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D. Barot
Sigma institute of pharmacy, Bakrol, Vadodara.

P. K. Pradhan
Sigma institute of pharmacy, Bakrol, Vadodara.

G. Patel
Sigma institute of pharmacy, Bakrol, Vadodara.

S. Shah
Sigma institute of pharmacy, Bakrol, Vadodara.

H. P. Parmar
Sigma institute of pharmacy, Bakrol, Vadodara.

S. Dey
Sigma Institute of Pharmacy, Bakrol, Baroda, India.

U. M. Upadhyay
Sigma Institute of Pharmacy, Bakrol, Baroda, India

Correspondence:
Prasanna Kumar Pradhan
Sigma institute of pharmacy, Bakrol, Vadodara.

Simultaneous UV spectrophotometric estimation of Olmesartane medoxomil and chlorthalidone in tablet dosage form

D. Barot, P. K. Pradhan, G. Patel, S. Shah, H. P. Parmar, S. Dey, U. M. Upadhyay

Abstract
A simple, rapid and accurate new UV spectroscopic is described for simultaneous estimation of Olmesartan Medoxomil (OLM) and Chlorthalidone (CLT) in synthetic mixture. The method depends on direct determination of OLM at 260 nm and absorption correction method for estimation of CLT at 215 nm. The method is accurate (% recovery 101.81 ± 0.001 and 101.53 ± 0.002, precise in the range 4 - 32 (LOD) and 2.5 – 20 (LOD) µg/ml for OLM and CLT respectively. The developed method was validated as per ICH guideline and the results were found to be satisfactory and successes fully marketed formulation.

Keywords: Olmesartan Medoxomil, Chlorthalidone, UV spectroscopy, absorption correction method.

1. Introduction
Olmesartan Medoxomil, chemically (5-methyl-2-oxo-2H-1,3-dioxol-4-yl)methyl 4-(2-hydroxypropan-2-yl)-2-propyl-1-({4-[2-(2*H*-1,2,3,4-tetrazol-5-yl]phenyl}methyl)-1*H*-imidazole-5-carboxylate (Fig 1) is a indicated for the treatment of hypertension. It may be used alone or in combination Olmesartan Medoxomil with other antihypertensive agents. Chlorthalidone, chemically (*RS*)-2-chloro-5-(1-hydroxy-3-oxo-2,3-dihydro-1H-isoondol-1-yl)benzene-1-sulfonamide (Fig 2) is often used the management of hypertension and edema [1, 2, 3, 4, 5, 6, 7, 8] Literature survey reveals various UV spectrophotometric method and HPLC for determination of drugs in combination with other drugs [9, 10, 11, 12, 13, 14, 15].

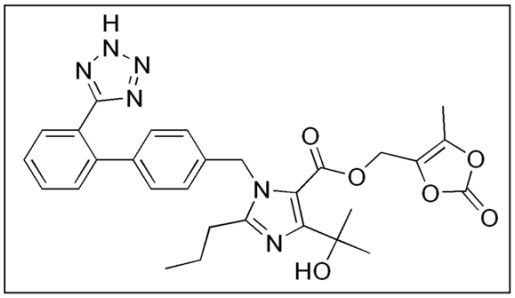

Fig 1: Chemical structure of Olmesartan Medoxomil

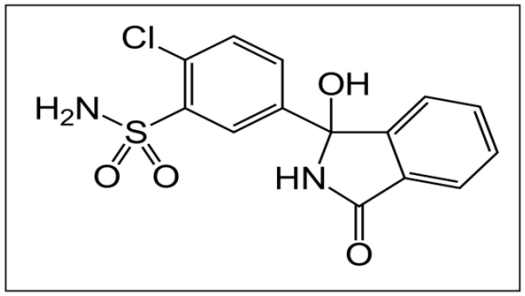

Fig 2: Chemical structure of Chlorthalidone

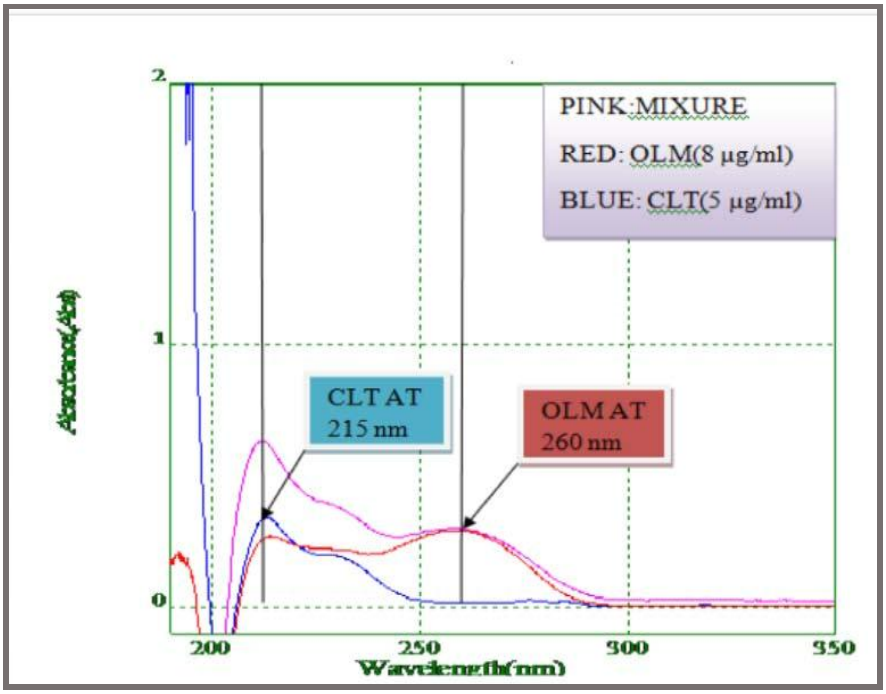

Fig 3: Overlain spectrum of OLM (8 µg/ml), CLT (5 µg/ml)

2. Materials and Method

Pharmaceutically pure sample of Olmesartan Medoxomil and Chlorthalidone were obtained as generous gifts from Zydus Cadila Healthcare Pvt. Ltd, Ahmedabad. and Shreeji Pharma Pvt. Ltd., Vadodara respectively. Both the drugs are used as a standard without further purification. Methanol AR grade (Merck Ltd., Mumbai, India) was used as solvent for the study. Double beam UV-visible spectrophotometer (Analytical, model 2080) having two matched quartz cells with 1 cm light path was used to measure absorbance of the resulting solution.

2.1 Preparation of Standard stock Solutions

Standards of 20 mg OLM and 12.5 mg CLT weighed accurately and transferred to 25 mL volumetric flask, dissolved with methanol and made up to mark with methanol to give solution of 800 µg/ml OLM and 500 µg/ml CLT respectively. 10 mL aliquots of each from standard stock solution were transferred to 100 mL volumetric flask separately and diluted up to the mark with methanol to give solution of 80 µg/ml OLM and 50 µg/ml CLT respectively.

2.2 Selection of analytical wavelength

For determination of analytical wavelength for measurement, standard solution of OLM (8 µg/ml) and CLT (5 µg/ml) and their mixture were prepared from above stock solution and scanned between 200-400 nm against methanol as blank. From the overlain spectra 260 nm was selected for direct determination of OLM and 215nm was selected for CLT, as at this wavelength the absorbance of CLT and absorbance of mixture after correction for OLM are coming out to be same. (**Fig 3**)

2.3 Linearity

Solutions for calibration were prepared by diluting aliquots of above stock solutions up to 10 ml with water to of OLM and CLT to prepare concentrations ranging from 4-32 µg/ml for OLM and 2.5-20 µg/ml for CLT. Six replicates for each solution at each level and absorbance was plotted against the corresponding concentration of the drug. (**Table 1**)

2.4 Repeatability

Repeatability was carried out using six replicates of 28 µg/ml concentrations of Olmesartan medoxomil and 17.5 µg/ml of Chlorthalidone were prepared and absorbance was measured at corresponding wavelength. RSD were calculated. (**Table 1**)

2.5 Precision

Precision of the method was evaluated by analyzing three different concentrations: 4, 16 and 28 µg/ml Olmesartan medoxomil and 2.5, 10 and 17.5 µg/ml Chlorthalidone were analyzed 3 times on the same day. For interday precision was assessed by analyzing similar solution three times over a period of three times over a period of three days. Finally, precision was expressed by respective RSD values. (**Table 2**)

2.6 Accuracy

Accuracy of the method was determined by OLM and CLT by standard addition method at three levels. Take powder equivalent to 160 mg Olmesartan medoxomil and 100 mg Chlorthalidone was accurately weighed and transferred to 100ml volumetric flask, sonicated for 10 min, diluted to mark, filtered. Base concentration of 8 µg/ml OLM and 5 µg/ml CLT were prepared. Then volumes were fortified with 50%, 100%, and 150% respective drugs from stock solution, diluted and analyzed. These procedures were repeated three times for each level of addition. (**Table 3**)

2.7 Assay of Tablets

Twenty tablets were weighed and finely powdered. An accurately weighed portion of the powder equivalent to 20 mg of OLM and 12.5 mg of CLT was transferred to 25 ml volumetric flask and sufficient Methanol was added and sonicated for 10 min. The solution was filtered through Whatman filter paper (No. 42). Take 10 mL into 100 mL

volumetric flask and then diluted up to volume with Methanol to get stock sample solution. Aliquot of 2.5 mL was pipetted out from above prepared solution and diluted up to 10 mL with Water to get the working sample solution. 6 replicates of these solutions were prepared. The solutions prepared in this manner were then subjected to analysis by developed method. % RSD of Olmesartan medoxomil and Chlorthalidone was calculated. (**Table 4**)

3. Result and Discussion

The methods were validated with respect to linearity, limit of detection (LOD), limit of quantification (LOQ), precision, accuracy and Robustness.

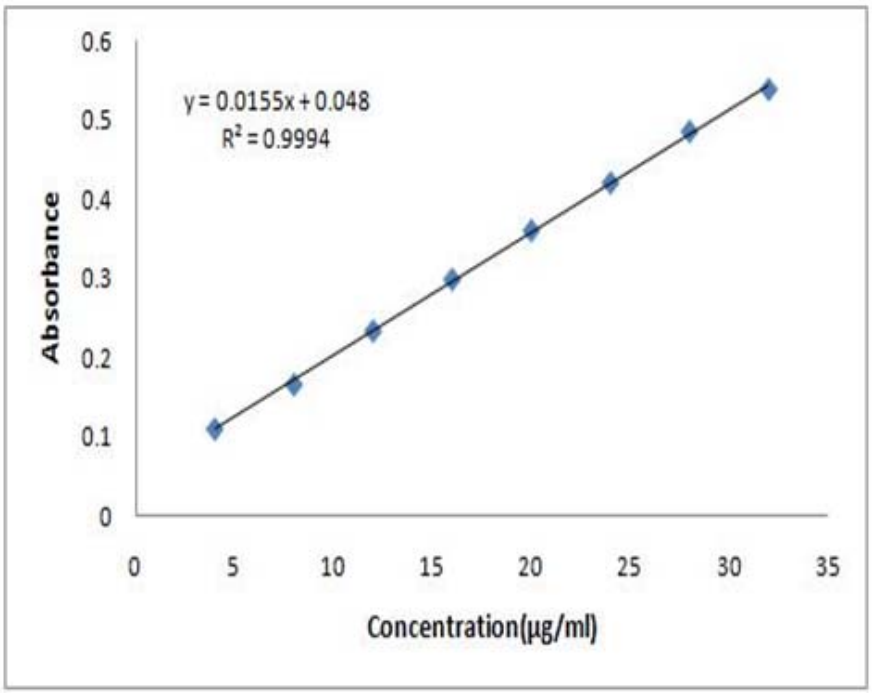

Fig 4: Calibration curve of Olmesartan medoxomil (at 260 nm)

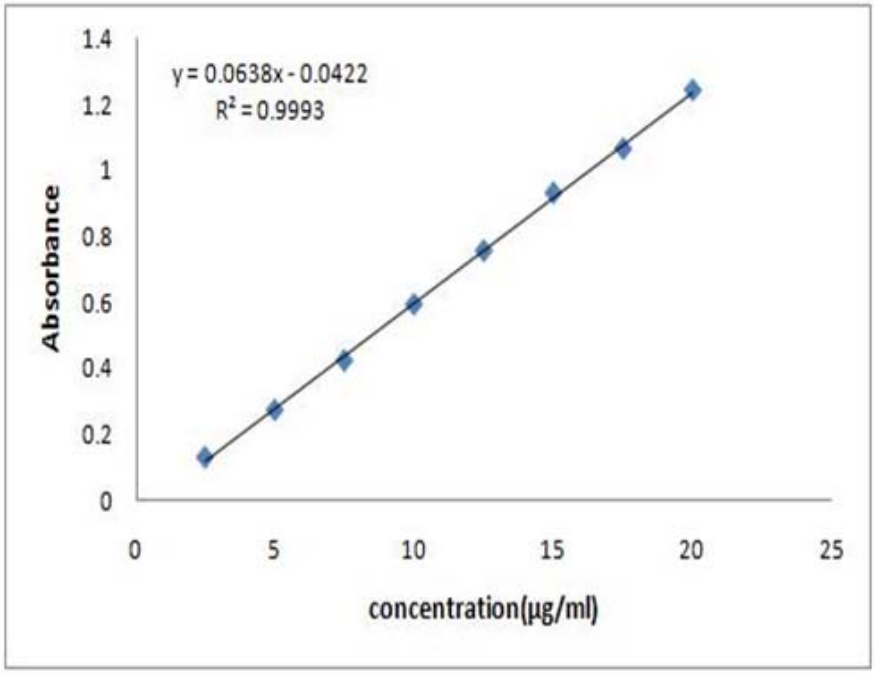

Fig 5: Calibration curve of Chlorthalidone (at 215 nm)

Table 1: Linearity and Range Data

Parameter	Olmesartan medoxomil	Chlorthalidone
Range (µg/ml)	4 -32	2.5 - 20
Linear equation	y = 0.0155x + 0.048	y = 0.0638x + 0.0422
r	0.9994	0.9993
Mean Slope (n=6)	0.01577 ± 0.00029	0.06286 ± 0.00032
Repeatability (% R.S.D.) (n=6)	0.056	0.081
LOD (µg/ml)	0.3287	0.0594
LOQ (µg/ml)	0.9961	0.1799

*(n=6 determinations)

Table 2: Precision Result of Olmesartan Medoxomil 260 nm and Chlorthalidone 215 Nm

	Interday precision		Intraday precision	
Target Conc. (µg/ml)	**Amt found (µg/ml) ± SD** (n=3)	**% RSD**	**Amt found (µg/ml) ± SD** (n=3)	**% RSD**
Olmesartan medoxomil				
4	4.005 ± 0.014	0.336	3.986 ± 0.027	0.683
16	16.053 ± 0.019	0.120	16.023 ± 0.048	0.297
28	28.088 ± 0.018	0.064	28.066 ± 0.039	0.138
Chlorthalidone				
2.5	2.543 ± 0.005	0.201	2.539 ± 0.01	0.384
10	10.279 ± 0.011	0.108	10.265 ± 0.024	0.236
17.5	17.654 ± 0.014	0.078	17.632 ± 0.033	0.185

Table 3: % Recovery of Olmesartan Medoxomil and Chlorthalidone

Conc. of preanalyzed sample (µg/ml)	Level of addition (%)	Amt of std spiked (µg/ml)	Amt of test taken (µg/ml)	Total conc. found (µg/ml)	Avg. Amt. Recovered (µg/ml) (n=3)	recovery Mean ± SD (%, n = 3)
Olmesartan Medoxomil						
8.09	50	4	12	12.105	4.02	100.38 ±0.54
	100	8	16	16.051	7.96	99.65 ± 0.37
	150	12	20	20.001	11.91	99.35 ± 0.26
Chlorthalidone						
4.95	50	2.5	7.5	7.475	2.53	100.99 ±0.52
	100	5.0	10	9.949	5.00	100.00 ±0.52
	150	7.5	12.5	12.512	7.56	100.83 ± 0.43

Table 4: Assay of Tablets

Synthesis Mixture	Actual amount (µg/ml)		Amount obtained (µg/ml) (n=3)		Assay ± SD (%, n = 3)	
	OLM	CLT	OLM	CLT	OLM	CLT
	20	12.5	20.362	12.691	101.81 ± 0.001	101.53 ± 0.002

The calibration curve was linear in a concentration range of 4-32 and 2.5-20 µg/ml with Regression coefficient 0.9994 and 0.9993 for OLM and CLT respectively. LOD, LOQ value for Olmesartan medoxomil was found to be 0.3287, 0.9961 and for Chlorthalidone it was found to be 0.5941, 0.1799 respectively. The % recovery was found 100.38 – 99.35 and 100.99 – 100. The developed method was validated as per ICH guideline and found to be accurate, precise, rapid and economical. The method was applied for analysis of Tablet dosage form. Assay results 101.81 ± 0.001 and 101.53 ± 0.002 for OLM and CLT respectively indicates that the proposed method can successfully estimations both the drugs. Hence the method can be applicable for routine analysis in pharmaceutical dosage form without any interference.

4. References

1. Drug Profile, Olmesartan medoxomil http://www.drugbank.ca/drugs/DB00275, 09, Dec, 2014.
2. Drug Profile, Olmesartan medoxomil http://www.drugs.com/monograph/olmesartan-medoxomil.html, 09, Dec, 2014.
3. Drug Profile, Chlorthalidone http://www.drugbank.ca/drugs/DB00310, 09, Dec, 2014.
4. Drug Profile, Chlorthalidone http://www.drugs.com/monograph/olmesartan-medoxomil.html, 09, Dec, 2014
5. Banerji P. "Symptoms of high blood pressure", 2009, http://www.tretment-for.com/high blood pressure symptoms.htm

6. Merck index, Merck research laboratories, division of Merck Company, NJ, USA, Edn 13, 2001, 5612.
7. Drug Bank. www.drugbank.ca/drugs/DB06725 acceded on 25 October.
8. Drug Update. www.drugsupdate.com acceded on 25 October.
9. Patela N, Patel JK. Simultaneous determination of azelnidipine and olmesartan medoxomil by first derivative spectrophotometric method. Der Pharm Let 2012; 4(4):1080-1084.
10. Patel DD, Patel MM. Simultaneous estimation of metoprolol succinate and olmesartan medoxomil in pharmaceutical dosage form by UV spectroscopy. Int J of Res in Pharm and Bio Sci 2012; 3(2):935-939.
11. Shah RM, Kakadia M, Patel J, Agola A, Saisivam S. Simultaneous estimation of meoprolol and olmesartan medoxomil by UV spectroscopy in fixed dose combination. An Int J of Pharm Sci 2012; 4.01:2516-2532.
12. Karajgi SR, Simpi CC, Kalyane NV. Simultaneous first derivative UV spectrophotometric estimation of ramipril and olmesartan. J of Pharm Sci 2012; 2(1):78-82.
13. Mhaske RA, Sahasrabudhe S, Mhaske AA, Garole DJ. "RP-HPLC method for simultataneous determination of irbesartan, losartan, medoxomil, hydrochlorothiazide and chlorthalidone. Int J of Pharm Sci and Res 2012; 3(4):1116-112.
14. Akiful HM, Nivedita G, Prashanth KK, Pradeep KT, Hasan AS, Prakash VD. Simultaneous estimation of atenolol and chlorthalidone as bulk and in tablet dosage form using UV- spectrophotometry. J of Pharm and Bio Sci 2012; 1:20-23.
15. Sahoo S, Mishra SK, Panda PK. HPLC method development for simultaneous estimation of telmisartan and chlorthalidone in tablet dosage form. Int J for Pharm Res Scholar 2012; 1:1-5.