RESEARCH ARTICLE

Exploiting the Diazotization Reaction of 8-hydroxyquinoline for Determination of Metoclopramide-hydrochloric acid in Pharmaceutical Preparations

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ABSTRACT

A sample, fast, precise and accurate spectrophotometric method to the quantitative determination of metoclopramide hydrochloride (MCP) in pure and pharmaceutical preparations, a simple, sensitive and high-purity method has been developed. This method is based on the diazotization of the primary amine group of metoclopramide hydrochloride by reaction hydrochloric acid with sodium nitrite followed by conjugation in an alkaline medium with 8-hydroxyquinoline against the reagent blank. The effect of several acids like hydrochloric, nitric, phosphoric, and sulfuriHc acid. That found hydrochloric acid the most excellent acid, to give the maximum absorption and sensitivity and the best volume $NaNO_2$ solution about 1 and 3 mL of an 8-hydroxyquinoline reagent gives high intensity and stability to the color formed, also azo dye give a maximum absorption and best sensitivity after 10 minutes and the color remains stable about 1-hour. Where the concentration range was 1-20 mg/L, it was found that it obeys law Beer-Lambert correlation coefficient (R2 =0.9997). They have a detection limit LoD (0.274 μg mL^{-1}) and limit of Quantitation LoQ (0.915 μg mL^{-1}), respectively. This method has also been used in many pharmaceutical preparations (capsules, tablets and syrup) to determine the drug metoclopramide.

Keywords: Metoclopramide hydrochloride, 8-hydroxyquinoline, Pharmaceutical, Diazotization reaction.

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INTRODUCTION

8-Hydroxyquinoline (8HQ) (Figure 1a), derivative of a quinolone originating in plants also from synthesis, has been utilized in agriculture as a fungicide and a preservative in the textile, paper and wood industries. 8-hydroxyquinoline possesses potent coordinating capacity and best metal estimate properties, which means it is most utilized of analytical and separation goal also of chelation metal.[1,2] Metoclopramide hydrochloride (MCP) that chemical formula ($C_{14}H_{22}ClN_3O_2$, HCl) and (354.3 gm/mol) molecular weight. IUPAC is 4-amino-5-chloro-N-(2- 17 diethyl amino) ethyl-2-methoxy benzamide,[3-5] as appear in Figure 1a. MCP drug is an odorless powder crystalline white. MCP about 1-mg at 25°C soluble in 0.7 gm of water, and 3 gm of it is ethanol soluble (96%), 55 gm in (90%) chloroform and soluble in diluted HCl that is practically soluble in ether. MCP drug have ionization constant by values of (pK1) 0.42 and (pK2) 9.71.[6-9] Different analytical methods have identified cited drugs, including chemometric-assisted tech high-performance liquid chromatography (HPLC), Spectrofluorimetric, spectro-photometric, potentiometric, GCMS and LCMS.[10-20] In this research, one spectral way was utilized to estimate MCP drug utilizing color reagents like diazotzil reaction by 8-hydroxyninol as a coupling agent to form azo-dye at room temperature.

MATERIALS AND METHODS

Reagents

All chemicals utilized were of analytical grade reagent. Metoclopramide hydrochloride solution (100 mg/L). prepare by dissolving of MCP about 0. 01 g in distilled water in a volume 100 mL an elementary flask. Appropriate dilution of the stander solution by DW prepared solution working of MCP drug. Solution of 8-Hydroxyquinoline (0.3%). It was prepared via dissolving of reagent 8- hydroxyquinoline 0.3 g in 5 mL acetic acid and completed the volume to 100 mL via distilled water. Solution Sodium nitrite the solution prepares

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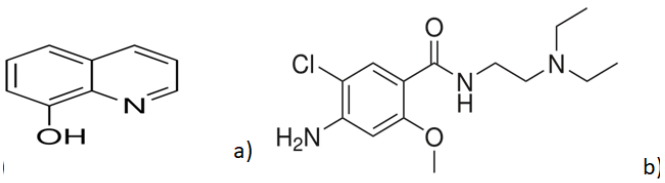


Figure 1: Chemical structure of a) 8-Hydroxyquinoline, b) Metoclopramide hydrochloride and

via dissolving sodium nitrite 0.1 g of in 100 mL distilled water solution of sulphamic acid solution, 3% (w/v). This solution was prepared via dissolving Sulphamic acid solution 3.0 g in 100 mL distilled water. A solution of concentration 0.1 N) was prepared from the HCl acid and base NaOH and NaNO2 in (100 mL) distilled water.

Sensitive

The proposed way's sensitivity was calculated by calculating a limit of Detection (LoD) and quantifying (LoQ) for a drug. Where the drug concentration is expressed as 3(S/N), and LOQ is also expressed 10(S/N) ratio, so it was calculated through the following equations

$$\text{LOD} = \frac{3\ SD\ of\ Y-Intercept}{\text{Slope of calibration curve}} \quad (1)$$

$$\text{LOQ} = \frac{10\ SD\ of\ Y-Intercept}{\text{Slope of calibration curve}} \quad (2)$$

Accuracy

Accuracy was calculated by measuring medication samples of 1.0 to 20.0 mg/L during one day, where one reading is repeated thrice. where accuracy is (RSD%) relative standard deviation

Precision

The relative error (Er%) was determined as well as the recovery rate for the results reached to obtain accurate results for the proposed method.

Selectivity

To make sure that the proposed method is highly selective through the use of common materials called excipients such as starch, glucose, cellulose, lactose and PVP, where their concentration is ten times the concentration of the drug used.

Calculation of the Calibration Curve

A series of solutions with a volume (10 mL) of MCP drug 1–20 mg/L was prepared, where 1-mL of hydrochloric acid solution and 1-mL of sodium nitrite were added. The mixture was shaken well for 2 minutes. After that 0.5 mL of sulphamic acid solution was added with occasional shaking for 5 minutes, followed by the addition of 3 mL 8-hydroxyquinoline, the solution agitated for 2 minutes at room temperature, and 2 mL of 1M NaOH were added. The volume was supplemented with distilled water to the mark where the maximum absorption of the formed azo dye was at a wavelength of 533 nm. Where through the calibration curve it was found that it obeys Law Beer-Lambert law, as shown in Table 1 and Figure 2.

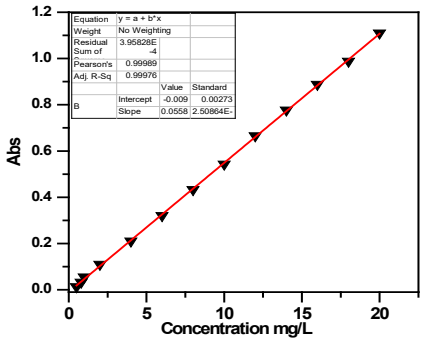


Figure 2: Calibration curve of metoclopramide hydrochloride

RESULT AND DISCUSSION

Preparation of Azo Dye

Metoclopramide hydrochloride MCP was reacted with a solution of $NaNO_2$ in an acidic medium, to form a diazonium salt through a reaction called a diazotization reaction. After the formation of the diazonium salt, it is combined with 8-hydroxyquinoline as a coupling agent in an alkaline medium, resulting in a color resulting from forming an azo dye as shown in Scheme 1.

Optimization of Reaction Conditions

Effect of concentration acid

different concentrations of acid about (0.2 - 0.9 M) of hydrochloride acid have been used for the common assay; it found the best absorbance and selectivity when using the 0.3 Mconcentration of hydrochloride acid as shown in Figure 3. The effect of several acids was too studied utilizing nitric, hydrochloric, phosphoric, sulfuric acid (0.3 M).[21-23] Found hydrochloride acid the most excellent acid, to give the maximum absorption and sensitivity as appeared in (Figure 4)

Effect of volume sodium nitrite

The effect of the amount of $NaNO_2$ was studied by taking different volumes (0.1–2) mL of sodium nitrite solution. Through the results shown in Figure 5, the volume of 1-mL $NaNO_2$ solution gives high intensity and stability to the color formed, so it was adopted reaction for the diazotization method.[1, 6, 24, 25]

Effect of amount 8-hydroxyquinoline

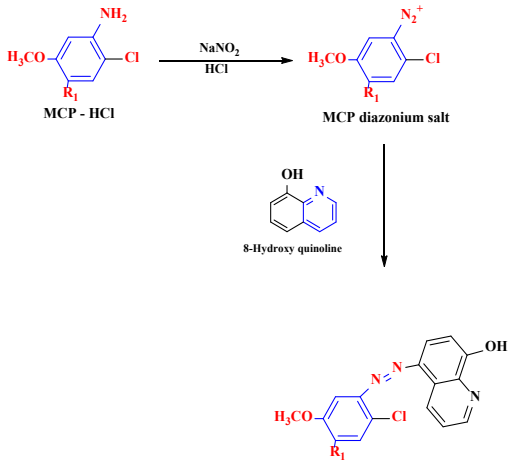
The effect of a 8-hydroxyquinolin reagent was studied through the use of different volumes (0.5–4) mL of the 8-hydroxyquinoline drug used. Through the results shown in Figure 6, the volume (3 mL) gives the best stability for the formed azo dye, and the color is stable, giving high absorbance and sensitivity[26-28]

Effect of time

The data appear in Figure 7 that explain, azo dye give maximum absorption and best sensitivity after 10 minute and the color remains stable about 1-hour, this means the high stability of the complex.[11]

Table 1: Statistical of calibration curve for several concentrations of Metoclopramide hydrochloride drug

Factors	*Proposed method*
λmax (nm)	533
Law Beer Lambert (mg/L)	1–20
Color	Orange
Regression equation	(Y = m X + C)
Intercept (C)	0.00927
Slope (m)	0.05582
Correlation coefficient (r2)	0.9997
standard deviation (SD)	0.511
(RSD%)	0.71
limit of Detection LOD (µg mL−1)	0.274
limit of Quantitation LOQ (µg mL−1)	0.915



Scheme 1: Proposed mechanism of the reaction between metoclopramide hydrochloride and 8-hydroxyquinoline to formation azo dye.

Table 2: Determination of MCP drug in several excipients utilizing the proposed and official method

Excipients	Conc. Of MCP (mg L^{-1})		E_{err} %	Recovery %
	present	Found		
glucose	10	10.2	1.96	101.9
starch	10	10.1	0.99	100.9
Lactose	10	9.9	-1.01	98.98
talc	10	10.3	2.91	102.9
PVP	10	10.4	3.84	103.8

Interference

The effect of several excipients that present with (MCP-HCl) in pharmaceutical preparations like glucose, lactose, talc, starch, and (PVP) was studied via utilizing solution having 10 mg/L of MCP drug but an excess quantity (excess 10-fold) of each excipient. The data appear in Table 2 and found none interference of the excipients.[15, 29, 30]

Application of the method

The proposed method was successfully useful to estimate MCP drug in its pharmaceutical preparations (syrup, tablet,

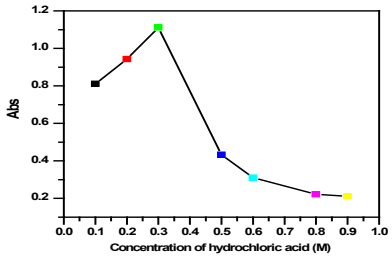


Figure 3: Effect of several concentration of hydrochloric acid

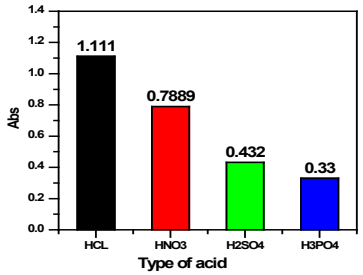


Figure 4: Effect of several type of acid

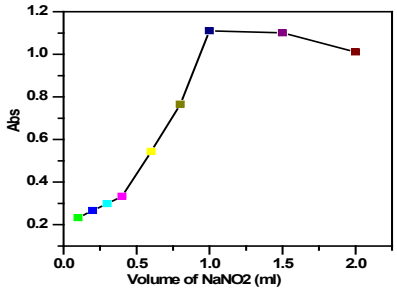


Figure 5: Effect of volume of $NaNO_2$

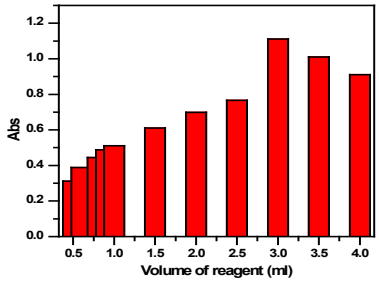


Figure 6: Effect of volume of 8-hydroxyquinoline reagent

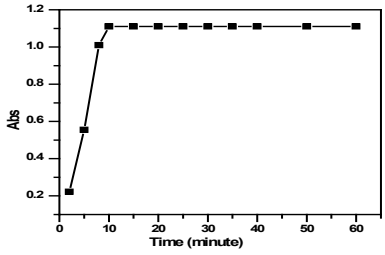


Figure 7: Effect stability time of color complex

Table 3: Determination of MCP in some formulations utilizing the official and proposed method

Pharmaceutical preparation	*Conc. Of MCP(mg L^{-1})*		*Eerr %*	*Recovery%*
	present	*Found*		
metoclopramide-hydrochloric acid tablets 5 mg , Iraq	5	4.911	-1.8122	98.18
	10	10.181	-1.777	101.7
	20	19.393	-3.129	96.87
metoclopramide-hydrochloric acid tablets 5 mg , Iran	5	4.933	-1.358	98.641
	10	10.183	1.797	101.79
	20	19.116	-4.6243	95.375
metoclopramide-hydrochloric acid capsule 10 mg Iran	5	5.166	3.213	103.21
	10	10.983	8.95	108.95
	20	20.123	0.611	100.61
metoclopramide-hydrochloric acid syrup 50 mg	5	5.250	4.761	104.7
	10	10.050	0.497	100.4
	20	19.523	-2.443	97.556

and capsule). The data in Table 3 indicate a best recovery and best relative error.[31, 32]

CONCLUSION

This study relied on developing a method for estimating MCP drug by spectrophotometric method, as the proposed method was inexpensive, sensitive, simple, and with higher selectivity. Through the calibration curve, it was found that it obeys Beer-Lambert. The volume 3 mL of 8-hydroxyquinoline gives the best stability for the formed azo dye, and the color is stable, giving high absorbance and sensitivity and the color remains stable for about 1-hour which means the complex's high stability plex.

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