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ORIGINAL ARTICLE

Applying green analytical chemistry for rapid analysis of drugs: Adding health to pharmaceutical industry

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Abstract Green RP-HPLC method for a rapid analysis of olmesartan medoxomil (OLM) in bulk drugs, self-microemulsifying drug delivery system (SMEDDS) and marketed tablets was developed and validated in the present investigation. The chromatographic identification was achieved on Lichrosphere 250 × 4.0 mm RP C_8 column having a 5 μm packing as a stationary phase using a combination of green solvents ethyl acetate:ethanol (50:50% v/v) as a mobile phase, at a flow rate of 1.0 mL/min with UV detection at 250 nm. The proposed method was validated for linearity, selectivity, accuracy, precision, reproducibility, robustness, sensitivity and specificity. The utility of the proposed method was verified by an assay of OLM in SMEDDS and commercial tablets. The proposed method was found to be selective, precise, reproducible, accurate, robust, sensitive and specific. The amount of OLM in SMEDDS and commercial tablets was found to be 101.25% and 98.67% respectively. The proposed method successfully resolved OLM peak in the presence of its degradation products which indicated stability-indicating property of the proposed method. These results indicated that the proposed method can be successfully employed for a routine analysis of OLM in bulk drugs and commercial formulations.

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1. Introduction

The pursuit in the field of green chemistry is growing dramatically and is becoming a grand challenge for chemists to develop new products, processes and services that achieve the necessary social, economical and environmental objectives due to an increased cognizance of environmental safety,

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checking environmental pollution, sustainable industrial ecology and cleaner production technologies worldwide. Many solvents used in the analytical methodologies are volatile organic compounds (VOCs), that are hazardous air pollutants (HAPs), flammable, toxic and/or carcinogenic [e.g., the majority of analytical methods certified by the US Environmental Protection Agency (EPA) and Food and Drug Administration (FDA) use corrosive and toxic chemicals, with no other options currently available] (Garrigues et al., 2010). They also pose serious environmental, health, and safety (EHS) concerns, including human and eco-toxicity issues, process safety hazards, and waste management issues.

Olmesartan medoxomil (OLM) is chemically 2,3 dihydroxy-2-butenyl 4-(1-hydroxy-1-methylethyl)-2-propyl-1-[*p*-(o-1H-tetrazol-5-ylphenyl)benzyl]imidazole-5-carboxylate, cyclic 2,3-carbonate as shown in Fig. 1 (Celebier and Altinoz, 2007a).

It is an ester prodrug which metabolizes to its active metabolite olmesartan (OL) after in vivo absorption (Bari and Rote, 2009). Pharmacologically, it belongs to angiotensin II receptor antagonist which is used in the treatment of hypertension either alone or in combination with other antihypertensive agents (Celebier and Altinoz, 2007a; Qutab et al., 2009; Amudhavalli et al., 2011).

An extensive literature survey revealed that many analytical methods have been reported for the analysis of OLM either alone or in combination with other antihypertensive drugs in pure drugs, marketed tablets and biological fluids. Several high performance liquid chromatography (HPLC) methods were reported for the analysis of OLM alone or in combination with other antihypertensive agents in pure drugs or tablet dosage forms (Patel et al., 2007; Sagirli et al., 2007; Bari and Rote, 2009; Bajerski et al., 2008; Murakami et al., 2008; Sultana et al., 2008; Birajdar et al., 2009; Rane et al., 2009; Sharma and Pancholi, 2009; Trivedi et al., 2009; Qutab et al., 2009; Godse et al., 2010; Kamble et al., 2010; Patil et al., 2010; Amudhavalli et al., 2011; Rao et al., 2012). Some spectrophotometric methods have also been reported for the quantitative analysis of OLM alone or in combination with other antihypertensive agents in pure drugs or pharmaceutical formulations (Celebier and Altinoz, 2007b; Patel et al., 2007; Bhosari et al., 2009; Hemke et al., 2010; Rote and Bari, 2010; Darwish et al., 2012). High performance thin layer chromatography (HPTLC) methods were also recorded for the analysis of OLM in tablet dosage forms (Shah et al., 2007; Bari and Rote, 2009; Kadukar et al., 2009; Kamble et al., 2010; Moussa et al., 2011). Ultra performance liquid chromatography (UPLC) methods have also been reported for quantification of OLM in pharmaceutical formulations (Kumar et al., 2012; Raj et al., 2012). The capillary zone electrophoretic (CZE) method was also used for the quantitative analysis of OLM in tablet dosage forms (Celebier and Altinoz, 2007b). Some analytical techniques like HPLC (Sultana et al., 2008; Tambe et al., 2010), HPTLC (Tambe et al., 2010) and liquid chromatography–mass spectrometry [LCMS] (Liu et al., 2007; Vaidya et al., 2008; Liu et al., 2010; Sengupta et al., 2010) methods have also been reported for the quantification of OLM in various biological fluids like plasma, serum and urine.

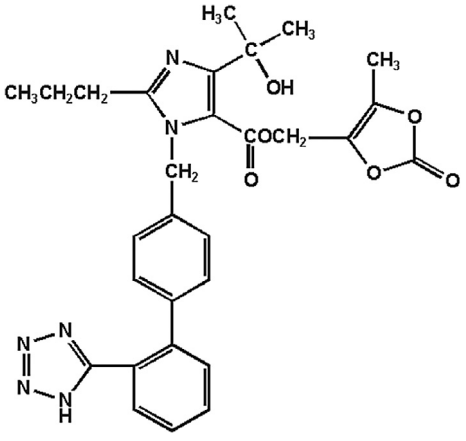

Figure 1 Chemical structure of OLM.

On analyzing the scientific articles of the past several years available for the assay of OLM, it becomes clear that organic and mixed aqueous-organic solvent systems have been found most useful for its analysis. Majority of these solvents are volatile organic compounds and pose a threat to the environment as they form low-level ozone and smog through free radical air-oxidation processes. The main goal of the green analytical chemistry is to take into consideration the amount and the toxicity of reagents consumed, and, consequently, the volume and the toxicity of wastes generated during method development and selection, thus reducing the environmental impact of the activities of analytical chemistry (Anastas and Warner, 1998; Sheldon, 2005). Green solvents or biosolvents are more an environment-friendly alternative to petrochemical solvents, which are derived from the processing of agricultural crops, for example, ethyl acetate and ethanol.

To our surprise, in spite of several favorable features such as non-toxicity, non-inflammability, non-aggressiveness, high biodegradability and cost effectiveness, the full potential of environmentally benign solvents (and their combinations) as eluents for the analysis of drugs/pharmaceuticals has not been exploited (Salvador and Chisvert, 2001; Vidotti et al., 2006).

To our knowledge, the stability-indicating green reverse phase HPLC (RP-HPLC) method using environmentally benign eluents (ethyl acetate and ethanol) has not been reported in the literature for the analysis of OLM in pharmaceutical formulations and biological fluids. Therefore, the aim of the present study was to develop and validate a simple, cost effective, rapid, facile, selective, precise, reproducible, accurate, robust and stability-indicating green RP-HPLC method coupled with UV detection for the rapid analysis of OLM in the self-microemulsifying drug delivery system (SMEDDS) and marketed tablets utilizing a combination of ethyl acetate and ethanol (50:50) as mobile phase and isocratic elution, taking into consideration a variety of international conference on harmonization (ICH) recommended test conditions (ICH, 2003).

The novelty of this method is that it used an environmentally benign mobile phase (ethyl acetate and ethanol) with C_8 RP-HPLC column for the rapid analysis of OLM. The developed method would also be utilized for studying the stability of OLM in various commercial and in-house developed pharmaceutical formulations.

Moreover, this study is advantageous because it protects analytical scientists and chemists from the exposure to volatile and corrosive organic solvents during experimentation.

2. Experimental

2.1. Chemicals and reagents

OLM (purity 99.2%) was obtained as a gift sample from Alfa Aesar, A Johnson Metthey Company (Ward Hill, MA). HPLC grade ethyl acetate and ethanol, hydrochloric acid, sodium hydroxide and hydrogen peroxide were purchased from BDH Laboratory supplies (Liverpool, UK). All other chemicals and reagents used were of analytical reagent (AR) grade. Commercial tablets were purchased from the local market of Riyadh, Saudi Arabia. OLM SMEDDS was prepared in the laboratory by the reported method using Capryol-90 as the oil phase, Tween-20, Tetraglycol, and distilled water as surfactant, cosurfactant and aqueous phase respectively (Lee et al., 2009).

2.2. Instrumentation and chromatographic conditions

Chromatographic identification was performed at room temperature (25 ± 1 °C), with Waters HPLC system (Waters, USA) equipped with a model 600 LC pump, model 717 autosampler, quaternary LC-10A VP pumps, a programable UV–visible variable-wavelength detector, SPD-10AVP column oven, a SCL 10AVP system controller (Shimadzu, Japan) and a vacuum degasser was used. The software used in the system was Millennium, version 32. The chromatographic identification was achieved on a Lichrosphere 250 × 4.6 mm RP C_8 column (Phenomenex, USA) having a 5 μm packing as a stationary phase. The green solvents ethyl acetate:ethanol (50:50% v/v) was used as an environmentally benign mobile phase. The elution was performed at a flow rate of 1.0 mL/min with UV detection at 250 nm. Samples (10 μL) were injected using a Waters auto sampler.

2.3. Preparation of drug stock solution for calibration curve

Calibration curve for OLM was prepared in the range of 0.1–200 μg/mL. Stock solution of 200 μg/mL concentration was prepared by dissolving 20 mg of OLM in a mobile phase. Serial dilutions from this stock solution were made by diluting the required aliquots with a mobile phase to get the concentration in the range of 0.1–200 μg/mL.

2.4. Method development

The selection of the solvent system was decided on the basis of the sensitivity of the assay, suitability for stability studies, time required for the analysis, peak parameter, ease of preparation and availability of cost effective green solvents. Based on the above criterion, we had tried ethanol, ethyl acetate, ethanol–water, ethyl acetate–ethanol, Tween-80, Tween 80–water, glycerol and glycerol–water alone as well as at different proportions. Out of the tried mobile phases for chromatographic identification, the environmentally benign combination of ethyl acetate and ethanol (50:50% v/v) was selected as the final mobile phase for further studies.

2.5. Validation studies

The proposed green RP-HPLC method was validated according to ICH guidelines for the linearity, selectivity, accuracy, precision, reproducibility, sensitivity, robustness and specificity.

Freshly prepared linearity solutions of different concentrations (0.1–200 μg/mL) were used for the construction of calibration curves. The mobile phase (ethyl acetate:ethanol 50:50% v/v) was delivered at 1.0 mL/min for column equilibration; the baseline was monitored continuously during this process. The detection was performed at 250 nm. The prepared dilutions were injected in triplicates and peak areas were recorded for each dilution, and the concentration was plotted against peak areas.

The selectivity of the green RP-HPLC method was determined by repeated injections of target concentration of OLM (20 μg/mL). The variations in retention time and peak area were recorded for selectivity determination.

Accuracy of the proposed method was determined by the standard addition method. The standard OLM solution (20 μg/ml) was spiked with 0, 50, 100 and 150% extra OLM standard solution and were reanalyzed by the proposed method. Experiments were performed in triplicates. Recovery (%), RSD (%), and standard error were calculated for each concentration.

Precision of the green HPLC method was determined as repeatability (intraday precision) and intermediate precision. Repeatability studies were performed by an analysis of four different concentrations of the drug (20, 30, 40 and 50 μg/mL) in triplicate on the same day. Intermediate precision of the method was checked by repeating the studies on three different days.

The reproducibility of the proposed method was evaluated by determining intraday and intermediate precision on a different instrument, analysis was performed by a different scientist in a different laboratory. For both intraday and intermediate variations, solutions of OLM at four different concentrations (20, 30, 40 and 50 μg/mL) were analyzed in triplicate.

Detection (LOD) and quantification (LOQ) limits of the green HPLC method were determined by the standard deviation (SD) method. For determination of LOD and LOQ, blank samples (samples without OLM) were injected in triplicate and the peak area of these blank samples was recorded. LOD and LOQ were determined from the slope (S) of the calibration curve and the standard deviation (SD) of the response by use of the formulae $LOD = 3.3 \times SD/S$ and $LOQ = 10 \times SD/S$.

The robustness of the green HPLC method was determined to evaluate the effect of the deliberate variation of chromatographic conditions on the determination of OLM. The target concentration (20 μg/mL) was selected for these studies. Robustness was determined by changing the mobile phase composition from 50:50 to 45:55 and 55:45, flow rate from 1.0 mL/min to 0.75 and 1.25 mL/min and wavelength of detection from 250 nm to 248 and 252 nm.

2.6. Forced degradation studies

In order to determine the stability-indicating property and specificity of the green HPLC method, force degradation studies were performed at various stress conditions such as acid stress, base stress, oxidative stress and thermal stress conditions.

For acid and base-induced degradation, the target concentration (20 μg/mL) of OLM was freshly prepared into a mobile phase for acid and base-induced degradation studies.

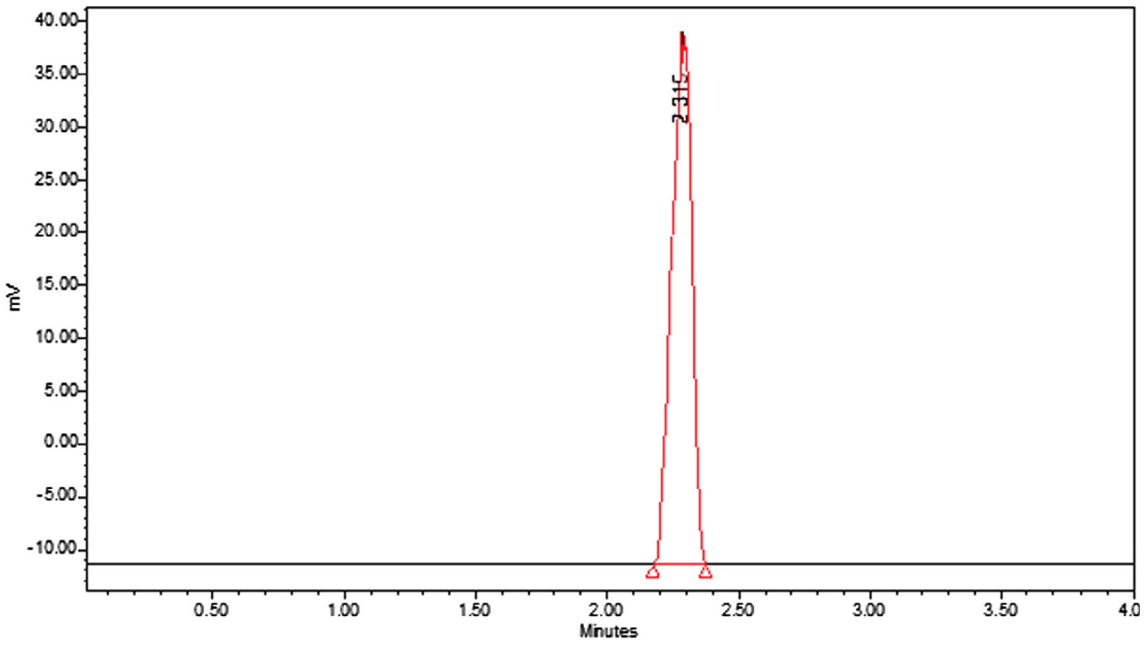

Figure 2 HPLC chromatogram of OLM in ethyl acetate:ethanol (50:50% v/v) with retention time of 2.13 min.

Table 1 Linear regression data for the calibration curves of OLM (n = 3).

Parameters	Values
Linearity range	0.1–200 μg/ml
Correlation coefficient (r^2 ± SD)	0.999 ± 0.0005
Regression equation	y = 9930x–19117
Slope ± SD	9930.00 ± 45.32
Confidence interval of slope*	9817.43–10042.56
Standard error of slope	26.16
Slope without intercept ± SD	9760.50 ± 39.14
Intercept ± SD	19117.00 ± 561.37
Confidence interval of intercept*	17722.32–20511.64
Standard error of intercept	324.11

* 95% confidence interval.

An aliquot of this solution (20 μg/mL) was exposed to acid and base hydrolysis by adding 4 mL of 1 M HCl and 4 mL of 1 M NaOH, respectively. These mixtures were kept in a hot air oven for 48 h at 50 °C and then reanalyzed by the green HPLC method for the determination of OLM in the presence of its acid and base degradation products respectively.

For oxidative degradation, the target concentration (20 μg/mL) of OLM was prepared into a mobile phase for oxidative degradation studies. An aliquot of this solution (20 μg/mL) was exposed to oxidative degradation by adding 4 mL of 30% hydrogen peroxide (H_2O_2). This mixture was kept in the hot air oven for 48 h at 50 °C and then analyzed by the green HPLC method for the determination of OLM in the presence of its oxidative degradation products.

For thermal degradation, an aliquot of target solution (20 μg/mL) was exposed to thermal degradation by exposing it in the hot air oven for 48 h at 50 °C and then analyzed by the green HPLC method for the determination of OLM in the presence of its thermal degradation products.

2.7. Solution stability studies

To ensure the reliability of the results in relation to handling and storage of stock standards, solution stability studies were performed at the target concentration (20 μg/mL) by a repeated analysis of the samples over a period of 72 h at ambient temperature (25 ± 1 °C) and at the refrigerated temperature (4 ± 0.5 °C).

Table 2 Selectivity of the green HPLC method (n = 6).

S. no.	Concentration (μg/ml)	Peak Area	Mean area ± SD	RSD (%)	R_t (min)	Mean R_t ± SD (% RSD)
1		185431			2.13	
2		176543			2.14	
3	20	172376	180239 ± 2050	1.13	2.13	2.14 ± 0.011 (0.51)
4		182312			2.15	
5		179865			2.14	
6		191412			2.16	

Table 3 Accuracy of the green HPLC method (% recovery, $n = 3$).

% of Drug added to analyte	Theoretical concentration (μg/ml)	Measured concentration (μg/ml) ± SD	RSD (%)	Standard error	% Recovery
0	20	19.66 ± 0.26	1.32	0.15	98.30
50	30	30.52 ± 0.54	1.76	0.31	101.73
100	40	40.32 ± 0.77	1.90	0.44	100.80
150	50	49.01 ± 0.85	1.74	0.49	98.02

Table 4 Precision of the green HPLC method (n = 3).

Concentration (μg/ml)	Repeatability (intra-day precision)			Intermediate precision (inter-day)		
	Mean area ± SD	RSD (%)	Standard error	Mean area ± SD	RSD (%)	Standard error
20	184346 ± 1134	0.61	654	172814 ± 1814	1.04	1047
30	271151 ± 1532	0.56	884	268978 ± 2032	0.75	1173
40	373214 ± 2832	0.75	1635	367865 ± 3725	1.01	2150
50	441087 ± 3498	0.79	2019	445432 ± 4172	0.93	2408

Table 5 Reproducibility of the green HPLC method ($n = 3$).

Concentration (μg/ml)	Repeatability (Intra-day precision)			Intermediate precision (Inter-day)		
	Mean area ± SD	RSD (%)	Standard error	Mean area ± SD	RSD (%)	Standard error
20	178415 ± 1321	0.74	762	170487 ± 2098	1.23	1211
30	268743 ± 1765	0.65	1019	264321 ± 2243	0.84	1295
40	370145 ± 3045	0.82	1758	364217 ± 3813	1.04	2201
50	437654 ± 3765	0.86	2173	441987 ± 4278	0.96	2469

Table 6 Robustness of the green HPLC method ($n = 3$).

Parameters	Mean area ± SD	RSD (%)	Standard error	Retention time ± SD	RSD (%)	Standard error
Mobile phase composition						
(55:45% v/v)	178751 ± 1605	0.89	926.67	2.16 ± 0.02	1.06	0.011
(45:55% v/v)	175108 ± 1819	1.03	1050.23	2.18 ± 0.01	0.52	0.005
Mobile phase flow rate						
(1.25 ml/min)	181043 ± 2213	1.22	1277.71	2.01 ± 0.02	1.14	0.011
(0.75 ml/min)	177876 ± 2341	1.31	1351.61	2.25 ± 0.03	1.37	0.017
Detection wavelength (nm)						
248	169032 ± 2554	1.51	1474.59	2.13 ± 0.02	1.09	0.011
252	185421 ± 2672	1.44	1542.72	2.14 ± 0.03	1.63	0.017

Table 7 Results of forced degradation studies of OLM at various stress conditions ($n = 3$).

Stress condition	Mean area ± SD	RSD (%)	Standard error	Number of degradation products (R_t)	OLM remaining (μg/ml)	OLM recovered (%)
1 M HCl	125632 ± 1542	1.22	890	1 (2.74)	14.57	72.85
1 M NaOH	61234 ± 623	1.01	359	1 (2.98)	8.09	40.45
30% H_2O_2	41234 ± 432	1.04	249	2 (0.84, 2.97)	6.07	30.35
Thermal	107613 ± 1231	1.14	710	1 (2.51)	12.76	63.80

2.8. Application of the proposed method for the assay of OLM in SMEDDS and marketed tablets

SMEDS formulation of OLM was prepared in the laboratory by the reported method using Capryol-90, Tween-20, Tetraglycol and distilled water as the oil phase, surfactant, cosurfactant and aqueous phase respectively (Lee et al., 2009). To determine the OLM content in SMEDDS (containing 20 mg/mL of OLM), 1 mL of SMEDDS was suitably diluted with the mobile phase to obtain 100 mL of stock solution. This solution was sonicated for 10 min then analyzed for drug content after suitable dilution with the mobile phase. The sample obtained was analyzed for

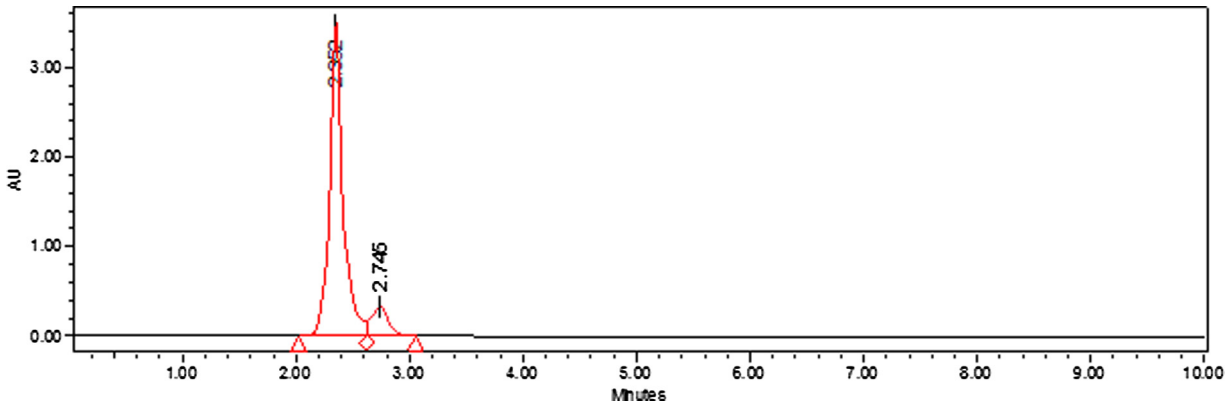

Figure 3 HPLC chromatogram of OLM in the presence of 1 M HCl.

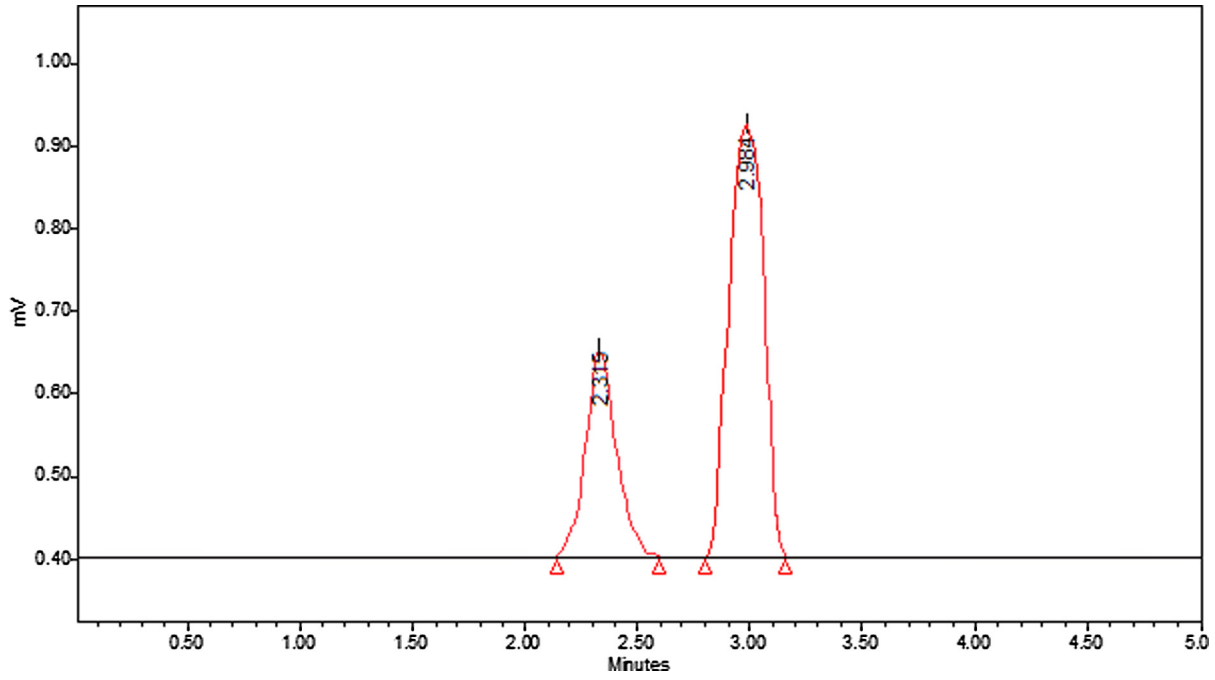

Figure 4 HPLC chromatogram of OLM in the presence of 1M NaOH.

drug content. The possibility of interference of SMEDDS components present in the formulation was studied. For the determination of the content of OLM in marketed tablets, 100 mL stock of each formulation was prepared and analyzed for drug content using the same procedure as used for SMEDDS.

3. Results and discussion

3.1. Method development

With the background to develop an environmentally benign RP-HPLC method for the rapid analysis of OLM in SMEDS and marketed tablets, various solvent systems as mobile phases were tried for the development of a green and environmentally benign RP-HPLC method for the rapid analysis of OLM.

During the method development step, use of ethanol or ethyl acetate or Tween-80 or glycerol alone as the mobile phase resulted in an asymmetric peak with a greater tailing factor (2.3) and a less number of theoretical plates. Further, Tween-80-water, ethanol–water and glycerol–water were tried at different proportions at a flow rate of 1.0 mL/min. A chromatograph was obtained with a very poor peak with greater asymmetry. In order to get a sharp peak with an asymmetry factor less than 2 and good sensitivity, ethyl acetate-ethanol as another mobile phase was tried. The detection wavelength for the analysis of OLM was set at 250 nm as reported previously (Murakami et al., 2008). The combination of ethyl acetate and ethanol (50:50% v/v) was found to be better with sharp peak, suitable retention time and good tailing factor/asymmetry (1.09). Therefore, this combination was selected as the final mobile phase to obtain a rapid and simple assay method for OLM with a reasonable run time (5 min), suitable retention time (2.31 ± 0.005 min) and the acceptable tailing or asymmetry factor (Fig. 2).

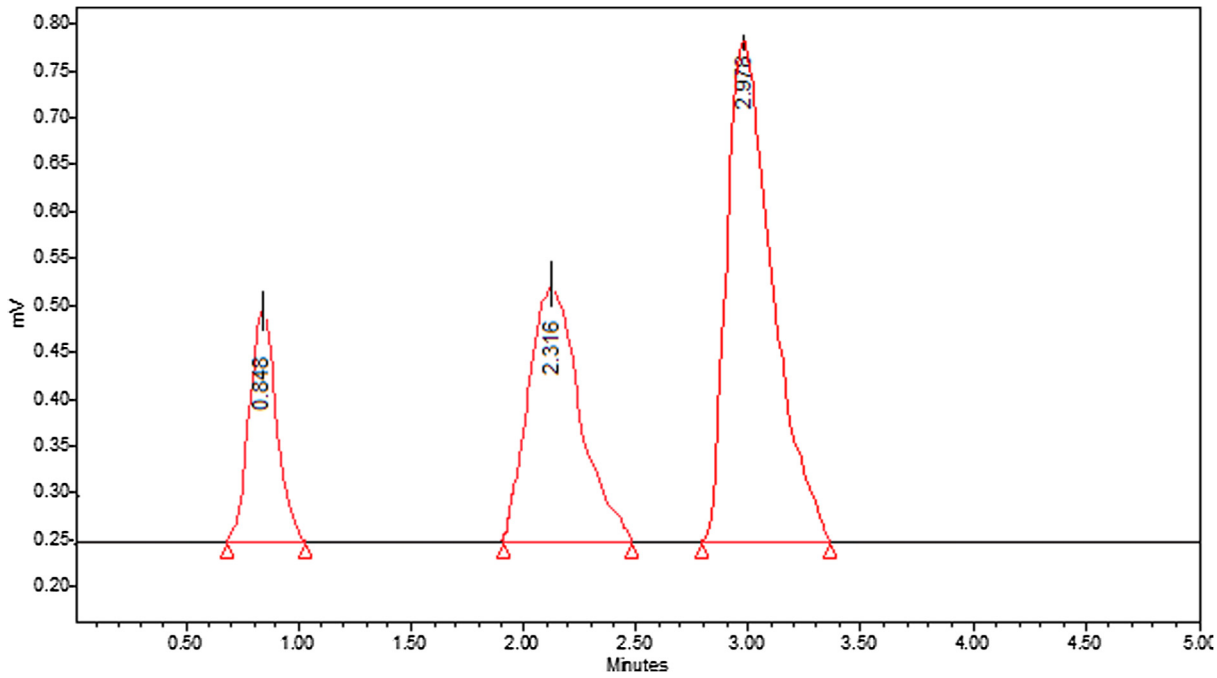

Figure 5 HPLC chromatogram of OLM in the presence of 30% H_2O_2.

3.2. Method validation

The calibration curve of the standard OLM was evaluated by the linear least square analysis. The calibration curve of peak area versus concentration was found to be linear in the concentration range of 0.1–200 μg/mL. The equation for the calibration curve was $y = 9930x–19117$. The correlation coefficient (r^2) of the calibration curve was found to be 0.999 ± 0.0005 (Table 1). The linear regression data for the calibration curve of OLM are shown in Table 1.

The selectivity of the green HPLC method was determined by repeated injections of OLM. The values of SD and % RSD in retention time and peak area were found to be very low (Table 2). The % RSD in retention time and peak area was found to be 0.38 and 1.13, respectively which indicated the selectivity of the green HPLC method.

The accuracy of the green HPLC method was determined as % recovery and is shown in Table 3. Good recoveries (98.02–101.73%) of the spiked drug were obtained at each concentration level. The standard deviation values at each concentration level were found be very low (0.26–0.85). The % RSD (1.32–1.90%) and standard error (0.15–0.49) of the method were also found to be very low which indicated the accuracy of the proposed method.

The results of intraday precision and interday/intermediate precision were expressed in terms of % RSD and are shown in Table 4. The developed method was found to be precise as the % RSD values for intraday and intermediate precision studies were found in the range of 0.56–0.79 and 0.93–1.04 respectively. Low value of % RSD is the indication of precision of the proposed method.

Reproducibility was evaluated by determining the precision of the proposed method in a different laboratory on a different Waters HPLC instrument with the analysis carried out by another person. Both intraday and intermediate precision were determined. No significant differences between RSD (%) values for intraday and intermediate precision were observed, which indicated the reproducibility of the method (Table 5).

LOD and LOQ for the proposed method were determined by the standard deviation of the blank response. The values of LOD and LOQ were found to be 0.06 and 0.18 μg/mL, respectively, which indicated the sensitivity of the proposed method.

For robustness, the SD, % RSD and standard error of the peak areas for the mobile phase composition, wavelength of detection and flow rate at a concentration level of 20 μg/mL are shown in Table 6. The low values of % RSD and standard error obtained after introducing small deliberate changes in the mobile phase composition, wavelength of detection and flow rate indicated the robustness of the proposed method.

3.3. Forced degradation studies

The stability-indicating property and specificity of the green RP-HPLC method was determined by exposing a target concentration of OLM (20 μg/mL) under various stress conditions. OLM was found to be degraded extensively under all stress conditions. Under acid stress conditions, 72.85% of OLM was remaining and 27.15% was degraded (Table 7 and Fig. 3). Therefore, OLM was found to be sufficiently unstable under acidic conditions. The acid-induced degradation products (peak 2 in Fig. 3) were found to be eluted with a retention time of 2.74 min.

However, under base stress conditions, only 40.45% of OLM was remaining and 59.55% was degraded (Table 7). The base-induced degradation products (peak 2 in Fig. 4) were found to be eluted with a retention time of 2.98 min.

The drug was also found to be degraded sufficiently under oxidative stress conditions (30% H_2O_2) (Fig. 5). The H_2O_2-induced degradation products (peak 1 and 3 in Fig. 5) were found to be eluted with a retention time of 0.84 and 2.97 min, respectively.

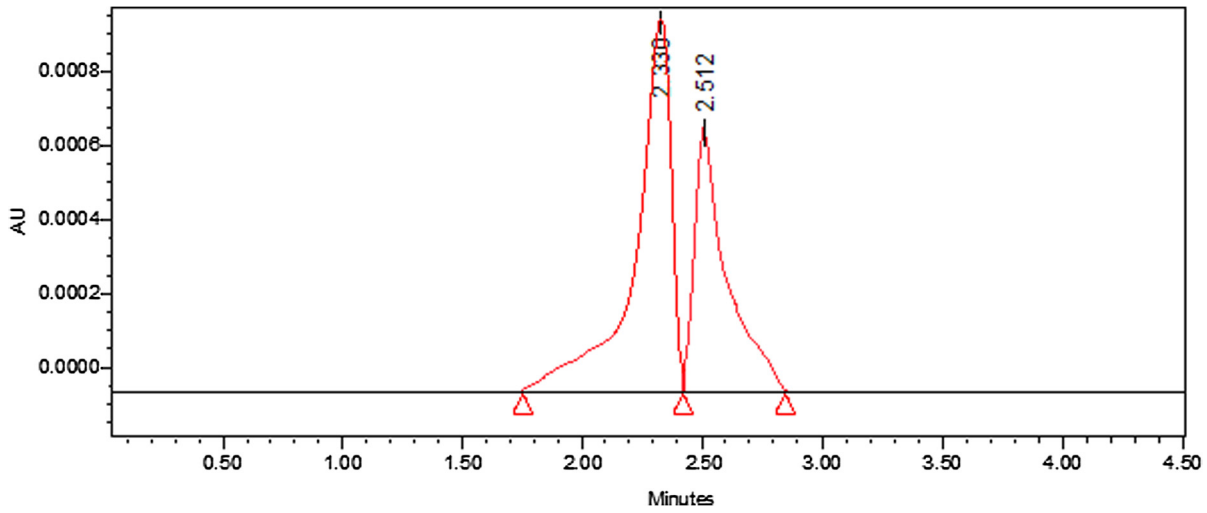

Figure 6 HPLC chromatogram of OLM under thermal condition.

However under thermal stress conditions, 63.80% of OLM was remaining and only 36.20% was degraded. The thermal-induced degradation product (peak 2 in Fig. 6) was found to be eluted with a retention time of 2.51 min.

Overall these results indicated that the proposed HPLC method was specific and stability-indicating.
Solution stability.

OLM was found to be stable when stored for 72 h at ambient temperature (25 ± 1 °C) and under refrigeration (4 ± 0.5 °C) in a combination of green ethyl acetate and ethanol (mobile phase). More than 99% of the OLM remained unchanged, on the basis of comparison of peak areas with those obtained from a freshly prepared solution of OLM.

3.4. Application of the proposed method for assay of OLM in SMEDDS and marketed tablets

The green RP-HPLC method developed was found to be rapid, selective, sensitive and suitable for the quantitative determination of OLM. Therefore this method was applied for the quantitative analysis of OLM in SMEDDS and marketed tablets. The amount of OLM in SMEDDS was found to be 101.25 ± 1.12%. Whereas, the amount of OLM in marketed tablets was found to be 98.67 ± 1.21%. These assay values were found within the range of ICH guidelines (98–102%). High assay values of OLM in SMEDDS and marketed tablets suggested that the method could be suitable for the routine analysis of OLM in various pharmaceutical formulations. The chromatogram of OLM extracted from the SMEDDS and marketed tablet was matching with that of pure OLM, showing the purity of peak in both formulations. There was no interaction between OLM and various excipients present in commercial tablets or SMEDDS formulation.

4. Conclusion

The proposed RP-HPLC method is simple, selective, rapid, accurate, precise, reproducible, robust, sensitive and stability-indicating. Therefore, the method was applied to the assay of OLM in SMEDDS and commercial tablets. A high assay value was obtained in both of the formulations. The method is also simple in terms of sensitivity, use of an environmentally benign mobile phase, lack of extraction procedures, lower retention time (rapid analysis), no internal standard and UV detection. All these factors make this method superior for the routine analysis of OLM in bulk drugs and various commercially available formulations of OLM. The method could also be applied for the prediction of shelf life in pharmaceutical formulations having OLM as an active ingredient because it is having stability-indicating properties. The replacement of widely-used traditional solvents and chemicals with new, innocuous, and less toxic ones provides environmentally benign alternatives to the more hazardous chemicals and processes in the field of drug/pharmaceutical analysis.

Conflict of interest

The authors report no conflict of interest.

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