화학공학소재연구정보센터

IP(Information Provider) 연구분야 보고서

Bio 분야에서의 Polyurethane의 응용

3장. Biostable 폴리우레탄의 연구 동향

• Biostable polyurethanes (PUs)

: 생 안정성 (biostable)은 인체내에서 장기적으로 사용되어지는 biomaterials의 주요한 요소 중의 하나이며, biostable 폴리우레탄 또한 꾸준히 연구되어져 왔다. 인체내에서 폴리우레탄은 주로 활성 산소 종에 의한 산화 stress나 효소에 의한 반응에 의하여 분해되어 저분자화 된다. 일반적으로 polyether-based 폴리 우레탄은 polyester-based 폴리 우레탄 보다 가수분해 반응에 대하여 더 안정하다. 또한 결정성 (degree of crystallinity)은 생안정성 고분자의 주요한 요소로써, 폴리 우레탄의 hard segment의 비율이 상대적으로 높고, 수소 결합 (hydrogen bonding)에 의한 배열이 더 잘 되어 있을 수록 안정한 특성을 보인다.

Figure 1. Potential Hydrogen Bonding in Polyurethanes.

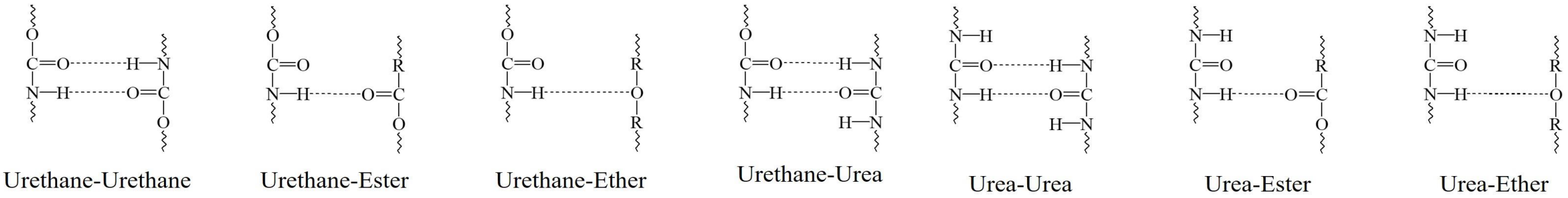

Table 1. Thermal Stability of Different Types of Urethanes.

Type of urethane group	Approximate upper Stability temperature (°C)
Alkyl—HN—CO—O—Alkyl	~ 250
Aryl—HN—CO—O—Alkyl	~ 200
Alkyl—HN—CO—O—Aryl	~ 180
Aryl—HN—CO—O—Aryl	~ 120

: 폴리 우레탄은 일반적으로 높은 열 안정성을 보여, 인체내에서의 열분해 가능성은 매우 낮다.

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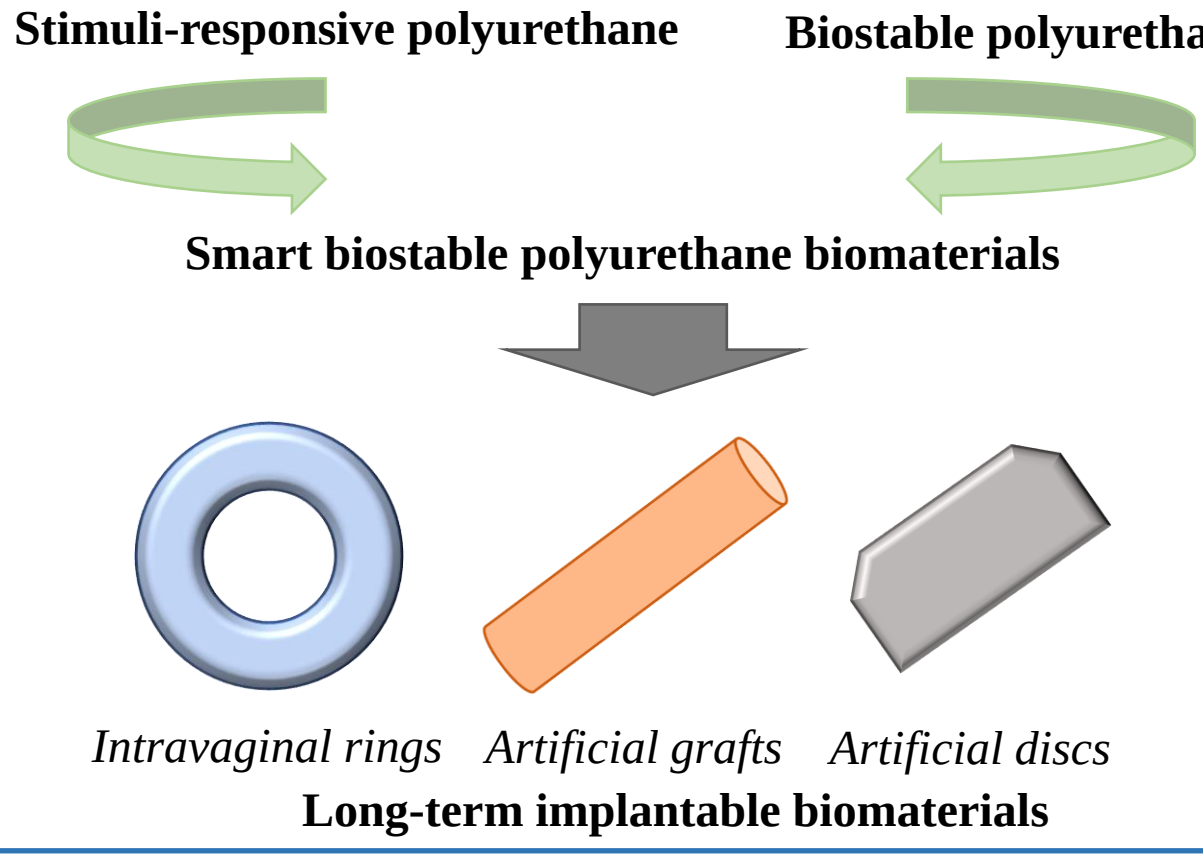
• Biostable polyurethanes (PUs)

: 생안정성 폴리우레탄은, 폴리우레탄의 자극감응성 물질로의 개질 가능한 특성과 더불어 응용되어, 인체내에 삽입 되어 장기적으로 사용될 수 있는 다양한 성능을 지닌 약물전달 기기나 인공 장기로 (e.g. intravaginal ring, artificial graft, and artificial disc) 개발되어 사용될 수 있다 .

Figure 2. Smart and Biostable Polyurethanes for Long-Term Implants.



ACS Biomaterials Science & Engineering, 4: 1479-1490, 2018

• Biostable PDMS-based polyurethanes (PUs) for blood-compatible biomaterials

: PDMS-based 폴리 우레탄은 polydimethylsiloxanes(PDMS) 의 특성 (low glass transition temperature, low surface energy, high gas permeability, a highly hydrophobic surface, and very good stability to heat and oxidative stress)과 폴리 우레탄의 특성 (elastomer, tunable physicochemical structural properties, and relatively good blood-compatibility)을 모두 지닐 것이라 기대되어 biostable polyurethane biomaterial로써 많은 연구가 진행 되어지고 있다.

특히, 양쪽성 이온 (zwitterion)을 지닌 PDMS-PU는 혈액적합성 생체재료서 (e.g. biostable vascular conduits, catheters, artificial lungs, and microfluidic device) 연구가 활발히 진행 되어지고 있다.

Scheme 1. example of synthesis of PDMS-based zwitterionic PU (PDMS-SB-UU).

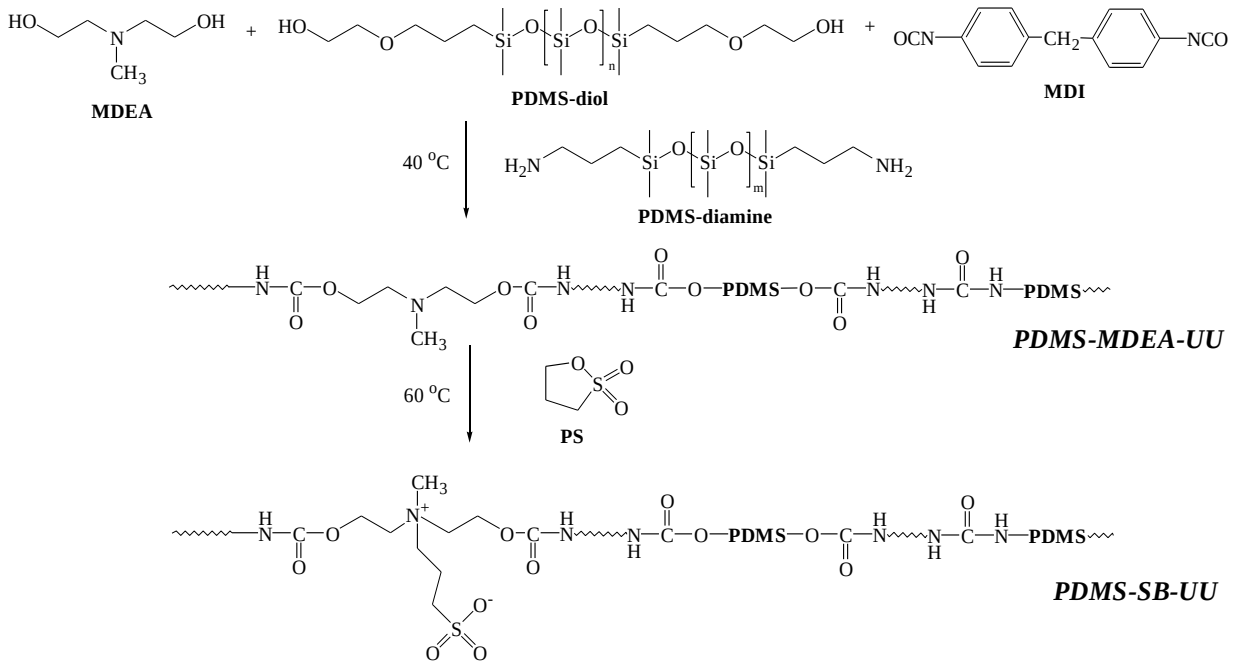


Table 2. Mechanical characteristics of PDMS-control, PDMS-SB-UU, and PDMS-SB-UU (n=3).

Polymer	Feed ratio of MDEA or SB (wt%)	Initial modulus (MPa)	Tensile strength (MPa)	Breaking Strain (%)
PDMS-Control	-	0.8 ± 0.1	2.0 ± 1.0	134 ± 36
PDMS-MDEA-UU	5	3.9 ± 0.3	8.7 ± 0.4	334 ± 25
PDMS-SB-UU	5	3.6 ± 0.3	6.1 ± 0.6	227 ± 21

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Figure 3. *In vitro* long-term stability studies by an enzyme using 100 U/mL lipase (A) and oxidative treatment using 30% H_2O_2 solution (B). Weight change versus exposed time was calculated for 8 weeks (n=3, $p < 0.05$ versus PDMS-Control).

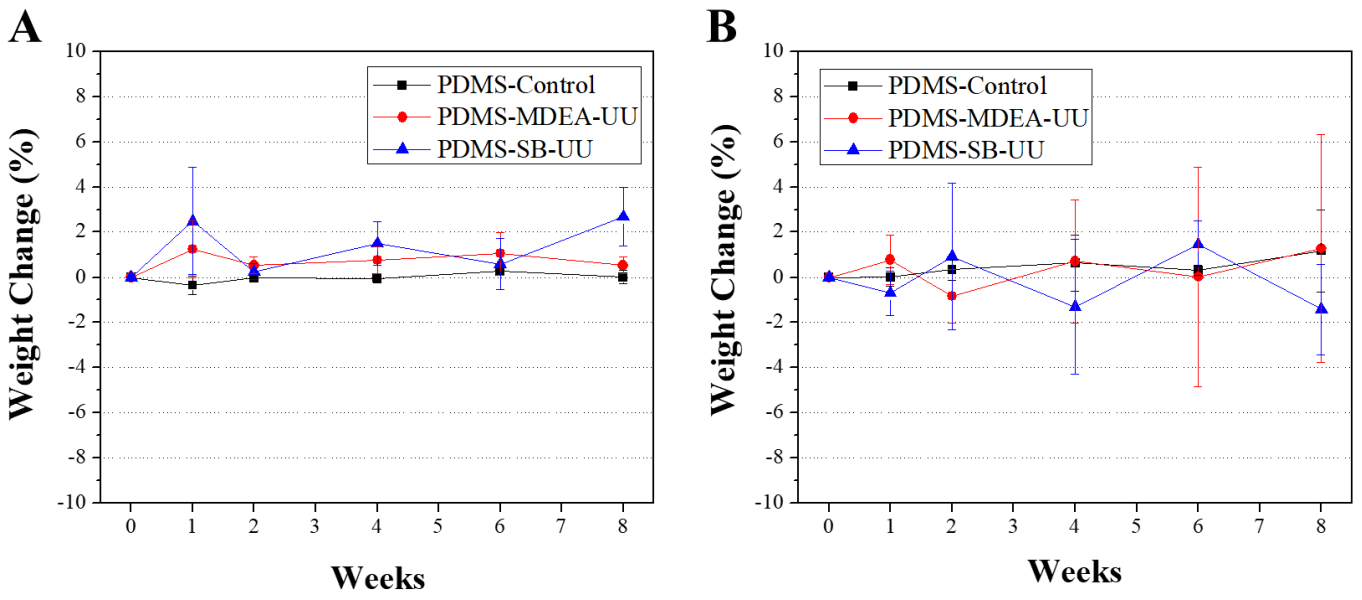

Figure 4. *X-ray diffraction (XRD) spectra of (A) control PDMS, (B) PDMS-MDEA-UU, and (C) PDMS-SB-UU solvent-cast films*

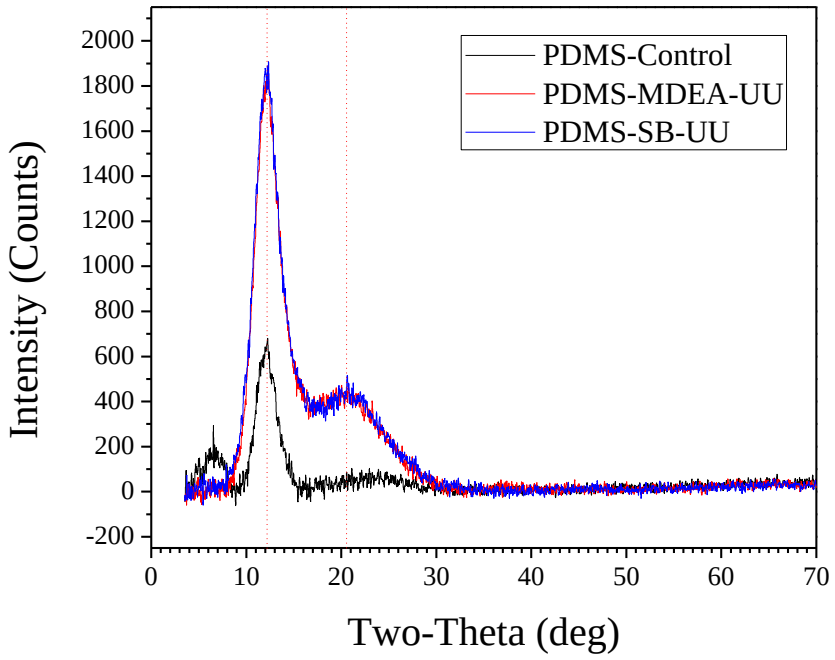

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Figure 5. *In vitro* (A) CO_2 and (B) O_2 permeability test using PDMS-SB-UU and PDMS-control films (n= 4, $p < 0.05$ versus PDMS-Control).

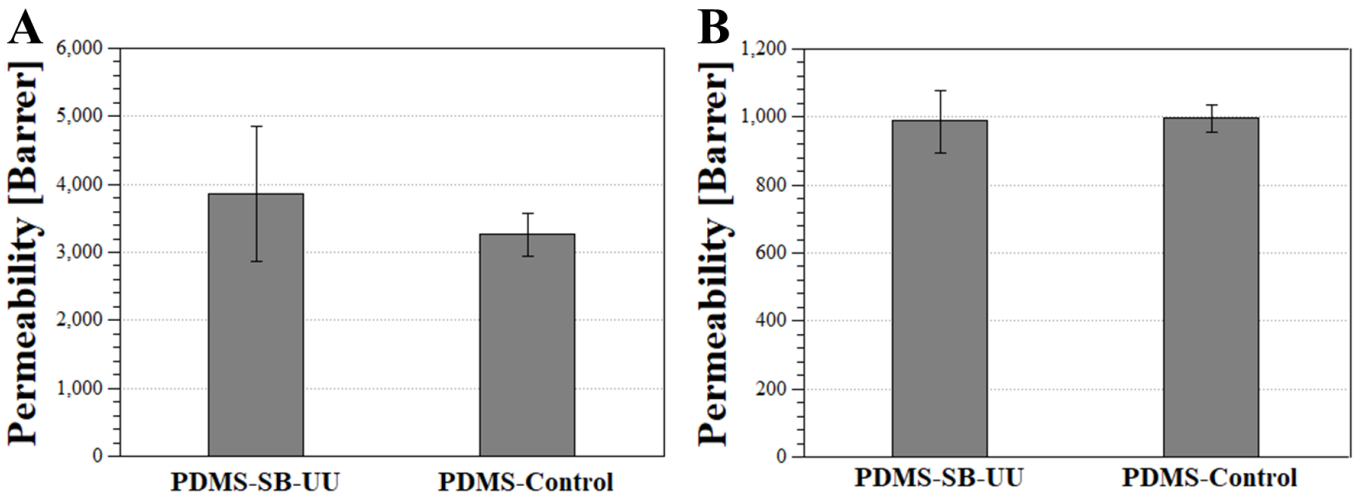

Figure 6. Protein (Fibrinogen) adsorption assay of (A) PDMS-control, (B) PDMS-MDEA-UU, (C) PDMS-SB-UU films (n=3, $p < 0.05$ versus PDMS-Control).

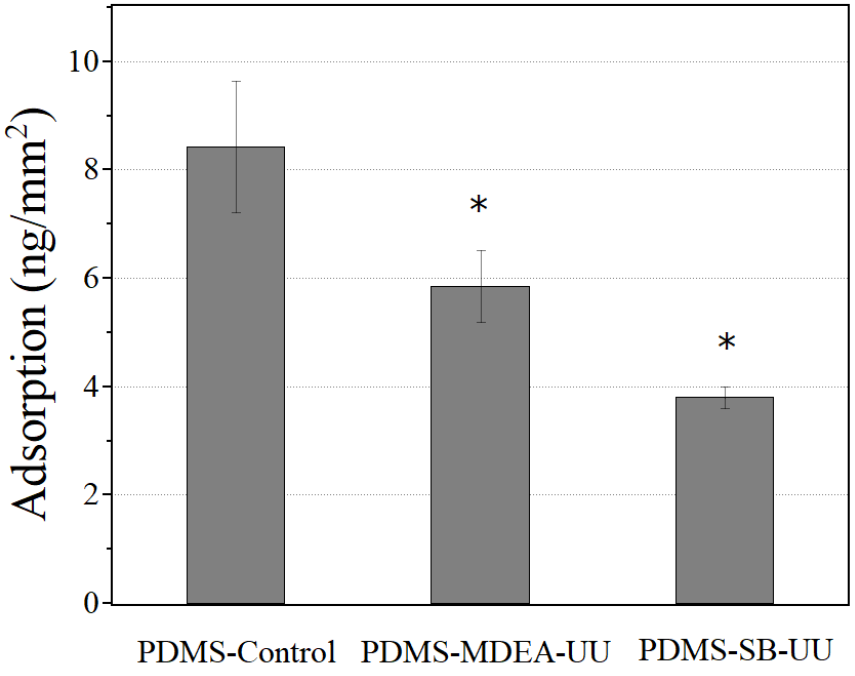

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Figure 7. Platelet deposition studies to (A) PDMS-control, (B) PDMS-MDEA-UU, (C) PDMS-SB-UU films observed by SEM after contact with ovine blood (citrated) for 3 h at 37 °C (n=3), and (D) deposited platelet number quantified by LDH assay (n=3, p<0.05)

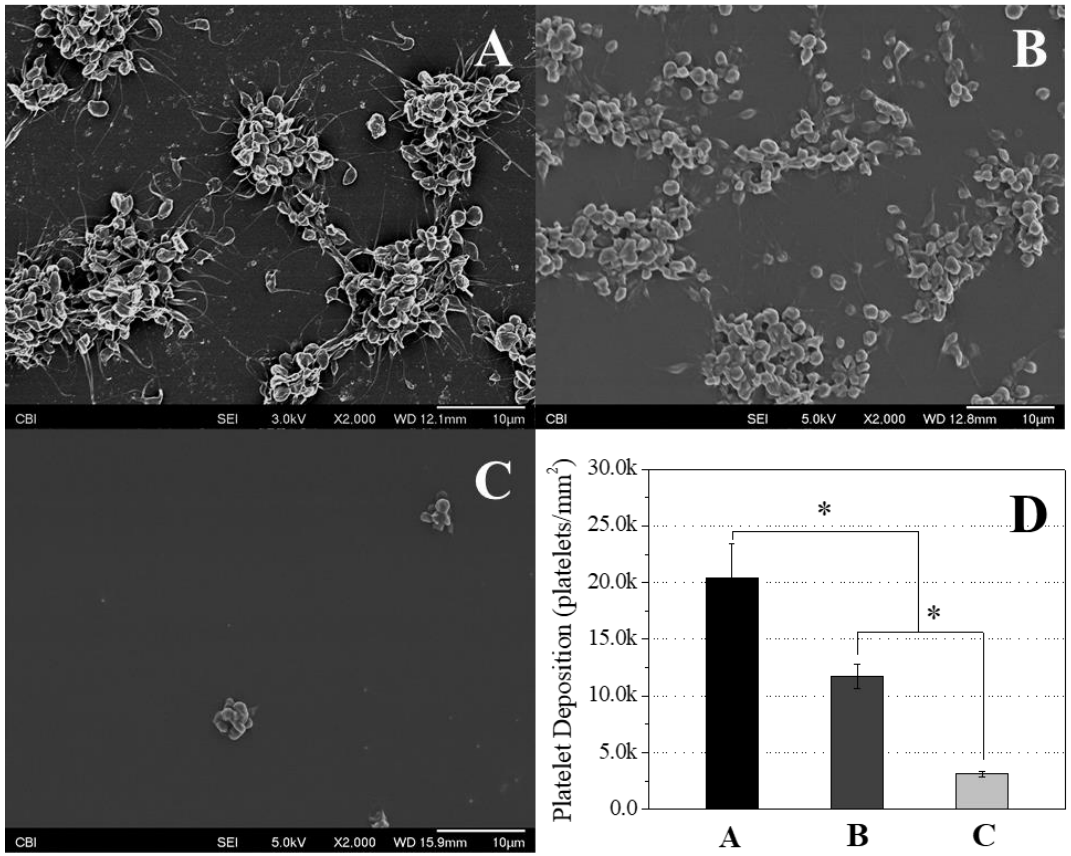

Figure 8. Hemolysis % of Negative control, PDMS-MDEA-UU film, PDMS-SB-UU film, and ePTFE graft against whole ovine blood (8 g/dL of hemoglobin). (n=3, p<0.05 versus negative control)

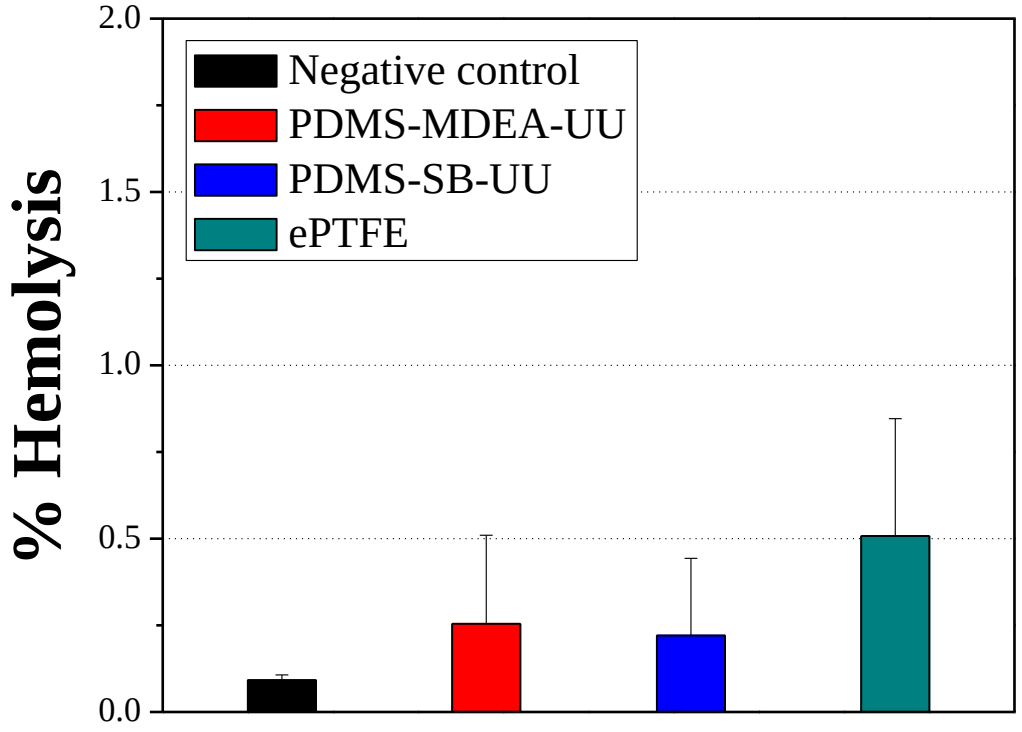

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Figure 9. *In vitro* cytotoxicity of PDMS-control, PDMS-MDEA-UU, and PDMS-SB-UU films tested with rat aorta smooth muscle cell (rSMC). MTS assay was conducted for analyzing cell viability. Data are normalized to the negative control and expressed as mean ± SD (n = 3, $p<0.05$ versus negative control). Negative control (N) includes the cells cultured in the medium only. To induce cell death in positive control (P), 1 M acrylamide dissolved in regular cell culture medium was used.

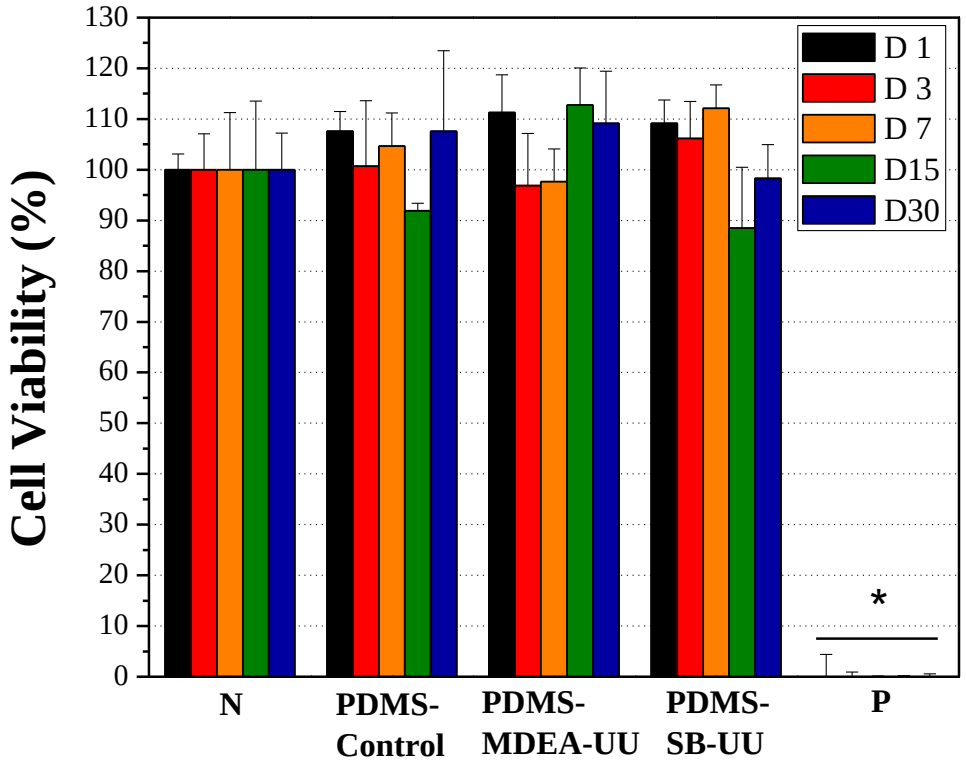
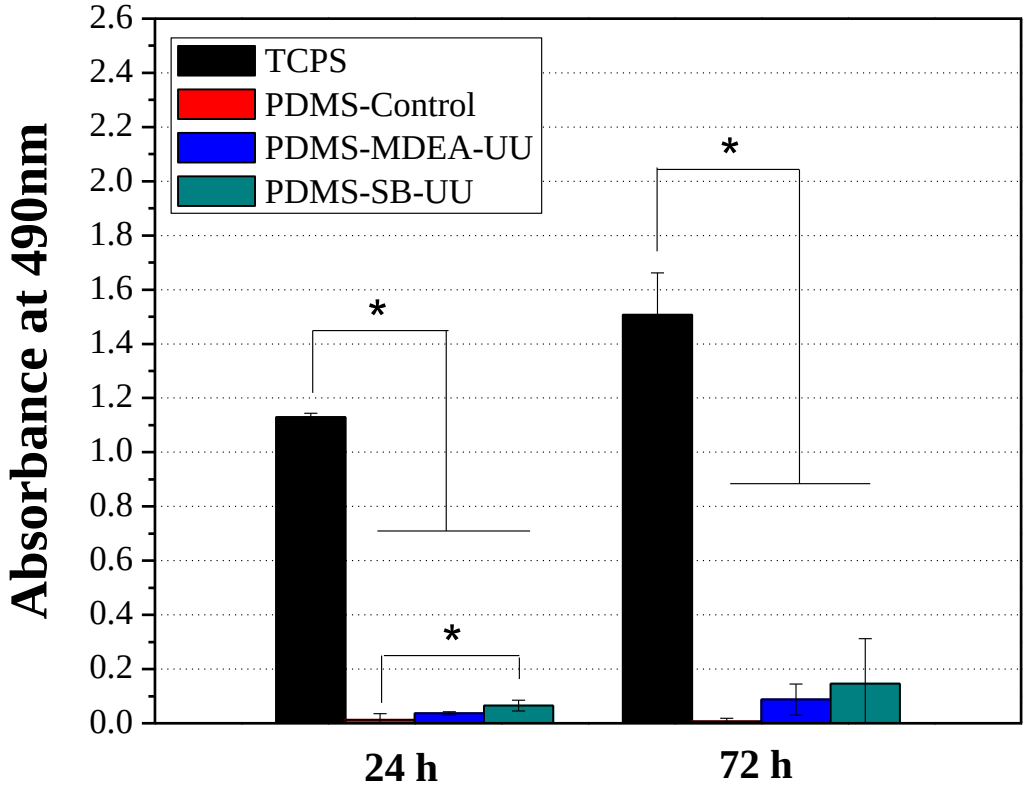


Figure 10. *Proliferation of rat aorta smooth muscle cell (rSMC) on tissue culture polystyrene (TCPS), PDMS-control, PDMS-MDEA-UU, and PDMS-SB-UU. MTS assay was performed for the evaluation. Data is expressed as mean ± SD (n = 3, p<0.05).*



- **Biostable PDMS-based polyurethanes (PUs) for blood-compatible biomaterials**

Figure 11. *Photo image (A) and SEM images (B-E) of electrospun small diameter (1.1 ± 0.1 mm) PDMS-SB-UU conduit*

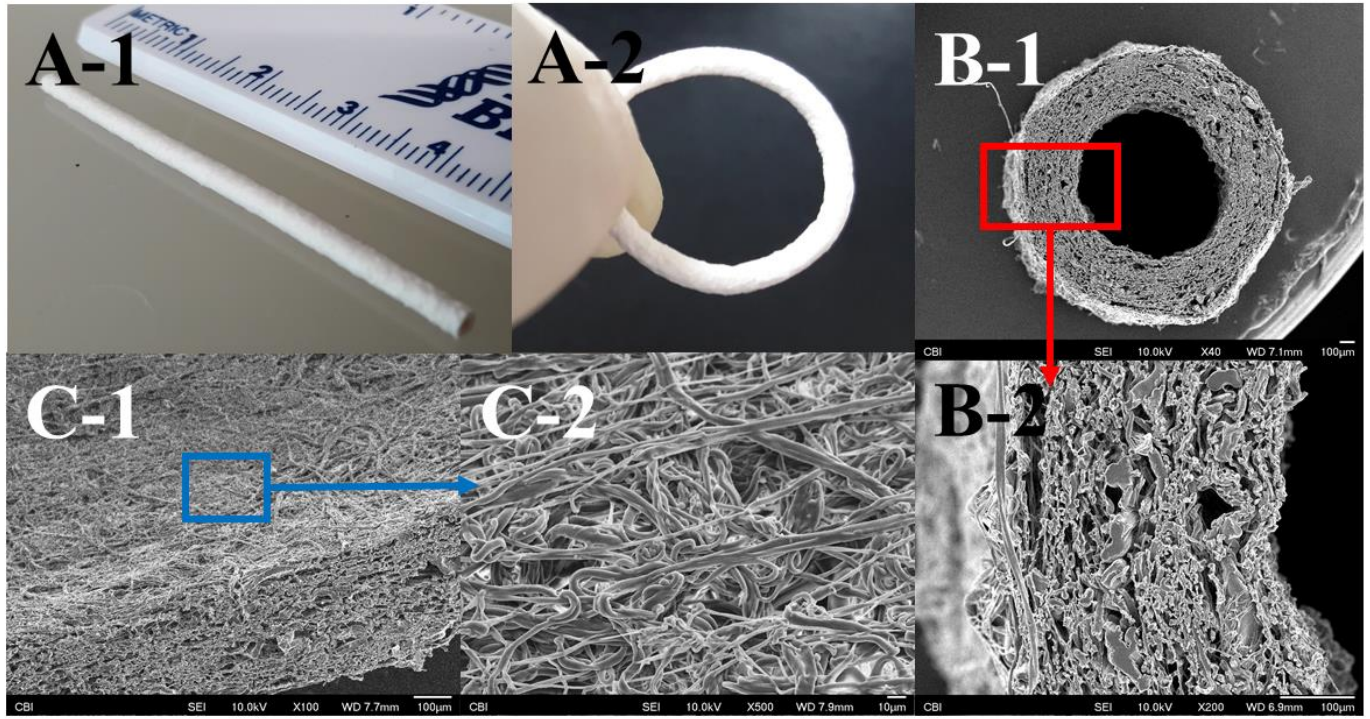


Figure 12. *suture retention test of electrospun PDMS-SB-UU conduit. Ti-CronTM coated Braided polyester (5x18”) was sutured at a distance of 3 mm from the sample’s (thickness: 300 µm) free end. Test Speed: 25 mm/min.*

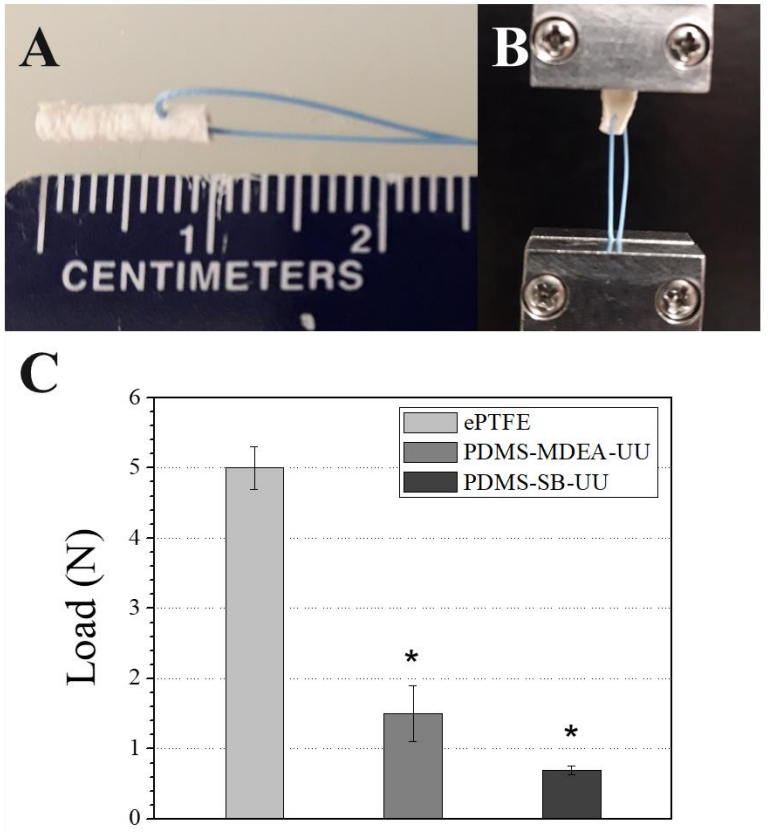


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Figure 13. (A) A two-way silicone foley catheter and an electron micrograph of PDMS-SB-UU coated the silicone catheter surface, (B) SEM images of PDMS-SB-UU coated silicone catheter treat with 30% H_2O_2 for 14 days, and (C) SEM images of PDMS-SB-UU coated silicone catheter treat with lipase for 14 days.

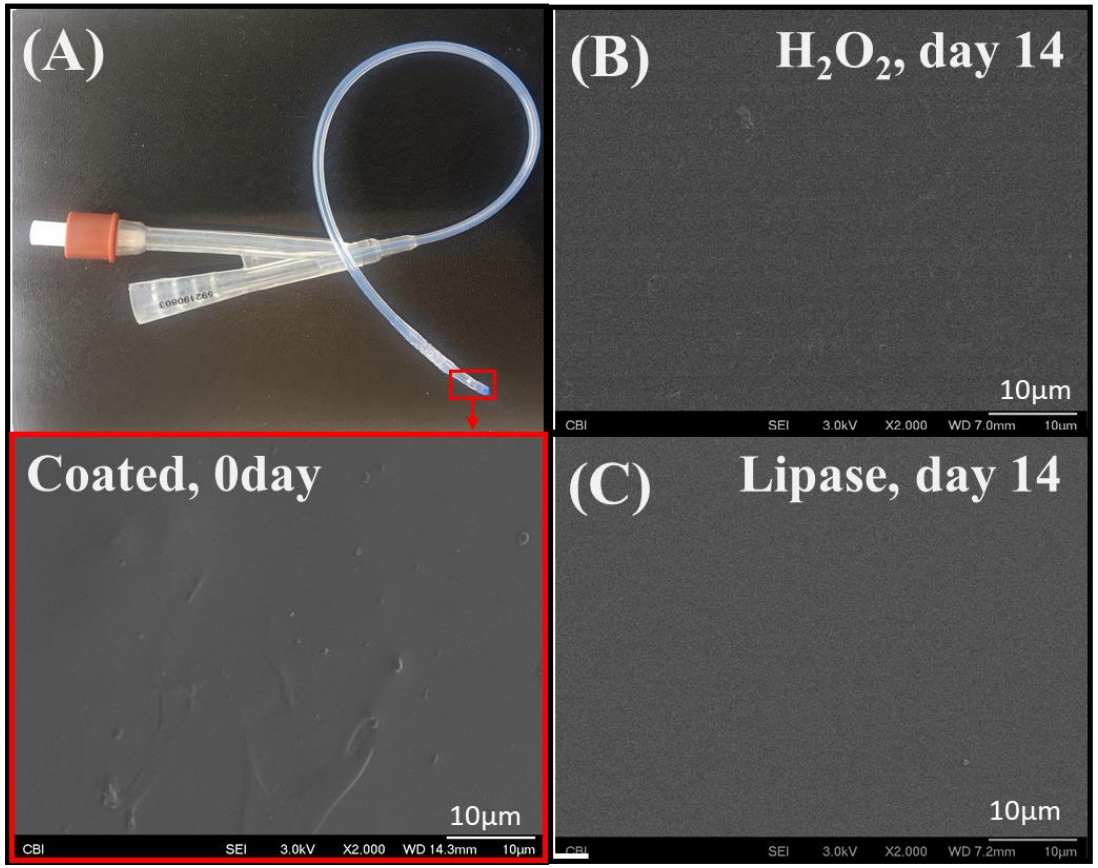
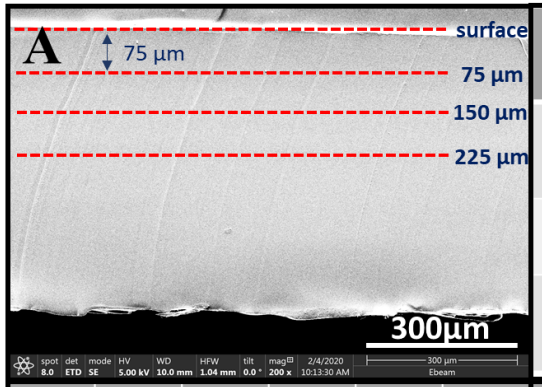


Figure 14. PDMS-control coating with PDMS-SB-UU (A) cross-section image for analysis, (B) atomic % of non-coating, (C) atomic % of dip-coating using 2 %(wt/vol) in HFIP, and (D) atomic % of dip-coating using 2%(wt/vol) in HFIP/DCM(1/1). Data are expressed as mean ± SD.



B	C K (%)	N K (%)	O K (%)	Si K (%)	S K (%)
0 to 75	37 ± 8	0	17 ± 5	15 ± 4	0
75 to 150	47.9 ± 0.1	0	25.4 ± 0.3	21.8 ± 0.2	0
150 to 225	43 ± 8	0	22 ± 5	18 ± 4	0

C	C K (%)	N K (%)	O K (%)	Si K (%)	S K (%)
0 to 75	41.8 ± 0.3	7.9 ± 0.2	25.6 ± 0.3	24.5 ± 0.1	0.10 ± 0.03
75 to 150	41.6 ± 0.3	8.2 ± 0.1	26.1 ± 0.9	23.9 ± 0.5	0.10 ± 0.03
150 to 225	41.9 ± 0.1	8.1 ± 0.3	25.9 ± 0.1	24.0 ± 0.2	0.06 ± 0.02

D	C K (%)	N K (%)	O K (%)	Si K (%)	S K (%)
0 to 75	41.2 ± 0.1	7.9 ± 0.1	25.3 ± 0.2	25.3 ± 0.2	0.13 ± 0.04
75 to 150	41.2 ± 0.2	7.66 ± 0.05	24.5 ± 0.2	26.62 ± 0.04	0.10 ± 0.03
150 to 225	41.2 ± 0.3	7.7 ± 0.3	25.1 ± 0.2	25.87 ± 0.06	0.10 ± 0.06

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• Biostable polyurethanes (PUs) for biosensing applications

: 폴리우레탄은 스마트 센서 (smart electronic sensing devices)를 만드는데 유용한 물리화학적 특성을 지녔다. 이러한 특성은 폴리우레탄의 원료 물질, 구조적 개질, soft segment와 hard segment의 개질, 합성 시 NCO:OH의 비율, 나노 섬유의 분산도, 그리고 화학적 기능도의 선택과 조절을 통하여 얻어진다. 지난 몇 세기 동안 폴리우레탄은 센서의 용량과 선택도를 향상시키는데 주요한 역할을 해 왔다. 구조적 및 화학적으로 개질 된 폴리우레탄은 센서의 특정 부위(세포, 효소, DNA 등의 신호와 자극에 반응)에만 적용되었음에도, 센서의 성능을 향상 시켜 온 것이다.

한 예로, 폴리 우레탄 기반의 Molecularly imprinted polymers (MIPs)은 바이러스 센서의 성능 향상을 위하여 연구 되어져 왔다.

Table 3. The basic quality assurance parameters of PU-based biosensors against viruses.

No.	Receptor	Template/Target	Detection limit
1	Surface imprinted MIP-PU	Tobacco mosaic virus (TMV)	100 ng/L to 1 mg/L
2		Parapox ovis virus (PPOV)	5 x 10^5 virus particles/mL
3		Tobacco mosaic virus (TMV)	10-100 mg/mL
4		Tobacco mosaic virus (TMV)	8 ng/mL
5		(Human rhinovirus) HRV 1A, HRV 2, HRV 14	100 mg/mL

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Table 4. Basic quality assurance parameters of PU-based biosensors against (a) glucose and (b) urea.

NO.	Materials	Fabrication route	Detection limit (mM)	Response time	Stability
A-1	asymmetric hydrophilic PU	Direct mixing (dip-coating)	1-10	~500 s	60 days
A-2	Hybrid (NO) sol-gel/PU	Sol-gel chemistry	0-12	65 s	18 days
A-3	Nafion-PU/enzyme-crosslinked electrode	Solution casting	4	-	10 h
A-4	Epoxy/PU	Solution casting	1-25	20-200 s	10-56 days in rats
A-5	Epoxy/PU hydrogels	Solution casting	2-30	4 min 20 ± 3s	60 days
A-6	NO-releasing silica modified/PU	Solution casting	159.1 ± 79.1	11.4 ± 12.8 s	-
A-7	Porous tecophilic PU	Electrospinning	1-30	32.1 ± 7.2 s	-
A-8	Epoxy/PU	Electrospinning	2-30	-	84 days
A-9	Porous PU	Dip-coating	0-5.55	8 ± 3 min	-
A-10	Dex/PU	Solution mixing	0-0.026	20 ± 8 min	20 days
A-11	PANi/PU/Epoxy-PU	Dip-coating	1-20	30 s	53 days
A-12	NO-releasing silica modified/PU	Solution-casting	1-21	-	~14 days
B-1	asymmetric hydrophilic PU	Direct mixing (dip-coating)	0.01-100	5 s	60 days
B-2	Photocurable PU-acrylate	Solution mixing	0.04-36	60 s	7-10 days
B-3	ammonium containing PVC/PU	LBL	0.01-100	3-8 min	3 days
B-4	ammonium containing PVC/PU	Solution casting	0.01-2	16-20 s	-

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