Buffer for dissolution and permeation was KRB, pH 7.4. Test tablets contained 10 mg of propranolol HCl. Caco-2 cells were cultivated according to routine cell culture protocols (TEER>350 Ω•cm). Flow in the dissolution module (Apparatus 4, USP) was 6.5 ml/min and 1.0 ml/min in the permeation module; both modules were connected via a stream splitter. For quantification of dissolved and permeated propranolol HCl, a FIAlab 3500 system together with a FIAlab fluorescence detector PMT-FL (λ EXC 260 nm) was used. It was shown that none of the excipients interfered with the analysis.

**Objectives**

To implement an entire automation for an apparatus assessing permeability of solid oral dosage formulations based on a Caco-2 monolayer and a flow through dissolution cell as described by Motz et al. [Motz et al., Eur J Pharm Biopharm, 2006, accepted] in order to widen the bottleneck formed by time and labor consumptive sampling and quantification.

**Experimental Methods**

Buffer for dissolution and permeation was KRB, pH 7.4. Test tablets contained 10 mg of propranolol HCl. Caco-2 cells were cultivated according to routine cell culture protocols (TEER>350 Ω•cm). Flow in the dissolution module (Apparatus 4, USP) was 6.5 ml/min and 1.0 ml/min in the permeation module; both modules were connected via a stream splitter. For quantification of dissolved and permeated propranolol HCl, a FIAlab 3500 system together with a FIAlab fluorescence detector PMT-FL (λ EXC 260 nm) was used. It was shown that none of the excipients interfered with the analysis.

**Results and Discussion**

Since the concentrations to be assessed with SIA analysis are differing strongly, two independent calibrations have been performed. For relative high concentrations at sampling port D, 25 µl of sample were injected into the fluorescence detector, and therefore, calibration was done via of first order polynomial equation (Figure 2) (R²>0.9999). For the lower concentrations at sampling port B, 50 µl of sample were injected. Here, limit of quantification was 40 ng·ml⁻¹ (10σ). Lower injection volumes (25 µl) yielded corresponding results. Measurement in sextuple showed a standard deviation for the lowest standard (0.05 µg·ml⁻¹) 2.35 % and for the highest standard (80 µg·ml⁻¹) 1.63 %; regression line exhibited an R² > 0.999.

Dissolution measurement revealed complete dissolution of the 10 mg propranolol HCl tablets (98.7 % ± 4.0%, n = 7) after 120 min (Figure 3). Caco-2 monolayers retained their integrity throughout the experiments.

**Conclusion**

Automation by means of SIA successfully yielded the required results.

1) Number of data points was increased by factor two, costs for manpower, sampling, and analysis were tremendously decreased.

2) The automated apparatus yielded comparable results to those obtained with manual sampling (similar dissolution and permeation profile).

Therefore, an important step has been done order to investigate the new tool for assessing permeability of solid dosage forms.

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