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Research article

Spectrophotometric simultaneous determination of efonidipine hydrochloride ethanolate and telmisartan in synthetic mixture by first order derivative method

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ABSTRACT

The established method represents the development and validation of a straight forward, precise, accurate, specific and reproducible method for the simultaneous estimation of Efonidipine Hydrochloride Ethanolate and Telmisartan in synthetic mixture. First order derivative of the overlay spectra was used for quantification of both drugs. This method involving the determination of both drugs at their respective zero crossing point working wavelength was observed 231.00 nm (Zero crossing point of Telmisartan) for Efonidipine hydrochloride ethanolate and 238.60 nm (Zero crossing point of Efonidipine Hydrochloride Ethanolate) for Telmisartan using methanol as diluent. International conference on harmonization (ICH) (Q2R1) guideline was used for method validation. The Beer-Lambert's law obeyed in the concentration range of 2-18 µg/ml and 4-36 µg/ml for Efonidipine Hydrochloride Ethanolate and Telmisartan, respectively. The percentage recovery was found in the range of 98-101 % of Efonidipine Hydrochloride Ethanolate and 98.46-99.77% of Telmisartan. The % relative standard deviation of precision and repeatability study was found beneath 1%. This simple and precise method can be used of both drugs in quality control laboratories.

Keywords: Efonidipine Hydrochloride Ethanolate, First order derivative, ICH Q2 (R1), Telmisartan, UV spectroscopy.

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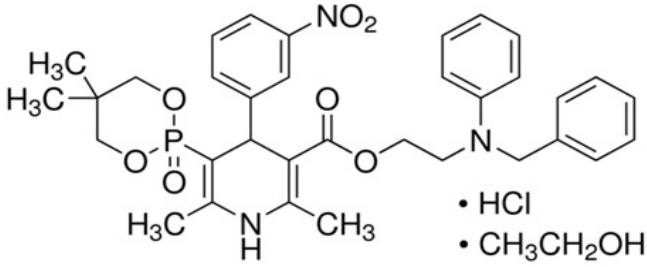
INTRODUCTION

Efonidipine Hydrochloride Ethanolate is a 2-[Benzyl(phenyl) amino] ethayl-1,4-dihydro-2,6-dimethayl-5-(5,5-dimethayl-2-oxo-1,3,2-dioxaphosphorinan-2-yl)-4-(3-nitrophenyl)-3-pyridine carboxylate hydrochloride ethanol. Chemical structure of Efonidipine Hydrochloride Ethanolate (EFO) shown in (Figure 1). EFO is a 1,4 dihydropyridine derivative calcium channel blocker, which inhibits both L- and T-type of calcium channel. Also increase the glomerular filtration rate without increasing intraglomerular pressure and prevents hypertension induced renal damage [1,2].

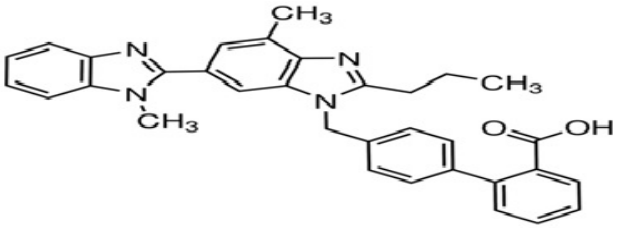
Telmisartan is benzimidazole derivative angiotensin II receptor antagonist and chemically comprised of 4′-{[4-methyl-6-(1-methyl-1H-benzimidazole-2-yl)-2-propyl-1H-benzimidazole-1-yl] methyl]}-biphenyl carboxylic acid [3,4]. Chemical structure of Telmisartan (TELMI) shown in (Figure 2). It inhibits the renin-angiotensin system (RAS), in addition acts as a selective agonist of peroxisome proliferative activated receptor gamma (PPAR-γ), a regulate the insulin and glucose metabolism in skeletal muscle. That dual mode of action may provide protective benefits against the vascular and renal damage caused by diabetes and cardiovascular disease [5]. Several studies have reported for quantification of EFO and TELMI individually as well as in combination with another drug; HPLC [6,7], LC-MS [8-10], UV spectroscopy [11-13], HPTLC [14], UPLC [15] method.

Figure 1: Structure of efonidipine hydrochloride ethanolate



Literature indicates one spectroscopic method available for simultaneous estimation in their synthetic mixture [16]. In published spectroscopic method shows lack of sensitivity. Also, drug ratio is not mention. This research objectives were to established and validate a simple, sensitive, efficient, precise and accurate first order derivative uv-visible spectroscopic method for simultaneously quantification of EFO and TELMI in synthetic mixture using 1:2 respective drug ratio. This developed method was validated in accordance with international conference on harmonization (ICH) Q2R1 guidelines [17]. The current research was found to be more sensitive, selective, accurate and precise for the analysis.

Figure 2: Structure of telmisartan



MATERIALS AND METHODS

Chemicals and Reagents

Efonidipine Hydrochloride Ethanolate and Telmisartan were provided by as a gift sample from Zuventus Healthcare Ltd. (Mumbai, India). HPLC grade Methanol, Acetonitrile and Water were used of Finar Pvt. Ltd.

Instrumentation

The study was done on a Shimadzu (model no.80387) UV-Visible double beam spectrophotometer with 1 cm Quartz match cells and data were processed using UV probe software. Electronic balance was used for weighing purpose (MAB 220 wensar).

Method Development

Preparation of primary standard stock solution EFO and TELMI were prepared by dissolving 20 mg and 40 mg respectively in 100 ml volumetric flask containing 30 ml methanol and sonication for 5 min. After sonication volume was made up to the mark with methanol to obtained concentration of 200 µg/ml of EFO and 400 µg/ml of TELMI.

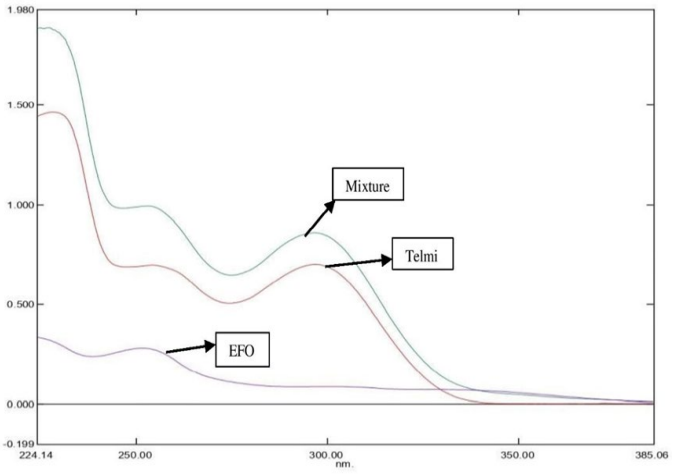
Preparation of secondary standard stock solutions

Appropriately diluted Primary standard stock solution with diluent methanol to obtain a concentration of 100 µg/ml and 200 µg/ml for EFO and TELMI, respectively.

Selection of wavelength

To prepare 10 µg/ml of EFO and 20 µg/ml of TELMI were individually from secondary stock solution and scanned in UV range between 200-400 nm.

Figure 3: Zero order spectra of efonidipine hydrochloride ethanolate, telmisartan and mixture



The obtained absorption spectra of both drugs were converted to their respective first order derivative spectra using the inbuilt software (Simadzu UV probe 2.6). After converting first order derivative spectra of EFO and TELMI, zero crossing point (ZCP) of both drugs were selected. The first working wavelength selected 231.00 nm (ZCP of TELMI), Where EFO showed reasonable absorbance. The second working wavelength selected 238.60 nm (ZCP of EFO), Where TELMI showed reasonable absorbance. The zero order absorption and first order derivative spectra is given in (Figure 3 and 4).

Method Validation

Analytical validation parameters for the analysis of the proposed method were determined according to ICH (Q2R1) guideline [17].

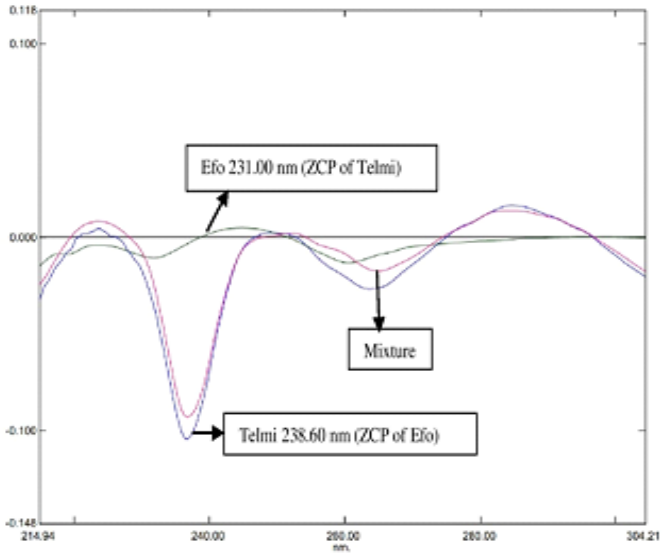
Linearity

From the secondary standard stock solution aliquots 0.2 to 1.8 ml solution to obtain nine solution of different concentration were dilution done by methanol. To obtain series of concentration of 2-18 µg/ml of EFO and 4-36 µg/ml TELMI was used for linear calibration plot respectively.

Specificity

Specificity test was performed using excipient. The solution of 8 µg/ml of EFO and 16 µg/ml TELMI were six times scanned, with and without the addition of excipient to check the interference of excipient.

Figure 4: First order derivative spectra of efonidipine hydrochloride ethanolate, telmisartan and mixture



Accuracy

The recovery of the method determined by solid addition method. The assay concentration was spiked at three different concentration levels of 80 %, 100 % and 120 % (6.4, 8, 9.6 µg/ml of EFO and 12.8, 16, 19.2 µg/ml of TELMI). The accuracy of the method was evaluated by calculating percentage recovery.

Precision

Repeatability of method checked by scanned six solution of same concentration at 8 µg/ml and 16 µg/ml of EFO and TELMI respectively. The Intra-day and Inter-day precision study were

performed at three times on the three different time intervals on same day and three different day at concentration levels 80 %, 100 %, 120 % (6.4, 8, 9.6 µg/ml of EFO and 12.8, 16, 19.2 µg/ml of TELMI. The result is express in term of % relative standard deviation (RSD).

Robustness

The capacity of the method was checked to remain unaffected by small variation of experimental parameter. The variation made for wavelength at EFO (230.00, 231.00, 232.00 nm) and TELMI (239.60, 238.60, 240.60 nm).

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

The sensitivity of the method was done based on the formula given in ICH (Q2R1) guideline [17]. From the five-calibration curve, deviation of the intercepts and slope were used to calculated LOD and LOQ according to formula.

LOD = 3.3 x Standard deviation/ Slope

LOQ = 10 x Standard deviation/ Slope

Analysis of a synthetic mixture

Synthetic mixture was prepared by equivalent to take 20 mg for EFO and 40 mg for TELMI with common tablet excipient (Talc, HPMC, Starch, Mg stearate, Lactose, PVP) in adequate amount. This synthetic mixture was diluted with methanol to make concentration 8 µg/ml for EFO and 16 µg/ml for TELMI**.**

RESULTS AND DISCUSSION

The objective of the method development was to quantification of drugs without spectral interference. Highly overlapping zero order absorption spectra shows the wavelength of both drugs were very closed to each other so they interfere for the estimation of each other analytes. So, objective of proposed method was to eliminate spectral interference, thus the first order derivative spectroscopic method was developed.

Linearity

The calibration curve was follows Beer's low over a given concentration range of 2-18 µg/ml for EFO and 4-36 µg/ml for TELMI. The data for linearity is shown in (Table 1). The calibration curve for EFO and TELMI is given in (Figure 5 and 6).

Table 1: Linearity data for efonidipine hydrochloride ethanolate and telmisartan

Concentration (µg/ml)	Absorbance dA/dλ	Concentration (µg/ml)	Absorbance dA/dλ
EFO		TELMI	
2	0.004	4	0.026
4	0.007	8	0.045
6	0.009	12	0.061
8	0.012	16	0.079
10	0.015	20	0.098
12	0.017	24	0.115
14	0.020	28	0.134
16	0.022	32	0.150
18	0.025	36	0.167

Specificity

Excipient hindrance were not observed at the working wavelength of EFO and TELMI. The UV spectroscopic system presented in this study is specific for EFO and TELMI. Specificity data of method are presented in (Table 2).

Figure 5: First order derivative linearity spectra of efonidipine Hydrochloride ethanolate (2-18 µg/ml)

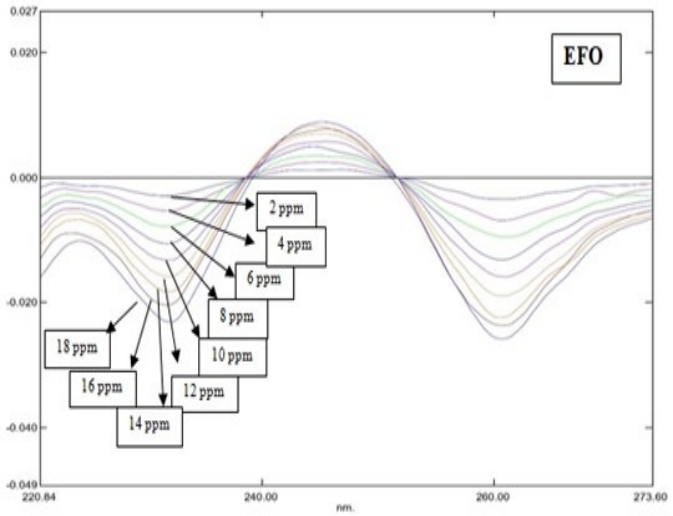


Figure 6: First order derivative linearity spectra of telmisartan (4-36 µg/ml)

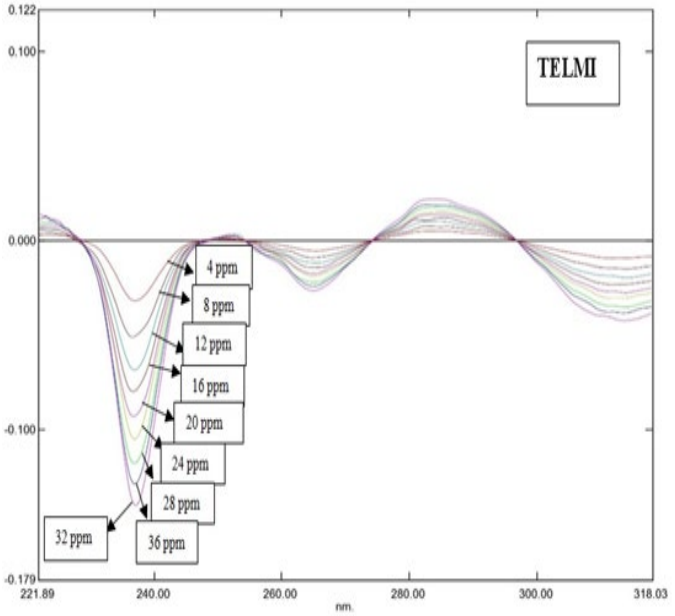


Figure 7: Linearity graph of efonidipine hydrochloride ethanolate

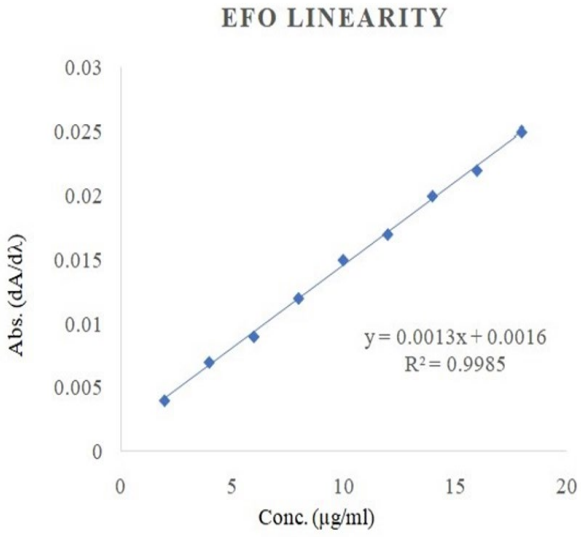


Figure 8: Linearity graph of telmisartan

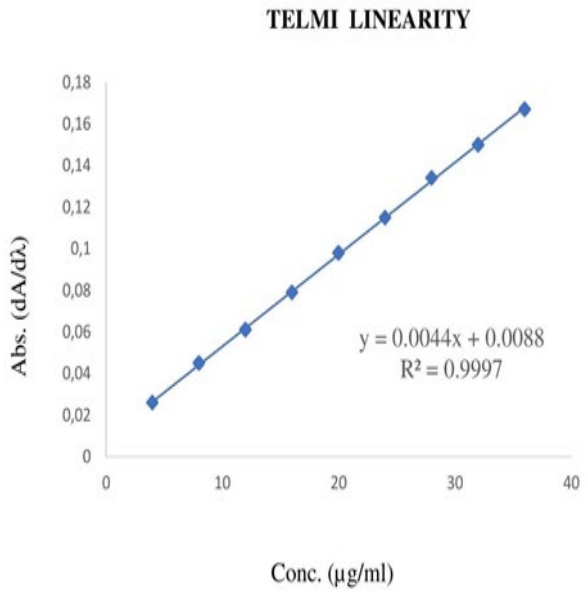


Table 2: Specificity data for efonidipine HCl ethanolate and telmisartan

Drug	Conc. (µg/ml)	Without Excipient		With Excipient		Mean % Interference
		Abs. Mean	Mean Conc. (µg/ml)	Abs. Mean	Mean Conc. (µg/ml)	
EFO	8	0.0123	8.26	0.0122	8.23	0.480
TELMI	16	0.0798	16.14	0.0796	16.09	0.307

Accuracy

When used for evaluation of recovery at three concentration level 80 %, 100 %,120 % after spiking with standard the proposed method showed % recovery between 98-120 % for EFO and TELMI. The recovery data are shown in (Table 3).

Table 3: Recovery data for efonidipine hydrochloride ethanolate and telmisartan

% Level	Target Conc.(µg/ml)		Spiked Conc.(µg/ml)		% Recovery	
	EFO	TELMI	EFO	TELMI	EFO	TELMI
80 %	8	16	6.4	12.8	100.07 %	98.53 %
100 %	8	16	8	16	99.67 %	100.53 %
120 %	8	16	9.6	19.2	99.36 %	99.61 %

Precision

Repeatability and intermediate precision expressed in terms of % RSD. The proposed system indicates acceptable limit in variation. Therefore, the current method was precise.

Table 4: Repeatability data for efonidipine HCl ethanolate and telmisartan

Drug	Confound (µg/ml)	Abs.Mean ± SD (n=6)	RSD
EFO	8	0.012 ± 1.90029	1.58
TELMI	16	0.079 ± 0.00089	1.13

Table 5: Intra-day and Inter-day data for efonidipine hydrochloride ethanolate and telmisartan

Drug	% Level	Intraday precision		Interday precsion	
		Abs. ± SD (µg/ml)	RSD	Abs. ± SD (µg/ml)	RSD
EFO	80 %	0.0096 ±0.0000	0.00	0.0097 ±0.0001	1.96
	100 %	0.0112 ±0.0001	1.17	0.0124 ± .0001	1.54
	120 %	0.0144 ±0.0001	1.30	0.0145 ± .0001	1.32
TELMI	80 %	0.068 ± 0.0010	1.57	0.068 ± 0.0011	1.70
	100 %	0.079 ± 0.0013	1.74	0.087 ± 0.0006	0.85
	120 %	0.091 ± 0.0011	1.26	0.091 ± 0.0010	1.17

Limit of Detection (LOD) and Limit of Quantification (LOQ)

LOD and LOQ of EFO and TELMI were determined by equation according to ICH guideline. LOD and LOQ were found to be 0.40 µg/ml and 1.21 µg/ml for EFO and 0.11 µg/ml and 0.34 µg/ml for TELMI respectively.

Roubstness study

Making a deliberate change in wavelength were take place and RSD was plant to be lower than 2, specify that the method is robust. The results are shown in (Table 6).

Table 6: Roubstness data for efonidipine hydrochloride ethanolate and telmisartan

Analysis of Synthetic mixture

The assay of synthetic mixture was found to be 100 % and 99.95 % for both the method respectively.

Drugs	Wavelength	Mean Abs. ± SD	RSD
EFO	230.00	0.009 ± 0.0001	1.11
	231.00	0.018 ± 0.0002	1.70
	231.00	0.015 ± 0.0099	0.57
TELMI	237.60	0.0876 ± 0.0110	1.31
	238.60	0.0796 ± 0.0011	1.44
	239.60	0.0536 ± 0.0005	1.07

Table 7: Assay of synthetic mixture

Drug	Conc. Added (µg/ml)	Abs. (n=3) Mean ± SD	Conc. Found (µg/ml)	% Content
EFO	8	0.012 ± 1.7	8	100 %
TELMI	16	0.079 ± 0.008	15.98	99.95 %

CONCLUSIONS

From the above research work, it can be concluded that the proposed method is sensitive, specific, and robust, with good delicacy and perfection. The 1st order derivative spectroscopy was developed to analysed the mixture, provide advantage that improved resolution and used to eliminate the spectral interference by broad band discrimination. The major advantage of this technique is that it is developed for synthetic mixture and helpful for experiment to develop for its combined dosage form. So that method can be implemented for quantification of commercially available dosage form by the pharmaceutical industry and analytical laboratories in future.

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CONFLICT OF INTEREST

There is no conflict of interest to expose.

REFERENCES

1. Shimizu M, Ogawa K, Sasaki HM, et al, 2003. Effects of Efonidipine, an L- and T-Type Dual Calcium Channel Blocker on Heart Rate and Blood Pressure in Patients with Mild to Severe Hypertension: An Uncontrolled, Open-Label Pilot Study, CTR. 64, pages-707-714.
2. Koichi HK, Takao ST, Goto Y, 2010. Impact of renal function on cardiovascular events in elderly hypertensive patients treated with efonidipine Renal Subset Analysis of the Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients (JATOS), Hypertens, Res. 33, pages-1211-1220.
3. Indian Pharmacopoeia, 2018. Government of India, Ghaziabad: Ministry of Health and Family Welfare, published by The Indian Pharmacopeia Commission, Delhi, pp 1604.

4. Akhrass PR, McFarlane SI, 2011. Telmisartan and cardioprotection, Vasc Health Risk Manag. 7, pages- 677-683.
5. Kusunoki H, Taniyama Y, Azuma J, et al, 2012. Telmisartan Exerts Renoprotective Actions via Peroxisome Proliferator-Activated Receptor-/Hepatocyte Growth Factor Pathway Independent of Angiotensin II Type 1 Receptor Blockade, HPRTDN. 59, pages-308-316.
6. Rajput AS, Jha DK, Gurram S, et al, 2020. RP-HPLC method Development and validation for the quantification of Efonidipine Hydrochloride in HMF Processed Solid Dispersion, Futur J Pharm Sci.6, pages- 1-9.
7. Kumar A, Shoni SK, Dahiya M, et al, 2017. Development and validation of liquid chromatography methodology for estimation of Efonidipine HCl Ethanolate, Pharm Anal Acta. 8, pages-1-6.
8. Man Liu, Zhao H, Tong Y, et al, 2014. Determination of efonidipine in human plasma by LC-MS/MS for pharmacokinetic application, J Pharm Biomed Anal. Pages -1-6.
9. Man Liu, Deng M, Zhang D, et al, 2016. A chiral LC-MS/MS method for spectrospecific determination of efonidipine in human plasma, J Pharm Biomed anal. 122, pages 35-41.
10. Pandya CP, Rajput SJ, 2020. Forced degradation study of efonidipine HCl ethanolate, characterization of degradation product by LC-Q-TOF–MS and NMR, J Appl Pharm Sci. 10, pages - 075-099.
11. Rathod SD, Patil PM, Waghmare SSA, et al, 2021. UV-Spectrophotometric Method for Estimation of Telmisartan in Bulk and Tablet Dosage Form, Int J Pharm Sci Res, 3, pages-3936-3939.
12. Chavhan V, Lawande R, Salunke J, et al, 2013. UV spectrophotometric method development and validation for telmisartan in bulk and tablet dosage form, Asian J Pharm Clin Res.6, pages-19-21.
13. Modi DV, Patel PU, et al, 2016. Development and validation of simultaneous equation method for simultaneous estimation of Telmisartan and Nifedipine in synthetic Mixture, Int Res J Pharm. 7(5), pages- 6-9.
14. Prabhu C, Subramanian GS, Karthik A, et al, 2007. Determination of Telmisartan by HPTLC-A stability indicating Assay, J Planar Chromatogr. 20, pages- 477-481.
15. Sahu K, Sahu S, Shaharyar M, et al, 2012. Comparative Study of Forced Degradation Behavior Of Telmisartan by UPLC and HPLC and Development of Validated Stability Indicating Assay Method according to ICH Guidelines, J Chromatogr Sep Tech. 3, pages-1-6.
16. Adeshra SD, Patel GH, Meshram DB, et al, 2012. Development and validation of three novel UV Spectrophotometric methods for simultaneous estimation of Efonidipine Hydrochloride Ethanolate and Telmisartan in their synthetic mixture and its comparison using ANOVA, J Med Chem Sci. 4 (2), pages-145-153.
17. ICH – Harmonized Tripartite Guideline, 2005. Validation of analytical procedure: text and methodology Q2 (R1). International Conference on Harmonization, IFPMA, Geneva, Switzerland.

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