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## **Comparative *in-vitro* dissolution study of Rosuvastatin Calcium and Telmisartan by RP-HPLC**

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### **ABSTRACT**

*The in vitro dissolution rates of 10 and 40 mg Rosatel Tablets (Rosuvastatin Calcium and Telmisartan) as sample from in house production of Company and Sample of Innovator were measured in various Dissolution Medias using the rotating paddle apparatus. The Similarity factor and dissimilarity factor for both drugs was found out and release profile media as well chromatographic conditions were found out. The results were encouraging indicating similar dissolution pattern of Innovator and Sample formulated.*

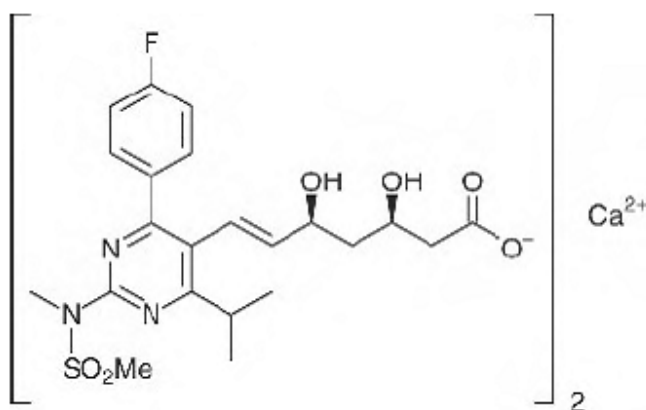
**Key words:** Rosuvastatin Calcium and Telmisartan.

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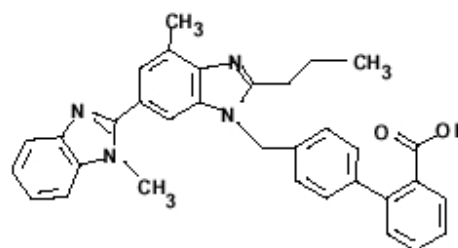
### **INTRODUCTION**

Rosuvastatin is a member of the drug class of statins, used to treat high cholesterol and related conditions, and to prevent cardiovascular disease. Rosuvastatin calcium [1] (Fig 1) and Telmisartan [2] (Fig 2) is a fixed dose combination containing Rosuvastatin 5 mg as Lipid Lowering agent and Telmisartan 10 mg as Anti Hypertensive agent. Chemically Rosuvastatin is bis[(E)-7-[4(4-fluorophenyl)-6-isopropyl-2-methyl (methylsulfonyl) amino] pyrimidin-5-yl](3R, 5S)-3, 5-dihydroxyhept-6-enoic acid] calcium salt. Chemically Telmisartan is 4'-[(1,4'-dimethyl-2'-propyl [2, 6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid. 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 coenzyme A to mevalonate, which is a rate limiting step in hepatic cholesterol synthesis. 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[3] Telmisartan interferes with the binding of angiotensin II to the angiotensin II AT<sub>1</sub>-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 analytical methods have been reported for simultaneous analysis of both the drugs together so following experiment was performed.



**Fig 1 Rosuvastatin Calcium**



**Fig 2 Telmisartan**

### Experimental Work[1-2]

#### Instrument:

#### Dissolution Apparatus (USP-II Paddle):

Model: TDT-06T ELECTROLAB.

RPM: 25, 50, and 75,100,125,150 Resolution: 1 R.P.M.

Accuracy: +/-1 R.P.M.

Temperature: Digital display 37.0 C to 37.20 C

Timer: 1 Min. to 99 Hrs. 59 mm. Micro-com. based. Power: 230 V AC 50 Hz.

Dimensions: 56cm x 65cm x 94cm

#### High Performance Liquid Chromatography

Model: Series 200

Make: Perkin Elmer, USA.

Column: Inertsil ODS 3V

Particle size: 2.27µm

Length: 250mm

Diameter: 4.6mm

**Pump:** Isocratic system. Flow rate 0.01ml/min variable operating back pressure 5000psi.

**Injector:** Rhenodyne valve with 20µl fixed loop.

**Detector:** Diode array detector (UV-visible) with isocratic pump.

Deionised Water plant

Make: Millipore

Model: Elix- 3 system (water output 3L)

Model: Milli Q Academic (water output 1.5L)

Model: Elix-10 system (water output 10L)

Analytical Balance

Model: BP211D

Make: Sartorius Gottingen AG, Germany.

Maximum: 210g

**Sonicator**

Model: TEC-4

Roop Telesonic Ultrasonix

Compact Ultrasonic Cleaner

**PH meter**

Model: Testonix 35 420 A (ORION)

**Materials**

Rosuvastatin Calcium - Dr Reddy's Lab., Hyderabad, India

Telmisartan - Hetro Drugs Ltd., India

Acetonitrile (HPLC Grade - E. Merck (India) Ltd., Mumbai

Water (HPLC Grade)- Milli Q

Lichrosolv<sup>®</sup>- E. Merck (India) Ltd., Mumbai

Orthophosphoric Acid (A.R. Grade)- E. Merck (India) Ltd., Mumbai

**Marketed Preparation**

**Rosatel Tab.** (Rosuvastatin Calcium and Telmisartan Tablets 10mg + 40mg, were procured from Zydus Cadila Ltd.)

**Innovator**

**Ros T Tab.**(Rosuvastatin Calcium Tablets 10mg and Telmisartan 40mg was procured from a renowned Pharma Company.)

**Development of Dissolution Method**[3-4]:

Dissolution of Rosuvastatin Calcium and Telmisartan was tried in various medias like 0.1N HCl, pH 6.8 Phosphate buffer , pH 4.5 Acetate Buffer, Water and release of drug was noticed in all the medias and compared to Innovator sample.

**Dissolution Method Parameters Using 0.1N Hcl as Media** [4-5]:

Dissolution Media: 0.1N HCL, pH= 1.2

Volume: 900ml

Apparatus: USP-II (Paddle)

Rpm: 50

Time Points: 10, 20, 30, 45, 60 minutes

Volume Withdrawn: 10ml Method of Analysis: HPLC.

**Dissolution Method Parameter Using 6.8 Phosphate Buffer as Media:**

Dissolution Media: Phosphate Buffer, pH = 6.8

Volume: 900ml  
Apparatus: USP-II  
rpm: 50  
Time Points: 10, 20, 30, 45, 60 minutes  
Volume Withdrawn: 10ml Method of Analysis: HPLC

**Dissolution Method Parameter Using 4.5 Acetate Buffer as Media[6-8]:**

Dissolution Media: Phosphate Buffer,  $\text{pH} = 6.8$   
Volume: 900ml  
Apparatus: USP-II  
Rpm: 50  
Time Points: 10, 20, 30, 45, 60 minutes  
Volume Withdrawn: 10ml Method of Analysis: HPLC.

**Dissolution Method Parameter Using Water as Media[9-11]:**

Dissolution Media: Phosphate Buffer,  $\text{pH} = 6.8$   
Volume: 900ml  
Apparatus: USP-II  
Rpm: 50  
Time Points: 10, 20, 30, 45, 60 minutes  
Volume Withdrawn: 10ml Method of Analysis: HPLC

**Chromatographic Conditions[12-14]:**

Column : Inertsil ODS 3V C-18 (250 x 5.1 mm), 5  $\mu$   
Detector : 298 nm  
Injection Volume : 10  $\mu$ l  
Flow Rate : 5.5 ml/min  
Temperature : 40°C  
Run Time : 20 minute  
Mobile Phase : Buffer: Methanol (35:65)  
Diluent : Methanol

**Estimation of Rosuvastatin Calcium and Telmisartan by Dissolution method[15-18]:*****Preparation of standard stock solution: Rosuvastatin Calcium standard stock solution: (200 $\mu$ g/ml)***

A 20mg of standard Rosuvastatin Calcium was weighed and transferred to a 100ml volumetric flask and dissolved in 50ml of Diluent. The flask was sonicating for 15min. and volume was made up to the mark with Diluent. From this stock solution working standard solution was prepared by Further 3.0ml was transferred in 50ml volumetric flask and Dissolution Media was added up to the mark to give a solution containing 12 $\mu$ g/ml Rosuvastatin Calcium (Fig.-3)

***Telmisartan standard stock solution: (800 $\mu$ g/ml)***

A 80 mg of standard Telmisartan was weighed and transferred to a 100ml volumetric flask and dissolved in 100ml of Diluent. The flask was sonicating for 15min. and volume was made up to the mark with Diluent. From this stock solution working standard solution was prepared by

Further 3.0ml was transferred in 50ml volumetric flask and Dissolution Media was added up to the mark to give a solution containing 10 $\mu$ g/ml Telmisartan (Fig.-4)

**Preparation of sample solution:**

**Rosuvastatin Calcium & Telmisartan sample solution:**

An intact tablet (containing both Rosuvastatin Calcium and Telmisartan) was dissolved in dissolution media and set dissolution condition as per above. After 10,20,30,45 min. inoculate 10ml by syringe and filter it through 0.45  $\mu$ m HVLP filter. Then transfer into HPLC vials (Fig.-5)

**Comparative Dissolution Study by Using Similarity ( $f_2$ ) and Dissimilarity**

**Factor ( $f_1$ ):**

A simple model independent approach uses a difference factor ( $f_1$ ) and a similarity factor ( $f_2$ ) to compare dissolution profiles (Moore 1996). The difference factor ( $f_1$ ) calculates the percent (%) difference between the two curves at each time point and is a measurement of the relative error between the two curves:

$$f_1 = \{[\sum_{t=1}^n |R_t - T_t|] / [\sum_{t=1}^n R_t]\} * 100$$

$$f_2 = 50 * \log \{ [1 + (1/n) \sum_{t=1}^n (R_t - T_t)^2]^{-0.5} * 100 \}$$

Where  $n$  is the number of time points,  $R$  is the dissolution value of the reference (Pre change) batch at time  $t$  and  $T$  is the dissolution value of the test (post change) batch at time  $t$ . The similarity factor ( $f_2$ ) is a logarithmic reciprocal square root transformation of the sum of squared error and is a measurement of the similarity in the percent (%) dissolution between the two curves.

## RESULTS AND DISCUSSION

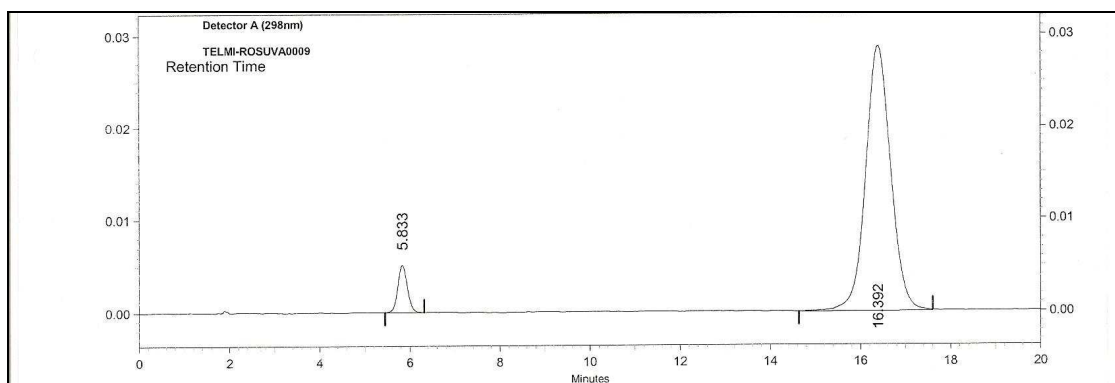
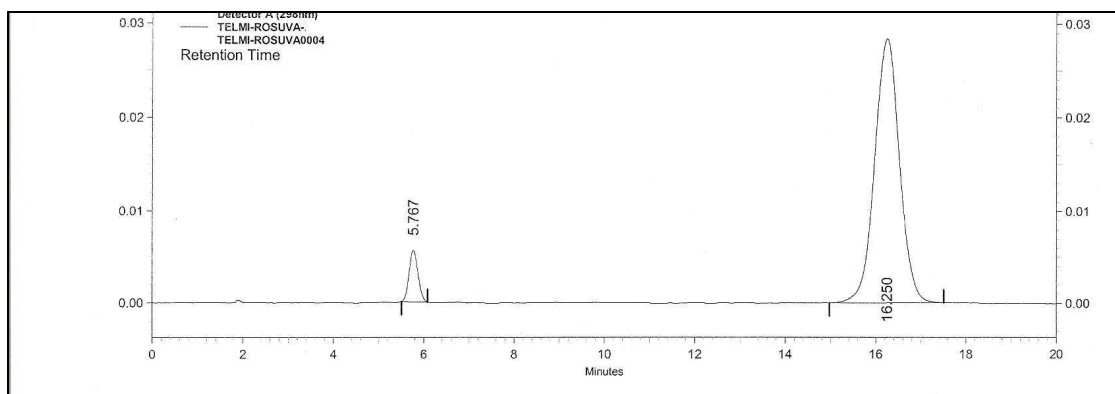


Figure 1: Chromatogram of Rosuvastatin and Telmisartan (Innovator)



**Figure 2: Chromatogram of Rosuvastatin and Telmisartan Sample**

**Table 1: Data Derived From Sample of Rosatel Tab. (Rosuvastatin Calcium-5mg): Dissolution Profile 6 Tablets**

Rosuvastatin Calcium				
Average Release of 6 Tablets				
Time (Min)	Water	0.1N HCL	4.5 Acetate Buffer	6.8 Phosphate Buffer
10	48.63%	15.20%	20.23%	30.50%
20	68.62%	20.30%	40.63%	49.23%
30	70.12%	38.40%	58.10%	64.32%
45	78.65%	46.20%	62.15%	78.22%
60	84.60%	47.65%	70.20%	99.23%

**Table 2: Data Derived From Sample of Rosatel Tab. (Telmisartan 80mg): Dissolution Profile 4 Point, 6 Tablets**

Telmisartan				
Average Release of 6 Tablets				
Time (Min)	Water	0.1N HCL	4.5 Acetate Buffer	6.8 Phosphate Buffer
10	10.22%	26.23%	28.23%	28.23%
20	12.28%	40.30%	30.63%	48.23%
30	14.23%	68.40%	32.10%	65.32%
45	22.23%	86.20%	46.15%	78.22%
60	24.26%	98.65%	56.20%	99.65%

**Table 3: Data Derived From Innovator: Dissolution Profile, 6 Tablets**

Innovator Sample Dissolution Studies		
pH 6.8 Phosphate Buffer		
Time (min)	Rosuvastatin Calcium	Telmisartan
Time (Min)	% Average Release	% Average Release
10	29.86%	29.50%
20	48.23%	48.63%
30	65.32%	66.32%
45	79.22%	78.19%
60	99.63%	100.23%

### Acknowledgement

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**CONCLUSION**

Thus proposed method was found to be simple, accurate, precise selective and economical for simultaneous routine analysis of Rosuvastatin Calcium and Telmisartan in tablet dosage form

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