

# 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 <https://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

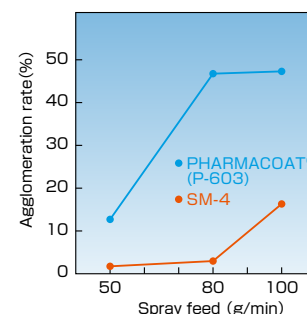
Grade*		Generic name	Methoxy content (%)	Hydroxypropoxy content (%)
SM	4, 15, 25, 100, 400, 1500, 4000	Methylcellulose	26.0 - 33.0	-
60SH	50, 4000, 10000	Hypromellose 2910	28.0 - 30.0	7.0 - 12.0
65SH	50, 400, 4000	Hypromellose 2906	27.0 - 30.0	4.0 - 7.5
90SH	4000, 15000, 100000	Hypromellose 2208	19.0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



Prevention of agglomeration of pellet coating using SM-4

<Sustained release agent>

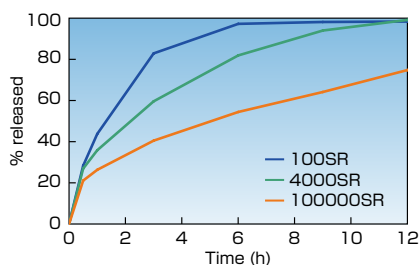
**METOLOSE® SR** Hypromellose USP, EP, JP

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	D20 : 20 - 40 D50 : 50 - 80 D80 : 100 - 160
	4000SR	3000 - 5600				
	15000SR	11250 - 21000				
	100000SR	75000 - 140000				

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

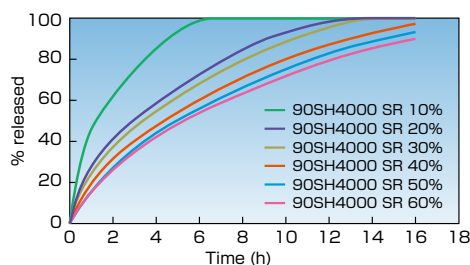
**Features:**

- 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.



Drug release from matrix tablets with Metolose® SR (viscosity grade)

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



Drug release from matrix tablets with Metolose® SR (content)

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

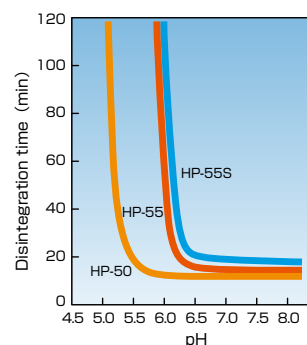
Grade	Phthalyl content (%)	Viscosity (mPa·s)*	pH Solubility
HP - 50	21.0 - 27.0	44 - 66	≥ 5.0
HP - 55	27.0 - 35.0	32 - 48	≥ 5.5
HP - 55S		136 - 204	

\*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



Solubility of HP-50, HP-55 and HP-55S films

# 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

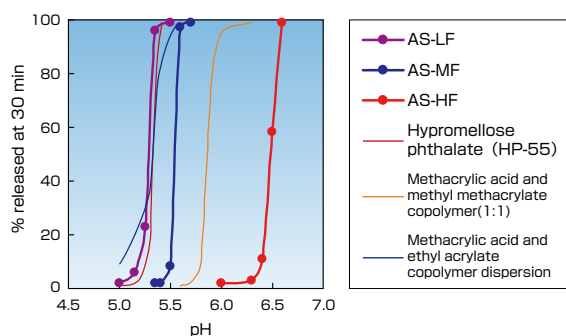
\*\*D<sub>50</sub>: NMT10 μm, D<sub>90</sub>: NMT20 μm by laser diffraction method

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

Abbreviation; HPMCAS

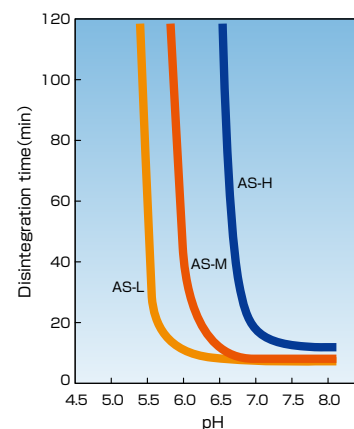
### Features:

- 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.



Drug release vs pH

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~)



Film solubility of various HPMCAS

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

- 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

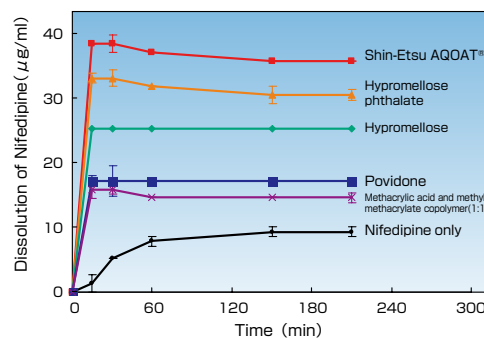
HPMCAS (all grades)	122°C
HPMCP (HP-55)	138°C
HPMC (PHARMACOAT <sup>®</sup> 606)	150°C

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



Dissolution of nifedipine from solid dispersions with various carriers

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>

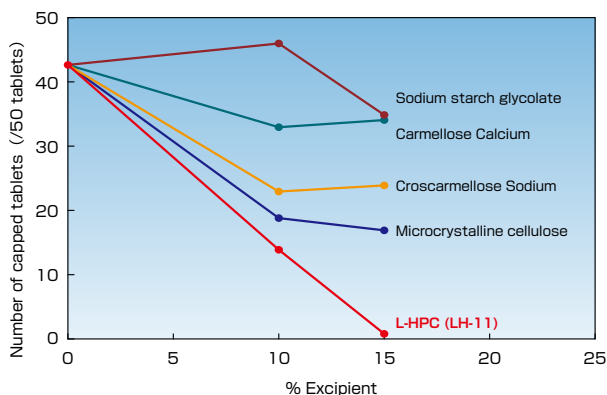
**L-HPC** Low-Substituted Hydroxypropyl Cellulose, NF, EP, JP

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

\*In-house Laser diffraction method

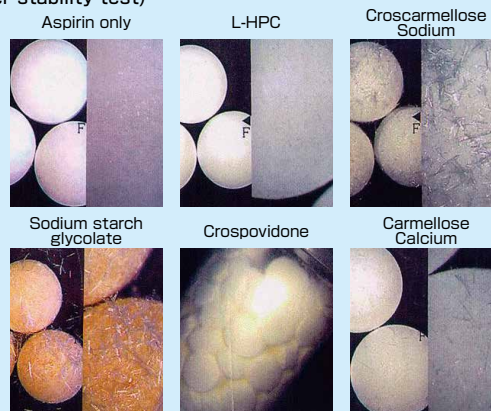
**Features:**

- Water insoluble, swells in water and works as dual functional ingredient, 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.



Anti-capping effect of L-HPC

Pictures of aspirin tablets with various excipients (After stability test)



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 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 advantages over other co-processed excipients is that SmartEx<sup>®</sup> contains L-HPC and therefore gives excellent stability.

Grade	Particle size D <sub>50</sub> ( μ m)*	Application
Plus	55 - 85	DC, ODTs

\*Laser diffraction method.

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



# Shin-Etsu Pharmaceutical Excipients Guide to Application

VS=Very suitable S=suitable

		PHARMACOAT®				METOLOSE®				METOLOSE® SR		HPMCP		Shin-Etsu AQOAT®				SmartEx®							
		603	645	606	615	SB-4	SM-4	Other SM	60SH	65SH	90SH	All Grades	All Grades	F Grades	MP Grades	G Grades	LH-11	LH-21, 22	LH-B1	LH-31, 32	NBD-020	NBD-021	NBD-022	Plus	
Solid Dosage Forms: Tablets and Pellets	Tablet coating	S	S	VS	S																				
	Pellet coating	S	S	S			VS																		
	Taste masking		S	VS	VS		VS						VS	S		VS									
	Enteric/delayed release coating (solvent)												VS			VS									
	Enteric/delayed release coating (aqueous dispersion* & dry)													VS											
	Enteric/delayed release coating (aqueous solution**)															VS									
	Sugar coating binder						VS																		
	Sustained release (matrix tablets)								S	S	S	VS													
	Binder solution (WG)	VS	S	S			VS																		
	Anti capping																VS	S			S				
	Dissolution improvement for WG																	S	VS						
	Disintegraton improvement for WG																		VS						
	Binding for WG																VS	S		S	VS	S	S		
	Disintegraton improvement for DC																		S			S	VS		
	Binding for DC																	S		S	VS	VS	VS		
	Binding for RC																			S	VS	VS	VS		
	Pellet extrusion																	S		VS					
	Dissolution improvement from drug layer																				S	VS			
ODT																				S	S	S	VS	VS	
Capsules	Capsule shell		VS	VS	S																				
	Dispersing aid for capsule filling															S		VS		S					
Amorphous Solid Disintegration	Solvent free methods	VS	VS	S								S		VS	S										
	Solvent methods	VS	VS	S									VS		VS										
Liquid and Others	Thickening							VS	VS	S	S														
	Eye Drops***								S																
	Suspending							VS	S	S	S														
	Dry syrup	VS	S	S	S			S																	
	Plaster/ dermal patch							S	S		S	S													
	Oral films		S	VS	S	S	S		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  
4-1, Marunouchi 1-chome, Chiyoda-ku, Tokyo, 100-0005  
Japan  
TEL: 81-3-6812-2441 FAX: 81-3-6812-2443  
<https://www.metolose.jp/en>

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