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Simultaneous HPTLC Estimation of Omeprazole and Cisapride in Pharmaceutical Dosage Form

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A simple, rapid, reproducible and economical high performance thin layer chromatographic method for simultaneous estimation of omeprazole and cisapride in capsule has been developed. It was performed on Kieselghur 60, F254 thin layer chromatographic plates using mobile phase comprising of propanol:toluene (1:3) and the detection was carried out at 276 nm showing R_f value 0.34 for omeprazole and 0.56 for cisapride. The calibration curve response was observed between 0.1-0.4 µg for omeprazole and 0.075-0.2 µg for cisapride by height and area. The per cent drug estimated for omeprazole and cisapride from marketed formulation was found to be 99.63 ± 0.93, 102.82 ± 0.82 by height and 100.47 ± 1.40,103.71 ± 1.05 by area, respectively. The per cent recovery by height and by area was found to be 100.16 ± 2.21 and 98.53 ± 3.38 for omeprazole and 100.24 ± 1.20 and 99.66 ± 0.88 for cisapride. The method was validated with the determination of accuracy, precision, specificity, linearity detector response and ruggedness.

Key Words: Omeprazole, Cisapride, HPTLC and Validation.

INTRODUCTION

Omeprazole (OMP) is a proton pump inhibitor which is used as antiulcer and antisecretory agent. It is chemically 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1*H*-benzimidazole[1]. Cisapride (CSP) is a prokinetic drug which increases the GI motility. It is chemically *cis*-4-amino-5-chloro-N-[1-[3-(4-fluorophenoxy)propyl]-3-methoxy-4-piperidinyl]-2-methoxy benzamide[2]. Literature survey reveals that the several methods such as UVspectrophotometric and chromatographic[3-7] have been reported for estimation of OMP in pharmaceutical formulation[8-12] and certain spectrophotometric[13-17] and chromatographic[18-21] have been reported for estimation of CSP There is no HPTLC method reported for simultaneous estimation of the OMP and CSP in combined dosage form, but in present experiment the efforts were done to develop method which will show good resolution, separation and estimation. The method was validated to show the sensitivity and reproducibility.

EXPERIMENTAL

The instrument used in present study was Camag-HPTLC system comprises Camag Linomat IV automatic sample applicator, Camag TLC Scanner III with CATS 4.0 software, Camag Twin trough glass chamber. The chemicals and reagents used throughout the project work were HPLC grade. The solvents used were methanol, propanol and toluene.

Standard solution of OMP (0.05 mg/mL) and CSP (0.025 mg/mL) were prepared in methanol.

Mixed standard solution (sample solution): Solution containing both the drugs *i.e.*, OMP and CSP - 0.05 and 0.025 mg/mL, respectively prepared in methanol.

Experimental chromatographic conditions: Standard experimental conditions were followed during the present experimental study. Stationary phase-Kieselghur 60, F254 TLC precoated aluminum foiled plates, mobile phase propanol:toluene (1:3), saturation time 0.5 h, thickness of plate 250 mm, sample application 6 mm band, separation technique ascending, temperature 24 ± 2 ºC, relative humidity 50-60 %, migration distance 70 mm, scanning mode absorbance/reflectance, detection wavelength 276 nm, the detection wavelength was selected from overlain spectra of both the drugs in methanol (Fig. 1).

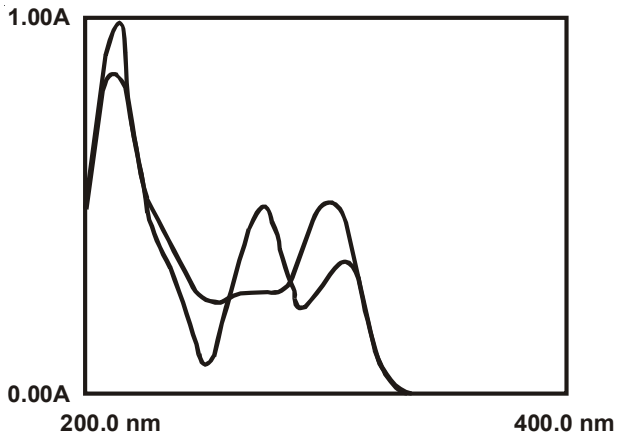

Fig. 1. Selection of the wavelength for densitometric evaluation of omeprazole and cisapride

Calibration curve response: OMP (0.05 µg/µL) and CSP (0.025 µg/µL) solution ranging from 2-8 µL were applied on TLC plate by microliter syringe with the help of automatic sample applicator. The plates were developed, dried and densitometrically scanned at 276 nm. Peak height and areas were recorded for each concentration of drugs and curves (concentration *versus* peak height/area) were constructed.

System suitability test: The system suitability test was performed by applying 6.0 µL of mixed standard solution containing (0.05 µg/µL) of OMP and (0.025 µg/µL) of CSP. The mean value, standard deviation and coefficient of variance were calculated for peak height and peak area.

Standard laboratory mixtures: Different laboratory mixtures were prepared in the same manner as that of a standard preparation to get the final concentration of OMP 0.05 µg/µL CSP 0.025 µg/µL. A 6.0 mL of each mixed standard solution (duplicate) and laboratory mixture (quadruplet) were applied on TLC plate in the form of 6.0 mm band. Plates were then developed in presaturated twin trough chamber with mobile phase. After development the plates were dried with the help of hot air dryer and evaluated desitometrically at wavelength of 276 nm.

Validation of proposed method: The proposed method was validated by considering following parameters.

Accuracy: The accuracy of proposed method was ascertained by carrying out recovery studies by standard addition method. The recovery study was performed to determine if there are positive or negative interference from excipients present in formulation. The method was ascertained on the basis of recovery study by standard addition method to preanalyzed sample (Table-1).

TABLE-1
PER CENT ESTIMATION OF DRUG FROM LABORATORY MIXTURE, MARKETED FORMULATION RECOVERY STUDY

Sample	% Estimation of labeled claim*				% Recovery			
	OMP		CSP		OMP		CSP	
	By height	By area	By height	By area	By height	By area	By height	By area
Standard lab mixture	101.20	101.74	99.75	99.88	–	–	–	–
	0.26	0.26	0.41	0.27	–	–	–	–
	0.26	0.25	0.41	0.27	–	–	–	–
Marketed formulation	99.63	100.47	102.82	103.71	100.16	98.53	100.24	99.66
	0.92	1.40	0.82	1.85	2.21	3.38	1.20	1.88
	0.93	1.39	0.80	1.01	2.21	3.43	1.20	1.88

*Mean, SD and CV of four observations.

Precision: Precision of an analytical method is expressed as SD or RSD of series of measurement. It was ascertained by replicate estimation of both the drugs by proposed method (Table-1).

Specificity: The specificity of the method was ascertained by analyzing standard drug and sample. The spot for OMP and CSP in sample was confirmed by comparing the R_f and spectra of the spot with that of standard. The peak purity of both the drugs was assessed by comparing the spectra at three different levels *i.e.*, peak start (S), peak apex (M) and peak end (E) positions of the spot.

Linearity detector response: The study was performed by application of different volume of mixed standard and response was obtained densitometrically (Table-2).

TABLE-2
RESULTS OF LINEARITY DETECTOR RESPONSE

Sample	Linearity range		Coefficient of correlation	
	By height	By area	By height	By area
OMP	0.100-0.4	0.100-0.4	0.9971	0.9976
CSP	0.075-0.2	0.075-0.2	0.9983	0.9959

Ruggedness: Ruggedness was carried out under the different conditions *i.e.*, different days and different analysts (Table-3).

TABLE-3
RESULTS OF RUGGEDNESS STUDY

Days	% Labeled claim			
	OMP		CSP	
	By height	By area	By height	By area
D-1	99.86	98.57	99.74	100.47
D-4	100.14	100.10	100.65	99.47
D-7	100.85	100.35	100.24	100.14
Mean	100.28	99.67	100.21	100.06
± SD	0.5100	0.9636	0.4557	0.5710
CV	0.5089	0.9602	0.4540	0.5700
Different analyst				
Days	% Labeled claim			
	OMP		CSP	
	By height	By area	By height	By area
A-1	100.24	100.26	100.46	100.63
A-2	100.36	99.64	99.92	100.46
A-3	99.83	100.46	99.63	100.35
Mean	100.14	100.12	100.00	100.48
± SD	0.2780	0.4240	0.4210	0.1410
CV	0.2770	0.4230	0.4210	0.1400

RESULTS AND DISCUSSION

Before preceding to the experiment both the drugs were standardized by the official methods. Various pure solvents and mixtures in varying proportion were tried as mobile phase. However, mobile phase consisting of propanol:toluene (1:3) was found to be more suitable for better separation of OMP and CSP with R_f value 0.34 and 0.56, respectively with saturation period of 0.5 h at 276 nm. The selection of wavelength was based on nearly equal absorbance by both the component of mixture for optimum sensitivity (Fig. 1). The calibration curves were drawn with peak height and peak area for each concentration of drugs.

The above-observed results evidenced that the proposed method is simple, accurate, specific, rapid and can be used for simultaneous estimation of OMP and

CSP in combined dosages form. The value within the limit of standard deviation and coefficient of variance signifies high precision of method. The proposed method can be used for the routine analysis OMP and CSP in their combined dosage form.

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