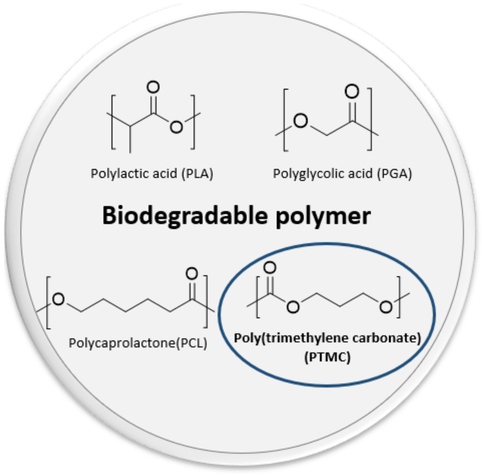
Urea-functionalized poly(trimethylene carbonate) derivative for biological function

Lee Yae Tan, Nalinthip Chanthaset*, Hiroharu Ajiro*
Nara Institute of Science and Technology (NAIST, Japan)

Introduction

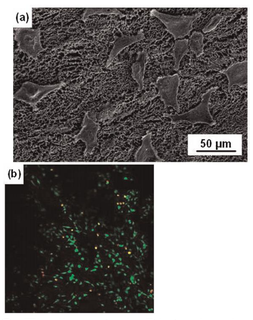
Biodegradable polymers



Biodegrability
Free from retention implant material in the body after healing period

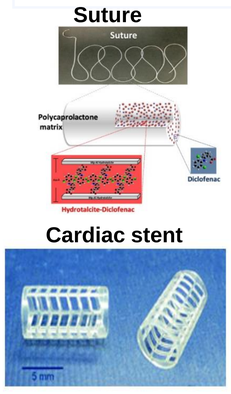
Biomaterial applications

Scaffold



S. Theiler, et al., Biotechnol. Bioeng. **2011**, 108, 694.

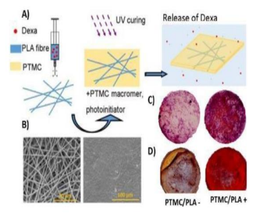
Suture



Cardiac stent

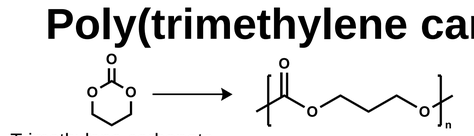
K. Fukushima, *et al.*, *Biomater. Sci.*, **2016**, 4, 9

Drug release



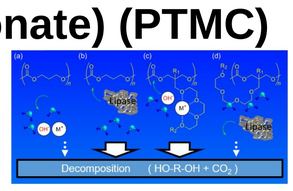
O. Guillaume, *et al., eCM Periodical & eCM Conferences .*, **2017**, 20

Poly(trimethylene carbonate) (PTMC)



Merits of PTMC
- Biodegradability
- Flexibility
- Low toxicity

Challenge/development of PTMC
- Lack of functionalities for practical use in biomaterial

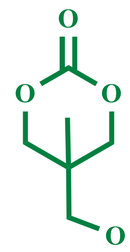


Y. Haramiishi, et al., *Poly Degra & Stability.* **2016**, *130*, 78.

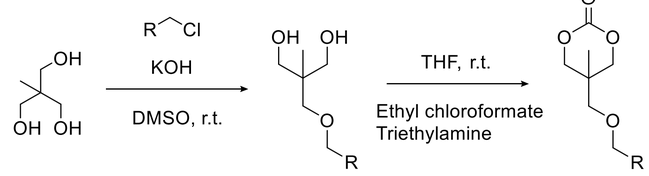
Low toxicity of degradation product

This work

(I) Synthetic ester-free TMC derivatives

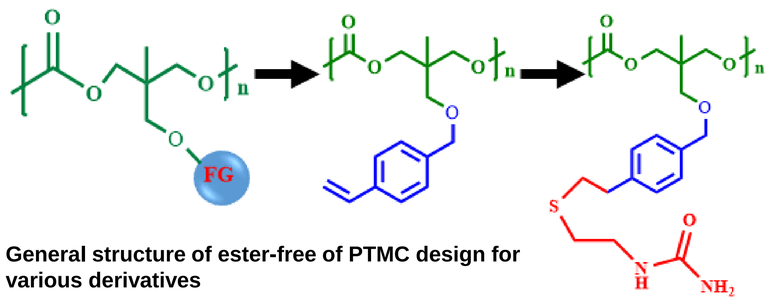


- ✓ Biodegradability
- ✓ Flexible
- ✓ Low toxicity
- ✓ Functionalities



Two steps of syntheses

(II) Urea-functionalized PTMC derivatives



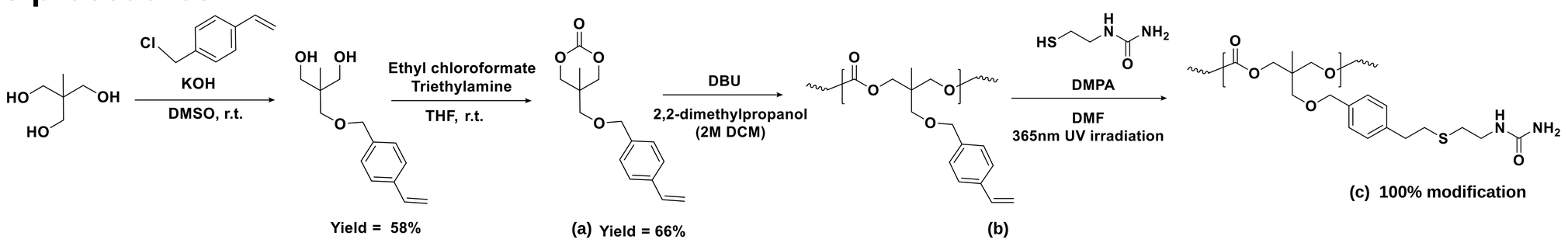
General structure of ester-free of PTMC design for various derivatives

- ❖ Investigate the interaction with potential drug (Cilostazol).
- ❖ Wettability of coating surface.
- ❖ Protein adsorption on coating surface.

- **Biodegradability**
- **Hydrogen bonding**
- **Hydrophilicity**

Results & Discussion

Synthesis procedures



Scheme 1. Synthesis of (a) TMCM-VB monomer, (b) polymerization of PTMC-VB and (c) post-polymerization modification of PTMCM-SU.

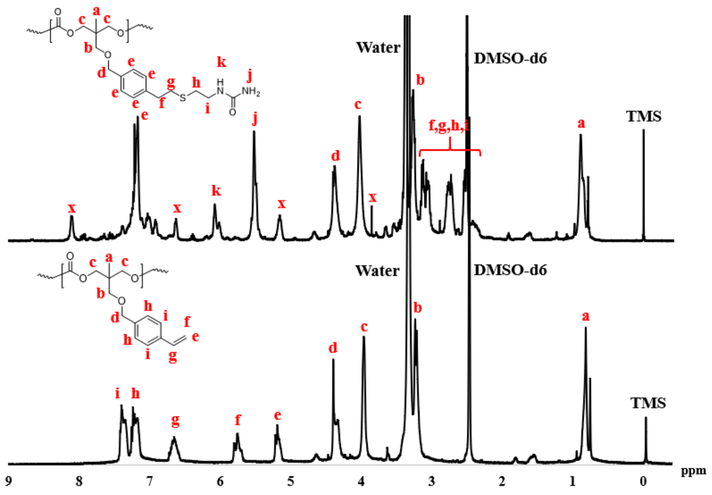


Figure 1. ^{1}H NMR spectra ($CDCl_3$, 400 MHz, r.t) of (a) PTMCM-SU and (b) PTMCM-VB.

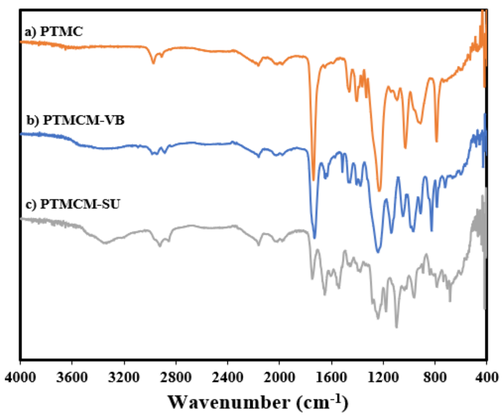
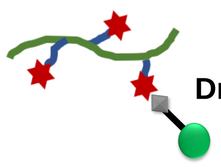
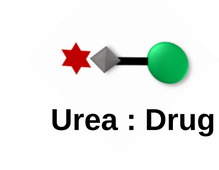


Figure 2. FTIR spectra of (a) PTMC (b) PTMCM-VB (c) PTMCM-SU.

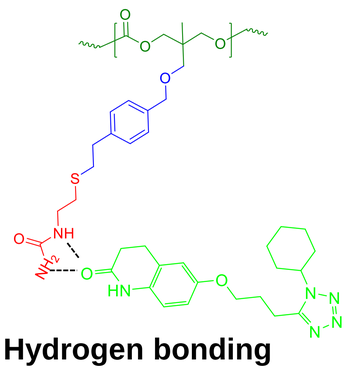
Cilostazol drug/polymer interaction



Drug-urea interaction



Urea : Drug



Hydrogen bonding

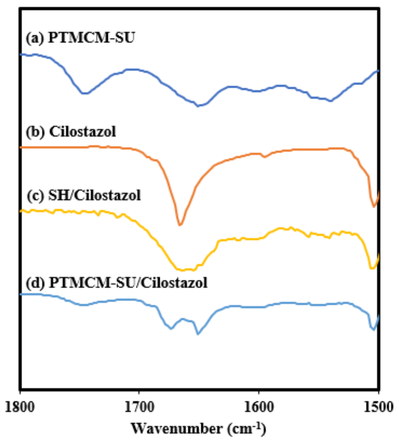
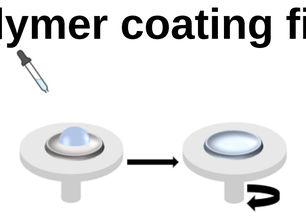


Figure 3. FTIR spectra of (a) PTMC-SU (b) Cilostazol (c) Precursor SU/Cilostazol (d) PTMCM-SU/cilostazol..

Polymer coating film (Roughness)



Polymer solutions (80 µl) spin on the glass substrate at 1000 rpm for 30 s

- Surface morphology
- Contact angle
- Protein adsorption

Surface morphology

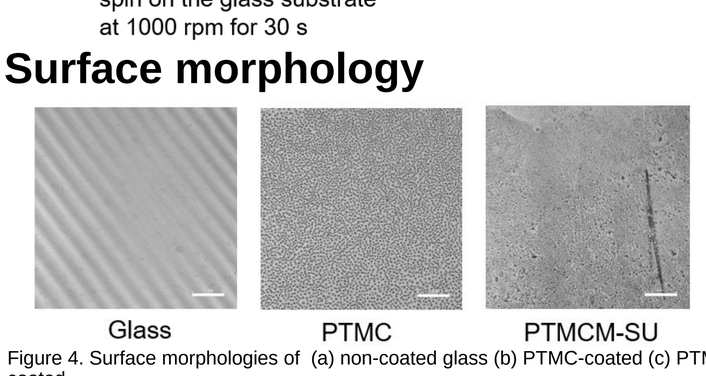


Figure 4. Surface morphologies of (a) non-coated glass (b) PTMC-coated (c) PTMCM-SU-coated .

Contact angle (Wettability)

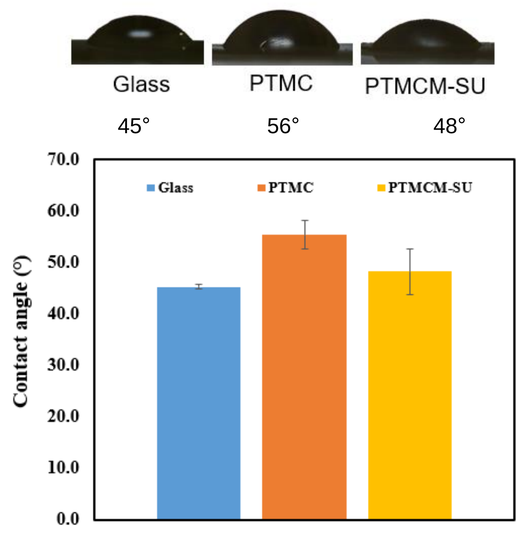


Figure 5. Contact angles of (a) non-coated glass (b) PTMC-coated (c) PTMCM-SU-coated .

Protein adsorption (Interaction)

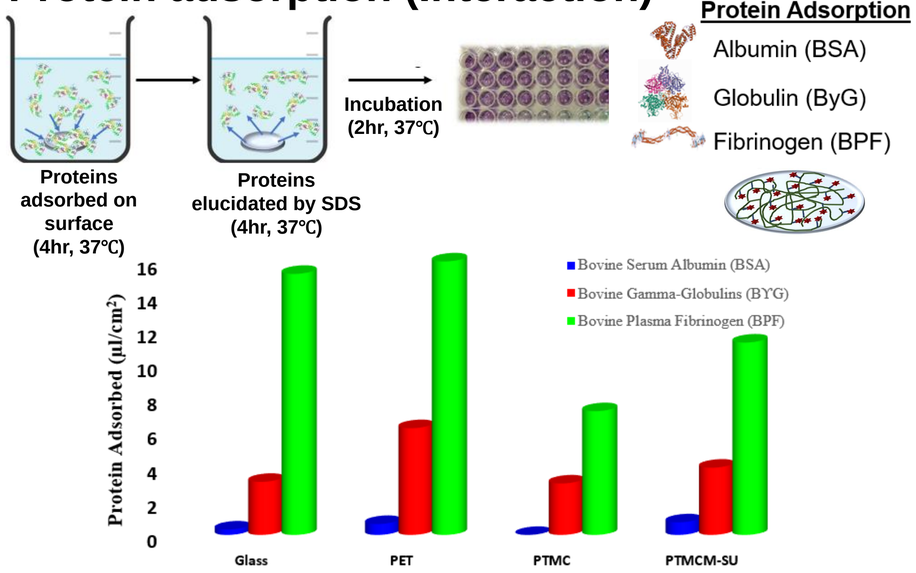


Figure 6. Protein adsorptions of non-coated glass, non-coated PET, PTMC-coated glass, PTMCM-SU-coated glass .

Conclusions

1. **Ester-free PTMC with urea derivative have successfully synthesized for biomaterials such as drug delivery control.**
2. **Hydrogen bonding induced between polymer PTMCM-SU and drug cilostazol could be useful for prolong drug release rate.**
3. **PTMCM-SU possessed hydrophilicity and high protein affinity, improved bioactivity of PTMC derivatives.**

Future Work

1. **Perform in-vitro drug release experiment with cilostazol.**
2. **Study biodegradability behaviour of polymer.**