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Research Article

Analytical Method Development and Validation of Ondansetron and Telmisartan in Tablet Dosage Form by RP-UPLC Method

Khushnuma Siddiqui*[1], Bhavana Dubey[2]

[1] Research Scholar, Department of Pharmaceutical Chemistry, Saroj Institute of Technology and Management, Lucknow (U.P.) 226002, India

[2]Assistant Professor, Department of Pharmaceutical Chemistry, Saroj Institute of Technology and Management, Lucknow (U.P.) 226002, India

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*Address for Correspondence:

Khushnuma Siddiqui, Research Scholar, Department of Pharmaceutical Chemistry, Saroj Institute of Technology and Management, Lucknow (U.P.) 226002, India

Contact No. 9026041053

Abstract

The objective of the present analysis was the improvement of easy, exact as well as reproducible and precise verifies reversed phase Liquid Chromatography with High Performance [UPLC] assays for Telmisartan and Ondansetron. The chromatographic splitting up was done on Acuity UPLC BEH C 18 (50×2.1mm and1.7µm) column with gradient elution. The injection amount was 1µl and also the detection was performed at 214 nm by utilizing photo diode array detector. The evolved as well as a validated UPLC way of Telmisartan and Ondansetron in tablet dosage styles based on ICH tips was precise and accurate, therefore it may be utilized for equally evaluation scientific studies of medications. This process demonstrated the repeatability of outcomes with regard to accuracy, scientific studies, robustness, and then program - suitability problems.

Keywords: UPLC, Ondansetron, chromatography, Telmisartan, accuracy, robustness

INTRODUCTION

Ondansetron is used-to cure sickness as well as vomiting brought on by radiotherapy, and surgical procedure[1]. It's believed that its results are experienced on peripheral and central nervous feelings. One particular portion is reducing the pastime on the vagus nerve, a nerve which triggers the vomiting facility within the medulla oblongata. The next is an obstruction of serotonin receptors within the chemoreceptor bring about zone. Ondansetron is a medication used to treat nausea and vomiting caused by emetogenic cancer chemotherapy, surgery, and radiation[1,2]. It is soluble in water and alcohol, mildly soluble in methanol, and slightly soluble in methylene chloride. In healthy people, the mean bioavailability after a single 8-mg oral dosage is around 56%.

Ondansetron is a selective antagonist of the serotonin 5 HT3 receptor, not proven to get pastime at additional recognized serotonin receptors along with lower affinity for dopamine receptors[3]. The antiemetic task on the medication is brought regarding via the inhibition of 5HT3 receptors that are each centrally (medullary chemoreceptor zone) as well as peripherally (GI tract). Headache, Constipation, Flushing, Hiccups, Alteration of outcomes of liver functionality examinations, Hypotension (low blood pressure), discomfort in the chest, bradycardia (slow heartbeat), and seizures[4].

The medication is administered every day, with respect to the seriousness of sickness and also vomiting. It's likewise employed off label for treating hyper emesis gravid arum within women that are pregnant, but there's simply no conclusive information situated on the safety of its for pregnancy. The standard serving for children and adults throughout the era of twelve is eight mg at first, accompanied by way of another serving of eight mg, 8 several hours later on[5]. The medication class known as angiotensin receptor blockers include telmisartan (ARBs).The ARBs reduce blood pressure in animal models as well as in humans. Their principal applications are for the treatment of congestive

heart failure, diabetic nephropathy, and hypertension (high blood pressure)[6].

Angiotensin II receptor antagonist (ARB) telmisartan is used to treat hypertension. High affinity ARBs bind to Angiotsin II type 1 (AT1) receptors, inhibiting Angiotenedin II's effects on vascular smooth muscle, which eventually lowers arterial blood pressure[7]. Its structural formula is as follows, and it could also possess PPAR-gamma agonistic qualities that might offer advantageous metabolic benefits.

An oral non-peptide angiotensin II antagonist that works on the AT1 receptor subtype is telmisartan. According to recent research, it may also possess PPAR agonistic qualities that might potentially have positive metabolic benefits. Clinical trials are now looking into this observation. Typical adverse effects might be:. Nasal congestion, back ache, sinus pain, diarrhoea, and little to no urinationating[8].

Telmisartan is used to treat high blood pressure (hypertension), as well as to lessen the risk of stroke, heart attack, or death from cardiovascular disease in adults older than 55 who have risk factors for severe heart conditions[9]. If you use the medication in your second or third trimester of pregnancy, the unborn child might suffer harm or perhaps pass away. Hypotension, tachycardia, and dizziness may result from an overdose[10].

Analytic techniques are supposed to set the identity, virginity, actual physical qualities as well as potency of all of the medicines which we make use of. HPLC evaluation technique is created to recognize, amount or even filtering ingredients of fascination. The following types of detectors are available: UV/Visible, photodiode array, fluorescence, conductivity, refractive index, electrochemical, mass spectrometer, and evaporative gentle scattering. Movable stage make up (or maybe solvent strength) plays a crucial part of RP HPLC splitting up. The appropriate variety of pH. is a crucial instrument for splitting up of ionizable elements[11].

Tetrahydrofuran (THF), acetonitrile (ACN), and methanol are frequently suggested solvents. Splitting up of a lot of samples could be increased by choosing the proper column heat. The validated span is defined by IUPAC as "the interval of analyte focus in just that the technique could be viewed as validated". The requirements of every kind of validation will obviously be is its own beast together with the validation amount needed. The different validation variables are linearity, robustness, precision, accuracy, as well as selectivity or even a specificity[12].

Chromatography may be the collective phrase for a pair of lab methods because of the splitting up of mixtures. Splitting up of 2 test parts in chromatography is grounded on the different distribution of theirs concerning 2 non miscible phases. For dedication of technique robustness, a selection of chromatographic details, injection volume, column temperature, flow rate, and quantitative impact of the variables is set[13]. Adsorption chromatography relies on a movable fluid or maybe gaseous stage which is adsorbed upon the surface area associated with a fixed good stage. Fluid chromatography is a favorite quantitative analytical method used in a number of parts of substance, pharmaceutical and biomedical sciences[14].

It uses the particular interaction involving a single form of solute particle as well as another particle which is immobilized for a fixed stage. Different modes of liquid chromatography have developed for analyses of a wide range of ingredients in several kinds of matrices. In normal-phase fluid chromatography, the fixed stage is a polar great adsorbent according to specks of silica gel, carbon or alumina[15]. The movable stage is made up of non polar, natural solvents (dehydrated), for instance methanol, ethanol, 2 propanol, acetonitrile, co2 tetrachloride or maybe hexane. Whichever method is selected for advancement of a specific technique, it's crucial that some requirements for technique validation are fulfilled[16].

Reversed-phase LC differs from NPLC in it's dependant on a nonpolar fixed stage. The most used column packing substance is octadecyl silyl silica (ODS C18), whereby silica is covalently modified by C18 purposeful team. Drinking water as well as water miscible natural solvents for example methanol, acetonitrile as and tetrahydrofuran are usually utilized. A rise within the heat by 18C decreases the retention period by 13% for a specific solute[17].

UPLC involves utilizing smaller sized specks of dust, quickness and also peak capability (number of peaks solved a device time) that is usually given to brand new limitations that is recognized as Ultra Performance[18]. Within the UPLC process, elevated temperature chromatography likewise enables increased flow prices by decreasing the viscosity of movable stage, that considerably cuts down on the column backpressure. The Van Deemter curve, governed by a situation with 3 parts reveals the functional flow assortment for a great effectiveness with little diameter debris is a lot in excess of for bigger diameters. The C phrase is because of kinetic opposition to equilibrium within the splitting up operation. The use of UPLC generated the detection of extra medication metabolites, exceptional splitting up as well as enhanced spectral quality[19].

The UPLC pump is regarded as just about the most vital parts inside a fluid chromatography process that must make a consistent frequent flow on the eluent through the UPLC injector, detector, and column[20]. A finding mechanism works on a probe to get into test places as well as draw test via them. The column heater is associated with a modular style and the foot print of its is the exact same to that particular of the test supervisor. The ACQUITY UPLC BEH Shield RP18 columns are created to offer selectivity's which enhance the C18 as well as C8 phases. This particular reduced pH balance is coupled with the higher pH. balance on the 1.7 µm BEH particle to supply probably the widest functional pH. running span. The 2 solvents are mixed within the mixer to produce the particular movable stage make up which is presented towards the column as time passes[21].

MATERIAL AND METHOD

The solubility of Ondansetron and Telmisartan was determined by taking about 1 mg of sample in vial, added 0.5ml of water and sonicated for few minutes[22]. Weighed about 1.0mg of each drug sample in 10ml clean and dry volumetric flask add about 7ml of acetonitrile: water (50:50 v/v) to a 1ml glass vial. For the selection of molecular weight, both drugs were injected in mass spectrometer. Pipette out 1 ml of TFA into a 1000ml volumetric flask and diluted up to the mark with water. Add 70ml of premix solution and sonicated to dissolve it completely[23].

Different chromatographic conditions were tried to optimize the method, which include the following:. Column: Acquity BEH C-18 (50 x 2.1mm, 1.7µm particle size). 41.15 mg (equivalent to 2.0 mg of standard) tablet powdered of Ondansetron right into a 10ml neat and dried out volumetric flask pour approximately 7ml of premix remedy and then sonicated to break down it entirely. Common remedies of fifty, 200, 150, 100, 250 as well as 300µg/ml had been ready.

Various samples were injected into the chromatographic system and then measured the good region. A graph was plotted of good location as opposed to focus (on X axis focus as well as on Y axis good region) and also calculates the correlation coefficient. 9.90ml of this particular remedy was spiked with 0.10ml hundred µg/ml of regular fix. 41.15 mg (equivalent to 2.0 mg of standard) tablet powder of Ondansetron. Add about 7ml of premix solution and sonicated to dissolve it.

Further pipette out 5ml of this solution in 10.0 ml volumetric flask. Measure the peak area of each sample using chromatographic system. All work performed by different analyst. The analysis was completed using both the approach described in the method of analysis and the modifications. The Sample Solution was held at 25°C, or room temperature, for a whole day. The mean of all of these data yields the achieved percent RSD value. Six injections of the standard solution and two replication injections of the sample were administered[24].

Pipette 1 ml of TFA into a 1000 ml volumetric flask, then add water to dilute it to the proper concentration. To make up the volume, add 700 ml of water, sonicate it to thoroughly dissolve it, and then filter it using a 0.45 Nylon membrane filter. To improve the process, several chromatographic settings were investigated. Preparation of Mobile Phase: Ammonium acetate buffer: methanol in linear gradient system. Preparation of Linearity Solutions:

Linearity standard solutions of 25, 50, 75, 100, 125 and 150µg/ml were prepared. Mix 60:40 ratios at 0 min, 10:90 ratios at 2 min, 50:50 ratio at 2.2 min and 30:40 ratio at 1.5 min for each phase. Make up the volume to 1000 ml using milli-Q water that has been degassed and filtered using a 0.2-inch nylon membrane filter. 41.9mg tablet powder of Telmisartan was added to a 100ml clean and dry volumetric flask with 7ml of methanol solution and sonicated to dissolve it, and 9.90ml of this solution was spiked with 0.10ml 150µg/ml of standard solution.

The analysis was completed using both the approach described in the method of analysis and the modifications. The Sample Solution was kept at room temperature i.e. 25°C for 24 hrs. and the Buffer Concentration from 5 to 2 mM.

The absorption peaks at 246 nm were seen throughout the 200–400 nm UV scan of the ondansetron standard solution (fig. 1).

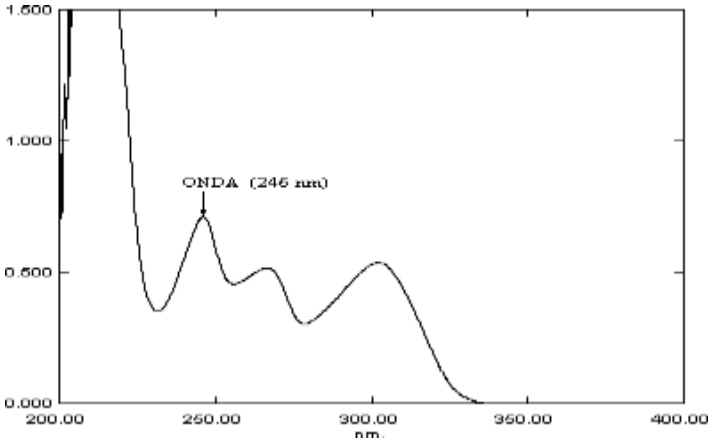

Fig. 1: Ondansetron's UV spectrum[25]

The picture below illustrates the absorption maxima at 229 nm from the UV scan of the typical telmisartan solution between 200 and 400 nm.

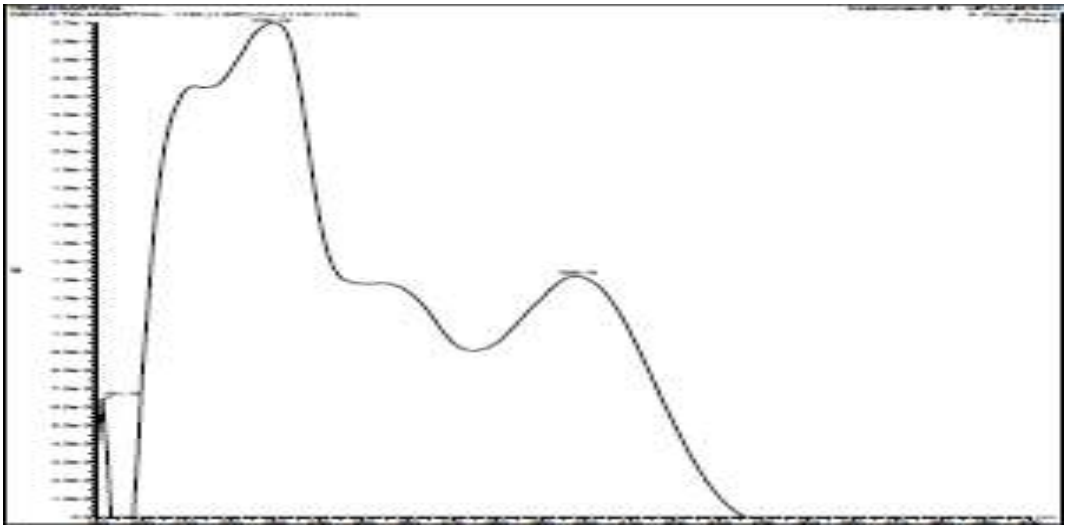

Fig. 2: UV spectra of Telmisartan[26]

Drug identification by Mass Spectroscopy

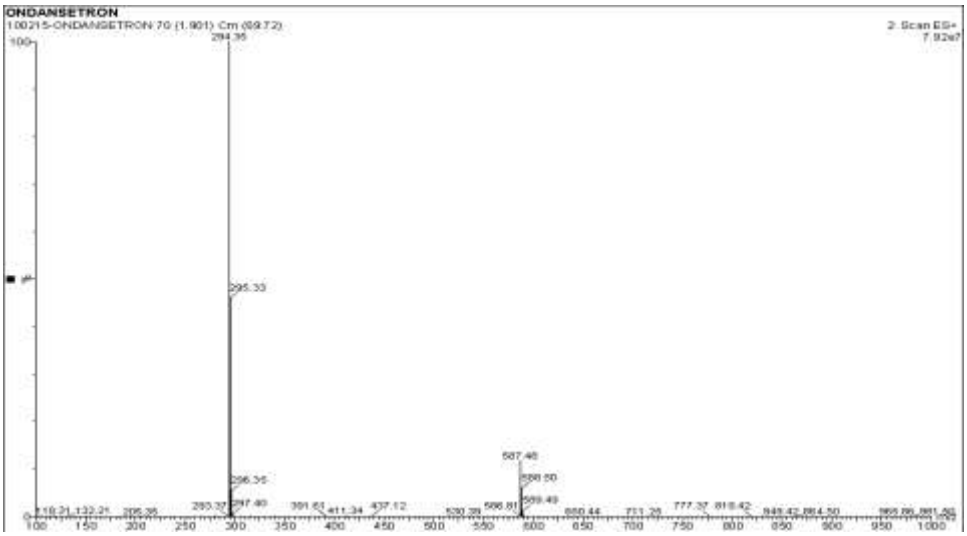

Fig. 3: Mass spectra of Ondansetron[27]

The molecular weight of Ondansetron was found to be 293.4 and telmisartan was found be 514.6 g/mol.

Mass spectra of telmisartan Purity and Molecular Weight of Drug by UPLC-MS

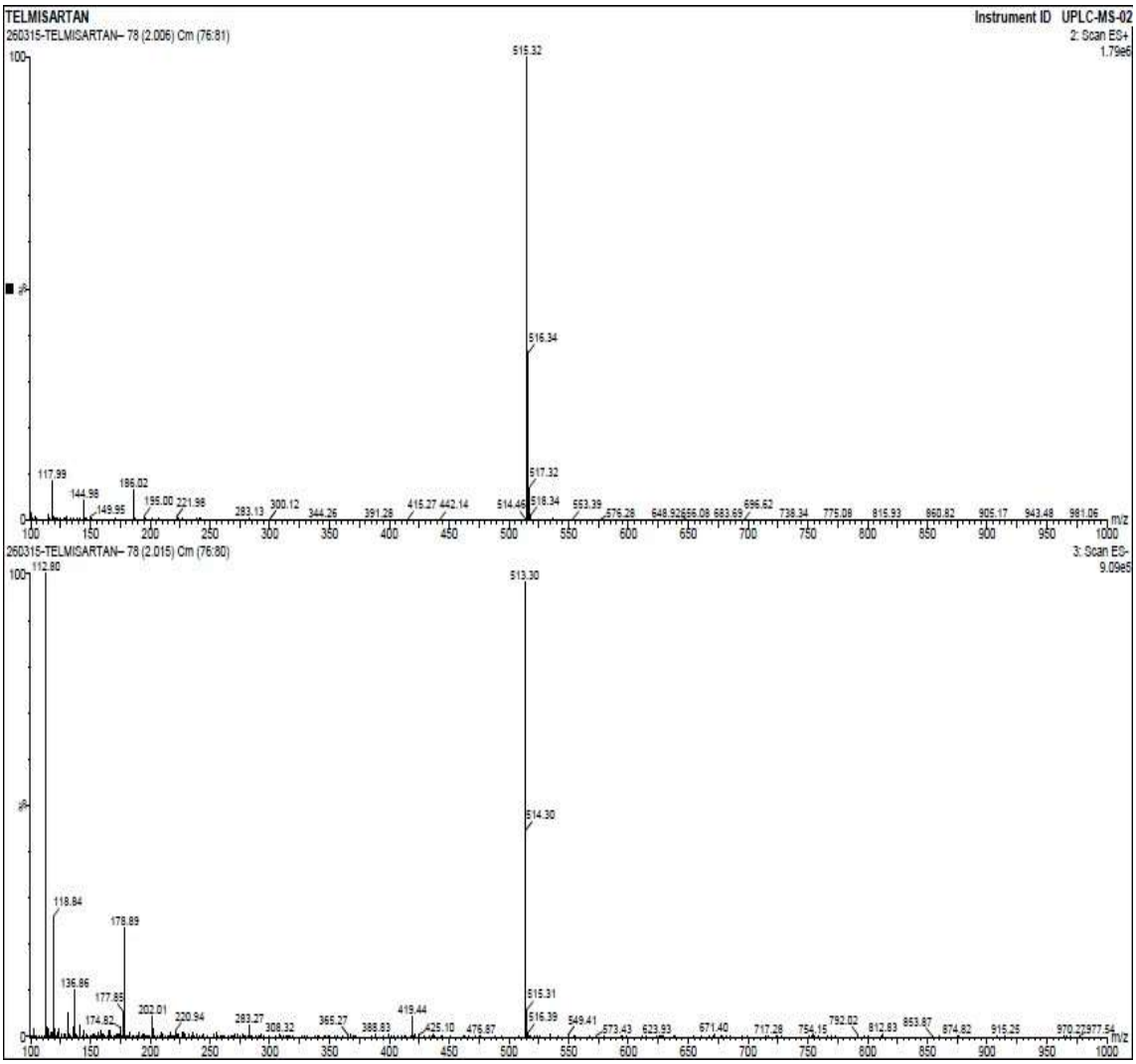

Fig. 4: Mass spectra of telmisartan Purity and Molecular Weight of Drug by UPLC-MS[28]

The purity of Ondansetron was found 99.83% and telmisartan was found 100.

UPLC-MS spectra of Ondansetron

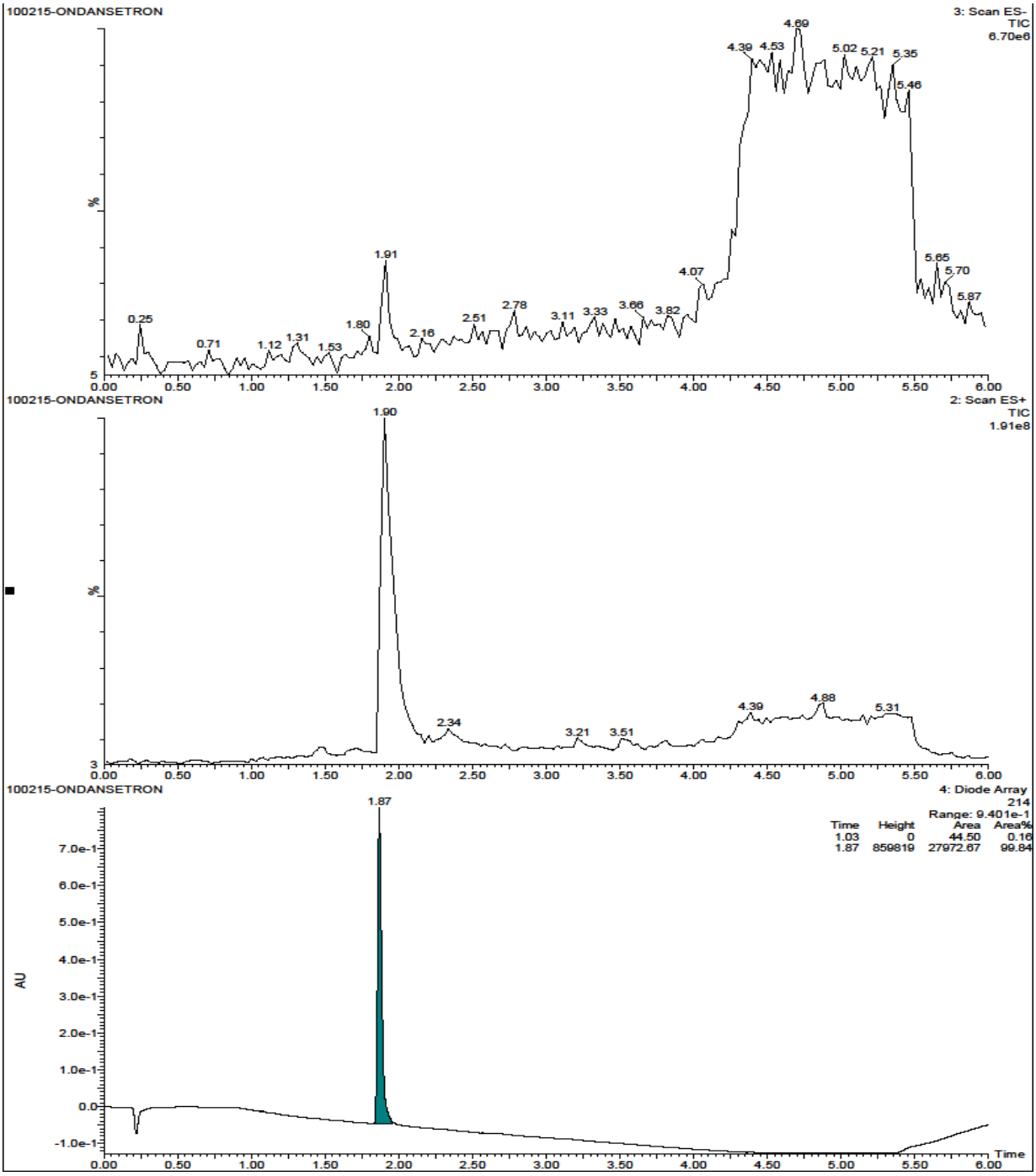

Fig. 5: UPLC-MS spectra of Ondansetron[29]

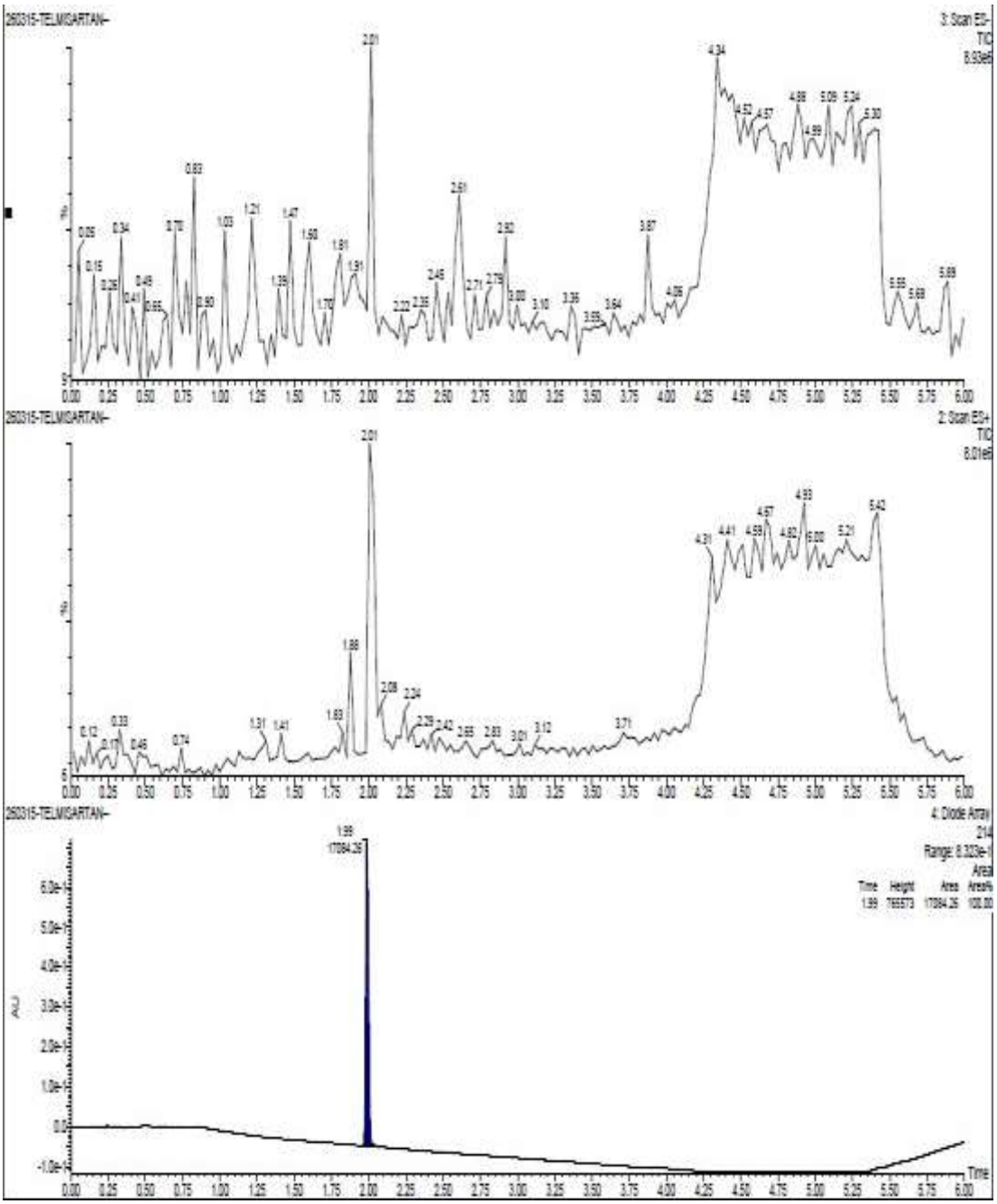

Fig. 6: UPLC-MS spectra of Telmisartan[30]

Analytical Method Formulation and Validation of Ondansetron

Analytical Method Development of Ondansetron

UPLC chromatograms of various trails are shown below figure

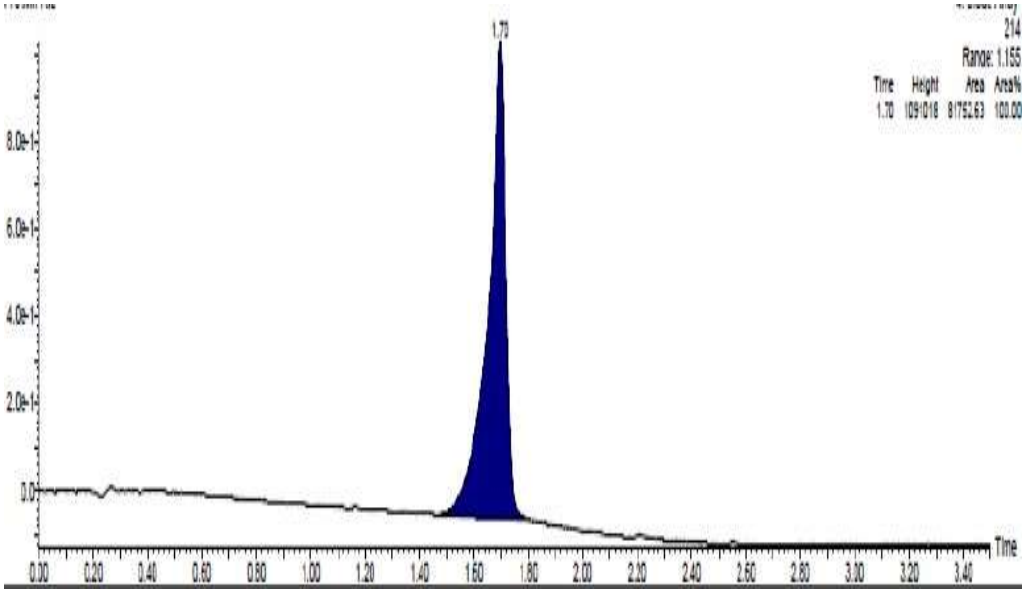

Fig. 7: UPLC chromatogram of Ondansetron under Trail-1 chromatographic condition[31]

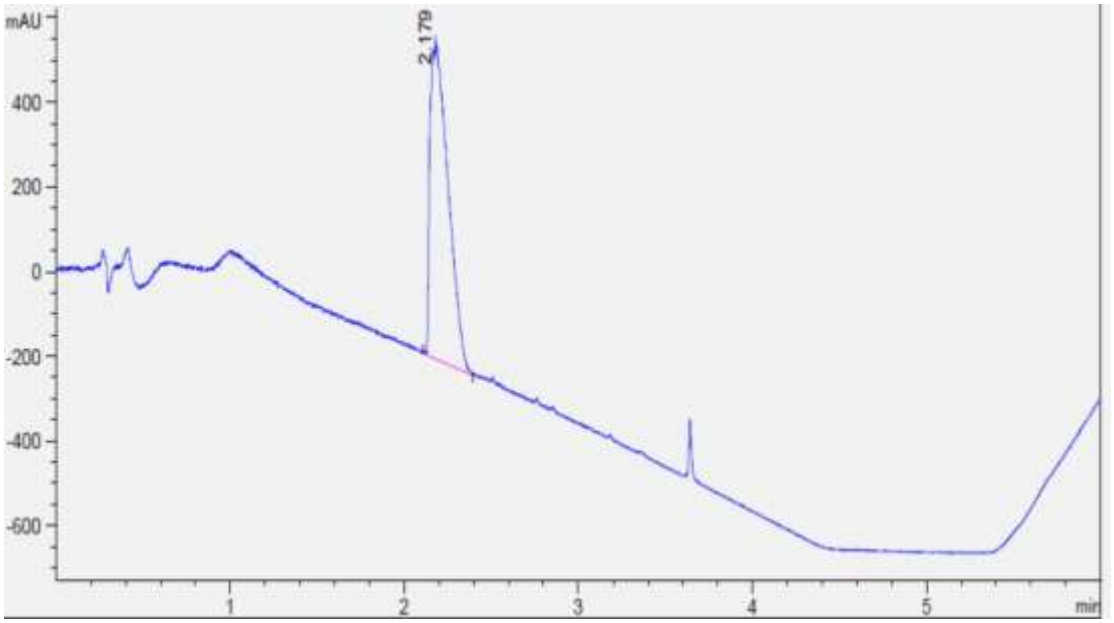

Fig. 8: UPLC chromatogram of Ondansetron under Trail-2 chromatographic condition[32]

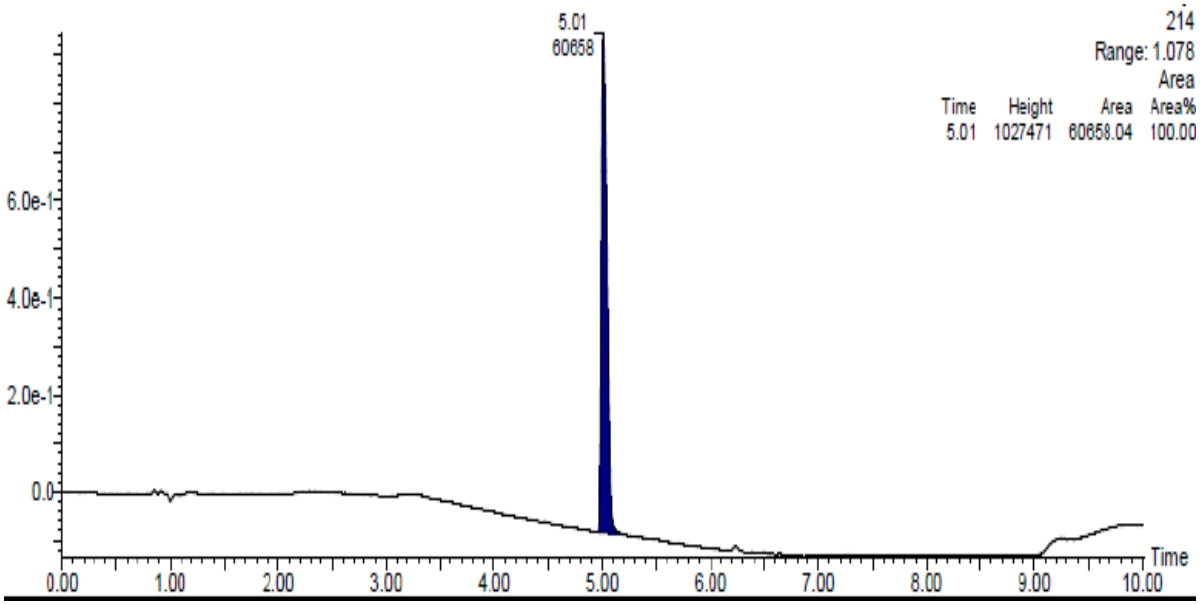

Fig. 9: UPLC chromatogram of Ondansetron under Trail-3 chromatographic condition[33]

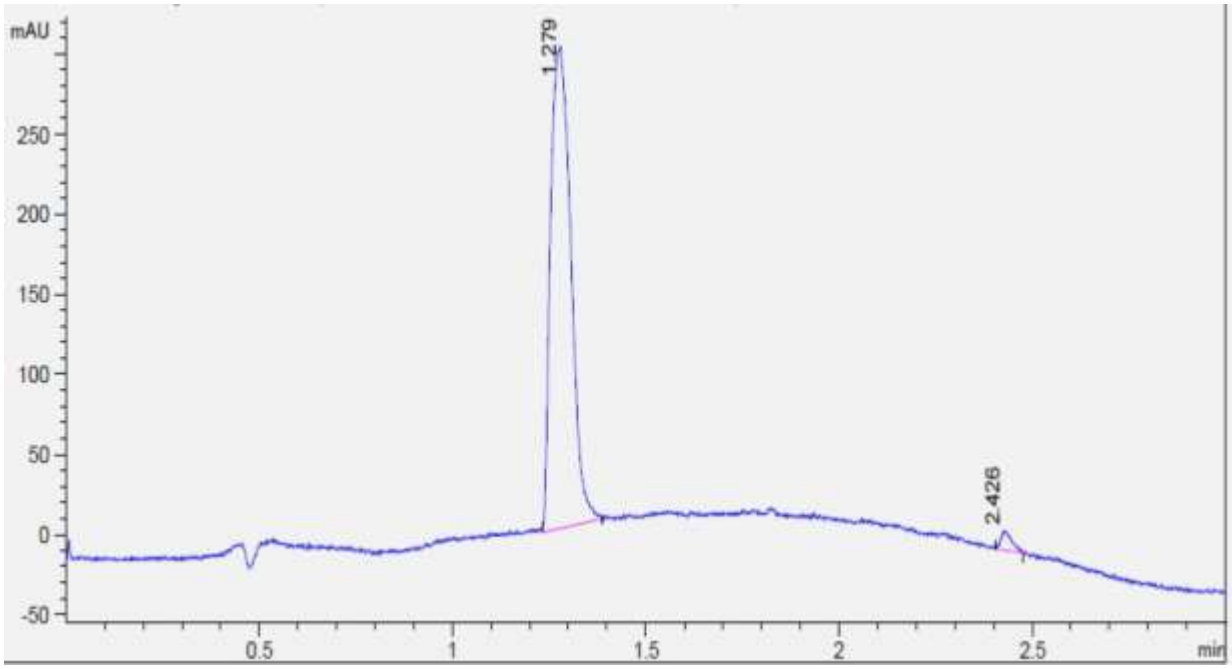

Fig 10.: UPLC chromatogram of Ondansetron under Trail-4 chromatographic condition[34]

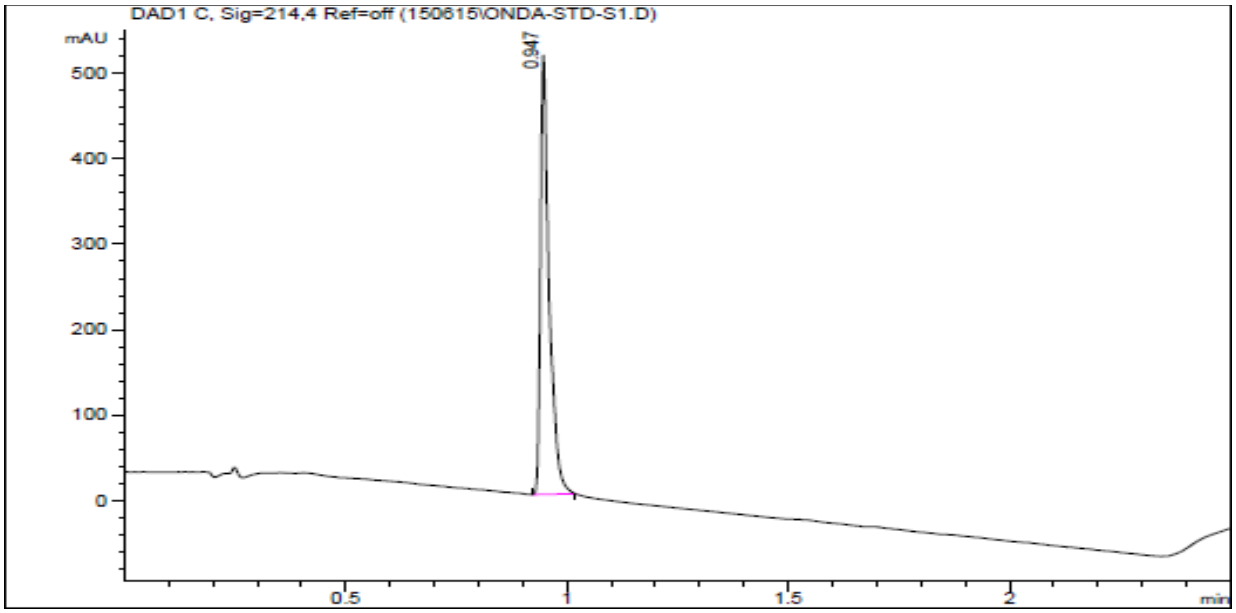

Fig. 11: UPLC chromatogram of Ondansetron under Trail-5 chromatographic condition[35]

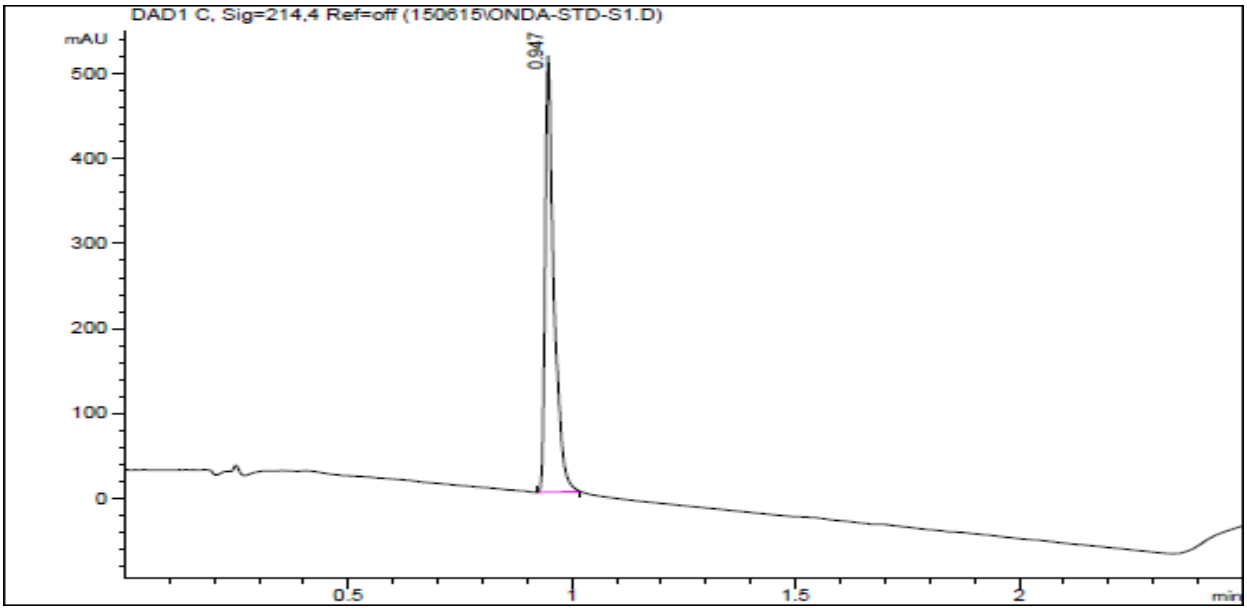

Fig. 12: UPLC chromatogram of Ondansetron standard for specificity[36]

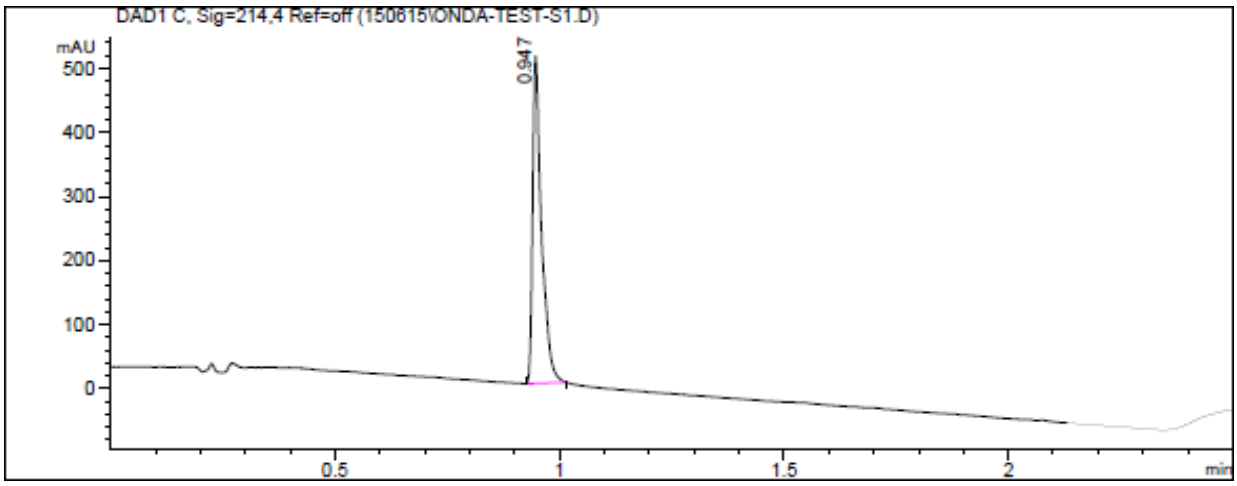

Fig. 13: UPLC chromatogram of Ondansetron Sample for specificity[37]

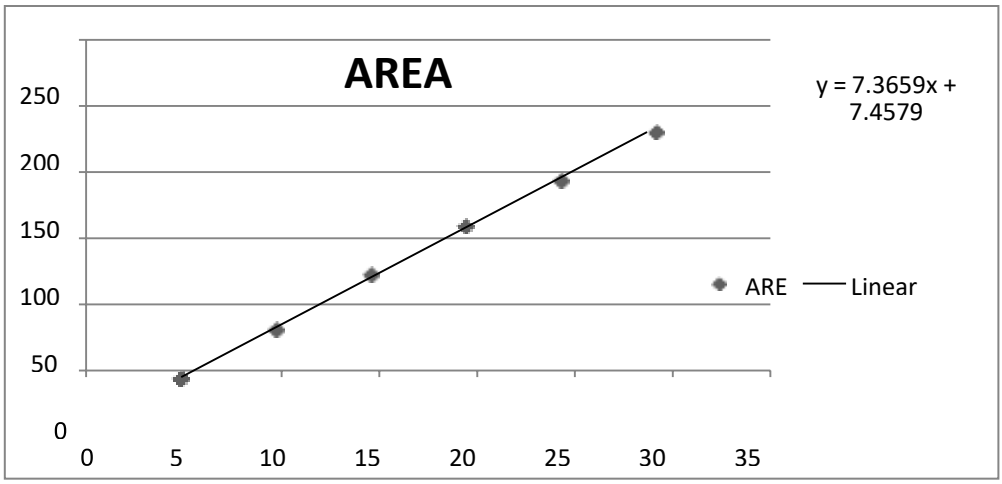

Fig. 14: Calibration curve of Ondansetron in UPLC[38]

Observation

Due to blanks and other interfering substances, there was no interference seen during the retention duration of ondansetron. Six duplicate injections of the standard solution showed a 0.09 relative standard deviation for the peak area response. The regression coefficient was found to be **0.999.**

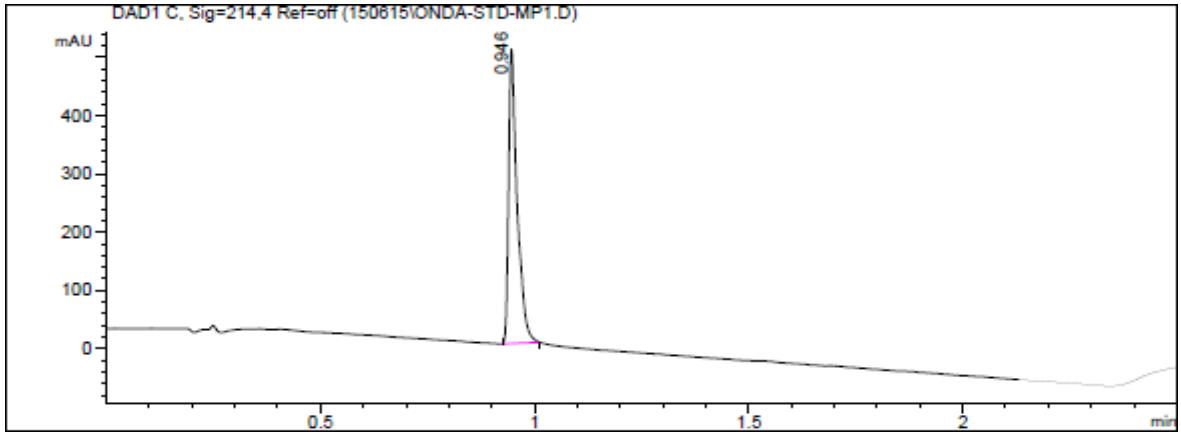

Fig. 15: UPLC chromatogram of Ondansetron Standard for method precision[39]

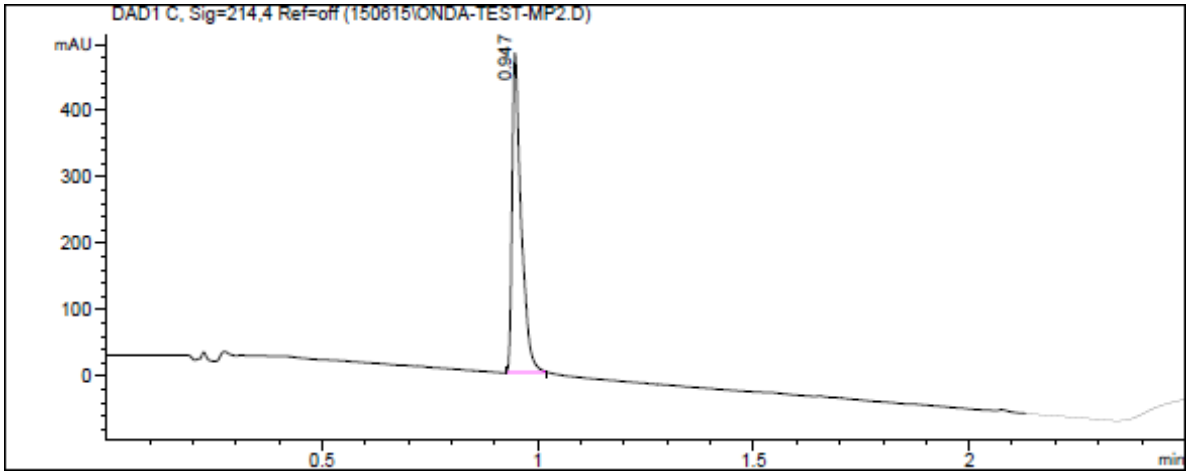

Fig. 16: UPLC chromatogram of Ondansetron Sample for method precision[40]

Solution Stability

Table 1: Solution Stability data of Ondansetron for analytical method validation by UPLC[41]

S.No.	Standard (100 µg/ml)	RT	Area
1	Replicate-1	0.949	708.759
2	Replicate-2	0.949	708.204
3	Replicate-3	0.949	709.986
4	Replicate-4	0.950	708.487
5	Replicate-5	0.948	707.432
6	Replicate-6	0.948	706.794
	Mean	**0.9**	**708.3**
	Standard Dev.	**0.00**	**0.78**
	% RSD	**0.05**	**0.11**

STANDARD INFORMATION

Table 2: Sample Information[42]

Hours	RT	Sample Area	Average Area	% Assay
		(100 µg/ml)		
0 Hr	0.949	705.071	705	**99.2**
	0.950	704.00		
2 Hr	0.948	706.722	706	**99.4**
	0.948	705.106		
4 Hr	0.948	706.578	705.6795	**99.4**
	0.948	704.781		
8 Hr	0.948	704.087	705.19	**99.3**
	0.948	706.293		
12 Hr	0.948	705.349	705.328	**99.3**
	0.948	705.307		
24 Hr	0.947	705.293	705.0595	**99.3**
	0.948	704.826		

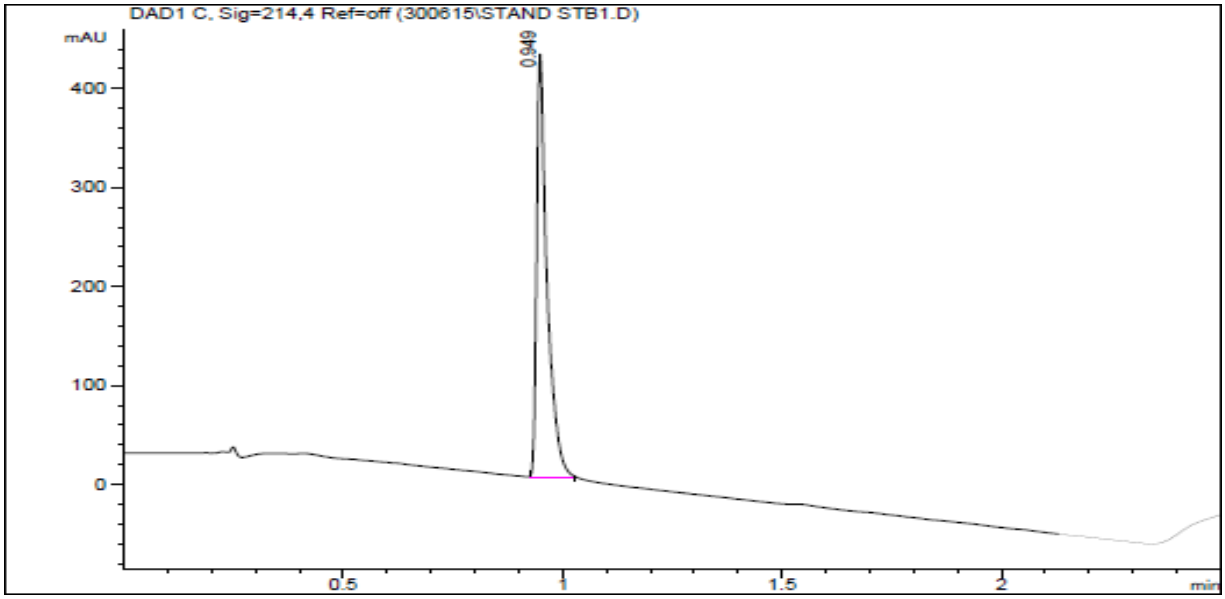

Fig 17: UPLC chromatogram of Ondansetron Standard for solution stability[43]

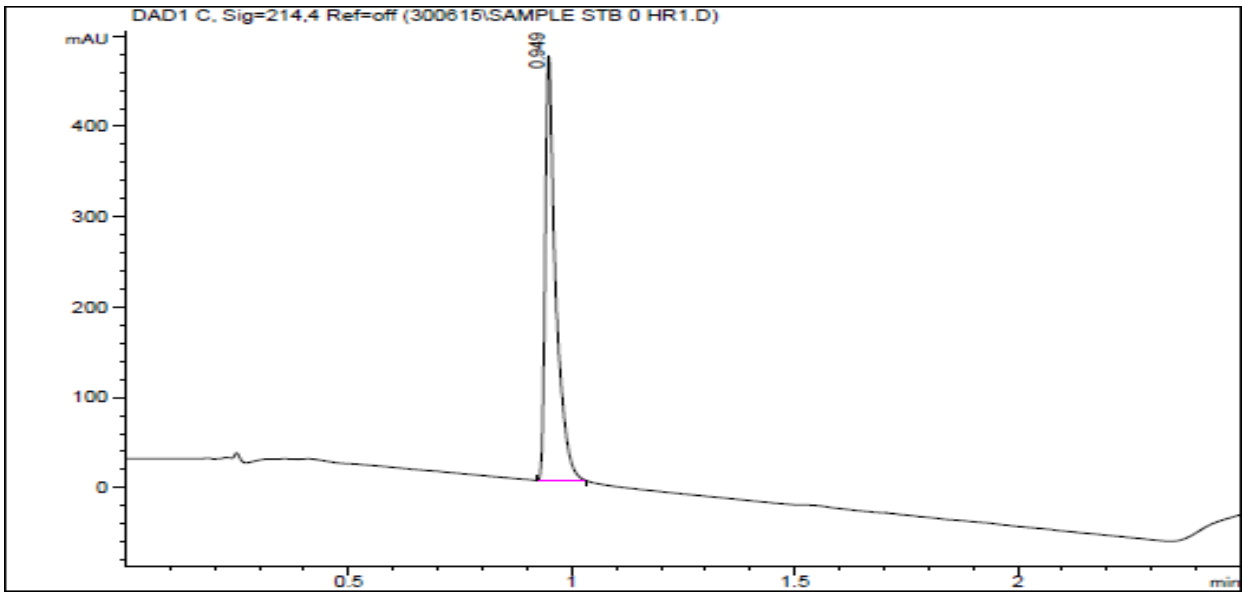

Fig. 18: UPLC chromatogram of Ondansetron Sample for solution stability[44]

Observation

Due to blanks and other interfering substances, there was no interference seen during the retention duration of ondansetron. Six duplicate injections of the same standard solution yielded 0.11 as the relative standard deviation for the peak area response. Six duplicate injections of the peak dose of ondansetron in the standard were found to have a 0.05 relative standard deviation for retention time.

Development of an Analytical Method and Validation of Telmisartan

Telmisartan Analytical Method Development

UPLC chromatograms of various trials are shown below in figure.

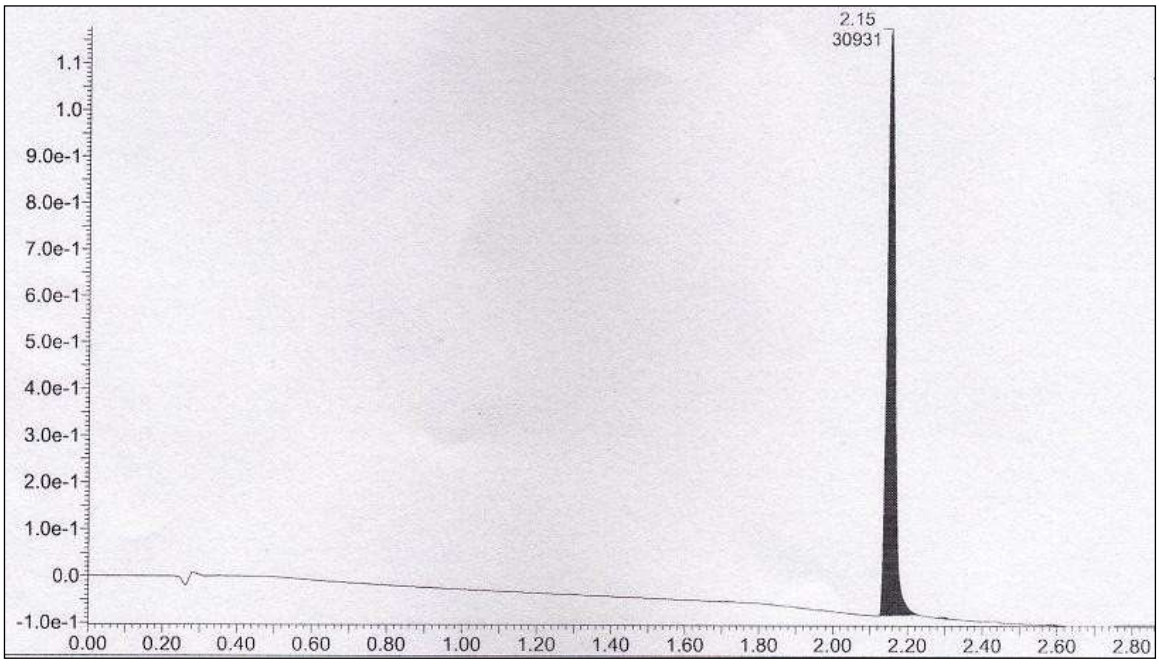

Fig. 19: UPLC chromatogram of Telmisartan under Trail-1 chromatographic condition[45]

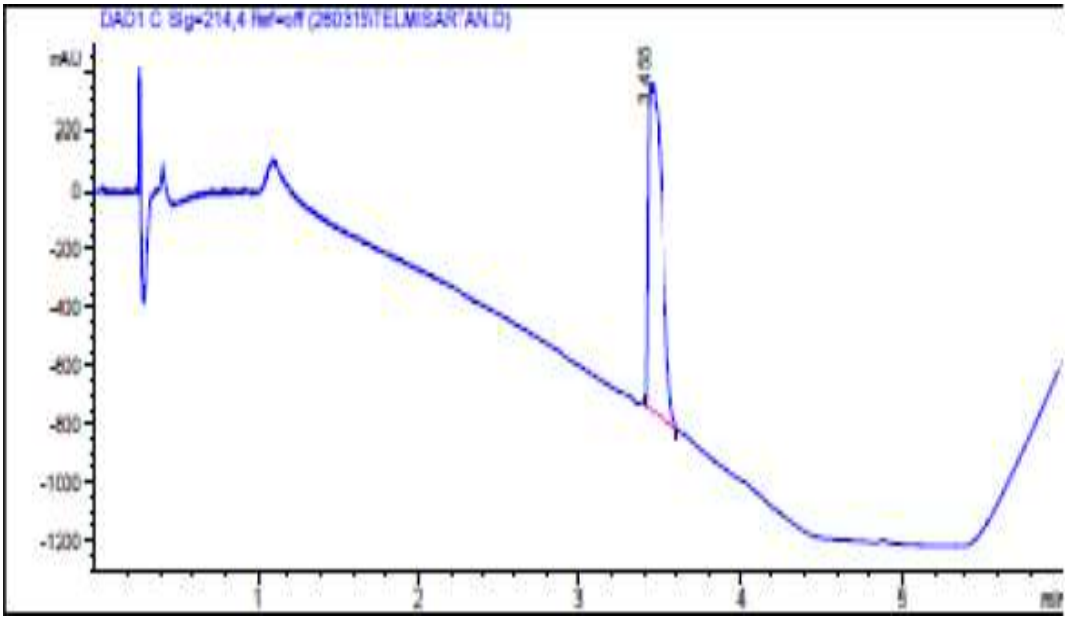

Fig. 20: UPLC chromatogram of Telmisartan under Trail-2 chromatographic condition[46]

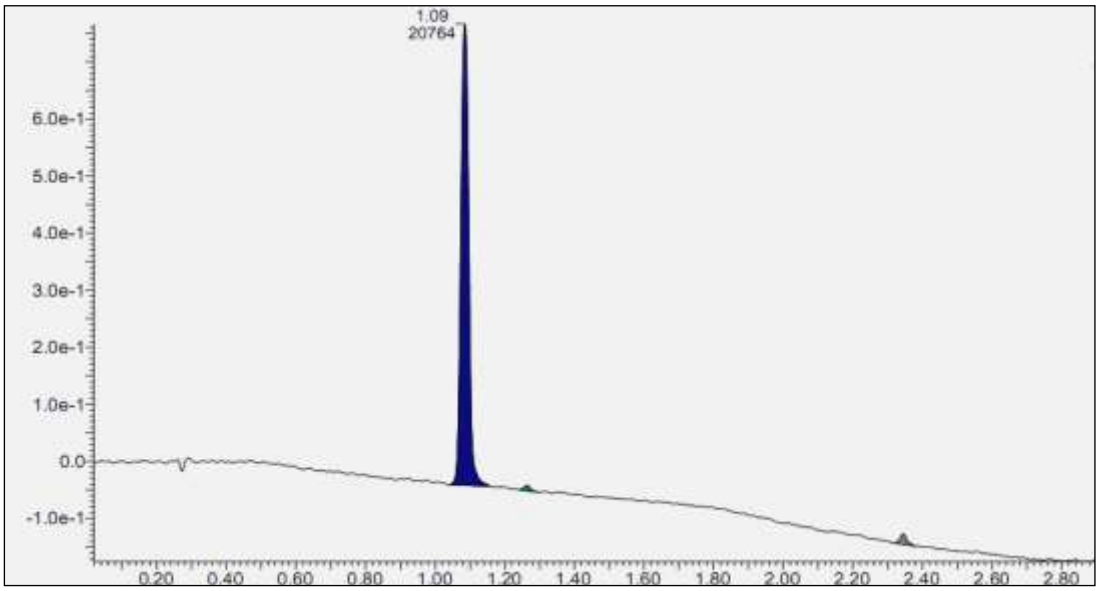

Fig. 21: UPLC chromatogram of Telmisartan under Trail-3 chromatographic condition[47]

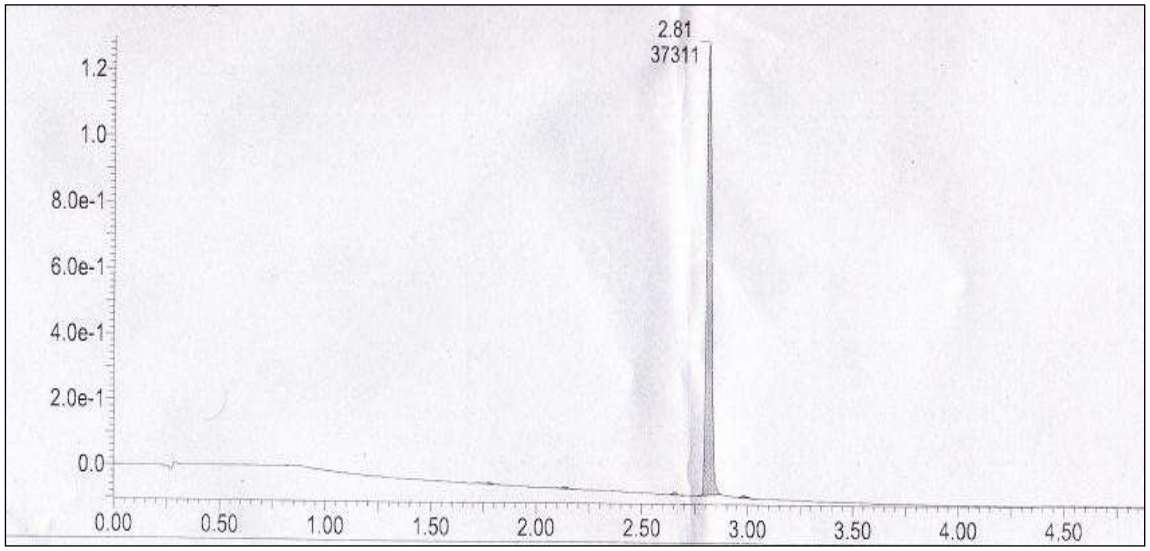

Fig. 22: UPLC chromatogram of Telmisartan under Trail-4 chromatographic condition[48]

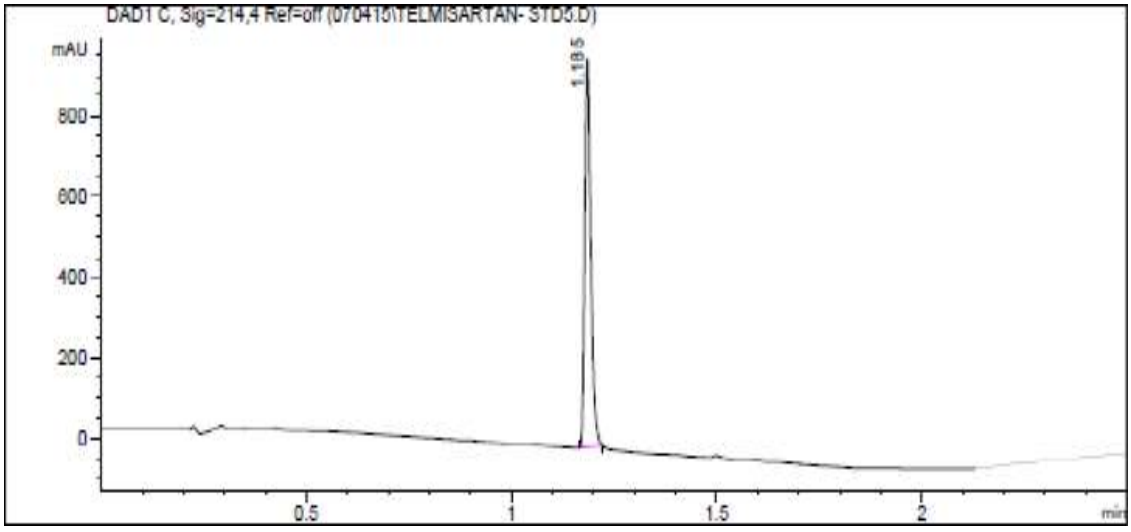

Fig. 23: UPLC chromatogram of Telmisartan under Trail-5 chromatographic condition[49]

Table 3: Observation of chromatogram during various trails in method development of Telmisartan is listed below:[50]

S.No.	Observation	Correction to next trial
Trial 1	Peak eluted in non-polar region	Column and Buffer needs to be changed, Flow rate decreased.
Trial 1	Peak shape is not good.	Column and Buffer needs to bechanged.
Trial 2	Peak tailing and Interferences observed	Column need to be changed
Trial 3	Run time longer, Peak shape good	Run time must be less
Trial 4	Run time longer, Peak shape good	Run time must be less
Trial 5	Peak shape, Base line, Sharpness of peak is fine, Run time is optimum. Finalized method	

Conclusion

The evolved as well as a validated UPLC way of Telmisartan and Ondansetron in tablet dosage styles based on ICH tips was precise and accurate, therefore it may be utilized for equally evaluation scientific studies of medications. This process demonstrated the repeatability of outcomes with regard to accuracy scientific studies, robustness, and then program - suitability problems. The % RSD was discovered to become a bit less compared to two % in all of the instances and also the regular deviation is to the boundaries.

Conflict of Interest

The authors have no conflict of interest.

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