

Anti-Precipitation of Hardly Soluble Drugs by Zwitterionic Polymers

Sae Matsuoka,^a Yuya Matsuda,^a Takeru Ishizaki,^a Kosuke Kuroda,^{a,*}

^aFaculty of Biological Science and Technology, Institute of Science and Engineering, Kanazawa University, Kanazawa, Japan

*kkuroda@staff.kanazawa-u.ac.jp

For drug evaluation in cell culture media, drugs are first dissolved in dimethyl sulfoxide (DMSO) and then, drugs/DMSO solutions are diluted with media to 0.1 wt% or less.¹ Hardly soluble drugs precipitate when diluting, and this causes inaccuracy in drug evaluation.² In this study, we propose new additives that is soluble in DMSO and inhibit drug precipitation. We focused on zwitterionic polymers as additives because they have low cytotoxicity.³ However, poly(ZI) we have developed (Fig.1a) was insoluble in DMSO. Then, we evaluated the ability to inhibit drug (ezetimibe) precipitation by diluting ezetimibe/DMSO solution with the aqueous poly(ZI) solution. Poly(ZI) did not inhibit ezetimibe precipitation (Fig.1b). For the improvement of DMSO solubility, we introduced oligoether chains into the poly(ZI), poly(ZI-OE₁₃) (Fig.1a). Poly(ZI-OE₁₃) was soluble in DMSO, but it could not inhibit ezetimibe precipitation sufficiently (Fig.1b). For the improvement of the ability to inhibit ezetimibe precipitation, we introduced long alkyl chains into the poly(ZI), poly(ZI-C₁₆) (Fig.1a). Poly(ZI-C₁₆) showed high inhibiting ability (Fig.1b), but it was insoluble in DMSO. We expect that the polymer which contains ZI, OE₁₃, and C₁₆ units to be soluble in DMSO and inhibit drug precipitation.

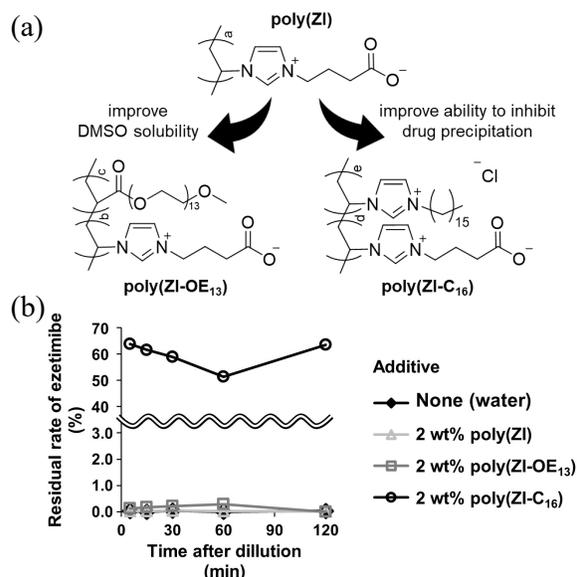


Fig 1. (a) Structures of zwitterionic polymers. (b) Residual rate of ezetimibe after 100-times dilution by water with 2 wt% zwitterionic polymers from ezetimibe/DMSO solutions.

References

1. Lipinski, A. C Lipinski *et al. Adv. Drug Deliv. Rev.* **2001**, *46*, 3.
2. Di, L. *et al. Drug Discov. Today.* **2006**, *11*, 446.
3. Kato, Y. *et al. Commun. Chem.* **2023**, *6*, 260



Sae Matsuoka (sae.matsu_2002@stu.kanazawa-u.ac.jp)

I am a second-year Master of Engineering student at Kanazawa University in Japan. I previously completed my Bachelor of Engineering with a major in bioengineering and minor in materials chemistry from Kanazawa University, in 2024. I have been awarded a scholarship from the Ushio Foundation. I have also participated in two conferences. My research interest is to contribute to drug development by using zwitterionic polymer as an additive to inhibit drug precipitation.