5 Conclusions

5.1 Conclusions on testing and selecting tubing material

The method for testing microdialysis tubing presented in this dissertation is suitable for selecting materials for pharmacokinetic applications.

The parameter Ae (Amount eluted) is a good indicator of reversible compound binding, and is a good descriptor for material comparison.

Using the suggested approach, tubes that elute less than 3 pmol/cm^2 can be used for monitoring rapid concentration changes, when used with a suitable microdialysis probe. For tubes with an Ae > 3 pmol/cm^2, a graphical appraisal remains essential to determine if the tube of interest may still be satisfactory for the intended use.

With the hydrophilic compound ZK 894, FEP, FEP/Teflon and fused silica tubes can be recommended for pharmacokinetic applications. The PEEK and silicone tubing show slight adhesion of ZK 894 (individual Ae of up to 11 pmol/cm^2), but may still be suitable for monitoring slow concentration changes.

With the lipophilic compound ZK 975, only fused silica can be recommended for pharmacokinetic applications. All other tubing materials tested (FEP, FEP/Teflon, PEEK and silicone) have a clearly higher individual Ae of 17 to 61 pmol/cm^2.

5.2 Conclusions on testing and selecting microdialysis probes

The method for testing microdialysis probes presented in this dissertation is suitable for selecting materials for pharmacokinetic applications.

The known parameters REC (recovery) and K (mass transfer coefficient) are important quantitative descriptors of compound diffusion through a membrane, provided they are shown to have been determined at steady-state. Since they do not give an indication as to the time needed to reach this steady-state, further parameters are necessary to describe a probe's ability to monitor (rapid) concentration changes.

The suggested parameter %iAUD (the percentage of the hypothetical ideal area under the data achieved) is a good indicator of probe responsiveness to increasing concentrations. Based on the presented data, probes with a %iAUD of ≥ 95% are suitable for monitoring rapidly increasing concentrations. Microdialysis probes with a %iAUD between 85 and 95% may still be satisfactory for monitoring slow increases in concentrations, or for infusion studies, where observations are made at steady-state. Probes with a %iAUD of less tan 85% are in general unsuitable for (semi-) quantitative microdialysis studies.

The suggested parameter Ae (amount eluted) is a good indicator of probe responsiveness to decreasing concentrations, and of the extent of compound adhesion to the membrane. Probes with an Ae of < 5 pmol/mm^3 are suitable for monitoring rapidly decreasing concentrations. For probes with a higher Ae, a graphical appraisal is still necessary to asses the suitability of these probes for the intended use.

For both compounds tested, the cellulose-derived membranes cuprophane (CMA/11 and MAB 4 probes) and cellulosic (MBR-4 probe) can be recommended for pharmacokinetic applications, with %iAUD = 98 - 100%, Ae = 0 - 1.6 pmol/mm^3 and K = 0.09 - 0.21 µL/min/mm^2 for both compounds tested (ZK 975 and ZK 894).

With the lipophilic compound ZK 975, no other material can be recommended. Only the two smallest probes tested with the 6 kDa PES membranes (MAB 4 and MAB 8 probes) may still be suitable for monitoring slow concentration changes.

With the hydrophilic compound ZK 894, the PES-membrane can generally also be recommended for pharmacokinetic applications. The PC-membrane (CMA/12 probe) may still be suitable for monitoring slow concentration changes, the PAN-membrane however (BR-4 probe) is unsuitable for pharmacokinetic applications.

THE END (Better late than never)