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A Simple, Sensitive Spectrophotometric Determination of Mosapride in Pharmaceutical Preparations Using Novel Reagent

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Abstract: A rapid, selective and sensitive spectrophotometric method for the determination of mosapride in either pure form or in its formulations in pharmaceutical preparations is described. The method is based on the diazotization coupling reaction of mosapride with 1-naphthol in acidic medium to give red azo dye product with the λ_{\max} of 500 nm and is stable for more than 12 hours at optimum condition. Beer's law is obeyed at concentration of 0.2 to 12 $\mu\text{g mL}^{-1}$ at the wavelength of maximum absorbance. Common excipients used as additives in pharmaceutical preparations do not interfere in the proposed method. The developed method is highly reproducible and applied to wide variety of pharmaceutical formulation and the results were compared favourably with the reported method.

Keywords: Mosapride citrate, 1-Naphthol, Diazotization, Spectrophotometer, Pharmaceutical preparations.

Introduction

Mosapride citrate ¹(I), (+/-)- 4-amino-5-chloro-2-ethoxy-N[[4-(4-fluorobenzyl)-2-morpholinyl] methyl]Benzamide citrate dihydrate² is used in gastrointestinal symptoms associated with chronic gastrointestinal symptoms associated with chronic gastritis. This drug is a selective 5-HT₄ receptor agonist³⁻⁵. Spectrophotometric parameters were established for standardisation of the methods including statistical analysis of data⁶. There is no sensitive and simple analytical method in literature for the quantitative determination of mosapride in bulk drug and formulations. Few authors have developed spectrophotometric determination of mosapride in pharmaceutical preparations. But these methods offer certain disadvantage like, sensitivity and stability, for its determination. Therefore the authors have made some attempts to develop a highly sensitive method for determination of mosapride,

based on diazotization coupling reaction to form red azo dye with λ_{max} of 500 nm. The method has been successfully employed for determination of mosapride in pharmaceutical preparations and compared with reported method in literature⁷ in terms of sensitivity and stability.

Experimental

Materials and Methods

Analytical grade reagents were used. Double distilled water was used throughout the experiments. 1-naphthol was purchased from S.D fine Chemicals (INDIA) and used without further purification. Hydrochloric acid (AR), Sodium nitrite were used. Commercial dosage was purchased from local sources.

A HITACHI 2000 UV-Visible spectrophotometer with 1.0 cm matched quartz cell was employed to obtain electronic spectral measurements.

Solutions

Standard solution of mosapride ($1000 \mu\text{g mL}^{-1}$) was prepared by dissolving 100 mg of mosapride in 10 mL of absolute alcohol and then diluted to the mark in 100 mL standard flask. A working standard solution of each $25 \mu\text{g mL}^{-1}$ was prepared by further dilution. 0.2% solution of freshly prepared 1-naphthol in 5.0 mL of 1N Sodium hydroxide. 5 N Hydrochloric acid and 3% Sodium nitrite solution were used for the experiments.

Procedure

Aliquots of working standard solution of mosapride (0.2 to 14 μg) were transferred into a series of 100 mL calibrated flask. To each flask, 15 mL of Hydrochloric acid (5 N) and 2 mL of 3% Sodium nitrite solution were added and kept to stand for 10 min at room temperature. Then 2 mL of aqueous solution of ammonium sulphamate (0.5 % W/V) was added and the solution was shaken thoroughly. After 2 min, 1 mL of coupling agent, 1-naphthol was added and diluted to mark with distilled water. The absorbance was measured at 500 nm against the corresponding reagent blank and calibration graph was constructed.

Procedure for the assay of dosage of mosapride in commercial Samples

Five tablets were powdered and a known weight of the powdered sample was dissolved in 5.0 mL absolute alcohol and filtered. The working standards were prepared by suitable dilution and the standard procedure was followed for the determination of mosapride in Tablets.

Result and Discussion

Spectral Characteristics

The proposed method involves diazotization coupling reaction of 1-naphthol with mosapride in acidic medium to produce the red coloured azo dye product with λ_{max} of 500 nm as shown in Figure 2.

Optimisation of Reagent Concentration

Various concentration and volume ranges for all the reagents were studied in detail. It was found that 1-naphthol in the range of 1-2 mL, 3 mL of mosapride, 1-2 mL of ammonium sulphamate, 5 N Hydrochloric acid in the range of 10-15 mL and 3% Sodium nitrite solution in the range of 1-2 mL were necessary to obtain a stable coloured product with maximum colour intensity. Required volumes of the reagents were hence used as noted in the standard procedure.

Stability

The coloured product of mosapride formed by the proposed method was found to be stable for more than 12 h at room temperature. Reproducible results were obtained in the temperature range of 31- 43°C. An increase in temperature of above 43°C and below 30°C, decreases the absorbance data, indicating the decomposition of the product. However a temperature of 31- 43°C is recommended for the absorbance measurements of the coloured product.

Optical characteristics

Beer's law is obeyed over the mosapride concentration range over 0.2 to 12 $\mu\text{g mL}^{-1}$ for 1-naphthol as coupling agent. Limit of Quantification (LOQ) were determined by taking the standard deviation (σ) of the blank with respect to water and slope of calibration curve's multiplied by a factor 10. That means, LOQ is approximately 3.3 times Limit of Detection (LOD). Normally the LOQ slightly crosses the lower limit of Beer's law. But LOD is well below the lower limit of the Beer's law range. The upper limit of Beer Lambert law is determined by plot of absorbance against concentration at the value of λ_{max} 500 nm. Beyond this limit, the correlation results were really affected. Hence the measurements were excluded above these limits to keep the linear relationship. The optical characteristic and precision data are presented in Table 1.

Table 1 Optical characteristics and precision data of mosapride

Optical Characteristics and Precision data	Value
Beer's law range ($\mu\text{g mL}^{-1}$)	0.2 – 12
λ_{max} (nm)	500 nm
Stability	more than 12h
Colour of the product	Red azo dye
Limit of detection ($\mu\text{g mL}^{-1}$)	0.621
Limit of quantification ($\mu\text{g mL}^{-1}$)	0.2638
Sandell's Sensitivity ($\mu\text{g cm}^{-2}$)	0.032
Molar absorptivity ($1 \text{ mol}^{-1} \text{ cm}^{-1}$)	3.61×10^4
Regression equation (Y^a)	5.71×10^{-2}
Slope (a)	0.75×10^{-2}
Intercept (b)	
Correlation coefficient (r)	0.9980
% Relative standard deviation ^b	0.8936
% Error ^c	± 0.0017
Optimum range by photometric determination ($\mu\text{g mL}^{-1}$)	0.18 to 15

^a $Y = bx+a$; where x is the concentration in $\mu\text{g mL}^{-1}$ ^bn=10 ^cTen replicates

Reaction Sequence

The 1-naphthol reacts with mosapride in acidic medium (HCL+NaNO₂) to produce red coloured azo dye product with λ_{max} of 500 nm. The reaction mechanism for the formation of product is shown in Figure 1.

Interference

Under the diazotization coupling reaction condition, problem of interference does not arise in the analysis of commercially available mosapride. The effects of additives associated with mosapride in its formulations were investigated using the developed method. The method does not suffer from common excipients and other substances

Application

Reproducibility of the method was checked out by 10 replicate determination at $6 \mu\text{g mL}^{-1}$. The application of the method for assay of pharmaceutical preparations was examined. The results of assay of the available tablets of mosapride are presented in Table 2. The actual weight of individual tablet is 5 mg. The analysis of the tablet was conducted from original state. The results are highly reproducible and assay of tablets were cross checked by reported method⁷ which agree favourably.

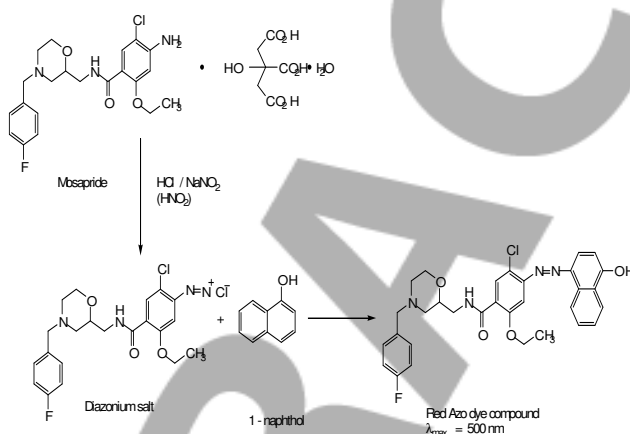


Figure 1. Reaction mechanism of mosapride with 1-naphthol

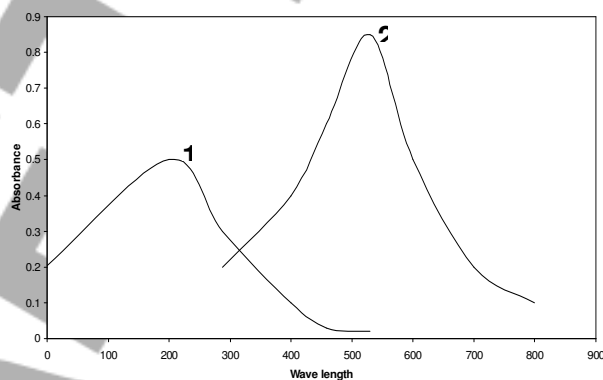


Figure 2. Absorption spectra of 1 Mosapride + reagent blank

Table 2. Determination of mosapride in pharmaceutical preparation

Samples	Label claim (mg)	Amount of drug found ^b in mg	
		Proposed Method	Reported Method ⁷
Tablet I ^a	5	4.98	4.95
Tablet II ^a	5	4.97	4.96

^b Average of ten determination.

Conclusion

The proposed method is simple, selective and highly sensitive than the spectrophotometric method available in literature⁷. The statistical parameter and recovery study data clearly indicates the reproducibility and accuracy of the method. Thus, the method can be adopted as an alternative to the existing spectrophotometric methods. Analysis of the authentic samples containing mosapride showed no interference from the common additives and excipients. Hence recommended procedure is well suited for the assay and evaluation of drugs in pharmaceutical preparations in assure of high standard of quality control.

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