Spectrophotometric determination of 3-hydroxy-3-methylglutaryl coenzyme-A reductase inhibitors in pharmaceutical preparations

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Abstract: Simple and accurate spectrophotometric methods are presented for the determination of five 3-hydroxy-3-methylglutaryl coenzyme-A (HMG-CoA) reductase inhibitors (statins), namely atorvastatin, fluvastatin, pitavastatin, rosuvastatin, and simvastatin, in pharmaceutical preparations. The methods are based on the reaction of drugs as n-electron donor with 7,7,8,8-tetracyanoquinodimethane as π-acceptors to give highly colored complex species. All variables were studied in order to optimize the reaction conditions. Beer’s law was obeyed in the concentration ranges 4–20 μg mL⁻¹, 4–12 μg mL⁻¹, 0.8–2.4 μg mL⁻¹, 4–14 μg mL⁻¹, and 2.5–20 μg mL⁻¹ for atorvastatin, fluvastatin, pitavastatin, rosuvastatin, and simvastatin, respectively. The proposed methods were successfully applied to the pharmaceutical preparations without any interference from excipients.

Key words: HMG-CoA reductase inhibitors, spectrophotometric determination, charge-transfer reaction, TCNQ, pharmaceutical preparations

1. Introduction

The discovery of 3-hydroxy-3-methylglutaryl coenzyme-A (HMG-CoA) reductase inhibitors, called statins, was a breakthrough in the prevention of hypercholesterolemia and related diseases. Statins specifically inhibit HMG-CoA reductase by competition, the enzyme that catalyzes the conversion of HMG-CoA to mevalonate, which is an early rate-limiting step in cholesterol biosynthesis in the body. These agents are highly effective in reducing total cholesterol and the low-density lipoprotein levels in several forms of hypercholesterolemia.¹⁻⁴

Statins have been available in the market for the past 30 years.⁵,⁶ Lovastatin is a natural product; simvastatin and pravastatin are semisynthetic products; and atorvastatin, fluvastatin, rosuvastatin, and pitavastatin are completely synthetic compounds.

Since lovastatin is not a major cholesterol-lowering drug used therapeutically in the treatment of hypercholesterolemia and pravastatin is not currently used in Turkey, these drugs were not included in this study.

Atorvastatin calcium (ATV) [R-(R, R*)]-2-(4-fluorophenyl)-β,δ-dihydroxy-5(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrole-1-heptanoic acid, calcium salt, fluvastatin sodium (FLV) [R*,S*-(E)]-[(±)-7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-6-heptenoic acid, monosodium salt, pitavastatin calcium (PTV), monocyclic bis (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolyl]-3,5-dihydroxy-6-heptenoate, rosuvastatin calcium (RSV), bis[(E)-7[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methyl-sulphonyl)]

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amino|pyrimidin-5-yl|(3R,5S)-3,5-dihydroxyhept-6-enio acid| calcium salt, and simvastatin (SMV), 2, 2-dimethyl-1, 2, 3, 7, 8, 8a-hexahydro-3, 7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)-ethyl]-1-naphthalenyl ester (Figure 1) are the most commonly used statins in the treatment of hyperlipidemia. Several analytical methods such as spectrophotometric, high performance liquid chromatographic (HPLC), high performance thin layer chromatography (HPTLC) and electroanalytical techniques are reported for the determination of these drugs simultaneously or alone in bulk drug and formulations.

To the best of our knowledge, there is no report available on the spectrophotometric determination of these drugs based on a charge transfer reaction with 7,7,8,8-tetracyanoquinodimethane (TCNQ).

A significant advantage of spectrophotometric methods, unlike other analytical methods, is the simplicity and low cost of the instrument. The sensitivity in terms of molar absorptivity and the precision of the methods

![Chemical structures of statins](image)

**Figure 1.** Chemical structure of statins, (A): ATV, (B): FLV, (C): PTV, (D): RSV, (E): SMV.
are very suitable for the determination of drugs in pure and dosage forms. Therefore, we decided to develop visible spectrophotometric determination of these drugs using TCNQ reagent. TCNQ has been widely used as the reagent for visible spectrophotometric methods of a number of n-electron donor drugs. These methods are based on the blue colored TCNQ•− radical anion formed by interaction of the drugs (as base) with the reagent in acetonitrile at room temperature. Because of the wide applicability of the proposed method, it is suggested for routine quality control assay of the drugs in pure form and its pharmaceutical preparations.

2. Experimental

2.1. Apparatus

Spectrophotometric measurements were carried out using a Shimadzu UV-160 A spectrophotometer with 1-cm glass cells.

2.2. Reagents and solutions

ATV and its pharmaceutical preparation Ator film tablet®, containing 20 mg of atorvastatin calcium per tablet, were kindly supplied by Sanovel Pharmaceuticals (İstanbul, Turkey). FLV and its pharmaceutical preparation Lescol capsule®, containing 40 mg of fluvastatin per capsule, were kindly supplied by Novartis Pharmaceuticals (İstanbul, Turkey). PTV and its pharmaceutical preparation Livalo film tablet®, containing 2 mg of PTV per tablet, were kindly supplied by Kowa Pharmaceuticals (Japan). RSV and its pharmaceutical preparation Crestor film tablet®, containing 20 mg of RSV per tablet, were kindly supplied by Astra Zeneca Pharmaceuticals (İstanbul, Turkey). SMV and its pharmaceutical preparation Zocor film tablet®, containing 20 mg of SMV per tablet, were kindly supplied by Nobel Pharmaceuticals (İstanbul, Turkey). TCNQ was obtained from Merck (Darmstadt, Germany). All chemicals and reagents were of analytical-reagent grade.

Stock solutions were prepared by dissolving 100 mg of ATV, FLV, PTV, RSV, and SMV (equivalent to 100 mg of these drugs' bases) in acetonitrile (RSV, SMV), methanol (FLV), acetonitrile–methanol mixture (4:1) (ATV), and methanol–water mixture (4:1) (PTV) in a 100-mL volumetric flask to give a concentration of 1.0 mg mL⁻¹ of drugs.

The drugs' base solutions were prepared. For this purpose, appropriate volumes of the stock solutions were transferred to a stoppered tube and 1 mL of 5 N NaOH (for ATV and RSV) and 0.1 M acetate buffer solution pH 4 (for PTV and SMV) were added. Two 5-mL portions of chloroform (for ATV, RSV) and two 5-mL portions of methyl tertiary butyl ether:ethyl acetate (1:1) mixtures (for PTV, SMV) were added for the extraction. Extracts were dried using anhydrous Na₂SO₄ and evaporated to dryness under nitrogen with mild heating. The residues were dissolved with acetonitrile in 20-mL volumetric flasks using an ultrasonic bath. Acetonitrile was added to the mark (100 μg mL⁻¹ as the base). FLV's base solution was not prepared since it gave the reaction directly with TCNQ reagent.

In acetonitrile 0.2% TCNQ solution was prepared. The solution was stable for 1 week at 4 °C.

2.3. Choice of solvent

Different solvents, namely chloroform, acetonitrile, acetone, ethanol, 1,4-dioxan, methanol, and methylene chloride, were investigated in order to select the most suitable one.
2.4. Reagent concentration

The effect of TCNQ concentration (%, w/v) on its reaction with the statins was investigated. For this purpose, various concentrations (%, w/v) of TCNQ solution were added to a fixed concentration of statins.

2.5. Reaction time and temperature

The optimum reaction time was determined by following the color development at room temperature and 60–80 °C.

2.6. Stoichiometry of the reaction

The molar ratio of TCNQ to given drugs in the reaction mixture was studied according to Job’s method of continuous variation.45

2.7. General procedure

Aliquots of 0.02–0.240 mL of the stock (for FLV) or drugs’ base solutions were pipetted into a series of 5.0-mL volumetric flasks, 1.0 mL of TCNQ solution was added, and acetonitrile was added to make them up to the volume. The reaction mixture was allowed to stand for 5 min at room temperature and then the absorbance of the resulting solutions was measured at 843 nm against a reagent blank treated similarly.

2.8. Assay procedure for pharmaceutical preparations

Ten capsules or tablets were weighed and powdered using a pestle and mortar. An accurately weighed portion of the powder, equivalent to 1 tablet weight for each drug, was transferred into a 100-mL volumetric flask. Then a 50-mL portion of acetonitrile (for RSV and SMV), methanol (for FLV), acetonitrile–methanol mixture (4:1) (for ATV), methanol–water mixture (4:1) (for PTV) was added into the flask containing powdered drug substance. The mixture was shaken mechanically for 5 min, sonicated in an ultrasonic bath for 30 min, diluted to the volume with solvent above, mixed, and filtered through a filter. Drug base solutions were prepared (except SIM) as described in the Reagents and Solutions section with an appropriate aliquot of the filtrate and assayed as described in the General Procedure section.

2.9. Method validation

Validation studies were performed according to International Conference on Harmonization guidelines.46

Selectivity of the method was studied with a mixture of commonly tablet excipients such as starch, magnesium stearate, lactose, glucose, fructose, sucrose, talc, cellulose, and titanium dioxide.

The calibration graph was constructed by considering the absorbance measured at 5 concentration levels of each of statins (5 determinations for each level).

The limits of detection (LOD) and limits of quantitation (LOQ) were determined using the formula: LOD or LOQ = \( \kappa \) SD\( a \)/b, where \( \kappa = 3 \) for LOD and 10 for LOQ, SD\( a \) is the standard deviation of the intercept, and b is the slope.

The inter- and intra-day precision were examined by analysis of standards for the same day and 5 consecutive days (each \( n = 5 \)).

To check the accuracy of the proposed methods, the standard addition technique was applied. A different amount of pure sample solution was added to 3 different concentrations of the standard drug solutions and
assayed. The percent recovery of the added standard to the assay samples was calculated from:

\[
\text{Recovery \%} = \left[ \frac{(C_t - C_u)}{C_a} \right] \times 100
\]

where \( C_t \) is the total concentration of the analyte found, \( C_u \) is the concentration of the analyte present in the formulation, and \( C_a \) is the concentration of the pure analyte added to the formulation.

The robustness of the proposed method was examined by evaluating the influence of small variations in the procedure variables, such as time of the reaction (5 ± 0.5 min) and added reagent volume (1.0 ± 0.05 mL).

The applicability of the proposed method was tested by the determination of drugs in their pharmaceutical preparations.

3. Results and discussion

ATV, FLV, PTV, RSV, and SMV are the most common statins used in hyperlipidemia. To the best of our knowledge, visible spectrophotometric determination of these drugs in tablets based on a charge transfer reaction with TCNQ has not been described. Therefore, visible spectrophotometric analyses using TCNQ reagent were developed for the determination of these drugs in tablets. The developed methods are based on the reaction of these statins as n-electron donors with TCNQ as a \( \pi \)-acceptor to give highly colored complex species. \( \pi \)-Acceptors are known to yield charge transfer complexes and radical anions with a variety of electron donors. The drug–TCNQ charge transfer complexes in polar solvent are given in the Scheme.

\[
\begin{align*}
\text{Scheme} \\
\tilde{D} + A & \rightarrow (D - A) \xrightarrow{\text{polar solvent}} \tilde{D} + \tilde{A} \\
\text{Donor} & \quad \text{Acceptor} \\
\text{Radical anion} & 
\end{align*}
\]

The interaction of statins with TCNQ in acetonitrile yielded a bluish-green colored chromogen, which absorbs maximally at wavelength 843 nm (Figure 2).

The influence of different parameters on color development was studied to determine optimum conditions.

3.1. Choice of solvent

Acetonitrile is considered an ideal solvent for the color reaction as it offers solvent capacity and gives the highest yield of the radical as indicated by high \( \varepsilon \) values.

3.2. Reagent concentration

It is found that when various concentrations (by volume) of TCNQ solution were added to a fixed concentration of statins 1.0 mL of 0.2\% (w/v) TCNQ was sufficient for quantitative determination of statins (Figure 3).

3.3. Reaction time and temperature

Complete color development was attained after 5 min at room temperature (Figure 4). The resultant complexes were stable up to 24 h at room temperature in the dark.
3.4. Stoichiometry of the reaction

Utilizing equimolar solution of drugs and TCNQ, the reaction stoichiometry was found to be close to 1:1 ratio (drug to reagent), confirming that 1 molecule of these drugs reacts with 1 molecule of TCNQ (Figure 5).

3.5. Method validation

Experiments showed that there was no interference from the additions and excipients, e.g., lactose, glucose, fructose, magnesium stearate, and starch.

A linear relationship was found with between the absorbance at $\lambda_{\text{max}}$ and the concentration of the drug in the ranges 4–20 $\mu$g mL$^{-1}$, 4–12 $\mu$g mL$^{-1}$, 0.8–2.4 $\mu$g mL$^{-1}$, 4–14 $\mu$g mL$^{-1}$, and 2.5–20 $\mu$g mL$^{-1}$ for ATV, FLV, PTV, RSV, and SMV, respectively. Regression equations of the developed methods are given in Table 1.

While LOD values were 1.3863, 0.3097, 2.2341, 0.0428, and 0.0852 $\mu$g mL$^{-1}$; LOQ values were 4.6210, 1.0322, 7.4471, 0.1427, and 0.2840 $\mu$g mL$^{-1}$ for ATV, FLV, RSV, PTV, and SMV, respectively.
Table 1. Regression equations of developed methods.

<table>
<thead>
<tr>
<th>Regression equation*</th>
<th>Slope ± SD</th>
<th>Intercept ± SD</th>
<th>Correlation coefficient, r</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV ( A = 0.0495C - 0.0182 )</td>
<td>0.0495 ± 0.0012</td>
<td>-0.0182 ± 0.0059</td>
<td>0.9994</td>
</tr>
<tr>
<td>RSV ( A = 0.0677C - 0.2468 )</td>
<td>0.068 ± 0.002</td>
<td>-0.2467 ± 0.005</td>
<td>0.9997</td>
</tr>
<tr>
<td>FLV ( A = 0.0752C - 0.2262 )</td>
<td>0.0736 ± 0.0026</td>
<td>-0.2233 ± 0.0078</td>
<td>0.9986</td>
</tr>
<tr>
<td>SMV ( A = 0.0405C + 0.0137 )</td>
<td>0.0405± 0.0002</td>
<td>0.0139 ± 0.0012</td>
<td>0.9994</td>
</tr>
<tr>
<td>PTV ( A = 0.3838C - 0.036 )</td>
<td>0.3807 ± 0.0043</td>
<td>-0.0361 ± 0.0055</td>
<td>0.9998</td>
</tr>
</tbody>
</table>

\* \( A = a + bC \) (where \( C \) is the concentration of drug in \( \mu g \text{ mL}^{-1} \), \( A \) is the absorbance at \( \lambda_{\text{max}} \)).

In the precision study, the RSD values were 0.88%–3.02% for intra-day precision and 1.22%–3.42% for inter-day precision. The obtained results indicate good precision and are summarized in Table 2.

The standard addition method was applied for recovery studies and the results obtained are shown in Table 3. The average percent recoveries obtained were 100.12%–100.81%, indicating good accuracy of the methods.

The proposed methods were stable to small variations in the procedure variables such as time of the reaction (5 ± 0.5 min) and added reagent volume (1.0 ± 0.05 mL).

Table 2. The results of validation parameters for proposed methods.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Statins</th>
<th>ATV</th>
<th>FLV</th>
<th>RSV</th>
<th>PTV</th>
<th>SMV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linearity range ( a ) (( \mu g \text{ mL}^{-1} ))</td>
<td></td>
<td>4.0–20.0</td>
<td>4.0–12.0</td>
<td>4.0–14.0</td>
<td>0.8–2.4</td>
<td>2.5–20.0</td>
</tr>
<tr>
<td>Intra-day ( b ), RSD %</td>
<td></td>
<td>1.77</td>
<td>1.09</td>
<td>1.58</td>
<td>1.38</td>
<td>0.88</td>
</tr>
<tr>
<td>Inter-day ( c ), RSD %</td>
<td></td>
<td>1.90</td>
<td>1.54</td>
<td>1.77</td>
<td>1.73</td>
<td>1.22</td>
</tr>
<tr>
<td>LOD (( \mu g \text{ mL}^{-1} ))</td>
<td></td>
<td>0.3553</td>
<td>0.3097</td>
<td>0.2225</td>
<td>0.0428</td>
<td>0.0852</td>
</tr>
<tr>
<td>LOQ (( \mu g \text{ mL}^{-1} ))</td>
<td></td>
<td>1.1842</td>
<td>1.0322</td>
<td>0.7416</td>
<td>0.1427</td>
<td>0.2840</td>
</tr>
</tbody>
</table>

\( ^a \)Average of 6 determinations, \( ^b \) \( n = 5 \) corresponds to replicate analysis for each level

\( ^c \)Results of 5 different days

The applicability of the proposed method was tested by the determination of drugs in their pharmaceutical preparations. The results obtained were satisfactorily accurate and precise as indicated by the excellent % recovery and RSD < 2 (Table 4).

The results obtained were compared statistically by Student’s t-test (for accuracy) and the variance ratio F-test (for precision) with those obtained by the official methods for FLV\(^{47}\), SMV\(^{47}\), and ATV\(^{48}\), and reference methods for RSV\(^{21}\) and PTV\(^{30}\). The values of t- and F-tests obtained at 95% confidence level did not exceed the theoretical tabulated values, indicating no significant difference between the methods compared (Table 5).
Table 3. The results of recovery studies obtained with standard addition method.

<table>
<thead>
<tr>
<th>Statins</th>
<th>Total amount found* (μg mL⁻¹) (Mean ± S.D.)</th>
<th>Recovery (%)</th>
<th>RSD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV¹</td>
<td>2.0 10.031 ± 0.051</td>
<td>100.31</td>
<td>0.51</td>
</tr>
<tr>
<td></td>
<td>4.0 12.031 ± 0.04</td>
<td>100.26</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td>6.0 14.057 ± 0.03</td>
<td>100.41</td>
<td>0.22</td>
</tr>
<tr>
<td>FLV²</td>
<td>2.0 6.044 ± 0.033</td>
<td>100.74</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>4.0 8.047 ± 0.026</td>
<td>100.59</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>6.0 10.024 ± 0.020</td>
<td>100.25</td>
<td>0.20</td>
</tr>
<tr>
<td>RSV³</td>
<td>2.0 8.032 ± 0.053</td>
<td>100.41</td>
<td>0.66</td>
</tr>
<tr>
<td></td>
<td>4.0 10.061 ± 0.074</td>
<td>100.61</td>
<td>0.73</td>
</tr>
<tr>
<td></td>
<td>6.0 12.060 ± 0.030</td>
<td>100.50</td>
<td>0.24</td>
</tr>
<tr>
<td>PTV⁴</td>
<td>0.2 1.209 ± 0.006</td>
<td>100.81</td>
<td>0.54</td>
</tr>
<tr>
<td></td>
<td>0.4 1.401 ± 0.007</td>
<td>100.12</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>0.8 1.807 ± 0.003</td>
<td>100.40</td>
<td>0.22</td>
</tr>
<tr>
<td>SMV⁵</td>
<td>3.0 8.048 ± 0.037</td>
<td>100.61</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>5.0 10.056 ± 0.049</td>
<td>100.56</td>
<td>0.49</td>
</tr>
<tr>
<td></td>
<td>7.0 12.048 ± 0.062</td>
<td>100.40</td>
<td>0.51</td>
</tr>
</tbody>
</table>

¹Ator tablet®, containing 20 mg of ATV per tablet  
²Lescol tablet®, containing 40 mg of FLV per tablet  
³Crestor tablet®, containing 20 mg of RSV per tablet  
⁴Livalo tablet®, containing 2 mg of PTV per tablet  
⁵Zocor tablet®, containing 20 mg of SMV per tablet  
*Five independent analyses, †Standard deviation

Table 4. The results of analysis of drugs in tablets.

<table>
<thead>
<tr>
<th>Statins</th>
<th>Mean* ± S.D. †</th>
<th>Recovery (%)</th>
<th>RSD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV¹</td>
<td>19.96 ± 0.185</td>
<td>99.65</td>
<td>0.927</td>
</tr>
<tr>
<td>FLV²</td>
<td>40.574 ± 0.359</td>
<td>101.436</td>
<td>0.884</td>
</tr>
<tr>
<td>RSV³</td>
<td>19.69 ± 0.277</td>
<td>98.437</td>
<td>1.406</td>
</tr>
<tr>
<td>PTV⁴</td>
<td>1.988 ± 0.033</td>
<td>99.390</td>
<td>1.659</td>
</tr>
<tr>
<td>SMV⁵</td>
<td>20.023 ± 0.273</td>
<td>100.115</td>
<td>1.363</td>
</tr>
</tbody>
</table>

¹Ator tablet®, containing 20 mg of ATV per tablet  
²Lescol tablet®, containing 40 mg of FLV per tablet  
³Crestor tablet®, containing 20 mg of RSV per tablet  
⁴Livalo tablet®, containing 2 mg of PTV per tablet  
⁵Zocor tablet®, containing 20 mg of SMV per tablet  
*Five independent analyses, †Standard deviation
**Table 5.** Statistical evaluations of the results obtained by proposed and reference methods for the assay of drugs in pharmaceutical preparations \((n = 5)\).

<table>
<thead>
<tr>
<th>Statistical value</th>
<th>ATV</th>
<th>FLV</th>
<th>RSV</th>
<th>PTV</th>
<th>SMV</th>
<th>Ref. Method&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Ref. Method&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Ref. Method&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Ref. Method&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Ref. Method&lt;sup&gt;e&lt;/sup&gt;</th>
<th>Ref. Method&lt;sup&gt;f&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD</td>
<td>19.98 ± 0.167</td>
<td>20.01 ± 0.345</td>
<td>39.93 ± 0.367</td>
<td>20.31 ± 0.375</td>
<td>19.94 ± 0.298</td>
<td>20.04 ± 0.023</td>
<td>20.07 ± 0.198</td>
<td>19.88 ± 0.256</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recovery (%)</td>
<td>99.9</td>
<td>100.05</td>
<td>99.82</td>
<td>101.55</td>
<td>100.2</td>
<td>101.4</td>
<td>100.35</td>
<td>99.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RSD (%)</td>
<td>0.835</td>
<td>1.72</td>
<td>0.919</td>
<td>1.846</td>
<td>1.147</td>
<td>1.923</td>
<td>0.986</td>
<td>1.287</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t-test of significance **</td>
<td>1.13</td>
<td>1.12</td>
<td>0.29</td>
<td>1.28</td>
<td>1.13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F-test of significance **</td>
<td>1.28</td>
<td>0.703</td>
<td>2.37</td>
<td>1.39</td>
<td>1.28</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tbody>
</table>

<sup>a</sup>Ator tablet® (20 mg ATV)  <sup>b</sup>Lescol tablet® (40 mg FLV)  <sup>c</sup>Crestor tablet® (20 mg RSV)  <sup>d</sup>Livalo tablet® (2 mg PTV)  <sup>e</sup>Zocor tablet® (20 mg SMV)

<sup>f</sup>Five independent analyses  <sup>**</sup><sup>P = 0.05, t = 2.23, F = 5.05</sup>
4. Conclusion

The aim of this study was to develop simple, fast, validated, and very economical spectrophotometric methods for analyzing ATV, FLV, RSV, PTV, and SMV in their pharmaceutical preparations. The developed methods were based on a charge transfer reaction with TCNQ reagent. The proposed methods are nearly the same or more sensitive\textsuperscript{11,16,18} and time saving\textsuperscript{9,13,14} than other published spectrophotometric methods. Moreover, the proposed methods are less expensive than the application of HPLC techniques.\textsuperscript{20–30} The described methods are suitable for the determination of statins in pharmaceutical formulations without interference from excipients and could be easily applied in quality control laboratories for the routine analysis of these drugs in raw material and pharmaceutical formulations.

References