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Research Article

DEVELOPMENT OF ANALYTICAL METHOD FOR METOCLOPROMIDE USING UV-SPECTROPHOTOMETRY

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ABSTRACT

A simple, sensitive, specific, spectrophotometric method has been developed for the detection of metoclopromide in pure form and pharmaceutical dosage forms. The optimum condition for the analysis of the drug metoclopromide was established. Metoclopromide exhibiting absorption both at 272 nm and obeyed beers law in the concentration range from 0.4 to 2.0 µg/ml. The lower limit of detection was found to be 0.06 µg/ml and the limit of quantification was found to be 0.22 µg/ml. The regression equation was found to be y = 0.427x – 0.021 with the regression coefficient of 0.999. The precision of the method was found to be 10.696 ± 0.059 mg against the label claim of 10 mg. The percentage recovery was found to be 100.638 ± 0.829. The sample solution was stable more than 24 hours. The assay results were found to be in good agreement against the label claim. The proposed method was simple sensitive, precise, accurate and easy for routine quality control analysis.

Keywords: Spectrophotometry,Metoclopromide, Estimation.

INTRODUCTION

Metoclopramide hydrochloride is a white or almost white, crystalline power which is very soluble in water. Its chemical name 4-amino-5-chloro-N-(2-(diethylamino)ethyl)-2-methoxybenzamide hydrochloride. The structure of the compound is shown as figure 1. It is used as dopamine receptor antiemetic and antagonist[1, 2]. It is also used in the prevention of cancer chemotherapy induced emesis. There are many pharmaceutical preparations available for metoclopromide hydrochloride from different manufacturing due to its wide application in both experimental and clinical medicine[3]. Hence it is needed that an accurate and simple method for its quantitative determination. The British Pharmacopoeia[1] recommended a non aqueous acid-base titration with potentiometric detection of the end-point for the evaluation of the raw material. As for formulation of tablet and injection recommended a chromatographic method, while for oral solution recommended a spectrophotometric method based on azo-coupling reaction with N-(1-naphthyl)ethylenediaminedihydrochloride.

Various analytical method includes colorimetry[4], UV spectrophotometry[5-9], spectrofluorimetric[10,11], liquid chromatography[12-15], electrochemical[16-19] and flow injection analysis[20-23]. The aim of present work was to develop a simple, sensitive, and selective spectrophotometric method using material on solvent for the determination of metoclopromide hydrochloride in bulk as well as pharmaceutical formulation.

MATERIALS AND METHODS

Experimental

Instrumentation

For the development process we used UV-visible spectrophotometer (Systronics2202), spectrofluorimeter(PerkinElmer LS55), sonicator(Branson 2510) andelectronic balance (Mettler Toledo).

Chemicals and Reagents

Pure metoclopromide has been obtained as gift sample from madras health centre and was used as such for further analysis. Formulations were purchased from the local pharmacies and used for analysis.Methanol (HPLC grade) and water (double distilled water) and all other chemicals used in the analysis were AR grade.

Procedure

Preparation of stock solution

100mg of pure drug metoclopromidewas weighed and transferred to a 100ml volumetric flask.50ml of methanol was added to the above flask, mixed well to ensure the complete solubility and the volume was made up with methanol.

Preparation of sample solution

The average weight of the tablets was determined by weighing 20 tablets and these were powdered. Tablet powder equivalent to 25 mg of metoclopromide was weighed and transferred to a 100 ml volumetric flask. About 10 ml of methanol was added and sonicated for 15min for complete dissolution of drug.The volume was made up with methanol and filtered through whatmanfilterpaper. Dilutions were made with methanol to attain a concentration of 1.2µg/ml. Six replicate analysis were carried out with sample weighed individually and the average weight of tablet was found to be 0.143 g.

Method validation

The developed method is to determine the metoclopromidein pure form and in tablet dosage form was validated asper ICH guidelines.

Linearity

The method was validated according to ICH Q2B guidelines, for the validation of analyticalprocedures in order to determine the linearity, sensitivity, precision and accuracy of the analyte[24-27]. For metoclopromide, five point calibration curve was generated with the appropriate volumes ofthe working standard solutions for the method. The linearity was evaluated by the least-squareregression method using uncorrected data.

Precision

Precision is the degree of repeatability of an analytical method under normal operational conditions. The precision of the assay was determined by repeatability(intra-day) and intermediate precision (inter-day) and reported as SD % for a statisticallysignificant number of replicate measurements [27]. The intermediate precision was studied bycomparing the assays on three different days and the results are documented as the standarddeviation and SD %.

Recovery study

Accuracy is the percent of analyte recovered by assay from a known added amount of drug. Data from nine determinations over three concentration levels covering the specified range were obtained. The accuracy was determined with standard quality control samples prepared in triplicate at three different concentration levels (80%, 100% and 120%) covering the entire linearity range with the pre-estimated formulation by standard addition method.

LOD and LOQ

The limit of detection (LOD) is defined as the lowest concentration of an analyte that ananalytical process can reliably differentiate from back-ground levels. The limit of quantification (LOQ) is defined as the lowest concentration of the standard curve that can be measured with an acceptable accuracy, precision and variability.In this study, LOD andLOQ were determined based on the standard deviation of the response and the slope of the correspondingcurve using the following equations.

$$\mathbf{LOD = 3.3\ s/m;\ LOQ = 10\ s/m.}$$

Where S, the noise of estimate, is the standard deviation of the absorbance of the sample and m isthe slope of the related calibrations graphs[27].

Stability

The stability of metoclopromide in methanol solution was studied by the UV spectrophotometric method. Sample solutions wereprepared in triplicate, stored at 25°C and analysed at 30, 60,90,120min and 24 hrs.

RESULTS AND DISCUSSION

The development of a simple, rapid, sensitive and accurate analytical method for the routine quantitative determination of samples will reduce unnecessary tedious sample preparations, the cost of materials and labour. Metoclopromideis a UV-absorbing molecule with specific chromophores inthe structure that absorb at a particular wavelength and this fact was successfully employed fortheir quantitative determinations using the UV spectrophotometric method. It was found that three absorption maximum (λ_{max}) was

observed at 213, 272 and 307. Since at 272 nm the absorbance of the compound is high, this wavelength was used for the determination of the metoclopromide, because at this wavelength the concentration requirement is low.The absorption spectrum of metoclopromidein methanol is shown in figure 2.

Calibration curve data were constructed in the range of the expected concentrations of 0.4 μg/ml to 2.0μg/ml. Beer's law was obeyed over this concentration range. The regression equation was found to be y = 0.427x – 0.021. The correlation coefficient (r^2)of the standard curve was found to be greater than0.999.The stock solutions and workingstandards were made in methanol. The (λ_{max})of the drug for the analysis was determined bytaking scan of the drug sample solution in the entire UV region. Calibrated data waspresented in table1and figure 3.

A replicate analysis of the standard solution was used to assess the precision andreproducibility of the proposed methods. The selected concentration within the calibration rangewas prepared in methanol and analyzed. With the relevant calibration curves to determine theintra and inter-day variability were determined. The intra and inter-day precision were determined by using SD %. The precision, accuracy and reproducibility of the results are givenin table 2, which demonstrate a good precision, accuracy and reproducibility.

The proposed methods can be successfully applied for metoclopromide assay in tablet dosage forms withoutany interference. The assay showed the drug content of this product is to be in accordance with the label claim of 10mg. The obtained result presented in the table 2 demonstrates the validityand accuracy of the proposed method for the determination of all drugs in pharmaceutical dosageforms. These results reveal that the developed method have an adequate precision, accuracyand consistency. Consequently, it can be applied to the determination of metoclopromide in pure form andpharmaceuticals without any interference from the excipients.The values of LOD and LOQ were determined by the statistical method and presented in table2**.** The stability of the drug solutions which was taken from the linearity study was used for thestability studies and found that it is stable up to 24 hrs.

CONCLUSION

The developed spectrophotometric method was simple, sensitive, and specific, for the detection of metoclopromide in pure form and pharmaceutical dosage form. It could be precisely quantify and LOD was found to be 0.06 μg/ml and the limit of quantification to be 0.22μg/ml. The entirecalibration curve shows the linear relationship with the absorbance and concentration and coefficientcorrelation was higher than 0.999. Precision of the method was found to be10.696 ± 0.059 against the label claim of 10 mg. The percentage recovery was found to100.638 ± 0.829. The sample solution was stable up to 24 hrs.The proposed method will be suitable for the analysis of metoclopromide in pure and pharmaceutical dosageform.

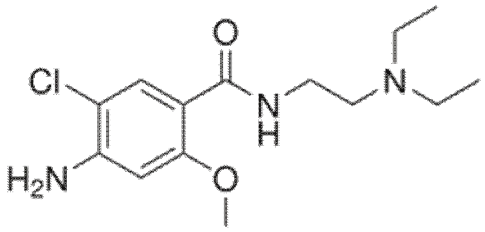

Fig. 1: Structure of metoclopromide

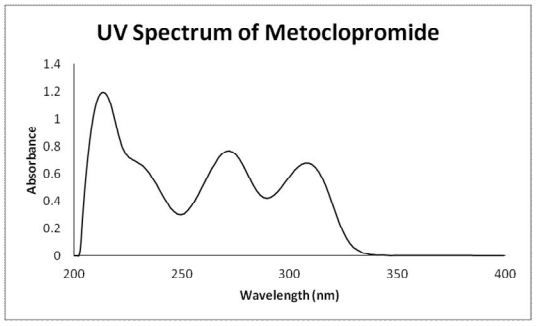

Fig. 2: Absorption spectrum for metoclopramide

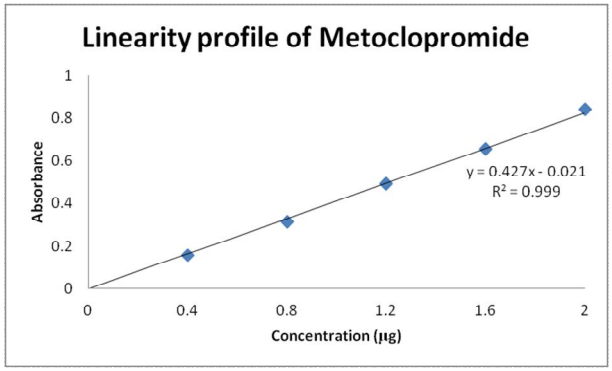

Fig. 3: Linearity for metoclopromide

Table 1: Linearity data for metoclopromide

Concentration (µg/ml)	Absorbance
0.4	0.157
0.8	0.313
1.2	0.491
1.6	0.658
2.0	0.839

Table 2: Validation parameters

Parameters	Values
Linearity range (µg/ml)	80-480 (µg/ml)
Precision (%)	100.696 ± 0.059
Accuracy (%)	100.638 ± 0.829
80 (%)	100.546 ± 1.085
100 (%)	101.083 ± 0.724
120 (%)	104.473 ± 7.968
LOD (µg/ml)	0.06 µg/ml
OQ (µg/ml)	0.22 µg/ml

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