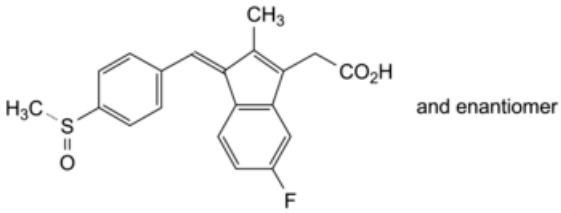
Edition: BP 2025 (Ph. Eur. 11.6 update)

Sulindac

General Notices

(Ph. Eur. monograph 0864)



and enantiomer

$C_{20}H_{17}FO_3S$ 356.4 *38194-50-2*

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

Preparation

Sulindac Tablets

Ph Eur

DEFINITION

[(1*Z*)-6-Fluoro-3-[[4-[(*RS*)-methanesulfinyl]phenyl]methylidene]-2-methyl-3*H*-inden-1-yl]acetic acid.

Content

99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance

Yellow, crystalline powder.

Solubility

Very slightly soluble in water, soluble in methylene chloride, sparingly soluble in ethanol (96 per cent). It dissolves in dilute solutions of alkali hydroxides.

It shows polymorphism (*5.9*).

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison sulindac CRS.

If the spectra obtained show differences, dissolve the substance to be examined and the reference substance separately in the minimum volume of hot methanol R, evaporate to dryness and record new spectra using the residues.

TESTS

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 0.10 g of the substance to be examined in the mobile phase and dilute to 50.0 mL with the mobile phase.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Reference solution (b) Dissolve 4 mg of sulindac for system suitability CRS (containing impurities B, C and D) in the mobile phase and dilute to 2 mL with the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: silica gel for chromatography R (10 µm).

Mobile phase glacial acetic acid R, ethanol (96 per cent) R, ethyl acetate R, methylene chloride R (1:4:100:400 *V/V/V/V*).

Flow rate 2 mL/min.

Detection Spectrophotometer at 280 nm.

Injection 20 µL.

Run time 2.5 times the retention time of sulindac.

Identification of impurities Use the chromatogram supplied with sulindac for system suitability CRS and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities B, C and D.

Relative retention With reference to sulindac (retention time = about 10 min): impurity C = about 0.20; impurity B = about 0.25; impurity D = about 0.7.

System suitability Reference solution (b):

— resolution: minimum 2.0 between the peaks due to impurities C and B.

Calculation of percentage contents:

— *correction factor*: multiply the peak area of impurity C by 2;

— for each impurity, use the concentration of sulindac in reference solution (a).

Limits:

— *impurity C*: maximum 0.5 per cent;

— *impurity B*: maximum 0.4 per cent;

— *impurity D*: maximum 0.2 per cent;

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 1.0 per cent;

— *reporting threshold*: 0.05 per cent.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C at a pressure not exceeding 0.7 kPa.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.300 g in 50 mL of *methanol R*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M sodium hydroxide* is equivalent to 35.64 mg of $C_{20}H_{17}FO_3S$.

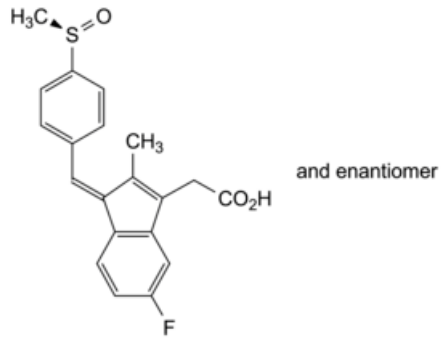
STORAGE

Protected from light.

IMPURITIES

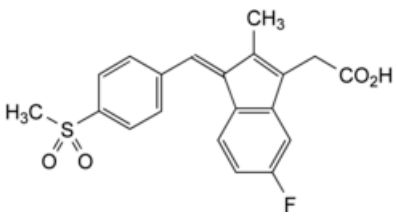
Specified impurities B, C, D.

Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) A.

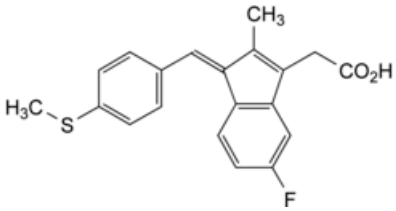


and enantiomer

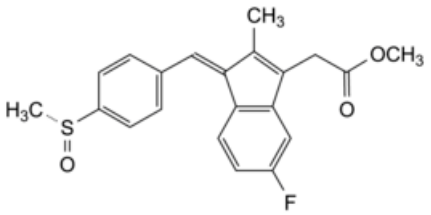
A. [(1*E*)-6-fluoro-3-[[4-[(*RS*)-methanesulfinyl]phenyl]methylidene]-2-methyl-3*H*-inden-1-yl]acetic acid,



B. [(1*Z*)-6-fluoro-3-[[4-(methanesulfonyl)phenyl]methylidene]-2-methyl-3*H*-inden-1-yl]acetic acid,



C. [(1*Z*)-6-fluoro-2-methyl-3-[[4-(methylsulfanyl)phenyl]methylidene]-3*H*-inden-1-yl]acetic acid,



and enantiomer

D. methyl [(1*Z*)-6-fluoro-3-[[4-[(*RS*)-methanesulfinyl]phenyl]methylidene]-2-methyl-3*H*-inden-1-yl]acetate.

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