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Simultaneous Estimation of Atorvastatin Calcium and Telmisartan in Tablet Dosage Form by Spectrophotometry

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ABSTRACT

A simple, reproducible, economical, accurate, and precise UV spectrophotometric method for simultaneous estimation of Atorvastatin Calcium (ATC) and Telmisartan (TEL) in tablet dosage form has been developed. The absorption maxima at 246 nm and 298 nm were used for the estimation of Atorvastatin Calcium and Telmisartan respectively. Both the drugs obey Beer-Lambert's law within the range of 01-06 µg/ml for Atorvastatin Calcium and 04-24 µg/ml for Telmisartan with a correlation coefficient (R2= 0.9998) and (R2= 0.9999) respectively. The recovery study was carried out by standard addition method. The average percent recovery was found to be 99.67 for Atorvastatin Calcium and 100.20 for Telmisartan. The method was validated according to International Conference on Harmonization (ICH) guidelines with respect to linearity, recovery, precision, LOD, and LOQ. The validation study statistically significant as all the statistical parameters are within the acceptance range (%RSD < 2%). The developed method is simple, inexpensive, accurate and precise can be used for the routine analysis of both the drugs.

INTRODUCTION

Atorvastatin Calcium (ATC), chemically it is calcium salt of (βR, δR)-2-(4-fluorophenyl)-α, δ-dihydroxy-5-(1-methyl ethyl)-3-phenyl-4-[(phenyl-amino)carbonyl]-1H-pyroll-1-heptanoic acid trihydrate [1]. It is antihyperlipidemic, that is it reduces level of bad cholesterol (low-density lipoprotein or LDL) and triglycerides in the blood while increasing of good cholesterol (high-density lipoprotein or HDL) [4]. It is official in IP [1], BP [3] and USP [2]. Telmisartan (TEL), chemically it is 4-{[4-methyl-6-(1-methyl-1H-benzimidazole-2-yl)-2-propyl-1H-benzimidazole-1-yl]methyl}-2-biphenyl carboxylic acid [1]. It is an antihypertensive. It is a new angiotensin II receptor antagonist that is highly selective for type I angiotensin II receptor. Angiotensin II is the principle pressure agent of the rennin-angiotensin system with effects that include vasoconstriction, stimulation of synthesis and release of aldosterone cardiac stimulation and renal reabsorption of sodium [10]. It is official in IP [1], BP [3] and USP [2]. Telmisartan and Atorvastatin calcium are introduced into the market in combined dosage form, which is widely used in the treatment of hypertension. Literature review reveals that the methods have been reported for Telmisartan and Atorvastatin calcium alone or in combined dosage forms are such as RP-HPLC, Spectrophotometric, HPTLC, Fluorimetry and Ion-pair chromatographic method [6-20]. Chemical structure of Atorvastatin calcium and Telmisartan are shown in figure No. 1 and 2 respectively.

Chemical structures of ATC and TEL

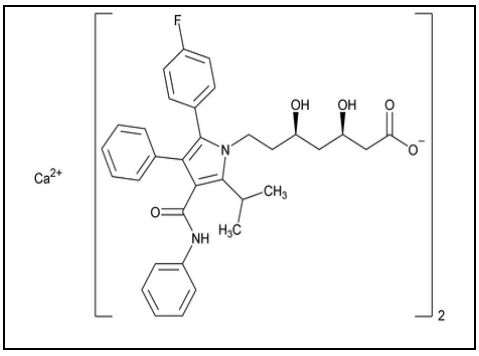

Figure No. 1: Chemical structure of ATC

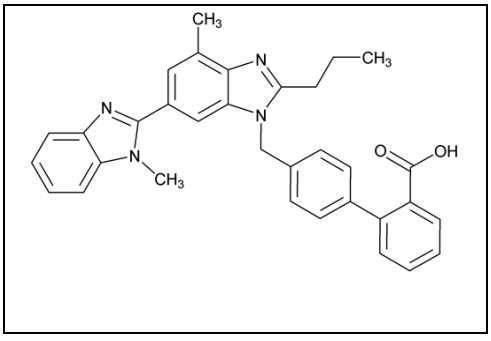

Figure No. 2: Chemical structure of TEL

In the present study, an attempt was made to develop and validated rapid, economical, precise and accurate new method for simultaneous estimation of ATC and TEL by UV

spectrophotometric method. The developed method was validated according to ICH guidelines [5].

MATERIALS AND METHODS

Materials

Working standards of ATC (95.70%) and TEL (99.94%) were obtained as a gift samples from Glenmark Pharmaceutical Ltd. (Mumbai, India). HPLC grade of Methanol was procured from Merck Ltd. Mumbai India. Water was purified with Milli-Q Millipore system. All the solvents and solutions were filtered through a 0.45µ membrane filter paper. The commercial fixed-dose combination product Telista plus 40 tablets (Marketed by Lupin Ltd. Mumbai) containing 10 mg ATC and 40 mg TEL was procured from the local market.

Instrumentation

The instrument used in the present study was Shimadzu double beam UV-Vis spectrophotometer (Model No.1800) with 1 cm matched quartz cells, and UV probe 2.32 software was used. Calibrated analytical balance Mettler Toledo was used for weighing purposed. All statistical calculations were carried out using Microsoft excel 2007 as an analytical tool.

Standard solution

A stock solution of Atorvastatin Calcium (250 µg/ml) was prepared by dissolving equivalent to 25 mg of Atorvastatin working standard into 100 ml volumetric flask, to this 50 ml diluent was added and dissolved in it by sonication for 5 minutes and volume was made up by diluent up to the mark with diluent (solution A). 5 ml solution A was transferred to 50 ml volumetric flask and the volume was made up to the mark by diluent (solution B). A stock solution of Telmisartan (1000 µg/ml) was prepared by dissolving 100 mg of Telmisartan into 100 ml volumetric flask, to this 50 ml diluent was added and dissolve it by sonication for 5 minutes and volume was made up to the mark by diluent (solution C). 5 ml solution C was transferred to 50 ml volumetric flask with the help of pipette and the volume was made up to the mark by diluent (solution D). Further dilution was performed by taking 3 ml of solution B and solution D into 25 ml volumetric flask and the volume was made up to the mark with diluent.

Sample solution

20 tablets of (Telista plus 40 Tablet) each contained 10 mg of ATC and 40 mg of TEL were accurately weighed. Their average weight determined and finally powdered. The quantity of the powder containing weight equivalent to 25 mg ATC and 100 mg TEL were transferred into 100 ml volumetric flask, to this 50 ml diluents was added followed by sonication for 10 minutes and made up the volume up to the mark with diluent (solution X). The resulting solution was stirred for 1 hour and then centrifuged at 5000 RPM for 10 minutes. 5 ml solution X was taken in 50 ml volumetric flask and the volume was made up to the mark by diluent (solution Y). Further dilution was performed by taking 3 ml of solution Y into 25 ml volumetric flask and made up volume up to the mark by diluent (solution Z).

METHOD VALIDATION

The developed method was validated according to ICH (Q2) B guidelines for validation of analytical procedures. As per the ICH guidelines, the method validation parameters checked were linearity, accuracy, precision, robustness, LOD, and LOQ.

Linearity (Calibration Curve)

For constructing calibration curve, series of six dilutions in the concentration range 01-06 (01, 02, 03, 04, 05, and 06) µg/ml for ATC and 04-24 (04, 08 12, 16, 20, and 24) µg/ml for TEL was taken. Calibration curve was constructed by plotting absorbance vs. concentration of ATC and TEL and regression equation calculated from straight line equation. Linearity curves for ATC and TEL showed in figure No. 5 and 6 respectively.

Accuracy (% Recovery)

The accuracy of the method was determined by calculating recovery of ATC and TEL by the standard addition method. Known amounts of standards solutions of ATC and TEL added at 80,100 and 120% level to prequalified sample solution of ATC and TEL. Three samples were prepared for each recovery level solutions were then analyzed and the percentage recovery was calculated by using formula.

Precision

The precision of analytical method expresses the degree of agreement among individual test when the procedure is applied repeatedly to multiple sampling of homogenous samples. Precision is considered at three levels that is system precision, method precision (repeatability) and intermediate precision (reproducibility).

System precision

The system precision was checked by taking absorbance repeatedly (n =6) of standard solutions of ATC and TEL under the same spectrophotometric condition and calculate the % RSD of absorbance which should not be more than 2%.

Method precision (Repeatability)

The method precision of the analytical method was determined by analyzed six sets of sample preparation against the same standard. Assay of all six sample preparation was determined and mean % assay, standard deviation and %RSD for the same was calculated.

Intermediate Precision (Reproducibility)

Intermediate precision of the analytical method was determined by performing method precision on another day by another analyst using different instrument under same experimental conditions. Assay of all replicate sample preparation was determined and mean % assay, standard deviation and %RSD for the same was calculated.

Precision study was established by evaluating system precision, method precision, and intermediate precision.

Robustness

The robustness of the analytical method is a measure of its capacity to remain unaffected by small but deliberate variations in the method parameters and provides an indication of its reliability during normal usage.

Robustness of the method was determined by performing assay of sample preparation at change of wavelength (±1 nm). The robustness of the method was evaluated by calculating %

assay of test solution which is not more than ±2.0% from mean value of method precision and system suitability parameters meet the requirements.

Limit of Detection & Limit of Quantification

Limit of Detection (LOD) is the lowest concentration of analyte in the sample that could be detected under the stated experimental condition and Limit of Quantification (LOQ) is the lowest concentration of the active ingredients in a sample that could be determined with accepted precision and accuracy. According to ICH recommendation, the approach based on the standard deviation (SD) of the response and slope (M) was used for determining the detection and quantification limits. LOD can be calculated according to formula LOD = 3.3 (SD/M) and LOQ = 10(SD/M). The signal to noise ratio was determined. The LOD was regarded as the amount for which the signal to noise ratio was 3:1 & LOQ as the amount for which the signal to noise ratio was 10:1.

RESULTS AND DISCUSSION

The developed method was validated according to International conference on harmonization ICH (Q2)B guidelines for validation of analytical procedures. As per the ICH guidelines, the method validation parameters checked were linearity, accuracy, precision, assay, robustness, LOD and LOQ.

In the present work, an analytical method based on UV spectrophotometry was developed and validated for assay of ATC and TEL in tablet formulation. The basic spectrophotometric condition used for this method was designed to be simple, easy to use and reproduce. The analytical conditions were selected after testing the different parameters that influence of wavelength, diluent, and other spectrophotometric parameters. Methanol was used as a diluent because both drugs were soluble in it and it had no interference while performing analysis. ATC showed wavelength maxima at 246 nm and TEL showed wavelength maxima at 298 nm.

1] The method showed a good linear response in the concentration range 01-06 µg/ml for ATC) & 04-24 µg/ml for TEL. The response of the drug was found to be linear in the concentration range and the linear regression equation was y = 0.042x + 0.003 for ATC and y = 0.051x + 0.004 for TEL where x is the concentration in µg/ml and y is the absorbance. The

correlation coefficients (R^2) were 0.9998 and 0.9999 for ATC and TEL respectively. The calibration curve obtained during linearity study are shown in Figure No. 5 and 6.

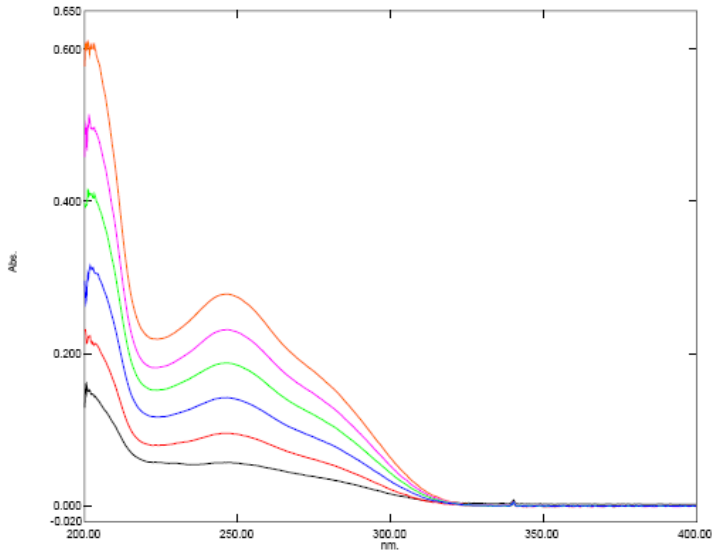

Figure No. 3: Overlain spectra of Atorvastatin Calcium for linearity study

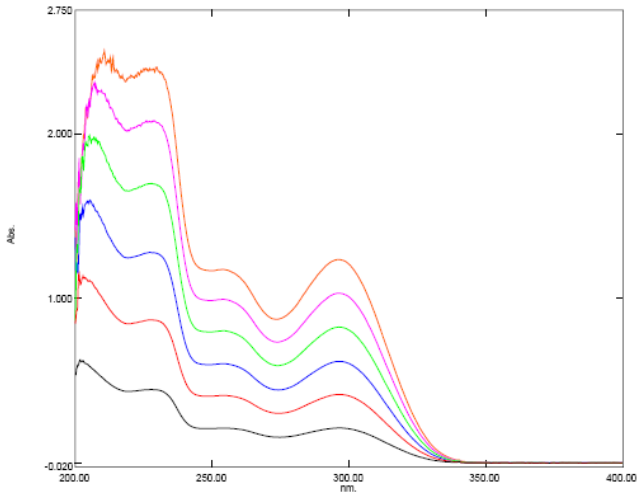

Figure No. 4: Overlain spectra of Telmisartan for linearity study

Table No. 1: Linearity study of ATC and TEL

Sr. No.	Concentration (µg/ml)		Absorbance	
	ATC	TEL	ATC at 246 nm	TEL at 298 nm
1	01	04	0.047	0.210
2	02	08	0.087	0.417
3	03	12	0.132	0.625
4	04	16	0.173	0.834
5	05	20	0.217	1.042
6	06	24	0.258	1.241

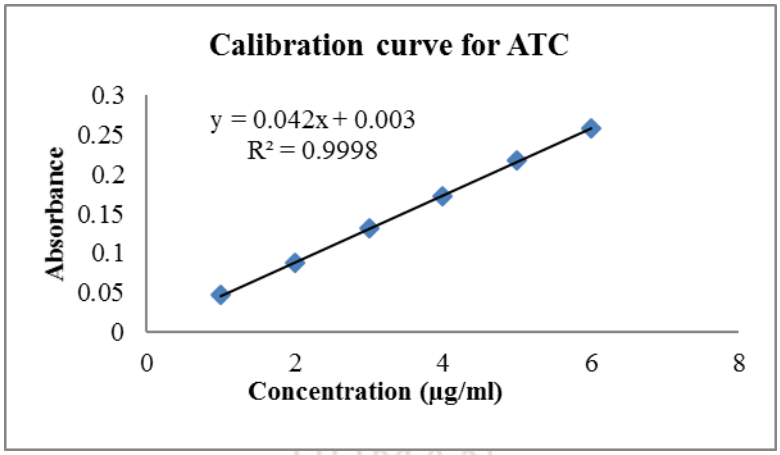

Figure No. 5: Linearity curve of Atorvastatin Calcium

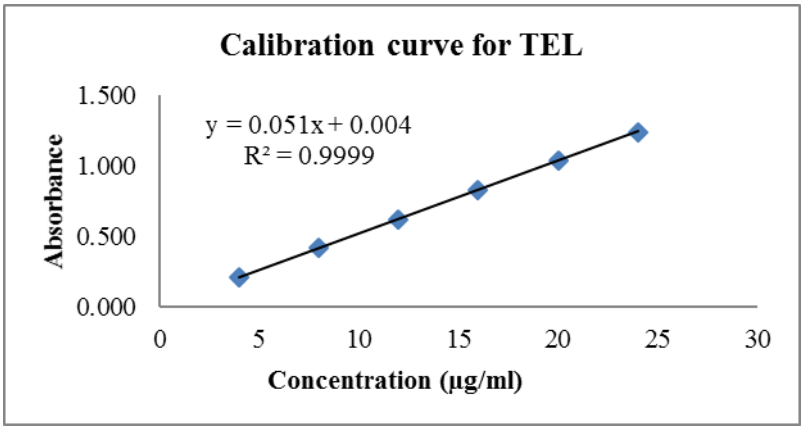

Figure No. 6: Linearity curve of Telmisartan

Table No. 2: Regression parameters of calibration curve

Parameters	**ATC**	**TEL**
Linear range (µg/ml)	01-06	04-24
Slope	0.042	0.051
Intercept	0.003	0.004
Correlation Coefficient (R^2)	0.9998	0.9999

2] The method was found to be precise and RSD was found to be less than 2%.

Table No. 3: Results of system precision study

Sr. No.	**Absorbance of ATC**	**Absorbance of TEL**
1	0.497	0.435
2	0.499	0.437
3	0.497	0.436
4	0.498	0.435
5	0.499	0.437
6	0.497	0.438
Mean	**0.498**	**0.436**
Standard deviation	**0.001**	**0.001**
%RSD	**0.197**	**0.278**

Table No. 4: Results of method precision study

Sr. No.	**Wt of sample in mg**	**Avg. Area of ATC**	**Avg. Area of TEL**	**% Assay of ATC**	**% Assay of TEL**
1	669.21	0.508	0.440	98.8	101.7
2	673.25	0.510	0.436	98.6	100.3
3	670.58	0.516	0.438	100.1	101.2
4	671.23	0.512	0.431	99.3	99.3
5	672.28	0.518	0.438	100.3	100.9
6	669.12	0.520	0.431	101.1	99.8
Mean				**99.7**	**100.5**
Standard Deviation				**0.983**	**0.897**
%RSD				**0.986**	**0.892**

Table No. 5: Results of intermediate precision study

Sr. No.	Wt of sample in mg	Avg. Area of ATC	Avg. Area of TEL	% Assay of ATC	% Assay of TEL
1	668.73	0.513	0.437	99.7	101.2
2	675.90	0.512	0.439	99.5	100.6
3	671.40	0.513	0.426	101.8	98.3
4	673.17	0.518	0.436	99.7	100.2
5	668.92	0.520	0.429	98.6	99.3
6	672.88	0.510	0.441	101.2	101.5
Mean				**100.2**	**100.2**
Standard Deviation				**1.194**	**1.214**
%RSD				**1.192**	**1.211**

3] The results of recovery of ATC and TEL with the % RSD are given in below table.

Table No. 6: Results of Accuracy study of ATC

Accuracy level	Set No.	Amount added (µg/ml)	Amount found (µg/ml)	Recovery (%)	Mean recovery (%)	SD	RSD (%)
80%	1	2	1.99	99.4	**99.4**	**0.875**	**0.880**
	2	2	2.01	100.3			
	3	2	1.97	98.5			
100%	1	2.5	2.47	98.8	**100.1**	**1.247**	**1.246**
	2	2.5	2.53	101.2			
	3	2.5	2.51	100.4			
120%	1	3	2.95	98.5	**99.5**	**0.921**	**0.926**
	2	3	3.01	100.3			
	3	3	2.99	99.6			

Table No. 7: Results of Accuracy study of TEL

Accuracy level	Set No.	Amount added (µg/ml)	Amount found (µg/ml)	Recovery (%)	Mean recovery (%)	SD	RSD (%)
80%	1	8	8.05	100.7	**99.8**	**0.927**	**0.929**
	2	8	7.91	98.8			
	3	8	8.00	100.1			
100%	1	10	10.09	100.9	**100.6**	**1.165**	**1.158**
	2	10	9.93	99.3			
	3	10	10.16	101.6			
120%	1	12	12.02	100.2	**100.2**	**0.735**	**0.734**
	2	12	12.11	100.9			
	3	12	11.93	99.4			

4] Assay of ATC and TEL showed in table number 8.

Table 8: Results of assay of ATC and TEL

Drugs	Label claim (mg/tab)	Amount of drug estimated (mg/tab)	% Amount found
ATC	10.0	9.84	98.4
TEL	40.0	40.76	101.9

5] LOD and LOQ value of ATC and TEL were determined by residual standard deviation method. The results are given in table number 9.

Table 9: LOD and LOQ of ATC and TEL

Drugs	**LOD (µg/ml)**	**LOQ (µg/ml)**
ATC	0.059	0.177
TEL	0.104	0.316

6] Robustness was evaluated by varying different parameters. The results of these variations are given in table number 10.

Table 10: Results of robustness study of ATC and TEL

Parameter	Variation	Assay of ATC (%)	Variation	Assay of TEL (%)
Wavelength	245	100.5	297	100.3
	246	101.7	298	98.8
	247	98.9	299	99.2

CONCLUSION

A validated UV-Spectrophotometry method has been developed for the determination of Atorvastatin calcium and Telmisartan in tablet dosage form. The developed method is simple, rapid, linear, accurate, precise and specific. Results from the validation experiments showed that the method is reliable and accurate therefore it can be successfully applied for the routine quality control analysis of Atorvastatin calcium and Telmisartan in pharmaceutical dosage form.

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REFERENCES

1. Indian Pharmacopoeia, volume III, Ministry of Health and Family Welfare Government of India, published by Indian Pharmacopoeia Commission, Ghaziabad, 2010; vol. II & vol. III: 849-850 & 2186-2187.
2. The United state Pharmacopoeia, the United state Pharmacopoeia Commission, America. 2012; USP 35 NF 30: 2263 & 4776.
3. The British Pharmacopoeia, the British Pharmacopoeia Commission, London. 2012; vol. I & II; 2191 & 2154.
4. www. Drugs. Com. Cerner Multum *et al.* Inc. Version. 2000-2015;
5. ICH Harmonized Tripartite Guideline, Validation of analytical procedure text and methodology Q2 [R1]. In International Conference on Harmonization of technical requirements for registration of pharmaceuticals for human use. 2005.
6. U. P. Patil, S. V. Gandhi, M. R. Sengar and V.S. Rajmane. Simultaneous determination of Atorvastatin calcium and Telmisartan in tablet dosage form by spectrophotometry International journal of ChemTech research. 2009; 1(4): 970-973.
7. Napa Delhi raj, Socalingam Anbazhagan. Validated HPTLC method for the estimation of antihypertensive drugs in pharmaceutical combined dosage forms. International Journal of Research and Reviews in Pharmacy

and Applied Science. 2012; 2(5): 959-964.N. Mukuntha Kumar, Sumathi V. Rao, Konde abbulu, B. Venkata Narayana, I. Sukumar. International journal of scientific research. 2014; 3(11): 357-359.
8. N. Mukuntha Kumar, Sumathi V. Rao, *et al.*, RP-HPLC method development and validation for the simultaneous determination of Telmisartan and Atorvastatin in bulk and pharmaceutical dosage form. International Journal of Scientific Research. 2014; 3(11): 357-359.
9. K.U. Chaudhari, P.D. Gaikwad, V.H. Bankar, S.P. Pawar. Development and validation of UV-spectrophotometric method for simultaneous estimation of Telmisartan and Atorvastatin calcium in bulk and tablet dosage form. International journal of pharmacy and technology. 2010; 2(2): 255-264.
10. R. Vijayamirtharaj, J. Ramesh, B. Jayalakshmi, Hanas Bin Hasim. Development and validation of RP-HPLC method for the simultaneous estimation of Telmisartan and Atorvastatin calcium in tablet dosage forms. Pharmacie Globale International Journal of Comprehensive Pharmacy. 2010; 1(04): 1-4.
11. Saurabh K Sinha, Prabhat K Shrivashtava, Sushant K Shrivastava. Development and validation of a HPLC method for the simultaneous estimation of Amlodipine and Telmisartan in pharmaceutical dosage form. Asian Pacific Journal of Tropical Biomedicine. 2012; S312-S315.
12. M. Anusha, D. Meena Bharathi, B Chandra Priyanka, Buchi N. Nalluri. Simultaneous estimation of Metoprolol Succinate and Telmisartan in bulk and pharmaceutical dosage forms by RP-HPL-PDA method. International Journal Pharmaceutical Sciences Review and Research. 2012; 16(2): 111-115.
13. N. Delhi raj, P. Ashok, U. Ravikiran, P. Abhinandhana. A review of various analytical methods on Atorvastatin. Indian Journal of Research in Pharmacy and Biotechnology. 2013; 1(6): 786-792.
14. Panchal PJ, Suhagia BN. simultaneous determination of Atorvastatin calcium and Ramipril in capsule dosage forms by high-performance liquid chromatography and high-performance thin layer chromatography. Journal of the Association of Official Analytical Chemists. 2010; 93(5): 1450-1457.
15. Patole S. Khodke A. Potale L. Damle M. J. Youngpharm. A validated densitometric method for analysis of Atorvastatin calcium and Metoprolol tartrate as bulk drugs and in combined capsule dosage forms. Journal of Youngpharm. 2011; 3(1): 55-59.
16. Pilli NR, Inamadugh JK, Mullangi R, Karra VK, Vaidya JR, Rao JV. Simultaneous determination of Atorvastatin, Amlodipine, Ramipril and Benazepril in human plasma by LC-MS/MS and its applications to a human pharmacokinetic study. Biomedical Chromatography. 2011; 25(4): 439-449.
17. Shah Y. Iqbal Z. Ahmad L. Khan A. Khan MI. Nazir S. Nazir F. Simultaneous determination of Rosuvastatin and Atorvastatin in human serum using RP-HPLC/UV detection: method development, validation and optimization of various experimental parameters. Journal of Chromatography B Analytical Technologies in the Biomedical and Life Sciences. 2011; 879 (9-10): 557-563.
18. R. A. Mhaske, D. J. Garole, A. A. Mhaske and S. Sahasrabudhe. RP-HPLC method for simultaneous determination of Amlodipine Besylate, Valsartan, Telmisartan, Hydrochlorothiazide and Chlorthalidone: application to commercially available drug products. International Journal of Pharmaceutical Sciences and Research. 2012; 3(1): 141-149.
19. Lakshmi Sivasubramanian, KS Lakshmi. H-point standard addition method for simultaneous spectrophotometric determination of Irbesartan, hydrochlorothiazide and Telmisartan in tablet. International Journal of Research in Pharmacy and Chemistry. 2014; 4(2): 373-380.
20. Asha B. Thomas, Sheetal N. Jagdale, Shweta B. Dighe, Rabindra K. Nanda. Simultaneous spectrophotometric estimation of Amlodipine Besylate and Telmisartan in tablet dosage form. International Journal of Pharma Tech. 2010; 2(2): 1334-1341.