Detection: spray with *anisaldehyde solution R* using 10 ml for a plate 200 mm square and heat at 100-105 °C for 10 min.

Results: see below the sequence of the zones present in the chromatograms obtained with the reference solution and the test solution. Furthermore, other zones are present in the lower third and upper part of the chromatogram obtained with the test solution.

Top of the plate	
	A bluish-purple zone
———	———
	A pale green zone
Thymol: a pink zone	A pink zone (thymol)
Carvacrol: a pale violet zone	A pale violet zone (carvacrol)
———	———
	A pale purple zone
	A grey zone
	A pale green zone
	A bluish-purple zone
	An intense brown zone
Reference solution	**Test solution**

TESTS

Water (*2.2.13*): maximum 120 ml/kg, determined on 20.0 g of the powdered drug (355) (*2.9.12*).

Total ash (*2.4.16*): maximum 15.0 per cent.

Ash insoluble in hydrochloric acid (*2.8.1*): maximum 4.0 per cent.

ASSAY

Essential oil (*2.8.12*). Use 30.0 g of the drug to be examined, a 1000 ml round-bottomed flask and 400 ml of *water R* as the distillation liquid. Distil at a rate of 2-3 ml/min for 2 h without *xylene R* in the graduated tube.

Carvacrol and thymol. Gas chromatography (*2.2.28*): use the normalisation procedure.

Test solution. Filter the essential oil obtained in the assay of essential oil over a small amount of *anhydrous sodium sulphate R* and dilute to 5.0 ml with *hexane R* by rinsing the apparatus and the anhydrous sodium sulphate.

Reference solution. Dissolve 0.20 g of *thymol R* and 50 mg of *carvacrol R* in *hexane R* and dilute to 5.0 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: *nitrogen for chromatography R* or *helium for chromatography R*.

Flow rate: 1.5 ml/min.

Split ratio: 1:100.

Temperature:

	Time (min)	Temperature (°C)
Column	0 - 45	40 → 250
Injection port		190
Detector		210

Detection: flame ionisation.

Injection: 0.2 µl.

Elution order: order indicated in the composition of the reference solution; record the retention times of these substances.

System suitability: reference solution:

– *resolution*: minimum of 1.5 between the peaks due to thymol and carvacrol.

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

Determine the percentage content of the sum of carvacrol and thymol.

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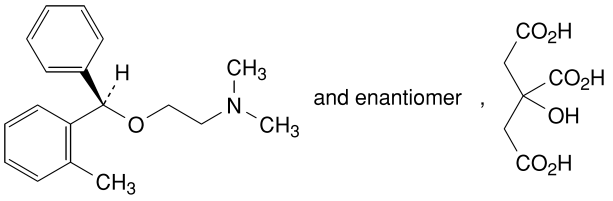
corrected 6.0

ORPHENADRINE CITRATE

Orphenadrini citras



$C_{24}H_{31}NO_8$ M_r 461.5
[4682-36-4]

DEFINITION

(*RS*)-*N*,*N*-Dimethyl-2-[(2-methylphenyl)phenylmethoxy]ethanamine dihydrogen 2-hydroxypropane-1,2,3-tricarboxylate.

Content: 98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: sparingly soluble in water, slightly soluble in alcohol.

mp: about 137 °C.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *orphenadrine citrate CRS*.

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and its absorbance (*2.2.25*) at 436 nm has a maximum of 0.050.

Dissolve 1.0 g in a 3.6 per cent *V/V* solution of *hydrochloric acid R* in *alcohol R* and dilute to 10.0 ml with the same acid solution.

Related substances. Gas chromatography (*2.2.28*): use the normalisation procedure.

Test solution. Dissolve 0.500 g of the substance to be examined in *water R* and dilute to 50 ml with the same solvent. Add 2 ml of *concentrated ammonia R* and shake with 3 quantities, each of 10 ml, of *toluene R*. To the combined upper layers add *anhydrous sodium sulphate R*, shake, filter and evaporate the filtrate, at a temperature not exceeding 50 °C, using a rotary evaporator. Take up the residue with *toluene R* and dilute to 20.0 ml with the same solvent.

Reference solution. Dissolve 30 mg of *orphenadrine citrate CRS* and 30 mg of *orphenadrine impurity E CRS* in 20 ml of *water R*. Add 1 ml of *concentrated ammonia R* and shake with 3 quantities, each of 5 ml, of *toluene R*. To the combined upper layers add *anhydrous sodium sulphate R*, shake, filter and evaporate the filtrate, at a temperature not exceeding 50 °C, using a rotary evaporator. Take up the residue with *toluene R* and dilute to 20.0 ml with the same solvent.

Column:

– *size*: *l* = 60 m, Ø = 0.32 mm,

– *stationary phase*: *poly(dimethyl)(diphenyl)siloxane R* (film thickness 1.0 µm).

Carrier gas: *helium for chromatography R.*

Flow rate: 1 ml/min.

Split ratio: 1:25.

Temperature:

– *column*: 240 °C,

– *injection port and detector*: 290 °C.

Detection: flame ionisation.

Injection: 2 µl.

Run time: 1.3 times the retention time of orphenadrine.

System suitability: reference solution:

– *resolution*: minimum of 1.5 between the peaks due to orphenadrine and to impurity E.

Limits:

– *any impurity*: maximum 0.3 per cent,

– *total*: maximum 1.0 per cent,

– *disregard limit*: 0.02 per cent.

Heavy metals (*2.4.8*): maximum 10 ppm.

2.0 g complies with limit test C. Prepare the standard using 2 ml of *lead standard solution (10 ppm Pb) R.*

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 3 h.

Sulphated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

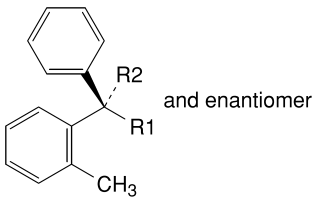
Dissolve 0.350 g in 50 ml of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 ml of *0.1 M perchloric acid* is equivalent to 46.15 mg of $C_{24}H_{31}NO_8$.

STORAGE

Protected from light. If the substance is sterile, store in a sterile, airtight, tamper-proof container, protected from light.

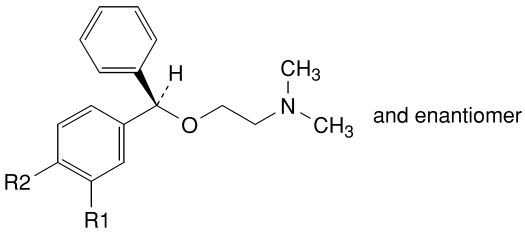
IMPURITIES



A. R1 = OH, R2 = H: (*RS*)-(2-methylphenyl)phenylmethanol (2-methylbenzhydrol),

B. R1 + R2 = O: (2-methylphenyl)phenylmethanone (2-methylbenzophenone),

C. R1 = O-CH_2-CH_2-NH_2, R2 = H: (*RS*)-2-[(2-methylphenyl)phenylmethoxy]ethanamine,



D. R1 = R2 = H: diphenhydramine,

E. R1 = CH_3, R2 = H: (*RS*)-*N,N*-dimethyl-2-[(3-methylphenyl)phenylmethoxy]ethanamine (*meta*-methylbenzyl isomer),

F. R1 = H, R2 = CH_3: (*RS*)-*N,N*-dimethyl-2-[(4-methylphenyl)phenylmethoxy]ethanamine (*para*-methylbenzyl isomer).

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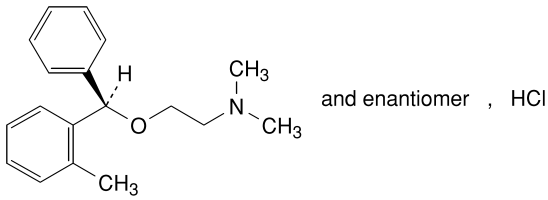
corrected 6.0

ORPHENADRINE HYDROCHLORIDE

Orphenadrini hydrochloridum



$C_{18}H_{24}ClNO$ M_r 305.9
[341-69-5]

DEFINITION

(*RS*)-*N,N*-Dimethyl-2-[(2-methylphenyl)phenylmethoxy]ethanamine hydrochloride.

Content: 98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: freely soluble in water and in alcohol.

mp: about 160 °C.

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).
Preparation: discs.
Comparison: *orphenadrine hydrochloride CRS.*

B. It gives reaction (a) of chlorides (*2.3.1*).

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and its absorbance (*2.2.25*) at 436 nm has a maximum of 0.050.

Dissolve 0.70 g in *alcohol R* and dilute to 10.0 ml with the same solvent.

Related substances. Gas chromatography (*2.2.28*): use the normalisation procedure.

Test solution. Dissolve 0.300 g of the substance to be examined in *water R* and dilute to 50 ml with the same solvent. Add 2 ml of *concentrated ammonia R* and shake with 3 quantities, each of 10 ml, of *toluene R*. To the