Supporting Information

1,4-Bis(2-hydroxyethyl)piperazine-derived water-dispersible and antibacterial polyurethane coatings for medical catheters

Anchal Gupta[1], Simran Kaur Rainu[2], Manleen Kaur[2], Mahipal Meena[1,3], Neetu Singh[2], and Josemon Jacob[1*]

[1]Department of Materials Science and Engineering, Indian Institute of Technology, Delhi, New Delhi, 110016, India

[2]Centre for Biomedical Engineering, Indian Institute of Technology, Delhi, New Delhi, 110016, India

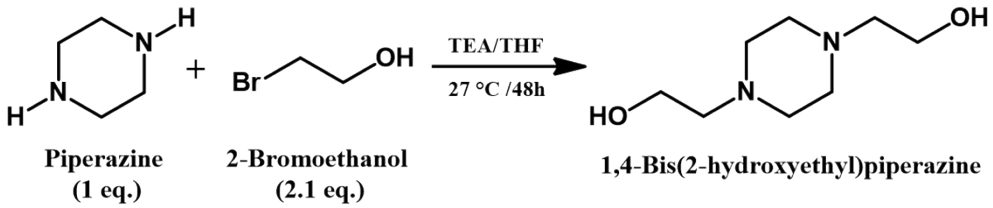
[3]Centre for Fire, Explosive and Environment Safety, DRDO, Delhi, 110054, India

*Corresponding author, E-mail: jacob@mse.iitd.ac.in

Experimental section

Synthesis of 1,4-bis(2-hydroxyethyl)piperazine (HEPZ)

Pre-dried piperazine (2 g, 23.22 mmol) and triethylamine (9.7 ml, 69.67 mmol) were added to distilled THF (30 ml) in a 100 ml schlenk round bottom flask under nitrogen at room temperature and stirred until a homogeneous solution was obtained. Then, 2-bromoethanol (3.5 ml, 49.04 mmol) dissolved in distilled THF (10 ml) was added dropwise for 15 min in an ice bath. The reaction was stirred at room temperature for 48 h, the precipitated salt was then separated by filtration, and the solvent was removed on a rotary evaporator. The obtained residue was washed with THF thrice and dried in a vacuum oven for 1 h. The dried product HEPZ (**Scheme S1**) was obtained as a white crystalline powder (2.5 g, 62%). ^{1}H NMR (500 MHz, D_2O): δ 3.61 (t, 4H, J = 6.2 Hz, O-C**H$_2$**), 2.47 (t, 12H, J = 6.3 Hz, N-C**H$_2$**) **(Fig. 1a)**. ^{13}C NMR (125 MHz, D_2O): δ 58.78, 58.10, 51.90 **(Fig. 1b)**. GC-MS (m/z 174.24) **(Fig. S1)**.



Scheme S1: Synthesis of HEPZ.

Characterization of HEPZ

GC-MS analysis showed a single compound at a retention time of 17.1 min with a molecular weight of m/z 174.12 confirming its formation (**Fig. S1**). In the ^{1}H NMR spectrum (**Fig. S2a**),

a triplet of 12 protons corresponding to the methylene protons attached to nitrogen at 2.50 ppm and a triplet of 4 protons intensity corresponding to the methylene protons attached to the hydroxyl group at 3.60 ppm is observed. In the ^{13}C NMR spectrum (**Fig. S2b**), the signals at 58.78 and 58.10 ppm are attributable to the carbon atoms attached to the hydroxyl groups and the carbon atoms next to nitrogen, respectively. The signal at 51.90 ppm corresponds to the carbon atoms of the piperazine ring further confirming the structure of HEPZ.

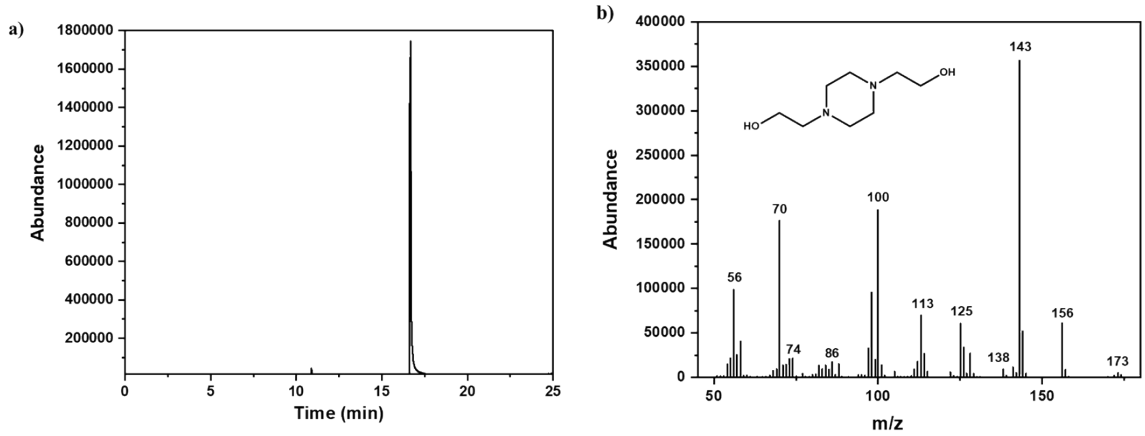


Fig. S1: a) Mass spectrum and b) gas chromatogram of HEPZ.

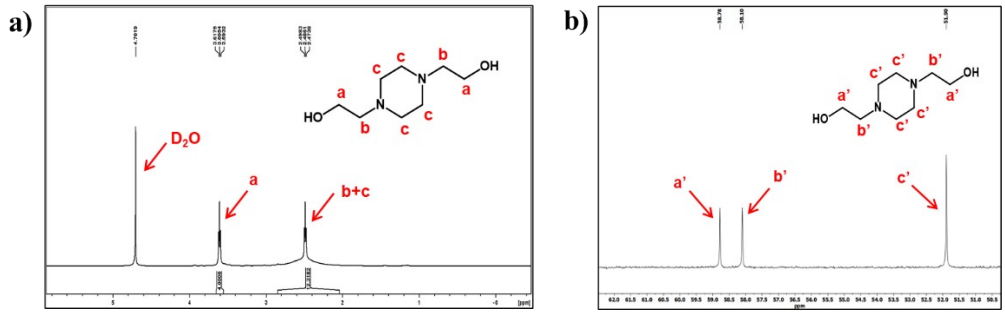


Fig. S2: a) ^{1}H NMR spectrum and b) ^{13}C NMR spectrum of HEPZ.

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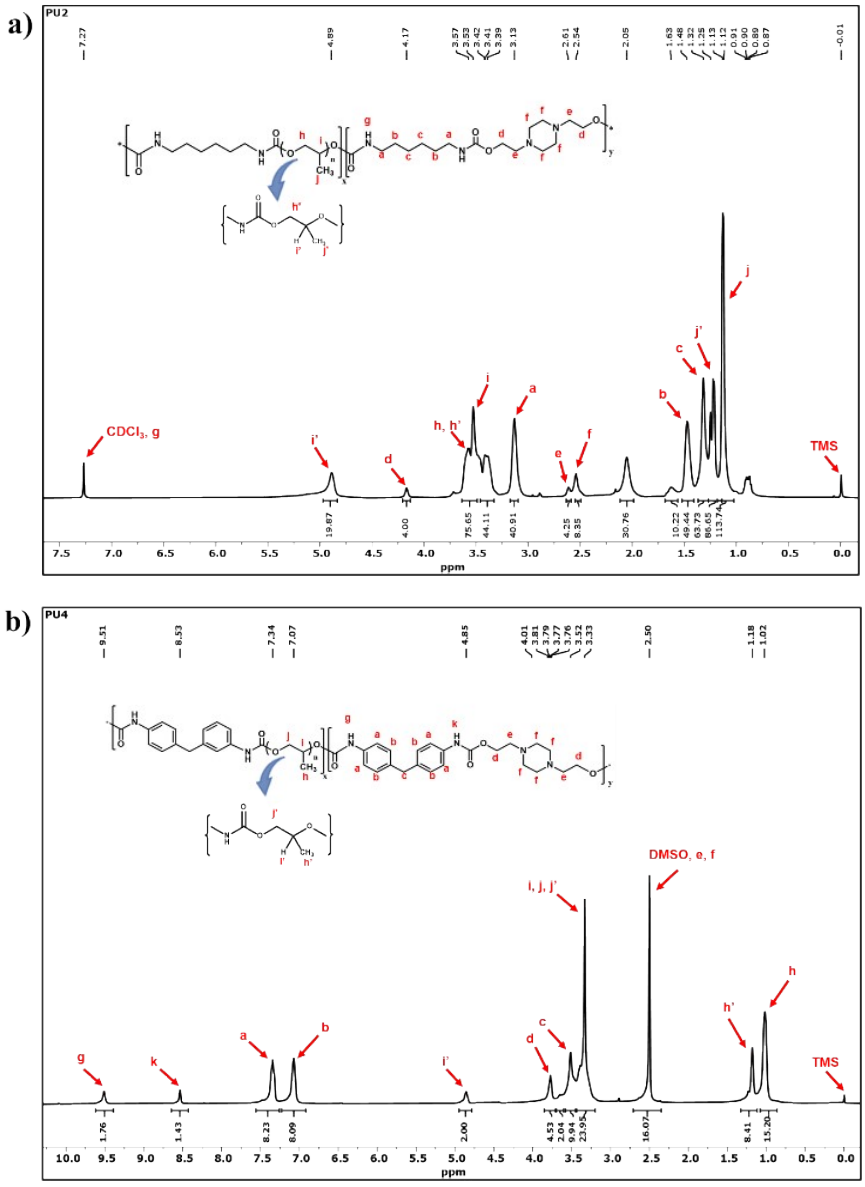

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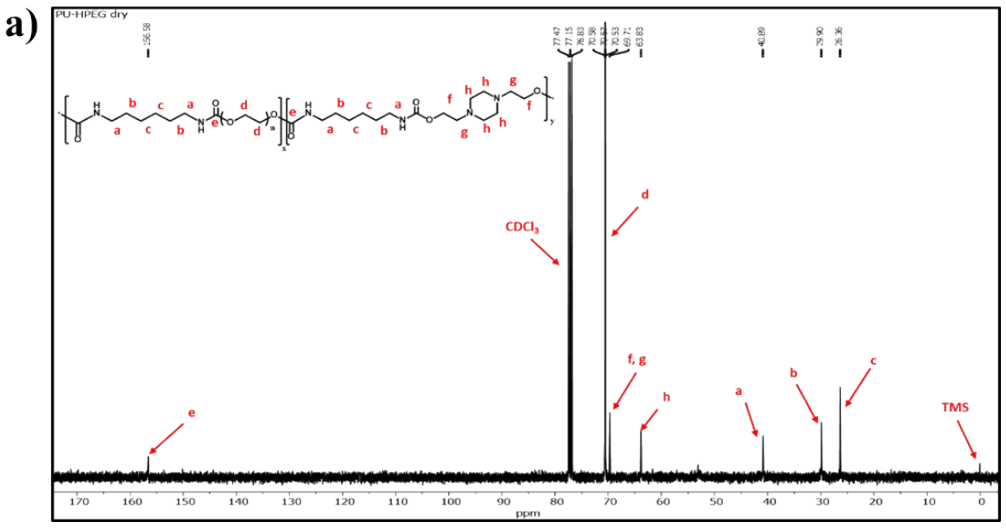
43 **Fig. S3:** ^{1}H NMR spectra of a) PU2 and b) PU4.



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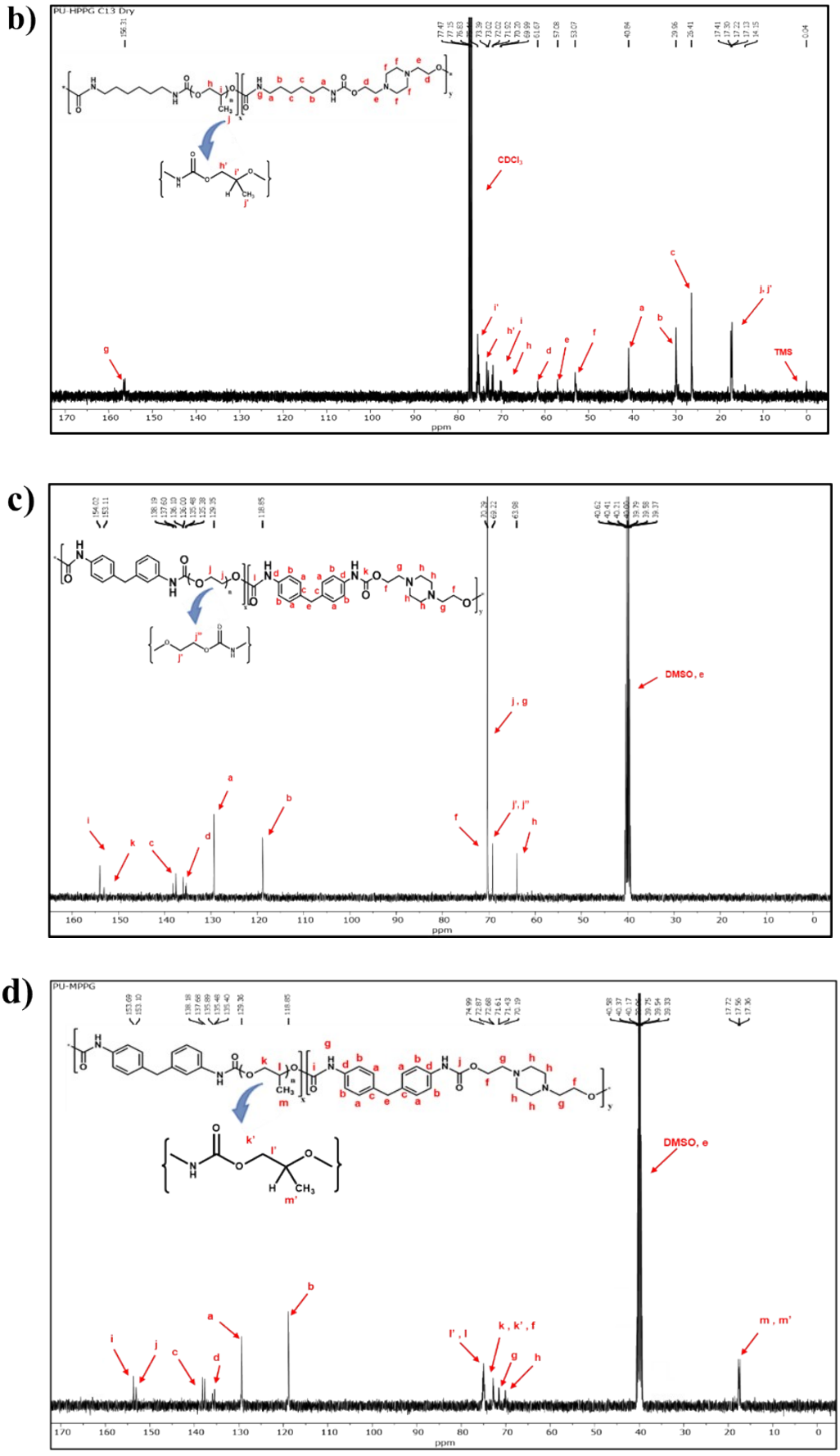


Fig. S4: ^{13}C NMR spectra of a) PU1, b) PU2, c) PU3, and d) PU4.

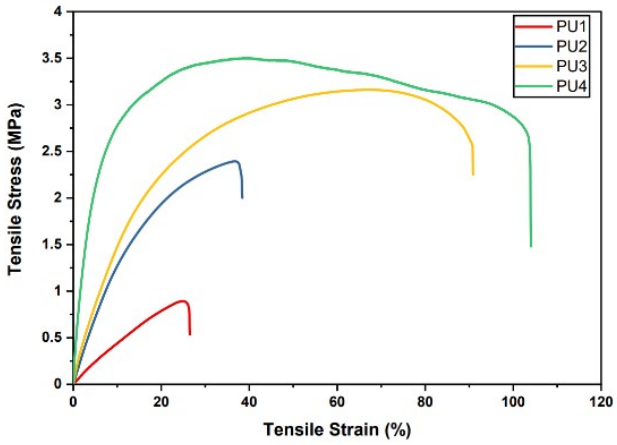
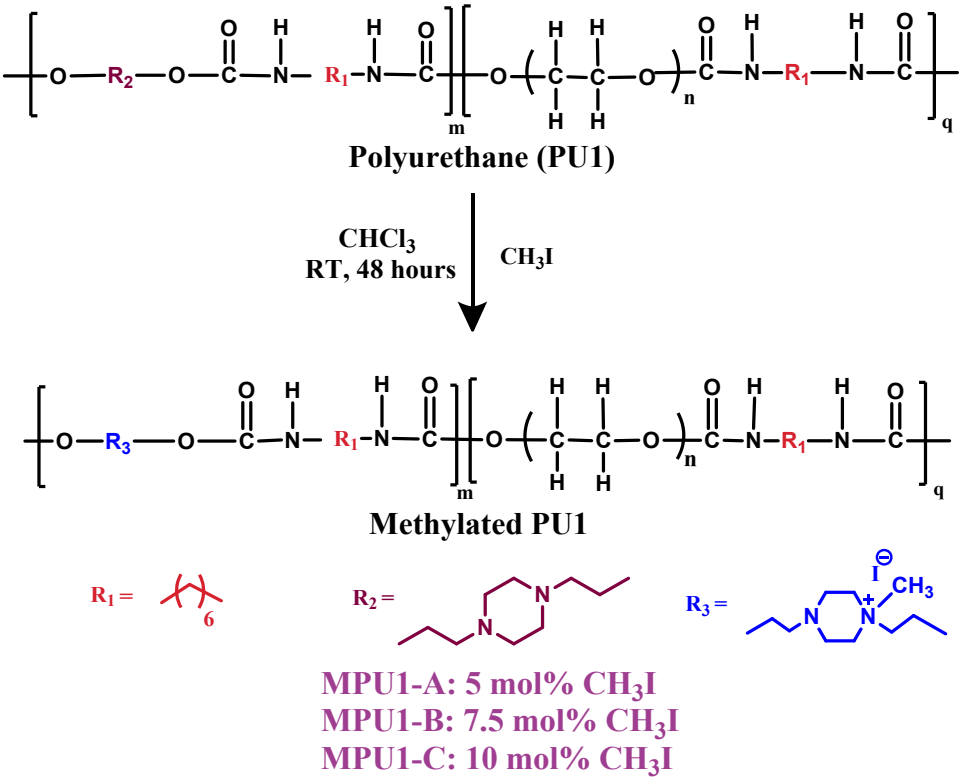


Fig. S5: Stress-Strain curves of PU1-PU4.

Preparation of methylated PU1

The methylation of PU1 was performed using 5, 7.5, and 10 mol% of MeI, and named MPU1-A, MPU1-B, and MPU1-C as shown in **Scheme S2** to perform the cytotoxicity studies.



Scheme S2: Synthetic route of methylation of PU1.

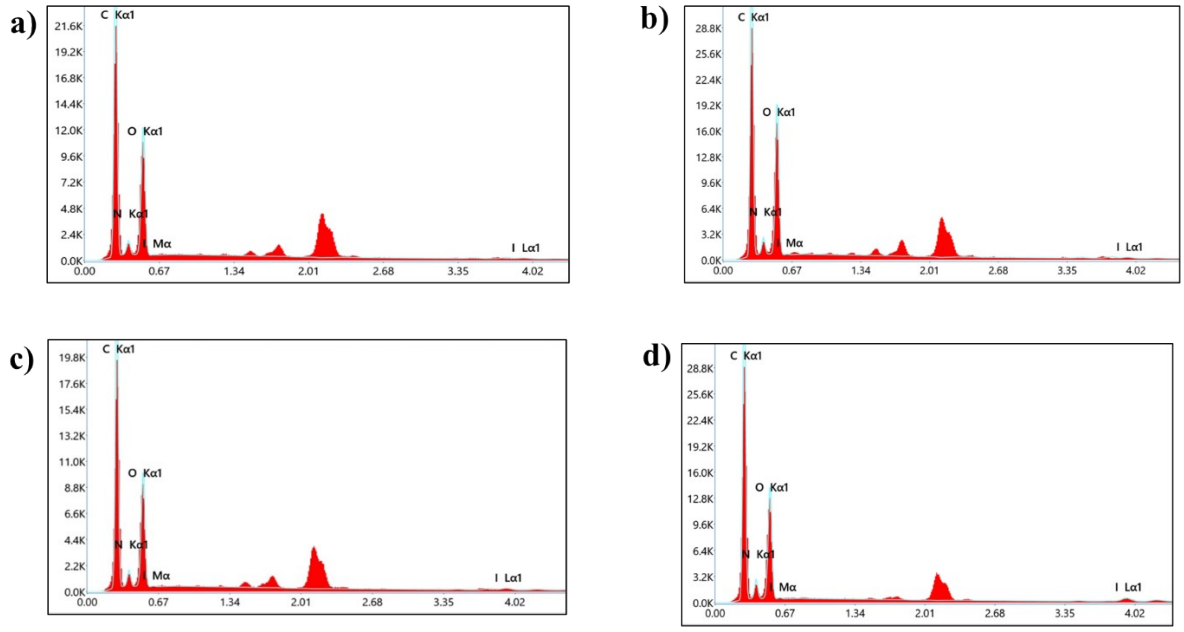
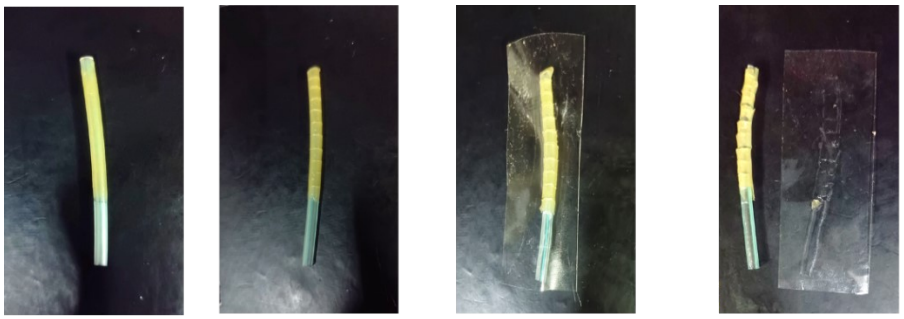


Fig. S6: EDX results of a) MPU3-A, b) MPU3-B, c) MPU3-C, and d) MPU3-D.

Table S1: Chemical resistance of MPU3-D films for one month.

Chemical environments	**% Weight loss** **Drying time: 5 h (RT)+ 10 h (50 °C)**			
	Week 1	Week 2	Week 3	Week 4
10 wt% NaCl aq. solution	1.9	0.5	0.4	0.1
20 % EtOH aq. solution	14.5	5.3	3.4	1.2
1 % NaOH aq. solution	14.8	9.8	6.0	1.3
10 % HCl aq. solution	5.6	3.8	1.9	1.0
Tap water	19.4	3.4	0.1	0.0



a) Coated PVC catheter **b) Incisions containing Coated PVC catheter** **c) Adhesive tape was applied over incisions** **d) Adhesive tape was pulled rapidly from cathter**

Fig. S7: Adhesion measurement of MPU3-D coating using peel-off tape adhesion test.

Table S2: Comparison of chitosan and silver-based antibacterial WPU coatings with HEPZ-derived WPU coatings.

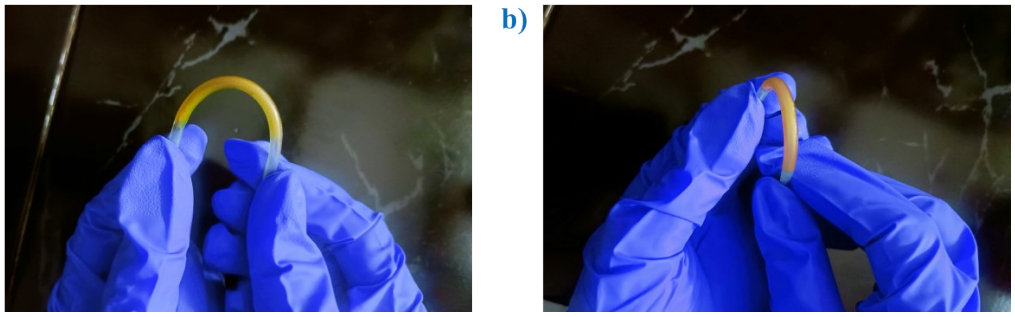
WPU coatings	Antibacterial Efficacy	References
Chitosan-based	N. Arshad et al. investigated the antibacterial activity of both dyed and printed fabrics treated with 2% and 4% chitosan-embedded water-dispersible PUs against gram-positive and gram-negative bacteria. They observed the greater inhibition zones in 4% chitosan-treated fabrics between 8 mm to 14 mm.	[1]
	N. Sukhawipat et al. determined the antibacterial activity of cationic water-dispersible polyurethane and protonated chitosan suspension against *E.coli* and observed 18.52 mm and 19.02 mm zones of inhibition when loaded with 0.5 and 0.7 wt% protonated chitosan.	[2]
	F. Naz et al. studied the antimicrobial activities of dyed and printed textiles coated with chitosan-derived water-dispersible PUs against *B. subtilis* and *S. aureus* (gram-positive bacteria) and *P. aeruginosa* and *E. coli* (gram-negative bacteria). They observed the inhibition zones ranging from 10.5 mm to 12.5 mm for dyed and printed fabrics upon increasing the molar ratio of chitosan in the polymer backbone.	[3]
Silver-based	Atay et al. observed that the PU matrix with 0.1% Ag nanoparticles showed inhibition zones of 7.5 mm and 1.25 mm against *S. aureus* and *E.coli*, respectively which increases on increasing loading of Ag nanoparticles to 1% but further increase to 10-30% lowered the antibacterial activity due to agglomeration of the nanoparticles.	[4]
	Daniel Ramirez and Franklin Jaramillo examined the effect of surface-modified silver nanoparticles in thermoplastic polyurethane nanocomposites over antibacterial activity. They observed that 1.5 wt% silver nanoparticles containing nanocomposites showed the highest inhibition zone of 9.3 mm against *E. coli* bacteria.	[5]

HEPZ-based	The antibacterial activity of HEPZ-based methylated PUs was tested against *S. aureus* and *E.coli* bacterial strains and no zones of inhibition were detected with lower alkylated PUs (MPU3-A and MPU3-B). In contrast, 8 mm and 7 mm inhibition zones were observed for highly alkylated MPU3-C (42.5%) and MPU3-D (72.5%).	–

Table S3: Pearson correlation analysis of samples vs % cell viability

Figure number	**Pearson r**			**P value**		
	r	95% confidence interval	R squared	P (Two-tailored)	P value summary	Significant? (alpha = 0.05)
7 (a)	-0.6988	-0.9781 to 0.4784	0.4884	0.1892	ns	No
7 (d)	-0.9717	-0.9970 to -0.7577	0.9442	0.0012	**	Yes

a) b)



Bending test of MPU3-D.mp4

Fig. S8: Manual bending test of MPU3-D coated catheters with a) front and b) upside-view with the attached video clip for reference.

Sample	**Hemolysis (%)**
Positive control	100
Negative control	0
MPU3-D	0.4 ± 0.2

Table S4: Hemolysis test results of MPU3-D with positive and negative control.

References

[1] N. Arshad, K.M. Zia, F. Jabeen, M.N. Anjum, N. Akram, M. Zuber, Synthesis, characterization of novel chitosan based water dispersible polyurethanes and their potential deployment as antibacterial textile finish, Int J Biol Macromol 111 (2018) 485–492. https://doi.org/10.1016/j.ijbiomac.2018.01.032.

[2] N. Sukhawipat, A. Suwan, E. Kalkornsurapranee, A. Saetung, N. Saetung, Cationic waterborne polyurethane–chitosan based on natural rubber as new green antimicrobial coating, Prog Org Coat 161 (2021). https://doi.org/10.1016/j.porgcoat.2021.106497.

[3] F. Naz, M. Zuber, K. Mehmood Zia, M. Salman, J. Chakraborty, I. Nath, F. Verpoort, Synthesis and characterization of chitosan-based waterborne polyurethane for textile finishes, Carbohydr Polym 200 (2018) 54–62. https://doi.org/10.1016/j.carbpol.2018.07.076.

[4] H.Y. Atay, I. Yaşa, E. Çelik, Antibacterial polymeric coatings with synthesized silver nanoparticles, Synthesis and Reactivity in Inorganic, Metal-Organic and Nano-Metal Chemistry 45 (2015) 784–798. https://doi.org/10.1080/15533174.2013.843561.

[5] D. Ramirez, F. Jaramillo, Improved mechanical and antibacterial properties of thermoplastic polyurethanes by efficient double functionalization of silver nanoparticles, J Appl Polym Sci 135 (2018). https://doi.org/10.1002/app.46180.