

Novel Flash Instrument Improves Sample Purity and Productivity

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Flash chromatography is the primary tool used to purify synthesized compounds in drug discovery. Current technology relies almost exclusively on ultraviolet (UV) detection. However, UV cannot see compounds that lack chromophores, and UV response relates to the strength of the chromophore (the extinction coefficient) rather than the quantity of the compound. Exploiting the benefits of different detection options for early stage purifications improves quantification and purity of compounds entering the screening pipeline.

Addressing the limitations of UV-based flash purifications is not as simple as connecting an external detector, such as an ELSD, to an existing flash system. Along with the significant increase in bench space required, there are a number of complications with fluidics, fraction collection, and data analysis.

The Reveleris™ flash purification system with RevealX™ detection technology (patents pending) addresses these challenges. By combining the strengths of ultraviolet and light scattering technologies into a single detection mechanism, and processing multiple signals to precisely control fraction collection, this technology results in optimal peak volumes, sample purity and recovery, solvent flexibility and waste reduction, and overall faster purifications.

See Non-Chromophoric Compounds

UV detectors miss non-chromophoric contaminants, causing inaccurate assessments of purity and misleading results in bioassay screening. To address this, medicinal chemists often collect all possible fractions for extensive post purification

workup, potentially creating significant delays and custody issues.

The Reveleris™ system detects both chromophoric and non-chromophoric compounds providing more information about complex mixtures.

Better Mass Balance

During synthetic transformations, chemists continuously monitor their reactions using TLC spotting and manual UV detection as indicators of reaction completion. RevealX™ technology represents mass balance better than UV alone, giving the chemist more confidence about the relative amounts of the target compound being synthesized, unreacting starting materials, and reaction by-products being collected.

Smart Fraction Collection

Complementing UV with light scattering detection reveals important information about a sample mixture. However, without the ability to collect fractions based on all detection signals simultaneously and as peaks are eluting, the medicinal chemist would still have to collect everything and spend significant time on post-run fraction workup.

The RevealX™ detection technology is more than just multiple detectors – it uses advanced signal processing and software algorithms to synchronize the signals so that the fraction collector knows which peaks are which, and collects accordingly.

Advanced Fluidics

To add a stand alone detector, the chemist must address complicated issues such as flow splitting and adjusting split ratios for each run. The proprietary splitting design of the Reveleris™ system eliminates the

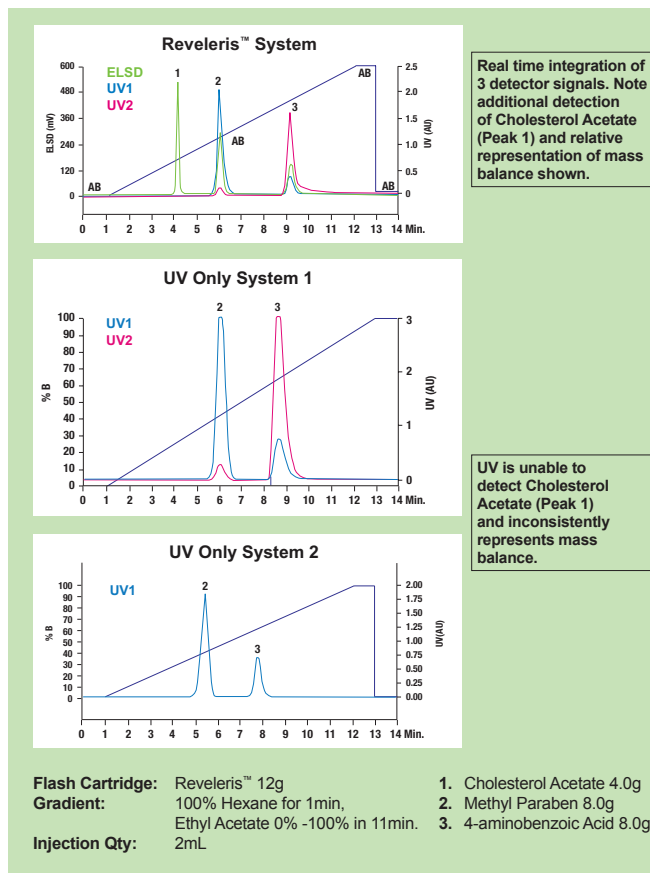


Figure 1: A three-component mixture shows the advantage of the Reveleris™ system over other flash systems. Note the additional peak, the relative mass balance, and the alignment of all three detector signals for fraction collection.

variability surrounding flow rates, sample volumes, and solvent conditions. This also simplifies solvent choices – the chemist can choose the best solvents (including chromophoric solvents such as toluene and acetone) for their flash purification needs rather than their detector's needs. The Reveleris™ system also optimizes delay volumes to minimize sample loss and improve overall yield.

Conclusion

The Reveleris™ system has the ability to detect non-chromophoric compounds, synchronize three detection signals for smart fraction

collection, and more accurately represent mass balance and reaction yields. This gives the medicinal chemist the ability to gather more information about their reaction mixtures in a single run and pass more promising drug candidates to downstream laboratories. In addition, the Reveleris™ system can optimize fraction collection and eliminate time-consuming post-purification work-up. The end result is an overall acceleration of the drug discovery and development pipeline, allowing pharmaceutical companies to bring important new drugs to market more quickly.