Xanthan Gum

1 Nonproprietary Names

BP: Xanthan gum
PhEur: Xanthani gummi
USPNF: Xanthan gum

2 Synonyms

Corn sugar gum; E415; *Keltrol*; polysaccharide B-1459; *Rhodigel*; *Vanzan NF*; *Xantural*.

3 Chemical Name and CAS Registry Number

Xanthan gum [11138-66-2]

4 Empirical Formula Molecular Weight

The USPNF 20 describes xanthan gum as a high molecular weight polysaccharide gum. It contains D-glucose and D-mannose as the dominant hexose units, along with D-glucuronic acid, and is prepared as the sodium, potassium, or calcium salt.

The molecular weight is approximately 2×10^6.

5 Structural Formula

Each xanthan gum repeat unit contains five sugar residues: two glucose, two mannose, and one glucuronic acid. The polymer backbone consists of four β-D-glucose units linked at the 1 and 4 positions, and is therefore identical in structure to cellulose. Trisaccharide side chains on alternating anhydroglucose units distinguish xanthan from cellulose. Each side chain comprises a glucuronic acid residue between two mannose units. At most of the terminal mannose units is a pyruvate moiety; the mannose nearest the main chain carries a single group at C-6. The resulting stiff polymer chain may exist in solution as a single, double, or triple helix that interacts with other xanthan gum molecules to form complex, loosely bound networks.[1,2]

6 Functional Category

Stabilizing agent; suspending agent; viscosity-increasing agent.

7 Applications in Pharmaceutical Formulation or Technology

Xanthan gum is widely used in oral and topical pharmaceutical formulations, cosmetics, and foods as a suspending and stabilizing agent.[3,4] It is also used as a thickening and emulsifying agent. It is nontoxic, compatible with most other pharmaceutical ingredients, and has good stability and viscosity properties over a wide pH and temperature range; *see* Section 11.

When xanthan gum is mixed with certain inorganic suspending agents, such as magnesium aluminum silicate, or organic gums, synergistic rheological effects occur.[5] In general, mixtures of xanthan gum and magnesium aluminum silicate in ratios between 1:2 and 1:9 produce the optimum properties. Similarly, optimum synergistic effects are obtained with xanthan gum:guar gum ratios between 3:7 and 1:9.

Although primarily used as a suspending agent, xanthan gum has also been used to prepare sustained-release matrix tablets.[6–8]

Xanthan gum is also used as a hydrocolloid in the food industry, and in cosmetics it has been used as a thickening agent in shampoo.[9]

8 Description

Xanthan gum occurs as a cream- or white-colored, odorless, free-flowing, fine powder.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for xanthan gum.

Test	PhEur 2002	USPNF 20
Identification	+	+
Characters	+	—
pH	6.0–8.0	—
Viscosity	≥600 mPas	≥600 mPas
Propan-2-ol	≤750 ppm	≤0.075%
Other polysaccharides	+	—
Loss on drying	≤15.0%	≤15.0%
Total ash	6.5–16.0%	6.5–16.0%
Microbial contamination	+	+
Bacteria	$\leq 10^3$/g	—
Fungi	$\leq 10^2$/g	—
Pyruvic acid	—	≤1.5%
Arsenic	—	≤3 ppm
Lead	—	≤5 ppm
Heavy metals	—	≤0.003%
Organic volatile impurities	—	+
Assay	—	91.0–108.0%

10 Typical Properties

Acidity/alkalinity: pH = 6.0–8.0 for a 1% w/v aqueous solution.
Freezing point: 0°C for a 1% w/v aqueous solution.
Heat of combustion: 14.6 J/g (3.5 cal/g)
Melting point: chars at 270°C.
Particle size distribution: various grades with different particle sizes are available; for example, 100% less than 180 μm in size for *Keltrol CG*; 100% less than 75 μm in size for *Keltrol CGF*; 100% less than 250 μm, 95% less than 177 μm in size for *Rhodigel*; 100% less than 177 μm, 92% less than 74 μm in size for *Rhodigel 200*.
Refractive index: n_D^{20} = 1.333 for a 1% w/v aqueous solution.
Solubility: practically insoluble in ethanol and ether; soluble in cold or warm water.
Specific gravity: 1.600 at 25°C
Viscosity (dynamic): 1200–1600 mPa s (1200–1600 cP) for a 1% w/v aqueous solution at 25°C.

11 Stability and Storage Conditions

Xanthan gum is a stable material. Aqueous solutions are stable over a wide pH range (pH 3–12), although they demonstrate maximum stability at pH 4–10 and temperatures of 10–60°C. Xanthan gum solutions of less than 1% w/v concentration may be adversely affected by higher than ambient temperatures: for example, viscosity is reduced. Solutions are also stable in the presence of enzymes, salts, acids, and bases.

The bulk material should be stored in a well-closed container in a cool, dry place.

12 Incompatibilities

Xanthan gum is an anionic material and is not usually compatible with cationic surfactants, polymers, or preservatives as precipitation occurs. Anionic and amphoteric surfactants at concentrations above 15% w/v cause precipitation of xanthan gum from a solution.

Under highly alkaline conditions, polyvalent metal ions such as calcium cause gelation or precipitation; this may be inhibited by the addition of a glucoheptonate sequestrant. The presence of low levels of borates (<300 ppm) can also cause gelation. This may be avoided by increasing the boron ion concentration or by lowering the pH of a formulation to less than pH 5. The addition of ethylene glycol, sorbitol, or mannitol may also prevent this gelation.

Xanthan gum is compatible with most synthetic and natural viscosity-increasing agents. If it is to be combined with cellulose derivatives, then xanthan gum free of cellulase should be used to prevent depolymerization of the cellulose derivative.

The viscosity of xanthan gum solutions is considerably increased, or gelation occurs, in the presence of some materials such as ceratonia, guar gum, and magnesium aluminum silicate.[5] This effect is most pronounced in deionized water and is reduced by the presence of salt. This interaction may be desirable in some instances and can be exploited to reduce the amount of xanthan gum used in a formulation; *see* Section 7.

Xanthan gum solutions are stable in the presence of up to 60% water-miscible organic solvents such as acetone, methanol, ethanol, or propan-2-ol. However, above this concentration precipitation or gelation occurs.

Xanthan gum is incompatible with oxidizing agents, some tablet film-coatings,[4] carboxymethylcellulose sodium,[10] dried aluminum hydroxide gel,[11] and some active ingredients such as amitriptyline, tamoxifen, and verapamil.[3]

13 Method of Manufacture

Xanthan gum is a polysaccharide produced by a pure-culture aerobic fermentation of a carbohydrate with *Xanthomonas campestris*. The polysaccharide is then purified by recovery with propan-2-ol, dried, and milled.[12,13]

14 Safety

Xanthan gum is widely used in oral and topical pharmaceutical formulations, cosmetics, and food products and is generally regarded as nontoxic and nonirritant at the levels employed as a pharmaceutical excipient.

The estimated acceptable daily intake for xanthan gum has been set by the WHO at up to 10 mg/kg body-weight.[14]

LD_{50} (dog, oral): >20 g/kg[14]
LD_{50} (rat, oral): >45 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection and gloves are recommended.

16 Regulatory Status

GRAS listed. Accepted for use as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (oral solutions, suspensions, and tablets; rectal and topical preparations). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

—

18 Comments

Xanthan gum is available in several different grades that have varying particle sizes, e.g., *Rhodigel EZ*, *Rhodigel* and *Rhodigel 200* (Rhodia) where *Rhodigel EZ* is the coarsest and *Rhodigel 200* the finest material. Fine-mesh grades of xanthan gum are used in applications where high solubility is desirable since they dissolve rapidly in water. However, fine-mesh grades disperse more slowly than coarse grades and are best used dry blended with the other ingredients of a formulation. In general, it is preferable to dissolve xanthan gum in water first and then add the other ingredients of a formulation.

When added to liquid opthalmics, xanthan gum delays the release of active substances, increasing the therapeutic activity of the pharmaceutical formulations.[15]

Xanthan gum has also been used to produce directly compressed matrices that display a high degree of swelling due to water uptake, and a small amount of erosion due to polymer relaxation.[16]

The USPNF 20 also includes a monograph for xanthan gum solution.

The EINECS number for xanthan gum is 234-394-2.

19 Specific References

1 Jansson PE, Kenne L, Lindberg B. Structure of extracellular polysaccharide from *Xanthamonas campestris*. *Carbohydr Res* 1975; **45**: 275–282.
2 Melton LD, Mindt L, Rees DA, Sanderson GR. Covalent structure of the polysaccharide from *Xanthamonas campestris*: evidence from partial hydrolysis studies. *Carbohydr Res* 1976; **46**: 245–257.
3 Bumphrey G. 'Extremely useful' new suspending agent. *Pharm J* 1986; **237**: 665.
4 Evans BK, Fenton-May V. Keltrol [letter]. *Pharm J* 1986; **237**: 736–737.
5 Kovacs P. Useful incompatibility of xanthan gum with galactomannans. *Food Technol* 1973; **27**(3): 26–30.
6 Talukdar M, Van der Mooter G, Augustijus P. *In vivo* evaluation of xanthan gum as a potential excipient for oral controlled-release matrix tablet formulation. *Int J Pharm* 1998; **169**: 105–113.
7 Lu MF, Woodward L, Borodkin S. Xanthan gum and alginate based controlled release theophylline formulations. *Drug Dev Ind Pharm* 1991; **17**: 1987–2004.
8 Dhopeshwarkar V, Zatz JL. Evaluation of xanthan gum in the preparation of sustained release matrix tablets. *Drug Dev Ind Pharm* 1993; **19**: 999–1017.
9 Howe AM, Flowers AE. Introduction to shampoo thickening. *Cosmet Toilet* 2000; **115**: 63–66, 68–69.
10 Walker CV, Wells JI. Rheological synergism between ionic and non-ionic cellulose gums. *Int J Pharm* 1982; **11**: 309–322.

11 Zatz JL, Figler D, Livero K. Fluidization of aluminum hydroxide gels containing xanthan gum. *Drug Dev Ind Pharm* 1986; **12**: 561–568.
12 Jeanes AR, Pittsley JE, Senti FR. Polysaccharide B-1459: a new hydrocolloid polyelectrolyte produced from glucose by bacterial fermentation. *J Appl Polym Sci* 1961; **5**(17): 519–526.
13 Godet P. Fermentation of polysaccharide gums. *Process Biochem* 1973; **8**(1): 33.
14 FAO/WHO. Evaluation of certain food additives and contaminants. Twenty-ninth report of the joint FAO/WHO expert committee on food additives. *World Health Organ Tech Rep Ser* 1986; No. 733.
15 Hoepfner E, Reng A, Schmidt PC, eds. *Fielder Encyclopedia of Excipients for Pharmaceuticals, Cosmetics and Related Areas*, 5th edn. Aulendorf: Edito Cantor Verlag, 2002: 1690.
16 Munday DL, Cox PJ. Compressed xantham and karaya gum matrices: hydration, erosion and drug release mechanisms. *Int J Pharm* 2000; **203**: 179–192.

20 General References

Gamini A, De Bleijer J, Leute JC. Physicochemical properties of aqueous solutions of xanthan: an NMR study. *Carbohydr Res* 1991; **220**: 33–47.
Kelco Division of Merck & Co Inc. Technical literature: *Xanthan gum—natural biogum for scientific water control*, 3rd edn, 1991.
Rhodia. Technical literature: *Rhodigel—food grade xanthan gum*, 1998.
Shatwell KP, Sutherland IW, Ross-Murphy SB. Influence of acetyl and pyruvate substituents on the solution properties of xanthan polysaccharide. *Int J Biol Macromol* 1990; **12**(2): 71–78.
Whitcomb PJ. Rheology of xanthan gum. *J Rheol* 1978; **22**(5): 493–505.
Zatz JL. Applications of gums in pharmaceutical and cosmetic suspensions. *Ind Eng Chem Prod Res Dev* 1984; **23**: 12–16.

21 Author

SA Daskalakis.

22 Date of Revision

30 August 2002.