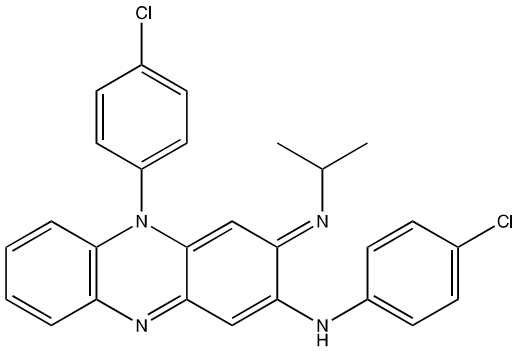
Supporting Information

Design and Solidification of Fast-releasing Clofazimine Nanoparticles for Treatment of Cryptosporidiosis

Yingyue Zhang[1], Jie Feng[1], Simon A. McManus[1], Hoang D. Lu[1], Kurt D. Ristroph[1], Eugene J. Cho[1], Ellen L. Dobrijevic[1], Hak-Kim Chan[2], Robert K. Prud'homme[1]*

1. Department of Chemical and Biological Engineering, Princeton University, Princeton, New Jersey 08854, United States



Scheme S1. Clofazimine Chemical Structure. Molecular weight: 473.4. Log P: 7.66. Chemical formula: $C_{27}H_{22}Cl_2N_4$.

Table S1: Specifications of AFFINISOL HPMCAS (provided by Dow at http://www.dow.com/en-us/pharma/products/affinisol)

AFFINISOL™ HPMCAS			
	716	912	126
Hydroxypropyl	5.0 – 9.0 %	5.0 – 9.0 %	6.0 – 10.0 %
Methoxyl	20.0 – 24.0 %	21.0 -25.0 %	22.0 – 26.0 %
Viscosity*	2.4 – 3.6 cP	2.4 – 3.6 cP	2.4 – 3.6 cP
Residue on Ignition	< 0.20 %	< 0.20 %	< 0.20 %
Loss on Drying	< 5.0 %	< 5.0 %	< 5.0 %
Free Acids	< 1.0 %	< 1.0 %	< 1.0 %
Acetate Substitution	5.0-9.0 %	7.0 – 11.0 %	10.0 – 14.0 %
Succinate Substitution	14.0-18.0 %	10.0 – 14.0 %	4.0 – 8.0 %
Acetic Acid	0.5 %	0.5 %	0.5 %

* Viscosity determined as a 2 % solution in NaOH solution

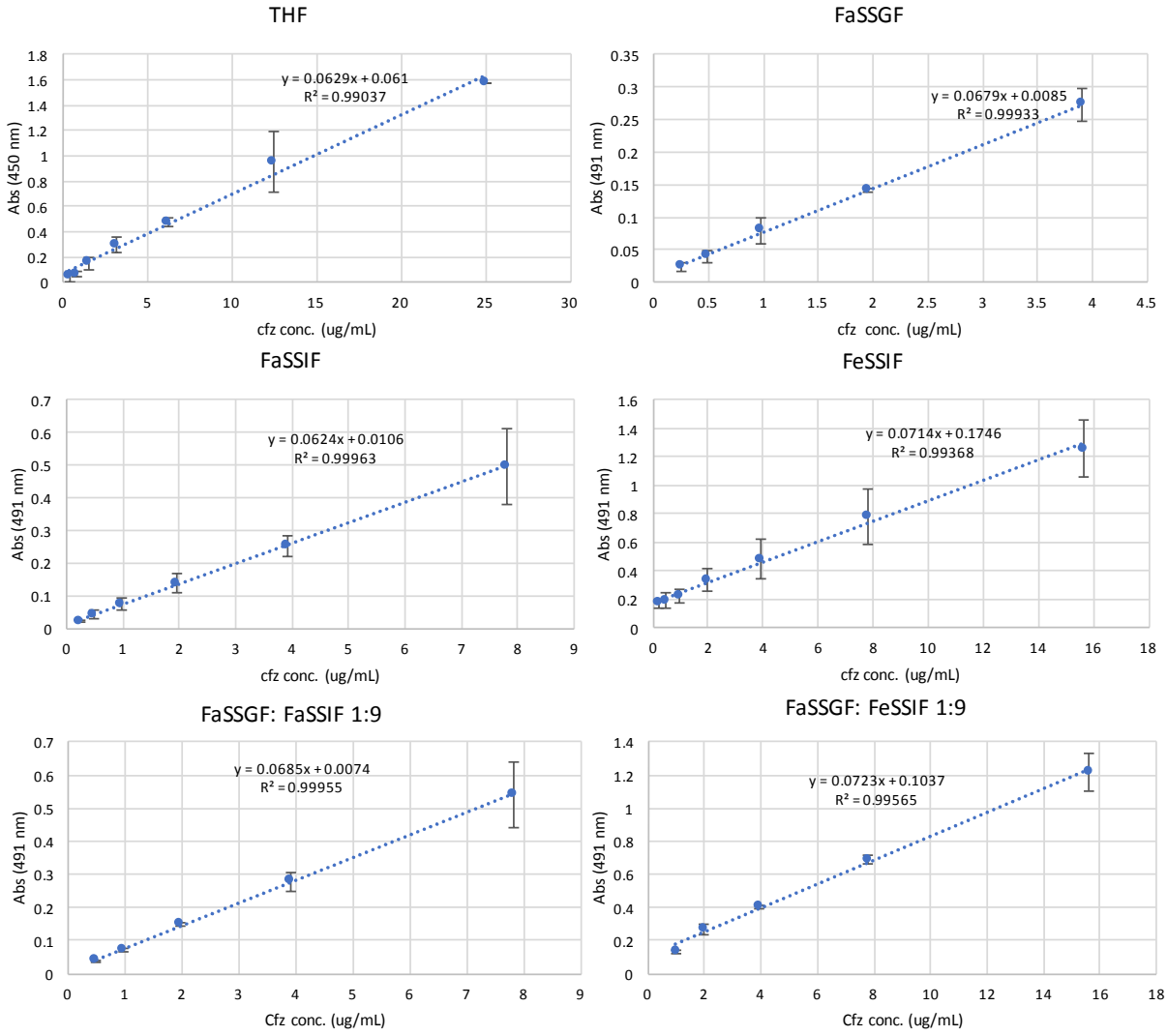


Figure S1. Clofazimine calibration curves in THF, FaSSGF, FaSSIF, and FeSSIF for determining clofazimine powder solubility. Clofazimine calibration curves in FaSSGF:FaSSIF 1:9 and FaSSGF: FeSSIF 1:9 for determining clofazimine release rate *in vitro*.

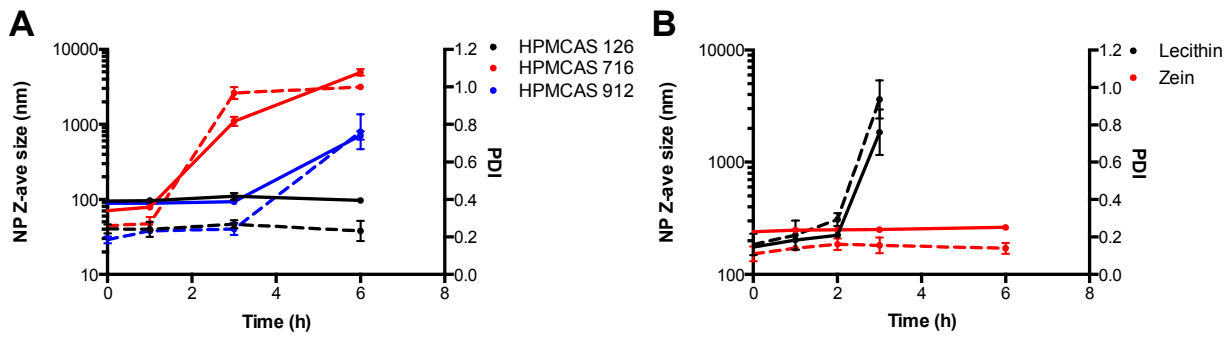


Figure S2. Size stability of clofazimine nanoparticles with various surface coatings in 10 vol% organics (A: HPMCAS, B: lecithin and zein). Solid line and dashed line represent nanoparticle Z-ave size and PDI, respectively.

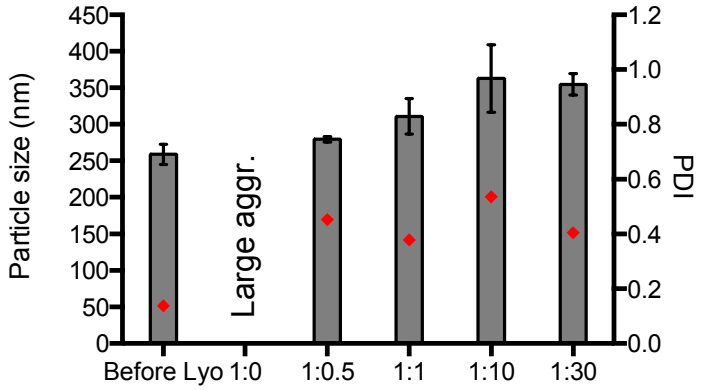


Figure S3. Particle size and PDI of clofazimine zein nanoparticles after lyophilization with different concentrations of mannitol as cryoprotectant. Grey bar represents particle size while red dot denotes corresponding PDI value.

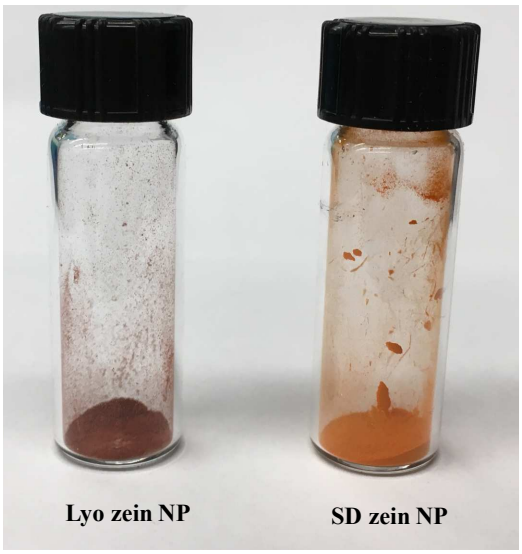


Figure S4. Appearance of lyophilized and spray-dried zein nanoparticles.

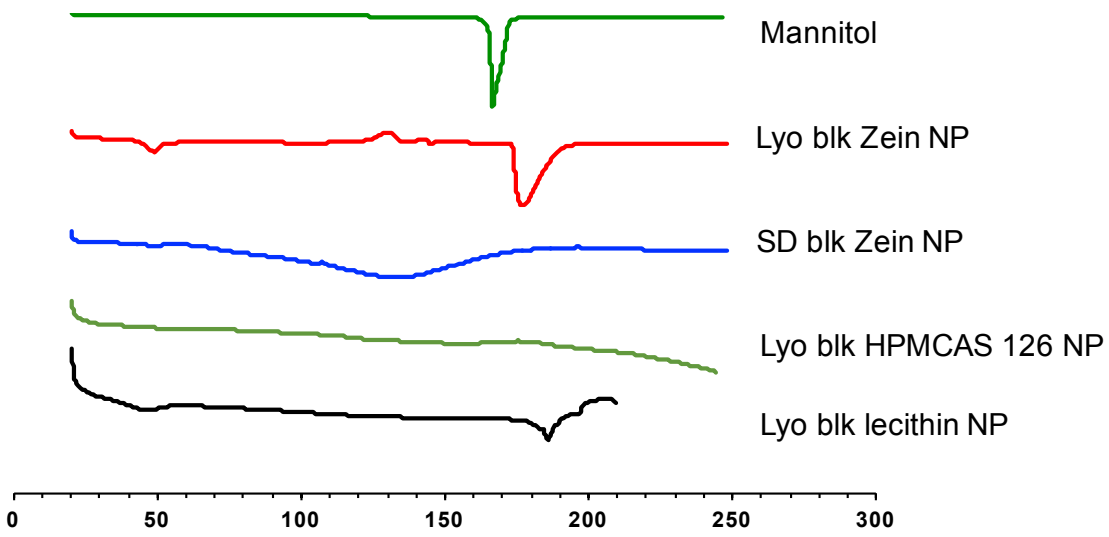


Figure S5. DSC traces of control samples. Blank nanoparticles were produced by FNP and lyophilized or spray-dried with same conditions as their corresponding clofazimine encapsulated nanoparticles.

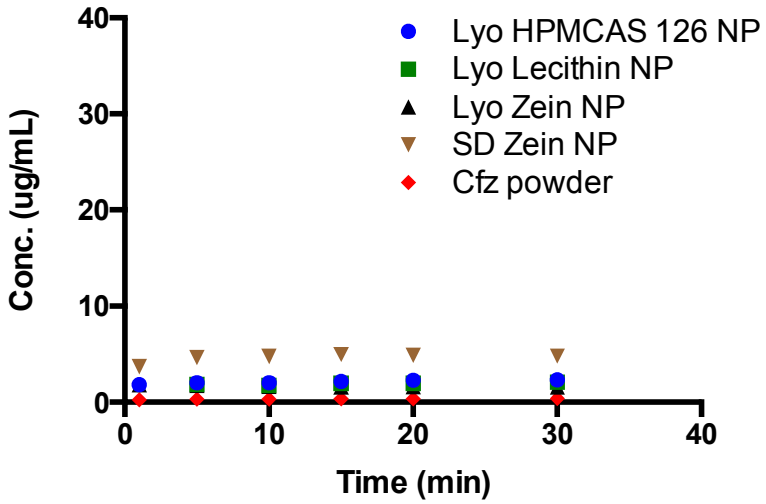


Figure S6. Dissolution of clofazimine nanoparticles with different stabilizers compared with free clofazimine (Cfz) powder in DI water at 37 ˚C.