applied sciences

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Supplementary Materials

Injectable Vaginal Hydrogels as a Multi-drugs Carrier for Contraception

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21 **Table S1.** Preparation of simulated vaginal fluid solution by using different chemicals

Component	Concentration (g/L)
NaCl	3.51
KOH	1.40
$Ca(OH)_2$	0.222
Bovine Serum Albumin	0.018
Lactic Acid	2.00
Acetic Acid	1.00
Glycerol	0.16
Urea	0.4
Glucose	5.0

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Table S2. Fitting parameters of various drug release models

Sample numbers		Zero-order kinetic model			First-order kinetic model			Higuchi kinetic model		
		Slope	Intercept	R^2	Slope	Intercept	R^2	Slope	Intercept	R^2
IMC	1	67.185	355.106	0.951	0.0634	6.042	0.691	0.0442	-0.0331	0.996
	2	128.945	660.980	0.938	0.0658	6.634	0.670	0.0769	-0.0601	0.993
	3	256.150	1335.91	0.939	0.06539	7.335	0.669	0.1664	-0.1280	0.993
GSD	1	6.474	22.469	0.929	0.0792	3.267	0.626	0.0907	-0.0918	0.986
	2	6.903	23.421	0.954	0.0738	3.444	0.686	0.1106	-0.1106	0.990
	3	13.443	49.912	0.965	0.0700	4.212	0.714	0.1860	-0.1768	0.996
EE	1	9.460	34.287	0.906	0.0182	3.599	0.596	0.0302	-0.0304	0.977
	2	19.967	50.789	0.941	0.0810	4.298	0.677	0.0626	-0.0699	0.974
	3	37.401	159.921	0.976	0.0589	5.492	0.811	0.1533	-0.1225	0.941

[1] CP-1, LA/GA mol ratio = 9; [2] CP-2, LA/GA mol ratio = 3; [3] CP-3, LA/GA mol ratio = 1. All samples with middle drug content.

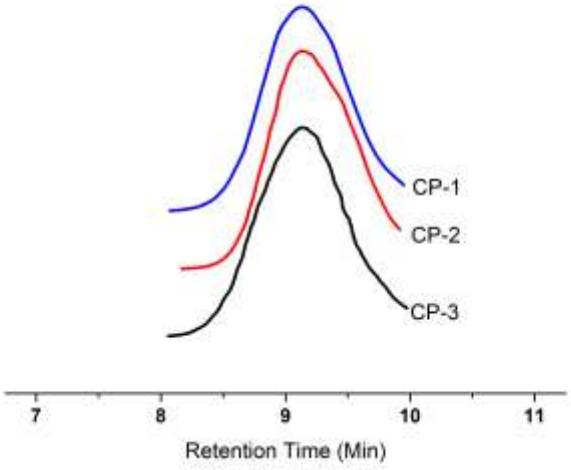

Figure S1. GPC traces of prepared CP-1, CP-2 and CP-3 block copolymers.

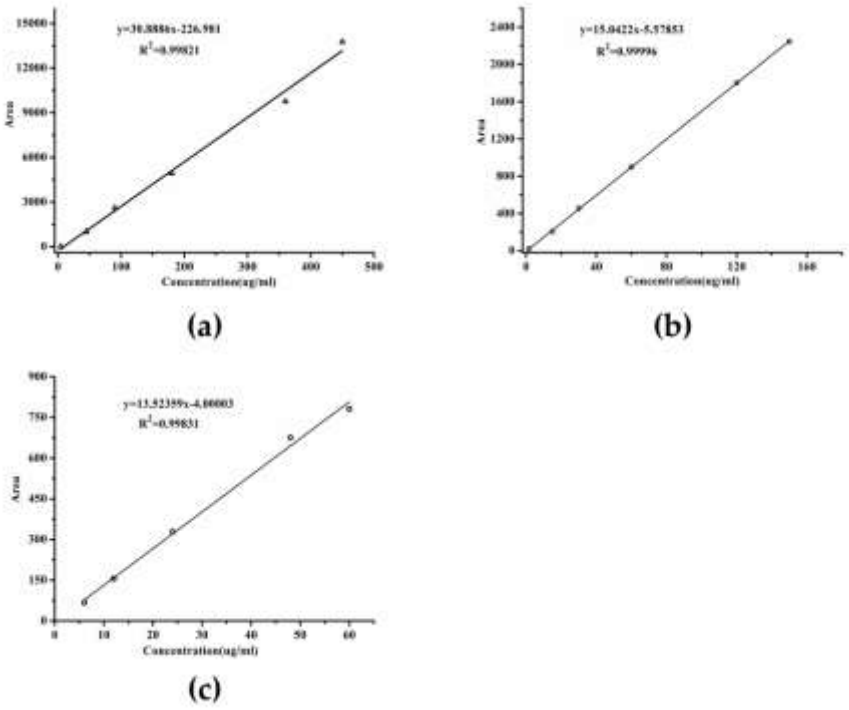

Figure S2. Standard curves of (**a**) IMC, (**b**) GSD and (**c**) EE. The regression equation was calculated in the form of $y = ax + b$, where y and x were the values of peak area and concentration of each reference compound, respectively.

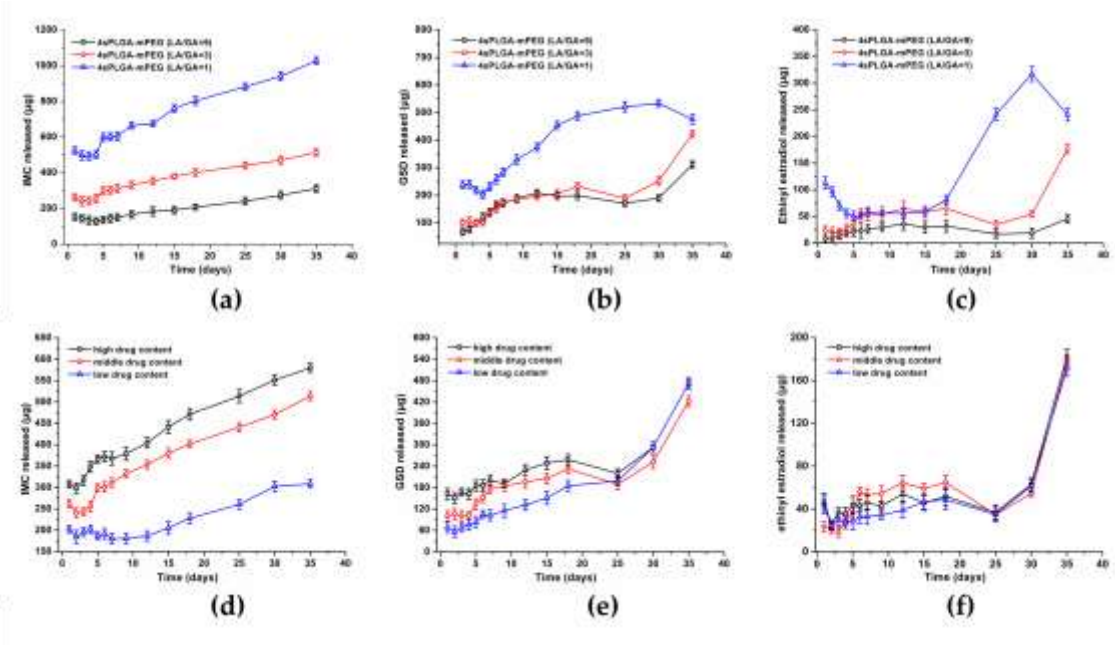

Figure S3. The release amounts of IMC, GSD and EE from prepared 4sPLGA-mPEG block copolymer hydrogels. Release amounts of IMC (**a**), GSD (**b**) and EE (**c**) packed by copolymer hydrogel with the same middle drug content and various LA/GA mol ratios at different days. Release amounts of IMC (**d**), GSD (**e**) and EE (**f**) loaded by CP-2 copolymer (LA/GA = 3) hydrogel with various drug contents (high, middle, and low) at different days. Copolymer concentration was 30 wt%.

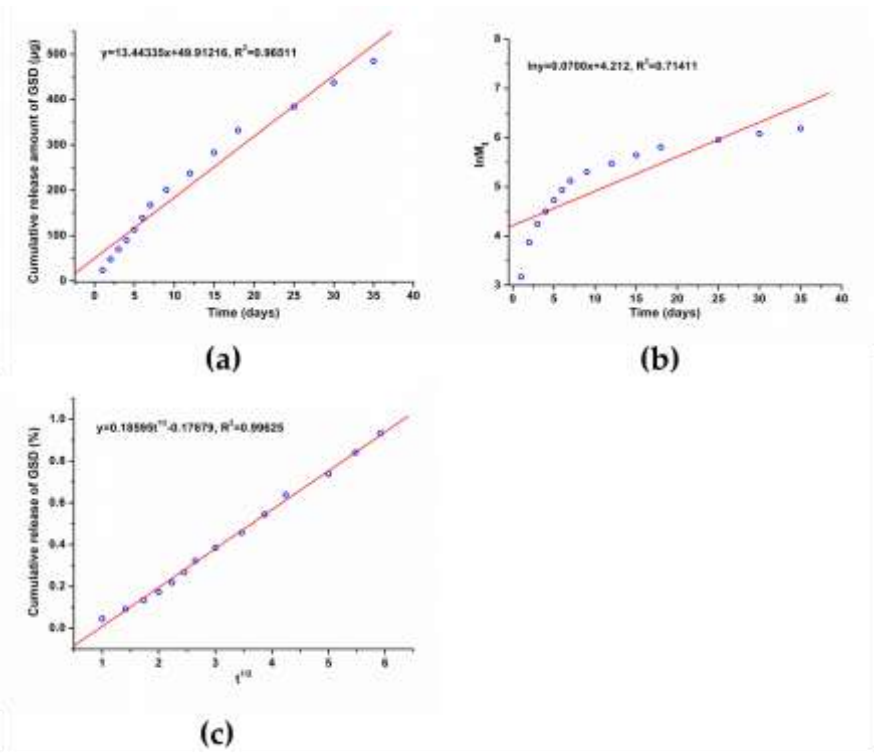

Figure S4. Fitting curves of cumulative release of GSD using different release kinetic models: (**a**) zero-order kinetic model, (**b**) first-order kinetic model, (**c**) Higuchi kinetic model. The CP-3 copolymer hydrogels were used with middle dosage content, the copolymer concentration is 30 wt%.

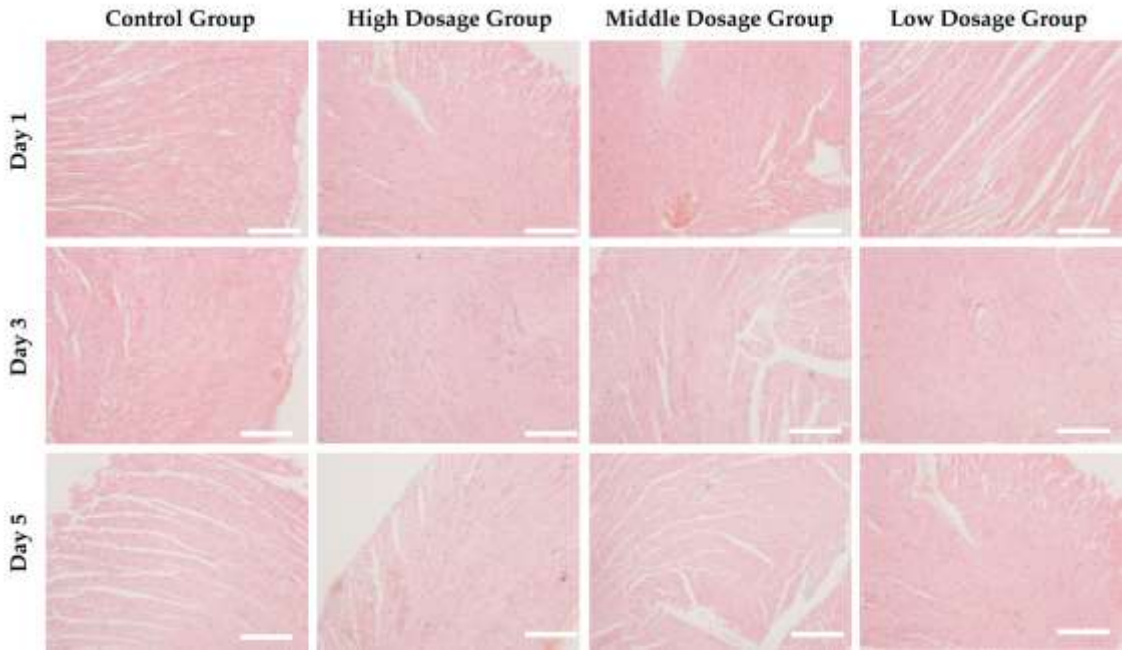

Figure S5. HE staining of SD rat hearts at day 1, 3, and 5 after injecting hydrogels with different drug dosages into vagina (high dosage, middle dosage, and low dosage). The CP-3 block copolymer solution at the concentration of 30 wt% was used. The volume of drug-loaded copolymer solution injected into vagina is 0.2 mL. Copolymer solutions without loading drug were injected in the vagina of SD rats as control group, scale bar: 5 μm.

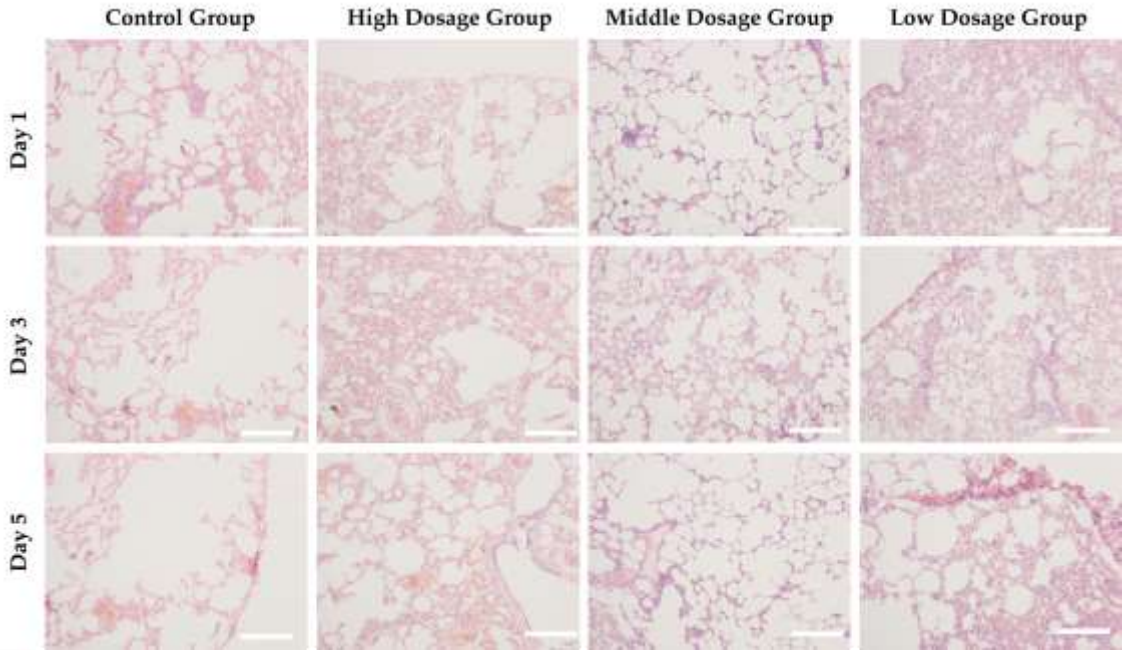

Figure S6. HE staining of SD rat lungs at day 1, 3, and 5 after injecting hydrogels with different drug dosages into vagina (high dosage, middle dosage, and low dosage). The CP-3 block copolymer solution at the concentration of 30 wt% was used. The volume of drug-loaded copolymer solution injected into vagina is 0.2 mL. Copolymer solutions without loading drug were injected in the vagina of SD rats as control group, scale bar: 5 μm.

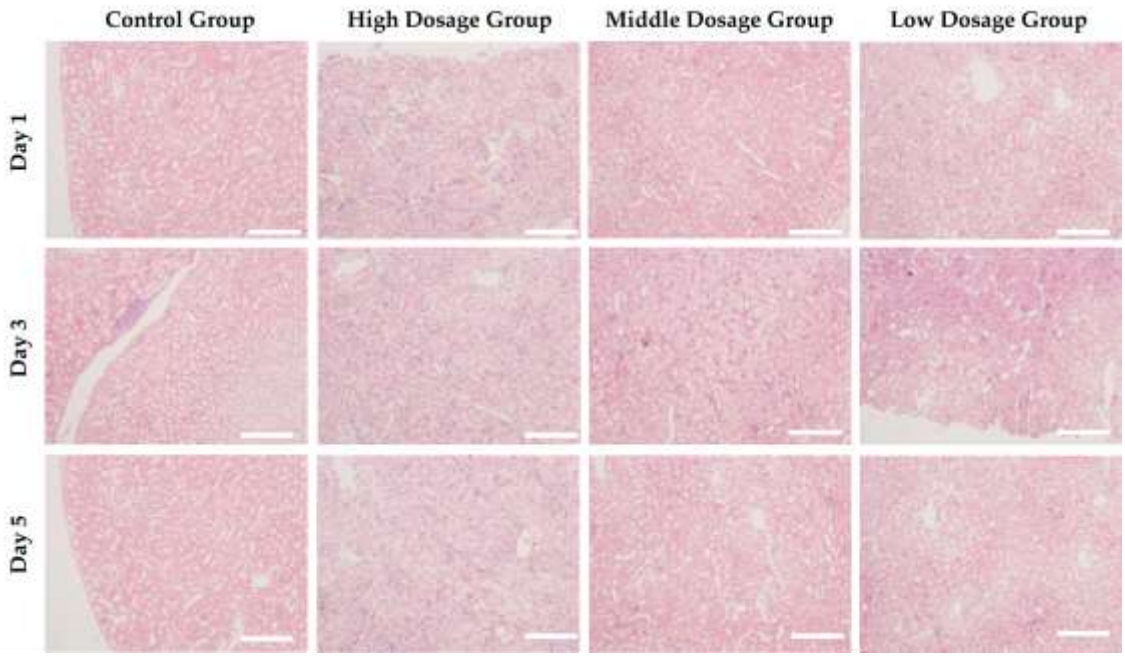

Figure S7. HE staining of SD rat kidneys at day 1, 3, and 5 after injecting hydrogels with different drug dosages into vagina (high dosage, middle dosage, and low dosage). The CP-3 block copolymer solution at the concentration of 30 wt% was used. The volume of drug-loaded copolymer solution injected into vagina is 0.2 mL. Copolymer solutions without loading drug were injected in the vagina of SD rats as control group, scale bar: 5 μm.

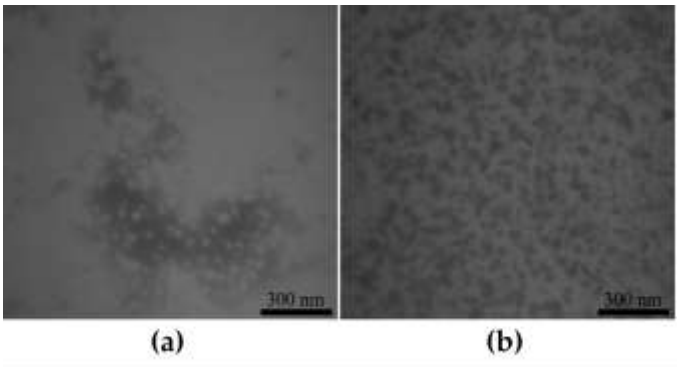

Figure S8. TEM of CP-3 block copolymer solution at concentration (**a**) 1 wt% and (**b**) 2.5 wt%, the micellar particles were observed.