Examination of a new method for analysing identity and concentration of drugs in ready-to-use preparations – proof of concepts of the DrugLog® system

B. Witter, C. Kock-Hauser, A. Liekweg

Background and importance
The increasing awareness of the necessity of safety in drug therapy and at the same time immense skills shortages pose new challenges for hospital pharmacies. The number of ready-to-use preparations increase especially in high risk fields such as Oncology and Pediatric medicine. For the immediate quality control in accordance with the German and European Pharmacopoeias, there is a need for analytical methods which do not require large volumes for testing and which were safety and fast by processing accurate results. Pharmacolog (Upsala, Sweden) promotes the UV/Vis spectrometer DrugLog® (figure 1) with these features.

Aims and objectives
The aims of examining DrugLog® were to test the reliability and precision of the method as well as process optimization in the quality control department. As part of this, the sample extraction without further processing in terms of everyday usability and safety, especially in the analysis of cytostatic drugs was examined.

Material and methods
The drugs norepinephrine, midazolam, atropine and cytarabine were tested during the first step. Standard curves of each drug were created in the system (table 1). Samples of ready-to-use preparations (pre-filled syringes (pfs) and infusion-flasks (inf.fl)) were analysed without further processing with 0.5 ml sample volumes each in micro UV single-use cuvettes with a lid. For preparations of cytarabine special cuvettes with Luer-Lock-lid were used (figure 2). The content as well as the identity of the drugs were determined simultaneously in the instrument.

Results
All tested substances could be analysed reliably with the new method, even atropine in the minimum concentration of 0.05 mg/mL with low UV absorption (not shown as figure). The total time required for analyses was reduced by 50-75% compared to the established UV-Vis analysis depending on the analysed drug. The cytostatic ingredient cytarabine could be analysed without cytotoxic contamination of staff or equipment.

Measurement of cytostatic ingredients (Cytarabine)

<table>
<thead>
<tr>
<th>Preparation Concentration Labeled [µg/mL]</th>
<th>Measured value [µg/mL]</th>
<th>Amount found [%]</th>
<th>Amount found after volume correction [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>395,3</td>
<td>373,4</td>
<td>94,5</td>
</tr>
<tr>
<td>B</td>
<td>384,3</td>
<td>371,8</td>
<td>96,8</td>
</tr>
<tr>
<td>C</td>
<td>393,4</td>
<td>379,0</td>
<td>96,3</td>
</tr>
<tr>
<td>Ø</td>
<td>391,0 µg/mL</td>
<td>374,7 µg/mL</td>
<td>95,9 %</td>
</tr>
</tbody>
</table>

Conclusion and relevance
DrugLog® simplifies processing, provides maximum work safety when dealing with cytotoxic drugs and ensures valid results for the tested drugs. Each drug requires a separate calibration. For substances without UV activity or very similar spectra, the methodology has limitations. Future investigation is planned in particular for the application in pediatric settings.

References:
- S. Kromidas: Validierung in der Analytik; 2. Auflage 2011; Wiley-VCH Verlag
- European Pharmacopoeia; Edition 3.0