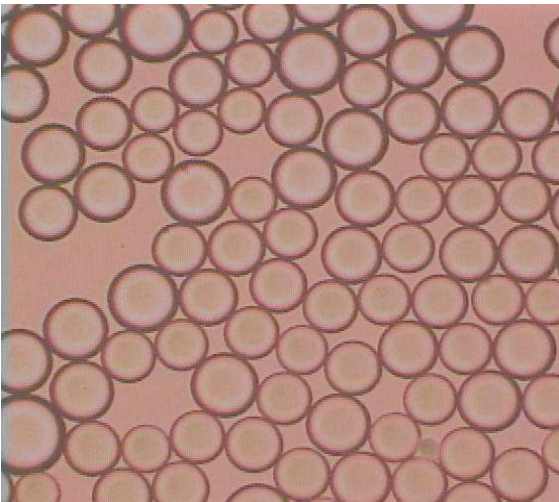


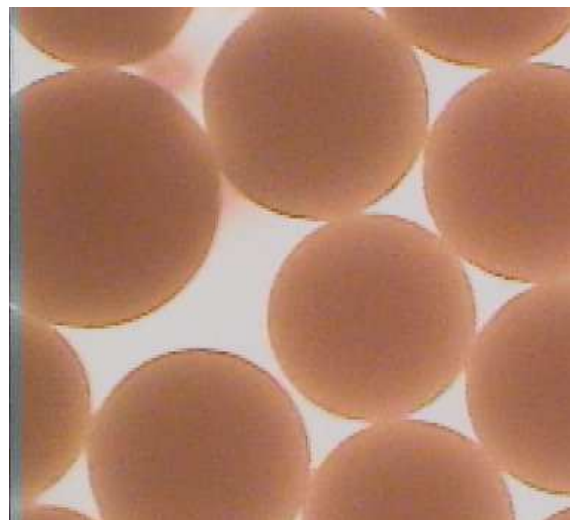
SPG Membrane Emulsification

Technical Bulletin



Monodisperse emulsion (O/W)

Double emulsions (W/O/W)



SPG Technology Co., Ltd.



e-mail:spg@spg-techno.co.jp

http://www.spg-techno.co.jp



< About SPG Membrane Emulsification >

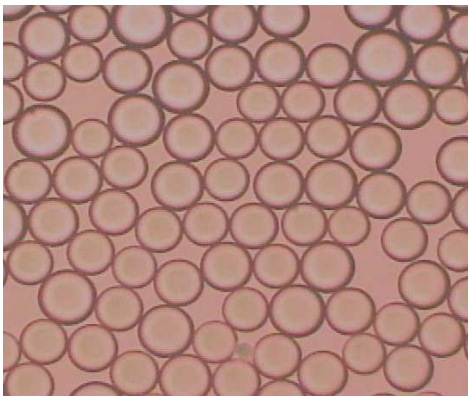
The method of preparing an emulsion by extruding an emulsion liquid from narrowly distributed SPG membrane pores is called "SPG membrane emulsification". Since the beginning of SPG membrane development, it has been studied to be applicable to various fields as an application utilizing the characteristics of SPG membrane.

< Special feature >

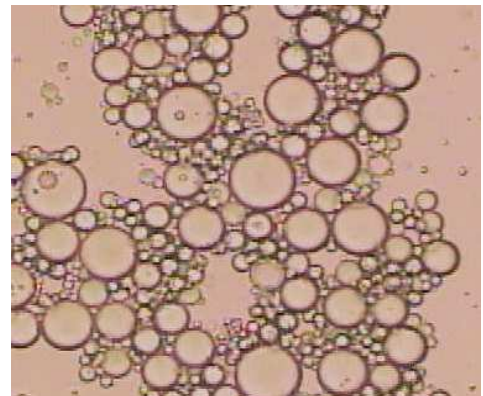
- : Preper to easy monodisperse emulsion
- : The particle size can be adjusted by changing the SPG membrane pore size.
- : Compatible with single emulsions (O/W and W/O).
- : Compatible with double emulsions (W/O/W and O/W/O).
- : Applicable to emulsion containing fine particles such as S/O/W.
- : Applicable to various fields such as medicine, chemistry, cosmetics, food
- : Energy saving and hardly affected by heat

< Comparison with other emulsification methods >

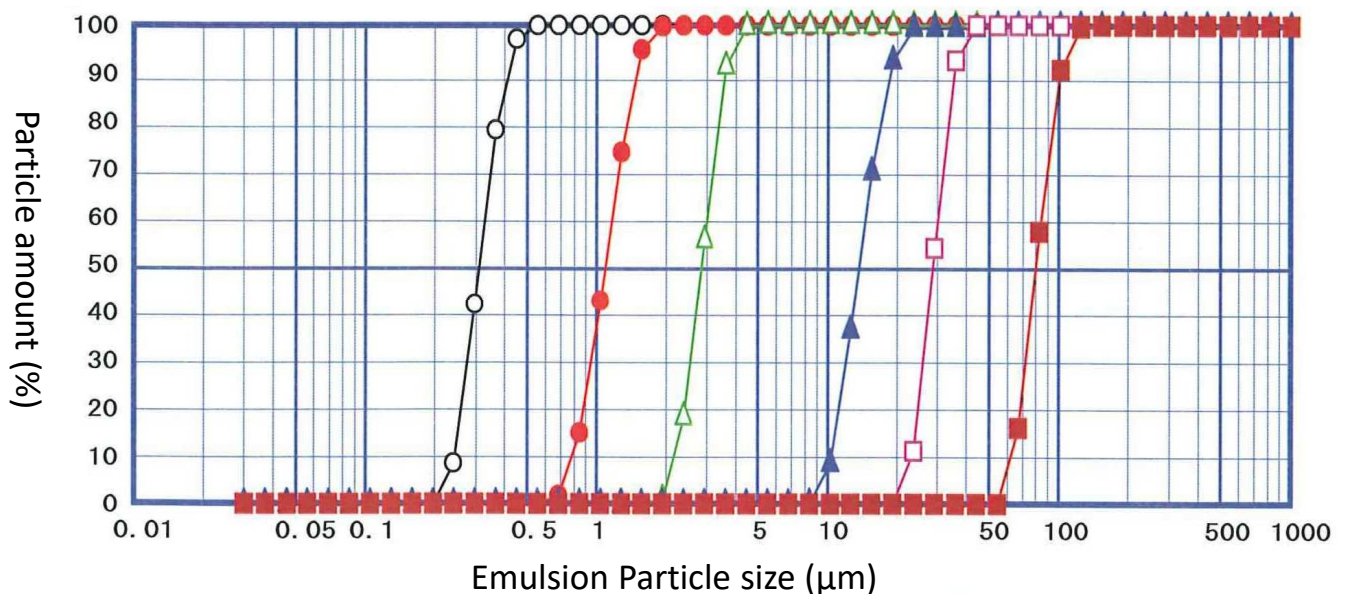
SPG Membrane Emulsification
(Direct Emulsification)



High speed shearing homogenizer
(IKA Homogenizer)



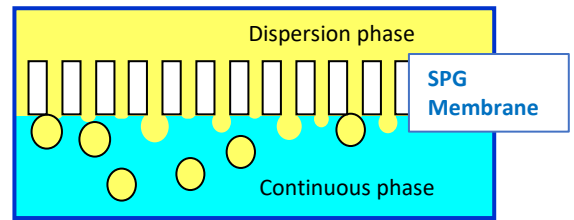
< Emulsion distribution by SPG membrane emulsification > (Direct Emulsification)



< Type of SPG membrane emulsification >

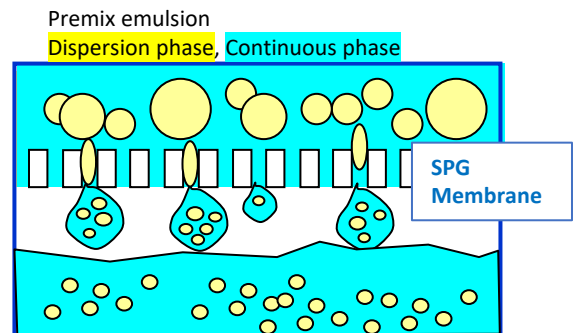
1. Direct Emulsification

This emulsification method disperses the dispersion phase directly from the SPG membrane into the continuous phase. The emulsion size is 3 - 4 times the SPG membrane pore size (D_m). And monodisperse emulsion can be obtained with high accuracy. In addition, the emulsion particle size can be controlled by changing the pore size of the SPG membrane.



2. High speed Emulsification (Premix)

This emulsification method allows the premixed emulsion liquid to permeate through the SPG membrane at a high flow rate, shearing the emulsion and aligning the particle size. The emulsion size is less than 1 times the SPG membrane pore size (D_m), and the emulsion flux speed is very fast. As with direct membrane emulsification, the emulsion size can be controlled by changing the SPG membrane pore size.



< Comparison of emulsification type >

	Direct Emulsification	High speed Emulsification (Premix)
Emulsification principle	Disperse	Shear
Emulsion size The emulsion size can be changed by changing the SPG pore size.	SPG pore size \times 3-4 times	SPG pore size \times 1 time or less
Emulsification time	Very slow e.g) Use 3 μ m SPG membrane to make 10 μ m emulsion with internal pressure micro kit. The flow rate of the dispersed phase at that time is "3ml/h".	Very fast e.g) Use 15 μ m SPG membrane to make 10 μ m emulsion with internal pressure micro kit. The flow rate of the premix emulsion at that time is "1ml/sec".
Monodispersity	◎ Direct emulsification can adjust monodisperse emulsion with higher accuracy.	○ Compared with other emulsification methods (High speed stirring, high pressure homogenizer, etc.), a highly accurate monodisperse emulsion can be obtained.
Practicality	It is suitable for producing monodisperse emulsions with a small amount and high added value.	It is suitable for emulsifying a large amount with monodispersity. In actual production, continuous emulsification is also possible.

< Type of Emulsion >

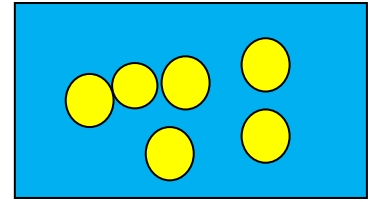
1. O/W (Oil in Water)emulsion

Dispersion phase = Oil or Hydrophobic solvent

Continuous phase = Aqueous solution with surfactant

: Uses “**Hydrophilic**” SPG membrane

: Can be prepared by “Direct emulsification” or “High-speed emulsification”



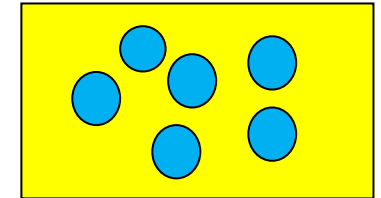
2. W/O (Water in Oil)emulsion

Dispersion phase = Water solution

Continuous phase = Oil or Hydrophobic solvent with surfactant

: Uses “**Hydrophobic**” SPG membrane

: Can be prepared by “Direct emulsification” or “High-speed emulsification”



3. W/O/W (Water in Oil in Water)emulsion

Inner Water (W1) = Water solution

Oil phase = Oil or Hydrophobic solvent with surfactant

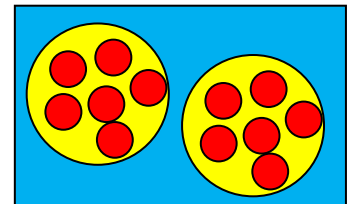
Outer water phase (W2) = Water solution with surfactant

: Manufacturing flow

① Primary emulsification = W/O emulsion is prepared

② Secondary emulsification = W/O prepared by primary emulsification is used as dispersed phase and emulsified with **hydrophilic** SPG membrane.

: Can be prepared by “Direct emulsification” or “High-speed emulsification”



* The primary emulsified W/O emulsion particles are desirably 1/10 or less of the pore size of the SPG membrane used in the secondary emulsification. When W/O particles are large, they are filtered through an SPG membrane.

* **High encapsulation rate**

The membrane emulsification method can efficiently enclose the inner aqueous phase.

4. S/O/W (Solid particle) in Oil in Water)emulsion

Solid particle

Oil phase = Oil or Hydrophobic solvent

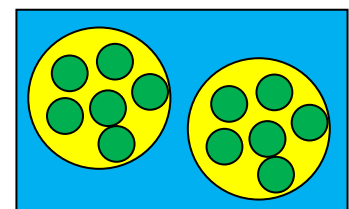
Outer water phase = Water solution with surfactant

: Manufacturing flow

① S/O preparation = Disperse S in Oil

② Emulsification = S/O is used as dispersed phase and emulsified with **hydrophilic** SPG membrane.

: Can be prepared by “Direct emulsification” or “High-speed emulsification”



* The Solid particles are desirably 1/20 or less of the pore size of the SPG membrane used in the emulsification. When Solid particle is large, they are filtered through an SPG membrane.

< Remarks >

* **Emulsified composition**

: Amphiphilic liquids cannot be used.

: Liquids that react with the SPG membrane (silicon oil, etc.) cannot be used.

* **Surfactant**

: Usable : Anionic nonionic surfactant

: Unusable : Cationic. Including proteins such as lecithin

* The SPG membrane surface is negatively charged. Therefore, it cannot be used with a positive charge.

Application examples of SPG membrane emulsification

1. O/W emulsion with "PLGA "

: Method = Direct Emulsification

: Device = Internal pressure micro kit (MN-20)

: Composition

; Dispersion phase ; PLGA (dl-lactic-co-glycolic acid)

; Continuous phase ; 0.35wt% PVA (polyvinyl-alcohol) solution

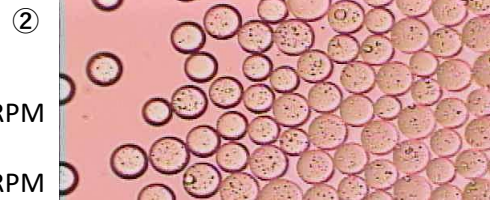
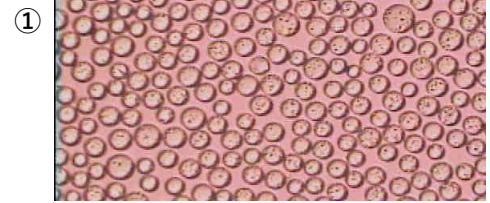
: Emulsification Conditions / Results

① SPG membrane pore size = 6.1 μ m \rightarrow Emulsion size = 14 μ m

(Emulsification pressure = 8kPa, Continuous phase stirring speed = 300 RPM)

② SPG membrane pore size = 10.8 μ m \rightarrow Emulsion size = 24 μ m

(Emulsification pressure = 2kPa, Continuous phase stirring speed = 300 RPM)



2. W/O/W emulsion with "Anticancer drugs "

: Method = Direct Emulsification

: Device = Filter kit (CP-20)

: Composition

Inner Water (W1) = Epirubicin (60mg) + 10wt% Lactose water 3ml

Oil phase = Lipiodol® Ultra Fluid 5ml + 10wt/vol% PGCR

Outer water phase (W2) = 0.7wt% HCO60 + 0.4wt% NaCl solution 7.5ml

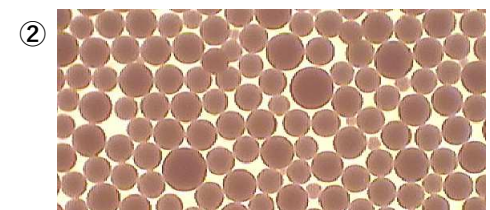
: Emulsification Conditions / Results

① Primary emulsification

* Emulsification with high speed stirring \rightarrow Emulsion size = 1 - 3 μ m

② SPG membrane pore size = 20 μ m \rightarrow Emulsion size = 70 μ m

(Dispersion speed (syringe speed) = 10ml/h, Continuous phase stirring speed = 300 - 1100 RPM)



3. W/O emulsion with "Sodium Silicate Solution "

: Method = Direct Emulsification

: Device = External Pressure micro kit (MG-20)

: Composition

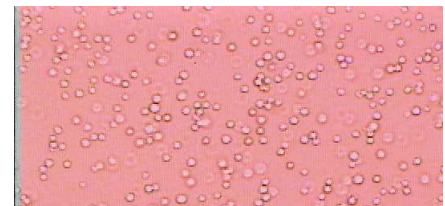
; Dispersion phase ; Sodium Silicate Solution

; Continuous phase ; kerosene + 1wt% PGCR

: Emulsification Conditions / Results

① SPG membrane pore size = 1.3 μ m \rightarrow Emulsion size = 4.5 μ m

(Emulsification pressure = 28kPa, Continuous phase stirring speed = 400 RPM)



4. O/W emulsion with "Styrene Monomer"

: Method = High speed Emulsification (Premix)

: Device = High speed mini kit (KH-125)

: Composition

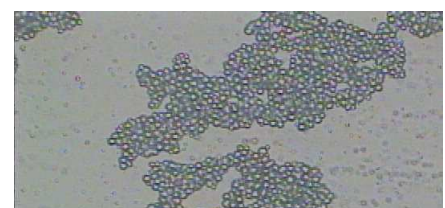
; Dispersion phase ; Styrene Monomer + 2wt% Peroxybenzoic acid

; Continuous phase ; 0.5wt% SDS solution

: Emulsification Conditions / Results

① SPG membrane pore size = 4.2 μ m \rightarrow Emulsion size = 3.7 μ m

(Emulsification pressure = 150kPa)





SPG Membrane Emulsification

DEVICES

for Laboratory

: Disposable Device

: Micro scale Device

: Mini scale Device

Scale up Equipment

SPG Technology Co., Ltd.



< e-mail >

[e-mail:spg@spg-techno.co.jp](mailto:spg@spg-techno.co.jp)

<http://www.spg-techno.co.jp>



< HP >

< Devices List for Laboratory > For "Direct Emulsification" Devices

Line up	Emulsification Effective area	Emulsion preparation amount		(μm)		(μm)	
		Dispersion phase	Continuous phase	Min	Max	Min	Max
Direct connector (DC)	0.4cm ²	2.5ml *2	5ml *3	1	50	3	200
Filter kit (CP-10K)	2.5cm ²	2ml or more (max 5ml)	6ml	1	50	3	200
Filter kit (CP-20K)	5.6cm ²	2ml or more (max 7ml)	8ml	1	50	3	200
Internal pressure micro kit (MN-20)	3.2cm ²	Min 3ml Max 10ml *4	10ml or more*3	0.3	20	1	80
External pressure micro kit (MG-20)	3.2cm ²	Min 3ml Max 10ml *4	30ml or more*3	0.1	20	0.3	80
High Speed mini kit (KH-125)	33cm ²	Min 50ml Max 200ml *4	500ml or more*3	0.1	20	0.3	80

*1 : D_p (Emulsion size) = D_m (SPG Pore size) × 3-4 Times

: Minimum is 3 times, Maximum is 4 times

These may not be applied when composition of emulsification is different. Please think as a standard.

*2 : It depends on the size of the syringe used.

*3 : It depends on the size of the continuous phase container used.

*4 : It can be increased by increasing the size of the dispersed phase tank as a special order.

For "High Speed Emulsification (Premix)" Devices

Line up	Emulsification Effective area	Emulsion preparation amount Total = Dispersion phase + Continuous phase	SPG Pore size (μm)		Emulsion size (μm) *1	
			Min	Max	Min	Max
Pumping connector (PC)	0.4cm ²	2.5ml *2	5	50	2.5	50
Internal pressure micro kit (MN-20)	3.2cm ²	Min 3ml Max 10ml *3	8	50	4	50
External pressure micro kit (MG-20)	3.2cm ²	Min 3ml Max 10ml *3	5	50	2.5	50
High Speed mini kit (KH-125)	33cm ²	Min 50ml Max 200ml *3	2	50	1	50

*1 : D_p (Emulsion size) = D_m (SPG Pore size) × 1 Time or less

: Minimum is 0.5 times, Maximum is 1 times

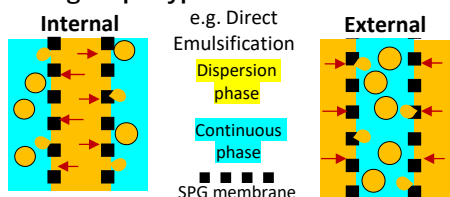
These may not be applied when composition of emulsification is different. Please think as a standard.

*2 : It depends on the size of the syringe used.

*3 : It can be increased by increasing the size of the dispersed phase tank as a special order.

about "Internal pressure" and "External pressure"

Using "Pipe type 10mm" of SPG membrane



The emulsification device (lab scale (micro kit, mini kit), bench scale) uses "pipe type 10 mm" SPG membrane that has high strength and can secure a wide SPG membrane emulsification effective area. There are two types of usage, "internal pressure type" and "external pressure type", and the working pressure differs greatly depending on the method of fixing the SPG membrane and the strength derived from the shape of the SPG membrane.

	Internal pressure	External pressure
Emulsification	The dispersed phase (or emulsion) is pressed from the inner face of the SPG membrane pipe to make an emulsion on the outer face.	The dispersed phase (or emulsion) is pressed from the outer face of the SPG membrane pipe to make an emulsion on the inner face.
Use Pressure	Max 0.3MPa	Max 0.98MPa (0.5MPa) *1
SPG membrane Pore size *2	<ul style="list-style-type: none"> Direct emulsification : 0.3 μm or more High speed emulsification : 8 μm or more 	<ul style="list-style-type: none"> Direct emulsification : 0.1 μm or more High speed emulsification : 2 (5) μm or more
Characteristic	<ul style="list-style-type: none"> It is easy to confirm the emulsification dispersion from the surface of the SPG membrane. Easy to emulsify with a small amount of continuous phase. 	<ul style="list-style-type: none"> Since it can be used up to a high pressure as compared with the internal pressure, a small pore size can be used and a smaller emulsion can be prepared. When using a long length SPG for direct emulsification, continuous phase transfer by a pump is required.

• 1: The maximum working pressure varies depending on the device used.

• *2: The usable pore size changes depending on the viscosity and concentration of the emulsion.

Disposable Device

Suitable for emulsification of small volumes from a few ml to a dozen ml.

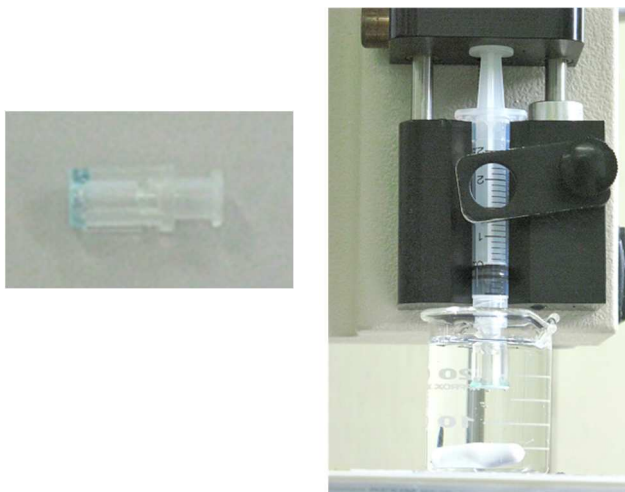
① Pumping Connector (PC)

Emulsification	High speed emulsification (premix)
SPG membrane	<ul style="list-style-type: none"> • Disc type $\Phi 7\text{mm} \cong 0.4\text{cm}^2$ • Pore size 5, 10, 20, 30, 50 μm • Hydrophilic or Hydrophobic
Emulsion preparation amount	Dispersion phase + Continuous phase = 2.5ml (It depends on the syringe used.)
Material	PVC, PMMA, Silicone resin (Hydrophobic coating)
Recommended syringe	2.5ml Luer lock type
Remarks	Non-sterilize (EOG sterilization is possible as an option)



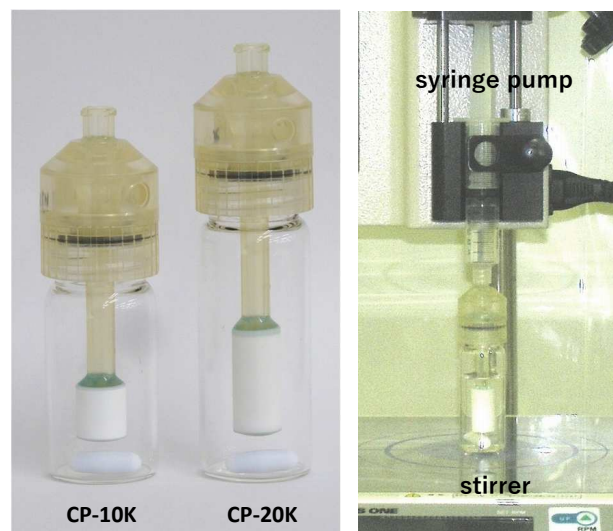
② Direct Connector (DC)

Emulsification	Direct emulsification
SPG membrane	<ul style="list-style-type: none"> • Disc type $\Phi 7\text{mm} \cong 0.4\text{cm}^2$ • Pore size 1, 3, 5, 10, 20, 30, 50 μm • Hydrophilic or Hydrophobic
Emulsion preparation amount	Dispersion phase = 2.5ml, Continuous phase = 5ml or more (It depends on the syringe and continuous phase container used.)
Material	PVC, PMMA, Silicone resin (Hydrophobic coating)
Recommended syringe	2.5ml Luer lock type
Remarks	Non-sterilize (EOG sterilization is possible as an option)



③ Filter Kit (CP-10K, CP-20K)

Emulsification	Direct emulsification
SPG membrane	<ul style="list-style-type: none"> • Pipe Type 10mm : CP-10K L10mm (effective Length L8mm) $\cong 2.5\text{cm}^2$: CP-20K L20mm (effective Length L18mm) $\cong 5.6\text{cm}^2$ • Pore size 1, 3, 5, 10, 20, 30, 50 μm • Hydrophilic or Hydrophobic
Emulsion preparation amount	Dispersion phase = 2~5ml(CP-10K), 2~6ml(CP-20K) Continuous phase = 6ml(CP-10K), 8ml(CP-20K)
Material	PVC, PMMA, Silicone resin (Hydrophobic coating) Silicone rubber, FKM
Recommended syringe	2.5ml Luer lock type
Remarks	Non-sterilize (EOG sterilization is possible as an option)



Note

* Not medical device.

Disposable devices are not medical devices. Please use it after understanding.

* About Direct Emulsification

A syringe pump and stirrer are required for direct emulsification with the direct connector or the filter kit. It is recommended that these are digital displays that allow detailed settings. Also, prepare a stand, clamp, jack, etc. to fix these.

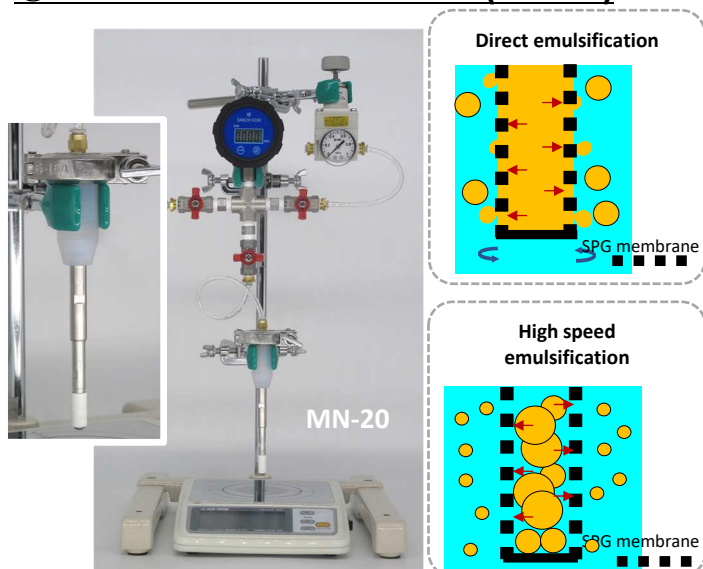
* About Chemical Resistance

Disposable devices are made of resin and rubber. Before using, check whether these materials are resistant to the emulsifying composition. **Pay particular attention to organic solvents.**

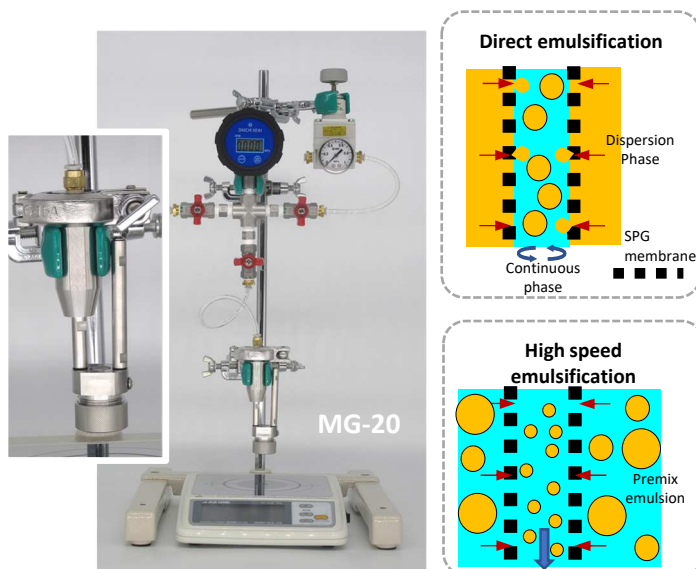
Micro Scale Device

- Since only the SPG membrane can be replaced, emulsions of various sizes can be prepared with one unit.
- Suitable for preparing small volume emulsions of several ml to 100 ml.
- Since it uses stainless steel, Teflon, and fluororubber, which have high chemical resistance, it can be used for preparing various types of emulsions.

① Internal Pressure Micro Kit (MN-20)



② External Pressure Micro Kit (MG-20)

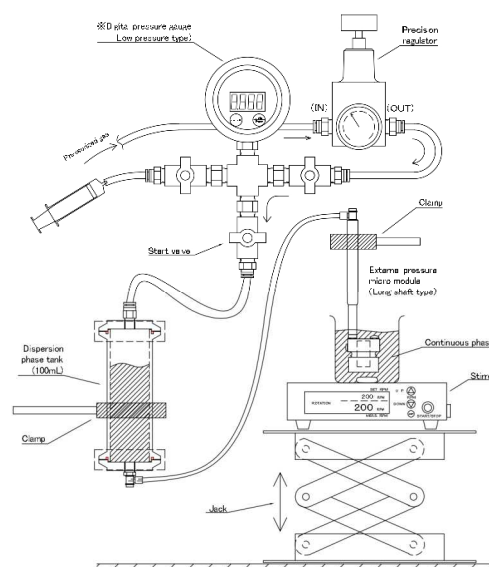


Model	Internal MN-20	External MG-20
Pressurization	Internal pressure	External pressure
Use Pressure	Max 0.3MPa	Max 0.5MPa
Emulsification	Direct emulsification High speed Emulsification (Premix)	
SPG membrane	· Pipe Type 10mm Length 10mm (effective Length L10mm) ≅ 3.2cm ²	
SPG Pore size *1	Direct emulsification : 0.3~20(50) μm *2 High speed Emulsification : 8~50 μm	Direct emulsification : 0.1~20(50) μm *2 High speed Emulsification : 5~50 μm
Dispersion phase Tank *3	10ml	
Material	SUS304, SUS303, PFA, FKM	
Emulsion preparation amount *4	Direct emulsification : Dispersion phase = 3-10ml : Continuous phase = 10ml or more High speed Emulsification : Dispersion phase + Continuous phase = 10ml	Direct emulsification : Dispersion phase = 3-10ml : Continuous phase = 30ml or more High speed Emulsification : Dispersion phase + Continuous phase = 10ml
Accessories	Secondary pressure regulator (digital pressure gauge, precision regulator, valve), Stirrer, Stand set	
Remarks	Customers are requested to prepare a continuous phase container (beaker, etc.), a pressurized gas cylinder, an air compressor, and a regulator for primary pressure.	

Note

* Specification changes (custom order available)

- Tank capacity (50ml, 100ml, 200ml, etc.)
- Low pressure type : Suitable for "Direct emulsification" using SPG pore size of 10 - 50 μm. : Separate tank, low pressure type pressure gauge



e.g) Low pressure type MG-20 : 100ml Separate tank

* about Chemical resistance

Stainless steel (SUS304, SUS303), fluoro resin (PFA), and fluororubber (FKM) are used for the wetted parts of MN-20 and MG-20. Make sure these materials are resistant to the emulsifying composition.

O-ring (fluororubber FKM) can be changed to "Perfluoroelastomer (FFKM)", which has high chemical resistance.

*1: The usable pore size varies depending on the viscosity and concentration of the emulsion.

*2: When performing direct emulsification, 20 μm or less is recommended. If the viscosity of the dispersed phase is low and the SPG pore size is large, the dispersed phase may come out from the SPG due to the weight of the dispersed phase (head pressure) and emulsification may not be possible.

*3: It is also possible to change to a custom tank of 20 ml, 50 ml, 100 ml, etc.

*4: The capacity can be increased by increasing the size of the dispersion tank and the size of the continuous phase container.

Mini Scale Device

- Since only the SPG membrane can be replaced, emulsions of various sizes can be prepared with one unit.
- Suitable for preparing emulsions with a volume of several hundred ml to 2 L.
- Since it uses stainless steel, Teflon, and fluororubber, which have high chemical resistance, it can be used for preparing various types of emulsions.

① High Speed Mini Kit

Model	KH-125
Pressurization	External pressure
Use Pressure	Max 0.98MPa
Emulsification	<ul style="list-style-type: none"> • Direct emulsification • High speed Emulsification (Premix)
SPG membrane	Pipe type 10mm, Length 125mm(effective Length L105mm) \approx 33cm ²
SPG Pore size *1	Direct emulsification : 0.1~20 μ m High speed Emulsification : 2~50 μ m
Dispersion phase Tank *2	200ml
Material	SUS304, SUS303, SUS316, PFA, FKM, ETFE, SIC, Carbon fiber
Emulsion preparation amount *3	<ul style="list-style-type: none"> • Direct emulsification : Dispersion phase = 50 - 200ml • Continuous phase = 500ml or more • High speed Emulsification : Dispersion phase + Continuous phase = 50 - 200ml
Accessories	<ul style="list-style-type: none"> • Secondary pressure regulator (digital pressure gauge, precision regulator, valve), • Continuous phase circulation pump (pump, inverter) • Stand set
Remarks	Customers are requested to prepare a continuous phase container (beaker, etc.), a pressurized gas cylinder, an air compressor, and a regulator for primary pressure.

*1 : The usable pore size varies depending on the viscosity and concentration of the emulsion.

*2 : It is also possible to change to a custom tank of 500ml, 1L, 2L, 5L, etc.

*3 : The capacity can be increased by increasing the size of the dispersion tank and the size of the continuous phase container.

Note

• Specification changes (Custom order available)

- Tank capacity (500ml, 1L, 2L, 5L, etc.)
- Change of Tank shape : Stirrer stirring tank (flat bottom) : with Hot water jacket, etc.
- Change of SPG membrane module : Length L250 mm, L500 mm, etc.
- Dedicated device for high speed emulsification (premix) : Non circulation pump
- Filtration (cross flow, dead end) specificati

* about Chemical resistance

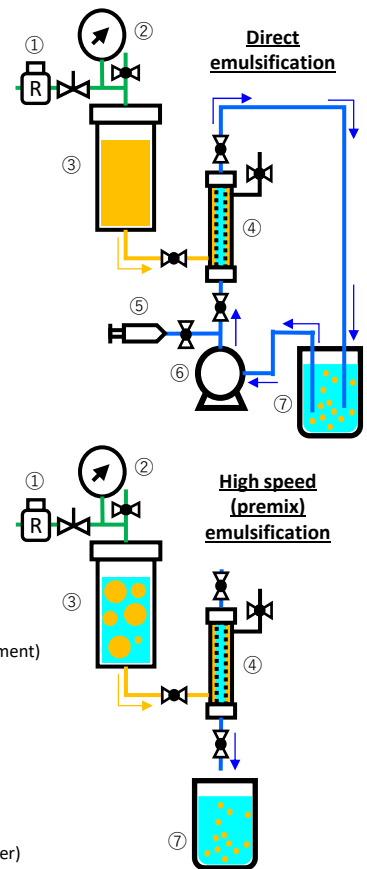
Stainless steel (SUS304, SUS303), fluororesin (PFA), ETFE, SIC, Carbon fiber and fluororubber (FKM) are used for the wetted parts of KH-125. Make sure these materials are resistant to the emulsifying composition.

O-ring (fluororubber FKM) can be changed to "Perfluoroelastomer (FFKM)", which has high chemical resistance.

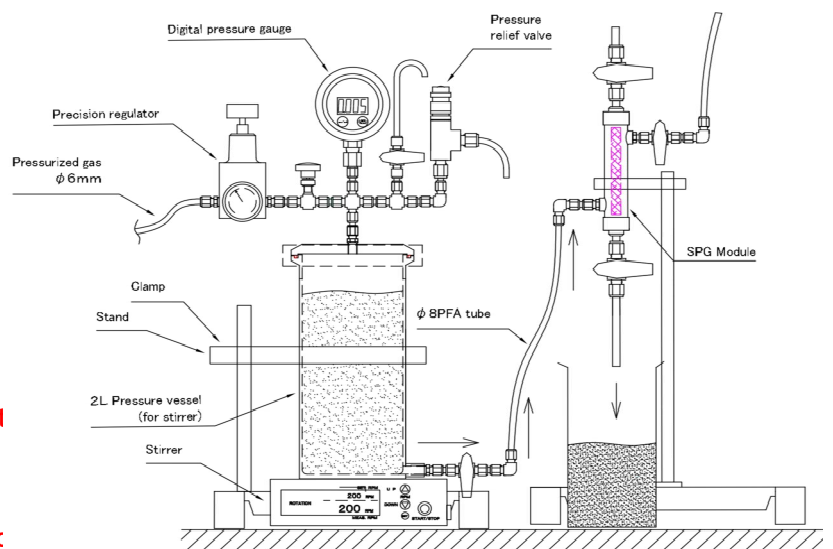


KH-125

Emulsification flow diagram



- ① Precision regulator (secondary pressure adjustment)
- ② Digital pressure gauge
- ③ Dispersed phase tank / Premix emulsion tank
- ④ SPG membrane module
- ⑤ Syringe for pump air bleeding
- ⑥ Continuous phase circulation pump
- ⑦ Continuous phase container (emulsion container)



e.g) Dedicated device for high speed emulsification (premix) : 2L Stirrer stirring tank

Scale up – equipment

Bench scale, Pilot scale, Manufacturing equipment

SPG devices are compatible with bench scales, pilot scales and production machines.

It will conduct a test on a laboratory scale, and based on the data (emulsification rate, etc.), it will specially design the device according to the effective area of the SPG membranes (= SPG membrane length and quantity) required when scaling up.

Flux speed of SPG membrane emulsification is proportional to the ability of per SPG membrane effective area. If it want to double the amount of emulsification, double the effective area of SPG membrane.

< Example >

Direct connector (0.4㎡) × 6 times ≙ Filter kit CP-10K (2.5㎡)

External pressure micro kit (3.2㎡) × 10 times ≙ High speed mini kit (33㎡)

If it want to increase the emulsification amount, in how many times the emulsifying effective area, please select the device.

< Scale up >

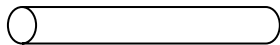
The scale-up equipment is too the same.

For example, to perform an experiment with “High-speed mini kit (KH-125)” and scale up to 30 times the size, it is as follows.

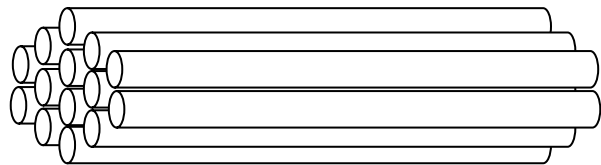
High speed mini kit (Effective length 105mm(33cm²)) × 30 times = 3,210mm(1,000cm²)

≙ Length 250mm (effective length 230mm (72cm²)) × 14 pcs

And it will manufacture an SPG membrane module that can fix 250 mm x 14 pcs SPG membranes, and select accessories of equipment.



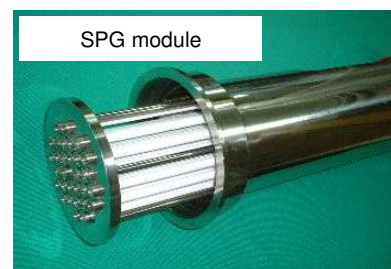
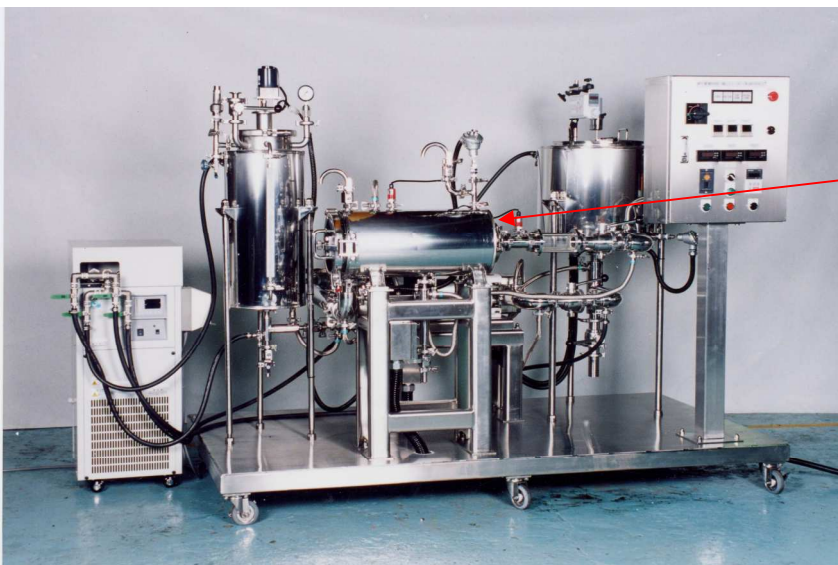
× 30Times



SPG membrane (Pipe Type 10mm) 125mm
Effective length = 105mm Effective area = 33㎡

SPG membrane (Pipe Type 10mm) 250mm
Effective length = 230mm Effective area = 72㎡
× 14 pcs ≙ 1,000㎡

Scale up – equipment (Bench scale)



- :SPG L500mm 30pcs Module
- : Dispersion phase Tank
=Capacity 20L
- : Continuous phase Tank
=Capacity 50L
- :Production=7.2L/h
- *Flax is dispersion phase
- *Pore size=5μm
- *Direct Emulsification

The scale-up equipment is custom made.

We design according to customer's request.