Hyphenated Techniques for Supercritical Fluid Chromatography: Analysis and Purification in New Drugs Discovery

Dr. Denis Berger
Mettler-Toledo AutoChem, Chemin du Prêche, P. O. Box 141, CH-1264 St-Cergue

Supercritical Fluid Chromatography (SFC) is a normal phase liquid chromatography technology in which the mobile phase is replaced by a pressurized, liquefied gas. It almost always uses liquid CO_2 as the main fluid in mobile phase to perform gradient elution, thus changing its composition with a polar modifier, usually methanol. The transition from/to supercritical state produces only minor, continuous changes in fluid density and viscosity, and has no impact onto the chromatographic process.

The compressibility of CO_2 varies with mobile phase composition, pressure and temperature, and, therefore, requires a sophisticated SFC pumping system to accurately deliver the selected flow rate and composition at any temperature and pressure. This is achieved through a specific control algorithm and feed back mechanism, which automatically and dynamically compensate for variation of compressibility during chromatographic runs.

The physical properties of such a liquefied gas (faster diffusion and lower viscosity) allow higher speed and throughput, faster re-equilibration and lower pressure drop on longer columns, as compared to reverse phase HPLC.

Standard UV-Visible with high pressure cell, mass spectrometer interfaced with atmospheric pressure chemical ionization or electro spray, evaporative light scattering and nitrogen detectors are used routinely. In addition, optimized GC detectors like flame ionization or electron capture can be used for specific agro- or petrochemical applications. It has also been shown that more complex detection systems can be used, either as stand-alone or installed in series, including infrared and atomic emission, or polarimetric devices.

The main advantages of SFC are best exploited by the pharmaceutical industry. In new drugs discovery, using both high throughput analytical SFC-MS and preparative SFC, the technology allows to recover purified compounds in very small amount of pure modifier, easy to evaporate. SFC is also recognized as the method of choice for chiral separations, including automatic methods development, preparation of pure enantiomers or measurement of enantiomeric excess.