Facing the Challenges of Aging SFC Equipment

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Introduction

Over the past 15 years, GSK has employed SFC for routine achiral and chiral method development as well as preparative scale-up. Early work with SFC in our labs started with the Hewlett Packard systems, eventually evolving into Berger SFC, which comprises the majority of our analytical SFC instrumentation to date. As systems begin to deteriorate with age, a limited supply of spare parts, numerous vendor acquisitions, and manufacturers no longer in existence to support such equipment, users are now faced with the challenge of replacing aging, outdated instrumentation.
We have chosen to move forward by implementing a procedure that guides us in the selection of newer, manufacturer supported systems. During this process, our group only considered manufacturers that offered both analytical and preparative systems; thereby, enabling us to transition from the Berger/Thar SFC era toward new advances in SFC development and technology. Demonstrated is an overview of current instrumentation and highlights of new purchases.

New Equipment Considerations

Criteria	PIC Analytic Assessment
1. Solvent Compatibility –alkanes, alcohols, & halogenated solvents	All components (i.e. valves, pumps, seals) are comprised of stainless steel and/or Teflon
2. Carry-Over – assessment of injector/autosampler	No carry-over exhibited
3. Software-user friendly and reliable (Fig 1-4)	•Operating parameters clearly displayed •Easy method/sequence creation •Fast column screening set-up •Easy data manipulation and multi-chromatogram viewing
4. Column Oven Design – easy access to columns (Fig. 5)	Unique door design and column organization
5. Hardware accessibility – ability to easily access components for maintenance (Fig. 6)	•Unit is divided into 3 accessible sections •Sections accessible from front and back
6. Reproducibility- reliability and consistency of pumps (Fig. 7)	Standard test mix reveals acceptable pumping capability (%RSD < 1.5%)

Current Analytical SFC Instrumentation

Specifications	Berger 1200	Berger 1200	Thar
Maximum Flow	10 ml/min	10 ml/min	10 ml/min
Column Size	4.6-10mm ID	4.6-10mm ID	4.6-10mm ID
Column Positions	6	6	10
Co-Solvent	6	1	6
Maximum Pressure	400 bar	400 bar	400 bar
Detection	DAD	DAD	VWD/MS
Software	Pronto	Chemstation	MassLynx

Newly Purchased SFC Instrumentation

SFC-PICLAB Analytic	Specifications
Maximum Flow Rate	20mL/min
Column Size	4.6 - 10 mm ID
Column Positions	Up to 10 columns
Co-Solvent	Up to 6 solvents
Maximum Pressure	350 bar
Injection	Automatic (116 vials) and manual
Detection	DAD Detector (Knauer)

Semi-Preparative Add-On Components
Additional CO_2 Pump
Fraction collector assembly

Software

•Control Module

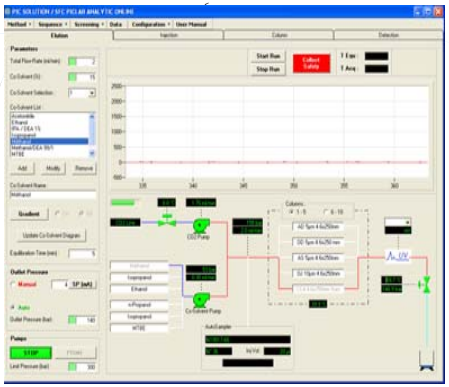


Fig. 1 One page system for monitoring and changing operating conditions

•Method Creation

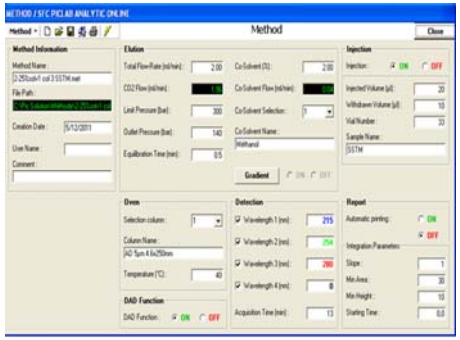


Fig. 2 Versatile method creation-one page set-up allowing the user to make a single injection without requiring a sequence

•Screening Builder

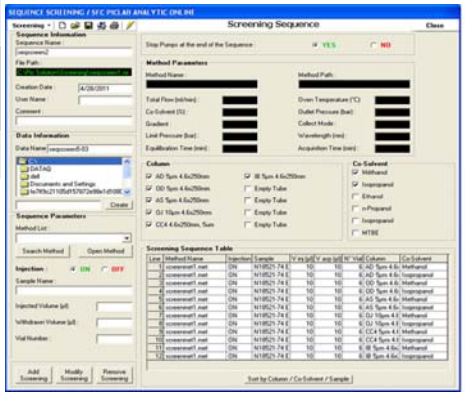


Fig. 3 Select multiple solvents and /or columns with a few clicks for routine screening

•Multi-Chromatogram Viewer

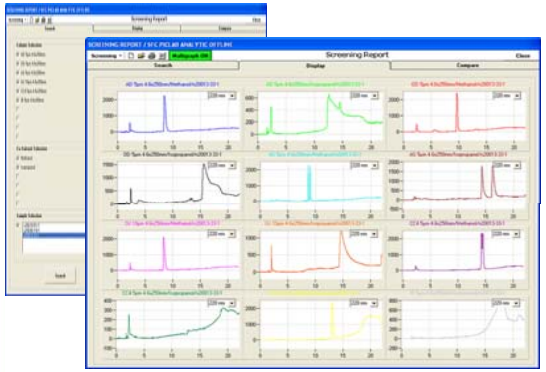


Fig. 4 Quick search option and view of complete screen

Column Oven Design

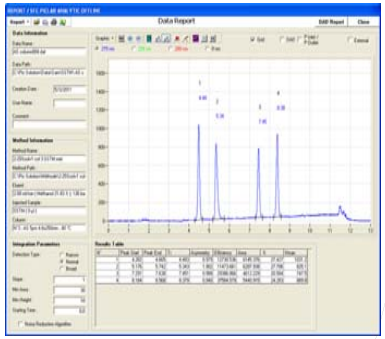
Fig. 5 Door access to 10 (4.6mm ID) and 2 semi-preparative (10mm ID) columns

Hardware Accessibility

Fig. 6 Three accessible sections housing components allows for easy maintenance and troubleshooting

System Reproducibility

Standard Suitability Test Mix	Instrument Parameters
Trans-stilbene oxide 4'-ethyoxayacetanilide 4'-hydroxyacetanilide	2-25% MeOH, 2 mL/min, 140 bar, 40 C, 4.6 x 250mm, 5µm, ASH



N=10	Peak 1	Peak 2	Peak 3	Peak 4
Avg	4.246	5.121	7.286	8.277
St Dev	0.014	0.014	0.026	0.013
%RSD	0.336	0.276	0.351	0.156

Fig. 7 Reproducibility of test mix

Vendor Considerations

Specifications	Jasco	Sepiatec	Waters
Maximum Flow	10 ml/min	6 ml/min	4ml/min
Column Size	4.6-10mm ID	4.6-10mm ID	2.1-4.6mm ID
Column Positions	6	8 (in parallel)	2-4
Co-Solvent	6	18	8
Maximum Pressure	400 bar	400 bar	413 bar
Detection	UV, PDA, CD, MS, ELSD	PDA	PDA, MS
Semi-Prep Capability	Yes	No	No

Conclusion

The decision to replace outdated instrumentation with a newer manufacturer is never an easy process; however, outlining a procedure for selection, has afforded an easier transition. Key features have been highlighted to demonstrate aspects of the system that we found particularly interesting and are a welcomed update to our laboratory. Such features include an easily accessible column oven which can house semi-preparative and analytical columns, easy set-up for column screening, and multi-chromatogram views for easy data manipulation. Also, future semi-preparative capability requiring minor modifications is possible. We have found a system that can easily support our current workflow, from analytical to preparative scale, and gives us the flexibility to expand in the future.

Acknowledgements

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