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Research Article

SPECTROPHOTOMETRIC DETERMINATION OF CETIRIZINE AND MONTELUKAST IN PREPARED FORMULATIONS

KAMYAR POURGHAZI[1,*], ZAHRA MONSEF KHOSHHESAB[2], ALIREZA GOLPAYEGANIZADEH[2,3], MAHMOUD REZA SHAPOURI[3], HOSSEIN AFROUZI[3]

[1] Faculty of Chemistry, Tarbiat Moalem University, 49 Mofateh Avenue, Tehran, Iran, [2] Department of Chemistry, Faculty of Science, Payam Noor University, Qazvin, Iran, [3] Quality Control laboratory, Darou Pakhsh Mfg. Co. Tehran, Iran

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ABSTRACT

The spectrophotometric method including first derivative (^{1}D) ultraviolet spectrophotometry was developed for determination of Cetirizine as a long acting antihistamine and Montelukast as an antileukotriene in pharmaceutical dosage forms. The method was performed at 217 and 335 nm for Cetirizine and Montelukast respectively. The regression analysis data for the calibration plot showed good linear relationship in the concentration range of 2-20 µg/ml (R^2 = 0.9991) for Cetirizine and 6-28 µg/ml (R^2 = 0.9976) for Montelukast. The relative standard deviation <0.4 was obtained. The LODs were found to be 112 and 10.3 ng ml^{-1} for Cetirizine and Montelukast respectively. Statistical analysis proves that the method is reproducible and selective for the simultaneous determination of Cetirizine and Montelukast.

Keywords: Cetirizine, Monetlukast, First derivative Spectrophotometry, Quantitative Analysis.

INTRODUCTION

Montelukast (**MON**), figure 1a, is a potent leukotriene receptor antagonist used for the treatment of seasonal allergic rhinitis and asthma [1]. Its empirical formula is $C_{35}H_{36}ClNO_3S$. Leukotriene inhibitors are a new pharmacological class of compounds for asthma management.

Various analytical methods have been reported for the assay of **MON** in the dosage forms or in plasma. Although most of them rely on the use of chromatographic methods such as HPLC [2-3], HPLC with fluorescence detection [4] and HPTLC [5]. other methods including capillary electrophoresis and voltametric determination were also used [6-7].

Cetirizine(**CET**), figure 1b, is a long acting antihistamine with some mast-cell stabilizing activity widely used in the comprehensive management of allergic rhinitis, the symptoms of which include itching, sneezing and nasal congestion. Its molecular formula is $C_{21}H_{27}Cl_3N_2O_3$.

Literature reveals a variety of analytical methods for determination of **CET** such as HPLC [8-10], TLC [11], and spectrophotometry [12]. There are numbers of investigations that compare the efficacy and safety of **CET** and **MON** used for the treatment of pediatric perennial allergic rhinitis, seasonal allergic rhinitis and thyroid eye disease, alone and with combination [13-15]. The results of the studies demonstrate that

combined **MON**/**CET** were more effective than **CET** alone in preventing eye itching rhinorrhea and nasal itching and delay appearance of AR symptoms [14-15].

No reports were in literature on the determination of **MON** and **CET** simultaneously. Here we describe the development of a rapid and simple second derivative spectrophotometric method for the determination of **MON** and **CET**. The proposed method is also useful for routine analysis of prepared formulations.

EXPERIMENTAL

Materials and Reagents

MON and **CET** standards were received as a gift from faculty of pharmacy, Tehran university. All the chemicals and reagents used were analytical and purchased from Merck.

Instrumentation

A double-beam UV-Visible spectrophotometer (Cary 100 CONC) connected to a compatible computer (software version 3.00) was used. The spectral bandwidth was 2 nm and the scanning speed was 600nm min^{-1}. The absorption spectra of solutions was recorded in 1-cm quartz cell over the range of 200-400 nm. The first derivatives of the measured spectra were obtained using accompanying software with $\Delta\lambda$= 4 nm.

Preparation of standard solutions

Stock standard solutions of **MON** and **CET** were prepared by dissolving 20 mg of each substances in 100 ml methanol. 0.5, 1, 2, 3, 4, 5, 6 and 7 ml of the stock standard solutions were diluted to 50 ml with methanol.

Preparation of sample solutions

Twenty tablets of **MON** and **CET** weighted, their mean weight was calculated and finely powdered. A portion of powder equivalent to sum of the mean weight of **MON** and **CET** were weighted and dissolved in 100 ml methanol. Then 10 ml of solution was diluted to 50 ml. The sample solution was filtered. Final concentrations of **MON** and **CET** were 10µg/ml and 20µg/ml respectively.

^{1}D method

Absorption spectra of the standard solutions were recorded over the range of 200-400 nm. The second derivatives of the measured spectra were obtained. The values of the ^{1}D amplitudes were measured at 217 nm (zero-crossing of **MON)** and 335 nm (zero-crossing of **CET**).

RESULTS AND DISCUSSION

The main instrumental parameters that affect the shape of derivative spectra are the wavelength increment ($\Delta\lambda$), wavelength scanning speed and smoothing. Generally the noise level decreases with an increase in $\Delta\lambda$. However if the value of $\Delta\lambda$ is too large, the spectral resolution is very poor. Some values of $\Delta\lambda$ were tested and $\Delta\lambda$=4 nm and wavelength scanning speed 600 nm min^{-1} were selected. Proper selection of zero crossing point in derivative spectra completely eliminates the interference of unwanted component and thus concentration of two components can be easily calculated without prior separation of compounds from combined dosage form.

MON possesses a very large absorption in the UV region while **CET** exhibits a low absorption in the same region (figure 2). The ^{1}D value at 217 nm (zero crossing of **MON**) has been used for quantitation of **CET** and the ^{1}D value at 335 nm (zero crossing of **CET**) has been used for quantitation of **MON (**figure 3). the plots of the absolute values of second derivative at 335 nm against concentrations of

MON showed a linear relationship in the range of 6-28 µg ml^{-1}. For **CET,** the linearity range was in the range of 2-20 µg ml^{-1}(table 1). The LODs were found to be 10.3 and 112 ng ml^{-1} for **MON** and **CET** respectively. The LOQs were found to be 34.33 and 373.33 ng ml^{-1} for **MON** and **CET** respectively, which indicate the good sensitivity of the method.

Precision

The intra-day and inter-day variations for determination of **MON** and **CET** were carried out five times in the same day and five consecutive days. Low values of the %RSD(0.4%) suggested An excellent precision of the method(table 2).

Accuracy

Accuracy of method was studied by applying the method to samples which known amount of **MON** and **CET** corresponding to 50, 100 and 150% of drug label claims had been added. Five determinations were performed for each level. Percent recovery for **MON** and **CET** was found in the range of 98.73% to 100.90% (table 3).

Analysis of prepared formulation

The method was applied to the determination of **MON** and **CET** in sample solutions. The amounts (%) of two drugs (table 4) were calculated by use of linear equation obtained from the calibration curves. The % recovery of **MON** and **CET** were well within the limits (label claim ± 5%).

(a) **(b)**

Fig. 1: Chemical structures of Montelukast (a) and Cetirizine (b).

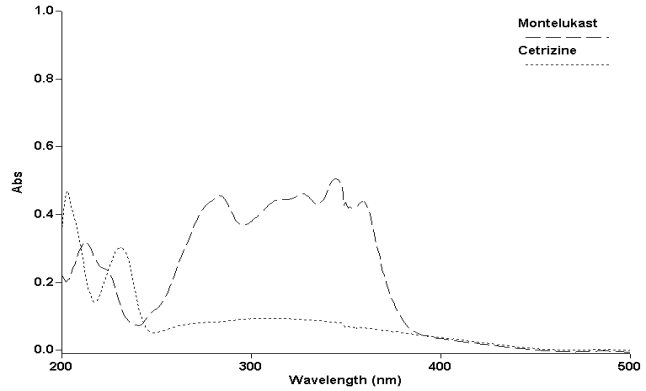

Fig. 2: UV absorption spectra of CET (4 µg ml^{-1}) and MON (10 µg ml^{-1}) in methanol.

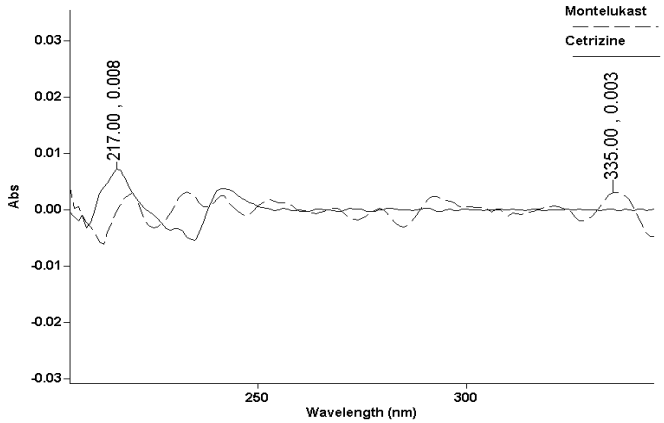

Fig. 3: First derivative spectra of CET and MON in methanol.

Table 1: Characteristic parameters for linear regression equation of MON and CET of the first derivative method

Parameter	MON	CET
Linearity range (µg ml^{-1})	6-28	2-20
Regression equations (Y)*	$Y = 0.0001 + 0.2901X$	$Y = 0.0003 + 0.8021X$
First regression coefficient (b)	0.2901	0.8021
Standard deviation of the first regression coefficient (S_b)	19.32×10^{-2}	18.15×10^{-2}
Intercept (a)	0.0001	0.0003
Standard deviation of the Intercept (S_a)	1.07×10^{-4}	1.01×10^{-4}
Correlation coefficient	0.9991	0.9976
Standard error of estimation	3.01×10^{-3}	2.83×10^{-3}

* $Y = a + bX$ Where X is the concentration of the drug in µg ml^{-1} and Y is the amplitude at the specified wavelength.

Table 2: Precision of ^{1}D method (n=5)

Drug	% label claim estimated (mean ±rds)	
	Inter-day	Intra-day
MON	99.87 ± 0.37	99.61±0.21
CET	99.46 ± 0.12	100.39 ± 0.17

Table 3: Accuracy of ^{1}D method (n=5)

Level[%]		Theoretical content		Amount added[mg		Mean amount found[mg]	
		MON	CET	MON	CET	MON	CET
5	10	2.5	5	7.46	14.81	99.46±0.51	98.73±0.37
5	10	5	10	10.09	20.11	100.90±0.32	100.55±0.21
5	10	7.5	15	12.58	24.94	100.64±0.28	99.76±0.12

Table 4: Determination of MON and CET in sample solutions

Amount (µg ml^{-1})	Recovery (mean* ±RSD)
MON	100.13±0.72
CET	99.5±1.10

*Average of five determination

CONCLUSION

The proposed ^{1}D method provides simple, accurate and reproducible quantitative analysis for simultaneous determination of **MON** and **CET** in tablets. The ^{1}D method has some advantages over other methods (e.g. HPLC) such as a short analysis time, easiness and good accuracy.

REFERENCES

1. A. Nayak, Expert opin. Pharmacother., 5(2004) 679-686.
2. R. D. Amin, H. Cheng, J. D. Rogers, J. Pharm. Biomed. Anal., 15(1997)631-638.-638.
3. S. Patil, Y.V. Pore, B.S. Kuchekar, A. Mane, V.G. Khire, Indian J. Pharm. Sci. 71(2009) 58-61.
4. Al. Rawithi S, Al-Gazlan S, Al-Ahmadi W, Al-Showaier I, Yusuf A, Raines D, J. Chromatogr. B Biomed. Sci. Appl., 754(2001) 527-531.
5. R. T. Sane, A. Menezes, M. Mote, A. Moghe, G. Gundi, J. planar Chromatogr. Modern TLC,17(2004)75-78.
6. Y. Shakalisava, F. Regan, J. Sep. Sci., 31(2007)1137-1143.
7. Alsarra,M. Al-omar, E. A. Gadkariem, F. Belal, IL Pharmaco, 60(2005) 563-567.
8. M. S. Arayne, N. Sultana, M. Nawaz, J. Anal. Chem., 63(2008) 881-887.
9. M. Ma, F. Feng, Y. Sheng, Sh. Cui, H. Liu, J. Chromatogr. B, 846(2007) 105-111.
10. M. F. Zaater, Y. R. Tahboub, N. M. Najib, J. Pharm. Biom. Anal., 22(2000)739-744.
11. S. N. Makhija, P. R. Vavia, J. Pharm. Biomed. Anal., 25(2001)663-667.
12. B. G. Gowda, M. B. Melwanki, J. Seetharamappa, J. Pharm. Biomed. Anal., 25(2001)1021-1026.
13. J. C. Hsieh, K. H. Lue, D. Sh. Lai, H. L. Sun, Y. H. Lin, Pediatric Asthma, Allergy and Immunology, 17(2004)59-69.
14. M. L. Pacor, G. D. Lorenzo, R. Corrocher, Clinical and Experiment Allergy, 31(2001)1607-1614.
15. M. Kurowski, P. Kuna, P. Gorski, Allergy, 59(2004) 280-288.