Recycling of CO_2 on a Supercritical Fluid Chromatography (SFC) Pilot Unit

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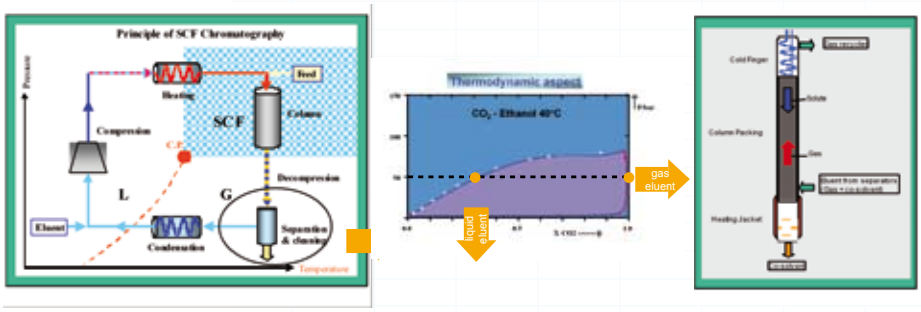
Introduction

Except for analytical and semi-prep instruments, eluent recycling after solute separation should be an ordinary feature of any supercritical fluid extraction and chromatographic equipment. But it should be stressed, that gaseous eluent from separators always contains some traces of solute and co-solvent, entrained as particles or vapor. Hence, in order to recycle the CO_2 and reuse it, the gas leaving the separators must be further purified. This purification step must provide clean CO_2 at the same pressure as a fresh fluid delivered from the supply unit (40 to 50 bar).



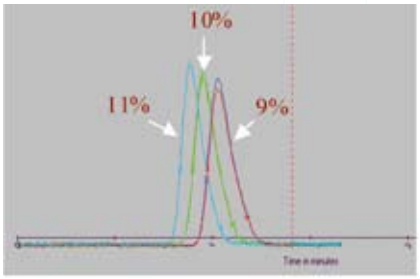
Practical Aspects

The purification of CO_2 is achieved in a gas scrubber. The system removes co-solvent and solute traces entrained from cyclonic separators. The remaining co-solvent dissolved in gaseous CO_2 is very low (< 0.3% under typical conditions) and is stable. Therefore, it has no influence on the chromatographic separation.

Impact on the Chromatograhy Separation

In SFC, even a small change in eluent composition typically conducts to a visible change in peak retention time.
Preparative chromatography involve multiple injections (10's to 1000's) and automatic collections of purified products. Therefore, any instability of the retention time would be detrimental to the purity and recovery yield. The performance of the recycling was demonstrated as shown in the figure on the right.

Conclusion: A perfect reproductibility is obtained at each CO_2/co-solvent composition tested.



Overlay of 3 pairs of chromatograms obtained with 3 co-solvent contents

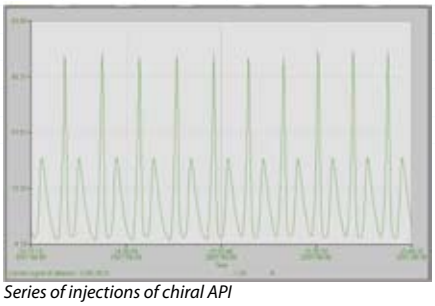
SuperSep™: A compact SFC unit
Capacity: kg(s) of product/day

Impact on the solvent consumption

System Type Column Size	HPLC 80 mm I.D.	SFC 50 mm I.D.	SFC 50 mm I.D.
Productivity (kg product/day/kg CSP)	0.240	2.2	2.2
Organic Solvent (L/kg of feed)	3100 (n-heptane/IPA 98/2)	352 (IPA+DMEA)	352 (IPA+DMEA)
CO_2 consumption (kg/kg of feed)	NA	1700 **(Without CO_2 recycling)**	170 **(With CO_2 recycling)**
Productivity (time to purify 1 kg)	100 h	36 h	36 h
Manufacturing cost comparaison (on hundred basis)	100	49	8.8

Separation of cyclopenta [b] Indol Amino derivative (B.Bonnier -R&D Sr Scientist, Eli Lilly, Belgium)

Recycling the CO_2 reduces the required quantities of fresh CO_2 necessary for semi-prep to preparative separation by 10 to 20 times. This can be easily translated by the reduction of the dimension of the CO_2 furniture, and therefore **the reduction of the capital expenditure** and the logistics involved.



Series of injections of chiral API

Conclusion

SFC is a powerful separation tool to all chemists. With CO_2 as eluent, SFC separates fast, and well.

The advantages of the technique are:

- High productivity
- Low amounts of organic solvents (5 to 20 times less than HPLC)
- Concentrated purified products (Size reduction of evaporators)

What does CO_2 recycling bring to your SFC?

- Reduction of CO_2 storage dimensions
- Decrease of global investments
- Reduction of operating costs
- Reduction of the risks associated with large CO_2 volumes