

Cellulose Acetate Phthalate

1 Nonproprietary Names

BP: Cellacefate

JP: Cellacefate

PhEur: Cellulose Acetate Phthalate

USP–NF: Cellacefate

2 Synonyms

Acetyl phthalyl cellulose; *Aquacoat CPD*; CAP; cellacefate; cellulose acetate benzene-1,2-dicarboxylate; cellulose acetate hydrogen 1,2-benzenedicarboxylate; cellulose acetate hydrogen phthalate; cellulose acetate monophthalate; cellulose acetophthalate; cellulose acetylphthalate; cellulosi acetas phthalas.

3 Chemical Name and CAS Registry Number

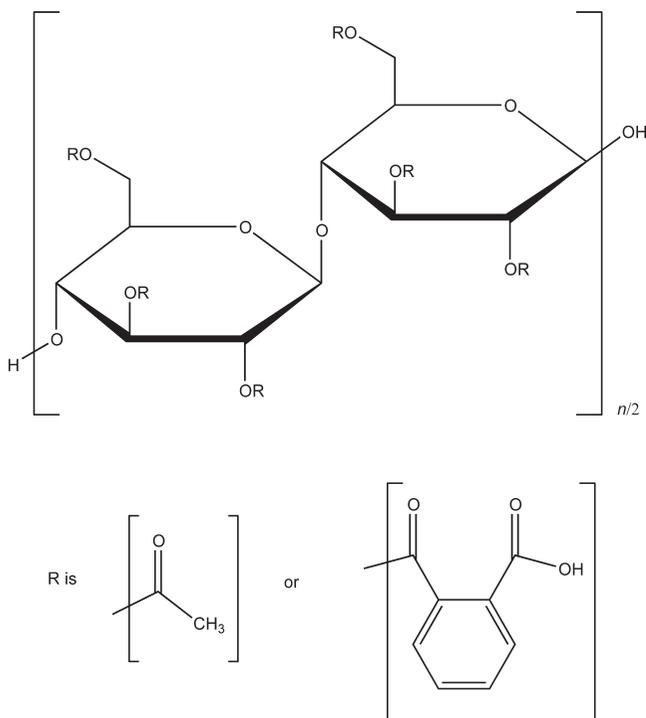
Cellulose, acetate, 1,2-benzenedicarboxylate [9004-38-0]

4 Empirical Formula and Molecular Weight

Cellulose acetate phthalate is a cellulose in which some of the hydroxyl groups are acetylated and some are phthalylated.

5 Structural Formula

Cellulose acetate phthalate is a reaction product of phthalic anhydride and a partial acetate ester of cellulose. It contains 21.5–26.0% of acetyl (C_2H_3O) groups and 30.0–36.0% of phthalyl (*o*-carboxybenzoyl, $C_8H_5O_3$) groups, calculated on the anhydrous acid-free basis.



6 Functional Category

Coating agent; microencapsulating agent; tablet and capsule binder.

7 Applications in Pharmaceutical Formulation or Technology

Cellulose acetate phthalate is used as an enteric film-coating material, as a microencapsulation agent, or as a matrix binder for tablets and capsules.^(1–8) Such coatings resist prolonged contact with the strongly acidic gastric fluid, but dissolve in the mildly acidic or neutral intestinal environment.

Cellulose acetate phthalate is commonly applied to solid-dosage forms either by coating from organic or aqueous solvent systems, or by direct compression. Concentrations generally used are 0.5–9.0% of the core weight. The addition of plasticizers improves the water resistance of this coating material, and formulations using such plasticizers are more effective than when cellulose acetate phthalate is used alone.

Cellulose acetate phthalate is compatible with many plasticizers, including acetylated monoglyceride; butyl phthalylbutyl glycolate; dibutyl tartrate; diethyl phthalate; dimethyl phthalate; ethyl phthalylethyl glycolate; glycerin; propylene glycol; triacetin; triacetin citrate; and tripropionin. It is also used in combination with other coating agents such as ethyl cellulose in controlled-release preparations.

8 Description

Cellulose acetate phthalate occurs as a hygroscopic, white to off-white, free-flowing powder, granule, or flake. It is tasteless and odorless, or might have a slight odor of acetic acid.

9 Pharmacopeial Specifications

The pharmacopeial specifications for cellulose acetate phthalate have undergone harmonization of many attributes for JP, PhEur, and USP–NF.

See Table I. See also Section 18.

Table I: Pharmacopeial specifications for cellulose acetate phthalate.

Test	JP XVII	PhEur 9.2	USP 40–NF 35 S1
Identification	+	+	+
Characters ^(a)	+	+	–
Free acid	≤3.0%	≤3.0%	≤3.0%
Heavy metals ^(a)	≤10 ppm	–	≤0.001%
Residue on ignition	≤0.1%	–	≤0.1%
Sulfated ash	–	≤0.1%	–
Viscosity (15% w/v solution)	45–90 mPa s	45.0–90.0 mPa s	45.0–90.0 mPa s
Water	≤5.0%	≤5.0%	≤5.0%
Assay	+	+	+
Acetyl groups	21.5–26.0%	21.5–26.0%	21.5–26.0%
Phthalyl (<i>o</i> -carboxybenzoyl) groups	30.0–36.0%	30.0–36.0%	30.0–36.0%

(a) These tests have not been fully harmonized at the time of publication.

10 Typical Properties

Density (bulk) 0.260 g/cm³

Density (tapped) 0.266 g/cm³

Melting point 192°C. Glass transition temperature is 160–170°C.⁽⁹⁾

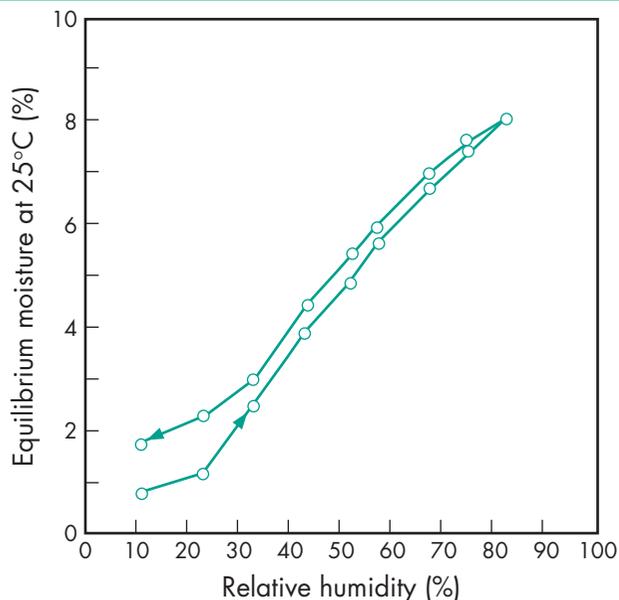


Figure 1: Sorption-desorption isotherm of cellulose acetate phthalate.

Moisture content Cellulose acetate phthalate is hygroscopic and precautions are necessary to avoid excessive absorption of moisture. Equilibrium moisture content has been reported as 2.2%, but moisture content is a function of relative humidity.⁽¹⁰⁾

See also Figure 1.

Solubility Practically insoluble in water, alcohols, and chlorinated and nonchlorinated hydrocarbons. Soluble in a number of ketones, esters, ether alcohols, cyclic ethers, and in certain solvent mixtures. It can be soluble in certain buffered aqueous solutions as low as pH 6.0. Cellulose acetate phthalate has a solubility of $\leq 10\%$ w/w in a wide range of solvents and solvent mixtures; see Table II and Table III.

Table II: Examples of solvents with which cellulose acetate phthalate has $\leq 10\%$ w/w solubility.

Acetone
Diacetone alcohol
Dioxane
Ethoxyethyl acetate
Ethyl glycol monoacetate
Ethyl lactate
Methoxyethyl acetate
 β -Methoxyethylene alcohol
Methyl acetate
Methyl ethyl ketone

Table III: Examples of solvent mixtures with which cellulose acetate phthalate has $\leq 10\%$ w/w solubility.

Acetone : ethanol (1 : 1)
Acetone : water (97 : 3)
Benzene : methanol (1 : 1)
Ethyl acetate : ethanol (1 : 1)
Methylene chloride : ethanol (3 : 1)

Spectroscopy

IR spectrum see Figure 2.

NIR spectrum see Figure 3.

Raman spectrum see Figure 4.

Viscosity (dynamic) A 15% w/w solution in acetone with a moisture content of 0.4% has a viscosity of 50–90 mPa s

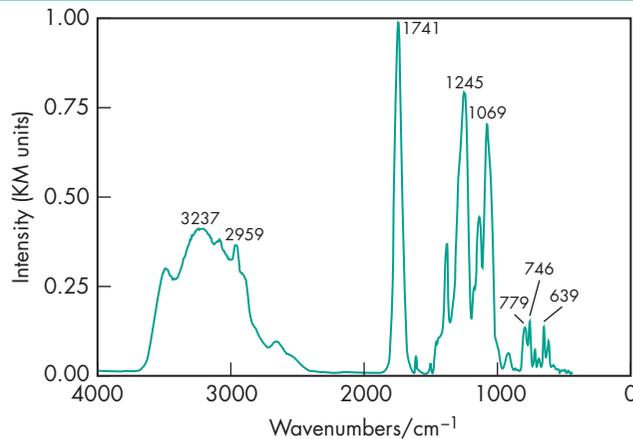


Figure 2: Infrared spectrum of cellulose acetate phthalate measured by diffuse reflectance. Adapted with permission of Informa Healthcare.

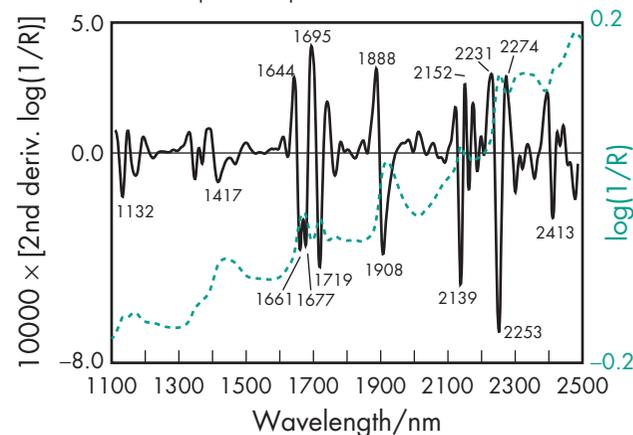


Figure 3: Near-infrared spectrum of cellulose acetate phthalate measured by reflectance.

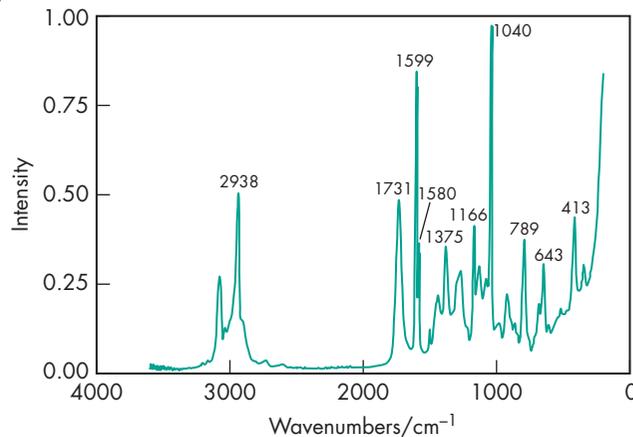


Figure 4: Raman spectrum of cellulose acetate phthalate measured in the 180° reflectance mode. Adapted with permission of Informa Healthcare.

(50–90 cP). This is a good coating solution with a honey-like consistency, but the viscosity is influenced by the purity of the solvent.

11 Stability and Storage Conditions

Slow hydrolysis of cellulose acetate phthalate will occur under prolonged adverse conditions such as high temperatures and high humidity, with a resultant increase in free acid content, viscosity, and odor of acetic acid. However, cellulose acetate phthalate is stable if stored in a well-closed container in a cool, dry place.

12 Incompatibilities

Cellulose acetate phthalate is incompatible with ferrous sulfate, ferric chloride, silver nitrate, sodium citrate, aluminum sulfate, calcium chloride, mercuric chloride, barium nitrate, basic lead acetate, and strong oxidizing agents such as strong alkalis and acids.

13 Method of Manufacture

Cellulose acetate phthalate is produced by a reaction between the partial acetate ester of cellulose and phthalic anhydride in the presence of a tertiary organic base such as pyridine, or a strong acid such as sulfuric acid.

14 Safety

Cellulose acetate phthalate is widely used in oral pharmaceutical products and is generally regarded as a nontoxic material, free of adverse effects. However, it may be irritant to the eyes, mucous membranes, and upper respiratory tract.

Results of long-term feeding in rats and dogs have indicated a low oral toxicity. Rats survived daily feedings of up to 30% in the diet for up to 1 year without showing a depression in growth. Dogs fed 16 g daily in the diet for 1 year remained normal.

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Cellulose acetate phthalate should be handled in a well-ventilated environment; use of a respirator is recommended when handling large quantities. Eye protection and gloves are recommended.

16 Regulatory Status

Included in the FDA Inactive Ingredients Database (oral tablets). Included in nonparenteral medicines licensed in the UK. Included in the Canadian Natural Health Products Ingredients Database.

17 Related Substances

Cellulose acetate; hypromellose phthalate; polyvinyl acetate phthalate.

18 Comments

Cellulose acetate phthalate has undergone harmonization of many attributes for JP, PhEur, and USP–NF by the Pharmacopeial Discussion Group. For further information see the General Chapter 5.8 in PhEur, along with the ‘State of Work’ document on the PhEur EDQM website, and also the General Information Chapter G10 in the JP.

Any plasticizers that are used with cellulose acetate phthalate to improve performance should be chosen on the basis of experimental evidence. The same plasticizer used in a different tablet base coating may not yield a satisfactory product.

In using mixed solvents, it is important to dissolve the cellulose acetate phthalate in the solvent with the greater dissolving power, and then to add the second solvent. Cellulose acetate phthalate should always be added to the solvent, not the reverse.

Cellulose acetate phthalate films are permeable to certain ionic substances, such as potassium iodide and ammonium chloride. In such cases, an appropriate sealer subcoat should be used.

A reconstituted colloidal dispersion of latex particles rather than solvent solution coating material of cellulose acetate phthalate is also available. This white, water-insoluble powder is composed of solid or semisolid submicrometer-sized polymer spheres with an average particle size of 0.2 μm . A typical coating system made from this latex powder is a 10–30% solid-content aqueous dispersion with a viscosity in the 50–100 mPa s (50–100 cP) range.

Therapeutically, cellulose acetate phthalate has been reported to exhibit experimental microbicidal activity against sexually transmitted disease pathogens, such as the HIV-1 retrovirus.^(11,12)

19 Specific References

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22 Date of Revision

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