Meeting Reports

Chromatographic Society Meetings Round-Up

"Current Method Development Strategies in Separation Science"

Chromatographic Society Spring Symposium, 19th and 20th May 2010, Merck Sharp and Dohme, Hoddesdon,Herts.

by E A Adlard

The topic of this meeting was "Current Method Development Strategies in Separation Science" although a more accurate title would have been "Current Method Development Strategies in HPLC in the Pharmaceutical Industry" since this was the theme of all the papers except for one on SFC. To one who has been in the field for a long time and can now afford the luxury of an overview the current situation in HPLC seems to bear a resemblance to GC in the days of packed columns when there were hundreds of stationary phases available, many of them giving identical separation. This dilemma was rationalised in GC with the development of high efficiency silica capillary columns and to a certain extent HPLC is following the same road with the development of uHPLC. However, HPLC has many more parameters that can be changed than GC so that arriving at optimum separation is a much more complicated process.

The opening talk was by Dr Chris Welch on "Chiral Chromatographic Method Development". Chiral stationary phases (CSP) may be extremely expensive to prepare but Dr Welch has developed methods of microscale, multiparallel method development with a "coffee-break cycle time" (scientific) evaluation requiring only a few milligrams of material. This allows more CSP including experimental ones to be evaluated, thus ensuring that it is the very best chiral separation that progresses towards preparative work. Also, loading studies to optimise up-scale throughput may be carried out on the microscale systems.

The next keynote lecture was given by Dr John Dolan, well-known for his articles on various aspects of liquid chromatography in LC-GC. He emphasised that many of the columns on the market from different suppliers and different names were in fact very similar in their separation abilities. This in itself, is not necessarily a bad thing since it means that equivalent replacements are available if a particular supplier ceases to market a given column but orthogonal separations require columns with a widely different separation

capabilities as possible. The use of test probes enabled an "F factor" (a fitting similarity) to be obtained. Values of F less than 3 means that columns are essentially the same and those with a factor greater than 60 are very different. Dr Dolan recommended consultation of the RQRI (Product Quality Research Institute) database in which 476 RP phases were compared. This should allow identification of similar and different columns to allow the orthogonal separation of difficult pairs. There was no mention of time in this argument since it might be quicker to run mixtures quickly on two different columns rather than seek good separation on one column in a longer net time.

The next session consisted of three presentations, the first of which was by Dr Tom van de Goor of Agilent (the principal sponsoring company of the meeting). Dr van de Goor pointed out that method development is an ongoing task in many analytical labs especially those involved in the development of new drugs and regulatory requirements often result in demands for better sensitivity, resolution and speed of analysis. Method development is a laborious and time –consuming task and automated method development reduces the time required and permit screening of many more separation conditions.When an optimised method has been developed in one location it may need to be transferred to other labs using different instruments. De Goor proposed a new approach that simplifies transfer from uHPLC to HPLC and vice versa without changes to the method or instrument modification.

This was followed by a paper presented by Tony Edge of Thermo Fisher on the optimisation of SPE clean-up before final separation by HPLC and mass spectrometric detection. Examples were given of how this approach could be used for the analysis of a range of pharmaceutical compounds in biological matrices. The final two talks of the day were by speakers on the analysis of drugs and intermediates for genotoxic impuritites. A number of groups and organic fragments had been recognised as potentially genotoxic and these were identified as either occurring in intermediates or as impurities in final products by both GC and HPLC. It is to be hoped that the fact that both these papers were by speakers from the

Netherlands was just coincidence and that UK pharmaceutical companies are also working on this topic. (Editor's Note: it IS a coincidence! For example, Andrew Teasdale (AstraZeneca, Charnwood) is an authority on this topic and has edited a book on "Genotoxic Impurities: strategies for isolation and control")

The second day of the meeting continued with the theme of column selection and optimisation of conditions with the first paper presented by Dr Roman Szucs of Pfizer UK, this year's winner of the Chromatographic Society's Jubilee Medal. He started his talk by pointing out the vast effort required in the search for new drugs. In any given year a company may examine up to 10,000 candidate compounds but after three or four years of preclinical and animal testing this will be reduced to perhaps 250 compounds. Phase II trials on volunteers takes another five or six years and reduces the number of candidate compounds to five for Phase III clinical testing so that after final regulatory approval fifteen years of effort and a billion dollars have been expended. Even after this it is not unknown for a drug to be withdrawn. Dr Szucs pointed out that resolution depended on both plate numbers and on separation factors and for optimum efficiency retention factors should lie in the range of about 2-5. Applying cluster analysis showed that examination of many commercial phases showed many phase giving similar separation with perhaps a dozen outliers giving quite different behaviour. Mathematical modelling required input for physico-chemical properties, solvation parameters (Abraham coefficients) and molecular descriptors. Combination of all of these can produce good correlation between experimental and predicted results. Another of the talks in this "industrial perspectives" session was from Adrian Clarke (AstraZeneca, Charnwood). This talk developed the theme introduced by Patrick Petersson in the previous Society meeting at Alderley Edge in March, further showcasing the almost seamless manner in which AstraZeneca have been able to introduce and adopt uHPLC.

As on the previous day there was a session with presentations by vendors on specific aspects of their products relevant to the overall topic of the meeting. These presentations made general contributions to the theme of the meeting. For example, a paper from Dionex specifically on the development of a method for the determination of diuretics was a good illustration of the use of ion-exchange, an obvious orthogonal, but perhaps under-utilised, mode of LC to RPLC. The morning session ended with a two hour break for lunch, exhibition and the Society's AGM. At the AGM, the President Mr Alan Handley pointed out that the Society was always willing to consider ideas for future meetings.

The two afternoon closing sessions consisted of another four papers again on the overall theme of the meeting, with talks by de Beer and Lesellier dealing with stationary phase selectivity, the latter in the context of supercritical fluid chromatography. De Beer dealt with several aspects of stationary-phase optimised LC including gradient elution on multiple stationary phase systems, the use of small particles and the use of high temperature to minimise bacl pressure problems. Lesellier noted that in SFC as in LC, porous graphitic carbon and fluorophenyl stationary phases are amongst the phases that show a significant difference from C18 phases. Perhaps the most intriguing talks of the day were left for last. GSK speakers Nigel Howes and Steve Mount dealt with Quality by Design for analytical methods. It was notable how for this approach to work it was necessary for close liaison between R&D and Production throughout the development of the methodology. Howes and Mount worked together closely as a team in dealing with questions which was good evidence for those that doubted that this coordinated approach was feasible in practice. It was also evident that, counter to the sentiment of the rest of the meeting, that effective method development in this way could often result in older, simpler technology being used.

A final thank you must go to MSD for hosting the meeting, to all the exhibitors who generously supported the meeting, to the Vice-President of the Society, Dr Paul Ferguson and the Treasurer Dr Greg Jonas, who organised this successful event in collaboration with the host MSD scientists.

HPLC 2010 - June 19-24, 2010 Boston, MA, USA

Hynes Convention Center and Sheraton Boston Hotel

AFTER the social event - macro-array LC?

Pete Carr, 2010 Martin Medal award winner, was keen that his research group shared the limelight with him

HPLC is clearly not a Chromatographic Society meeting but it would be remiss of us to allow the 'main event' of the year to go without comment or mention of the Society's involvement. Importantly, Pete Carr, our 2010 Martin Medal awardee was presented with his medal at the opening ceremony on the Sunday evening (to tumultuous claps of thunder from outside the building!). Following the award ceremony Professor Carr gave a virtuoso plenary lecture covering his contributions to the field of two-dimensional chromatography. This proved to be highly appropriate given that, while in Baltimore in 2008 all the talk was of U-HPLC and fused-core particles, in Boston the 'buzz' had moved on to 2D-LC and the analysis of biopharmaceuticals. During the week, Dwight Stoll, a Pete Carr collaborator gave a highly informative tutorial session on 2D-LC. Such sessions are clearly popular and useful and now seem

to be bedded in as permanent fixtures in the HPLC programme. Also very popular (and not just for those who like to o-d on cookies at the back of the room!) are the lunchtime vendor sessions. Delegates are clearly very interested in announcements of the latest introductions from the key players. Where there used to be Acquity and Infinity there now seems to be a bewildering range of U-HPLC instruments. "New column chemistries" often means the same old column chemistries but on smaller particles. However, to their credit, Waters were able to present on a new range of stationary phases in which the surface has been 'doped' to prevent the band broadening that can come with increasing load of basic compounds on even the best of reversed-phase materials.

UK delegates at opening social mixer getting ready for trekking on the hippie highway?

ISC 2010 - September 12 – 16, Valencia, Spain

External view of the Valencia Conference Ceter

Organisers of ISC 2010, Joan.O.Grimalt (L) and Yolanda Picot (R)

ISC 2010 is also not a Chromatographic Society meeting but at least the Society was one of the three national societies from UK, Germany and France responsible for staging meetings in the ISC series every two years. ISC 2010 was an important meeting and the principal Spanish organisers, Joan Grimalt and Yolanda Pico are to be congratulated on bringing a distinctive Mediterranean flavour to the series. There were large numbers of young presenters and a strong emphasis on electrophoresis and applications such as food and environmental which perhaps do not get as prominent a showcase as they might deserve in major separation science meetings.

Probably just as important as the meeting itself was what was going on behind the scenes. The final discussions took place in changing the organisational structure behind the ISC series so that the Permanent Scientific Committee will now include representatives from South Europe, North Europe and Central/East Europe and EuSSS as well as from UK, France and Germany. With this widening of participation it is hoped that this very long-running series will now go on from strength to strength. ISC 2012 was confirmed for Torun, Poland and the nomination of Salzburg, Austria for ISC 2014 was accepted.

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