# Chromatography Today talks to Kevin Altria (GSK (Harlow)

## "CE Expert" and 2006 Chromatographic Society Jubilee Medallist

*by John Lough*

In this latest in a series of occasional interviews with Chromatographic Society medallists it is only appropriate that for this issue the subject of the interview should be an individual who has made a substantial contribution to the field of electrophoresis. In the UK, and indeed much further afield, the name Kevin Altria and the technique capillary electrophoresis (CE) are inextricably linked. Perhaps it is an indication that CE is still in rude health that this is the second interview that Kevin has given on CE in recent months. However, rather than dwell on the future of CE, Chromatography Today's interest in this Chromatographic Society medallist and outstanding leader in the field was more on his own involvement in the technique and his reflections on the development of the technique.

*Presentation in 2006 of the Jubilee medal to Kevin (left) by Chris Bevan (Chrom Society President)*

**I understand that your intimate relationship with CE began right in the very early days for CE in the UK. Can you tell us how you first became involved with CE?**

I performed my PhD studies into CE at Birkbeck College at the University of London using home-made equipment in 1985. The equipment would never have been acceptable in today Health and Safety environment – the carbon electrode was taped onto the high voltage cable using insulation tape! It was the first system in the UK and I was the first to report pharmaceutical analysis by CE. It was easy to follow the literature then as there were only a dozen papers! I used to present posters at HPLC meetings and people looked very mystified by the work. I spent some time collaborating with Kings College where I built a radioactivity detector and analysed radio-labelled pharmaceuticals which involved trips along the Kings Road carrying canisters of radio-active material.

I left university and moved into Glaxo R&D where I continued my CE interest by assembling a homemade system there – modifications to the UV detector I had included use of a band saw to cut a slot through the casing – not very elegant but it worked OK. I showed that CE could be applied to Glaxo drugs and products and was able to support purchase of early commercial equipment – I also worked on equipment prototypes and provided early input to CE manufacturers.

One of early activities that had a significant impact was a series of 3 inter-company collaborations exercises which I co-ordinated with other UK based pharmaceutical companies. Method details and samples were sent to 7/8 different companies who replicated the separations and performed quantitative analysis with good precision obtained across all the companies. We performed chiral separations, quantified paracetamol content in capsules and determined the metal counter-ion of an acidic drug salt. I helped to train 100 FDA scientists in their Washington HQ using these methods as well and the methods were successful then also which really helped gain regulatory acceptance of CE.

**In the early days did you feel that capillary-zone electrophoresis(CZE) was quite limiting and then that the introduction of modes such as micellar electro-kinetic chromatography (MEKC) and micro-emulsion electrokinetic chromatography (MEEKC) were much needed boons to allow you to adequately tackle the complete range of pharmaceutical applications?**

CZE is simply the use of buffers to separate charged species so did limit the range a lot. In particular closely related species such as cis- and trans-isomers could not be resolved as they had identical charge/mass ratios. The use of MEKC and MEEKC expanded the resolving power available as selectivity is also based on solubility. MEKC and MEEKC expanded the range to include insoluble and neutral species such as steroids. MEEKC in particular proved useful when dealing with highly insoluble samples such as creams which can be directly dissolved in the microemulsions used for the separation.

**At the height of the interest in CE for the analysis of small molecule active pharmaceutical ingredient and drug product in R&D, it seemed that you were pulling off the impossible by focussing your research on company needs yet still being able to publish prolifically. Was there a complete overlap of experiments required here or did**

**you have to do much burning of the midnight oil to keep publishing?**

Much midnight oil was burnt… the majority of my work was company confidential so could not be published. If we developed a new approach or application we then applied it to compounds/products that we could publish. I also supervised a number of PhD and MSc students and so had company in the lab during the evening and weekend sessions. In the mid 1990's I was publishing 20 odd papers per year and with no internet – we had to send 3 copies of the papers and a floppy disk when we submitted a paper and have to wait months while the copies were posted to the reviewers etc. it's a lot less painful now with on-line submission.

**Given the high resolving power of CE, there was an interest in the use of "generic run buffers". Did you find that you could often carry out a large proportion of your applications with just one run buffer?**

The use of a single set of MEEKC separating conditions has given us, and other researchers, much success. The method is able to cope with a highly diverse range of charged and neutral insoluble or soluble species. Standard buffers such as 50mM phosphate pH 2.5 and 15mM borate are also very useful generic buffers for basic and acidic drugs respectively. Generic run buffers have been commercialised for inorganic anion and metal ion analysis which has popularised these applications.

**Did you enjoy giving presentations/ tutorials/workshops and get something out of them or did they sometimes just become an interference?**

Transferring knowledge was vital in the early days of CE. The technical complexity and skills associated with running routine CE were not really available and so early practitioners really struggled to make CE reliable in their labs which gave the technique bad press. I enjoyed giving motivational presentations that showed that CE could provide useful data and was reliable and robust. I did get more satisfaction from the tutorials and workshops where I passed on the tricks of the trade. In particular it was gratifying when I could solve a technical issue that an attendee had struggled with.

**For several years it looked as though capillary electro-chromatography (CEC) might supersede CE, perhaps being more attractive to those steeped in the ways of LC. Was this a technique with which you ever had a dalliance?**

I did spend a short period of time working on CEC with one of my student – it was a painful and expensive time. The columns were expensive, very fragile and prone to air bubble and blockages. We were fortunate to have collaboration with Norman Smith who had great CEC knowledge and enthusiasm and we did obtain some results and a publication but we did not pursue CEC any further.

**I understand that your career is now more related directly to management activities - do you still maintain an involvement in research into CE?**

I do still maintain a limited involvement in research. I am co-supervising a PhD student in Waterford Institute of Technology in Ireland and involved in a research program in Sao Paulo Brazil. Our research is mainly focussed on MEEKC and use of microemulsions as an eluent in HPLC for use in pharmaceutical analysis. I am also still writing "CE Currents" in LCGG magazine. I have recently published 2 papers concerning with continuous improvement (Lean Sigma) as I am concerned with that in GSK as part of my role.

**There is a school of thought that CE has not lived up to expectations, at least for small molecule pharmaceutical R&D, and another that it is now an invaluable technique used for a wide range of applications. There is a school of thought that CE has not supplanted LC simply because it was developed AFTER CE and another school of thought that it has not been as widely used as it could have been because it lacks reliability and robustness. What are your thoughts? For example, in the hands of an 'expert' such as yourself, is questionable reliability and robustness simply not an issue?**

It is true that CE suffered initially and was criticised as it was always compared to HPLC where equipment was more mature and reliable. There was also a wealth of experience and training to access in HPLC. This is gradually changing with CE as it is now included in many college/university courses. I believe that the use of CE for specific applications such as chiral analysis and inorganic anion and metal ion analysis is simpler, cheaper and more rapid than HPLC and other techniques and CE has found a routine niche here supported by commercial reagent kits. CE has struggled in the workhorse applications of assay and impurities for small ion molecules and HPLC continues to predominate.

Reliability and robustness have been improved significantly in recent years as equipment manufacturers have factored this into equipment design improvements.

CE will have its day though in pharmaceutical analysis and that day is dawning now… it's in the area of biopharmaceuticals. Biopharmaceuticals – proteins, DNA etc. is a big area of focus for traditional pharmaceutical companies such as GSK. CE methods such as isoelectric focussing are routinely used for characterisation of biopharmaceuticals and CE methods are often the first technique of choice. Bespoke instruments and kits are available for applications with built in robustness/ ruggedness – almost black-box operation. A series of inter-company collaboration on the analysis of biopharmaceuticals is part way though completion.

*We thank Kevin for giving up his valuable time and, interestingly, very nicely setting up the next issue of Chromatography Today which, amongst other features, will cover the theme of ……. biopharmaceuticals.*

Illustrative references for further reading:

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