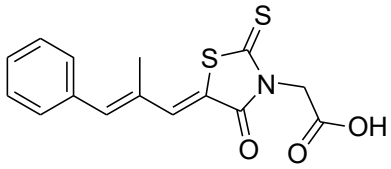
Epalrestat



$C_{15}H_{13}NO_3S_2$ Mol. Wt. 319.4

Epalrestat is 2-{(5Z)-5-[(2E)-2-Methyl-3-phenylprop-2-en-1-ylidene]-4-oxo-2-thioxothiazolidin-3-yl}acetic acid.

Epalrestat contains not less than 98.0 per cent and not more than 101.0 per cent of $C_{15}H_{13}NO_3S_2$, calculated on the dried basis.

Category. Antidiabetic.

Description. A yellow to orange crystalline powder. It shows polymorphism (2.5.11).

Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *epalrestat IPRS* or with the reference spectrum of epalrestat.

B. When examined in the range 200 nm to 400 nm (2.4.7), a 0.0005 per cent w/v solution in *methanol* shows absorption maxima and minima at the same wavelength as that of *epalrestat IPRS* prepared in the same manner.

Tests

Related substances. Determine by liquid chromatography (2.4.14).

Note- Carryout the tests protected from light.

Test solution. Dissolve 25 mg of the substance under examination in 10.0 ml of *N,N-dimethylformamide.*

Reference solution. A 0.0025 per cent w/v solution of *epalrestat IPRS* in *N,N-dimethylformamide.*

Chromatographic system
- a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- mobile phase: a mixture of 70 volumes of a buffer solution prepared by dissolving 6.8 g of *potassium dihydrogen phosphate* and 7.09 g of *disodium hydrogen phosphate* in 1000 ml of *water,* adjusted to pH 6.5, and 35 volumes of *acetonitrile,*
- flow rate: Adjust, so that the retention time of epalrestat is about 12 minutes,
- spectrophotometer set at 280 nm,
- injection volume: 3 µl.

Inject the reference solution. The test is not valid unless the column efficiency in not less than 6000 theoretical plates, the tailing factor is not more than 1.5, and relative standard deviation for replicate injection is not more than 2.0 per cent.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the area of any secondary peak is not more than 0.2 times of the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent) and the sum of the areas of all the secondary peaks is not more than the area of the principal peak in the chromatogram obtained with the reference solution (1.0 per cent).

Heavy metals (2.3.13). 2.0 g complies with the limit test for heavy metals, Method B (10 ppm).

Sulphated ash (2.3.18). Not more than 0.1 per cent.

Loss on drying (2.4.19). Not more than 0.2 per cent, determined on 1.0 g by drying under vacuum over silica gel at 60° for 3 hours.

Assay. Determine by liquid chromatography (2.4.14).

NOTE- Carryout the tests protected from light.

Internal standard solution. A 1.0 per cent v/v solution of *propyl parahydroxy benzoate* in *N,N-dimethylformamide.*

Test solution. Dissolve 20 mg of the substance under examination in 2.0 ml of internal standard and dilute to 10.0 ml with *N,N-dimethylformamide.* Dilute 1.0 ml of the solution to 10.0 ml with *N,N-dimethylformamide.*

Reference solution. Dissolve 20 mg of *epalrestat IPRS* in 2.0 ml of internal standard and dilute to 10.0 ml with *N,N-dimethylformamide.* Dilute 1.0 ml of the solution to 10.0 ml with *N,N-dimethylformamide.*

Use chromatographic system as described under Related substances.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation of the ratio of peak area of epalrestat and internal standard for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{15}H_{13}NO_3S_2$ using the ratio of peak area of epalrestat and internal standard.

Storage. Store protected from light and moisture, at a temperature not exceeding 30°.

Solubility (2.4.26). Soluble in *N,N-dimethylformamide*, slightly soluble in *methanol* and in *ethanol*, and practically insoluble in *water.*
