



ULTRAVIOLET ASSAY OF METOCLOPRAMIDE. HCL IN PHARMACEUTICAL FORMULATIONS APPLICATION TO CONTENT UNIFORMITY TESTING

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ABSTRACT

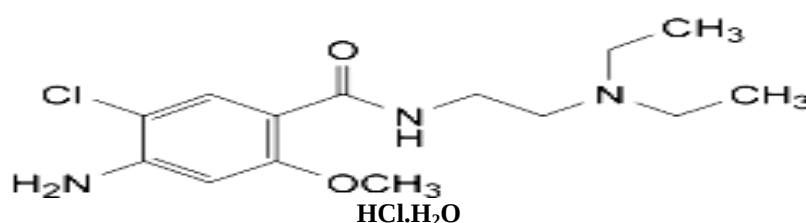
A simple, accurate, precise, rapid, economical and sensitive ultra violet spectrophotometric method has been developed for the estimation of metoclopramide. HCL in pharmaceutical preparations and environmental wastewater samples, which shows maximum absorbance at 310 nm in distilled water. Beer's law was obeyed in the range of 2-25 μ g/ml, with molar absorptivity of 1.25×10^4 L.mol⁻¹.cm⁻¹, relative standard deviation of the method was less than 1.8%, and accuracy (average recovery %) was 100 ± 1.0 . The method was successfully applied to the estimation of metoclopramide. HCL in pharmaceutical formulations, content uniformity testing and industrial wastewater samples. The proposed method was validated by sensitivity and precision which proves suitability for the routine analysis of metoclopramide. HCL in true samples.

KEYWORDS: Metoclopramide. HCL, Ultra violet, Pharmaceutical preparations.

INTRODUCTION

Metoclopramide hydrochloride (Figure. 1) is Benzamide, 4-amino-5-chloro-N-[2-(diethylamino) ethyl]-2-methoxy-, mono hydrochloride, monohydrate; 4-Amino-5-chloro -N-[2-(diethylamino) ethyl]-o-anisamide mono hydrochloride monohydrate.^[1]

Symptomatic treatment of nausea and vomiting including that associated with acute migraine Delayed (but not acute) chemotherapy-induced nausea and vomiting Radiotherapy-induced nausea and vomiting Prevention of postoperative nausea and vomiting.^[2,3]



$C_{14}H_{22}ClN_3O_2 \cdot HCl \cdot H_2O$ MW= 354.3 g.mol⁻¹

Figure 1: Chemical Structure of Metoclopramide hydrochloride.

The literature survey reveals that various methods has been reported for estimation of Metoclopramide hydrochloride these include potentiometric titration method^[4], visible spectrophotometric^[5-8], potentiometric^[9] spectrofluorimetric^[10], Flow-injection chemiluminescent^[11], LC-ESIMS^[12], HPLC^[13], and quenched continuous fluorescence.^[14] These methods are required expensive or sophisticated instruments and not simple for routine analysis. The present paper reports the development of a new UV method for estimation of metoclopramide. HCL in pharmaceutical formulations (tablets) and content uniformity testing.

EXPERIMENTAL

Apparatus

Shimadzu UV- 1700 pharm aspect (double beam) spectrophotometer with 1.0 cm quartz cells was used for absorption measurement.

Reagents

All chemical used were of analytical or pharmaceutical grade and metoclopramide. HCL standard material and pharmaceutical preparations (tablets) was provided from AL-Hokamaa company for pharmaceutical industries (HPI) Mosul-Iraq.

Distilled water was used as a solvent.

Metoclopramide. HCL standard solution 100ppm

This solution was prepared by dissolving 10 mg of metoclopramide. HCL in 100 ml of distilled water in calibrated flask.

Estimation of absorption maxima

The standard solution of metoclopramide. HCL(20µg/ml) was scanned in the range of 200-400 nm

which shows maxima located at 213,270 and 310 nm. Since 310 nm wavelength was selected for the construction of calibration curve because at this wavelength the absorbance low but more selective. Figure 2.

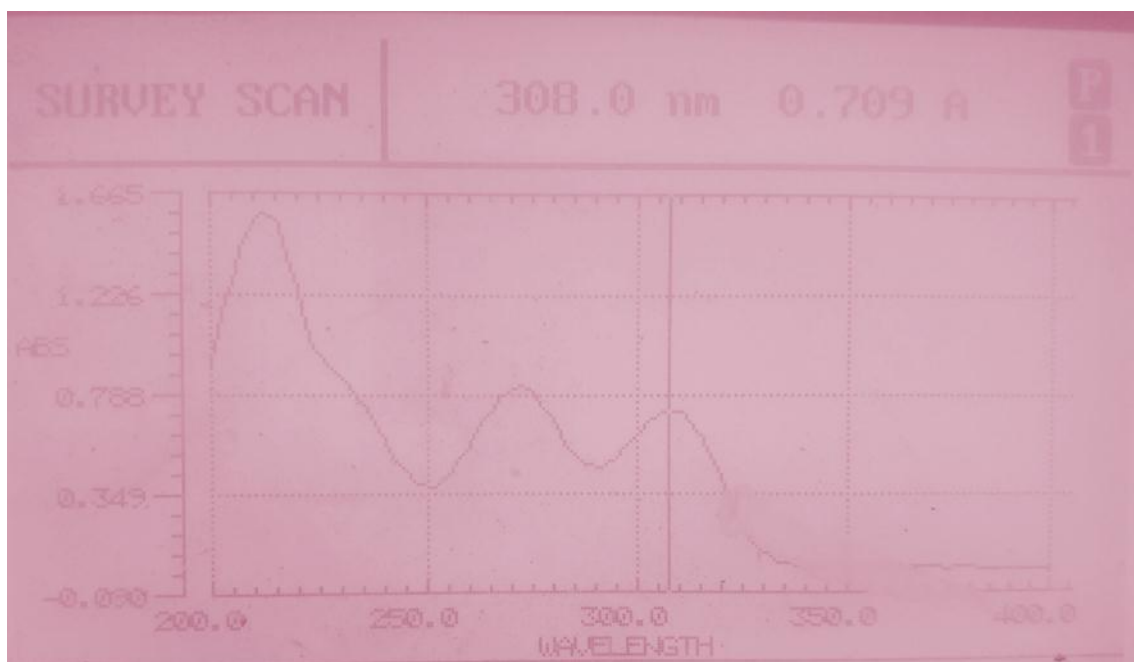


Figure 2: Absorption spectra of 20µg /ml of Metoclopramide hydrochloride.

Recommended procedure

From the absorption maxima, calibration curve was prepared in the concentration range of 2-25 µg/ml. The absorbance was measured at 310 nm against distilled water as a blank. The concentration of the sample solution can be determined by using the calibration curve.

Procedures for pharmaceutical preparations (Tablets)

To minimize a possible variation in the composition of the tablets(containing 5mg of Metoclopramide hydrochloride /tablet were provided from AL-Hokamaa company for pharmaceutical industries (HPI) Mosul-Iraq). The mixed content of 20 tablets were weighed and grounded, then the powder equivalent to 10 mg of Metoclopramide hydrochloride in about 70 ml of distilled water was stirred well for 30 min and then filtered through whatman No. 42 filter paper and the filtrate solution was diluted to 100ml by distilled water and different volume of this solution was treated as described above under general procedure. The drug content of the sample was calculated by using regression analysis.

Procedures for pharmaceutical preparations (Syrups and drops)

Take a volume of syrups or drops containing 10 mg of Metoclopramide hydrochloride in to 100 mL volumetric flasks and diluted with mobile phase to the volume, and the amount of Metoclopramide hydrochloride was calculated by using regression analysis.

Procedure for real water samples

To demonstrate the practical applicability of the proposed method, real water samples were analyzed by this method. Industrial waste water from AL-hokamaa company for pharmaceutical industries (HPI) Mosul-Iraq, were fortified with the concentrations in the range of 5,10,25 µg/ml of Metoclopramide hydrochloride. The fortified water samples were analyzed as described above for recommended procedure and the concentration was calculated by using the calibration curve of this method.

RESULTS AND DISCUSSION

UV- Visible spectrophotometry is still considered to be a convenient and low cost method for the estimation of pharmaceuticals.^[15-17] This method used for the estimation of metoclopramide. HCL in pharmaceutical preparations and environmental wastewater samples was found to be sensitive, simple, accurate, and reproducible.

Beer's law was obeyed in the concentration range of 2-25 µg/ml Figure 3 with correlation coefficient of 0.9986, intercept of 0.1313 and slope of 0.0353. The conditional molar absorptivity was found to be 1.25×10^4 l/mol.cm.

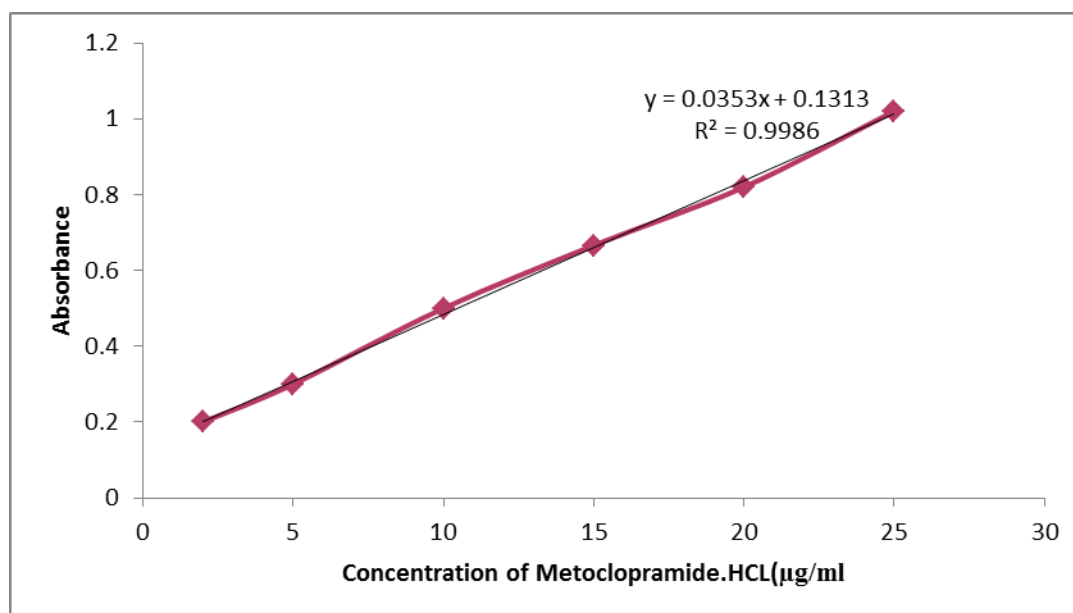


Figure 3: Calibration curve for metoclopramide. HCL potassium.

The accuracy and precision of the method, a pure drug solution was analyzed at three different concentrations, each estimation being repeated six times. The relative error(%) and relative standard deviation values are

summarized in (Table 1). From table 1 the values of standard deviation were satisfactory and the recovery studies were close to 100%. The RSD% value is 1.8% indicative of accuracy of the method.

Table I: Accuracy and precision of the proposed method.

(Metoclopramide. HCL taken(µg/ml)	Er (%) ^a	RSD (%)
5	1.0	1.4
10	0.91	1.8
25	0.88	1.8

a: Mean of six estimations.

Analytical application

The proposed method was successfully applied to the analysis of Metoclopramide hydrochloride in pharmaceutical formulation (tablets, syrups and drops) and spiked distilled water samples. The result of analysis for pharmaceutical formulation (Table. 2) which reveals

that there was close agreement between the results obtained by the proposed method and label claim, and the results of industrial waste water samples (table.3) show that the recovery values obtained were close to 100%.

Table 2: Assay of Metoclopramide. HCL in pharmaceutical formulations.

Pharmaceutical formulation supplied by HPI	Amount of Metoclopramide hydrochloride* Proposed method	Label claim	%Recovery
Tablet 5mg	4.98 mg	5 mg	99.6
Syrups 5mg/5ml	5.04 mg/5ml	5mg/5ml	100.8
Oral Drops 4mg/ml	4.03 mg/ml	4mg/ml	100.75

*Mean of ten determinations.

The results of industrial waste water samples Table 3. Show that the recovery values obtained were closed to 100%.

Table 3: Determination of metoclopramide .HCL in industrial wastewater samples.

Water sample	metoclopramide. HCL($\mu\text{g/ml}$)★ Taken Found		Recovery%
Industrial waste water	5	5	100
	15	15.1	100.6
	25	25.2	100.8

★ Mean of ten determinations.

The proposed method was compared with other reported UV spectrophotometric methods and found to be superior over other methods, (Table 4).

Table 4: Comparison of the existing UV spectrophotometric methods with the proposed method for metoclopramide. HCL.

Parameters	Method 1	Method 2	Method 3	. Method 4
Ref	18	19	20	Proposed
$\lambda\text{Max}(\text{nm})$	272	270	272	310
Solvents	0.1N HCL	0.1N HCL	Methanol	Distilled Water
Linear range $\mu\text{g/ml}$	2-20	5-30	0.4-2	2-25
RSD%	less than 2	1.75	Less than 2	Less than 1.8
Application	Tablets, Capsules,	Injections	Tablets	Tablets, Syrups, Oral drops, content uniformity testing, Industrial waste water

Application of the proposed method to content uniformity^[21-23]

Content uniformity or the Uniformity of dosage unit was defined as the degree of uniformity in the amount of active substance among dosage units. The risk assessment strategy underlying content uniformity testing is the assumption that some pre-specified limits exist where safety and efficacy outcomes may change if content uniformity fails. The proposed method proved to

be suitable for the content uniformity test, where a great number of assays on individual tablets are required. Data presented in table 4 indicate that the proposed method can accurately and precisely quantitative metoclopramide. HCL in its commercially available tablets. The mean percentage (with RSD) of the labeled claim found in ten tablets was 100.06(0.3132%) which fall within the content uniformity limits specified by the United State Pharmacopeia.^[22]

Table 5: Content uniformity testing of tablets using the Proposed method.

Parameter	% of the label claim
Tablet No.1	100.6
Tablet No.2	99.6
Tablet No.3	100.4
Tablet No.4	100.3
Tablet No.5	99.5
Tablet No.6	100.2
Tablet No.7	99.8
Tablet No.8	100.2
Tablet No.9	100.2
Tablet N0.10	99.8
Mean(X)	100.06
%RSD	0.3132
Max. allowed unit value ^[22]	$\pm 15\%$

CONCLUSION

The developed method is found to be high sensitive, accurate, simple, precise and economical, and can be used for routine quality control analysis of metoclopramide. HCL in pure form, pharmaceutical formulations, industrial waste water samples and application to content uniformity testing.

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