Sensitivity increase thanks to stationary phase changing in GC

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Introduction

In the pharmaceutical industry, purity norms about drugs are very strict because of their use. Impurities should be detected only at extremely low levels (in terms of few % to few ppm). Therefore, sensitive analytical methods are needed for detection.
Sensitivity can be improved by increasing the sample concentration, or by changing method parameters, such as the column stationary phase.
To be sure the product is in accordance with health authorities' norms, a "quantification limit" is performed. This also tests if the studied impurity can be seen at the limit quantity.

Experimental conditions

A mixture of four fumaric acid impurities: (monomethylfumarate (MM), monoethylfumarate (ME), dimethylfumarate (DM) and diethylfumarate (DE)) were used for the test. Decan was used as an internal standard (EI).

GC:	Agilent 6890
Detectors:	FID
Inlet:	Split 1/50 ; T1 = 250°C ; T2 = 220°C
First column tested:	DB-5 J&W 10m; 0.15mm; 1.2µm
Secondary column:	DB-FFAP J&W 15m; 0.25mm; 0.25µm
Carrier gas:	He; 1.2mL/min
	Oven temperature: (1)100°C (0min), 15°C/min to 160°C (0min) and (2) 100°C (2min), 10°C/min to 130°C (0min), 20°C/min to 200°C (4min).

Results and discussion

Comparison between chromatogram 1a and 1b (DB-5) (1b is 10 times more concentrated than 1a) details the positions of all fumarates.
On the first chromatogram, the two mono fumarates (at 0.1% relative content) were not detected. On the contrary, when the DB-FFAP column was used (2), all peaks could be seen. The sensitivity of the two mono fumarates was around five times better than that obtained on a DB-5. This can be explained by the fact that monofumarates have an acid function, for which a FFAP column is better adapted.

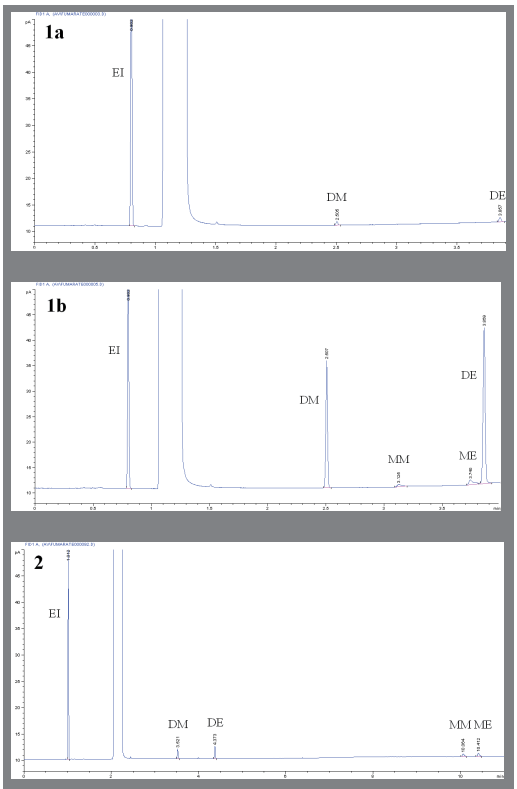

Figure 1 : (1a) Quantification limit : 0.1% of fumarate ; DB-5 column. (1b) Quantification solution : 1% of fumarate ; DB-5 column. (2) Quantification limit : 0.1% of fumarate ; DB-FFAP column

Conclusion

This paper demonstrates that the nature of the film affects sensitivity. Monoethyl and monomethyl fumarates can be detected at 0.1% only on the DB-FFAP column.
So, it is important to study the structure of molecules and to choose an appropriate column to separate compounds.

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