NOF CORPORATION

Biocompatible Materials
for Life Science

LIPIDURE®

Product Catalog Ver.3

Contents

From the Biosphere to Outer Space

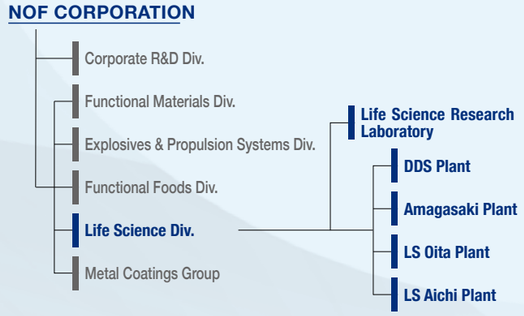
The NOF Group, pursues multi-faceted business development in five divisions of activities based on its own technologies. NOF Group endeavors to realize its management philosophy of "Contributing to humanity and society as a corporate group that creates new value through the power of chemistry, from the biosphere to outer space." by focusing particularly on the fields of "life science", "electronics and information" and "environment and energy"

Corporate Overview

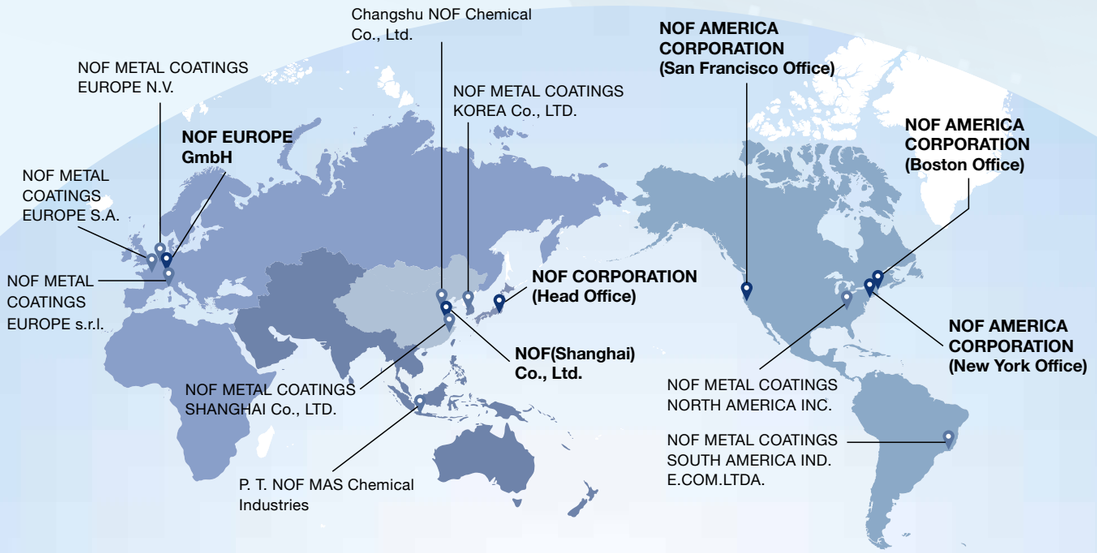
Head Office : Shibuya-ku, Tokyo, Japan
Establishment : June 1, 1937 (Incorporated on July 1, 1949)
Capital : 17,742 million JPY (as of March 31, 2025)
Employees : 3,997 (as of March 31, 2025)
Sales : 238,310 million JPY (April 1, 2024- March 31, 2025)

Corporate Organization

Life Science Products Division has been expanding into the fields of eye care, pharmaceuticals, medical devices, and diagnostics, etc., using our biocompatible material Lipidure® (MPC (2-Methacryloyloxyethyl Phosphorylcholine) derivatives) as a key material. Life Science Products Division integrated with DDS Development Division in April, 2023 and became new division named "Life Science Division". Life Science Division will continue to contribute globally for the technical evaluation in pharmaceutical and medical fields with its sophisticated biocompatible materials.



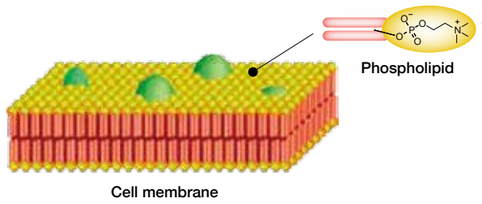
Overseas Subsidiaries and Joint Ventures

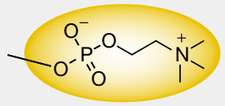


Product overview

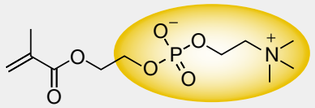
Key material, MPC

MPC represents 2-Methacryloyloxyethyl Phosphorylcholine, a key material of LIPIDURE®. NOF CORPORATION (NOF) succeeded in world's first industrial production of MPC in 1990, and we have continuously supplied quality MPC globally up to today.
MPC consists of phosphorylcholine group and methacrylic group. Phosphorylcholine group is the hydrophilic part of phospholipid, which exists on cell membrane of living organisms.
Phosphorylcholine group can impart following functions: high biocompatibility, high hydrophilicity, high lubricity, and high antithrombogenicity. Methacrylic group enables polymerizing MPC with various comonomers, providing limitless possibility to make various MPC polymer suitable for modifying various base materials, with various purposes. MPC and related products are chemically synthesized substances, so that the products have little lot-to-lot variation and little biohazardous risk.



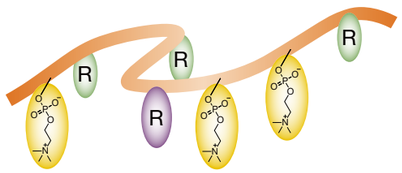


Phosphorylcholine (PC)
- High biocompatibility
- High hydrophilicity
- High lubricity
- High antithrombogenicity

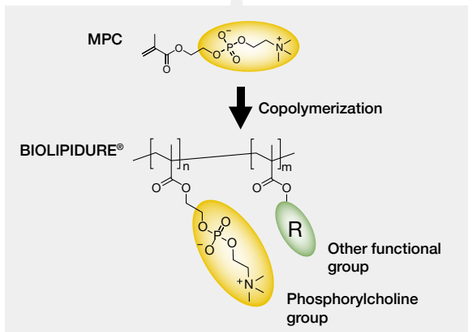


MPC (2-Methacryloyloxyethyl Phosphorylcholine)
- Providing functions of phosphorylcholine
- Polymerizable with various comonomers.
- Little lot-to-lot variation
- Little biohazardous risk

01 Additives for diagnostics, BIOLIPIDURE®, LIPIDURE®-SF



BIOLIPIDURE® is a series of MPC-based polymers that is useful for designing In Vitro Diagnostics (IVD) and biochemical assay reagents.
BIOLIPIDURE® has efficacy for suppression of non-specific adsorption of protein, stabilization of protein and enhancement of sensitivity. Also, BIOLIPIDURE® has little lot to lot variation because it is fully synthetic polymer (i.e. not derived from animal origin).
We provide rich variation of BIOLIPIDURE®, that helps you find out a suitable product to meet your particular application. LIPIDURE®-SF is a Zwitterionic surfactant.



Feature
- MPC-based polymer designed for IVD additives and assay reagent
- Rich variation in physical property derived from monomer composition
- 5 wt% aqueous solution (5% polymer and 95% water)
- 10 g / 100 g / 1 kg package available

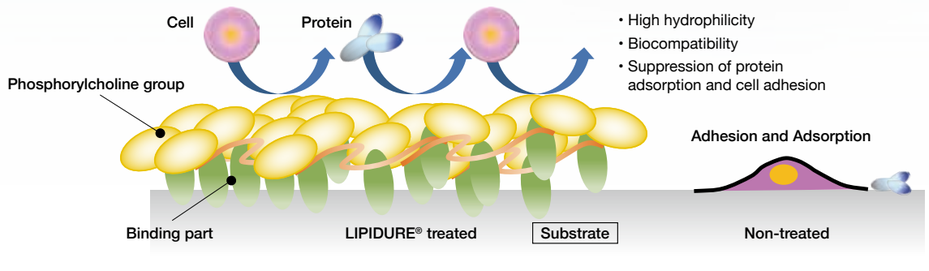
Basic Function
- Suppression of non-specific adsorption of protein
- Stabilization of protein
- Sensitization in immunoassays

Advantage
- Little lot-to-lot variation
- Little biohazardous risk

➡ Superior to protein-based reagent

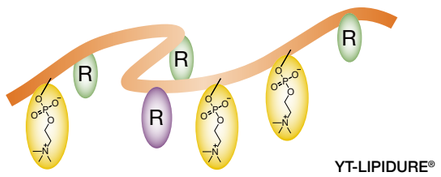
02 Coating agent for medical devices, LIPIDURE®

LIPIDURE® can be used as coating agent for various kinds of medical devices such as artificial heart, lung, joint and catheter. LIPIDURE® has three functions: 1) high hydrophilicity, 2) high biocompatibility and 3) suppression of protein adsorption and cell adhesion. Also, LIPIDURE® has little lot-to-lot variation because it is fully synthetic polymer (not derived from animal origin).
We have several types of products depending upon the binding strength and targeted substrate.



03 Additives for eye drops, YT-LIPIDURE®

YT-LIPIDURE® series are additives for eye drops which are useful for dry eye care. YT-LIPIDURE®-EL is our standard product containing a biocompatible MPC polymer like an Artificial Cell Membrane. It has been used for artificial tear eye drops which relieve dry eye symptom because of its higher wettability. It has three main functions: 1) Stabilization of tear film, 2) Suppression of moisture evaporation from eye and 3) Protection of cornea from irritants. YT-LIPIDURE®-LS is a new product containing a biocompatible MPC polymer similar to YT-LIPIDURE®-EL but it forms nanoparticle-like steric structure in water and make it higher lubricity and durability as well as wettability on eye which could contribute to higher comfort.



Feature
- Dry eye score improvement
- Protective effect against preservatives
- Prevention of tear film break-up
- Stabilization of tear film
- Moisturizing
- Possible to apply on wearing hard and soft contact lenses
- Approved as additives by MHLW in Japan

*MHLW : Ministry of Health, Labour and Welfare

01 Additives for diagnostics, BIOLIPIDURE®

BIOLIPIDURE® is a series of MPC-based polymers that is useful for designing In Vitro Diagnostics (IVD) and biochemical assay reagent.
BIOLIPIDURE® exhibits multiple functions, such as suppression of non-specific adsorption of protein, stabilization of protein, sensitization in immunoassays, and so on. As BIOLIPIDURE® is fully synthetic materials, the products are provided with high stability (at least 1 year in a cold storage), little lot-to-lot variation, and little biohazardous risk. With these features, BIOLIPIDURE® is superior to protein-based reagents, namely bovine serum albumin (BSA), casein, etc.
BIOLIPIDURE® is provided as 5 wt% aqueous solution (5% polymer and 95% water) with no preservatives or other subspecies. Standardized product content is 10 g / 100 g / 1 kg. Quality assurance period: 1 year after shipment (BIOLIPIDURE®-204: Six months after shipment)

Product line-up

subseries	Product name	Feature	Adoption example
100	BIOLIPIDURE®-103	Very hydrophilic	Latex agglutination Lateral flow test
200	BIOLIPIDURE®-203	Moderately hydrophobic	Blocking in ELISA/CLEIA Latex agglutination Lateral flow test Protein stabilizer
	BIOLIPIDURE®-204	Moderately hydrophobic	
	BIOLIPIDURE®-205 *	Relatively hydrophobic	
	BIOLIPIDURE®-206	Relatively hydrophobic	
400	BIOLIPIDURE®-401 *	Very hydrophilic (Anionic)	Lateral flow test Metal surface modification
	BIOLIPIDURE®-402 *	Very hydrophilic (Anionic)	
	BIOLIPIDURE®-403	Very hydrophilic (Anionic)	
	BIOLIPIDURE®-405	Very hydrophilic (Anionic)	
	BIOLIPIDURE®-405L *	Very hydrophilic (Anionic)	
	BIOLIPIDURE®-406 *	Very hydrophilic (Anionic)	
	BIOLIPIDURE®-407 *	Very hydrophilic (Anionic)	
500	BIOLIPIDURE®-502	Very hydrophilic (Cationic)	Lateral flow test
	BIOLIPIDURE®-504 *	Very hydrophilic (Cationic)	
700	BIOLIPIDURE®-702	H-bond acceptor	–
800	BIOLIPIDURE®-802	Relatively hydrophobic	Blocking in ELISA/CLEIA Lateral flow test Protein stabilizer Solbilizer
	BIOLIPIDURE®-803 *	BSA-like physical property	
	BIOLIPIDURE®-804 *	BSA-like physical property	
1000	BIOLIPIDURE®-1002	Moderately hydrophobic	Blocking in ELISA/CLEIA Colorimetric assay Solbilizer
	BIOLIPIDURE®-1003	BSA-like physical property	
1200	BIOLIPIDURE®-1201	Moderately hydrophobic	Blocking in ELISA/CLEIA Latex agglutination
1300	BIOLIPIDURE®-1301	Moderately hydrophobic	–
1700	BIOLIPIDURE®-1701	Reactive group (NH2・HCl)	Covalently bonding blocker for immunoassay
1800	BIOLIPIDURE®-1801	Very hydrophilic (Anionic)	–

(*) Prototype

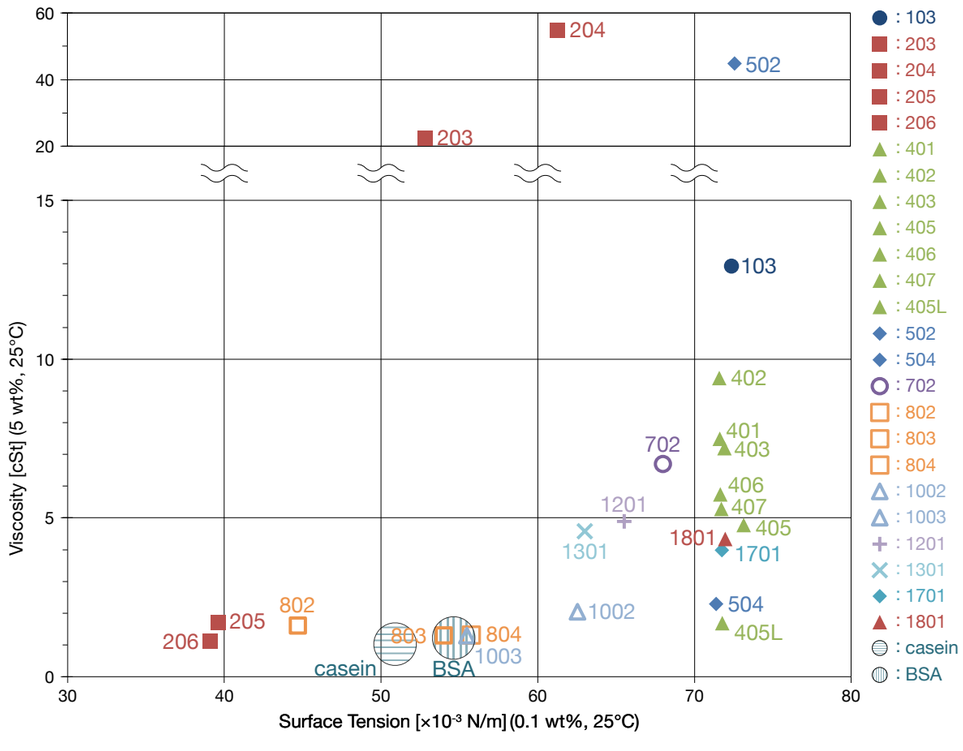
Guide to BIOLIPIDURE® Selection

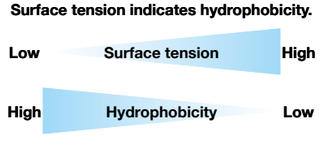
We recommend choosing appropriate BIOLIPIDURE® for the initial evaluation according to assay and purpose as follows.

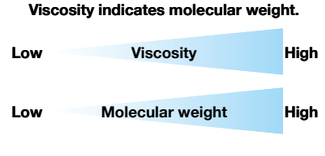
Assay	Blocking	Stabilizing	Sensitizing
Latex agglutination	200, 800 and 1200 series	800 series and SF08	103, 400 series
ELISA/CLEIA (microplate)	200, 800, 1000 and 1200 series	203, 800 series and SF08	–
CLEIA (magnetic beads)	200 and1000 series	800 series and SF08	–
Lateral flow (with latex)	200 and 800 series	800 series	103
Lateral flow (with gold nano-particle)	200 and 800 series	800 series	400 series

Physical Property of BIOLIPIDURE®

Each BIOLIPIDURE® has unique feature in terms of monomer composition, molecular weight, or resulting physical property. The figure below shows the physical property map of BIOLIPIDURE®. The horizontal axis is for the surface tension, indicating the polymer's hydrophobicity, and the vertical for the viscosity, indicating the molecular weight.
We offer a wide range of BIOLIPIDURE® with various physical properties, enabling you to find the best product that meets your specific application.





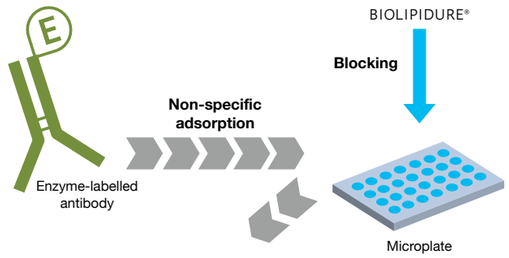


Blocking in Immunoassays

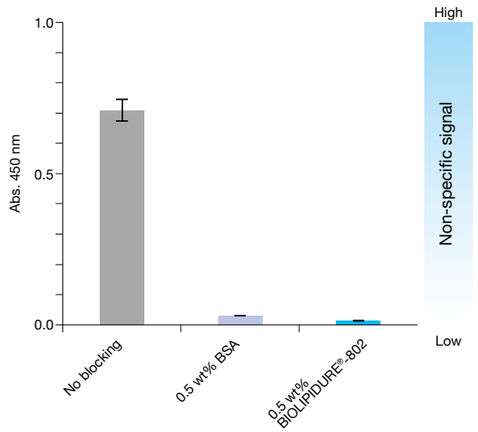
Suppression of Non-Specific Protein Adsorption

BIOLIPIDURE® can effectively suppress the non-specific adsorption of protein on microplate or magnetic beads.
Three experiments were carried out to demonstrate the ability of BIOLIPIDURE® to suppress the non-specific adsorption of protein.

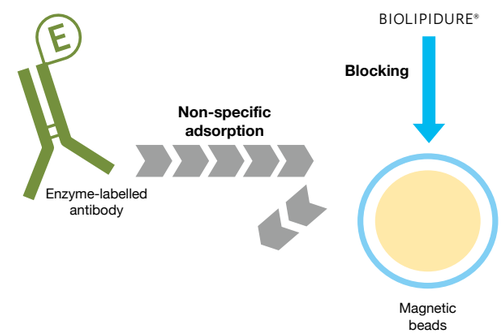
[By coating microplate]



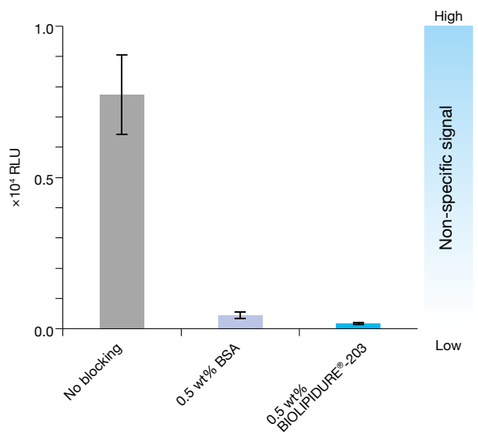
1. MaxiSorp (Thermo Fisher Scientific) 8-well strip plate was blocked with 10-fold diluted BIOLIPIDURE® (0.5 wt% final, diluted with PBS).
2. The plate was aspirated and dried over night at RT.
3. HRP-labelled goat anti-mouse IgG was added, and incubated for 1 hr at RT.
4. Washing with PBS-T.
5. Colorimetric substrate (TMB) was added, and reacted for 10 min at RT.
6. Stop solution (sulfuric acid) was added, followed by measuring Abs. at 450 nm.



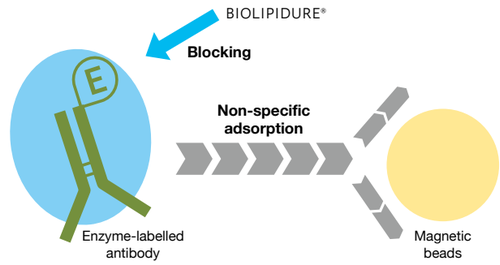
[By coating magnetic beads]



1. 8.5 µg of magnetic beads (Magnosphere™ MX100, JSR) was suspended in 100 µL of TBS containing 10-fold diluted BIOLIPIDURE® (0.5 wt% final).
2. After 1 hr of incubation at RT, the beads was washed with TBS.
3. TBS containing 10 ng of AP-labelled goat anti-human IgG was added, and incubated 1 hr at RT, followed by washing with TBS-T.
4. Chemiluminescent substrate (CDP-*Star*, Roche) was added and reacted for 10 min at RT to measure relative light unit (RLU).

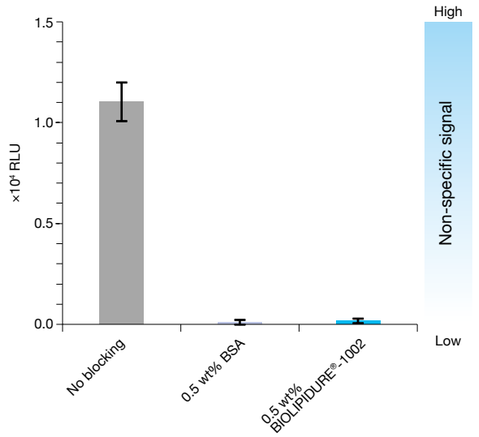


[By adding to antibody solution]



1. 100 ng/mL of AP-IgG solution containing 0.1 times the volume of BIOLIPIDURE® (0.5 wt% final) was prepared.
2. 8.6 µg of magnetic beads (Magnosphere™ MX100, JSR) was suspended in the AP-IgG solution.
3. After 1 hr of incubation at RT, the beads was washed with TBS-T.
4. Chemiluminescent substrate (CDP-*Star*, Roche) was added and reacted for 10 min at RT to measure relative light unit (RLU).

The methods of the second and third experiments are developed by Dr. Kumada of Kyoto Institute of Technology, and shared with NOF CORPORATION.



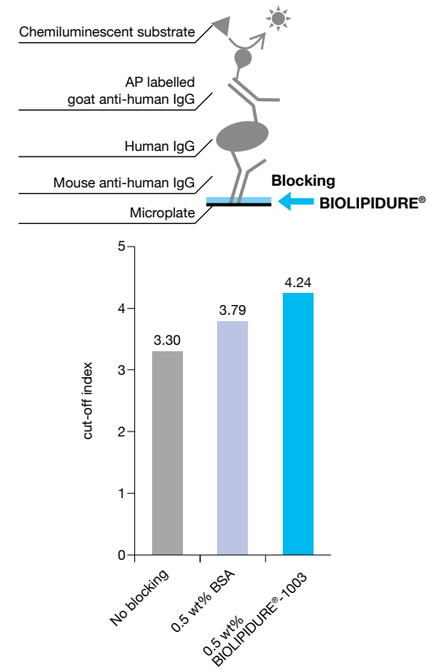
Application to Sandwich CLEIA

The protein-adsorption suppressing function of BIOLIPIDURE® is exhibited in sandwich CLEIA, making whole range of the assay more sensitive. Plate-based, and magnetic bead-based sandwich CLEIA detecting human IgG were carried out to demonstrate the performance of BIOLIPIDURE®.

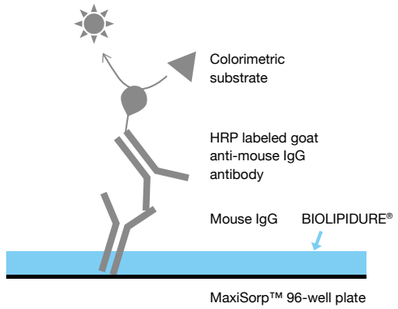
[Microplate-based assay]

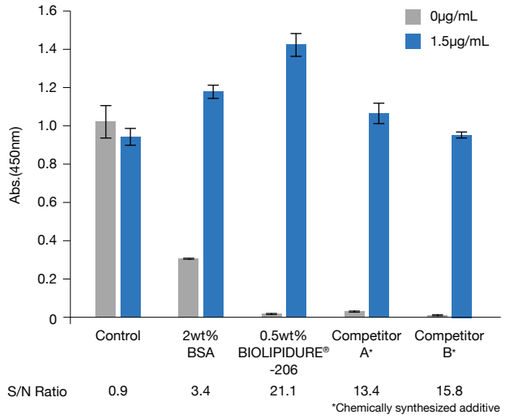
1. Mouse anti-human IgG monoclonal antibody was immobilized on Maxisorp(TM) 8-well plate (Thermo Fisher Scientific).
2. The plate was washed with TBS.
3. **10-fold diluted BIOLIPIDURE®** (0.5 wt%, diluted with TBS) was added, followed by 1 hr incubation at RT.
4. Human IgG standard was added, followed by 1 hr incubation at RT.
5. The plate was washed with TBS-T.
6. AP-labelled goat anti-human IgG polyclonal antibody was added, followed by 1 hr incubation at RT.
7. The plate was washed with TBS-T.
8. Chemiluminescent substrate (CDP-*Star*, Roche) was added and reacted for 15 min at RT to measure relative light unit (RLU).

BIOLIPIDURE® significantly enhanced the signal intensity in sandwich CLEIA.



[Comparison with competitors' products]





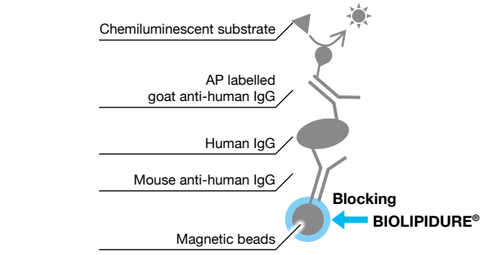
1. Mouse IgG was immobilized on Maxisorp (TM) 96-well plate (Thermo Fisher Scientific).
2. The plate was washed with PBS-T.
3. **10-fold diluted BIOLIPIDURE®** (0.5 wt%, diluted with PBS) was added, followed by 1hr incubation at RT.
4. The plate was aspirated and dried overnight in desiccator.
5. HRP-labeled goat anti-mouse IgG antibody was added, followed by 1hr incubation at RT, then washed with PBS-T.
6. Colorimetric substrate (TMB) was added and reacted for 10 min at RT.
7. Stop solution (sulfuric acid) was added, followed by measuring Abs. at 450 nm.

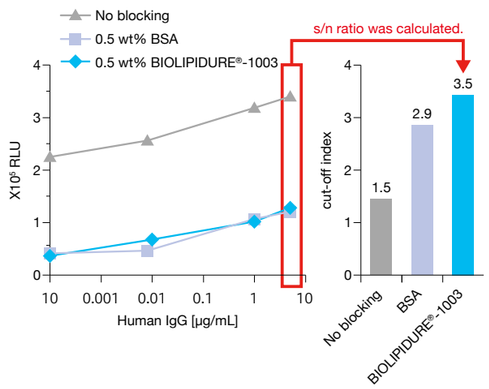
*Competiter's product A and B were used based on their instructions.

[Magnetic beads-based assay]

1. Mouse anti-human IgG monoclonal antibody was covalently immobilized on magnetic beads (Magnosphere MX100, JSR).
2. The beads was washed with MES buffer (pH 5.0).
3. **10-fold diluted BIOLIPIDURE®** (0.5 wt% final) was added, followed by 1 hr incubation at RT.
4. Human IgG standard was added, followed by 1 hr incubation at RT.
5. The beads was washed with TBS-T.
6. AP-labelled goat anti-human IgG polyclonal antibody, followed by 1 hr incubation at RT.
7. The beads was washed with TBS-T.
8. Chemiluminescent substrate (CDP-*Star*, Roche) and enhancer (Sapphire-II, Invitrogen) was added, and reacted for 1 min at RT to measure relative light unit (RLU).

BIOLIPIDURE® significantly enlarge the s/n ratio in sandwich CLEIA, as well as BSA.





Protein Stabilization

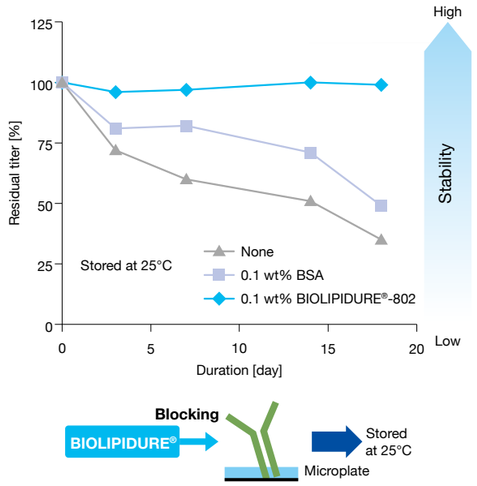
BIOLIPIDURE® can effectively stabilize protein both on solid phase and in liquid phase. It is considered that BIOLIPIDURE® and its hydrated water surround the protein to optimize the hydrophobic balance, and suppresses denaturation, aggregation, or nonspecific adsorption to inside wall of container.
Two experiments were carried out to demonstrate the protein stabilizing function of BIOLIPIDURE®.

Stabilization of Immobilized Antibody

The surface of microplate which primary antibody was immobilized on was treated with BIOLIPIDURE®. After storing the plate, the titer of the immobilized antibody was determined by ELISA.

1. Anti-mouse IgG antibody (Primary antibody) was immobilized on Maxisorp(TM) 8-well strip plate (Thermo Fisher Scientific).
2. The plate was blocked with **50-fold diluted BIOLIPIDURE®** (0.1 wt%).
3. The plate was washed with PBS-T, and dried over night at RT.
4. The plate was stored for 18 days at 25°C.
5. Titer of the antibody was determined by sandwich ELISA. Residual titer is expressed taking the initial titer as a base of 100%.

By using BIOLIPIDURE®, 100% of antibody titer has been maintained for 18 days.

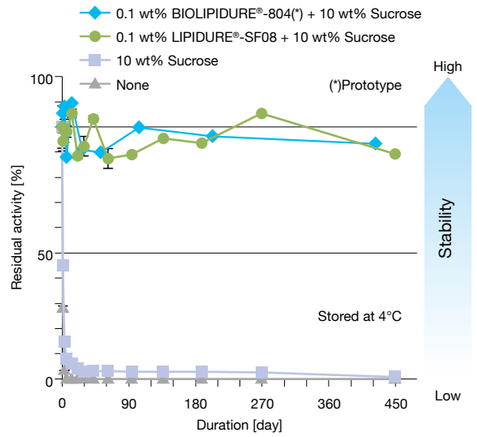


Stabilization of Diluted Enzyme Conjugate

BIOLIPIDURE® was added to diluted solution of enzyme labelled antibody. After storing the solution, the enzyme activity was measured.

1. HRP-labelled secondary antibody (Bio-Rad, Cat#170-6516) was diluted 20,000-fold with PBS containing **0.02 times the volume of BIOLIPIDURE®** (0.1 wt% final) or LIPIDURE®-SF08, and sucrose (10 wt% final).
2. The antibody solution was put into 2-mL plastic tube, and stored at 4°C for more than 1 year.
3. 8 μL of the solution was sampled and HRP activity was measured using colorimetric substrate (TMB).
4. Residual activity is expressed taking the initial activity as a base of 100%.

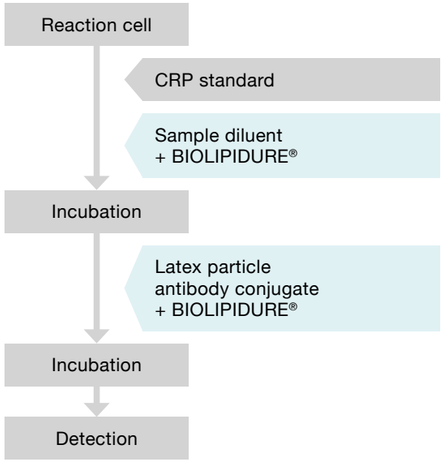
By using BIOLIPIDURE®, 100% of enzyme activity has been maintained more than 400 days.

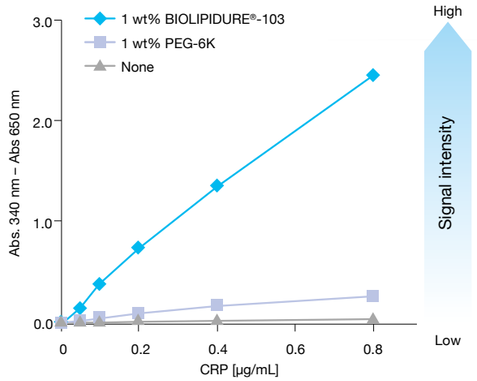


Sensitizing in Immunoassays

Application to Latex Agglutination Test

BIOLIPIDURE® can sensitize latex agglutination test. A latex agglutination test detecting CRP (C-reactive protein) was carried out to evaluate the performance of BIOLIPIDURE®.
The test was performed using 7070 automated analyzer (Hitachi). BIOLIPIDURE®-103 was added to both sample diluent and latex particle suspension (1 wt% final for each).

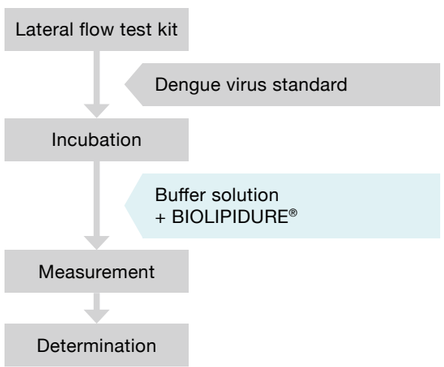


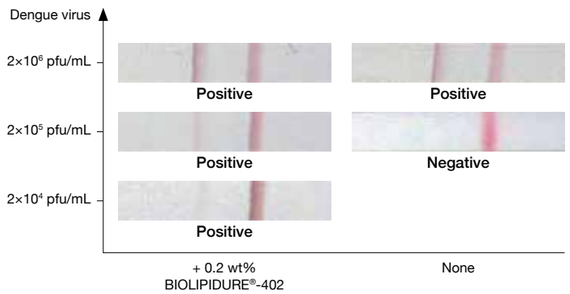


By using BIOLIPIDURE®, the sensitivity of latex agglutination test was significantly improved.

Application to Lateral Flow Test

BIOLIPIDURE® can sensitize lateral flow test. A lateral flow test detecting Dengue virus was carried out to evaluate the performance of BIOLIPIDURE®.
A Colloidal Gold Method lateral flow test kit was manufactured, and BIOLIPIDURE®-402 was added (0.2 wt% final) to developing solution.

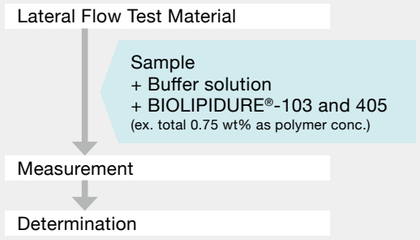




By using BIOLIPIDURE®, the sensitivity of lateral flow test was significantly improved.

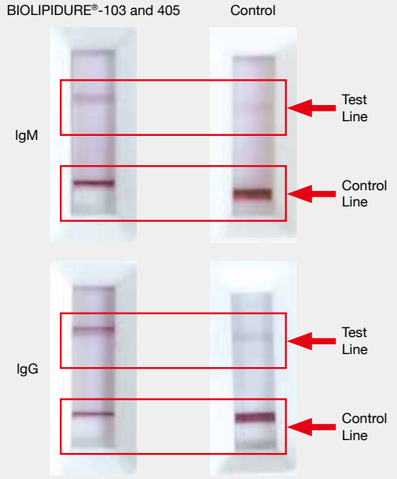
COVID-19

A lateral flow test detecting COVID-19 IgM and IgG was carried out respectively to evaluate the performance of BIOLIPIDURE®. The sensitivity of lateral flow test kit (Colloidal Gold Method) was improved by using combination of BIOLIPIDURE®-103 and BIOLIPIDURE®-400 series(e.g.405). The best condition (e.g. BIOLIPIDURE® combination, mix ratio, total polymer concentration) may vary depending on individual lateral flow test system.



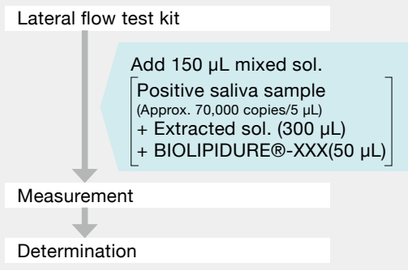
Material

- Novel Coronavirus (SARS-CoV-2) IgM Antibody Detection Kit (Colloidal Gold Method) (Cat#CG-CoV-IgM, Ray Biotech Co.)
- Novel Coronavirus (SARS-CoV-2) IgG Antibody Detection Kit (Colloidal Gold Method) (Cat#CG-CoV-IgG, Ray Biotech Co.)
- COVID-19 Serum Sample (Cat#CoV-PosM-S-100, CoV-PosG-S-100, Ray Biotech Co.)

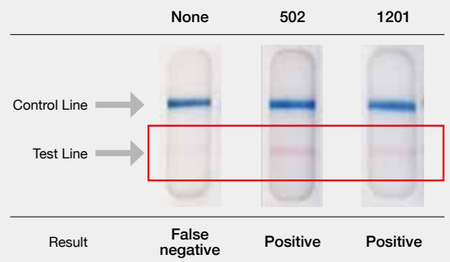


The sensitivity of lateral flow test was significantly improved by using BIOLIPIDURE®

BIOLIPIDURE® also has potential to sensitize COVID-19 lateral flow antigen test with saliva sample.
Saliva sample often causes false negative results in lateral flow test.
In this case, we evaluate lateral flow antigen test that do not recommend saliva, with saliva sample.



The positive concordance rate when using approximately 70,000 copies/5µL of nasopharyngeal swab samples with : 97%.



By using BIOLIPIDURE®, determination is improved from false negative result to positive.

Determination assistance from Dr. Yanagihara, Dr. Ota and Dr. Nabeshima of Nagasaki University Hospital

Application to component of Lateral Flow Test

The sensitivity of lateral flow test was significantly improved by treating the sample/conjugate pad with BL405L in advance.

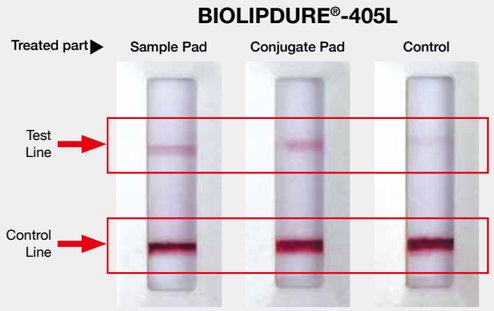
Lateral Flow Test Kit

- Sample/Conjugate pad treated with undiluted BIOLIPIDURE®-405L solution (add 100/10 µL BIOLIPIDURE®-405L, and drying overnight at RT or vacuum drying at 50°C for 2 hours)
- Capture membrane
- Absorbent sink

Sample
+ Buffer solution

Measurement

Determination



Material

- Novel Coronavirus (SARS-CoV-2) IgM Antibody Detection Kit (Colloidal Gold Method) (Cat#CG-CoV-IgM, Ray Biotech Co.)
- COVID-19 Serum Sample (Cat#CoV-PosM-S-100, Ray Biotech Co.)

Application to Lateral Flow Test with Color Latex Beads

The sensitivity of lateral flow test was significantly improved by using BIOLIPIDURE® and BL405L.

Lateral Flow Test Kit

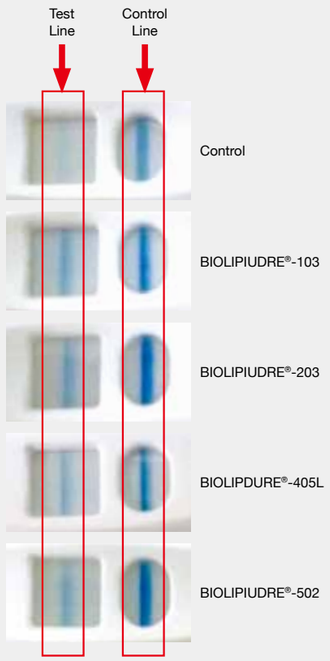
Sample (30 mIU/mL as final conc.)
+ PBS *LOD : 50 mIU/mL
+ BIOLIPIDURE®-XXX
(0.5 wt% as polymer conc.)

Measurement

Determination

Material

- Clearblue (pregnancy test) (6-685-01, OMRON Co.)
- Human chorionic gonadotropin (hCG) (approval number: 21300AMZ00678, Fuji Pharma Co., Ltd.)



Application to Lateral Flow Test with Cellulose Nano-beads

The sensitivity of lateral flow test using cellulose nano-beads was significantly improved by using BIOLIPIDURE® and BL405L.

Lateral Flow Test Kit

Sample (200 mIU/mL as final conc.)
+ Saline *LOD : 200 mIU/mL
+ BIOLIPIDURE®-XXX
(0.5 wt% as polymer conc.)

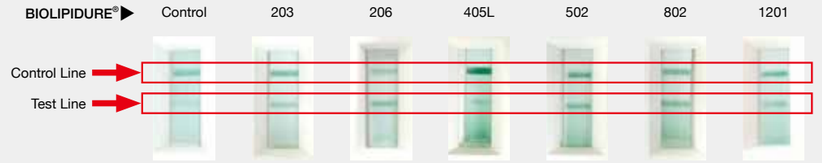
Measurement

Determination

Material

- Cellulose nano-beads (green)
- Anti-hCG antibody (mouse)
- Human chorionic gonadotropin (hCG) (Fuji Pharma Co., Ltd.)

Efficacy for enhancement of sensitivity



Recommended Combination (A+B) for SARS-CoV-2

Assay	Solution A	Solution B
Types of BIOLIPIDURE®	103, 203, 802	401*, 402*, 403, 405 and 407*
Range of concentration in final formulation (wt% as polymer conc.)	0.1 - 0.5	0.1 - 0.5
Total polymer conc. (wt%)	0.2 - 1.0	

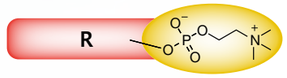
(*) Prototype

LIPIDURE®-SF
Zwitterionic Surfactant

LIPIDURE®-SF08

Product name	Adoption example
LIPIDURE®-SF08	Latex agglutination Nondenaturing solubilizer

Feature
- Zwitterionic surfactant
- MPC-based, synthetic surfactant
- 5 wt% aqueous solution
- Size:10 g / 100 g



[Solubilization of water-insoluble compound by LIPIDURE®-SF08 (Procedure)]

Procedure

1. 20 mg/mL ethanol solution of Cholecalciferol was prepared.
2. 3 µL of the solution prepared in step 1 was added to 100 µL of 0.05 wt% LIPIDURE®-SF08 aqueous solution.
3. After stirring the mixture for 1 min, the turbidity of the mixture at 450 nm was measured.
4. The turbidity ratio to PBS was calculated from the turbidity of Cholecalciferol aqueous solution dispersed in PBS and the turbidity of the mixed solution measured in step 3 as follows.

$$\text{Turbidity ratio to PBS}[\%] = 100 \times \frac{\text{Turbidity of LIPIDURE®-SF08 and cholecalciferol mixture}}{\text{Turbidity of PBS and cholecalciferol mixture}}$$

5. In the case of myristic acid and lauric acid being dissolved by solubilizing agents, the turbidity ratios to PBS ware also caluculated. Test solution ware prepared by mixing 100 ng/mL ethanol solution of each solute and 100 µL LIPIDURE®-SF08.
6. The turbidity ratios to PBS in the case of using LIPIDURE®-SF08 were compared to those of TritonX-100 and Tween20.

Solubilizing agent	HLB*	CMC (wt%)	Solubilizing effect**		
			Cholecalciferol	Myristic acid	Lauric acid
LIPIDURE®-SF08	8.3	0.100	○	○	○
TritonX-100	13.5	0.015	△	○	○
Tween20	16.7	0.007	△	○	△
HPC***	13.6	9.000	NA	NA	NA

*HLB: Hydrophilic Lipophilic Balance (Griffin method)
**The solubilization effect was evaluated as follows.
「○」: Soluble (Turbidity less than 10%), 「△」: Partially soluble (Turbidity 10% - 50%),「×」: Insoluble (Turbidity more than 50%)「NA」: Not available yet.
***Hexyl Phosphorylcholine (Prototype)

Prototypes

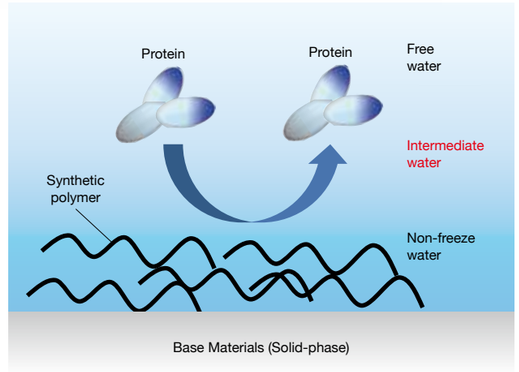
Highly-Durable Blocking Reagent “NOF-NB001”

Product name	Adoption example
NOF-NB001	Blocking in ELISA/CLEIA

Feature
- Highly-durable blocking reagent
- High durability against washing step
- High applicability to plastic-based material
- High suppressibility of biomolecule adsorption to NOF-NB001 treated surface.
- 5 wt% aqueous solution
- Size:10 g / 100 g

Principle

NOF-NB001 contains our novel synthetic polymer. The polymer forms an “intermediate water layer”, along with strongly coating the surface of base materials; PS, PP, etc. The intermediate water layer is only found in biocompatible polymer (e.g. protein, polysaccharide, and nucleic acid) and acts like a physical barrier against the adsorption of biomolecule such as protein.



LIPIDURE®-GD series
new additives suitable for PCR application

Feature of LIPIDURE®-GD

Product name	Sensitivity	Stability
LIPIDURE®-GD100	++	+
LIPIDURE®-GD200	+	+
LIPIDURE®-GD300	+	++
LIPIDURE®-GD400	++	++
LIPIDURE®-GD500	+	++

Efficacy
+ : high
++: higher

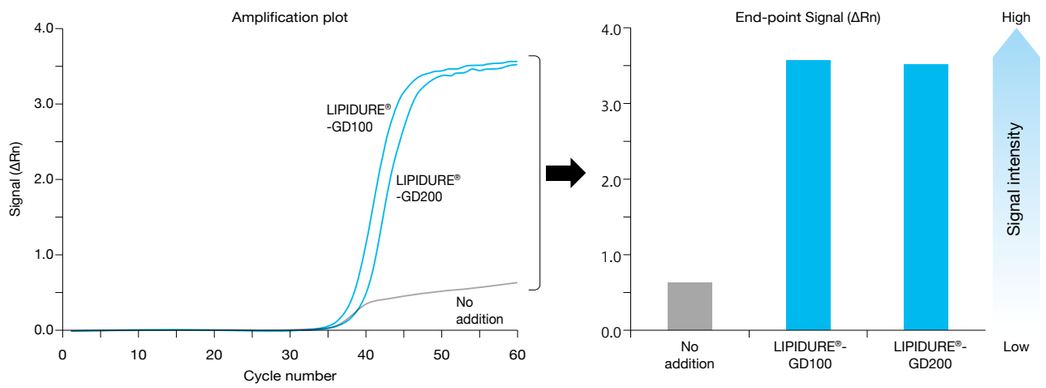
Value
LIPIDURE®-GD will:
- Enable a challenging detection of tiny amount of the target by PCR system.
- Save your time to optimize your PCR system.

Function
By just putting LIPIDURE®-GD into your master mix, the PCR system gets:
- Stronger end-point signal
- Improved limit of detection
- Better preservation stability

Sensitizing in PCR

[Enhancing the end-point signal]

Evaluation
1. A commercially available COVID-19 RT-qPCR kit (Japanese NIID method) was prepared.
2. LIPIDURE®-GD100 or -GD200 was added to the master mix respectively (2 vol% final as GD100, 1 vol% final as GD200).
3. Control RNA (50 copy of N set No.2) was added.
4. One-step RT-qPCR was conducted.

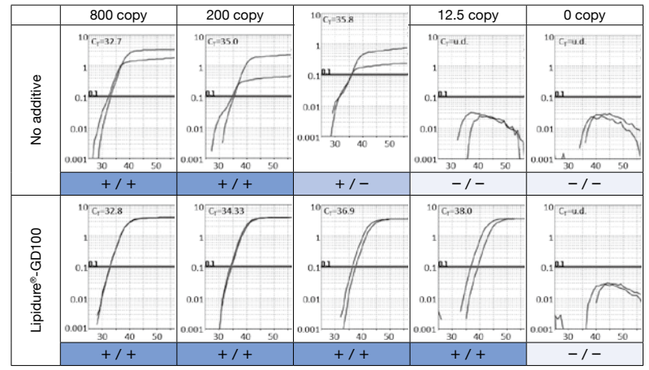


LIPIDURE®-GD significantly enhances the end-point signal intensity.

[Improving the limit of detection]

Evaluation
1. A commercially available COVID-19 RT-qPCR kit (Japanese NIID method) was conducted with LIPIDURE®-GD100 added to the master mix (2 vol% final as GD100).
2. Positive control RNA (N set No.2) and Negative control (PCR grade purified water) were used.
3. The result was deemed to be positive (+) when the amplification plot exceeded the threshold, otherwise to be negative (-).

LIPIDURE®-GD significantly improves the limit of detection.

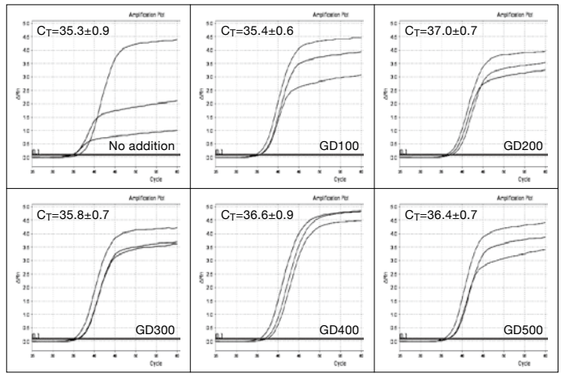


X axis: cycle number, Y axis: signal (ΔRn), Threshold: ΔRn=0.3

[Comparison among LIPIDURE®-GD]

Evaluation
1. A commercially available COVID-19 RT-qPCR kit (Japanese NIID method) was conducted with LIPIDURE®-GD added to the master mix.
2. Positive control RNA (500 copies/test of N set No.2)

The effect on amplification curve by adding each LIPIDURE®-GD was evaluated.
Best product may vary with individual PCR system.



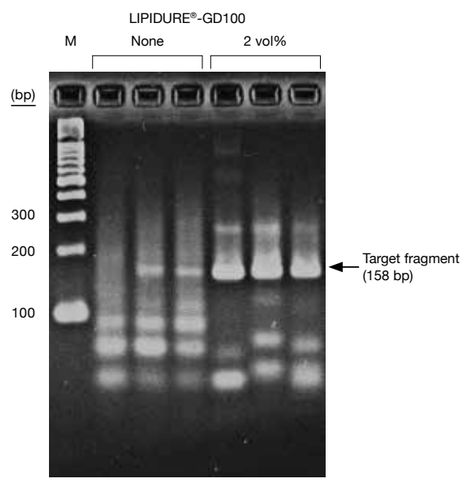
X axis: cycle number, Y axis: signal (ΔRn), Threshold: ΔRn=0.3

[DNA amplification enhancement]

An agarose gel electrophoresis was conducted to confirm if LIPIDURE®-GD enhances DNA amplification, or just enhances fluorescent signal.

Evaluation
1. A commercially available COVID-19 RT-qPCR kit (Japanese NIID method) was prepared.
2. LIPIDURE®-GD100 was added to the master mix (2 vol% final as GD100).
3. Positive control RNA (200 copies/test of N set No.2) was added.
4. One-step RT-qPCR was conducted.
5. The crude RT-qPCR product was developed by agarose gel electrophoresis.
   Apply volume = 5 μL
   Gel/Buffer = 3%(w/v) agarose / 0.5x TBE

Amplification of target fragment can be significantly increased by using LIPIDURE®-GD



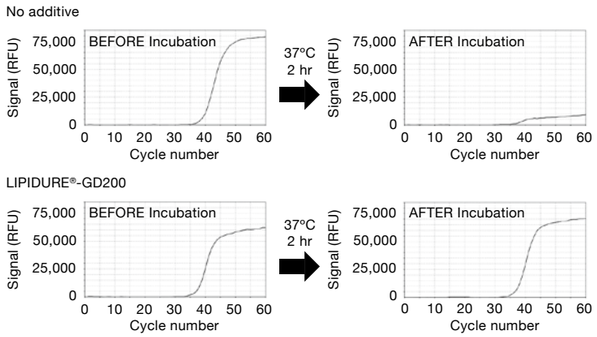
Stabilization in PCR

[Stabilizing master mix]

Evaluation

1. A commercially available COVID-19 RT-qPCR kit (Japanese NIID method) was prepared with LIPIDURE®-GD added to the master mix.
2. The master mix was incubated at 37°C for 2 hrs as an accelerated aging test.
3. One-step RT-qPCR was conducted using master mix BEFORE and AFTER incubation respectively. Positive control RNA (50 copy of N set No.2) was used as template.

LIPIDURE®-GD significantly improves the preservation stability of the master mix.



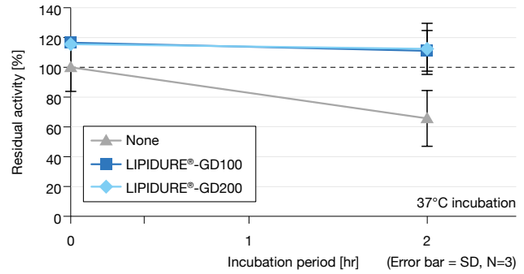
[Storage stability improvement]

As a practical evaluation from another perspective, storage stability of the RT-qPCR master mix was examined.

Evaluation

1. A commercially available COVID-19 RT-qPCR kit (Japanese NIID method) was prepared with LIPIDURE®-GD added to the master mix.
2. The master mix was incubated at 37°C for 2 hr as an accelerated aging test.
3. One-step RT-qPCR was conducted using master mix BEFORE and AFTER incubation respectively. Positive control RNA (500 copies of N set No.2) was used as template.

$$\text{Residual activity [\%]} \stackrel{\text{def}}{=} \frac{\text{(Endpoint } \Delta\text{Rn)}}{\text{(Endpoint } \Delta\text{Rn of no LIPIDURE® control at 0 hr)}} \times 100$$

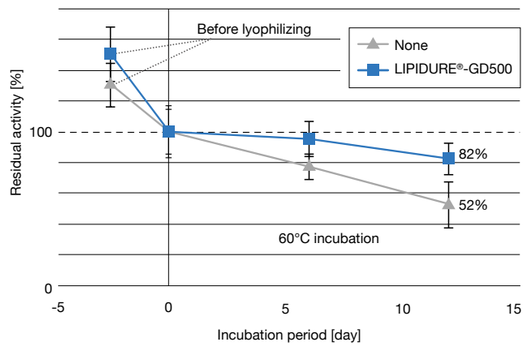


[Lyophilizing resistance improvement]

Evaluation

1. A commercially available COVID-19 RT-qPCR kit (Japanese NIID method) was prepared with LIPIDURE®-GD added to the master mix.
2. The master mix was lyophilized and incubated at 60°C as an accelerated aging test.
3. One-step RT-qPCR was conducted using master mix BEFORE and AFTER incubation respectively. Positive control RNA (500 copies of N set No.2) was used as template.

$$\text{Residual activity [\%]} = \frac{\text{(Endpoint signal)}}{\text{(Endpoint signal at 0 day)}} \times 100$$

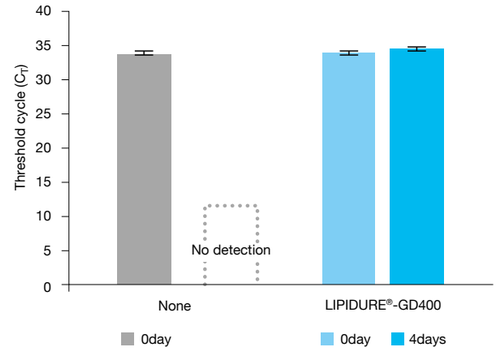


[Stabilizing Nucleic acid]

Evaluation

1. Nucleic acid solution (10 copies/μL) was prepared with LIPIDURE®-GD added to the Nucleic acid .
2. Nucleic acid solution was incubated at 4°C for 14 days.
3. After the master mix was prepared, one-step RT-qPCR was performed with nucleic acid solution BEFORE and AFTER incubation respectively.

LIPIDURE®-GD significantly improves the preservation stability of the Nucleic acid solution.

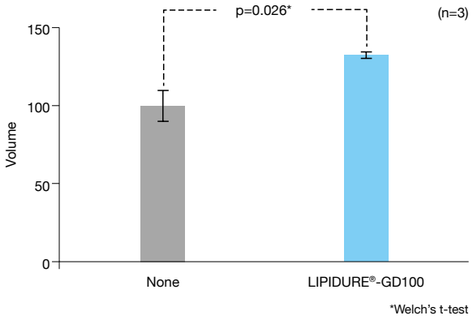


Application to DNA-dependent PCR

Evaluation

1. A master mix was prepared to amplify A, B, C and E protein coding regions of λ DNA.
2. LIPIDURE®-GD100 was added to the master mix (1vol% final as GD100).
3. PCR was conducted.
4. The crude PCR product was developed by agarose gel electrophoresis.
   Apply volume: 5 μL
   Gel/Buffer: 1 %(w/v) agarose / 1x TAE
5. The amplification amount of the target fragment was quantified.

The amplification of the target fragment was significantly increased.

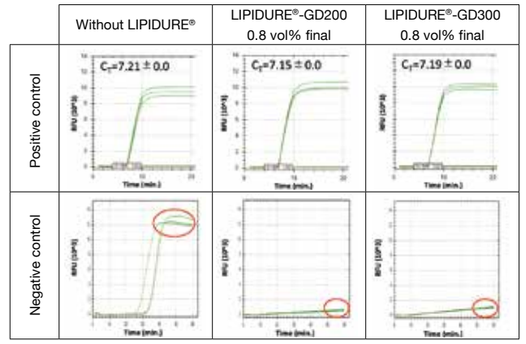


Application to LAMP

Evaluation procedure

1. A commercially available LAMP kit was prepared.
2. LIPIDURE®-GD was added to the LAMP master mix.
3. PCR was conducted.
4. Positive control DNA or water* as negative control was added.
5. Isothermal amplification was conducted to compare the amplification curve.

*Water, Nuclease free



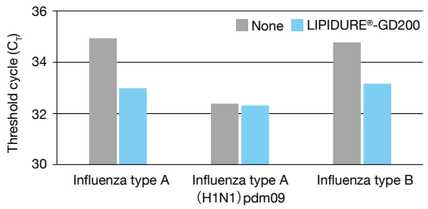
LIPIDURE®-GD suppressed non-specific amplification in negative control.

Application to Multiprex PCR

Evaluation

1. A commercially available LAMP kit was prepared.
2. LIPIDURE®-GD200 (1 vol% final) was added to the master mix.
3. Control DNA was added.
4. Multiplex PCR was conducted to compare the threshold cycle (C_T) values in each detection item.

C_T values can be significantly improved by using LIPIDURE®-GD.



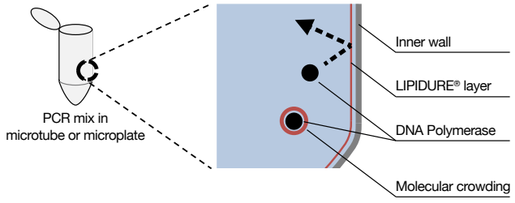
Hypothetical mechanism of LIPIDURE®-GD

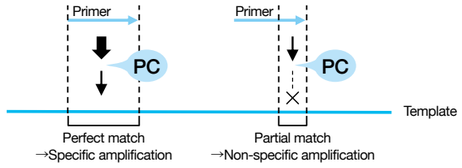
(A) Interaction with DNA polymerase

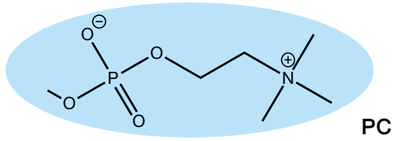
- LIPIDURE® can block the adsorption of protein to the surface of reaction tube.
- LIPIDURE® may enhance the enzyme activity of DNA polymerase by molecular crowding effect.

(B) Interaction with nucleic acid

- LIPIDURE® polymer has chaotropic phosphorylcholine (PC) group.
- The chaotropic group may improve specificity of primers and probes, resulting from weakening hydrogen bonds between Watson-Click base pair. i.e. when a primer anneals to the target region of the template, there must be perfect match of nucleic acid sequence, which forms enough strong affinity to maintain the hybridization even if PC group weakens the hydrogen bond between Watson-Click base pairs.







PC group

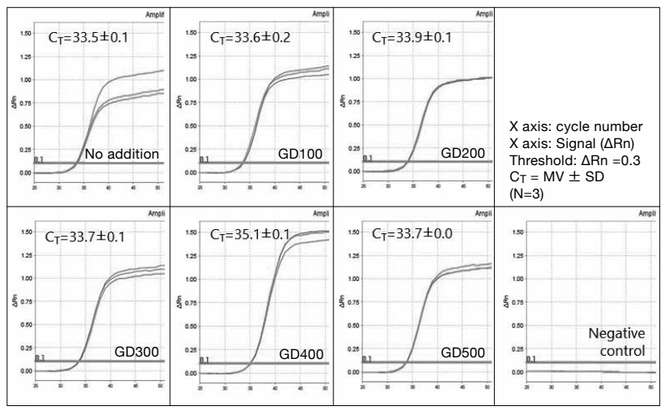
Case Study

This section presents a case study on sensitivity enhancement of a PCR system.

STEP 1 Selection of LIPIDURE®-GD

Evaluation

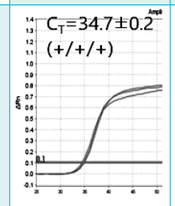
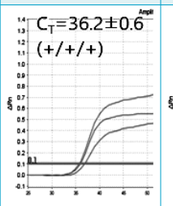
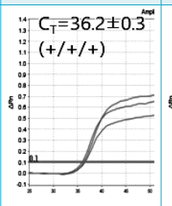
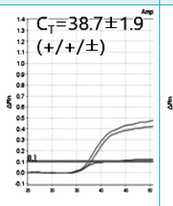
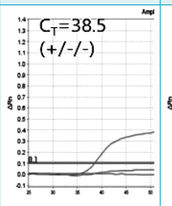
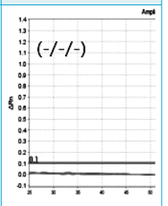
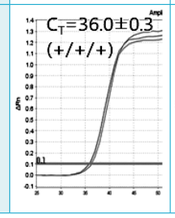
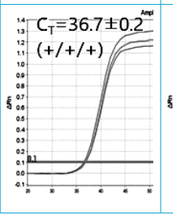
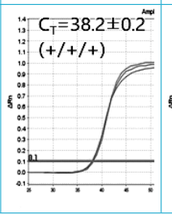
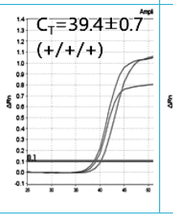
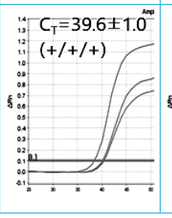
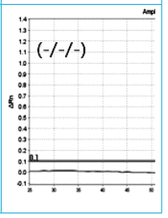
1. A commercially available COVID-19 RT-qPCR kit (a modified Japanese NIID method) was prepared.
2. LIPIDURE®-GD was added to the master mix. (1.0 vol% final)
3. Positive control RNA (500 copies/test of N set No.2) or negative control was added.
4. One-step RT-qPCR was conducted to compare the amplification plot.



The most suitable LIPIDURE®-GD for this PCR system was GD400 in terms of end-point enhancement.

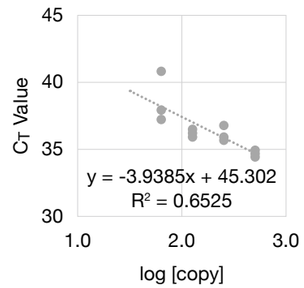
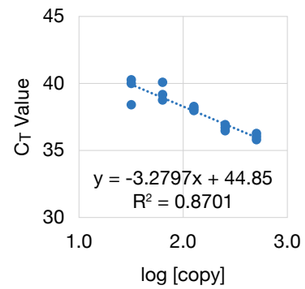
*The optimal LIPIDURE®-GD polymer may vary depending on the individual PCR system.

STEP 2 Confirmation of the effect of LIPIDURE®-GD400

	500 copies/test	250 copies/test	125 copies/test	62.5 copies/test	31.3 copies/test	0 copies/test
PW						
GD400						

In this case, LIPIDURE®-GD400 did enhance the sensitivity of the PCR system, and better limit of detection was observed.

STEP 3 Additional effect of LIPIDURE®-GD400

	No addition	LIPIDURE®-GD400
Calibration curve		
Slope	-3.938	-3.280
Amplifying efficiency	**79%**	**102%**

In this case, LIPIDURE®-GD400 also enhanced the quantifiability and the amplifying efficiency of the PCR system.

FAQ (Frequently Asked Questions)

<BIOLIPIDURE®>

Protocol

Q : What is the recommendation for the concentration of BIOLIPIDURE®?

A : We recommend using BIOLIPIDURE® with 10-50 times dilution. For your initial evaluation, our recommendation is 10 times dilution. Please note that BIOLIPIDURE® is 5 wt% aqueous solution, therefore, the final concentration of BIOLIPIDURE® should be 0.1 – 0.5 wt% in case of 10-50 times dilution.

Q : What is the recommendation to choose suitable BIOLIPIDURE® for blocking, stabilization of antibody or enhancement of sensitivity?

A : Please refer to page 7 of this catalog.

Q : What is the effect of combination of a couple of BIOLIPIDURE® types?

A : We don't have enough data for the combination of different BIOLIPIDURE®, however, two different types of BIOLIPIDURE® could be added to two separate reagents respectively and finally these two reagents are mixed and used together in some cases.

Q : When we diluted BIOLIPIDURE® with ethanol, the solution became cloudy and polymer was precipitated. How should I dilute BIOLIPIDURE®?

A : Some of BIOLIPIDURE® like 200 series could not be dissolved in ethanol. Please dilute BIOLIPIDURE® with water or buffer solution.

Quality

Q : What is the stability and shelf life of BIOLIPIDURE®?

A : MPC polymer in BIOLIPIDURE® is stable chemically but our guarantee period for BIOLIPIDURE® is 1 year after shipment at 2-10°C without opening the package because BIOLIPIDURE® is aqueous solution but does not contain any preservatives.

Q : How is the stability of BIOLIPIDURE®-400 series (anionic type) in buffer and durability against pH change and temperature change?

A : BIOLIPIDURE®-400 series are stable in general buffer around neutral pH. We have stability data for BIOLIPIDURE®-405 for 3 years at 4°C with unopened condition. We don't have data for different pH and temperature.

Others

Q : Is there a possibility to use BIOLIPIDURE® as a solubilizer for hydrophobic compounds?

A : Yes. BIOLIPIDURE®-206 and 1002 could be recommended.

Q : Do you sell higher concentrated BIOLIPIDURE® or even powder?

A : We have not established powder form of BIOLIPIDURE® as regular products. Technically, lyophilized sample could be available for some types of BIOLIPIDURE®.

Physical property

Q : What is the chemical structure and molecular weight for each BIOLIPIDURE®?

A : The information for chemical structure and molecular weight is confidential. However, you can refer to the physical property map on page 7 of this catalog for viscosity which shows molecular weight and surface tension which shows hydrophilic-hydrophobic interaction.

Q : What is difference among same types of BIOLIPIDURE®, for example 400 series?

A : All products in the BIOLIPIDURE®-400 series contain both MPC groups and anionic groups; however, they differ in monomer ratios and average molecular weights. The products, listed in order of increasing anionic ratio, are 407, 406, 401, 402, 403, and 405.

<LIPIDURE®-SF08>

Q : With regard to LIPIDURE®-SF08, is the efficacy for stabilization of enzyme-conjugated antibody related to stabilization of enzyme or antibody?

A : SF08 should work for improvement of stability for both enzyme and antibody.

References

1) Yasunori Kinoshita, Takahiro Tayama, Koichiro Kitamura, Md Salimullah, Hidekazu Uchida, Miho Suzuki, Yuzuru Husimi & Koichi Nishigaki. Novel concept microarray enabling PCR and multistep reactions through pipette-free aperture-to-aperture parallel transfer. BMC Biotechnology. 10, 2010

2) Jong-Won Park, Shigeru Kurosawa, Hidenobu Aizawa, Shin-ichi Wakida, Satoshi Yamada, Kazuhiko Ishihara. Comparison of stabilizing effect of stabilizers for immobilized antibodies on QCM immunosensors. Sensors and Actuators B: Chemical. 91(1-3), 158-162, 2003

3) Jong-Won Park, Shigeru Kurosawa, Hidenobu Aizawa, Shin-ichi Wakida, Satoshi Yamada, Kazuhiko Ishihara. Stabilizing effect of artificial stabilizers for binding activity of QCM immunosensors. IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control. 50(10), 1234-1235, 2003

4) Takayuki Minekawa , Akira Kambegawa, Kumiko Shindome, Hiroshi Ohkuma, Katsushi Abe, Hiroaki Maekawa, Hidetoshi Arakawa. Development of bioluminescent enzyme immunoassay for s-equol using firefly luciferase and its application to the assessment of equol-producer status. Chem. Pharm. Bull. 59(1), 84-87, 2011

5) Nozomu Matsunaga, Nodoka Narukawa, Tsutomu Yamasaki, Seiichi Katayama, Yasuo Hitsumoto. Inhibition of the interaction between fibronectin and dermatopontin by Clostridium perfringens fibronectin-binding proteins. Microbiology and Immunology. 65(8), 333-341, 2021

6) Masafumi Sakono, Tamotsu Zako, Masafumi Yohda, Mizuo Maeda. Amyloid oligomer detection by immobilized molecular chaperone. Biochemical Engineering Journal. 61(15), 28-33, 2012

7) Tomozumi Noda, Masaru Matsuda, Hirotaka Suzuki, Yusuke Okawa and Motohiro Mitani. Effective Blocking and Stabilizing Methods Using Synthetic Polymer on ELISA. ELISA Methods and Protocols, Methods in Molecular Biology. 5, 59-71, 2023

02 Coating agent for medical devices, LIPIDURE®

LIPIDURE® can be used as coating agent for various kinds of medical devices such as artificial heart, lung, joint and catheter. LIPIDURE® has three functions: 1) high hydrophilicity, 2) high biocompatibility and 3) suppression of protein adsorption and cell adhesion. Also, LIPIDURE® has little lot-to-lot variation because it is fully synthetic polymer (not derived from animal origin).

We have several types of products depending upon the binding strength and targeted substrate.

Quality assurance period: 1 year after shipment (LIPIDURE®-NH01: Six months after shipment)

Feature of LIPIDURE® series

Product name	Solubility	Binding method	Feature
LIPIDURE®-CM5206	Ethanol	Physical binding	• Biocompatibility • Suppression of protein adsorption and cell adhesion • Easy process for coating
LIPIDURE®-CM1102	Ethanol	Physical binding	• Biocompatibility • Hydrophilicity • Suppression of protein adsorption and cell adhesion • Easy process for coating
LIPIDURE®-CR2001	Ethanol, Water	Chemical binding	• Biocompatibility • Hydrophilicity • Suppression of protein adsorption and cell adhesion • Lubricity • Higher durability
LIPIDURE®-CR3001	Ethanol, Water	Chemical binding	• Biocompatibility • Hydrophilicity • Suppression of protein adsorption and cell adhesion • Lubricity • Higher durability
LIPIDURE®-NH01	Water	Chemical binding	• Biocompatibility • Hydrophilicity • Suppression of protein adsorption and cell adhesion • Higher durability

LIPIDURE® series and applicable substrate

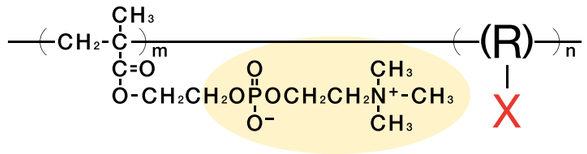
Product name	Coating type	Product name							Glass	Silicone	Metal
		PE	PS	PP	PU	PC	PEEK	PET			
LIPIDURE®-CM5206	Physical binding	○	○	○	○	○	–	○	○	NA	○
LIPIDURE®-CM1102	Physical binding	○	○	○	○	○	–	○	○	NA	○
LIPIDURE®-CR2001	Chemical binding	○	○	○	○	–	○	○	–	NA	–
LIPIDURE®-CR3001	Chemical binding	○*	○*	○*	–	○*	–	○*	○*	○*	○*
LIPIDURE®-NH01	Chemical binding	○*	–	–	–	–	–	–	–	–	–

*Pretreatment is necessary

○ : Applicable, NA : Not applicable, – : Not tested

Product Line-up

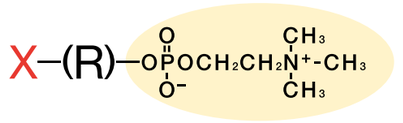
[Physical coating polymers]



Phosphorylcholine(PC)

Product	Functional Group ; X	Size	Appearance
LIPIDURE®-CM5206	Hydrophobic	1 g, 10 g, 100 g	White powder
LIPIDURE®-CM1102	Hydrophobic	1 g, 10 g, 100 g, 1 kg	White powder

[Reactive PCs]

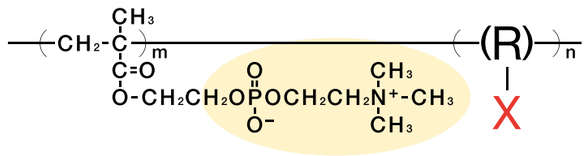


Phosphorylcholine(PC)

Product	Reactive Group ; X	Size	Appearance
LIPIDURE®-PC	CH_2=C(CH_3)COO	10 g, 100 g, 500 g, 1 kg, 4 kg	white powder
LIPIDURE®-PC02*	CH_2=CHCOO	10 g, 100 g	white powder
LIPIDURE®-PC03*	CH_2=CHCONH	10 g, 100 g	white powder

(*) Prototype

[Reactive PC polymers]



Phosphorylcholine(PC)

Product	Reactive Group ; X	Size	Appearance
LIPIDURE®-CR2001*	Photoreactive	1 g, 10 g	White powder
LIPIDURE®-CR3001	Alkoxy silane	1 g, 10 g, 100 g	White powder
LIPIDURE®-NH01	NH_2	10 g, 100 g, 1 kg	5 wt% aqueous solution

*LIPIDURE-CR2001 should be stored at room temperature and protected from light.
(*) Prototype

Coating with LIPIDURE® by physical binding

LIPIDURE®-CM5206

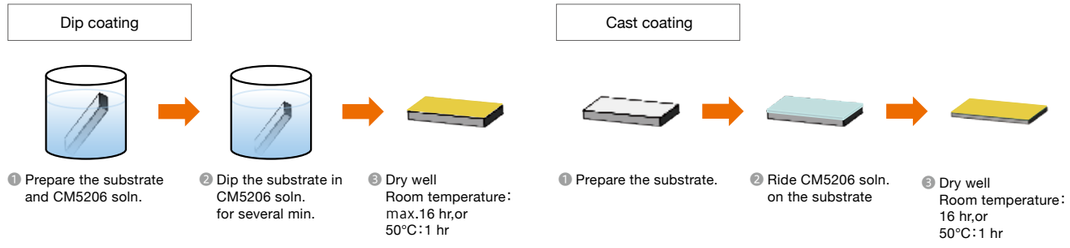
[Procedure of dissolution for LIPIDURE®-CM5206]

❶ Prepare closable vessel
❷ Weigh CM5206
❸ Add Ethanol
❹ Stir until CM5206 is fully dissolved at room temperature.
*It might take up to 16 hr or more.

Concentration :
For initial evaluation, we recommend 0.5 wt%

Solvent :
Ethanol

[Coating process of LIPIDURE®-CM5206]



[Hydrophilization of substrate surface]

Substrate : Acrylic plate
Coating solution : 0.5 wt% LIPIDURE®-CM5206 EtOH soln.
Standby time for water in sessile drop method : 3 sec.
Standby time for air in air bubble method : 10 sec.

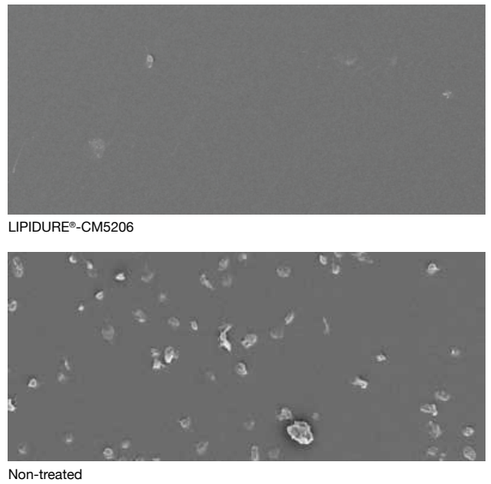
Contact angle/ by water, in air		Contact angle/ by bubble, in water	
Not-treated	LIPIDURE®-CM5206 treated	Not-treated	LIPIDURE®-CM5206 treated
99°	114°	99°	149°
	Hydrophobic		Hydrophilic

[Suppression of platelet adsorption]

Procedure

❶ Dissolve LIPIDURE®-CM5206 in ethanol at 0.5 wt%.
❷ Add 100 µL/well of LIPIDURE®-CM5206 soln. to 384 well tissue culture plate.
❸ Remove all soln. Dry at room temperature.
❹ Centrifuge rabbit whole blood. (4°C, 1,500 rpm, 20 min)
❺ Collect platelet-rich plasma (PRP) and add 50 µL/well.
❻ Incubate at room temperature for 1 hr.
❼ Remove the PRP and wash 3 times with Hanks's buffer soln. and immobilize with 2.5% Glutaraldehyde.
❽ Incubate at room temperature for 2 hr.
❾ Wash with distilled water.
❿ Observe under SEM after freeze drying and gold vapor deposition.

Result



LIPIDURE®-CM5206

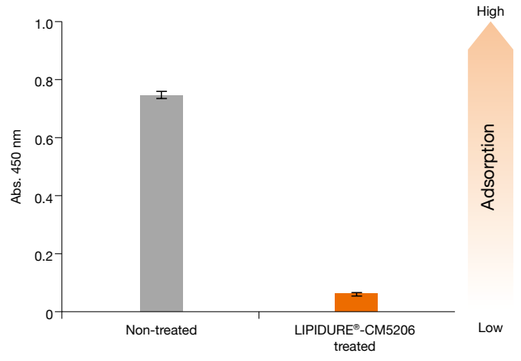
Non-treated

[Suppression of protein adsorption]

Procedure

❶ Dissolve LIPIDURE®-CM5206 in ethanol at 0.5 wt%.
❷ Add equal or more than 200 µL/well LIPIDURE®-CM5206 soln. to 96-well flat bottom plate.
❸ Remove all soln. Dry at room temperature.
❹ Add 100 µL/well HRP labeled IgG conjugate soln. (24000 times dilution by PBS)
❺ Incubate at room temperature for 1 hr.
❻ Wash with 0.05% Tween 20-PBS.
❼ Add 100 µL/well HRP substrate soln.
❽ Incubate at room temperature for 10 min.
❾ Add 2N H_2SO_4 50 µL/well to stop the HRP reaction.
❿ Measure the absorbance at 450 nm.

Result

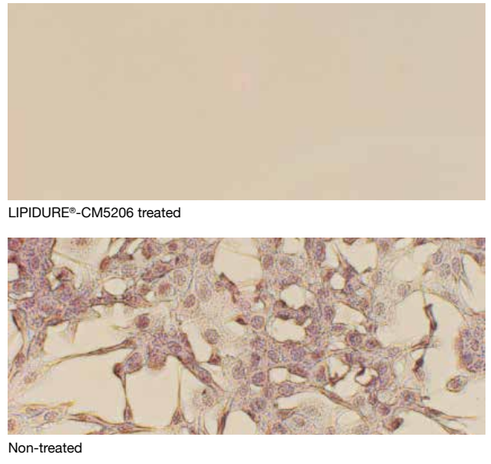


[Suppression of cell adhesion]

Procedure

❶ Dissolve LIPIDURE®-CM5206 in ethanol at 0.5 wt%.
❷ Add 100 µL/well LIPIDURE®-CM5206 soln. to 384 well tissue culture plate.
❸ Remove all soln. Dry at room temperature for max. 16 hr.
❹ Seed NIH3T3 cells (used DMEM media containing 10%-Calf Serum) at 10,000 cells/well.
❺ Culture for 18 hr.
❻ Remove the media.
❼ Add 50 µL/well hematoxylin soln.
❽ Incubate at room temperature for 10 min.
❾ Wash with pure water. Dry in air.
❿ Observe under microscope.

Result



LIPIDURE®-CM5206 treated

Non-treated

[Summary of safety data for LIPIDURE®-CM5206]

Test Items	Result
Test for In Vitro Cytotoxicity (Based on ISO10993-5)	Negative
Test for Skin Sensitization (Based on ISO10993-10)	Negative
Tests for Systemic Toxicity (Based on ISO10993-11)	Negative

Test Items	Result
Tests for Interactions with Blood (Based on ISO10993-4)	Non-hemolytic
Tests for Intracutaneous reactivity (Based on ISO10993-10)	Negative
Bacterial Reverse Mutation Test (Based on ISO10993-3)	Negative

[Thickness of coating layer with LIPIDURE®]

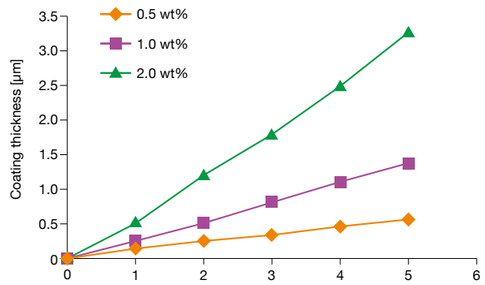
Procedure

1. Dipping the base material into the CM5206 solution for 1 min.
2. Drying for max. 16 hr (overnight) at room temperature or 1 hr at 50°C.

Thickness of coating layer with LIPIDURE® onto polystyrene plate against the number of times of dip-coating*.

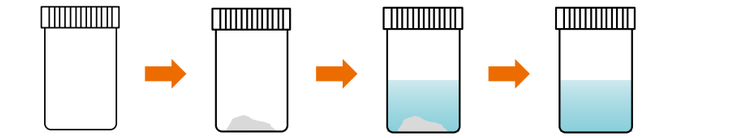
*Thickness of coating layer with LIPIDURE®- coating is calculated by weight measurement.

Result

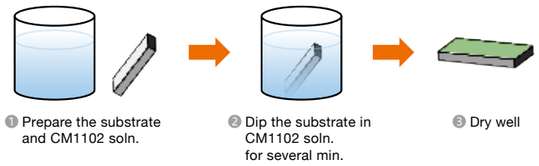


LIPIDURE®-CM1102

[Preparation and coating method for LIPIDURE®-CM1102]



Coating process



[Hydrophilization of substrate surface]

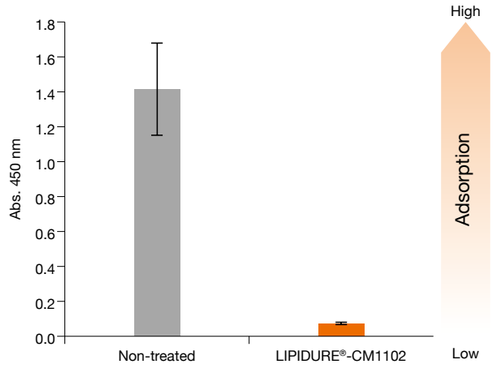
Substrate : Acrylic plate
Coating solution : 0.5 wt% LIPIDURE®-CM1102 EtOH soln.
Standby time for water in sessile drop method : 3 sec.
Standby time for air in air bubble method : 10 sec.

Contact angle/ by water in air		Contact angle/ by bubble in water	
Not-treated	LIPIDURE®-CM1102 treated	Not-treated	LIPIDURE®-CM1102 treated
99°	61°	119°	134°
	Hydrophilic		Hydrophilic

[Suppression of protein adsorption]

Procedure

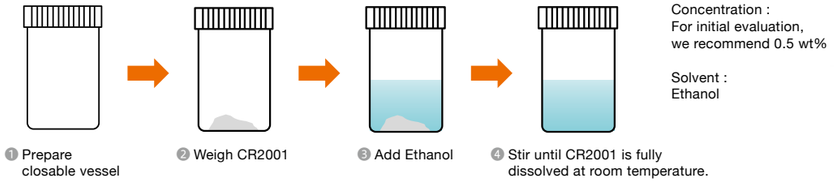
1. Dissolve LIPIDURE®-CM1102 in ethanol at 0.5 wt%.
2. Add 200 μL/well or more of LIPIDURE®-CM1102 soln.
3. Remove all soln.
4. Dry at room temperature.
5. Add 100 μL/well HRP labeled IgG conjugate soln. (24,000 times dilution by PBS)
6. Incubate at room temperature for 1 hr.
7. Wash with 0.05% Tween 20-PBS
8. Add 100 μL/well HRP substrate soln.
9. Incubate at room temperature for 10 min.
10. Add 2N H_2SO_4 50 μL/well to stop the HRP reaction.
11. Measure absorbance at 450 nm.



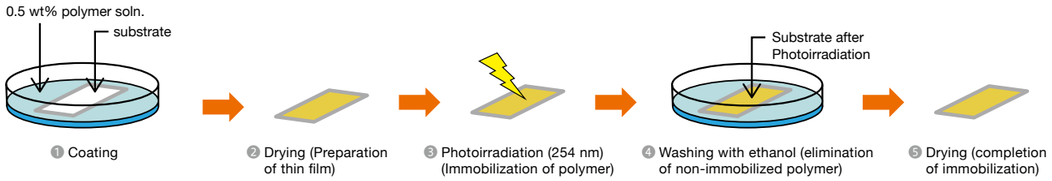
Coating with LIPIDURE® by chemical binding

LIPIDURE®-CR2001

[Procedure of dissolution for LIPIDURE®-CR2001]



[Coating process of LIPIDURE®-CR2001]

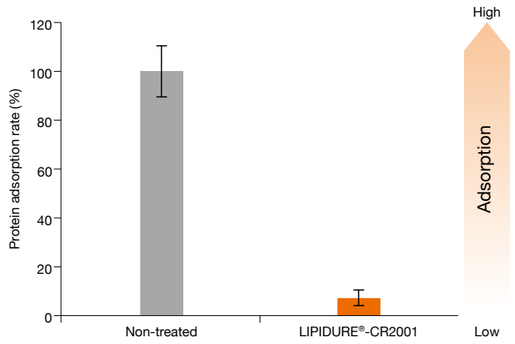


[Suppression of protein adsorption]

Protein adsorption is significantly reduced by immobilization of LIPIDURE®-CR2001.

#Protein:
Peroxidase labeled IgG conjugate
(diluted 24000-fold)
#Color developing system:
TMBz (tetramethylbenzidine) method

Result



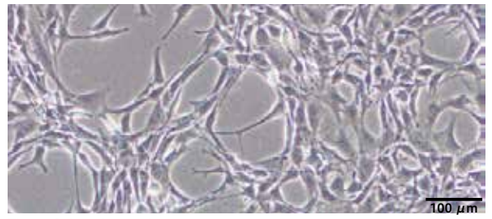
[Suppression of cell adhesion]

Procedure

❶ Immobilize LIPIDURE®-CR2001 on the 6-well tissue culture treated plate.
❷ Seed NIH3T3.
*Seeding density : 50,000 cells/well (2 mL/well)
Media : DMEM containing 10%CS and antibiotics.
❸ Incubate for 3 days in 37°C , 5% CO_2 incubator.
❹ Discard media and washing with 2 mL/well D-PBS(-) 3 times.
❺ Observe with phase-contrast microscope.

Result

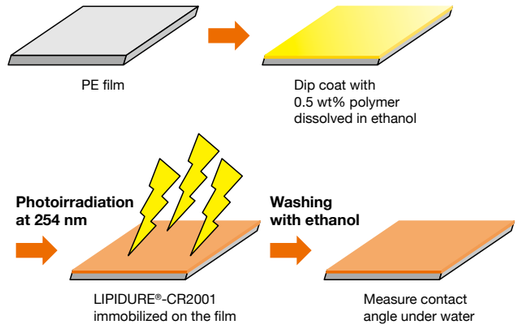
LIPIDURE®-CR2001



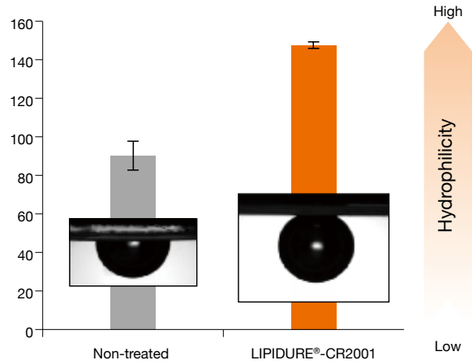
Tissue Cultured treated

[Coating and Immobilizing Procedure]

Procedure



Result



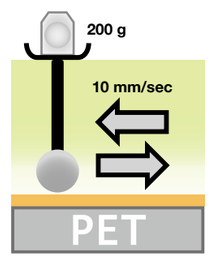
[Improvement of Lubricity]

Procedure

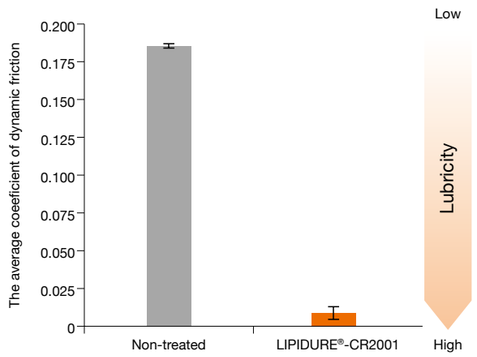
❶ Cast coat (0.12 mg/cm^2) and Immobilize with LIPIDURE®-CR2001 on the PET slide.
❷ Set the Surface Property Tester. (SHINTO scientific co., Ltd.)
❸ Measure the dynamic friction coefficient on the surface in physiological saline.

Measurement condition

Travel speed : 10 mm/sec
Travel distance : 20 mm
Contact : 10 mm stainless ball (point contact)
Weight of a load : 200 g
Load converter : 9.8 N
Number of measurement : 5 cycles (1 cycle = going and returning)

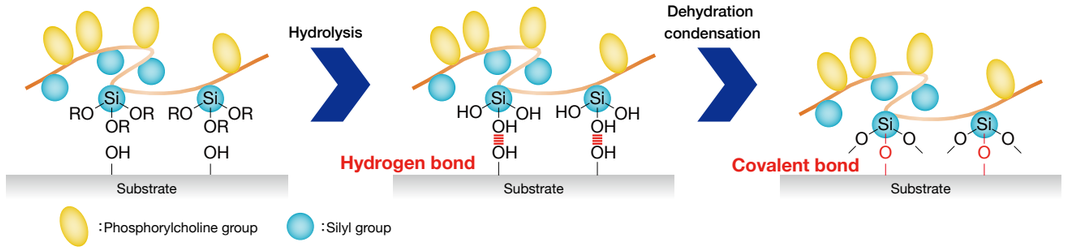


Result



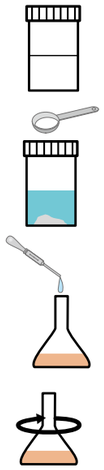
LIPIDURE®-CR3001

LIPIDURE®-CR3001 is a surface modifier imparting excellent hydrophilicity and excellent biocompatibility on substrate such as silicone and metal. LIPIDURE®-CR3001 polymer has alkoxy silane group, which can bind the polymer onto such substrate by making strong hydrogen bond and covalent bond.



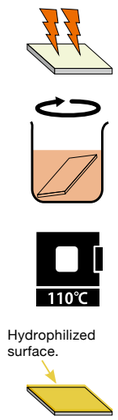
[Procedure of coating on silicone with LIPIDURE®-CR3001]

Preparation of coating solution



1. Prepare ethanol.
2. Dissolve CR3001 in the ethanol.
   * CR3001/ethanol = 1.0 - 4.0 wt%
3. Add CR3001 solution into 0.1 mM HCl aq. soln. with stirring.
   * CR3001 soln./HCl soln. = 1/1 (wt)
4. Stir at RT for 30 min to completely activate CR3001.
   * Proceed to surface modification step instantly.

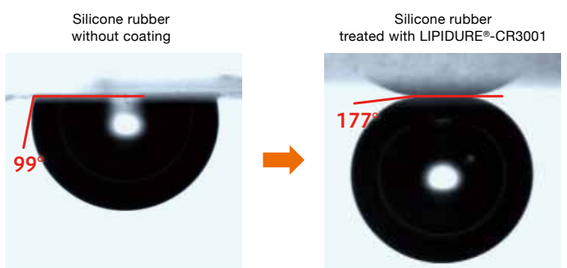
Surface modification step



1. Perform surface oxidation treatment.
   * O_2 plasma, UV ozone, or corona discharge treatment recommended.
   * Water contact angle to be ≈30°.
2. Dip coat with the coating solution.
   * The coating liquid should be prepared immediately before use.
3. Dry in an oven at 110°C for 30 min. to immobilize LIPIDURE®-CR3001 on the substrate
4. Complete.
   * Residual LIPIDURE®-CR3001 can be removed by rinsing with water.

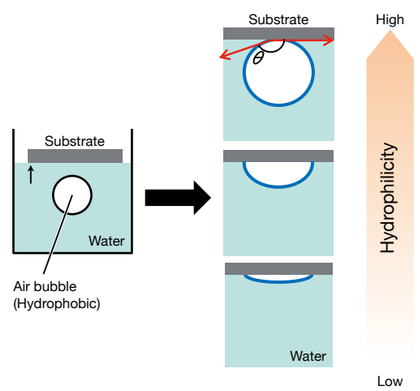
[Hydrophilic coating for silicone]

A silicone rubber sheet was modified with LIPIDURE®-CR3001. Contact angle (air in water) of the CR3001-modified surface was measured to confirm the improvement of hydrophobicity.



Hydrophilization of silicone rubber surface

[Principle of contact angle measurement]



[Coating procedure for metal and surface hydrophilicity]

A metal foil, SUS 304 was used as an example, was modified with LIPIDURE®-CR3001.

Contact angle of the substrate modified with CR3001 was measured to confirm the improvement of hydrophobicity.

Coating solution: LIPIDURE®-CR3001 EtOH solution was dropped into the same weight of hydrochloric acid (pH≈4) with stirring, immediately before use.

Concentration: Final concentration of CR3001 was 2.0 wt%

SUS 304

- Cleaned by Ultra sonication in organic solvent.
- Treated with 35% nitric acidto form oxide film.
- Dip coated with coating solution

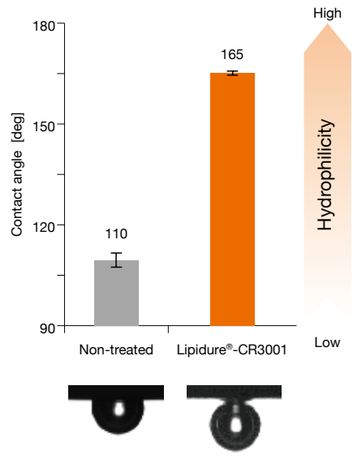
SUS 304 + adsorbed CR3001

- Dried in an oven at 110°C for 30 min to silanize the surface.

SUS 304 + immobilized CR3001

- Washed with purified water.

Evaluation
Contact angle was measured.
(Captive bubble method in water)



LIPIDURE®-CR3001 impart excellent hydrophilicity on SUS 304 surface.

[Suppression of protein adsorption]

Metal foils modified with LIPIDURE®-CR3001 were characterized in terms of protein adsorption property.

SUS 304 or titanium (1 cm X 1 cm)

- Modified with LIPIDURE®-CR3001 in the same procedure as descrived above

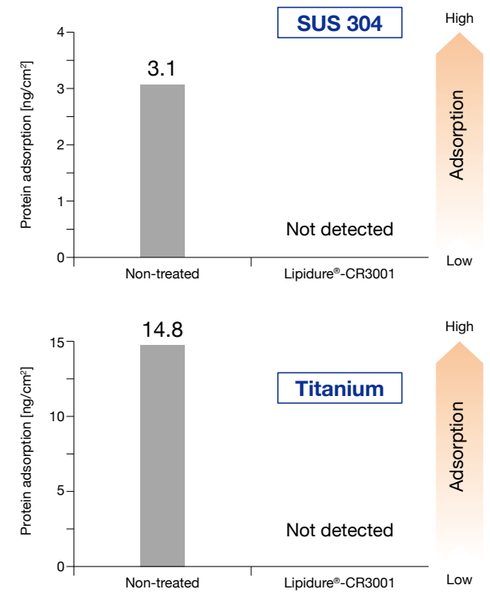
CR3001 treated

- Set in a 12-well plate

- 2 mL of Horseradish peroxidase (Wako Pure Chemical) was added. (10 mg/mL for SUS, 3 mg/mL for Ti)
- Gently shaken for 15 min in a room temperature
- Washed three times with 2 mL of PBS containing 0.05% Tween 20
- Set in a new plate

- Colorimetric substrate was added and reacted in a room temperature for 10 min.
- Quenched with sulfuric acid.

Evaluation
Absorbance at 450 nm was measured



LIPIDURE®-CR3001 completely suppressed protein adsorption on SUS 304, and titanium.

[Procedure 2 of coating on substrate with LIPIDURE®-CR3001]

If the coating by procedure 1 is difficult, please try coating by procedure 2.

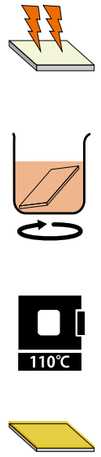
Preparation of coating solution

❶ **Dissolve LIPIDURE®-CR3001 in ethanol.**
・CR3001/ethanol = 0.5 - 2.0 wt%

❷ **Add 250 mM HCl aq. into LIPIDURE®-CR3001 ethanol soln. with stirring.**
・CR3001 soln./ HCl aq. = 100/ 1 (w/w)

❸ **Stir at RT for 30 min to completely activate CR3001.**
・Proceed to surface modification step instantly.

Surface modification step



❶ **Perform surface oxidation treatment.**
・O2 plasma, UV ozone, or corona discharge treatment recommended.
・Water contact angle to be ≈ 30°.

❷ **Dip coat with the coating solution.**
・The coating liquid should be prepared immediately before use.

❸ **Dry in an oven at 110 °C for 30 min. to immobilize LIPIDURE®-CR3001 on the substrate.**

❹ **Complete.**
・Residual LIPIDURE®-CR3001 can be removed by rinsing with water.

[Alternative test regarding suppression effect of virus adhesion]

*Phage was used as modelvirus in this evaluation.

Immobilize LIPIDURE®-CR3001 on glass.
(refer to Procedure 2 of coating with LIPIDURE®-CR3001)

↓ Put the glass into 24-well plate and sterilize by UV over night.

Add 0.5 mL of bacteriophage solution to each well.

↓

Incubate at ①37°C or ②25°C for 3 hr.

↓ Wash the glass with distilled water.

Transfer the glass to conical tube and add 1.0 mL of medium.

↓ Shake for 1 min.

After removal of the glass, mix 0.1 mL of medium (containing phage) remaining in the conical tube with 0.9 mL of normal medium.

↓

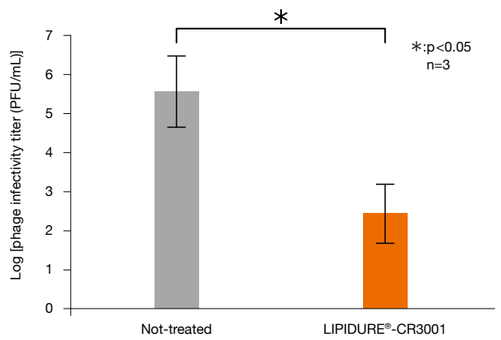
Mix 0.1 mL of phage-containing medium prepared as described above, 0.1 mL of bacterial solution and 3 mL of agar medium and then add all of the mixture to the agar medium plate.

↓ Incubate at ①37°C or ②25°C overnight.

Count viral plaque and calculate phage infectivity titer.

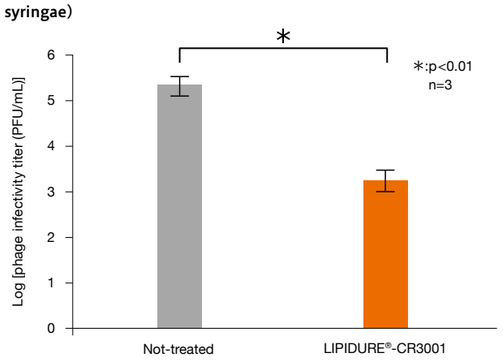
①Non-enveloped virus

(phage:Escherichia coli phage Qβ, bacteria:Escherichia coli)



②Enveloped virus

(phage:Pseudomonas syringae phage ϕ6, bacteria:Pseudomonas syringae)

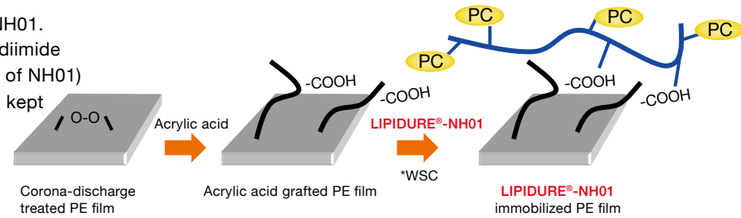


LIPIDURE®-NH01

[Coating procedure]

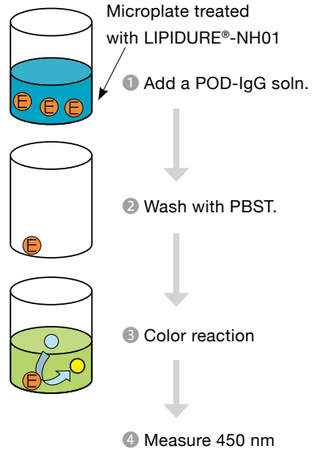
❶ Dissolve 1 wt% of WSC* to LIPIDURE®-NH01. (1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide Hydrochloride (1 g) is dissolved into 99 g of NH01)
❷ Base material is put into the solution and kept at room temperature for 24 hr.
❸ After the reaction, the sample is washed with water.

*Water Soluble Carbodiimide

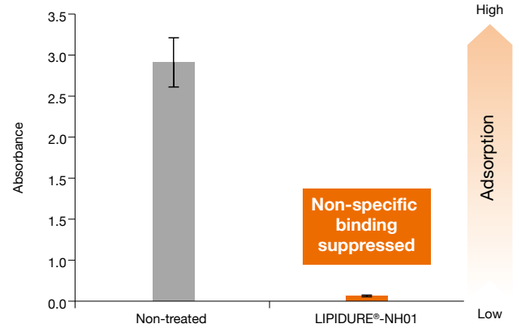


[Suppression of protein adsorption]

Procedure



Result



POD-IgG adsorption on carboxy-plate treated with LIPIDURE®-NH01

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03 Additives for eye drops, YT-LIPIDURE®

[Function of YT-LIPIDURE®]

- Dry eye score improvement
- Protective effect against preservatives
- Prevention of tear film break-up
- Stabilization of tear film
- Moisturizing
- Possible to apply on wearing hard and soft contact lenses
- Approved as additives by PMDA* in Japan

*PMDA = Pharmaceuticals and Medical Devices Agency

Product Line-up

Product	Type	Size (Package)	Appearance
YT-LIPIDURE®-EL	Low Endotoxin	1 kg, 10 kg (Polyethylene bottle)	5% polymer aqueous solution without preservatives
YT-LIPIDURE®-PMB-H*	High Viscosity	1 kg, 10 kg (Polyethylene bottle)	5% polymer aqueous solution without preservatives
YT-LIPIDURE®-LS*	High Lubricity	1 kg, 10 kg (Polyethylene bottle)	1% polymer aqueous solution without preservatives

(*) Prototype : These products above are under development we don't warrant that it will not infringe any laws, regulations or patents.

YT-LIPIDURE®-EL

[Safety Data]

Product	Result
Primary skin irritation test	No irritation
Cumulative skin irritation test	No irritation
Skin sensitization test	Negative
Cytotoxicity test	No stimulation

Product	Result
Eye irritation test	No irritation
Single-dose toxicity test	LD50>2000 mg/kg
Human patch test	Negative
Reverse mutation test	Negative

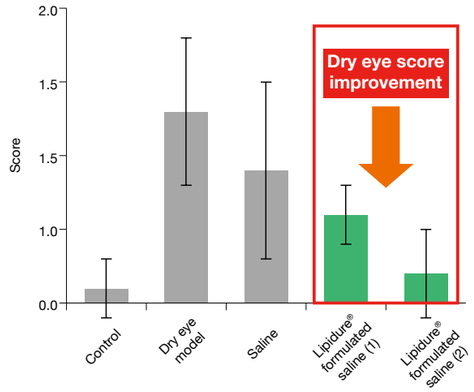
[Dry Eye Score Improvement]

Method

1. Prepare dry eye model (n = 3).
2. Forcibly open eyes for 3 hr.
3. Instill each test solution into eyes every 30 min. (total:6 times).
4. Dye cornea with Methylene blue.
5. Score dyed cornea status.

Score

Dyed status of cornea	Score
Not dyed with dye	0
Dyed small part of cornea lightly	0.5
Dyed less than 1/4 of cornea area	1
Dyed between 1/4 and 1/2 of cornea area	2
Dyed between 1/2 and 3/4 of cornea area	3
Dyed more than 3/4 of cornea area	4

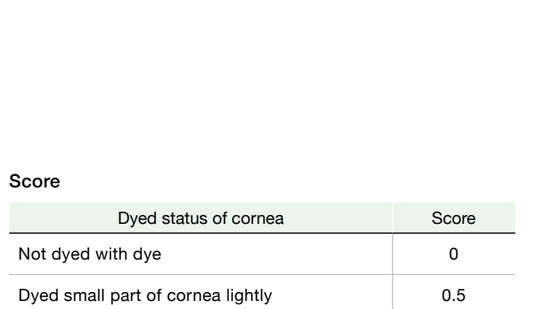


[Protective Effect of LIPIDURE® Against Preservatives]

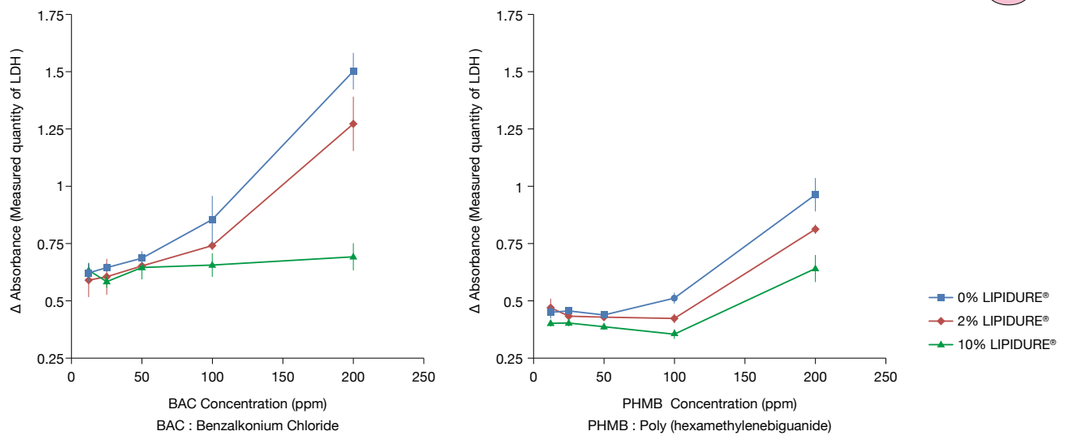
Method

Evaluate the effect of LIPIDURE® against damages by BAC and PHMB.

Lactate dehydrogenase (LDH) is an endogenous enzyme, which comes out of a cell when the cell is damaged.



Result



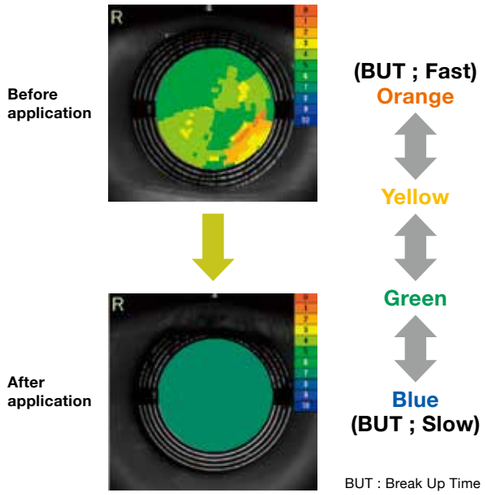
LIPIDURE® significantly decreases the LDH levels induced by preservatives.

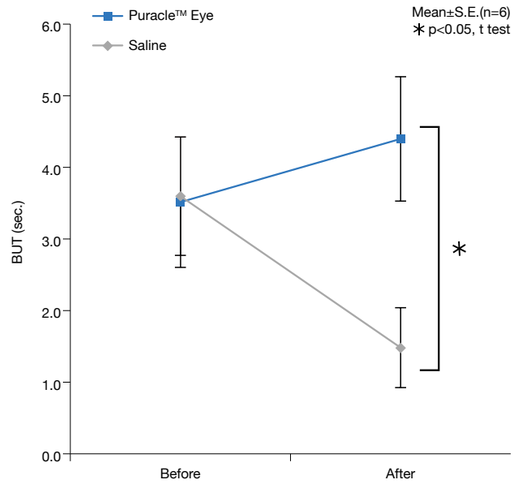
[Application to Eye Drops]

Puracle™ Eye Artificial Tear

- Category : 3rd category pharmaceutical product by PMDA* in Japan
  *PMDA = Pharmaceuticals and Medical Devices Agency
- Actives : Sodium Chloride, Potassium Chloride
- Additives : LIPIDURE®, PHMB etc.
- Dosage : Apply 1 to 3 drops, 1 to 6 times a day
- Advantages
  Effective for eye fatigue, tear supplement (dry eye), improve discomfort on wearing hard and soft contact lens and blurred vision (when much eye mucus is discharged
- Volume : 10 mL
- Sold & Distributed by Nitto Medic Co., Ltd.
- Manufactured by NOF CORPORATION

[Prevention of Tear Film Break-up]





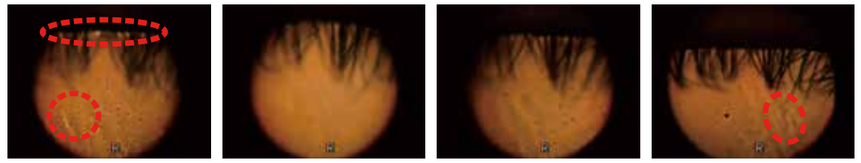
[Stabilization of Tear Film]

Method

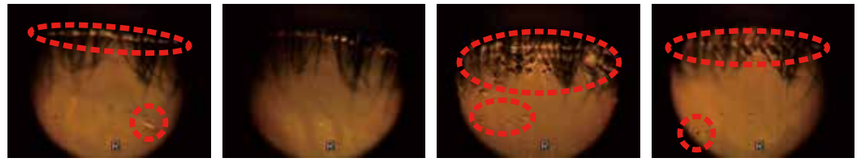
1. Apply eye drops or saline on soft contact lens wearers.
2. Measure Non-Invasive tear film Break Up Time (NIBUT).

Result

Puracle™ Eye

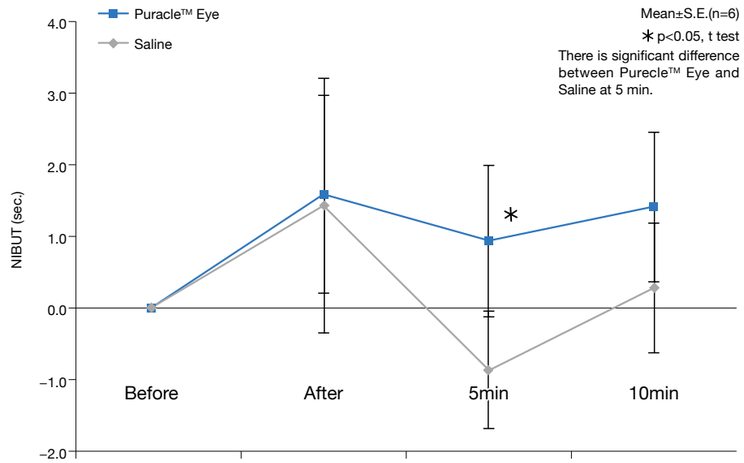


Saline



*Pictures taken at 5 sec after blink

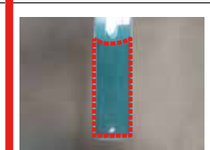
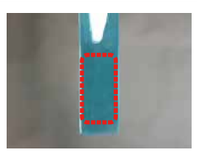
: Soft Contact Lens surface



[Moisturizing Effect for RGP Lens]

Method

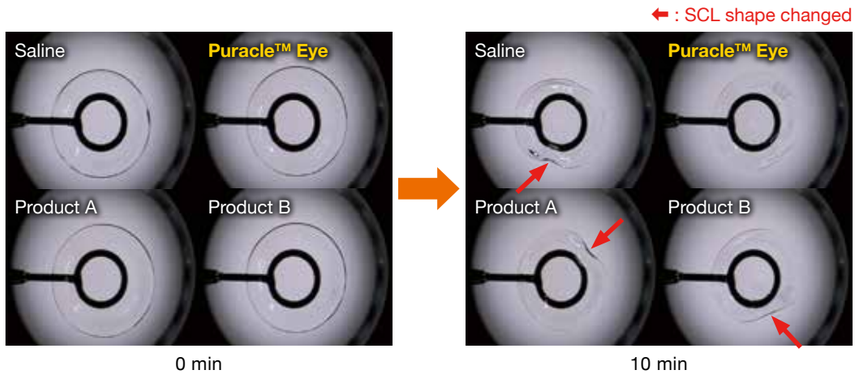
1. Soak Rigid Gas Permeable (RGP) lens in each eye drops for 1 min.
2. Take RGP lens out of the eye drops.
3. Measure break up time.

Saline	Puracle™ Eye	Product A	Product B
BUT 0 sec	BUT 24 sec	BUT 0 sec	BUT 18 sec
			

[Moisturizing Effect for Soft Contact Lens]

Method

1. Soak Soft Contact Lens (SCL) in eye drop and take them out from eye drop.
2. Observe lens shape for 10 min.

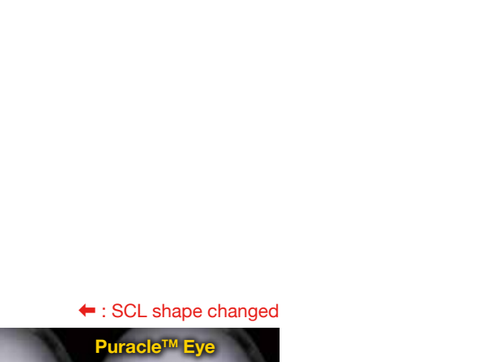


YT-LIPIDURE®-PMB-H

[Viscosity of ophthalmic agents]

Procedure: Kinematic viscosity of ophthalmic agents (contains: product;2.0 wt%, hypromellose [active ingredient];0.1 wt%, pH adjuster, buffer) was measured (Mean±S.D., n=3) Tukey-Kramer test (vs Control, **:p<0.01; vs Contains low Mw product • Contains medium Mw product, +:p<0.05)

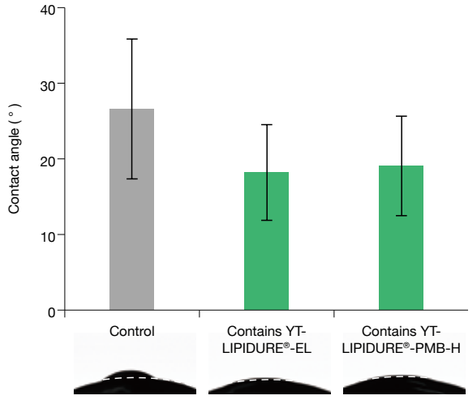
YT-LIPIDURE®-PMB-H significantly increases the viscosity of agents



[Wettability (Contact angle on lens)]

Procedure: Ophthalmic agents (contains product;2.0 wt%, hypromellose [active ingredient];0.1 wt%, pH adjuster, buffer) was dropped into a commercial contact lenses, and the contact angle was measured after 2 sec (Mean±S.D., n=3). The dotted line in the figure indicates the lens shape.

YT-LIPIDURE®-PMB-H improves surface wettability same as YT-LIPIDURE®-EL

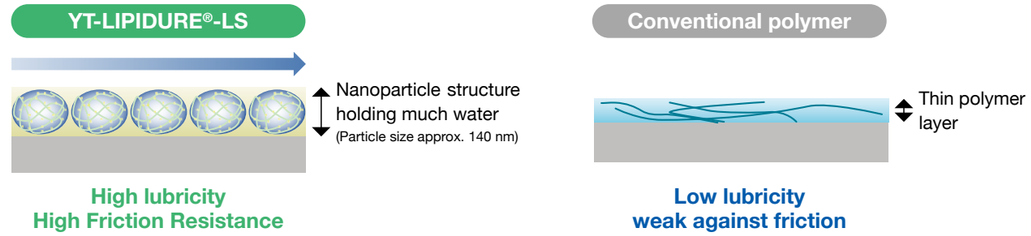


YT-LIPIDURE®-LS

[Product information]

Product information	: YT-LIPIDURE®-LS
Product Form	: 1 wt% aqueous solution
Character	: Light blue, slightly turbid solution
pH	: Approx. 5.0
NET	: 10 kg, 1 kg (Container material : PE)
Cautions	: Store at room temperature. Seal the container, store away from heat source and direct sunlight.
Recommended conc.	: 1.0 ~ 10 vol% as YT-LIPIDURE®-LS

[Lubricious hydrophilic layer with YT-LIPIDURE®-LS]



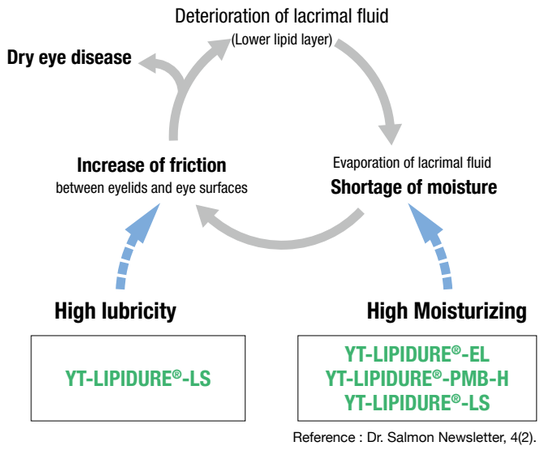
YT-LIPIDURE®-LS has high moisturizing property and lubricity.

[Safety Data]

Test items	Results
Primary skin irritation test	No irritation
Cumulative skin irritation test	No irritation
Skin Sensitization test	Negative
Cytotoxicity test (V79 cells, SIRC cells)	No stimulation
Eye irritation test	No irritation
Continuous ocular mucosal irritation test	No irritation
Single-dose toxicity test	> 2,000 mg/kg
Human patch test*	Safe
Reverse mutation test	Negative
Chromosomal aberration test	Negative

*T. Sugai, Journal of Japanese Cosmetic Science Society, 19, 49-56(1995).

How to occur and care the dry eye disease



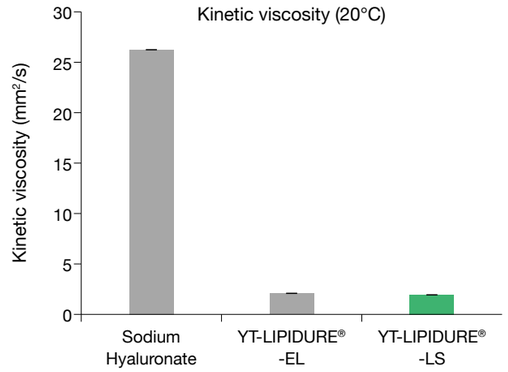
Reference : Dr. Salmon Newsletter, 4(2).

Supplement of lubricity and moisture is effective for dry eye care.

[Kinetic viscosity]

Polymer conc. 0.1 wt%

Mean±S.D.(n=3)



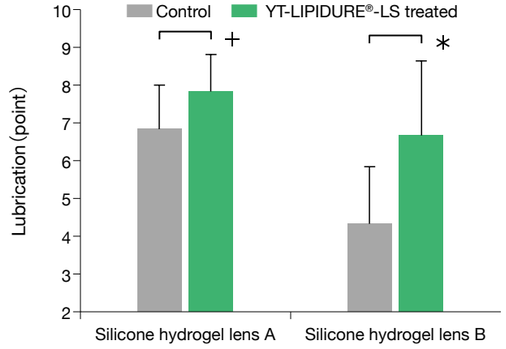
[Evaluation of lubricity improvement effect]

After replacing the packing solution of commercial contact lenses with saline, lenses were immersed in YT-LIPIDURE®-LS diluted to 10-fold with saline for 2 hr and then autoclaved. Rubbed lens with fingers and evaluated its slipperiness.

Polymer conc. 0.1 wt%

Mean±S.D.(n=6)
＋ p=0.14, ∗ p<0.05, Student's t-test

Lubricity is rated on a scale of 1 to 10. (polymacon: 2 points, Omafilcon A: 8 points)

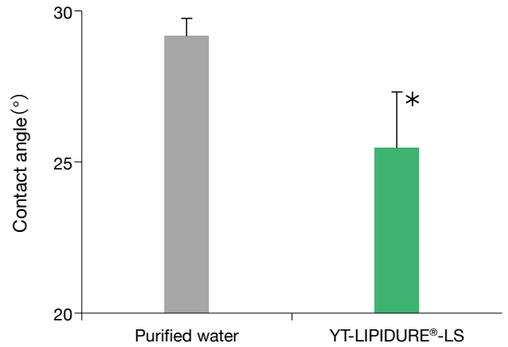


[Wettability (Contact angle measurement)]

YT-LIPIDURE®-LS was diluted 10-fold with purified water. Then the contact angle was measured by the sessile drop method (drop: 1 μL, subject: slide glass).

Polymer conc. 0.1 wt%

Mean±S.D.(n=3)
∗ p<0.05, Student's t-test



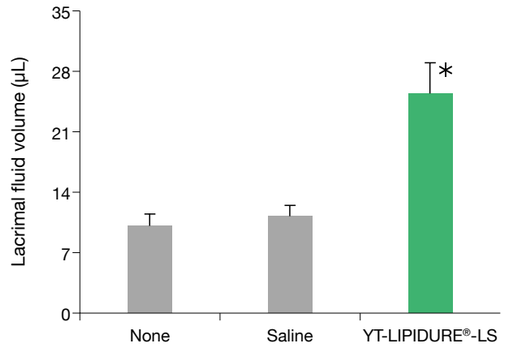
[Evaluation of dry eye improvement effects ① Lacrimal fluid volume]

YT-LIPIDURE®-LS (10-fold dilution) and saline were instilled into *N*-acetylcysteine-treated dry eye model rabbits once a day for 5 days. Then the lacrimal fluid volume was measured by schirmer test paper.

Polymer conc. 0.1 wt%

Mean±S.D.(n=9-12)
∗ p<0.05, Dunnett's test vs Saline

Research report by Noriaki Nagai of KINDAI UNIVERSITY
N. Nagai et al. "MPC Polymer Promotes Recovery from Dry Eye via Stabilization of the Ocular Surface.", Pharmaceutics, 13,no2(2021):168

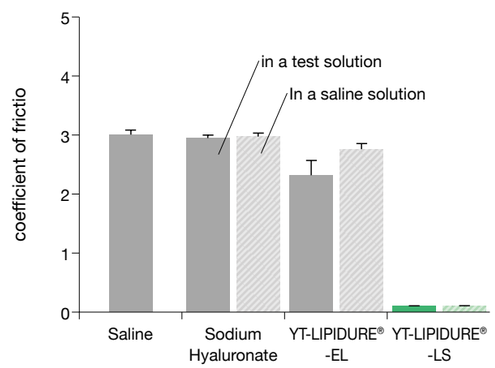


[Lubricity and its durability (HEMA/MAA gel)]

Immerse the gel plate in the test solution for 2 hr. Measure the coefficient of friction using a friction tester with a silicone probe. Then immerse the gel plate in a saline solution and measure the coefficient of friction.

Polymer conc. 0.1 wt%

Mean±S.D.(n=3)



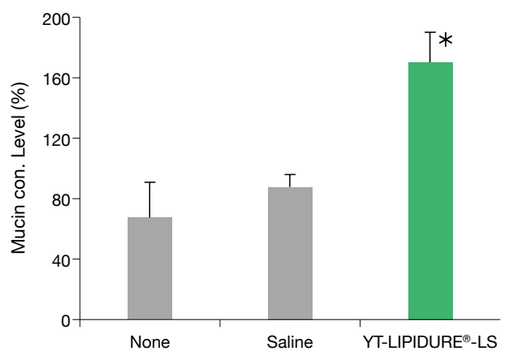
[Evaluation of dry eye improvement effects ② Mucin level in lacrimal fluid]

YT-LIPIDURE®-LS (10-fold dilution) and saline were instilled into *N*-acetylcysteine-treated dry eye model rabbits once a day for 5 days. Then the concentration of extracted mucin from lacrimal fluid was measured by fluorescence intensity.

Polymer conc. 0.1 wt%

Mean±S.D.(n=9-12)
*Mucin con. level in the normal model as 100%.
∗ p<0.05, Dunnett's test vs Saline

Research report by Noriaki Nagai of KINDAI UNIVERSITY
N. Nagai et al. "MPC Polymer Promotes Recovery from Dry Eye via Stabilization of the Ocular Surface.", Phrmaceutics, 13,no2(2021):168

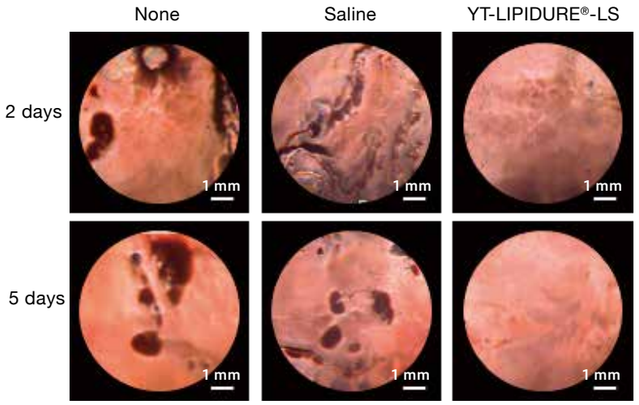


[Evaluation of dry eye improvement effects ③ Stabilization of lacrimal fluid]

YT-LIPIDURE®-LS (10-fold dilution) and saline were instilled into *N*-acetylcysteine-treated dry eye model rabbits once a day for 5 days. The ocular surface was monitored by using a dry eye monitor.

Polymer conc. 0.1 wt%

Research report by Noriaki Nagai of KINDAI UNIVERSITY
N. Nagai et al. “MPC Polymer Promotes Recovery from Dry Eye via Stabilization of the Ocular Surface.”, Phrmaceutics, 13,no2(2021):168



The dark parts of the images reflect break-up states of the lacrimal fluid layer

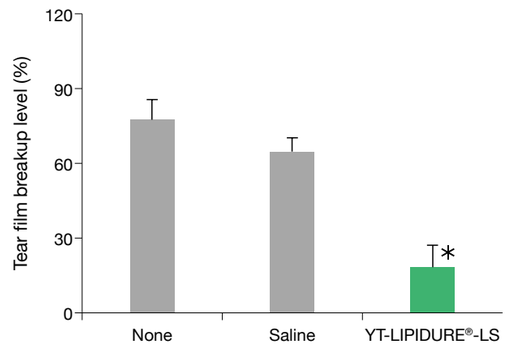
[Evaluation of dry eye improvement effects ④ Tear film breakup level]

YT-LIPIDURE®-LS (10-fold dilution) and saline were instilled into *N*-acetylcysteine-treated dry eye model rabbits once a day for 5 days. The tear film breakup level on the ocular surface was measured by a dry eye monitor.

Polymer conc. 0.1 wt%

Mean±S.D.(n=9-12)
*Tear film breakup level in the normal model as 100%.
∗ p<0.05, Dunnett’s test vs Saline

Research report by Noriaki Nagai of KINDAI UNIVERSITY
N. Nagai et al. “MPC Polymer Promotes Recovery from Dry Eye via Stabilization of the Ocular Surface.”, Phrmaceutics, 13,no2(2021):168



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YT-LIPIDURE®-EL

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2) K. Ishihara “New Biomaterials for Use in Contact Lenses” Journal of Japan Contact Lens Society 61 (1), 2-8, 2019

3) R. Ando-Kobayashi, M Tsuchida et al. “Reducing the Cytotoxicity of Polyhexamethylene Biguanide (PHMB) by Formulation with an MPC Polymer” Journal of Japan Contact Lens Society 52 (4), 265-269, 2010

YT-LIPIDURE®-LS

1) N. Nagai et al. “MPC Polymer Promotes Recovery from Dry Eye via Stabilization of the Ocular Surface.”, Pharmaceutics, 13, no2(2021):168

2) M Minami, M Yamaguchi et al. “Effect of MPC Polymer on Corneal Toxicity and Corneal Drug Permeation of Benzalkonium Chloride in Corneal Epithelial Cells” Journal of the eye 37 (10), 1309-1314, 2020

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