

---

(Mini Review)

## **A brief review of various analytical methodologies for quantitative analysis of telmisartan and rosuvastatin calcium in different matrices.**

Alaa Ahmed Mostafa <sup>1,\*</sup>, Michael Gamal Fawzy <sup>1</sup>, Abdalla Shalaby <sup>2</sup>, Rania Adel Sayed <sup>2</sup>

<sup>1</sup> *Pharmaceutical Chemistry Department, Faculty of Pharmacy, Egyptian Russian University, Badr City, Cairo 11829, Egypt.*

<sup>2</sup> *Analytical Chemistry Department, Faculty of Pharmacy, Zagazig University, Zagazig 44519, Egypt.*

\*Corresponding author: Alaa Ahmed Mostafa, E-mail: Alaa-azzam@eru.edu.eg, Tel: +201015810943.

*Received 12<sup>th</sup> July 2023, Revised 31<sup>st</sup> December 2023, Accepted 26<sup>th</sup> April 2024*

DOI: 10.21608/erurj.2024.221466.1052

### **ABSTRACT**

Cardiovascular diseases including hypertension and hypercholesterolemia considered to be two of the most chronic, age-related risk factors. Both risk factors controlling process may require a combination of lifestyle modification and pharmaceutical medication either single or combined. Appropriate lifestyle changes may help to control some forms of hypertension as excess body fat is a major contributor to hypertension, along with dietary salt, alcohol, and inactivity. Most cases of hypertension accompanied by hypercholesterolemia require a single or combination of antihypertensive agents e.g. diuretics, angiotensin-converting enzyme inhibitors, calcium channels blockers, and/or angiotensin II receptor blockers with antihyperlipidemic agents e.g. fibrates, or statins. The pharmaceutical product contains telmisartan (TMS) and rosuvastatin calcium (RVS) in one tablet under the trade name of Telrose<sup>®</sup> used for the treatment of cardiovascular including hypertension and hypercholesterolemia. This study examines various analytical approaches, such as UV-visible spectroscopy, spectrofluorimetric, chromatographic, electrochemical, and capillary electrophoresis techniques, for quantifying TMS and RVS in their fixed-dose pharmaceutical formulation and other matrices. The comparative use of various analytical methods for quantifying TMS and RVS is discussed

in this review. Further analytical research for estimating TMS and RVS may be successfully conducted using the information presented in this review paper.

*Keywords: Telmisartan; rosuvastatin calcium; HPLC; spectrophotometry; cardiovascular.*

## 1. Introduction

Chronic, ubiquitous, and age-related, hypertension accompanied by Hypercholesterolemia frequently has crippling cardiovascular and renal effects. Typically, hypertension is reported together with other cardiovascular risk factors (1).

Both economically developed and developing nations contend with hypertension as a major public health issue(2). Nowadays, more people suffer from hypertension and hyperlipidemia, especially in low- and middle-income countries. Estimates show that 31.1% of adults globally have hypertension. In low and middle-income countries adult hypertension was more prevalent than in high-income ones (28.5%)(3).

The cardiovascular condition controlling process may require a combination of lifestyle modification and pharmaceutical medication either single or combined. Appropriate lifestyle changes may help to control some forms of hypertension as excess body fat is a major contributor to hypertension, along with dietary salt, alcohol, and inactivity(4).

Most cases of hypertension accompanied by hyperlipidemia require a single or combination of antihypertensive agents e.g. diuretics, angiotensin-converting enzyme inhibitors (ACEIs), calcium channels blockers (CCBs), and/or angiotensin II receptor blockers (ARBs)(5) with antihyperlipidemic agent e.g. fibrates, or statins.

TMS (Figure, 1A), under the chemical name of 4c-[4-Methyl-6-(1-methyl-1H-benzimidazol-2-yl)-2-propyl-1H-benzimidazol-1-yl] methyl] Biphenyl-2-carboxylic acid. A long-acting nonpeptide antagonist of the angiotensin II type 1 (AT1) receptor that is used to treat essential hypertension. It achieves this specifically and irreversibly prevents the activation of the AT1 receptor by angiotensin II without affecting other receptor systems involved in cardiovascular regulation(6). The medicine may have the therapeutically significant advantage of having good tissue penetration because of telmisartan's unusually high lipophilicity and high volume of distribution(7).

TMS is a white or slightly yellowish, crystalline powder. Sparingly soluble in methylene chloride, slightly soluble in methanol, and practically insoluble in water. It dissolves in 1 M sodium hydroxide with a molecular weight (514.6 g/mol)(8,9).

RVS (Figure, 1B), under the chemical name of Calcium (3R,5S, E)-7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methylmethylsulfonamido) pyrimidine-5-yl)-3,5-dihydroxyhept-6-enoate salt. A synthetic lipid-lowering medication for high cholesterol. It is a competitive inhibitor of 3-hydroxy-3-methylglutaryl reductase that is selective.

A preliminary and speed-limiting stage in the production of cholesterol(10). This inhibition lowers the levels of low-density lipoprotein in the blood through two different mechanisms: first, by lowering mevalonate levels, which decreases the regulatory sterol pool and causes an increase in the hepatic low-density lipoprotein receptors, which are responsible for removing low-density lipoprotein from the blood; and second, by blocking the synthesis of very low-density lipoprotein in the liver(11). RVS white crystals or crystalline powder. Soluble in organic solvents such as DMSO, and dimethyl formamide. slightly soluble in water and aqueous buffers with a molecular weight (1001.1 g/mol) (8,9).

The review aimed to determine the percentage of analytical methods (chromatographic, spectrophotometric, fluorometric, and electrochemical) that were utilized for the defemination of TMS (Figure, 2) and RVS (Figure, 3). Also, the review illustrated the methods utilized for the determination of the binary pharmaceutical dosage form.

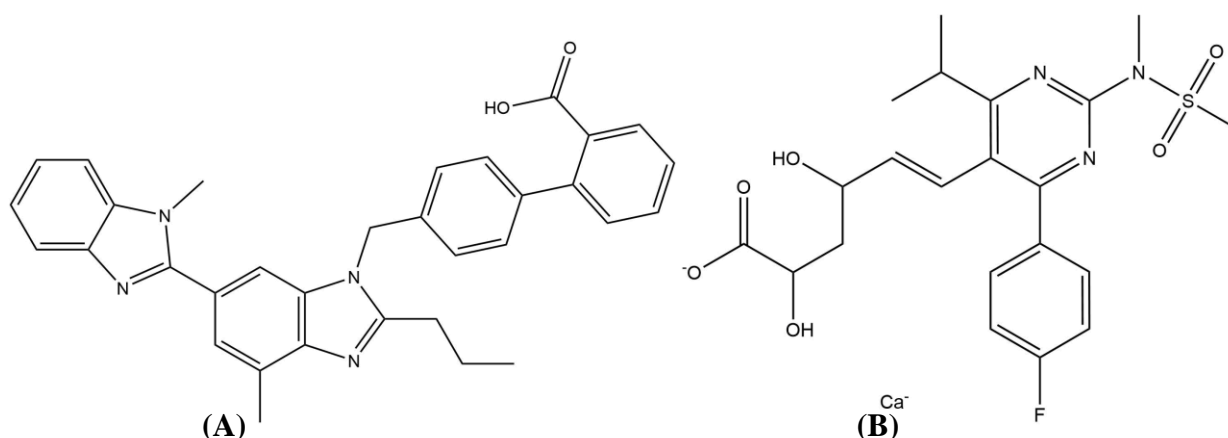


Figure 1: Chemical structures of (A) telmisartan, and (B) rosuvastatin calcium.

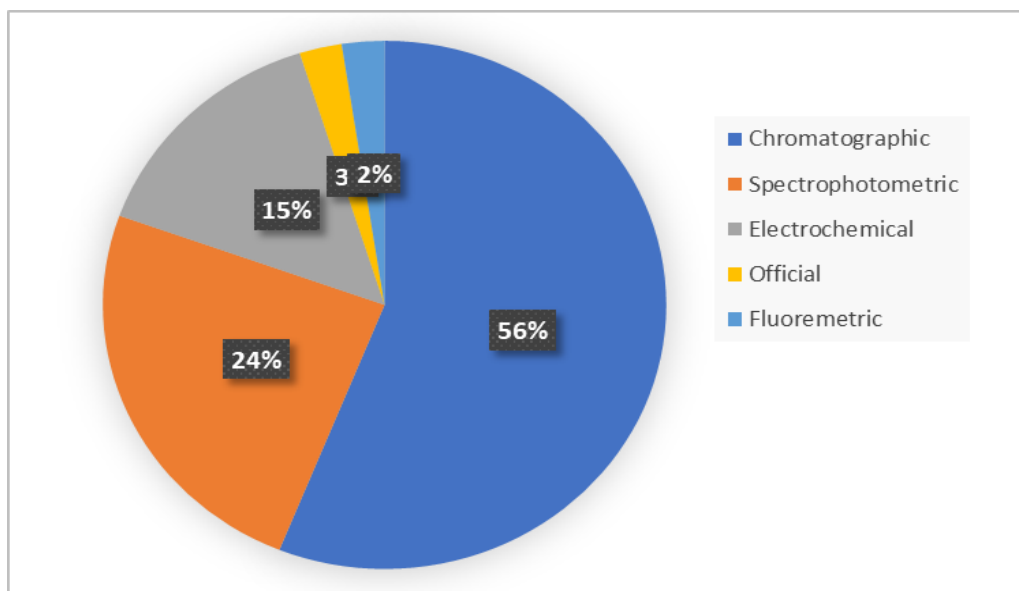


Figure 2: The pie chart represents the percentage of different analytical methods for TMS determination.

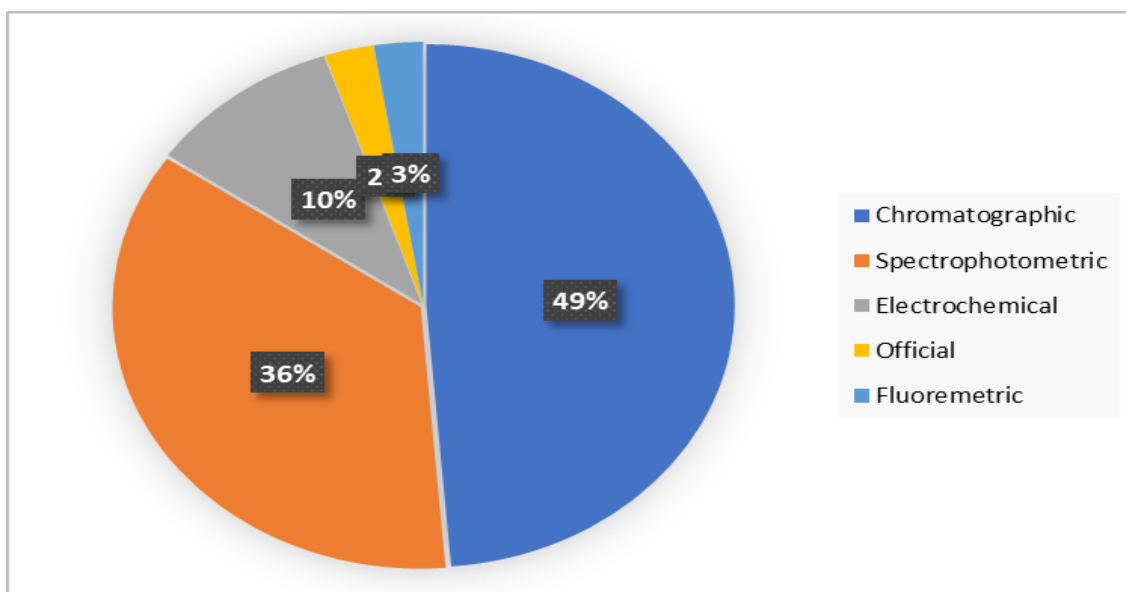


Figure 3: Pie chart represents the percentage of different analytical methods for RVS determination.

## 2. Analytical techniques

### 2.1. Official and reported analytical methods for the analysis of TMS

#### 2.1.1. Official analytical method

TMS is identified in BP by Infrared absorption spectrophotometry by dissolving in alcohol and evaporating the solution while the spectrum of the residue is examined. It is determined in USP by titration of where telmisartan is dissolved in 5 ml anhydrous formic acid and diluted with 75 ml of acetic anhydride and titrated against 0.1 M perchloric acids.

#### 2.1.2. Reported analytical methods

##### a. Spectroscopic methods

###### *UV spectrophotometric methods*

- Ten spectrophotometric methods were reported for the estimation of TMS in bulk and tablet (12–21) by utilizing different solvents and different absorbance maxima.
- Four spectrophotometric methods were reported for the estimation of TMS in bulk (22), pharmaceutical dosage form (23,24), and urine samples (25) by colored complex formation.

###### *Spectrofluorimetric method*

- The spectrofluorimetric method was developed for TMS determination. The method measured excitation 336 nm at and emission at 475nm utilizing 0.1M NaOH as a solvent (26).

##### b. Electrochemical methods

- The conductimetric method was developed for the determination of TMS in pure and tablet formulations. The method depends on the weak acid properties of TMS which can be quantified by measuring its conductance in alcoholic media (27).
- The square wave adsorptive stripping voltammetric method was developed for the determination of TMS in tablets and human plasma. The method was applied at pH 10.38 (28).
- The voltammetric method was developed for the determination of TMS. The method was applied using sodium dodecyl sulfate-modified pyrolytic graphite surface (29).
- The cathodic adsorptive stripping voltammetric method was developed for the determination of TMS in pharmaceuticals and biological fluids. The method was applied at pH 10.00 (30).

### c. Chromatographic methods

#### *High-performance thin-layer chromatography*

- Two HPTLC methods were developed for the determination of TMS in tablets. The methods utilized silica Gel 60 F254 TLC for separation. The first method used a solvent system comprised of Toluene: Methanol (7:3 v/v/v). The UV detector was adjusted to 299 nm for the detection of TMS (31). The second method utilized a solvent system comprised of ethyl acetate: dichloromethane: methanol (6:2:1 v/v). The UV detector was adjusted to 295 nm for the detection of TMS (32).

#### *High-performance liquid chromatography*

**Table 1:** The reported chromatographic methods for simultaneous determination of TMS.

Column	Mobil phase	Flow rate	Detector	Sample matrix	Ref
Shimadzu - C18	0.025M potassium dihydrogen phosphate: acetonitrile: methanol (45:50:5, v: v: v).	1.0 ml/min.	UV at 216 nm	Bulk and tablet formulation.	(33)
Chromosil -C18	Methanol: 0.1% Orthophosphoric acid: acetonitrile in the ratio of (80:05:15 v/v/v).	1.5 ml/min.	UV at 256 nm	Tablet formulation.	(34)
sun fire - C18	Pentane sulphonic acid sodium salt monohydrate with Triethyl amine: Methanol in the ratio (40: 60 v/v).	1.2 ml/min.	UV at 230 nm	Bulk and tablet formulation.	(35)
Prontosil ODS -C18	Acetonitrile: Buffer in proportion of (90:10 v/v).	1.0 ml/min.	Fluorescence at 259 nm excitation and 399 nm emission	Bulk and tablet formulation.	(36)
Hypersil - C18	Methanol: water 80:20 (v/v).	1.0 ml/min.	UV at 225 nm	Bulk and tablet formulation.	(37)

Column	Mobil phase	Flow rate	Detector	Sample matrix	Ref
Xterra - C8	Buffer: methanol 40: 60 (v: v)	0.5 ml/min.	UV at 230 nm	Bulk and tablet formulation.	(38)
Chromolith - C18	0.1% trifluoroacetic acid and acetonitrile (83.7:16.3, v/v)	0.5 ml/min.	UV at 230 nm	Drug and related impurities	(39)
Inertsil ODS -C18	Potassium dihydrogen orthophosphate buffer with Triethylamine and phase B of use filter and degas acetonitrile.	1.0 ml/min.	UV at 246 nm	Drug and related impurities	(40)
Waters symmetry - C18	10 mM potassium dihydrogen phosphate: acetonitrile (64:40, v: v).	1.0 ml/min.	UV at 230 nm	Drug and degradation products.	(41)
Kromasil C18	0.1 % ammonium hydroxide solution with acetonitrile: methanol (80:20, v: v).	1.0 ml/min.	UV at 230 nm	Drug and related substances.	(42)
Lichrosphere - C18	20 mM ammonium acetate containing 0.1% (v/v) Triethyl and acetonitrile.	1.0 ml/min.	UV at 254nm	Drug and related compounds.	(43)
Chromosil - C18	Acetonitrile: methanol: sodium dihydrogen orthophosphate (0.01 M) in the ratio of (41:10:49, v: v: v).	1.0 ml/min.	UV at 291 nm	Bulk and plasma.	(44)
Phenomenex Luna - C8	Methanol and acetonitrile (70:30 %v/v).	1.0 ml/min.	UV at 290 nm	Rat plasma.	(45)
Hypurity - C18	Acetonitrile: Ammonium format buffer 2 mM (70:30 v/v).	0.5 ml/min.	MS/MS 513.2/469.3 m/z.	Human plasma.	(46)

Column	Mobil phase	Flow rate	Detector	Sample matrix	Ref
UPLC-MS/MS BEH- C18	Acetonitrile: 8 mM ammonium acetate containing 0.15 % formic acid (70:30, v: v).	0.3 ml/min.	515.27→2 76.13 m/z.	Human plasma.	(47)
UPLC- BEH - C18	Acetonitrile: methanol : water (75 : 15 : 10 v/v/v).	0.33mL/min	UV at 235	Bulk and its forced degradation products.	(48)
UPLC- Waters Aquity BEH - C18	10mM Ammonium acetate with the addition of 1mL Triethyl amine, and Acetonitrile in the ratio (90:10, v/v);	0.3 mL/min	UV at 235	Bulk and tablet formulation and its related substances.	(49)

## 2.2. Official and reported analytical methods for the analysis of RVS

### 2.2.1. Official analytical method

RVS is determined in USP by high-performance layer chromatographic method where the mobile phase consisted of acetonitrile 1%, aqueous trifluoroacetic acid, and water (29:1:70), and the ratio changed to (75:1:24) after 50 minutes. The drug was dissolved in acetonitrile. Elution utilized 3.0-mm × 15-cm; 3-µm packing L1 column at temperature 40° with UV detector at 242 nm. Injection volume 10µL and flow rate 0.75 ml/minute.

### 2.2.2. Reported analytical methods

#### a. Spectroscopic methods

##### *UV spectrophotometric methods*

- Three spectrophotometric methods for determination of RVS in bulk and pharmaceutical dosage form. The drug was measured at 244 nm (50), at 242.8 nm (51), at 242 nm (52), and at 234.6: 251 nm (53).
- Five spectrophotometric methods were developed for the determination of RVS in pure form and pharmaceutical dosage form by the formation of the ion-pair complex (54–58) utilizing different agents and different absorbance maxima.



- One stability-indicating spectrophotometric method for the estimation of RVS and its oxidative degradation products (59).

#### *Spectrofluorimetric method*

- Spectrofluorimetric method for estimation of RVS in bulk and pharmaceutical dosage form. The method depends on the reaction of RVS with sulphuric acid. The drug was measured at excitation 227 nm and emission at 370 nm (60).

### **b. Electrochemical methods**

- The square wave voltammetric method was developed for the determination of RVS in pharmaceuticals and biological fluids (61–64). The methods utilized different pretreated types of electrodes.
- The cyclic voltammetric method was developed for the determination of RVS in human plasma. The method utilized hanging mercury electrode novel nanocomposites prepared from spinel copper ferrite and reduced graphene oxide (65).
- The cyclic voltammetric method was developed for the determination of RVS in human plasma. The method utilized reduced graphene oxide and silver nanocomposite (66).

### **c. Chromatographic methods**

#### *High-performance thin-layer chromatography*

- Stability-indicating HPTLC methods for determination of RVS and its oxidative degradation products utilizing mobile phases: Ethyl acetate: methanol: ammonia (7:3:0.01, v/v/v) (59), Chloroform: n-hexane: methanol: glacial acetic acid (8:10.4:1.5:0.1 v/v/v/v) (67). The drug was detected at 245 nm in both methods.
- Stability-indicating HPTLC method for determination of RVS in tablets. Acetonitrile: Ethyl Acetate: Toluene (6:1:3 v/v/v) was utilized as a mobile on silica gel 60 F<sub>254</sub> as a stationary phase. The drug was detected at 245 nm (68).

*High-performance liquid chromatography***Table 2:** The reported chromatographic methods for simultaneous determination of RVS.

Column	Mobil phase	Flow rate	Detector	Sample matrix	Ref
Luna - C18	Buffer: Acetonitrile: methanol (45:25:35, v: v: v).	1.0 ml/min	UV at 248 nm	Bulk and tablet formulation.	(69)
Nucleodur - C8	Ethanol: methanol: ethyl acetate (6:3:1 v/v)	1.0 ml/min	UV at 254nm	Bulk and tablet formulation.	(70)
Thermo Hypersil - C18	Methanol: water (90:10, v: v)	0.9 ml/min	UV at 243 nm	Bulk and tablet formulation.	(71)
Thermo scientific C8	Methanol: acetonitrile: water (40:40:20, v/v).	1.0 ml/min	UV at 248 nm	Bulk and tablet formulation.	(72)
YMC - C8	Acetonitrile: water (40:60, v/v).	1.5 ml/min	UV at 242 nm	tablet formulation.	(73)
Nucleodur - C8	0.1M formic acid and methanol (25:75, v/v).	1.0 ml/min	UV at 280 nm	Bulk and tablet formulation.	(74)
Kromasil -C8	Acetonitrile and water (75:25 v/v).	1.0 ml/min	PDAD at 240 nm	Bulk and tablet formulation.	(75)
Phenomenex -C 18	Acetonitrile and buffer (50:50, v: v).	1.0 ml/min	UV at 254nm	Bulk and tablet formulation.	(76)
Phenomenex, Synergi - C18	Acetonitrile: water (40:60, v: v).	1.0 ml/min	Fluorescence at 366 nm excitation and 410 nm emission.	Bulk and tablet formulation.	(77)
Eclipse XDB - C8	Sodium dihydrogen phosphate: acetonitrile (50:50 v/v)	1.2 ml/min	UV at 248 nm	Bulk and tablet formulation.	(78)

Column	Mobil phase	Flow rate	Detector	Sample matrix	Ref
Princeton - C18	A mixture of water and methanol in the ratio (20:80, v: v).	1.0 ml/min	UV at 240 nm	Bulk and tablet formulation with degradation products.	(79)
Sunfire - C18	10 mM ammonium acetate and acetonitrile: methanol (50:50 v/v).	1.0 ml/min	UV at 242 nm	Drug and its lactone impurity.	(80)
C18	Water: acetonitrile: methanol (40: 40: 20, v: v: v).	1.0 ml/min	UV at 245 nm	Drug and its oxidative degradation products.	(59)
Waters Acquity UPLC -C18	Methanol and 0.1% trifluoroacetic acid (50:50, v: v).	0.3 ml/min	UV at 240 nm	Drug and its related impurities.	(81)
LC-MS/MS - Diamonsil C18	Acetonitrile-methanolic acid (0.1%) (60:40, v/v).	0.8 ml/min	MS/MS 482.1 → 258.1 m/z.	Human plasma.	(82)
HiChrom C18	0.1% formic acid in acetonitrile and 0.1% formic acid in water (70:30 v/v).	0.3 ml/min	MS/MS 482.1 → 258.1 m/z.	Human plasma.	(83)
Zorbax-SB Phenyl column.	0.1% v/v glacial acetic acid in 10% v/v methanol in water and 40% v/v methanol in acetonitrile.	0.35 ml/min	MS/MS 470.2 → 276.2 m/z.	Human plasma.	(84)
Xterra - C18	15 µmol/L ammonium acetate in water and methanol.	0.4 ml/min	MS/MS 480.1 → 418.1 m/z.	Human plasma.	(85)
Phenomenex Kinetex- C18	0.1% v/v glacial acetic acid in Aqueous formic acid (0.1%) and methanol.	0.2 ml/min	MS/MS 482.3→258.2 m/z.	Human blood.	(86)
Xterra - C18	A mixture of acetonitrile and 10 mM ammonium acetate (55:45, v: v).	0.3 ml/min	MS/MS 481.3→256.0 m/z.	Human blood.	(87)

### 2.3. Recently reported analytical methodologies for the determination of TMS and RVS in binary mixtures

#### a. Spectroscopic methods

##### *UV spectrophotometric methods*

- Two spectrophotometric methods were developed for the simultaneous determination of TMS and RVS pharmaceutical dosage forms. The first method depends on measuring the absorbance at 243.8nm and 295.3nm for RVS and TMS, respectively (88). The second method utilized four mathematical and ratio spectra manipulations to resolve severely overlapped spectra (89).

#### b. Chromatographic methods

##### *High-performance liquid chromatography*

Table 3: The reported chromatographic methods for simultaneous determination of TMS and RVS in binary mixtures

Column	Mobil phase	Flow rate	Detector	Sample matrix	Ref
Oyster ODS3 - C18	10 mM phosphate buffer with 1.1 g octane-1-sulfonic acid sodium salt and acetonitrile, (50:50, v/v).	1.0 ml/min	UV at 242 nm.	tablet formulation.	(90)
Kinetex C18	ammonium phosphate monobasic buffer and methanol at a ratio of (30:70, v/v).	1.0 ml/min	UV at 242 nm.	tablet formulation.	(91)

### 3. Conclusion

The current study provides an overview of the many analytical approaches for TMS and RVS detection in various matrices, including pharmaceutical formulations and serum and plasma samples, that have been reported in the literature. Analytical methods such as spectroscopy, chromatography, and electrochemical processes were used to quantify TMS and RVS both individually and in bulk tablet formulation. According to the results of this study, various methodologies were reported for estimation of TMS and RVS as a single in addition just a few analytical techniques based on UV-Vis spectrophotometry and HPLC are accessible for estimation of the binary mixture. HPLC with UV detection is also the method most frequently used to assess both medicines in the pharmaceutical matrix and other biological matrices since it delivers correct findings with minimal effort, according to the data for TMS and RVS analysis. A suggested HPLC fluorescence or UV could be applied in pharmaceutical dosage forms or biological fluids by utilizing a mobile phase consisting of acetonitrile and *o*-phosphoric acid.

- **Conflict of Interest**

The Authors declare no conflict of interest.

### 4. References

1. Staessen JA, Wang J, Bianchi G, Birkenhäger WH. Essential hypertension. *Lancet*. 2003;361(9369):1629–41.
2. Wong ND, Lopez V, Tang S, Williams GR. Prevalence, treatment, and control of combined hypertension and hypercholesterolemia in the United States. *Am J Cardiol*. 2006;98(2):204–8.
3. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. *Nat Rev Nephrol*. 2020;16(4):223–37.
4. Beilin LJ, Puddey IB, Burke V. Lifestyle and hypertension. *Am J Hypertens*. 1999;12(9):934–45.
5. Guerrero-García C, Rubio-Guerra AF. Combination therapy in the treatment of hypertension. *Drugs Context*. 2018;7.
6. Bakheit AHH, Abd-Elgalil AA, Mustafa B, Haque A, Wani TA. Telmisartan. *Profiles drug Subst excipients Relat Methodol*. 2015;40:371–429.
7. Wienen W, Entzeroth M, van Meel JCA, Stangier J, Busch U, Ebner T, et al. A review on telmisartan: a novel, long-acting angiotensin II-receptor antagonist. *Cardiovasc Drug Rev*.

2000;18(2):127–54.

8. The British Pharmacopoeia. London, UK: Her Majesty's Stationary Office, 2021.
9. United States Pharmacopoeia. Washington, 2021.
10. Dudhipala N, Veerabrahma K. Improved anti-hyperlipidemic activity of Rosuvastatin Calcium via lipid nanoparticles: Pharmacokinetic and pharmacodynamic evaluation. *Eur J Pharm Biopharm.* 2017;110:47–57.
11. Quirk J, Thornton M, Kirkpatrick P. Rosuvastatin calcium. *Nat Rev Drug Discov.* 2003;2(10):769–70.
12. Sonia K, Lakshmi KS. Validation of Telmisartan by UV Spectrophotometry Method. *Res J Pharm Technol.* 2019;12(5):2413–5.
13. Kumar M, Kumar C, Bhatt S, Pandurangan A, Kaushik V, Malik A, et al. Dissolution method development and validation for tablet dosage form of Telmisartan using UV spectrophotometric method. *J Chem Pharm Res.* 2018;10(5):148–56.
14. Susmitha AS, Kokilambigai KS, Lakshmi KS. Spectrophotometric quantification of Telmisartan employing multivariate calibration technique in bulk and pharmaceutical formulations. *Res J Pharm Technol.* 2019;12(4):1799–805.
15. Nagar MK, Dhabale PN, Hosmani AH. Validated Spectroscopic Method for Estimation of Telmisartan from Tablet Formulation. *Asian J Res Chem.* 2011;4(11):1664–5.
16. Vobbilireddi SK, Sujana K, Rani AP. New Validated UV-Spectrophotometric Method for the Determination of Telmisartan in Bulk and Dosage Form. *Analyst.* 2012;2(9):9.
17. Nagabathula R, Madhuri G, Devi UR, Vamsi A, Bhavani K. UV Spectroscopic method for estimation and validation of Telmisartan in bulk and tablet dosage forms. *World J Pharm Sci.* 2019;113–7.
18. Pandey A, Sawarkar H, Singh M, Kashyap P, Ghosh P. UV-spectrophotometric method for estimation of telmisartan in bulk and tablet dosage form. *Int J ChemTech Res.* 2011;3(2):657–60.
19. Chivate ND, Patil SM, Saboji JK, Chivate AN. Development of UV spectrophotometric method for estimation and validation of telmisartan as a pure API. *J Pharm Res.* 2012;5(6):3331–3.
20. Pradhan KK, Mishra US, Sahoo A, Sahu KC, Mishra D, Dash R. Method development and validation of Telmisartan in bulk and pharmaceutical dosage forms by UV Spectrophotometric method. 2011;
21. Tsvetkova D, Obreshkova D, Ivanova S, Yankov V, Atanasov P, Hadjieva B. Telmisartan quality

- control by validation of UV-spectrophotometric method. *Int J Innov Res Med Sci.* 2016;1(04).
22. Saiyed SA, Jadeja P, Mashru R. Development and Validation of Extractive Spectrophotometric Methods for the Estimation of Telmisartan by Using Smartphone Application. *J Drug Deliv Ther.* 2022;12(3-S):178–90.
  23. Bais S, Singh C, Singhvi I, Joshi Y, Patel B, Chandewar A. Novel method for quantitative estimation of Telmisartan from Tablet formulation by Colorimetric Method. *Asian J Pharm Anal.* 2014;4(2):54–6.
  24. Srihari G. Spectrophotometric Determination of Telmisartan Sulphate in Pharmaceutical Dosage Forms. *Asian J Pharm Heal Sci.* 2011;1(3).
  25. Kumbhar ST, Chougule GK, Gajeli GB, Tegeli VS, Thorat YS, Shivsharan US. Visible spectrophotometric determination of telmisartan from urine. *Int J Pharm Sci Res.* 2011;2(5):1254.
  26. Jamkhandi CM, Disouza JI, Bhagwat DA. Development of Newer Fluorimetric Method for Estimation of Telmisartan. *Inter J Pharm Pharm Sci.* 2010;2(4):209–11.
  27. Jamkhandi CM, Salunkhe SR, Disouza JI, Bhagwat DA, Kuchekar CP. DEVELOPMENT OF NEWER CONDUCTOMETRIC METHOD FOR ESTIMATION OF TELMISARTAN IN PURE AND FORMULATION. *J Drug Deliv Ther.* 2014;4(3):110–2.
  28. Alarfaj NA. Square-wave adsorptive stripping voltammetric determination of antihypertensive agent telmisartan in tablets and its application to human plasma. *J Anal Chem.* 2013;68(4):335–40.
  29. Kumar N, Goyal RN. A simple and highly selective determination of telmisartan at sodium dodecyl sulfate modified pyrolytic graphite surface. *Electroanalysis.* 2018;30(5):892–900.
  30. Taşdemir İH, Akay MA, Erk N, Kılıç E. Voltammetric behavior of telmisartan and cathodic adsorptive stripping voltammetric method for its assay in pharmaceutical dosage forms and biological fluids. *Electroanalysis.* 2010;22(17-18):2101–9.
  31. Chandurkar SN, Phoujdar MS. Development and validation of HPTLC method for determination of Telmisartan in API and pharmaceutical dosage form. *World J Pharm Sci.* 2017;195–9.
  32. Vekariya NR, Patel GF, Dholakiya RB. Stability-indicating HPTLC determination of telmisartan in bulk and tablets. *Res J Pharm Technol.* 2010;3(3):900–4.
  33. Upendra B, Hemant D, Kumar DA. RP-HPLC Method Development and Validation For Estimation of Telmisartan in Bulk and Tablet Dosage Form. *Int J Drug Regul Aff.* 2013;1(2):61–4.

34. Rao MB, Nagendrakumar A, Sivanadh M, Rao GV. Validated RP-HPLC method for the estimation of telmisartan in tablet formulation. *Pharm Res.* 2012;2(2):50–5.
35. Surekha ML, Swamy GK, Ashwini GL. Development and Validation of RP-HPLC method for the estimation of Telmisartan in bulk and tablet dosage Form. *Int J Drug Dev Res.* 2012;4(4):0.
36. Patel BA, Captain AD. DEVELOPMENT AND VALIDATION OF RP-HPLC METHOD FOR ESTIMATION OF TELMISARTAN IN BULK AND FORMULATION USING FLUORESCENCE DETECTOR. *J Biomed Pharm Res.* 2014;3(2):44–8.
37. Londhe S V, Kaul N, Agrawal H, Mahadik KR. Stability-indicating RP-HPLC method for analysis of telmisartan in the bulk drug and in formulations. *Acta Chromatogr.* 2010;22(4):539–48.
38. Sujana K, Gowri Sankar D, Bala Souri O, Swathi Rani G. Stability indicating RP-HPLC method for the determination of telmisartan in pure and pharmaceutical formulation. *Int J Pharm Pharm Sci.* 2011;3(2):164–7.
39. Dobričić V, Vukadinović D, Jančić-Stojanović B, Vladimirov S, Čudina O. AQbD-oriented development of a new LC method for simultaneous determination of telmisartan and its impurities. *Chromatographia.* 2017;80(8):1199–209.
40. Patel KM, Patel UR, Patel AD. Development and Validation of a Reversed-Phase HPLC Method for the Simultaneous Determination of Telmisartan and Its Related Compound B (Positional Isomers) in the Bulk Drug. *Int J Anal Appl Chem.* 2015;1(2):12–23.
41. Gupta A, Charde RM, Charde MS. Determination of Telmisartan and forced degradation behavior by RP-HPLC in tablet dosage form. *J Pharm Res.* 2011;4(4):1270–3.
42. Gholave J V, Gadhari NS, Patil SS, Upadyay SS, Patil VR, Shelke KF. Development and Validation of a Stability-indicating RP-HPLC Method for the Simultaneous Determination of Telmisartan and its Related Substances in Telmisartan Bulk Drug Substance. *Anal Chem Lett.* 2020;10(5):577–89.
43. Rao RN, Prasad KG, Naidu CG, Maurya PK. Development of a validated liquid chromatographic method for determination of related substances of telmisartan in bulk drugs and formulations. *J Pharm Biomed Anal.* 2011;56(3):471–8.
44. KAUR L, SINGH G, DHAWAN RK, KAUR N, GUPTA GD. Development and Validation of Rapid RP-HPLC Method for the Detection and Quantification of Telmisartan Incorporated in Dosage Forms and Plasma. *J Pharm Res Ther.* 2020;1(2):78–83.



45. Patel JM, Dhingani AP, Garala KC, Raval MK, Sheth NR. Development and validation of bioanalytical HPLC method for estimation of telmisartan in rat plasma: application to pharmacokinetic studies. *Dhaka Univ J Pharm Sci.* 2012;11(2):121–7.
46. Terish JD, Kumar SS, Ramesh N, Sasijith SL. Estimation of telmisartan in human plasma by reversed phase liquid chromatography coupled with tandem mass spectrometry-a bioequivalence study application. *Der Pharm Lett.* 2011;3:289–98.
47. Wani TA, Zargar S. New highly-sensitive ultra-performance liquid chromatography-mass spectrometry method for quantification of telmisartan in human plasma. *Trop J Pharm Res.* 2015;14(3):511–8.
48. Dhekale NH, Bindu KH, Kirankumar KY, Gore AH, Anbhule P V, Kolekar GB. Development and optimization of a multivariate RP-UPLC method for determination of telmisartan and its related substances by applying a two-level factorial design approach: application to quality control study. *Anal Methods.* 2014;6(14):5168–82.
49. Bhavani V, Rao TS, Raju SVN, Madhusudan B, Begum J. Stability indicating UPLC method for the estimation of telmisartan related substances in tablets formulation. *Int J Sci Res Publ.* 2013;3(2).
50. Singh H, Gupta RD, Gautam G. Determination of Rosuvastatin Calcium in bulk and Pharmaceutical dosage forms by using UV-Spectrophotometric method. *Asian J Pharm Pharmacol.* 2018;4(1):45–8.
51. Katkade PN, Saudagar RB. Spectroscopic Determination and Validation of Rosuvastatin Calcium Concentration in Bulk and Dosage form. *Analyst.* 2016;1(20):19–80.
52. Patil A, Maste MM, Suryawanshi SS, Patil N. Green Solvent Assisted UV-Spectrophotometric Method for Estimation of Rosuvastatin in Bulk and Pharmaceutical Dosage Forms. *Res J Pharm Technol.* 2022;15(2):587–90.
53. Jain PS, Kale NK, Surana SJ. Quantitative estimation of Rosuvastatin in bulk and tablet dosage form by using area under curve method. *J Pharm Bioanal Sci.* 2013;4:128–33.
54. Ramadan AA, Mandil H, Alsayed-Ali R. Spectrophotometric determination of rosuvastatin in pure form and pharmaceutical formulations through ion-pair complex formation using bromocresol green. *Int J Pharm Pharm Sci.* 2015;7(11):191–8.
55. Lima MF, Cassella RJ, Pacheco WF. Spectrophotometric determination of rosuvastatin in pharmaceutical formulations using quinalizarin. *Brazilian J Pharm Sci.* 2017;53.

56. Prajapati PB, Bodiwala KB, Marolia BP, Rathod IS, Shah SA. Development and validation of extractive spectrophotometric method for determination of rosuvastatin calcium in pharmaceutical dosage forms. *J Pharm Res.* 2010;3(8):2036–8.
57. Ramadan AA, Mandil H, Alshelhawi N. Spectrophotometric determination of rosuvastatin calcium in pure form and pharmaceutical formulations by the oxidation using iodine and formation triiodide complex in acetonitrile. *Int J Pharm Pharm Sci.* 2014;6(5):579–85.
58. A Wani T, A Darwish I, Y Khalil N. Novel microwell-based spectrophotometric assay for the determination of rosuvastatin calcium in its pharmaceutical formulations. *Curr Pharm Anal.* 2013;9(1):54–60.
59. Badawy AM, Mostafa NM, Lamie NT, El-Aleem A. 10. Stability Indicating Methods for the Determination of Rosuvastatin Calcium in the Presence of its oxidative Degradation Products. *Future.* 2012;1:1.
60. Braga VSM, Mancilha TP, Cassella RJ, Pacheco WF. Determination of rosuvastatin in urine by spectrofluorimetry after liquid–liquid extraction and derivatization in acidic medium. *J Fluoresc.* 2013;23(1):49–55.
61. Silva TA, Pereira GF, Fatibello-Filho O, Eguiluz KIB, Salazar-Banda GR. Square-wave voltammetric determination of rosuvastatin calcium in pharmaceutical and biological fluid samples using a cathodically pretreated boron-doped diamond electrode. *Diam Relat Mater.* 2015;58:103–9.
62. Silva TA, Zanin H, Vicentini FC, Corat EJ, Fatibello-Filho O. Electrochemical determination of rosuvastatin calcium in pharmaceutical and human body fluid samples using a composite of vertically aligned carbon nanotubes and graphene oxide as the electrode material. *Sensors Actuators B Chem.* 2015;218:51–9.
63. Altınöz S, Uyar B. Electrochemical behaviour and voltammetric determination of rosuvastatin calcium in pharmaceutical preparations using a square-wave voltammetric method. *Anal Methods.* 2013;5(20):5709–16.
64. Nhu-Trang T-T, Nguyen H-N, Thach T-X, Nguyen H-N, Nguyen C-H, Do MH. A simple electrochemical method for determination of rosuvastatin calcium in cholesterol-lowering medical products. In: *AIP Conference Proceedings.* AIP Publishing LLC; 2022. p. 60002.
65. El-Wakil MM, Abdelhady KK, Salam RAA, Hadad GM, Ali R. Facile synthesis of novel nanocomposite prepared from spinel copper ferrite and reduced graphene oxide in the presence of

- anti-fouling agent diethyl ammonium acid sulphate for ultrasensitive detection of rosuvastatin in human plasma. *Microchem J.* 2019;147:1133–40.
66. El-Zahry MR, Ali MFB. Enhancement effect of reduced graphene oxide and silver nanocomposite supported on poly brilliant blue platform for ultra-trace voltammetric analysis of rosuvastatin in tablets and human plasma. *RSC Adv.* 2019;9(13):7136–46.
  67. Belal F, Ibrahim F, Khedr A, Elawady T. Stability indicating TLC method for the determination of rosuvastatin and identification of some degradation products using electrospray ionization mass spectrometry. *J Liq Chromatogr Relat Technol.* 2014;37(8):1114–32.
  68. Karkanis V V, Parikh V, Panchal R. Estimation of Rosuvastatin calcium in tablet dosage form by HPTLC method. *Tablet.* 2011;400:100–74.
  69. Donthula S, Kumar MK, Teja GS, Kumar M, Janapati YK. A new validated RP-HPLC method for determination of Rosuvastatin calcium in bulk and pharmaceutical dosage form. 2011;
  70. Haq N, Shakeel F, Alanazi F, Alshora DH, Ibrahim MA. Development and validation of a green RP-HPLC method for the analysis of rosuvastatin: a step towards making liquid chromatography environmentally benign. *Green Process Synth.* 2018;7(2):160–9.
  71. Hazra K, Chowdary A, Devgan M, Shukla R, Sarkar B, Suryawanshi A. Development and validation of rp-hplc method for estimation of rosuvastatin calcium solid dispersions tablets. *Asian J Pharm Res Vol.* 2014;4(3):122–5.
  72. Jana K, Mahanti B. Development and Validation of a new improved RP-HPLC Method for estimation of Rosuvastatin calcium in Pharmaceutical dosage form. *Res J Pharm Technol.* 2020;13(6):2886–92.
  73. 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.
  74. Ashour S, Omar S. Validated high-performance liquid chromatographic method for the estimation of rosuvastatin calcium in bulk and pharmaceutical formulations. *Int J Biomed Sci IJBS.* 2011;7(4):283–8.
  75. Dhamdhare RB, Vijayalakshmi A. Implementation of Quality by Design Approach to the Analytical Method Development and Validation for the Estimation of Rosuvastatin Calcium.
  76. Madiha M, Sidra A, Najia R, Tariq A, Wajiha I, Lubna B, et al. High performance liquid chromatographic method validation for determination of rosuvastatin calcium in tablet dosage forms. 2018;

77. Caglar S, Toker S. Determination of rosuvastatin at picogram level in serum by fluorimetric derivatization with 9-Anthryldiazomethane using HPLC. *J Chromatogr Sci.* 2013;51(1):53–8.
78. Hassouna ME, Salem HO. Stability indicating new RP-HPLC method for the determination of rosuvastatin calcium in pure and tablets dosage forms. *Int J Appl Pharm Bio Res.* 2017;2:11–27.
79. PIMPALE A, KAKDE R. STABILITY-INDICATING METHOD DEVELOPMENT AND VALIDATION FOR THE ESTIMATION OF ROSUVASTATIN CALCIUM IN PHARMACEUTICAL DOSAGE FORM BY REVERSE PHASE-HIGH PERFORMANCE LIQUID CHROMATOGRAPHY. 2020;
80. Moodbidri PV, Dhayanithi V, Manjunathashastry GB, Pati HN, Vasireddy P. A new simultaneous determination of Rosuvastatin calcium and its Lactone impurity by reverse phase HPLC method. *Asian J Pharm Res.* 2015;5(4):175–82.
81. Reddy GVR, Reddy BV, Haque SW, Gautam HD, Kumar P, Kumar AP, et al. Development and validation of a stability-indicating UPLC method for rosuvastatin and its related impurities in pharmaceutical dosage forms. *Quim Nova.* 2011;34:250–5.
82. Zhang D, Zhang J, Liu X, Wei C, Zhang R, Song H, et al. Validated LC-MS/MS method for the determination of rosuvastatin in human plasma: application to a bioequivalence study in Chinese volunteers. *Pharmacol Pharm.* 2011;2(4):341–6.
83. Shah Y, Iqbal Z, Ahmad L, Nazir S, Watson DG, Khuda F, et al. Determination of Rosuvastatin and its Metabolite N-Desmethyl Rosuvastatin in Human Plasma by Liquid Chromatography–High Resolution Mass Spectrometry: Method Development, Validation, and Application to Pharmacokinetic Study. *J Liq Chromatogr Relat Technol.* 2015;38(8):863–73.
84. Macwan JS, Ionita IA, Akhlaghi F. A simple assay for the simultaneous determination of rosuvastatin acid, rosuvastatin-5S-lactone, and N-desmethyl rosuvastatin in human plasma using liquid chromatography–tandem mass spectrometry (LC-MS/MS). *Anal Bioanal Chem.* 2012;402(3):1217–27.
85. Lee HK, Ho CS, Hu M, Tomlinson B, Wong CK. Development and validation of a sensitive method for simultaneous determination of rosuvastatin and N-desmethyl rosuvastatin in human plasma using liquid chromatography/negative electrospray ionization/tandem mass spectrometry. *Biomed Chromatogr.* 2013;27(11):1369–74.
86. Moon SJ, Lee SE, Kwak Y-G, Kim M-G. Validation of LC-MS/MS method for determination of rosuvastatin concentration in human blood collected by volumetric absorptive microsampling

- (VAMS). *Transl Clin Pharmacol*. 2021;29(3):125.
87. Siddartha B, Babu IS. Estimation and validation for determination of rosuvastatin in human plasma by LC/MS/MS method. *J Glob Trends Pharm Sci*. 2014;5(3):1979–88.
88. Jose E, Nair AC, Kuttichan M. Development and Validation of a Solvent Extraction UV Spectrophotometric Method for the Estimation of Rosuvastatin Calcium and Telmisartan in Combined Dosage Form. *Res J Pharm Technol*. 2022;15(5):2065–9.
89. Fawzy MG, Mostafa AA, Shalaby A, Sayed RA. Green-assisted spectrophotometric techniques utilizing mathematical and ratio spectra manipulations to resolve severely overlapped spectra of a cardiovascular pharmaceutical mixture. *Spectrochim Acta Part A Mol Biomol Spectrosc*. 2023;295:122588.
90. Gholve R, Pekamwar S, Wadher S, Kalyankar T. Stability-indicating RP-HPLC method development and validation for simultaneous estimation of telmisartan and rosuvastatin calcium in bulk and in tablet dosage form. *Futur J Pharm Sci*. 2021;7(1):1–15.
91. Choi MN, Park YJ, Kim JE. Development and Validation of a Reversed-phase High Performance Liquid Chromatography Method for the Simultaneous Estimation of Rosuvastatin Calcium and Telmisartan in Fixed-Dose Complex Dual-Layer Tablets in Six Dosage Forms. *Indian J Pharm Sci*. 2021;83(3):451–64.