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DEVELOPMENT AND VALIDATION OF SPECTROPHOTOMETRIC METHODS FOR DETERMINATION OF MOSAPRIDE CITRATE IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

Three simple and sensitive visible spectrophotometric methods (A, B and C) have been developed for the quantitative estimation of mosapride citrate in bulk drug and pharmaceutical dosage forms (tablets). In method A, mosapride citrate undergoes oxidation followed by complex formation reaction with 1,10–phenanthroline in presence of ferric chloride to form orange red coloured chromogen exhibiting absorption maximum at 508.8 nm and obeyed Beer's law in the concentration range of 2–10 µg/mL. Method B is also based on the oxidation followed by complex formation reaction of drug with 2,2'–bipyridine in presence of ferric chloride to form red coloured chromogen exhibiting absorption maximum at 520.2 nm and Beer's law is obeyed in the concentration range of 2–10 µg/mL. Method C is based on the reaction of mosapride citrate with Folin–Ciocalteu (FC) reagent in alkaline condition to form stable blue coloured chromogen with absorption maximum at 721 nm and Beer's law is obeyed in the concentration range of 20–60 µg/mL. The results of analysis for the three methods have been validated statistically and by recovery studies. The results are compared with those obtained using UV spectrophotometric method in alcohol at 272 nm.

Key words : Mosapride, Validation, Spectrophotometric

INTRODUCTION

Mosapride citrate[1–7] (**1**) is chemically (±)–4–amino–5–chloro–2–ethoxy–N–{[4– (4–fluorobenzyl)–2–morpholinyl] methyl} benzamide citrate dihydrate and is used in gastrointestinal symptoms associated with chronic gastritis. This drug is a selective 5–HT_4 receptor agonist. Very few analytical reports are found in literature for its quantitative estimation by HPLC[8], HPTLC[9] and spectrophotometry[10–12]. In the present work, three simple and sensitive visible spectrophotometric methods (A, B and C) have been developed for the quantitative estimation of mosapride citrate in bulk drug and pharmaceutical dosage forms.

In method A, mosapride citrate (**1**) undergoes oxidation followed by complex formation reaction with, 1,10–phenanthroline in presence of ferric chloride to form orange red coloured chromogen (**2**) exhibiting absorption maximum at 508.8 nm and Beer's law is obeyed in the concentration range of 2–10 µg/mL. The orange red coloured complex resulting from mosapride with 1,10–phenanthroline in presence of Fe (III) may be due to the fact that an unshared pair of electrons can be shared with Fe (II) ion (formed by reaction of mosapride with Fe (III). Three such molecules of 1,10–phenanthroline attach themselves to the metallic ion. In the similar way, method B is based on oxidation followed by coupling reaction of drug with 2,2–bipyridine in presence of ferric chloride to form red coloured chromogen (**3**) exhibiting absorption maximum at 520.2 nm and Beer's law is obeyed in the concentration range of 2–10 µg/mL. Method C is based on the reaction of mosapride citrate with Folin–Ciocalteu (FC) reagent in alkaline condition to form blue coloured chromogen with absorption maximum at 721 nm and Beer's law is obeyed in the concentration range of 20–60 µg/mL. The blue coloured complex formed is due to the reduction[13,14] of 1, 2 and 3 oxygen atoms of FC reagent and the formation of molybdenum blue or tungsten blue. Spectrophotometric parameters are established for standardisation of the methods including statistical analysis of data. These methods have been successfully extended to the pharmaceutical dosage forms (tablets) containing mosapride citrate.

EXPERIMENTAL

All spectral measurements were done on Systronics 119 UV/visible spectrophotometer.

Reagents

Analytical grade reagents were used. Commercially available samples were purified.

1. Absolute alcohol.
2. Aqueous ferric chloride (0.03 M and 0.5% w/v, Loba Chemie)
3. 1,10–Phenanthroline (0.1 M in alcohol, Merck)
4. 2,2'–Bipyridine (0.5% w/v in alcohol, Merck)
5. Na_2CO_3 solution (20% in water, Glaxo)
6. FC Reagent (1N, Loba Chemie)
7. Double distilled water.

Working standard of drug solution

About 100 mg of mosapride citrate was accurately weighed and dissolved in 20.0 mL of absolute alcohol in a 100.0 mL volumetric flask and diluted upto the mark with absolute alcohol (1 mg/mL). The final concentration of mosapride was brought to 100.0 µg/mL with alcohol.

Sample preparation

Two brands of commercial tablets were analyzed by the proposed methods. Thirty tablets of formulation each containing 5 mg of mosapride were accurately weighed and powdered. Weight of tablet powder equivalent to 100.0 mg of drug was taken in 40.0 mL of alcohol and shaken for 15 min, filtered into 100.0 mL volumetric flask through cotton wool and the remaining amount of alcohol was added through tablet powder to make upto 100.0 mL. Final concentration was brought upto 100.0 µg/mL with alcohol.

Assay

Method A

Aliquots of mosapride citrate ranging from 0.2–1.0 mL (1.0 mL = 100 µg) were transferred into a series of 10.0 mL volumetric flasks. To each flask 0.5 mL of $FeCl_3$ (0.03 M) and 1.0 mL of 1,10–phenanthroline (0.1 M) were added and heated on water bath for 20 min and then cooled to room temperature. The volumes were made upto the mark with water. The absorbance of the orange red coloured solutions was measured at 508.9 nm against reagent blank. The orange red coloured chromogen was stable for more than 3 h. The amount of mosapride citrate present in the sample was computed from calibration curve.

Method B

Aliquots of mosapride citrate ranging from 0.2–1.0 mL (1.0 mL = 100.0 µg) were transferred into a series of 10.0 mL volumetric flasks. To each flask 0.75 mL of ferric chloride (0.5 % w/v) and 2.0 mL of 2,2'–bipyridine (0.5% w/v) were added and heated on water bath for 30 min and then, cooled to room temperature. The volumes were made upto the mark with water. The absorbance of the red coloured solutions was measured at 520.2 nm against reagent blank. The red coloured chromogen was stable for more than 4 h. The amount of mosapride citrate present in the sample was computed from calibration curve.

Method C

Aliquots of mosapride citrate ranging from 2.0–6.0 mg (1.0 mL=100.0 µg) were transferred into a series of 10.0 mL volumetric flasks. To each flask 2.0 mL of Na_2CO_3 solution (20% w/v) and 1.0 mL of FC reagent (1 N) were added and heated on water bath for 45 min and then cooled to room temperature. The volumes were made upto the mark with water. The absorbance of the blue coloured solutions was measured at 721 nm against reagent blank. The blue colured chromogen was stable for more than 3 h. The amount of mosapride citrate present in the sample was computed from calibration curve.

The results of the above methods are compared with results obtained with UV spectrophotometric method. In UV method[10], solution of mosapride in alcohol either pure or formulation (100.0 µg/mL) was prepared. Aliquots of mosapride ranging from 0.2–1.0 mL (1.0

mL = 100.0 µg) were transferred into a series of 10.0 mL volumetric flasks. The volumes were made upto the mark with alcohol and the absorbance of the solutions was measured at 272 nm against solvent blank. The amount of mosapride was computed from calibration curve.

RESULTS AND DISCUSSION

The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and Sandell's sensitivity are presented in Table 1. The regression analysis using the method of least squares was made for the slope (b), intercept (a) and correlation (r) from different concentrations and the results are summarised in Table 1. The percent relative standard deviation and percent range of error (0.05 and 0.01 level of confidence limits) calculated from the eight measurements, $^{3}/_{4}$ of the upper Beer's law limits of mosapride are given in Table 1. The results showed that these methods have reasonable precision. Comparison of the results obtained with the proposed and UV methods for dosage forms (Table 2) confirm the suitability of these methods for pharmaceutical dosage forms. The optimum conditions for colour development for methods A, B and C were established by varying the parameters one at a time and keeping the other parameters fixed and observing the effects of product on the absorbance of the coloured species and incorporated in the procedures.

Table 1. Optical characteristics and precision

	Method A	Method B	Method C
λ_{max} (nm)	508.8	520.2	721
Beer's law limits (µg/mL) (C)	2–10	2–10	20–60
Molar absorptivity (lit, mole^{-1} cm^{-1})	4.576 x 10^4	3.347 x 10^4	0.553 x 10^4
Sandell's sensitivity (µg/cm^2 0.001 absorption units)	0.024	0.036	0.043
Regression equation (Y*)			
Slope (b)	0.0699	0.0509	0.0100
Intercept (a)	0.0015	0.0007	0.0585
Correlation co–efficient (r)	1.001	1.001	1.000
% RSD	0.558	0.805	0.855
Range of errors**			
Confidence limits with 0.05 level	± 0.0019	± 0.0020	± 0.0023
Confidence limits with 0.01 level	± 0.028	± 0.0030	± 0.0034

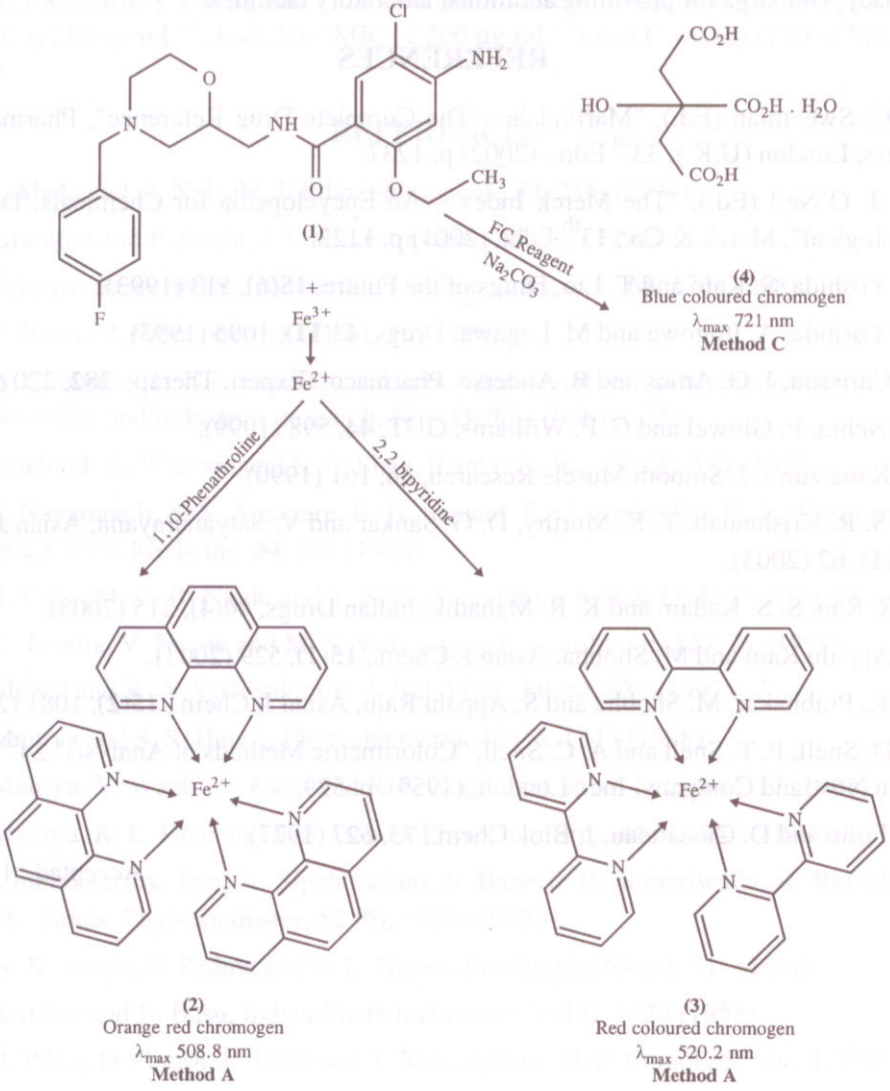
* Y = bc + a where C is the concentration of Mosapride in µg/mL and Y is the absorbance at the respective λ_{max}. ** For eight measurements.

In order to justify the reliability and suitability of the proposed methods, known quantities of pure mosapride citrate was added to its various preanalysed formulations and the mixtures were analysed by the proposed methods. The results of recovery experiments are also summarised in Table 2. The other active ingredients and excipients usually present in pharmaceutical dosage forms did not interfere.

Table 2. Evaluation of mosapride citrate in pharmaceutical dosage forms

Sample*	Labelled amount (mg)	Amount obtained (mg)				Percentage recovery**		
		Proposed Method			Reference Method UV			
		A	B	C		A	B	C
T_1	5	4.95	4.93	4.92	4.97	99.21	99.35	99.42
T_2	5	4.96	4.91	4.93	4.96	99.18	99.24	99.17

* T_1, T_2 are tablets from different manufacturers. ** Average of 8 determinations.



Scheme

The proposed methods are found to be simple, sensitive, selective, economical, accurate and precise and can be used in the determination of mosapride in bulk drug and its pharmaceutical dosage forms in a routine manner.

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