Edition: BP 2025 (Ph. Eur. 11.6 update)

Gelatin[1]

General Notices

(Ph. Eur. monograph 0330)

Action and use

Excipient.

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DEFINITION

Purified protein obtained from collagen of animals by partial alkaline and/or acid hydrolysis and/or enzymatic hydrolysis, or by thermal hydrolysis.

The hydrolysis leads to gelling or non-gelling product grades. This monograph covers both the gelling grade and the non-gelling grade (also called hydrolysed gelatin).

♦ CHARACTERS

Appearance

— *gelling grade*: faintly yellow or light yellowish-brown solid, usually occurring as translucent sheets, shreds, granules or powder;

— *non-gelling grade*: faintly yellow or white granules or powder.

Solubility

— *gelling grade*: practically insoluble in common organic solvents; gelling grades swell in cold water and give on heating a colloidal solution which on cooling forms a more or less firm gel;

— *non-gelling grade*: soluble in cold or warm water, practically insoluble in common organic solvents.

Different gelatins form aqueous solutions that vary in clarity and colour. For a particular application, a suitable specification for clarity and colour may be required.♦

IDENTIFICATION

Gelling grade: A, B.

Non-gelling grade: A, B, C.

A. To 2 mL of solution S (see Tests) add 0.05 mL of *copper sulfate solution R*. Mix and add 0.5 mL of *dilute sodium hydroxide solution R*. A violet colour is produced.
B. In a test-tube about 15 mm in internal diameter, place 0.5 g of the substance to be examined and add 10 mL of *water R*. Allow to stand for 10 min, heat at 60 °C for 15 min and keep the tube upright at 2-8 °C for 6 h. Invert the tube; the

contents flow out immediately for non-gelling grades and do not flow out immediately for gelling grades.
C. To 0.5 g in a 250 mL bottle, add 10 mL of *water R* and 5 mL of *sulfuric acid R*. Place the bottle, partly but not completely closed (for example, using a watch glass), in an oven at 105 °C for 4 h. Allow to cool and add 200 mL of *water R*. Adjust to pH 6.0-8.0 using a 200 g/L solution of *sodium hydroxide R*. Place 2 mL of the solution in a test-tube and add 2 mL of a solution prepared immediately before use containing 14 g/L of *chloramine R* in *phosphate buffer solution pH 6.8 R*. Mix and allow to stand for 20 min. Add 2 mL of *dimethylaminobenzaldehyde solution R9*. Mix and place in a water-bath at 60 °C for 15 min. A red to violet colour develops.

TESTS

Solution S

Dissolve 1.00 g in *carbon dioxide-free water R* at about 55 °C, dilute to 100 mL with the same solvent and keep the solution at this temperature to carry out the tests.

pH (*2.2.3*)

3.8 to 7.6 for solution S, measured at 55 °C.

Conductivity (*2.2.38*)

Maximum 1 $mS\text{-}cm^{-1}$, determined on a 10.0 g/L solution at 30 ± 1.0 °C (without the use of a temperature compensation device).

Sulfur dioxide (*2.5.29*)

Maximum 50 ppm.

Peroxides

Maximum 10 ppm, determined using *peroxide test strips R*.

Peroxidase transfers oxygen from peroxides to an organic redox indicator which is converted to a blue oxidation product. The intensity of the colour obtained is proportional to the quantity of peroxide and can be compared with a colour scale provided with the test strips, to determine the peroxide concentration.

Suitability test Dip a test strip for 1 s into *hydrogen peroxide standard solution (2 ppm H_2O_2) R*, such that the reaction zone is properly wetted. Remove the test strip, shake off excess liquid and after 15 s compare the reaction zone with the colour scale provided. The test strips are suitable if the colour matches that of the 2 ppm concentration.

Test Weigh 20.0 ± 0.1 g of the substance to be examined in a beaker and add 80.0 ± 0.2 mL of *water R*. Stir to moisten all the gelatin and allow the sample to stand at room temperature for 1-3 h. Cover the beaker with a watch-glass. If dissolution is not complete, place the beaker for 20 ± 5 min in a water-bath at 65 ± 2 °C to dissolve the sample. Stir the contents of the beaker with a glass rod to achieve a homogeneous solution. Dip a test strip for 1 s into the test solution, such that the reaction zone is properly wetted. Remove the test strip, shake off excess liquid and after 15 s compare the reaction zone with the colour scale provided. Multiply the concentration read from the colour scale by a factor of 5 to calculate the concentration in parts per million of peroxide in the substance to be examined.

Gel strength (Bloom value)

80 per cent to 120 per cent of the nominal value stated on the label for the gelling grade.

The gel strength is expressed as the mass in grams necessary to produce the force which, applied to a plunger 12.7 mm in diameter, makes a depression 4 mm deep in a gel having a concentration of 6.67 per cent *m/m* and matured at 10 °C.

Apparatus Texture analyser or gelometer with:

— a cylindrical piston 12.7 ± 0.1 mm in diameter with a plane pressure surface with a sharp bottom edge;

— a bottle 59 ± 1 mm in internal diameter and 85 mm high.

Adjust the apparatus according to the manufacturer's manual. Settings are: distance 4 mm, test speed 0.5 mm/s.

Method Place 7.5 g of the substance to be examined in a bottle. Add 105 mL of *water R*, close the bottle and allow to stand for 1-4 h. Heat in a water-bath at 65 ± 2 °C for 15 min. While heating, stir gently with a glass rod. Ensure that the solution is uniform and that any condensed water on the inner walls of the bottle is incorporated. Allow to cool at room temperature for 15 min and transfer the bottle to a thermostatically controlled bath at 10.0 ± 0.1 °C, fitted with a device to ensure that the platform on which the bottle stands is perfectly horizontal. Close the bottle and allow to stand for 17 ± 1 h. Remove the bottle from the bath and quickly wipe the water from the exterior of the bottle. Centre the bottle on the platform of the apparatus so that the plunger contacts the sample as near to its midpoint as possible and start the measurement.

Iron

Maximum 30 ppm.

Atomic absorption spectrometry (*2.2.23, Method II*).

Test solution To 5.00 g of the substance to be examined, in a conical flask, add 10 mL of *hydrochloric acid R*. Close the flask and place in a water-bath at 75-80 °C for 2 h (if necessary for proper solubilisation, the gelatin may be allowed to swell after addition of the acid and before heating, the heating time may be prolonged, and a higher temperature may be used). Allow to cool and adjust the contents of the flask to 100.0 g with *water R*.

Reference solutions Prepare the reference solutions using *iron standard solution (8 ppm Fe) R*, diluting with *water R*.

Wavelength 248.3 nm.

Chromium

Maximum 10 ppm.

Atomic absorption spectrometry (*2.2.23, Method II*).

Test solution Test solution described in the test for iron.

Reference solutions Prepare the reference solutions using *chromium standard solution (100 ppm Cr) R*, diluting with *water R*.

Wavelength 357.9 nm.

Zinc

Maximum 30 ppm.

Atomic absorption spectrometry (*2.2.23, Method II*).

Test solution Test solution described in the test for iron.

Reference solutions Prepare the reference solutions using *zinc standard solution (10 ppm Zn) R*, diluting with *water R*.

Wavelength 213.9 nm.

Loss on drying (*2.2.32*)

Maximum 15.0 per cent, determined on 5.000 g by drying in an oven at 105 °C for 16 h.

Microbial contamination

TAMC: acceptance criterion 10^3 CFU/g (*2.6.12*).

TYMC: acceptance criterion 10^2 CFU/g (*2.6.12*).

Absence of *Escherichia coli* (*2.6.13*).

Absence of *Salmonella* (*2.6.13*).

STORAGE

Protected from heat and moisture.

LABELLING

The label states the gel strength (Bloom value) or that it is a non-gelling grade (also called hydrolysed gelatin).

◊ FUNCTIONALITY-RELATED CHARACTERISTICS

This section provides information on characteristics that are recognised as being relevant control parameters for one or more functions of the substance when used as an excipient (see chapter 5.15). Some of the characteristics described in the Functionality-related characteristics section may also be present in the mandatory part of the monograph since they also represent mandatory quality criteria. In such cases, a cross-reference to the tests described in the mandatory part is included in the Functionality-related characteristics section. Control of the characteristics can contribute to the quality of a medicinal product by improving the consistency of the manufacturing process and the performance of the medicinal product during use. Where control methods are cited, they are recognised as being suitable for the purpose, but other methods can also be used. Wherever results for a particular characteristic are reported, the control method must be indicated.

The following characteristic may be relevant for gelling grade gelatin used as viscosity-increasing agent, binder or used for microencapsulation.

Gel strength (Bloom value)

(see Tests).◊

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1 This monograph has undergone pharmacopoeial harmonisation. See chapter *5.8 Pharmacopoeial harmonisation*.