

Proline

1 Nonproprietary Names

BP: Proline
JP: L-Proline
PhEur: Proline
USP-NF: Proline

2 Synonyms

AjiPure; P; Pro; prolinum; 2-pyrrolidinecarboxylic acid.

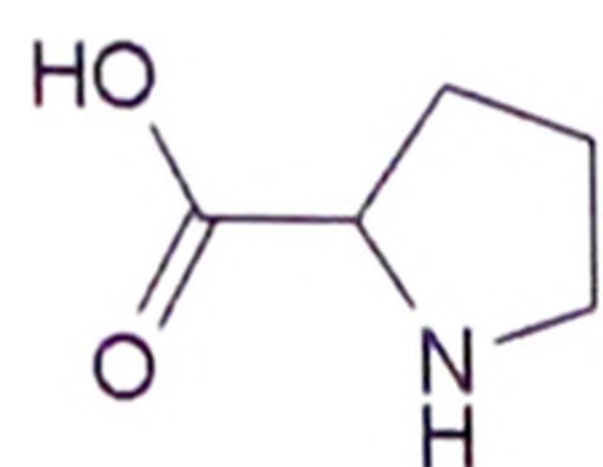
3 Chemical Name and CAS Registry Number

L-Pyrrolidine-2-carboxylic acid [147-85-3]

4 Empirical Formula and Molecular Weight

C₅H₉NO₂ 115.1

5 Structural Formula



6 Functional Category

Dispersing agent.

7 Applications in Pharmaceutical Formulation or Technology

Proline is used as a stabilizer in liquid formulations for injection or infusion. It is more effective than glycine at controlling dimer formation^(1,2) and aggregation, maintaining antibody function and reducing discoloration in liquid intravenous immunoglobulin preparations.⁽¹⁾ These stabilizing effects are attributable to proline's amphiphilic properties.^(1,3) It has been used in intravenous immunoglobulin preparations at concentrations of 250 mmol/L and at pH 4.8.⁽³⁾

8 Description

Proline is an amphiphilic amino acid and occurs as white crystals or crystalline powder and has a sweet taste. It is deliquescent.

9 Pharmacopeial Specifications

See Table I.

10 Typical Properties

Dissociation constants

$$pK_1 = 1.99$$

$$pK_2 = 10.60$$

Partition coefficient $\log P$ (octanol:water) = -2.54

Solubility See Table II.

11 Stability and Storage Conditions

Store protected from light in well-closed containers.

12 Incompatibilities

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Table I: Pharmacopeial specifications for proline.

Test	JP XVII	PhEur 9.2	USP 40–NF 35 S1
Identification	+	+	+
Characters	+	+	—
Appearance of solution	—	+	—
Specific rotation	-84.0° to -86.0°	-84.0° to -86.0°	-84.3° to -86.3°
pH	5.9-6.9	—	—
Ninhydrin-positive substances	—	+	—
Chlorides	≤0.21%	≤200 ppm	≤0.05%
Sulfates	≤0.028%	≤300 ppm	≤0.03%
Ammonium	≤0.02%	≤0.02%	—
Iron	≤10 ppm	≤10 ppm	≤30 ppm
Heavy metals	≤10 ppm	—	≤15 ppm
Related substances	+	—	≤2.0%
Loss on drying	≤0.3%	≤0.5%	≤0.4%
Sulfated ash	—	≤0.1%	—
Residue on ignition	≤0.1%	—	≤0.4%
Assay	99.0-101.0%	98.5-101.0%	98.5-101.5%

Table II: Solubility of Proline.

Solvent	Solubility
Butanol	Insoluble
Ethanol	1.55% at 35°C
Ether	Insoluble
Isopropanol	Insoluble
Water	1 in 0.80 at 0°C 1 in 0.62 at 25°C 1 in 0.48 at 50°C 1 in 0.42 at 65°C

13 Method of Manufacture

Proline is synthesized from glutamic acid.

14 Safety

Proline is mostly well-tolerated. Hemolysis-related adverse reactions have been reported in patients given proline-stabilized intravenous immunoglobulins. However, incidences of renal adverse effects were low for proline-stabilized intravenous immunoglobulins, particularly compared with sucrose-stabilized preparations.⁽⁴⁾

Preparations containing proline are contraindicated in patients with hyperprolinaemia.

Increases in amino acid concentrations have been found to induce sister-chromatid exchanges in human lymphocytes. This mutagenic effect was not found to be dose-dependent.⁽⁵⁾

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. When heated to decomposition,