Metamorphosis of Supercritical Fluid Chromatography to SFC

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Abstract

SFC, commonly expanded as \textit{Supercritical Fluid Chromatography}, is described as a normal-phase chromatographic technique which employs supercritical CO\textsubscript{2} as mobile phase to achieve separation. Both the words - "normal-phase" and "supercritical", unfortunately create some negative impressions about the technique. The word supercritical often creates an aura of some bizarre phenomena, whereas normal-phase creates the perception of niche, difficult processes which are employed when more common techniques e.g. reversed-phase liquid chromatography (RPLC), fail. In this tutorial we will address such misplaced perceptions and demonstrate why SFC should be considered at par with RPLC in terms of versatility, robustness and ease-of-use.

The prefix "supercritical" is misleading in describing modern SFC. The modus operandi now is to employ CO\textsubscript{2} as a principal solvent in a liquid-like mobile-phase. The motivation is to benefit from some wonderful properties of CO\textsubscript{2} in enhancing separation performances. Regarding being normal-phase, SFC works with all sorts of stationary-phases (not only polar) and it does not suffer from the major problems faced in normal-phase liquid chromatography - e.g. difficulty with column equilibration, lesser effectiveness of solvent gradient, slow equilibration etc. Modern SFC works like RPLC in terms of (a) using solvent gradients to develop faster and optimized separation, (b) employing organic additives, e.g. TFA, ammonium acetate etc. in the mobile-phase for improving peak shapes and/or MS detection.

Critically speaking, SFC has advantages over RPLC because of the wide miscibility range of CO\textsubscript{2} with a varied range of organic solvents with different polarities, e.g. methanol, acetonitrile, DCM etc. The mobile phase composed of CO\textsubscript{2} and a co-solvent in all proportions (from 100\% CO\textsubscript{2} to 100\% co-solvent) can seamlessly work with both normal and reversed-phase columns, chiral and achiral chemistries, bringing unique versatility to chromatography. RPLC-like solvent gradient techniques can be now used with polar columns creating selectivities orthogonal to RPLC. Many separations which normally need multiple methods involving different forms of LC can be done in a single SFC run.

In this tutorial we will explain these unique capabilities of modern SFC, detailing upon the currently expanding areas of applications where it has advantages over LC and GC, and why it should be viewed as a complementary technique to RPLC.