Clinical Chemistry

Removing the purification bottleneck

Improvements in the power and sophistication of software controlling HPLC/MS systems now make it possible to develop a streamlined purification process for a broad range of previously difficult to resolve target compounds. These technologies uncover new avenues in molecular entity discovery.

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Purification of target compounds from crude synthetic mixtures has always been a rate limiting step in the new molecular entity discovery process. Typical technologies employed either have limited resolving power, but simple guiding principles (Flash Chromatography, TLC) or high resolving power but no simple universal rules (Mass-directed HPLC).

During the last 20 years, however, the power and sophistication of the software controlling HPLC/MS systems - analytical as well as preparative - has improved significantly and made it possible to develop a streamlined purification process applicable to a wide range of synthetic mixtures.

Flash chromatography limits

In early drug discovery research, the goal is to get as many compounds into screening as possible in the shortest possible time. Today most medicinal chemists use flash chromatography as the primary tool for purifying the target compounds. The problem with this approach is that it limits the number of samples a chemist can process weekly. Chemistries need to perform relatively well to achieve successful separation even if the flash chromatography system is equipped with a mass spectrometer.

Specialised learning

When synthetic chemists face challenging separations, or need to purify a large number of compounds, they seek help from specialised laboratories. To support a wide array of purification requests, companies like Rilas Technologies set out to find robust analytical and purification systems equipped with software which makes easy to generate focused purification gradients from simple analytical runs. It was concluded that Agilent's 1290 Infinity II Preparative LC/MSD system controlled by automated purification software was the best fit for these types of requests.

Every incoming crude mixture is analysed by our acidic (0.1% formic acid in a water/acetonitrile gradient) and basic method (0.1% ammonium hydroxide in water/acetonitrile gradient) using Agilent's 1290 Infinity II Analytical-Scale LC Purification system equipped with diode array detector and a

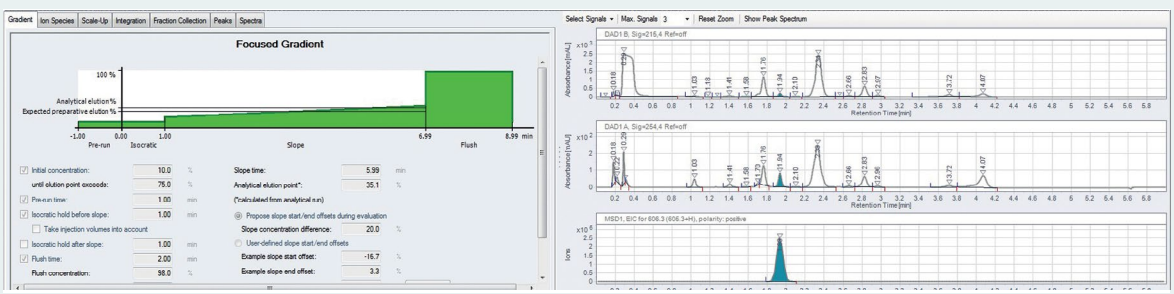
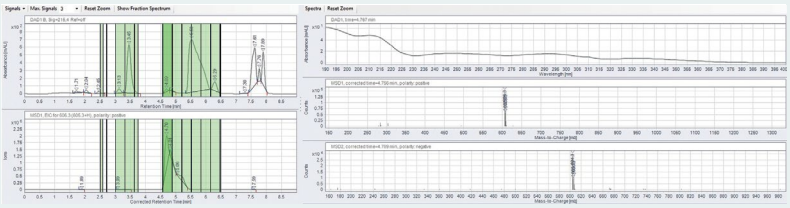


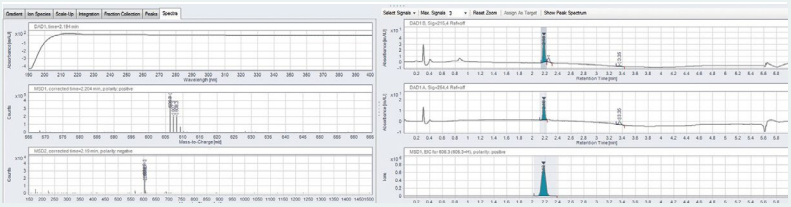
Figure 1: PreQC of a crude mixture Column: Waters XSelect C18, 5µm, 4.6 x 50mm, Mobile Phase A: 0.1% formic acid in water, Mobile Phase B: 0.1% formic acid in acetonitrile Flow Rate: 2.5ml/min. Gradient: 5 to 95% B in 4 minutes



single quad mass spectrometry detector. The resulting PreQC chromatograms are then analysed by the automated purification software resulting in sample specific focused purification gradients. Representative PreQC, preparative and FinalQC chromatograms are depicted on Fig 1 through 3.

This process allows us to purify hundreds of samples weekly without knowing the structures of the target molecules. We only need to know the exact mass of each compound of interest. Figure 4 depicts a snapshot of the summary of several hundred purifications, clearly showing that the process works with great success and we strongly believe that it can be adapted by non-experts to remove the purification bottleneck.

Figure 2: Purification of a crude mixture Column: Waters XSelect C18, 5µm, 19 x 100mm Mobile Phase A: 0.1% formic acid in water; Mobile Phase B: Acetonitrile; Flow rate: 40ml/min; Gradient: 18.4% B to 38.4% B in 6 minutes



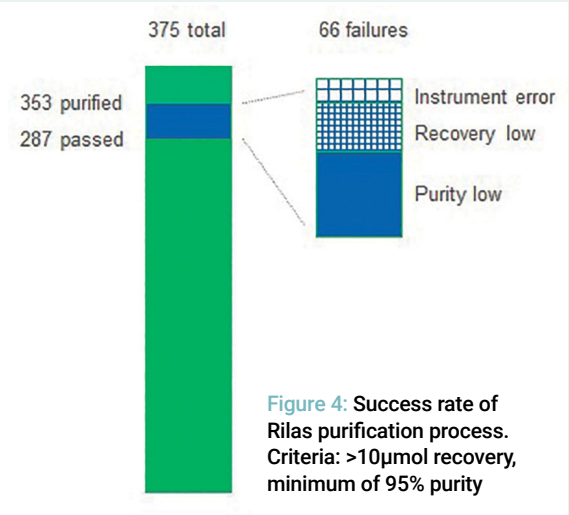


Figure 3 (ABOVE): FinalQC. Column: Acquity CSH C18, 2.1 x 30mm, 1.7µm; Mobile Phase A: 0.1% Formic acid in water. Mobile phase B: 0.1% Formic Acid in acetonitrile. Flow Rate = 0.8mL/min. Gradient: 5% B to 95% in 1.7 minutes

Figure 4: Success rate of Rilas purification process. Criteria: >10µmol recovery, minimum of 95% purity

Secure sanitisation of confidential health data

With increasing rates of cybercrime and large penalties for data breaches, the protection of highly confidential health data is a challenge for many laboratory professionals. **Philip Bridge** explains why laboratories should invest in cetified destruction services...

Overlooking end-of-life data and the incorrect management of data procedures, including the disposal of computers and IT assets can become a serious threat to the security of healthcare information; it also opens up the potential risk for penalties and breaches of privacy legislation, which can cause irreparable damage to a laboratory's image and reputation.

Invisible content isn't deleted content

Decommissioning, disposing or reusing of IT assets is one of the most vulnerable moments for data. Many wrongly believe that native deletion options, such as choosing to 'Empty Trash' or 'Format' the drive are all secure sanitisation solutions, capable of eliminating all traces of deleted files permanently. Unfortunately, the fact that the content is no longer visible does not mean that it is no longer present on the storage media system. The introduction of global data privacy laws has attempted to standardise and update the protection of personal data to face the new challenges of the digital era. It is now critical for laboratory professionals to put secure erasure processes in place for both end-of-life media and through-life data during the lifecycle of all devices.

Budget for 'end-of-life' data disposal upfront

For businesses, the easiest way to implement this is to set a budget aside at the time of purchasing any new hardware, and then use a secure service when the device needs to be disposed of or reused. Outsourcing this service to qualified third parties offering a certified data destruction process can mitigate the risk of exposing sensitive confidential health data.

Philip Bridge is President of Ontrack and has over twenty years data and storage technology experience