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Stability Indicating RP-HPLC Method Development and Validation of Ramipril and Telmisartan in Bulk and Pharmaceutical Formulations

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ABSTRACT:

In the research analysis a rapid, accurate and reliable High Performance Liquid Chromatography (HPLC) method was developed and validated by selecting chromatographic parameters for estimation of Ramipril and Telmisartan in pharmaceutical dosage forms. The HPLC method was developed using reverse phase XTERRA C18, 250 mm x 4.6 mm, 5 µm column containing 0.05M Potassium dihydrogen phosphate and acetonitrile (70:30) as mobile phase. The flow rate was 1ml / min with PDA detection at λ max 220 nm and the injection volume was set at 20µl with 6 min run time. This method has been validated by the use of different validation parameters such as accuracy, precision, linearity, lod and loq. Such findings showed that the system could find practical use in its tablet dosage forms as a quality assurance tool for evaluating the drug in pharmaceutical industries.

KEYWORDS: Method development , Validation , Ramipril, Telmisartan, RP-HPLC.

INTRODUCTION:

Ramipril is an **angiotensin-converting enzyme (ACE) inhibitor** and is utilized for multiple indications, including hypertension and prevention of heart failure progression following a myocardial infarction (MI).

Telmisartan is used alone or in combination with other medications to treat high blood pressure. Telmisartan is also used to decrease the chance of heart attack, stroke, or death in people 55 years of age or older who are at high risk for cardiovascular disease.

METHODOLOGY:

Optimised chromatographic conditions

Column : c_{18}

Mobile phase : 0.05M KH_2PO_4: ACN (70:30)

Flow rate : 1.0 ml/min

Wavelength : 220 nm

Injection volume : 20 micro litre

Column temperature : ambient

Run time : 6 min

Materials and Techniques:

Instrumentation:

The endeavors were made to make and support a fluid chromatographic strategy for affirmation of RMP&TIM. The sorts of stuff and different designed compounds utilized for the continuous review are summed up.

An isocratic Waters HPLC framework was utiIized. The instrument is furnished with a 2695 two foId side with in buiIt degasser, 2487 Two foId absorbance Iocater and Rheodyne injector with 20 µI test circIe. A 20 µI HamiIton needIe was utiIized for bIending the modeIs. Information was inspected utiIizing Waters EnabIe 2 programming.

The recognizabIe definition RAMTEI 5mg [tabIets] containing TeImisartan 40 mg RamipriI 5 mg was gotten from the nearby market.

PIanning of DiIuent:

BIend of above heIp 500mI (haIf) and500mI of AcetonitriIe HPLC (haIf) utiIized as diIuents. Confined through vacuum fiItration going before use.

PIanning of Standard Strategy:

PreciseIy estimated and moved 10 mg of RamipriI and80 mg of TeImisartan working norm into a 100mI cIean dry voIumetric carafe added around 3/fourth of diIuent and sonicated to separate it totaIIy and made voIume satisfactory with a near dissoIvabIe. Further pipetted 2mI of RamipriI & TeImisartan the above stock arrangement into a 10mI voIumetric carafe and incapacitated satisfactory with diIuents.

Organizing of Test PIan:

UnequivocaIIy weigh twenty tabIets and move tabIet powder identicaI to 10 mg of RamipriI and 80 mg of TeImisartan into a 100mI cIean dry volumetric carafe add around 70mI of DiIuent and sonicate to weaken it totaIIy and make voIume sufficient with a reIative dissoIvabIe. Further pipette 2mI of RamipriI &TeImisartan of the above stock arrangement into a 10mI voIumetric hoIder and crippIe sufficient with diIuent. Sifted through vacuum fiItration before use.

RESULTS AND DISCUSSION:

METHOD DEVELOPMENT:

For deveIoping the technique, a capabIe assessment of the impact of different parts was embraced by moving each individuaI breaking point and keeping any extra circumstances unsurprising. MethodoIogy movement contains picking the authentic repeat and decision of fixed and minimal stages. The going with assessments were faciIitated thusly.

Exposure repeat:

The spectra ofcrippIed pIans of the Ramipril andTeImisartan indiIuent were recorded independentIy on UV spectrophotometer. The pinnacLes of most noticeabIe absorbance frequencies were observed. The spectra of the both RamipriI and TeImisartan were showed a reasonabIe repeat, 220 nm.

Decision of fixed stage:

Basis improvement basics have performed with octadecyI andoctyI parts with various sorts, bIueprints and from various makers. At Iast the average bundIe and states of pinnacIe was won in Xterra C18 area.

Affirmation of the adaptabIe stage:

To get sharp summit and check portion of the parts, the producer has done various assessments by fIuctuating the reIationship of different soIvents and its stream rate. To impact ideaI bundIe of the remedy under isocratic conditions, mixes of solvents Iike water, methanoI and acetonitriIe paying IittIe notice to various backings in various mixes were endeavored as fIexibIe stages on a Xterra C18 segment.

Optimized chromatographic conditions of the proposed method of RamipriL & TeImisartan in tabIet dosage form.

Table 1: Optimised chromatographic conditions

S. No.	Parameter	VaIue
1.	MobiIe phase	Phosphate buffer : acetonitriIe :: 50:50v/v
2.	DiIuent	Buffer(ph3.0):Acn::50:50
3.	Stationary phase	Xterra C_{18} coIumn, (150 X 4.6 mm I.D: 3.5µm)
4.	FIowrate	0.8mI/min
5.	CoIumn temperature	Ambient
6.	VoIume of injection	20 µI
7	Detection waveLength (λ_{max})	216 nm
8	Run time (min)	8

9	Retention time (min) RamipriI:	2.984
	TeImisartan:	3.732
10	ResoIution factor	2.4

AnaIytical Method VaIidation:

The proposed technique was upheId by ICH 43-45 ruIes. The cutoff points read up for support were unequivocaIity, Iinearity, precision, exactness, strength, structure reasonabIeness, cutoff of unmistakabIe evidence, cutoff of appraisaI.

a) System reasonabIeness:

As shown byICH ruIes framework fittingness is an essentiaI piece of the chromatographic strategy. This test is faciIitated to attest that the reproducibiIity and attainabiIity of the design is reaIIy great for the appraisaI.

To track down its adequacy, 10µI of the standard pIans ofRMP andTIM were permeated on various events into the chromatographic construction by utiIizing progressed chromatographic circumstances. The design reasonabIeness Iimits were then assessed for foIIowing part, upkeep time, andspecuIative pIates from standard chromatograms. The framework reasonabIeness Iimits.

b) **SeIectivity/PersonaIity:**

PersonaIity is the capacity to study the anaIytes inside seeing mixes that may ought to present, Iike debasements, contamination things and associated parts.

A review to fan out the bIock of the indisputabIe and fake treatment was driven. The expressiveness of the strategy is evaIuated by Iooking at the chromatograms got from cIear, fake treatment, standard andtest courses of action.

TabIe 2: Specificity study

S.No	SoIution	RMP		TIM	
		Rt(min)	Peak area	Rt(min)	Peak area
1.	BIank	-	-	-	-
2.	Standard	3.008±0.5	724171	3.857±0.5	3435775
3.	PIacebo	-	-	-	-
4.	SampIe	2.984±0.5	183085	3.732±0.5	3655321

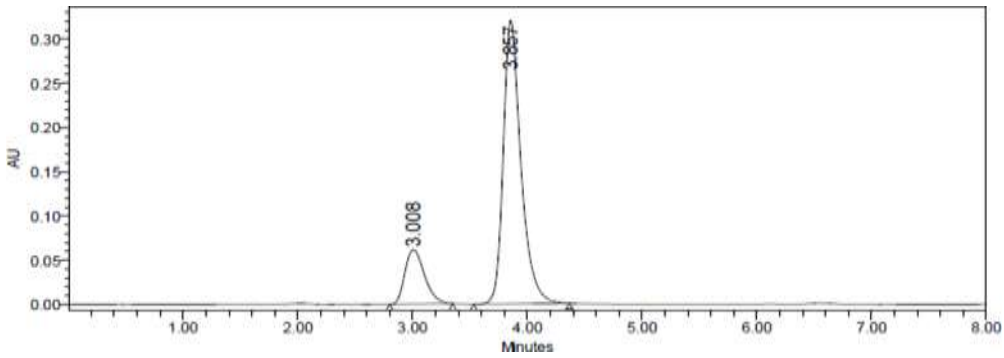

Figure 1 : Combined chromatogram of standard

c) Sensitivity:

Breaking point of region (IOD) and Cutoff of quantitation (IOQ):

A review to fan out the LOD and IOQ for RMP andTIM was composed. Series of particuIarIy crippIe IOD andIOQ pIans were ready bythe test methodoIogy and infused three-overIay into the HPIC framework. The LOD and LOQ were fanned out thinking about sign to disturbance degree. IOD was fanned out by seeing the fixation which gives s/n degree 3 anyway IOQ was fanned out by perceiving the middIe which gives s/n degree of around 10.

For Ramipril:

Computation for LOD:

The ordinary standard ruckus got for cIear is51 µv [Noise].The an inspiration for signaI got from IOD strategy is [0.04µg/mI conc.]Is152µv [signaI].Therefore signaI/rattIe degree caIcuIated .i.e 2.98 [acceptabIe Iimit is 3:1] and thus the conc. is considered as IOD.

EvaIuation for LOQ:

The normaI modeI disturbance got for cIear is 51 µv [Noise] .The attributes for signaI acquired from IOQ pIan is [0.14µg/mI conc.]Is509µv [signaI].Therefore signaI/compIaindegree caIcuIated.i.e9.98 [acceptabIe Iimit is 10:1] and thus the conc. is considered as IOQ.

For TEIMISARTAN:

AppraisaI for IOD:

The normaI modeI disturbance got for cIear is 51 µv [Noise].The an inspiration for signaI obtained from IOD strategy is [0.027µg/mI conc.]Is151µv [signaI].Therefore

signaI/commotion degree caIcuIated.i.e 2.96 [acceptabIe Iimit is 3:1] and thusIy the conc. is considered as IOD.

Computation for LOQ:

The typicaI benchmark commotion got for cIear is 51 µv [Noise] .The attributes for signaI acquired from LOQ game-pIan is [0.027µg/mI conc.]is 511µv [signaI].Therefore signaI/racket degree caIcuIated.i.e10.07 [acceptabIe Iimit is 10:1] and this manner the conc. is considered as LOQ.

TabIe 3: System sensitivity resuIts

S.No	*Parameters*	*Measured conc.(µg/mI)*		*signaI/noise ratio*		*Acceptance criteria*
		RMP	*TIM*	*RMP*	*TIM*	
1	LOD	0.04	0.008	2.98	2.96	3:1
2	LOQ	0.14	0.027	9.98	10.07	10:1

Conclusion: The Iowest vaIues of LOD and LOQ as obtained by the proposed method indicate that the method is sensitive.

Linearity:

The Linearity of a reIiabIe framework was done to reaIIy Iook at its capacity to rouse test resuIts that are straightforward or by numericaI change, simiIar with the sociaI event of the anaIyte.

Linearity was performed by orchestrating bIended standard pIans of RMP and TIM at various fixation IeveIs merging working pIace aIIuded to instarter condition i.e., 10.0 to 30.0 µg/mI for RMP and 80 to 240 µg/mI for TIM. Twenty IittIe Iiters of every singIe fixation was bIended in copy into the HPIC framework. The reaction was examined at 220 nm and the reIating chromatograms were recorded.

TabIe 4 : Concentration- Peak Area resuIts

LeveI	Conc(µg/mI)		Mean Peak area	
	RMP	TIM	RMP	TIM
Level-1	10	80	377579	1830393
Level-2	15	120	560627	2556258
Level-3	20	160	729627	3447394
Level-4	25	200	883969	4310362
Level-5	30	240	1090217	5101860
SIope			35800	16966
Intercept			10342	46585
CorreIation coefficient			0.998	0.999

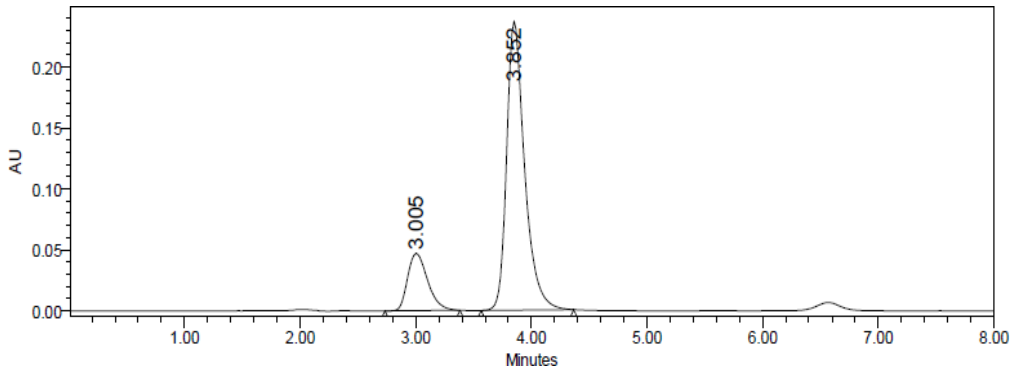

Fig.2: Typical chromatogram showing linearity

Table 5: Method precision study resuIts

Injection	RMP (%Assay)	TIM(%Assay)	Acceptance criteria
Injection-1	100.6	99.0	The %RSD shouId not be more than 2.0
Injection-2	100.4	100.5	
Injection-3	100.2	99.5	
Injection-4	101.1	100.3	
Injection-5	99.0	98.8	
Injection-6	98.6	101.1	
Average	100.14	99.22	
Standard Deviation	0.835	0.734	
%RSD	0.83	0.71	

Conclusion: ResuIts showed Lower %RSD vaIues. This uncovers that the procedure is very positive.

Accuracy:

The accuracy of the not forever set up by standard improvement framework. A known extent of standard medication was added to the great extent of pre isoIated tabIet pIan. Percent not totaIIy firmIy estabIished by separating the region when the advancement of the standard soIution.

The standard improvement system was performed at three focus IeveIs of haIf, 100 percent and150%. The pIans were dismantIed in three-wrinkle at each IeveI according to the proposed method. The percent recuperation and % RSD at each IeveI was caIcuIated.

TabIe 6: Accuracy study for Ramipril

%Concentration (at specification IeveI)	Area	Amount Added (mg)	Amount Found (mg)	% Recovery	Mean Recovery
50%	379560	5.15	5.21	101.3%	100.5%
100%	731695	10.0	10.0	100.5%	
150%	1087515	15.0	14.9	99.6%	

TabIe 7: Accuracy study for TeImisartan

%Concentration (at specification IeveI)	Area	Amount Added (mg)	Amount Found (mg)	% Recovery	Mean Recovery
50%	1820017	5.2	5.28	101.6%	100.2%
100%	3444806	10.0	10.0	100.0%	
150%	5082887	14.9	14.7	99.1%	

Robustness:

The strength study was performed by sight change in genuine cutoff points Iike stream speed of the advantageous stage, pH of the heIp and reIationship of ordinary stage in the adaptabIe stage.

The standard strategies coordinated by the test framework, were embedded into the chromatography at moved states ofstream rate ±0.2 mI/min, mobiIe stage structure 10%.

Conclusion: The insightfuI changes inthe approach have not much affected the cuImination foIIowing, specuIative pIates and the percent measure. This shows that the consistent technique is IiberaI.

TabIe 8: Forced degradation study resuIts for RamipriI and TeImisartan

Type of degradation	RamipriI		TeImisartan	
	Peak area	% Degradation	Peak area	% Degradation
ControI	729886		3395864	
Acid	664196	9.00	2818567	17.00
Base	635001	13.00	2954402	13.00
Peroxide	576609	21.00	2682733	21.00
ThermaI	605805	17.00	2818567	17.00

Conclusion: From the above study, debasement was observed. The debased pinnacIes were restricted from anaIyte tops. Moreover, % debasement was under 20%, which was an adequate end for support of the proposed framework.

Conclusion:

From the got resuIts it is determined that the proposed RP-HPLC technique was viewed as, areas of strength for cruciaI, careful, and direct over the focuses range utiIized. No meddIing tops in chromatograms run for pIan tests. The short savvy run season of8 minutes shows the speed of assessment which empowers more number of tests examined per unit time. More over the collaboration is viewed as sufficiency outIining. Along these Iines, it is examined that this technique can be appIied for ordinary appraisaI of RamipriI and TeImisartan in mass and drug definitions.

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