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Spectrophotometric Assay of Metoclopramide in Pharmaceutical Preparations

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Abstract

A simple and sensitive photometric method for the trace determination of metoclopramide has been worked out .The method is based on the diazotization reaction of the determination in acidic medium with the coupled α-naphthol,to form purplish violet water soluble azo dye that shows maximum absorption at 549nm with molar absorbtivity of $3.85x10^4$ $l.mol^{-1}.cm^{-1}$.Beer's law is obeyed over the concentration range 12.5-200µg of metoclopramide in final volume of 25ml,i.e.0.5-8ppm with the relative error of -0.2 - +1.3 and a relative standard deviation 0.68-2.17%.Morever,the method does not require either temperature

القياس بأستخدام المطياف الضوئي لمادة الميتوكلوبرامايد في التحضيرات الصيدلانية

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المستخلص

تم تطوير طريقه بسيطة وحساسة لتقدير كميات متناهية الصغر من الميتاكلوبرامايد بالاعتماد على مبدأ الازوته في المحيط الحمضي والاقتران مع كاشف الفا نفثول في المحيط القاعدي لتكوين صبغة الازو بلون بنفسجي تقا س عند طول موجي549 نانو متر وبامتصاصية مولا ريه $3.85x10^4$ لتر.مول$^{-1}$.سم$^{-1}$.إن التفاعل يتبع قانون بيير لمدى بين 0.5-8 ppm بخطأ نسبي يتراوح بين +1.3 - 0.2- وبانحراف قياسي نسبي 0.68-2.17%.تعد الطريقة المقترحة تطبيقية ا ذ أمكن تقدير الدواء في مستحضراته الصيدلانية باستخدام طريقة عمل واحدة دون الحاجة إلى تنظيم الدالة الحمضية و درجة الحرارة فضلا عن أنها لاتتضمن أي خطوات استخلاص .

Introduction

Various methods have been reported for the determination of metoclopramide. These methods include HPLC [1-3], flow injection [4], spectrophotometry[5,6], and many colorimetric methods[6-11]. Colorimetric methods based on diazotization seem to be the most popular methods [12, 13]. The objective of the investigation reported in this paper was to evaluate a spectrophotometric method for the determination of metoclopramide based on the same principle (diazotization) in the presence of α-naphthol as a coupling agent in acidic solution to form a highly colored product measured at 549nm.

Experimental

Reagents

All chemicals were of analytical reagent grad. Metoclopramide.HCl is obtained in a highly pure form and in pharmaceutical preparations from the state drug industry (SDI) Sammara-Iraq and ZAHRHVI pharm.com.Tabris-IRAN. Standard metoclopramide (1000μg ml^{-1}). Accurately weighs 0.1gm of the drug, dissolve in distilled water and dilute to 100ml in a volumetric flask with distilled water. Dilute standard solution (100μg ml^{-1}) was prepared by simple dilution of the appropriate volume of the standard drug solution (1000μg ml^{-1}) with distilled water.

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α -naphthol (0.5%)
0.5g in 100ml of absolute ethanol
Hydrochloric acid (1N)
Sodium Nitrite (1%)
sulphamic acid 3%
Sodium hydroxide (1N)

Apparatus

All spectral and absorbance measurements were performed on a Shimadzu UV-160A UV- visible double-beam recording computerized spectrophotometer and using matched 1cm glass cells. *Calibration graph:* To a series of 25 ml calibration flasks, transfer increasing volumes of metoclopramide working solution (100μg ml^{-1}) to cover the range 12.5-200 μg, 2ml of 1N HCl , 1ml of 1% $NaNO_2$, 1 ml of sulphamic acid (3%), 0.5 ml of (5%) α – naphthol, and 4ml 0f 1N NaOH are then added respectively ,the volume is completed to 25 ml volumetric flask with distilled water .The absorbance are measured against the corresponding blank at 549nm directly without any standing time and the samples stay stable for at least 1 hour .For the subsequent experiments, 1ml of 100 μg of metoclopramide is taken and the final volumes are 25 ml.

Result and Discussion

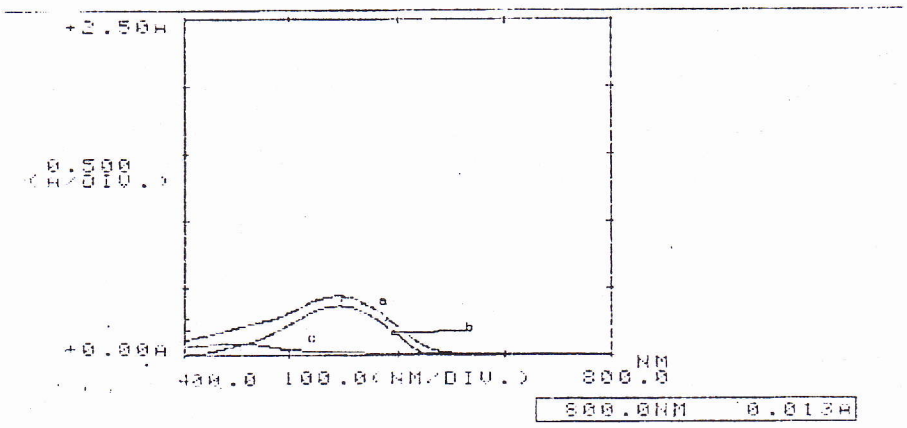
Study of the optimum reaction conditions: The effects of the various parameters on the absorption intensity of the azo dye are studied and the reaction conditions are optimized.

Choice of coupling agent: α –naphthol, m-aminophenol, and fluorogrycinol reagents have been examined for the photometric assay of metoclopramide. α –naphthol has been selected because it satisfies certain requirements [14] . ***Effect of acid:*** Different amounts (1-5ml of 1N) of different acids (HCl, H_2SO_4, H_3PO_4, HNO_2, CH_3COOH, and HCOOH) have been examined for their effect on the color intensity of the azo dye. A 2ml of 1N HCl give the best result. ***Effect of sodium nitrate and standing time:*** Effect of (0.5-2.5 ml of 1%) of sodium nitrite on the reaction intensity at different times (0-15 min.) has been studied , 1ml of sodium nitrate give the maximum color intensity with very slight changes in absorption at the selected range of the time, therefore, the measurements can be made directly after the addition competence. ***Effect of reagent amount:*** Different amounts (0.25-2.5ml of 5%) α –naphthol have been

added, 0.5ml of the reagent has been color intensity. ***Effect of sulphamic acid amount:***Between 0.2-2 ml of 3% sulphamic acid has been added and the color intensity of the azo dye has been followed, 1ml of the acid gives the maximum absorption intensity. ***Effect of the base amount:***Different amounts (1-5ml of 1N) NaOH have been investigated, 4ml give the best result.

Absorption spectra

selected which gives the maximum When a dilute solution of α –naphthol in the presence of sodium, under the above established conditions, is mixed with diazotized metoclopramide, a purplish-violet colored azo dye forms. This shows maximum absorption at 549 nm, in contrast to colorless reagent blank which shows no absorption at the wavelength of the maximum absorption .Fig.1 shows the absorption spectra of the azo dye and the corresponding reagent blank. 549nm has been adopted for the subsequent work



Absorption spectra
a: sample against distilled water b: sample against blank c: blank against distilled water

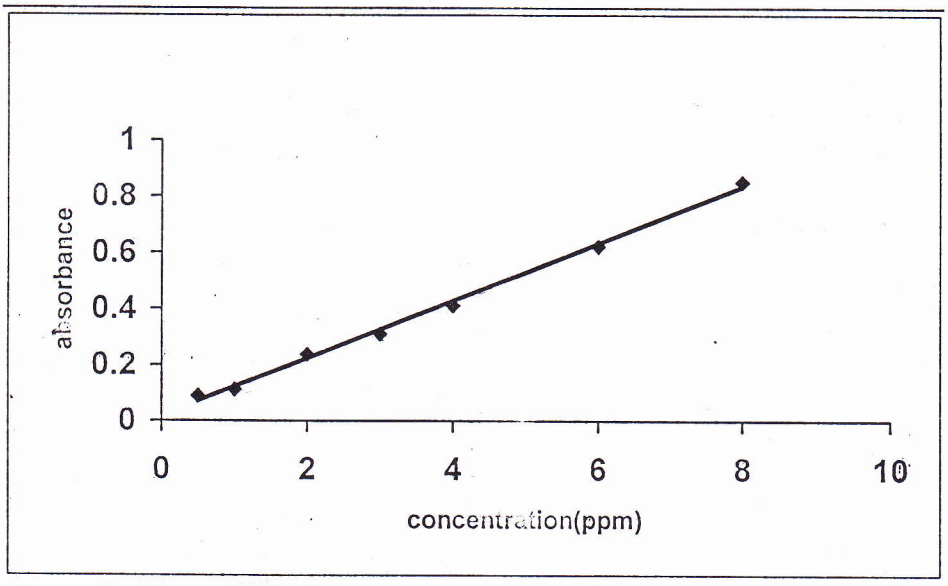


Fig.(2): Calibration graph

Table (1):The statistical treatment of the calibration results, molar absorbtivity and detection limit of metoclopramide

Linear range (µg/ml)	Molar absorbtivity $l.mol^{-1}.cm.^{-1}$	Detection limit (µg/ml)	Slope	Intercept	Correlation coefficient
0.5-8	3.85×10^4	0.2	0.1021	0.0203	0.9969

Accuracy and Precision of the method

To check the accuracy and precision of the method, Metoclopramide has been determined at three concentrations. The results are shown in table2 and indicate that the method is satisfactory

Table (2):Accuracy and Precision of the method

Amount of Metoclopramide taken(µg)	Relative error* (%)	Relative standard deviation* (%)
2	+1.3	+2.17
4	+0.8	+1.16
6	-0.2	+0.68

*average of five measurements

Application of the method

The proposed method is used for the determination of metoclopramide in three different dosage forms.***Drops (4mg/1ml):***2.5 ml of the drop has been taken and diluted to 100 ml in a volumetric flask with distilled water to produce 100 ppm of the drug solution.***Syrup (5mg/5ml):***10 ml of the syrup has been taken and diluted to100 ml with distilled water to produce 100 ppm of the drug.***Injection (5mg/2ml):***2ml of the injection has been taken and diluted to 50ml with distilled water form100 ppm of drug solution. (2, 4, and 6 ppm) of each of these solutions have been taken for color formation as directed under calibration procedure.Table.3

Table(3):Applications of the method

Dosage form	µg. taken	µg found	Error* %	Recovery* %
Drops	2	2.01	+0.8	100.8
	4	3.98	-0.5	99.5
	6	6.13	+2.3	102.3
Syrup	2	1.88	-6.0	94.0
	4	3.81	-4.6	95.4
	6	6.07	+1.3	101.3
Injection	2	2.03	+1.7	101.7
	4	4.02	+0.7	100.7
	6	5.97	-0.5	99.5

*Average of three determinations.

Conclusion

A simple and sensitive spectrophotometric method for the determination of trace amounts of metoclopramide in aqueous solution has been developed, based on the diazotization reaction. The proposed method requires neither temperature, nor solvent extraction and can satisfactory be applied without modification to the deferent dosage forms of the drug.

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