

Approaches towards implementation of supercritical fluid chromatography-mass spectrometry (SFC-MS) for high-throughput separations of pharmaceutical compounds

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Introduction

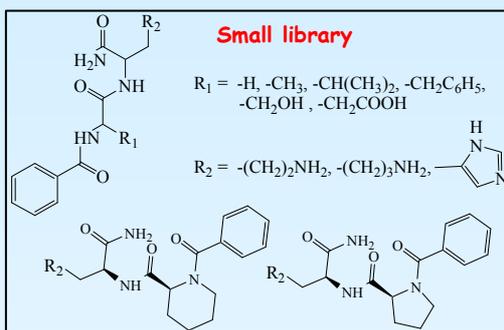
High performance liquid chromatography (HPLC) is the most widely used separation technique within the pharmaceutical industry. Due to the growing need for high speed and high quality separations other techniques such as SFC are now being considered. A key advantage of SFC is minimal solvent waste, which is particularly important in preparative SFC, leading to fast sample recovery. Hence it is important to explore whether SFC, which also promises to be cheaper and more environmentally friendly than conventional HPLC, can be applied more widely as a complementary method.

Objectives

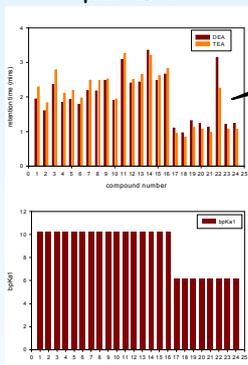
- Develop generic method
- Compare SFC and HPLC
- Focus on speed - use of smaller 50mm columns
- Identify trends in physico-chemical properties

Possible trends

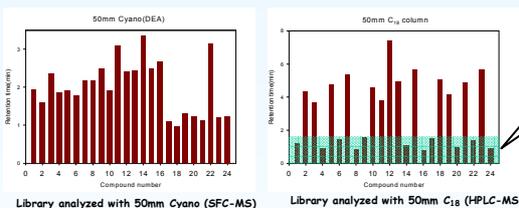
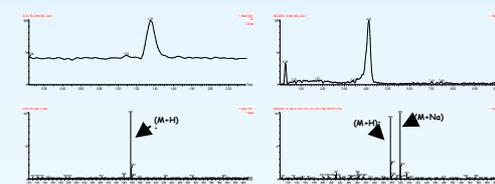
- Log P ☹
- Log D ☹
- pKa 😊 ?



SFC & HPLC



- bpKa1 low, less retained
- Exception possibly due to presence of acid functionality (R₁=CH₂COOH)



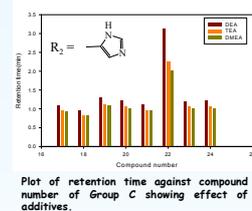
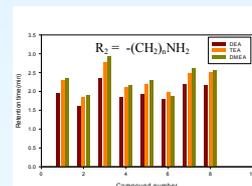
- SFC gives greater coverage for the focussed library as the data suggests
- Less than 50% (11 of 24) not compatible with generic HPLC method, elute with the solvent front

Experimental approach

- Diverse training set (20 compounds)
- Small library of compounds with similarity in structures
- Direct comparison of SFC and HPLC
- Predictor- Map data retention against physico-chemical property

Additive comparison

- Diethylamine
- Triethylamine
- Dimethylethylamine



- Secondary amine additive: Compounds with aliphatic substructure less retained
- Retention less affected by the identity of tertiary amine

Conclusions

- SFC gives greater coverage and is significantly faster compared to HPLC for this class of compounds
- The identity of an amine has little or no effect on the retention times
- Cyano column gives good results on addition of additive analytically acceptable but could cause difficulty preparative chromatography
- Physico-chemical property predictor - not yet but maybe

Acknowledgements