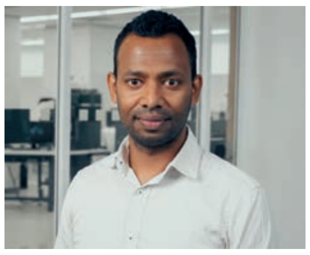

APGC: A Better Future with Nitrogen

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Atmospheric pressure ionisation gas chromatography mass spectrometry can help solve the increasing difficulties of economically sourcing helium by opening the door to the use of nitrogen carrier gas with uncompromised performance.

Helium is an inert gas that is obtained from natural gas well sources where helium recovery infrastructure is installed. Over several decades, helium has evolved to be the GC carrier gas of choice because of its availability and good chromatographic performance. This has most notably been the case for GC-MS using electron ionisation (EI) and instruments have been optimised for its use. But helium is non-renewable; its availability is linked to petroleum production and therefore to the vagaries of that troubled market. Additionally, helium is under high demand in several areas including medical diagnostics, which often take a priority over chromatographic use. Consequently, the global helium infrastructure is facing great challenges, including geopolitical influence, natural events, dwindling sources, and technical issues at extraction facilities.

In short, helium availability is severely impacted, which ultimately means increasing costs and increasingly a lack of availability for end users.

The increasing pressure of the helium shortage has led many to consider other options. We have seen increased use of hydrogen and nitrogen as alternative carrier gases. Hydrogen's optimum linear velocity is greater than helium, which can increase sample throughput through decreased analysis times. However, its combustible nature and general safety concerns have hampered its adoption. Additionally, hydrogen is a reducing gas and often results in chemical changes of fragmentation ions which can negatively impact operation in mass spectrometry. And finally, the use of hydrogen can cause discrimination and other issues related to its reactivity in the injection port of the GC as well.

Nitrogen has been described as a 'slow gas' because its optimum linear velocity is lower than helium, and is often overlooked as a helium alternative, due to historic issues which are no longer limitations. In GC-MS applications, many commercial systems have evolved to using helium and electron ionisation which occurs in vacuum. For successful operation, high vacuum must be maintained, and instruments and vacuum pumps have been optimised for helium gas operation for most manufacturers. This leads to an issue when they might consider nitrogen as a possible replacement gas as a result of helium supply concerns.

But when we utilise atmospheric pressure ionisation for ion formation, the downsides of nitrogen disappear. In atmospheric pressure gas chromatography (APGC), where we are dealing with a high-pressure environment for ionisation, the presence or absence of nitrogen as the GC carrier gas makes no difference to either sensitivity or specificity. Additionally, the atmospheric chemical ionisation process already utilises nitrogen for the initial formation of charged species. Therefore, use of nitrogen as the carrier gas in fact simplifies the system because we are only introducing nitrogen from an additional source through the column, effectively removing helium from the equation altogether.

The Game-Changer

Although the coupling of GC and MS with atmospheric pressure ionisation (API) appeared in published papers as early as the 1970s, the commercial interest in coupling GC with an atmospheric pressure ion source has only expanded in the last decade. The need to preserve highly diagnostic molecular ions for some applications has made 'soft' ionisation (which causes less fragmentation) more desirable than 'hard' ionisation techniques that can extensively fragment molecules but are, nevertheless, the expectation with traditional GC-MS. The crux of the matter is that reduced fragmentation yields higher sensitivity and specificity, simplifying precursor ion selection for targeted MS/MS applications using MRM acquisitions.

At Waters, we promote APGC as an ion source for multiple models of mass spectrometer. Options exist for highly sensitive GC-MS/MS performance as well as high-resolution and even ion mobility separations. Furthermore, it is straight forward to swap between APGC-MS/MS and UPLC-MS/MS in a matter of minutes. For this, no venting is required, and UPLC-MS/MS and GC-MS/MS can be performed using the same mass spectrometer. Finally, it's worth noting that APGC analysis are not flow-rate limited as is the case for most EI-based GC-MS/MS systems. This allows for a wider range of compatibility for GC column flow and carrier gas type.

The introduction of APGC expanded the scope of our analytical platforms, offering unique and data-rich experiments that extend their reach beyond previous capabilities. Using APGC, we can harness a combination of sensitivity, mass accuracy, resolution, and ion mobility to give levels of selectivity that will thoroughly characterise samples and yield data at an entirely different and exciting level.

In short, APGC is robust, sensitive, and very well suited to the identification and determination of a wide variety of compounds. With APGC, unlike EI, the molecular ion is typically well preserved, resulting in higher sensitivity and selectivity. Then, of course, there is the cost. The ability to use nitrogen as the carrier gas has an immediate impact on costs and this alone is a big driver for adopting APGC. If you're not concerned about cost, you probably are worried about the volatility of the helium supply chain; the supply-and-demand equation is certainly tipped heavily toward demand. We've seen suppliers limiting the volumes of helium sold to any one laboratory, making it increasingly important for labs to have alternative options to ensure effective and agile responses to supply chain interruptions.

Jumping on the API bandwagon

We are now beginning to see other manufacturers looking to API techniques and, although they are a little less mature than ours, we anticipate rapid growth over the next decade. Due to the combination of positive performance characteristics of APGC we fully expect the rapid growth in use of the technique across the coming decade.

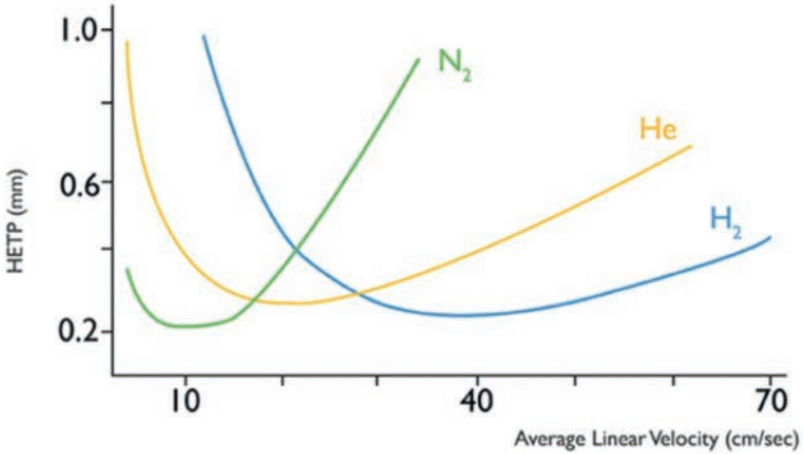

Figure 1. van Deemter curves for the three common GC carrier gasses.

We can find a good analogy for APGC in the LC-MS world, which began using electrospray ionisation to the point where, with MS/MS in particular, it became the gold standard for small molecule analysis. Why? Because ESI delivered high sensitivity and specificity for MS/MS. APGC looks set to follow the same path - and the helium issue will simply act as a catalyst. Overall, APGC-MS/MS offers an affordable, well-suited alternative to GC-MS/MS with electron ionisation for the determination of organic compounds at ultra-trace levels.

Final thoughts

The APGC system is a significant step up in terms of analytical performance relative to what we can currently achieve with EI systems. It represents a change in technology that aims to alleviate some of the biggest challenges the field currently faces. And, specifically with respect to helium shortages, APGC offers a simple plug-and-play solution for swapping to nitrogen - an affordable, renewable alternative that delivers results without any analytical compromise. We truly believe it is a gamechanger, and hope users will, too.