Chemical Methodologies 5(2021) 317-323

Chemical Methodologies

Journal homepage: http://chemmethod.com

Original Research Article

Development and Validation of UV-Spectroscopic First Order Derivative Method for Simultaneous Estimation of Rosuvastatin Calcium and Teneligliptin Hydrobromide Hydrate in Synthetic Mixture.

Amitkumar Vyas[1], Jayshree Godhaniya [1*], Ashok Patel[1], Ajay Patel[1], Nilesh Patel[1], Sunny Shah[1], Devang Sheth[2]

[1]*B.K. Mody government Pharmacy College, Government polytechnic campus, Near Ajidam, Rajkot-36003, Gujarat, India*

[2]*L.M. College of pharmacy, Ahmedabad-38009, Gujarat, India*

ARTICLE INFO

Article history

Submitted: 2021-04-01
Revised: 2021-05-14
Accepted: 2021-05-26
Manuscript ID: CHEMM-2104-1325
Checked for Plagiarism: **Yes**
Language Editor:
Dr. Behrouz Jamalvandi
Editor who approved publication:
Dr. Hasan Karimi Maleh
DOI: 10.22034/chemm.2021.131260

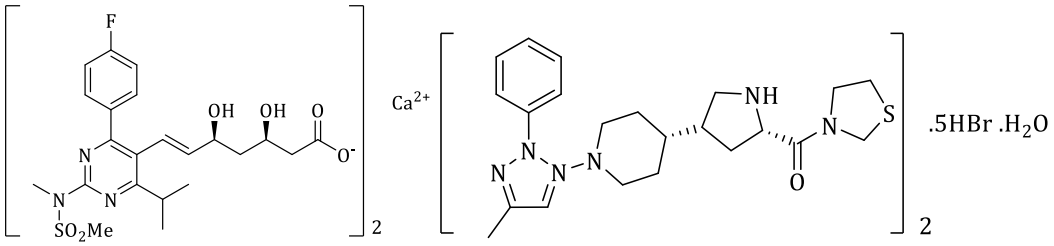
KEYWORDS

Rosuvastatin calcium
Teneligliptin hydrobromide hydrate
First order derivative method
UV spectrophotometry
ICH guideline

ABSTRACT

This work aimed to develop and validate a simple, accurate, precise, and reproducible spectroscopic method for simultaneous estimation of rosuvastatin calcium and teneligliptin hydrobromide hydrate by UV-Visible first-order derivative method. According to our present knowledge, no UV method was reported for combination of rosuvastatin and teneligliptin. So, in this work, it was decided to performed the first-order derivative method and it was validated as per ICH(Q2 R1) guideline. Rosuvastatin calcium and teneligliptin hydrobromide hydrate showed absorbance at the working wavelength of 230.03 nm (Zero crossing point of rosuvastatin calcium) and 222.66 nm (Zero crossing point of rosuvastatin calcium), respectively, using methanol as diluent. Linearity was found over the concentration range of 1-42 µg/ml for both drugs and correlation coefficients was 0.9995 and 0.9994, respectively. Accuracy was found between 98.91%-101.13% and 99.38%-100.25% for rosuvastatin calcium and teneligliptin hydrobromide hydrate, respectively. LOD was found to be 0.213µg/ml and 0.120 µg/ml for rosuvastatin calcium and teneligliptin hydrobromide hydrate respectively. LOQ was found to be 0.646 µg/ml and 0.3648 µg/ml for rosuvastatin calcium and teneligliptin hydrobromide hydrate, respectively. The result revealed that the developed method is suitable for analysis of determining rosuvastatin calcium and teneligliptin hydrobromide hydrate in a binery mixture.

GRAPHICAL ABSTRACT



* Corresponding author: Jayshree Godhaniya
✉ E-mail: jayshreegodhaniya1@gmail.com Phone:+7202071247

Introduction

Rosuvastatin calcium is (E)-(3R, 5S)-7-{4-(4-flourophenyl)-6-isopropyl-2-[methyl (sulphonylamino)] pyrimidin-5-yl}-3,5-dihydroxyhepten-6-oic acid calcium, is a synthetic lipid-lowering agent which acts on plasma lipids [1]. It is an inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A, an enzyme responsible for the conversion of HMG-CoA to mevalonate, which was a rate-limiting step in cholesterol biosynthesis [2]. The structure of rosuvastatin calcium is given in Figure 1.

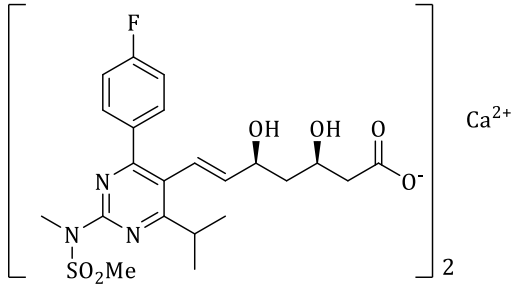


Figure 1: Rosuvastatin calcium

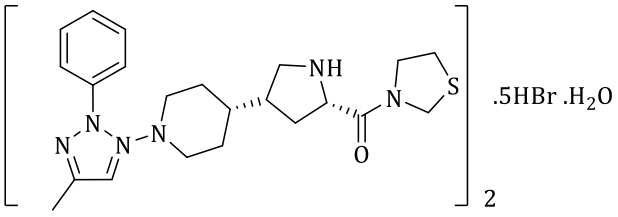


Figure 2: Teneligliptin hydrobromide hydrate

Teneligliptin hydrobromide hydrate belongs to an antidiabetic class. It increases incretin levels (GLP-1 and GIP), which reduces glucagon release, and ultimately increases insulin secretion, decreases gastric emptying, and blood glucose levels. Oral teneligliptin, a dipeptidyl peptidase-4 inhibitor, is indicated for the treatment of adults with type 2 diabetes (T2DM) [3, 4]. Structure of teneligliptin is given in Figure 2.

This combination is used in the treatment of a patient suffering from dyslipidemia associated with type 2 Diabetes Mellitus. Diabetes, and increasing resistance to insulin, even in persons considered to have ‘‘normal’’ insulin sensitivity, has been associated with higher concentrations of cholesterol and TG and lower concentrations of HDL cholesterol [4,5].

Various analytical methods are available to determine the rosuvastatin calcium and teneligliptin hydrobromide hydrate individually, which include HPLC method for rosuvastatin calcium[6,7], teneligliptin [8,9], HPTLC method for rosuvastatin calcium[10], HPTLC method for teneligliptin[11], LC-MS method for rosuvastatin calcium[12], LC-MS method for teneligliptin hydrobromide hydrate[13], UV method for rosuvastatin calcium[14,15] and UV method for teneligliptin[16-18]. But there is no method available that can simultaneously detect both in combination.

To the best of our knowledge, there is no UV method available for this combination. Therefore, in this study, it was decided to carry out the first-order derivative method. This method was validated to comply with the ICH(Q2R1) [19]. First-order derivative method spectroscopy was found to be more selective, accurate, precise, and simple for the estimation.

Material and methods

Chemicals and Reagents

Teneligliptin hydrobromide hydrate and rosuvastatin calcium and methanol were provided by B. K. Mody Government Pharmacy College. UV visible spectrophotometer (UV-1800 Shimadzu) was used; data were processed using UV probe (version 2.6) software. The experiment was carried out at B.K. Mody Government Pharmacy College in 2021.

Instrumentation

The proposed work was done on a Shimadzu UV-visible spectrophotometer (model UV-1800 series), which possesses a double beam double detector configuration with a 1cm quartz matched cell. All weighing was done on electronic balance (MAB 220 Wensar).

Selection of Solvents

Based on the solubility study, methanol was selected as the solvent for dissolving teneligliptin hydromide hydrate and rosuvastatin Calcium.

Preparation of standard stock solution

A standard stock solution of 100 µg/ml of rosuvastatin calcium and 100 µg/ml teneligliptin hydrobromide hydrate was prepared in methanol as diluents.

Selection of wavelength

From appropriate dilution of the working standard stock solution, 10µg/ml of Rosuvastatin calcium and teneligliptin hydrobromide hydrate were separately prepared and scanned in the UV range 200-400 nm. The overlain zero-order absorption spectra of both drugs were obtained. These absorption spectra were converted to 1st order derivative spectra by using UV probe software. After observing overlay 1st order derivative spectra with Δλ 16 and scaling factor 1 for Rosuvastatin calcium and teneligliptin hydrobromide hydrate, zero-crossing points of both drugs were selected. The first wavelength selected was 222.66 nm (Zero crossing of Rosuvastatin calcium), where teneligliptin hydrobromide hydrate showed considerable absorbance. The second wavelength selected was 230.03 nm (Zero crossing of teneligliptin hydrobromide hydrate), where Rosuvastatin calcium showed considerable absorbance.

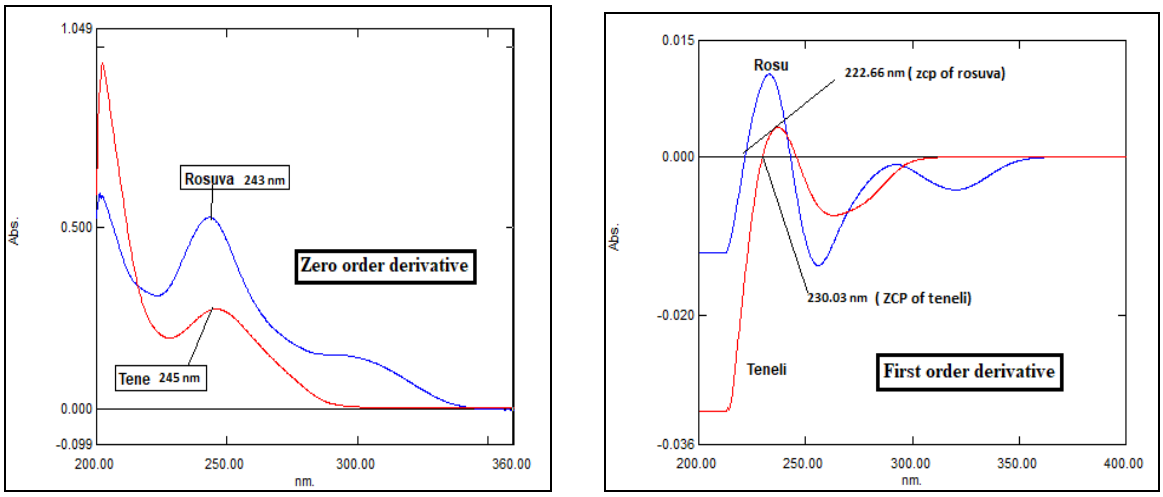


Figure 3,4: Wavelength selection of rosuvastatin calcium and teneligliptin hydrobromide hydrate
Both drugs are highly overlapping so, 1st order derivative method was performed

Method validation

Linearity

The standard stock solution was diluted with methanol properly to obtain the concentration of 1, 6, 12, 18, 24, 30, 36, and 42 µg/ml for both rosuvastatin calcium and teneligliptin hydrobromide hydrate.

Specificity

Specificity was performed under 6 replicates at 15 µg/ml of rosuvastatin calcium and teneligliptin hydrobromide hydrate with and without the addition of excipients to check the interference of excipients.

Accuracy

The accuracy of the method was performed in triplicate at three different concentration levels of 80%,100% and 120% (12, 15, and 18 µg/ml) for both drugs rosuvastatin calcium and teneligliptin hydrobromide hydrate. The accuracy was performed by spiking of the stated concentration in assay concentration. The accuracy of the method was checked by calculating percentage recovery.

Precision

Repeatability was performed under 6 replicates at a concentration of 15µg/ml of Teneligliptin hydrobromide hydrate and rosuvastatin calcium. Intra-day and inter-day variations of Teneligliptin hydrobromide hydrate and rosuvastatin calcium were performed in triplicate at three different concentration levels 80%, 100%, 120% (12, 15, and 18µg/ml). The results are expressed in the form of RSD.

Robustness

The robustness of the method was carried out by introducing a small change in experimental conditions like a wavelength. The changes made in wavelength ± 1 nm (229.30, 230.03, and 231.03 nm) for rosuvastatin calcium and (221.66, 222.66, and 223.66) was for teneligliptin hydrobromide hydrate.

LOD and LOQ

The limit of detection (LOD) and limit of quantification (LOQ) were calculated by the formula. The calibration curve was repeated and five deviations (SD) of the intercepts were calculated.

LOD = 3.3 × Standard deviation / Slope

LOQ = 10 × Standard deviation / Slope

Assay of a synthetic mixture

Synthetic mixture was prepared by equivelant to take 20mg for both ROSU and TENELI with common tablet excipent in adequate amount. This synthetic mixture was diluted with methanol to make concentration 15 µg/mL for both drugs.

Result and Discussion

Linearity

Linear responses were obtained in the concentration range of 1-42 µg/ml for both drugs. The data for linearity is shown in Tables 1 and 2. The calibration curve for rosuvastatin calcium and teneligliptin hydrobromide hydrate at 230.03 and 222.66 nm is given in Figure 5 and 6.

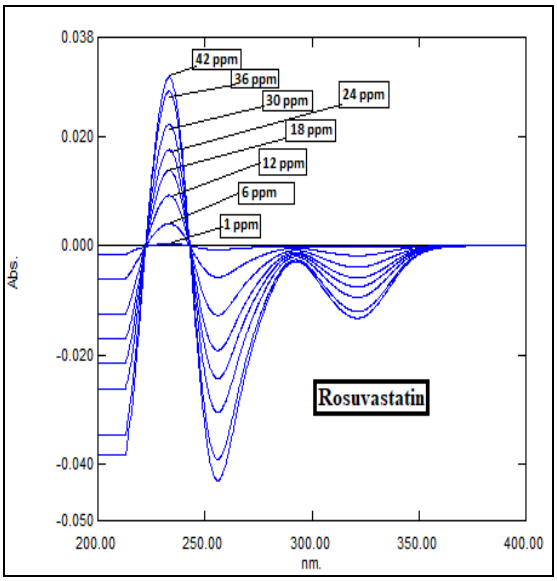


Figure 5: Calibration curve of ROSUVA

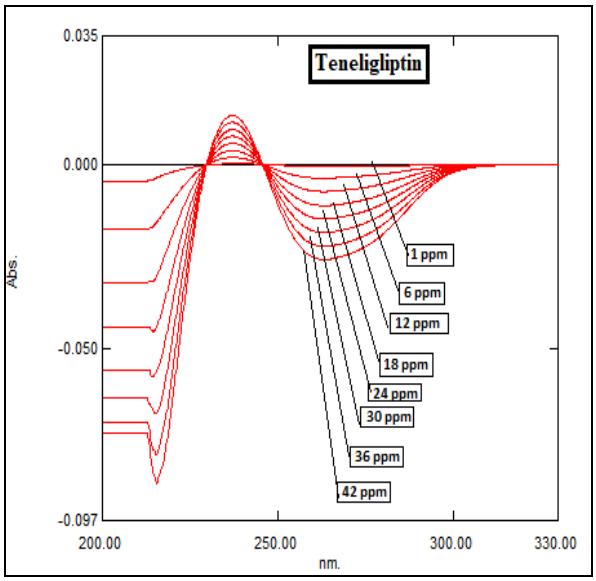


Figure 6: Calibration curve of TENELI

Table 1: Linearity of ROSUVA

LINEARITY OF ROSUVA (230.03nm)	
CONC.(µg/ml)	dA/dλ
1	0.001
6	0.005
12	0.009
18	0.014
24	0.018
30	0.023
36	0.027
42	0.032

Table 2: Linearity of TENELI

LINEARITY OF TENELI (222.66nm)	
CONC.(µg/ml)	dA/dλ
1	0.001
6	0.005
12	0.01
18	0.015
24	0.02
30	0.025
36	0.03
42	0.034

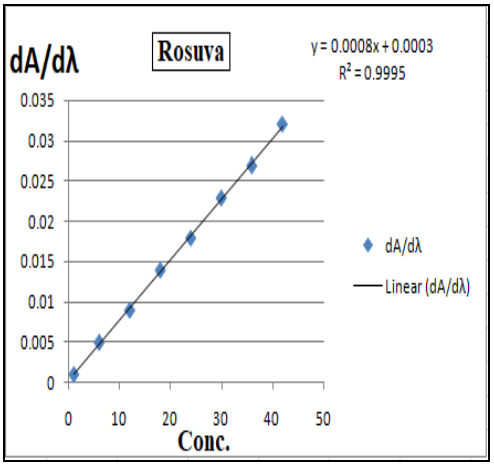


Figure 7: Calibration curve of rosuvastatin

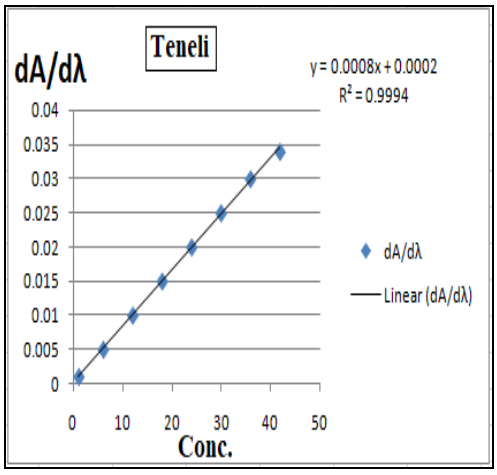


Figure 8: Calibration curve of teneligliptin

Specificity

Excipient interference is not observed at the working wavelength of 230.03nm for Rosuvastatin calcium and 222.66 for teneligliptin hydrobromide hydrate. The UV spectroscopic method presented in this study is specific for rosuvastatin calcium and teneligliptin hydrobromide hydrate.

Table 3: Specificity data of ROSUVA and TENELI

Drug.	Conc (µg/ ml)	Without Exepient		With excipient		Mean Diff.	Mean %Interference
		Mean Abs. (Before)	Mean Conc.	Mean Abs. (After)	Mean Conc.		
Rosuva	15	0.0119	14.5	0.0118	14.45	0.005	0.0333
Teneli	15	0.0124	14.56	0.0120	14.52	0.002	0.0266

Accuracy

When used for evaluation of recovery at three concentration levels, 80%, 100%, and 120% after spiking with standard, the proposed method showed % recovery between 98% – 102% for both drugs.

Table 4: Recovery study of ROSUVA and TENELI

Target Conc.	Level (N=3)	Amt Added	Total Amt	Mean absorbance	Mean concentration	Mean %Recovery
ROSUVASTATIN CALCIUM						
15	80%	12	27	0.02166	26.70	98.91%
15	100%	15	30	0.023	30.041	100.13%
15	120%	18	33	0.027	33.375	101.13%
TENELIGLIPTIN HYDROBROMIDE HYDRATE						
15	80%	12	27	0.02166	26.83	99.38%
15	100%	15	30	0.024	29.75	99.16%
15	120%	18	33	0.0266	33.083	100.25%

Precision

Repeatability and intermediate precision expressed in terms of RSD revealed that the proposed method provided an acceptable intraday and interday variation.

Table 5: Intraday and interday precision of ROSUVA and TENELI

Precision		Intraday precision		Interday precision	
Wavelength	(%)	Mean abs ± SD	RSD	Mean abs ± SD	RSD
At 230.03nm (Rosuva)	80	0.008556±0.0001624	1.898	0.009167±0.000167	1.818
	100	0.011111±0.0001924	1.732	0.011444±0.000192	1.681
	120	0.014444±0.0001924	1.332	0.014778±0.000143	0.796
At 222.66nm (Teneli)	80	0.009778±0.0001924	1.968	0.010222±0.000192	1.888
	100	0.013444±0.0001924	1.431	0.013222±0.000183	0.187
	120	0.01555±.0001924	1.23	0.015444±0.000143	0.926

Table 6: Repetability of ROSUVA and TENELI

Sr no.	Rosuvastatin calcium		Teneligliptin hydrobromide hydrate	
	Concentration	Absorbance	Concentration	Absorbance
1	15	0.011	15	0.013
2	15	0.011	15	0.014
3	15	0.011	15	0.013
4	15	0.012	15	0.013
5	15	0.011	15	0.013
6	15	0.011	15	0.013
MEAN	0.01126667		0.01316667	
SD	0.00020825		0.00020825	
%RSD	1.8483		1.58164	

LOD and LOQ

LOD and LOQ of rosuvastatin calcium and teneligliptin hydrobromide hydrate were determined by equation according to ICH guideline. LOD of ROSUVA and TENELI was found to be 0.2131 and 0.1204 respectively. And LOQ was found to be 0.646 and 0.3648 for ROSUVA and TENELI, respectively.

Robustness study

Deliberate change in different parameter wavelengths showed a relative standard deviation of absorbance less than 2%, indicating that the method was robust.

Table 7: Robustness study of ROSUVA and TENELI

Drugs	Wavelength	Mean abs ± SD	RSD
Rosuvastatin calcium	229.03	0.00933±0.000177	1.896
	230.03	0.01133±0.000177	1.561
	231.03	0.01333±0.000177	1.327
Teneligliptin hydrobromide hydrate	221.66	0.01766±0.000237	1.341
	222.66	0.01266±0.000237	1.871
	223.66	0.00896±0.000237	1.943

Assay of synthetic mixture:

% Drug content of synthetic mixture of rosuvastatin and teneligliptin was found between 95.55-100.2778%.

Table 8: Assay of ROSUVA and TENELI mixture

Conc. (Rosu:Teneli) (µg/ml)	Abs.(N=5) Mean abs ± SD		Conc. Found Mean±SD		% Drug content	
	ROSU	TENELI	ROSU	TENELI	ROSU	TENELI
15:15	0.012333± 0.000577	0.011667± 0.000577	15.04166± 0.721687	14.33333± 0.721687	100.2778	95.5555

Conclusion

The proposed method is rapid, sensitive, precise and accurate for the determination of rosuvastatin calcium and teneligliptin hydrobromide hydrate in a synthetic mixture. This method was validated as per ICH Q2(R1) guideline. This method is free from the interference of the other active ingredients and other additives used in the synthetic mixture. This method can be recommended for routine and quality control analysis of rosuvastatin calcium and teneligliptin hydrobromide hydrate in a synthetic mixture. All the validation parameters complied with its acceptable limit given in the guideline.

Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

We have no conflicts of interest to disclose.

References

[1]. Pharmacopoeia I., *Government of India. Ghaziabad: Ministry of Health and Family Welfare, Published by The Indian Pharmacopoeia Commission*, Delhi: Controller of Publications, 1996, **2**:448 [Google scholar]

[2]. Lemke T.L. Williams D.A., *Foye's principles of medicinal chemistry*; Walters Kulwer Pvt Ltd: New Delhi, 2013 [Google scholar], [Publisher]

[3]. Drug profile and information of teniligliptin hydrobromide hydrate, November 2020, https://pubchem.ncbi.nlm.nih.gov/compound/Teneligliptin-hydrobromide-hydrate

[4]. Patil M., Jani H., Khoja S., Pirani N., Khoja S., *pharmaTutor.*, 2017, **5**:24 [Google scholar], [Publisher]

[5]. Ronald M.K., Siri P.W. *Med. Clin. North A.,* 2004, **88**:897 [Crossref], [Google scholar], [Publisher]

[6]. Pandya C.B., Channabasavaraj K.P., Chudasama J.D., Mani T.T., *Int. J. Pharm. sci. Rev. Res.,* 2010, **5**:82 [Google scholar]

[7]. Gadilohar N. R, Girase A. M, Suryawanshi H. P, Pawar S. P., *Asian. J. of Pharm. Res.*, 2018, **8**:170 [Crossref], [Google scholar], [Publisher]

[8]. Bansode AS., Devhadrao NV., Shinde VC., Gaikwad DD. *World J. Pharm. Sc*i., 2017, **5**:37 [PDF], [Google scholar], [Publisher]

[9]. Lokhande P.*Int. j. Trend sci. Res.,* 2019, **3**:259 [Crossref], [Google scholar], [Publisher]

[10]. Chitlange S.S., Rawat D.P.,Gandhi S.P., *Anal. Chem. Lett.*, 2017, **4**:556 [Crossref], [Google scholar], [Publisher]

[11]. Raj H.A., Rajput S.J., Dave J.B., Patel C.N., *Int. J. ChemTech Res.*, 2009, **1**:677 [Crossref], [Google scholar], [Publisher]

[12]. Shah Y., Iqbal Z., Ahmad L., Khan A., Khan, M.I., Nazir S., Nasir F., *J. Chromatogr. B,* 2011, **879**:557 [Crossref], [Google scholar], [Publisher]

[13]. Park J.W., Kim K.H., Park J.Y., *J. Biomed. Chromatogr.*, 2019, **34**:e4721 [Crossref], [Google scholar], [Publisher]

[14]. Singh H., Gupta RD., Singh GG., Gautam G. *Asian J Pharm pharmacol.*, 2018, **4**:45 [Crossref], [Google scholar], [Publisher]

[15]. Gupta A., Mishra P.,Shah K.*J.E. J. Chem.*, 2009, **6**:89 [Google scholar], [Publisher]

[16]. Poulami P., Gosh S., Roy T., Kumar R.B.V.V., *J. Drug Deliv. Ther.*, 2019, **9**:95 [Crossref], [Google scholar], [Publisher]

[17]. Jain P.S., Patil P.S., Sonawane S.J., Surana S.J., *Acta Sci. Pharma. Sci.*, 2019, **3**:43 [PDF], [Publisher]

[18]. Kshirsagar S.A. Mane S.B., Hanchate Y.S., Katte A.S., *Int. j. Pharm. Res. Scholars.*, 2018, **7:**1 [PDF], [Publisher]

[19]. *ICH Q2(R1) Validation of analytical procedures*: Geneva, 2005 [PDF], [Google scholar], [Publisher]

HOW TO CITE THIS ARTICLE

Amitkumar Vyas, Jayshree Godhaniya, Ashok Patel1, Ajay Patel, Nilesh Patel, Sunny Shah, Devang Sheth. Development and Validation of UV-Spectroscopic First Order Derivative Method for Simultaneous Estimation of Rosuvastatin Calcium and Teneligliptin Hydrobromide Hydrate in Synthetic Mixture., Chem. Methodol., 2021, 5(4) 317-323
DOI: 10.22034/chemm.2021.131260
URL: http://www.chemmethod.com/article_131260.html