Determination of Gliclazide in Pharmaceutical Preparations by Capillary Gas Chromatography with Cool On-Column Injection and Elimination of the Matrix Effect

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Conditions were established for the identification and quantitation of gliclazide in pharmaceutical preparations by capillary gas chromatography with flame ionization detection and cool on-column injection. Gliclazide was extracted with methanol and, after filtration, assayed on a (25 m × 0.25 mm id, 0.2 μm film thickness) CP-WAX 58 (FFAP)–CB WCOT fused silica column. Because the available preparations were of various origins and, therefore, could differ in auxiliary substances and their qualitative parameters, the influence of the matrix constituents on the analytical results was taken into account. Good separation conditions were established for the developed method. The retention time of gliclazide is about 36 min and differs from the retention times of the internal standard (approximately 29 min) and additional peaks present in chromatograms (20–26 min), which were assigned to matrix constituents. The recoveries of gliclozide were high and reached 96.5%. The developed method is characterized by selectivity and precision (relative standard deviation 0.38–1.26%), a wide range of linearity (0.1–10.0 mg/mL), and a limit of detection of 30 ng. In addition, the results of chromatographic analyses calculated in 3 ways were compared with those obtained by UV spectrophotometry. The suggested technique of cool on-column injection, in contrast with split-splitless injection (used in preliminary investigations), reduces to a minimum the possibility of thermal decomposition of gliclazide.

Gliclazide belongs to a new group of second-generation hypoglycemic drugs, thiourea derivatives, used in medicine in the form of oral drugs having various degrees of active-substance release. In contrast with the first-generation drugs, the gliclazide preparations are of very high efficiency, so treatment doses are several times lower.

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TRACE, ver. 1.06, for data acquisition, calculations, and chromatogram registration; Microsoft Office 97 Standard, Statistica 5.1 edition '97, CorelDRAW® (Merck KGaA, Darmstadt, Germany).

(e) **UV-visible spectrophotometer.**—CARY 1E (Varian, San Fernando, CA), equipped with quartz glass cuvette (1 cm pathlength).

### Reagents

(a) **Carrier gas.**—Helium of purity class 5.0 (BOC Gazy, Siewierz, Poland), additionally passed through an OT3-2 oxygen/moisture trap filter (R&D Separations, Inc., Rancho Cordova, CA). The chromatograms were recorded at a constant pressure of carrier gas, 100 kPa, as a mode of the mobile phase flow during the entire GC oven program.

(b) **Gases fed to the detector.**—Synthetic air: Synthetische Luft KW-Frei 20.0000% Sauerstoff (350 mL/min); hydrogen (35 mL/min) and nitrogen (make-up gas, 30 mL/min) of purity class 5.0 (Linde Gaz Polska, Kraków, Poland).

(c) **Methanol, gradient grade, for LC.**—LiChrosolv® (Merck KGaA, Darmstadt, Germany).

(d) **Standards.**—(1) **Gliclazide.**—Meeting the specifications of the European Pharmacopoeia (Cat. No. EP G0326000, Promochem Sp. Z. o. o., Warszawa, Poland. (2) **Phenazone.**—Meeting the specifications of the European Pharmacopoeia (Cat. No. EP P0800000, Promochem Sp. Z. o. o.).

(e) **Standard solutions.**—(1) **Gliclazide standard solutions.**—Gliclazide standard was weighed with an accuracy of ±0.1 mg and dissolved in 10.0 mL methanol to obtain gliclazide concentrations of 1.0–10.0 mg/mL. (2) **Internal standard solution.**—A 10.0 mg/mL methanol solution of phenazone was used. (3) **Standard solutions for the internal standard method.**—Amounts of 30.5 ± 0.3 mg gliclazide standard were weighed with an accuracy of ± 0.1 mg, added to 10.0 mL volumetric flasks containing 500 μL internal standard solution and 2.3 mL methanol, dissolved, and then the solutions were diluted to volume with methanol.

### Preparation of Sample Solutions

Ten tablets, each containing 80 mg gliclazide declared, were ground, and amounts equivalent to the averaged mass of 1 tablet

### Table 1. Validation parameters and results obtained for the GC method

<table>
<thead>
<tr>
<th>Method parameter</th>
<th>Measured for</th>
<th>Mean ± 95% confidence interval</th>
<th>SD</th>
<th>RSD, %</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>tR, min</td>
<td>Phenazone</td>
<td>29.39 ± 0.0222</td>
<td>0.095</td>
<td>0.323</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Gliclazide</td>
<td>35.82 ± 0.0276</td>
<td>0.118</td>
<td>0.329</td>
<td>7</td>
</tr>
<tr>
<td>RRT, min</td>
<td>Gliclazide</td>
<td>1.219 ± 0.00134</td>
<td>0.0057</td>
<td>0.468</td>
<td>7</td>
</tr>
<tr>
<td>Peak height</td>
<td>Phenazone</td>
<td>13023.9 ± 8034.7</td>
<td>28987.3</td>
<td>22.6</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Gliclazide</td>
<td>113381.9 ± 5657.6</td>
<td>20411.1</td>
<td>18.0</td>
<td>7</td>
</tr>
<tr>
<td>Peak area</td>
<td>Phenazone</td>
<td>42548946.1 ± 70259.3</td>
<td>2526367.0</td>
<td>5.42</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Gliclazide</td>
<td>82451939.8 ± 1352033.4</td>
<td>4877811.0</td>
<td>5.92</td>
<td>7</td>
</tr>
<tr>
<td>RF</td>
<td>Peak height</td>
<td>0.136 ± 0.00347</td>
<td>0.00469</td>
<td>3.45</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Peak area</td>
<td>0.3240 ± 0.00327</td>
<td>0.00442</td>
<td>1.36</td>
<td>7</td>
</tr>
<tr>
<td>R</td>
<td>Gliclazidephenazone</td>
<td>5.33 ± 0.29</td>
<td>1.03</td>
<td>20.0</td>
<td>7</td>
</tr>
</tbody>
</table>

* tR = retention time; RRT = relative retention time; RF = response factor; R = resolution.
* SD = standard deviation.
* RSD = relative standard deviation.
* n = 50.
* n = 7.
Figure 2. Chromatograms recorded under the specified conditions by using an internal standard: (A) gliclazide standard; (B)–(H) pharmaceutical preparations analyzed. Peaks: 1 = phenazole; 2 = gliclazide.
were weighed with an accuracy of ±0.1 mg; 25.0 mL methanol was added to each amount, and the mixtures were shaken for 15 min. The suspensions obtained were filtered through filter paper with medium-wide pores (No. 389, 9 cm diameter; FILTRAK®, Niederschlag, Germany).

For the internal standard method, at this point in the procedure 10.0 mL volumetric flasks each containing 500 µL internal standard solution were diluted to volume with appropriate filtrate.

**Pharmaceutical Preparations Analyzed**

The following randomly selected gliclazide preparations, available in the marketplace, originated from various manufacturers: (B)–(H) as in Figure 2 when (A) refers to gliclazide standard. The numbers represent lot number and expiration date, respectively (B) DIABEZIDUM 80 mg GLICLAZIDUM, Jelfa (Poland), 20999 (09 2001); (C) Glinormax® Gliclazidum 0.08 g, Polfa Kutno S.A. (Poland), 93040031 (05 2004); (D) diamicron gliclazide gliclazida 80 mg, servier (France), 021701194, 9 F 0764 (06 2004); (E) diamicron gliclazide 80 mg, servier (Belgium), 02151194, 9 F 0764 (06 2004).

**Preliminary GC Analyses and Results**

During preliminary investigations performed by 2 independent analysts, the conditions for the chromatographic separation of gliclazide were checked, and preliminary validation parameters were determined to establish the optimum conditions of analysis (16).

**Effect of parameter changes on the measurement of results.**—The solutions of standard and pharmaceutical preparations for chromatography were fed into the chromatographic column at a constant flow rate (1.0–2.0 mL/min, 26–43 cm/s) or at a constant pressure (70–120 kPa) of carrier gas within different ranges of detector sensitivity, isothermally or with the temperature program for the GC oven in the range of 40–275°C, while the rate of temperature increase changed from 5 to 20°C/min and the duration of the initial and final temperatures covered a wide range.

Samples were injected by using the air plug technique (17) with control of the injection volume before and after injection.

The initial measurements with split were performed at an inlet temperature in the range of 150–275°C and a split ratio ranging from 1:10 to 1:50 (split-vent flow rate, 10–50 mL/min). A volume of 1.0–3.0 µL was injected.

The secondary cooling (17) time of the cold on-column injector was changed over the range of 0.05–0.2 min. A volume of 1.0 µL was injected.

Because each individual measurement took on average ca 40 min, the measurements were made in cycles consisting of 6 or 9 analyses; 3 chromatograms were obtained for each sample. Each measuring cycle was preceded by a system leak check, an evaluation of the chromatographic column, and a baseline stability check for any given program. For each analysis cycle for a pharmaceutical preparation, a chromatogram was obtained for one of the standard solutions. The chromatograms were recorded with baseline compensation.

The chromatograms shown in Figure 1, a and b, were obtained for a standard solution of gliclazide with the use of 2 radically different injection techniques, split-splitless (Figure 1a) and cool on-column (Figure 1b). The first chromatogram, in contrast with the other, contains several additional peaks, which could be due to the thermal decomposition of the analyte. That difference in the behavior of the analyte, depending on the injection technique used, accounts for the choice of cool on-column as a mode of injection for further examination.

The main peaks in all recorded chromatograms were characterized by repeatable retention times, shapes, and areas, but their heights were different (Table 1). Therefore, the internal standard method was chosen for further analyses.

### Table 2. Levels (%) of matrix constituents in gliclazide pharmaceutical preparations analyzed

<table>
<thead>
<tr>
<th>Pharmaceutical preparation (country of origin)</th>
<th>Mean ± 95% confidence interval</th>
<th>Range</th>
<th>SD&lt;sup&gt;b&lt;/sup&gt;</th>
<th>RSD, %&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabezidum (Poland)</td>
<td>8.94 ± 0.17</td>
<td>8.63–9.09</td>
<td>0.21</td>
<td>2.39</td>
</tr>
<tr>
<td>Glinormax (Poland)</td>
<td>2.95 ± 0.05</td>
<td>2.88–3.02</td>
<td>0.06</td>
<td>2.16</td>
</tr>
<tr>
<td>Diamicron (France)</td>
<td>1.17 ± 0.09</td>
<td>1.06–1.36</td>
<td>0.12</td>
<td>10.13</td>
</tr>
<tr>
<td>Diamicron (Belgium)</td>
<td>2.55 ± 0.06</td>
<td>2.48–2.65</td>
<td>0.08</td>
<td>2.97</td>
</tr>
<tr>
<td>Diabrezide (Italy)</td>
<td>6.83 ± 0.20</td>
<td>6.59–7.15</td>
<td>0.26</td>
<td>3.73</td>
</tr>
<tr>
<td>Diamicron (UK)</td>
<td>2.35 ± 0.13</td>
<td>2.17–2.56</td>
<td>0.16</td>
<td>6.84</td>
</tr>
<tr>
<td>Diaprel (France)</td>
<td>6.70 ± 0.17</td>
<td>6.31–6.91</td>
<td>0.21</td>
<td>3.15</td>
</tr>
</tbody>
</table>

<sup>a</sup> n = 6; the GC area% method was used for calculations.

<sup>b</sup> SD = standard deviation.

<sup>c</sup> RSD = relative standard deviation.
The resolution \((R; 18)\) of the gliclazide and phenazone peaks was calculated to control the conditions of the chromatographic separation. The criterion \(R \geq 4\) was used.

The results of the experiments described above are shown in Table 1.

**Selectivity and specificity of the method.**—The selectivity of the method was determined by establishing the effect of potential constituents of the matrix on the gliclazide determination under specified conditions. Chromatograms of gliclazide standard and appropriate preparations were recorded to compare the individual peaks obtained (Figure 2). The proper peak and matrix constituents were defined on the basis of retention time and peak area.

The following retention times were obtained: gliclazide, ca 36 min; and phenazone (internal standard), ca 29 min; the range of retention times of the additional peaks was ca 20–26 min.

The position of the gliclazide peaks in the Figure 2 chromatograms, defined by retention times and their relative values, relative retention times (RRTs; Table 1), is repeatable and, therefore, enables easy identification.

For gliclazide the phenazone peak was the reference peak for the RRT; a criterion of \(\pm 0.5\%\) was used.

To illustrate the levels of the matrix constituents (as percentages) in the gliclazide preparations analyzed, the relationship between the gliclazide peak area and additional peaks areas (excluding the phenazone peak area) was examined. The

\[
A = 1200E2 + 7387E4 \cdot c
\]

correlation: \(r = 0.9858\)

![Figure 3. Relationship between peak areas and gliclazide concentrations.](image_url)

![Figure 4. Chromatograms of gliclazide solutions used for determining (a) the detection limit and (b) the quantitation limit.](image_url)
Table 3. Results from analyses of pharmaceutical preparations by the 3 methods used

| Pharmaceutical preparation (country of origin) | Found, mg |  |  |  |  |  |  |  |
|-----------------------------------------------|-----------|---|---|---|---|---|---|
| | Range     | Mean ± 95% confidence interval | SD | RSD, % | E_{rel}, % | Precision |
| Direct GC (measurement of peak area)          |           |   |   |   |   |   |
| Diabezidum (Poland)                          | 76.2–79.6 | 77.7 ± 1.15 | 1.44 | 1.85 | 2.88 | 77.7 ± 1.15 |
| Glinormax (Poland)                           | 60.2–79.8 | 72.1 ± 6.23 | 7.80 | 10.8 | 9.88 | 72.1 ± 6.26 |
| Diamicron (France)                           | 78.4–82.0 | 79.4 ± 1.13 | 1.40 | 1.78 | 0.75 | 79.4 ± 1.13 |
| Diamicron (Belgium)                          | 71.0–79.3 | 74.8 ± 2.49 | 3.10 | 4.15 | 6.50 | 74.8 ± 2.49 |
| Diabrezide (Italy)                           | 72.7–85.9 | 79.6 ± 4.10 | 5.10 | 6.44 | 0.50 | 79.6 ± 4.10 |
| Diamicron (UK)                               | 67.0–73.4 | 69.8 ± 2.36 | 3.00 | 4.23 | 12.8 | 69.8 ± 2.36 |
| Diaprel (France)                             | 59.5–76.7 | 68.3 ± 5.47 | 6.80 | 10.0 | 14.6 | 68.3 ± 5.47 |
| GC with internal standard (measurement of peak height) | | | | | | |
| Diabezidum (Poland)                          | 73.2–76.5 | 75.3 ± 1.03 | 1.29 | 1.71 | 5.88 | 75.3 ± 1.03 |
| Glinormax (Poland)                           | 73.9–77.7 | 75.8 ± 1.34 | 1.67 | 2.21 | 5.25 | 75.8 ± 1.34 |
| Diamicron (France)                           | 76.4–80.8 | 79.0 ± 1.25 | 1.56 | 1.97 | 1.25 | 79.0 ± 1.25 |
| Diamicron (Belgium)                          | 82.6–89.0 | 87.3 ± 1.96 | 2.45 | 2.81 | 9.13 | 87.3 ± 1.96 |
| Diabrezide (Italy)                           | 73.3–87.0 | 79.8 ± 3.76 | 4.70 | 5.90 | 0.28 | 79.8 ± 3.76 |
| Diamicron (UK)                               | 84.9–94.6 | 91.8 ± 2.89 | 3.61 | 3.93 | 14.72 | 91.8 ± 2.89 |
| Diaprel (France)                             | 78.4–83.1 | 81.2 ± 1.37 | 1.71 | 2.10 | 1.25 | 81.2 ± 1.37 |
| GC with internal standard (measurement of peak area) | | | | | | |
| Diabezidum (Poland)                          | 78.9–80.2 | 79.4 ± 0.38 | 0.47 | 0.59 | 0.70 | 79.4 ± 0.38 |
| Glinormax (Poland)                           | 73.9–75.2 | 74.7 ± 0.56 | 0.70 | 0.94 | 6.67 | 74.7 ± 0.56 |
| Diamicron (France)                           | 76.5–77.5 | 77.0 ± 0.27 | 0.34 | 0.44 | 3.69 | 77.0 ± 0.27 |
| Diamicron (Belgium)                          | 77.8–78.5 | 78.1 ± 0.24 | 0.30 | 0.38 | 2.38 | 78.1 ± 0.24 |
| Diabrezide (Italy)                           | 79.0–81.5 | 80.1 ± 0.81 | 1.01 | 1.26 | 0.14 | 80.1 ± 0.81 |
| Diamicron (UK)                               | 75.5–77.7 | 76.7 ± 0.75 | 0.94 | 1.22 | 4.12 | 76.7 ± 0.75 |
| Diaprel (France)                             | 73.5–75.6 | 74.3 ± 0.67 | 0.84 | 1.13 | 7.11 | 74.3 ± 0.67 |
| UV spectrophotometry (measurement of absorbance) | | | | | | |
| Diabezidum (Poland)                          | 78.8–80.3 | 79.5 ± 0.62 | 0.77 | 0.97 | 0.58 | 79.5 ± 0.62 |
| Glinormax (Poland)                           | 81.9–82.1 | 82.0 ± 0.08 | 0.10 | 0.12 | 2.50 | 82.0 ± 0.08 |
| Diamicron (France)                           | 79.9–80.3 | 80.1 ± 0.11 | 0.14 | 0.17 | 0.17 | 80.1 ± 0.11 |
| Diamicron (Belgium)                          | 74.3–79.8 | 77.3 ± 2.22 | 2.77 | 3.59 | 3.44 | 77.3 ± 2.22 |
| Diabrezide (Italy)                           | 76.6–77.3 | 77.0 ± 0.28 | 0.35 | 0.45 | 3.81 | 77.0 ± 0.28 |
| Diamicron (UK)                               | 83.3–89.5 | 86.2 ± 2.54 | 3.18 | 3.69 | 7.79 | 86.2 ± 2.54 |
| Diaprel (France)                             | 77.9–82.4 | 80.2 ± 1.94 | 2.43 | 3.03 | 0.19 | 80.2 ± 1.94 |

\(^a\) Declared content of all preparations = 80.0 mg.

\(^b\) \(n = 6\).

\(^c\) SD = standard deviation.

\(^d\) RSD = relative standard deviation.

\(^e\) E_{rel} = relative error.

\(^f\) Y = x ± 2SD.

\(^g\) Absolute calibration method.
the peak height was containing an appropriate amount of analyte (Figure 4a). Sim-
chronatographic analyses were established.

The limits of detection and quantitation were found to be 30
and 60 ng, respectively.

The precision has been defined as the degree of consist-
tency between the measurements repeated many times. To
check the measurements for consistency, the values of the
RSD and absolute SD were used, with the assumption that the
result of single measurements was y = x ± 2 SD (95% confi-
dence level).

The precision, calculated for n = 6, was as follows: y =
3.048 ± 0.0344 mg/mL (x_{min} = 3.03 mg/mL, x_{max} =
3.07 mg/mL, SD = 0.0172, and RSD = 0.564%).

The chromatograms of the examined solutions were used
for the identification and determination of gliclazide.

As a result of these examinations, the conditions of the
chromatographic analyses were established.

Quantitative Analyses

The following 3 analytical methods were used: absolute
calibration method (direct GC), internal standard method (GC
with an internal standard), and UV spectrophotometric
method (for comparison).

Quantitative GC Analyses

A 1.0 μL aliquot of the appropriate solution of standard or
pharmaceutical preparation was fed into the column through
the cold on-column injector. The secondary cooling time of
the injector was 0.1 min. The chromatograms were recorded at
a constant carrier gas pressure of 100 kPa and with the follow-
ing temperature program for the GC oven: from 75°C (hold
for 5 min) to 240°C at 10°C/min (hold for 18 min).

The chromatograms of standard solutions were used for
linearity checking and determination of retention times, re-

donse factors (RFs), and gliclazide concentrations in the
pharmaceutical preparations.

The chromatograms of the examined solutions were used
for the identification and determination of gliclazide.

The absolute calibration method, based on calculations
with peak areas obtained by direct GC, and the internal stan-
dard method, based on calculations with peak areas or peak
heights with “averaged RF” multilevel calibration, were used,
together with the software capabilities.

Spectrophotometric Analyses

For spectrophotometric measurements, the standard and
the pharmaceutical preparations under study were dissolved in
methanol so that solutions of concentrations ranging from 5 to
20 μg/mL were obtained. The absorbance (A) was measured
at \( \lambda_{\text{max}} = 227 \) nm. The relationship between absorbance and
concentration, \( A = f(c) \), was linear in compliance with the
Lambert-Beer law. The concentration of gliclazide was calcu-
lated from absorbances recorded at \( \lambda_{\text{max}} \) for relevant solutions
of the standard and pharmaceutical preparations.

The results of the analyses by the 3 methods are presented
in Table 3.

Results and Discussion

The chromatograms of the standard (gliclazide) and the
individual pharmaceutical preparations under study were re-
corded under the conditions specified above.

The results of quantitative analysis are presented in
Figure 2. There are 2 base peaks visible in chromatograms
A–H. One is for gliclazide (retention time, approximately
36 min), and the second is for the internal standard phenazone
(retention time, about 29 min).

The chromatograms differ from each other by the presence
of additional peaks of various heights and areas, but similar re-
tention times. It should be noted that no additional peaks are
present in chromatogram A of the standard. Thus, it can be con-
cluded that the additional peaks observed in chromatograms
B–H are due either to impurities in the active substance or to
auxiliary substances present in the pharmaceutical preparations.

The position of the gliclazide peaks in the Figure 2
chromatograms, defined by retention times and RRT values
(Table 1), is repeatable and enables their easy identification.

By considering the heights of the additional peaks recorded
in the chromatograms, it would be possible to assess the purity
of each preparation, if the peaks were identified. Because such
identification was not performed in this study, it can be con-
cluded only that the areas of the additional peaks recorded in
chromatograms C, D, E, and G are larger than those of the ad-
ditional peaks in chromatograms B, F, and H, and that these
results suggest various impurity levels (Table 2).

Regardless of the origin of the additional peaks, the aim of this
study, i.e., to develop a method for the determination of the active
substance without matrix constituents, appears to be achieved;
because the gliclazide peak recorded under established condi-
tions differs significantly in retention time from the additional
peaks, the active substance can be determined independently.

Although the peaks obtained under the established condi-
tions are not symmetrical, the results presented in Table 3 are
repeatable, as shown by the statistical evaluation. The prelimi-
nary validation procedure confirmed the credibility of the de-
veloped method, which guarantees that reliable analytical re-
sults can be obtained.
The relationship between peak area and concentration indicates a wide linearity range from 0.1 to 10 mg/mL. The equation describing the calibration line contains a small value of parameter b (Figure 3).

The developed method is also characterized by high gliclazide recoveries averaging 96.5% and low detection and quantitation limits of 30 and 60 ng, respectively.

Determination of the gliclazide content of tablets by the GC direct method produced divergences between declared content and found that were greater than those obtained by UV spectrophotometry or by the GC with internal standard method (Table 3). Much better results were obtained when the calculations for the GC with internal standard method were based on peak area rather than on peak height.

Under the established conditions of the GC analysis with the use of the internal standard and calculations based on peak areas, the values for relative error (Erel), RSD, and 95% confidence interval were lower than those obtained by direct GC or by the GC with internal standard method with calculations based on peak heights (Table 3). Thus, it appears that the developed method—the GC with internal standard method with calculations based on peak area—produces the best results and should be recommended for the determination of gliclazide.

The results for gliclazide determination obtained by UV spectrophotometry (Table 3) are consistent with those obtained by the GC with internal standard method with calculations based on peak area. The former are higher for preparations G and H only, probably because of the effect of matrix constituents on direct UV measurements. However, this explanation was not confirmed by the results for preparations B and F, both of which have additional chromatographic peaks that are similar to those of G and H. Therefore, it can only be concluded that preparations G and H also contain other matrix constituents that increase the UV absorbance but are undetectable in chromatograms.

Conclusions

Conditions were established for the identification and determination of gliclazide in pharmaceutical preparations by capillary GC. The most accurate and repeatable results were obtained by the GC with internal standard method with calculations based on peak area, regardless of the origin of the drugs. These results indicate the high selectivity and precision of the proposed method. Any influence of matrix constituents was eliminated under the specified conditions.

Results confirmed that the developed method can also be used to assess drug purity, provided that the additional chromatographic peaks are identified. These peaks might indicate manufacturing impurities or decomposition products of the active substance.

The developed method is characterized by high recovery (96.5%) and low limits of detection and quantitation (30 and 60 ng, respectively). Furthermore, the method is linear within a wide concentration range (0.1–10.0 mg/mL). The results of the quantitative analyses as well as the statistical data clearly demonstrate that the developed method is precise.

The cool on-column injection mode contributed greatly to the satisfactory analytical results.

References