Shin-Etsu

Methylcellulose USP
Hypromellose USP

METOLOSE®
METOLOSE®SR

Water soluble cellulose ether
Sustained release agent for matrix system

CONTENTS

Introduction

Shin-Etsu Chemical Co., Ltd. began to produce water soluble cellulose ethers in 1962, with the trade name METOLOSE®. METOLOSE® consists of Methylcellulose (methylcellulose USP) and three substitution types of Hydroxypropylmethylcellulose (Hypromellose USP) each available in several grades differing in viscosity.

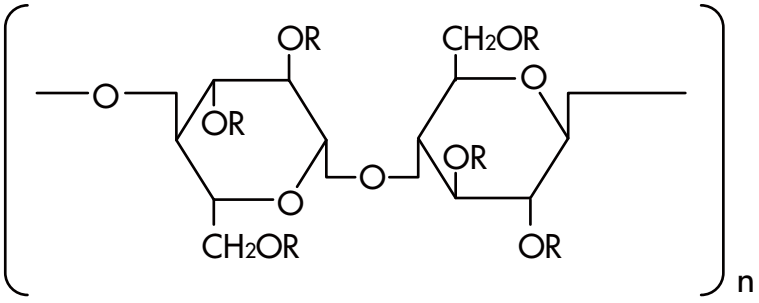
METOLOSE® can be used as a binder for solid dosage forms such as tablets and granules. It also provides a variety of functions such as water retention, thickening, protective colloid, surface activity, etc.

It also can be used as a hydrophilic matrix agent. The hydrophilic matrix system is the simplest sustained release technology for oral dosage forms, consisting essentially of a drug and a water soluble highly viscous polymer. Recent advances in this hydrophilic matrix system have allowed more controllable and reproducible drug release by controlling the chemical and physical properties of the polymer. METOLOSE® SR is especially suitable for this application, and provides a genuine consistency in the final products.

This brochure briefly describes the properties of METOLOSE® and METOLOSE® SR.

If you are interested in its characteristics and application, or have any question, please contact us for further information.

Description

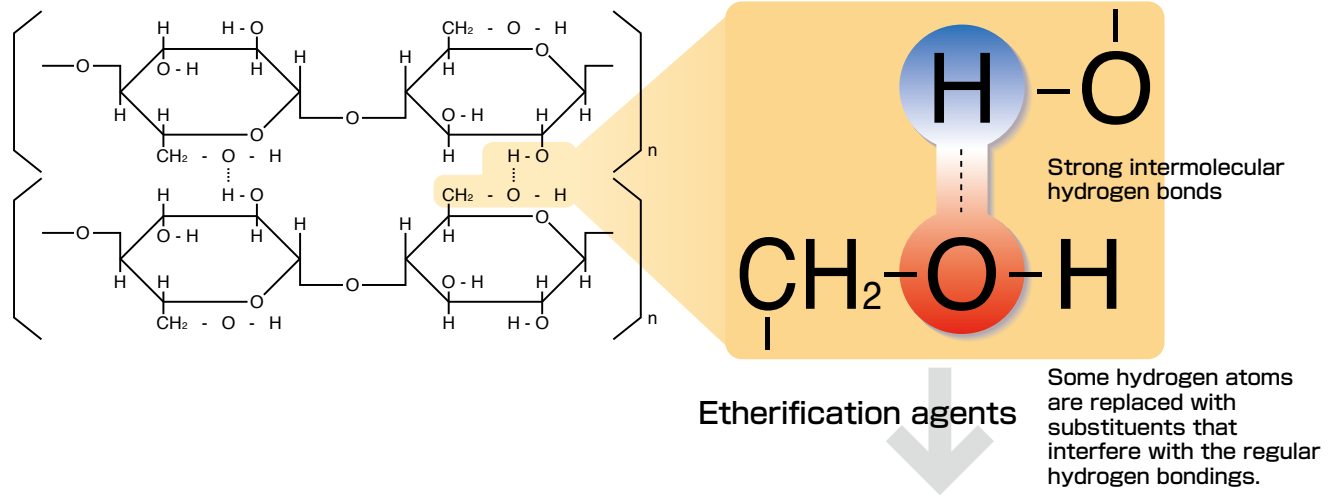
Trade name	METOLOSE® SM	METOLOSE® SH
Generic name	Methylcellulose	Hypromellose (Hydroxypropylmethylcellulose)
Abbreviation	MC	HPMC
IUPAC name	Cellulose, methyl ether	Cellulose, 2-hydroxypropyl methyl ether
CAS RN®	9004-67-5	9004-65-3
Compendial status	USP (The United States Pharmacopoeia) EP (European Pharmacopoeia) JP (Japanese Pharmacopoeia)	
Structure		

R = -H
-CH_3
-$CH_2CH(CH_3)OH$ ..... not included in Methylcellulose

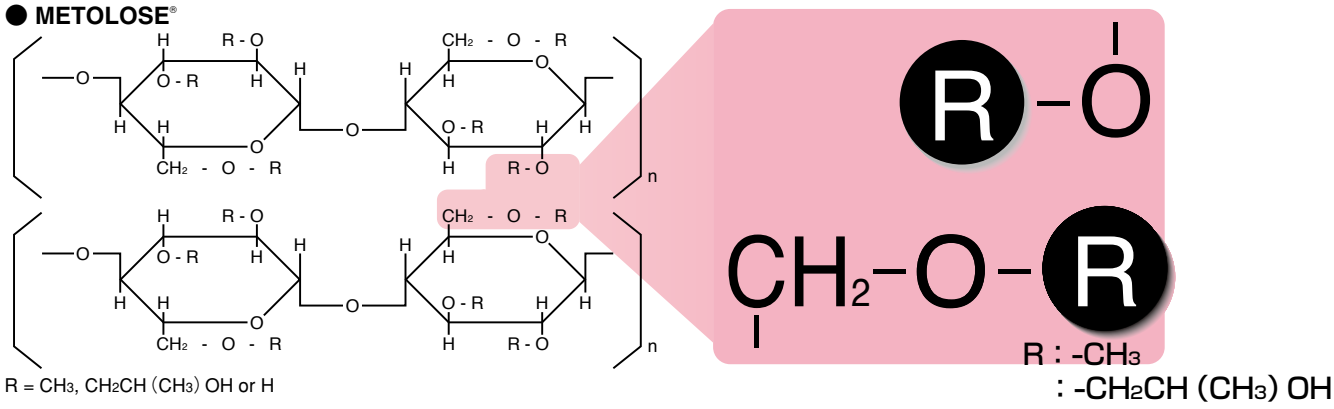
What is METOLOSE®?

METOLOSE® is a nonionic water-soluble cellulose ether which is derived from pulp. To produce METOLOSE®, the pulp is first treated with caustic soda to obtain alkali-cellulose, and this is etherified with chloromethane or with the combination of chloromethane and propylene oxide at high temperature. Cellulose is not soluble in water due to its crystalline structure with strong intermolecular hydrogen bondings between OH groups. When the hydrogen atoms of some of the OH groups are substituted with methyl or hydroxypropyl groups, the resulting methoxy and hydroxypropoxy groups interfere with the intermolecular hydrogen bondings, so that the polymer chains are less strongly bound to each other. This allows water to penetrate into the intermolecular spaces of cellulose, and the polymer becomes water-soluble. This is the reason why METOLOSE® is soluble in water while pulp, the source of METOLOSE®, is not.

● **Cellulose (Pulp)**

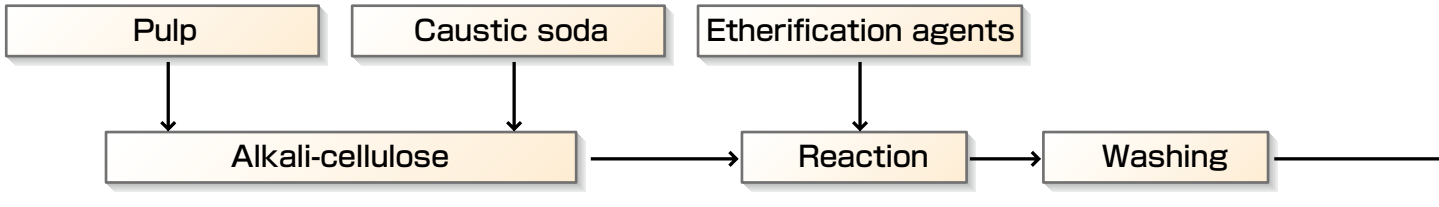


● **METOLOSE®**



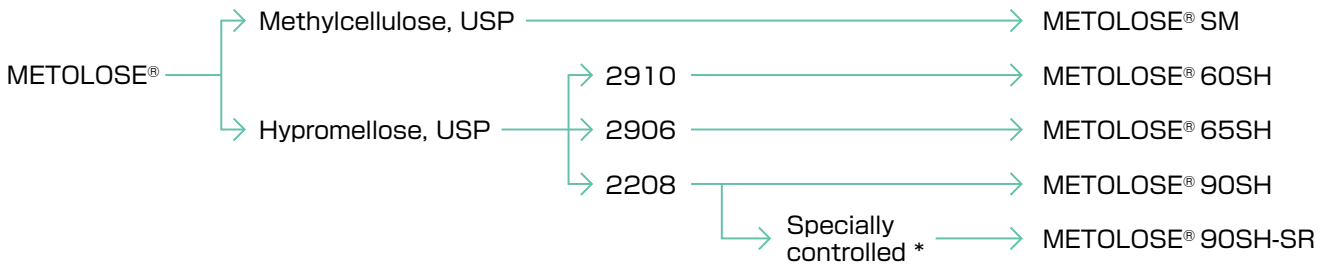
R = CH_3, $CH_2CH(CH_3)OH$ or H

● **Production flow diagram**



Substitution Types

METOLOSE® includes several types with different levels and kinds of substitution.
The available types are SM, 60SH, 65SH and 90SH. Their substitution levels are shown below.



* Please refer to Table 2 in the next page

Table 1. Types of METOLOSE®

● **Typical substitution levels of METOLOSE®**

Type	SM	60SH	65SH	90SH	90SH-SR
Name in the USP	Methylcellulose	Hypromellose, 2910	Hypromellose, 2906	Hypromellose, 2208	
CAS registry number	9004-67-5	9004-65-3			
Methoxy, D.S.*	1.8	1.9	1.8	1.4	
Hydroxypropoxy, M.S.*	-	0.25	0.15	0.25	
Features and main application	Low thermal gelation temp. Less sticky. Binder. Dispersing agent.	Clear solution. Thickener for clear solution.	Better dispersibility. Dispersing agent.	Availability of higher viscosity. Hydrophilic and better compatibility with surfactants. Cataplasm	Finer particle. Tighter specification of substituent. Hydrophilic matrix tablets for sustained release.

*D.S. = Degree of substitution, i.e. the average number of substituted hydroxyl groups in the anhydrous glucose unit.
M.S. = Molar substitution, i.e. the average number of substituents in the anhydrous glucose unit.

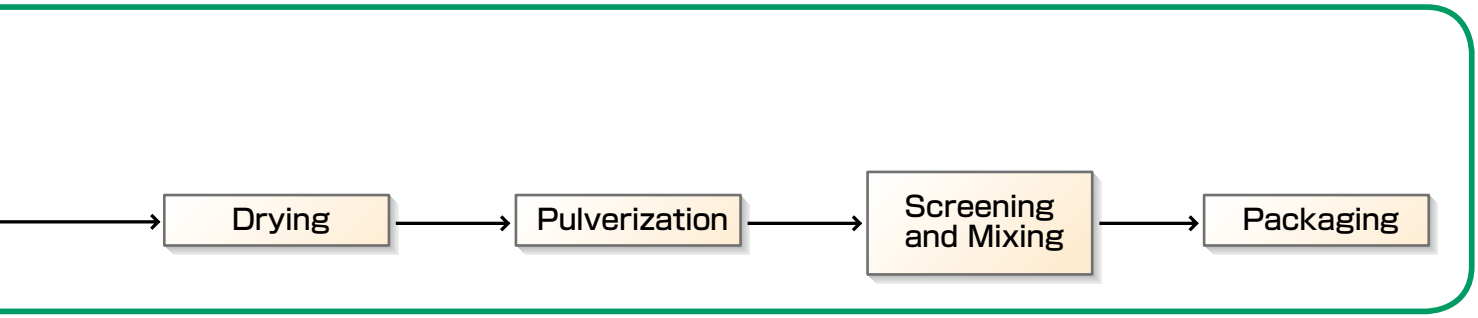


Table 2. Types of METOLOSE®

Grade	Substitution type	Methoxy content (%)	Hydroxypropoxy content (%)	Particle size (μm)
SM	Methylcellulose	26.0 – 33.0	-	-
60SH	Hypromellose 2910	28.0 – 30.0	7.0 – 12.0	
65SH	Hypromellose 2906	27.0 – 30.0	4.0 – 7.5	
90SH	Hypromellose 2208	19.0 – 24.0	4.0 – 12.0	
90SH-SR		22.0 – 24.0	8.5 – 10.5	D20; 20-40 D50; 50-80 D80; 100-160

Each type of METOLOSE® includes several viscosity grades as shown below.

Table 3. Available grades and viscosity specifications

Available grades and viscosity specifications

Labeled Viscosity	USP Specification (mPa·s)*1	SM	60SH	65SH	90SH	90SH-SR
4	3.2 — 4.8	○				
15	12.0 — 18.0	○				
25	20.0 — 30.0	○				
50	40.0 — 60.0		○	○		
100	80 — 120	○				○
400	320 — 480	○		○		
1500	1125 — 2100	○				
4000	3000 — 5600	○	○	○	○	○
10000	7500 — 14000		○			
15000	11250 — 21000				○	○
100000	75000 — 140000				○	○

*1 Viscosity is measured with 2% aqueous solution at 20 ℃. Viscosity ranges are 80% - 120% for labeled viscosity less than 600 mPa·s and 75% - 140% for labeled viscosity 600 mPa·s and higher, respectively. (Viscosity is harmonized item among the USP, EP and JP).

Nomenclature

Substitution type	Labeled viscosity	Other (Special powder property, etc.)
SM-	15	
60SH-	50	
90SH-	4000	SR

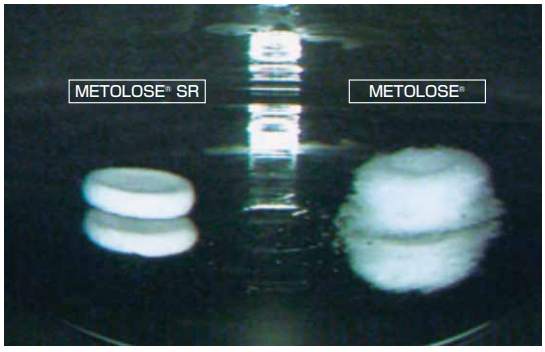
Package

Packaging material: Double-layered polyethylene bag in fiber drum
Net weight: Depending on grades*

*Below pictures are examples of representative grades and net weight depends on grades. Please contact us for further information.

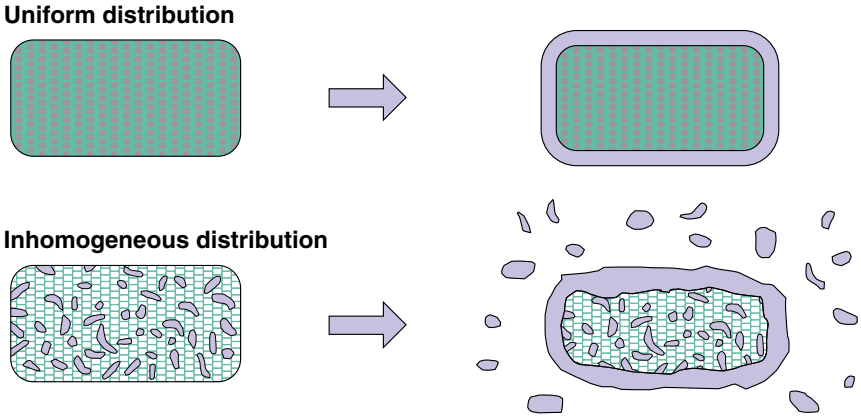
Sustained Release Application with METOLOSE®

There are several ways to control drug release and one of them is hydophilic matrix tablet which can work in the wide range of digestive tracts and available even for poorly soluble drugs. From the manufacturing and economical standpoints, it is clearly desirable to simply mix the components such as drugs and matrix agents and to compress into tablets. Hypromellose is one of the common agent for this application due to its hydrophilic nature and variation of the chemical quality.
In this section, sustained release application with METOLOSE® 90SH-SR series (Hypromellose 2208) is introduced.



What is hydrophilic matrix tablet?

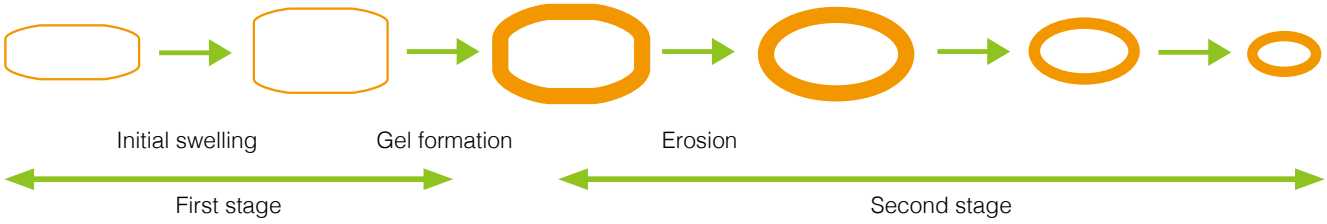
Hydrophilic matrix system controls the drug release through a gel layer which is formed from the hydration of hypromellose. The formulation is very simple, basically consists from drug and hypromellose. Therefore it is easy to control the dissolution profile by selecting a specific grade of METOLOSE®. Compared with the control release by polymer coating, the dissolution from matrix tablet is very robust, as it can be controlled by the formulation. However it is also said that the selection and the quality of hypromellose is very important.
Additionaly, homogeneity of hypromellose particle in the tablet is also the important aspect for gel formation. If it is not uniform, it takes longer time for gel layer hydration and partial disintegration happens, resulted in the deviation of the dissolution. Upper picture shows the difference of the hydration between tablets with general METOLOSE® grade and METOLOSE® SR grade. METOLOSE® SR can prevent initial swelling and disintegration.



Dissolution process of hydrophilic matrix tablet

Below picture illustrates the schematic dissolution pfrofile of the matrix tablet. After the administration, hydrophilic matrix tablets made with METOLOSE® SR hydrate to form a gel layer on the surface of the tablet as the first stage. At the second stage, after the gel layer is completed, the dissolution of drug is stabilized. At the same time, the gel layer dissolves and disappears from the surface and water is penetrated into the inside of the tablets. Finally the tablet disappears by dissolving.

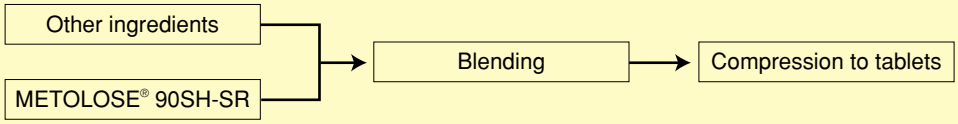
Schematic dissolution profile on the matrix tablet



How to use METOLOSE® for matrix tablets

Hydrophilic matrix tablets with METOLOSE® can be prepared by following methods.

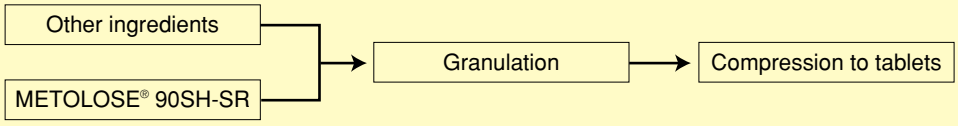
Direct compression (DC)



DC can be applied if the other ingredients such as drugs have the following properties.
-Sufficient flowability
-Sufficient compressibility
-Miscibility with METOLOSE®

METOLOSE® itself has sufficient flowability and compressibility. Therefore, prior to blending process, other ingredients had better to be processed such as granulation beforehand.

Wet granulation (WG), Dry granulation



For granulations process, normal granulation processes and equipments are available such as a high-shear mixer, a fluidized bed granulator and a roller compactor.
For high shear mixer granulation, mixture of water and ethanol solution (20:80 by wt.) can be recommended as a solvent.

Formulation design

Formulation can be decided with following process. As you see, the formulation design is very simple.
Due to this simple formulation, the process is very robust.

Requirements for drugs	→	Requirements for solid dosage forms
-Dose -Desirable dissolution profile		-Tablet size -Amount of hypromellose -Grade of hypromellose

Factors affecting to drug release of matrix tablets

The formulation of hydrophilic matrix tablets using hypromellose is very simple, required ingredients are just drug and hypromellose. Therefore the dissolution profile is affected by the formulation and the quality of hypromellose.
Several considarable factors were studied and each effect to the dissolution profiles is introduced.
Generally, critical control parameters (CCPs) for hydrophilic matrix formulation with hypromellose are drug solubility, viscosity, substitution levels, particle size and content of hypromellose.

Selection of METOLOSE® grades

Effect of drug solubility

For a highly water-soluble drug : drug release is regulated by diffusion through the gel layer. In the first 30 minutes an excess amount of drug in the gel layer can be released. The dissolution profile is shown in Figure 1.
For a poorly water-soluble drug : drug release is regulated by erosion of the matrix tablet. The dissolution curve is comparatively linear as compared with highly soluble drugs. The dissolution profile is shown in Figure 2.

Effect of viscosity

Viscosity of HPMC affects gel strength, hydration speed in the first stage and erosion rate of the gel in the second stage. The higher viscosity grade has stronger gel strength and slower dissolution (Figure 2). By selecting the viscosity grade, the dissolution profile can be easily controlled.

Effect of substitution type

Substitution type of METOLOSE® affects hydration speed of HPMC particles and gel strength, which can influence the dissolution profile (Figure 3). In case of Methylcellulose almost no gel layer formation, because it takes much longer hydration time compared with hypromellose.

Effect of particle size

Larger particle requires longer hydration time, resulted in longer time for completion of gel layer. Therefore, at this initial swelling stage, drug is released (Figure 4). METOLOSE® SR has an average particle size around 70 μm, which is an ideal particle size for matrix application.

Effect of HPMC content

The content of HPMC in the matrix tablet significantly affects the initial erosion of the tablet in the first stage (Figure 5). To obtain the delayed release, the content of HPMC should be 20 % or higher.

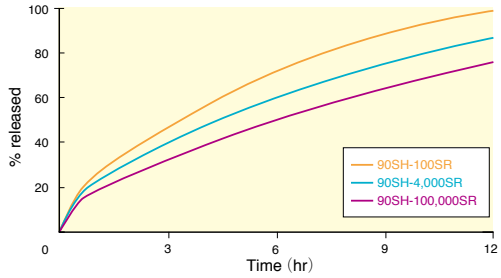
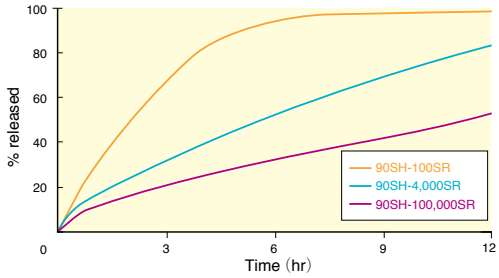


Figure 1. Dissolution profile: High solubility in water



Formulation (Fig. 1) :

Chlorpheniramine maleate	191 mg
METOLOSE® SR	286 mg
Mg-stearate	3 mg
Total	480 mg / Tab

Formulation (Fig. 2) :

Theophylline	382 mg
METOLOSE® SR	95 mg
Mg-stearate	3 mg
Total	480 mg / Tab

Figure 2. Dissolution profile: Low solubility in water

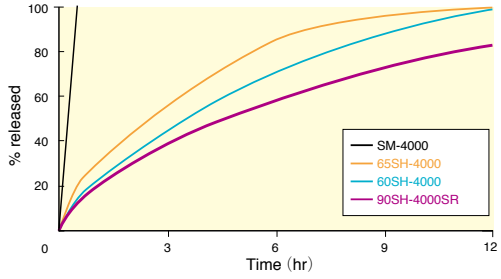
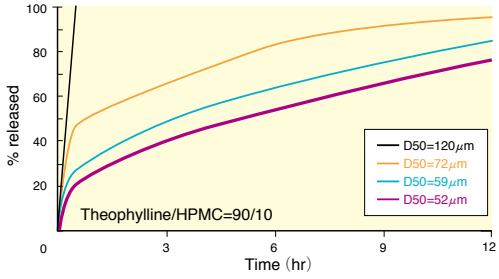


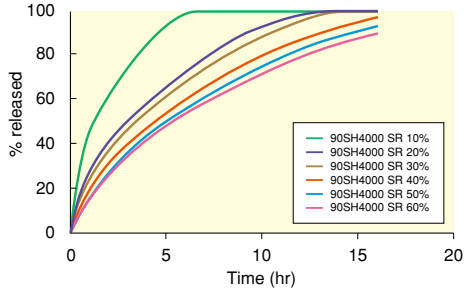
Figure 3. Effect of various substitution types



Formulation (Figs. 3 and 4) :

Theophylline	429.3 mg
METOLOSE® SR	47.7 mg
Mg-stearate	3 mg
Total	480 mg

Figure 4. Effect of particle size



Formulation:

Theophylline	10 mg
METOLOSE® SR	467 mg
Lactose	
Mg-stearate	3 mg
Total	480 mg/tab

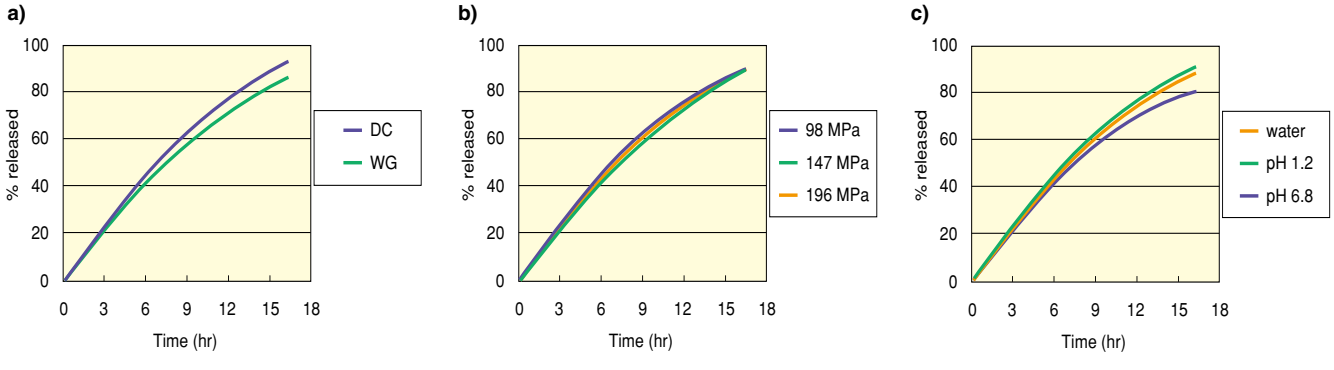
Compression: 11.3 mm flat, 480 mg / Tab, 80 MPa
Dissolution: According to the USP paddle method; paddle rotation: 100 min^{-1}; 900 mL of purified water; test period: 12 hours; detection: UV.

Figure 5. Effect of HPMC content

Effect of the way of preparation (direct compression (DC) or wet granulation (WG)), tablet hardness and dissolution media

In order to see the impact of the way of preparation (DC or WG), tablet hardness and dissolution media, same formulation was tested.

As a results, these parameters didn't affect to the dissolution profiles with this formulation.



Formulation:

Theophylline	264 mg
90SH4000 SR	64.5 mg
Mg-stearate	1.5 mg
Total	330 mg/tab

Figure 6. Effect of a) preparation method, b) tableting pressure and c) dissolution media on drug release profile. Tablets were prepared by DC in b) and c).

Ⅱ Formulation examples

1) Theophylline (direct compression)

Direct compression is the simplest technique to prepare matrix tablets. This essentially consists of drug substance and METOLOSE®. Drug substance, which usually shows poor flowability, is primarily granulated in a fluidized-bed granulator.

1-1) Formulation of tablet

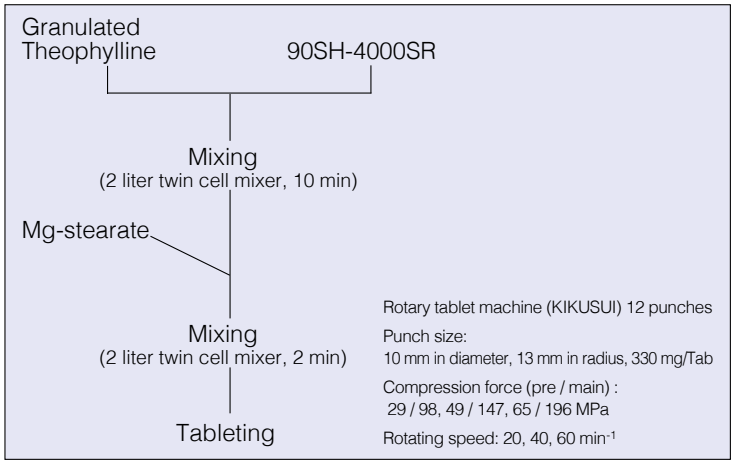
Ingredient	mg/Tablet
Theophylline*	264
90SH-4000SR	64.5
Mg-stearate	1.5
Total	330 mg/Tab

*Theophylline powder was granulated by a fluidized-bed. (Mixing rate : Theophylline 97%, Pharmacoat® 606 3%) The obtained theophylline granules showed good flowability and mixing ability to METOLOSE® powders.

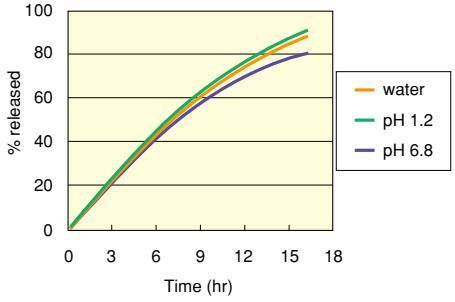
Fluidized bed granulation
Machine: Fluidized-bed Flowcoater FLO-5 (Freund)
Charge: 3 kg of Theophylline
Supply drying air temperature: 80℃
Exhaust air temperature: 35℃
Binder solution: Pharmacoat® 606 7% aq. soln.
Spray feed rate: 60 g/min

Powder properties of granule
Bulk density: 0.34 g/mL
Tapped density: 0.47 g/mL
Average particle size: 170 μm

1-2) Mixing procedure of the powders for compression



1-3) Results



Dissolution test: According to the USP method(Paddle method)
Dissolution medium: Purified water, pH 1.2, pH 6.8; 900 mL
Paddle rotation: 100 min-1
Test periods: 16 hours

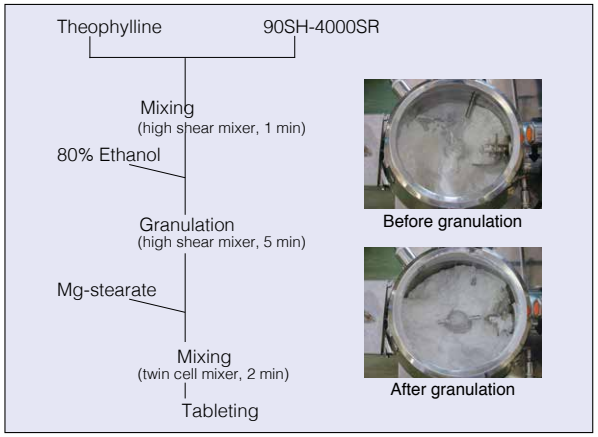
Figure 7.
Dissolution profiles of Theophylline tablets in different buffer solutions and water

2) Theophylline (wet granulation)

2-1) Mixing procedure of the powders for compression

Formulation was same as 1-1), however powder theophylline was used. 80% Ethanol was used as a kneading liquid in order to avoid sticky mass attached to the vessel's wall.

2-2) Mixing procedure of the powders for compression



Granulation with alcoholic solvent mixture improved powder handling and compressibility of the powders. 80 to 90% Ethanol is suitable for the granulation.

Wet granulation
Machine: High shear mixer Vertical granulator FM-VG-15 (Powrex)
Charge: 300 g
Agitation (blade / chopper): 600 / 1000 min-1
Kneading liquid: 80% ethanol, 180 g

Powder properties of granule
Bulk density: 0.35 g/mL
Tapped density: 0.48 g/mL
Average particle size: 122 μm

2-3) Results

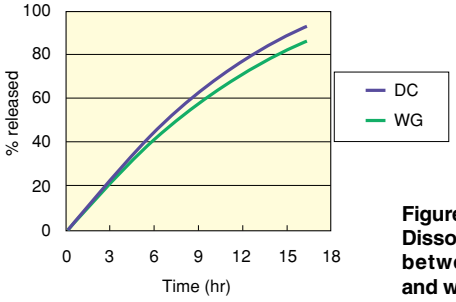


Figure 8.
Dissolution profiles comparison between direct compression and wet granulation

Film Coating of Pellets and Fine Granules using SM-4

Aqueous film coating for pellets and fine granules has more difficulties compared with tablet film coating, because of the problem of sticking during fluidized bed operation. Our METOLOSE® SM-4, which is an extremely low viscosity methylcellulose (4 mPa·s), is suitable for this application. Methylcellulose loses its adhesiveness at relatively high moisture content and film coating for pellets and fine granules could be achieved without agglomeration with a reasonable spray feed rate. The coated pellets and fine granules were covered with a continuous film of methylcellulose.

1) Pellets coating

Extruded and spheronized theophylline pellets, which diameter is 1 mm, were coated with 7 % aqueous solution of SM-4 with mentioned coating parameters. As a comparative study, same experiment was performed with 7% aqueous solution of Pharmacoat® 603 (Hypromellose 2910).

Machine	: Flowcoater FLO-5(fluidized bed)
Coating solution	: 7 % aqueous solution
Coating amount	: 8 % as polymer
Charge	: 5 kg theophylline pellet
Spray gun	: Air spray Nozzle 1.2 mm
Spray air	: 300 kPa, 210 mL/min
Gun position	: 40 cm from pellet bed (top spray)
Supply air flow	: 4.0 m³/min.
Supply air temp	: 80 ℃
Spray feed rate	: 50, 80, 100 g/min
Exhaust air temp.	: 47, 39, 35 ℃
Pellet temp.	: 51, 44, 39 ℃

Results

In order to see the agglomeration rate, coated pellets were sieved with 16 mesh (aperture is 1.2 mm). SM-4 reduced agglomeration rate even at the higher spray rate. Additionally continuous layer of SM-4 was confirmed by SEM observation.

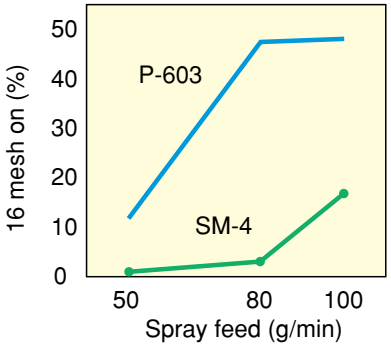
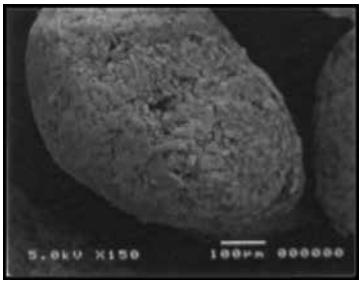
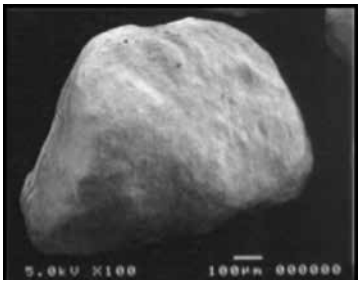


Figure 9. Agglomeration rate of coated pellets



Uncoated pellet



Coated pellet

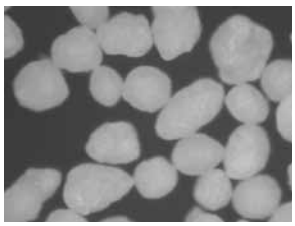
2) Fine granules coating

MCC (Microcrystalline cellulose) spheres, which diameter is 160 μm, were coated with 7% aqueous solution of SM-4 with mentioned coating parameters. In fludized-bed, wurster column was used.
As a comparative study, same experiment was performed with 7 % aqueous solution of Pharmacoat® 603 (P-603, Hypromellose 2910).

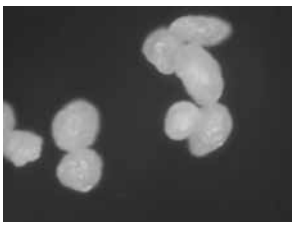
Machine	: Glatt GPCG-1
Coating solution	: 7 % aqueous solution
Coating amount	: 8 % as polymer
Charge	: 2 kg
Spray gun	: Air spray Nozzle 1.0 mm (bottom spray)
Supply air	: 3 bar
Supply air flow	: 50 m³/min.
Supply air temp	: 85 ℃
Spray feed rate	: 15 g/min
Exhaust air temp.	: 50 ℃
Pellet bed temp.	: 50 ℃

Results

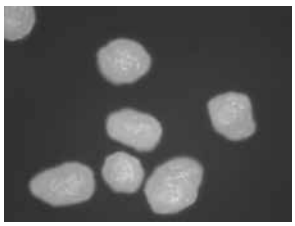
Coated granules were observed with SEM. SM-4 was effective to prevent agglomeration as diameter of the coated granules were not significantly increased.



Core
D50: 160 μm D90: 200 μm



Coated granules with P-603
D50: 184 μm D90: 298 μm



Coated granules with SM-4
D50: 175 μm D90: 208 μm

Properties of METOLOSE® Powder

Appearance	White or slightly off-white powder, fibrous powder or granules.
True density	1.26-1.31 g/mL
Bulk density Tapped density	0.20-0.45 g/mL 0.35-0.65 g/mL
Angle of repose	35-50°
Degradation temperature Self ignition temperature	280-300 ℃ approx. 360℃
Hygroscopicity	Depends on substitution type. See Fig. 12-14
Dust explosion	Kst = approx. 100 bar・m/s 1 bar = approx. 0.1 MPa

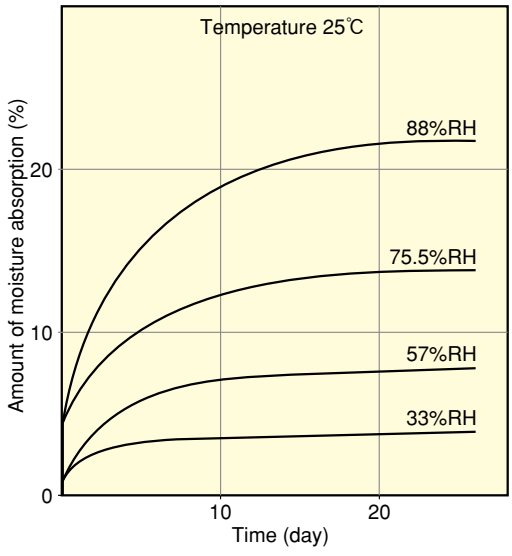


Figure 10. Moisture absorption rate of 60SH-4000

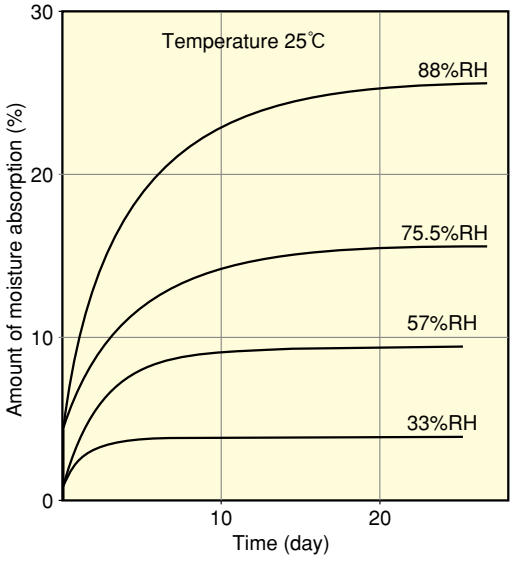


Figure 11. Moisture absorption rate of 90SH-4000

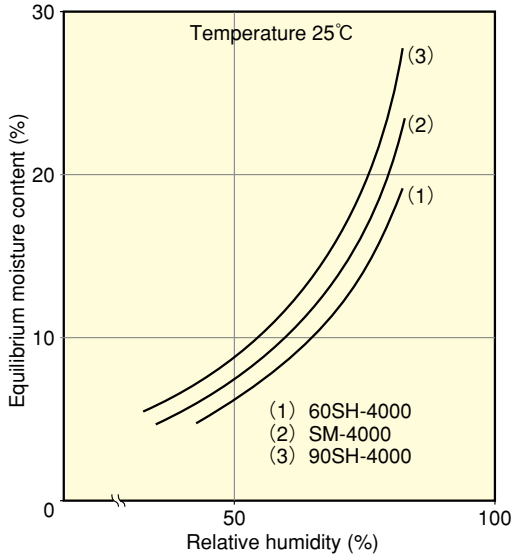


Figure 12. Equilibrium moisture content of METOLOSE®

Properties of METOLOSE® Solution

I Preparation of solution

How to dissolve METOLOSE®

The direct addition of METOLOSE® to water results in the formation of lumps due to incomplete wetting of the powder. This increases the preparation time. The methods shown below are therefore recommended. The appropriate one should be chosen depending on the application.

1. Hot water method

This method takes advantage of the insolubility of METOLOSE® in hot water.

1 Place about 1/2 up to all of the required amount of water at 70℃ or above in a vessel. Gradually add METOLOSE® while stirring.

2 At first METOLOSE® floats on the surface of the hot water, but it will gradually disperse to form a uniform slurry. Continue stirring and dispersing until all particles are thoroughly wetted in the hot water.

3 Add the rest of water as cold water or ice water while stirring.

4 Cool the resultant mixture while stirring until it becomes transparent.

5 A clear aqueous solution of METOLOSE® is obtained.

In order to dissolve METOLOSE® using the hot water method, sufficient cooling is essential. The temperature at which complete dissolution occurs depends on substitution type.

2. Organic solvent method

This method can be applied when a organic solvent which can be mixed with water such as ethanol. Disperse or wet the METOLOSE® powder in ethanol in advance, and then add water to the dispersion while stirring.
Please note that to add cellulosic powder to organic solvent directly may not be safe. Please take enough prevention on handling the material.

Ⅱ Thermal gelation

An aqueous solution of METOLOSE® changes to a gel when heated to a certain temperature. This thermal gelation results from formation of crosslinking caused by the intermolecular hydrophobic interaction between the high substituent portions where 3 hydroxyl groups are all substituted with the methoxyl groups. Different substitution types have different gelation behaviors. The gel reverts to its original solution form when it is cooled down. The thermal gelation of METOLOSE® has various applications. For more information on the thermal gelation, refer to the article by *Takahashi et al., Japanese Journal of Polymer Science and Technology, Vol. 38, No. 3, p 133-137.*

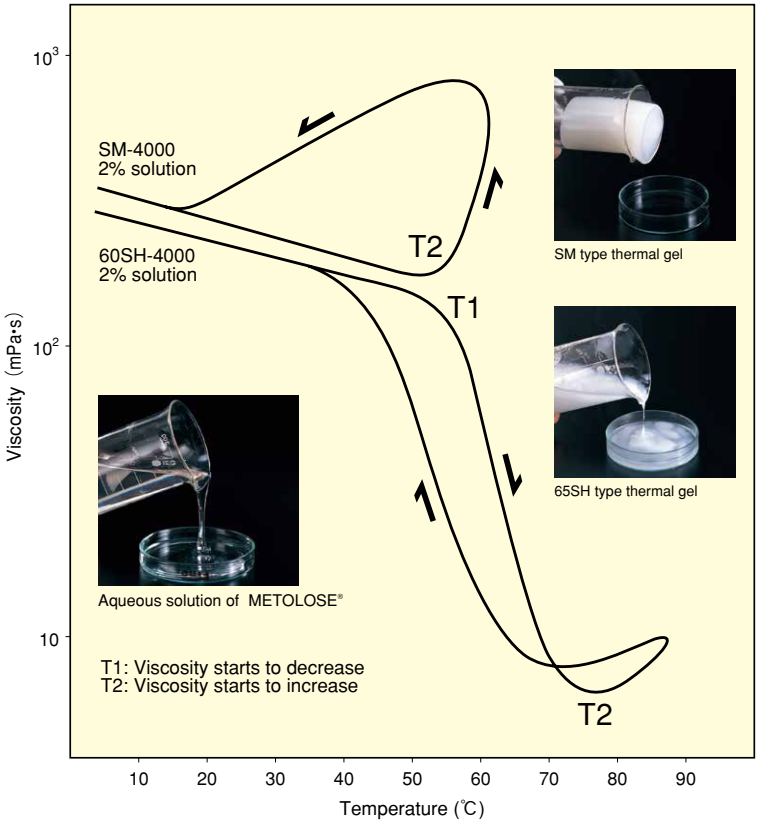


Figure 13. Thermal gelation behavior

Test method:
An aqueous solution of METOLOSE® was heated and subsequently cooled at a constant rate. During the heating and cooling, its viscosity was measured using a torsion oscillation viscometer (Nametre). Heating rate: 1 ℃ /min, cooling rate: 0.5 ℃ /min.

Type \ Item		Thermal gelation temperature (℃) T1	Thermal gelation temperature (℃) T2	gel texture
SM		—	Approx. 55	Hard
SH	60SH	Approx. 55	Approx. 75	Relatively soft
SH	65SH	Approx. 60	Approx. 75	Relatively soft
SH	90SH	Approx. 70	Approx. 85	Soft

The effect of additives on the thermal gelation temperature of METOLOSE® (2 % aq.)

Added Substance \ Type	※ % Added	SM-4000	60SH-4000		90SH-4000	
		T_2	T_1	T_2	T_1	T_2
No additive	0	55	55	75	70	85
NaCl	5	40	45	70	50	60
NaOH	5	40	25	45	45	70
Na_2SO_4	5	Salting out	Salting out	Salting out	25	30
$Na_2CO_3 \cdot 10H_2O$	5	40	30	45	45	60
$Al_2(SO_4)_3 \cdot 18H_2O$	5	45	40	50	50	65
$FeCl_3$	5	50	50	65	65	75
$MgCl_2$	5	55	50	65	60	75
Glucose	5	55	55	75	70	85
Glycerin	5	55	55	75	70	85
Ethanol	5	65	55	80	75	95
Polyethylene glycol	5	55	50	80	70	90

※Weight % based on solution weight.

Other properties

1. Viscosity

The viscosity of solutions of METOLOSE®, as well as other water-soluble polymers, is considered to reflect tangling of long polymeric chains in the solution. Therefore, the viscosity of METOLOSE® solution is related to molecular weight. The molecular weight of METOLOSE® is controlled in the manufacturing process. The following figures show the relationships of viscosity to concentration and temperature.

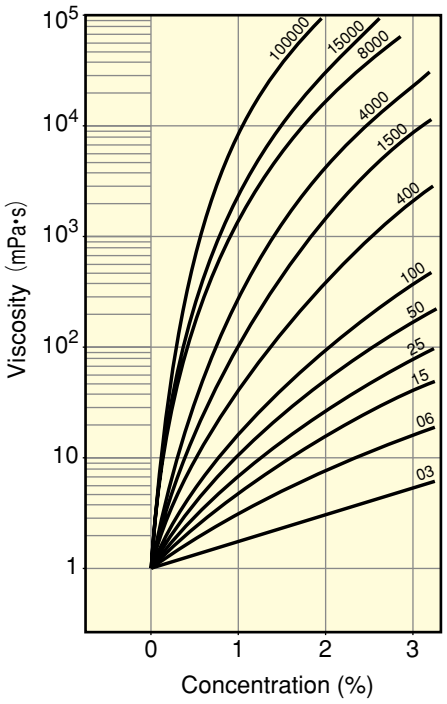


Figure 14. Concentration / viscosity relationship (20℃)

2. Blend of METOLOSE® grades

METOLOSE® products of different viscosity grades can be blended to obtain an intermediate viscosity grade. It can be seen from Fig. 15, for example, that 35 % of 400 mPa·s and 65 % of 1500 mPa·s would give a 1000 mPa·s product.

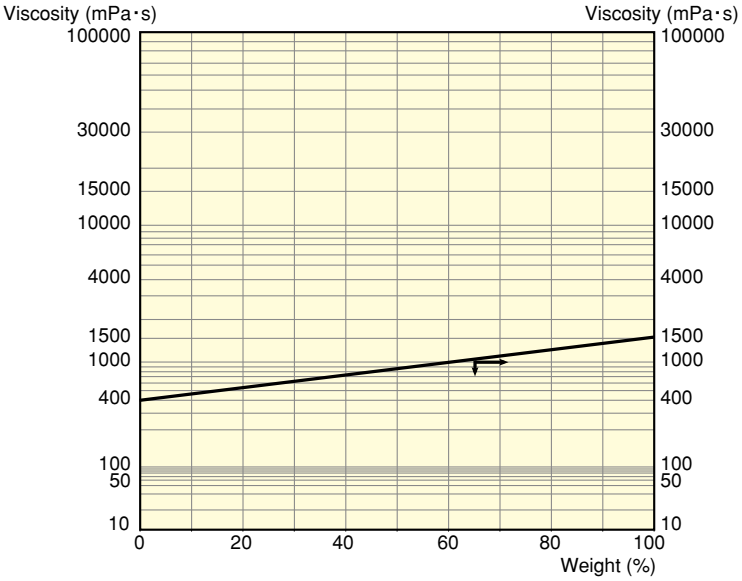
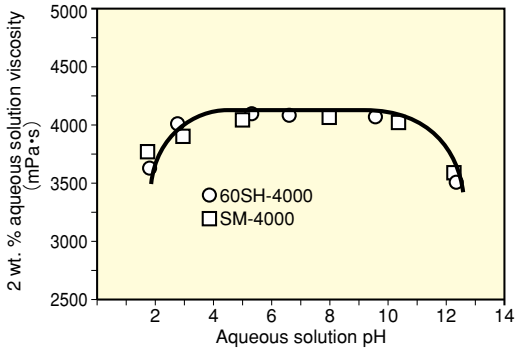


Figure 15. Blending chart for intermediate viscosity

3. Stability at various pH values

METOLOSE® solution maintains a constant viscosity over the pH range of 3-11. At pH outside of this range, the viscosity will be lower. If a METOLOSE® solution is stored at low pH (acidic), its viscosity will be gradually decreased due to depolymerization.

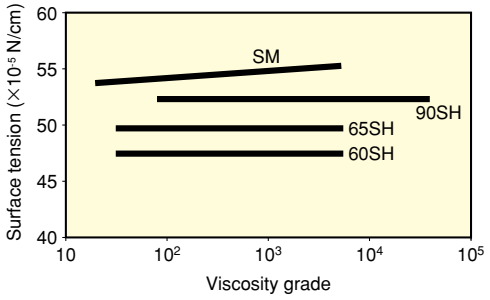


Test method:
A solution was prepared by the hot water method. The pH was adjusted by adding a calculated amount of HCl or NaOH prior to cooling down. Sample concentration: 2 wt%. Viscosity and pH were measured at 20 ℃ .

Figure 16. Effect of pH on viscosity

4. Surface activity

METOLOSE® can be considered as a non-ionic surfactant, as it has both hydrophilic and hydrophobic groups in the molecule. Due to such characteristics, it functions as a superior protective colloid, being effective for stabilization of emulsions, suspensions and foams.



Test method:
Ring method. Concentration: 0.2 wt %.

Figure 17. Surface tension of a 0.2 wt.% aqueous solution of METOLOSE®

5. Solubility in organic solvents

METOLOSE® is a water-soluble polymer and it also dissolved in some organic solvents. Among the substitution types, 60SH has the best solubility in organic solvents. METOLOSE® is insoluble in 100% ethanol.

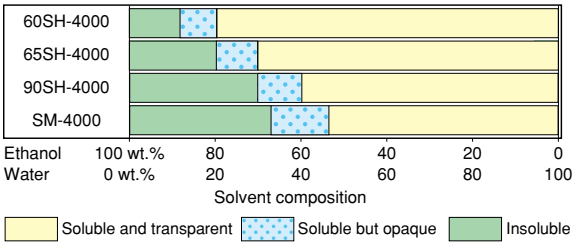
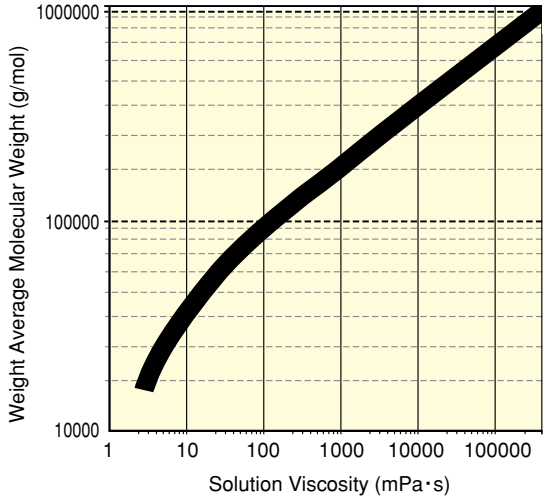


Figure 18. Solubility of each type in organic solvents (2 component system)

6. Molecular weight



Analytical method (GPC-MALLS technique)

-Equipments
Pump: DS-4, Shodex, Tokyo, Japan
MALLS (Muliple angle- laser light scattering detector):
DAWN DSP, Wyatt Technology Corp.
Reflective index detector:RI-71, Shodex, Tokyo, Japan
-Analytical condition
Column: SB-806MHQ, Shodex, Tokyo, Japan at 40℃
Elution: 0.1 M $NaNO_3$ aqueous solution 1.0ml/min.
Sample: 0.1 M $NaNO_3$ aqueous solution
Injected volume: 200 micro liter
-Equation
$Mw = 40000 \times (\mathrm{Log}\ \eta) + 880 \times (\mathrm{Log}\ \eta)^4$
η : solution viscosity

Figure 19. Relationship between the viscosity and molecular weight

Precautions for Safe Handling

Warning: May form flammable or Explosive dust-air mixtures.

When handling, avoid accumulation and suspension of dust in the air.
Store away from heat sources, sparks, and flame. Do not permit grinding, welding, or smoking near this material.
General precautions outlined in the National Fire Protection Association's NFPA654 "Standard for the Prevention of Fire and Dust Explosions from the Manufacturing, Processing, and Handling of Combustible Particulate Solids" and NFPA 77 "Recommended Practice on Static Electricity" are recommended.
(Minimum Explosive Concentration: 30 g/m^3, Methylcellulose)

CAUTION: Spilled powder becomes slippery when wet. May cause eye irritation.

Avoid contact with eyes, skin and clothing.
Wash thoroughly after handling.
Wash contaminated clothing before re-use.
Use only with adequate exhaust ventilation.
Follow and organized house keeping plan.
Keep floors and equipment clean.

Emergency and first aid procedures

If inhaled: Remove to fresh air. Give artificial respiration if breathing stops. Get immediate medical attention.
In case of eye contact: Flush eyes with plenty of fresh water while holding eyelids open. Get immediate medical attention.
In case of skin contact: Wash off with flowing water.

In case of material spills and leakages

The following steps should be taken.
- Wear an approved respirator, rubber gloves, rubber boots and safety goggles.
- Vacuum or sweep up spillage.
  Prevent dust generation. Place spillage in an appropriate container for waste disposal.
- Ventilate area and wash spill site.
- Wash contaminated clothing before reuse.
- If spillage is viscous solution, scrape up as much as possible before flushing it with plenty of water.
  Place the scraped spillage in an appropriate container for waste disposal.

Storage

Keep dry. Store away from excess heat and sunlight. Store in sealed containers.

Disposal

Contents: Dispose of unused contents in accordance with all applicable federal, state and local laws.
Consult the distributor for further information.
Container: Do not re-use container. Dispose of empty container by incineration or the procedures approved by federal, state and local authorities.

****

Carefully read and understand the safety data sheet (SDS) before using this product.

N O T E :

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