

Supporting Information for

A Combinative Assembly Strategy Inspired Reversibly Borate-Bridged Polymeric Micelles for Lesion-Specific Rapid Release of Anticoccidial Drugs

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Supplementary Figures

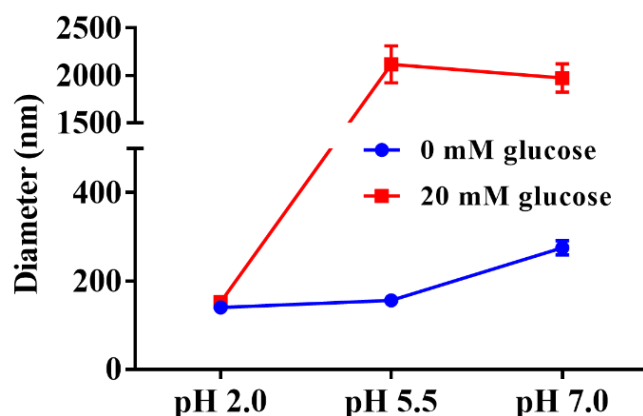


Fig. S1 Diameter variations of S_{0.1}P_{1.0}CS/DIC micelles at pH values of 2.0, 5.5 and 7.0, with the presence and absence of glucose (20 mM). Data are expressed as mean±SD, n=3

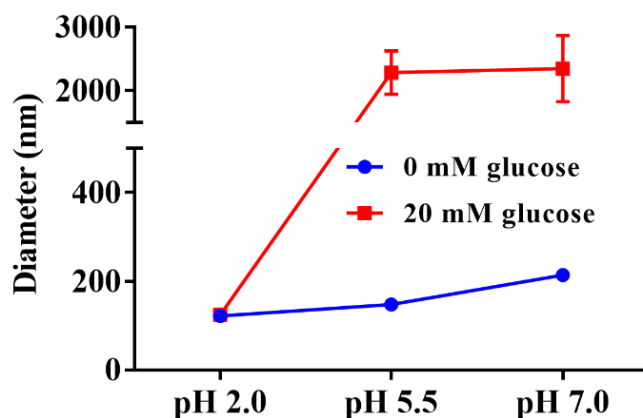


Fig. S2 Diameter variations of S_{0.1}P_{1.5}CS/DIC micelles at pH values of 2.0, 5.5 and 7.0, with the presence and absence of glucose (20 mM). Data are expressed as mean±SD, n=3

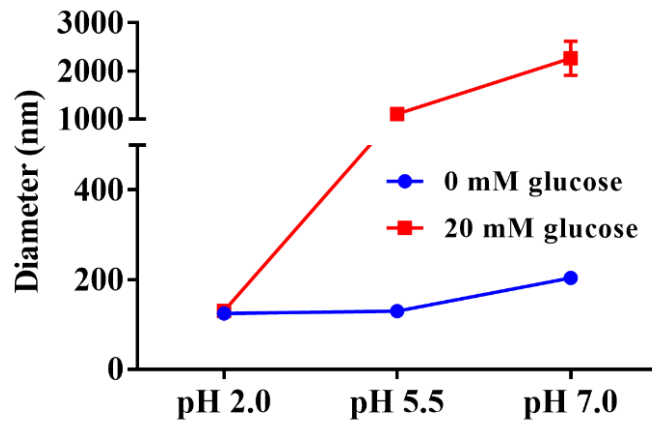


Fig. S3 Diameter variations of S_{0.2}P_{1.5}CS/DIC micelles at pH values of 2.0, 5.5 and 7.0, with the presence and absence of glucose (20 mM). Data are expressed as mean±SD, n=3

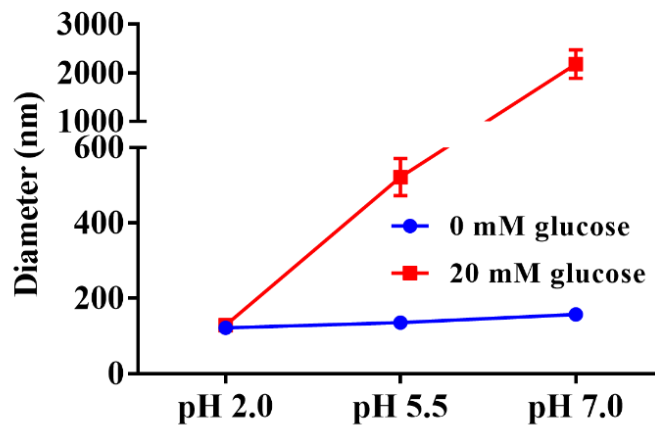


Fig. S4 Diameter variations of S_{0.5}P_{1.5}CS/DIC micelles at pH values of 2.0, 5.5 and 7.0, with the presence and absence of glucose (20 mM). Data are expressed as mean±SD, n=3

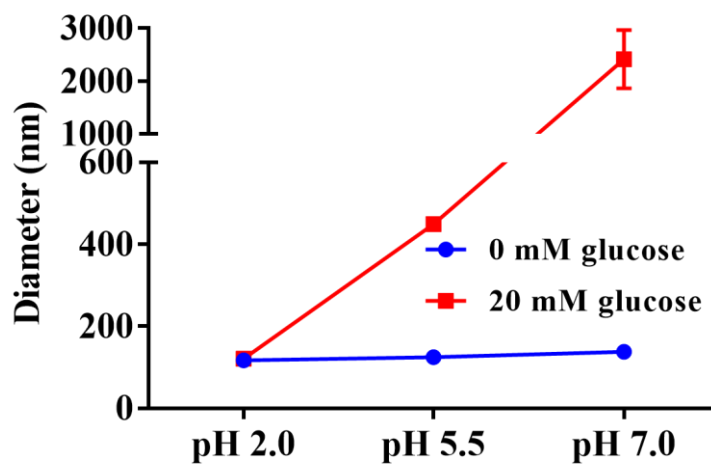


Fig. S5 Diameter variations of S_{1.0}P_{1.5}CS/DIC micelles at pH values of 2.0, 5.5 and 7.0, with the presence and absence of glucose (20 mM). Data are expressed as mean±SD, n=3

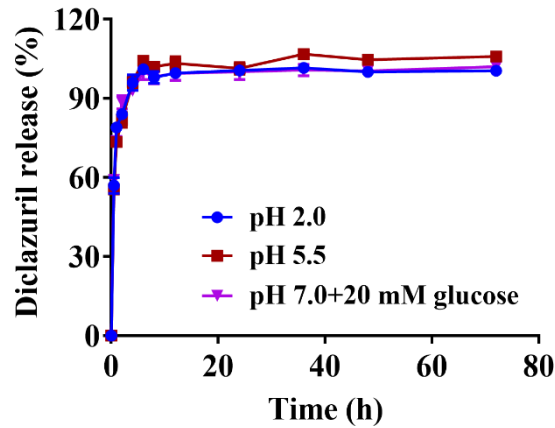


Fig. S6 Free DIC release profile from the dialysis bag at different pH values of 2.0, 5.5, and in the presence of glucose (20 mM) at pH 7.0. Data are expressed as mean \pm SD, n=3

Table S1 Graft ratio of PBA moieties in P_xCS copolymers, where x is the ratio of PBA molecules to CS monomers. Data are presented as mean \pm SD, n = 3

Type of P _x CS	PBA: CS (n/n)	Graft ratio (%)
P _{0.5} CS	0.5	11.93 \pm 1.56
P _{1.0} CS	1.0	35.13 \pm 3.89
P _{1.5} CS	1.5	40.45 \pm 2.14
P _{2.0} CS	2.0	41.38 \pm 3.24

Table S2 Graft ratio of SA moieties in S_yP_{1.0}CS copolymers, where y is the ratio of SA moieties to PBA molecules. Data are presented as mean \pm SD, n = 3

Type of S _y P _{1.0} CS	SA: PBA (n/n)	Graft ratio (%)
S _{0.1} P _{1.0} CS	0.1	4.57 \pm 1.16
S _{0.2} P _{1.0} CS	0.2	14.56 \pm 3.58
S _{0.5} P _{1.0} CS	0.5	21.31 \pm 2.79
S _{1.0} P _{1.0} CS	1.0	25.05 \pm 4.18

Table S3 Graft ratio of SA moieties in S_yP_{1.5}CS copolymers, where y is the ratio of SA moieties to PBA molecules. Data are presented as mean \pm SD, n = 3

Type of S _y P _{1.5} CS	SA: PBA (n/n)	Graft ratio (%)
S _{0.1} P _{1.5} CS	0.1	4.14 \pm 0.93
S _{0.2} P _{1.5} CS	0.2	10.68 \pm 2.76
S _{0.5} P _{1.5} CS	0.5	16.67 \pm 2.63
S _{1.0} P _{1.5} CS	1.0	17.01 \pm 3.32

Table S4 Characterization of series of DIC-loaded micelles. Data are presented as mean \pm SD, n = 3. *p < 0.05 and ***p < 0.001

Samples	Size (nm)	PDI	DL (%)	EE (%)
SPCS/DIC	124.1 \pm 0.9	0.092 \pm 0.008	13.4 \pm 1.16*	74.3 \pm 4.2***
PCS/DIC	139.5 \pm 1.1	0.153 \pm 0.013	8.97 \pm 1.59	59.1 \pm 4.3

Table S5 Pharmacokinetics parameters following a single oral administration (15 mg/kg of DIC) of DIC suspension and SPCS/DIC micelles. Data are presented as mean \pm SD, n = 6. *p < 0.05 and ****p < 0.0001 as compared to DIC suspension

Parameters	Unit	DIC suspension	SPCS/DIC
AUC _{0-t}	$\mu\text{g}\cdot\text{mL}^{-1}\text{h}$	140.40 \pm 7.07	236.10 \pm 28.69*
C _{max}	$\mu\text{g}\cdot\text{mL}^{-1}$	8.90 \pm 1.20	7.50 \pm 0.63
T _{max}	h	0.48 \pm 0.03	8.25 \pm 0.35****
t _{1/2}	h	64.56 \pm 10.55	85.85 \pm 7.59*
CL	$\text{mL}\cdot(\text{h}\cdot\text{g})^{-1}$	0.063 \pm 0.0034	0.041 \pm 0.0026*

Table S6 Body weight determined at the initial and the end of the experiment, and relative body weight gain (%), feed conversion ratio (FCR). Data are expressed as mean \pm SD, n=10

Groups	Body weight		Weight gain (%)	Relative body weight gain (%)	Feed conversion ratio (FCR)
	Before challenge (g)	After challenge (g)			
Negative control	95.8 \pm 5.7	173.3 \pm 13.8	81	100	3.06
Positive control	96.4 \pm 4.8	138.2 \pm 14.3	43	53	5.42
SPCS/DIC (H)	92.8 \pm 7.6	154.5 \pm 9.2	67	82	3.63
SPCS/DIC (M)	94.7 \pm 5.9	163.0 \pm 27.6	72	89	3.66
SPCS/DIC (L)	93.9 \pm 7.0	151.4 \pm 16.1	61	76	4.02
PCS/DIC	96.4 \pm 7.2	153.9 \pm 21.6	60	74	3.88
DIC	96.3 \pm 5.8	141.0 \pm 17.9	46	57	4.92

Table S7 Bloody faeces counted during 5-7 days after challenge with Eimeria tenella. Data are expressed as pooled bloody faeces from 10 chicks in each group

Groups	Days after challenge			Total bloody faeces
	5	6	7	
Negative control	0	0	0	0
Positive control	11	6	6	23
SPCS/DIC (H)	6	3	3	12
SPCS/DIC (M)	5	5	3	13
SPCS/DIC (L)	4	6	7	17
PCS/DIC	4	6	6	16
DIC	6	8	5	19

Table S8 Intestinal lesions examined at 8 days after challenge with *Eimeria tenella*. Data are expressed as mean \pm SD, n=10

Groups	Intestinal lesion ranks					Lesion scores (mean \pm SD)
	0	1	2	3	4	
Negative control	8	0	0	0	0	0.00 \pm 0.00
Positive control	5	1	2	0	0	0.62 \pm 0.92
SPCS/DIC (H)	7	1	0	0	0	0.12 \pm 0.35
SPCS/DIC (M)	7	1	0	0	0	0.12 \pm 0.46
SPCS/DIC (L)	6	1	1	0	0	0.38 \pm 0.46
PCS/DIC	5	3	0	0	0	0.37 \pm 0.35
DIC	5	0	2	0	0	0.51 \pm 0.71

Table S9 Grade estimation of coccidiostats according to ACI values

ACI	>180	160-180	120-160	<120
Grade of coccidiostats	Highly effective	Moderately effective	Inefficient	Invalid