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Research Paper

ANALYTICAL METHOD VALIDATION FOR ESTIMATION OF TELMISARTAN AND ROSUVASTATIN CALCIUM IN THE COMBINATION

Krishan Kumar Yadav*, Sulekha Mandal

Dept. of Pharmaceutical Quality Assurance, Mahatma Gandhi College of Pharmaceutical Sciences, Jaipur - 302022

In this research work, an attempt has been made to develop a validated stability-indicating method for TLS and RST. The peaks of telmisartan and rosuvastatin were eluted at 2.553 min and 4.505 min, respectively, with the resolution of 9.40 between them. During the system suitability and system repeatability testing, the parameters like retention time (min), theoretical plate count, tailing factor, resolution, % RSD, and % RD were checked to ensure reproducibility of the chromatographic system. The specificity of the method was established by verifying blank interference The value of squared correlation coefficient (R2) was found 1.000 for TLS and 0.999 for RST, indicating the method is linear and suitable to use in the studied concentration range. Recovery results show the method is accurate and with no interference from excipients.

The method is repeatable and precise as the % RSD results below 2.0. The SS and SR parameters are used for establishing the robustness of change in chromatographic parameters; the results within the acceptance limits indicate its robustness.

Keywords: Telmisartan, Rosuvastatin calcium, RP-HPLC and Validation

INTRODUCTION

Telmisartan is chemically described as 2-(4- {[4-methyl-6-(1-methyl-1H-1,3-benzodiazol-2-propyl-1H- 1,3benzodiazol-1-yl] methyl}phenyl) benzoic acid. It is used as an angiotensin II receptor antagonist (AT1) in the management of hypertension.1 It selectively antagonizes angiotensin II binding to the AT1 subtype receptors. It is commonly administered through the oral route (Fig. 1B).[1-2]

Rosuvastatin calcium is chemically calcium: (E,3R,5S)-7-[4-(4-fluorophenyl) -2- [methyl (methyl sulfonyl) amino] -6-propan-2-ylpyrimidin-5-yl]-3,5-dihydroxyhept-6-enoate. It belongs to a class of drugs called statins, which are employed in lowering hypercholesterolemia, its related conditions and preventing cardiovascular diseases (Fig. 1A).[3-4]

Pharmacologically Rosuvastatin Calcium is a lipid lowering agent. It is a competitive inhibitor of HMG-Co A reductase. It catalyses the reduction of 3-hydroxyl-3-methylglutaryl coenzymeA to mevalonate, which is a rate limiting step in hepatic cholesterole synthesis. [5]

Mevalonate is a small molecule used in the synthesis of cholesterol and other mevalonate derivatives. In this way, it lowers the amount of cholesterol and LDL- cholesterol. Pharmacologically Telmisartan interferes with the binding of angiotensin II to the angiotensin II AT1-receptor by binding reversibly and selectively to the receptors in vascular smooth muscle and the adrenal gland. As angiotensin II is a vasoconstrictor, which also stimulates the synthesis and release of aldosterone, blockage of its effects results in decreases in systemic vascular resistance. Telmisartan does not inhibit the angiotensin converting enzyme, other hormone receptors, or ion channels. This is a new combination is market and so far no suitable analytical methods have been reported for simultaneous analysis of both the drugs together.[6-7]

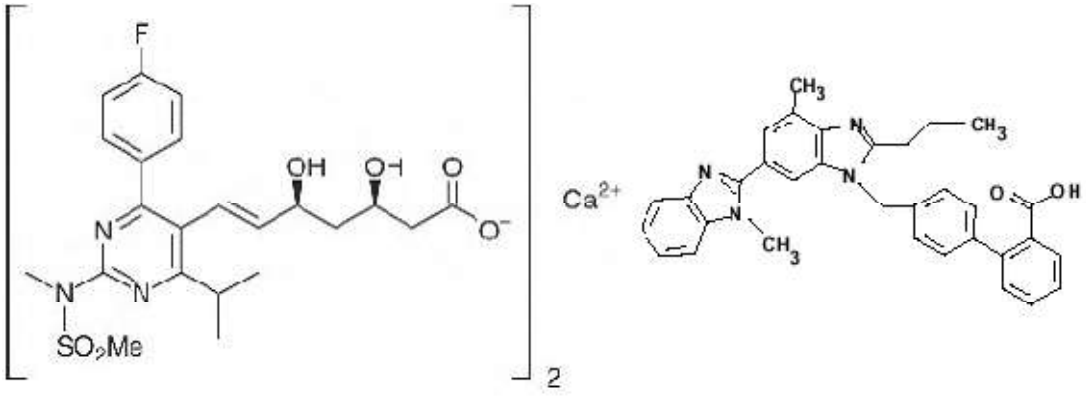

Fig. 1: Chemical Structure of (A) Rosuvastatin Calcium and (B) Telmisartan[8]

Materials Used:

Rosuvastatin – Zydus CadilaHealthCare Ankleshwar

Telmisartan - Hetro Drugs Ltd., India.

Chemicals and Reagents:

Diluent: Methanol (HPLC Grade) E. Merck (India) Ltd.,Mumbai

Milli-Q Water: In-house production of company.

Ortho-Phosphoric Acid: AR grade, Spectrochem. India

Instrument

Analytical weighing balance (CY204) made by Citizon The digital pH meter (LT-49) made by Labtronic Laboratory Photostability chamber (SRLPHSC- 11-A) made by S R Lab Instruments India Pvt. Ltd., The Oyster ODS3 (5 µm, 4.6 × 150 mm) column of Merck & Co. was joined to a Shimadzu HPLC (SCL-10Avp) instrument, and injection volume of 20 µL with UV detector was used for method development.

Chromatographic conditions

Parameters	Results
Type of system	HPLC with UV detector or equivalent
Pump mode	Isocratic
Mobile phase	10 mM phosphate buffer with 1.1 g octane-1-sulfonic acid sodium salt having pH 2.5 (adjusted with 5% OPA) and Acetonitrile (500:500, v/v)
Column	Oyster ODS3 (5 µm, 4.6 × 150 mm) P/N: S670153 (Make: Merck & Co.)
Injection volume	20 µL
Run time	9 min
Flow rate	1.0 mL/min
Detection	242.0 nm
Column temperature	Ambient (about 25 °C)
Blank	Diluent

Standard solution

40.0 mg telmisartan and 10.4 mg of rosuvastatin calcium (equivalent to 10 mg of rosuvastatin) were weighed and transferred into a 200-mL dry volumetric flask; 140 mL diluent was introduced to it and sonicated for 10 min with intermediate shaking to dissolve. Subsequently, the cooled solution was filled up to the mark by diluent and mixed thoroughly which gave the concentration of telmisartan (200 µg/ml) and rosuvastatin (50 µg/mL). The standard solution suitability was established with two different preparations.

Sample solution

Twenty telmisartan and rosuvastatin tablets 40/10 mg (TELLZY®-RS) were weighed and crushed, and 278.2 mg powder (equivalent to 40 mg telmisartan and 10 mg rosuvastatin) was transferred into a 200-mL dry volumetric flask; 140 mL diluent was introduced to it and sonicated for 20 min with intermediate shaking to completely dissolve the content. Subsequently, the cooled solution was filled up to the mark by diluent and mixed thoroughly. Finally, it was filtered using Whatman filter paper by discarding the initial 5 mL filtrate, and then, the sample was analyzed with HPLC.

Method validation

The proposed method was validated as per the ICH guideline Q2(R1).

RESULTS AND DISCUSSION:

Specificity

The interference from blank absent at telmisartan and rosuvastatin peak shows the method is specific (Fig. 2A & 2B). The peaks due to degraded product generated during stress study did not interfere with TLS and RST peak. The mass balance data established for acid and photolytic-stressed RST show a decrease in response with the generation of major degradant at 8.955 min and 6.280 min, respectively. The mass balance data established for TLS and RST in the drug product sample show that the response of RST decreased in acid, thermal, and photolytic stressed conditions with the generation of major degradant at 8.687, 1.811, and 6.134 min, respectively.

The mass balance data show that TLS is stable in all stressed conditions as no degradant is generated for it. As a product containing two active components TLS and RST, it is not possible to apply the more harsh stress condition to achieve the degradation of TLS because they may cause severe degradation as well as generation of secondary degradant of RST.

Linearity

The method was linear in concentration range 99.9073–299.7218 µg/mL for telmisartan (R^2 = 1.000) and 23.6841–71.0522 µg/mL for rosuvastatin (R^2 = 0.999), showing its fitness for analysis.

DL and QL

The DL was 1.1066 µg/ml for TLS and 0.6932 µg/ml for RST, respectively, indicating that even little amounts of TLS and RST can be detected. The QL was 3.3532 µg/mL TLS and 2.1005µg/ml for RST, respectively, indicating that even small amounts of TLS and RST can be quantified.

Accuracy

At each level of 50, 100, and 150%, the average results of % recovery were found to be 100.51, 99.76, and 99.14% for TLS and 99.68, 99.72, and 98.56% for RST, showing the method is accurate and free from excipients interference.

Precision

The developed method is repeatable and precise, as the % RSD value for the assay was below 2.0 for both TLS and RST in method repeatability and intermediate precision.

Robustness

Results of the sample filtered using Nylon SF (0.45 µm) and PVDF SF (0.45 µm) met the acceptance criteria (% RD = ≤ 3.0%) with results Whatman filter paper (as per method). Therefore, in addition to Whatman filter paper, the Nylon SF (0.45 µm) and PVDF SF (0.45 µm) are helpful in sample filtration.

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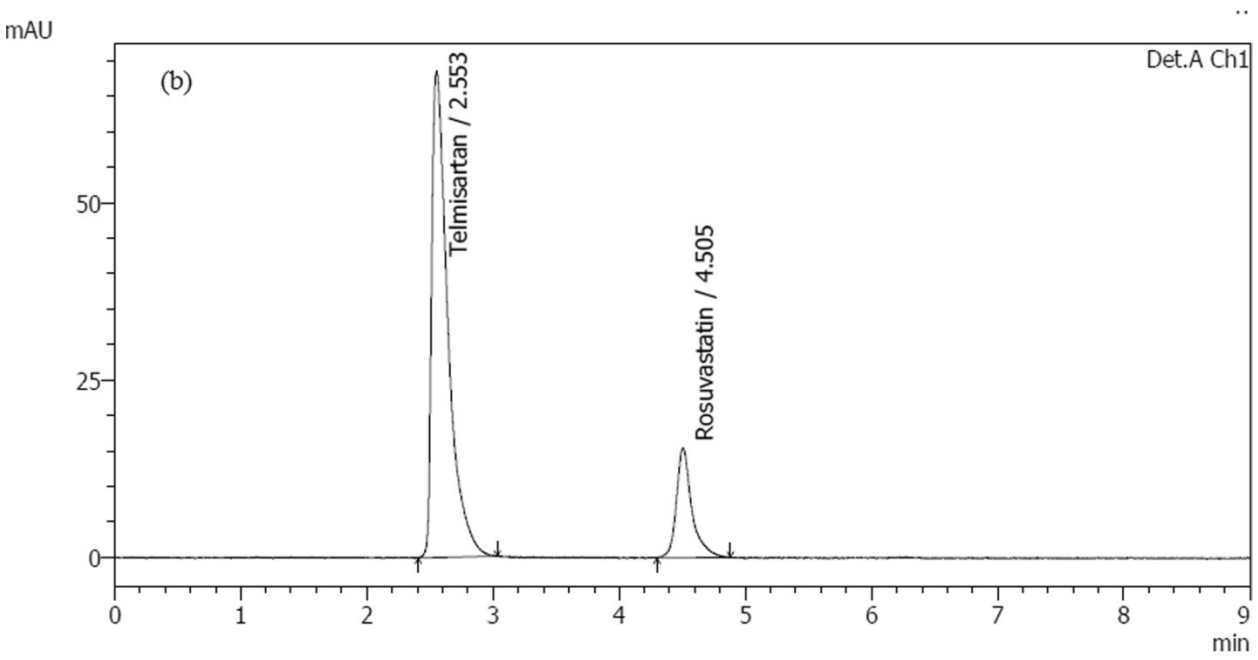

Fig. 2 A: Chromatogram of Standard

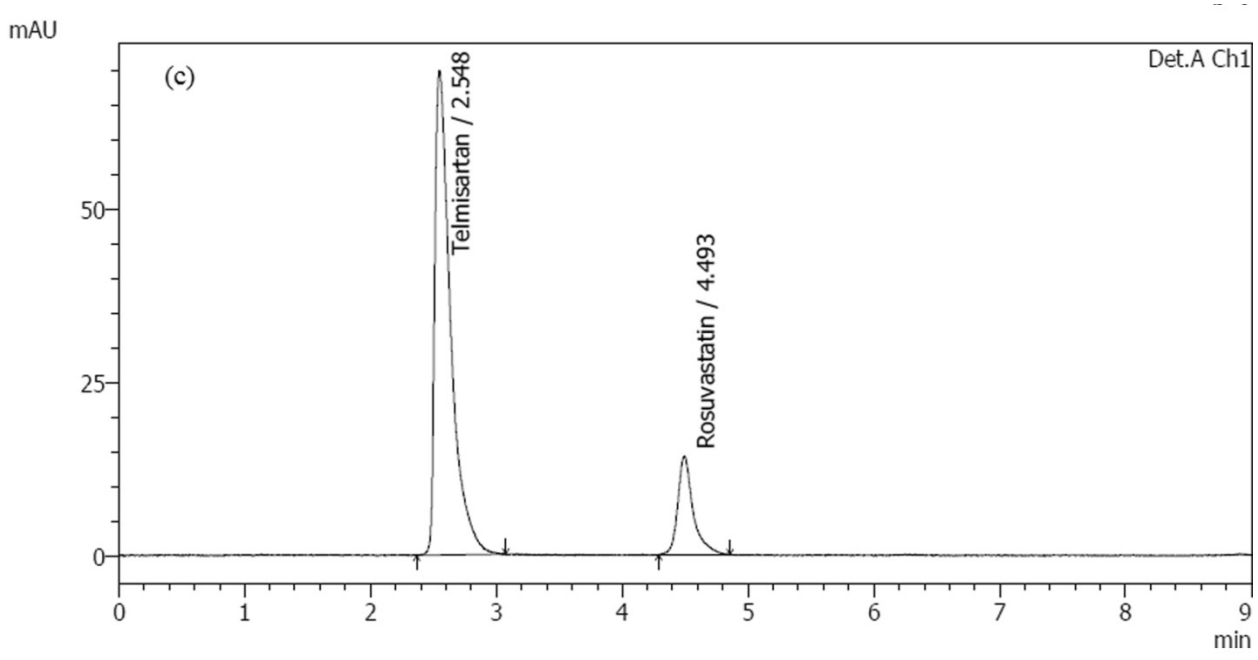

Fig. 2 B: Chromatogram of Sample

CONCLUSION:

The stability-indicating method was validated according to the ICH guidelines for simultaneous estimation of TLS and RST in bulk by RP-HPLC. Results of validation study show the proposed method is simple, specific, precise, accurate, and robust as well as linear in set concentration range.

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