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Determination of some drugs by micellar electrokinetic capillary chromatography

The pseudo-effective mobility as parameter for screening

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ABSTRACT

In contrast to capillary zone electrophoresis, micellar electrokinetic capillary chromatography can be applied to the determination of compounds that are uncharged and almost insoluble in water. As a screening parameter, the pseudo-effective mobility is to be preferred to the capacity factor $k'$ because it can be calculated if $t_{MC}$ is unknown, and because it gives a better indication of whether components can be separated or not. Special attention should be paid, however, to the composition of the sample solution. The use of organic solvents to dissolve the sample can influence the separation enormously. Calibration graphs were constructed for some drugs and as an example dapsone in tablets was determined.

INTRODUCTION

Since the introduction of micellar electrokinetic capillary chromatography (MECC) by Terabe and co-workers [1,2], it has proved to be a highly efficient separation method. Amongst others, many compounds of pharmaceutical interest have been separated by MECC, such as vitamins, cephalosporins, penicillins, antipyretic and analgesic preparations, barbiturates and optical isomers of drugs [3-9]. Most papers, however, only present qualitative data and little attention has been paid to quantitative aspects or screening possibilities.

In classical capillary zone electrophoresis with aqueous electrolyte systems, components can only be separated if they are charged and soluble in water. In MECC, however, uncharged compounds and, because of the hydrophobic character of the micelles, compounds that are almost insoluble in water can also be separated.

In this work, we studied the applicability of MECC to the qualitative and quantitative separation of some drugs that are uncharged and almost insoluble in water. Further, the advantage of the use of "pseudo-effective mobility" as a parameter for screening over the use of capacity factors ($k'$) and the effect of methanol in the sample were examined.

THEORETICAL

MECC is a separation technique based on the partitioning of the components over two phases, just as in chromatographic techniques. However, two mobile phases are used, viz., an electroosmotically pumped aqueous mobile phase and the hydrophobic interior of micelles. Often an analogue of the capacity factor, $k'$, is used, which can be calculated according to the equation [1,2]

$$k' = \frac{n_{MC}}{n_w} = \frac{t_S - t_{EOF}}{t_{EOF} \frac{1 - t_S}{t_{MC}}}$$

(1)
where \( n_{MC} \) and \( n_s \) are the total moles of solute in the micelles and in the aqueous phase, respectively, and \( t_s, t_{EOF} \) and \( t_{MC} \) are the migration times of the solute, an appropriate marker (insolubilized component) for the determination of the electroosmotic flow (EOF) and the micelles, respectively.

Application of this concept of \( k' \) in MECC shows that for higher values of \( k' \) very low values of the resolution, \( R_s \) [2], result. Further, a slight inaccuracy in the determination of \( t_s \) leads to a large difference in the calculated \( k' \) value, especially for \( t_s \) values near the \( t_{MC} \). This means that the use of \( k' \) values for screening purposes is limited whereas the suggestion that a large difference between higher values of \( k' \) leads to a separation is false.

Moreover, the EOF can change with time and therefore the \( t_{EOF} \) and the \( t_{MC} \) have to be measured in each experiment in order to calculate the appropriate \( k' \). The \( t_{MC} \) can be obtained by applying a micelle (MC) marker such as Sudan III or anthracene [2,10] or by methods such as extrapolation with iteration or frontal analysis [11]. However, especially when organic co-solvents are used, it is still a subject of discussion how to obtain the "true \( t_{MC} \)". If the velocity of the micelles is small or even negative, \( t_{MC} \) cannot be measured and, according to eqn. 1, \( k' \) can not be calculated, even when the components show normal migration behaviour. For all these reasons \( k' \) is often not suitable for use in MECC.

Another way to describe the migration behaviour of components in MECC is in terms of mobilities [12]. The velocity of the aqueous mobile phase is determined by the mobility of the EOF, \( m_{EOF} \), and that of the micelles by the apparent mobility of the micelles, \( m_{app,MC} \), defined as

\[
m_{app,MC} = m_{eff,MC} + m_{EOF}
\]

where \( m_{eff,MC} \) is the effective mobility of the micelles. The mobilities are negative for anions and positive for cations. For ionic species \( m_{eff} \) can be obtained from the mobility at infinite dilution, correcting for relaxation and retardation effects according to the Debye–Hückel–Onsager theory. For micelles, \( m_{eff,MC} \) will also be strongly dependent on the composition of the micellar phase.

For a given surfactant concentration in a specific electrolyte system, a constant composition of the micellar phase can be expected, through which the effective mobility of the micelles and the \( k' \) for the components must be constant.

In CZE the effective mobility can be used as a parameter for screening [13]. In MECC often uncharged particles with no electrophoretic mobility are analysed. As they are solubilized in the charged micelles for \( k'/(k' + 1) \) part of the time, they will acquire a net velocity of

\[
v_S = \frac{k'}{1 + k'} v_{MC} + \frac{1}{1 + k'} v_{EOF}
\]

or

\[
v_S = \frac{k'}{1 + k'} (m_{eff,MC} + m_{EOF}) E + \frac{1}{1 + k'} m_{EOF} E
\]

or

\[
v_S = \left( \frac{k'}{1 + k'} m_{eff,MC} + m_{EOF} \right) E
\]

where \( v_S, v_{MC} \) and \( v_{EOF} \) are the velocities of the solubilized sample component, the micelle marker and the EOF marker, respectively.

From eqn. 5, it is clear that for uncharged particles pseudo-mobilities can be defined, similar to the mobilities of charged particles, satisfying the conditions

\[
v_S = m_{app,S} F
\]

and

\[
m_{app,S} = m_{app,S} + m_{EOF}
\]

A great advantage of working with pseudo-effective mobilities compared with \( k' \) is that for the calculation of the pseudo-effective mobilities \( t_{MC} \) or \( m_{eff,MC} \) is not required, as can be seen from the equation

\[
m_{eff,S} = m_{app,S} - m_{EOF} = \frac{l_d}{l_d} - \frac{l_d}{l_{EOF}}
\]

where \( l_s \) and \( l_d \) are the total length of the capillary and the length of the capillary from injection to detection, respectively, and \( V \) is the applied voltage.

To demonstrate the effect of a small inaccuracy in the determination of migration times on \( k' \) and pseudo-effective mobilities, we calculated the values of \( k' \) and \( m_{eff,S} \) for several values of \( t_{EOF}, t_s \) and \( t_{MC} \).
with an accuracy in the determination of the $t_s$ of 0.5%. In Table I all calculated values are given.

From Table I, it can be concluded that especially for $t_s$ values near the $t_{MC}$ values a dramatic change in $k'$ results, whereas the pseudo-effective mobilities are nearly constant for small differences in $t_s$.

EXPERIMENTAL

Instrumentation

For all experiments the P/ACE System 2000 HPCE instrument (Beckman, Palo Alto, CA, USA) was used. All experiments were carried out in a fused-silica capillary from Polymicro Technologies (Phoenix, AZ, USA), 50 μm I.D., total length 27.65 cm, distance between injection and detection 20.85 cm. The capillary was treated with 10 A4 hydrochloric acid for 5 h at 160°C in order to obtain a high $m_{EoF}$. The wavelength of the UV detector was 214 nm. All experiments were carried out applying a constant voltage of 10 kV with the anode at the inlet and the cathode at the outlet side. Data analysis was performed using the laboratory-written data analysis program CAESAR.

Separation conditions

For all analyses an electrolyte system of 0.02 M tris(hydroxymethyl)aminomethane (Tris) with 100 mM sodium dodecyl sulphate (SDS) at pH 8.5 adjusted by adding boric acid was used. It must be noted however, that owing to difficulties in preparing reproducible electrolyte compositions, differences can occur in $k'$ or $m_{EoF,s}$ using different batches. In all experiments the sample was introduced by pressure injection for 5 s.

If the capillary tube is filled with a solution of SDS, the UV signal of a solution of 0.001 M mesityl oxide in SDS introduced by pressure injection can be observed after 192 s. This means that with a separation volume of about 410 nl, the volume injected with a 5-s pressure injection is about 11 nl. Although the minimum injection time with our apparatus is 1 s, we chose a pressure injection time of 5 s for the sake of reproducibility.

Chemicals

All drugs were kindly donated by the State Institute for Quality Control for Agricultural Products (RIKILT, Wageningen, Netherlands). Dapsone tablets (OPGFarma 89c08-90067) were obtained at a local pharmacy.

RESULTS AND DISCUSSION

In order to study the applicability of MECC to the analysis of water-insoluble components we selected eight drugs, the structural formulae of which are given in Fig. 1.

For the preparation of a sample mixture, water cannot be used as solvent and therefore we first studied the effect of the presence of methanol in a sample on the separation.

Effect of the presence of methanol in the sample

In order to study the effect of methanol in the sample on $t_{EOF}$ and $t_{MC}$, we prepared three sample solutions of creatinine (which proved to be uncharged and an insolubilized component in this electrolyte system) and Sudan III in 100 mM SDS solution and added methanol to concentrations of 0, 10 and 20%. Three separations were carried out, injecting twice in each separation. The first injection was the sample (a) without, (b) with 10% and (c) with 20% methanol. After a separation for 3 min at 10 kV we injected the sample mixture without methanol in all three instances, whereafter the separation was completed. The three electropherograms are shown in Fig. 2.

As can be seen in Fig. 2a, the time differences between $t_{EOF}$ and $t_{MC}$ of the first injection ($t_1$) and that of the second injection ($t_2$) are equal. By the addition of only 10% methanol to the sample in the first injection (case b), $t_1$ decreases whereas $t_2$ is nearly constant, and in case c a strong decreasing effect on $t_1$ can be seen at constant $t_2$.

The fact that the time intervals between the two $t_{EOF}$ values are nearly constant in all instances means that by the addition of methanol to a sample the velocity of the EOF is not influenced. The sample components, however, show a different migration behaviour. They tend to remain in the methanol plug (EOF) for a longer time, resulting in shorter migration times, owing to a strong solubility effect and a local breakdown of the micelles. The results of this effect on the efficiency of the separations are demonstrated in Fig. 3, where the electropherograms are given for the separation of a mixture of phenol, $p$-cresol and 2,6-xylenol (all at $10^{-4} M$, in all...
TABLE I
CALCULATED CAPACITY FACTORS, $k'$, AND PSEUDO-EFFECTIVE MOBILITIES, $10^5 m_{et}s$ (cm$^2$/V·s) FOR SEVERAL VALUES OF THE MIGRATION TIMES (min) FOR THE EOF MARKER, $t_{EOF}$, A SAMPLE COMPONENT, $t_s$, AND THE MC MARKER, $t_{MC}$

The accuracy in the determination of $t_s$ is taken as 0.5% ($l_c = 27$ cm, $l_q = 20$ cm, applied voltage 10 kV).

<table>
<thead>
<tr>
<th>Fixed values</th>
<th>$t_s$</th>
<th>$k'$</th>
<th>$m_{et}s$</th>
<th>$t_s - 0.5%$</th>
<th>$t_s + 0.5%$</th>
<th>$t_s - 0.5%$</th>
<th>$t_s + 0.5%$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$t_{EOF} = 2$ min; $t_{MC} = 10$ min</td>
<td>8.00</td>
<td>14.61</td>
<td>15.00</td>
<td>15.41</td>
<td>$-33.69$</td>
<td>$-33.75$</td>
<td>$-33.81$</td>
</tr>
<tr>
<td>$t_{EOF} = 10$ min; $t_{MC} = 20$ min</td>
<td>11.0</td>
<td>0.21</td>
<td>0.22</td>
<td>0.24</td>
<td>$-0.78$</td>
<td>$-0.92$</td>
<td>$-0.96$</td>
</tr>
<tr>
<td>$t_{EOF} = 10$ min; $t_{MC} = 50$ min</td>
<td>20.0</td>
<td>1.64</td>
<td>1.67</td>
<td>1.69</td>
<td>$-4.48$</td>
<td>$-4.50$</td>
<td>$-4.52$</td>
</tr>
</tbody>
</table>

Sample solutions) with the MC marker Sudan III, with an increasing percentage of methanol in the sample.

It can be clearly seen that, although $t_{EOF}$ (methanol) is nearly constant in all electropherograms, the migration times of all components strongly decrease and the separation efficiency declines dramatically. The addition of methanol to sample solutions for solvation effects or as an EOF marker generally must be avoided, as it can greatly affect the separation, as shown before. A better way to dissolve water-insoluble components is to use an SDS solution.

In Table II, the calculated values for $k'$ according to eqn. 1 are given for the components of the sample used for the electropherograms in Fig. 3 (up to 70% methanol). It is clear that the $k'$ values depend strongly on the presence of methanol in the sample. In Table III the average $k'$ values (standard deviation) from ten experiments are given for a sample of eight drugs dissolved in SDS without methanol and containing 20% methanol. Although the $k'$ values are affected by the presence of methanol in the sample, the repeatability is fairly good at a given methanol concentration, hence the $k'$ values can be monitored for screening purposes by this means.
Fig. 1. Structural formulae of drugs insoluble in water (nicarbazin is a 1:1 mixture of the two given components).

\[ \text{**k' values versus pseudo-effective mobilities**} \]

In the theoretical part we discussed some advantages in the use of the \( m_{\text{eff},s} \) over \( k' \). The most important advantage was that \( m_{\text{eff},s} \) can also be calculated if \( t_{\text{MC}} \) values are unknown. To demonstrate this advantage we carried out eight experiments with a sample mixture of the eight drugs for different \( m_{\text{EOF}} \) varying between 50 \( \cdot \) 10\(^{-5}\) and 40 \( \cdot \) 10\(^{-5}\) cm\(^2\)/V\( \cdot \)s. In order to change the \( m_{\text{EOF}} \), the capillary was rinsed extensively with 1 \( M \) HCl and/or KOH, followed by a rinsing step with distilled water. Fenbendazole was used as an MC marker. In Table IV the average calculated values with standard deviations of \( k' \) and \( m_{\text{eff},s} \) are given for the five experiments in which \( t_{\text{MC}} \) could be measured (high EOF) and three experiments (low EOF) without \( t_{\text{MC}} \). The \( m_{\text{eff},s} \) values obtained from both series of experiments agree, whereas in the latter instance no \( k' \) values could be calculated.
Fig. 2. Electropherograms for the determination of creatinine (C) and Sudan III (S) with and without methanol in the sample. In each experiment two injections were made, the first injection (a) without, (b) with 10% and (c) with 20% methanol in the sample and the second injection without methanol in the sample in all instances. A separation step for 3 min at 10 kV was performed between the two injections. In all instances the sample contained 0.15 mg/ml of creatinine and 0.035 mg/ml of Sudan III and the injection volume was about 11 nl. For further explanation, see text.

Quantitative analysis
To study the quantitative possibilities of MECC, experiments were carried out with a sample mixture consisting of 0.30 mg/ml of nicarbazin, dimetridazole, carbadox and furaltadone, 0.15 mg/ml of sulphadimidine, sulphadiazine and dapsone and 0.030 mg/ml of fenbendazole dissolved in a 100 mM SDS solution. This sample was diluted 1.2-, 1.5-, 2-, 3-, 6- and 10-fold. All these dilutions were measured

TABLE II
CALCULATED CAPACITY FACTORS, $k'$, FOR PHENOL, p-CRESOL AND 2,6-XYLENOL FOR SAMPLES WITH INCREASING AMOUNTS OF METHANOL IN THE SAMPLE

<table>
<thead>
<tr>
<th>Methanol (%)</th>
<th>$k'$ Phenol</th>
<th>$k'$ p-Cresol</th>
<th>$k'$ 2,6-Xylenol</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>0.98</td>
<td>2.59</td>
<td>4.72</td>
</tr>
<tr>
<td>20</td>
<td>0.92</td>
<td>2.43</td>
<td>4.38</td>
</tr>
<tr>
<td>30</td>
<td>0.85</td>
<td>2.20</td>
<td>4.06</td>
</tr>
<tr>
<td>40</td>
<td>0.81</td>
<td>2.05</td>
<td>3.76</td>
</tr>
<tr>
<td>50</td>
<td>0.77</td>
<td>1.85</td>
<td>3.46</td>
</tr>
<tr>
<td>60</td>
<td>0.78</td>
<td>1.72</td>
<td>3.14</td>
</tr>
<tr>
<td>70</td>
<td>0.79</td>
<td>1.60</td>
<td>2.98</td>
</tr>
</tbody>
</table>

Fig. 3. Electropherograms for the separation of (1) phenol, (2) p-cresol, (3) 2,6-xylanol and (4) Sudan III with increasing amounts of methanol in the sample. The concentration of all sample components was 0.0001 M and the injection volume was about 11 nl.
TABLE III
AVERAGE VALUES OF THE CAPACITY FACTORS, $k'$, FOR THE SAMPLE COMPONENTS WITH STANDARD DEVIATIONS (IN PARENTHESES) FOR TEN EXPERIMENTS

<table>
<thead>
<tr>
<th>Component</th>
<th>$k'$ Without methanol</th>
<th>$k'$ With 20% methanol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicarbazin</td>
<td>0.375 (0.002)</td>
<td>0.398 (0.037)</td>
</tr>
<tr>
<td>Dimetridazole</td>
<td>0.565 (0.004)</td>
<td>0.563 (0.007)</td>
</tr>
<tr>
<td>Sulphadimidine</td>
<td>0.852 (0.005)</td>
<td>0.797 (0.009)</td>
</tr>
<tr>
<td>Sulphadiazine</td>
<td>1.833 (0.025)</td>
<td>1.570 (0.026)</td>
</tr>
<tr>
<td>Carboxol</td>
<td>2.137 (0.012)</td>
<td>1.905 (0.023)</td>
</tr>
<tr>
<td>Furaltadone</td>
<td>3.061 (0.012)</td>
<td>2.787 (0.023)</td>
</tr>
<tr>
<td>Dapsone</td>
<td>5.378 (0.018)</td>
<td>4.754 (0.038)</td>
</tr>
<tr>
<td>Fenbendazole</td>
<td>$\infty$</td>
<td>$\infty$</td>
</tr>
</tbody>
</table>

TABLE IV
AVERAGE CALCULATED VALUES WITH STANDARD DEVIATIONS (IN PARENTHESES) FOR $k'$ AND $10^5 \; m^{\text{eff,s}} \; (\text{cm}^2/\text{V} \cdot \text{s})$ FOR EIGHT DRUGS IN EXPERIMENTS WITH VARYING $m_{\text{EOF}}$

<table>
<thead>
<tr>
<th>Compound</th>
<th>$k'$ $(n = 5)$</th>
<th>$m^{\text{eff,s}}$ $(n = 5)$</th>
<th>$m^{\text{eff,s}}$ $(n = 3)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>EOF</td>
<td>0</td>
<td>45.71 (2.87)</td>
<td>41.13 (0.47)</td>
</tr>
<tr>
<td>Nicarbazin</td>
<td>0.271 (0.005)</td>
<td>8.06 (0.20)</td>
<td>8.25 (0.04)</td>
</tr>
<tr>
<td>Dimetridazole</td>
<td>0.447 (0.006)</td>
<td>11.68 (0.24)</td>
<td>11.04 (0.07)</td>
</tr>
<tr>
<td>Sulphadimidine</td>
<td>0.714 (0.004)</td>
<td>15.75 (0.22)</td>
<td>16.09 (0.03)</td>
</tr>
<tr>
<td>Sulphadiazine</td>
<td>1.615 (0.052)</td>
<td>23.35 (0.56)</td>
<td>22.72 (1.11)</td>
</tr>
<tr>
<td>Carboxol</td>
<td>1.890 (0.031)</td>
<td>24.73 (0.42)</td>
<td>24.60 (0.70)</td>
</tr>
<tr>
<td>Furaltadone</td>
<td>2.756 (0.021)</td>
<td>27.75 (0.36)</td>
<td>28.10 (0.03)</td>
</tr>
<tr>
<td>Dapsone</td>
<td>4.875 (0.070)</td>
<td>31.38 (0.43)</td>
<td>31.81 (0.04)</td>
</tr>
<tr>
<td>Fenbendazole</td>
<td>$\infty$</td>
<td>37.81 (0.44)</td>
<td></td>
</tr>
</tbody>
</table>

TABLE V
AVERAGE MIGRATION TIME, $t$ (min), $10^5 \; m^{\text{eff,s}}$ (cm$^2$/V · s), SLOPE AND INTERCEPT (ARBITRARY UNITS) AND CORRELATION COEFFICIENT OF CALIBRATION GRAPHS FOR THE DIFFERENT SAMPLE COMPONENTS WITH STANDARD DEVIATIONS IN PARENTHESES

<table>
<thead>
<tr>
<th>Compound</th>
<th>$t$ $(n = 5)$</th>
<th>$m^{\text{eff,s}}$ $(n = 5)$</th>
<th>Slope</th>
<th>Intercept</th>
<th>Correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicarbazin</td>
<td>2.57 (0.020)</td>
<td>-11.73 (0.096)</td>
<td>78.96</td>
<td>-0.40</td>
<td>0.999</td>
</tr>
<tr>
<td>Dimetridazole</td>
<td>2.86 (0.026)</td>
<td>-15.46 (0.076)</td>
<td>123.70</td>
<td>-0.63</td>
<td>0.999</td>
</tr>
<tr>
<td>Sulphadimidine</td>
<td>3.17 (0.043)</td>
<td>-18.71 (0.194)</td>
<td>133.85</td>
<td>-1.43</td>
<td>0.998</td>
</tr>
<tr>
<td>Sulphadiazine</td>
<td>4.37 (0.058)</td>
<td>-27.03 (0.196)</td>
<td>195.33</td>
<td>-0.24</td>
<td>0.999</td>
</tr>
<tr>
<td>Carboxol</td>
<td>4.04 (0.065)</td>
<td>-26.33 (0.130)</td>
<td>92.43</td>
<td>-1.36</td>
<td>0.997</td>
</tr>
<tr>
<td>Furaltadone</td>
<td>3.56 (0.081)</td>
<td>-31.10 (0.125)</td>
<td>119.19</td>
<td>-1.50</td>
<td>0.999</td>
</tr>
<tr>
<td>Dapsone</td>
<td>6.66 (0.127)</td>
<td>-34.69 (0.141)</td>
<td>429.19</td>
<td>-2.54</td>
<td>0.999</td>
</tr>
<tr>
<td>Fenbendazole</td>
<td>11.30 (0.342)</td>
<td>-40.60 (0.137)</td>
<td>258.87</td>
<td>-2.62</td>
<td>0.997</td>
</tr>
</tbody>
</table>
three times and using the measured peak areas calibration graphs were constructed. In Table V all measured migration times and calculated \( m_{\text{eff}} \) values for the components, the slopes, intercepts and the correlation coefficients of the calibration graphs are given, with standard deviations. From Table V it can be concluded that linear calibration graphs (nearly passing through the origin) are obtained. In Fig. 4 the calibration graphs obtained by applying the average values of the three experiments for all dilutions are shown.

**Determination of dapsone in tablets by MECC**

As an application we determined the amount of dapsone in a tablet of mass 202.8 mg stated to contain 100 mg of dapsone per tablet. The tablet was pulverized and 15.4 mg were dissolved in 50 ml of 100 mM SDS solution containing about 0.1 mg fenbendazole as \( t_{\text{sec}} \) marker. As duplicate, a 2-fold diluted solution was used. From the calibration graph, we found 104.5 mg (S.D. = 1.2 mg) and 105.8 mg (S.D. = 1.4 mg) of dapsone, respectively, in the tablet, showing that MECC is suitable for the determination of dapsone in tablets. In Fig. 5 the electropherogram of the standard sample mixture with the eight drugs and the electropherogram of the sample mixture from the tablet are given. Although the migration times for peaks 7 and 8 differ consider-ably, owing to a small difference in \( t_{\text{EOF}} \), the calculated \( m_{\text{eff}} \) values are nearly identical.

**CONCLUSIONS**

In MECC the capacity factor, \( k' \), provides fundamental information concerning the distribution coefficient over the aqueous and the micellar phase,
which can give a guide to improving the resolution according to the resolution equation of micellar electrokinetic capillary chromatography. For screening purposes, pseudo-effective mobilities are to be preferred to capacity factors because they can be calculated even if $t_{MC}$ is unknown and because they are less sensitive to inaccuracies in the determination of the migration times. Moreover, pseudo-effective mobilities give a better indication of whether components can be separated or not. The addition of an organic solvent to the sample affects the values of $k'$ and pseudo-effective mobilities and the resolution of the separation. Although in our experiments a large injection volume was applied in order to examine in detail the effect of methanol in the sample, a better way is to dissolve in water-insoluble components in an SDS solution. Linear calibration graphs were obtained for the different drugs and the results for the determination of dapsone in tablets without any sample pretreatment were satisfactory.

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