# Visible Spectrophotometric Methods for the Estimation of Metoclopramide Hydrochloride in Tablets

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Two simple, sensitive, accurate, and rapid visible spectrophotometric methods have been developed for the estimation of metoclopramide hydrochloride in tablets. Method A is based on the reaction of drug with 4-dimethyl amino-benzaldehyde (Ehrlich reagent) to yield a yellow colour Schiff's base, which shows maximum absorbance at 438 nm against reagent blank, while method B is based on diazotisation of primary amine group of metoclopramide hydrochloride with sodium nitrite and hydrochloric acid followed by coupling with ß-napthol (in alkaline medium) to form a red colour dye, which shows maximum absorbance at 553 nm against reagent blank. Beer's law was obeyed in the concentration range of 10-100 µg/ml in method A and 1-10 µg/ml in method B. Results of the analysis were validated statistically and by recovery studies.

Metoclopramide hydrochloride has got central antidopaminergic effect and is used mainly as antiemetic and antinauseant. Chemically, metoclopramide is 4-amino-5-chloro-N-[(2-diethylamino) ethyl]-2-methoxy benzamide.[1] Literature survey reveals the estimation of metoclopramide hydrochloride in pharmaceutical formulations by various HPLC[2-7] and spectrophotometric[8-10] methods. The present work describes two new, simple visible spectrophotometric methods involving metoclopramide hydrochloride with reagents such as 4-dimethyl amino-benzaldehyde (Ehrlich reagent) in method A, while sodium nitrite, concentrated hydrochloric acid, and β-napthol (in alkaline medium) in method B.

Recovery experiments were performed by adding known amount of drug to the preanalyzed formulation and reanalyzing the mixture by proposed method. Results were validated statistically and the % recovery was found in the range of 98.7 to 100.2. The proposed methods are new, simple, sensitive, accurate, and precise and can be successfully employed in the routine analysis of metoclopramide hydrochloride in pharmaceutical dosage forms.

A Shimadzu 1601 UV/Vis spectrophotometer with 1 cm matched quartz cells was used for absorbance measurements. Metoclopramide hydrochloride drug powder procured from IPCA Labs (P) Ltd., Mumbai, was used in this study. The tablets used for the above studies were procured from a local pharmacy. For method A, 1% solution of Ehrlich reagent and 0.1 N sulphuric acid solutions were prepared in methanol. For method B, 1% w/v sodium nitrite solution was freshly prepared in distilled water, and 0.1% alkaline β-napthol solution was prepared by dissolving 4.0 g NaOH and 0.1 gm β-napthol in distilled water and the solution then diluted to 100 ml with distilled water.

A standard solution containing 1 mg/ml of metoclopramide hydrochloride was prepared by dissolving 100 mg of pure drug in 100 ml of (methanol in method A/distilled water in method B. It was further diluted to obtain 500 µg/ml with methanol for method A and with distilled water to obtain 100 µg/ml for method B). Twenty tablets were weighed and powdered. Powder equivalent to 100 mg of metoclopramide hydrochloride was accurately weighed and dissolved in methanol (method A) and distilled water (method B) to make 100 ml. The solutions were filtered through Whatman filter paper No.41 and were further diluted to 500 µg/ml with methanol for method A and 100 µg/ml with distilled water for method B.

In the method A, aliquots of standard stock solution (0.2-

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**TABLE 1: RESULTS OF ANALYSIS OF METOCLOPRAMIDE HYDROCHLORIDE IN TABLETS**

| Formulation | Label claim (mg/tab) | Method | % of label claim ± S.D | % CV | S.E.M | % recovery*± S.D |
|---|---|---|---|---|---|---|
| Tablet 1 | 10 | A | 100.4±1.08 | 1.07 | 0.540 | 99.4±0.76 |
| | | B | 99.2±0.76 | 0.77 | 0.380 | 99.3±0.69 |
| Tablet 2 | 10 | A | 99.3±0.93 | 0.94 | 0.465 | 98.7±0.49 |
| | | B | 98.7±0.49 | 0.50 | 0.245 | 100.2±0.79 |
| Tablet 3 | 10 | A | 99.2±0.53 | 0.54 | 0.265 | 99.3±0.69 |
| | | B | 99.3±0.63 | 0.64 | 0.315 | 99.6±0.63 |

*Mean of five determinations, The commercial preparations used were – Tablet 1: PERINORM, IPCA Labs (P) Ltd.; Tablet 2: MEXERON, WALLACE Pharmaceuticals Ltd.; Tablet 3: REGLAN, CFL, Pharmaceuticals Ltd.

2.0 ml, 10-100 μg/ml) or sample solution (1.0 ml) were transferred to a series of 10 ml corning volumetric flasks. To each flask, 1.0 ml of Ehlrich reagent solution and 0.5 ml of methanolic sulphuric acid solution was added and mixed. The mixture was kept aside for 2.0 min for the development of colour and the volume in each flask was adjusted to 10.0 ml with methanol. The absorbance of the resulting solution in each flask was measured at 438 nm against the reagent blank and the calibration curve was plotted. The amount of metoclopramide hydrochloride was determined with reference to the calibration curve.

In the method B, aliquots of standard stock solution (0.1-1.0 ml, 1-10 μg/ml) or sample solution (0.5 ml) were transferred to a series of 10 ml corning volumetric flasks. To each flask 2.0 ml of freshly prepared 1% sodium nitrite solution and 1.0 ml of concentrated hydrochloric acid was added. A reaction time of 15 min at 0-5° was given for the completion of reaction. Then 0.5 ml of 0.1% alkaline β-napthol solution was added to the above mixture, and the volume in each flask was adjusted to 10.0 ml with distilled water. The absorbance of the resulting solution in each flask was measured at 553 nm against the reagent blank and the calibration curve was plotted. The amount of metoclopramide hydrochloride was determined with reference to the calibration curve.

To test the accuracy and reproducibility of the proposed methods, recovery experiments were carried out by adding known amount of the drug to the preanalyzed formulation and reanalyzing the mixture by proposed methods. The results of the same are shown in Table 1.

The developed methods were optimized using different parameters such as Ehrlich reagent concentration, methanolic sulphuric acid concentration in method A; and sodium nitrite concentration, concentration of alkaline β-napthol solution in method B for development of maximum colour intensity. One ml of 1% Ehrlich reagent in methanol, 0.5 ml of 0.1 N methanolic sulphuric acid in method A; and 2.0 ml of 1% sodium nitrite solution, 1.0 ml concentrated hydrochloric acid, and 0.5 ml of 0.1% alkaline β-napthol solution in method B was found to be optimum for the development of maximum colour intensity. Stability study of the chromogen was carried out by measuring the absorbance values at time intervals of 10.0 min for 2.0 h and was found to be stable for 1.5 h in both the methods. The optimized method was validated statistically and by recovery studies. The results are summarized in Table 2. The proposed method was successfully applied for the determination of metoclopramide hydrochloride in pharmaceutical dosage forms.

The analysis results of tablets are in good agreement with the labelled claim. The reproducibility, repeatability, and accuracy of these methods were found to be good, which is evidenced by low standard deviation. The percent recovery obtained was 98.7-100.2, which indicates non-interference from the common excipients and colour used in the formulations. The developed visible spectrophotometric methods were simple, sensitive, accurate, precise, and reproducible and can be successfully applied for the routine estimation of metoclopramide hydrochloride in bulk and pharmaceutical dosage forms.

**TABLE 2: OPTICAL CHARACTERISTICS AND PRECISION OF THE METHODS**

| Parameters | Method | |
|---|---|---|
| | A | B |
| $\lambda_{max}$ (nm) | 438 | 553 |
| Beer's Law limits (μg/ml) | 10-100 | 1-10 |
| Sandell's sensitivity (μg/cm$^2$/0.001 A.U.) | 0.1392 | 0.0123 |
| Molar extinction coefficient (l/mol.cm) | $2.119\times10^3$ | $2.741\times10^4$ |
| Correlation coefficient ($r^2$) | 0.9927 | 0.9975 |
| Regression equation (b+ac) | | |
| Slope (a) | 0.005 | 0.0662 |
| Intercept (b) | 0.0337 | 0.0922 |
| % Coefficient of variance (%CV) | 0.418 | 0.423 |
| Standard error of mean (S.E.M) | ±0.170 | ±0.190 |
| % range of error | | |
| Confidence limit with 0.05 level | ±0.417 | ±0.489 |
| Confidence limit with 0.01 level | ±0.343 | ±0.384 |

Sensitivity and the percentage range of error (95% level confidence limit) calculated from five replicate readings are incorporated in Table 2. The Molar absorptivity and Sandell's sensitivity values show the sensitivity of both the methods. The precision is confirmed by % CV (coefficient of variance) values, which are less than 2%, and is indicated in Table 2. The analysis results of marketed formulations (tablets) are in good agreement with the labelled claim. The reproducibility, repeatability, and accuracy of these methods were found to be good, which is evidenced by low standard deviation. The percent recovery obtained (98.7-99.4 for method A, and 99.3-100.2 for method B) indicates non-interference from the common excipients used in the formulations. Thus these methods developed in the present investigation are simple, sensitive, accurate, and precise and can be successfully applied for the routine estimation of metoclopramide hydrochloride in bulk and pharmaceutical dosage forms.

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**Accepted 18 June 2006**
**Revised 6 August 2005**
**Received 30 January 2004**
**Indian J. Pharm. Sci., 2006, 68 (3): 397-399**