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Development and Validation of Spectrophotometric Method For Simultaneous Estimation of Rosuvastatin Calcium and Aspirin In Bulk and Pharmaceutical Dosage Form

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ABSTRACT

Rosuvastatin calcium and Aspirin combination is used in the treatment of Cardio vascular diseases. Rosuvastatin calcium is HMG Co-A reductase inhibitor and Aspirin is Antiplatelet agent. Literature survey revealed one UV Spectrophotometric method for simultaneous estimation of Rosuvastatin calcium and Aspirin in combined dosage form. Therefore simple, sensitive, rapid and precise spectrophotometric method has been developed and validated for simultaneous estimation of Rosuvastatin calcium and Aspirin from bulk and its pharmaceutical dosage form. These drugs were estimated in formulation by Q-absorption method in which wavelengths selected were 257nm as iso-absorptive point and 244nm as λ_{max} of Rosuvastatin calcium. Linearity was observed in the concentration range of 10-50 µg/ml and 40-120 µg/ml for Rosuvastatin calcium and Aspirin respectively. Percentage purity and accuracy were in the limit of 98-102% and precision was less than 2 for both drugs. Limit of Detection for Rosuvastatin calcium & Aspirin was found to be 1.6730µg/ml & 7.4278µg/ml respectively. Limit of Quantitation for Rosuvastatin calcium & Aspirin was found to be 5.0696µg/ml & 22.5083µg/ml respectively. Validation study revealed that the method is simple, rapid, specific, accurate, precise, reproducible, robust and economic and can be used for routine quantitative analysis of Rosuvastatin calcium and Aspirin in pure and combined pharmaceutical dosage form.

KEY WORDS; Rosuvastatin calcium, Aspirin, Q-absorption method, Methanol.

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INTRODUCTION

Rosuvastatin calcium, (E)-(3R,5S)-7-[4-(4-fluorophenyl)-6-isopropyl-2{methyl(methylsulphonyl amino)}pyrimidin-5-yl]-3,5-dihydroxyhepten-6-oic acid calcium, is a HMG Co-A Reductase inhibitor which is used in Hyperlipidemia[1,2]. Literature survey revealed that various UV, HPLC and HPTLC methods reported for the estimation of Rosuvastatin calcium in pharmaceutical formulations[2-10]. Aspirin, 2-acetobenzoic acid, is a Non-steroidal anti-inflammatory, Antirheumatic, Antithrombotic which is used in pain; fever; inflammatory conditions; reduction of MI[1,2]. Literature survey revealed that there are titration, difference and HPLC methods are available for estimation of Aspirin in pharmaceutical dosage form[2,11-18]. Extensive literature survey reveals, only one UV method is available for simultaneous estimation of Rosuvastatin calcium and Aspirin in their combined dosage form[23]. Aim of present work was to develop simple, precise, accurate and economical spectrophotometric methods for simultaneous determination of Rosuvastatin calcium and Aspirin in their combined dosage form. The proposed method was optimized and validated in accordance with International Conference on Harmonization (ICH) guidelines.

MATERIALS AND METHOD

MATERIALS USED

Rosuvastatin Calcium (gift sample from Zydus Cadila Pharmaceuticals Ltd., Ankleshwar)

Aspirin (gift sample from West-Coast Pharmaceutical Works LTD, Ahmedabad)

Formulation of Rosuvastatin Calcium and Aspirin (UNISTAR, Unichem Laboratories Ltd, Mumbai: 10mg of Rosuvastatin calcium + 75mg of Aspirin)

REAGENT USED

Methanol: AR grade (Finar Chemicals Pvt. Ltd, Ahmedabad, India)

APPARATUS AND INSTRUMENTS USED

Double beam UV-visible Spectrophotometer: ELICO SL218 (ELICO Ltd., Hyderabad, India)

Weighing balance: Shimadzu AX 200 (Shimadzu Corporation, Kyoto, Japan)

Sonicator: Ultrasonic Cleaner FS_4 (Frontline Electronics & Machinary Pvt. Ltd., Ahmedabad)

PREPARATION OF PURE STOCK SOLUTION OF ROSUVASTATIN CALCIUM (100µg/ml)

100 mg of drug was accurately weighed and transferred to a 100 ml volumetric flask, dissolved in methanol to obtain first stock solution and from resulting stock solution 10 ml of sample transferred

to a 100 ml volumetric flask and make up to 100 ml with methanol to get concentration 100µg/ml as a second stock solution.

PREPARATION OF PURE STOCK SOLUTION OF ASPIRIN (1000µg/ml)

100 mg of drug was accurately weighed and transferred to a 100 ml volumetric flask, dissolved in methanol to get concentration 1000µg/ml as a stock solution.

STUDY OF OVERLAIN SPECTRA AND SELECTION OF WAVELENGTH

The stock solution of Rosuvastatin calcium diluted with methanol to obtain 10-50µg/ml of Rosuvastatin calcium. The stock solution of Aspirin diluted with methanol to obtain 40-120µg/ml of Aspirin. Calibration curve were plotted of both that is Rosuvastatin calcium and Aspirin.

In quantitative assay of two components by Q-absorption method, absorbances were measured at the iso-absorptive wavelength and maximum absorption of one of the two components. From overlain spectra of Rosuvastatin calcium and Aspirin, absorbances were measured at the selected wavelengths i.e. 257nm (iso-absorptive wavelength) and 244nm (wavelength of maximum absorption of Rosuvastatin calcium).

PREPARATION OF SAMPLE SOLUTION

Weigh the content of capsule equivalent to 10 mg of ROS and 75 mg of ASP and transfer in to a 100-ml volumetric flask. Add 50 ml of methanol and sonicate it for 30 min. and filter it through whatman filter paper no.41. Transfer 10.0ml of filtrate into 100ml volumetric flask and add methanol up to mark to get final concentration of ROS 10µg/ml and ASP 75µg/ml. The absorbance of solutions were measured at 257nm and 244nm using methanol as blank. From the following sets of equations, the concentration of each component in sample can be calculated.

Concentration of Aspirin (C_X) = ($Q_M - Q_Y / Q_X - Q_Y$) × A_2 / ax_2

Concentration of Rosuvastatin Calcium (C_Y) = $A_2 / ax_2 - C_X$

Where,

A_1 and A_2 = Absorbance of sample solution at 257nm and 244nm

$Q_M = A_2 / A_1$

$Q_X = ax_2 / ax_1$

$Q_Y = ay_2 / ay_1$

VALIDATION OF THE METHOD[24]

The developed method was validated in terms of parameters like accuracy, precision, linearity, LOD and LOQ.

ACCURACY

In order to ensure the suitability and reliability of proposed method, recovery studies were carried out. To an equivalent quantity of formulation powder, a known quantity of standard Rosuvastatin calcium and Aspirin added at 80%, 100% and 120% level and the contents were re-analysed by the proposed method. The %recovery and %RSD were calculated.

PRECISION

Precision of the method was confirmed by interday and intraday analysis i.e. the analysis of formulation was repeated three times in the same day and on three successive days. The amount of drugs was determined and %RSD also calculated.

LINEARITY

For both drugs, appropriate dilutions of standard stock solutions were analysed as per the developed method. Calibration curve was plotted in the concentration range of 10-50 µg/ml for Rosuvastatin calcium and 40-120 µg/ml for Aspirin.

LIMIT OF DETECTION (LOD) AND LIMIT OF QUANTITATION (LOQ)

The LOD and LOQ of Rosuvastatin calcium and Aspirin by proposed method were determined using calibration standards. LOD and LOQ were calculated as 3.3 σ/S and 10 σ/S respectively, where S is the slope of the calibration curve and σ is the standard deviation of response.

RESULTS AND DISCUSSION

The proposed method was based on spectrophotometric absorption for the simultaneous estimation of Rosuvastatin calcium and Aspirin in UV region using methanol as solvent for Q-absorption method. Wavelengths 257nm and 244nm were selected as isoabsorptive point and λ_{max} of Rosuvastatin calcium respectively. Two drugs individually followed Beer-Lambert's law over the concentration range of 10-50 µg/ml and 40-120 µg/ml for Rosuvastatin calcium and Aspirin respectively. Coefficient of correlation for Rosuvastatin calcium at 244nm was found to be 0.997, for Aspirin coefficient of correlation at 257nm was found to be 0.998. The value of correlation coefficient suggests the level of precision of the method.

Drug content in formulation was directly found from the above mentioned equation. Standard deviations, %RSD was calculated and given in table 3. Percentage estimation in formulation was 99.034 and 99.392 (%RSD < 2) for Rosuvastatin calcium and Aspirin respectively.

The method was validated according the ICH guidelines for validation of analytical procedures. The value of slope, intercept and correlation coefficient value are given in table 1. Limit of Detection (LOD) and Limit of Quantitation (LOQ) were determined by using the formula and are mentioned in table 2.

To study the validation parameters accuracy, reliability and interference, recovery experiment was carried out by standard addition. The recovery of added standard was calculated at different concentration levels. From the total amount of drug found, the percentage recovery was calculated which was between 99-102%w/w (%RSD < 1).

Table 1: Data of optical characteristics for Rosuvastatin calcium and Aspirin

Parameters		Observed Value			
		Rosuvastatin calcium		Aspirin	
Wavelength		244nm	257nm	244nm	257nm
Beer's Law Limit (µg/ml)		10-50 µg/ml		40-120 µg/ml	
Molar absorptivity (lit./mole/cm)		1.6939×10^4	1.091×10^4	0.1657×10^4	0.6991×10^4
Sandell's sensitivity (µg cm^{-2}/0.001 absorbance unit)		0.05910	0.0917	0.1086	0.02577
Correlation coefficient (r^2)		0.997	0.9966	0.9994	0.998
Regression Equation (y=mx + c)	Slope	0.0176	0.0117	0.0088	0.0034
	Intercept	-0.0169	-0.0203	0.0333	0.0351

Table 2: Data of validation parameters for Rosuvastatin calcium and Aspirin

Parameters	Observed Value	
	Rosuvastatin calcium	Aspirin
Accuracy (%Recovery)	99.53834	99.78707
Intraday precision (%RSD)	0.46121	0.07769
Interday precision (%RSD)	0.49064	0.08119
Linearity (r^2)	0.9992	0.9973
Ruggedness (%RSD)	0.7111	0.10373
LOD (µg/ml)	1.6729	7.4277
LOQ (µg/ml)	5.0696	22.5083

Table 3: Data from the analysis of capsule formulation (n=3)

Tablet Components	Labeled Claim (mg/tab)	Amount Found (mg/tab)	% Purity	SD	%RSD
Rosuvastatin Calcium	10.0	9.903	99.034	0.2062	0.2082
Aspirin	75.0	74.544	99.392	0.0475	0.0478

Table 4: Data from recovery study of Rosuvastatin calcium and Aspirin (n=3)

Levels (%)	Mean %Recovery±SD	
	Rosuvastatin calcium	Aspirin
80	98.68±0.9762	99.86±0.1346
100	99.15±0.4947	98.67±0.1065
120	98.90±0.1025	98.88±0.1155

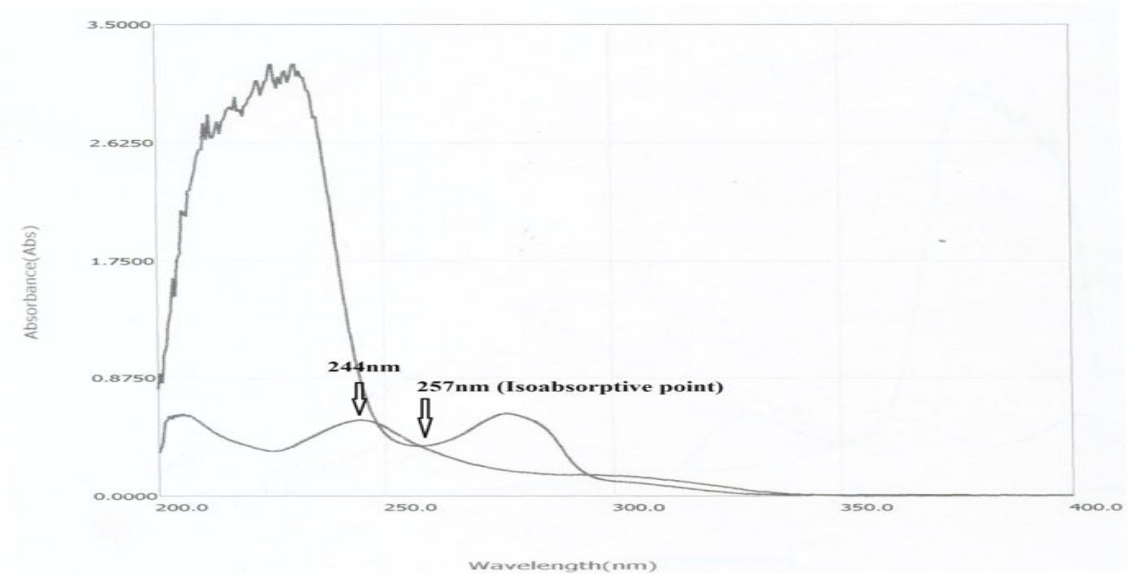

Fig. 1: Overlain Spectra of Rosuvastatin calcium and Aspirin

CONCLUSION

The proposed method is simple, precise, and accurate for the rapid for simultaneous determination of PARA and LOX in combined tablet dosage forms and this method may be successfully applied in control laboratories for their determination in combined dosage form.

REFERENCES

1. Tripathi KD. Essential of medical pharmacology. 6th edition. Jaypee brothers: Medical publishers pvt. Ltd.; 2008. 608-609, 614-615.
2. Indian Pharmacopoeia 2010, Indian Pharmacopoeia commission, Ghaziabad, Published by Government of India, Rosuvastatin calcium, III. 2072-2073. Aspirin, II. 842-843.
3. Rajkondwar VV, Maini P, Vishwakarma M. Characterization and Method Development for Estimation and Validation of Rosuvastatin Calcium by UV–Visible Spectrophotometry. Int J Theo App Sci 2009; 1(1): 48-53.
4. Gupta A, Mishra P, Shah K. Simple UV Spectrophotometric Determination of Rosuvastatin Calcium in Pure Form and in Pharmaceutical Formulations. E-J Chem 2009; 6(1): 89-92.

5. Donthula S, Meriga K, Teja SG, Mohan KY, Yasodha KJ, Ramesh D. A New Validated RP-HPLC Method for Determination of Rosuvastatin calcium in Bulk and Pharmaceutical dosage form. Schol Res Lib 2011; 3(3): 350-356.
6. Kaila HO , Ambasana MA , Thakkar RS , Saravaia HT , Shah AK. A New improved RP-HPLC Method for Assay of Rosuvastatin calcium in Tablets. Indian J Pharm Sci 2010; 72(5): 592-598.
7. Pandya CB, Channabasavaraj KP, Chudasama JD, Mani TT. Development and Validation of RP-HPLC Method for Determination of Rosuvastatin calcium in Bulk and Pharmaceutical dosage form. Int J Pharm Sci Rev Res 2010; 5(1): 82-86.
8. Devi US, PushpaLatha E, Guptha NCV, Ramalingam MRP. Development and Validation of HPTLC Method for Estimation of Rosuvastatin Calcium in Bulk and Pharmaceutical Dosage Forms. Int J Pharm Bio Sci 2011; 2(2): 134-140.
9. Chaudhari BG, Patel NM, Shah PB. Determination of Simvastatin, Pravastatin sodium and Rosuvastatin calcium in Tablet dosage forms by HPTLC. Indian J Pharm Sci 2007; 69(1): 130-132.
10. Sane RT, Kamat SS, Menon SN, Inamdar SR, Mote MR. Determination of Rosuvastatin calcium in its Bulk drug and Pharmaceutical preparations by High-Performance Thin-Layer Chromatography. J Planar Chrom- Modern TLC 2007; 18, Number-103: 194-198.
11. United States Pharmacopoeia, Asian edition, The US Pharmacopoeial Convention, Rockville; 2008, Aspirin, II. 1447-1448.
12. British Pharmacopoeia, London- The Stationary Office; 2010. Aspirin, I. 182-183.
13. Maheswari RK, Chandrawanshi HK, Gupta N. Quantitative Estimation of Aspirin in Tablets and Bulk sample using Metformine hydrochloride as Hydrotropic agent. Int J Pharm Pharm Sci 2010; 2(1): 20-23.
14. Maheshwari RK, Saxena M, Gahlot M, Chaki M, Kinariwalw M, Jagwani Y. Novel Application of Hydrotropic Solubilising Additives in the Estimation of Aspirin in Tablets. Indian J Pharm Sci 2010; 72(5): 649-651.
15. Bhattacharyya I, Bhattacharyya SP, Talukdar S, Medya S. Development of Difference Spectroscopic Method for the Estimation of Aspirin in Formulation using Hydrotropy. Int J Res Pharm Sci 2011; 2(1): 84-87.
16. Sureshkumar S, Jamadar LD, Bhat K, Musmade PB, Vasantharaju SG, Udupa N. Analytical Method Development and Validation for Aspirin. Int J ChemTech Res 2010; 2(1): 389-399.
17. Gujar pp, Kulkarni AA, Shaha AP, Gandhi SM, Mohite SK, Magdum CS. Development and Validation of Method for Simultaneous Estimation of Rosuvastatin calcium and Aspirin in

Combined Capsule dosage form by UV Spectrophotometry. Inventi Rapid: Pharm Ana Qual Assur 2011.

18. ICH, Guideline on Analytical method validation, in proceeding of International Convention on Quality for the Pharmaceutical Industry, 2002.