

# Pharmaceutical Excipients

## **METOLOSE®**

Methylcellulose  
Hypromellose

USP, EP, JP

## **METOLOSE® SR**

Hypromellose

USP, EP, JP

## **PHARMACOAT®**

Hypromellose

USP, EP, JP

## **HPMCP**

Hypromellose Phthalate

NF, EP, JP

## **Shin-Etsu AQOAT®**

Hypromellose Acetate  
Succinate

NF, JP

## **L-HPC**

Low-Substituted  
Hydroxypropyl Cellulose

NF, EP, JP

**SmartEx®**

# Product Information

Shin-Etsu Chemical supplies the following various excipients for pharmaceutical industry.  
Color vs indication

Grade	Specification	Reference data
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Please find the detailed information in the individual brochure.  
Each brochure can be obtained at <http://www.metolose.jp/en>.

## <Film coating agent, binder>

### PHARMACOAT® Hypromellose USP, EP, JP

Grade	Viscosity (mPa·s)*	Substitution type	Methoxy content (%)	Hydroxypropoxy content (%)
603	2.4 - 3.6	2910	28.0 - 30.0	7.0 - 12.0
645	3.6 - 5.1			
606	4.8 - 7.2			
615	12.0 - 18.0			

\*Viscosity of 2 w/w % aqueous solution at 20°C

#### Features:

- Low viscosity, suitable for film coating with water or solvent (co-solvent of water and ethanol) coating system.
- Water soluble and non-ionic, less interaction with active pharmaceutical ingredient (API).
- Applicable as a binder in wet granulation. Low viscosity and soluble polymer, helpful to obtain granules with uniform particle size and good flowability.
- Applicable also as a solid dispersion carrier.

## <Sugar coating binder>

### SB-4 Hypromellose USP, EP, JP

Grade	Viscosity (mPa·s)*	Substitution type	Methoxy content (%)	Hydroxypropoxy content (%)
SB - 4	3.2 - 4.8	2208	19.0 - 24.0	4.0 - 12.0

\*Viscosity of 2 w/w % aqueous solution at 20°C

#### Features:

- Applicable as a binder for sugar coating as an alternative of gelatin. Compared to gelatin, SB-4 has a better stability.

## <Thickener>

### METOLOSE® Hypromellose, Methylcellulose USP, EP, JP

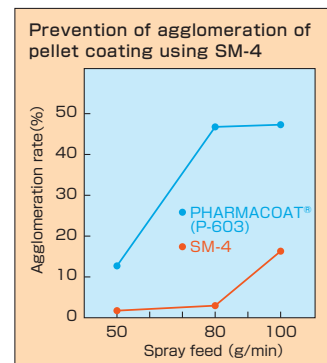
Grade*		Generic name	Methoxy content (%)	Hydroxypropoxy content (%)
SM	4, 15, 25, 100, 400, 1500, 4000	Methylcellulose	26.0 - 33.0	-
60SH	50, 4000, 10000	Hypromellose 2910	28.0 - 30.0	7.0 - 12.0
65SH	50, 400, 4000	Hypromellose 2906	27.0 - 30.0	4.0 - 7.5
90SH	4000, 15000, 100000	Hypromellose 2208	19.0 - 24.0	4.0 - 12.0

\*Values in the table are viscosities of 2 w/w % aqueous solution at 20°C

#### Features:

- Non ionic and water soluble polymer with various viscosity.
- Applicable as film strips and dispersant of liquid formulation.
- SM-4 is recommendable for pellet coating as it is less sticky. The thermal gelling helps to prevent agglomerations during the coating process even at the higher spray speed.

Pellets which were extruded from 1.0 mm- diameter die were coated with 7% aqueous solution of SM-4 and the result was compared with PHARMACOAT® 603 (P-603) in fluidized bed granulator. The ratio of agglomerated pellets was analyzed from the weight retained on #16 sieve, when the spray speed was changed from 50 g/min to 100 g/min.



<Sustained release agent>

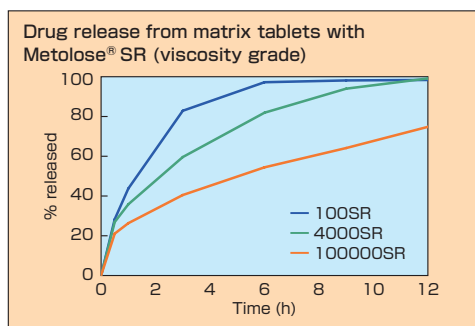
**METOLOSE® SR** Hypromellose USP, EP, JP

Grade		Viscosity (mPa·s)*	Substitution type	Methoxy content (%)	Hydroxypropoxy content (%)	Particle size (μm)
90SH	100SR	80 - 120	2208	22.0 - 24.0	8.5 - 10.5	<i>D</i> <sub>20</sub> : 20 - 40 <i>D</i> <sub>50</sub> : 50 - 80 <i>D</i> <sub>80</sub> : 100 - 160
	4000SR	3000 - 5600				
	15000SR	11250 - 21000				
	100000SR	75000 - 140000				

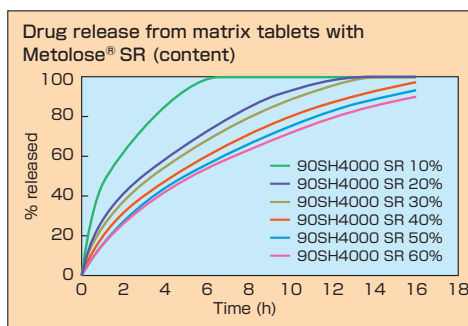
\*Viscosity of 2 w/w% aqueous solution at 20°C

**Features:**

- For Hydrophilic matrix formulation of API and METOLOSE® SR to extend the dissolution. The dosage forms can be obtained by direct compression or granulation process.
- METOLOSE® SR has specifications of particle size which can be suitable for sustained release application.
- Dissolution profile can be easily adjusted by selecting appropriate grade.
- Recommendable amount of METOLOSE® SR is more than 20% in the formulation in order to form the stable gel layer.



Formulation : Theophylline ..... 429 mg  
 METOLOSE® SR ..... 48 mg  
 Mg stearate ..... 3 mg  
 Preparation : Direct compression  
 Tested medium : water



Formulation : Theophylline ..... 10 mg  
 METOLOSE®4000 SR } ..... 467 mg  
 Lactose }  
 Mg stearate ..... 3 mg  
 Preparation : Direct compression  
 Tested medium : water

<Enteric coating agent, solid dispersion carrier>

**HPMCP** Hypromellose Phthalate, NF, EP, JP

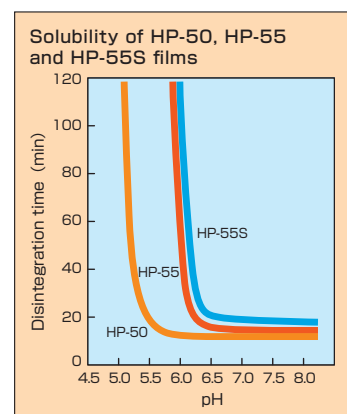
Grade	Phthaly content (%)	Viscosity (mPa·s)*	pH Solubility
HP - 50	21.0 - 27.0	44 - 66	≥ 5.0
HP - 55	27.0 - 35.0	32 - 48	≥ 5.5
HP - 55S		136 - 204	

\*Viscosity of 10 w/w% solution of methanol and dichloromethane at 20°C

**Features:**

- Suitable for solvent coating system. As co-solvents, mixture of ethanol and water (80/20 w/w%) or mixture of acetone and water (95/5 w/w%) are recommendable.
- Relatively stable, due to less hydrolysis.
- Available as a solid dispersion carrier for solubility enhancement.

According to the disintegration test method, dissolution time was measured for cast film from organic solvent (thickness: 100 μm; size: 10 x 10 mm)  
 ~ pH 5.6: USP Phthalate buffer  
 pH 5.8 ~: USP Phosphate buffer



# Product Information

<Enteric coating agent, solid dispersion carrier>

## Shin-Etsu AQOAT<sup>®</sup> Hypromellose Acetate Succinate, NF, JP

Grade	Viscosity* (mPa · s)	Methoxy content (%)	Hydroxypropoxy content (%)	Acetyl content (%)	Succinoyl content (%)	Particle	pH Solubility
AS - LF	2.4 - 3.6	20.0 - 24.0	5.0 - 9.0	5.0 - 9.0	14.0 - 18.0	Fine**	≥ 5.5
AS - LMP						Medium***	
AS - LG						Coarse	
AS - MF	2.4 - 3.6	21.0 - 25.0	5.0 - 9.0	7.0 - 11.0	10.0 - 14.0	Fine**	≥ 6.0
AS - MMP						Medium***	
AS - MG						Coarse	
AS - HF	2.4 - 3.6	22.0 - 26.0	6.0 - 10.0	10.0 - 14.0	4.0 - 8.0	Fine**	≥ 6.5
AS - HMP						Medium***	
AS - HG						Coarse	

\*Viscosity of 2 w/w% solution of sodium hydroxide aqueous solution at 20°C

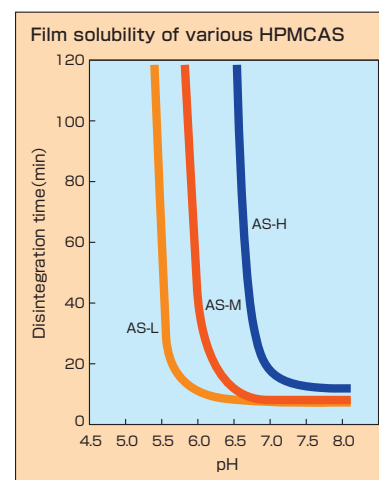
\*\*D<sub>50</sub>: NMT10 μm, D<sub>90</sub>: NMT20 μm by laser diffraction method

\*\*\*D<sub>50</sub>: 70 - 300 μm by laser diffraction method

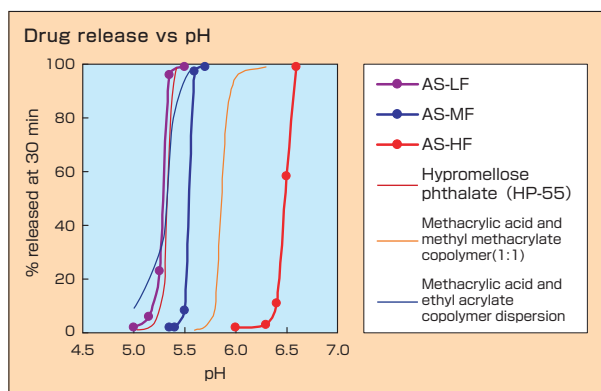
Abbreviation: HPMCAS

### Features:

- For enteric coating, various coating methods can be applied such as aqueous, organic solvent, ammonia neutralized and dry coating. Coating methods can be selected depending on the characteristic of API. For example, dry coating is suitable for water and solvent sensitive API.



According to the disintegration test method, dissolution time was measured for cast film from organic solvent (thickness: 100 μm; size: 10 x 10 mm)  
 ~ pH 5.6: USP Phthalate buffer  
 pH 5.8 ~: USP Phosphate buffer



Riboflavin granules were coated with various enteric coating agents. Percent release of riboflavin at 30 minutes was measured in USP Phthalate buffer (~pH 5.6) and USP Phosphate buffer (pH 5.8~)

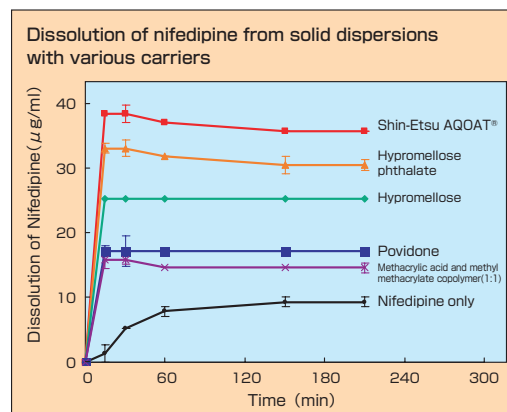
- Shin-Etsu AQOAT<sup>®</sup> is also used in solid dispersion for solubility and bioavailability enhancement.

In order to prepare solid dispersion, various methods are applicable such as spray dry, spray coating, hot melt extrusion (HME), coprecipitation etc. As Shin-Etsu AQOAT<sup>®</sup> can dissolve into various organic solvents and has relatively low glass transition temperature (T<sub>g</sub>), it is one of the most suitable polymers in solid dispersion. Numerous scientific papers reported that Shin-Etsu AQOAT<sup>®</sup> was able to enhance the drug solubility more effectively compared to other polymers.

### T<sub>g</sub> of various cellulosic polymers

HPMCAS (all grades)	122°C
HPMCP (HP-55)	138°C
HPMC (PHARMACOAT <sup>®</sup> 606)	150°C

T<sub>g</sub> was determined by DSC experiment under the following test condition;  
 Equipment: DSC Q2000 (TA Instruments, Japan),  
 Heating rate: 10°C/min,  
 Referred to the second heating run N<sub>2</sub> gas atmosphere  
 Sample size: 3 mg



Nifedipine (NP) and various carriers were dissolved into organic solvents with the ratio of NP/carrier=1/2 by weight and sprayed, dried and milled. Dissolution test was done with simulated intestinal fluid (pH 6.8).

<Disintegrant, binder, anti-capping agent>

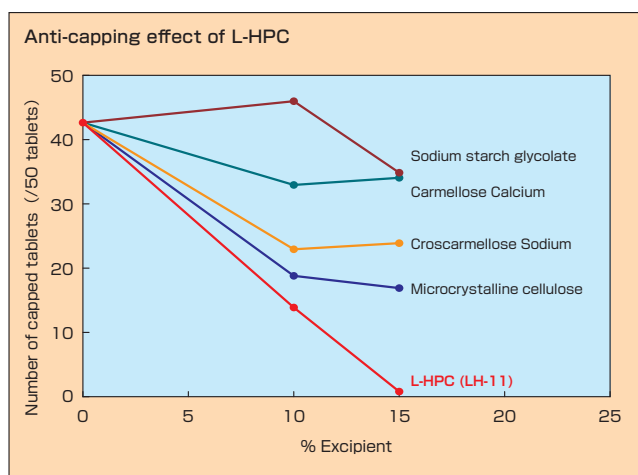
**L-HPC** Low-Substituted Hydroxypropyl Cellulose, NF, EP, JP

Grade	Hydroxypropoxy content (%)	Mean particle size* ( $\mu\text{m}$ )	90% cumulative particle size * ( $\mu\text{m}$ )	Application
LH - 11	10.0 - 12.9	45 - 65	150 - 200	Direct compression (DC), anti-capping
LH - 21		35 - 55	100 - 150	DC, granulation (high shear)
LH - 22	7.0 - 9.9			DC, granulation (high shear)
LH - B1	10.0 - 12.9	45 - 65	100 - 150	DC, granulation (fluid bed)
LH - 31		17 - 23	40 - 100	Granulation (high-shear, extrusion), layering
LH - 32	7.0 - 9.9			Granulation (high-shear, extrusion), layering
NBD - 020	13.0 - 15.9	35 - 55	70 - 130	Granulation (high shear)
NBD - 021	10.0 - 12.9			DC, granulation (high shear)
NBD - 022	7.0 - 9.9			DC, orally disintegrating tablets

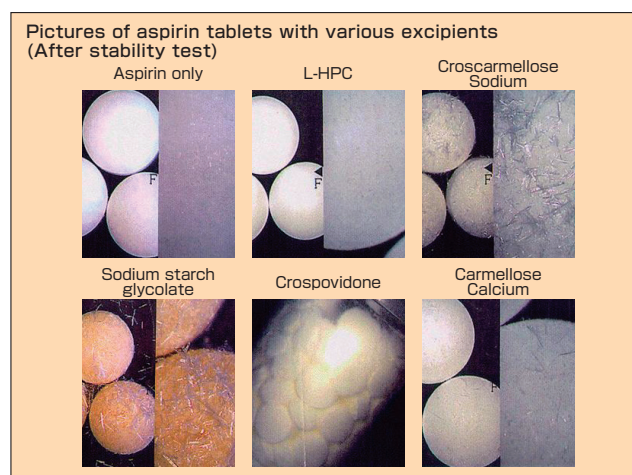
\*In-house Laser diffraction method

**Features:**

- Water insoluble, swells in water and works as dual functional ingredients, disintegrant and binder for tablets and pellets.
- Suitable grade can be selected depending on process and API characteristics.
- Non-ionic polymer which has less interaction with API and better stability.



Ethenzamide tablets were prepared with various ratio of excipients and friability test was implemented in accordance with USP method.



Aspirin tablets with 20% excipients were stored in closed plastic bottle at 50°C for 3 months.

**SmartEx<sup>®</sup>**

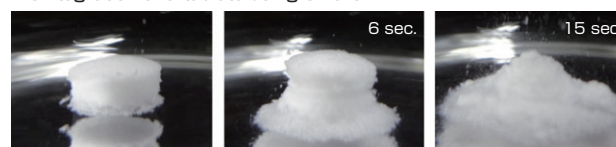
SmartEx<sup>®</sup> is a co-processed excipient which consists of L-HPC, D-mannitol and fully hydrolyzed polyvinyl alcohol (PVA) and it specially designed for orally disintegration tablets (ODTs) and also immediate release tablet formulation by direct compression.

All the excipients are widely used in pharmaceutical industry. One of the main advantage over other co-processed excipients is that SmartEx<sup>®</sup> contains L-HPC and therefore gives excellent stability.

Grade	D50 ( $\mu\text{m}$ )*	Feature
QD - 50	45 - 75	Quicker disintegration
QD - 100	85 - 125	Higher compressibility

\*In-house laser diffraction method, different from the product specification

Disintegration of a tablets using SmartEx<sup>®</sup>



# Shin-Etsu Pharmaceutical Excipients Guide to Application

		Solid Dosage Forms: Tablets and Pellets														Capsules			Amorphous Solid Dispersion		Liquid and Others												
		Tablet coating	Pellet coating	Taste masking	Enteric/delayed release coating	Enteric/delayed release coating (aqueous dispersion* & dry)	Enteric/delayed release coating (aqueous solution**)	Sugar coating binder	Sustained release (matrix tablets)	Anti capping	Dissolution improvement for WG	Disintegrator improvement for WG	Binding for WG	Disintegrator improvement for WG	Binding for DC	Binding for RC	Pellet extrusion	ODT	Dissolution improvement from drug layer	Capsule shell	Dispersing aid for capsule filling	Solvent free methods	Solvent methods	Thickening	Eye Drops***	Suspending	Dry syrup	Plaster/ dermal patch	Oral films				
PHARMACOAT®	603	S	S						VS											VS	VS					VS							
	645	S	S	S					S											VS	VS	VS				S		S					
	606	VS	S	VS					S											VS	S	S				S		VS					
	615	S		VS																S						S		S					
	SB-4										VS																			S			
METOLOSE®	SM-4		VS	VS					VS																					S			
	Other SM																						VS		VS	S	S			S			
	60SH								S														VS	S	S		S		VS				
	65SH								S														S		S								
METOLOSE® SR	All Grades							VS																			S						
HPMCP	All Grades			VS	VS																S	VS											
Shin-Etsu AQOAT®	F Grades			S		VS																											
	MP Grades																					VS											
	G Grades			VS	VS		VS															S	VS										
L-HPC	LH-11								VS			VS								S													
	LH-21, 22								S	S		S		S		S																	
	LH-B1									VS	VS		S								VS												
	LH-31, 32											S		S	S	VS	S	S															
	NBD-020								S			VS		VS	VS		VS	S			S												
	NBD-021											S	S	VS	VS			S															
SmartEx®	QD-50, 100																																VS

\* Shin-Etsu AQOAT® is dispersed in the coating dispersion and not dissolved (aqueous dispersion and partly neutralized methods).

\*\* Shin-Etsu AQOAT® is dissolved in the aqueous coating solution (fully neutralized method).

\*\*\*Eye drops : This application may require specialized properties. Please contact our sales department for assistance. Bulk drug GMP is not applicable.

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Cellulose & Pharmaceutical Excipients Department  
6-1, Ohtemachi 2-chome, Chiyoda-ku, Tokyo, 100-0004  
Japan  
TEL: 81-3-3246-5261 FAX: 81-3-3246-5372  
<http://www.metolose.jp/e>