Quantification of allergic component with E-Nose
Application with DiMethylFumarate

Results obtained at Alpha MOS Laboratory, Toulouse, France

Application Note

Europe has to face a new public health problem related to the presence of dimethylfumarate discovered in certain products (sofas, shoes, and more) generating recalling and proceedings by concerned retailers.
Dimethylfumarate (DMF) is a fungicide that manufacturers use, during transport of goods imported from Southeast Asia, to prevent fungal proliferation linked with an especially intense rain season.
The DMF can cause acute dermatitis, eczema, and general fatigue to the persons who have been in contact with this substance.

Objective

The anti-fungal in cause was identified as dimethyl fumarate (Figure 1), an ester which is also used to treat psoriasis.

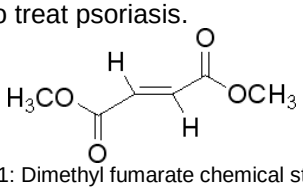
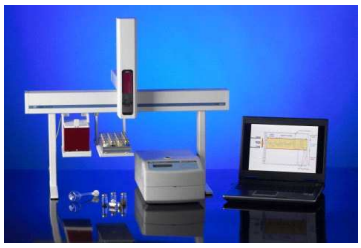


Figure 1: Dimethyl fumarate chemical structure

Dimethyl fumarate has been found to be a sensitizer at very low concentrations, producing extensive, pronounced eczema. Concentrations as low as 1 ppm may produce allergic reactions.
Alpha M.O.S. Heracles system can be suitable to rapidly access the presence of dimethyl fumarate in goods with fast response and good sensitivity.
The aim of this application note is to validate the performance of Heracles e-nose system for the quantification of dimethyl fumarate in products such as shoes.

Flash Gas Chromatography

The HERACLES Electronic Nose includes two short columns (2m) of different polarities (DB5 apolar and DB1701 slightly polar), coupled to two Flame Ionization Detectors (FID). Therefore, the two chromatograms obtained simultaneously, allow an improved identification of chemical compounds.



Ultra Fast GC based HERACLES Electronic Nose

With high heating rates (up to 20°C/second), the time of analysis is very short (some seconds) and an analysis can be run every 4 minutes.
Tenax trap located before columns allows pre-concentrating the injected fraction to assume high sensitivity.

Samples & analytical conditions

Two brand new pairs of shoes were tested: women shoes and children shoes.
The woman shoes were tested in a sampling-bell after equilibrium for approximately 8 hours (Figure 2). The children shoes were tested in their commercial box, which was punctured for SPME sampling.

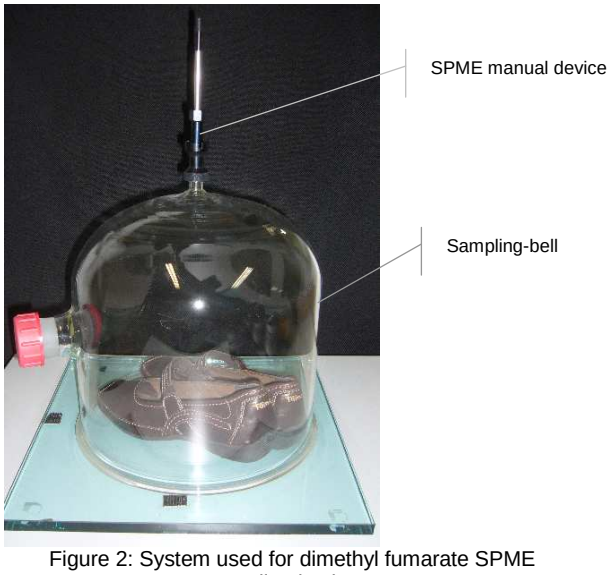


Figure 2: System used for dimethyl fumarate SPME sampling in shoes

Parameter	Set point
Adsoption conditions	
Adsorption time	10 min
Heracles e-nose conditions	
Injection temperature	300°C
Trap ready temperature	40°C
Sampling time	120 s
Trap prepurge time	1 s
Trap desorption temperature	250°C
Trap cleanout time	50s
Injection time	3000 ms
Columns temperature program	40°C(2s) to 270°C (2s) @ 5°C/s
Pressure column programm	16 psi
Detectors temperature (FID)	250°C
Acquisition parameters	
Acquisition time	50 s
Time between two injections	30 min

Table 1: Analytical parameters

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The sampling was performed using a manual SPME (Solid Phase Micro Extraction) system fitted with a fiber of bonded Carboxen/PDMS 85µm (Supelco. Ref 57336-U).
Each sample injection was done according to the following sequence:

- SPME adsorption phase (10 min) and Heracles clean up in parallel
- SPME desorption and Heracles analysis (3 min)
- SPME conditioning in the Heracles injector (7 min)
- SPME cooling and Heracles clean up in parallel (10 min)

Calibration

The calibration was realized using commercial dimethyl fumarate (Aldrich, ref. 242926). The standard samples were prepared in air by dilution of headspace of a septum-capped flask containing dimethyl fumarate powder and incubated in a water-bath set at 25°C.
As the volatility data of dimethyl fumarate were not available, the data of dimethyl maleate, an isomer, were used to calculate the concentration in headspace at equilibrium. At 25°C, the concentration of dimethyl maleate in headspace at atmospheric pressure is around 339 ppm (mol/mol).
The samples used for calibration were prepared in septum-capped 250-ml Schott bottles maintained at 40°C. The true volume of these flasks was estimated to 300 ml. Samples of dimethyl fumarate used in calibration were thus prepared by successive additions of 0.9 ml headspace of stock gas sample immerged in a water-bath at 25°C, which correspond to a concentration of approximately 1 ppm.

The analysis of the dimethyl fumarate calibration gas showed a peak on each column, well discriminated from background volatile compounds (Figure 3).

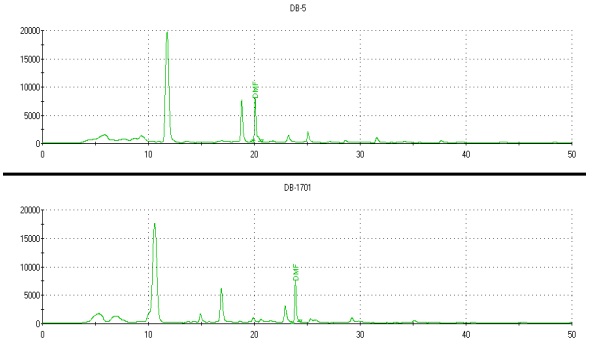

Figure 3: Heracles e-nose chromatogram for dimethyl fumarate at 4 ppm in air

Linearity
The calibration was measured on the range 0 to 5 ppm of dimethyl fumarate in air on both Heracles columns (Figure 5).

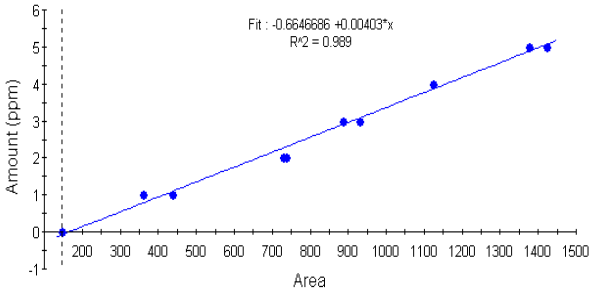

Figure 4: Dimethyl fumarate calibration line on DB5 column of Heracles e-nose

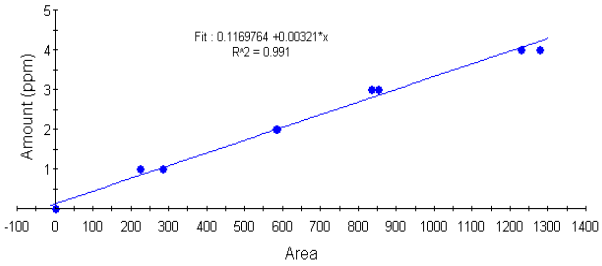

Figure 5: Dimethyl fumarate calibration line on DB1701 column of Heracles e-nose

The linearity is good but requires very strict respect of analytical sequence. Indeed, each sequence has to be strictly identical to obtain good results. A timer was used for each step.
Furthermore, the SPME system can damage the Heracles septum very rapidly. Thus, the septum should be changed very regularly.

Limit of detection
The detection limit of the method was estimated at 0.2 ppm.

Results & Discussions

The quantification of dimethyl fumarate in women's shoes showed some new volatile compounds. One of these molecules showed interference with dimethyl fumarate on column DB5 but not on DB1701 (Figure 6). The amount of dimethyl fumarate quantified in these shoes is very close to detection limit and probably come from insufficient fiber conditioning.

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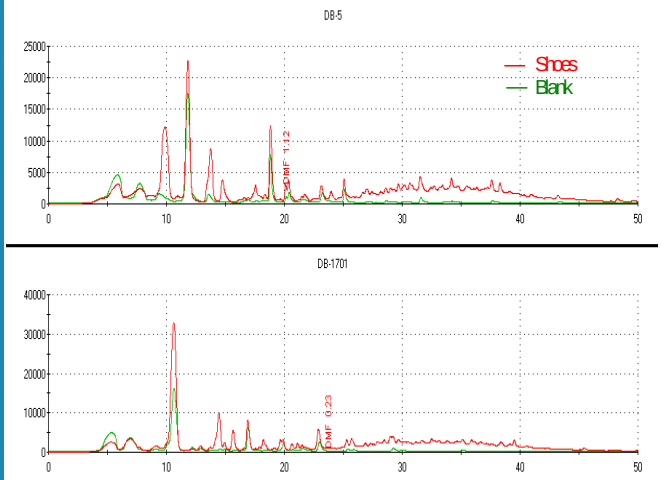

Figure 6:. Dimethyl fumarate quantification in woman shoes on Heracles e-nose

The same kind of results was obtained on children shoes (Figure 7).

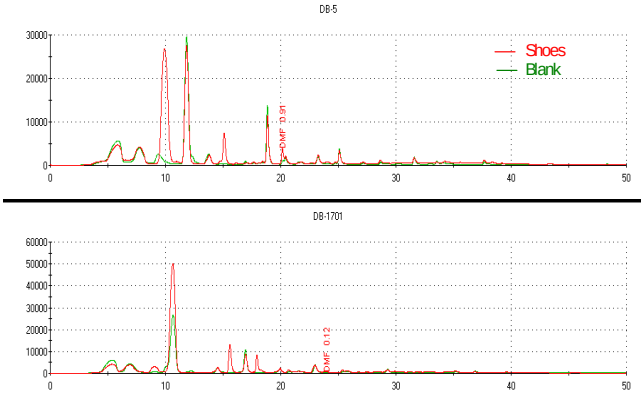

Figure 7: Dimethyl fumarate quantification in child shoes on Heracles e-nose

This analysis shows that the dimethyl fumarate level in the two pairs of shoes is far lower than the limit of 1 ppm that could show allergic problem.

Repeatability test

The repeatability of the measurement was determined on calibration samples (Table 2). The mean RSD is close to 10%. This value is relatively high but still acceptable. It can be explained by the use of manual SPME.

Table 2: Mean RSD (%) in calibration samples

Standard	n	Mean value (ppm)	SD (ppm)	RSD (%)
1 ppm	4	0.94	0.15	16
2 ppm	4	2.14	0.17	8
3 ppm	4	2.91	0.13	4
4 ppm	4	4.29	0.52	12

Conclusion

All importers and/or retailers are responsible of the launching of their products. Recognized quality problems endanger their corporate brand, risk proceedings from consumers, and can potentially create high costs to these companies from various Public and Private Health organizations.

To avoid risk, an analytical method has been developped and the quantification of dimethyl fumarate in shoes can be conducted via SPME sampling followed by Heracles e-nose analysis.

The analysis of dimethyl fumarate in shoes can be done directly by puncture of the commercial box and sampling with the manual SPME device. The method can be automated using SPME fiber exchange systems. The same system could be used to evaluate the presence of dimethyl fumarate in sofas. These should however be contained in a hermetic (or almost) plastic bag or cardboard box.

This method is simple and will indicate rapidly whether the product presents a risk for the customer. Indeed, if dimethyl fumarate is measured over 1 ppm the product can induce grave allergy for its user.

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