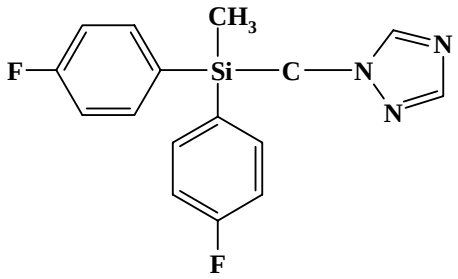
FLUSILAZOLE
435



ISO common name	Flusilazole
Chemical name	Bis-(4-fluorphenyl)-methyl-(1*H*-1,2,4-triazol-1-yl-methyl)-silan (IUPAC); 1-[[Bis(4-fluorophenyl)methyl-silyl]methyl]-1*H*-1,2,4-triazole (CA; *85509-19-9*)
Empirical formula	$C_{16}H_{15}F_2N_3Si$
RMM	315.4
m.p	53 °C
v.p.	3.9×10^{-5} Pa at 25 °C
Solubility	In water: 54 mg/l (pH 7.1), 900 mg/l (pH 1.1) at 20°C; readily soluble in many organic solvents
Description	Colourless crystals
Stability	Stable under normal storage conditions
Formulations	Water dispersible granules, emulsifiable concentrates and emulsions in water

FLUSILAZOLE TECHNICAL

[*] **435**/TC/(M)/-

1 Sampling. Take at least 100 g.

2 Identity tests

2.1 GLC. Use the GLC method below. The retention time of flusilazole for the sample solution should not deviate by more than 0.2 min from that of the calibration solution.

2.2 Infrared. Prepare potassium bromide discs from the sample and from flusilazole standard containing approximately 1 % of material. Scan the discs from 400–4000 cm^{-1}. The spectrum produced from the sample should not differ significantly from that of the standard.

3 Flusilazole

OUTLINE OF METHOD Flusilazole is determined by capillary gas chromatography using flame ionisation detection and benzophenone as internal standard.

REAGENTS

Acetonitrile

Flusilazole standard of known purity

Benzophenone internal standard, purity at least 990 g/kg

Internal standard solution. Weigh into a volumetric flask (1000 ml) benzophenone (3.0 g) and add acetonitrile (about 900 ml). Place the flask in an ultrasonic bath for 5 min; allow to cool to room temperature, dilute to the mark with acetonitrile, and mix well.

Calibration solution. Weigh (to the nearest 0.1 mg) 40, 60 and 80 mg of flusilazole standard into three separate volumetric flasks (50 ml). Add by pipette to each flask internal standard solution (10.0 ml), add acetonitrile (30 ml), place the flasks in an ultrasonic bath for 7 min. Allow to cool to room temperature, dilute to the mark with acetonitrile and mix well. (Solutions C_A, C_B, and C_c). The solutions are known to be stable for at least 5 d). Filter the solutions through a 0.45 μm PFTE filter into sample vials.

[*] Provisional CIPAC method 1997. Prepared by a Committee chaired by: Mrs C Schaller. Based on a method supplied by DuPont de Nemours France.

APPARATUS

Gas chromatograph permitting use of 0.53 mm 'megabore" columns and equipped with on-column injection and temperature programming facilities and a flame ionisation detector
Column fused silica, 10 m × 0.53 mm (i.d.) and 2.0 μm film thickness, coated with crosslinked 50 % phenylmethylsiloxane (HP-17 or equivalent)
Integrator or *electronic data system*
Filtering apparatus with 0.45 μm filter (Acrodisc-CR PFTE or equivalent)
Ultrasonic bath

PROCEDURE

(a) Operating conditions (typical):

Column	Fused silica, 10 m x 0.53 (i.d.) mm and 2.0 μm film thickness coated with crosslinked 50% phenylmethylsiloxane (HP-17 or equivalent)
Detector	Flame ionisation
Temperatures	
Column oven	150 to 265°C at 15°C/min; hold at 265 °C for 4 min. *Do not exceed 280 °C to prevent column deterioration.*
Injection port	250 °C
Detector	300 °C
Gas flow rates	
Carrier gas (helium)	20 ml/min
Hydrogen	50 ml/min) or as recommended for the
Air	300 ml/min) particular instrument
Injection volume	1 μl
Retention times	flusilazole: about 6 min benzophenone: about 3 min

(b) Sample preparation. Weigh (to the nearest 0.1 mg) into a volumetric flask (50 ml) enough sample to contain about 55-65 mg (*w* mg) of flusilazole. Add by pipette internal standard solution (10.0 ml) using the same pipette as for the preparation of the calibration solutions. Add acetonitrile (30 ml), and place the flask in an ultrasonic bath for 7 min. Allow to cool to room temperature and mix well (Solution S). Filter the solution through a 0.45 μm PFTE filter into a sample vial.

(c) System equilibration. Set proper flow rates, and allow the column to equilibrate at 150 °C. Inject 1 μl quantities of acetonitrile to confirm the temperature program and check if a stable baseline has been obtained. Adjust

the carrier gas flow rate to obtain the required retention times and resolution.

(d) Determination. Inject in duplicate 1 µl portions of the calibration and the sample solutions. In the following sequence: C_{A1}, C_{A2}, S_1, C_{B1}, C_{B2}, S_2, C_{C1}, C_{C2}, and so on for other sample solutions. Measure the relevant peak areas and calculate the average flusilazole to benzophenone peak area ratio for each calibration and sample solution. Prepare a calibration curve by plotting the average peak area ratio for each calibration solution versus the mass of flusilazole (mg) in the calibration solutions. Using the least-squares method calculate the line that best fits the experimental data. The correlation coefficient should be 0.998 or better. If not, repeat the calibration. Determine the mass of flusilazole (mg) in the sample solution using the equation of the calibration curve.

(e) Calculation

$$\text{Flusilazole content} = \frac{(R - b) \times P}{a \times w} \text{ g/kg}$$

where:

R	=	average flusilazole to benzophenone ratio of the sample solution
a	=	slope of calibration curve
b	=	intercept of calibration curve
P	=	purity of the flusilazole standard (g/kg)
w	=	mass of sample taken (mg)

Repeatability r = 35 g/kg at 918 g/kg active ingredient content
Reproducibility R = 52 g/kg at 918 g/kg active ingredient content

Based on a study with 10 participants and 40 results.

FLUSILAZOLE WATER DISPERSIBLE GRANULES

[*] **435/**WG/(M)/-

1 Sampling. Take at least 1 kg.

2 Identity tests

2.1 GLC. As for flusilazole technical **435**/TC/(M)/2.1.

2.2 Infrared. Extract the sample with acetonitrile, filter and evaporate the solvent in a stream of clean dry air. Continue as for flusilazole technical

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435/TC/(M)/2.2.
3 Flusilazole. As for flusilazole technical **435**/TC/(M)/3 except add:

REAGENTS

Tetrabutyl ammonium phosphate. Store in a desiccator.
Tetrabutyl ammonium phosphate (TBAP) 0.25 % reagent. Weigh into a volumetric flask (1000 ml) tetrabutyl ammonium phosphate (2.5 g). Add water (200 ml) and acetonitrile (about 700 ml). Place in an ultrasonic bath for 10 min, allow to cool to room temperature, dilute to the mark with acetonitrile and mix well.

and substitute:
(b) Sample preparation. Weigh (to the nearest 0.1 mg) into a volumetric flask (50 ml) enough sample to contain about 55–65 mg (*w* mg) of flusilazole. Add by pipette internal standard solution (10.0 ml), add 0.25 % TBAP solution (35 ml), and place the flask in an ultrasonic bath for 45 min shaking the flask two to three times during this period to disperse the formulation. Allow to cool to room temperature. Fill to the mark with 0.25 % TBAP solution, and mix well. (Solution S). Filter the solution through a 0.45 μm PFTE filter into a sample vial.

Repeatability r = 7 g/kg at 197 g/kg active ingredient content
Reproducibility R = 16 g/kg at 197 g/kg active ingredient content

4 Suspensibility (Draft method)

REAGENTS AND APPARATUS As for **435**/TC/(M)/3 and MT 168.

PROCEDURE

(a) Preparation of suspension. MT 168.

(b) Determination of sedimentation. MT 168.

(c) Determination of flusilazole in the bottom 25 ml of suspension. After removal of the top 225 ml of suspension transfer the 25 ml remaining quantitatively a volumetric flask (50 ml), add by pipette internal standard solution (10.0 ml), add 0.25 % TBAP solution (35 ml), and place the flask in an ultrasonic bath for 45 min shaking the flask two to three times during this period to disperse the formulation. Allow to cool to room temperature. Fill to the mark with 0.25 % TBAP solution, and mix well. (Solution S). Filter the solution through a 0.45 μm PFTE filter into a sample vial.
Proceed as for **435**/TC/(M)/3

(d) Calculation

$$Q = \frac{(R - b) \times P}{a \times 10^{-6}}$$

$$\text{Suspensibility} = \frac{111(\,c - Q\,)}{c}\ \%$$

where:

R = average flusilazole to benzophenone ratio of the sample solution
a = slope of calibration curve
b = intercept of calibration curve
P = purity of the flusilazole standard (g/kg)
c = mass of active ingredient in sample actually taken (g)
Q = mass of active ingredient in the 25 ml remaining in the cylinder (g)

FLUSILAZOLE EMULSIFIABLE CONCENTRATES

[*] **435**/EC/(M)/-

1 Sampling. Take at least 500 ml.

2 Identity tests

2.1 GLC. As for flusilazole technical **435**/TC/(M)/2.1.

3 Flusilazole. As for flusilazole technical **435**/TC/(M)/3.

Repeatability r	= 12 g/kg at 257 g/kg active ingredient content
	= 16 g/kg at 396 g/kg active ingredient content
Reproducibility R	= 16 g/kg at 257 g/kg active ingredient content
	= 25 g/kg at 396 g/kg active ingredient content

Based on a study with 12 participants and 48 results.

[*] Provisional CIPAC method 1997. Prepared by a committee chaired by: Mrs C Schaller. Based on a method supplied by DuPont de Nemours, France.

FLUSILAZOLE OIL IN WATER EMULSIONS
* **435**/EW/(M)/-

1 Sampling. Take at least 500 ml.

2 Identity tests
2.1 GLC. As for flusilazole technical **435**/TC/(M)/2.1.

3 Flusilazole. As for flusilazole technical **435**/TC/(M)/3.

Repeatability r	= 5 g/kg at 96.7 g/kg active ingredient content
	= 9 g/kg at 244 g/kg active ingredient content
Reproducibility R	= 7 g/kg at 96.7 g/kg active ingredient content
	= 14 g/kg at 244. g/kg active ingredient content

Based on a study with 11 participants and 44 results.

* Provisional CIPAC method 1997. Prepared by a committee chaired by: Mrs C Schaller. Based on a method supplied by DuPont de Nemours, France