PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY A MATHEMATICAL, PHYSICAL & ENGINEERING SCIENCES

Optimization Strategies in Chiral Liquid Chromatography

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Phil. Trans. R. Soc. Lond. A 1990 **333**, 159-160
doi: 10.1098/rsta.1990.0145

Synopses from the poster exhibition

Optimization strategies in chiral liquid chromatography

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The advent of new LC column technology for the separation of chiral drugs and metabolites has transformed the practice of enantiomer separation for the quality control of chiral drugs and for biological studies on chiral entities. The wide variety of separation principles now exploited for chiral analysis has led to the development of more than 40 different columns, plus the complementary technology where a chiral mobile phase additive is used with a regular reversed-phase column.

The multiplicity of choice for chiral separations can present major difficulties in selecting a suitable starting point for a particular enantiomer separation. However, for a particular chiral modality, the problem is then to rapidly assess its suitability for a given analyte, and then the optimize the enantiomeric resolution observed. These objectives can be achieved by using a combination of systematic optimization strategies, together with diagnostic tests for peak resolution and homogeneity. Thus factorial design (Berridge 1985) can be used to assess the practical range and extent of interaction of those eluent parameters that determine chiral resolution. This can then be followed by computer-aided sequential simplex optimization to establish the conditions for the best available resolution on the specific chiral system selected (Fell *et al.* 1989). The central composite (factorial) design requires $(2k+2k+1)$ experiments for k factors, and permits a second-order polynomial to be fitted to the data, with the advantage that the model so developed can be used predictively (Berridge 1985). Simplex lattice design is a form of simultaneous optimization design based on isoeluotropic mixtures of mobile phase to generate data that allow a linear model to be developed for predictive purposes (Schoenmakers 1986).

Computer-based methods using photodiode array detectors (with or without laser-based polarimetric detectors) permit reliable peak recognition using multivariate data. They also permit peak homogeneity assessment in cases of potential interference from the sample or biological matrix (Fell *et al.* 1989). A valuable diagnostic for detecting incipient separation of enantiomers (in cases where no resolution is visually apparent) is offered by transforming the chromatogram to its second derivative (Fasanmade & Fell 1989). The peak separation function gives an excellent and robust criterion for method development, better in many cases than resolution R_s or alpha values. These approaches have been applied in a number of separations of chiral drugs involving chiral quality control and chiral bioanalysis. The problem of column selection, however, remains complex and may well require an expert systems approach for its satisfactory solution.

Phil. Trans. R. Soc. Lond. A (1990) **333**, 159–172
Printed in Great Britain

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Trace analysis: soils

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Determinations of constituents present in soils and soil solutions at trace concentrations are conducted primarily because of interest in soil as a medium for plant growth or because of its influence upon the solute chemistry of fresh waters and ground waters. Interest may arise from concern over potential toxicity effects or over adverse effects of deficiency of trace nutrient elements essential to soil or freshwater biota.

In the above context, total amounts of elements present in soil are generally of less interest than water-soluble or labile, plant available forms (Marr & Cresser 1983). Rhizosphere soil may be more relevant than bulk soil in assessing plant availability. Over recent decades, optimal chemical extractants (such as EDTA or DTPA for Zn and Cu) have been selected which reflect plant availability of trace elements in terms of high correlations between plant tissue and soil extract concentrations. Occasionally full speciation is conducted. M. S. Cresser & E. El-Sayad (unpublished results), for example, have measured water-soluble, exchangeable and organically bound trace elements, and those in carbonate and amorphorus and crystalline iron and manganese oxides, and residual sand, silt and clay minerals. Such detailed analysis is valuable in elucidation of soil pedogenesis (El-Sayad *et al.* 1988).

No single, low-cost technique is applicable to all the elements of interest at the concentrations normally found, especially in deficiency studies. Flame AAS is useful for Mn, Fe and Zn and sometimes for Cu. For Cd, Co, Cr, Ni and Pb, however, preconcentration is invariably needed (Cresser 1983), or furnace AAS may be used, with a matrix modifier and preferably a L'vov platform. ICPAES provides adequate sensitivity for several, but not all, trace elements (Cresser *et al.* 1990). The more recently introduced ICPMS has great potential, but cost is a limitation. For Hg, cold vapour AFS is suitable, and hydride generation AAS is used for As and Se.

Ion chromatography is invariably used for measuring Cl^-, F^-, NO_2^-, NO_3^-, PO_4^{3-} and SO_4^{2-} in soil solutions, but sometimes NO_2^-, NO_3^- and PO_4^{3-} are determined by manual or automated (segmented flow or flow injection) colorimetric analysis. Boron is best determined fluorimetrically at very low concentration. Microprocessor-controlled dispenser–diluters are excellent for low-cost, high-sample-throughput colorimetric or fluorimetric analysis.

In deficiency studies and speciation studies, contamination, including impurities in reagents, may become a major limitation in some working environments.