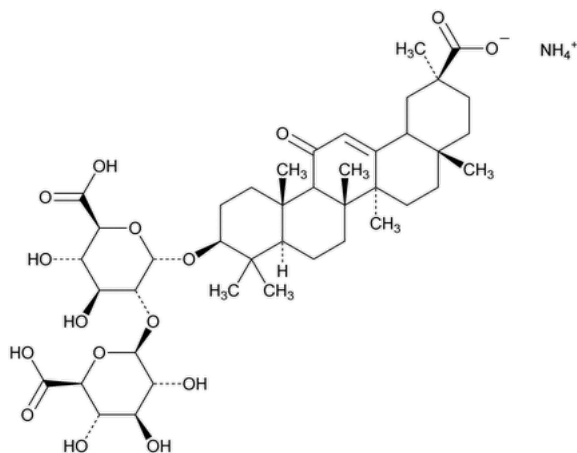


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Ammonium Glycyrrhizate

Change to read:



$C_{42}H_{62}O_{16} \cdot NH_3$ ▲839.97 ▲ (ERR 1-Jul-2022)

Monoammonium glycyrrhizinate;

Glycyrrhizic acid ammonium salt;

α -D-Glucopyranosiduronic acid, (3 β ,20 β)-20-carboxy-11-oxo-30-norolean-12-en-3-yl 2-O- β -D-glucopyranuronosyl-, ammonium salt (1:1);

α -D-Glucopyranosiduronic acid, (3 β ,20 β)-20-carboxy-11-oxo-30-norolean-12-en-3-yl 2-O- β -D-glucopyranuronosyl-, monoammonium salt CAS
 RN®: 53956-04-0.

DEFINITION

Ammonium Glycyrrhizate is a mixture of ammonium 18 α - and 18 β -glycyrrhizate (ammonium salt of (20 β)-3 β -[[2-O-(β -D-glucopyranosyluronic acid)- α -D-glucopyranosyluronic acid]oxy]-11-oxoolean-12-en-29-oic acid), and the 18 β -isomer is the main component. It contains NLT 78.0% and NMT 102.0% of ammonium 18 α - and 18 β -glycyrrhizate, on the anhydrous basis.

IDENTIFICATION

• **A.** The retention times of the peaks of 18 α - and 18 β -glycyrrhizic acid from the *Sample solution* correspond to those from the *System suitability solution*, as obtained in the *Content of Ammonium 18 α - and 18 β -Glycyrrhizate*. [NOTE—The peak of 18 α -glycyrrhizic acid could be absent in the *Sample solution*.]

• **B.** [IDENTIFICATION TESTS—GENERAL, Ammonium \(191\)](#).

Acceptance criteria: Meets the requirements

ASSAY

Change to read:

• **CONTENT OF AMMONIUM 18 α - AND 18 β -GLYCYRRHIZATE**

Mobile phase: Acetonitrile, glacial acetic acid, and water (38:1:61)

Standard solution: 0.5 mg/mL of [USP Glycyrrhizic Acid RS](#) in *Mobile phase*

System suitability solution: 0.5 mg/mL of [USP Ammonium Glycyrrhizate RS](#) in *Mobile phase*

Sample solution: 0.5 mg/mL of Ammonium Glycyrrhizate in *Mobile phase*

Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm \times 30-cm analytical column; 5–10 μ m packing L1

Flow rate: 2.0 mL/min

Injection volume: 10 μ L

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times of 18β-glycyrrhizic acid and 18α-glycyrrhizic acid are about 1.0 and 1.2, respectively, *System suitability solution*.]

Suitability requirements

Resolution: NLT 2.0 between the peaks due to 18β-glycyrrhizic acid and 18α-glycyrrhizic acid, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution*, *System suitability solution*, and *Sample solution*

Determine the peak areas for each isomer (18α-glycyrrhizic acid or 18β-glycyrrhizic acid).

Calculate the percentage of ammonium 18α-glycyrrhizate (or ammonium 18β-glycyrrhizate) in the portion of Ammonium Glycyrrhizate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{W(\text{Salt})}/M_{W(\text{Acid})}) \times 100$$

r_U = peak area of the 18α-glycyrrhizic acid (or 18β-glycyrrhizic acid) in the *Sample solution*

r_S = peak area of the 18β-glycyrrhizic acid in the *Standard solution*

C_S = concentration of the [USP Glycyrrhizic Acid RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of the *Sample solution* (mg/mL)

$M_{W(\text{Salt})}$ = molecular weight of ammonium glycyrrhizate, ▲839.97▲ (ERR 1-Jul-2022) g/mol

$M_{W(\text{Acid})}$ = molecular weight of glycyrrhizic acid, ▲822.94▲ (ERR 1-Jul-2022) g/mol

Acceptance criteria: The total percentage of ammonium 18α-glycyrrhizate and ammonium 18β-glycyrrhizate is 78.0%–102.0%, and the percentage of ammonium 18α-glycyrrhizate is NMT 13.0%, on the anhydrous basis.

IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#).

Sample: 1.0 g

Acceptance criteria: NMT 0.5%

- **LIMIT OF ORGANIC IMPURITIES**

Mobile phase, System suitability solution, and Chromatographic system: Proceed as directed in *Content of Ammonium 18α- and 18β-Glycyrrhizate*.

Sample solution: 1.0 mg/mL of Ammonium Glycyrrhizate in the *Mobile phase*

Reference solution A: 0.05 mg/mL of Ammonium Glycyrrhizate in the *Mobile phase*, prepared from the *Sample solution*

Reference solution B: 0.057 mg/mL of Ammonium Glycyrrhizate in the *Mobile phase*, prepared from the *Sample solution*

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for 24-hydroxyglycyrrhizinic acid, 18β-glycyrrhizic acid, and 18α-glycyrrhizic acid are about 0.7, 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 2.0 between the peaks due to 18β-glycyrrhizic acid and 18α-glycyrrhizic acid

Analysis

Samples: *System suitability solution*, *Reference solution A*, *Reference solution B*, and *Sample solution*

Acceptance criteria: See [Table 1](#).

Table 1

Name	Relative Retention Time	Acceptance Criteria
24-Hydroxy glycyrrhizinic acid ^a	0.7	NMT the sum of the areas of the peaks in the chromatogram from <i>Reference solution B</i> , corresponding to NMT 5.7%
Any other impurity	—	For each impurity, NMT 0.4 times the sum of the areas of the peaks in the chromatogram from <i>Reference solution A</i> , corresponding to NMT 2.0%

Name	Relative Retention Time	Acceptance Criteria
Sum of other impurities	—	NMT 1.6 times the sum of the areas of the peaks in the chromatogram from <i>Reference solution A</i> , corresponding to NMT 8.0%
Disregard limit	—	0.04 times the sum of the areas of the peaks in the chromatogram from <i>Reference solution A</i> , corresponding to 0.2%

^a (4β,20β)-3β-[[2-O-(β-D-Glucopyranosyluronic acid)-α-D-glucopyranosyluronic acid]oxy]-23-hydroxy-11-oxoolean-12-en-29-oic acid.

SPECIFIC TESTS

Change to read:

- **OPTICAL ROTATION, *Specific Rotation*** [▲](781S) [▲]-(ERR 1-Jul-2022)

Sample solution: 10.0 mg/mL of Ammonium Glycyrrhizate in 50% ethanol

Acceptance criteria: [▲]+49.0° [▲](ERR 1-Jul-2022) to [▲]+55.0° [▲](ERR 1-Jul-2022) on the anhydrous basis

- **WATER DETERMINATION, *Method Ia***(921).

Sample: 0.25 g

Acceptance criteria: NMT 6.0%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, and store in a cool, dry place.

- **USP REFERENCE STANDARDS** (11).

[USP Ammonium Glycyrrhizate RS](#)

[USP Glycyrrhizic Acid RS](#)

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
AMMONIUM GLYCYRRHIZATE	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: [Chromatographic Database](#)

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