Synergistic Spectrophotometric strategies for precise Sartans quantification in Pharmaceuticals: Unifying UV Derivative and AUC approaches with solvent consistency

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Olmesartan Medoxomil (OLM), Telmisartan (TEL), Valsartan (VAL), Derivative spectroscopy.

ABSTRACT:
This study aims to develop and validate a Ultra violet spectroscopic analytical method for accurately measuring Olmesartan Medoxomil (OLM), Telmisartan (TEL), and Valsartan (VAL), three common antihypertensive drugs. These medications block angiotensin II at the AT1 receptor, reducing blood pressure through vasodilation and decreased water retention. UV spectrophotometry offers a simple and cost-effective approach for drug quantification. The objective is to establish specific wavelengths for each drug and evaluate derivative and AUC techniques for precise measurement. A diluent of 0.1N sodium hydroxide and distilled water (3:7) was used, yielding wavelengths of 248 nm for OLM, 295 nm for TEL, and 250 nm for VAL in zero-order analysis. First-order derivative peaks were identified at 264 nm, 284 nm, and 267 nm, while second-order derivatives showed 252 nm, 241 nm, and 239 nm for OLM, TEL, and VAL, respectively. AUC analysis further refined ranges for each compound. The method was validated for accuracy, precision, sensitivity, and detection limits using this solvent system. Results demonstrated that the UV spectrophotometric method was effective for the precise quantification of OLM, TEL, and VAL. The common solvent system ensured efficiency in routine quality control. In pharmaceutical settings, this approach offers a dependable, rapid, and economical technique for monitoring these drugs.

1. Introduction

Olmesartan Medoxomil (OLM), Telmisartan (TEL), and Valsartan (VAL) are medications classified as Angiotensin II receptor antagonists (AT1), commonly used to manage high blood pressure [1] either alone or in combination with other drugs. By reducing blood pressure, they lower the risk of non-fatal heart events such as strokes and heart attacks. These drugs work by blocking the hormone angiotensin-II at the AT1 receptor, which in turn relaxes blood vessels and reduces water excretion by the kidneys [2]. The primary aim of our current investigation was to develop and validate four distinct spectroscopic methods namely, derivative [3-5] (zero, first order, second order, and AUC methods) for the quantitative assessment and approval of Olmesartan Medoxomil, Telmisartan and Valsartan in pharmaceutical formulations. In-depth scrutiny of existing literature unveiled the existence of few analytical techniques, including spectroscopic [6-13], RP-HPLC [14-19], UPLC [20], and LC-MS [21,

22] methods [23-31], which have been utilized for the estimation of these drugs. However, it was noted that derivative UV-spectrophotometric techniques employing the same solvent solution have not been documented for the quantification of these medicinal products. By designing and validating these novel spectroscopic methods, we aimed to provide a robust and reliable approach for the quantitative assessment and approval of Olmesartan Medoxomil, Telmisartan, and Valsartan in pharmaceutical formulations. Our research contributes to the advancement of analytical chemistry by introducing innovative methods that offer enhanced accuracy and precision in the quantification of these sartans. Additionally, the development of derivative UV-spectrophotometric techniques utilizing the same solvent solution adds to the versatility and applicability of analytical methods available for routine analysis.

2. Methods

Materials

The reference standard of Olmesartan Medoxomil, Telmisartan, and Valsartan API were procured from MSN Laboratories. Sodium hydroxide and water are used as reagents were of AR grade. 0.1N Sodium hydroxide and distilled water in a ratio of 3:7 as a diluent.

Instruments

For Spectro Analysis of the Instrument Shimadzu 1800 was applied with UV Probe 2.34 Software for data analysis and interpret the compound. In 1cm quartz cells, abs spectra of reference, test solutions, measured over the 200–400 nm range.

Preparation of stock solution

The three drugs 25 milli gram was dissolved in 3ml of 0.1 Normality Sod Hydroxide and make up the volume to 25 ml to get 1000 micro gram per ml concentration above stock solution 2.5 ml 1/4th pipette and made the volume to 25 ml and the concentration is 100 and further dilutions made with distilled water.

Preparation of sample solution

Weigh 20 tablets, OLM, TEL and VAL with label claim of 40 mg, 80 mg and 80 mg and powdered each drug individually. Then transfer the analyte equivalent to 25 mg into 25 ml volumetric flask and add 3 ml of 0.1 N sodium hydroxide add 7 ml of distilled water and sonicate for 5 minutes. Filter through 0.45µ Whatman filter paper and make up to 25 ml with distilled water. To prepare 12 and 5 micro gram per ml 1.2 ml and 0.5ml was taken from the sec stock solution the main concentration prepared to 100 microgram per ml by taking 2.5 ml and made the volume to 25 ml.

Zero order UV derivative spectroscopic method[3]

Prepare a series of dilutions in the concentration range of 3-16, 4-20 and 1-9 µg/ml were examined within the range of wavelengths 200-400 nm using distilled water as blank. The UV spectrum of OLM, TEL and VAL showed their λmax at 248, 250, 290 nm.

Preparation of calibration curve

Absorbances at 248, 250, 290 nm were plotted vs concentration. The technique displays an excellent linearity range of 3-15 µg/ml for OLM, 4-20 microgram per ml for TEL, for VAL 1-9 µg/ml.

First-order UV derivative spectroscopic method[3]

Its conversion of the normal spectrum into first 1^{ST} derivative spectrum. Spectra were derivatized using first order, delta lambda 16000 and scaling factor 10. The first order derivative spectrum of (OLM, TEL and VAL) showed a sharp peak at 264, 284 and 267 nm respectively. The absorbance difference at n = 1 ($dA/d\lambda$) was calculated. The amplitudes were measured for all the solutions and plotted against concentration to get calibration curve. During the developed method formulation and Pharmaceutical Laboratory preparations are successfully analyze.

Preparation of calibration curve

The amplitudes at 219and 250 nanometer plot with the continuous concentration of OLM, TEL and VAL. The method shows good linearity range of 3-15 micro gram /ml for OLM, 3-15 micro gram /ml for TEL and 4-20 micro/ml for VAL.

Second-order UV derivative spectroscopic method[3]

In this Spectrophotometric method, the original spectra were derivatized using Second order, delta lambda 16000 and scaling factor 10 to get second order Derivative spectra. The $d^2A/d\lambda^2$ of corresponding crests of OLM, TEL and VAL were measured at 252.43, 239, 241 nm and plotted against concentrations to give calibration curve and regression equation was calculated.

Preparation of calibration curve

The absorption spectra of OLM, TEL and VAL were reported in the range of 200-400nm. The amplitudes at 252, 241 and 239 nm were plotted vs concentration of OLM, TEL and VAL. The method shows good linearity sequence limit of 3-15, 3-15 micro gram/ml, 4-20, 2^{nd} OLM, TEL and VAL.

Area under curve method (AUC) [3]

To the integrated values of the absorbance the two WL of the dosage forms λ1 (239.2) and λ2 (257.8) on Olmesartan medoxomil (OLM), on Telmisartan (TEL), λ1 (240.8) and λ2 (258.8) and λ1 (273.2) and λ2 (317) on Valsartan (VAL) absorption spectra. Area calculating recorded to the horizontal axis area to, after calculating areas of different concentrations (3-15, 3-15, 4-20 µg/ml) calibration graph was plotted using areas. Similarly, areas at λ1, λ2, were calculated from Assay spectrum and substituted in linear regression equation.

Preparation of calibration curve

The max absorption spectra of working std solution of OLM, TEL and VAL were reported in range, 200-400nm. The areas from 239.2-257.8 nm, 240.8-258.8 nm and 273.2-317 nm, were plotted vs concentration of OLM, TEL and VAL. The method shows good linearity range of 3-15 µg/ml, 3-15 µg/ml for OLM and TEL and 4-20 µg/ml for VAL.

3. Results

Linearity and Range

Zero order derivative method

OLM, TEL and VAL got the linear within the prepared dilutions for 4-20 µg/ml and 1-9 µg/ml with correlation co-efficient, slope and intercept 0.9996, 0.0432 and 0.0214, 0.9995, 0.0484 and 0.0214 and 0.9997, 0.0338 and 0.0023.

First order derivative method

OLM, TEL and VAL showed linearity within the range of concentration for with correlation co-efficient, slope and intercept of 3-15 µg/ml 1, 0.0144 and 0.0054, 3-15 µg/ml, 0.9995, 0.0060 and 0.0116 and 4-20 µg/ml, 0.9997, 0.0092 and 0.0010 for first order derivative method.

2nd order derivative method

OLM, TEL and VAL showed linearity within the range of concentration for with correlation co-efficient, slope and intercept of 3-15 µg/ml, 0.0017 and 0.0009, 3-15 µg/ml, 0.9995, 0.0074 and 0.0055 and 4-20 µg/ml, 0.9995, 0.0019 and 0.0011 for second order derivative method.

AUC method

OLM, TEL and VAL showed linearity within the range of concentration for with correlation co-efficient, slope and intercept of 3-15 µg/ml, 0.9996, 0.0523 and 0.0354, 3-15 µg/ml, 0.9995, 0.52300.2221 and 4-20 µg/ml, 0.9998, 0.0208 and 0.0051 for second order derivative method.

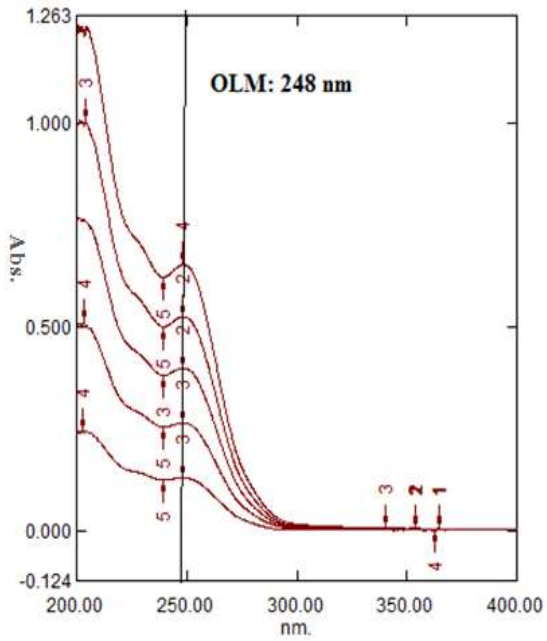

Figure 1: Zero order absorption spectra of Olmesartan

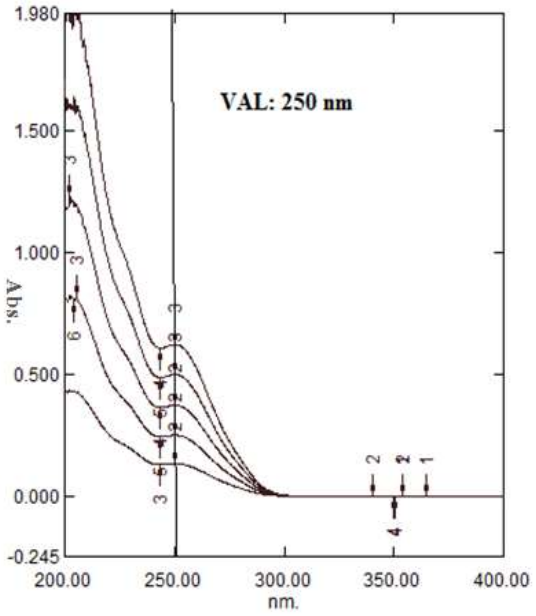

Figure 2: Zero order absorption spectra of Valsartan

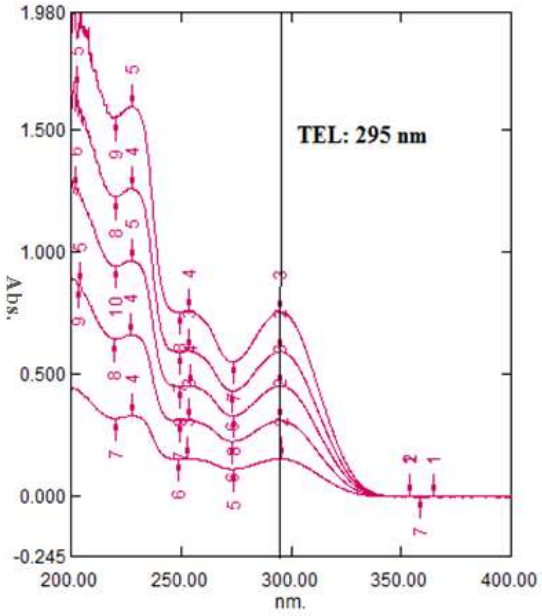

Figure 3: Zero order absorption spectra of Telmisartan

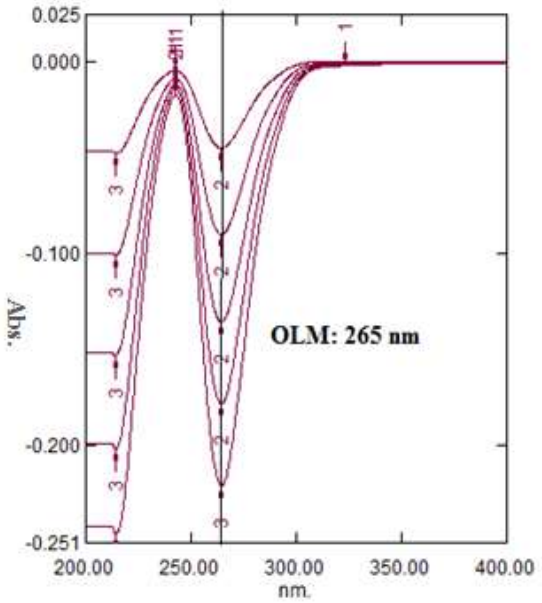

Figure 4: First order absorption spectra of Olmesartan

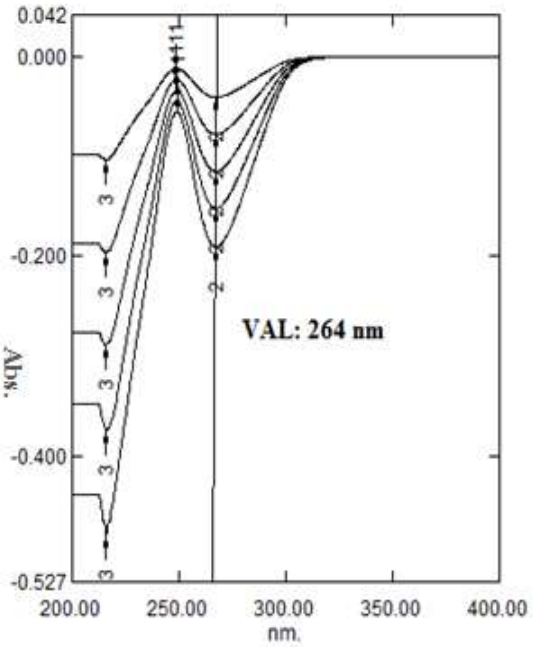

Figure 5: First order absorption spectra of Valsartan

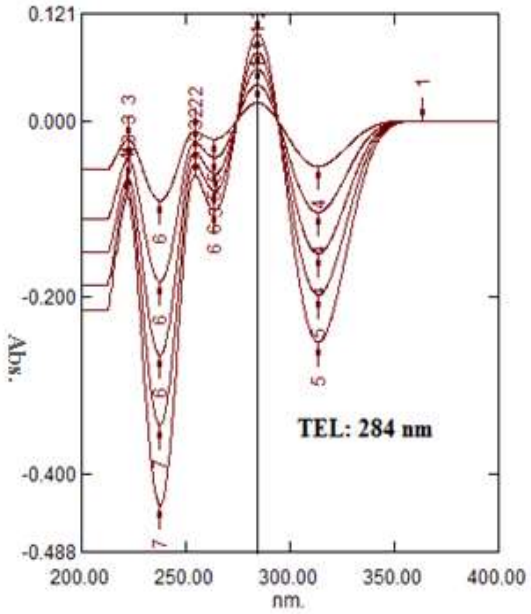

Figure 6: First order absorption spectra of Telmisartan

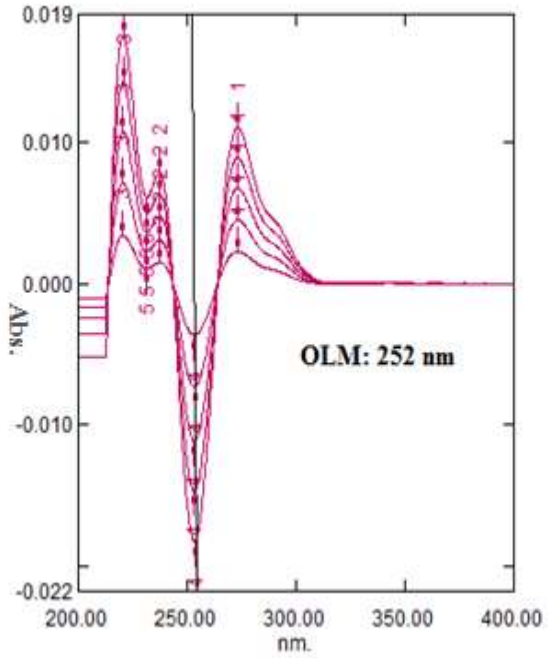

Figure 7: 2nd order absorption spectra of Olmesartan

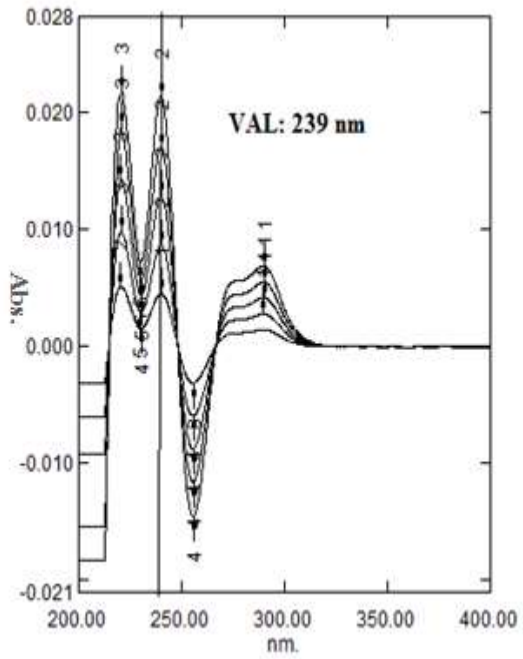

Figure 8: Second order absorption spectra of Valsartan

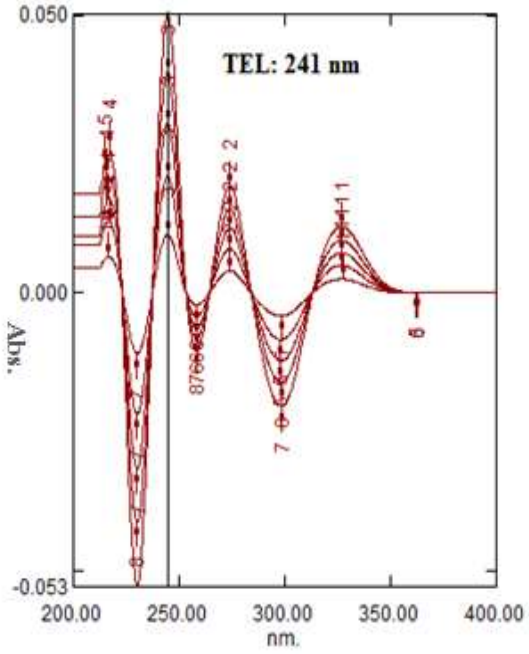

Figure 9: Second order absorption spectra of Telmisartan

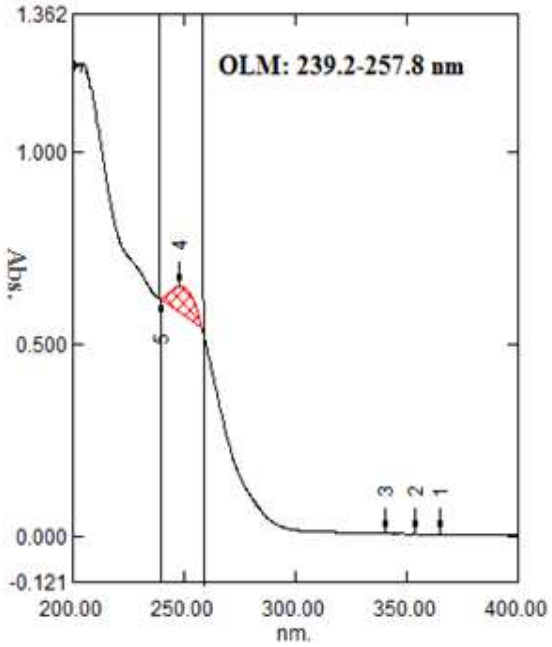

Figure 10: Absorption spectra of AUC Olmesartan

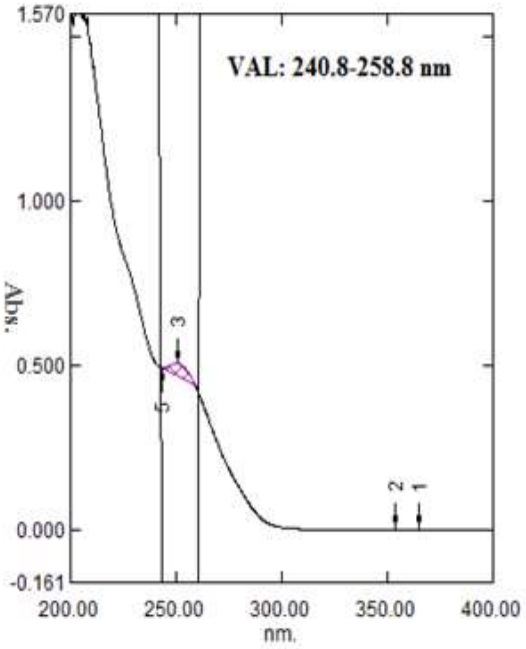

Figure 11: Absorption spectra of AUC Valsartan

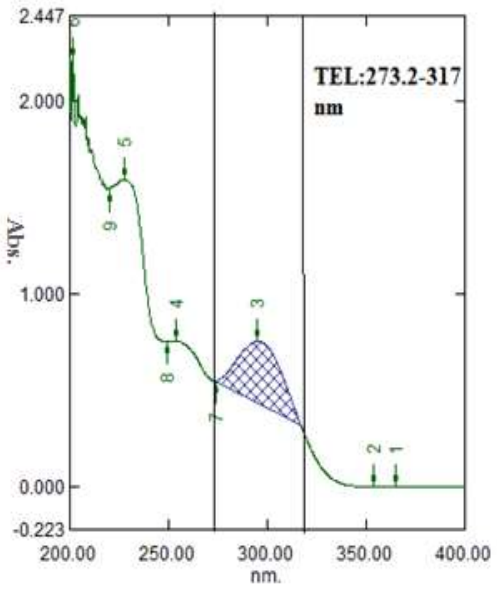

Figure 12: Absorption spectra of AUC method of Telmisartan

Accuracy

Accuracy of the method was confirmed by recovery study form marketed formulation at three levels of concentration i.e. 50%, 100%, and 150% of label claim by standard addition technique.

LOD and LOQ

Calibration study was repeated for five sequences and (SD) of the intercepts was calculated.
LOD =3.3*SD/slope of CC Curve
LOQ= 10*SD/ slope of CC curve
SD= SD of intercepts.

Table 1: Zero and First order derivative spectroscopic methods- Validation parameters

Parameters assessed	Zero order			First order		
	OLM	TEL	VAL	OLM	TEL	VAL
Beer's law range (µg /ml)	3-15	3-15	4-20	3-15	3-15	4-20
Wavelength (nm)	248	295	250	264	284	267
Correlation Coefficient (r^2)	0.9996	0.9995	0.9997	1.000	0.9995	0.9997
Slope	0.0432	0.0484	0.0338	0.0144	0.0060	0.0092
Intercept	0.0038	0.0214	0.0023	0.0054	0.0116	0.0010
LOD	0.496	0.457	0.125	0.236	3.437	0.282
LOQ	0.670	1.719	0.356	0.358	8.050	1.374
Intra-day precision (%RSD)	1.624	1.633	0.384	1.764	1.122	0.849
Inter-day precision (%RSD)	1.838	1.544	0.148	1.761	1.183	1.446

Table 2: Second order derivative and AUC methods- Validation parameters

Parameters assessed	Second order			AUC		
	OLM	TEL	VAL	OLM	TEL	VAL
Beer's law range (µg /ml)	3-15	3-15	4-20	3-15	3-15	4-20
Wavelength (nm)	252	241	239	239.2-257.8	273.2-317	240.8-258.8
Correlation Coefficient (r^2)	1.000	0.9995	0.9995	0.9996	0.9995	0.9998
Slope	0.0017	0.0074	0.0019	0.0523	0.5230	0.0208
Intercept	0.0009	0.0055	0.0011	0.0354	0.2221	0.0051
LOD	1.4323	1.786	1.172	0.144	0.340	0.344
LOQ	4.3403	13.055	5.084	1.507	0.806	1.418
Intra-day precision (%RSD)	1.416	1.131	1.44	1.701	1.170	1.485
Inter-day precision (%RSD)	1.589	1.001	1.118	1.865	1.069	1.305

Table 3: Recovery studies

Derivative spectroscopic method	% addn of label claimed	Amount of standard added (µg/ml)	Obtained amount (µg/ml)	Recovery%± SD
Zero order OLM	50	1.5	10.71	102.02±0.35
	100	3	12.30	102.58±0.47
	150	4.5	13.67	101.30±0.20
Zero order TEL	50	1.5	10.942	104.21±0.25
	100	3	12.512	104.27±0.32
	150	4.5	14.041	104±0.36
Zero order VAL	50	2	13.54	96.72±0.30
	100	4	15.37	96.09±0.41
	150	6	17.68	98.24±0.20
First order OLM	50	1.5	10.25	97.61±0.26
	100	3	11.84	98.72±0.41
	150	4.5	13.23	98.04±0.25
First order TEL	50	1.5	10.233	97.46±0.26
	100	3	11.566	96.38±0.15
	150	4.5	13.233	98.02±0.30
First order VAL	50	2	14.23	101.70±0.35
	100	4	15.86	99.18±0.11
	150	6	18.36	102.05±0.15
	50	1.5	10.058	95.79±0.20

Second order OLM	100	3	11.823	98.52±0.37
	150	4.5	13	96.29±0.32
Second order TEL	50	1.5	10.337	98.45±0.17
	100	3	11.985	99.88±0.23
	150	4.5	13.394	99.21±0.20
Second order VAL	50	2	14.15	101.12±0.25
	100	4	16.26	101.64±0.26
	150	6	18.36	102.04±0.30
AUC OLM	50	1.5	10.73	102.24±0.36
	100	3	12.43	103.61±0.32
	150	4.5	13.82	102.41±0.15
AUC TEL	50	1.5	10.715	102.0±0.20
	100	3	11.895	99.12±0.25
	150	4.5	13.420	99.41±0.15
AUC VAL	50	2	14.08	100.58±0.32
	100	4	15.62	97.62±0.25
	150	6	17.54	97.46±0.26

*Amount of OLM, TEL and VAL in the pre-analyzed samples are 9,5 and 12 Micro gram per ml

Analysis of marketed formulation

Applicability of the suggested technique was investigated by examining the samples that were sold commercially.

Table 4: Results of Assay of formulation

Method	Drug	Labeled claim	Amount obtained	% Found*±SD
Zero order	OLM	40 mg	40.61	101.543±0.25
	TEL	80 mg	83.452	104.31±0.20
	VAL	80 mg	79.54	99.43 ±0.35
First order	OLM	40 mg	40.25	97.61±0.26
	TEL	80 mg	77.703	97.12±0.25
	VAL	80 mg	80.43	100.54±0.15
Second order	OLM	40 mg	39.19	99.56±0.45
	TEL	80 mg	82.28	102.85±0.25
	VAL	80 mg	80.46	100.5±0.25
AUC	OLM	40 mg	40.96	102.41±0.26
	TEL	80 mg	83.42	104.28±0.15
	VAL	80 mg	78.664	98.3±0.26

*Average of three experiments

4. Discussion

The UV spectrophotometric methods displayed strong linearity across specific concentration ranges for Olmesartan Medoxomil (OLM), Telmisartan (TEL), and Valsartan (VAL). The derivative and AUC methods exhibited linearity from 4-20 micro gram /ml for OLM and VAL, and 3-15 micro gram /ml for TEL. 248 nm for OLM, 295 nm for TEL, and 250 nm for VAL in zero order. First-order derivative analysis yielded absorbance peaks at 264 nm, 284 nm, and 267 nm for OLM, TEL, and VAL respectively. Second-order derivative analysis revealed peaks at 252 nm, 241 nm, and 239 nm, while AUC methods showed ranges of 239.2-257.8 nm, 273.2-317 nm, and 240.8-258.8 nm for OLM, TEL, and VAL respectively. Precision assessments showed consistent intra-day and inter-day variability, indicating reliable reproducibility. Accuracy, as determined through recovery studies, demonstrated nearly 100% recovery rates across varying concentration levels. The amount of standard drug added is in between 1.5 to 6 µg/ml. The labelled claim for OLM is 40mg, TEL 80mg and VAL 80mg Calculated limits of detection and quantification were within acceptable ranges. In summary, these UV spectrophotometric methods provide efficient and cost-effective approaches for quantifying OLM, TEL, and VAL.

5. Conclusion

Derivative Spectrophotometric (Zero, first, second order, and AUC) techniques have been devised and accepted in order to examine each dose form of Olmesartan Medoxomil (OLM), Telmisartan (TEL), and Valsartan (VAL). The developed spectrophotometric techniques for the quantitative estimation were validated in accordance with ICH guidelines and repeatability of reliable results and close to related value, and cost-effective. They can be used in Quality Control Laboratories for routine analysis. The study highlights how using the same solvent can influence the spectrum properties of important organic compounds found in pharmaceuticals. Statistical analysis demonstrates the method's selectivity and reproducibility for analysis. A common solvent was utilized in this research to validate a UV spectrometric approach for determination. The findings showed that the techniques for the testing of Olmesartan Medoxomil, Telmisartan, and Valsartan are reliable, fast, robust, and accurate.

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