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Eastman C-A-P enteric coating material

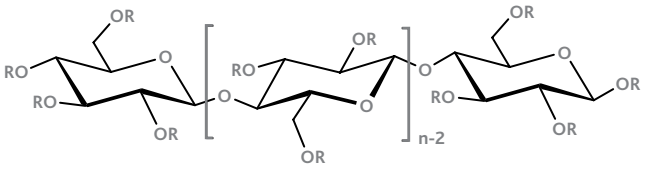
(Cellulose acetate phthalate or cellacefate, NF)

Cellulose esters are part of a large family of cellulose derivatives that have a long history of use in pharmaceutical applications. Cellulose esters fall into two categories: enteric and nonenteric. Enteric esters are those, such as cellulose acetate phthalate (C-A-P), which are insoluble in acidic conditions (e.g., in the stomach) but soluble in mildly acidic to slightly alkaline conditions (e.g., in the small intestine). Nonenteric esters, such as cellulose acetate (CA) and cellulose acetate butyrate (CAB), do not show pH-dependent solubility characteristics.

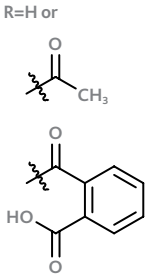
Eastman esterifies cellulose to produce cellulose acetate phthalate. See Figure 1 for structural formula. The structure of cellulose consists of repeating anhydroglucose units. Each anhydroglucose unit (AGU) has three hydroxyl groups that are esterified to yield cellulose esters. The amount of esterification can be expressed as weight percent of acyl group or degree of substitution (DS). DS = 3 means all three hydroxyl groups are esterified; DS = 1 means one out of three groups is esterified. Because DS is a statistical mean value, a value of 1 does not assure that every AGU has a single substituent. In some cases, there can be unsubstituted anhydroglucose units, some with two substituents, and some with three substituents. More often than not, the value will be a non-integer.

Figure 1. Structural formula of cellulose acetate phthalate

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



anhydroglucose unit



Eastman C-A-P enteric coating is designed for pharmaceutical tablets or granules.

Eastman C-A-P enteric coating material is a pH-sensitive cellulose derivative designed for coating pharmaceutical tablets or granules. It may also be used as a matrix material in solid dosage forms. Eastman C-A-P enteric coating material withstands prolonged contact with acidic gastric fluids but dissolves readily in the mildly acidic to neutral environment of the small intestine. It can be applied to tablets or granules from solutions of organic solvents.

C-A-P meets the National Formulary (NF) compendial specifications found in the cellacefate monograph. The Japanese Pharmacopeia and European Pharmacopeia have also implemented the harmonized text of this monograph. Confidential information on C-A-P to support pharmaceutical applications is maintained in a Drug Master File (DMF) with the U.S. Food and Drug Administration.

Table 1. Typical properties[a]

Physical form	White powder or pellets[b]
Composition	
Phthalyl, %	30.0–36.0
Acetyl, %	21.5–26.0
Moisture, %	< 5.0 wt%
Free acid (as phthalic acid), %	< 3.0 wt%
Viscosity,[c] cP at 25°C	45–90
pH solubility in USP buffer solutions	≥ 6.2

[a]Properties reported here are typical of average lots. Eastman makes no representation that the material in any shipment will conform exactly to the value listed. Specifications are available on request.
[b]Pelletized C-A-P exhibits slower dissolution time in poor solvents such as ethyl acetate/isopropanol blends. Acetone or acetone blends are the preferred solvents for C-A-P pellets.
[c]Centipoises,15% C-A-P in an acetone solution

Table 2. Organic solvent systems

The following solvent systems can be used to dissolve Eastman C-A-P.

System	C-A-P
Acetone	100
Acetone:ethyl alcohol	50:50
Acetone:isopropyl alcohol	50:50
Acetone:methyl alcohol	50:50/25:75
Acetone:methylene chloride	50:50/25:75
Methylene chloride:ethyl alcohol	75:25
Ethyl acetate:ethyl alcohol	50:50
Ethyl acetate:isopropyl alcohol	50:50/75:25
Ethyl alcohol:water	—

Note: *In using acetone blends, it is important to dissolve the powder in acetone before adding the second solvent.*

Increasing alcohol or water content will change the solubility of C-A-P in the solvent system and could retard the drying rate. For the most rapid dissolution and to obtain gel-free solutions in organic solvent, the enteric polymer should be added slowly to the solvent mixture while stirring. It is recommended that the coating solution be filtered prior to use.

Modification with plasticizers

The properties of coatings made with C-A-P enteric polymer may be modified by adding a plasticizer to the polymer solution before coating. Plasticizers add film flexibility (increased resistance to chipping or cracking) while lowering the glass transition temperature (T_g) of the polymeric film. In general, the optimum concentration of plasticizer is the minimum amount which provides the necessary flexibility to form a continuous coating.

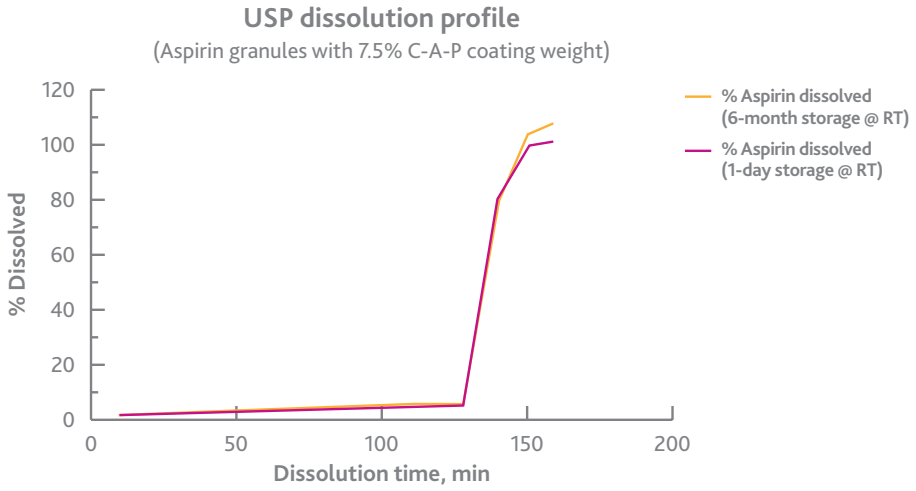
The commonly used plasticizers for C-A-P are polyethylene glycol (PEG), triacetin, diethyl phthalate, and triethyl citrate (TEC). The amount of plasticizer used can be up to 35% of the polymer weight.

Dissolution profile for aspirin granules coated with C-A-P

Aspirin granules were coated with C-A-P using a Glatt GPCG-5 fluidized bed sprayer. The coating solution consisted of 7.5% C-A-P, 2.5% triacetin, and 90% acetone and was filtered prior to use. The aspirin particles had a coating weight of 7.5%.

Samples were evaluated by USP dissolution testing for enteric properties. See Figure 2. Samples were tested after 1 day of storage at room temperature and after 6 months of storage at room temperature.

Figure 2. Comparison of dissolution profiles for C-A-P-coated aspirin granules



The dissolution data show no significant changes in release profiles for freshly coated aspirin granules and coated aspirin granules stored for 6 months at room temperature.

Stability and handling

Eastman C-A-P enteric coating material is packaged and sealed in moisture-resistant fiber drums equipped with polyethylene inner liners and reusable metal closures. Drums held in cool, dry storage should be brought to room temperature before opening to prevent condensation on inside surfaces. Under prolonged storage at high temperatures or high humidity, C-A-P will slowly hydrolyze, increasing the free acid content.

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Eastman Chemical Company
Corporate Headquarters
P.O. Box 431
Kingsport, TN 37662-5280 U.S.A.

U.S.A. and Canada, 800-EASTMAN (800-327-8626)
Other Locations, +(1) 423-229-2000

www.eastman.com/locations

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