

TORAY

Innovation by Chemistry

Hollow Fiber Dialyzer

TORAY FILTRYZER™ NF-U series



Adsorption & *Anti-thrombogenicity*

Characteristics of TORAY FILTRYZER NF series

The membrane having the property of protein adsorption and suppressing structural change of adsorbed proteins

Design concept of a new PMMA membrane

PMMA has an adsorption property of several kinds of proteins. As the one of the reasons for the occurrence of coagulation during hemodialysis, it is considered that platelets are activated by adhesion on membrane surface because of recognizing protein structure which was

changed by adsorption on membrane (Fig.1 a). In TORAY FILTRYZER™ NF (NF), we aimed at suppressing platelet adhesion on membrane surface by preventing proteins adsorbed on membrane from structural changes (Fig.1 b).

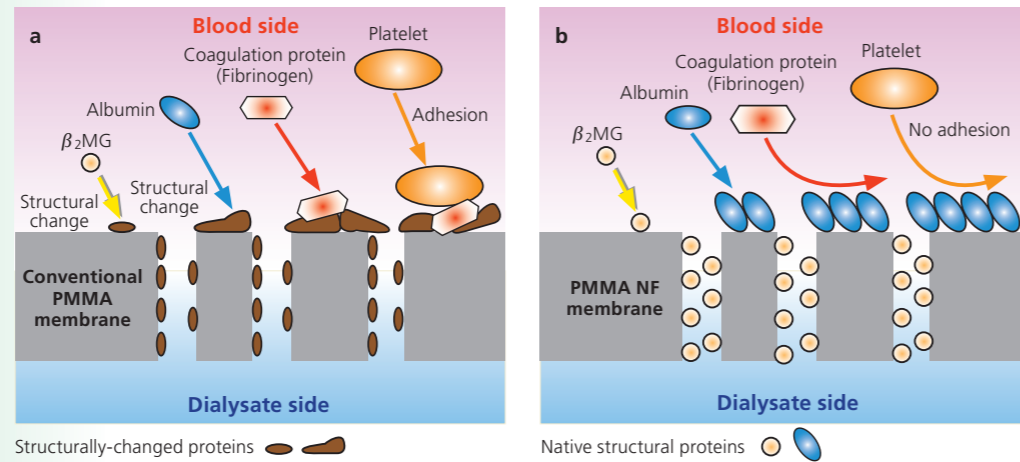


Fig.1 Schema of the protein adsorption mechanism on the PMMA membrane¹⁾

Structural change of adsorbed proteins

Structural change of albumin adsorbed on membrane was analyzed by using "Attenuated total reflection Fourier transform infrared spectroscopy (ATR-FTIR)". Peak of amide bond of albumin adsorbed on NF membrane was closer to that of native albumin than that on conventional PMMA membrane (Fig.2).

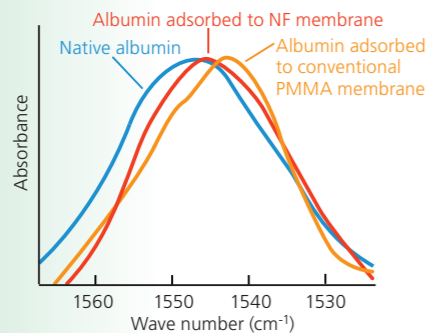


Fig.2 ATR-FTIR spectra of albumin adsorbed on the NF and conventional PMMA membranes, and native human serum albumin¹⁾
(Data were obtained from in vitro investigation using human albumin solution and hollow fiber sliced in half lengthwise.)

Improvement of anti-thrombogenicity

Platelet adhesion on the NF membrane surface was lower than the conventional PMMA membrane (Fig.3). The amounts of fibrinogen adsorbed on the NF membrane were lower than the conventional PMMA membrane (Fig.4).

Suppression of platelet adhesion on membrane

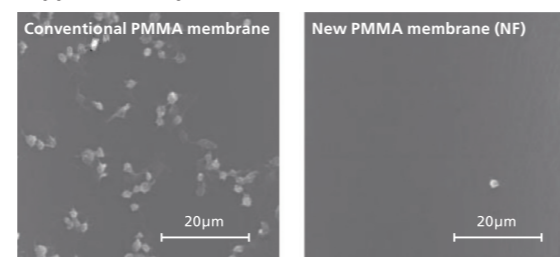


Fig.3 Platelet adsorption on membrane surface in vitro²⁾
(SEM image obtained from in vitro investigation using human blood.)

Suppression of fibrinogen adsorption on membrane

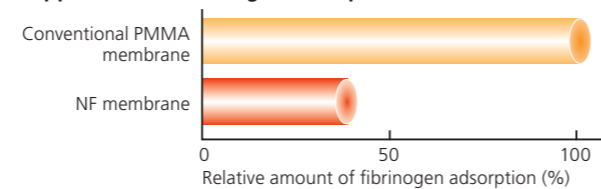


Fig.4 Adsorption amounts of fibrinogen^{2) #)}
* The amount of conventional PMMA membrane is set as 100%

Unique membrane structure and protein adsorption property

PMMA membranes have a homogeneous structure, in which pores on both blood and dialysate surfaces are almost similar in size. The whole PMMA membrane acts as both a separating layer and an adsorption site for

solute (Fig.5). PMMA membranes have adsorption properties and adsorb about 8 times the amount of proteins adsorbed by polysulfone (PS) (Fig.6, in vitro study).

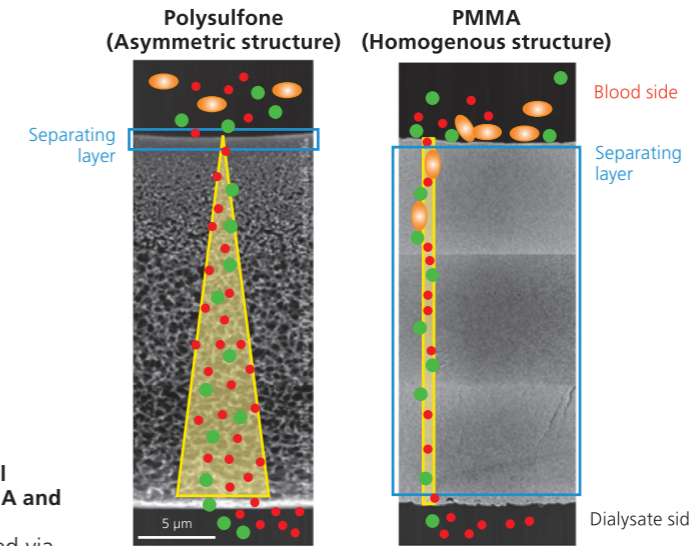
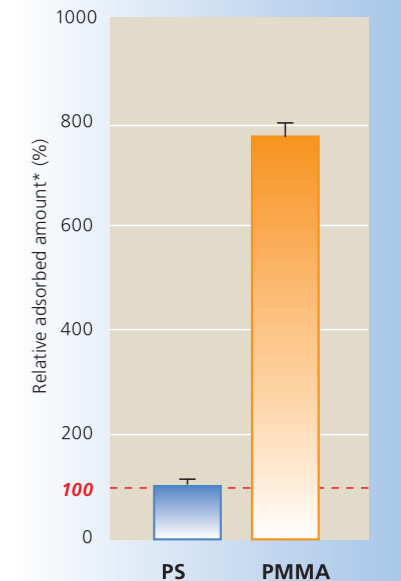


Fig.5: Cross-sectional image of PMMA and polysulfone.
Images were obtained via electron microscopy.

MW: molecular weight, PBUTs: protein-bound uremic toxins

- Small MW solutes (ex. Urea, Creatinine etc.)
- Low MW proteins (ex. β_2 -microglobulin etc.)
- Middle and high MW solutes (ex. Albumin, PBUTs etc.)



* The amount of PS is set as 100%

Fig.6: Comparison of the amounts of proteins adsorbed by PMMA and polysulfone³⁾.

The PMMA-specific adsorption property

It is confirmed that platelet adhesion is suppressed in NF while adsorption performance in NF is almost equal to conventional PMMA (Fig. 7, 8).

Protein adsorption

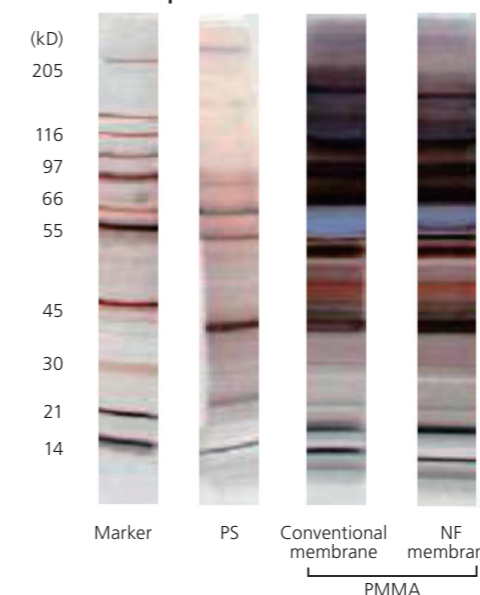


Fig.7 Electrophoretic patterns of proteins adsorbed by membrane^{2) #)}

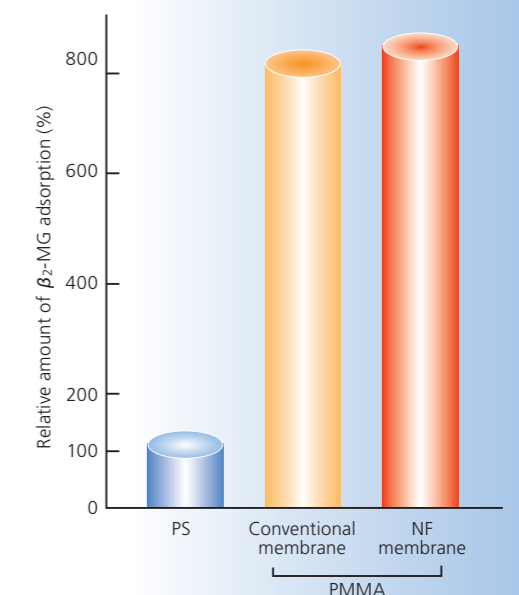


Fig.8 Adsorption amounts of β_2 -microglobulin^{2) #)}
* The amount of PS is set as 100%

1) Oshihara W et al., Contrib Nephrol. 2017;189:230-236.

2) Takahashi H et al., Kidney and Dialysis (suppl.) High Performance Membrane '13 2013;75:230-236.

3) Sugaya H et al., Kidney and Dialysis (suppl.) High Performance Membrane '06 2006;61:19-23.

4) Masakane I et al., Renal Replacement Therapy 2017;3:32

5) Uchiuni N et al., Renal Replacement Therapy 2018;4:32

#: Results were obtained from in vitro investigation using human plasma

Expected effect of albumin leakage controlled dialyzer NF-U series.

Characteristics of PMMA Membrane

- Excellent Biocompatibility¹⁾
- Protein adsorption properties and it can remove large molecular weight proteins.
- Good removal balance of small uremic toxins and high-molecular weight substances.

Expected characteristics of Filtryzer NF Series

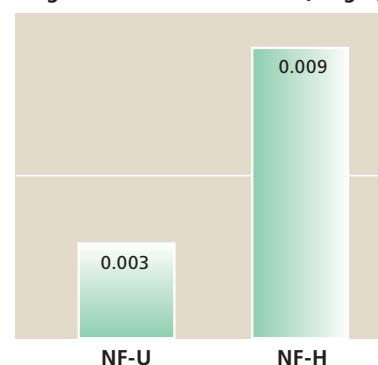
By modifying the membrane surface that suppresses the structural change of the adsorbed protein, we succeeded in suppressing platelet adhesion and further improving biocompatibility.

Various clinical reports on NF Series

- 1) Suppression of platelet activation.
- 2) Improvement of dialysis pruritus and unidentified side-effects⁴⁾⁵⁾.
- 3) Improvement of nutritional condition of patients⁵⁾.

NF-U has a feature of minimized albumin leakage, and it also allows to use comfortably for patients who are concerned about malnutrition.

Sieving Coefficient of Albumin (Target)



Specifications		NF-U Series			
Type		NF-1.3U	NF-1.6U	NF-1.8U	NF-2.1U
Fibers	Effective surface area (m ²)	1.3	1.6	1.8	2.1
	Effective length (mm)	195			
	Inside diameter (μm)	200			
	Membrane thickness (μm)	30			
Blood volume (mL)		83	103	118	135
Clearance (mL/min)*	Urea	233	246	254	260
	Creatinine	200	217	225	231
	Phosphate	182	198	208	217
	Vitamin B ₁₂	110	128	140	149
	Inulin	62	72	77	85
UFR in vitro (mL/hr/mmHg) **		32	38	45	48

* Clearance are typical data with aqueous solution. (Q_B: 300 mL, Q_D: 500±10 mL/min, Q_F: 10±2 mL/min, Temp.: 37±1 °C)

** UFRs are typical data with bovine blood. (Ht: 32±3 %, TP: 6.0±0.5 g/dL, Q_B: 300 mL/min, TMP: 50 mmHg, Temp.: 37±1 °C)

TORAY

Manufacturer:

Toray Industries, Inc.

1-1, Nihonbashi-Muromachi 2-chome,
Chuo-ku, Tokyo 103-8666, JAPAN

Exporter:

Toray Medical Co., Ltd.

4-1, Nihonbashi-Honcho 2-chome,
Chuo-ku, Tokyo 103-0023, JAPAN



Toray International Italy S.r.l.

Via Mecenate 86, 20138 Milan, ITALY