Monoammonium Glycyrrhizinate 35 mg, Glycine 25 mg, DL-Methionine 25 mg Tablets

Dissolution <6.10> Perform the test with 1 tablet of Monoammonium Glycyrrhizinate 35 mg, Glycine 25 mg, DL-Methionine 25 mg Tablets at 50 revolutions per minute according to the Paddle method, using 900 mL of water as the dissolution medium. Withdraw not less than 20 mL of the medium at the specified minute after starting the test, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 10 mL of the filtrate, and use the subsequent filtrate as the sample solution (1). Pipet 1 mL of the sample solution (1), add water to make exactly 10 mL, and use this solution as the sample solution (2).

The requirements are met if Monoammonium Glycyrrhizinate 35 mg, Glycine 25 mg, DL-Methionine 25 mg Tablets conform to the dissolution requirements.

Glycyrrhizic acid

Weigh accurately about 25 mg of Glycyrrhizic Acid RS (previously determine the water <2.48>), and dissolve in dilute ethanol to make exactly 50 mL. Pipet 5 mL of this solution, add dilute ethanol to make exactly 100 mL, and use this solution as the standard solution.

Perform the test with exactly 20 μL each of the sample solution (1) and standard solution as directed under Liquid Chromatography <2.01> according to the following conditions, and determine the peak areas, A_{Ta} and A_{Sa}, of glycyrrhizic acid.

Dissolution rate (%) with respect to the labeled amount of glycyrrhizic acid ($C_{42}H_{62}O_{16}$)
$= M_{Sa} \times A_{Ta}/A_{Sa} \times 1/C_a \times 90$

M_{Sa}: Amount (mg) of Glycyrrhizic Acid RS, calculated on the anhydrous basis
C_a: Labeled amount (mg) of glycyrrhizic acid ($C_{42}H_{62}O_{16}$) in 1 tablet

Operating conditions —

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 20ºC.

Mobile phase: A mixture of diluted acetic acid (31) (1 in 15) and acetonitrile (3:2).

Flow rate: Adjust the flow rate so that the retention time of glycyrrhizic acid is about 10 minutes.

System suitability —

System performance: Dissolve 5 mg of Glycyrrhizic Acid RS in dilute ethanol to make 20 mL. When

the procedure is run with 20 μL of this solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of glycyrrhizic acid are not less and 2000 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of glycyrrhizic acid is not more than 2.0%.

Glycine, DL-Methionine

Weigh accurately about 25 mg of Glycine RS, previously dried at 105ºC for 3 hours, and dissolve in water to make exactly 100 mL. Pipet 10 mL of this solution, add water to make exactly 100 mL, and use this solution as the glycine standard stock solution. Separately, weigh accurately about 25 mg of DL-Methionine RS, previously dried at 105ºC for 3 hours, and dissolve in water to make exactly 100 mL. Pipet 10 mL of this solution, add water to make exactly 100 mL, and use this solution as the DL-methionine standard stock solution. Pipet 1 mL each of the glycine standard stock solution and DL-methionine standard stock solution, add water to make exactly 10 mL, and use this solution as the standard solution. Perform the test with exactly 20 μL each of the sample solution (2) and standard solution as directed under Liquid Chromatography <2.01> according to the following conditions, and determine the peak areas, A_{Tb} and A_{Tc}, of glycine, and A_{Sb} and A_{Sc}, of DL-methionine.

Dissolution rate (%) with respect to the labeled amount of glycine ($C_2H_5NO_2$)

$= M_{Sb} \times A_{Tb}/A_{Sb} \times 1/C_b \times 90$

Dissolution rate (%) with respect to the labeled amount of DL-methionine ($C_5H_{11}NO_2S$)

$= M_{Sc} \times A_{Tc}/A_{Sc} \times 1/C_c \times 90$

M_{Sb}: Amount (mg) of Glycine RS

M_{Sc}: Amount (mg) of DL-Methionine RS

C_b: Labeled amount (mg) of glycine in 1 tablet

C_c: Labeled amount (mg) of DL-methionine in 1 tablet

Operating conditions —

Detector: A fluorophotometer (excitation wavelength: 350 nm, fluorescence wavelength: 450 nm)

Column: A stainless steel column 6.0 mm in inside diameter and 10 cm in length, packed with strongly acidic ion-exchange resin for high-pressure liquid chromatography composed with a sulfonated polystyrene copolymer (5 μm in particle diameter).

Column temperature: A constant temperature of about 60ºC.

Reaction coil: A stainless steel coil 0.5 mm in inside diameter and 2 m in length.

Reaction coil temperature: A constant temperature of about 60ºC.

Mobile phase: Dissolve 8.4 g of citric acid monohydrate and 11.8 g of trisodium citrate dihydrate in water to make exactly 1000 mL.

Reaction reagent: Dissolve 1 g of *N*-acetyl-L-systeine and 0.8 g of *o*-phthalaldehyde in ethanol (99.5) to make 15 mL. To this solution add 4 mL of a solution of 10% polyoxyethylene (23) lauryl ether, and add an aqueous solution containing 384 mmol/L of sodium carbonate, 216 mmol/L of boric acid and 108 mmol/L of potassium sulfate to make exactly 1000 mL.

Flow rate of the mobile phase: 0.4 mL per minute.

Flow rate of the reaction reagent: 0.3 mL per minute.

System suitability —

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, glycine and DL-methionine are eluted in this order with the resolution between these peaks being not less than 1.5.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviations of the peak areas of glycine and DL-methionine are not more than 2.0%, respectively.

Dissolution Requirements

	Labeled amount	Specified minute	Dissolution rate
Monoammonium Glycyrrhizianate (as Glycyrrhizic Acid)	35 mg (25 mg)	60 minutes	Not less than 80%
Glycine	25 mg		Not less than 85%
DL-Methionine	25 mg		Not less than 85%

Glycine RS Glycine (JP). When dried, it contains not less than 99.0% of glycine ($C_2H_5NO_2$).

***N*-Acethyl-L-Cysteine** Acetylcysteine. When dried, it contains not less than 98.0% of acetylcysteine ($C_2H_9NO_3S$).

DL-Methionine RS $C_5H_{11}NO_2S$: 149.21

(2*RS*)-2-Amino-4-(methylsulfanyl)butanoic acid. It meets the following requirements:

Description —DL-Methionine RS occurs as white crystals or crystalline powder. It has a characteristic odor a slight sweet taste.

Identification —Determine the infrared absorption spectrum of DL-Methionine RS, previously dried, as directed in the potassium bromide disk method under Infrared Spectrophotometry <*2.25*>: it exhibits

absorption at the wave numbers of about 2930 cm^{-1}, 1650 cm^{-1}, 1580 cm^{-1}, 1414 cm^{-1} and 1340 cm^{-1}.

Related substances—Dissolve 0.10 g of DL-Methionine RS in 10 mL of water, and use this solution as the sample solution. To exactly 1 mL of this solution add water to make exactly 50 mL. Pipet 5 mL of this solution, add water to make exactly 20 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under Thin-layer Chromatography <2.03>. Spot 5 μL each of the sample solution and standard solution on a plate of silica gel for thin-layer chromatography. After air-drying, immediately develop the plate with a mixture of 1-butanol, water and acetic acid (100) (3:1:1) to a distance of about 10 cm, and dry the plate at 80ºC for 30 minutes. Spray evenly a solution of ninhydrin in acetone (1 in 50) on the plate, and heat at 80ºC for 5 minutes: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

Loss on drying <2.41>: not more than 0.30% (1g, 105ºC, 3 hours).

Content: not less than 99%. Assay—Weigh accurately about 0.15 g of DL-Methionine RS, previously dried, dissolve in 3 mL of formic acid, add 50 mL of acetic acid (100), and titrate <2.50> with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination in the same manner, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 14.92 mg of $C_5H_{11}NO_2S$