

New RP-HPLC Method for Simultaneous Estimation of Olmesartan Medoxomil and Hydrochlorothiazide in Combined Pharmaceutical Dosage Forms

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Abstract: A simple RP-HPLC method developed for simultaneous estimation of Olmesartan medoxomil and Hydrochlorothiazide in combined pharmaceutical dosage forms. This method validated as per ICH guidelines. This method was simple, specific, precise, linear, accurate, robust and ruggedness for simultaneous analysis of both Olmesartan medoxomil and Hydrochlorothiazide.

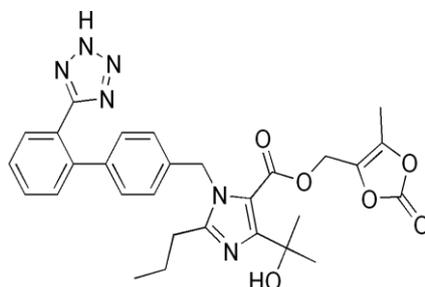
Keywords: Olmesartan medoxomil, Hydrochlorothiazide, RP-HPLC.

I. Introduction

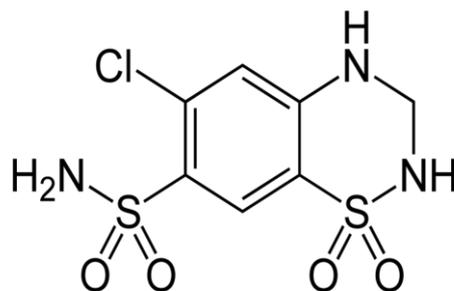
Olmesartan medoxomil is angiotensin II receptor blocker approved for use as an alternative therapeutic anti-hypertensive agent. Chemically, it is (5-methyl-2-oxo-2H-1, 3-dioxol-4-yl) methyl, 4-(2-hydroxypropan-2-yl)-2-propyl- 1-({4- [2- (2H- 1, 2, 3, 4-tetrazol -5-yl)phenyl]phenyl)methyl)-1H-imidazole-5-carboxylate. It is shown in figure-1. It works by blocking a substance in the body that causes blood vessels to tighten. As a result, olmesartan relaxes blood vessels. This lowers blood pressure and increases the supply of blood and oxygen to the heart [1].

Hydrochlorothiazide is one of the oldest and widely used diuretics which is also used in the treatment of hypertension [2]. Chemically, it is 6-chloro-1, 1-dioxo-3,4-dihydro-2H-1,2, 4-benzothiazine-7-sulfonamide. It is shown in figure-2. Hydrochlorothiazide is a diuretic medication often used to treat high blood pressure and swelling due to fluid buildup other uses include diabetes insipid us, renal tubular acidosis, and to decrease the risk of kidney stones in those with high calcium level in the urine. For high blood pressure it is often recommended as a first line treatment. It is taken by mouth and may be combined with other blood pressure medications as a single pill to increase the effectiveness.

Several analytical HPLC methods have been found for the determination of individual and simultaneous estimation of Olmesartan medoxomil and Hydrochlorothiazide [3]-[7]. So, the work has been done to develop a simple, precise and accurate RP- HPLC method for simultaneous estimation of Olmesartan medoxomil and Hydrochlorothiazide in pharmaceutical formulations.



(Figure 1: Olmesartan medoxomil)



(Figure 2: Hydrochlorothiazide)

II. Materials and Methods

Apparatus: HPLC (Model: Alliance 2695 separation module with UV-Visible detector, Make: Waters, Software: Empower-2), Digital pH meter (Model: LP-1393, Make: POLMAN), Sonicator (Model: Soltec, Make: Sonica), Electronic Weighing Balance (Model: ML204 Ia01, Make: Mettler Toledo).

Chemicals and Reagents: Acetonitrile (HPLC grade, Make: Qualigens fine chemicals), Sodium dihydrogen orthophosphate (AR grade, Make: S.D Fine Chem. Ltd), Water (HPLC grade), Orthophosphoric acid (AR grade, Make: Rankem), Olmesartan medoxomil (Richer Pharmaceuticals, Hyderabad, India), Hydrochlorothiazide (Richer Pharmaceuticals, Hyderabad, India).

Chromatographic Conditions: This separation achieved by isocratically using Hypersil C18 column (150 X 4.6mm, 5 μ m), column oven temperature 30 °C, flow rate 1.0mL/min, UV at 254nm. Mobile phase was 0.1M mono basic sodium phosphate buffer (pH: 3.0 \pm 0.1) adjusted with orthophosphoric acid and acetonitrile at 70:30 ratio. Diluent was water and acetonitrile in the ratio of 90:10(v/v). Run time was 10min.

Preparation of mobile phase: 13.8g of Sodium dihydrogen orthophosphate weighed and transferred in to 1000mL volumetric flask and make up to the mark with water and adjusted pH: 3.0(\pm 0.1)with diluted Orthophosphoric acid solution. This buffer and acetonitrile were taken in the ratio of 70:30 and mixed well then filtered through 0.45 μ m Millipore filter paper and sonicated using sonicator up to 15min.

Preparation of standard solution: Weighed 20mg of Olmesartan medoxomil and 12.5mg of Hydrochlorothiazide working standards in 100mL volumetric flasks and dilute with 30mL of diluent and made up to the mark with diluent for standards stock solution. Transferred 10mL of the standards stock solution in to 100mL volumetric flask and made up to the mark with diluent. This standards solution used to sample analysis.

Preparation of sample solution: 10 tablets of Olmesartan medoxomil and Hydrochlorothiazide powdered using mortar. 200mg of this powder sample weighed and transferred in to 100ml volumetric flask and dissolved in 30mL of diluent then made up to the mark with diluent. This sample solution filtered then used as a sample stock solution. 10mL of this sample stock solution transferred in to 100mL volumetric flask and made up to the mark with diluent. This solution is used for sample analysis.

Sample analysis: Injected 20 μ L of blank (diluent), standard solution and sample solution in HPLC for sample analysis. Retention time for Hydrochlorothiazide 1.99 and Retention time for Olmesartan medoxomil 4.93.

Method Validation

Specificity and Selectivity: The specificity of the method was checked by injecting blank solution and sample solution. There was no interference from blank and excipients at the retention time of analytes peaks.

System suitability: Injected the system suitability solution and checked the system suitability. The tailing factor value was less than 2.0, theoretical plate's value was more than 2000 and resolution value was more than 2.0.

Linearity: Linearity was checked by preparing of five concentrations of the substance ranging from 25% to 150% level of the target. A concentration of 20ppm solution was proposed in the procedure as a 100% for Olmesartan medoxomil, 12.5ppm solution was proposed in the procedure as a 100% for Hydrochlorothiazide. Estimations were carried out as per the procedure mentioned. Observations were recorded and a linearity curve was prepared using regression analysis. The correlation coefficient was 0.999 for Olmesartan medoxomil and 0.999 for Hydrochlorothiazide. Linearity graphs were shown in Figure 4 and Figure 5.

Accuracy: The accuracy of the method was determined by % of recovery method for the spiked concentration levels of 50%, 100% and 150%. A concentration of 20ppm solution was proposed in the procedure as a 100% for Olmesartan medoxomil, 12.5ppm solution was proposed in the procedure as a 100% for Hydrochlorothiazide. The accuracy results were shown in table1 table 2.

Precision: The method precision and system precision were performed. The results were within limits for both Olmesartan medoxomil and Hydrochlorothiazide. The results were shown in table3.

Robustness of the Method: Changing with the flow rate (\pm 0.1mL/minute) and column oven temperature (\pm 5°C) and calculated RSD. The results were within limits.

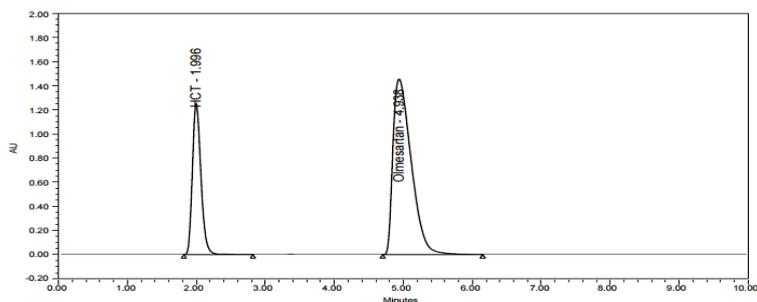
Ruggedness of the Method: The ruggedness of the method was performed with different analyst and different day analysis and calculated RSD. The results were within limits.

LOD and LOQ: This method was having limit of detection value for Olmesartan medoxomil 1.2ppm, for Hydrochlorothiazide 3.6ppm. The method was having limit of quantification value for Olmesartan medoxomil 3.0ppm, for Hydrochlorothiazide 9.0ppm.

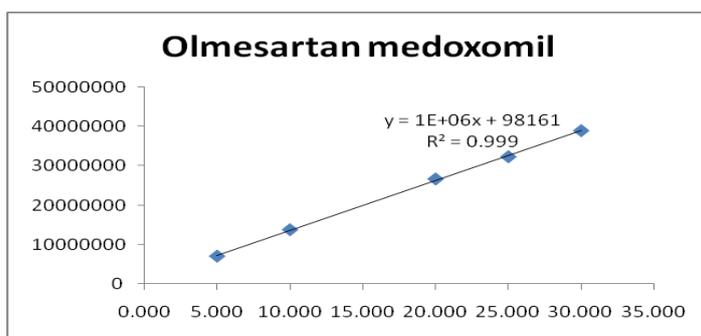
III. Results And Discussions

The developed method was validated as per ICH guidelines for specificity, linearity, accuracy, precision, robustness and ruggedness. The results were within limits.

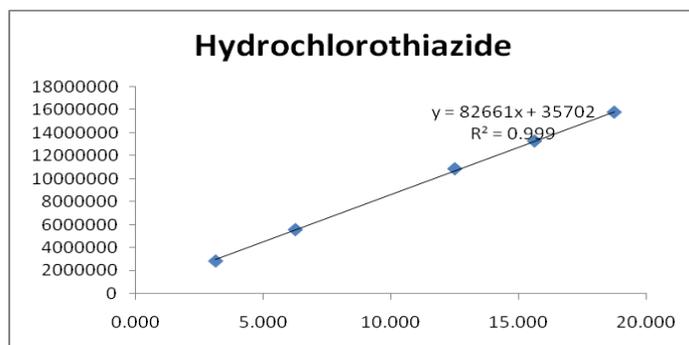
IV. Figures And Tables



(Figure 3: Chromatogram of Olmesartan Medoxomil and Hydrochlorothiazide)



(Figure 4: Linearity graph for Olmesartan Medoxomil)



(Figure 5: Linearity graph for Hydrochlorothiazide)

Concentration Level(spike)	Recovery
50%	100.97%
100%	100.02%
150%	100.71%

Table1: Accuracy for Olmesartan medoxomil

Concentration Level(spike)	Recovery
50%	101.78%
100%	100.73%
150%	99.42%

Table2: Accuracy for Hydrochlorothiazide

Precision	Olmesartan medoxomil	Hydrochlorothiazide
System Precision	0.34%	0.28%
Method Precision	0.42%	0.21%

Table3: Precision for Olmesartan medoxomil and Hydrochlorothiazide

V. Conclusion

The developed Reverse Phase HPLC method was very simple, selective and reproducible method for simultaneous analysis of Olmesartan medoxomil and Hydrochlorothiazide in combined pharmaceutical dosage forms. This method was having very low run time. It was accurate, precise, linear, robust and ruggedness method. As per best of my knowledge this method was very simple method for simultaneous determination of Olmesartan medoxomil and Hydrochlorothiazide in combined pharmaceutical dosage forms.

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