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LAVENDER OIL

Lavandulae aetheroleum

DEFINITION

Essential oil obtained by steam distillation from the flowering tops of *Lavandula angustifolia* Miller (*Lavandula officinalis* Chaix).

CHARACTERS

Appearance: colourless or pale yellow, clear liquid.

It has a characteristic odour.

IDENTIFICATION

First identification: B.

Second identification: A.

A. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 20 µl of the substance to be examined in 1 ml of *toluene R.*

Reference solution. Dissolve 10 µl of *linalol R* and 10 µl of *linalyl acetate R* in 1 ml of *toluene R.*

Plate: *TLC silica gel plate R.*

Mobile phase: *ethyl acetate R, toluene R* (5:95 *V/V*).

Application: 10 µl as bands.

Development: twice, 5 min apart, over a path of 10 cm.

Drying: in air.

Detection: spray with *anisaldehyde solution R* and heat at 100-105 °C for 5-10 min. Examine immediately in daylight.

Results: see below the sequence of zones present in the chromatograms obtained with the reference solution and the test solution. Furthermore, other violet-red or greenish-brown zones are present in the chromatogram obtained with the test solution above the zone of linalyl acetate up to the solvent front.

Top of the plate	
	Several violet-red or greenish-brown zones
———	———
Linalyl acetate: a violet to brown zone	
	A violet to brown zone (linalyl acetate)
	A violet-red zone
	Possibly a weak violet-brown zone (cineole)
———	———
Linalol: a violet to brown zone	A violet to brown zone (linalol)
	A weak brownish-green zone
	Several unresolved zones
Reference solution	**Test solution**

B. Examine the chromatograms obtained in the test for chromatographic profile.

Results: the characteristic peaks in the chromatogram obtained with the test solution are similar in retention time to those in the chromatogram obtained with reference solution (a).

TESTS

Relative density (*2.2.5*): 0.878 to 0.892.

Refractive index (*2.2.6*): 1.455 to 1.466.

Optical rotation (*2.2.7*): – 12.5° to – 7.0°.

Acid value (*2.5.1*): maximum 1.0, determined on 5.0 g of the substance to be examined dissolved in 50 ml of the prescribed mixture of solvents.

Chromatographic profile. Gas chromatography (*2.2.28*): use the normalisation procedure.

Test solution. The substance to be examined.

Reference solution (a). Dissolve 0.1 g of *limonene R*, 0.2 g of *cineole R*, 0.2 g of *3-octanone R*, 0.05 g of *camphor R*, 0.4 g of *linalol R*, 0.6 g of *linalyl acetate R*, 0.2 g of *terpinen-4-ol R*, 0.1 g of *lavandulyl acetate R*, 0.2 g of *lavandulol R* and 0.2 g of *α-terpineol R* in 5 ml of *hexane R.*

Reference solution (b). Dissolve 5 mg of *3-octanone R* in *hexane R* and dilute to 10 ml with the same solvent.

Column:

- *material*: fused silica,
- *size*: *l* = 60 m , Ø = 0.25 mm,
- *stationary phase*: *macrogol 20 000 R* (film thickness 0.25 µm).

Carrier gas: *helium for chromatography R.*

Flow rate: 1.5 ml/min.

Split ratio: 1:100.

Temperature:

	Time (min)	Temperature (°C)
Column	0 - 15	70
	15 - 70	70 → 180
Injection port		220
Detector		220

Detection: flame ionisation.

Injection: 0.2 µl.

Elution order: order indicated in the composition of reference solution (a). Record the retention times of these substances.

System suitability: reference solution (a):

- *resolution*: minimum 1.4 between the peaks due to terpinen-4-ol and lavandulyl acetate.

Using the retention times determined from the chromatogram obtained with reference solution (a), locate the components of reference solution (a) in the chromatogram obtained with the test solution.

Determine the percentage content of each of these components. The percentages are within the following ranges:

- *limonene*: less than 1.0 per cent,
- *cineole*: less than 2.5 per cent,
- *3-octanone*: 0.1 per cent to 2.5 per cent,
- *camphor*: less than 1.2 per cent,
- *linalol*: 20.0 per cent to 45.0 per cent,
- *linalyl acetate*: 25.0 per cent to 46.0 per cent,
- *terpinen-4-ol*: 0.1 per cent to 6.0 per cent,
- *lavandulyl acetate*: more than 0.2 per cent,
- *lavandulol*: more than 0.1 per cent,
- *α-terpineol*: less than 2.0 per cent.
- *disregard limit*: area of the peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Chiral purity. Gas chromatography (*2.2.28*).

Test solution. Dissolve 0.02 g of the substance to be examined in *pentane R* and dilute to 10 ml with the same solvent.

Reference solution. Dissolve 10 µl of *linalol R*, add 10 µl of *linalyl acetate R* and 5 mg of *borneol R* in *pentane R* and dilute to 10 ml with the same solvent.

Column:

– *material*: fused silica,
– *size*: *l* = 25 m, Ø = 0.25 mm,
– *stationary phase*: *modified β-cyclodextrin for chiral chromatography R* (film thickness 0.25 µm).

Carrier gas: *helium for chromatography R*.

Flow rate: 1.3 ml/min.

Split ratio: 1:30.

Temperature:

	Time (min)	Temperature (°C)
Column	0 - 65	50 → 180
Injection port		230
Detector		230

Detection: flame ionisation.

Injection: 1 µl.

System suitability: reference solution:

– *resolution*: minimum 5.5 between the peaks due to (*R*)-linalol (1st peak) and (*S*)-linalol (2nd peak), minimum 2.9 between the peaks due to (*S*)-linalol and borneol (3rd peak) and minimum 2.7 between the peaks due to (*R*)-linalyl acetate (4th peak) and (*S*)-linalyl acetate (5th peak).

Calculate the percentage content of the specified (*S*)-enantiomers from the following expression:

$$\frac{A_S}{A_S + A_R} \times 100$$

A_S = area of the peak due to the corresponding (*S*)-enantiomer,

A_R = area of the peak due to the corresponding (*R*)-enantiomer.

Limits:

– *(S)-linalol*: maximum 12 per cent,
– *(S)-linalyl acetate*: maximum 1 per cent.

STORAGE

In a well-filled, airtight container, protected from light, at a temperature not exceeding 25 °C.

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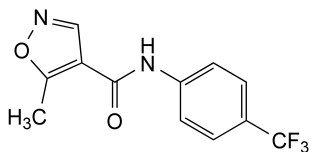
LEFLUNOMIDE

Leflunomidum



$C_{12}H_9F_3N_2O_2$ M_r 270.2

DEFINITION

5-Methyl-*N*-[4-(trifluoromethyl)phenyl]isoxazole-4-carboxamide.

Content: 98.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white powder.

Solubility: practically insoluble in water, freely soluble in methanol, sparingly soluble in methylene chloride.

It shows polymorphism (*5.9*).

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Preparation: heat the substance to be examined and the reference substance at 130 °C for 10 min.

Comparison: *leflunomide CRS*.

TESTS

Related substances. Liquid chromatography (*2.2.29*). *Store all solutions protected from light.*

Test solution (a). Dissolve 25.0 mg of the substance to be examined in 5 ml of *acetonitrile for chromatography R* and dilute to 50.0 ml with the mobile phase.

Test solution (b). Dissolve 0.125 g of the substance to be examined in 5 ml of *acetonitrile for chromatography R* and dilute to 50.0 ml with the mobile phase.

Reference solution (a). Dilute 5.0 ml of test solution (a) to 50.0 ml with the mobile phase. Dilute 1.0 ml of this solution to 100.0 ml with the mobile phase.

Reference solution (b). Dissolve 12.5 mg of *leflunomide impurity A CRS* in 5 ml of *acetonitrile for chromatography R* and dilute to 100.0 ml with the mobile phase. Dilute 10.0 ml of the solution to 100.0 ml with the mobile phase. Dilute 2.0 ml of this solution to 100.0 ml with the mobile phase.

Reference solution (c). Dissolve 25.0 mg of *leflunomide CRS* in 5 ml of *acetonitrile for chromatography R* and dilute to 50.0 ml with the mobile phase.

Reference solution (d). Dissolve the contents of 1 vial of *leflunomide for peak identification CRS* (containing impurities B and C) in 2.0 ml of the mobile phase and sonicate for 10 min.

Column:

– *size*: *l* = 0.125 m, Ø = 4.0 mm;
– *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: mix 5 volumes of *triethylamine R* with 650 volumes of *water for chromatography R*, adjust to pH 3.4 ± 0.1 with *phosphoric acid R* and add 350 volumes of *acetonitrile for chromatography R*.

Flow rate: 1.0 ml/min.

Detection: spectrophotometer at 210 nm.

Injection: 20 µl of test solutions (a) and (b) and reference solutions (a), (b) and (d).

Run time: twice the retention time of leflunomide.

Identification of impurities: use the chromatogram supplied with *leflunomide for peak identification CRS* and the chromatogram obtained with reference solution (d) to identify the peaks due to impurities B and C.

Relative retention with reference to leflunomide (retention time = about 25 min): impurity B = about 0.2; impurity A = about 0.4; impurity C = about 0.9.