Supercritical Fluid Chromatography; Recent Developments and New Directions

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Within analytical chemistry, chromatography is by far the most widely used analytical technique. Gas chromatography (GC) and (high-performance) liquid chromatography (HPLC) have gained widespread acceptance in numerous application areas. As both gases and liquids can be used as the mobile phase in chromatography, extending the range of mobile phases to the supercritical region is but a logical step. Since supercritical fluids combine many characteristics of gases and liquids it is not surprising that SFC can be seen as an intermediate technique between GC and HPLC. Potential advantages of (carbon-dioxide-based) SFC in comparison with LC include the compatibility with various GC detectors and the increased speed of analysis. In comparison with GC, SFC is advantageous for the analysis of high relative molecular mass or thermally labile components.

History of SFC
SFC is by no means a new technique. The first experiments using supercritical fluids as the mobile phase were performed by Klesper, Corwin and Turner as far back as 1962, well before the introduction of HPLC. After the initial period of interest in SFC in the 1960s, the progress of SFC slowed down. The developments in SFC doubtlessly continued but clearly did not reach the exponential development curve that is characteristic for the development of new techniques and methods. In part, the slow development was due to early experimental problems, the lack of commercially available instrumentation and the fact that SFC development was overshadowed by the simultaneous development of HPLC and capillary GC.

In the 1970s, SFC was in a dormant state. Research interest in SFC was limited. A strong revival of the interest in SFC occurred in the early 1980s. Two important aspects were the introduction of the first commercial instrument by Hewlett-Packard and the introduction of open-tubular columns in SFC by Novotny et al. in 1981. From then on SFC developed along two lines, i.e., the old line of packed columns and the newer line of open-tubular columns.

Packed and Open-tubular Columns
After the introduction of open-tubular columns, considerable debate arose on which of the two column types should be preferred for SFC. Later, the consensus was reached that both column types have their own unique advantages and disadvantages.

In general, open columns possess a high efficiency. As diffusion in supercritical fluids is much slower then in gases, the inner diameter of open columns in SFC has to be much smaller than in GC. Typically, 50 μm open columns are used. The use of these narrow columns imposes severe restraints on the instrumentation. Injection and detection are highly critical. Apart from the limitation imposed by extra column band broadening, the sensitivity of the detection device requires special consideration due to the strongly reduced sample capacity of narrow-bore open columns. Packed columns are generally much easier to operate. Furthermore, columns packed with sub-10 μm particles are more time efficient than contemporary open columns. A fundamental problem of packed columns in SFC is the inherently high pressure drop which limits the maximum obtainable plate number.

The choice of the column type in SFC is determined by a number of parameters. The most important of these are the required plate number and analysis speed, sample loadability, detection limits and the injector and detector compatibility. Packed columns are superior over open-tubular columns with regard to the speed of analysis, the sample capacity, the injector compatibility and the detection limits. Open columns are to be preferred in terms of the maximum obtainable plate number. In addition, open columns are more favourable for combination with various detectors because a large variety of components can be eluted with pure carbon dioxide as the mobile phase.

Instrumental Developments
Numerous improvements have been published on various aspects of instrumentation for SFC. As instrumentation for open-tubular SFC is far more complicated than for packed-column SFC, technological improvements have centred on open-tubular SFC. Areas of special interest were injection techniques and detector couplings.

Nowadays, a wide variety of injection devices is available for open-tubular SFC. Flow split, timed split and combined split injection techniques allow the introduction of nanolitre sample sizes on to open columns with inner diameters below 50 μm. Total injection without splitting enables the introduction of several microlitres of sample but is not yet applicable in routine analysis. Further research is needed to develop easy to operate and reliable systems for the introduction of large sample sizes in SFC.

Over the past several years a number of fixed restrictor designs have been developed. In particular, the polished ‘integral’ tapered restrictor and the frit restrictor are now widely used. Variable restrictors have been described. These systems are, however, not yet applicable in daily practice. Progress in detection techniques for SFC has been extremely rapid. Existing detectors, such as the ultraviolet (UV) detector and the flame ionization detector (FID), have been further developed and adapted to suit the specific requirements of SFC. Low-volume detection cells have been developed for UV detection and photodiode-array UV detection in open-tubular SFC. Other detectors which have proved extremely useful in GC, such as the electron capture detector, the nitrogen/phosphorus detector and the flame photometric detector, have been introduced in SFC. Powerful identification possibilities for unknown compounds are provided by the compatibility of SFC with mass spectrometry (MS) and Fourier transform infrared spectroscopy (FTIR). Research work in the future should focus on the development of more sensitive and modifier-compatible detectors.

Mobile and Stationary Phases
During recent years a large number of potential mobile phases for SFC has been thoroughly investigated. Key features in these studies were: (i) the applicability of the mobile phase for the elution of polar solutes and (ii) the detector compatibility. Despite the problems often encountered when trying to elute polar solutes, carbon dioxide is still, by far, the most widely used mobile phase in SFC. In open-tubular SFC, fairly polar solutes can be eluted with pure carbon dioxide as the mobile phase.
packed-column SFC, however, most of the separations require modified mobile phases. The development of stationary phases for packed-column SFC has concentrated and will continue to concentrate on preparing more homogeneous materials which exhibit a reduced silanol influence. Although still far from perfect, polymeric stationary phases are definitely an improvement over conventional hydrocarbonaceous packing materials.10

Open-tubular SFC clearly benefited from the progress in GC column technology. Nowadays a wide variety of stationary phase material is available. The selectivity can be optimized by choosing from a series of stationary phases with various polarities. In the case of extremely complex samples, multidimensional SFC with series coupled columns of different selectivities provides enhanced separation power.11 The use of multidimensional chromatographic techniques is expected to increase in the future owing to the ever increasing complexity of the samples to be analysed.

Applications
Despite the potential advantages of SFC listed above, the number of unique applications that can neither be solved using GC nor LC but can be solved using SFC is limited. It is clear that this range of applications does not provide sufficient right to exist for SFC. A much larger number of applications exists, however, in which SFC should be the method of choice because it is simply easier, more sensitive, more rugged or faster than either GC or LC.

A typical example of an analytical problem that can be solved using either of the three chromatographic techniques but where SFC is the most favourable technique is the analysis of polymer additives. These compounds cannot be analysed using normal gas chromatography but require the use of high-temperature GC. In general, if an analytical problem can be solved using GC, GC is very often the technique that should be chosen. This is, however, no longer true when high-temperature GC columns are very susceptible to breakage. Furthermore, on-column injection, which is difficult to automate, and the use of a retention gap are mandatory. Coupling of the retention gap to the analytical column is by no means trivial. Last, but not least, the current generation of high-temperature GC columns are very susceptible to breakage. Especially in routine analysis, SFC is a better alternative for the analysis of high relative molecular mass components than is high-temperature GC. For the particular example of polymer additives, analysis by LC requires gradient elution. This leads to relatively long total analysis times. Also, the detection limits of UV detection are generally poor. The analysis of liquid crystals used in liquid crystal displays is a second example of an analytical problem that can be solved using (high-temperature) GC, LC and SFC. Again, SFC is the most reliable, most rugged and fastest method. An example where GC cannot be used is the analysis of poly(methylhydro- siloxanes). At higher temperatures these components tend to react with the stationary phase and the column wall of the GC column. LC can be used but generally does not provide sufficient resolution to separate the individual isomers. Moreover, detection in LC is cumbersome. For this particular example open-tubular SFC is preferable as a complete separation of the individual isomers requires an extremely high plate number. For many other applications packed columns are clearly advantageous over open columns.

Conclusions
The number of chromatographic applications that can neither be solved by GC nor by LC, but can be solved using SFC, is limited. For a fairly large number of applications in which high relative molecular mass components or components of limited thermal stability have to be determined, however, SFC is to be preferred over GC and LC because it is easier, faster, more rugged or more reliable. Hence it is clear that SFC is a useful technique which definitely deserves a place among the other chromatographic techniques. An application area where SFC holds remarkable potential is the separation of chiral samples. As a result of numerous instrumental improvements, experimental difficulties are now seldom a major obstruction to the application of SFC.

References

Photoionization Detection is 30 Years Old. The Story So Far Plus ‘Son of Photoionization Detection’: Far-ultraviolet Adsorption

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Photoionization, as a means of detection, has been with us for about 30 years. Robinson1 first reported the development of a photoionization detector in 1957. At the same time, groups in various parts of the world2 were working on the development of flame ionization techniques. This latter technique became very popular and was rather quickly licensed to a number of commercial gas chromatography (GC) manufacturers since the detector was very sensitive and easy to build. Lovelock3 became interested in the photoionization technique and published a review of ionization techniques in 1961.4

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