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Original Article

Method Development and Validation of Olmesartan Medoxomil by Using RP-HPLC

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ABSTRACT

Background: Olmesartan (OLM) is a drug used to treat hypertension, or elevated blood pressure. Controlling high blood pressure lowers the chance of further strokes, renal problems and heart attacks. **Materials and Methods:** The article presents a comprehensive overview of the drug's pharmacological characteristics and therapeutic effectiveness. A UV spectrophotometric technique was used to determine the solubility of Olmesartan medoxomil in a range of solvent ratios, including ethanol, methanol, acetonitrile, chloroform, pyridine, acetone, ethyl ether and distilled water. This was carried out since parameter analysis, drug validation and HPLC technique development all heavily depend on the solubility of the drug. The dissolution rates of several compounds were measured in a number of solvents, including distilled water, ethanol, methanol, acetonitrile, acetone, chloroform and pyridine. For every solvent, the UV spectra were measured between 200 and 400 nm. The λ_{max} values for several solvents were analyzed and recorded. **Results and Discussion:** The study revealed that Olmesartan medoxomil is very soluble in methanol and ethanol. A wavelength of 256 nm for methanol and an absorbance of 0.291 were used. The C_{18} (4.6×250 mm, 5 µ) particle size column in our approach was filled with water (containing 5% ammonium acetate) and methanol (5%:95%) at room temperature and 1.0/min flow rate using 10-min runtime. Olmesartan medoxomil eluted with a retention time of exactly 2.3 min. **Conclusion:** Using 10 min runtime, Olmesartan medoxomil eluted with a retention time of exactly 2.3 min.

Keywords: Olmesartan medoxomil, Hypertension, Validation, RP-HPLC.

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INTRODUCTION

Olmesartan is used to treat hypertension, or elevated blood pressure. Reducing hypertension can help avert heart attacks, strokes and renal issues. One drug that belongs to the Angiotensin Receptor Blocker (ARB) class is olmesartan. In order to facilitate easier blood flow, it relaxes blood vessels. The molecular formula for olmesartan medoxomil is 2, 3-dihydroxy-2-butenyl 4-(1-hydroxy-1-methylethyl).2-propyl-1-[benzyl p-(o-1H-tetrazol-5-ylphenyl)] imidazole cyclic 2, 3-carbonate, 5-carboxylate. Chemical structure of Olmesartan medoxomil is shown in Figure 1.

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Drug Profile

Angiotensin II receptor antagonist olmesartan medoxomil is mostly used to treat hypertension, or high blood pressure. The following is a comprehensive medication profile that includes important details about olmesartan medoxomil:

Olmesartan medoxomil belongs to the class of medications known as Angiotensin II Receptor Blockers (ARBs) or Angiotensin Receptor Blockers (ARBs). It works by blocking the action of angiotensin II, a hormone that causes blood vessels to narrow. By inhibiting angiotensin II, olmesartan medoxomil relaxes blood vessels, thereby reducing blood pressure (Arora *et al.*, 2020; Gopani *et al.*, 2017; Ghante *et al.*, 2019; Celebier *et al.*, 2014). The principal indication for Olmesartan medoxomil is the treatment of hypertension (high blood pressure) in adults and children six years of age and older (Dhole *et al.*, 2013). The recommended starting dose for most adults is usually 20 mg once daily. The dosage can be increased to 40 mg based on the individual patient's response (Beg *et al.*, 2016). For paediatric patients (6-17 years old), the starting dose is weight-dependent

(Jain *et al.*, 2011). It is typically administered orally in the form of tablets. Olmesartan medoxomil is a prodrug and once ingested, it is rapidly converted to its active form, olmesartan, in the gastrointestinal tract (Thomas *et al.*, 2022). The peak plasma concentration is reached about 1-2 hr after oral administration (Biagini *et al.*, 1998). Olmesartan is primarily eliminated via the hepatic (liver) route. It is excreted in faeces (about 35%) and urine (about 60%) (Rump *et al.*, 2004). Common side effects may include dizziness, light headedness, diarrhoea, or flu-like symptoms. Serious side effects are rare but may include kidney problems, allergic reactions and low blood pressure (Fogari *et al.*, 2010). It is important to monitor blood pressure regularly. Patients with impaired liver function may require dose adjustments. Caution is advised in patients with renal impairment (Wabkhede *et al.*, 2007). Olmesartan medoxomil may interact with certain medications, including potassium-sparing diuretics, Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and lithium (Brunner, 2002). Olmesartan medoxomil is contraindicated in pregnancy (especially in the second and third trimesters) due to the risk of harm to the foetus and its use should be avoided in breastfeeding women (Laeis *et al.*, 2001).

Importantance of Analytical Method and its Validation

The process of confirming that the method works as intended is called validation. Validation requires a series of experiments to check the performance of the method. The method should be able to produce reliable and accurate results after it is developed. The only way to assess the validity of a method is to perform laboratory tests. Validation experiments involve measuring different aspects of the method to evaluate its suitability. The key parameters of Validation are as follows:

Specificity

To make sure the analytical technique can measure the analyte properly in the presence of other factors that might interfere with the analysis, specificity tests are carried out. For example, excipients should not affect the analytical process when it comes to specificity investigations (Srikanth *et al.*, 2023).

Linearity

The concept of linearity of analytical method refers to a methods ability to show a linear relationship between observed responses and various concentrations (Sandhu *et al.*, 2016). To investigate linearity, a response vs concentration graph is employed. Regression analysis is one of the statistical approaches that must be utilized to establish whether the analytical process is linear or not (Dhole *et al.*, 2012).

Precision

Precision investigations assess how closely the observed values match up at the same concentrations and under the same circumstances (Dubey and Ghosh, 2015). The standard deviation and relative and standard deviation of the observed value are calculated for this research (Shah *et al.*, 2022).

Limit of detection

The Limit of Detection (LOD) in analytical method is the smallest amount of the analyte that can be accurately and precisely detected under ideal circumstances by the proposed analytical method (Al-Masri and Al-Mardini, 2005).

Limit of quantitation

The Limit of Quantification (LOQ) is the lowest analyte concentration that can be quantitatively detected with a stated accuracy and precision (Amim, 2012).

Robustness

These parameters, which involve a little adjustment to the ideal chromatographic conditions such column temperature, flow rate and pH, are verified on various instruments and operators. In this method flow rate parameter was used (Mahaparale *et al.*, 2013).

Ruggedness

Ruggedness test is determined between two different days and two different analysts and instruments (Bharti *et al.*, 2022).

Accuracy

A threefold precision is employed: 80%, 100% and 120% of the intended concentration (Singh, 2015). A low % recovery and relative standard deviation number show how accurate the spectrophotometric and HPLC methods (McDowall, 2005).

MATERIALS AND METHODS

Instruments Condition

Ultraviolet-visible (UV-vis) spectrophotometer: Model UV-1800 (Shimadzu).

HPLC system

The Waters-HPLC (Model-2489) was equipped with a manual injector port with 10 µL fixed loop, a Waters 515 HPLC Pump and a Waters 2489 UV/visible detector. The Waters C-18 (4.6×250 mm, 5 µm) column was utilized and data were collected using the Empower^{-3} programming software.

Additional equipment used in the study included a sonicator (Remi Instrument Ltd., Mumbai, 10A) for sample dissolution, an analytical balance from Mettler-Toledo International Inc. Greifensee (Switzerland) for precise weighing and a highly precise hot air oven (Labman Scientific). Samples were injected into the HPLC system using a Hamilton micro syringe.

Chromatographic parameters

Column: Waters C-18 (4.6×250 mm, 5 µm).

Detector: Waters 2489 UV/visible detector.

Wavelength: 256 nm.

Flow Rate: 1.00 mL/min^{-1}.

Mobile Phase: Ammonium acetate buffer: methanol (5%: 95%).

Reagent: (For API).

Olmesartan medoxomil (API) was obtained as generous gift sample. Acetonitrile (ACN), Methanol (MeOH), Ammonium acetate and water was used. All reagents were HPLC analytical grade and were procured from Thermo Fisher Scientific India Pvt. Ltd.

Reagent: (For Market Formulation)

The tablet of Olmesartan Medoxomil (Olmetime™ Batch No. J5IAV005, Mfg. Date. 10/2022, Exp. Date. 09/2024) containing 40 mg Olmesartan Medoxomil, with Colour: Titanium Dioxide IP was taken for studies. They were procured from Medical Store.

Mobile phase selection and optimization (pilot scale-up study)

Optimization Method 1

Standard stock solution of 200 ppm, 20 mg of olmesartan medoxomil was prepared in a 100 mL volumetric flask. Acetonitrile (100%) was added and sonicated for better dissolution. The volume was made up to mark with diluent and final concentration was made and Acetonitrile (100%) was chosen as a mobile phase.

Optimization Method 2

Standard stock solution of 200 ppm, 20 mg of olmesartan medoxomil was prepared in a 100 mL volumetric flask. ACN: Methanol (90%:10%) was added and sonicated for better dissolution. The volume was made up to mark with diluent and final concentration was made and ACN: DW (70:30) was chosen as a mobile phase.

Optimization Method 3

Standard stock solution of 200 ppm, 20 mg of olmesartan medoxomil was prepared in a 100 mL volumetric flask. Methanol (100%) was added and sonicated for better dissolution. The volume was made up to mark with diluent and final concentration was made and Acetonitrile: Ammonium acetate buffer (95%:5%) was chosen as a mobile phase.

Optimization Method 4

Standard stock solution of 200 ppm, 20 mg of olmesartan medoxomil was prepared in a 100 mL volumetric flask. Methanol (100%) was added and sonicated for better dissolution. The volume was made up to mark with diluent and final concentration was made and Methanol: Distilled water (95%:5%) was chosen as a mobile phase.

Final optimization

Standard stock solution of 200 ppm, 20 mg of olmesartan medoxomil was prepared in a 100 mL volumetric flask. ACN: Methanol (9:1) was added and sonicated for better dissolution. The volume was made up to mark with diluent and final concentration was made and Ammonium acetate buffer: methanol (5%: 95%) was chosen. We check the peaks (chromatograms) and finalise the solvent mobile phase based on the peak in the chromatogram with its retention time.

Preparation of buffer

The buffer was prepared freshly; the accurately weighed 0.577 g ammonium acetate was transferred in 250 mL volumetric flask, followed by volume make-up to the mark with Methanol and ACN (90:10). After the preparation of 0.1N ammonium acetate,

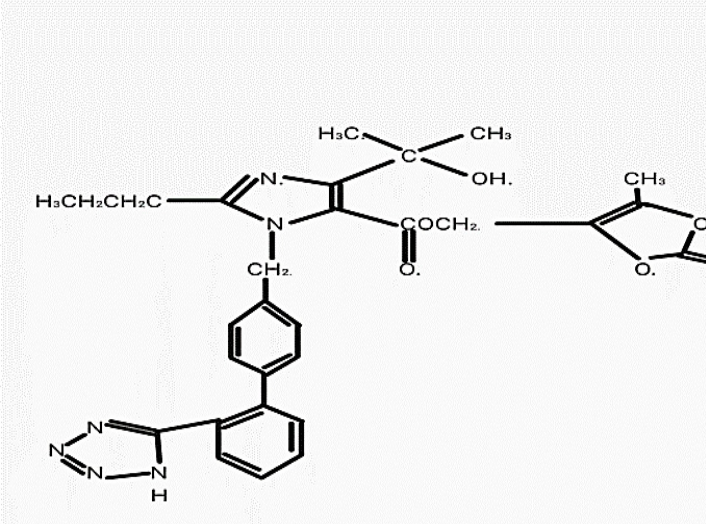

Figure 1: Structure of Olmesartan medoxomil.

Table 1: Results of System suitability, Linearity, LOD, LOQ and Accuracy % Recovery for chosen Active Pharmaceutical Ingredients and (API) Olmetime-40 Market Formulation.

System Suitability											
Sl. No.	CONC. (PPM)	Chosen Active Pharmaceutical Ingredients (API)					Olmetime-40 (market formulation)				
		RT	AUC	Height	Tailing	Plate Count	RT	AUC	Height	Tailing	Plate Count
1	100	2.376	4873543	767752	1.686495	2918.024935	2.373	5192554	884986	1.832349	4330.702933
2	100	2.385	4897196	744166	1.461483	3116.82822	2.392	5116936	815944	1.892317	2427.847396
3	100	2.383	4804471	690368	1.547809	2224.288415	2.356	5090015	806883	1.711417	2577.520328
4	100	2.389	4950114	786362	1.501971	2808.261451	2.384	4996373	783603	1.574545	2737.726276
5	100	2.388	4863286	730781	1.386625	2973.38569	2.352	5149318	713273	1.770358	1621.540456
6	100	2.392	4748685	674349	1.379183	2504.159749	2.384	5079907	737555	1.764371	1332.271637
	SUM	14.313	29137295	4393778	8.963566	16544.94846	14.241	30625103	4742244	10.545357	15027.60903
	MEAN	2.3855	4856215.833	732296.3333	1.493927667	2757.49141	2.3735	5104183.833	790374	1.7575595	2504.601504
	SD	0.00561249	70833.41813	43449.42902	0.114702161	332.4347326	0.0163187	66966.10093	61086.92156	0.10916656	1053.978754
	RSD	0.23527504	1.458613467	5.933312382	7.677892529	12.05569422	0.68753743	1.311984504	7.728862736	6.211258264	42.08169451
Linearity											
Sl. No.	CONC. (PPM)	Chosen Active Pharmaceutical Ingredients (API)					Olmetime-40 (market formulation)				
		RT	AUC	Height	Tailing	Plate Count	RT	AUC	Height	Tailing	Plate Count
1	2	2.373	114435	17203	1.783776	3597.869152	2.354	112758	14528	1.765339	2167.812283
2	4	2.389	212905	29177	1.844863	2576.460249	2.353	187852	24355	1.733275	2117.375404
3	8	2.401	447689	58018	1.509785	2096.278067	2.363	411105	56388	1.634408	2630.673969
4	16	2.414	776482	119059	1.360768	3183.131246	2.363	750673	102468	1.655323	2542.207064
5	32	2.413	1517046	209631	1.253817	2222.856721	2.356	1555487	202547	1.663266	2320.672767
6	64	2.39	2982125	506372	1.725336	4736.836151	2.355	3115737	396266	1.694085	2128.391062
	SUM	14.38	6050682	939460	9.478345	18413.43159	14.144	6133612	796552	10.145696	13907.13255
	MEAN	2.39666667	1008447	156576.6667	1.579724167	3068.905264	2.35733333	1022268.667	132758.6667	1.690949333	2317.855425
	SD	0.01580717	1091281.78	185444.6643	0.241738424	997.9125921	0.00450185	1152187.269	146141.2843	0.050135101	222.1706393
	RSD	0.65954818	108.2140935	118.4369729	15.30257176	32.51689141	0.19097221	112.7088511	110.0804098	2.964908547	9.585181067
LOD											
Sl. No.	CONC. (PPM)	Chosen Active Pharmaceutical Ingredients (API)					Olmetime-40 (market formulation)				
		RT	AUC	Height	Tailing	Plate Count	RT	AUC	Height	Tailing	Plate Count
1	0.00001	2.341	34908	5015	1.688663	2507.082667	2.377	24702	2946	1.970714	1556.136891
2	0.00001	2.348	26970	3757	2.033837	2526.800643	2.358	35909	4475	1.907563	1923.47954
3	0.00001	2.35	21133	2685	1.84999	2293.9395	2.358	29562	3557	1.812289	1384.493297
	SUM	7.039	83011	11457	5.57249	7327.82281	7.093	90173	10978	5.690566	4864.109728
	MEAN	2.34633	27670.33333	3819	1.857496667	2442.607603	2.36433333	30057.66667	3659.333333	1.896855333	1621.369909
	SD	0.00473	6914.152611	1166.236683	0.172709395	129.1272758	0.01096966	5619.917823	769.619603	0.079753437	275.3507809
	RSD	0.20141	24.98760144	30.53775027	9.297965269	5.28645189	0.46396398	18.69711939	21.03168891	4.204508158	16.98260091
LOQ											
Sl. No.	CONC. (PPM)	Chosen Active Pharmaceutical Ingredients (API)					Olmetime-40 (market formulation)				
		RT	AUC	Height	Tailing	Plate Count	RT	AUC	Height	Tailing	Plate Count
1	0.00003	2.352	54820	7479	1.650556	2590.983581	2.369	14351	1683	1.690691	1374.430763
2	0.00003	2.35	22861	3074	1.950121	2615.431869	2.355	17532	2026	1.896505	772.690756
3	0.00003	2.349	17677	2245	1.88678	2479.922979	2.359	17937	1713	1.717447	597.864041
	SUM	7.051	95358	12798	5.487457	7686.338429	7.083	49820	5422	5.304643	2744.98556

System Suitability											
Sl. No.	CONC. (PPM)	Chosen Active Pharmaceutical Ingredients (API)					Olmetime-40 (market formulation)				
		RT	AUC	Height	Tailing	Plate Count	RT	AUC	Height	Tailing	Plate Count
	MEAN	2.35033	31786	4266	1.829152333	2562.11281	2.361	16606.66667	1807.333333	1.768214333	914.9951867
	SD	0.00153	20115.72348	2813.243146	0.157878144	72.22053652	0.0072111	1963.932365	189.9640317	0.111905506	407.3719206
	RSD	0.06499	63.28485332	65.94569025	8.631219002	2.818788316	0.30542578	11.82616839	10.5107358	6.328729712	44.52175558
Accuracy% Recovery											
Sl. No.	% CONC (CONC. (PPM)	Chosen Active Pharmaceutical Ingredients (API)					Olmetime-40 (market formulation)				
		RT	AUC	Height	Tailing	Plate Count	RT	AUC	Height	Tailing	Plate Count
	80% (24)	2.352	1372097	178640	1.528456	2438.77495	2.378	1268529	218173	1.656363	3815.99845
		2.362	1375821	181475	1.317694	2809.822627	2.379	1252459	215006	1.724329	4706.88849
		2.36	1362109	183562	1.372468	3012.265744	2.378	1239666	209835	1.675258	4028.9473
	SUM	7.074	4110027				7.135	3760654			
	MEAN	2.358	1370009				2.378	1253551.333			
	SD	0.005291503	7090.454428				0.00057735	14462.47165			
	%RSD	0.224406388	0.517548018				0.024275414	1.153719937			
1	100% (32)	2.368	1741199	248006	1.595919	3371.709312	2.345	1578444	239308	1.870573	2496.08201
2		2.354	1755363	257185	1.485511	3436.741541	2.368	1552029	285810	2.098004	6612.28417
3		2.384	1750267	232813	1.353827	2590.326779	2.374	1579601	285312	1.888932	5646.38485
	SUM	7.106	5246829				7.087	4710074			
	MEAN	2.369	1748943				2.362	1570024.667			
	SD	0.015011107	7174.22163				0.01530795	15595.43768			
	%RSD	0.633736575	0.410203285				0.64800127	0.993324373			
1	120% (40)	2.379	2204264	302499	1.475903	1114.617367	2.367	1868169	372443	1.971175	7825.28124
2		2.383	2226910	296720	1.368281	896.478926	2.38	1843281	359128	1.950297	7719.7097
3		2.383	2172505	267822	1.311181	2105.008782	2.381	1830481	318291	1.781865	3883.77944
	SUM	7.145	6603679				7.128	5541931			
	MEAN	2.382	2201226.333				2.376	1847310.333			
	SD	0.002309401	27329.40853				0.00781025	19164.36749			
	%RSD	0.096965755	1.24155377				0.328714212	1.037420034			

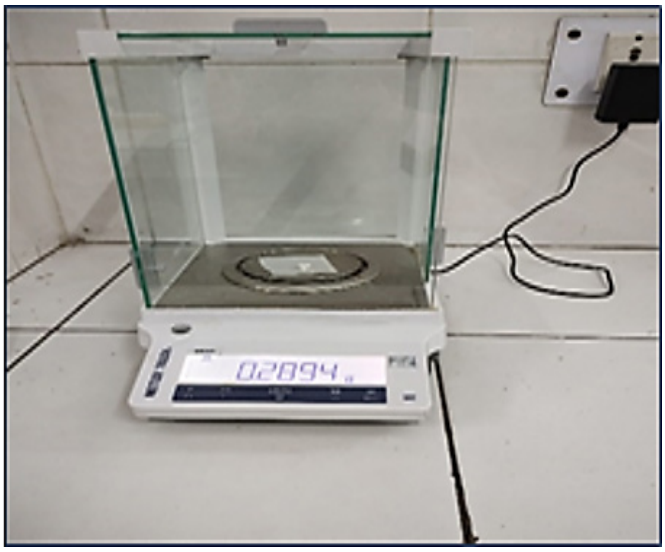

Figure 2: Olmesartan medoxomil tablet.

Table 2: Results of Ruggedness of chosen Active Pharmaceutical Ingredients (API) for 32 ppm & Olmetime - 40 Market Formulation.

		Chosen Active Pharmaceutical Ingredients (API)						Olmetime-40 (market formulation)					
		Interday 1		Interday 2		Interday 3		Interday 1		Interday 2		Interday 3	
Sl. No.	CONC. (PPM)	Mean±SD	%RSD	Mean±SD	%RSD	Mean±SD	%RSD	Mean±SD	%RSD	Mean±SD	%RSD	Mean±SD	%RSD
1	2	177332.5± 5335.120	3.008	174937±748.118	0.427	175670±393.151	0.223	174335±4147.888	2.379	178422±3054.701	1.712	176360.5±658.316	0.373
2	4	356996±2805.799	0.785	361581±2345.473	0.648	361825.5±4629.428	1.279	261441±2296.682	0.878	259440±4505.684	1.736	264873.5±89.802	0.033
3	8	549230.5±7128.3434	1.297	539168.5±11986.167	2.223	538356±1035.204	0.192	518390.5±1750.089	0.337	517627±1673.014	0.323	500628±8198.196	1.637
4	16	1019060.5±2822.063	0.276	1027466.5±344.361	0.033	998769±15832.120	1.585	888573±5293.401	0.595	889726±13873.435	1.559	887560.5±12659.332	1.426
5	32	2032484.5±8313.454	0.409	2028810±1639.073	0.080	1966491.5±4359.313	0.221	1669611±15225.423	0.911	1649432±12331.942	0.747	1677359±12310.729	0.733
6	64	4035070±66014.074	1.636	4044463.5±50937.851	1.259	4067503.5±91334.861	2.245	3416847.5±44077.501	1.290	3450709±26763.991	0.775	3335549.5±24547.211	0.735

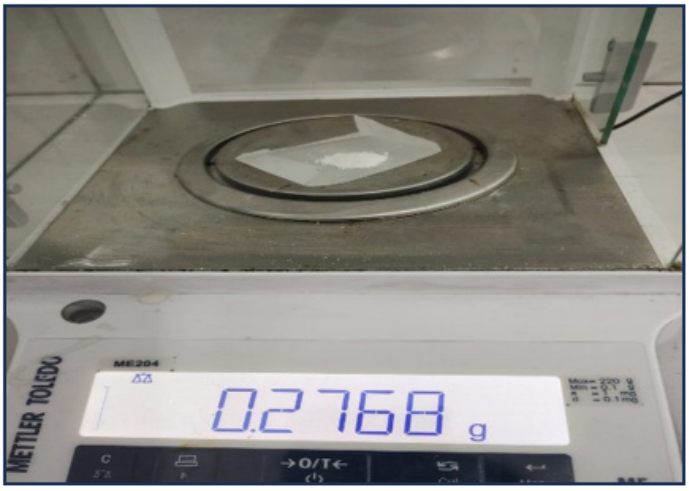

Figure 3: Olmesartan medoxomil crushed tablet.

the filtration of the buffer solution was done by using A0.22 µ/mL pour size membrane filter.

Preparation of Standard solution

Standard stock solution of 200 ppm, 20 mg of olmesartan medoxomil was prepared in a 100 mL volumetric flask. ACN: Methanol (9:1) was added and sonicated for better dissolution. The volume was made up to mark with diluent and final concentration was made.

Preparation of Sample solution

To analyse the medicament in tablet, 1 tablet 0.2894 g was precisely weighed and the coarse powder was triturated in the mortar to get a fine powder. The equivalent of 0.2768 g tablet powder was weighed, transferred to a 100 mL volumetric flask and diluent 10% Acetonitrile and 90% Methanol was added to make up the mark and mixture was sonicated for 15 min. The tablet solution was diluted to a final concentration. Olmesartan medoxomil tablet shown in Figure 2 and crushed tablet shown in Figure 3.

Analytical Method Validation of HPLC

The procedures provided above were validated in accordance with the ICH Q2 standard (R1). Robustness, analyte stability in solution, linearity, precision, limit of detection, limit of quantitation, accuracy/recovery, selectivity/specificity and ruggedness were among the many qualities that were examined for method validation. The ICH criteria were followed in terms of approach (ICH guideline Q2 (R1 and R2).

System Suitability

An evaluation of the systems suitability is necessary for best results of analytical procedures. In order to find out whether the system was suitable, six standard analyte solutions of pure drug Olmesartan medoxomil were injected at a concentration of 200 ppm. Several parameters were assessed, including the USP

tailing factor, theoretical plate count, peak asymmetry factor and percentage Relative Standard Deviation (%RSD). Based on the results obtained, the suitability of the system was assessed. Six duplicate injections were used to acquire the %RSD of the region. A comparison was made between the recommendation and the observed outcomes.

Specificity/selectivity

An injectable sample must be able to distinguish the target analyte from any other drugs or adulterants in order to demonstrate specificity. By injecting a blank and a placebo, the HPLC technique was used to analyze these parameters.

Linearity

A fresh 200 ppm stock of pure drug Olmesartan medoxomil was used to dilute the compound to eight various concentrations using a 90%:20% mixture of methanol and acetonitrile. We used least squares regression to examine the collected data.

System precision

In order to assess the repeatability, six repeats were performed on the same day using three distinct Olmesartan medoxomil concentrations (2 ppm, 4 ppm, 8 ppm, 16 ppm, 32 ppm and 64 ppm) in a 9:1 combination of methanol and acetonitrile. We obtained an intermediate level of accuracy by measuring the same concentration with six separate samples on same day but different times. For three times, the dilution was determined to have remained stable in terms of accuracy. To ascertain the repeatability, three distinct Olmesartan medoxomil concentrations (24 ppm, 32 ppm and 40 ppm) were examined using an RP-HPLC. The concentration estimates derived from the standard curve were accompanied by the following statistics for each dataset: confidence interval, standard deviation and percentage Relative Standard Deviation (%RSD).

Accuracy

A threefold precision was employed: 80%, 100% and 120% of the intended concentration. A low % recovery and relative standard

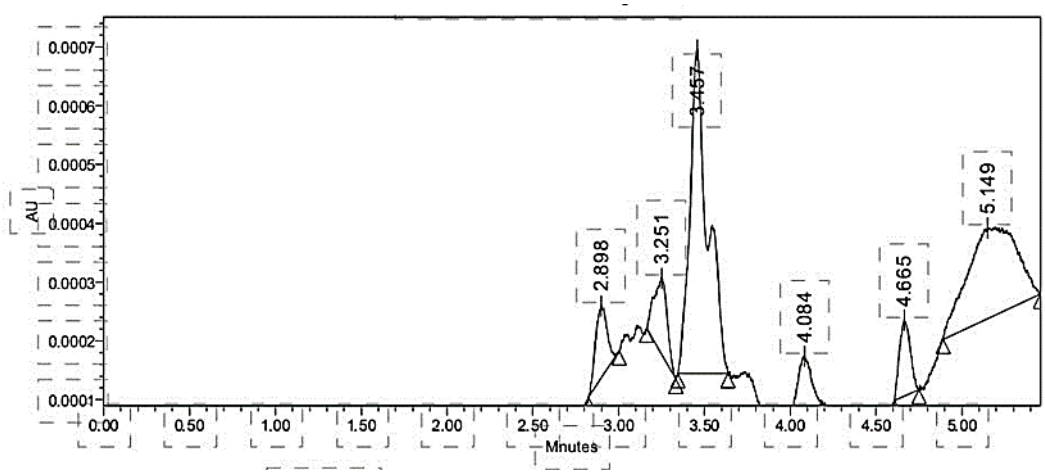

Figure 4: Optimization Method 1: Standard stock solution of 200 ppm, 20 mg of olmesartan medoxomil was prepared in a 100 mL volumetric flask. Acetonitrile (100%) was added and sonicated for better dissolution.

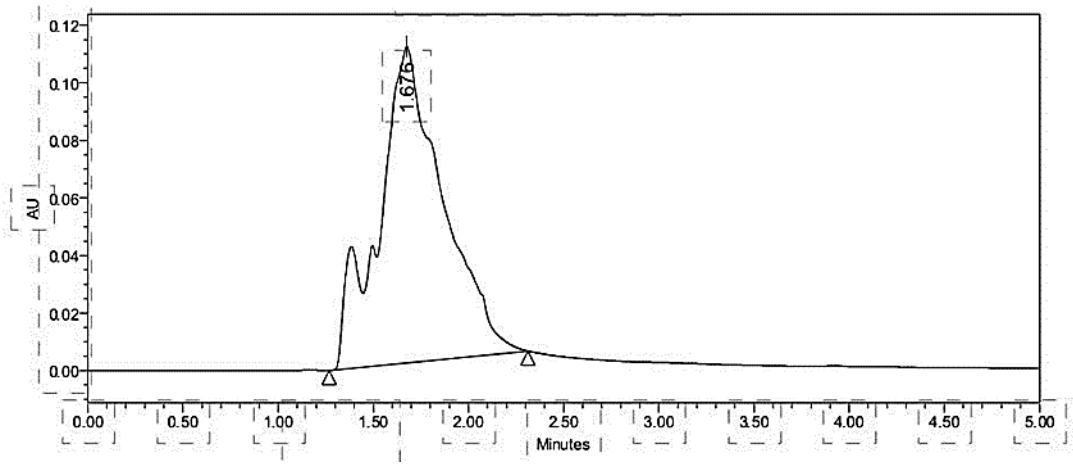

Figure 5: Optimization Method 2: Standard stock solution of 200 ppm, 20 mg of olmesartan medoxomil was prepared in a 100 mL volumetric flask. ACN: Methanol (90%:10%) was added and sonicated for better dissolution.

Table 3: Results of robustness of chosen Active Pharmaceutical Ingredients (API) and Olmetime-40 Market Formulation.

Robustness Flow													
		Chosen Active Pharmaceutical Ingredients (API)						Olmetime-40 (market formulation)					
Sl. No.	CONC. (PPM)	RT	AUC	Height	Tailing	Plate Count	Flow Rate	RT	AUC	Height	Tailing	Plate Count	Flow Rate
1	64	2.579	3397385	461348	1.635149	2454.230613	0.9	2.361	1804851	285467	1.62023	2229.748327	0.9
2	64	2.594	3366571	468796	1.54737	2560.272527		2.361	1801559	282857	1.555257	2191.542183	
3	64	2.582	3363063	486909	1.617792	2970.446311		2.36	1794377	281568	1.434481	2491.739229	
4	SUM	5.176	6729634	955705	3.165162	5530.718838		4.721	3595936	564425	2.989738	4683.281412	
5	MEAN	2.588	3364817	477852.5	1.582581	2765.359419		2.3605	1797968	282212.5	1.494869	2341.640706	
6	SD	0.00849	2480.53	12807.82513	0.049795874	290.0366641		0.000707107	5078.4409	911.4606409	0.085401529	212.2713669	
7	RSD	0.32787	0.07372	2.6802884	3.146497635	10.48820859		0.029955805	0.2824545	0.322969621	5.712977432	9.065069905	
8	64	2.325	3174274	507485	1.619216	3128.102084	1	2.368	1748355	281188	1.52841	2720.224491	1
9	64	2.33	3137648	519219	1.62414	3646.396121		2.365	1791534	304575	1.485634	2516.825068	
10	64	2.334	3114861	480990	1.561366	2826.632917		2.36	1789445	280826	1.506127	2693.688829	
11	SUM	6.989	9426783	1507694	4.804722	9601.131122		7.093	5329334	866589	4.520171	7930.738388	
12	MEAN	2.32967	3142261	502564.6667	1.601574	3200.377041		2.364333333	1776444.67	288863	1.506723667	2643.579463	
13	SD	0.00451	29973.9	19583.70165	0.034908078	414.6331869		0.004041452	24348.7784	13608.19492	0.021394241	110.5714374	
14	RSD	0.19356	0.9539	3.896752587	2.179610667	12.95576058		0.170934099	1.3706466	4.710951185	1.419918036	4.182640959	
15	64	2.134	2762214	448633	1.647781	2670.305363	1.1	2.118	1670119	271744	1.524661	1927.439504	1.1
16	64	2.16	2725217	450309	1.57482	2904.509193		2.169	1645576	273006	1.569252	2888.527126	
17	64	2.137	2735679	493230	1.583216	3637.627851		2.149	1688336	284443	1.537683	2779.269798	
18	SUM	6.431	8223110	1392172	4.805817	9212.442407		6.436	5004031	829193	4.631596	7595.236428	
19	MEAN	2.14367	2741037	464057.3333	1.601939	3070.814136		2.145333333	1668010.33	276397.6667	1.543865333	2531.745476	
20	SD	0.01422	19071.5	25278.16458	0.039921672	504.6495808		0.025696952	21457.8484	6995.977582	0.022929354	526.1877724	
21	RSD	0.66355	0.69578	5.447207222	2.49208443	16.43373902		1.197806953	1.28643378	2.531127584	1.485191296	20.78359682	

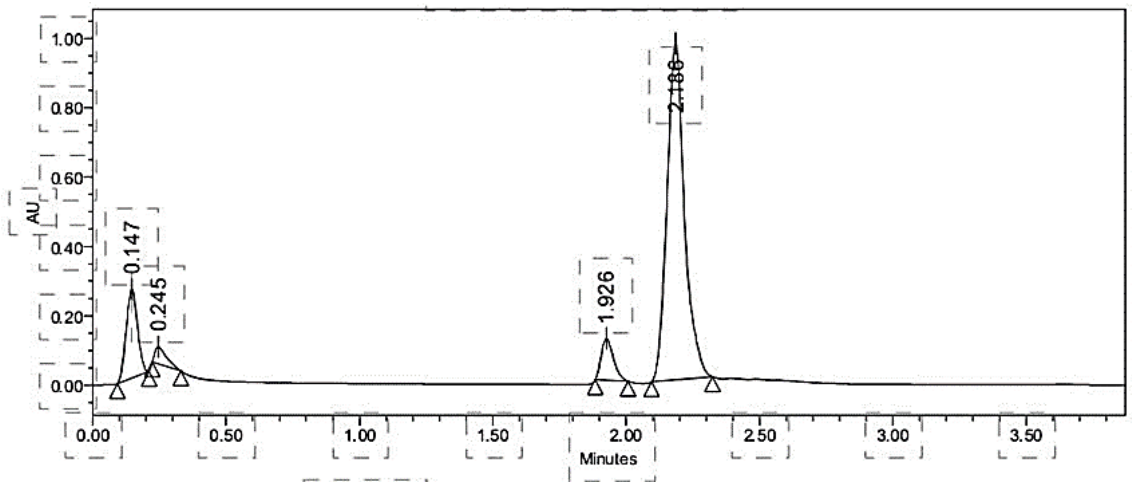

Figure 6: Optimization Method 3: Standard stock solution of 200 ppm, 20 mg of olmesartan medoxomil was prepared in a 100 mL volumetric flask. Methanol (100%) was added and sonicated for better dissolution.

deviation number exhibited how accurate the spectrophotometric and HPLC methods are.

Robustness

The robustness of the approach validation was determined by seeing no significant difference between flow rates. The relative standard deviation as a percentage was less than 2, which is within the allowed range.

Ruggedness

The Ruggedness of the approach validation was determined by seeing no significant difference between analyst A and analyst B.

The relative standard deviation as a percentage was less than 2, which is within the allowed range.

Limit of detection

In order to determine the limit of detection, the sample was diluted to a known concentration of 0.00001 ppm. The computed area percentage RSD was less than 2%, which is below the limit.

Limit of quantitation

In order to determine the limit of quantitation, the sample was diluted to a known concentration of 0.00003 ppm. The computed area percentage RSD was less than 2%, which is below the limit.

RESULTS

Optimization method

The mobile phase of the final solvent is chosen by taking into account the retention period of the peak in the chromatogram. The outcomes of the optimization procedure are shown in Figures 4-7. The final optimization method result for API is presented in Figure 8.

System suitability

The system suitability is determined by the several parameters. Tailing factor, retention time and AUC were studied for the drug Olmesartan medoxomil. The observations obtained were analysed after administering six injections of 100 ppm. The tailing factor was under the limit, as less than 2 and retention time and AUC %RSD was less than 2%. Results of System suitability of API and market formulation are presented in Tables 1 and 2 respectively.

Linearity

The concentration range of 2ppm to 64ppm was shown to be linear in the standard calibration curve. In calibration curve chart peak area was plotted on the X-axis and concentration on the Y-axis. After performing a linear regression analysis, the correlation coefficients (R^2) value was found to be 0.9997. The equation for the calibration curve-based peak area and concentration ppm was y=45992x-42605. Linearity data of API and market formulation are shown in Table 1 and calibration curve chart is shown in Figure 3 and Figure 4 respectively. The market formulation (R^2) value was found to be 0.9998. The equation for the calibration curve-based peak area and concentration ppm was y=48562x-2466.9.

Limit of detection

In order to determine the limit of detection, the sample was diluted to a known concentration of 0.00001 ppm. The computed area percentage RSD is less than 2%, which is below the limit. The results of LOD of API and market formulation are presented in Table 1.

Limit of quantitation

In order to determine the limit of quantitation, the sample was diluted to a known concentration of 0.00003 ppm. The computed area percentage RSD is less than 2%, which is below the limit. The result of LOQ of API and market formulation are presented in Table 1.

Accuracy

To evaluate the techniques' dependability, we conducted recovery experiments. Standards are added to the sample solution at concentrations of 24 ppm, 32 ppm and 40 ppm to guarantee accuracy. Results of Accuracy of API and market formulation are presented in Table 1.

Precision

Precision determines random errors on reproducibility and repeatability. This method is quantified using the terms %RSD (Relative Standard Deviation). % RSD of less than 2% is acceptable. The precision investigations for the developed analytical

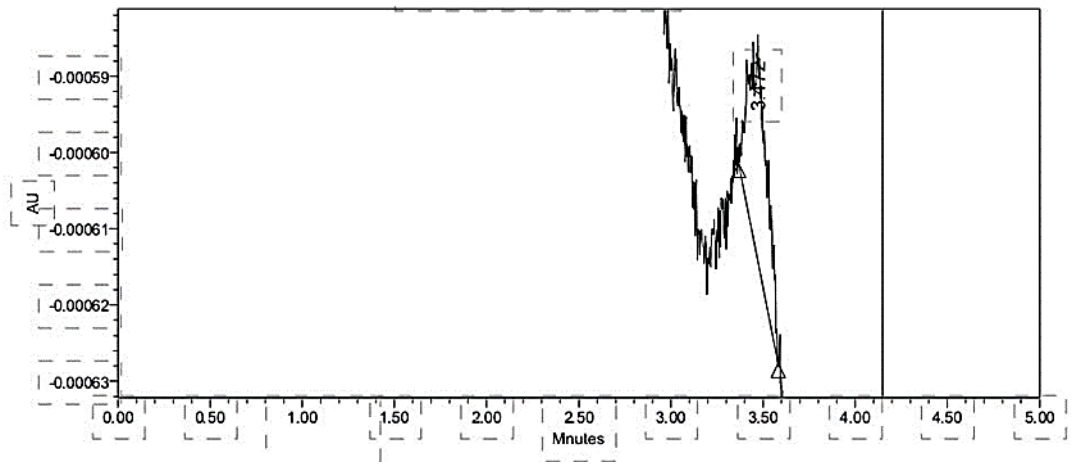

Figure 7: Optimization Method 4: Standard stock solution of 200 ppm, 20 mg of olmesartan medoxomil was prepared in a 100 mL volumetric flask. Methanol (100%) was added and sonicated for better dissolution.

Table 4: Results of Ruggedness of chosen Active Pharmaceutical Ingredients (API) for 32 ppm.

Ruggedness 32PPM												
	Sl. No.	CONC. (PPM)	Chosen Active Pharmaceutical Ingredients (API)					Olmetime-40 (market formulation)				
			RT	AUC	Height	Tailing	Plate Count	RT	AUC	Height	Tailing	Plate Count
ana1	1	32	2.379	1808685	259059	1.432205	1163.332146	2.367	1819629	281428	1.561194	3287.591355
	2	32	2.403	1799886	241416	1.386868	2047.204868	2.364	1770540	272936	1.48617	2752.023114
	3	32	2.38	1843247	245403	1.326169	2202.526143	2.369	1779903	275447	1.485382	2526.712694
Ana2 Ishu	4	32	2.37	1815814	271882	1.517527	2716.31341	2.406	1806744	231022	1.398102	1764.157253
	5	32	2.382	1812145	209718	1.364483	1738.15627	2.37	1794671	268202	1.735213	2964.642854
	6	32	2.366	1793765	260370	1.905857	3713.560249	2.395	1774473	263398	1.675256	2639.359673
		SUM	14.28	10873542	1487848	8.933109	13581.09309	14.271	10745960	1592433	9.341317	15934.48694
		MEAN	2.38	1812257	247974.6667	1.4888515	2263.515514	2.3785	1790993.333	265405.5	1.556886167	2655.747824
		SD	0.012884099	17209.29854	21731.40328	0.214596576	876.8775793	0.017512852	19472.3696	17935.08405	0.127402094	512.984152
		RSD	0.541348686	0.949605853	8.763557816	14.41356479	38.73963195	0.736298189	1.087238531	6.757615818	8.183134831	19.31599632
Ruggedness 64PPM												
	Sl. No.	CONC. (PPM)	Chosen Active Pharmaceutical Ingredients (API)					Olmetime-40 (market formulation)				
			RT	AUC	Height	Tailing	Plate Count	RT	AUC	Height	Tailing	Plate Count
ana1	1	64	2.379	3119043	427936	1.372296	1566.184283	2.348	2822747	453127	1.656767	3015.543632
	2	64	2.376	3138552	423993	1.406869	1158.949624	2.361	2796699	489384	1.566919	4263.653623
	3	64	2.377	3171639	3171639	1.373177	2286.996959	2.372	2908752	492793	1.54388	3863.286109
Ana2 Ishu	4	64	2.362	3122037	459529	1.392897	1668.175256	2.415	2818992	481206	1.749786	4373.364064
	5	64	2.373	3157269	445893	1.300978	2294.410634	2.379	2921601	517852	1.789451	4469.110563
	6	64	2.372	3165029	454584	1.417903	2816.465669	2.37	2894010	492229	1.708549	3550.611427
		SUM	14.239	18873569	5383574	8.26412	11791.18243	14.245	17162801	2926591	10.015352	23535.56942
		MEAN	2.373167	3145594.83	897262.3333	1.377353333	1965.197071	2.374167	2860466.83	487765.1667	1.669225333	3922.594903
		SD	0.006047	22368.927	1114302.396	0.041553016	605.6505714	0.022675	53671.7279	20956.47077	0.098816832	562.6410048
		RSD	0.254809	0.71111914	124.1891423	3.016874075	30.8188212	0.955082	1.87632757	4.296426272	5.919921642	14.3435919

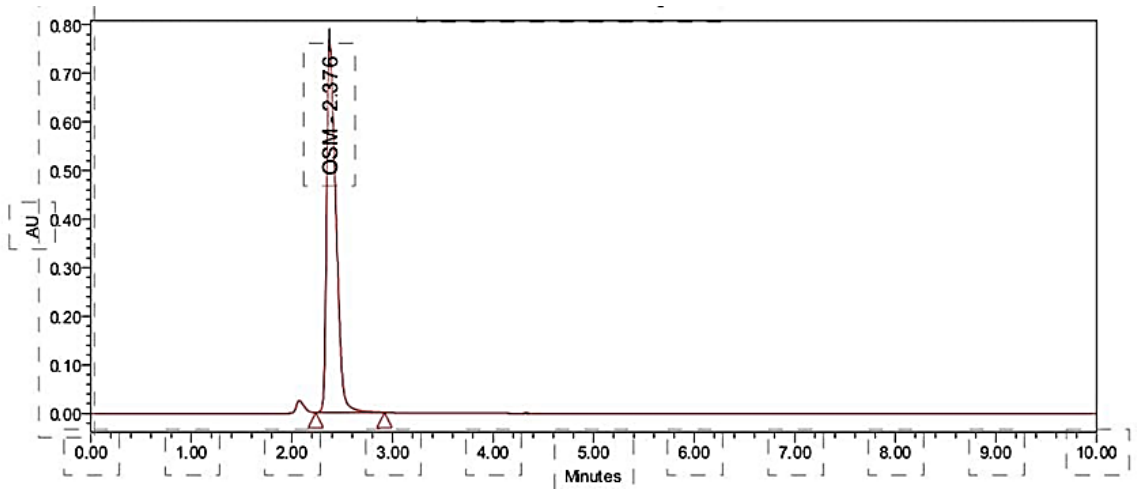

Figure 8: Final Optimization Method : Standard stock solution of 200 ppm, 20 mg of olmesartan medoxomil was prepared in a 100 mL volumetric flask. ACN: Methanol (9:1) was added and sonicated for better dissolution. The volume was made up to mark with diluent and final concentration was made and Ammonium acetate buffer: methanol (5%: 95%) was chosen.

techniques included assessing both intra-day and inter-day precision. To determine accuracy, experiments were conducted in terms of repeatability, interday and intraday precision. The results were found to have %RSD in acceptable limit, as not more than 2%. These results for API and market formulation are presented in Table 2.

Robustness

The robustness of the approach validation was determined by seeing no significant difference between flow rates. The relative standard deviation as a percentage is less than 2, which is within the allowed range. The results of robustness of API and market formulation are presented in Table 3.

Ruggedness

The Ruggedness of the approach validation was determined by seeing no significant difference between analyst A and analyst B. The relative standard deviation as a percentage is less than 2, which is within the allowed range. The ruggedness result of API and market formulation are presented in Tables 4 for 32 ppm and 64 ppm.

DISCUSSION

I have completed my work by following the ICH guidelines and all the results are mentioned above. The study revealed that Olmesartan medoxomil is very soluble in methanol and ethanol. A wavelength of 256 nm for methanol and an absorbance of 0.291 were used. The C18 (4.6×250 mm, 5 µ) particle size column in our approach was filled with water (containing 5% ammonium acetate) and methanol (5%:95%) at room temperature and 1.0/min flow rate using 10-min runtime.

CONCLUSION

The C18 (4.6×250 mm, 5 µ) particle size column in our approach was filled with water (containing 5% ammonium acetate) and methanol (5%:95%) at room temperature and 1.0mi/min flow rate. Using 10 min runtime, Olmesartan medoxomil eluted with a retention time of exactly 2.3 min. The developed approach was reliable and reproducible based on the ICH guidelines with all relevant parameter's studies such as linearity, accuracy, robustness, ruggedness, limit of detection, limit of quantitation. Hence the same methodology of approach for analytical method development and validation may be adopted for Olmesartan formulation in near future as the retention time was lower (Rt=2.3 min) as compared with the previous reported literature having retention time of 7 min.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

OLM: Olmesartan; **RSD:** Relative Standard Deviation; **mg:** Milligram; **i.e.:** That is; **LOQ:** Limit of Quantitation; **LOD:** Limit of Detection.

REFERENCES

Al-Masri, R., & Al-Mardini, M. A. (2005, December 31). Stability-indicating HPLC assay method of lovastatin. Bulletin of Pharmaceutical Sciences. Assiut, 28(2), 185–189. https://doi.org/10.21608/bfsa.2005.65287

Amin, M. (2012, September 1). Spectrophotometric Determination of fenoterol in Pure form and Pharmaceutical Formulation. Al-Azhar Journal of Pharmaceutical Sciences, 46(2), 25–38. https://doi.org/10.21608/ajps.2012.7115

Beg, S., Katare, O. P., Saini, S., Garg, B., Khurana, R. K., & Singh, B. (2016, June 1). Solid self-nanoemulsifying systems of olmesartan medoxomil: Formulation development, micromeritic characterization, *in vitro* and *in vivo* evaluation. Powder Technology, 294, 93–104. https://doi.org/10.1016/j.powtec.2016.02.023

Bharti, S., Sharma, S., Singh, B., & Bharti, N. (2022, April 1). Vitrector-assisted anterior capsulorhexis in adult intumescent cataract. Indian Journal of Ophthalmology, 70(4), 1408–1409. https://doi.org/10.4103/ijo.IJO_1626_21

Biagini, M., Lombardi, A., Perelli, P., Roscio, G., & Rocchi, A. (1998). Effects of losartan on 24-hr blood pressure and its variability in mild to moderate hypertension. American Journal of Hypertension, 11(Suppl. 4), 262A–.

Brunner, H. R. (2002, May). The new oral angiotensin II antagonist olmesartan medoxomil: A concise overview. Journal of Human Hypertension, 16(2)(Suppl. 2), S13–S16. https://doi.org/10.1038/sj.jhh.1001391

Çelebier, M., Kaynak, M. S., Altınöz, S., & Şahİn, S. (2014). UV spectrophotometric method for determination of the dissolution profile of Rivaroxaban. Dissolution Technologies, 21(4), 56–59. https://doi.org/10.14227/DT210414P56

Dhole, S. M., Khedekar, P. B., & Amnerkar, N. D. (2012, July 1). Comparison of UV spectrophotometry and high performance liquid chromatography methods for the determination of repaglinide in tablets. Pharmaceutical Methods, 3(2), 68–72. https://doi.org/10.4103/2229-4708.103875

Dhole, S. M., Khedekar, P. B., & Amnerkar, N. D. (2013). Development and validation of hptlc densitometry method for simultaneous estimation of rosiglitazone and glimepiride in fixed tablet dosage form. Journal of the Chilean Chemical Society, 58(2), 1663–1666. https://doi.org/10.4067/S0717-97072013000200004

Dubey, R., & Ghosh, M. (2015, March). Simultaneous determination and pharmacokinetic study of losartan, losartan carboxylic acid, ramipril, ramiprilat and hydrochlorothiazide in rat plasma by a liquid chromatography/tandem mass spectrometry method. Scientia Pharmaceutica, 83(1), 107–124. https://doi.org/10.3797/scipharm.1410-15

Fogari, R., Taddei, S., Holm-Bentzen, M., Baszak, J., Melani, L., & Schumacher, K. (2010, September). Efficacy and safety of olmesartan medoxomil 40 mg/hydrochlorothiazide 12.5 mg combination therapy versus olmesartan medoxomil 40 mg monotherapy in patients with moderate to severe hypertension: A randomized, double-blind, parallel-group, multicentre, multinational, phase III study. Clinical Drug Investigation, 30(9), 581–597. https://doi.org/10.2165/11536710-000000000-00000

Gopani, C. T., Patel, A. V., & Panchal, P. I. Phase estimation techniques for FMCW radar.

MR G, SD S, SG J, VS N. RP-HPLC and HPTLC method development and validation for estimation of dolutegravir in bulk and tablet dosage form. (2019, May 1). Indian Drugs, 56(5).

Jain, P. S., Chaudhari, A. J., Patel, S. A., Patel, Z. N., & Patel, D. T. (2011, July 1). Development and validation of the UV-spectrophotometric method for determination of terbinafine hydrochloride in bulk and in formulation. Pharmaceutical Methods, 2(3), 198–202. https://doi.org/10.4103/2229-4708.90364

Laeis, P., Püchler, K., & Kirch, W. (2001, June 1). The pharmacokinetic and metabolic profile of olmesartan medoxomil limits the risk of clinically relevant drug interaction. Journal of Hypertension. Supplement, 19(1), S21–S32. https://doi.org/10.1097/00004872-200106001-00004

Mahaparale, S. P., Gonjari, I. D., & Jayaveera, K. N. (2013, December 1). Validated stability indicating RP-HPLC method for simultaneous determination of metoprolol succinate and olmesartan medoxomil in tablet dosage form. Journal of Pharmaceutical Research, 12(4), 122–127. https://doi.org/10.18579/jpcrkc/2013/12/4/79319

McDowall, R. D. (2005, September). Effective and practical risk management options for computerised system validation. The quality assurance journal: The quality assurance journal for pharmaceutical, health and environmental professionals, 9(3), 196–227.

Rump, L. C., Stegbauer, J., & Laeis, P. (2004, February 1):S197. The effect of the combination of the oral angiotensin II-antagonist olmesartan medoxomil and atenolol on the pharmacokinetics, safety and tolerability in healthy male subjects. Journal of Hypertension, 22(Suppl. 1). https://doi.org/10.1097/00004872-200402001-00843

Sandhu, P. S., Beg, S., Katare, O. P., & Singh, B. (2016, September 1). QbD-driven development and validation of a HPLC method for estimation of tamoxifen citrate with improved performance. Journal of Chromatographic Science, 54(8), 1373–1384. https://doi.org/10.1093/chromsci/bmw090

Shah, P., & Dhaduk, B. (2022, July 1). RP-HPLC *In Vitro* Dissolution Method Development and Validation for Determination of Olmesartan Medoxomil, Chlorthalidone and Cilnidipine Drug Combinations. Current Pharmaceutical Analysis, 18(6), 629–641. https://doi.org/10.2174/1573412918666220131114138

Singh, J. (2015, September). Singh J. International conference on harmonization of technical requirements for registration of pharmaceuticals for human use. Journal of Pharmacology and Pharmacotherapeutics, 6(3), 185–187. https://doi.org/10.4103/0976-500X.162004

Srikanth, A., Yedlapalli, G., Srikanth, G., Harathi, G. L., & Anil, S. S. (2023). Development and validation for the simultaneous estimation of olmesartan medoxomil and hydrochlorothiazide by using RP-HPLC methods. World Journal of Advanced Research and Reviews, 17(2), 686–696. https://doi.org/10.30574/wjarr.2023.17.2.0247

SumitKArora, S. K., MaviyaHussain, M., SubhashRYende, S. R., KeshavMoharir, K., Pande, V., & Ittadwar, A. (2020). Bauhinia purpurea: An Updated Pharmacological Profile. Journal of Ayurvedic and Herbal Medicine, 6(2), 81–85. https://doi.org/10.31254/jahm.2020.6213

Thomas, M., Meena, K. C., Shrivastava, A., & Tripathi, N. (2022). *In vitro* assessment of cytotoxic effects of guggul in L929 mouse skin fibroblast cells. Annals of Phytomedicine, 11(2), 332–338. https://doi.org/10.54085/ap.2022.11.2.39

Wankhede, S. B., Tajne, M. R., Gupta, K. R., & Wadodkar, S. G. (2007, March 1). RP-HPLC method for simultaneous estimation of Telmisartan and Hydrochlorothiazide in tablet dosage form. Indian Journal of Pharmaceutical Sciences, 69(2). https://doi.org/10.4103/0250-474X.33164

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