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SIMULTANEOUS UV SPECTROPHOTOMETRIC ESTIMATION OF OLMESARTAN MEDOXOMIL, CHLORTHALIDONE AND AMLODIPINE BESYLATE BY SIMULTANEOUS EQUATION METHOD

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ABSTRACT

A latest, uncomplicated, error – free, low-cost UV Spectrophotometric method has been flourished for the simultaneous estimation of Olmesartan medoxomil, Chlorthalidone, Amlodipine besylate in bulk and in combined tablet dosage form employing simultaneous equation method. The stock solution was composed by methanol followed by the further required with distilled water. This method involves the formation and solving of simultaneous equations at 256 nm, 227 nm and 237 nm, as absorbance maxima of Olmesartan Medoxomil, chlorthalidone and amlodipine besylate, respectively. Beer's law obeyed the concentration range of 14-26 µg mL^{-1}, 8.75-16.25 µg mL^{-1}, and 10.5–19.5 µg mL^{-1}, for Olmesartan Medoxomil, Chlorthalidone and Amlodipine besylate respectively. The results of analysis were validated for various parameters according to ICH guidelines.

Keywords: UV Spectrophotometric, Olmesartan medoxomil, Chlorthalidone, Amlodipine besylate, ICH guidelines, Simultaneous estimation

INTRODUCTION

Olmesartan medoxomil (OLM) (Figure 1) [1-3]is chemically 5-methyl – 2 – oxo - 1,3 – dioxol – 4 – yl) methyl 4 – (1 – hydroxyl – 1 – hydroxyl – 1 – methyl ethyl) – 2 – propyl – 1 – {[2' – (1H – tetrazole – 5 – yl) biphenyl – 4 –yl] methyl} – 1 H – imidazole – 5 – carboxylate with molecular formula of $C_{29}H_{30}N_6O_6$ and a relative

molecular mass of 558.6 . It's an angiotensin II type I receptor blocker and is employed to take care of hypertension. OLM may be a Synthetic Imidazole derivative with an antihypertensive property.

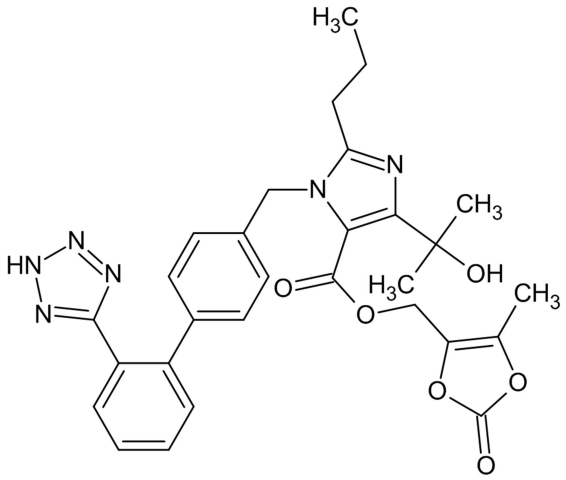

Figure 1: Chemical structure of OLM

Chlorthalidone (CHL) (Figure 2)[1-3] is chemically (2 – chloro – 5 – (1 – hydroxy – 3 – oxo – 2,3 – dihydro – 1H - isoindol– 1 – yl) benzenesulfonamide. CHL has the formula of $C_{14}H_{11}ClN_2O_4S$ and a relative molecular mass of 338.8. It is a NACL Symporter inhibitor and is employed as an antihypertensive agent and diuretic. CHL is examined as a thiazide – like diuretic.

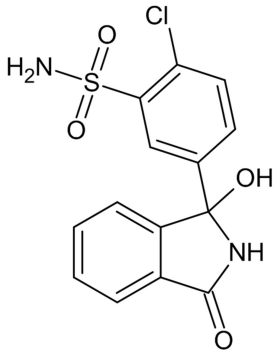

Figure 2: Chemical structure of CHL

Amlodipine Besylate (AML) (Figure 3) [1-3] is chemically 3 – ethyl 5 – methyl (4RS) – 2 – [(2 – aminoethoxy) methyl] – 4 – (2 – chlorophenyl) – 6 – methyl – 1, 4 – dihydropyridine – 3,5 – dicarboxylate benzenesulfonate. AML features a formula of $C_{26}H_{31}ClN_2O_8S$ and a relative molecular mass of 567.1. It's a calcium-channel blocker and is employed as an antihypertensive. AML may be a long-acting dihydropyridine calcium channel blocker and is effective in treating Angina Pectoris.

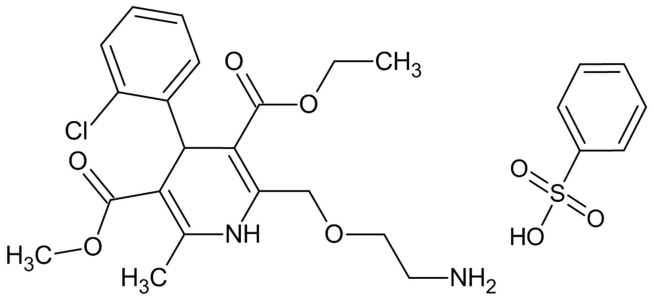

Figure 3: Chemical structure of AML

According to the literature review, there are numerous approaches for estimating OLM, CHL, and AML individually and in combination with other drugs. The literature review further says that there were two HPLC methods **[4, 5]** and a LCMS method **[6]**. There were no UV Spectrophotometric methods for the simultaneous estimation of OLM, CHL, and AML. Hence, the aim of the proposed work is to develop a UV Spectrophotometric method for the simultaneous estimation of OLM, CHL, and AML.

MATERIALS AND METHODS

Instruction

Lab India double beam spectrophotometer model UV 3092 was employed with 1.00 cm quartz cells. The scan was administered within the range of 200 to 400 nm at 0.1 nm intervals. UV Win5 Software v5.2.0.1104 was employed.

Reference sample

AML, CHL, OLM, active pharmaceutical ingredients with a purity of 99.73%, 99.69%, and 99.85% w/w, respectively, were offered by Ideal Analytical and Research Institution, Puducherry, India.

Marketed formulation

TRIOLMEZEST CH20 tablets containing 20 mg of OLM, 12.5 mg of CHL, and 5 mg of AML per tablet (manufactured by Synokem Pharmaceuticals Ltd, Haridwar, India and marketed by Sun Pharma Laboratories, Mumbai, India) were purchased from a Medplus chain store in Guduvancherry, India.

Chemicals

Methanol of HPLC Gradient grade was picked-up from Finar Limited, Ahmedabad, Gujarat, India.

The standard stock solution of analyte

Individual standard stock solutions of OLM, CHL and AML (1000 µg mL^{-1}) were drawn by dissolving 10 mg in 10 mL of methanol.

Methodology of simultaneous equation spectrophotometric method

Overlay Spectroscopy and Wavelength Selection

Stock solutions were diluted individually with methanol to form 10 µg mL^{-1} solutions

for each OLM, CHL, and AML. The produced solutions were scanned versus methanol as a reference at 200 to 400 nm. OLM, CHL, and AML had peak absorptions of 256, 209, and 360 nm, respectively. At the maximum of the others, every pharmaceutical has ideal absorbance. The λmax of CHL was found to be at 209 nm, which is not suitable since there may be a lot of interference due to noise. Hence the measurement was taken at 227 nm for where suitable absorbance is obtained for OLM and AML. Standard solutions of 20 μg mL^{-1} for OLM, 12.5 μg mL^{-1} for CHL, and 15 μg mL^{-1} for AML were generated by appropriate dilution from the stock solution and zero order spectrum scanned between 200 to 400 nm. The absorptivity was calculated for OLM (X) at λ1, λ2 and λ3 (ax1, ax2 and ax3); CHL (Y) at λ1, λ2 and λ3 (ay1, ay2 and ay3) and AML (Z) at λ1, λ2 and λ3 (az1, az2 and az3). The absorbance of sample solutions was measured at 256 nm (λ1), 227 nm (λ2) and 237 nm (λ3). The zero order spectrum of

Solution Stability

Stability in the solution was evaluated by the standard solution and the test preparation. The solution was stored at ambient temperature without protection from light and tested after 6, and 12 hrs. The matured solutions' responses were compared to those of newly created solutions. The stability of the stored standard solution and test preparation was investigated, and it was discovered that the formulations were stable for up to 12 hours. Without discernible loss, the tester readings after 12 hours were statistically similar to the original value.

Analysis of Pharmaceutical Formulation

Ten TRIOLMEZEST CH20 pills were carefully weighed, then broken into powder and well blended. The amount of tablet powder 20 mg OLM (12.5 mg CHL, and 5 mg AML) was transferred to a 100 ml volumetric flask, and 75 millilitres of methanol was added and thoroughly mixed. The mixture was sonicated for 10 minutes before being structured to volume with methanol and thoroughly mixed. This solution was further diluted in a 10 mL volumetric flask with methanol to generate an answer containing 20 μg mL^{-1} OLM, 12.5 μg mL^{-1} CHL, and 5 μg mL^{-1} AML. The Spectrum of AML was enriched utilizing the spectrum addition approach by adding a 10μg mL^{-1} zero order spectrum of pure standard AML through spectrophotometers software. Each drug's concentration was determined using simultaneous equation method. After subtracting the added concentration (AML spectrum) (10 μg mL^{-1}), the claimed concentration of AML is calculated.

Method Validation

The method was validated with reference to linearity, precision, and accuracy **[7]**.

Linearity

Aliquots equivalent to 14 - 26 µg mL^{-1} OLM, 8.75 – 16.25 µg mL^{-1} CHL, and 10.5 – 19.5 µg mL^{-1} are precisely transferred from their stock solutions (1000 µg mL^{-1}) into three different series of 10 mL volumetric flasks, then methanol filled to volume. From 200 to 400 nm, the spectra of the created internal standard are evaluated and saved on the computer. The LOD and LOQ values were calculated from the data's obtained from Linearity.

Precision

Consistency & intermediate precision were also used to assess the tactic's precision. The consistency was assessed using seven samples of the very same concentration. For the measurement of intermediate precision, inter-day and intra-day assays were conducted at 100% of test concentration in triplicates for the same concentration, on the same day, and for the next three days. The relative standard deviation was calculated as a percentage.

Accuracy

Analytical recovery experiments were administered using the standard addition method at three distinct strengths (80 %, 100% and 120%) to verify the correctness of the devised tactics and to verify the interference of formulation excipients. The percent recovery was computed using the total amount of medication detected. For each concentration, the technique was done three times. The percent RSD was determined.

RESULTS AND DISCUSSION

A quick, sensitive, inexpensive, precise, and accurate analytical approach was developed and tested for simultaneous detection of OLM, CHL, and AML in purified API and mixed tablet dose form.

The suggested approach uses a UV spectrophotometric simultaneous equation method using methanol as the solvent for simultaneous estimation of OLM, CHL and AML. Figure 4 shows the overlain spectra of 10 µg mL^{-1} OLM, CHL, and AML.

The overlay spectrum of the standard solutions 10 µg mL^{-1} each of OLM, CHL, and AML recorded in the zero-absorbance mode, as shown in **Figure 4**, revealed that the simultaneous equation method was suitable for concurrent estimation of OLM, CHL, and AML. Wavelength of 256, 227, and 237 nm were selected to determine OLM, CHL, and AML as all the three drug showed absorbance at the selected wavelength of the other two drugs. The spectra obtained by tablet formulation is presented in **Figure 5** and obtained values presented in **Table 1**.

The corresponding absorbance values obtained for solution stability of standard and assay samples solutions showed no considerable variation in the absorbance for 12 hrs. The assay results found for solution stability were within ± 2 % compared with

the new solution and shown in **Table 1**. The calibration curves of OLM, CHL, and AML were linear in the series and specified wavelength. The regression equation, correlation coefficient, calculated values of LOD and LOQ were presented in **Table 1**. The % RSD values obtained with the system, inter, and intraday precision was less than 2%, indicating good precision, while the % recoveries for accuracy **(Figure 6)** were within limits. The summary of validation parameters and results obtained is presented in **Table 1**.

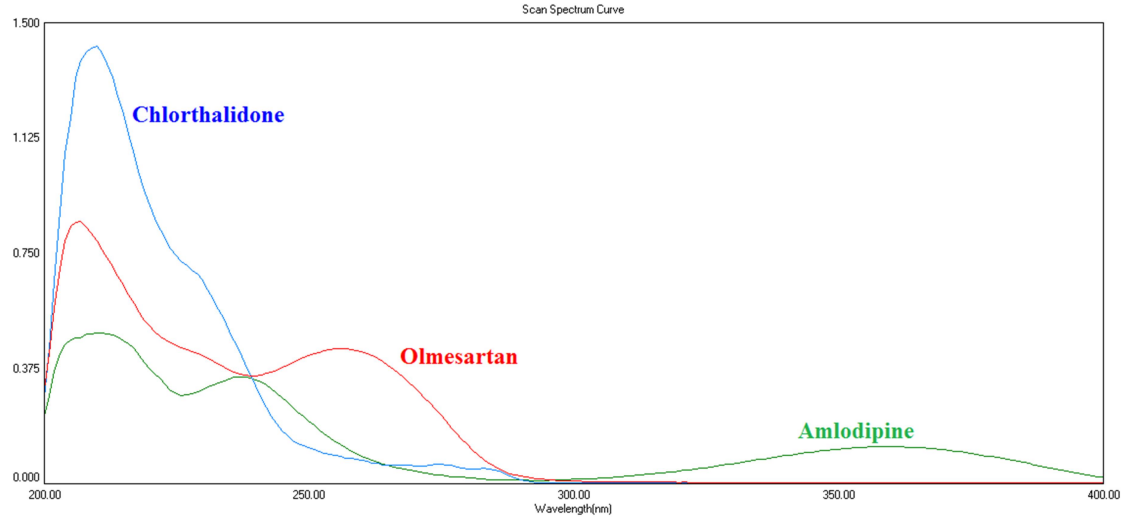

Figure 4: Overlain spectra of 10 µg mL^{-1} OLM, CHL, and AML.

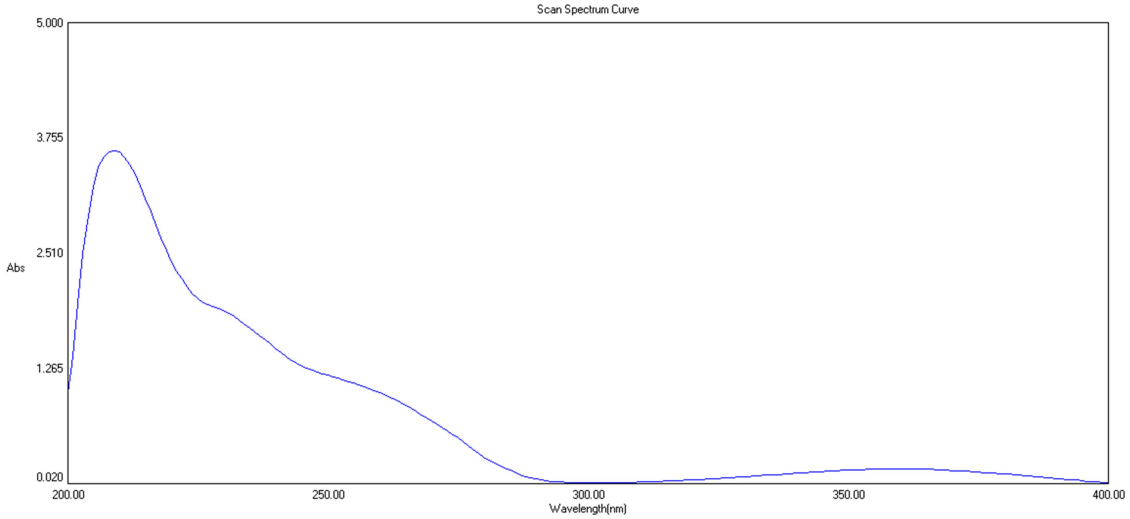

Figure 5: Spectrum obtained from the tablet formulation after spectral addition of 10 µg mL^{-1} of AML

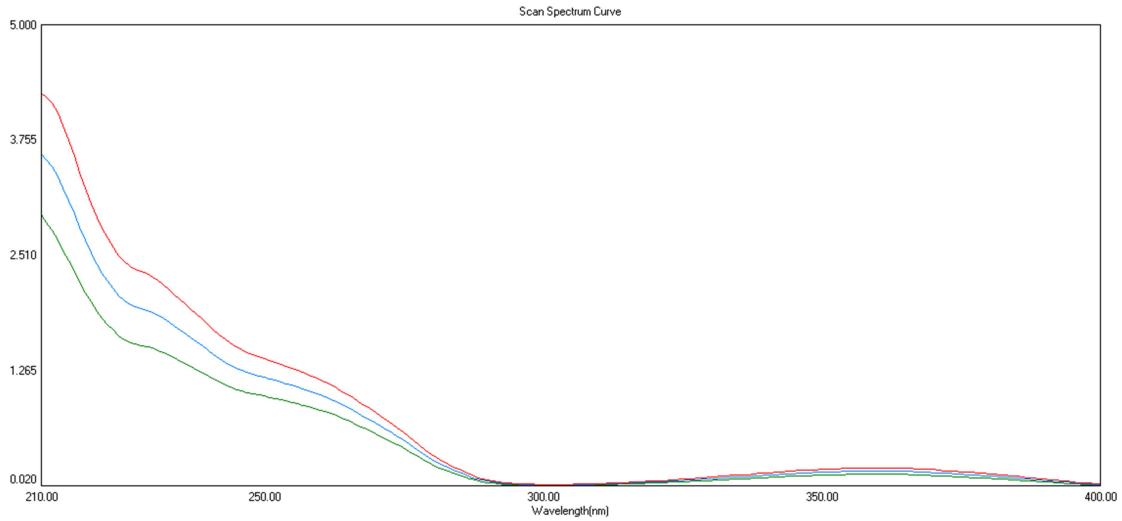

Figure 6: Overlay spectrum for accuracy studies

Table 1: Validation parameters and results obtained by the developed UV spectrophotometric method for the simultaneous determination of OLM, CHL and AML

Description	Observations		
	OLM	CHL	AML
Detection wavelength (nm)	256	227	237
Solution stability standard, (% RSD)	0.51	0.49	0.81
Linearity[a] (µg mL^{-1})	14 – 26	8.75 – 16.25	10.5 – 19.5
LOD (µg mL^{-1})	0.82	0.48	0.64
LOQ (µg mL^{-1})	2.49	1.45	1.94
Slope	0.0395	0.0651	0.0330
Standard deviation of the slope	0.0007	0.0011	0.0006
Confidence limit of the slope 95%	0.0395 ± 0.0006	0.0651 ± 0.001	0.0330 ± 0.006
Intercept	0.0028	-0.0806	0.0226
Standard deviation of the Intercept	0.0088	0.0088	0.0088
Confidence limit of the Intercept	0.0028 ± 0.008	-0.0806 ± 0083	0.0226 ± 0.005
Regression coefficient (r^2)	0.9986	0.9996	0.9999
System precision[b], (% RSD)	0.32	0.29	0.76
Confidence limit for System precision	0.80 ± 0.002	0.73 ± 0.002	0.51 ± 0.003
Intraday precision[b], (% RSD)	0.43	0.37	0.44
Confidence limit for Intraday precision	99.36 ± 0.34	99.30 ± 0.29	99.40 ± 0.35
Interday precision[c], (% RSD)	0.48	0.51	0.54
Confidence limit for Interday precision	99.16 ± 0.22	99.14 ± 24	99.20 ± 0.26
Accuracy[d], % w/w	99.21 – 101.10	99.20 – 100.50	99.13 – 100.60
Confidence limit for accuracy	99.78 ± 0.57	99.75 ± 0.42	99.78 ± 0.49
Assay[d] ± SD	99.70 ± 0.48	99.89 ± 0.24	98.60 ± 1.44

[a]mean of five replicates; [b]mean of six determinations; [c]mean of 18 findings in three consecutive days; [d]mean of three findings at each level

CONCLUSION

A new UV spectrophotometric procedure employing simultaneous equation method has been developed for the simultaneous estimation of OLM, CHL and AML in pharmaceutical formulation. The developed method is rapid and validated as per ICH norms. Hence the proposed technique will be highly useful in routine quality control of OLM, CHL and AML in pharmaceutical formulation.

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