N–Acetyl–L–Cysteine(EX) *1
: For Manufacturing, Processing or Repacking

N–Ac–L–Cys(EX)

$C_5H_9NO_3S$:163.19

N-Acetyl-L-Cysteine(EX), when dried, contains not less than 98.5 percent and not more than 101.0 percent of N- Acetyl-L-Cysteine ($C_5H_9NO_3S$).

Description: White crystals or crystalline powder; strongly acid taste. Freely soluble in water, soluble in ethanol (96).

Identification: Compare the infrared absorption spectrum <NP TEST 35> of the sample with that of the standard by potassium bromide disc method.

Specifications:

Item	Limit	Test Method
Specific rotation $[\alpha]^{20}_D$	+21.3 to +27.0°	NP TEST 1 [dried sample, C=5, phosphate buffer solution*2]*3
State of solution	clear and colorless	NP TEST 2 [0.5g in 10mL of H_2O,
(Transmittance)	not less than 98.0%	spectrophotometer, 430nm, 10mm cell thickness]
Heavy metals(Pb)	not more than 10ppm	NP TEST 7 [1.0g, (3), ref: 1.0mL of Pb Std. (0.01mg/mL)]
Zinc(Zn)	not more than 10.0ppm	EP
Related substances	not more than 0.2%of L-cysteine not more than 0.3% of *N, N'*-diacetyl-L-cystine not more than 0.15% of *N, S*–diacetyl-L-cysteine not more than 0.10% of other impurity (each) not more than 0.5% of total impurities	EP*4
Loss on drying	not more than 1.00%	NP TEST 11 [1g, in vacuum, at 70℃ for 4 hours]

Item	Limit	Test Method
Residue on ignition (sulfated)	not more than 0.20%	NP TEST 13 [1g, at 550℃ to 650℃ for 3 hours]
Assay	98.5 to 101.0%	EP
pH	2.0 to 2.8	NP TEST 33 [1.0g in 100mL of H_2O]

Endotoxin	less than 24.0EU/g	NP TEST 34 [C = 0.25, kinetic-turbidimetric technique]

＊1 : USP, EP

＊2 : In a 50mL volumetric flask mix 2.5g of the test sample, accurately weighed, with 2mL of disodium dihydrogen ethylenediaminetetraacetate solution (1→100), add 15mL of sodium hydroxide solution (1→25), and mix to dissolve. Dilute to volume with pH 7.0 buffer prepared by mixing 29.5mL of 1mol/L sodium hydroxide, 50mL of 1mol/L potassium dihydrogen phosphate, and sufficient water to make 100mL.

＊3 : Temperature coefficient of $[\alpha]^{t}_{D}$: −0.06°

＊4 : 1) Analytical condition

Detector: UV detector (220nm)

Column: ODS (4.0mm ø×0.25m)

Temperature: Constant temperature around 25℃

Mobile phase: Acetonitrile, water previously adjusted to pH3.0 with phosphoric acid (3:97 V/V)

Flow rate: 1.0mL/min

Injection volume: 20μL

Analytical time: Three times over the retention time for acetylcysteine

2) Solution preparation

i) Test solution

Take 800mg of sample and add 0.01mol/L hydrochloric acid solution to make 100mL.

ii) Reference solution(a)

Dilute 5.0mL of the test solution to 50.0mL with 0.01mol/L hydrochloric acid solution. Dilute 1.0mL of this solution to 100.0mL with 0.01mol/L hydrochloric acid solution.

iii) Reference solution (b)

Dissolve 80mg of L-cystine in 2mL of 1mol/L hydrochloric acid solution and dilute to 200mL with water.

iv) Reference solution (c)

Dissolve 100mg of L-cysteine in 100mL of 0.01mol/L hydrochloric acid solution (L-cysteine dilute solution).

Dissolve 5mg of N,N'-diacetyl-L-cystine and 2.5mg of N,S-diacetyl-L-cysteine in 0.01mol/L hydrochloric acid solution, mix with 3mL of L-cysteine dilute solution and 4mL of Reference solution (b) and dilute to 20mL with 0.01mol/L hydrochloric acid solution. Dilute 5mL of this solution to 50 mL with the test solution.

v) Reference solution (d)

Dissolve 4mg of sodium 2-methyl-2-thiazoline-4-carboxylate in 0.01mol/L hydrochloric acid solution and dilute to 100mL with 0.01mol/L hydrochloric acid solution.

3) Calculation

Impurity contents (percentage) are calculated according to following equations.

i) In case of L-cysteine, *N, N'*-diacetyl-L-cystine, *N, S*-diacetyl-L-cysteine

Each impurity (%) = (A1 / A2) × (m2 / m1) × 100 × correction factor

ii) In case of unspecified impurities

Each impurity (%) = (A3 / A2) × (m2 / m1) × 100

Where,

A_1: peak area of individual impurity (L-cysteine, *N,N'*-diacetyl-L-cystine and *N,S*-diacetyl-L-cysteine) in the chromatogram obtained with test solution.

A_2: peak area of acetylcysteine in the chromatogram obtained with reference solution (a).

A_3: peak area of unspecified impurity in the chromatogram obtained with test solution.

m_1: mass of the acetylcysteine in test solution (mg/mL)

m_2: mass of acetylcysteine in reference solution (a) (mg/mL)

correction factor: L-cysteine = 3.4

N,N'-diacetyl-L-cystine = 0.7

N,S-diacetyl-L-cysteine = 0.3

(Remark)

Following peaks are neglected;

ⅰ) Any peak originated from solvent used for mobile phase.

ⅱ) Peak due to 2-methyl-2-thiazoline-4-carboxilic acid, which is formed due to degralation of acetylcysteine in acidic solution.

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