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Xanthan Gum

General Notices

(Ph. Eur. monograph 1277)

11138-66-2

Action and use

Excipient.

Ph Eur

DEFINITION

High-molecular-mass anionic polysaccharide produced by fermentation of carbohydrates with *Xanthomonas campestris*. It consists of a principal chain of β(1→4)-linked D-glucose units with trisaccharide side chains, on alternating anhydroglucose units, consisting of 1 glucuronic acid unit included between 2 mannose units. Most of the terminal units contain a pyruvate moiety and the mannose unit adjacent to the principal chain may be acetylated at C-6.

Xanthan gum has a relative molecular mass of approximately 1×10^6. It exists as the sodium, potassium or calcium salt.

Content

Minimum 1.5 per cent of pyruvate acetal groups ($C_3H_3O_2$; M_r 71.1) (dried substance).

CHARACTERS

Appearance

White or yellowish-white, free-flowing powder.

Solubility

Soluble in water giving a highly viscous solution, practically insoluble in organic solvents.

IDENTIFICATION

A. In a flask, suspend 1 g in 15 mL of a 10.3 g/L solution of *hydrochloric acid R*. Close the flask with a fermentation bulb containing *barium hydroxide solution R* and heat carefully for 5 min. The barium hydroxide solution shows a white turbidity.
B. To 300 mL of *water R*, previously heated to 80 °C and stirred rapidly with a mechanical stirrer in a 400 mL beaker, add, at the point of maximum agitation, a dry blend of 1.5 g of *carob bean gum R* and 1.5 g of the substance to be examined. Stir until the mixture forms a solution, and then continue stirring for 30 min or longer. Do not allow the water temperature to drop below 60 °C during stirring. Discontinue stirring and allow the mixture to stand for at least 2 h. A firm rubbery gel forms after the temperature drops below 40 °C but no such gel forms in a 1 per cent control solution of the sample prepared in the same manner but omitting the carob bean gum.

TESTS

pH (*2.2.3*)

6.0 to 8.0 for a 10.0 g/L solution in *carbon dioxide-free water R*.

2-Propanol

Gas chromatography (*2.2.28*).

Internal standard solution Dilute 0.50 g of *2-methyl-2-propanol R* to 500 mL with *water R*.

Test solution To 200 mL of *water R* in a 1000 mL round-bottomed flask, add 5.0 g of the substance to be examined and 1 mL of a 10 g/L emulsion of *dimeticone R* in *liquid paraffin R*, stopper the flask and shake for 1 h. Distil about 90.0 mL, mix the distillate with 4.0 mL of the internal standard solution and dilute to 100.0 mL with *water R*.

Reference solution Dilute a suitable quantity of *2-propanol R*, accurately weighed, with *water R* to obtain a solution having a known concentration of 2-propanol of about 1 mg/mL. To 4.0 mL of this solution add 4.0 mL of the internal standard solution and dilute to 100.0 mL with *water R*.

Column:

— *size*: *l* = 1.8 m, Ø = 4.0 mm;

— *stationary phase*: *ethylvinylbenzene-divinylbenzene copolymer R* (149-177 µm).

Carrier gas *helium for chromatography R*.

Flow rate 30 mL/min.

Temperature:

— *column*: 165 °C;

— *injection port and detector*: 200 °C.

Detection Flame ionisation.

Injection 5 µL.

Relative retention With reference to 2-propanol: 2-methyl-2-propanol = about 1.5.

Limit:

— *2-propanol*: maximum 750 ppm.

Loss on drying (*2.2.32*)

Maximum 15.0 per cent, determined on 1.000 g by drying in an oven at 105 °C for 2.5 h.

Total ash (*2.4.16*)

6.5 per cent to 16.0 per cent (dried substance).

ASSAY

Test solution Dissolve a quantity of the substance to be examined corresponding to 120.0 mg of the dried substance in *water R* and dilute to 20.0 mL with the same solvent.

Reference solution Dissolve 45.0 mg of *pyruvic acid R* in *water R* and dilute to 500.0 mL with the same solvent.

Place 10.0 mL of the test solution in a 50 mL round-bottomed flask, add 20.0 mL of a 10.3 g/L solution of *hydrochloric acid R* and weigh. Boil on a water-bath under a reflux condenser for 3 h. Weigh and adjust to the initial mass with *water R*.

In a separating funnel mix 2.0 mL of the solution with 1.0 mL of *dinitrophenylhydrazine-hydrochloric solution R*. Allow to stand for 5 min and add 5.0 mL of *ethyl acetate R*. Shake and allow the solids to settle. Collect the upper layer and shake with 3 quantities, each of 5.0 mL, of *sodium carbonate solution R*. Combine the aqueous layers and dilute to 50.0 mL with *sodium carbonate solution R*. Mix. Treat 10.0 mL of the reference solution at the same time and in the same manner as for the test solution.

Immediately measure the absorbance (*2.2.25*) of the 2 solutions at 375 nm, using *sodium carbonate solution R* as the compensation liquid.

The absorbance of the test solution is not less than that of the reference solution, which corresponds to a content of pyruvoyl groups of not less than 1.5 per cent.

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 characteristics may be relevant for xanthan gum used as viscosity-increasing agent.

Viscosity

(*2.2.10*): typically minimum 600 mPa·s.

Add 3.0 g (dried substance) within 45-90 s into 250 mL of a 12 g/L solution of *potassium chloride R* in a 500 mL beaker stirring with a low-pitch propeller-type stirrer rotating at 800 r/min. When adding the substance take care that agglomerates are destroyed. Add an additional quantity of 44 mL of *water R*, to rinse any adhering residue from the walls of the beaker. Stir the preparation at 800 r/min for 2 h whilst maintaining the temperature at 24 ± 1 °C. Determine the viscosity within 15 min at 24 ± 1 °C using a rotating viscosimeter set at 60 r/min and equipped with a rotating spindle 1.78 mm high and 12.60 mm in diameter which is attached to a shaft 3.2 mm in diameter. The distance from the top of the cylinder to the lower tip of the shaft should be 25.60 mm and the immersion depth 50.0 mm.

The following characteristics may be relevant for xanthan gum used as matrix former in prolonged-release tablets.

Viscosity

See test above.

Particle-size distribution (*2.9.31* or *2.9.38*)

Powder flow (*2.9.36*)