RESEARCH ARTICLE

Determination of Metochloropramide Hydrochloride by Spectrophotometric Method by using Diazotized p-nitro aniline reagent

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ABSTRACT

New simple, sensitive, accurate, and inexpensive spectrophotometric technique has been developed for the estimation of Metochloropramide hydrochloride [MCP-HCl] in pure and pharmaceutical preparation. This technique is based on the diazotization of a primary amino group of Metochloropramide hydrochloride [MCP-HCl] with $NaNo_2$ and HCl followed by coupling with p-nitro aniline in alkaline medium to obtain a stable red-colored water-soluble azo-dye, show a maximum absorption (λ_{max}) at 513. 50nm. Bear's low is obeyed in the concentration range of (0.2–25) $\mu g.ml^{-1}$ with molar absorptivity of $2.313\times10^3 L.mol^{-1}.cm^{-1}$and sandall's sensitivity 0.0145 $\mu g.mL^{-2}$. The limit of detection (LOD) and limit of quantitative were 0.182 $\mu g.mL^{-1}$and 0.553 $\mu g.mL^{-1,}$ respectively. The proposed technique successfully applied to (tablets, syrup, and injection).

Keywords: Determination, Diazotization reaction, Dosage forms, Metochlorobromide, Spectrophotometric.

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INTRODUCTION

Metoclopramide hydrochloride [MCP-HCL] ($C_{14}H_{22}CL_2N_3O_2$). and name chemical is 4-amino-5-chloro-N- [2-(diethylamino) ethyl]-2-methoxybenzamide hydrochloride and molecular weight of 336.3g.mol^{-1} .White-colored crystalline and melting point of 183°C.[1]

Metochlorobromide hydrochloride is employed as antiemetic in the therapy of nausea, vomiting and to extend gastrointestinally. The drug used to be used for the control of sickness due to radiation therapy and chemotherapy.[2] Also, it used to relative positive belly and esophagus problems such as diabetic gastroparesis and gastroesophageal reflux disorder.[3] Several techniques have been reported for the estimation of [MCP.HCL] in various. They include some spectrophotometric method,[4-13] HPLC,[14,15] fellow injection analysis,[16] and electrochemical,[17,18] Spectrofluorometric[19,20] solid-phase extraction 20. Aim of the present work is to suggest a simple and sensitive spectrophotometry procedure for with determination of (MCP. HCl) in pure dosage forms and pharmaceutical preparation.

EXPERIMENTAL

Apparatus

A PG instrument, UV-visible spectrophotometer model T80 (Shimadzu, Japan) with 1 cm matched quartz cells was used for the absorbance measurement. Sartorius BL 210S electronic balance was used for weighing the samples. Hot plate with a magnetic stirrer, Ijlassco, India.

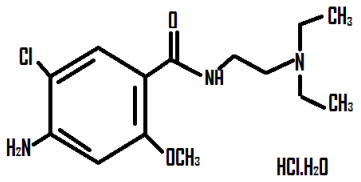
MATERIALS AND METHOD

The chemical used had been of analytical reagent grade BDH and pancreas.

Pharmaceutical grade Metochloropramide hydrochloride powder received in pure form (99.99%) was provided from the stabile company for drug industries and medical application samara- Iraq (SDI), India, and Emirate. All chemicals and reagents used were of analytical grade

Metoclopramide Hydrochloride stock solution [1000 $\mu g.ml^{-1}$]

The stock solution of (MCP. HCl) was prepared by dissolving accurate weighted 0.1000 g of pure drug in 10 mL of the



Scheme 1: The chemical structure of (MCP.HCL)

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distilled water and completed volume to the mark in volumetric flask 100ml with distilled water.

Metochloropramide Hydrochloride Working Solution [100 µg.ml^{-1}]

They are prepared by diluting 10mL of the stock to 100 mL solution in a volumetric flask with distilled water.

Diazotized p-nitroanline Reagent Solution, (DPNA), [0.02M]

p- Nitroanline (PNA) (0.5524) g was dissolved in 50ml distilled water, and 3.4mL 0f concentrated HCL was then added to this solution with stirring.

The mixture was heated to obtain a clear solution, transferred to 200 ml volumetric flask, and cooled to (0–5)°C in an ice –bath $NaNo_2$ (0.276) g was then added and the mixture was stirred vigorously. Five minutes later, the solution was made up to the mark with distilled water. The solution is kept in a brown bottle into a refrigerator and used after three hours of preparation. It is stable for at least 72 hours.

Sodium Hydroxide Solution (2.5M)

Prepared by dissolving (10.000) g of NaOH in 10 of distilled water and the volume was made up to the mark in 100 mL volumetric flask.

Solution for the analysis of Metochloropramide hydrochloride in pharmaceutical preparation

In Tablets

The content of 10 tablets was accurately weighed and grinded into a fine powder and mixed well. Then the average weight was calculated an amount of the powder equivalent to (0.1742) g and 0.1318 g (containing 0.01 g of the drug Metochloropramide hydrochloride in Premosan10mg and 10 mg, respectively was accurately weighed, dissolving in 5 mL of distilled water and stirred for 10 min to ensure complete dissolution of the drug, then transferred into100 mL volumetric flask and diluted to the mark with distilled water to get 1000 µg mL^{-1} of [MCP-HCl]. The solution was filtered by using Whatman filter paper No.4 1 to avoid any suspended or undissolved material before use.

Working solution (100 µg.ml^{-1}) was freshly prepared and analyzed by the recommended procedure

In syrup and Injection

Each 2 mL of syrup and injection of Premosan contains [5mg and 10 mg of (MCP-HCl)]. An accurately measured volume (2 mL)was transferred into a 100 mL volumetric flask, then added 10ml of distilled water, left to stand for 10mins and diluted to the mark with distilled water to get 20 µg.mL^{-1} (MCP-HCl) solutions. The solution was filtered by using Whatman filter paper No.4 1 to avoid any suspended or undissolved material before use.

The working solution (100 µg.ml^{-1}) was freshly prepared and analyzed by the recommended procedure.

General Recommended Procedure for Calibration

In a series of 10 mL volumetric flasks, 1 mL of 0.02 M of the diazotized p-nitro aniline solution, aliquots of working drug solution (100 µg.mL^{-1}) in the range (0.05, 0.1, 0.3, 0. 5….. 4.5) mL were added to each flask followed by using 1 mL of 2.5 M NaOH with shaking and allowed to stand for 5 minutes. The content material was diluted to the mark with distilled water and mixed well. After 5min, the absorbance of the red-colored azo-dye was measured at 513, 50 nm against the reagent blank prepared in the same manner without the analyte

RESULT AND DESICCATION

Absorption Spectra for Primary Test

The primary test for the present method involved diazotization p-nitro aniline, followed by coupling with Metochloropramide Hydrochloride. The test was done by adding 1mL of 0.01M diazotized p-nitro aniline 10 mL volumetric flask followed by the addition of 1 mL of (100µg .ml^{-1}) Metochloropramide hydrochloride with shaking. A 1 mL of 1 M NaOH was then added to the above mixture. The contents were diluted to the mark with distilled water. The absorbance and Λ_{max} of the red-colored azo-dye was once measured at 513, 50 nm against the reagent blank organized in the same manner without the analyte (Figure 1) shows that the maximum absorption was obtained at a wavelength 513.50 nm.

Optimization of Reaction Variables

The various parameters related to the color product formation have been studied by varying the parameters one at a time, controlling all other is fixed, and the optimum conditions have been selected.

Impact of the diazotized p-nitro aniline concentration

The optimum diazotized p-nitro aniline concentration was estimated by adding 1 mL of various concentrations [0.05-

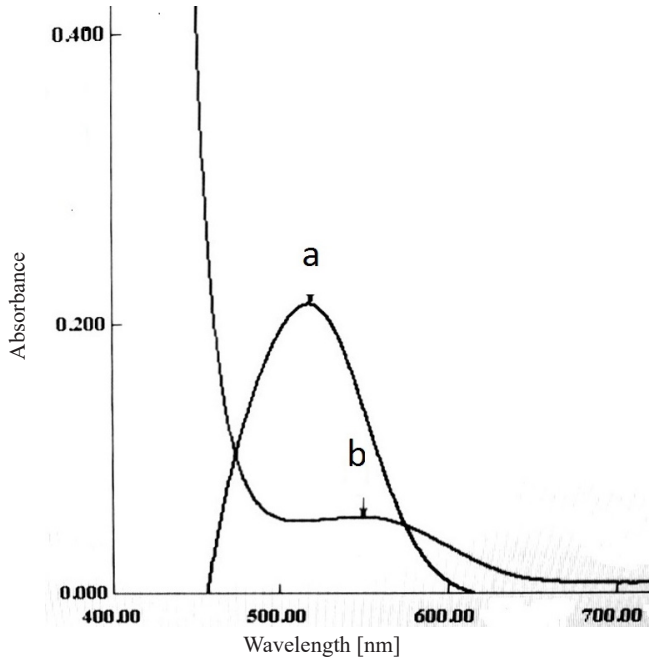


Figure 1: Absorption spectra of :(a) the complex of 10 µg.ml^{-1} (MCP.HCL) with diazotized p-nitro aniline against the reagent blank, (b) blank solution against to distilled water under the primary test conditions

0.03] M of diazotized p-nitro aniline reagent solution; the result showed that 0.02M, reagent solution is sufficient for the production of maximum and reproducible color intensity (Figure 2). Therefore the recommended concentration diazotized p- nitro aniline was chosen to be 1ml of 0.02M and used for all subsequent measurements.

Impact of Type Base

The impact of different alkaline solutions with a concentration of 1M on the absorption intensity of the colored azo dye formed was investigated. It was found that sodium hydroxide gave the most absorption intensity of the colored product, which is used for the subsequent work, Table 1.

Effect of Sodium Hydroxide Concentration

The stability of the formed azo-dye product depends upon the nature of the reaction medium.[17] The formed azo-dye was found to have responsible stability when the reaction medium was rendered alkaline by the addition of 1ml of 2.5 M sodium hydroxide solution which was optimum and recommended for the subsequent work, Figure 3.

Impact of Coupling Reaction Time (min)

The optimum time of coupling reaction time was determined by choosing different time periods [0-30] min for development

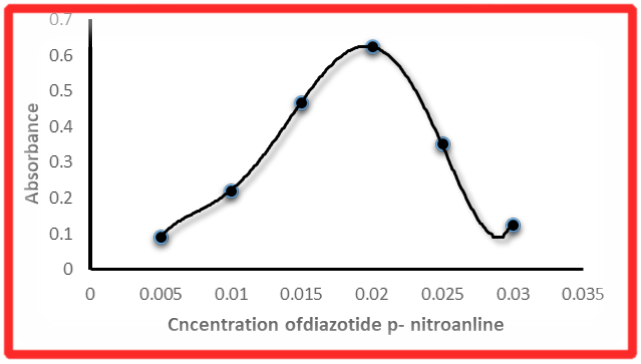


Figure 2: Effect of diazotized p-nitro aniline concentration on the coloration development in the estimation 10 µg.ml^{-1} (MCP. HCl)

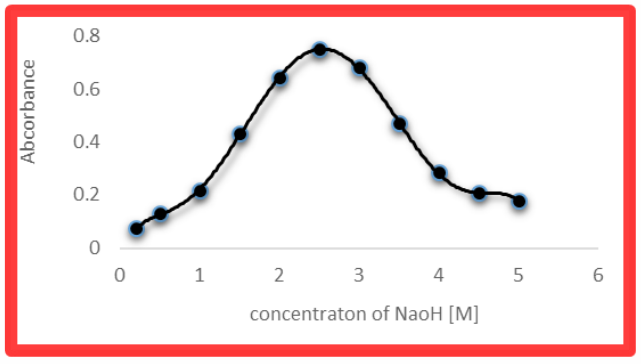


Figure 3: impact of sodium hydroxide concentration on the color development in the estimation 10 µg.ml^{-1} (MCP.HCL)

Table 1: Effect of different base

Alkaline medium [1M]	*Absorbance*
NaOH	0.217
KOH	0.187
Na_2CO_3	0.101
$NH+_4OH$	0.045

the collar of azo-dye at room temperature; it was found that 10 minutes' period was required for full. Color development as shown in Table 2

Impact of reagent mixing order 5

The effect of different orders of components addition on chromogen formation was investigated by changing the order of the addition of reactants three time as shown in Table 3. Results shows that mixing order number one was recommended and thus was followed in the subsequent experiments, since it resulted in obtaining maximum absorbance.

Stability

The impact of time on formed the azo- dye product was investigated by allowing the reaction to proceed by varying periods. It was found that the absorbance reaches to a maximum constant value after 35 minutes, and the color of the azo product was nearly stable for at least 60 min as shown as in Figure 4.

Final absorption spectra

When 10 µg.ml^{-1} (MCP.HCL) is treaded with diazotized p-nitro aniline reagent, below the aforementioned optimum conditions, an absorption peak optioned at 513. 50 nm the reagent blank showed almost nil absorption at the maximum wavelength ae shown in (Figure 5)

Calibration curve Procedure of analytical data

Employing the optimum experimental condition, the measured absorbance values at 513.50 nm Varus different standard concentration of (MCP-HCl) were plotted to construct a calibration curve. The linearity of the obtained plot of the

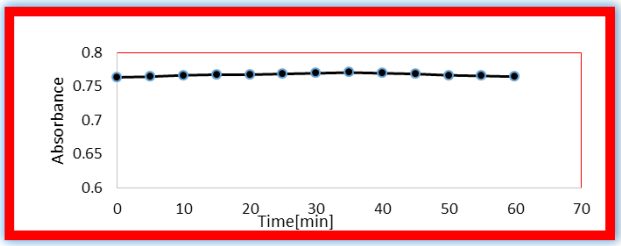


Figure 4: The stability of colored with reaction time

Table 2: Impact of coupling reaction time

Time (min)	*Absorbance*
0	0.744
2	0.755
5	0.761
10	0.771
15	0.752
20	0.741
25	0.681
30	0.666

Table 3: Variation of absorbance with a change of reactants addition order in the estimation of 10 µg.ml^{-1}(MCP-HCl)

Number	*Sequences*	*Absorbance*
1	Diazotized reagent+Drug+Base	0.771
2	Diazotized reagent+Base+Drug	0.568
3	Drug+Base+ Diazotized reagent	0.316

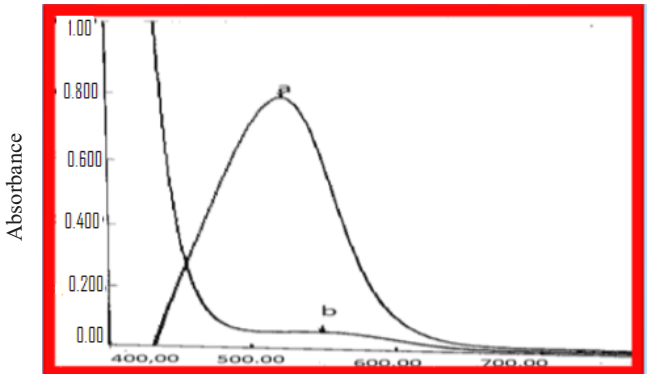


Figure 5: Absorption spectra (a) the complex of 10 µg.mL^{-1}) with diazotized p-nitro aniline versus reagent blank (b) blank solution against distilled water under the optimum conditions

(MCP. HCl) was the concentration range of (0.2-25.0) µg.mL^{-1}. As shown in Figure 6. The statistical treatment of the analytical data are summarized in Table 4.

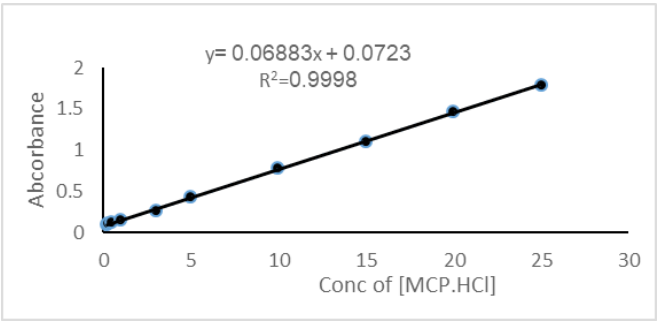


Figure 6: Calibration curve for the estimation of MCP-HCL under the optimum conditions.

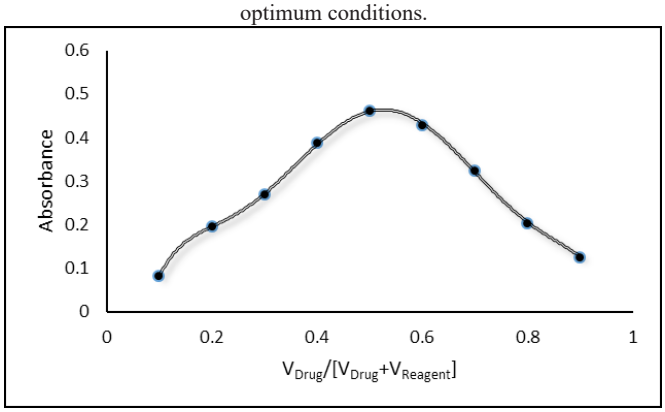


Figure 7: Continuous variation method for the reaction (MCP.HCL) with diazotized p-nitro aniline

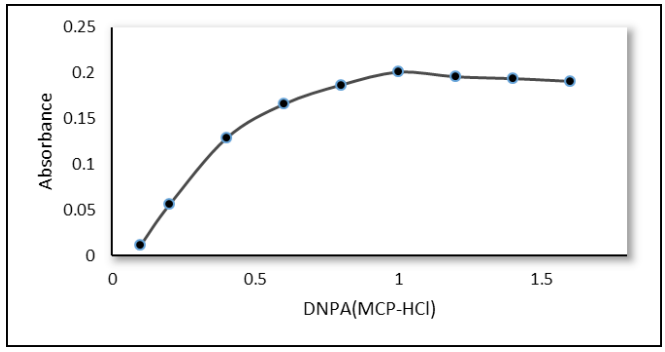


Figure 8: Molar ratio method for the reaction (MCP.HCL) with diazotized p-nitro aniline

Nature of Dye Product

Job's method[17] and molar ratio method[18] was used in the estimation of the reaction ratio of (MCP.HCL) with a p-nitro aniline reagent. The obtained results in (Figure 7 and 8) showed that 1:1 (MCP.HCL) to diazotized p-nitro aniline reagent ratio is obtained. Hence, the azo-dye may have the proposed mechanism illustrated in (Sheme 2).

Comparison of the Methods

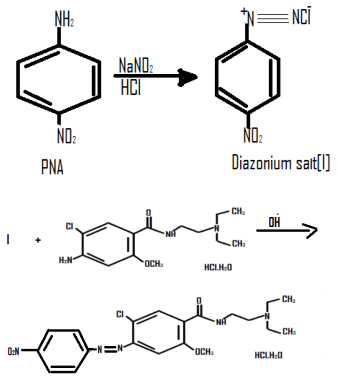
Table 5, shows a compression between some analytical variables of the present method with another spectrophotometric method in literature.

Accuracy and Precision

The accuracy and precision of the proposed method were tested by analyzing three replicate samples of (MCP-HCl) in three different concentration levels (within Beers law range). The result listed in Table 6 indicates an acceptable accuracy and precision of the method.

Interference Study

The effect of various excipients, which may be present in pharmaceutical products and influencing the reaction between [MCP.HCL] and reagent p-nitro aniline. The substance was present in a dosage that studied by adding different amounts of foreign substance to 10µg/mL of [MCP. HCl] as shown in Table 7 that studied foreign species did not interfere in the present method.



Scheme 2: Suggested reaction mechanism between DNPA and (MCP. HCl)

Table 4: Optical characteristics and statistical data for the determination of MCP-HCl

Parameter	*Value*
λ_{max} (nm)	513.50
color	red
Regression equation	Y = 0.0688 (MCP.HCL) + 0.0723
Linearity range (µg.ml^{-1})	0.2-25
Calibration sensitivity(µg.ml^{-1})	0.0688
Correlation coefficient(r)	0.9999
Correlation Linearity(R^2)	0.9998
Molar absorptivity (L.mol^{-1}.cm^{-1})	2.313×10^3
Shandell's sensitivity(µg.ml^{-2})	0.0145
L.O.D (µg.ml^{-1})	0.182
L.O.Q (µg.ml^{-1})	0.553

Table 5: Analytical parameters for the analysis of [MCP.HCL] by the proposed method comparing to method

Methods	*Linear Range (μg.ml^{-1})*	*(ε) L.mol^{-1}.cm^{-1}*	*Correlation coefficient (R)*	*C.V% range*	*Ref*
Propose method	0.2–25	$2.310*10^3$	0.9998	0.191–0.88	–
Spectrophotometric	0.1–10	$3.81*10^4$	0.9997	0.224–0.844	9
Spectrophotometric	10–50	–	o.9998	0.152–0.459	10
Spectrophotometric	5–30	$1.143*10^3$	0.999	0.869–1.17	11
Spectrophotometric	0.1–26	$4.124*10^4$	0.9994	≤0.44	12
Spectrophotometric	0.3–3.0	$2.25*10^5$	0.9995	0.029–1.50	13
Rp-HPLC	0.1–1000	–	0.9970	0.72–1.10	14
HPLC	48 –0.25	–	0.9988	0.19–1.44	15

Table 6: Evolution of the accuracy and precision of the proposed method for [MCP.HCL]

Concentration of [MCP.HCL] (μg.ml^{-1})			
Taken	*Found**	*Er%*	*C.V%*
5	5.053	-0.570	0.287
10	10.106	-0.482	0.363
20	20.126	-0.321	0.68

*Average of three measurement

Table 7: Recovery value for 10μg.ml^{-1} [MCP.HCL] in the presences of different excipients

Excipients		*Metochlorobromide. HCL Con.*		
Name	*Concentration (μg.ml^{-1})*	*Taken (μg.ml^{-1})*	*Found (μg.ml^{-1})*	*Recovery %*
Lactose	1000	10.000	10.036	100.630
Glucose			10.077	100.773
Sucrose			10.096	100.966
Starch			10.151	101.567

Average of three measurement

Table 8

	Concentration (μg.mg^{-1})*			
Sample	*Taken*	*Found**	*Recovery%*	*C.V%*
Parmosan tables (10mg)	5	5.024	100.48	0.577
		5.077	101.54	0.440
	10	10.159	101.54	0.2202
		10.111	101.11	0.286
	20	20.13	100.65	0.254
		20.125	100.628	0.191
Parmosan injection (10mg/2mL)	5	5.071	101.546	0.713
	10	10.121	101.21	0.443
	20	20.123	100.618	0168
Parmosan syrup (5mg)	5	5.033	100.66	0.88
	10	10.096	100.96	0.378
	20	20.121	101.21	0.302

Application in pharmaceutical

The application of the method for the assay of [MCP.HCL] in drugs has been applied successfully, and the results obtained were listed in (Table 8) for each sample in three replicates.

CONCLUSION

The proposed method rapid, simple, sensitive, and accurate determination of Metochloropramide hydrochloride. The method was found to be from interference by the excipients. The wide application of the new procedure for routine quality control was well established by the assay of [MCP-HCl] in pure and in pharmaceutical preparation

REFERENCE

1. Muhamed Y. Basheer, Ahmed. A Kashif , Abdalmajed Aljaliy, Musab M Ibrahim, Hind M Osman[1] Development and Validation of UV-Spectroscopic Method for Assay of Metochlorobromide hydrochloride in Bulk and Injectable DOSAGE form, American Journal of Research Communication, 2017, 5(3)22-33.
2. Hind A.W. AL-Azzaw, Faiz M. AL-Obadi and Theia'a N. Al Sabha[2] Spectrophotometric assay of Metochlorobromide hydrochloride in bulk and dosage form 1-British pharmacopoeia. 20 edition, The Stationary office, London2012 th
3. J. Ayman and K. Kasim, Spectrophotometric Method for the determination of Metochlorobromide hydrochloride in Bulk and pharmaceutical preparation Rafidaine J. Sci.2013, (5), 294-298

4. U. Deokate and G. Anjali, A Stability Indicating UV-Spectrophotometric Method for Assay of Metochlorobromide hydrochloride, INT. J. Pharm. Pharmaceut. Sci. 2014(6), 394-397
5. N. Dudhane, S Vidate, H, Borkar, T. Lohiya and J. Umekar, Simultaneous UV Spectrophotometric Estimation of Paracetamol and Metochlorobromide hydrochloride in sold Dosage form, J Pharmaceut. Sci.Res 2010(2)48-52
6. A. Lamya A. Salim, A Kasim, Spectrophotometric determination of Metochlorobromide hydrochloride in pharmaceutical Using Diazotization Reaction, Rafidaine J. Sci.,2011, (22), 76-88
7. D. Okrame, B. Kanakapure V. Kanakapure.R. Hosakere, determination of Metochlorobromide hydrochloride in pharmaceutical and Spiked Human Urine through Diazotization Reaction, J. food Drug analy.,2012. (20) 454-463
8. S. Raghad and S. Sadeem, Spectrophotometric determination of Metochlorobromide hydrochloride in Tablet Diazotization Coupling Reaction with phenol, Iraqi J. Sci., 2009(50) 136-134
9. S. Theia and H. Intesar Spectrophotometric determination of Metochlorobromide hydrochloride in Bulk and pharmaceutical preparation, Nat. J, Chem., 2006 (24) 561- 570
10. Abbas Noor Alshirif and Marowa H. Abbas, New Spectrophotometric Method for the determination of Metochlorobromide hydrochloride in pure and pharmaceutical on Coupling with Doxycycline Hyclate Int.J.Chem. Sci. 2015,13(3) 1093-1108
11. UADeokate, Anjali Macchinra Grode*Astablity indicating UV- Spectrophotometric for deamination Metochlorobromide hydrochloride, INT. Pharm. Pharmaceut. Sci. 2014 vol (6), issue 975-1491
12. Muhamed Y. Basheer[1], Ahmed. A Kashif[1], Abdalmajed Aljaliy[1], Musab M Ibrahim, Hind M Osman[1] Development and Validation of UV-Spectroscopic Method for Assay of Metochlorobromide hydrochloride in Bulk and Injectable DOSAGE form, American Journal of Research Communication, 2017, 5(3)22-33.
13. Hind A.W. AL-Azzawi[1,] Faiz M. AL- Obadi[1] and Theia'a N. Al Sabha[2] Spectrophotometric assay of Metochlorobromide hydrochloride in bulk and dosage form
14. Zuhair A-A. Khammas[*], Hawraa M. Abdul Kareem. Anew Visible Spectrophotometric Approach for Mutual determination of Metochlorobromide hydrochloride and Amoxicillin in pharmaceuticals After Could point Extraction., Science Journal of Analytical Chemistry 2016(4/5)66-77
15. Vamahikrishna. G[1*], Neelima.M[1], Bhaviani. M, Sreekanth.G[1 1], Shobha Rani. S[2]Asimple Rp –HPLC for Simultaneous Estimation of Paracetamol and Metochlorobromide hydrochloride in Tablet Dosage form, Isor Journal of Pharmacy and Biological Sciences 2014 (Nov-Dec.) ,69-78
16. Ahmed Khan[*1,] Jallat Khan[*2] Muhamed Irfan[3], Syed Barqir Shyum Naqvi[4] Gul Majid Khan[1]Muhammed Harris Shoaib[4], Rabia Ismail Yosaf[5]and Amjad Khan[6]Vlidation and application of high-performance liquid chromatography method for estimation of Metochlorobromide hydrochloride In plasma pak .J. pharm. Sci. 2017 Vol. 30, No,1 January (143-147)
17. Takahashi H, et al. Determination of Metochlorobromide hydrochloride and Glucuronide and sulphate Conjugates in Human Biological Fluids (plasma, Urine and Bile) by ion pair High Performance Liquid Chromatography., J, Chromatogr 1987, 419-243
18. N. Arfaj, Flow injection Chemiluminescent pharmaceutical Formulations and Biological Fluids using $[Ru(dipy)_3]^{+2}$-Permanganate System, Talanta. 2004, (62),255-263
19. Jop., p; Spectrochemical Methods of Analysis, Wiley, New York 1971;364
20. Chritian G.D.; Analytical Chemistry, fifth ed., Wiley, New York 1994;385-368