ISSN: 2320 - 4230

Journal of Drug Discovery and Therapeutics

Available Online at www.jddt.in

CODEN: - JDDTBP (Source: - American Chemical Society)

Volume 3, Issue 35, December: 2015, 01-04

Research Article

NEW SPECTROPHOTOMETRIC DETERMINATION OFMETOCLOPRAMIDE IN BULK AND PHARMACEUTICAL DOSAGE FORM

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Received 01 Dec 2015; Accepted 18 Dec 2015

ABSTRACT

The new, selective and sensitive visible spectrophotometric method have been developed for the estimation of Metoclopramide in bulk and in pharmaceutical preparations. The amino group in Metoclopramide is diazotized with sodiumnitrite and hydrochloric acid at 0^0C temperature. After diazotization, the diazonium salt is coupled with resorcinol. The orange coloured chromogen formed in the method is stable for more than 24 hours. The orange colouredchromogen is used to determine the Metoclopramide spectrophotometrically.

KEYWORDS: Spectrophotometric determination, Metoclopramide, Resorcinol and diazotization.

INTRODUCTION:

Metoclopramide chemically, 4-amino-5-chloro-N-(2-diethylaminoethyl) -2-methoxy benzamide. Metoclopramide is used as an antiemetic agent. Metoclopramide blocks central and peripheral dopamine receptors. The latter activity results in stimulation of plain muscle in the stomach and upper GI tract.

The results in rapid gastric emptying and faster intestinal transit. Lower oesophageal sphincter pressure is increased and this prevents oesophageal reflux. Central dopamine inhibition abolishes nausea and vomiting. Prolactin levels are increased and extrapyramidal side effects may be seen. It is used as antiemetic agent. It is soluble in ether, methanol and Benzene. The structure of metoclopramide is as follows .

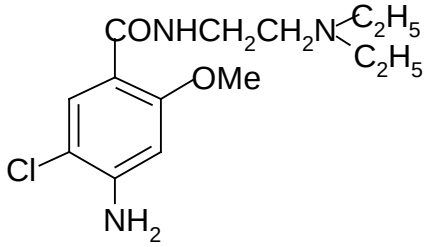

Figure 1: Metoclopramide

Uses: Metoclopramide is used as an antiemetic agent.

Adverse effects: Nausea, vomiting due to various causes except in motion, sickness delayed gastric emptying diabetic gastro paresis. Constipation or diarrhea, drowsiness, extra pyramidal reactions, Hypertensive crisis in patients with pheochromocyltoma, parkinsonism.

Various spectrophotometric methods are available in the literature for estimation of drugs by diazotisation and coupling reaction. The reagents such as acetylacetone[4], benzoyl acetone[5]dibenzyl methane[7], 1-naphthyl ethylene diamine[14] 1:1 ammonia: water solution[11], 2-napthol[40], 3-amino phenol[47], etc., are used for the estimation of drugs by diazotisation method. But all have certain limitations. In these methods more steps are involved, heating is necessary; the colour development is not instant and not reproducible values. The recently proposed method using 1:1 ammonia: water solution is less sensitive, time consuming and involves several steps.

No method is reported in the literature for estimation of the selected drugs by using resorcinol as the coupling reagent. Hence, it is proposed to use resorcinol as coupling reagent for the estimation of the selected drugs by spectrophotometry. The method is simple, rapid, reproducible, precise, and needs no extraction or heating, colour development is instantaneous, and the colour is stable for more than 24 hours. Further, the controlling of experimental conditions is minimum.

The proposed general procedure: The drug containing amino group is treated with cold solution of sodium nitrite in acidic medium at 0-5^{o}C temperature. The resultant solution is allowed to stand for five minutes for the diazotisation to complete. Then the drug is treated with resorcinol to produce coloured species. The

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absorbance of the coloured species is measured at the wavelength of maximum absorbance for each drug against the reagent blank (prepared in a similar manner devoid of drug solution) and the amount of drug is determined from the calibration curve made between the absorbance and the amount of drug.

EXPERIMENT: Spectrum of diazotised Metoclopramide treated with resorcinol:

The wavelength of maximum absorbance of the diazotised drug treated with resorcinol solution is ascertained by the following procedure.

1.0 ml of metoclopramide solution (100 µg/ml) is transferred into a 10 ml volumetric flask. To this, 2.0 ml of 0.1N hydrochloric acid and 1.0 ml of cold 0.1N sodium nitrite solution are added. The resultant solution is well mixed, and then allowed to stand for five minutes at 0-5^{o}C temperature for diazotisation. To this solution 1 ml of 1% urea solution is added and shaken frequently for nitrogen gas to escape. Then 1.0 ml of 0.5N sodium carbonate and 1ml of 1% resorcinol solution are added and the volume is made to 10 ml with methanol. The absorbance of the orange colour formed is measured in the wavelength range of 380 to 550 nm, against the reagent blank. The spectrum is given below.

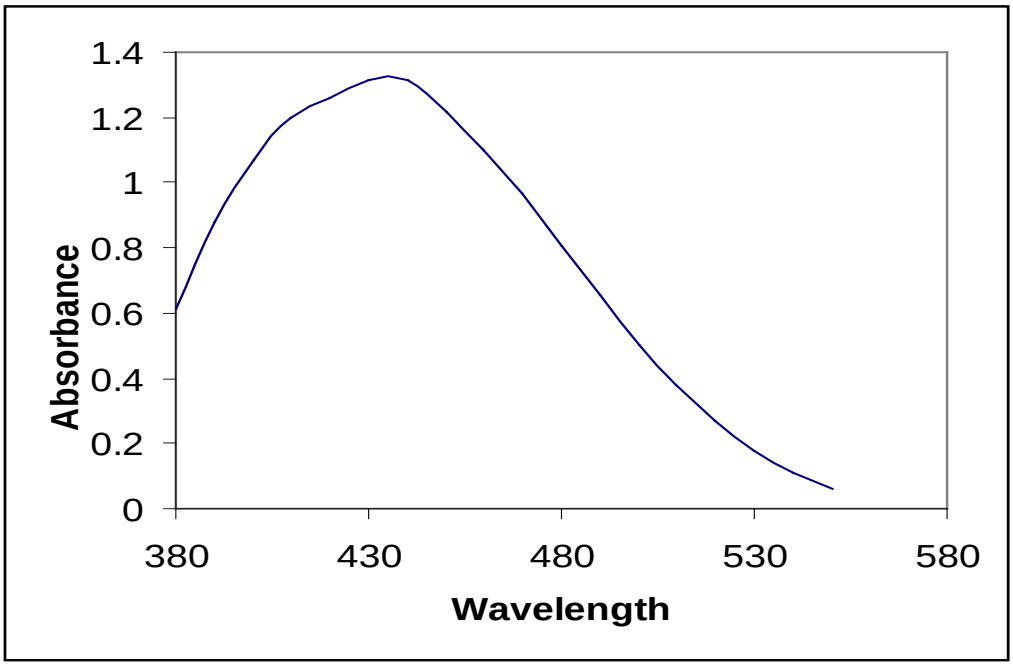

Figure 2: Spectrum of diazotisedmetoclopramide treated with resorcinol

From the above spectrum, it is clear that the diazotised drug treated with resorcinol solution has maximum absorbance at 440 nm. Hence, all further studies are made at 440 nm.

The optimal conditions for the determination of metoclopramide are arrived to by the following steps.

Assay procedure: Variousaliquots of the standard metoclopramide solution ranging from 0.2-1.0 ml are transferred into a series of 10 ml volumetric flasks. To each flask, 2.0 ml of 0.1N hydrochloric acid solution and 1.0 ml of cold 0.1N sodium nitrite solution are added. The resultant solution in each flask is well shaken and allowed to stand for five minutes at 0-5^{0}C temperature for diazotisation to complete. 1.0 ml of 1% urea solution is added to each flask and the solution is shaken frequently to allow nitrogen gas to escape. Then 1.0 ml of 0.5N sodium carbonate solution and 1.0 ml of 1% resorcinol solution are added and the volume in each flask is made upto 10 ml with methanol. A orange colour is formed. The maximum absorbance of the orange colour solution is measured at 440 nm against the reagent blank. Calibration graph is obtained by plotting absorbance values against the concentration of metoclopramide solution. The calibration curve is found to be linear over a concentration range of 20 to 100 µg/ml of metoclopramide. The amount of metoclopramide present in the sample is estimated from the calibration graph. The results are presented in the following graph.

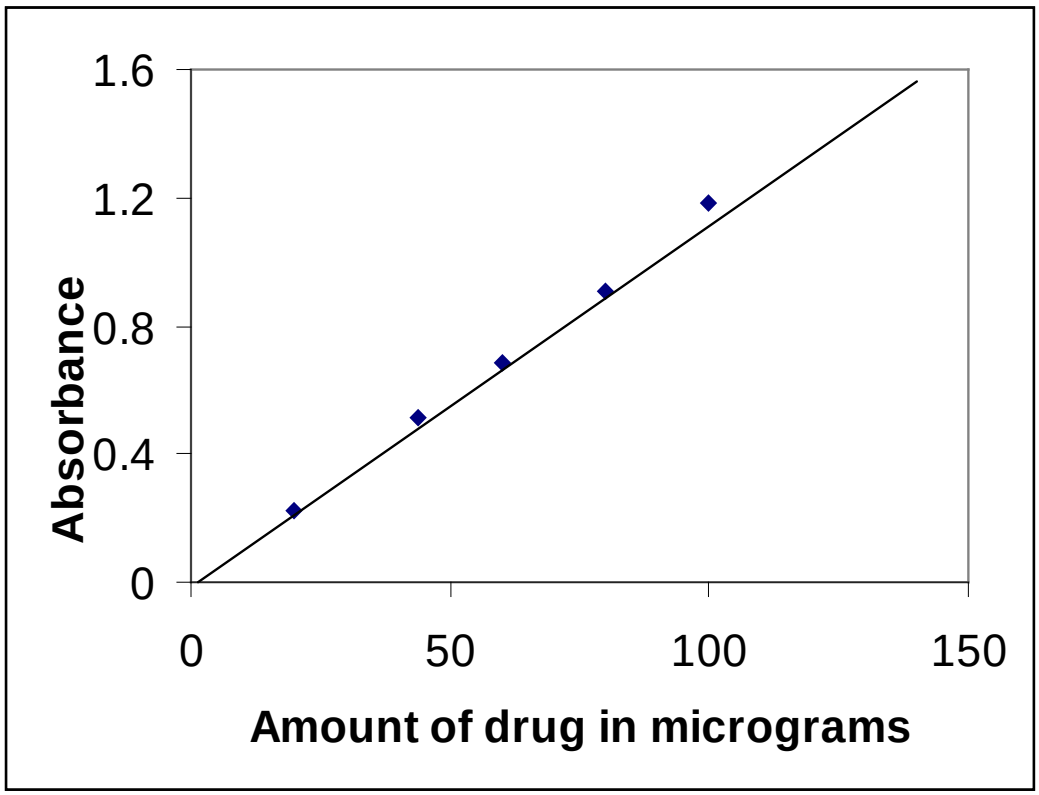

Figure 3: Calibration curve of metoclopramide

Assay of metoclopramide in pharmaceutical formulations:

The proposed procedure for the assay of metoclopramide is applied for its determination in commercial tablets.

Preparation of the sample solution:

Powdered tablet equivalent to 50 mg of the drug is weighed accurately and transferred into a 50 ml beaker and mixed well with 30 ml of methanol. The solution is filtered and transferred into a 50 ml volumetric flask and the volume is made up to 50 ml with methanol. The concentration of the drug solutions is now 1mg/ml. This stock solution is further diluted to obtain the working concentration of 100 μg/ml.

The pharmaceutical preparation as prepared above is analysed by the following procedure.

(H) Assay Procedure: Known volumes of the drug formulation prepare as above are transferred into a series of 10 ml volumetric flasks and 2.0 ml of 0.1N hydrochloric acid solution, 1.0 ml of 0.1N sodium nitrite solution are added. The resultant solution in each flask is shaken well and allowed to stand for five minutes at 0-5^{0}C temperature for diazotisation. Then 1.0 ml of 1% urea solution, 1 ml of 0.5N sodium carbonate and 1.0 ml of 1% resorcinol solution is added. The absorbance of the resultant solution is measured at 440 nm. The amount of metoclopramide in the pharmaceutical formulation is evaluated from the predetermined calibration plot. The results are present in the following table.

Table 1: Assay of metoclopramide in pharmaceutical formulations

Sample	Labelledamount (mg)	Amount Found ±S.D	Percentage of Label claim	t_{cal}
Tablet 1	10	9.96 ±0.23	99.6	0.3887
Tablet 2	10	10.08 ±0.34	100.8	0.5124
Tablet 3	10	10.02±0.28	100.2	0.1562
Tablet 4	10	9.98±0.39	99.80	0.1129

Results and discussion:

Metoclopramide undergoes diazotisation when treated with sodium nitrite and hydrochloric acid. The excess nitrous acid during the diazotisation is removed by the addition of urea solution. The solution was shaken frequently to allow the nitrogen gas to escape. The diazonium cation reacts with the coupling reagent, resorcinol by electrophilic substitution at the o-position of the coupling agent to producedaorangeazo product. This wine red product shows maximum absorbance at 440 nm. The colour of the product is stable for more than 24 hours. The calibration curve (concentration vs absorbance) is linear over the range of 20-100 µg/ml of metoclopramide. The standard deviation values are low indicateshigh accuracy and reproducibility of the method. The 't' calculated values are compares well with the theoretical value of 2.78 there by indicating that the precision of the method is good. There no effect of additives and excipients such starch, calcium lactose and glucose in the concentrations those present in general pharmaceutical preparations.

The proposed method is found to be simple, precise, accurate and time saving, reproducible and can be conveniently adopted for routine analysis of estimation of metoclopramide in bulk drugs samples and pharmaceutical formulations.

CONCLUSION:

The proposed method is found to be simple, precise, accurate and time saving, reproducible and can be conveniently adopted for routine analysis of estimation of Metoclopramide in bulk drugs samples and pharmaceutical formulations.

Acknowledgements:

The author is thankful to U.G.C.S.E.R.O., Hyderabad for financial Assistance for the sanction of M.R.P. (No.F-4689/14 SERO/UGC) .

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