

General name: Hydrophobically modified hydroxypropylmethycellulose

INCI name: Hydroxypropylmethylcellulose Stearoxy Ether

SANGELOSE®

New thickener of a Cellulose derivative

Ideal performance of thick gelation

Possible to combine with Vitamin C derivatives

Possible to combine with Salts



Manufacturer:



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【Product Name】 Hydrophobically modified hydroxypropylmethycellulose

【INCI name】 HYDROXYPROPYL METHYLCELLULOSE STEAROXY ETHER

【DMF】 Registered in 2009

【CAS】 141615-27-2

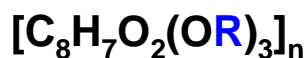
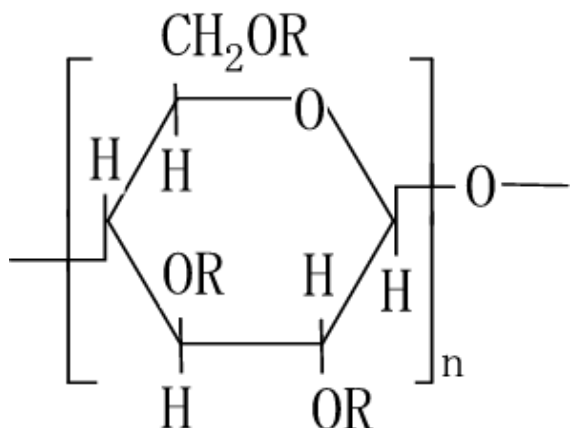
【Type】 60L、 60M、 90L、 90M

【Description】 White to yellowish white powder and transparent in liquid after mixing into a solution

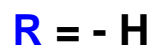
About SANGELOSE(2)



SANGELOSE (Hydroxypropylmethylcellulose Stearoxy Ether) is a pharmaceutical and cosmetic excipient in which C18 (stearyl group) was introduced to Hypromellose (HPMC).



Long chain group (hydrophobic group)



There are four kinds of SANGELOSE (60L,60M,90L,90M) where the molecular weight and the substitution degree of the hydrophobic group are different.

	Molecular weight	L Type	M Type
Hydrophobic group (wt%)		0.3 ~ 0.6	1.0 ~ 2.0
60 series	Middle	water soluble	water insoluble
90 series	High	water soluble	water insoluble



【Characteristic】 (Ideal performance for a thickener)

- **Good solubility**

 - Dissolves easily. Not dissolved in hot water.

 - Mixes well leaving no fisheye effect.

- **Thicken with small quantity**

 - Compared with HPMC, HEC etc, 1/2~1/3 quantity is enough to thicken the target.



- **Make thixotropic gel**, good shape stability and good stretch in application.
- With hydrophobic group, high skin affinity doesn't make gel sticky.
- **Compared with normal cellulose derivatives like HPMC, HEC etc, it has good sensory touch in use.**
- **Good combination with ionic composition.**
- **Good stability combined with various salts. The combination use with vitamin C derivatives is possible.**

Standard of SANGELOSE



Grade	60L	60M	90L	90M
Description	Confirm			
Identification (1)~(4)	Confirm			
Viscosity(mm ² /s)	72 ~ 108		160 ~ 240	
p H	5.5 ~ 7.5			
Purity test (1) Chloride (2) Heavy metals (3) Ether extract	Not more than 0.284% Not more than 10ppm Not more than 0.2%			
Loss on drying(%)	Not more than 5.0%			
Residue on ignition(%)	Not more than 0.10%			
(1) Methoxyl group(%)	27.0 ~ 30.0		21.5 ~ 24.0	
(2) Hydroxypropoxy group(%)	7.0 ~ 11.0		7.0 ~ 11.0	
(3) Stearyloxyhydroxypropoxyl group (%)	0.3~0.6	1.0~2.0	0.3~0.6	1.0~2.0

Safety tests SANGELOSE has passed



- **Single dose oral toxicity study in rats**
- **Single dose dermal toxicity study in rats**
- **Primary dermal irritation study in rabbits**
- **Primary eye irritation study in rabbits**
- **Dermal Photosensitivity study in guinea pigs**
- **Dermal sensitization study in guinea pigs**
- **30days dose repeated dose toxicity study in rats**
- **6 month repeated dose toxicity study (30days recovery) in rats**
- **Reverse mutation test in bacteria (Ames test)**
- **Chromosomal aberration test with mammalian cells in culture**
- **Micronucleus test in mice**
- **Patch test on human skin**



■ How to dissolve (in laboratory)

Add suitable quantity of SANGELOSE into hot water(over 70°C), mix it in about 1 min. Then, mix it in ice bath. Dissolved and thickened with bubble. (Add suitable quantity of alcohol after cooling for Sangelose M and H type)

■ Solubility for Water /Ethanol



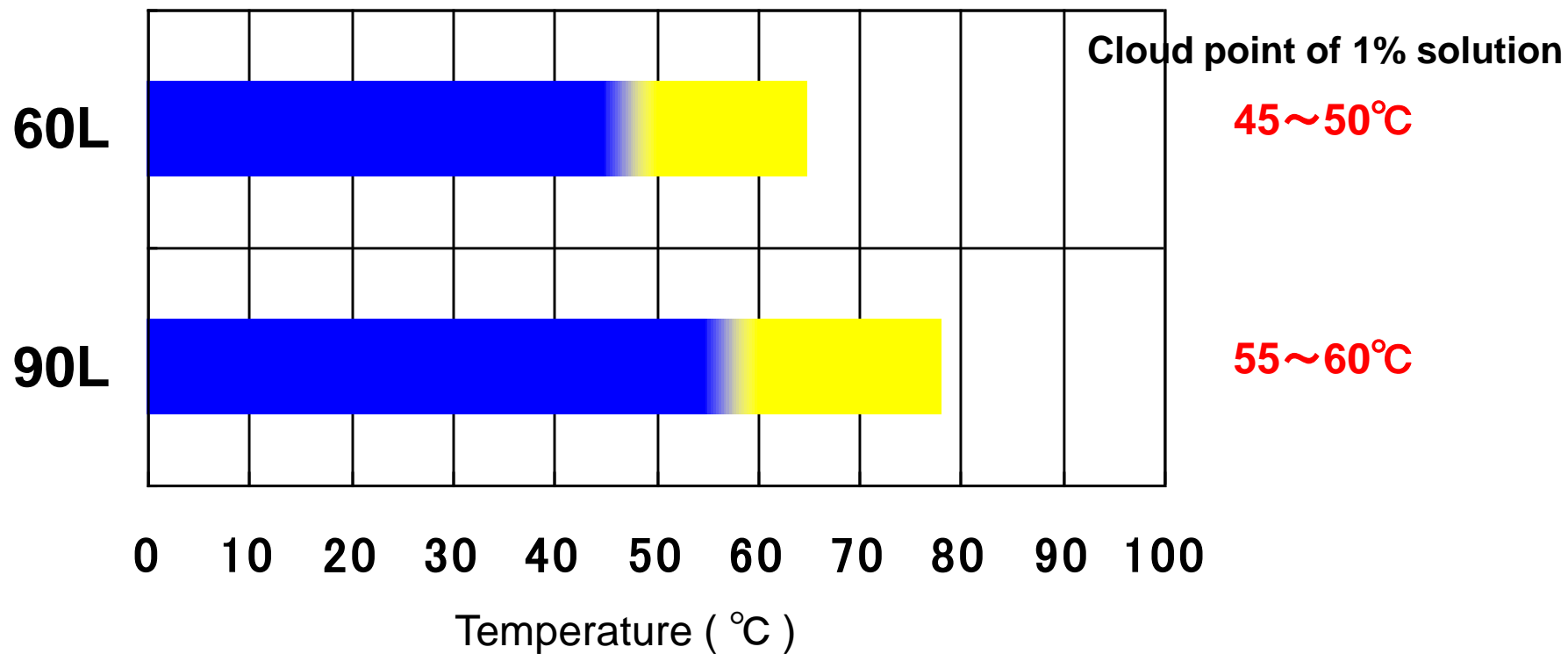
Type (Long chain alkyl group)		Conc. of ethanol in solution (%)										
		0	10	20	30	40	50	60	70	80	90	100
L type	60L	Soluble (Blue bar)										
	90L	Soluble (Blue bar) until 60%, Slightly cloudy (Yellow/Blue gradient) from 60% to 70%										
M type	60M	Slightly cloudy (Yellow/Blue gradient) until 20%, Soluble (Blue bar) from 20% to 80%										
	90M	Slightly cloudy (Yellow/Blue gradient) until 30%, Soluble (Blue bar) from 30% to 60%										

Solubility (2)

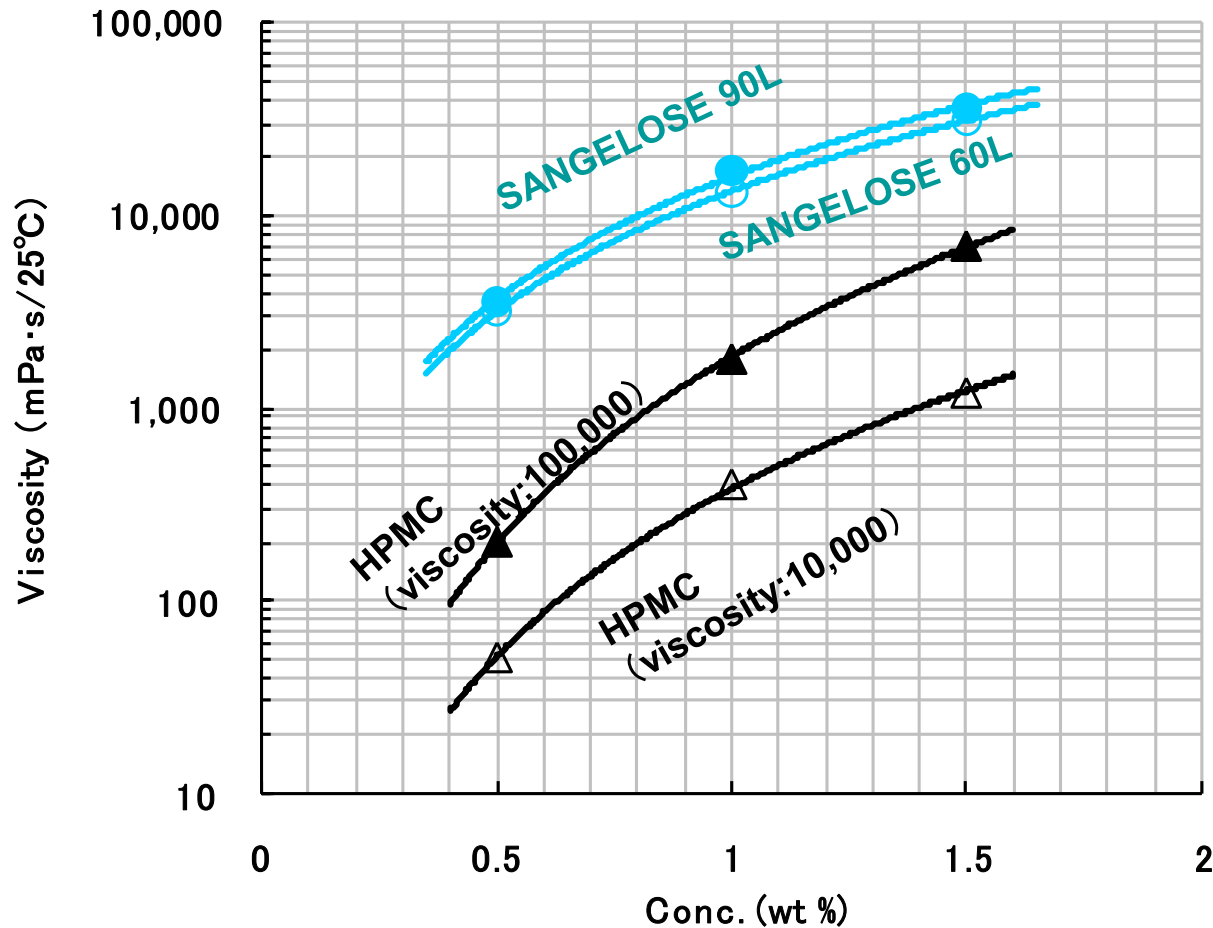
■ SANGELOSE solution change by temperature (1.0 wt%)



■ Soluble
■ Slightly cloudy

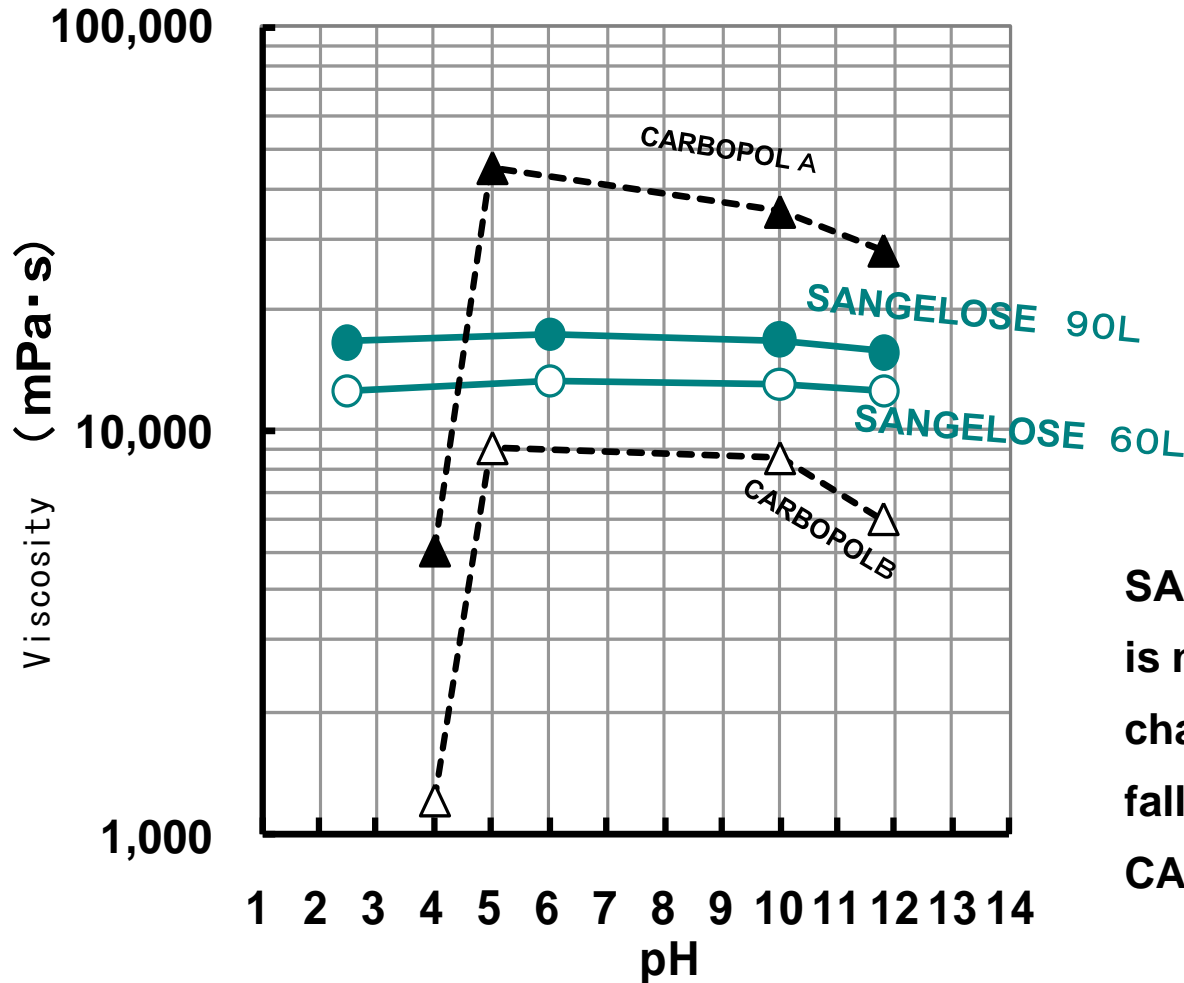


■ Relation of Concentration and Viscosity



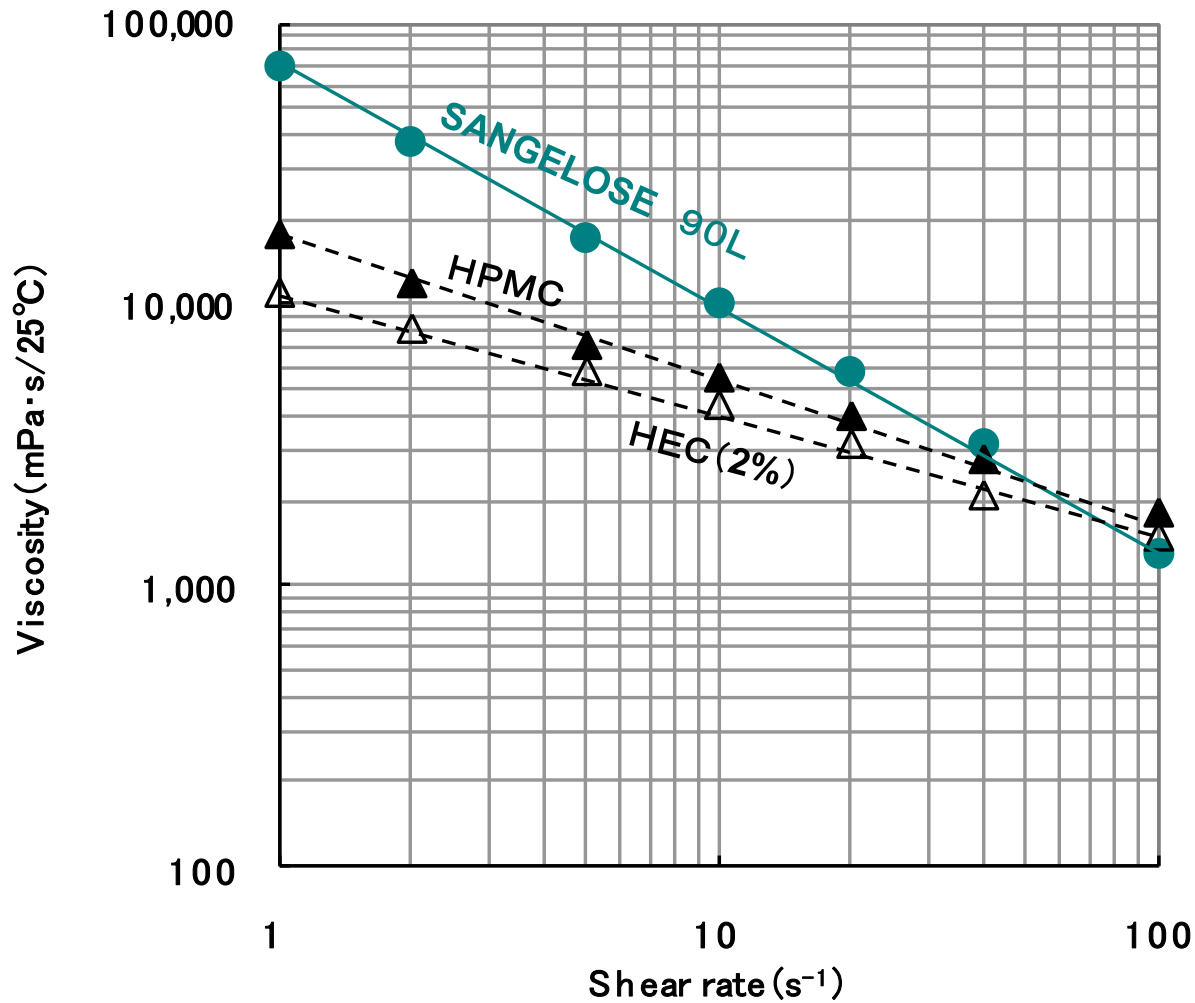
Compared with normal cellulose derivative, small quantity of SANGELOSE is enough to thicken.

■ Influence of pH on viscosity (1.0 wt% aq. 25°C)



SANGELOSE's viscosity is not influenced by pH change, though it one falls rapidly in case of CARBOPOL.

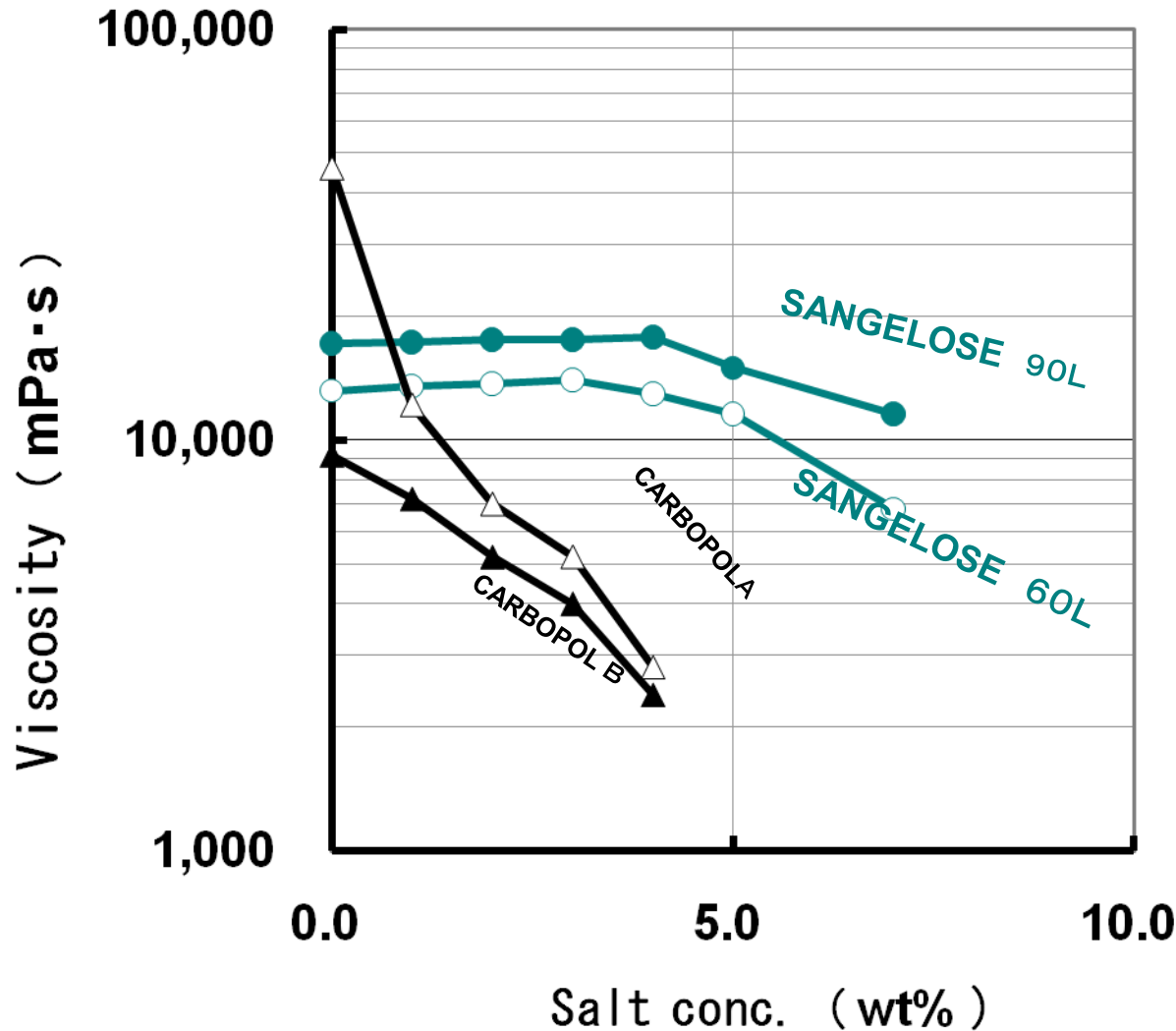
■ Relation of Shear rate and Viscosity (1.0 wt% aq.)



Compared with HPMC, HEC, SANGELOSE make thixotropic gel.



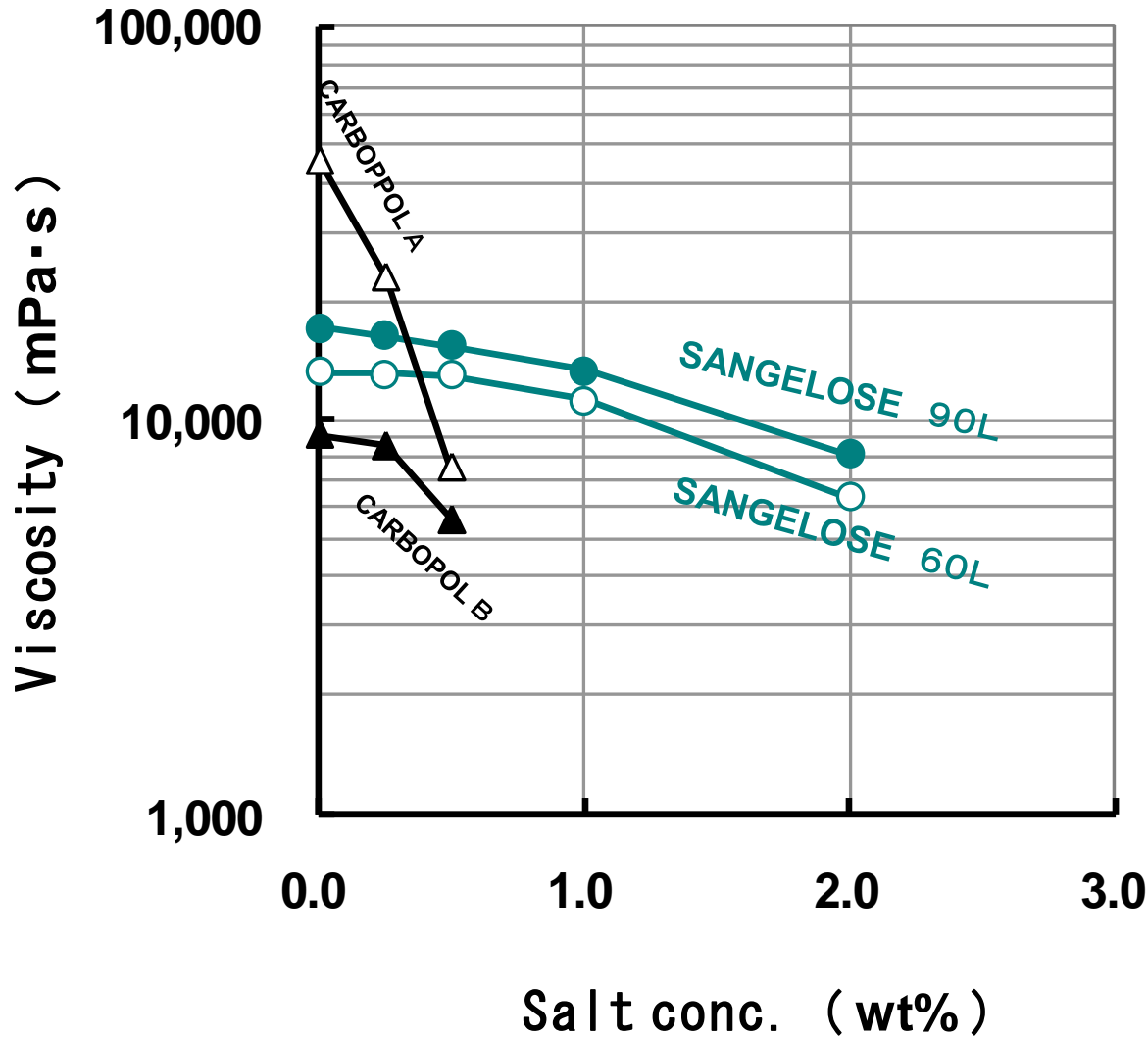
■ Viscosity influence in NaCl (1.0 wt% aq. 25°C)



SANGELOSE's viscosity is little influenced by NaCl.



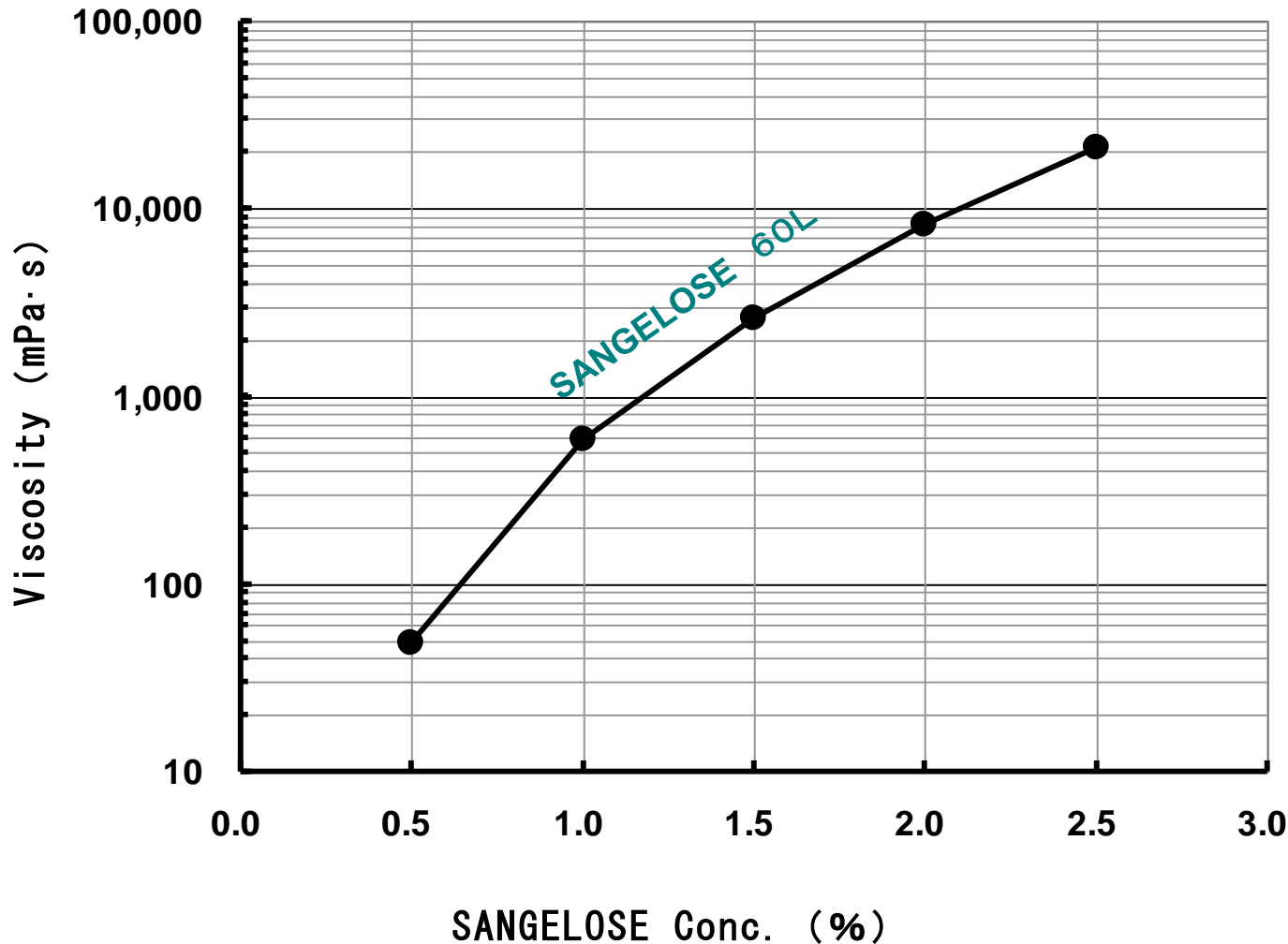
■ Viscosity influence in **MgSO₄** (1.0 wt% aq, 25°C)



SANGELOSE's viscosity is little influenced by MgSO₄.



■ Concentration-Viscosity curve in 50% ethanol solution (25°C)

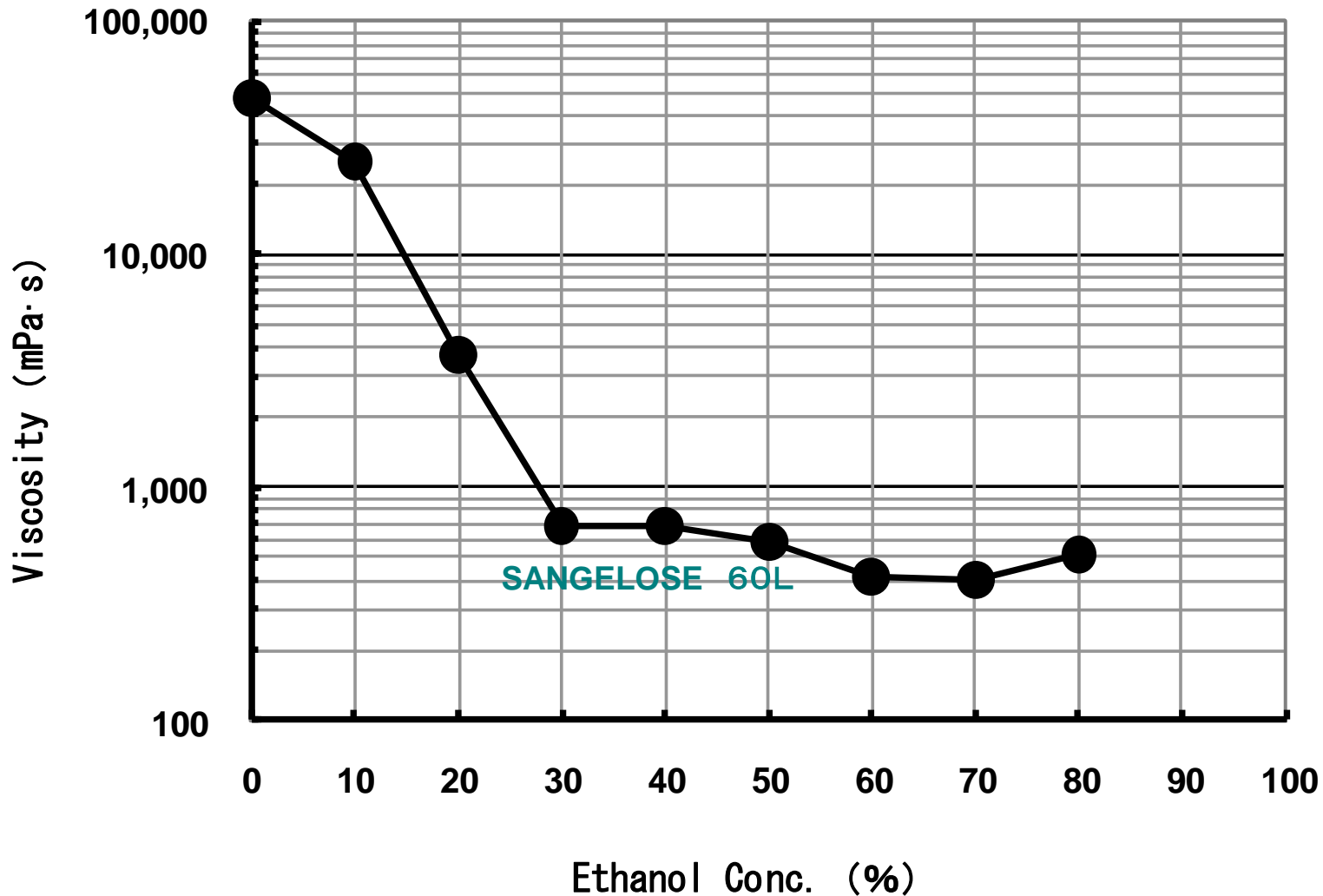


When added alcohol, the viscosity of **SANGELOSE** solution becomes thickened liquid to non-fluid gel, up to added quantity.

Viscosity character (7)



■ Influence of ethanol concentration on the viscosity of SANGELOSE 60L (1%, 25°C)





Composition for cosmetics with Vitamin C derivative(For whitening)

Because of BSE(Bovine Spongiform Encephalopathy), Placental Protein can't be used, and Vitamin C derivative is recognized suitable instead.

For example..

- Magnesium Ascorbyl Phosphate
- Sodium Ascorbyl Phosphate
- Ascorbic Acid 2-Glucoside

Though these derivatives with Carbopol are not stable in terms of color, **SANGELOSE doesn't affect color change and viscosity decline.** It can make stable cosmetics.

(Under consideration) Lotion or foundation cream with Vitamin C derivative.

SANGELOSE application(2)–1



- Stability with 3% Sodium Ascorbyl Phosphate (0.5%aq.)

40°C, after 4 weeks

With SANGELOSE



With Carbopol



SANGELOSE application(2)–2



■ Stability with 3% Sodium Ascorbyl Phosphate (0.5%aq. 25°C)

		After mix	1 week	2 weeks	4 weeks
SANGELOSE 90L	Color	Slightly yellow	Slightly yellow	Slightly yellow	Slightly yellow
	Absorbance	0.035	0.033	0.042	0.052
	Viscosity	3,120	3,060	3,140	3,170
Carbopol	Color	Yellow	Yellow	Yellow	Yellow
	Absorbance	0.107	0.180	0.231	0.302
Without thickener	Color	Slightly yellow	Slightly yellow	Slightly yellow	Slightly yellow
	Absorbance	0.005	0.005	0.008	0.013

Absorbance : 420nm

SANGELOSE application(3)



■ Stability with 3% Ascorbic Acid 2-Glucoside (0.5%aq. 25°C)

		After mix	1 week	2 weeks	4 weeks
SANGELOSE 60L	Color	Slightly yellow	Slightly yellow	Slightly yellow	Slightly yellow
	Absorbance	0.024	0.017	0.019	0.023
	Viscosity	1,800	1,780	1,720	2,060
SANGELOSE 90L	Color	Slightly yellow	Slightly yellow	Slightly yellow	Slightly yellow
	Absorbance	0.038	0.043	0.040	0.033
	Viscosity	1,720	2,020	1,860	2,060
Without thickener	Color	Slightly yellow	Slightly yellow	Slightly yellow	Slightly yellow
	Absorbance	0.004	0.010	0.014	0.030

Absorbance : 420nm



■ Composition for Moisturizing cream

O/W Gel Cream prescription example

A	Pure water	28.4
	1, 3-Butylene glycol	5.0
	Glycerolglycerin	2.5
	SANGELOSE 60L (1% water solution)	50.0
B	Cetearyl alcohol	1.0
	Dimethicone (6cs)	2.0
	Macadamia Oil	2.5
	Jojoba oil	2.5
	Squalane	2.5
	Tocopherol	0.1
	Emulium Delta	3.0
	Phenoxyethanol	0.5

100.0



■ Composition with TiO₂ (For UV protection)

Though nano size TiO₂ is used in cosmetics for UV protection, TiO₂ might be aggregated by Carbopol gel. However, SANGELOSE can make stable cream without such a problem.

■ Composition with cationic material (For hair care products)

Though HEC and HPC are used in combination with cationic materials for physical stability, its sensory touch is not good. SANGELOSE can make a thixotropic gel and its long alkyl group has a good affinity with skin lipids. Thus, SANGELOSE can make stable products which feel good to the touch.



■ Application for Hair care products (Sensory test)

Test : Ten subjects, 20 to 50 years of age, applied a 1 % content of various high polymer/water solutions (40g) in their hair. Leave in for 5min at room temperature. After, rinse with water and dry. Evaluate the sensory touch of hair in wet and dry conditions.

Sensory Touch Result (Wet condition) (Good ~ Poor =5 ~ 1)

	Stretch	Flexibility	Smoothness
1% SANGELOSE 90L	4.3	4.6	4.3
1% HEC	2.4	2.4	2.9
1% High polymerized PEG	4.0	1.4	1.4
1% Guar gum	2.4	2.6	3.0
1% Carrageenan	3.0	2.6	3.0
1% Glucomannan	3.1	3.0	3.0



Sensory Touch Result (Dry condition) (Good ~ Poor =5 ~ 1)

	Flexibility	Smoothness	Freshness
1% SANGELOSE 90L	4.6	4.6	3.6
1% HEC	1.4	2.9	1.4
1% High polymerized PEG	1.4	1.4	1.4
1% Guar gum	3.0	3.0	2.7
1% Carrageenan	3.1	3.0	2.7
1% Glucomannan	3.0	3.0	2.6

**Adopted application : Shampoo, Treatment, Conditioner,
Hair manicure etc.**



■ Other application examples

Good stability with Salt

⇒ Thickener for deep sea water cosmetics rich in minerals.

Good stability with Acid

⇒ Thickener for cosmetics with fruit acid.

Good compatibility with alcohol

⇒ Thickener for deodorants with alcohol

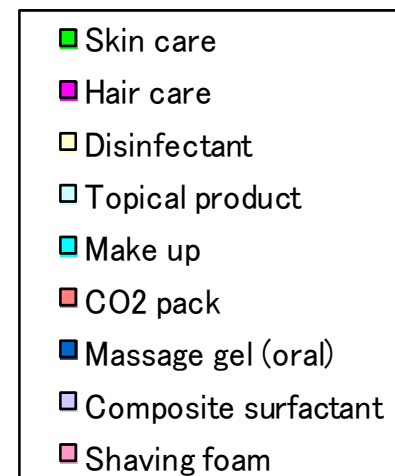
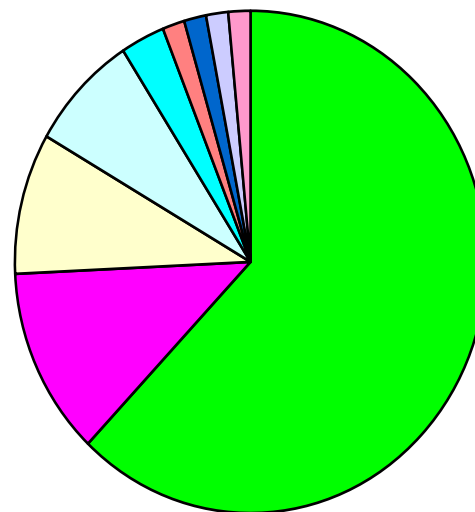
Water insoluble (Sangelose M type)

⇒ Ideal for eyeliners and eyebrow makeup having good stability against sweat and tears.



Current applications of SANGELOSE in the pharmaceutical and cosmetic fields

application	Applied numbers
Skin care	41
Hair care	8
Disinfectant	6
Topical product	5
Make up	2
CO2 pack	1
Oral gel	1
Composite surfactant	1
Shaving foam	1
total	66



Recent application (1)

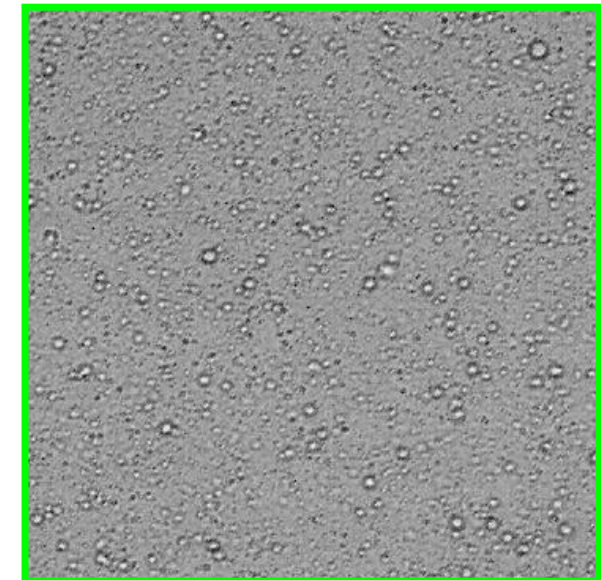
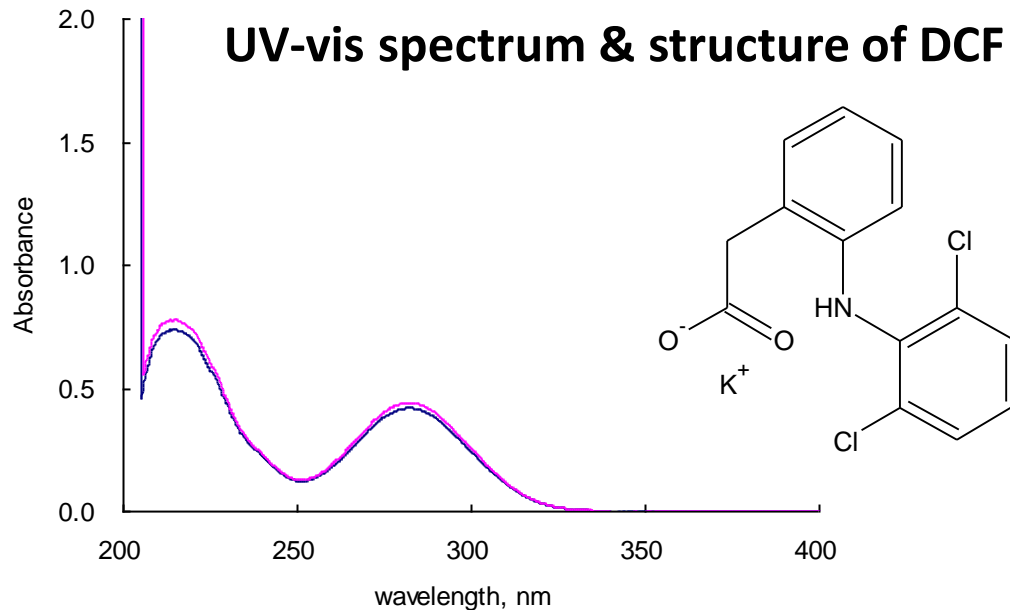


Preparation and Properties of Surfactant-free Diclofenac Emulgel Using SANGELOSE as the Gel Matrix

Hui Xu (徐暉), Dongchun Liu (劉東春), Sijie Zhang (張斯傑), Xing Tang (唐星)
(Shenyang Pharmaceutical University)

Toshio Shimamoto, Yasunari Inamoto (Daido Chemical Corporation)

The 28th The Society of Powder Technology, Japan / Division of Particulate Design and Preparations ,
Osaka, Japan-Oct 26, 2011



Microscopic image of
SANGELOSE Emulgels

4-1. The drug release and transdermal flux



The drug release percentages at 8h and steady-state flux of transdermal permeation of prepared emulgels and commercial gels

	$Q_{8h}, \%$	$J_{ss}, \text{mg cm}^{-2} \text{h}^{-1}$
90L	52.8 ± 7.6	0.138 ± 0.028 ↑
90L+T80	55.3 ± 6.4	0.034 ± 0.011
90L+LP	59.4 ± 3.6	0.069 ± 0.015
60L	63.4 ± 3.0	0.089 ± 0.034 ↑
HPMC+T80	60.2 ± 3.6	0.061 ± 0.010
Carbomer+T80	35.4 ± 5.2	0.024 ± 0.014
Pemulen	33.8 ± 1.1	0.046 ± 0.013
Voltaren®	22.5 ± 2.9	0.058 ± 0.007
Jiuning®	37.7 ± 4.0	0.048 ± 0.012

Recent application (2)



Preparation of nano-emulsion by using a microfluidizer

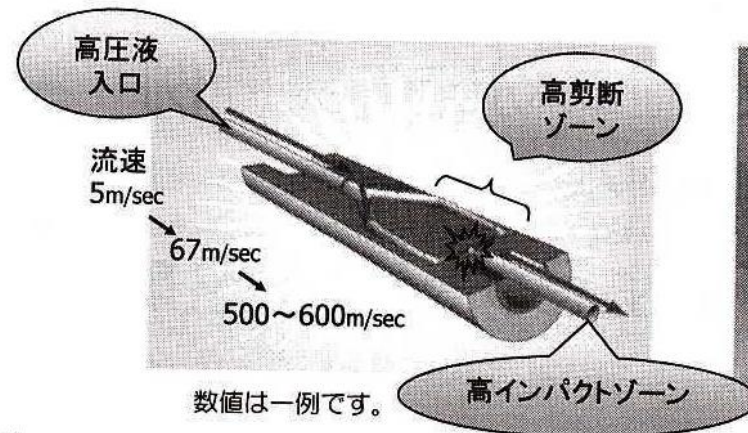
K. Miura, M. Fujii, S. Aiuchi, N. Koizumi, Y. Watanabe,
Showa Pharmaceutical University,
The Academy of Pharmaceutical Science and Technology, Japan (2010)

M-110-E/H



仕様

調圧範囲	(MPa)	21~172
処理量	(mL/min)	80~400
動力	(kW)	3.7



Slit diameter; 75µm

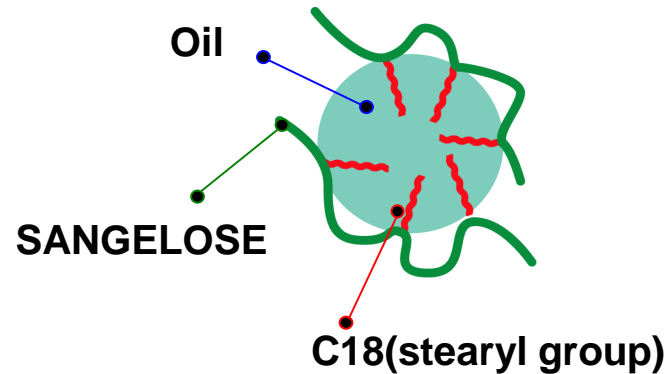
The nano-emulsion can be prepared by using a microfluidizer with an extremely high shearing rate.

Recently, by using SGL as an emulsifier (alternative surfactant), ca. 500nm of nano-emulsion was prepared by a microfluidizer.

4-2. Stability of a nano-emulsion by Microfluidizer



Recently, by using SGL as an emulsifier (alternative surfactant) ca. 500nm of nano-emulsion was prepared by a microfluidizer.



Tab. Stability results

Oil	0 day	7 day	60 day
LP (nm)	500	500	510
SO (nm)	520	450	500
MCT (nm)	500	520	530

Emulsifier ; SGL (1w/w%), Model drug ; Diphenhydramine

Preparation ; Microfluidizer (70MPa, 10pass)

Oil ; Liquid paraffin (LP), Soybean oil (SO), Middle chain fatty acid triglyceride(MCT)