WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 5, 1210-1218. Research Article ISSN 2277– 7105

# ABSORBANCE CORRECTION SPECTROPHOTOMETRIC METHOD FOR SIMULTANEOUS ESTIMATION OF SIMVASTATIN AND TELMISARTAN IN SYNTHETIC MIXTURE

**Ankit B. Patel* and Dipti B. Patel**

Department of Pharmaceutical Quality Assurance, Shree S. K. Patel College of Pharmaceutical Education & Research, Ganpat University, Kherva - 384012, Mehsana, Gujarat, India.

Article Received on
15 March 2017,

Revised on 05 April 2017,
Accepted on 25 April 2017

DOI: 10.20959/wjpr20175-8435

***Corresponding Author**
**Ankit B. Patel**
Department of Pharmaceutical Quality Assurance, Shree S. K. Patel College of Pharmaceutical Education & Research, Ganpat University, Kherva - 384012, Mehsana, Gujarat, India.

## ABSTRACT

A new, simple, accurate and sensitive UV - spectrophotometric absorption correction method has been developed for simultaneous determination of Simvastatin and Telmisartan in synthetic mixture. Methanol was used solvents. The method is based upon determination of Simvastatin at 237nm and Telmisartan 296nm, respectively. Beer's law obeyed the concentration range of 3-18 µg/ ml for both drugs. The percentage recovery was found in the range of 100.06-101.01% for Simvastatin and 100.6-101.4% for Telmisartan. The developed method was validated statistically and by recovery studies. The % RSD value was found to be less than 2. Thus the proposed method was simple, precise, economic, rapid and accurate and can be successfully applied for simultaneous determination of Simvastatin and Telmisartan in synthetic mixture.

**KEYWORDS:** Simvastatin, Telmisartan, Absorbance Correction.

## INTRODUCTION

Simvastatin (SIMVA) (Figure 1) is chemically, [(1S,3R,7S,8S,8aR)-8-[2-[(2R,4R)-4-hydroxy-6-oxooxan-2-yl]ethyl]-3,7-dimethyl-1,2,3,7,8,8a-hexahydronaphthalen-1-yl]2,2 dimethylbutanoate, The empirical formula is $C_{25}H_{38}O_5$[1], Simvastatin is a White to off-white crystalline powder. It is very slightly soluble in methanol. Simvastatin is soluble in n-hexanel, sparingly soluble in ethanol. Simvastatin is a lipid-lowering agent. Simvastatin is a prodrug in which the 6-membered lactone ring of simvastatin is hydrolyzed in vivo to generate the beta,

delta-dihydroxy acid, an active metabolite structurally similar to HMG-CoA (hydroxymethylglutaryl CoA). Once hydrolyzed, simvastatin competes with HMG-CoA for HMG-CoA reductase, a hepatic microsomal enzyme. Interference with the activity of this enzyme reduces the quantity of mevalonic acid, a precursor of cholesterol.[2]

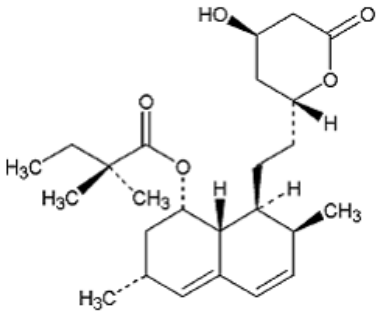


**Figure 1: Structure of Simvastatin**

Telmisartan is described chemically as 4'-[(1,4'-dimethyl-2'-propyl[2,6'-bi-1Hbenzimidazol]-1' yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid. The empirical formula is $C_{33}H_{30}N_4O_2$. Telmisartan is a white to yellowish powder. it is insoluble in water, but is sparingly soluble in methanol and soluble in strong acids and bases.[11] Telmisartan is an angiotensin-receptor blocker and Inhibition of angiotensin II binding to AT1 inhibits its AT1-mediated vasoconstrictive and aldosterone secreting effects and results in decreased vascular resistance and blood pressure.[12] The structural formula is shown in fig (2).

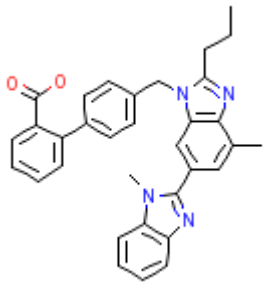


**Figure 2: Structure of Telmisartan**

## MATERIAL AND METHODS

### Instruments

A Shimadzu model 1700 (Japan) double beam UV/Visible spectrophotometer with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. Spectra were automatically obtained by UV-

Probe system software. A Sartorius CP224S analytical balance (Gottingen, Germany), an ultrasonic bath (Frontline FS 4, Mumbai, India) was used in the study.

**Materials and Reagents**

Pure sample of SIMVA was provided as a gift sample from Emcure pharmaceuticals limited and TELMI was obtained from Intas pharmaceuticals limited. Synthetic mixture (500 mg) of SIMVA (40 mg) and TELMI (80 mg) was prepared in laboratory using generally used excipients (380 mg) like lactose, talc, magnesium stearate. Methanol AR Grade was received form S.D fine Chemicals Ltd, Mumbai, India. Whatman filter paper no 41. All the chemicals used were of analytical grade.

**Preparation of Solutions**

**Preparation of standard stock solutions**

Accurately weighed standard SIMVA (10 mg) and TELMI (10 mg) powder was transferred to separate 100 ml volumetric flask and dissolve in methanol. The flasks were sonicated for 15 min. and diluted up to the mark with methanol to get (100 µg/ml) of standard stock solution of both the drugs (SIMVA and TELMI).

**Preparation of sample solution**

A quantity of the synthetic mixture equivalent to 40 mg of SIMVA and 80 mg of TELMI was transferred to a 100 ml volumetric flask. The content was combined with methanol (50 ml), sonicated for 20 minute to dissolve the drug as perfectly as desirable. The solution was filtered through a Whatman filter paper No. 41. The volume was fixed up to the mark with methanol. An aliquot of this solution (0.1 ml) was transferred in to a 10 ml volumetric flask and the volume was fixed up to mark with methanol.

**Absorbance Correction Method**

Standard solution of Simvastatin (10µg/ml) and Telmisartan (10µg/ml) were scanned in uv range of 200 to 400 nm for determination of wavelength for estimation of Simvastatin and Telmisartan, From the overlain spectra of Simvastatin and Telmisartan, the wavelength selected for the estimation of Telmisartan was 296 nm, where Simvastatin has no significant absorbance. For estimation of Simvastatin it was 237 nm, where absorbance of Telmisartan is corrected.

$A = a * b * c$

CX = A1 / a * b

CX = A1 / a1 * b..... 1

A2 = A (SIMVA) + A (TELMI)

A2 = (a2 * CX * b) + (a3 * CY * b)

A2 = (a2 * CX) + (a3 * CY)

CY = [A2 - (a2 * CX)] / a3..... 2

Where,

A1 = Absorbance of sample solution at 296 nm

A2 = Absorbance of sample solution at 237 nm

a1 = Absorptivity of Telmisartan at 296 nm

a2 = Absorptivity of Telmisartan at 237 nm

a3 = Absorptivity of Simvastatin at 237 nm

## METHOD VALIDATION

The developed method was validated with respect to linearity, accuracy, intraday and interday precision, limit of detection (LOD) and limit of quantitation (LOQ) and robustness in accordance with the ICH guideline.

### Linearity

The calibration curves were constructed over a concentration range of 3 – 18 µg/ml for both drugs. Accurately measured standard working solutions of SIMVA (0.3, 0.6, 0.9, 1.2, 1.5 and 1.8 ml) and TELMI (0.3, 0.6, 0.9, 1.2, 1.5 and1.8 ml) were transferred to a series of 10 ml of volumetric flasks and diluted to the mark with methanol and the absorbance was measured at 237 nm (λmax of SIMVA) and at 296 nm (λmax of TELMI). The calibration curves were assembled by constructing absorbances versus concentrations and the regression equations were calculated.

### Precision

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. Precision may be considered at three levels: repeatability, Intraday precision and Interday precision.

**Repeatability**

Repeatability of the method was determined by analyzing mixed standard solution of Simvastatin and Telmisartan (5 µg/ml) 6 times without changing the parameters of measurement. The results are reported in terms of relative standard deviation (RSD) in Table-1.

**Intermediate Precision**

The intraday and inter day precision of the proposed method was performed by analyzing the corresponding responses three times on the same day(intraday) and on three different days (interday) over a period of one week for three different concentrations of standard solutions of Simvastatin and Telmisartan. Result was showed in Table-1.

**Accuracy**

Accuracy was checked by recovery study at 3 different concentration levels, i.e., a multilevel recovery study. The tablet samples were spiked with an extra 80,100 and 120% of standard Simvastatin and Telmisartan and the mixtures were analyzed by proposed method. Results of the recovery study are shown in table 4 suggested that method was accurate for the simultaneous estimation of SIMVA and LOSA in synthetic mixture. Result was showed in Table-2.

**Limit of Detection and Limit of Quantitation**

The limit of detection (LOD) and limit of quantification (LOQ) were calculated using signal-to-noise (i.e. 3.3 for LOD and 10 for LOQ) ratio using following equations designated:

**LOD = 3.3 X σ/S**

**LOQ = 10 X σ/S**

Where, σ = the standard deviation of the response,

S = slope of the calibration curve.

**Determination of SIMVA and TELMI in synthetic mixture**

Synthetic mixture was prepared by mixing generally used excipients in the pure drugs in our laboratory. Sample solution was prepared as described previously. The responses of the sample solution were measured at 237 nm and 296 nm for determination of SIMVA and TELMI, respectively. The amounts of the SIMVA and TELMI present in the sample solution were estimated by absorption correction equations.

## RESULTS AND DISCUSSION

An attempt has been made to develop a rapid, sensitive, economic, precise and accurate analytical methods for simultaneous estimation of SIMVA and TELMI in synthetic mixture. The proposed methods are based on spectrophotometric absorption for the simultaneous estimation of SIMVA and TELMI in UV region using methanol as solvent. SIMVA and TELMI obeyed linearity in the concentration range of 3-18 µg/ml in methanol at their respective λ-max with correlation coefficient ($r^2$>0.99). The overlain absorption spectra of SIMVA and TELMI in methanol is shown in Figure 3.

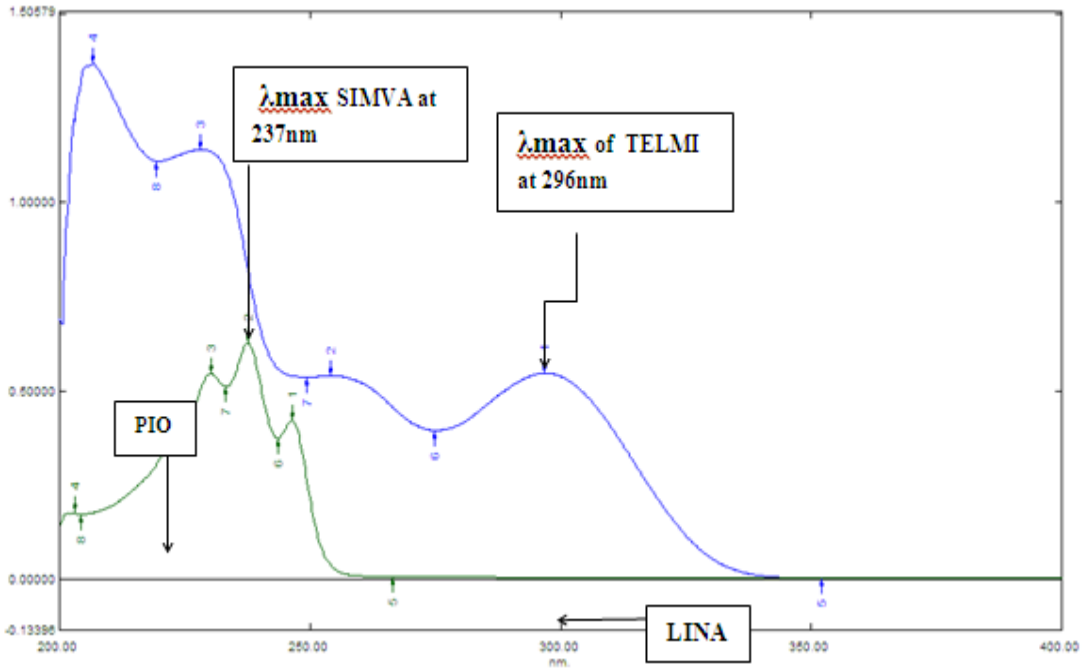


**Figure 3: Overlain Spectrum of SIMVA and TELMI (10µg/ml)**

**Table 1: Regression data of SIMVA and TELMI by Absorbance Correction Method**

| Parameters | | SIMVA (237nm) | TELMI (296nm) |
|---|---|---|---|
| Beer's law limit (µg /ml) | | 3-18 | 3-18 |
| Regression equation (y = mx +c) | | y= 0.0683x + 0.0126 | y = 0.0586x +0.0071 |
| Correlation coefficient ($r^2$) | | 0.9994 | 0.9998 |
| LOD (µg/ml) | | 0.7503 | 0.2626 |
| LOQ (µg /ml) | | 2.2736 | 0.7964 |
| Repeatability (% RSD, n = 6) | | 0.3466 | 0.8813 |
| Precision (% RSD, n = 3) | Intraday | 0.20-0.86 | 0.20-0.96 |
| | Interday | 1.03-1.52 | 1.45-1.54 |

**Table 2: Accuracy (% Recovery Study) data for SIMVA and TELMI**

| Drug | Level | Amount taken (µg/ml) | Amount added (%) | % Mean recovery ± S.D. (n=3) |
|---|---|---|---|---|
| SIMVA | I | 4 | 80 | 101.1 ± 1.07 |
| | II | 4 | 100 | 100.33 ± 0.57 |
| | III | 4 | 120 | 100.06 ± 0.47 |
| TELMI | I | 8 | 80 | 101.47 ± 0.60 |
| | II | 8 | 100 | 100.66 ± 0.38 |
| | III | 8 | 120 | 100.73 ± 0.58 |

**Table 3: Estimation of SIMVA and TELMI in synthetic mixture.**

| synthetic mixture. | Labeled claim (mg/ml) | | Amount found (mg/ml) | | % Labeled Claim ± S.D (n=6) | |
|---|---|---|---|---|---|---|
| | SIMVA | TELMI | SIMVA | TELMI | SIMVA | TELMI |
| | 40 | 80 | 40.4 | 80.36 | 100.58 ± 1.2213 | 100.45 ± 0.6053 |

The validation parameters were studied at all the selected wavelengths for the developed method. All the validation parameters were found to be within acceptable limits. The % recoveries were found to be in the range of 100.03-101.01 % for SIMVA and 100.66-101.47% for TELMI (Table 2). The precision of method was determined by repeatability, intraday and interday precision and was expressed as the % RSD which indicates good method precision (Table 1). The Limit of detection 0.75 µg/ml at 237 nm for SIMVA, 0.26 µg/ml at 296 nm for TELMI. Limit of quantification for SIMVA at 237 nm were 2.27 µg/ml and TELMI at 296 nm were 0.79 µg/ml (Table 1). The proposed spectrophotometric method was successfully applied to SIMVA and TELMI in synthetic mixture. SIMVA and TELMI content in synthetic mixture were found to be 100.58 % and 100.45 % respectively (Table 3).

## CONCLUSION

The absorbance correction method was developed for simultaneous determination of SIMVA and TELMI in binary mixture. Method was found to be precise and accurate as can be reflected from validation parameters data. Developed method was efficiently applied for determination of SIMVA and TELMI in pharmaceutical formulation and there for method can be extended for the regular QC analysis of both drugs in Synthetic mixture.

## ACKNOWALEDGEMENT

The authors wish to thank Emcure pharmaceuticals limited and Intas pharmaceuticals limited for providing SIMVA and TELMI pure drug powder as gift sample for research work. The authors are highly thankful to Shree S. K. Patel College of Pharmaceutical Education &

Research, Ganpat University, Kherva, Mehsana, Gujarat, India for providing all the facilities to carry out the work.

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