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 comparision 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,[1] 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.[2] 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.[3] Total injection without splitting enables the introduction of several microlitres of sample[4] 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[5] and the frit restrictor[6] are now widely used. Variable restrictors have been described.[7] 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)[8] and Fourier transform infrared spectroscopy (FTIR).[9] 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 experienced 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 CO_2 as the mobile phase. In

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 is needed. High-temperature GC still suffers from a number of practical problems. First of all the number of stationary phases available for high-temperature GC is limited. 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(methylhydrosiloxanes). 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.

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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. Robinson[1] first reported the development of a photoionization detector in 1957. At the same time, groups in various parts of the world[2] 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.

Lovelock[3] became interested in the photoionization technique and published a review of ionization techniques in 1961.[4]

This included the flame ionization detector (FID), the photoionization detector (PID), cross-section and electron capture detection (ECD).

The FID has become the most popular in the group as a result of its wide dynamic range, its selective response to organic compounds, its sensitivity and its simplicity of construction. While the ECD has also maintained a significant place as a selective detector for halogenated species, the cross-section detector has been forgotten.

During the 1960s and 1970s, a variety of papers[5–9] on photoionization were published using glow or microwave discharges as the ionizing source. Both types involved flowing high purity helium or argon through an electrical or microwave discharge to generate the source of energetic photons required to ionize the sample. With these early PIDs, the light source and ion chamber were not separated and, as a result, neither section could be optimized. The maximum lamp intensity occurs at low pressures while the maximum sensitivity for the ion chamber is at near atmospheric pressure. As a result, these early detectors were very pressure (or flow-rate) dependent. In general, these detectors were difficult to operate, mechanically complex, unstable and required a vacuum pump. The glow discharge detector had the continual problem of column bleed collecting on the discharge electrodes, resulting in problems with igniting the lamp. It is no wonder that the PID was replaced with the FID during the 1960s. By the late 1960s most researchers agreed that photoionization had become firmly entrenched as the detector of choice for analysis of carbon compounds.

In the period from 1973 to 1974, a major breakthrough in photoionization technology [separating the ion chamber from the ultraviolet lamp] was reported by Driscoll and Spaziani,[10] Sevcik and Krysul,[11] as well as Ostojik and Sternberg.[12] This design also eliminated many of the deficiencies of the glow discharge detector by allowing the ionization chamber to operate at atmospheric pressure and the lamp to be maintained at low pressures. This improved the sensitivity and simplified the operation of the detector. Now, after half a decade, photoionization appeared to be on the upswing again. The PID described by Driscoll and Spaziani[13] was offered commercially by HNU Systems in the spring of 1976. Since this was the first commercial PID, it attracted a great deal of interest because of its reported 50-fold improvement in sensitivity over the FID for aromatic hydrocarbons. Other features of the new PID that were interesting were its response to inorganic compounds, and its non-destructive nature. Within two years, however, the PID was replaced with a new model[14] that eliminated some of the deficiencies, such as temperature limitations and decomposition of thermally labile compounds on the inlet, which were inherent in the first PID.

Some recent applications of the PID for analysis of organic and inorganic compounds are described briefly. All applications and additional references in the text are to the PIDs with separated lamp and ionization chambers. The period covered is from 1976 to mid-1991.

Discussion

The PID detector is now in its third generation, has lower dead volumes for easier use with low flows and narrow diameter capillary columns. Its construction also allows easy interchange of lamps (8.3, 9.5, 10.2 and 11.7 eV) which facilitates use of the PID as a selective detector; only species with ionization potentials at or below the energy of the lamp being ionized are detected. The different lamps do, however, vary in photon output, the lowest detection limits being achieved with the 10.2 eV source.

In reviewing the role the PID detector had found in GC analysis, it is interesting to concentrate on the less well known, but arguably potentially very significant, applications for PID, particularly in industrial hygiene and emissions analysis. This is an area which has become much more important through the enactment of legislation, *e.g.*, in the UK Control Substances Hazardous to Health (COSHH) and the Environmental Protection Act with its focus on integrated pollution control. This is not just a UK phenomenon but is reflected in similar legislation throughout the industrial world.

PID traditionally has found most use as an aromatics detector, *e.g.*, in standard US Environmental Protection Agency (EPA) methods for waste and potable waters (EPA methods 601/602/501/503) due both to its selectivity and sensitivity. Lower detection limits for benzene are typically sub-pg. There is also new emphasis on this application with the development of portable GCs for soil gas and contaminated groundwater analysis with the instigation of such programmes as LUST (Leaking Underground Storage Tanks).

The PID has been the detector of choice for these applications due to its selectivity, low detection limits, the lack of gases, and its non-support-destructive nature which allow series detection, typically TCD or ECD, for environmental applications.

The almost non-destructive nature (typically only one in 10 molecules of the analyte are ionized) has also meant that many PIDs have been used in series with other detectors and other instrumentation, *e.g.*, with FID to determine which analytes are unsaturated or aromatic by comparison of relative response, or to determine the number of double bonds in a fatty acid. A growing number of PID detectors have been linked in series with mass spectrometers (MS); capillary GC–MS often does not allow sufficient eluent to 'split' the flow into a 'destructive' detector such as FID.

The largest growing applications area for PID has been the continuous analysis of workplace air for toxic compounds and emission/fence-line monitoring for compliance with regulatory limits. The PID has been successful in these areas, particularly as it has no support gas requirements and because of its long-term stability at high sensitivities.

The chromatograms listed below are all relatively common PID applications but seem to be not so well known to the analytical chemist, who typically perceives the PID to be an 'aromatics detector'. These applications are: (*i*) isocyanates to ppt levels; (*ii*) formaldehyde at ppb levels (new low 'control' levels are being set for this compound); (*iii*) low-level organic sulfur compounds [nuisance (Environmental Protection Act) and process/feedstock contamination]; (*iv*) ethylene oxide, a suspected carcinogen (*e.g.*, use as sterilization medium for medical disposables now has to be 'justified'); (*v*) arsine/phosphine at low ppb levels (the PID can detect a whole range of inorganics at trace levels).

In all the chromatograms mentioned so far, particularly of air samples, a negative peak can be observed; this is caused by strongly UV-absorbing compounds. The far-UV light from a PID source is in the range 105–145 nm (10.2 eV = 122 nm).

'Son of PID'

The effect mentioned above has been translated into the development of a new detector: far-UV adsorption ('Son of PID'). This new detector is now a second generation instrument, having been optimized by reduction in dead volume and the development of a new photodiode 'tuned' to the frequency range emitted by a 10.2 eV (122 nm) source.

Chromatograms for formaldehyde, anaesthesia gases, hydrocarbons, sulfur compounds and permanent gases have been obtained, together with data on initial lower levels of detection which are likely to be exceeded during the continuing development programme.

Conclusion

PID, one of the first GC detectors to be developed, is now undergoing a resurgence of interest due to its ease of use and low detection limits, for 'environmental' samples.

Far-UV (FUV) detectors appear to be able to offer a more sensitive (one to two orders of magnitude) alternative for many methods, such as landfill gas, currently analysed by TCD.

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