ORIGINAL RESEARCH ARTICLES

VALIDATED HPTLC METHOD FOR SIMULTANEOUS DETERMINATION OF OLMESARTAN MEDOXIMIL AND METOPROLOL SUCCINATE IN TABLET DOSAGE FORM

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ABSTRACT

A high performance thin layer chromatographic method has been developed for the simultaneous determination of olmesartan medoximil and metoprolol succinate from tablet dosage form. The mobile phase consisting of water-methanol-ammonium sulphate (4.5:4.5:1.5 v/v/v) and wavelength of detection 233 nm was used. The developed method was validated as per ICH guidelines.

Keywords: Olmesartan medoximil, Metoprolol succinate, HPTLC, Validation.

INTRODUCTION

Olmesartan medoximil (OLM) 2, 3-dihydroxy-2-butenyl-4(1-hydroxy-1-methyl ethyl)-2-propyl-1-[p-(o-1H-tetrazol-5-yl-phenyl) benzyl] imidazole-5-carboxylate, cyclic 2, 3-carbonate) is completely hydrolysed to active form, olmesartan which is an angiotensin II receptor antagonist with anti-hypertensive activity. Metoprolol succinate (MET) is (±)1-(isopropylamino)-3-[p-(2-methoxyethyl) phenoxy]-2-propanol succinate salt (2:1) is a beta adrenergic blocking agent, which reduces the chest pain and lowers the blood pressure[1, 2, 3]. Spectrophotometric and chromatographic methods for olmesartan medoximil, either in combination with other drugs or as a single drug have been reported[4, 5, 6, 7, 8, 9]. Survey of literature of metoprolol succinate, either single or in combination with other drugs revealed several methods based on HPLC and electrochemical methods in human plasma, urine and pharmaceutical formulation[10, 11, 12, 13]. However there is no HPTLC method for simultaneous determination of OLM and MET in tablet formulation. The proposed method was validated as per ICH guidelines.

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EXPERIMENTAL

Reagents

Methanol (AR grade), distilled water and ammonium sulphate (AR grade) were procured from Merck India Pvt. Ltd., Mumbai.

Pure Drugs (Working Standards)

Working standards of olmesartan medoximil and metoprolol succinate was obtained as a gift sample from Cipla Ltd., Mumbai and IPCA Ltd. respectively. OLESAR M-50 (claiming 20 mg of OLM and 50 mg of MET) was obtained from local market and analysed by proposed method.

Instrument

Camag HPTLC system consisting of Linomat 5 applicator, Camag TLC scanner 3 and Win CATS software V-1.4.4 was used for chromatographic separation.Spotting of samples was done by using Hamilton microliter syringe.

Procedure

Chromatographic condition

Methanol was used as a solvent for solution preparation. Stationary phase was aluminium HPTLC plate (20×10 cm) precoated with silica gel F_{254}. Mobile phase consisting of methanol:water:ammonium sulphate in the ratio 4.5:4.5:1.5 v/v/v was used. Linear ascending development was carried out in a 20×10 cm twin trough glass chamber using mobile phase. No saturation was required. The development distance was 7 cm which was achieved in 20 min. The TLC plates were removed from chamber and dried at 35^0 for 5 min. The wavelength of detection selected was 233 nm since both drugs showed optimum absorbance at that wavelength. The slit dimension of detection was kept 6.00 × 0.45 mm, scanning speed 20 mm/sec and data resolution 100 mcm/step. A typical densitogram of working standard solutions is as shown in Fig. 1.

Standard Preparation

Stock solutions each of 100 mcg/mL of olmesartan medoximil and metoprolol succinate were prepared by dissolving 10 mg of each drug in 25 mL methanol in separate volumetric flask and then the volume was adjusted to 100 mL with methanol separately.

Linearity of Detector Response

Varying concentrations of 100-700 ng/spot of olmesartan medoximil and metoprolol succinate were prepared from their respective stock solutions on the chromatographic plates. The plate was developed using mobile phase comprising of methanol:water:ammonium sulphate in the ratio 4.5:4.5:1.5 v/v/v in twin trough chamber to a distance of 7 cm. After removal from chamber, the plate was dried at 35^0 for 5 min. The plate was scanned and quantified at 233 nm. Peak area was recorded for

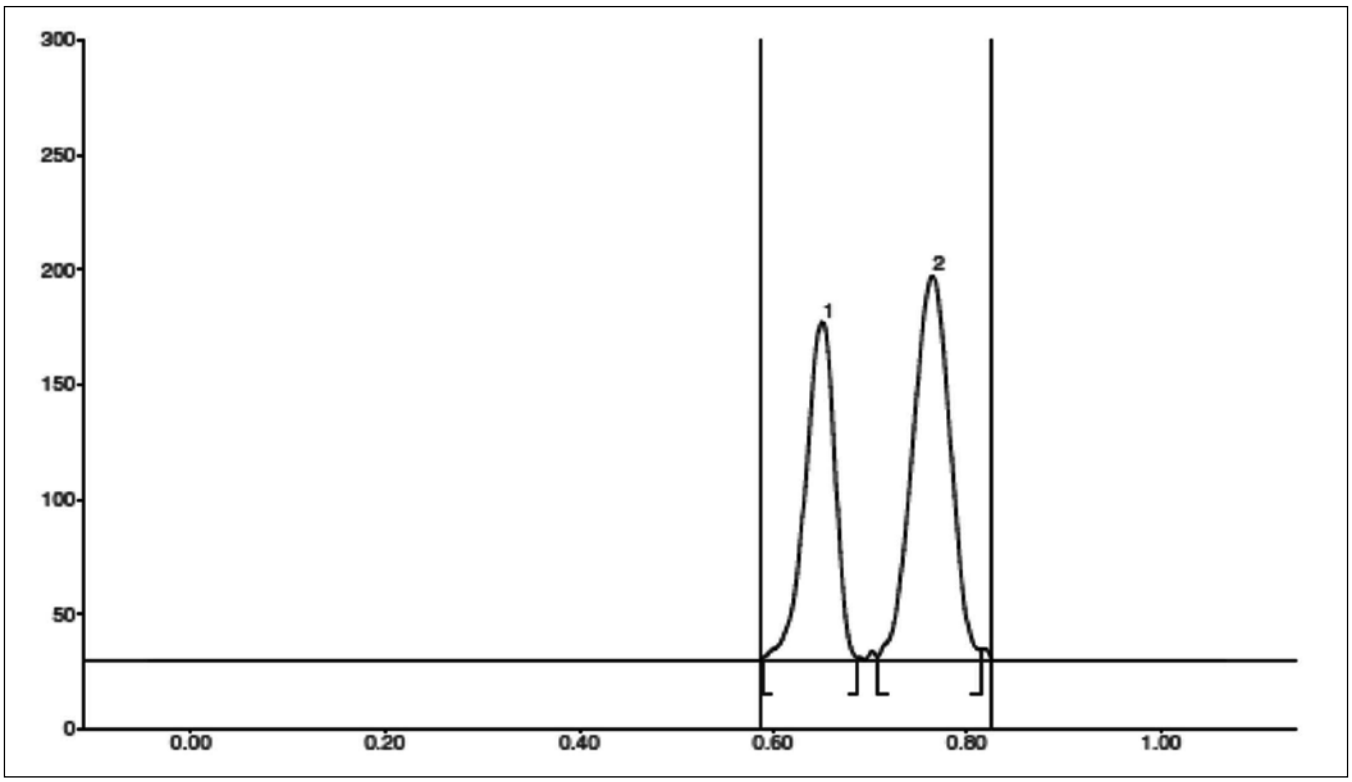

Fig. 1: Densitogram of olmesartan medoximil and metoprolol succinate

Table I: Analysis of marketed formulation

Sample	Label claim	% Label claim found*	Standard deviation*	%RSD*
Olmesartan medoximil	20	99.31	0.5008	0.5024
Metoprolol succinate	50	99.11	0.6667	0.6278

**average of six determinations*

Table II: Results of recovery study

% Level of recovery	Mean % recovery*		Standard Deviation		% RSD	
	OLM	MET	OLM	MET	OLM	MET
80	98.91	99.99	0.3818	0.4000	0.3860	0.4001
100	99.65	100.02	0.4924	0.4100	0.4941	0.4100
120	99.70	100.08	0.2645	0.0692	0.2653	0.0692

**average of three at each level of recovery*

Table III: Method validation parameters

Parameters	OLM	MET
Detection wavelength	233 nm	233 nm
Linearity range (ng/spot)	100-700	100-700
Correlation coefficient	0.9991	0.9992
Detection limit (ng/band)	12.07	17.3
Quantitation limit (ng/band)	37	51.7

olmesartan medoximil and metoprolol succinate. A linear relationship between peak area and concentration was observed for both olmesartan medoximil and metoprolol succinate in the range of 100-700 ng/spot. This range was selected as linear range for analytical method development of both the components.

Procedure for Analysis of Tablet Formulation

Marketed tablets containing 20 mg of olmesartan medoximil and 50 mg of metoprolol succinate were used. Twenty tablets were weighed and finely powdered. A quantity of powder equivalent to 20 mg of olmesartan medoximil and 50 mg of metoprolol succinate was weighed and transferred to a 50 mL volumetric flask containing 25 mL methanol, sonicated for 5 min, and the volume was made up to 50 mL with methanol. The solution was filtered using Whatmann filter paper no. 41. From the filtrate, appropriate aliquots were diluted to 10 mL to furnish sample stock solution of olmesartan medoximil 20 ng/mcL and metoprolol succinate 50 ng/mcL. From sample stock solution, 10 mcL was applied to an HPTLC plate to furnish final amounts of 200 ng per band for olmesartan medoximil and 500 ng per band for metoprolol succinate. After chromatographic development peak areas of the bands were measured at 233 nm and amount of each drug present per tablet was estimated from the respective calibration plots and presented in

Table I. The procedure was repeated six times for analysis of homogeneous samples.

Recovery Studies

The accuracy of proposed methods was checked by recovery study by addition of standard drug solution to preanalysed sample solution at three different concentration levels (80%, 100% and 120% of both API) within the range of linearity for both the drugs. Each being analysed in a manner similar to as described for assay and the recovery of added standard was calculated.The result of recovery study is reported in Table II.

Validation [14]

The developed method was validated as per ICH guidelines for specificity, linearity, accuracy, limit of detection, limit of quantitation. The method is found to be specific for olmesartan medoximil and metoprolol succinate, since it resolved the peak of both drugs (olmesartan medoximil; R_f=0.65 and metoprolol succinate; R_f=0.78) in presence of other excipients in the formulation (Fig. 1). To confirm the specificity of the proposed method, the solution of the formulation was spotted on the TLC plate, developed and scanned. It was observed that the excipients present in the formulation did not interfere with the peak of olmesartan medoximil and metoprolol succinate.

The correlation coefficient and other validation parameters are given in Table III. Deliberate alteration of the analytical conditions showed that areas of the peaks of interest remained unaffected by small change of the operating conditions confirming the robustness of the method.

RESULTS AND DISCUSSION

The method utilizes a precoated silica gel 60 F_{254} on aluminium foil. Different mobile phases containing different ratios of water, methanol and ammonium sulphate were examined. Finally the mobile phase with water-methanol-ammonium sulphate 4.5:4.5:1.5(v/v/v) was selected which gives good separation of olmesartan medoximil (R_f=0.65) and metoprolol succinate (R_f=0.78). The detector response for olmesartan medoximil and metoprolol succinate was found to be linear in the range 100-700 ng/spot. The correlation coefficient obtained for the linearity of both the drugs was 0.9991 and 0.9992 for olmesartan medoximil and metoprolol succinate respectively. The limit of detection and limit of quantitation for olmesartan medoximil and metoprolol succinate was found to be 12.07 ng per band and 17.3 ng per band, and 37 ng per band and 51.7 ng per band respectively. Low values of standard deviation and coefficient of variation are indicative of the high precision of the method.

CONCLUSION

The HPTLC method was found to be accurate and can be applied for routine quality control analysis of olmesartan medoximil and metoprolol succinate from their pharmaceutical preparation.

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