Excipients
NISSO HPC

NOTE #: DC-ODT-02
APPLICATION: Direct Compression/ ODT Formulation

# High Performance Dry Binding with HPC-SSL Super Fine Powder

APPLICATION NOTE

## Introduction

HPC-SSL-SFP (Super Fine Powder), a highly compressible grade of HPC, is introduced for dry binding applications. With a very fine particle size and low molecular weight, HPC-SSL-SFP imparts the expected HPC advantages in tablet hardness and friability at lower usage amounts and with faster dissolution when compared to regular HPC and other commonly used excipients.

CONTENTS PAGE

## 1. Features of HPC-SSL Super Fine Powder

- HPC-SSL-SFP is highly compressible, giving superior tablet properties at low usage levels in dry binding applications.
- HPC-SSL-SFP is super low viscosity and super fine particle size, allowing fast disintegration and fast dissolution times that are not possible with regular HPC grades.
- HPC-SSL-SFP provides HPC's well-known advantages in improved tablet hardness and friability.

## 2. Applications

- Direct compression
- Extra-granule dry addition
- Orally Disintegrating Tablet (ODT)
- Dry granulation/roller compaction
- High drug load binding
- Downsizing of tablet
- Anti-capping

## 3. Molecular Weight and Powder Properties

| | | Reference to other HPC grades | |
|---|---|---|---|
| | HPC-SSL-SFP (super fine powder) | HPC-SL-FP (fine powder) | HPC-L (regular powder) |
| Molecular weight | 40,000 | 100,000 | 140,000 |
| $D_{50}/D_{90}$ (μm) | 20/50 | 80/160 | 170/370 |
| Angle of repose (degree) | 53 | 47 | 45 |
| Bulk density (loose/packed) | 0.18/0.33 | 0.32/0.48 | 0.37/0.55 |

### Note on Methods used in this Application Note

Direct compression: Powder for tablet was prepared by dry-mixing of materials except Magnesium Stearate in PE bag for three minutes. This was followed by addition of Magnesium Stearate and further dry-mixing for 30 seconds. Laboratory scale rotary tablet press machine was used to compress tablet at 10 kN of compression force. Tablet weight and diameter were 200 mg and 8 mm respectively.

Wet granulation (Fluidized Bed): Acetaminophen, lactose and corn starch were pre-mixed in PE bag for three minutes and added to the granulator, followed by granulation with spraying 8% aqueous solution of HPC-SSL at spray speed of 5 mL/min and drying. Powder for tablet was prepared by dry-mixing granules of 30 mesh pass and Magnesium Stearate for 30 seconds. Laboratory scale rotary tablet press machine was used to compress tablet at 10 kN of compression force. Tablet weight and diameter were 200 mg and 8 mm respectively.

Tablet properties test methods: Tablet hardness was measured as average of 10 tablets per lot. Friability and disintegration time was measured according to JP method. Release rate of acetaminophen was also measured according to JP method and concentration of acetaminophen at each time point was determined by measurement of absorbance at 243 nm with UV spectrophotometer.

## 4. Comparison to Other Commonly Used Dry Binders

HPC-SSL-SFP is compared to several other commonly used dry binders in a direct compression acetaminophen.

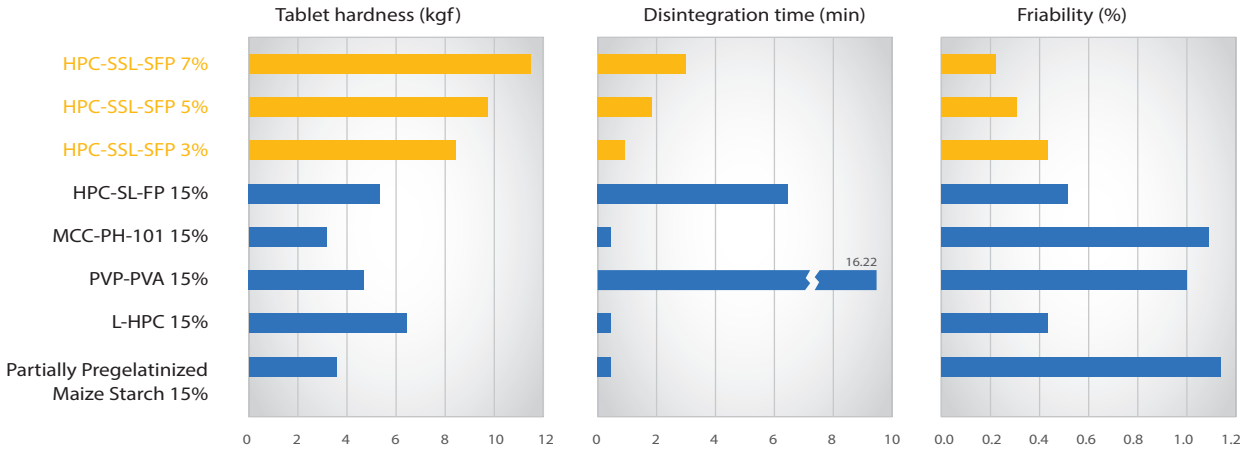
### a) Formulation

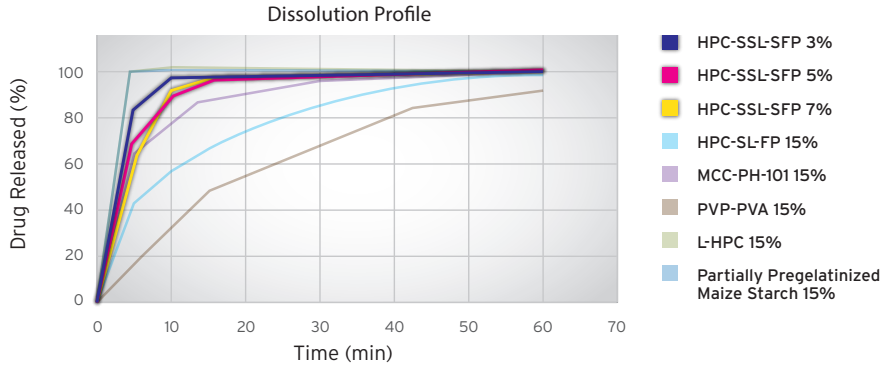
| | | HPC-SSL-SFP | | | Other binders |
|---|---|---|---|---|---|
| Acetaminophen | (%) | 60 | | | 60 |
| Lactose | (%) | 22.8 | 24.2 | 25.6 | 17.2 |
| Corn starch | (%) | 9.7 | 10.3 | 10.9 | 7.4 |
| HPC-SSL-SFP | (%) | 7 | 5 | 3 | - |
| Other binders | (%) | - | | | 15 |
| Magnesium Stearate | (%) | 0.5 | | | 0.5 |
| Silica | (%) | 0.5 | | | 0.5 |

Compression pressure 10 kN,
Tablet weight 200 mg

Other binders:
HPC-SL (FP), MCC PH-101,
PVP-PVA (PLASDONE S630),
L-HPC (LH-21),
Partially Pregelatinized
Maize Starch (Starch 1500)

### b) Results




### c) Conclusion

HPC-SSL-SFP is an excellent dry binder that can provide harder tablet hardness and less friability with much lower use level than other dry binders, while also having fast disintegration time and drug release.

## 5. Comparison of Direct Compression and Wet Granulation Methods

HPC-SSL-SFP is used as a dry binder in a Direct Compression acetaminophen formulation and is compared to the same formulation using HPC-SSL (regular type) as a wet binder in a fluidized bed granulation application. Tablet properties and drug release by both methods are evaluated.

### a) Formulation

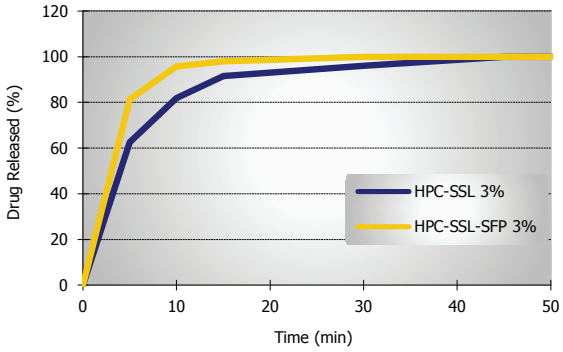
| | | Wet Granulation Method | Direct Compression Method |
|---|---|---|---|
| Acetaminophen | % | 30 | 30 |
| Lactose | % | 49 | 49 |
| Corn Starch | % | 21 | 21 |
| HPC-SSL-SFP | % | - | 3 |
| HPC-SSL | % | 3 | - |
| Silica | % | 0.5 | 0.5 |
| Magnesium Stearate | % | 0.5 | 0.5 |

### b) Results

Tablet Properties

| | Wet Granulation HPC-SSL | Direct Compression HPC- SSL-SFP |
|---|---|---|
| Hardness (kgf) | 10.63 | 9.57 |
| Friability (%) | 0.18 | 0.24 |
| Disintegration Time (min) | 2.28 | 1.33 |

Dissolution Profile




### c) Conclusion

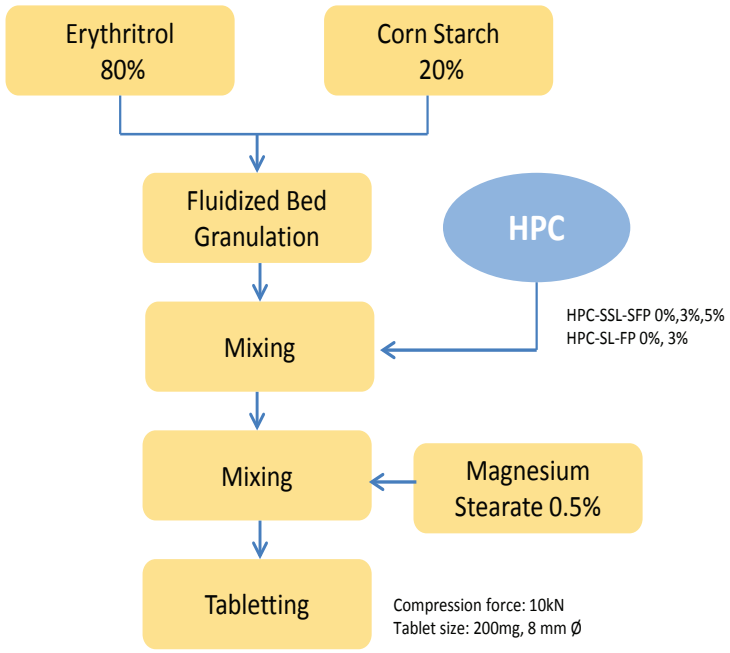
Direct Compression Method with HPC-SSL-SFP was found to provide equivalent properties to, and faster drug release than tablet prepared by fluidized bed method with HPC-SSL. It is suggested that formulations prepared by wet granulation method could also be done by DC method using HPC-SSL-SFP without deterioration of tablet properties or hindering drug release in the case of low drug load formulation.

## 6. Extra-Granule Addition Application

HPC-SSL-SFP is compared to a one of Nisso's other HPC grades to show the impact of moving to the super low viscosity and super fine particle size when HPC is added as an extra-granule dry powder.

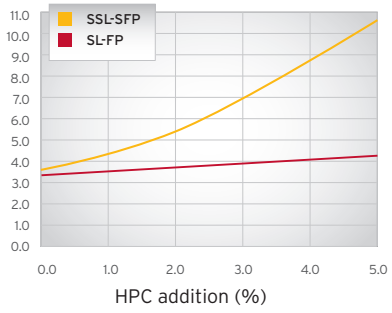
a) Formulation and process

- Granulation: Erythritol 80% + Corn Starch 20%
- Extra-granule HPC addition: 0-5%

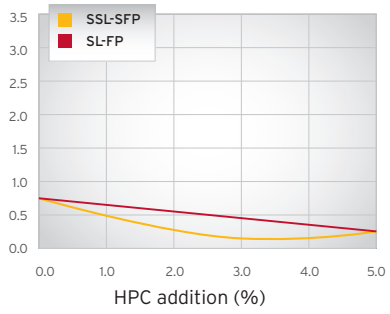



b) Results

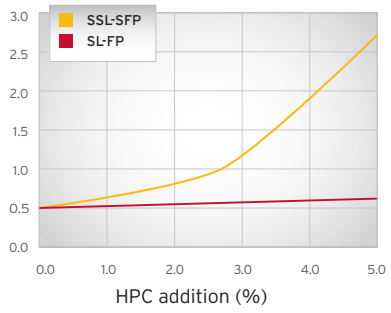
Tablet hardness (kgf)




Friability (%)




Disintegration Time (min)




c) Conclusion

The excellent compression formability of HPC-SSL-SFP is effective for improvement of tablet properties at low use level by extra-granule addition method.

## 7. Orally Disintegrating Tablet (ODT) application

A small amount of HPC-SSL-SFP is added to a conventional MCC-based ODT. Tablet properties and stability are evaluated for both formulations.

### a) Formulation

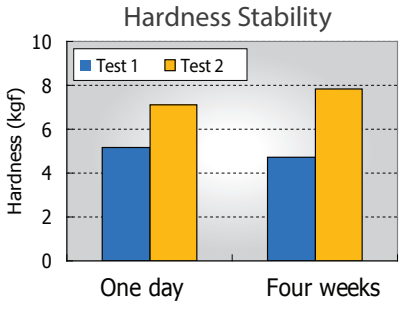
| | | Test 1 | Test 2 |
|---|---|---|---|
| Acetaminophen | % | 60 | 60 |
| MCC PH-102 | % | 37.5 | 34.5 |
| HPC-SSL-SFP | % | - | 3 |
| Crospovidone | % | 2 | 2 |
| Silica | % | 0.5 | 0.5 |
| Magnesium Stearate | % | 0.5 | 0.5 |

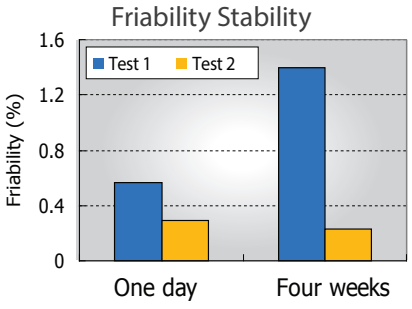
Compression pressure 10 kN,
Tablet weight 200 mg

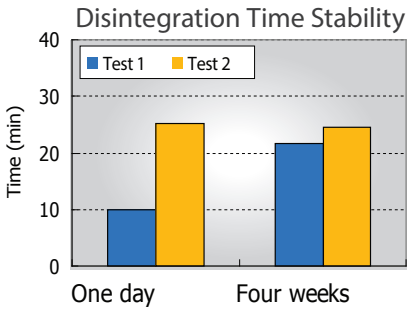
### b) Results

Tablet properties

| | | Test 1 | Test 2 |
|---|---|---|---|
| Hardness | (kgf) | 5.16 | 7.13 |
| Friability | (%) | 0.57 | 0.29 |
| Disintegration time | (sec) | 10 | 22 |




### c) Conclusion

The addition of a small amount of HPC-SSL-SFP to an ODT greatly improves the tablet properties and stability of those properties.

## 8. HPC-SSL-SFP Specifications

<USP/NF>

| Test Items | Unit | Specifications |
|---|---|---|
| Grade | | HPC-SSL-SFP |
| Viscosity (2% aqueous solution at 20° C) | mPa*s | 2.0–2.9 |
| Identification | | Conforms |
| pH | | 5.0–8.0 |
| Loss on drying | % | Not more than 5.0 |
| Residue on ignition | % | Not more than 0.2 |
| Lead | ppm | Not more than 10 |
| Heavy metals | ppm | Not more than 20 |
| Assay for Hydroxypropoxy groups | % | Not more than 80.5 |
| Particle size (45 µm pass) | % | Not less than 99% |

<Ph. Eur.>

| Test Items | Unit | Specifications |
|---|---|---|
| Grade | | HPC-SSL-SFP |
| Apparent viscosity (2% aqueous solution at 20° C) | mPa*s | 2.0–2.9 |
| Identification (A–F) | | Conforms |
| Appearance of solution | | Conforms |
| pH | | 5.0–8.5 |
| Silica | % | Not more than 0.6 |
| Chlorides | % | Not more than 0.5 |
| Heavy metals | ppm | Not more than 20 |
| Loss on drying | % | Not more than 7.0 |
| Sulphated ash | % | Not more than 1.6 |
| Particle size (45 µm pass) | % | Not less than 99% |

<JP>

| Test Items | Unit | Specifications |
|---|---|---|
| Grade | | HPC-SSL-SFP |
| Viscosity (2% aqueous solution at 20° C) | mPa*s | 2.0–2.9 |
| Description | | White to yellowish white powder |
| Identification (1)–(3) | | Conforms |
| pH | | 5.0–7.5 |
| Clarity of solution | | Conforms |
| Chloride | % | Not more than 0.142 |
| Sulfate | % | Not more than 0.048 |
| Heavy metals | ppm | Not more than 20 |
| Arsenic | ppm | Not more than 2 |
| Loss on drying | % | Not more than 5.0 |
| Residue on ignition | % | Not more than 0.5 |
| Assay (Hydroxypropxy group) | % | 53.4–77.5 |
| Particle size (45 µm pass) | % | Not less than 99% |

## 9. Cautions for handling

- Avoid raising excessive dust from powder. Ensure adequate ventilation.
- May form explosive dust-air mixtures. Keep away from heat, static and flame.
- Electrically ground and bond all equipment. Avoid contact with skin and eyes.
- Use gloves and safety glasses. Wash face and hands thoroughly after use.
- Refer to MSDS for complete safety handling instructions.

## 10. Stability and reactability

- Stable in normal conditions. Avoid strong oxidizing agents.
- Not flammable but combustible
- Dust explosion lower limit: 60 g/m$^3$

## 11. Packaging

- 10 kg box, double-lined PE bag
- 500 g box, double-lined PE bag

Nisso

www.nissoexcipients.com


Head Office

Nippon Soda Co., Ltd
2-1 2-Chome, Ohtemachi
Chiyoda-ku, Tokyo 100-8165 Japan
(T) 81-3-3245-6159
(F) 81-3-3245-6059
info@nippon-soda.co.jp

Chinese Distributor

Room No.1801, Tianxing Roosevelt Center, No.677 Yellow River Road, Shahekou Dist., Dalian, China.
Tel: 0411-8452-1177
Fax: 0411-8452-1199/2288
http://www.dalian-diligence.com