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The development of analytical methods to determine metoclopramide-hydrochloric acid in the standard raw and it compared with pharmaceuticals

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ABSTRACT

The three novel easy, to the prepare and sensitive spectral methods, were used to estimate metoclopramide in both standard and pharmaceuticals. The effective double-electron, was present in the metoclopramide compound helps to interact in an acidic medium with a reagent such as diazotide resorcinol and 8-hydroxyquinoline reagents. The present article was extended to find out three analytical methods with UV-V is the detector. In both A and B methods, two azo-dyes are formed, they are orange-red and red stable and have high water solubility, giving highest absorption values at 415 nm and 485 nm but the C method will depend on a complex colour configuration with the p-benzoquinone reagent, which has a maximum absorption at a wavelength of 285 nm. Beer's law was applied in a range of concentrations between 1 and 10 $\mu\text{g} / \text{ml}$, 2-20 $\mu\text{g} / \text{ml}$ and 1-30 $\mu\text{g} / \text{ml}$. The values of the molar absorption factors were (4.1224×10^4 , 3.0229×10^4 and 1.7373×10^4) $\text{L mol}^{-1}\text{cm}^{-1}$ with a sensitivity of Sandell's equal to 0.2606×10^{-4} , 0.9834×10^{-4} and $0.2568 \times 10^{-4} \mu\text{g cm}^{-2}$ to methods A, B respectively and LLOD values were 0.255, 0.553 and 0.158 $\mu\text{g} / \text{ml}$ to methods A, B and C. LLOQ 0.512, 0.898 and 0.455 $\mu\text{g} / \text{ml}$ to methods A, B, C respectively. The constant fixed Kf configuration was also calculated for the colored outputs of the reaction where it was found to be equal to 43.6435×10^8 , 54.6261×10^8 and $17.29099 \times 10^6 \text{L}^2 \text{mol}^{-2}$ to all methods A, B, C respectively. The values of G were calculated based on -43.9293 KJ / mol, -44.3735 and -51.2019. G values, molar absorption factor, Sandell sensitivity, detection limit.



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INTRODUCTION

The chemical formula to metoclopramide hydrochloride, $\text{C}_{14}\text{H}_{17}\text{ClN}_2\text{O}$ with molecular weight (354.3 gm /mol) the scientific name under the IUPAC system is 4-amino-5-chloro-N-(2-diethylamino) ethyl-2 ethyl-2 ethyl-2). Figure 1 shows the structural form of hydrochloride metoclopramide. Metoclopramide hydrochloride is an odourless white crystalline powder. 1 mg of metoclopramide is soluble in 0.7 gm of water at 25 C, and 3 gm of it is soluble in ethanol (96%), 55 gm in chloroform (90%) and soluble in diluted hydrochloric acid which is practically soluble in

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ether. Metoclopramide hydrochloride contains ionization constants with values of 0.42 (pK_1) and 9.71 (pK_2) (Yuvaraja and Khanam, 2014; Sawale et al., 2016; Shakeel et al., 2014; . et al., 2014; Zhai et al., 2017) . Metoclopramide strengthens the oesophageal muscle of the oesophagus and reduces gastric acid reflux. Metoclopramide hydrochloride is used to reduce nausea and vomiting when combined with chemotherapy, and it speeds up gastric emptying of harmful intestinal and liquid meals. It is an alternative benzamide drug that is used, because of its Kinetic properties to reduce disorders of gastrointestinal degeneration, such as ileal motility, stomach, oesophagus and reduce indigestion, vomiting and nausea (Adegoke, 2012; Satyanary and Nagesara, 2012; Okram et al., 2012) . Metoclopramide hydrochloride has been used because of its pro-gastrointestinal effects through cholinergic stimulation of gastrointestinal diseases caused by radiotherapy, chemotherapy and post-operative nausea. Several analytical methods were used to determine metoclopramide hydrochloride, such as High-performance liquid chromatography, gas chromatography, voltage measurement, voltage measurement method, chemical fluorescence. Metoclopramide and aspirin can be estimated together in human plasma and in pharmaceutical preparations by using chemical fluorescence and phosphorescence (Neha et al., 2015; Khaleel et al., 2011a; Vandenplas and Hauser, 2015) .

Most widely used methods to metoclopramide in pharmaceuticals are spectral, in which the metoclopramide is classified within the easy complexes, which can be readily estimated by the ultraviolet spectral method. The conjugation reaction can also be used to determine metoclopramide in the alkali medium. However, the best methods are used to estimate that metoclopramide hydrochloride and pyridoxine hydrochloride in human plasma are HPLC-UV methods. The electrolysis method was used to estimate metoclopramide by using a modified and electrode carbon. A sequential flow injection analysis can be performed to determine metoclopramide. (Patil and Nandibewoor, 2015; Gulsu et al., 2012; Dusane et al., 2011; Elmansi et al., 2016)

In this study, three spectral methods were used to determine metoclopramide hydrochloride using colour reagents such as diazotzil reaction with resorcinol, 8-hydroxyincol and p-benzoquinone as a coupling agent to form azo-dye in alkaline medium at room temperature (Alshirifi and Abbas, 2015; Aljarah and Obedagha, 2014) .

MATERIALS AND METHODS

Instrumentation:

Double beam UV-visible spectrophotometer (UV-Jenawa Model 1100) was used for absorbance with a 10 mm quartz cell.

Materials and reagents:

All reagents with a high degree of analytical purity, deionized water were also used. Metoclopramide hydrochloride was purchased from Merck. The pharmaceutical dosage used in this work Primperan tablets (metoclopramide tablets) with 10 mg of metoclopramide HCl / tablet contains 5 mg of metoclopramide (Sifar-Istanbul / Turkey) HCl / tablet and Metal Injection (Sanofi Aventis Egypt) contains 10 mg / 2 ml (Jawad and Kadhim, 2013) .

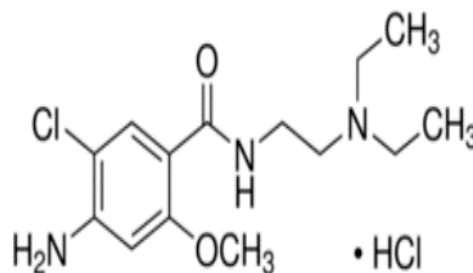


Figure 1: Structure of metoclopramide hydrochloride

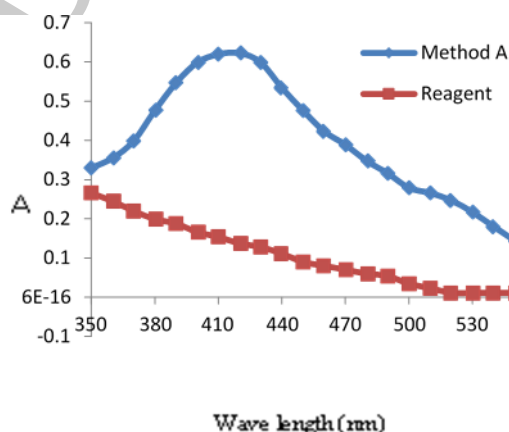


Figure 2: Absorption spectra of metoclopramide hydrochloride azo dye with the resorcinol reagent (5.0 µg/mL)

0.5% sodium nitrite solution.

The sodium nitrite reagent was supplied by BDH Chemicals Ltd. The solution is prepared by dissolving 0.5 g of NaNO_2 in a volumetric flask and supplemented with 100 ml of deionized water.

Sodium hydroxide solution 0.5 N:

This solution is prepared by taking the exact weight of the base and dissolving in 100 ml of deion-

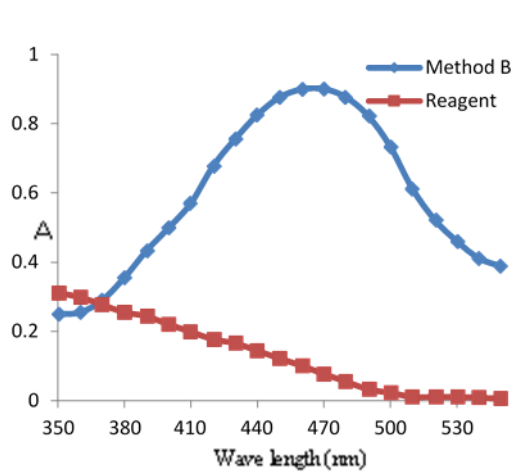


Figure 3: Absorption spectra of metoclopramide hydrochloride azo dye with the 8-hydroxyquinaldine reagent ($10.0 \mu\text{gmL}^{-1}$)

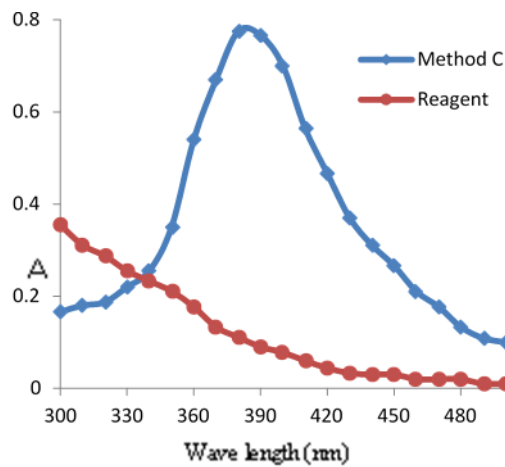


Figure 4: Absorption of metoclopramide hydrochloride with the p-benzoquinone reagent ($15.0 \mu\text{gmL}^{-1}$)

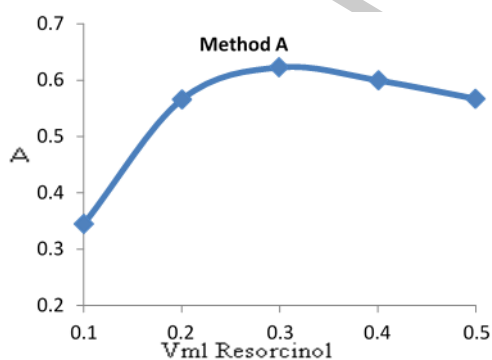


Figure 5: Effect of resorcinol reagent volume on absorbance

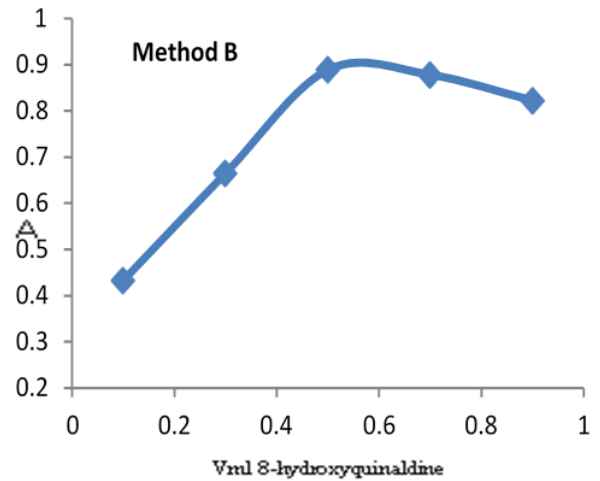


Figure 6: Effect of 8-hydroxyquinaldine reagent volume on absorbance

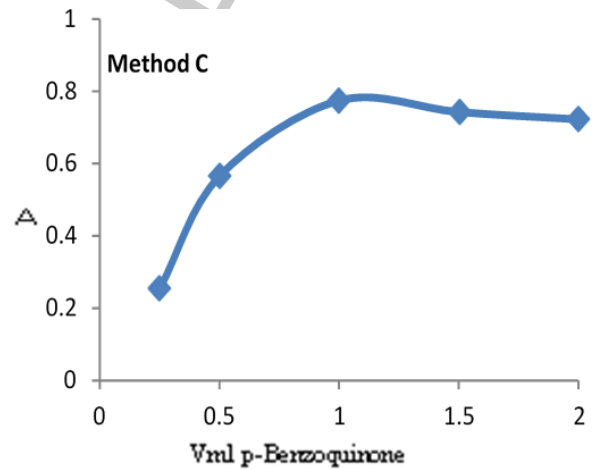


Figure 7: Effect of p-benzoquinone volume on absorbance

ized water to prepare 0.5 N solution by dissolving 2 g of substance in 100 ml of deionized water (Deokate and Gorde, 2014).

8-hydroxyquinaldine reagent solution 0.5%.

Pure reagent supplied by BDH Chemicals Ltd. This solution was prepared by dissolving 0.5 g of 8-hydroxyquinoline reagent in a 100 ml volumetric flask (Okram et al., 2012).

0.5% resorcinol.

0.5% resorcinol solution was prepared by dissolving 0.5 g of resorcinol (supplied by BDH Chemicals Ltd) in a 100 ml flask (Devi et al., 2016).

1% p-benzoquinone solution.

1% of the p-benzoquinone solution was prepared by dissolving 1 g in a minimum amount of ethanol and making the volume to 100 ml with ethanol (Malih et al., 2012).

Sodium hydroxide solution 0.5 N

120 This solution is suitably prepared by taking the ex-
 121 act weight of the base and dissolving it in 100 ml of
 122 deionized water to prepare a 0.5 N solution by dis-
 123 solving 2 g of substance in 100 ml of distilled wa-
 124 ter (Al-Rufaie, 2016b) .

125 **Hydrochloric acid solution 0,5 N**

126 This solution is prepared by diluting appropriately
 127 a 36% concentrated solution of hydrochloric acid in
 128 a 250 ml graduated flask with deionized water (Al-
 129 Rufaie, 2016a) .

130 **Metoclopramide hydrochloride standard solu-
 131 tion**

132 Metoclopramide hydrochloride was obtained from
 133 (SDI, Samara, Iraq). A solution of 1,000 µg /
 134 ml metoclopramide hydrochloride was prepared by
 135 dissolved 100 mg of metoclopramide hydrochloride
 136 in 100 ml of deionized water and diluted for final
 137 concentrations (Hemalatha et al., 2011) .

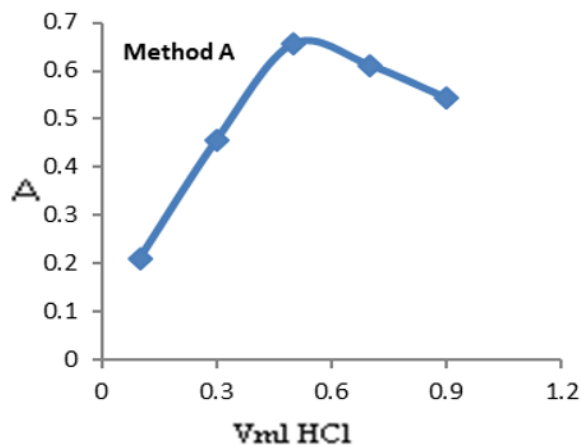


Figure 10: Effect of HCl (0.5N) volume on absorbance

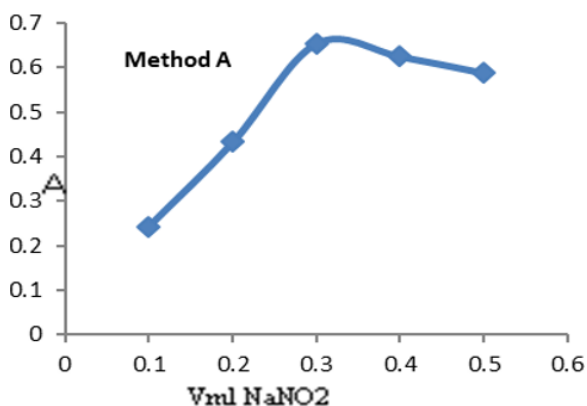


Figure 8: Effect of NaNO₂ volume on absorbance

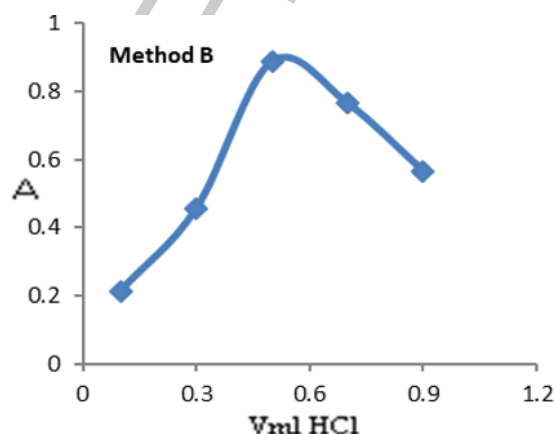


Figure 11: Effect of HCl (0.5N) volume on absorbance

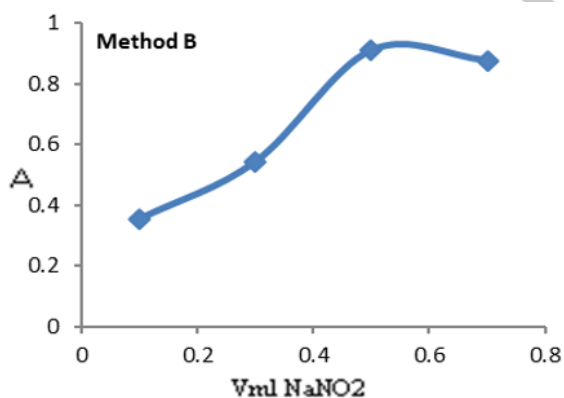


Figure 9: Effect of NaNO₂ volume on absorbance

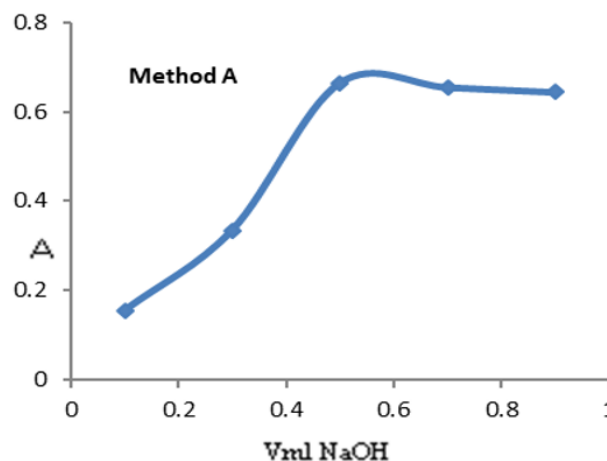


Figure 12: Effect of NaOH (0.5N) volume on absorbance

138 **Procedure:**

139 The three spectral methods have been used to anal-
 140 ysis of hydrochloric metoclopramide by using differ-
 141 ent coloured reagents:

142 Method A

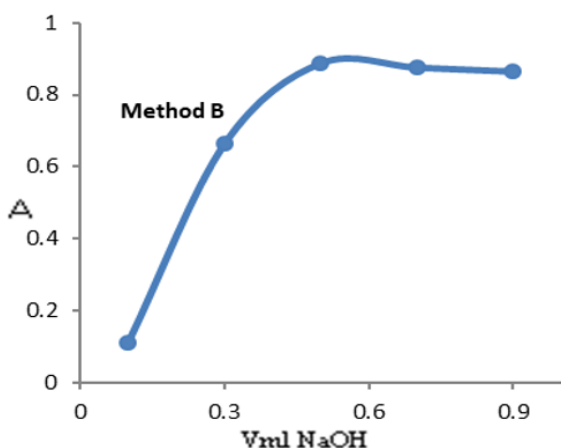


Figure 13: Effect of NaOH (0.5N) volume on absorbance

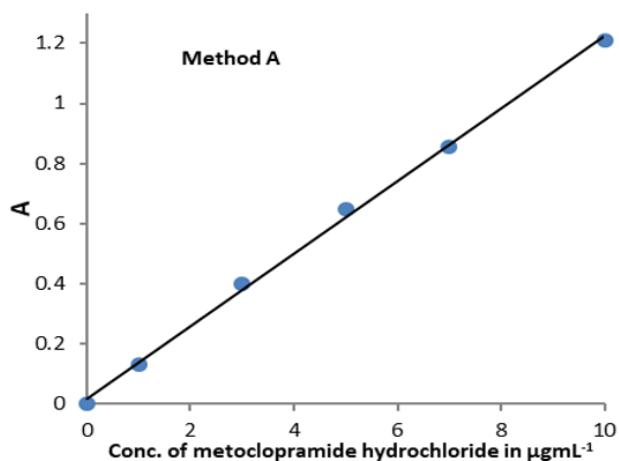


Figure 14: The calibration curve in method-A

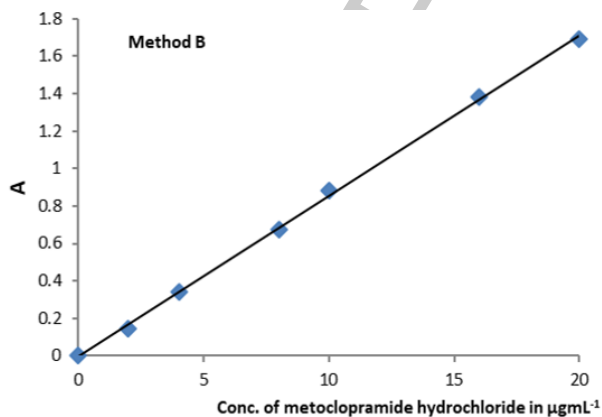


Figure 15: The calibration curve in method-B

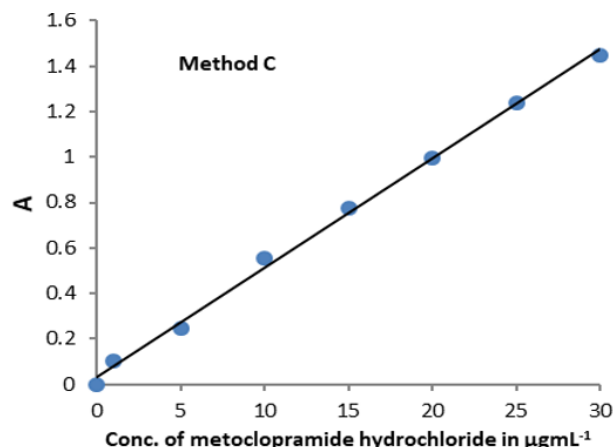


Figure 16: The calibration curve in method-C

Different concentrations in the range of 1-10 mg/ml (0.1 volumes, 0.3, 0.5 0.7, 0.9 and 1.0) ml of the standard solution of metoclopramide hydrochloride (100 $\mu\text{g} / \text{ml}$) were transferred and measured in the number of volumetric flasks with 10 ml volumes using a micro-pipette. To each flask were added 0.3 ml of 0.5% of NaNO_2 and 0.5 ml of 0.5 N of HCl. After three minutes, 0.3 ml of resorcinol was added 0.5% and 0.5 ml of 0.5 N NaOH solution and added with deionized water. The absorbance of the coloured product was measured after 10 minutes, the colour absorbance at 415 nm against the corresponding white reagent.

Various concentrations were prepared in the range 2.0-20 mg / ml volume (0.2,0.4,0.6,0.8,1.0,1.2,1.4,1.6,1.8 and 2.0) ml of the standard solution of metoclopramide hydrochloride (100 mg / ml) in a series of volumetric flasks (10 ml) by means of a micro-pipette. For each flask, 0.5 ml of 0.5% NaNO_2 solution and 0.5 ml of 0.5 N solution of 8-hydroxyquinoline and 0.5 ml of 0.5% solution of 0.5 N NaOH and diluted to the mark with deionized water. The absorbance of the coloured product was measured at 485 nm against the solvent as blank after 10 minutes.

Method C

In the series of volumetric flasks (10 ml), transfer concentrations of the standard solution of 100 $\mu\text{g} / \text{ml}$ of metoclopramide-HCl equivalent to 1.0-30 $\mu\text{g} / \text{ml}$, add one ml of p-benzoquinone solution, make up the volume to 10 ml with deionized water, then the absorbance was measured after 10 minutes at 385 nm against a blank. The calibration curve was constructed from the concentrations of metoclopramide hydrochloride ($\mu\text{g} / \text{ml}$) against absorbance.

The essay procedure to tablets of metoclopramide hydrochloride:

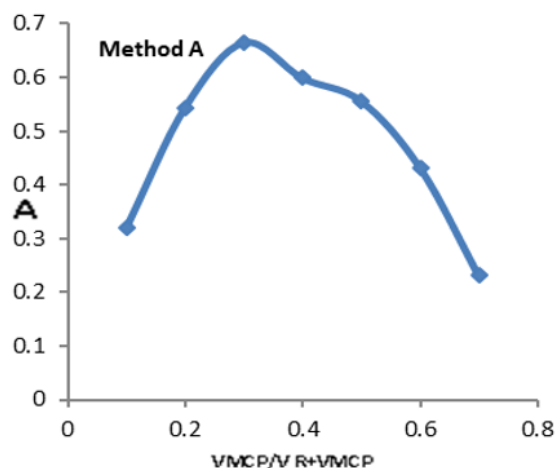


Figure 17: Job's method for method A

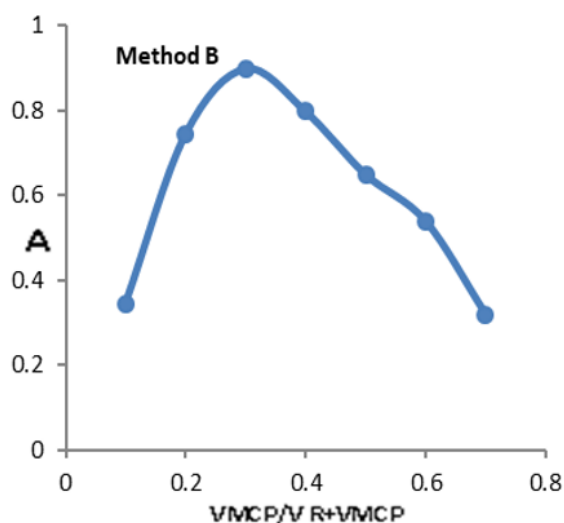


Figure 18: Job's method for method B

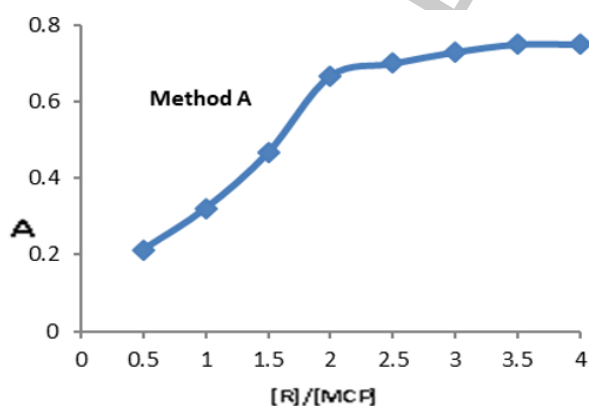


Figure 19: mole ratio method for method A

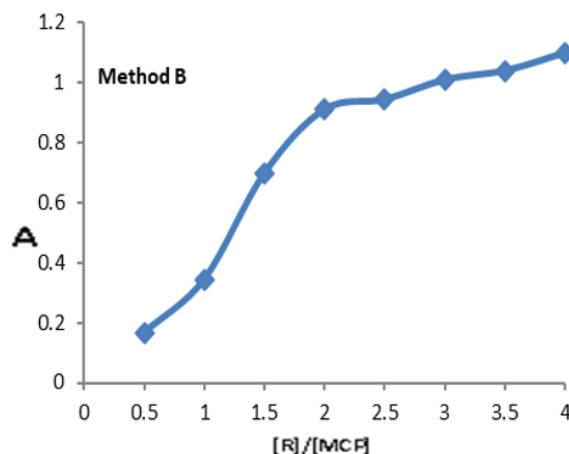


Figure 20: mole ratio method for method B

10 tablets were weighed and ground well, then mixed (5 mg and 10 mg). A fraction of the powder equivalent to 0.05 g of metoclopramide hydrochloride was weighed and dissolved in deionized water, mixed well and filtered using a filter paper. Then transfer to a 100 ml flask and complete to mark with deionized water. The solution was treated in the recommended way. The working solutions were prepared by diluting the resulting solution with deionized water.

RESULTS AND DISCUSSION

Determination of the Lambda max

The values of the absorption spectra of the coloured complexes of the reaction between the hydrochloride salt of metoclopramide and diazonium with the resorcinol or the 8-hydroxyquinoline reagent in acidic medium (in both methods A and B respectively) with respect to the reagent target. The sample shows the maximum absorption at 415 nm (method A) and 485 nm (method B). The reaction involved two steps to give a coloured product. Initially, metoclopramide hydrochloride is treated with sodium nitrite in an acid environment to give diazonium salt. In the second phase, the diazonium ion reacts with the coupling agent of resorcinol or 8-hydroxyquinoline (method A or B) to form an orange azo dye (method) and red colour (method B) in an alkaline medium. Method C, which includes the reaction between metoclopramide hydrochloride and p-benzoquinone, shows maximum absorption at 385 nm. The absorption spectra are shown in Figures 2, 3 and 4.

Optimal conditions for the reaction

The effect of the various parameters on the absorption intensity, was optimized. All the experimental parameters were optimized by using 5.0, 10.0 and

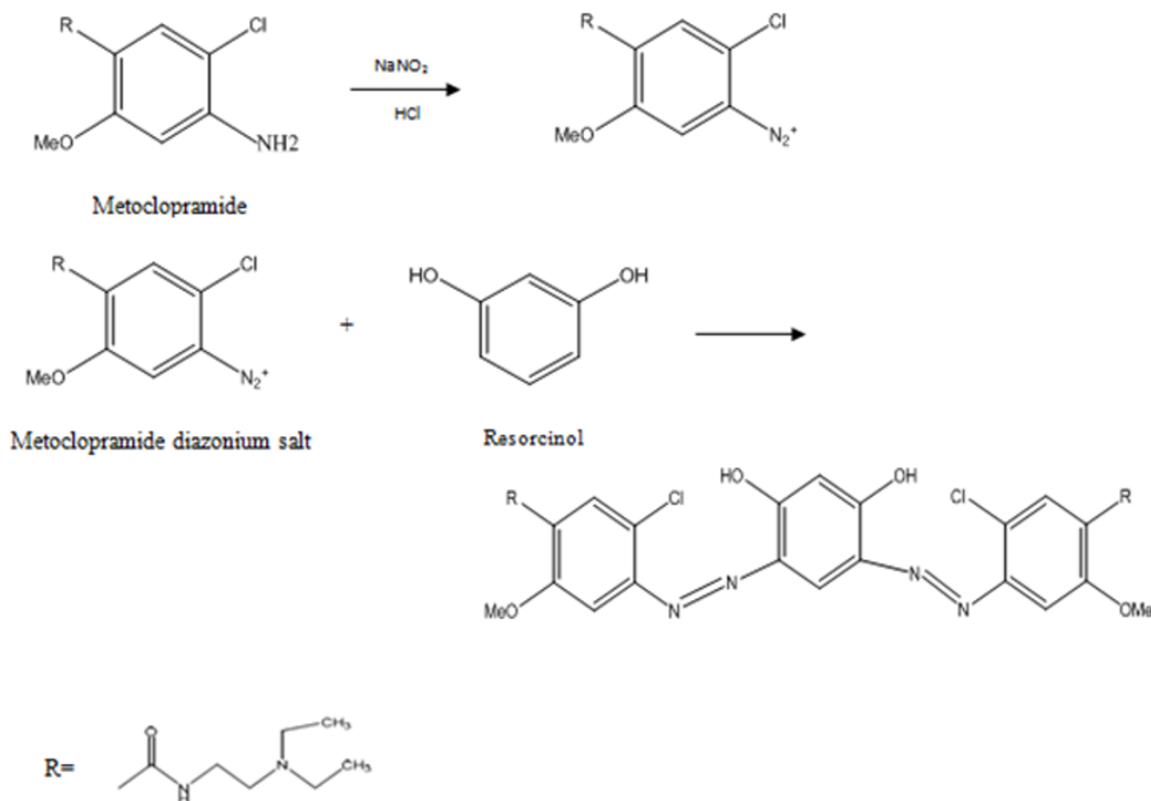


Figure 23: The proposed mechanisms of the products may be suggested as the following figures

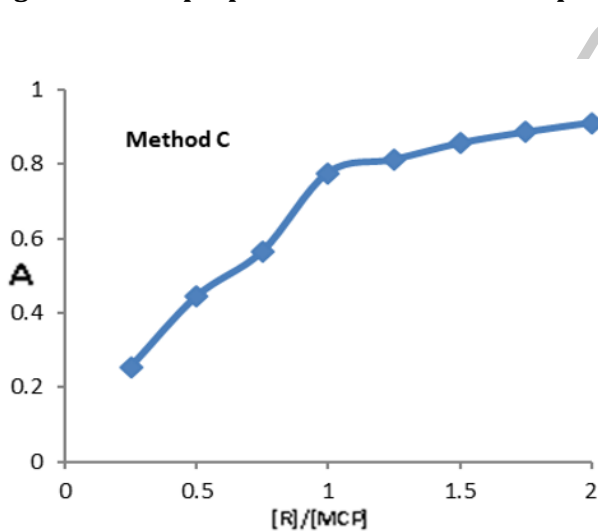


Figure 21: mole ratio method for method C

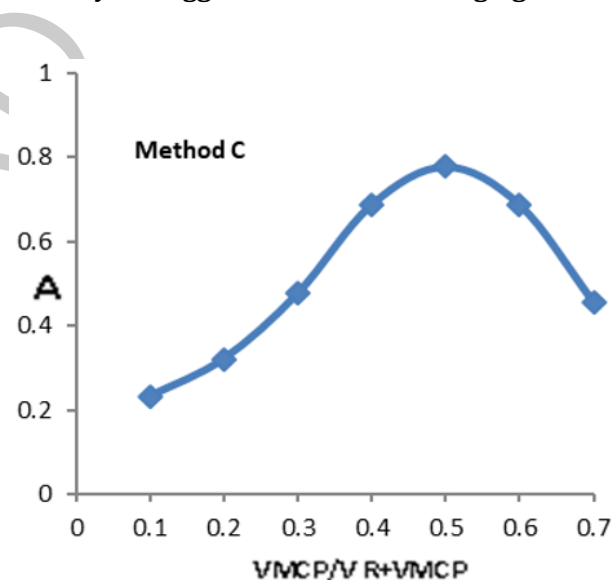


Figure 22: Job's method for method C

217 15.0 mg/ml metoclopramide hydrochloride with the
 218 three methods A, B, C respectively (Al-Rufaie *et al.*,
 219 2013) (Figures 23, 24 and 25).

220 The effect of reagent volumes.

221 The reagent volumes were tested in the range of
 222 0.1-0.5 mL and 0.5% resorcinol. The 0.3 ml were
 223 applied in subsequent experiments (method A) be-
 224 cause they obtained the maximum absorption and
 225 the other 8-hydroxyquinoline in the range of 0.1-0.9

ml at a concentration of 0.5%. The 0.5 ml volume
 226 was selected as the best volume that could be used
 227 for further studies due to this volume and focuses
 228 on the maximum absorption value (method B) as
 229 shown in Figure 5 and Figure 6 .
 230

The quantities were tested within 0.25-2.0 ml of p-
 231 benzoquinone at a concentration of 1% (Al-Abbasi
 232 *et al.*, 2011; Khaleel *et al.*, 2011b; Menaka and
 233

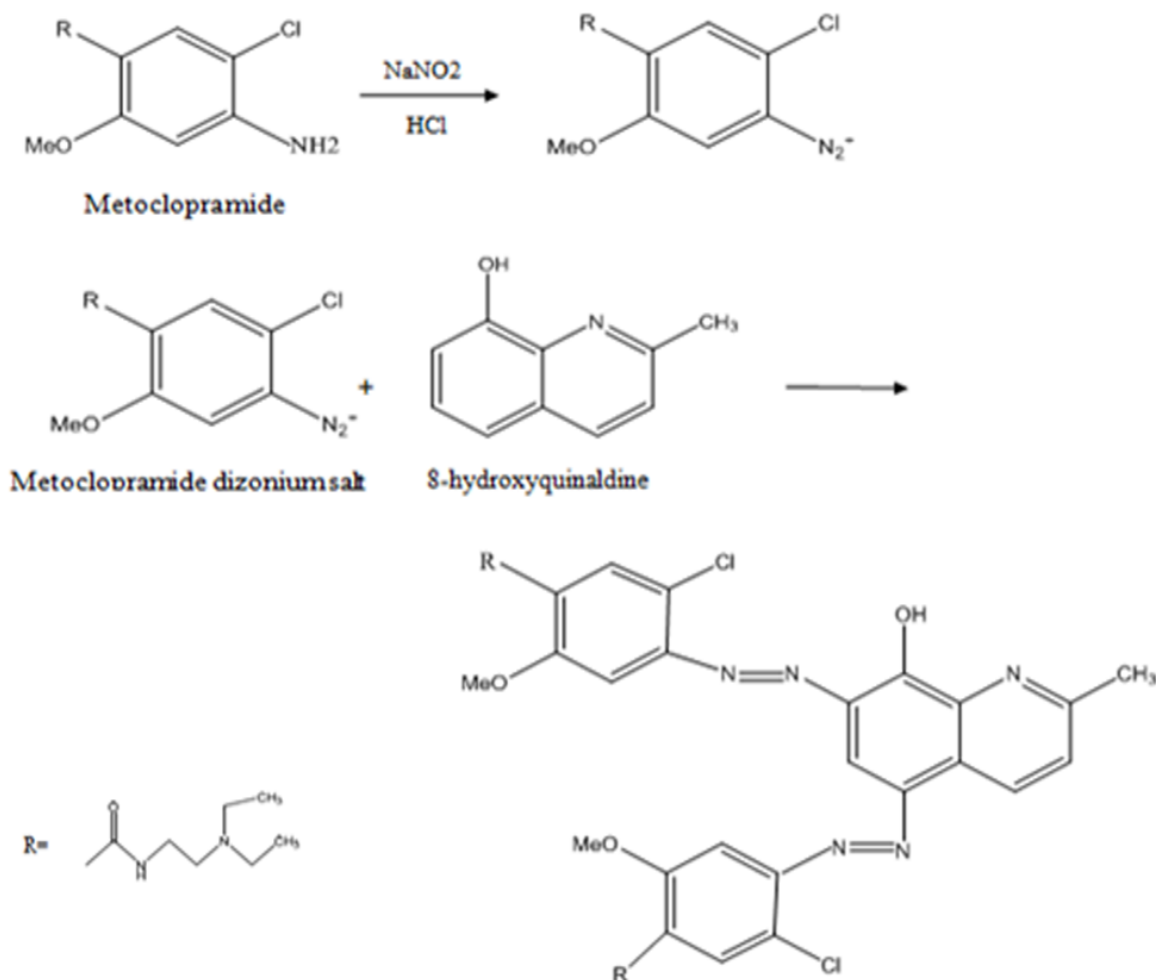


Figure 24: The probable reaction mechanism of the coupling reaction between metoclopramide and 8-hydroxyquinaldine (method-B)

234 Pandey, 2013). It was found that 1.0 ml was appropriate for application in subsequent experiments (method C), Figure 7.

237 Effect of sodium nitrite

238 The different volume of 0.5% in a range of 0.1-0.5 ml of NaNO₂ was tested in the absorption density. It was observed that the volume of 0.3 ml of sodium nitrite was the optimal absorption volume (method A) (Figure 8). The NaNO₂ volume of 0.5 ml was also selected for density absorption (method B) (Figure 9) (Rashmika et al., 2013).

245 Acid effect

246 Different acids such as H₂SO₄, HCl, HNO₃ and CH₃COOH were tested for absorption values in methods A and B. A 0.5 N concentration of 0.5 mL of hydrochloric acid was selected as this concentration gave the highest absorption of the measured product in both methods A and B (Jia et al., 2010) (Figure 10 and Figure 11).

253 Effect of reaction time.

254 The azo coupling reaction was completed at 10 minutes and at 15 minutes for methods A and B. The coloured products were more stable at 24 hours in methods A and B, on the other hand, coloured products using p-benzoquinone and metoclopramide hydrochloride found completely in 10 minutes and stable for 24 hours (Poddar et al., 2011).

261 The effect of temperature

262 The effect of temperature on absorption intensity was studied at different temperatures in the range 5-45°C. The results indicate that the absorbance values decrease at higher temperatures, probably due to the dissociation of the compound. The maximum absorbance was found in the range of 20 to 35 °C. Therefore all studies were conducted at room temperature (Adegoke and Nwoke, 2008).

270 The effect of Base volume :

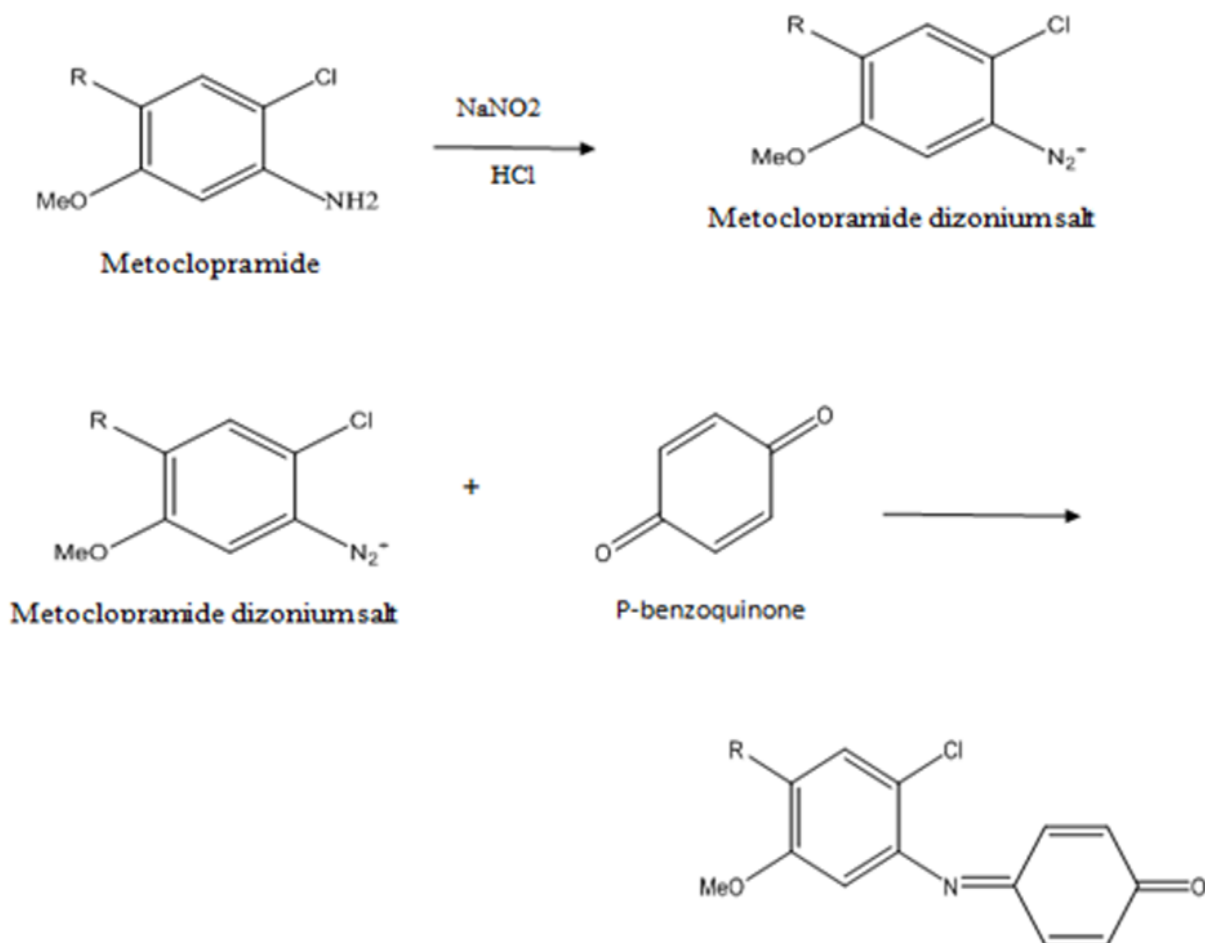


Figure 25: The probable reaction mechanism of the coupling reaction between metoclopramide and P-benzoquinone (methodC)

271 The effect of base concentration on the coloured
 272 product was tested by using different basic solu-
 273 tions, such as ammonium hydroxide, sodium acetate,
 274 potassium hydroxide, sodium carbonate and
 275 sodium hydroxide. The product of sodium hydroxide
 276 solution was given sensitivity and stability
 277 highly, so it was used in applied in subsequent
 278 experiments. different volumes of (0.1-0.9 ml) from
 279 0.5 M NaOH solutions were tested. The results
 280 showed that 0.5 ml of sodium hydroxide solution
 281 is sufficient to the production of maximum repro-
 282 ducible and absorption intensity in both methods A
 283 and B as shown in Figures 12 and 13 . Partial decol-
 284 orization of the product, maybe accruing in higher
 285 concentrations of the base (Annapurna *et al.*, 2009;
 286 Nancy *et al.*, 2018) .

287 The calibration curve:

288 Under optimal conditions studied, the
 289 metoclopramide-HCl calibration curves were
 290 designed for all methods A, B, C, illustrated in
 291 Figures 14 and 15 and Figure 16 , the linear

relationship between the concentrations of meto-
 292 clopramide HCl and absorbance and 1, 0-30 $\mu\text{g} / \text{ml}$
 293 to methods A, B, C, respectively, with a correlation
 294 coefficient of 0.988, 0.9999 and 0.9987 respectively
 295 to methods A, B, C. It was found that the molar
 296 absorption coefficients of the methods A, B, C are
 297 4.1224×10^4 , $3.0229 \times 1.7373 \times 10^4$ and 104 L
 298 $\text{mol}^{-1} \text{cm}^{-1}$ for methods A, B, C, respectively (Yadav
 299 *et al.*, 2010) . The Sandell's sensitivity was $0, 3606$
 300 $\times 10^{-4}$, 0.9834×10^{-4} and $0.2568 \times 10^{-3} \mu\text{g.cm}^{-2}$
 301 to methods A, B, C, respectively, all results are listed
 302 in Table 1 .

304 Stoichiometry

305 The stoichiometry of metoclopramide hydrochloride
 306 with diazonium salt and resorcinol or 8-
 307 hydroxyquinoline solutions was studied in methods
 308 A and B using the working method and the molar
 309 ratio method (Naggar *et al.*, 2009) as shown in Fig-
 310 ures 17 and 18 and Figure 22 . the results showed
 311 that 1: 2 was formed at 415 nm and 485 nm respec-
 312 tively for methods A and B, instead, the results show

Table 1: The analytical parameter for methods A, B and C

Method-C	Method-B	Method-A	Parameters
385	485	415	λ_{\max} , nm
1.0-30	2.0-20	1.0-10	Linear range ($\mu\text{g/mL}$)
1.7373x10 ⁴	3.0229x10 ⁴	4.1224x10 ⁴	Molar absorptivity coefficient (ϵ), (L mol ⁻¹ cm ⁻¹)
0.2568x10 ⁻³	0.9834x10 ⁻⁴	0.3606x10 ⁻⁴	Sandell sensitivity (Ng cm ⁻²)
0.033	0.003	0.018	Intercept (a)
0.048	0.085	0.120	Slope (b)
0.9979	0.9999	0.9988	correlation coefficient (R ²)
0.158	0.553	0.255	LOQ($\mu\text{g/mL}$)
0.455	0.898	0.512	LOD($\mu\text{g/mL}$)

Table 2: Accuracy and precision of the proposed methods

%RSD*	%(Recovery \pm SD)*	%Relative error*	The Amount was Found* ($\mu\text{g/mL}$)	Amount taken ($\mu\text{g/mL}$)	Method
0.58	101.50 \pm 0.24	1.40	2.03	2	A
1.01	100.80 \pm 0.51	0.80	5.04	5	
1.09	101.30 \pm 0.33	1.30	10.13	10	
0.91	100.80 \pm 0.23	0.80	5.04	5	
0.89	100.20 \pm 0.49	0.20	15.03	15	
0.97	99.45 \pm 0.15	0.55	19.89	20	
0.83	101.20 \pm 0.14	1.20	10.12	10	C
0.96	99.67 \pm 0.22	0.33	14.95	15	
0.77	100.68 \pm 0.42	0.68	25.17	25	

313 that a 1: 1 complex was formed at 385 nm method C
 314 using the Labor and method of molar relations (Fig-
 315 ures 19, 20 and 21).

316 The stability constant

317 The constant stability K_f of the colored products was
 318 calculated from the continuous variation data using
 319 the following equation (Wan *et al.*, 2012) :

$$320 K_f = \frac{A/A_m}{(1-A/A_m)^{n+1} C^n n^n}$$

321 Where: A and A_m are the maximum absorbance of
 322 the continuous variation curve and the absorbance
 323 corresponding to the union of the two tangents of
 324 the continuous variation curve, respectively. n is the
 325 number of reactant molecules in the reaction prod-
 326 uct, C is the molar concentration of metoclopramide
 327 hydrochloride at the maximum absorbance. K_f was
 328 found to be 43.6435×10^8 , 54.6261×10^{-8} and
 329 17.29099×10^6 L² mol⁻² for methods A, B and C
 330 respectively. This indicates a stable reaction prod-
 331 uct. The Gibbs free energy of the reaction (ΔG) was
 332 also calculated using the following equation (Tyagi
 333 and Dhillon, 2012) :

$$\Delta G = -2.303RT \log K_f$$

334 Where R is the universal gas constant (8.314 J mol⁻¹
 335 deg⁻¹). T is the absolute temperature (273 + 25 ° C),
 336 K_f is the reaction formation constant. It was found
 337 that ΔG values were -43.9293 kJ / mol, -44.3735 and
 338 -51.2019 for methods A, B and C, respectively (Fig-
 339 ures 23 and 24 and Figure 25). The negative value
 340 of ΔG refers to the spontaneity of the reaction.
 341

342 Precision and precision.

343 To study the accuracy and precision of the calibra-
 344 tion curve, solutions containing three different con-
 345 centrations of metoclopramide hydrochloride were
 346 designated in methods A, B and C (Suresh *et al.*,
 347 2012) . The results obtained, which are summarized
 348 in Table 2 indicate a good precision and accuracy for
 349 all methods.

350 Interference

351 The methods developed were successfully applied
 352 to the determination of metoclopramide hydrochlo-
 353 ride in its pharmaceutical formulation, and the re-
 354 sults are presented in Table 3 . The results obtained

Table 3: The application the methods for determination of metoclopramide hydrochloride in pharmaceutical preparations

METOCAL TION 10mg/2ml	Drugs brand name									Conce. ($\mu\text{g/ml}$)	Proposed methods		
	INGEC-			MECLODIN Tablets 5mg			Metoclopramide Tablets 10mg						
7.0	5.0	3.0	7.0	5.0	3.0	7.0	5.0	3.0	7.0	5.0	3.0	Taken conc. ($\mu\text{g/ml}$)	Method A
6.89	5.11	3.03	7.11	4.99	3.09	7.03	5.02	3.05	7.03	5.02	3.05	Found conc. ($\mu\text{g/ml}$)	
98.42	102.20	101.0	101.57	99.80	103.0	100.42	100.40	101.66	100.42	100.40	101.66	Recovery(%) n=3	Reference method
0.56	0.99	0.79	1.10	0.86	0.97	0.59	0.75	0.58	0.59	0.75	0.58	RSD(%),n=3	
99.73 \pm 0.08			100.05 \pm 0.04			101.22 \pm 0.02			101.22 \pm 0.02			(%Recovery \pm SD) n=5	
15.0	10.0	5.0	15.0	10.0	5.0	15.0	10.0	5.0	15.0	10.0	5.0	Taken conc. ($\mu\text{g/ml}$)	Method B
14.89	10.04	5.09	14.77	10.05	5.12	15.02	10.12	5.04	15.02	10.12	5.04	Found conc. ($\mu\text{g/ml}$)	
99.26	100.40	101.80	98.46	100.50	102.40	100.13	101.20	100.80	100.13	101.20	100.80	Recovery (%) n=3	Reference method
0.98	0.76	0.64	1.01	0.89	0.77	0.91	0.57	0.66	0.91	0.57	0.66	RSD(%),n=3	
100.60 \pm 0.06			101.13 \pm 0.05			100.05 \pm 0.03			100.05 \pm 0.03			%Recovery \pm SD n=5	
15.0	10.0	5.0	15.0	10.0	5.0	15.0	10.0	5.0	15.0	10.0	5.0	Taken conc. ($\mu\text{g/ml}$)	Method C
14.99	9.97	5.11	14.92	9.87	5.05	14.89	10.13	5.02	14.89	10.13	5.02	Found conc. ($\mu\text{g/ml}$)	
99.93	99.70	102.2	99.46	98.70	101.0	99.26	101.30	100.40	99.26	101.30	100.40	Recovery (%) n=3	Reference method
0.99	1.02	0.89	0.72	0.99	0.93	1.01	0.82	0.93	1.01	0.82	0.93	RSD(%),n=3	
100.72 \pm 0.01			99.9 2 \pm 0.05			101.22 \pm 0.04			101.22 \pm 0.04			%Recovery \pm SD n=5	

355 were compared statistically with the reference, the
 356 Student t-test values obtained with a 95% level of
 357 confidence and five degrees of freedom and did not
 358 exceed the theoretical tabulated value of $t = 2.77$,
 359 so it does not indicate a significant difference be-
 360 tween the compared methods. The F value (19.01)
 361 has also shown that there is no significant differ-
 362 ence between the accuracy of the proposed meth-
 363 ods and the reference method. The proposed meth-
 364 ods can be used for quality control and mass anal-
 365 ysis of metoclopramide hydrochloride, as well as in
 366 its dosage forms (Al-Salman, 2018a, 2019).

367 Analytical applications

368 The methods developed were successfully applied

369 to the determination of metoclopramide hydrochlo-
 370 ride in the pharmaceutical formulation, and the re-
 371 sults were presented in Table 3. The results were
 372 statistically compared with the reference values of
 373 the Student's t-test were obtained with a confidence
 374 level 95% and five degrees of freedom and did not
 375 exceed the theoretical tabulated value $t = 2.77$, so
 376 it does not indicate a significant difference between
 377 the compared methods. The F value (19.01) has
 378 also shown that there is no significant difference be-
 379 tween the accuracy of the proposed methods and
 380 the reference method. The proposed methods can
 381 be used for quality control and routine analysis of
 382 metoclopramide hydrochloride mass and in their
 383 dosage forms (Al-Salman, 2018b).

384 CONCLUSIONS

385 Simple, fast and precise spectrophotometric meth- 435
 386 ods have been a determination of metoclopramide 436
 387 hydrochloride in standard and pharmaceutical 437
 388 preparations. Methods A and B depended on the 438
 389 diazotation coupling reaction to form an azo dye 439
 390 with resorcinol reagent and 8-hydroxyquinoline 440
 391 azo dye absorbed at 415 nm and 485 nm respec- 441
 392 tively. Method C contains the reaction between 442
 393 the drug metoclopramide hydrochloride with p- 443
 394 benzoquinone to form a dye-absorbed product at 444
 395 385 nm. The completion of these procedures did 445
 396 not require the control of temperature, solvent 446
 397 extraction and even its precise and sensitive meth- 447
 398 ods. The proposed methods are able to determine 448
 399 metoclopramide hydrochloride in pharmaceutical 449
 400 formulations without any interference of excip- 450
 401 ients such as starch and glucose and commonly 451
 402 used products, suggesting easy application in the 452
 403 analysis of standard materials. Furthermore, these 453
 404 methods are extremely accurate and do not require 454
 405 the use of expensive instruments, which makes 455
 406 them suitable for routine measurement methods in 456
 407 laboratories. 457

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411 Contributions of the authors

412 This research was conducted individually in the lab- 462
 413 oratories of the Faculty of Pharmacy, University of 463
 414 Basrah. This investigation was completed during a 464
 415 4-month period with serious and continuous work 465
 416 and, therefore, excellent results were obtained by 466
 417 finding an easy and sensitive method to estimate 467
 418 metoclopramide hydrochloride. 468

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