



What Exactly did The British Chromatography Industry Bring to the Table?

At a recent meeting organised by The Chromatographic Society called to discuss the alarming drop in research funding, especially by government bodies, into the field of Separation Sciences the question of 'What is the track record of such funding actually resulting in products of tangible benefit to the bench chemist previously?' was muted. Many people are familiar with the role that chromatography plays in the field of aiding the drug development programme of every single block busting drug of the last 25 years yet there are numerous other application areas where discoveries made by British Scientists have allowed breakthroughs in areas such as Environmental, Food and Beverage, Oil and Gas and the bio-processing fields. Whether it be innovation or evolution UK scientists have been at the forefront with their skills in basic research and product development for many years benefiting not only the UK community but the global one also.. The difficulty when putting together a retrospective view such as this is not so much what to include but what to leave out. In addition since we are picking a relatively small number of items from a long list of products developed over a 30 years plus period of time some filtration is required. Products that are known, in the main, internationally and launched into the market pre-1990 were chosen on this occasion.

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INSTRUMENTATION

Here I have chosen one example of a GC instrument and one HPLC. For the GC instrument the seemingly ubiquitous Pye 104 was a fairly easy choice following its launch in the 1960's (illustrated in Figure 1 on the right, the instrument on the left is a 105, the Prep. Version) and many scientists learnt their trade on this Instrument. Available with a range of detectors, the FID (Flame Ionisation Detector) being the most popular, this machine was extremely rugged and quite easy to customise. The oven unit itself was spacious by today's standards and the unit as a whole was extremely heavy to move around the lab. This proved not to be a problem for most scientists of the day and such was its iconic status to scientists of a certain era, there exists a Pye 104 Club [1] as testimony to its longevity and wide appeal (www.chromsoc.com for more details on the club).



Figure 1. Pye 104 Gas Chromatograph.

As far as 'black box' HPLC instruments are concerned one of the most unique was developed by John Knox and Dick Wall at the Wolfson LC unit (WLCU) in Edinburgh University around the 1973-74 period. The example shown in Figure 2 belies its bulk, weight and robustness yet some of the characteristics built into it were many years ahead of their time. Dispersion was recognised a source of chromatographic inefficiency and design employed with the unit kept it to a minimum. During its short lifetime as a commercial product two pumps were utilised, the first being a constant pressure pump, pneumatically controlled but once limitations were realised with that approach an early version of twin piston constant flow pump, electronically

controlled was introduced (shown in Figure 2). As temperature was considered (running on from GC) a way of controlling separations an oven unit was included in the design capable of reaching 75°C. Although temperature control units have been commercialised since, the Shandon LC unit allowed the injection loop, much of the connection tubing, the column and detector cell itself to remain thermostated thus minimising thermal gradients which were to become an issue with other commercial and 'own made' units. Regrettably the unit was not so easy to repair and its UV lamp replacement protocol demanded that around 12 mirrors in the detector optics needed to be removed before access to the lamp was gained. These mirrors then had to be replaced and realigned which was a very specialised and tedious job. Nevertheless this optics system allowed very sensitive levels of detection to be obtained compared to instruments of that era. Inevitably, as with dinosaurs' its size ultimately was responsible for its demise along with a large influx of modular units from many suppliers which offered improved benefits to those the Shandon LC system offered.

As mentioned many other manufacturers brought products or sub-units to the market around that time yet it took a good 30 years to understand and visualise the benefits of using temperature in HPLC as a way of increasing the eluting properties of even pure water – Green chemistry anyone?

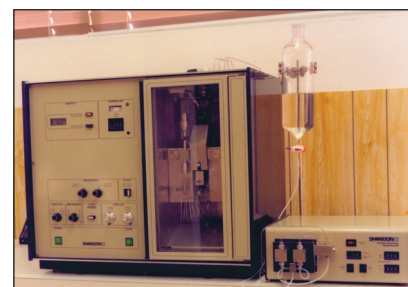


Figure 2. Shandon HPLC Unit with Column oven compartment.

MEDIA

During the 1970's and early 80's Britain had a spell where several world class media for separations scientists were developed and brought to the market place.

Totally porous spherical silica in the range of ten down to three microns in diameter suitable for chemical modification was made available from Phase Separations with the Spherisorb® range. The process originated from a project started at the Atomic Weapons Research Establishment at Harwell near Oxford where modelling studies of uranium particles in reactor tubes lead to the manufacture of several metal oxide products including silica. The process was then purchased by Phase Separations, Clwyd, UK who commercialised the product globally via the increasing range of column packing companies which were springing up at the time. The C18 phases offered within the line were of two types, ODS-1 and -2. The former interestingly enough did not have all residual silanols covered thus allowing an early form of mixed mode separations using reversed phase and ionic interactions to take place. The ODS-2 was a pure reversed phase material however. Such was the success of the product line that at one time it was the most often cited packing material in learned journals during the 1980's. The company was sold to Waters Corporation in the mid-late 1990's and products are still available as Waters® Spherisorb.

Around the same period in the mid 1970's a similar range of totally porous spherical silica products were being developed by Prof John Knox and co-workers at the Wolfson Liquid Chromatography Unit (WLCU) in Edinburgh and commercialised under the Hypersil® name by Shandon Southern Products, Cheshire, UK. It offered slightly different performance, in view of its manufacturing process, to the Spherisorb and in the early days it was the base silica of choice for many companies who used it as a starting point for their own produced series of bonded phases. Base Deactivated Silica (BDS), higher surface area silica (HS100) for Prep use and a high purity phase were all introduced sequentially. The company was sold to Thermo Instruments in 1997 and the products are still sold today.

Both of these micro particulate silica's were manufactured from a silica sol which by today's standards would be classed as relatively 'impure' compared to the high purity (in terms of metal content) silicas currently on the market. Interestingly enough the levels of contamination were actually central to the ability of the older phases being able to perform some separations, particularly in the clinical field, which have not been possible in today's products. Therefore the metal content should be viewed as a 'feature' and not always an undesirable characteristic of the product.

On the non-silica front two products both from University origins came onto the market in the 1970's and 80's and are still thriving today after being cited in many papers. PL Gel from Polymer Laboratories, now a part of Varian Inc. is a spherical polystyrene-divinylbenzene polymer which is used for non-aqueous Gel Permeation Chromatography (GPC). The original process was developed at the University of Loughborough in the UK and commercialised by Prof Ray Whetton and some ex- post grad students. The company built on its polymer chemistry knowledge base to produce other materials for chromatographic use such as the Aquagel size exclusion chromatography (SEC) columns and later a range of anion, cation and reversed phase columns based on different porosities and particle sizes. Due to the pH stability, the materials found favour at the process scale where in-situ cleaning at extremes of pH was possible as opposed to silica pH limitations.

A second material from the WLCU again commercialised by Shandon was the porous graphitic carbon sold as Hypercarb®. Although activated carbon had been used for GC applications previously, this was the first time that graphitic carbon had been made available in a form suitable for the pressures involved in HPLC and in a spherical form with surface and porosity characteristics giving acceptable retention times. The 2D graphitic structure (Figure 3) imparted a highly selective surface which allowed mixtures with compounds of similar molecular shape and functionality (e.g. diastereo- and geometric isomers) to be separated on relatively short columns.

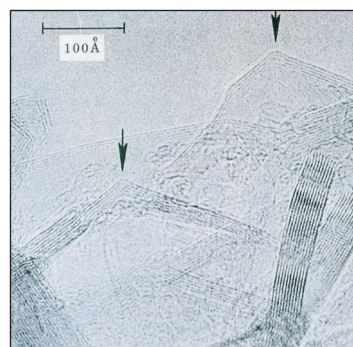


Figure 3. Electron micrograph of 2D porous graphitic particles showing layers of hexagonally linked carbon

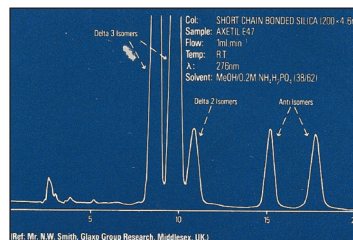


Figure 4a. Axetil isomers chromatographed on silica based column 200mm long.

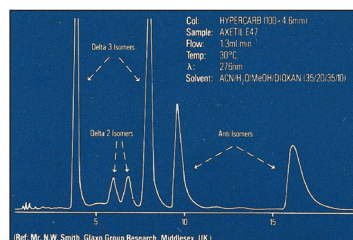
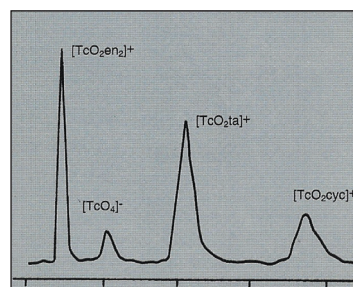


Figure 4b. Axetil isomers chromatographed on Hypercarb column 100mm long.



COLUMN:	Hypercarb® 100x4.6mm
MOBILE PHASE:	Acetonitrile: 1% TFA (2:98v/v) for 14 min, then changed to acetonitrile: 1% TFA (10:90 v/v) for 6 mins.
FLOW RATE:	1ml/min
DETECTOR:	Radiomatic
REFERENCES:	M. F. Emery and C. K. Lim, J. of Chrom. 497 (1989), 212.

Figure 5. Anions and Cations separated on the same column.

Coupled to the unique selectivity and pH stability (0 – 14) this allowed more or less any mobile phase to be used to effect a separation and some pretty unique separations (*Figures 4 and 5*) were achieved which had failed miserably on silica or polymer based columns.

Initially touted as the ideal stationary phase for LC, the reality failed to live up to the potential mainly due to a widespread lack of understanding of the mechanisms, and control of them, taking place during separations. None the less the product is 21 years old, still widely available and this year at HPLC2009 in Dresden (June 28th – July 2nd) a celebration will be held to mark the event.

The processes for all stationary phase production at that time were clouded in secrecy by manufacturers fearful of passing on trade secrets to the competition. Laboratory through to pilot plant and full production scale operations were claimed at various stages once Quality Management

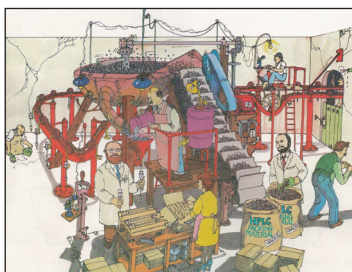


Figure 6. Common impression of media manufacturing plant, mid 1980's.

Programmes became important prerequisites in the Pharma. Industry for columns of choice. Customer base although the illustration in *Figure 6* is not intended to be representative of any particular manufacturer.

As a testimony to the efforts of the WLCU an image of a scientist working on an HPLC Instrument taken from a photograph from the laboratory is actually used on a Scottish £20 note (*Figure 7*). Can any other country boast their separation scientist's elevation to such exalted company?



Figure 7. Recognition for the British Chromatography Industry.

Coming soon – more products from the Halcyon days of the British Chromatography Industry.

Acknowledgements to those who supplied photographs and memories for the chosen products and apologies to those on a longer list, who for reasons of space did not have their products featured this time around.

REFERENCES

(1) I Wilson, *50th Anniversary Handbook of the Chromatographic Society*, ILM Publications 2006, 4-7

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