.0 | 0.035 |
| RSD% | ≤ 2.98 | < 1.2 |
| Determination coefficient | 0.9949 | 0.9989 |

## 4. Conclusions

Based on the results obtained, a simple and rapid method can be proposed for the determination of metoclopramide hydrochloride (METH) as pure and in pharmaceutical preparations, through oxidative coupling reaction with 2,5-dihydroxybenzoic acid, and in the presence of $KIO_4$. An orange-coloured product is formed that shows the highest absorption spectrum at 500 nm, and the intensity of this spectrum is proportional to the amount of METH in the sample .It gave values of recovery %, RE % and RSD % within the allowable range.

**References**

[1] World Health Organization. The international pharmacopoeia. Geneva :World Health Organization, Dept. of Essential Medicines and Pharmaceutical Policies,10th ed. (2008).

[2] A.Acosta, M.Camilleri, Prokinetics in gastroparesis gastroenterology clinics, Gastroenterol Clin North Am., 44 (2015) 97-111, https://doi.org/10.1016/j.gtc.2014.11.008

[3] H. Pakniat, F. Lalooha, F. Movahed, A. Boostan, , M. B. Khezri, C. Hedberg, M. A. Hosseini,. The effect of ginger and metoclopramide in the prevention of nausea and vomiting during and after surgery in cesarean section under spinal anesthesia, Obstetrics Gynecology Sci., 63 (2020) 173-180, https://doi.org/10.5468/ogs.2020.63.2.173

[4] W. A. Abd Alrada, I. D. Sulaiman,Determination of Metochloropramide Hydrochloride by spectrophotometric method by using diazotized p-nitroaniline reagent, International J Drug Del. Technol. ,10 (2020) 68–73, https://doi.org/10.25258/ijddt.10.1.11

[5] N. Zeb-un , S. Saira, R.Mehwish, F. Rasheeda, I. A.Saba, S. Shumaila, S. Hina, F.Tayyaba,et al., Estimation of equivalence for quality parameters of metoclopramide hydrochloride tablets used to treat emesis, Arch. Pharm. Pract.,12 (2021) 25-8, https://doi.org/10.51847/xuwqnWXsOY

[6] R. Ali, N. Othman,. Spectrophotometric determination of metoclopramide hydrochloride in pharmaceutical preparations via Schiff's base reaction. In 1st International Ninevah Conference on Medical Sciences (INCMS 2021) (2021) 63-69, https://dx.doi.org/10.2991/ahsr.k.211012.011

[7] E.S. Thanoon, A. Saeed, Development of green spectrophotometric method for determination of metoclopramide hydrochloride. Egypt. J. of Chem., 64( 2021) 3451-3456, https://dx.doi.org/10.21608/ejchem.2021.43857.2923

[8] S. M. Abbas, J.M.S. Jamur, A.M.Nasif, Spectrophotometric method for the determination of metoclopramide in pharmaceutical forms, J. Appl. Spectr., 88 (2021) 433–440. https://doi.org/10.1007/s10812-021-01191-7

[9] H. M. Abdulkareem , M.Al-Tameemi, I. H. Ibraheem, M. S. Hadi,. Surfactant cloud point extraction as a procedure of preconcentrating for metoclopramide determination using spectro analytical technique. Baghdad Sci. J., 17 (2020) 57-56, https://doi.org/10.21123/bsj.2020.17.1.0057

[10] B.A. Saleem, Spectrophotometric determination of some drugs using oxidation reduction reactions. Ibn AL-Haitham J. For Pure and Appl. Sci., 32 (2019) 43-55, https://doi.org/10.30526/32.3.2281

[11] K. Salman, Q. Qasim, A. AL-Rikabi, H. N. K. Al-Salman, The development of analytical methods to determine metoclopramide-hydrochloric acid in the standard raw and it compared with pharmaceuticals, Int. J. Res. Pharm. Sci.,10 (2019) 1-14, https://doi.org/10.26452/ijrps.v10i4.1663

[12] H. K. A. Taha, M. M. Al-Rufaie, Z.Y. Motaweq, Spectrophotometric determination of metoclopramide medicine in bulk form and in pharmaceuticals using orcinol as reagent, Ovidius Univ. Annals of Chem., 29 (2018), 85-89, https://doi.org/10.2478/auoc-2018-0012

[13] M.S. Mashkour, M.K. Kahlol, S.W. AL-Hasnawi, Colorimetric determination of metoclopramide hydrochloride and glutathione by using 1, 2- naphthaquinolinc-4-sulphonate sodium reagents, Res. J. Pharma. Technol., 11 (2018) 3290-3294, https://doi.org/10.5958/0974-360X.2018.00605.4

[14] N.R. Ahmed, N.C. Saadallah, A.I. Ahmed, Estimation of metoclopramide HCl in pharmaceutical preparations and environmental water samples,WJPPS, 9 (2019) 151-159. https://doi.org/10.20959/wjpps20201-15283

[15] M. Bilici, M.U. Badak, A. Zengin, Z. Suludere, N. Aktas, Synthesis of magnetic halloysite nanotube-based molecularly imprinted polymers for sensitive spectrophotometric detection of metoclopramide in urine samples. Mater. Sci. and Eng., C, 106 (2020) 110223, https://doi.org/10.1016/j.msec.2019.110223

[16] H. Marzouk, E. Ibrahim, M. Hegazy, S. Saad, Greenness profile assessment of selective liquid chromatographic methods for determination of a quaternary antimigraine combination along with three of their related official impurities, Biomed. Chroma., (2021) e5132. https://doi.org/10.1002/bmc.5132

[17] S. Kaukab, S. Hussain, G. Murtaza, Single dose pharmacokinetics of metoclopramide oral tablets utilizing HPLC-UV method, Current Pharma. Anal.,15 (2019) 703-709, https://doi.org/10.2174/1573412914666180425123202

[18] S.Valavala,N. Seelam, S. Kandagatla, LC-MS characterization of acid degradation products of metoclopramide: development and validation of a stability-indicating RP-HPLC method, Inter. J. Res. Pharma. Sci., 11 (2020) 781-789, https://doi.org/10.26452/ijrps.v11i1.1895

[19] S.G. Karaiskou, M.G. Kouskoura, C.K. Markopoulou, Modern pediatric formulations of the soft candies in the form of a jelly: determination of metoclopramide content and dissolution, Pharma. Devel. Tech., 25 (2020) 20-27, https://doi.org/10.1080/10837450.2019.1609499

[20] N.F. Farid, I.A. Naguib, N.S. Abdelhamid, B.H. Anwar, M.A. Magdy, Validated ecofriendly chromatographic method for quantitative determination of anti-migraine quaternary mixture, J. Separa. Sci.. 43 (2020) 2330-2337, https://doi.org/10.1002/jssc.202000256

[21] N. Kahali, J. Khanam, A Novel HPLC method validation based on analytical techniques of metoclopramide benzamide derivative (Metoclopramide Base) and its determination from solid dispersion by solvent evaporation method, J. Appl. Pharm. Sci, 8 (2018) 18-26, https://doi.org/10.7324/japs.2018.8203

[22] S.S. El-Mosallamy, K. Ahmed,H.G. Daabees,T. Wael, A microfabricated potentiometric sensor for metoclopramide determination utilizing a graphene nanocomposite transducer layer, Anal. Bioanal. Chem., 412 (2020) 7505–7514, https://doi.org/10.1007/s00216-020-02884-2

[23] A. A.N. Mahmoud, N.S. Rashed, M.M. Fouad, Simultaneous densitometric and UPLC methods for the determination of paracetamol and metoclopramide HCL, Asian J Appl. Chem. Res., 6 (2020) 56-67, https://doi.org/10.9734/ajacr/2020/v6i130154

[24] H. Elmansi, , S. Abo El Abass Mohamed, M. E. Fathy, Simultaneous determination of metoclopramide and aspirin by spectrofluorimetric technique: application to pharmaceutical formulations and human plasma, Anal. Methods, 8 (2016) 1281-1292, https://doi.org/10.1039/c5ay02777b

[25] O.S. Hassan, N.H. Ali, Determination of metoclopramide in pharmaceutical commercial using flow injection chemiluminescence technique, Sys. Rev. Pharm., 11 (2020) 503-507, https://doi.org/10.5530/srp.2020.3.64

[26] J. C. Abbar, M.D. Meti, S.T. Nandibewoor, Sensitive and selective voltammetric oxidation and determination of an antiemetic drug using gold electrode and its biomedical applications. Surf. and Int., 19 (2020) 100484, https://doi.org/10.1016/j.surfin.2020.100484

[27] F.Yang,W.Zhang,B.Liu,Y.Ji,Y.Zhao,K.Zhou,Optimizatio of electrochemilumin-escence experimental conditions for metoclopramide determination based on response surface methodology. ,Int. J. Electrochem. Sci., 15 (2020) 8145-8155, https://doi.org/10.20964/2020.08.79

[28] A.R. Mbaye,C. Foulon, M. Lecoeur, Capillary electrophoresis as a versatile tool for quality control and epidermis permeation studies of transdermal formulations. J. Pharma. Biomed. Anal., 193 (2021) 113732, https://doi.org/10.1016/j.jpba.2020.113732

[29] R.F. Hussein,S.N. Ali, M.M. Hammami, Rapid determination of metoclopramide level in human plasma by LC-MS/MS assay. Am. J. Pharm. Tech. Res.**,** 8 (2018) 190-200, https://doi.org/10.46624/ajptr.2018.v8.i6.018

[30] M.W.I. Nassar, K.A.S. M.Attia, A.A.A. Mohamad, R.A.M. Said, R.F.A. Gaber, Atomic absorbance spectrometric determination of metoclopramide hydrochloride using ammonium reineckate, World J. Pharm. Res., 7 (2018) 1-12, https://doi.org/10.20959/wjpr201817-13338

[31] R.T. Sawale, T. Kalyankar, R. George, S.D. Deosarkar, Molar refraction and polarizability of antiemetic drug 4-amino-5-chloro-N-(2-(diethylamino)ethyl)-2 methoxybenzamide hydrochloride monohydrate in {Aqueous-Sodium or Lithium Chloride} Solutions at 30$^{o}$C, J. Appl. Pharm. Sci, 6 (2016) 120-124, https://doi.org/10.7324/japs.2016.60321

[32] N. R. Ahmad, N. M. Ali, Spectrophotometric determination of metoclopramide in some pharmaceutical preparation via oxidative coupling reaction, J. Edu. and Sci., 18 (2006) 16-22, http://dx.doi.org/10.33899/edusj.2006.77240

**استخدام تفاعل الاقتران التأكسدي في التقدير الطيفي للميتوكلوبرامايد هيدروكلوريد في المستحضرات الصيدلانية**

ربيع محمد علي ياسين و نبيل صبيح عثمان

قسم الكيمياء/ كلية العلوم /جامعة الموصل /موصل /العراق

**المستخلص**

تم تطوير طريقة طيفية سهلة وحساسة وسريعة لتقدير الميتوكلوبرامايد هيدروكلوريد. اشتملت الطريقة على تفاعل الاقتران التأكسدي للميتوكلوبرومايد هيدروكلوريد مع 5,2-ثنائي هيدروكسي حامض البنزويك باستخدام بيريودات البوتاسيوم بوصفه عامل مؤكسد في وسط مائي وعند الدالة الحامضية 4.5 لإعطاء ناتج ملون .يعطي أعلى امتصاص عند الطول الموجي 500 نانوميتر. كان المدى الخطي لقانون بير ضمن نطاق التركيز 5-75 مايكروغرام / مل من ميتوكلوبرومايد هيدروكلوريد وقيمة معامل الامتصاص المولاري $2.196 \times 10^3$ لتر /مول .سم ودلالة ساندل للحساسية 0.0449 مايكروغرام/سم$^2$. كانت قيمة الانحراف القياسي النسبي اقل من 3.9 وتم حساب حد الكشف وحد التقدير النوعي وكانت قيمتهما على التوالي 0.059 و0.198 مايكروغرام /مل. تم تطبيق الطريقة المقترحة بنجاح في التقدير الطيفي لمستحضرات صيدلانية للميتوكلوبرامايد على شكل أقراص وحقن مع نسبة استعادة مقبولة.