# Try L-HPC (Low-Substituted Hydroxypropyl Cellulose) to Formulate Solid Dosage Forms with Good Stability.

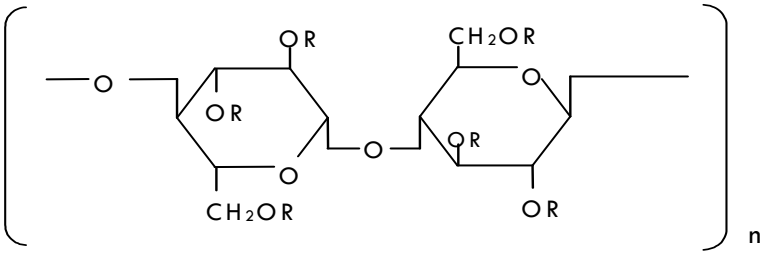
## Introduction

L-HPC (Low-substituted Hydroxypropyl Cellulose) was first approved in 1987 as a disintegrant/binder for pharmaceutical solid dosage forms in Japan. A recent survey shows that L-HPC is ranked as the first choice for tablet disintegrant by Japanese pharmaceutical companies. Not only a disintegrant, L-HPC also functions as binder due to its good compressibility. There are many cases that L-HPC solved problems of interactions with APIs other issues such as capping.

The key benefits of L-HPC include:

- Excellent compatibility with active ingredients
- Quick and fine disintegration leading to better dissolution
- Dual functions as both disintegrant and binder
- Anti-capping effect for tableting process
- Also suitable for pellet extrusion
- Variety of grades are available depending on application

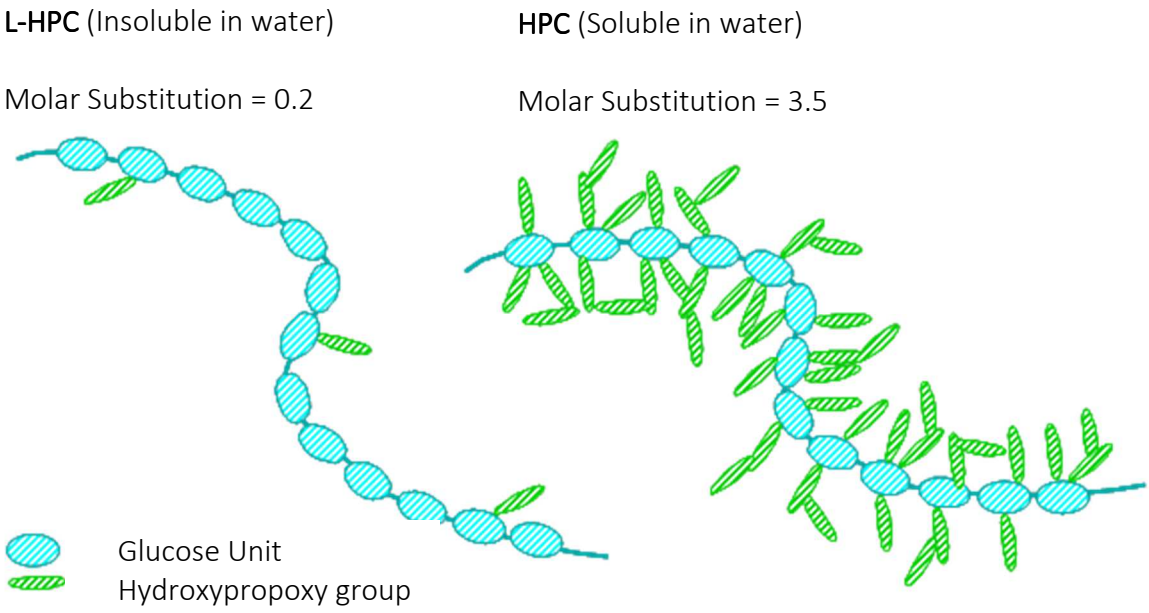
Structure of L-HPC




R = -H or -$CH_2CH(CH_3)OH$

## L-HPC is not the same as HPC….

Although sharing the same CAS number, L-HPC has different characteristics from Hydroxypropylcellulose (HPC), that is a binding agent widely used for solid dosage forms. L-HPC and HPC have separate monographs in pharmacopeia. While the regular HPC has a large amount of hydroxypropoxyl groups in the cellulose backbone, L-HPC has only a small level (See the picture below). Due to this chemical difference, HPC is soluble in water, but L-HPC is insoluble. HPC is typically used for granulation binding as an aqueous solution, but L-HPC cannot be used in this way. L-HPC is an effective disintegrant due to its swelling action in water, but this is not the case with HPC. Because L-HPC also has good compressibility, dry blending of this material produces hard tablets like those made from microcrystalline cellulose. In this application, L-HPC functions as a "dry binder."




## L-HPC is listed in:

- JP (Japanese Pharmacopeia)
- NF (US National Formulary)
- 21 CFR 172.870 (Code of Federal Register / Food Additive)

## Excellent Compatibility to APIs.

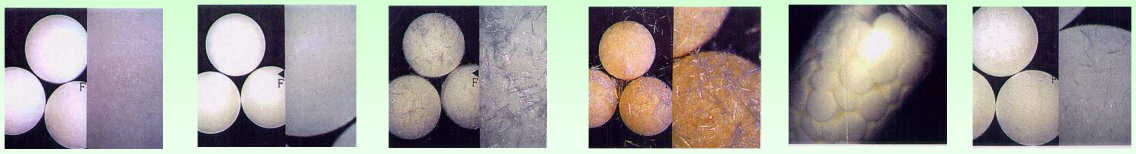
Because L-HPC is non-ionic, it is less reactive to API compared to other ionic excipients. This excellent compatibility is the best reason for the first-choice by Japanese pharma companies.

For example, aspirin tablets with L-HPC were stable under high temperature whereas ionic ingredients showed whisker of salicylic acid formed by hydrolysis (See pictures below).

Vitamin C tablets with L-HPC were also intact compared to the ionic disintegrants. The color stability was even better than microcrystalline cellulose which is another non-ionic ingredient under the same moisture level. Our further study suggests that this was due to the low water activity of L-HPC because water molecules are bound to the amorphous region of the polymer. All tablets were made by direct compression.

### Aspirin Tablets

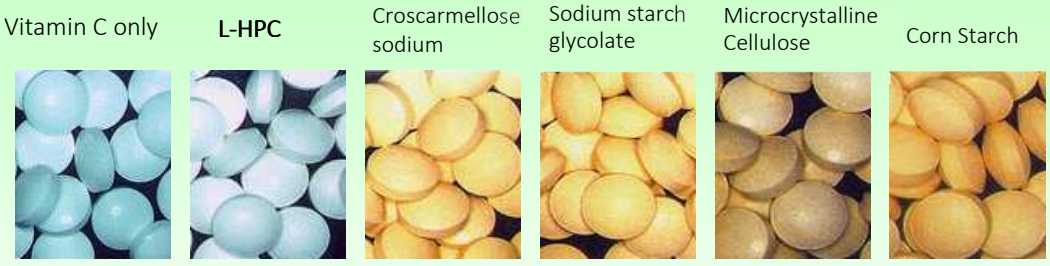
Excipient content: 20%. Stored at 50°C in closed bottle for 3 months.



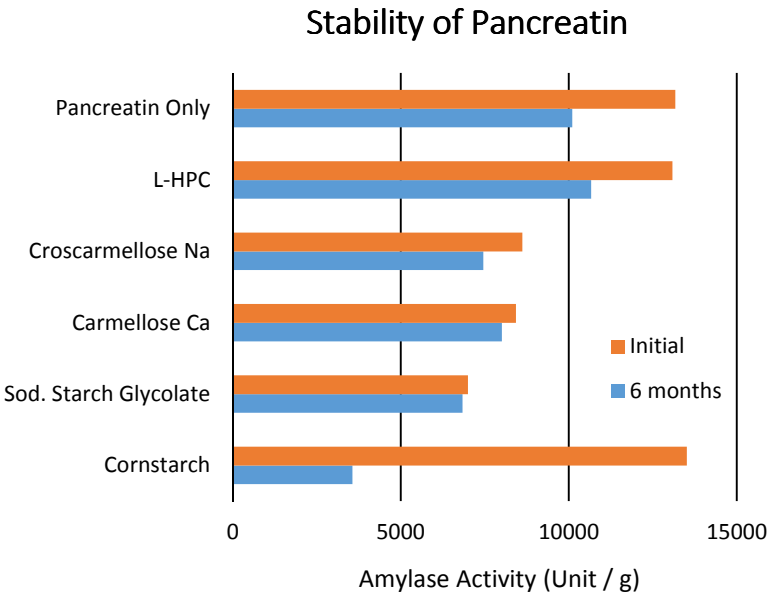

*Tablets were stuck in bottle.

### Vitamin C Tablets

Excipient content: 20%. Stored at 50°C in closed bottle for 2 months.



The following data is from a stability test of pancreatin (a digestive enzyme) that was simply blended with excipient (1:1). After six months of storage at 50 ˚C, amylase activity was measured. Please note that ionic excipients interacted with enzyme and reduced the activity at the initial stage. Cornstarch showed significant decrease after 6 months, but L-HPC formulation did not affect to the stability of enzyme.




## L-HPC does not contain peroxide.

There are no peroxides used in the manufacturing process of L-HPC. Therefore, peroxide is not detected in the final product of L-HPC, whereas other excipients such as crospovidone shows residual peroxide (see the following data). Such residual peroxide may cause interactions with APIs, but there is no concern with L-HPC.

### Peroxide Content in Excipients

| | Peroxide* (as $H_2O_2$) |
|---|---|
| Killidon CL (BASF) | 200 ppm |
| Kollidon CL-F (BASF) | 250 ppm |
| Polyplasdone XL (Ashland) | 100 ppm |
| L-HPC | Not Detected |

*Test Paper Kit, Hishe Chemicals, Japan

## Grades and Applications

A number of grades having different particle size, particle shape, and hydroxypropoxy content are available. The following table summarizes brief properties and suitable application for each grade of L-HPC. They can be used by dry blending followed by direct compression, wet granulation process (either internal and/or external addition) followed by drying and tabletting, wet granulation for pellet extrusion, or drug layering. Please contact Shin-Etsu technical experts to select a suitable grade for your application.

### L-HPC Grades

| Grade | $D_{50}$* (μm) | Particle Property | Hydroxypropoxy Content* (%) | Suitable for |
|---|---|---|---|---|
| LH-11 | 55 | Most Fibrous | 11 | Anti-Capping |
| LH-21 | 45 | Moderately Fibrous | 11 | Wet-Granulation |
| LH-22 | 45 | Moderately Fibrous | 8 | Wet-Granulation |
| LH-31 | 20 | Micronized | 11 | Pellet Extrusion, Drug Layering |
| LH-32 | 20 | Micronized | 8 | Pellet Extrusion, Drug Layering |
| LH-B1 | 55 | Non Fibrous, High Density | 11 | Fluid-Bed Granulation |
| NBD-020 | 45 | Non Fibrous | 14 | Wet-Granulation |
| NBD-021 | 45 | Non Fibrous | 11 | Direct Compession |
| NBD-022 | 45 | Non Fibrous | 8 | Orally Disintegrating Tablets |

* Typical Value. Not specification.

For more information on L-HPC, please contact: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