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DEVELOPMENT AND STATISTICAL VAIDATION OF SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF MOSAPRIDE IN PHARMACEUTICAL FORMULATION

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ABSTRACT: Three simple, precise and economical UV methods have been developed for the estimation of Mosapride in bulk and pharmaceutical formulations. Mosapride has the absorbance maxima at 309nm (Method A), and in the first order derivative spectra, showed zero crossing at 309 nm, with a sharp peak at 300 nm when n=1 (Method B), Method C applied was Area Under Curve (AUC) for analysis of Mosapride in the wavelength range of 300-320nm. Drug followed the Beer's Lamberts range of 5-40 µg/ml for the method A, B C. Results of analysis were validated statistically and by recovery studies and were found to be satisfactory.
KEYWORDS: Mosapride, UV Spectrophotometry, Derivative Spectroscopy, Area Under Curve.

INTRODUCTION

Mosapride is a selective serotonin 5-HT4 receptor agonist drug used for short-term treatment of erosion and ulceration of the esophagus caused by gastroesophageal reflux disease. Chemically Mosapride is (4-Amino-5-chloro-2-ethoxy-N-((4-(4-fluorobenzyl)-2-morpholinyl) methyl) benzamide (citrate dihydrate) (Figure 1). It is listed in Martindale-The complete drug reference[1]. Literature survey reveals plane HPLC[2] and spectrophotometric method[3] exists for estimation of Mosapride. No single UV method for Mosapride is reported till date using zero order, First order derivative spectroscopy and AUC method[6,7,9]. Hence an attempt has been made to develop new UV method for its estimation in bulk and pharmaceutical formulations with good accuracy, simplicity, precision and economy.

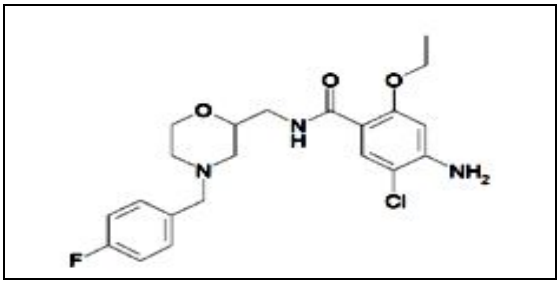

Figure 1: Chemical structure of Mosapride

EXPERIMENTAL

Pure sample of Mosapride was obtained from Torrent Pharmaceuticals, Mehsana, India as a gift sample. A Shimadzu UV-1700 UV/VIS Spectrophotometer was used with 1 cm matches quartz cell. Tablets of 5mg were procured from local pharmacy.

Preparation of standard solution:

The pure drug accurately about 5mg was weighed and dissolved 100 ml methanol to give the standard stock solution of concentration 50 µg/ml. Aliquots of standard stock solution were pipette out and suitably diluted with distilled water to get the final concentration of standard solutions.

Zero order spectroscopic method:

The solutions were scanned in the range from 400-200 nm (method A), and the peaks were observed at 240nm and 309 nm. The wavelength selected for the analysis of the drug was 309nm (Figure 2). The drug followed the Beer's- Lamberts law in the range of 5-35 µg/ml. using the calibration curve the concentration of the sample solution can be determined.

First order derivative spectroscopic method[6,7,8,9]:

The first order derivative spectra at n=1 (method B), showed a sharp peak at 300 nm (Figure 3).the absorbance difference at n=1 ($dA/d\lambda$) is calculated by the inbuilt software of the instrument which was directly proportional to the concentration of the standard solution.

The standard drug solution was diluted so as to get the final concentration in the range of 5-40 µg/ml and scanned in the first order derivative spectra. The calibration curve of dA/dλ against concentration of the drug showed linearity.

Area Under Curve Method (AUC):

The AUC (Area Under Curve) method[7,9] involves the calculation of integrated value of absorbance with respect to the wavelength between two selected wavelength 300nm and 320nm (Figure 4). Area calculation processing item calculates the area bound by the curve and the horizontal axis. The horizontal axis is selected by entering the wavelength range over which the area has to be calculated. The wavelength range is selected on the basis of repeated observations so as to get the linearity between area under curve and concentration. Suitable dilutions of standard stock solution (50µg/ml) of the drug were prepared and scanned in the spectrum mode from the wavelength range 400-200 nm and the calibration curve was plotted. All the three method were checked by analyzing the samples with known concentration. As the result obtained were satisfactory, the method was applied for the pharmaceutical formulations.

Analysis of the Tablet formulation:

For the estimation of Mosapride in tablet formulation by three methods, 10 tablets of brand were weighed and triturate to fine powder. Tablet powder equivalent to 5mg of Mosapride was weighed and then dissolved and further diluted with quantity sufficient with methanol. It was kept for ultrasonication for 30 min; this was filtered through Whatman filter paper no. 41 to get the stock solution of 50 µg/ml. Various dilutions of the tablet solution were prepared and analyzed for six times and the concentration was calculated by using the calibration curve for three methods.

Validation of the method:

All these methods were validated according to ICH guidelines[4, 5] by carrying out analysis of six replicate sample of tablet (Table 2). Recovery studies were carried out at three different levels i.e. 50%, 100%, and 150% by adding the pure drug to previously analyzed tablet powder sample. From the amount of drug found, percentage recovery was calculated (Table 2).

The ANOVA test i.e. Tukey-Kramer Multiple comparison test[7,8,9] was applied to determine whether there is significant difference between the results of analysis by three different analysis methods (Table 3)

RESULTS AND DISCUSSIONS

All the methods A, B, and C for the estimation of Mosapride in tablet dosage were found to be simple, accurate and reproducible. Beer- lambert's law was obeyed in the concentration range of 5-35 µg/ml in all these methods (Table 1). The accuracy of the method was assessed by recovery studies at three different levels i.e. 50%, 100%, 150%. The values of standard deviation were satisfactory and the recovery studies were close to 100%. The %RSD value is less than 2 indicative of accuracy of the method. The developed method was statistically compared using one way ANOVA. The P value was found to be 0.0863 and was greater than 0.05. Hence the results of the ANOVA indicate no significant difference between three methods. Hence these methods can be useful in routine analysis of Mosapride in bulk drug and pharmaceutical formulations.

Table 1: Optical characteristics and other parameters

Parameters	Method A	Method B	Method C
λmax (nm) / wavelength range (nm)	309	300	300-320
Beer's-Lambert's range (µg/ml)	5-35	5-35	5-40
Coefficient of Correlation	0.9988	0.9989	0.999032
Regression Equation Y = mx + c			
a. Slope(m)	0.03963	0.029484	0.5937
b. Intercept(c)	0.005485	0.011442	0.31071
LOD (µg/ml) LOQ (µg/ml)	0.10 0.30	0.15 0.45	0.25 0.75

Where,

A is zero order derivative spectrum method with n = 0.

B is first order derivative method with n = 1.

C is AUC method.

Table 2: Result of Analysis of Mosapride in Tablet and Recovery studies.

METHOD	Tablet	Label Claim	%estimated	%recovery	S.D.	%COV	S.E.
A	T1	5	99.84	101.36	0.924	0.944	0.542
	T2	5	100.56	101.26	0.638	0.442	0.365
B	T1	5	99.33	98.52	1.324	1.453	0.245
	T2	5	99.64	99.65	1.234	1.234	0.764
C	T1	5	98.35	100.12	0.643	0.435	0.257
	T2	5	99.83	100.80	0.355	0.523	0.256

Where,
A is zero order derivative spectrum method with n = 0.
B is first order derivative method with n = 1.
C is AUC method.
T1 is Mosapid
T2 is Mosid - MT

Table 3: One Way ANOVA (Tukey -Kramer multiple comparison test).

Comparison	Mean Difference	q value	P Value
Method A Vs Method B	2.120	5.342	ns P > 0.05
Method A Vs Method C	0.6650	2.467	ns P > 0.05
Method B Vs Method C	-1.840	3.474	ns P > 0.05

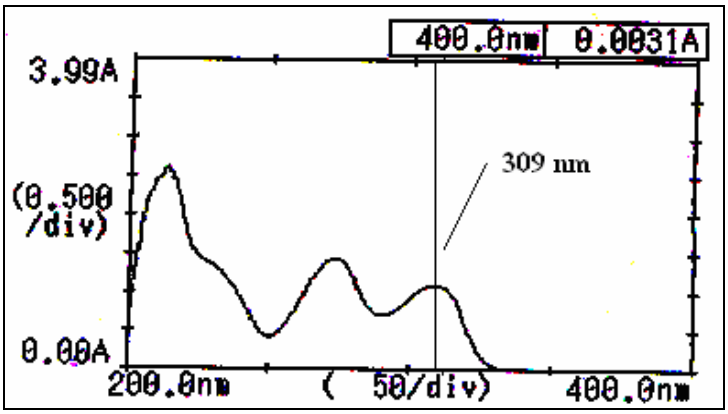

Figure 2: Zero order spectrum of Mosapride

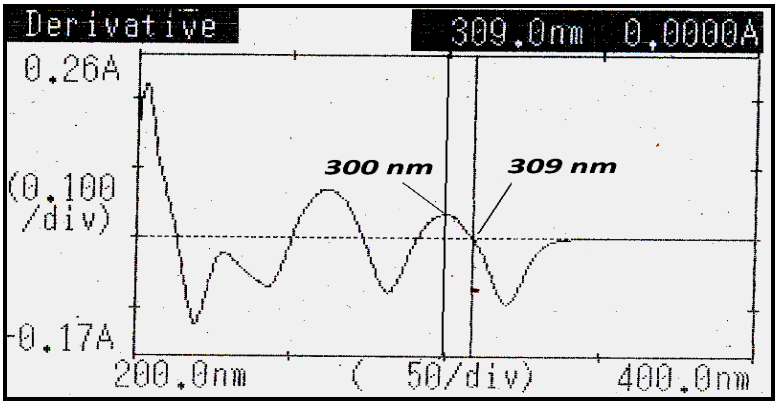

Figure 3: First order derivative spectrum of Mosapride with n=1

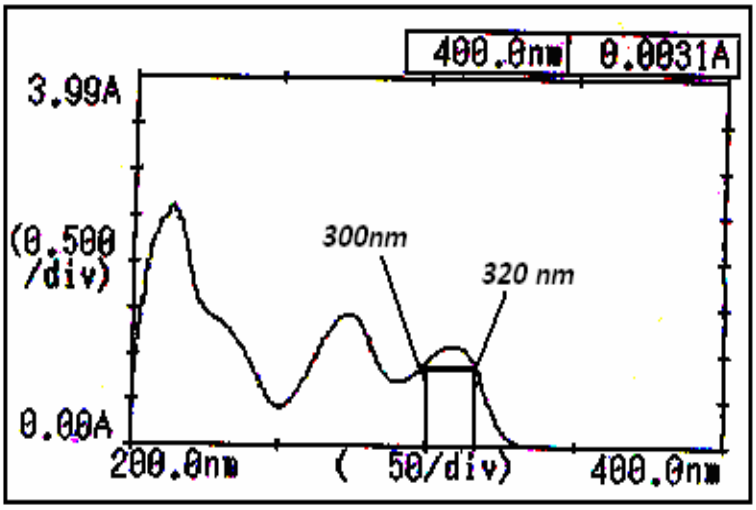

Figure 4: Wavelength range selected for AUC method of Mosapride

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