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# Capillary Electrophoresis Determination of Pravastatin and Separation of Its Degradation Products

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A capillary zone electrophoresis method for pravastatin determination was developed and validated. Rapid migration of negatively charged pravastatin molecule was obtained in alkaline buffer by the application of electric field of 30 kV. Influence of the pH value and ionic strength of running buffer, applied voltage and capillary temperature on mobility and sensitivity was evaluated. Detection wavelength was set to 237 nm. The method was applied to the determination of the drug in pharmaceutical dosage form. Pravastatin is a  $\delta$ -hydroxy acid, which is prone to lactonize and epimerize in a pH-dependent manner. Micellar electrokinetic chromatographic approach was chosen to develop a method able to separate pravastatin and its degradation products in acidic media. The proposed method allows baseline separation of hydroxy acid and neutral lactone forms of the drug that appear as interconversion products depending on the pH value.

*Keywords*  
pravastatin  
capillary zone electrophoresis  
pharmaceuticals  
micellar electrokinetic chromatography  
degradation products

## INTRODUCTION

Pravastatin is a cholesterol-lowering compound that competitively inhibits the microsomal enzyme 3-hydroxy-3-methylglutaryl-co-enzyme A (HMG-CoA) reductase, a rate-limiting enzyme in the cholesterol biosynthetic pathway. Although the HMG-CoA reductase inhibitors (statins) are structurally related, only pravastatin has a hydroxyl substituent on the hexahydronaphthalene nucleus (Figure 1). Pravastatin is characterized as one of the best statins due to the hydroxyl group which causes higher hydrophilicity than other statins.<sup>1</sup>

Pravastatin possesses an alkyl chain terminated with a carboxylic acid group and bearing two hydroxyl groups at the  $\beta$  and  $\delta$  positions with respect to the carboxylic acid group. The carboxylic acid group and the hydroxyl group at the  $\delta$  position are prone to lactonize, as shown

in Figure 1. Lactonizable compounds such as statins may exist in the free acid form or the lactone form or as an equilibrium mixture of both forms.<sup>2</sup> Lactonization causes processing difficulties in the manufacture of statin drugs. Consequently, great care must be exercised when handling lactonizable compounds in order to isolate them in high yields.

All statins share an HMG-like pharmacophore, which may be present in the active hydroxy-acid form or in the inactive prodrug lactone form. *In vivo*, prodrug lactones are enzymatically hydrolyzed to their hydroxy-acid pharmacophores.<sup>3</sup> Pravastatin is administered to patients in its active form as the hydroxyl acid sodium salt. The drug exists in solution with its lactone equilibrium product in a pH-dependent manner. At acidic pH, the hydroxy acid form of pravastatin can reversibly lactonize. Additional-

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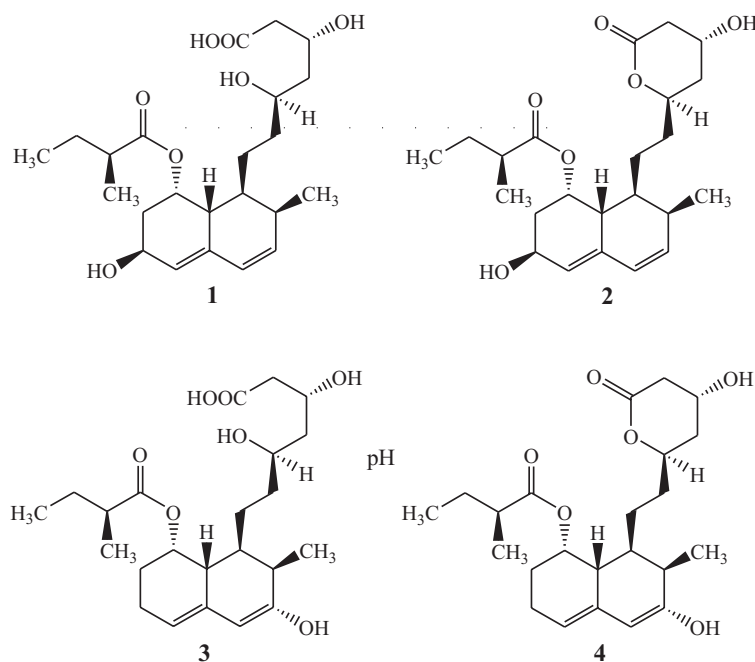


Figure 1. Structures of pravastatin (**1**), pravastatin lactone (**2**), C-6-epimer of pravastatin (**3**) and its lactone form (**4**).

ly, pravastatin is also susceptible to an isomerization reaction at acidic pH, which is relatively rapid.<sup>4</sup> The C-6 position is bis-allylic and, hence, the C-6 atom is prone to epimerize.

Statins are now among the most frequently prescribed drugs for reducing LDL cholesterol and triglyceride levels in the blood stream of patients at risk of cardiovascular disease.<sup>5</sup> For this reason, rapid and effective ways for the determination of these drugs are desirable. In addition, treatment with statins is very long and thus the purity of these drug substances is of great importance. Development of simple and selective methods for monitoring their potential impurities is highly required. Several HPLC methods for the analysis of pravastatin have been developed using UV,<sup>6–9</sup> fluorescence<sup>10</sup> and MS-MS detection.<sup>11–16</sup> Voltammetry was also used for drug quantitation.<sup>17</sup> However, capillary electrophoretic methods proposed for the determination of pravastatin are scarce.<sup>18</sup> Micellar electrokinetic chromatography (MEKC) has been used for its determination in production media.<sup>19</sup> Capillary electrophoresis has been applied to the screening of anionic impurities in bulk drug and determination of pravastatin  $pK_a$  value.<sup>20,21</sup> The official method in assay procedures of pravastatin listed in the European Pharmacopoeia and its pharmaceutical product described in USP is the HPLC method with UV detection (retention time about 21 min).<sup>22</sup>

Application of capillary zone electrophoresis (CZE) by the pharmaceutical industry is mainly due to the wide range of possible benefits that may be obtained compared to the well-established and widely used HPLC technique. Principal advantages include improvements in cost

efficiency and solvent avoidance. Capillary electrophoresis may be easier and faster for a number of analyses.

The present work was aimed at developing a reliable and simple method with a short run time for the determination of pravastatin using CZE. The proposed method has been applied to determination of the drug in a pharmaceutical formulation. MEKC approach was chosen to develop a method able to separate the drug and its interconversion products in acidic media.

## EXPERIMENTAL

### Materials

Pravastatin sodium, kindly supplied by Pliva (Zagreb, Croatia), was used without any purification. The quality of the drug is high enough to comply with the European Pharmacopoeia (98.1 %). Stock solution was prepared in water at a concentration of 0.1 mg mL<sup>-1</sup> and stored at 4 °C in a refrigerator.

Standard solutions were prepared daily by diluting the stock solution with water just before use in a concentration range from 1 to 100 µg mL<sup>-1</sup>. Water used for the preparation of standard solutions and running buffers was purified by a Milli-Q system. All the other chemicals used were of analytical reagent grade quality (Merck or Sigma).

### Apparatus

Capillary electrophoresis experiments were performed on an Agilent CE system (Agilent Technologies, Waldbronn, Germany), equipped with a diode array detector. The data were collected using the <sup>3D</sup>CE/MSD ChemStation software ver. A 10.02. Uncoated fused-silica capillaries (Agilent Techno-

logies) of 48.5 cm total length (effective length to detector 40 cm) and 50  $\mu\text{m}$  internal diameter were used. An alignment interface, containing an optical slit matched to the internal diameter, was employed and the detection wavelength was adjusted to 237 nm. The applied voltage was held constant at different values ranging within 10–30 kV. All the electrophoretic runs were carried out at constant temperature. The temperature inside the capillary cartridge was maintained within the 20–40  $^{\circ}\text{C}$  range.

### Analytical Procedure

At the beginning of each working day, the capillary was rinsed with 0.1 mol  $\text{L}^{-1}$  NaOH for 5 min under high pressure, followed by rinsing with water (10 min) and running buffer (5 min). Repeatability of migration times was found to be dependent on the rinse procedure. The capillary was flushed between the runs with BGE for 5 min to ensure assay reproducibility. As electrolysis of the background electrolyte solutions can change the electroosmotic flow, which leads to poor quantitative assays, the running buffer was replaced with a fresh electrolyte after three injections.

Samples were injected into the capillary on the anodic side by 50 mbar pressure for 4 s. Before the injection into the CE system, each solution (sample solutions and running buffer) was subjected to filtration through 0.2  $\mu\text{m}$  Acrodisc GHP filters (Gelman, Ann Arbor, USA). Electrophoresis was carried out by applying high voltage to the capillary, with the cathode being at the detector end.

The BGE solutions used for CZE were prepared from sodium tetraborate by adjusting to the desired pH with 0.1 mol  $\text{L}^{-1}$  hydrochloric acid or 0.1 mol  $\text{L}^{-1}$  sodium hydroxide.

Sample solution of pravastatin for monitoring its degradation products using capillary electrophoresis was prepared at a concentration of 75  $\mu\text{g mL}^{-1}$  in acidic media (pH = 2). Borate buffer (25 mmol  $\text{L}^{-1}$ , pH = 9.3) with 25 mmol  $\text{L}^{-1}$  sodium dodecyl sulphate (SDS) was used for micellar electrokinetic chromatographic measurements.

### Pharmaceutical Formulation Analysis

Pravastatin tablets (Pravachol, 20 mg) were purchased from the local market. Pravachol contains the following excipients: croscarmellose sodium, lactose, magnesium oxide, magnesium stearate, microcrystalline cellulose, povidone and yellow ferric oxide. A powdered sample of drug formulation equivalent to the average weight of one tablet was transferred into a 50 mL calibrated flask and purified water was added (30 mL). The mixture was sonicated for 5 min to provide complete dissolution and was made up to the mark with purified water. Appropriate solutions were prepared by taking suitable aliquots of the clear supernatant and diluting them with purified water to give a final analyte concentration (20, 35, 50 and 65  $\mu\text{g mL}^{-1}$ ). Tablet sample solutions were then analyzed in the same way as standard solutions by the proposed CZE method. Solutions were filtered through 0.2  $\mu\text{m}$  filters before injection to the CE system. For recovery experiments, known quantities of pure drug were added to the different pre-analyzed samples of a com-

mercial formulation. Total amount of the drug was then determined using the proposed CZE method and the amount of the added drug was calculated by the difference.

## RESULTS AND DISCUSSION

### Capillary Zone Electrophoresis

In an attempt to find the suitable pH value and ionic strength for the running buffer and considering the molecular structure of pravastatin that provides information on its acido-base properties, the influence of pH and buffer ionic strength on mobility, sensitivity and speed were carefully evaluated. Buffer pH has an influence on the degree of ionization of the molecules, their electrophoretic mobility as well as on the control of the electroosmotic flow. Pravastatin structure suggests that a capillary zone electrophoresis method could be used under alkaline conditions for determination of this drug. As reported in the literature,<sup>23</sup> pravastatin has a  $\text{pK}_a$  value of 4.2. The drug is completely in the anionic form above pH = 6. Therefore, the working pH has to be above this pH value, so that pravastatin can be ionized and analyzed using CZE. On the other hand, the alkaline buffer will generate strong electroosmotic flow, allowing for shorter analysis time. Borate buffer solutions in the pH range between 7.5 and 10 were investigated. Within the studied pH range, the best results were at pH = 9.3, which provided a good compromise among the migration time, peak shape and sensitivity of the method (Figure 2).

The effect of ionic strength of the buffer on analysis time was assessed at a constant pH of 9.3. As the concentration was changed from 20 to 30 mmol  $\text{L}^{-1}$ , a small increase in pravastatin migration time was obtained. It is suggested that this effect is related to lower electroosmotic flow, resulting from a decrease of the zeta potential at the capillary wall-solution interface.<sup>24</sup> Efficiency of the assay, expressed as the number of theoretical plates, was

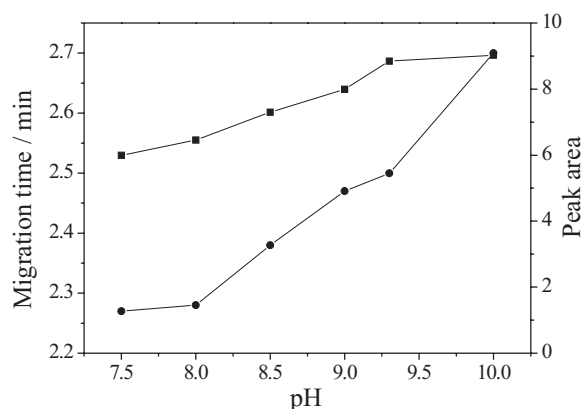


Figure 2. Effect of running buffer pH on the migration time (circles) and peak area (squares) of pravastatin (50  $\mu\text{g mL}^{-1}$ ). Operating conditions: 25 mmol  $\text{L}^{-1}$  borate buffer, voltage 30 kV, 20  $^{\circ}\text{C}$ , detection wavelength 237 nm, hydrodynamic injection 50 mbar, 4 s.

calculated using the formula  $N = 5.545 (l/w)^2$ , where  $N$  = number of theoretical plates,  $l$  = effective capillary length and  $w$  = peak width. A plot of  $N$  vs. borate concentration was constructed and  $25 \text{ mmol L}^{-1}$  was selected as the optimum borate concentration for running buffer with a maximum of 232 187 theoretical plates obtained. Addition of SDS as surfactant in the running buffer was also studied. Introduction of anionic detergent SDS ( $25 \text{ mmol L}^{-1}$ ) into borate buffer increases the migration time of pravastatin. This is the reason for choosing CZE instead of micellar electrokinetic chromatography for determination of pravastatin in bulk form and in pharmaceuticals.

The effect of the applied voltage on pravastatin migration time was examined over the range 10–30 kV. Using  $25 \text{ mmol L}^{-1}$  borate buffer at pH = 9.3, the increase of the applied voltage led to shorter migration time. As expected, increasing the applied voltage caused an increase in electroosmotic flow, leading to shorter analysis time of negatively charged pravastatin molecules. Pravastatin determination was performed at a voltage of 30 kV; the current was 45–47  $\mu\text{A}$  under these conditions.

The temperature inside the capillary cartridge also affects solute mobility and the electroosmotic flow. In addition, capillary temperature control is extremely important for assay reproducibility. Influence of temperature on the analysis was investigated for 20, 25, 30, 35 and 40 °C. On increasing the temperature, the migration time of pravastatin as well as the peak area decreased. The 20 °C temperature was chosen for suitable analysis time and good sensitivity.

Through the experiments described above, optimum conditions for the determination of pravastatin were defined. Strong UV absorption at 237 nm allows direct on-line detection by CZE. A typical electropherogram of pravastatin standard solution is given in Figure 3A. The strong electric field and alkaline running buffer generate strong electroosmotic flow, allowing drug determination within 2.55 min. Pravastatin retention time is about 21 min in the assay procedure listed in *Ph. Eur.* using the HPLC with UV detection.<sup>22</sup> Relatively short analysis time is the main advantage of the CZE method. Furthermore, the proposed method offers several advantages over HPLC, including low consumption of reagents and solvents, small sample size, simplicity and inexpensive capillaries.

### Method Validation

After development, experiments were carried out to evaluate the validity of the method for pravastatin determination in raw material and in tablets. In the developed CZE method, linearity of the detector response was established for pravastatin concentration ranging from 5 to  $75 \mu\text{g mL}^{-1}$ . The regression equation of the calibration curve was  $y = 187.64 x - 0.036$  with the correlation coefficient of 0.997 ( $n = 6$ ). The detection limit and the quantification limit were calculated from the calibration curve using the equations:  $\text{LOD} = 3s/m$  and  $\text{LOQ} = 10s/m$  (where  $s$  is the standard deviation of the intercept and  $m$  is the slope of the calibration curve).<sup>25</sup> LOD and LOQ were found to be 0.5 and  $1.8 \mu\text{g mL}^{-1}$ , respectively. Due to the small diameter of the capillary, volumes of the order of nanoliters were injected. For the same reason, the light path at the on-capillary detector window is very short, reducing the signal produced by the sample. Therefore, the detection and quantitation limits are approximately three orders of magnitude higher than LODs and LOQs for some chromatographic methods reported.<sup>26</sup> However, the detection sensitivity achieved using maxima at wavelengths 237 nm was sufficient for drug quantitation in commercially available formulations.

Method precision was determined by measuring repeatability or intra-day precision and inter-day precision of migration times and peak area. Multiple injections ( $n = 6$ ) of the same pravastatin sample solution were carried out to demonstrate the repeatability. The RSDs of migration times were found to be 0.41 % at the  $5 \mu\text{g mL}^{-1}$  level and 0.78 % at the  $25 \mu\text{g mL}^{-1}$  level. Replicate injections of the lowest level of concentration among the calibration graph solutions provided the RSD of the peak area of 1.68 %. Inter-day precision was also evaluated over three different days with newly prepared running buffer and samples by performing six successive injections of four replicate samples on each day. RSDs < 1.1 % were obtained for the inter-day migration times. Three different pravastatin concentrations in the linear range were analyzed in six independent series on the same day and six successive days. The data evaluated by the use of calibration plots are summarized in Table I.

TABLE I. Precision and accuracy of the developed CZE method for pravastatin analysis

Added $\mu\text{g mL}^{-1}$	Intra-day			Inter-day		
	Found <sup>(a)</sup> $\mu\text{g mL}^{-1}$	Precision RSD <sup>(b)</sup> %	Accuracy bias <sup>(c)</sup> %	Found <sup>(a)</sup> $\mu\text{g mL}^{-1}$	Precision RSD <sup>(b)</sup> %	Accuracy bias <sup>(c)</sup> %
10.0	10.09±0.14	1.39	0.90	10.14±0.21	2.07	1.40
25.0	24.89±0.21	0.84	-0.44	24.76±0.23	0.93	-0.96
50.0	50.04±0.47	0.94	0.08	49.95±0.39	0.78	-0.10

<sup>(a)</sup> Mean of five determinations ± SD, <sup>(b)</sup> RSD, relative standard deviation, <sup>(c)</sup> Bias %, [(found – added) / added] × 100



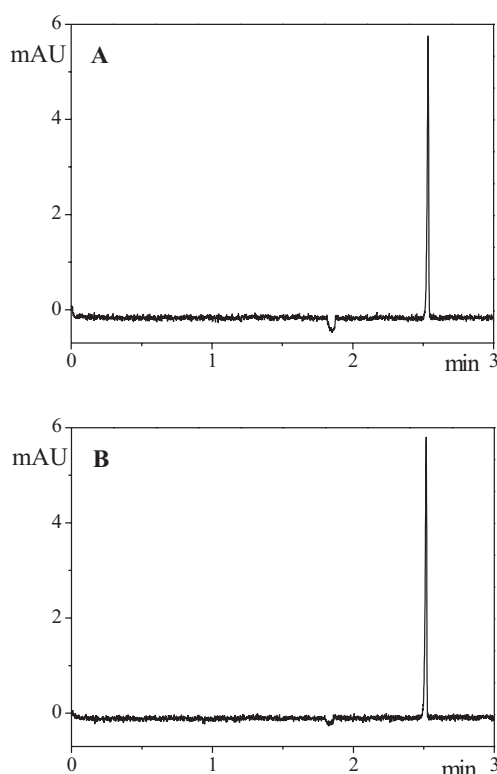


Figure 3. Electropherogram of pravastatin in 25 mmol L<sup>-1</sup> borate buffer, pH = 9.3, (A) in standard solution (25 µg mL<sup>-1</sup>) and (B) in tablet solution (25 µg mL<sup>-1</sup> pravastatin). Operating conditions: voltage 30 kV, 20 °C, detection wavelength 237 nm, hydrodynamic injection 50 mbar, 4 s.

Stability of standard solutions was maintained by leaving the pravastatin solutions (50 µg mL<sup>-1</sup>) in a tightly closed volumetric flask in the refrigerator at 4 °C. The solutions were measured at 6 h intervals for 2 days. They were found to be stable for the period studied.

#### Analytical Application

In order to establish the potentiality of the developed method, a pharmaceutical dosage form of pravastatin was assayed. It was noticed in formulation samples that excipients did not interfere with the peak of interest under the separation conditions (Figure 3B). In addition, the peak purity evaluation revealed that the UV spectra of different parts of the peak were identical, indicating homogeneity of the pravastatin peak in formulation samples. The peak purity factor was found to be 999.6 for pravastatin in the tablet solution. This is a measure of similarity in the shape of the spectra. Accuracy of the method, regarded as the closeness of agreement between the claimed content of tablets and the found value, was 99.2 % (RSD = 1.1 %,  $n = 5$ ). Accuracy was also verified by recovery studies analyzing samples fortified by known quantities of the drug. The assay results for pravastatin formulation are given in Table II. Application of CZE to pravastatin determination in a pharmaceutical prepara-

TABLE II. Determination of pravastatin in a pharmaceutical formulation

Added / µg mL <sup>-1</sup>	Mean recovery <sup>(a)</sup> / %	RSD / %
15.0	98.4	1.5
20.0	99.1	2.1
25.0	99.8	1.3
30.0	100.3	1.4
35.0	99.5	0.9
40.0	101.2	1.1

<sup>(a)</sup> Mean of five determinations

tion resulted in acceptable percent recoveries; therefore, the developed CZE method can be used as an alternative method for the analysis of pravastatin in bulk form and in pharmaceuticals. The best working concentrations are from 25–35 µg mL<sup>-1</sup>. Considering the data relating to the reproducibility in peak area and short and reproducible migration time, it is apparent that the proposed CZE method is a very promising alternative method for the determination of this drug.

#### Micellar Electrokinetic Capillary Chromatography

Pravastatin is a δ-hydroxy acid, which is prone to lactonize and epimerize in a pH-dependent manner. The hydroxy acid form of pravastatin can reversibly lactonize at acidic pH, so the drug exists in solution with its lactone equilibrium product. It was found in the literature that the extent of lactonization is < 6 % over the 30-min experimental period at pH = 2.<sup>27</sup> Pravastatin is also susceptible to an isomerization reaction at acidic pH, which is relatively rapid.<sup>4,28</sup> The above mentioned interconversion compounds of pravastatin represent its related impurities listed in *Ph. Eur* and are also potential biotransformation products.<sup>4,22</sup>

In capillary electrophoresis, the selectivity of the method is fundamentally based on charge-to-volume ratios. The free hydroxyl acid and the lactone forms of pravastatin have different polarities; therefore, capillary electrophoresis can be a procedure with totally different selectivity of these interconversion forms present in acidic solution. The MEKC method was developed for the separation of pravastatin and its degradation products in acidic media. Introduction of SDS in the background electrolyte solutions plays a key role for the separation of negatively charged hydroxyl acid forms and neutral lactone species that migrate at the same rate as the EOF in the CZE method. Separation of neutral pravastatin lactone from each other requires partitioning into charged micelles that migrate at a different rate from the EOF.

Aqueous samples of the drug were acidified (pH = 2) and analyzed immediately and after set intervals. Degradation at pH = 2 was monitored for a period of 4 hours at room temperature. To check the repeatability of drug

degradation, a pravastatin solution was divided into three aliquots. Each aliquot was acidified and analyzed. The presence of 25 mmol L<sup>-1</sup> SDS in the running borate buffer at pH = 9.3 produces very good separation of degradation products. A series of SDS concentrations were evaluated for their effect on the efficiency of degradation product resolution and migration time. The migration time of the compounds increased with an increase in SDS concentration. Further decrease in SDS concentration resulted in decreased efficiencies. Choosing a 25 mmol L<sup>-1</sup> borate buffer, pH = 9.3, addition of 25 mmol L<sup>-1</sup> SDS, applied voltage of 30 kV, and temperature of 20 °C resulted in a complete separation analysis of pravastatin and its degradation products in less than 6.5 min. Under these conditions, the recorded current was lower than 60 μA. The peak purity of separated compounds was obtained by overlaying the spectra captured at the apex, up and down the slope, using a diode-array detector, and no interference was noted. The recorded on-line spectra of the peaks of degradants were found to have the absorption maximum almost at the same wavelength as the pravastatin molecule.

Pravastatin molecule passed the detector window in 3.32 min with addition of 25 mmol L<sup>-1</sup> SDS used for the MEKC method. Significant decrease of pravastatin concentration at pH = 2 was observed within 2 min (Figure 4A). At the same time, new peaks at 2.93 min and 6.19 min were observed. Negative charge on the epimerized compound in alkaline buffer and the literature data<sup>19,27</sup> suggest that the first peak could be attributed to the C-6 epimer of pravastatin. Epimerization was relatively rapidly observed but the equilibrium of interconversion products was established after 70 min. The amount of pravastatin decreased by about 40 % within 20 min after sample acidification and new peaks at 2.82 and 5.44 min were observed (Figure 4B). Since lactone forms are devoid of any ionizable moiety, the slowest migrating compound can be attributed to neutral pravastatin lactone, which should have the highest affinity for the negatively charged micelles. We have therefore concluded that the degradation products observed with UV detection at 6.19 min could be assigned to pravastatin lactone.<sup>27</sup> Slower formation of lactone forms compared to the epimerization rate is also in agreement with literature data.<sup>4,28</sup> The peak at 5.44 min which appeared later, after 15 min of degradation time, could be attributed to the C-6 epimer of pravastatin lactone. Its peak area was found to increase with increasing concentration of the C-6 epimer of pravastatin over time (Figure 4C), so conversion of the C-6 epimer of pravastatin to its lactone form was assumed. Pravastatin and its C-6 epimer are fully charged at pH = 9.3, thus bearing a negative charge, which causes some degree of repulsion between the drug molecules and negatively charged micelles. The C-6 epimer of pravastatin elutes first suggesting, in agreement with previously

reported data, that the partition coefficient between SDS micelles and buffer solutions is different from that of pravastatin.<sup>19</sup> Both negatively charged analytes exhibited migration toward the cathode due to high electroosmotic velocity.

The proposed capillary electrophoresis method allows baseline separation of pravastatin and all its degradation products in acidic media. Separation time of 6.5 min was sufficient for the analysis. Thus the developed MEKC method has a shorter runtime compared to the reported HPLC method for separation of pravastatin related impurities using UV detection.<sup>22</sup> Peak identity was

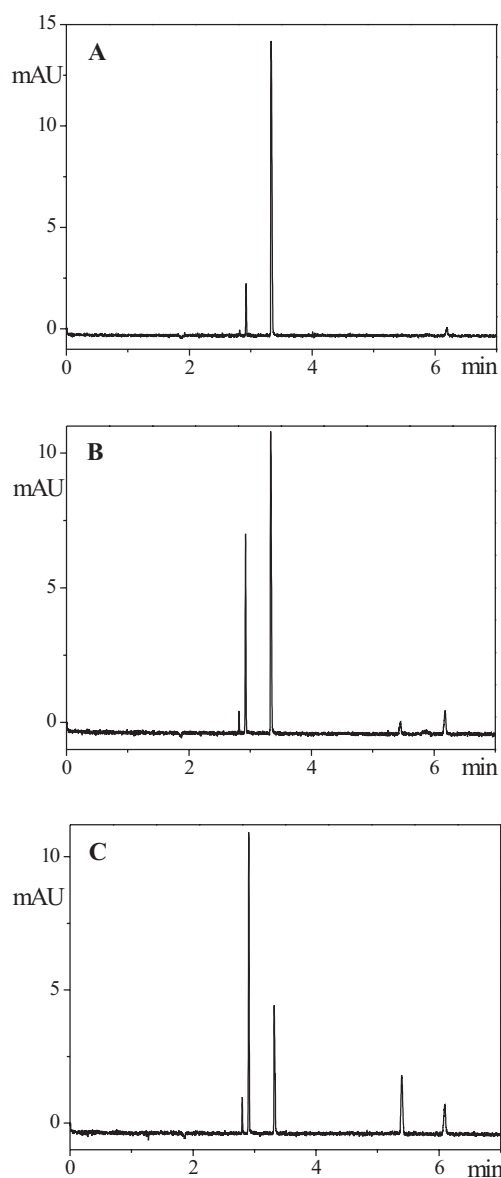


Figure 4. Separation of pravastatin (75 μg mL<sup>-1</sup>) exposed to acidic media (pH = 2) and its degradation products obtained after (A) 2 min, (B) 20 min and (C) 80 min. Separation conditions: 25 mmol L<sup>-1</sup> borate buffer, pH = 9.3, 25 mmol L<sup>-1</sup> SDS, voltage 30 kV, 20 °C, detection wavelength 237 nm, hydrodynamic injection 50 mbar, 4 s.

studied by the spectra recorded using a diode-array detector. However, the UV spectra of pravastatin, C-6 epimer of pravastatin and pravastatin lactones do not differ significantly. The exact identity of separated peaks could be known by comparing the migration time with each degradation product, because UV spectra of all compounds are very similar, or by mass detection, which will be the subject of further investigations. Analysis by MEKC coupling with mass spectrometry could confirm the assumption described above. Although the limit of quantitation of the pravastatin assay using CZE is still high, it is reasonable to predict that the MEKC method could be used for evaluation and quantitation of its degradation products at a low level by capillary electrophoresis using more sensitive mass spectrometric detection.

## CONCLUSIONS

A capillary zone electrophoresis method was developed for determination of pravastatin. The applied voltage of 30 kV and alkaline running buffer, pH = 9.3, generate strong electroosmotic flow that enables determination of a fully charged drug molecule within 2.5 min. Application of the CZE to pravastatin determination in a pharmaceutical dosage form resulted in acceptable deviation from the stated concentration. Therefore, the developed CZE method can be used as an alternative method for the quantitation of pravastatin in bulk form and in pharmaceuticals.

Micellar electrokinetic chromatographic approach was chosen to develop a method able to separate the drug and its degradation products in acidic media. The proposed method allows baseline separation of pravastatin, C-6 epimer of pravastatin and their lactone forms that appear as interconversion products depending on the pH value. The migration times of degradation compounds ranged from 2.8 to 6.2 min.

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**SAŽETAK****Određivanje pravastatina i odjeljivanje njegovih razgradnih produkata kapilarnom elektroforezom****Biljana Nigović i Ivana Vegar**

Razvijena je i validirana metoda kapilarne zonske elektroforeze za određivanje pravastatina. Dobivena je brza pokretljivost negativno nabijenih molekula pravastatina u lužnatom puferu primjenom električnog polja od 30 kV. Istraživan je utjecaj pH i ionske jakosti pufera, primijenjenog napona i temperature u kapilari, na pokretljivost analita i osjetljivost metode pri valnoj duljini detekcije 237 nm. Metoda je primijenjena za određivanje lijeka u farmaceutskom dozirnom obliku. Pravastatin je  $\delta$ -hidroksi kiselina koja je sklona laktonizaciji i epimerizaciji u ovisnosti o pH vrijednosti medija. U razvoju metode odjeljivanja pravastatina i njegovih razgradnih produkata u kiselom mediju korištena je micelarna elektrokinetička kromatografija. Predložena metoda omogućava odjeljivanje hidroksi kiselinskih i neutralnih laktonskih oblika lijeka koji se pojavljuju kao produkti prijelaza ovisno o pH vrijednosti.