RESEARCH ARTICLE

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Rp-Hplc Method for Estimation of Metoprolol Succinate and Olmesartan Medoxomil in Pharmaceutical Formulation with forced Degradation Studies

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ABSTRACT

A simple, specific, accurate, and precise RP-HPLC method was developed and validated for the simultaneous estimation of Metoprolol Succinate and Olmesartan Medoxomil in pharmaceutical formulation with forced degradation studies. The method was developed using Enable C 18G column (250 ×4.6 mm, 5 µm) with mobile phase consisting of methanol and water (pH adjusted to 3.5 with orthophosphoric acid in the ratio of 80: 20 % v/v with a flow rate of 1 mL/min. The UV detection was carried out at 240 nm. The retention time for Metoprolol Succinate and Olmesartan Medoxomil were found to be 3.986 and 6.092 min, respectively. The proposed method was validated for linearity, range, accuracy, precision, robustness, LOD, and LOQ. Linearity was observed over a concentration range 4-40 µg/mL for Metoprolol Succinate (r2 = 0.9999) and 5-60 µg/ml for Olmesartan Medoxomil (r2 = 0.9999). The % RSD for Intraday and Interday precision was found to be 0.57 and 0.68 for Metoprolol Succinate and 0.52 and 0.41 for Olmesartan Medoxomil. The LOD and LOQ were found to be 0.1143 µg/mL and 0.3565 µg/mL for Metoprolol Succinate and LOD and LOQ were found to be 0.0563 and 0.1782 µg/mL for Olmesartan Medoxomil respectively.

Key words: Forced Degradation, Metoprolol Succinate, Olmesartan Medoxomil and RP-HPLC.

1. INTRODUCTION

Metoprolol Succinate [Figure 1], chemically designated as (±) 1- (isopropylamino)-3-[*p*-(2-methoxyethyl) phenoxy]-2-propanol succinate (2:1). It is a cardioselective drug used alone or combination with other medicines to treat hypertension and various cardiovascular disorders The action of Metoprolol succinate is mediated through the β1-selective adrenoceptor blockage, thus causing a reduction in heart rate and cardiac output (Rajanit Sojitra et al., 2015). Literature survey reveals various analytical method are reported either alone or combination with other drugs includes spectrophotometric, HPLC in pure drug, pharmaceutical formulations, and biological fluids.

Olmesartan Medoxomil [Figure 2] chemically designated as Olmesartan medoxomil is described chemically as the (5-methyl-2-oxo-1,3-dioxol-4-yl) methyl ester of 4-(1-hydroxy-1-methyl ethyl) -2-propyl-1-{[20-(1H-tetrazol-5-yl)[1,10- biphenyl]-4-yl]methyl}-1H-imidazole-5-carboxylic acid. It is a pro-drug and hydrolyzed to olmesartan during absorption from the gastrointestinal tract. Olmesartan is a selective AT1 subtype angiotensin II receptor antagonist. The drug works by inhibiting the effects of angiotensin II, a potent vasoconstrictor and one of the key contributors to cardiovascular and renal disease. It is a selective angiotensin II receptor blocker approved by the US Food and Drug Administration (FDA) in 2002

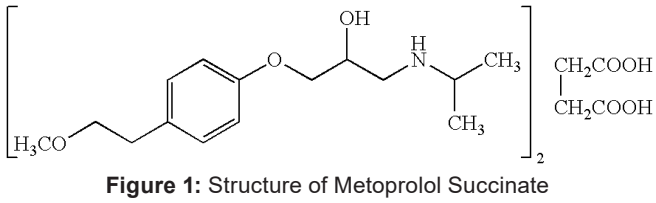

Figure 1: Structure of Metoprolol Succinate

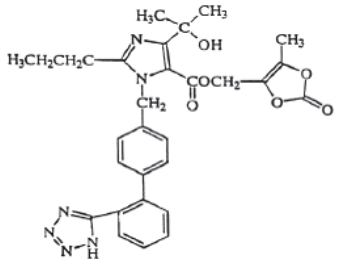

Figure 2: Structure of Olmesartan Medoxomil

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for the treatment of hypertension, used either alone or in combination with other drugs (Muralidharan et al., 2012). Several analytical methods have been reported for the determination of Olmesartan Medoxomil either alone or in combination with other drugs in pure drug, pharmaceutical dosage forms and in biological samples using spectrophotometry, HPLC, HPTLC and Electrophoresis methods. Both drugs are official in the British Pharmacopoeia and the United States Pharmacopoeia. The fixed-dose combination of Metoprolol Succinate and Olmesartan Medoxomil is effective in the treatment of mild to moderate hypertension. The combined dosage form was not only more effective than monotherapy with the individual components but the combination product allows a low-dose multidrug regimen as an alternative to high-dose monotherapy, thereby, minimizing the likelihood of dose-related side-effects. Various analytical methods were reported for simultaneous estimation of Metoprolol Succinate and Olmesartan Medoxomil in pure drug, pharmaceutical formulations and biological fluids by spectrophotometric (Vachhani and Patel , 2011; Chitlange *et al.*, 2012 and HPLC (Olabemiwo *et al.*, 2012; Patel and Patel , 2012; Raval *et al.*, Thakker *et al.*, 2012). Only one stability indicating RP-HPLC method was reported for the simultaneous estimation of both drugs in pharmaceutical formulation but the developed method has long retention time and complex mobile phase composition. Therefore in the present study, an attempt was made to develop a simple, precise, accurate RP-HPLC method with forced degradation studies for the analysis of Metoprolol Succinate and Olmesartan Medoxomil in pharmaceutical formulation.

2. METHODS

2.1 Materials and Chemicals

Metoprolol Succinate and Olmesartan Medoxomil standard were obtained as a gifted sample from-RA Chem Hyderabad. Metoprolol Succinate and Olmesartan Medoxomil tablets (OLMESAR M TABLETS) containing Olmesartan Medoxomil 20 mg and Metoprolol Succinate 25 mg were purchased from a local pharmacy. HPLC grade water was from MERCK India Ltd. HPLC grade methanol was from standard reagent pvt ltd Hyderabad. Analytical grade hydrochloric acid, sodium hydroxide, hydrogen peroxide, and orthophosphoric acid was from SD Fine chemicals Mumbai, India. Nylon membrane filters 0.2 µm and 0.45 µm were from PALL life sciences Mumbai, India. Ultrasonicator used was from LAB India Ltd Mumbai. p^H meter was of Elico LI 120 make. UV Spectrophotometer was of Elico SL 210 model consisted of spectral treats software.

2.2 Instrumentation

The chromatographic system used for the method development and validation consisted of Shimadzu HPLC comprising of LC-20AD binary gradient pump, a variable wavelength programmable SPD-20A detector and an SCL 20A system controller. A Rheodyne injector 7725i fitted with a 20 µL loop was used and data were recorded and evaluated by use of LC solutions software version 5.0.

2.3 Chromatographic Conditions

Chromatographic analysis was performed on Enable C18 G column (250 x 4.6 mm i.d, 5µ). The mobile phase consisted of methanol and water (p^H adjusted to 3.5 with orthophosphoric acid in the ratio of 80:20 %v/v. The flow rate was 1 mL/min, injection volume was 20 µL and detection was carried out at 240 nm using a UV detector.

2.4 Preparations of Metoprolol Succinate and Olmesartan Medoxomil stock solution

A stock solution of Metoprolol Succinate (1000 µg/mL) and olmesartan medoxomil (1000 µg/mL) was prepared separately by transferring accurately weighed 50 mg of metoprolol succinate and 50 mg of olmesartan medoxomil into a 50 mL volumetric flask and to it added a 20 mL methanol. The mixture was sonicated for 5 min to dissolve the drug and the solution was diluted up to the mark with methanol. Standard solutions of Metoprolol Succinate (100 µg/mL) and Olmesartan Medoxomil (100 µg/mL) were prepared by diluting 10 mL of standard stock solution to 100 ml in a volumetric flask with the mobile phase. To prepare a binary mixture of olmesartan medoxomil and metoprolol succinate appropriate volume of standard solution was transferred into a 100 mL volumetric flask and diluted with mobile phase to get a solution containing 20 µg/mL of olmesartan medoxomil and 25 µg/mL of metoprolol succinate.

2.5 Analysis of Metoprolol Succinate and Olmesartan Medoxomil in combined dosage form

Accurately weighed about twenty tablets and an average weight of tablet was determined. The tablets were transferred into a mortar and triturated to a fine powder form. An aliquot of the powder equivalent to 20 mg of Olmesartan Medoxomil and 25 mg of Metoprolol Succinate was transferred into a 100 mL volumetric flask. To it, 20 mL HPLC grade methanol was added and sonicated for 5 min to dissolve the drugs. The content of the flask was kept for 10 min at laboratory temperature and diluted up to mark with HPLC grade methanol this gives a concentration of olmesartan medoxomil 200 µg/mL and

metoprolol succinate 250 µg/mL. The above solution was filtered through 0.2 µ membrane filter. 1 mL of the filtrate was transferred into a 10 mL volumetric flask and diluted with mobile phase to get a concentration of 20 µg/mL and 25 µg/mL for olmesartan medoxomil and metoprolol succinate respectively.

2.6 Method Validation

The method was validated for accuracy, precision, linearity, specificity, robustness, the limit of detection, the limit of quantitation.

Linearity

Linearity was performed by preparing standard solutions of Olmesartan Medoxomil and Metoprolol Succinate at different concentration levels. Olmesartan Medoxomil was prepared in the concentration range of 5-60 µg/mL and 4-40 µg/mL for Metoprolol Succinate. Twenty microliters of each concentration from both drug solutions were injected in duplicate into the HPLC system. The response was carried out at 240 nm, and the corresponding chromatograms were recorded from these mean peak areas were calculated. The calibration curve was plotted by taking concentration on x-axis and peak areas on the y-axis for both the drugs.

Accuracy

The accuracy of the method evaluated by standard addition method in which a known amount of standard drug was added to the fixed amount of pre-analyzed tablet solution. Percent recovery of Olmesartan Medoxomil and Metoprolol Succinate was calculated at three concentration levels of 80%, 100%, and 120%. The solutions were analyzed in triplicate at each level. The percent recovery and % RSD at each level was calculated.

Precision

The precision of the method was evaluated as system precision and method precision.

For the study of system precision, six replicate standard solutions of Olmesartan Medoxomil and Metoprolol Succinate were analyzed. The percent relative standard deviation (%RSD) was calculated for both Olmesartan Medoxomil and Metoprolol Succinate.

Method precision of the analytical method was carried out on six preparations from the tablet formulation, and percentage amount of olmesartan medoxomil and metoprolol succinate in the tablet formulation was calculated. The intraday and interday precision study were conducted for both olmesartan medoxomil and metoprolol succinate. The mean % assay value, standard deviation, and percent relative standard deviation was calculated.

Limit of detection (LOD) and limit of quantitation (LOQ)

LOD was measured by serially diluting the standard solutions of olmesartan ledoxomil and metoprolol Succinate and determining the concentration were the response of sample peaks are three times the noise peak. LOQ was measured by serially diluting the standard solutions of olmesartan medoxomil and metoprolol succinate and determining the concentration were the response of sample peaks are ten times the noise peak.

Robustness

Robustness of the method was determined by making slight changes in the composition of organic phase ± 5%, p^H of mobile phase, flow rate by ± 0.1 mL/min and detection wavelength by ± 2 nm.

Specificity

The specificity of the proposed method was determined against blank and placebo applications. Here mobile phase was used as blank and excipients like starch, lactose, magnesium stearate were used as placebo.

2.7 Forced Degradation studies

Different stress conditions were used for the forced degradation studies of the formulation. These were also used to evaluate the specificity of the method. All the samples were diluted with mobile phase and filtered through 0.2 µ membrane filter.

Acidic conditions

Weighed accurately about twenty tablets and triturated it to a fine powder form. An aliquot of the powder equivalent to 20 mg of Olmesartan Medoxomil and 25 mg of Metoprolol Succinate was transferred into a 100 mL volumetric flask. To this add 50 ml of diluent and sonicated for 10 min to dissolve the drug completely. Then 10 mL of 5N HCl was added to it, refluxed for 6 hr at 60 ^{0}C, cooled to room temperature, neutralized with 5N NaOH and diluted up to the mark with the diluent. The above sample solution was filtered through 0.2 µ nylon membrane filter. Pipette out 1 ml of the above-filtered sample solution into a 10 mL volumetric flask and volume made up to the mark with diluent.

Alkaline conditions

Weighed accurately about twenty tablets and triturated

it to a fine powder form. An aliquOt of the powder equivalent to 20 mg of olmesartan medoxomil and 25 mg of metoprolol succinate was transferred into a 100 mL volumetric flask. To this added a 50 ml of diluent and sonicated for 10 min to dissolve the drug completely. Then 10 ml of 5N NaOH was added to it, refluxed for 6 hr at 60^0C, cooled to room temperature, neutralized with 5N HCl and diluted up to the mark with the diluent. The above sample solution was filtered through 0.2 µ nylon membrane filter. Pipette out 1 ml of the above-filtered sample solution into a 10 ml volumetric flask and volume made up to the mark with diluent.

Oxidative degradation

Weighed accurately about twenty tablets and triturated it to a fine powder form. An aliquot of the powder equivalent to 20 mg of Olmesartan Medoxomil and 25 mg of Metoprolol Succinate was transferred into a 100 ml volumetric flask. To this add 50 ml of diluent and sonicate for 10 min to dissolve the drug completely. Then 5 ml of 30 % hydrogen peroxide was added, refluxed for 2 hour at 60 ^{0}C, then cooled to room temperature and diluted up to the mark with diluents. The above sample solution was filtered through 0.2 µ nylon membrane filter. Pipette out 1 mL of the above-filtered sample solution into a 10 ml volumetric flask and volume made up to the mark with diluent.

Thermal degradation

Weighed accurately about twenty tablets and triturate it to a fine powder form. The powder sample was subjected to thermal stress at 105 ^{0}C for about 2 days. An aliquot of the powder equivalent to 20 mg of olmesartan medoxomil and 25 mg of metoprolol succinate was transferred into a 100 mL volumetric flask. To this added 50 mL of diluent and sonicated for 10 min to dissolve the drug completely and diluted up to mark with diluents. The above sample solution was filtered through 0.2 µ nylon membrane filter. Pipette 1mL of the above-filtered sample solution into a 10 mL volumetric flask and volume made up to the mark with diluent.

Photolytic Degradation

Weighed accurately about twenty tablets and triturate it to a fine powder form. The powder sample was subjected to UV light in a photostability chamber for about 10 days. An aliquot of the powder equivalent to 20 mg of olmesartan medoxomil and 25 mg of metoprolol Succinate was transferred into a 100 ml volumetric flask. To this, add 50 mL of diluent and sonicated for 10 min to dissolve the drug completely and diluted up to mark with diluents. The above sample solution was filtered through 0.2 µ nylon membrane filter. Pipette 1 mL of the above-filtered sample solution into a 10 ml volumetric flask and volume made up to the mark with diluent.

3. RESULTS AND DISCUSSION

Optimization of chromatographic conditions

In the present work, an analytical method based on RP-HPLC using UV detector was developed and validated for simultaneous estimation of Olmesartan Medoxomil and Metoprolol Succinate in pharmaceutical formulation. The selection of analytical conditions was based on the chemical nature of Olmesartan Medoxomil and Metoprolol Succinate. A systematic study of various factors was undertaken by varying one parameter at a time and keeping all other conditions constant for development of the analytical method. Both Olmesartan Medoxomil and Metoprolol Succinate were soluble in polar solvents; therefore, RP-HPLC was chosen. The selection of stationary phase has been done on the basis of back pressure, resolution, peak shape, theoretical plates, and day to day reproducibility in retention time resolution between Olmesartan Medoxomil and Metoprolol Succinate peaks. After evaluating all these factors Enable C18 G column (250 x 4.6 mm i.d, 5µ) was chosen for the analysis. For optimization of mobile phase preliminary trials were conducted under isocratic conditions using mobile phases composed of a mixture of solvents like water, methanol, and acetonitrile with or without orthophosphoric in different combinations. A mixture of Methanol and water (p^H 3.5) in the ratio of 80:20 v/v was found to be most suitable of all the combinations since the chromatographic peaks obtained were have good system suitability parameters. The Flow rate of mobile phase was optimized based on the resolution between chromatographic peaks and minimal solvent consumption. The flow rate of mobile phase was changed from 0.5-2 ml/min. It was found from trials that 1 ml/min flow rate was ideal for successful elution of both drugs. For the selection of analytical wavelength, standard solutions of both drugs were scanned in the wavelength range of 200-350 nm. A detection wavelength of 240 nm was selected. The chromatogram of the sample was shown in Figure 3

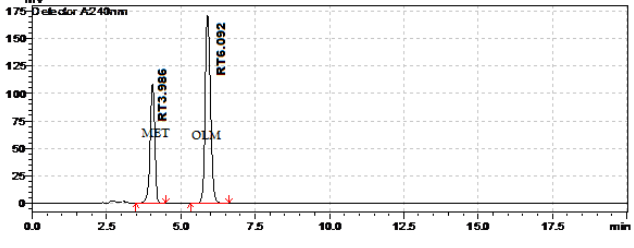

Figure 3: Chromatogram of Metoprolol Succinate and Olmesartan Medoxomil

Linearity

Linearity was studied by preparing standard solutions at different concentration levels. The linearity ranges for Metoprolol Succinate and Olmesartan Medoxomil were found to be 5-60 µg/mL and 4-40 µg/mL respectively. The linear regression equation for metoprolol succinate was found to be 6510x + 1410 with correlation coefficient 0.9982. The linear regression equation for Olmesartan Medoxomil was found to be 29518x + 2445 with correlation coefficient 0.9993. The calibration table for metoprolol succinate and olmesartan medoxomil was shown in Table 1 and 2, respectively. The calibration curve of metoprolol succinate and Olmesartan Medoxomil were shown in Figure 4 and 5, respectively.

Accuracy

The percent recovery of Olmesartan Medoxomil and Metoprolol Succinate was found to be 100.42-100.56 % and 99.84-100.58%. This indicates the accuracy of the method. The results are shown in Table 3 and 4.

Precision

System precision

The %RSD for Olmesartan Medoxomil was found to be 0.64 and for Metoprolol Succinate was found to be 1.44, which are within the acceptance criteria of not more than 2.0 indicates the precision of the method. Table 5.

Method Precision

The %RSD for Intraday and Interday precision assay results of six preparations for olmesartan medoxomil were found to be 0.52 and 0.41, respectively which are within the acceptance criteria of not more than 2.0 indicates the precision of method. The %RSD for Intraday and Interday precision assay results of six preparations for Metoprolol Succinate were found to be 0.57 and 0.68 respectively which are within the acceptance criteria of not more than 2.0 indicates the precision of the method Table 6.

Limit of detection and Limit of quantitatation

The LOD and LOQ were found to be 0.1143 µg/mL and 0.3565 µg/mL for Metoprolol Succinate and the LOD and LOQ for Olmesartan Medoxomil were 0.0563 µg/mL and 0.1782 µg/mL respectively.

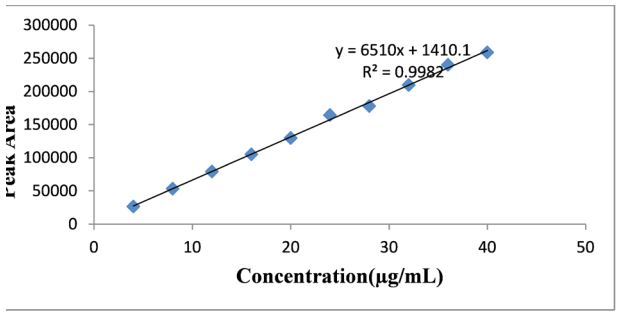

Figure 4. Linearity plot of Metoprolol Succinate

Table 1: Linearity data for Metoprolol Succinate

Level	*Concentration of Metoprolol Succinate(µg/mL)*	*Mean peak area*
Level-1	4	26843
Level-2	8	53688
Level-3	12	79351
Level-4	16	105371
Level-5	20	129980
Level-6	24	164521
Level-7	28	177901
Level-8	32	209793
Level-9	36	240031
Level-10	40	258830
Slope		6510
Intercept		1410
Correlation Coefficient		0.9982

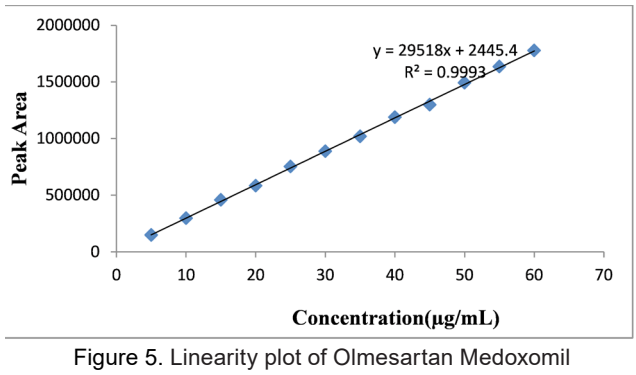

Figure 5. Linearity plot of Olmesartan Medoxomil

Table 2: Linearity data for Olmesartan Medoxomil

Level	*Concentration of Olmesartan Medoxomil (µg/mL)*	*Mean peak area*
Level-1	05	148603
Level-2	10	297211
Level-3	15	458291
Level-4	20	583824
Level-5	25	752518
Level-6	30	889163
Level-7	35	1019972
Level-8	40	1188341
Level-9	45	1298041
Level-10	50	1492418
Level-11	55	1635572
Level-12	60	1777459
Slope		29518
Intercept		2445
Correlation Coefficient		0.9993

Table 3: Accuracy results of Olmesartan Medoxomil

Accuracy level (%)	*Amount taken(µg/mL)*	*Amount found(µg/mL)*	*% Recovery*	*Mean Recovery*	*% RSD*
	16	15.94	99.62		
80	16	16.22	101.31	100.42	0.83
	16	16.08	100.52		
	20	20.12	100.63		
100	20	20.14	100.73	100.56	0.14
	20	20.09	100.41		
	24	24.16	100.60		
120	24	24.11	100.46	100.42	0.11
	24	24.06	100.21		

Table 4: Accuracy results of Metoprolol Succinate

Accuracy level (%)	Amount taken(µg/mL)	Amount found (µg/mL)	% Recovery	Mean Recovery	% RSD
	20	20.15	100.71		
80	20	20.03	100.12	100.58	0.40
	20	20.18	100.91		
	25	24.89	99.56		
100	25	24.91	99.64	99.84	0.43
	25	25.08	100.32		
	30	30.04	100.13		
120	30	30.12	100.40	100.29	0.13
	30	30.11	100.36		

Table 5: System precision results for olmesartan medoxomil and metoprolol succinate

Injection No.	*Peak area of olmesartan medoxomil*	*Peak area of metoprolol succinate*
1	583824	164521
2	587982	169910
3	581254	164731
4	589013	164440
5	581131	168351
6	588962	168202
Mean	585361	166692
SD	3749.5	2409
%RSD	0.640	1.44

Table 6: Method precision results for Olmesartan Medoxomil and Metoprolol Succinate

	Olmesartan Medoxomil(%Assay)		*Metoprolol Succinate(%Assay)*	
Set	*Intraday(n = 6)*	*Interday(n = 6)*	*Intraday(n = 6)*	*Interday(n = 6)*
1	100.15	100.46	99.98	100.74
2	100.47	100.40	100.69	100.16
3	100.84	100.29	100.09	99.13
4	99.66	100.12	99.34	99.52
5	99.96	99.69	100.72	100.84
6	99.41	100.96	100.82	100.38
Mean	100.08	100.32	100.27	100.12
SD	0.52	0.41	0.57	0.68
%RSD	0.52	0.41	0.57	0.68

Robustness

To evaluate the robustness of the developed method, small deliberate variations in optimized method parameters were made. The effect of change in flow rate, change in p^H, change in the composition of mobile phase, and detection wavelength on retention time, tailing factor, and theoretical plates were studied. The method was found to be unaffected by small changes in flow rate, change in pH, change in the composition of the mobile phase, and detection wavelength, as shown in Table 7 and 8.

Specificity

Specificity is the ability to unequivocally assess the analyte in the presence of components that may be expected to be present. Typically, these might include impurities, degradants, or matrix. The specificity of an analytical method is its ability to accurately and specifically measure the analyte of interest without interference from blank or placebo. The peak purities of metoprolol succinate and olmesartan medoxomil were assessed by comparing the retention times of standard metoprolol succinate and olmesartan medoxomil and the sample, and good correlation was obtained between the retention time of the standard and sample. Placebo and blank were injected, and there were no peaks. There is no interference of degradation peaks on drug peaks. Hence, the method is specific. The specificity results are shown in Table 9.

Analysis of commercial formulation

The proposed method was applied for the determination of Metoprolol Succinate and Olmesartan Medoxomil in marketed formulations available (OLMESAR M TABLETS). The % recovery was found to be 100.32±0.18 and 100.7±0.45 for Metoprolol Succinate and Olmesartan Medoxomil, respectively shown in Table 10.

Table 7: Robustness results for Metoprolol Succinate

		System Suitability parameters	
Conditions	*% Assay*	*Theoretical Plates*	*Tailing Factor*
Flow Rate 0.9 mL/min	99.89	6410	1.07
Flow Rate 1.1 mL/min	99.92	6321	1.09
Mobile Phase- Water(25):Methanol(65)	100.34	6341	1.08
Mobile Phase- Water(15):Methanol(85)	100.23	6372	1.08
Mobile Phase pH 3.7	100.58	6251	1.08
Mobile Phase pH 3.3	100.76	6299	1.08
Wavelength 242 nm	100.24	6373	1.08
Wavelength 238 nm	100.36	6364	1.09

Table 8: Robustness results for Olmesartan Medoxomil

		System Suitability parameters	
Conditions	*% Assay*	*Theoretical Plates*	*Tailing Factor*
Flow Rate 0.9 mL/min	100.35	8430	1.16
Flow Rate 1.1 mL/min	100.42	8678	1.19
Mobile Phase- Water(25):Methanol(75)	100.28	8689	1.18
Mobile Phase- Water(15):Methanol(85)	100.21	8474	1.18
Mobile Phase pH 3.7	100.57	8544	1.18
Mobile Phase pH 3.3	100.32	8466	1.18
Wavelength 242 nm	100.42	8615	1.18
Wavelength 238 nm	100.19	8720	1.17

Table 9: Specificity results of the method

Name of solution	*Retention Time*
Blank	No peaks
Placebo	No peaks
Olmesartan Medoxomil	6.092 min
Metoprolol Succinate	3.986 min

Table 10: Analysis of Metoprolol Succinate and Olmesartan Medoxomil in the commercial formulation

	Labelled claim(mg)		*Amount found*(mg)*		*%Recovery*±%RSD*	
Formulation	*Metoprolol Succinate*	*Olmesartan Medoxomil*	*Metoprolol Succinate*	*Olmesartan Medoxomil*	*Metoprolol Succinate*	*Olmesartan Medoxomil*
OLMESAR M TABLETS	25	20	25.08	20.14	100.32±0.18	100.7±0.45

*Average of three determinations

Table 11: Forced degradation studies of Olmesartan Medoxomil and Metoprolol Succinate

Stress Conditions	*Duration*	*%Drug Recovered*	*% Drug decomposed*	*Retention Time (min)*	*Theoretical Plates*	*Tailing Factor*
			Olmesartan Medoxomil			
Control Sample	----	100.7	----	6.092	8856	1.18
Acid Degradation	6 hr	100.49	0.21	6.016	8769	1.21
Alkaline Degradation	6 hr	80.51	20.19	6.092	8441	1.21
Oxidative Degradation	2 hr	91.69	9.01	5.606	8923	1.19
Thermal Degradation	2 days	95.52	5.18	6.092	8454	1.19
Photolytic Degradation	10 days	96.42	4.28	6.052	8621	1.18
			Metoprolol Succinate			
Control Sample	----	100.32	---	3.986	6372	1.08
Acid Degradation	6 hr	98.77	1.55	4.012	6453	1.07
Alkaline Degradation	6 hr	90.69	9.63	3.986	6478	1.08
Oxidative Degradation	2 hr	85.15	15.17	3.786	6509	1.09
Thermal Degradation	2 days	87.52	12.8	3.986	6435	1.08
Photolytic Degradation	10 days	93.77	6.55	3.982	6689	1.08

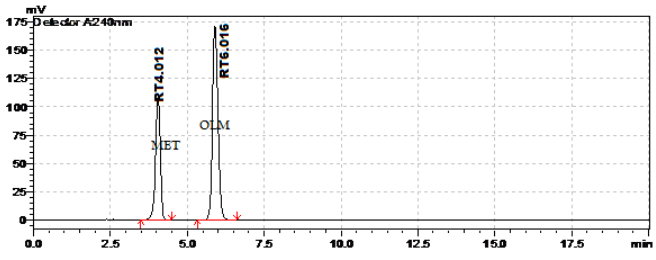

Fig 6. Acid degradation chromatogram

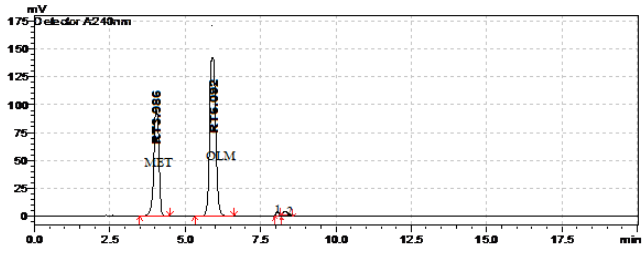

Figure 7: Base degradation chromatogram

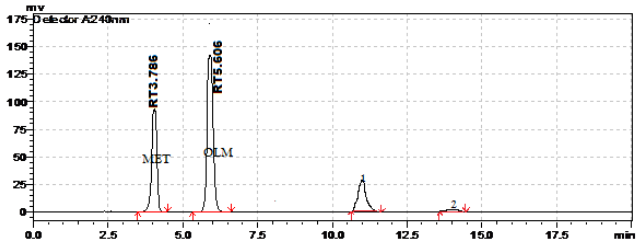

Figure 8: Oxidative degradation chromatogram

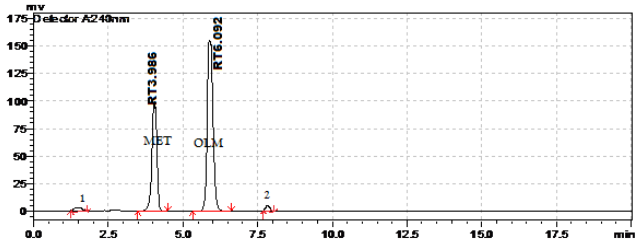

Figure 9: Thermal degradation chromatogram

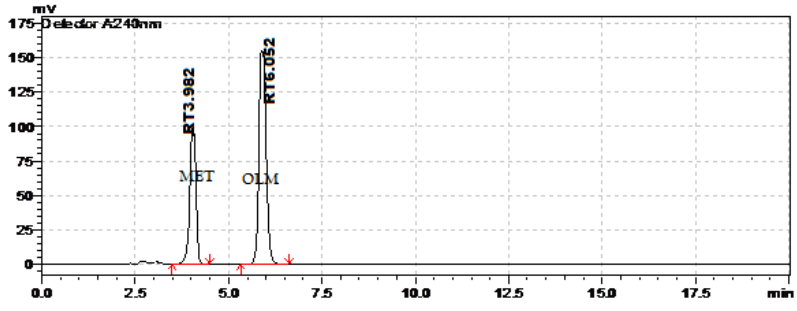

Fig 10: Photolytic degradation chromatogram

Results of Forced degradation studies

Under acidic conditions, metoprolol succinate degraded to 1.55 % and Olmesartan Medoxomil degraded to 0.21%. In these stress conditions, there is no appearance of degradation peak on the chromatogram. In basic conditions, Metoprolol Succinate degraded to 9.63 % and Olmesartan Medoxomil degraded to 20.19 %. Under these conditions,

two degradant peaks appear at retention times of 8.023 min and 8.601 min 2.321. In oxidative conditions, metoprolol succinate degraded to 15.17 % and olmesartan medoxomil to 9.01%. The degradant peak detected at retention times of 11.021 min and 14.201 min. In thermal conditions, Metoprolol Succinate degraded to 12.8 % and Olmesartan Medoxomil degraded to 5.18 %. The two degradant peaks appear at retention times of 1.603 min and 7.713 min on the chromatogram. In photolytic conditions, metoprolol succinate degraded to 6.55 % and olmesartan medoxomil degraded to 4.28 % here both the drugs degraded to a significant extent but no peaks were detected. From the degradation studies, it was concluded that both drugs showed stability towards an acidic condition wherein remaining conditions they degraded to a significant extent.

The proposed method for the simultaneous estimation of Metoprolol Succinate and Olmesartan Medoxomil validated as per the ICH guidelines, and it is simple, specific, and reliable. The data generated from the forced degradation studies enabled the evaluation of Metoprolol Succinate and Olmesartan Medoxomil stability under a variety of ICH recommended conditions. These data are valuable for the safety and potency assessment of a drug product. Furthermore, this simple and rapid RP-HPLC method can also be used successfully for the determination of Metoprolol Succinate and Olmesartan Medoxomil in pharmaceutical formulations without any interference from the excipient.

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