

# Changing from Helium to Hydrogen



## Things to Consider when Changing from Helium to Hydrogen Carrier Gas in GC Methods

Recently, there has been a significant number of publications discussing problems associated with the global supply and increased cost of Helium gas. Many of these have been produced by gas chromatography (GC) instrumentation and gas generator manufacturers, highlighting an expected increase in the use of Hydrogen as an alternative to Helium for use as a GC carrier gas. These articles focus mainly on the benefits of Hydrogen in terms of guaranteed continuity of supply, lower cost, and shorter GC analysis times. While the present discussion confirms these potential benefits, it will also consider some of the practical and regulatory concerns impacting the adoption of Hydrogen. GC method transition from Helium to Hydrogen is also featured here. Unfortunately, as will be shown, there are negative as well as positive issues to consider.

### Pharmacopeial Prescription and Regulatory Compliance

The type of carrier gas is not an allowable adjustment in either the PhEur or the USP and the corresponding general chromatography monographs have recently been harmonized. The prescription of Hydrogen in new and revised monographs will therefore have more impact on the use of Hydrogen than will the price and supply of Helium in the short term.

For the foreseeable future, Helium, Nitrogen, and Hydrogen will all be required as carrier gases based on compliance issues. There has recently been movement in the pharmacopeia. For example, in the revised USP monograph for Castor Oil (2019), the determination of fatty acids has been changed from a titration to a GC assay using Hydrogen as the carrier gas. Indeed, there are now several methods in both the PhEur and USP requiring Hydrogen. For methods using Nitrogen, there may be little sense in costly revalidation using Hydrogen. A measure of the speed of historical updates to compendial methods can be seen in the number of monographs still requiring the use of GC-packed columns using Nitrogen carrier gas.

Procedures, where any change of carrier gas would be ill-advised, include GMP testing which would require full revalidation of the method and especially where such methods are being used in a live stability study for obvious reasons.

## Technical Considerations Impacting the Use of Hydrogen rather than Helium

The following bullet points are listed to summarise the positive and negative impacts to be considered.

### Gas Chromatography (GC)

#### Pro's

- Running hydrogen at the same linear velocity as helium, with the same oven temperature program should give you almost identical results. Compare the last chromatogram using helium with the results with hydrogen. The peaks should elute at the same retention times but may have a slightly sharper shape.
- Hydrogen at an increased linear velocity will allow faster analysis times giving the same or better resolution due mainly to sharper peak shapes.
- The use of Hydrogen generators will greatly reduce costs, negate any continuity of supply issues, and will remove the safety risks and time associated with handling large gas cylinders, and the cost and environmental impact of transporting cylinders over long distances.
- If you are connecting a GC-Flame Ionisation Detection) GC-FID, you can supply both the carrier gas and fuel gas supply from a single gas cylinder or generator.

#### Con's

- Revalidation of existing methods will be required.
- Older GCs may need time-consuming physical recalibration requiring the use of a calibrated digital flow meter.
- Copper tubing that was used to supply Helium should be discarded or independent tubing for Hydrogen should be provided. If you use the same tubing to supply Hydrogen, you will see high background baselines and it will take longer to optimise the analysis.
- All fittings should be compression fittings. Do not use sealing agents or weld connections. These can introduce volatile organic compounds (VOCs) into the gas stream and contaminate the GC system.
- The principal unavoidable problem with the use of Hydrogen is that it may react with some of the sample components during chromatography.
- The flammability of Hydrogen requires oven leak sensors and gas flow controllers that will shut off the gas flow if Hydrogen is sensed or unexpected increases in flow due to back pressure drops are registered.
- Specific detectors such as Electron Capture (ECD), may not operate as effectively while using the required carrier flow rate of Hydrogen required for a packed column or mega-bore capillary analysis.

## Gas Chromatography-Mass Spectroscopy (GC-MS)

### Pro's

- The Pro's listed for GC apply, except for the GC-FID comment.
- You will need to connect just a single gas line between the Hydrogen generator and the GC.

### Con's

- The Con's listed for GC apply, except for the ECD comment.
- For optimal performance, there is a requirement to use a modified ion volume in the ion source and these are becoming available.
- While the problem with Hydrogen reacting with sample components during chromatography as for GC is equally relevant, it is especially pertinent to GC-MS when the aim is to identify unknown sample components.
- Another problem related to the last point is that the MS spectra obtained using Hydrogen may exhibit different ion fragment intensities from those of our current spectral libraries which were produced using Helium.

## Compliance Method Development Transition from Helium to Hydrogen Carrier Gas – An example

Although not from a Pharmaceutical source, let's look at a Fatty Acid Methyl Esters (FAMES) analysis of a 38-component standard mixture (Supelco F.A.M.E. mixture Catalogue # 18919-1AMP) with *trans*palmitelaidic acid methyl ester (purchased from Matreya, Catalogue # 1148)).

Figure 1 shows a section of the total chromatogram including the poorly resolved peaks 29-33 in the original method run using helium carrier gas. This method used a carrier flow rate of  $34 \text{ cm s}^{-1}$  with a  $20 \text{ mL min}^{-1}$  split flow (Table 1). The results of this analysis suggest that there is little opportunity for increasing sample throughput.

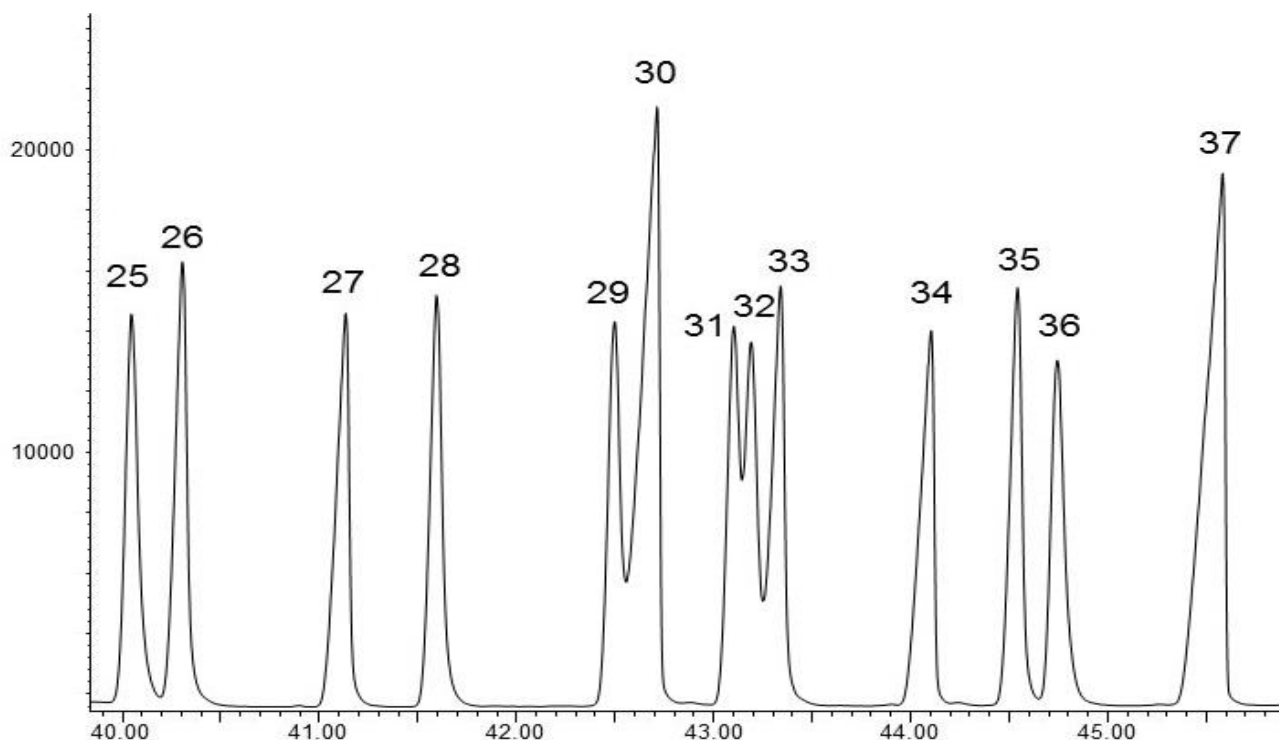


Figure 1.

Section of the total chromatogram of the 38 component FAME standard showing poorly resolved peaks 29-33.

Carrier Gas	Helium	Hydrogen	Hydrogen
Figure	1 + 2A + 3A	2B	3B
Inlet Pressure	16 psig	16 psig	7 psig
Carrier Flow	1.6 mL/min	3.4 mL/min	1.2 mL/min
Average Linear Velocity	33.96 cm/sec	75.37 cm/sec	33.92 cm/sec
Split Flow	20 mL/min	20 mL/min	5.6 mL/min
Injector temperature	250 °C		
Oven Parameters	40 °C (2 min hold), 4 °C/min to 250 °C (3 min hold)		
Detector	FID at 260 °C		
Column	Supelco 2380 (30m x 0.25mm x 0.2mm film)		

Table 1.

However, to see whether a translated method using hydrogen carrier gas would give similar results, the method parameters were kept the same, with only the carrier gas linear velocity altered as a result of changing the gas from helium to hydrogen (Table 1). Figure 2 shows the comparative results of using helium (2A) and hydrogen (2B) carrier gas. The increase in linear velocity resulted in a shorter analysis time, but co-elution of peaks 29-33 meant that method revalidation was required.

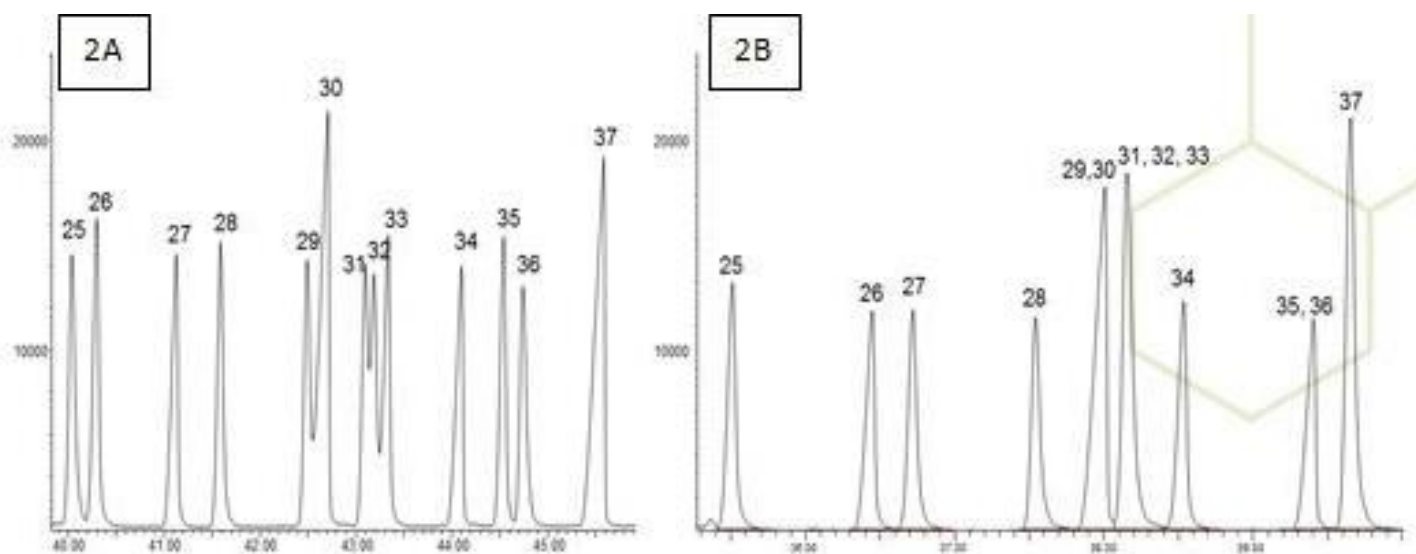


Figure 2.

2A shows a section of the chromatogram produced using the original helium method including poorly resolved peaks 29-33. Figure 2B shows co-elution of peaks 29-30 and 31-33 when running the sample using hydrogen carrier gas at a higher linear velocity.

The method was revalidated to match the linear velocity of hydrogen with that of the original helium method. This required reduction of the GC head pressure to reduce the flow rate of the carrier gas. This had the effect of reducing peak size because of the reduction of carrier flow rate combined with the relatively high split flow. Peak height was improved by reducing the split flow from 20 mLmin<sup>-1</sup> to 5.6 mLmin<sup>-1</sup> which increased the amount of analyte transferred onto the column (Table 1).

After revalidating the method to match the linear velocity of hydrogen to the linear velocity of helium in the original method, the results were almost identical to those obtained with helium (Figure 3). This meant no reduction in analysis time, but like-for-like results with an increase in peak height of samples run using hydrogen carrier gas because of improved efficiency associated with its use.

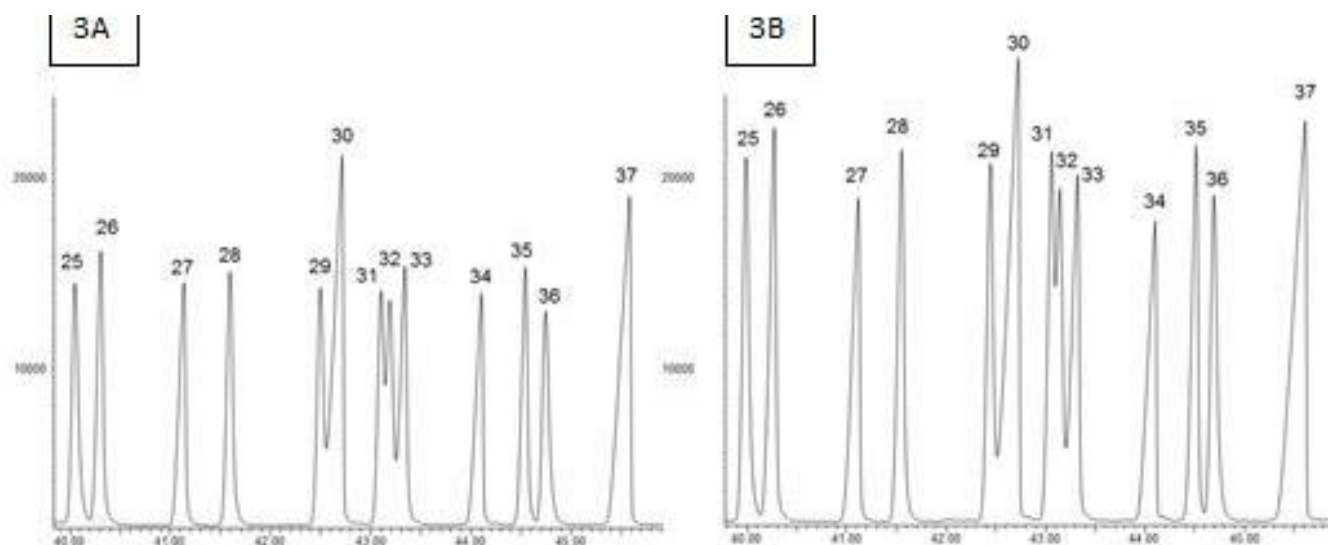


Figure 3.

Results of the original method using helium carrier gas (3A) and results of the revalidated GC method using hydrogen carrier gas (3B).

## Conclusion

Although hydrogen is often cited as a fast carrier gas, it is not always possible to speed up analysis because of a lack of peak resolution. Here we have shown that it is possible to revalidate your method by keeping the linear velocity of hydrogen the same as that of helium. This approach will ensure that compounds elute at the same retention time despite a change in the carrier gas. By adopting this approach, you can use a column with the same dimensions and will only need to make slight adjustments to the GC method. In this case, minimal validation is required.

## Author Biography



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Frank started his career at Kings and Co as a Senior Technician before joining Berridge Environmental Labs as Organic Analysis Team Leader in 1990. After a short spell with Pharmaco LSR in its Department of Aquatic Toxicology Studies, he joined the Chromatography Department of Butterworth Laboratories in 1994 and has progressed through various roles to his current position. Frank has spoken at JPAG meetings on Organic Volatile Impurities analysis.