SHIMADZU
Solutions for Science
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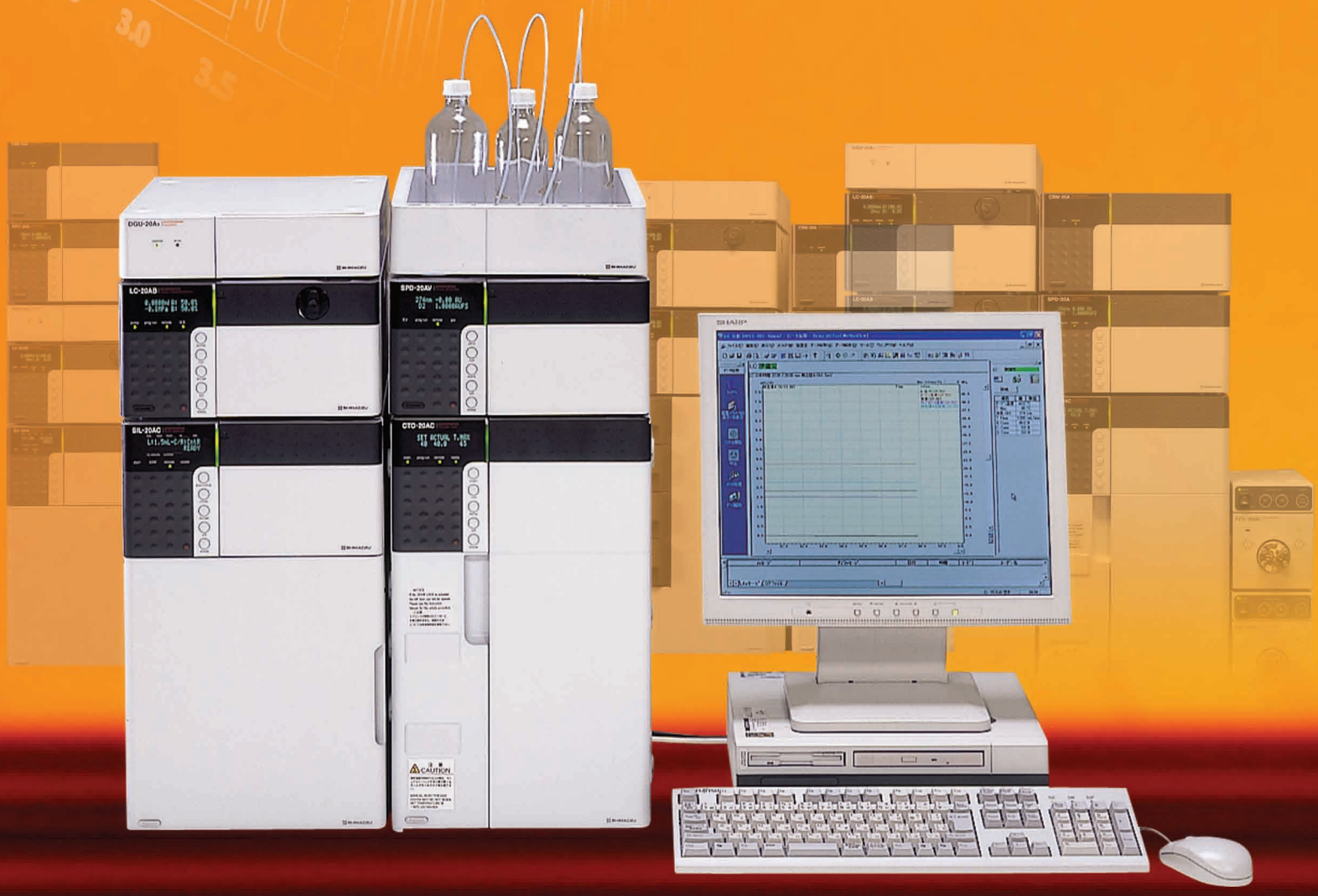
Summer 2005 / International Edition

LC World Talk

SHIMADZU'S NEWSLETTER FOR THE HPLC GLOBAL COMMUNITY

Prominence



"Contribute to society through

Greetings! My name is Shuzo Maruyama, and I am Shimadzu's LC Business Unit General Manager. Please allow me to offer my thanks for your continued support of Shimadzu's products.

Shuzo Maruyama, LC Business Unit General Manager

This year marks Shimadzu Corporation's 130th anniversary since its establishment in Kyoto in 1875, when it was founded by Genzo Shimadzu as a scientific equipment manufacturing sales enterprise. As a manufacturer of a comprehensive array of analytical instruments, Shimadzu manufactures and markets almost every type of analytical instrument required for chemical and physical analysis, and its reputation for innovation and excellence is ever growing.

Adhering to our corporate credo, "Contribute to society through science and technology", we are devoting our energies to research and development. Epitomizing our dedication to developing original technology is the discovery of the soft ionization method for which Koichi Tanaka received the Nobel Prize, and which has brought us high esteem.

Lead to Innovation

Incorporating a sub-10-second, ultra high-speed injection and a wealth of accumulated low-carryover technology, Prominence holds an impregnable position as an MS front end LC for the high-performance LC/MS/MS, which demands the highest LC perfomance.

Shimadzu has more than 30 years of history in the manufacture and sale of products in the HPLC line. Our LC-6A series, first placed on the market in 1984, was one of the world's first models based on a modular design, which is widely accepted as the standard for today's HPLC.

The Prominence series, first placed on the market in 2004, is our latest model of this modular-type LC. Incorporating a sub-10-second, ultra high-speed injection and a wealth of accumulated low-carryover technology, Prominence holds an impregnable position as an MS front end LC for the high-performance LC/MS/MS, which demands the highest LC performance.

The Web server function built into Prominence allows instrument control and monitoring via the web browser installed on co-networked PCs. With implementation of this latest networking technology, the many incorporated features of this instrument are efficiently exploited to greatly improve user convenience and productivity. It is with great pride that we put the finishing touches on this product, which is sure to admirably serve HPLC users everywhere.

As we look to the future, we intend to approach product development and manufacture with an adventurous spirit, and with the solution requirements of customers uppermost in mind, to effectively contribute to everyone's analytical requirements using our original technologies. With this commitment, we ask for your continued support and trust in Shimadzu's HPLC for many years to come.

1972–Introduction of LC-1A

1978–Technology Breakthrough!
LC-3A: Constant displacement quick return (CDQR) solvent delivery system

1982–Industry First! LC-5A: Dedicated HPLC system with 1 mm micro bore column

SPD-M1A: High resolution, high sensitivity dual lamp PDA detector

LC-5A

1984–Technology Breakthrough!
LC-6A: Compact, versatile HPLC system with modular design and centralized controller

LC-6A

science and technology”

Prominence: LC-20A Major Units Overview

Solvent delivery units

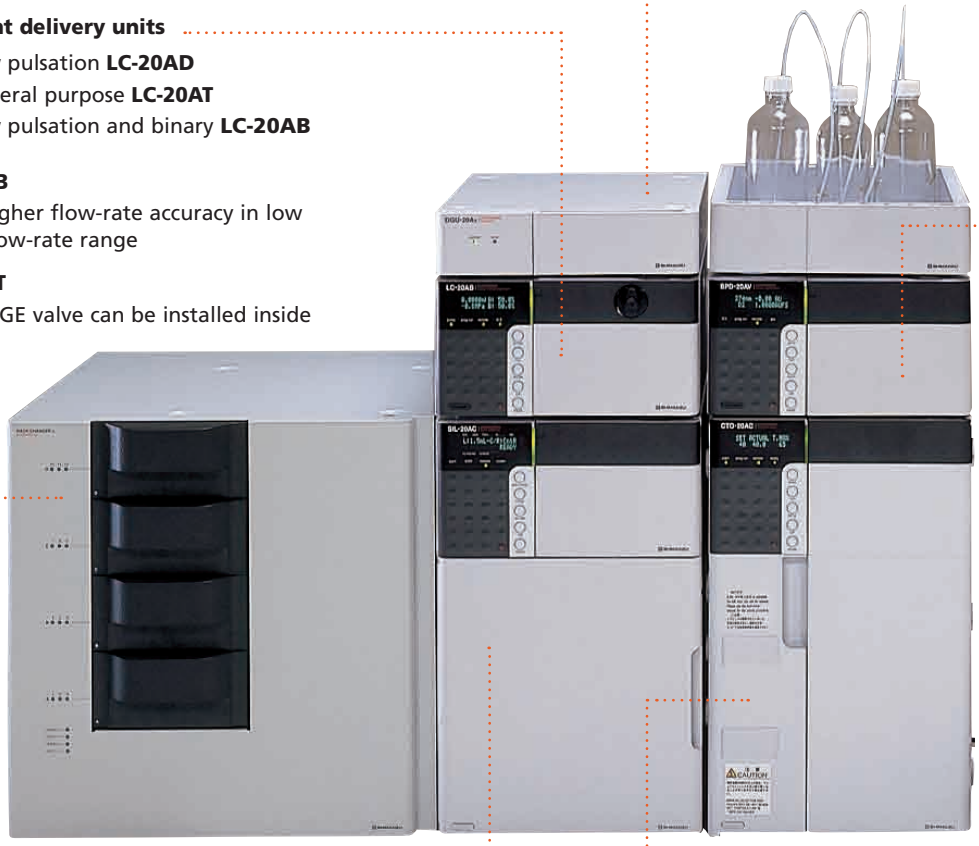
1. Low pulsation **LC-20AD**
2. General purpose **LC-20AT**
3. Low pulsation and binary **LC-20AB**

20AD/B

1. Higher flow-rate accuracy in low flow-rate range

20AD/T

2. LPGE valve can be installed inside



Low-volume degasser DGU-20A

1. Teflon AF®
2. Ghost peak reduction
3. 1/20 volume (3ch, 5ch, <400µL)

World's Highest Sensitivity!

High Sensitivity PDA SPD-M20A

1. Less noise (<1/2)
2. Less drift (1/2)
3. Temp-controlled cell standard
4. 4ch analog output standard

High Sensitivity UV-VIS SPD-20A/V

1. Less noise (less 30%)
2. Less drift (1/2)
3. Temp-contolled cell standard
4. Low pressure Hg lamp equipped

World's First!

Controller CBM-20A / CBM Lite

1. LAN adapter equipped
2. Web control capability
3. Card to be installed inside pump or SIL

Rack Changer

1. Max 12 MTP/DWP
2. Cooling option (type C)
3. Automatic rack change

World's Fastest!

Fast autosampler SIL-20A/C

1. Fast injection: 10 sec. cycle
2. Low sample carryover: New needle and valve design
3. Multi-rinse liquids applicable

Oven CTO-20A/C

1. CMD (Column Management Device) compatible
2. No sub-controller required for valve operation

1991-95–Unparalleled Worldwide Acceptance!
LC-10A: Advanced modular HPLC system with exclusive fiber optic interface. More than 50,000 LC-10A units shipped since introduction

LC-10A

1997-Technology Breakthrough!
LC-VP: Expanded validation and productivity, superb performance with high flexibility and expandability, best MS front end

2004–Innovative Breakthrough
LC-20A Prominence: World's first Web control, fastest sample injection, and the highest detection sensitivity performance to surpass current HPLC technology

LC-20A

by Tsuyoshi Morikawa, Naoki Osaka

The Dream of Universal Instrument Control

Combining HPLC systems and data systems to improve control, user interfaces and productivity in the lab

Innovative Network Compatibility

The world's first HPLC control by a web browser is available with the CBM-20A. Use any computer with Microsoft Internet Explorer 6.0 to control and monitor the Prominence HPLC system. Connection to the CBM-20A requires no special software to control and monitor HPLC systems on the network from the client PC.

Easily check the status of networked HPLC systems, or monitor consumable parts for increased work efficiency.

Naoki Osaka, Tsuyoshi Morikawa

THE LONG AND CONTINUING DEVELOPMENT of HPLC instrumentation has brought this analytical technology so far into the mainstream that it is now considered an indispensable laboratory tool. Further, the parallel development of computers and their networks has led to the inevitable logical leap: the merging of laboratory analysis and network communications. The widespread prevalence of the network in the lab and in the office is rapidly fueling the demand for easy access to the HPLC at any time from any location for convenient setting of instrument parameters, stopping and starting analysis, and monitoring of analysis status.

In client/server type chromatography data systems (CDS), any HPLC on the system can be accessed from any of the client PCs. However client software must be installed on each PC. Additionally, since any PC that is to operate under this environment must have the associated proprietary CDS control software built in, the HPLC instrument most suitable for the analyst's application quite often cannot be used.

In this current situation, we thought about how it might be possible to provide all users the ability to easily use any CDS on any HPLC irrespective of the time, place or environment. We reached the conclusion that the most desirable approach would be to devise a mechanism by which the HPLC system itself would incorporate a built-in control program that could be accessed via a Web browser (Internet Explorer) that is already universally installed on most computers.

By implementing this concept, information (including maintenance information) associated with all the instruments on the network would easily allow centralized administration. For example, the operational status and periodic maintenance logs for such items as seal and lamp replacement, etc. could be monitored for 200 HPLC units without leaving the office.

However, various problems emerged when development of the Web-based controller actually began. There are many examples of excellent internet home page designs, but in our case, all of the Web content had to be created in the Web server inside the controller.

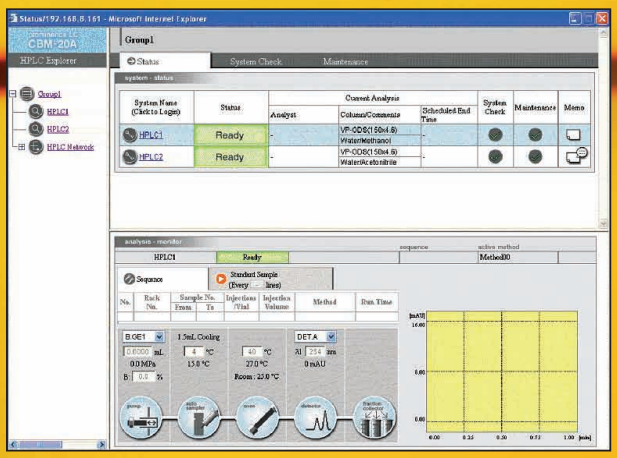


Figure 1: Instrument Monitor Screen

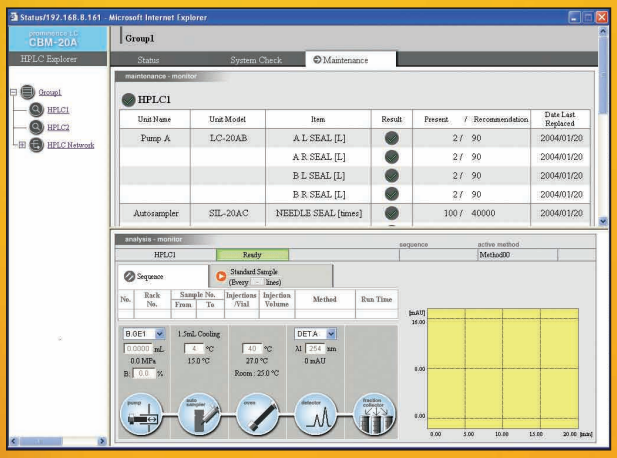


Figure 2: Maintenance Screen

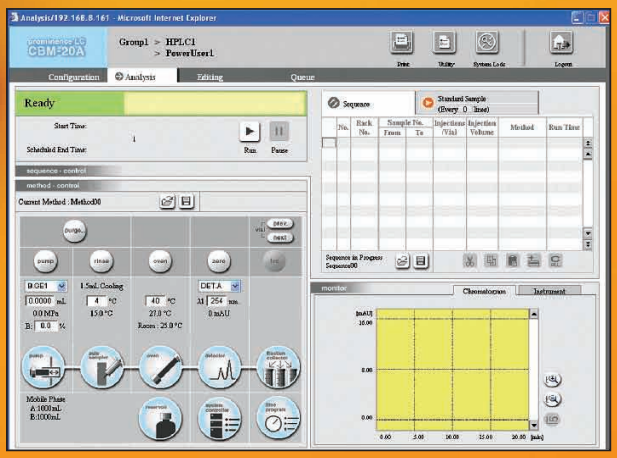


Figure 3: Analysis Start Screen

> "The widespread prevalence of the network in the lab and in the office is rapidly fueling the demand for easy access to the HPLC at any time from any location...

Generally, while the strong point of a Web server is the possibility to create Web content determined beforehand, it does not lend itself well to complicated adjustive control based on instrument configuration. Since an HPLC system can vary immensely in complexity, from a simple system consisting of a solvent delivery pump and detector, to a system with several pumps and detectors, an autosampler, column oven, valves, etc., we decided to start development by keeping the HPLC system configuration and control operation separate. That completed, we would then introduce technology specifically designed to create Web content dynamically. In this way, development was advanced by ensuring that the software and design elements developed by our in-house software and design departments engaged intimately with this type of new technology.

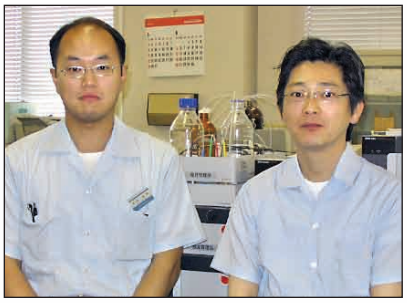
Another advantage of this system is that XML is used for the exchange of data between the PC and HPLC. Currently, standardization for sharing analytical information (AnIML project*) using XML is progressing. The goal of this project is to define the format and structure of analytical data obtained by different data systems so that these data can be shared among other data systems as well as general-use application software. We believe that it will become possible to control any HPLC using any data system by making the best use of this project's outcome, and we dream of the time that this will become a reality. When this is achieved, not only will it be possible to combine the HPLC system and data system as desired, but Universal Instrument Control will have been achieved through a uniform user interface, and productivity in the lab is expected to improve greatly.

*AnIML stands for the Analytical Information Markup Language, an XML–based data interchange format based on JCAMP-DX and ANDI ontologies. It is being developed via a collaborative effort between many groups and individuals worldwide and is sanctioned by the ASTM under subcommittee E13.15. For more information on this emerging standard please visit http://animl.sourceforge.net.

Vision of Next Generation Autosampler

by Nobuyuki Tatsumi, Yoshiaki Maeda

The spread of triple-stage LC/MS/MS for bioanalysis that started in the late 1990's brought about a dramatic change in the demand for HPLC. The high selectivity and high sensitivity of LC/MS/MS, on the one hand, reduced the necessity for separation between compounds of interest and, on the other hand, exposed the importance of shortening the analysis cycle and reducing carryover.



Yoshiaki Maeda, Nobuyuki Tatsumi

CARRYOVER is the term applied in relation to the occurrence of baseline fluctuation and peaks originating from the sample injected directly before the current one; however, it is known that along with the increasingly complicated structure of compounds of new drug candidates and the increase in hydrophobic and strongly basic compounds, these compounds are increasingly the source of carryover due to their strong adsorption in the HPLC flow lines and column.

Generally, in HPLC, the quantitation limit is most often limited by detection sensitivity (signal/noise ratio). However, in recent high sensitivity LC/MS/MS analysis, the quantitation limit is oftentimes determined by carryover. This is due to the fact that, while the instrument has sufficient sensitivity, the quantitation limit cannot be lowered because carryover peaks were observed. Despite developing appropriate analytical conditions to achieve adequate system sensitivity, there must be many metabolism researchers who have experienced the dilemma of not being able to use detected peaks for quantitation.

WHAT IS THE NEXT GENERATION AUTOSAMPLER?

It is widely known that the autosampler made the most notable contribution to analytical efficiency by shortening the analysis cycle and decreasing carryover. Due to its positive role in improving analysis operations by reducing analysis time and improving quantitation accuracy, there is a growing demand for higher performance using autosamplers. The performance enhancements desired from autosamplers can be consolidated as follows.

- Improved throughput with shorter analysis cycle
- Better low-carryover performance to eliminate the effects of sample properties like hydrophobicity and basicity
- Flexible rack formats that accommodate a wide range of sample containers from glass vials to microtiter plates
- Support for processing a greater number of specimens, from one day's worth of samples to 1 week's worth of samples

Moreover, basic performance features like measurement accuracy and instrument durability are considered to be critical factors in achieving the above with good reliability.

SIL-20A/C

BIRTH OF THE LOW–CARRYOVER AUTOSAMPLER

Development of an instrument can be characterized by periods of smooth progress and periods of convoluted turns. The process of infusing low-carryover attributes into this autosampler involved a circuitous, tortuous journey. In the late 90's, one of the largest pharmaceutical companies in Japan complained of large carryover from autosamplers operating as the front end for MS/MS systems. Initially, we thought of possible changes in the needle wash time and washing method, and every 3 months or so we installed corrective parts at the customer's site for evaluation (at that time, Shimadzu had no in-house LC/MS/MS for evaluation). Despite our efforts, there was no great improvement. After about a year of being frustrated at all our attempts to solve this carryover problem, I was at my wit's end. Thinking back, we really must express our gratitude to the customer for displaying such patience. The customer's patience in this situation was probably warranted, since there was really no low-carryover autosampler in existence which could have satisfied the requirement.

One night, I had a dream that I was conducting an experiment (probably because, at that time, I could not get the carryover problem out of my head). The instrument in my dream, for some reason or another, was providing excellent results, and I just happened to wonder why everything was going so swimmingly. I had no idea what the reason might be, but I just happened to notice that the needle had a special plating. This plating resembled the plating on an electrode that I had casually noticed on a completely different instrument the day before. The next day, with the sense of foreboding that I was "a drowning man clutching at a straw", I searched out the vendor that had plated the electrode, and requested that he plate the autosampler needle. On running a test analysis, there was a distinct improvement in performance, and applying this to the product, we found the solution. In wonderment, I experienced the realization that in product development, one could never know when or where an idea might emerge to break a seemingly impenetrable impasse.

Injection volume setting range	0.1 µL ~ 100 µL (standard) 1 µL ~ 2000 µL (option)
Injection accuracy	0.3 % RSD or less (with 10µL injection) (SIL-20A/20AC regularly shows RSD of about 0.1% with its high-accuracy measuring pump and highly airtight construction.)
Injection cycle speed	10 seconds (10 µL)
Carryover	0.005 % or less (naphthalene, chlorhexidine)
Number of samples accommodated	1 mL vial: 175 vials 1.5 mL vial: 105 vials (SIL-20A) 70 vials (SIL-20AC) 4 mL vial: 50 vials MTP/DWP: 2 plates (standard) 12 plates (w/rack changer) In addition to each of the above, 10 of the 1.5mL vials can also be used in the control rack
Sample Cooler	4°C ~ 40°C (SIL-20AC)

Table 1: Specifications for Prominence Series SIL-20A/C

NEXT GENERATION AUTOSAMPLER SIL-20A/C

The Prominence Series SIL-20A/C low-carryover autosampler was developed as a general-use autosampler that could be used for LC to LC/MS/MS. The main specifications for this instrument are shown in Table 1.

FUTURE AUTOSAMPLERS

Liquid phase chromatography is the core of analytical separation technology, and is widely employed throughout many fields of application. Accordingly, analytical separation technology based on liquid phase chromatography, although somewhat mature, has the strong potential to bring about transformation through its merging with new analytical techniques such as LC/MS/MS. Global information exchange is important for equipment manufacturers. For developers like myself, however, a flexible imagination together with knowledge as a base are also important to accurately translate new demands into concrete reality. I look forward to the development of instrumentation that can be used with greater satisfaction by researchers around the world.

Pathfinder® Column

Introduction of the Most Inert Silica-Based HPLC Column Technology

Reversed phase continues to be the dominant mode of high performance liquid chromatography (HPLC) because of the wide range of chemically diverse compounds that can be analyzed by this technique. However, some drawbacks remain, e.g. analysis of basic compounds can be hampered by ionic and other polar interactions of the basic analytes with residual silanols and other polar sites present on the silica surface. This can result in asymmetric peaks and irreproducible retention times. Many manufacturers of HPLC columns are now focusing on improving stationary-phase stability and reproducibility. Improved column stability — both chemical and thermal — offers new advantages, such as decreased analysis time and new methods of selectivity optimization.

Today, we are proud to introduce conceptually new HPLC packing materials developed by Shant Laboratories sa/nv and Shimadzu Europe. When the scientists at Shant Laboratories developed the Pathfinder® product line for the pharmaceutical industry, the goal was to produce columns with performance levels that surpassed all other products on the market. The result is Shant's new Polymer Encapsulated Silica Technology that yields a product with unique chromatographic characteristics and dramatically improved performance. We're very excited about this new technology, and believe that it will have a significant impact on the process of drug discovery, and on other applications in the bio/pharmaceutical industries.

Existing Technologies

Silica Modified Packings: Traditional silica-based reversed-phase packings are manufactured by derivatizing the surface of silica particles using silane reagents that react with silanol (Si-OH) groups. Because the silanes are considerably larger than the silanols, not all of the silanols are derivatized. Consequently, surface derivatization is always incomplete, and may leave large patches of unbonded surface. The residual silanols are acidic and cause peak tailing for basic compounds due to anion-exchange interaction. In addition, the underivatized regions of the surface are likely the sites where the silica particles begin to dissolve in high pH mobile phases.

Polymeric Packings: One approach for eliminating unwanted silanol interactions is the development of non-silica stationary phases. These column packings use polymeric particles instead of silica, but they account for only a small portion of the total LC-column business. Indeed, the silanol tailing and pH-stability problems of silica columns are absent from the polymeric columns. However, these polymer columns could not provide separations as good as the silica columns. In many cases, even with the desired selectivity obtained, plate numbers for polymer columns are much lower than the equivalent silica columns.

Hybrid Particle: The technological progress in stability has resulted from the use of alternative supports such as hybrid organic-inorganic particles, especially useful for high pH applications, an area in which silica gel has been in disfavor. The columns constructed from this material have proved to be more stable in alkaline conditions and have a 30% longer lifetime than the typical silica-based packings, but they suffer from poorer efficiency than silica gel. The rate of mass transfer in the bulk stationary phase appears to be slower than the mass transfer in a silica-gel packing.

Polymer Grafted Silica: During the final stage of silica manufacturing, a silicon-organic layer is subjected to react with the silanol groups of silica support, thereby generating an "anchored coating". This type of polymer coating is considered to be more homogeneous, but it is limited to the concentration of silanol groups on the surface. That can cause problems when considering bath-to-bath reproducibility issues. In addition, in this so-called soft polymer grafting, the silica support is not completely encapsulated during the cross-linking procedure. This results in non-complete coating and may lead in some cases to a poor chromatographic performance, especially for basic components.

Pathfinder Particle Engineering

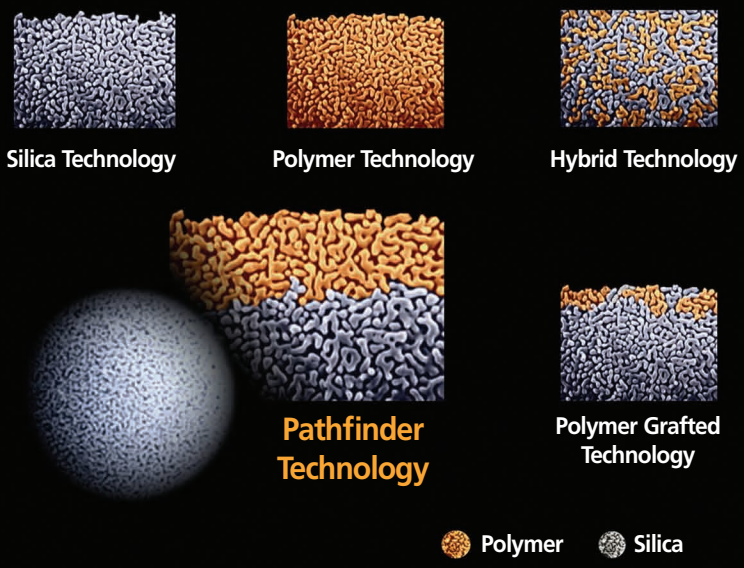
Pathfinder media is a new generation of HPLC packing material, made from organic and inorganic building blocks combined at the molecular level: one that forms the internal silica core, and another that forms the external chemically inert polymer capsule. Unlike novel hybrid materials, which have organic groups throughout their structure, these hybrid particles have organic groups only at their surface. As a result, the hybrid preserves the unique mass transfer characteristics of silica and shares the chemical inertness, temperature and pH stability of organic polymers.

Both porous and non-porous microspheric particles in a range of sizes can be produced with this innovative approach. Pathfinder technology ensures the absence of residual silanol groups on the surface and controllable batch-to-batch reproducibility caused by the total production process.

Technology

for More Powerful Method Development

by **Dr. George Abrahamian** (CEO, Shant Laboratories sa/nv)
and **Jan van Gils** (Sales Manager, Shimadzu Benelux)



For porous packing material, 5 different Pathfinder phases are available in 100 and 300 Angstrom pore sizes with a particle size of 2, 3 and 5 micron covering the complete range from fully hydrophilic to hydrophobic. Non-porous Pathfinder packing material is also available with 1.5 and 3 micron particles for ultra-fast HPLC applications.

Chemical Inertness

Pathfinder media are made through an advanced bonding chemistry process that yields a product with unique chromatographic characteristics. It is still primarily hydrophobic, but it has hydrophilic domains near the surface that can be wetted with polar eluents; hence, it retains the configuration of the bonded phase. Therefore, the columns can function well in 100% aqueous environments as well as with 100% organic mobile phases without shrinking or swelling.

Pathfinder hybrid packing material has no silanol activity due to the external polymeric block. The result is a silica-based stationary phase that has eliminated the negative effects of silanols on reversed-phase HPLC separations combined with chemical inertness at any temperature. The ultra-inert characteristic of Pathfinder HPLC columns makes them the ideal choice for separating polar basic compounds. When compared to other modern base-deactivated columns, the Pathfinder columns ultimately produce significantly better peak shape and innovative selectivity when separating basic solutes without any additives. Separation of highly basic compounds such as pyridine is accompanied by severe tailing on most commercially available base-deactivated columns due to the electrostatic interaction of this solute with residual silanols.

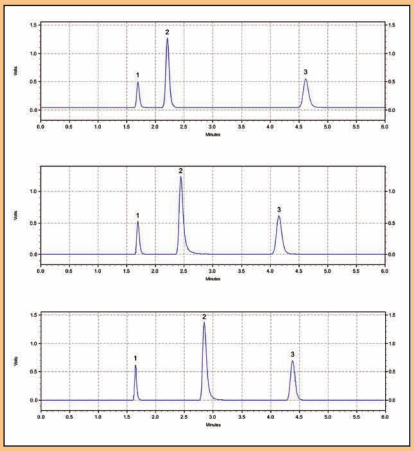


Figure 1: Separation of Basic Pyridine and Phenol Using Pathfinder AP, Xterra C18 and ACE C18 columns (150x4.6 mm column, 3.5 micron, 100 Å)

Samples: 1. Uracil, 2. Pyridine, 3. Phenol

The Pyridine test indicates a degree of silanophilic activity of silica C18 phases, measuring the selectivity factor for pyridine and phenol.

a= k pyridine/ k phenol

Typically, residual silanols will cause peak tailing and changes in retention for pyridine. Accordingly, the silanophilic activity of silica based RP phases is:

High if a > 1.00

Moderate if a is 0.50 to 0.99, and

Low if a < 0.50

According to the test, AP gives the best peak shape, highest column efficiency and lowest value for pyridine:

AP: 0.12, Xterra: 0.41, ACE: 0.45

Eluent: Methanol/Water 30:70

Flow rate: 1ml/min

Detection: UV@254nm

Temperature: 40°C

Flexibility in Packing Material Design

Most commercial C18 phases only contain 10-15% carbon, which means similar design criteria can lead to similar selectivity. This similarity can cause problems when a sample needs an alternative selectivity.

The potential value of Pathfinder technology is that it allows the design of stationary phases with well-defined properties, such as hydrophobicity and polarity of the stationary phase. Furthermore, it is possible to design tailor-made external polymer blocks, without restriction of the surface properties. In addition, the retentivity and the polarity of the stationary phases can be easily varied with different amounts of prepolymer before the definitive engineering of the external capsule takes place.

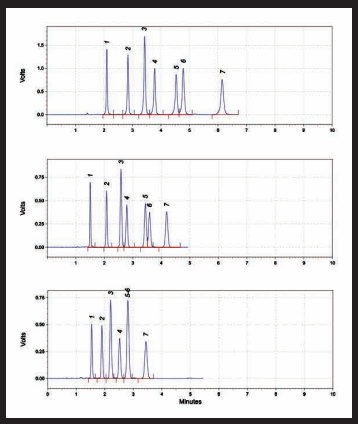


Figure 2: Comparative Data on Extended Selectivity using Pathfinder® MR, Gemini, and Xterra columns
1. MR 2. GEMINI 3. XTERRA
Conditions:
Column 1: Pathfinder MR
4.6 x 150 mm, 4um
Column 2: Gemini C18
4.6 x 150 mm, 5um
Column 3: Xterra C18
4.6 x 150 mm, 5um
Eluent: ACN/Water 50:50
Flow rate: 2ml/min UV@254nm
Temperature: 40°C
Samples:
1. Hydrocortisone
2. Dioxycorticosterone
3. 11-alfa-Hydroxyprogesterone
4. Cortisone Acetate
5. Corticosterone
6. 11-Ketoprogesterone
7. 17-alfa-Hydroxyprogesterone

Example: The Pathfinder C18 AS column is equivalent to a high-carbon (30%) C18 phase packing that is made through an advanced bonding chemistry process yielding a product with unique chromatographic characteristics. The octadecyl C18 functional groups are incorporated into the structure of the capsule to obtain a high-density C18 coverage. This results in longer retention for all compounds. The dense bonding in the Pathfinder C18 AS column gives the packing excellent efficiency and peak symmetry. It is highly stable, reproducible, and often more selective than ordinary C18 phases.

Besides the traditional hydrophobic separation model in silica C18 reversed-phase columns, polar separation models are becoming more and more important in research for innovative selectivity. The controllable polymer chemistry of Pathfinder technology makes the introduction of polar groups near the particle surface possible in many different ways. This results in five standard phases and possibilities for customized turnkey solutions. By active use of PH and temperature positive repulsion and dipole interactions, it becomes a separation tool along with the traditional hydrophobic reversed-phase separation model.

The Pathfinder method development kit with five different polar embedded C18 chemistries is a unique tool for the Shimadzu HPLC method development system using temperature-controlled column switching solutions.

Chemical Stability

Pathfinder products all have outstanding chemical stability. They can be used across the pH range from 1 to 12. The enhanced pH and thermal stability of Pathfinder® reversed-phase packing materials allow for the widest possible range of chromatographic conditions. For example, chromatographers can use high pH to suppress amine protonation and low pH to suppress the ionization of acidic solutes. Extreme chemical stability also enables the cleaning of fouled columns under very acidic conditions and the sterilization or depyrogenation of columns with alcoholic basic solutions. By using low-pH conditions, analysts can increase the retention of anions by protonating them, thereby avoiding the need for quaternary amine ion-pairing agents. Similarly, one can, in principle, increase the retention of positively charged amines by raising the pH to higher values.

Thermal Stability

Pathfinder Polar embedded RP columns can be routinely used up to 200°C due to the extremely high temperature specifications of the developed packing materials. The thermal stability of Pathfinder columns has its own distinct inherent advantages. It can enable analyses at higher column temperatures, which lower mobile-phase viscosity and lessen the mechanical wear and tear on LC pumping systems. Higher run temperatures also lower the retention of solutes in reversed-phase mode, and this process often results in faster analyses or the ability to reduce the necessary amount of organic modifier to elute the solutes.

With thermal stability of Pathfinder columns comes the freedom to use column temperature to optimize the separation, which can lead to a more robust separation or to beneficial selectivity changes. For example, the elevated temperature, when used in conjunction with adjustments in mobile-phase composition, can be a very powerful aid in optimizing separations. Thermal stability can also make method development easier because temperature is easily changed, whereas mobile-phase changes may require long equilibration periods after switching between drastically different organic modifiers. Elevated temperature liquid chromatography (ETLC) can most easily be described as an adaptation of HPLC where the major modification is the replacement of the traditional mobile phases, such as acetonitrile or methanol, with superheated water as the mobile phase.

The main advantage of superheated water is its ability to elute polar compounds. This ability can be successfully utilized to separate a number of compounds by ETLC, using water or aqueous buffers as the sole eluent.

Continued on back cover

Winner of the 2005 Pittcon Editors' Silver Award

Shimadzu introduces the first LCMS-IT-TOF Mass Spectrometer

FOR THE FIRST TIME, a tandem MS/MS spectrometer for use with HPLC, incorporating both ion trap and time-of-flight capabilities, is available. Hybrid mass spectrometers, such as Shimadzu's new LCMS-IT-TOF, have been embraced by the analytical community for their unique capabilities.

The combination of these two different mass spectrometry techniques results in capabilities beyond any single mass analyzing technology. Ion trap mass spectrometry allows target molecules to be selected and fragmented easily while time-of-flight MS allows for accurate mass determination.

For such uses as biomarker discovery, metabolite identification and human health research, the LCMS-IT-TOF couples atmospheric pressure ionization with Ion-Trap (IT) and Time-of-Flight (TOF) technologies, to deliver high mass accuracy and high mass resolution (10,000 at 1000 m/z) independent of MS mode. It allows more qualitative information about a sample to be collected in a single run, eliminating multiple analyses and the need to split samples between multiple instruments. The technologies used in the LCMS-IT-TOF allow molecules to be broken up into successively smaller fragments, and the masses of those fragments to be measured accurately enough to determine the likely empirical and structural formulae. With the new LCMS-IT-TOF, it will be possible to fragment the various component peaks found in a HPLC separation to determine formulae for each and where they come from. The new instrument incorporates a host of new technologies and enhancements, including:

- Compressed Ion Injection (patented)
- Ballistic Ion Extraction (patented)
- Dual-Stage Reflectron (patented)
- New ion transfer optics
- Temperature control of the flight tube

These technologies combine with other unique features to ensure the trap does not get overfilled or have difficulties with space-charge effects, and these technologies also improve long-term mass accuracy and stability. The source design, desolvation capillary and reduced collision ion focusing Q-Array were adapted from Shimadzu's successful single quad HPLC mass spectrometer.

The importance of the LCMS-IT-TOF instrument was recognized by the editors of industry trade publications and journals with the award of the Editors' Silver Award at Pittcon 2005. This was also the first time the instrument was shown at a major U.S. tradeshow.

The LCMS-IT-TOF mass spectrometer will change the way researchers deduce the structure of unknown compounds and contaminants. It represents a significant improvement over other mass spectrometry techniques because of the combination of high sensitivity and long-term stability of mass accuracy in an easy-to-use instrument for HPLC use.

Winner of the 2005 R&D 100 Award

Pathfinder® Column Technology

for More Powerful Method Development

Continued from page 10

Ultra-Fast High Selectivity Liquid Chromatography

Use of micro silica particle technology is becoming more and more popular for fast LC/LCMS analysis in combination with high selectivity. Two-micron particles packed in 2.1 and 1 mm ID column hardware configurations will result in high column backpressure, especially when the HPLC configuration is optimized for low dead-volume specifications.

Pathfinder 1.5 and 3 micron Non-Porous columns provide the possibility for ultra-fast and high-resolution analysis. Using temperature as an active separation parameter will create regular backpressures in combination with the chemical inert Pathfinder HPLC columns. Porous 2 micron fast HPLC Pathfinder® columns are available for higher column capacity applications at regular flow rates. In combination with the low dead-volume Shimadzu LC-20A Prominence HPLC system, fast analysis with high selectivity becomes available in a robust way.

Validated Batch-to-Batch Reproducibility

Batch-to-batch reproducibility for silica-based reversed-phase columns is largely dependent on the concentration of the silanol groups of silica particles with known limitations. Batch-to-batch differences in Pathfinder technology are eliminated because of the new polymer chemistry and controlled silica particle production approaches. The quality assurance protocol for Pathfinder columns involves producing and testing these columns under strict documented processes. Several key characteristics are measured to make certain that each piece is designed and manufactured to strict customer and industry specifications. The company's manufacturing methods ensure column reproducibility, which means they've eliminated variations in column performance from batch to batch.

A variety of quality assurance tests developed by leading HPLC scientists are performed in the manufacturing process to confirm batch-to-batch and column-to-column reproducibility. Pathfinder HPLC columns are guaranteed to provide the best reproducibility of any reversed-phase HPLC column.

For more information

For more information regarding Pathfinder technology please reply to pathfinder@shimadzu.de

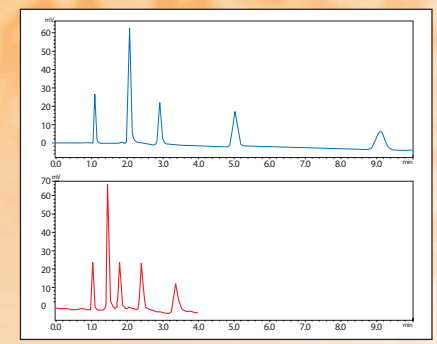


Figure 3: "Green" HPLC using 100% water. Top: 1 ml/min water at 150°C; test mix: Uracil, Acetophenone, Benzene, Toluene, Ethylbenzene. Bottom: 1 ml/ water at 200°C with Prominence.

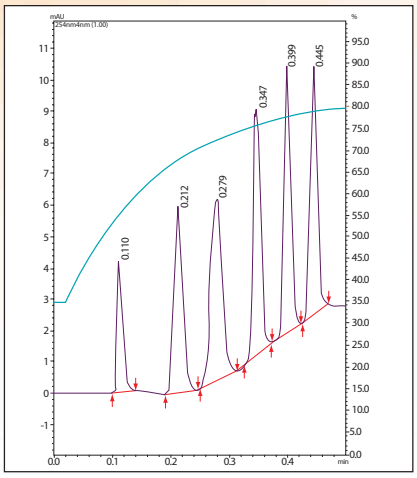


Figure 4: Shark fin™ ultra-fast gradient LC analysis with Prominence; Pathfinder EP non-porous 3µm 4.6 x 33 mm; PDA@254; Flow: 5 ml/min; A: H_2O, B: Acetonitrile, T: 60°C, BP: 300 bar. Elution order: Uracil, Phenol, Methylparaben, Ethylparaben, Propylparaben, Butylparaben.

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