Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Supporting Information for:

A strategy for developing effective orally-delivered nanoparticles through modulation of the surface "hydrophilicity/ hydrophobicity balance"

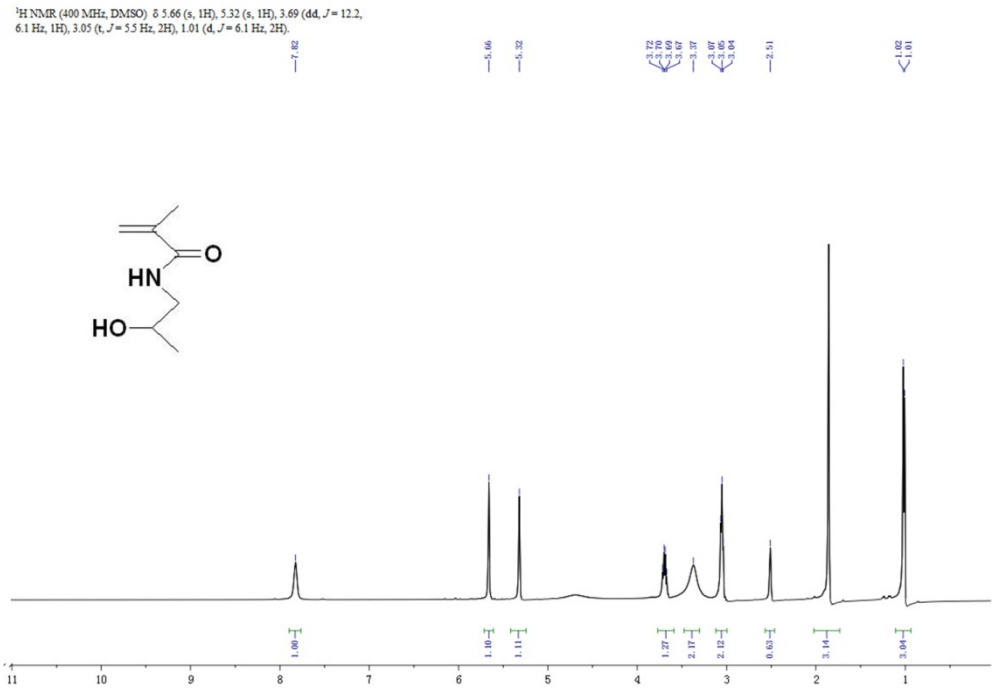
Yi Cui [1], Wei Shan [1], Min Liu, Lei Wu, Yuan Huang *

Key Laboratory of Drug Targeting and Drug Delivery System (Ministry of Education), West China School of Pharmacy, Sichuan University, No. 17, Block 3, Southern Renmin Road, Chengdu 610041, China

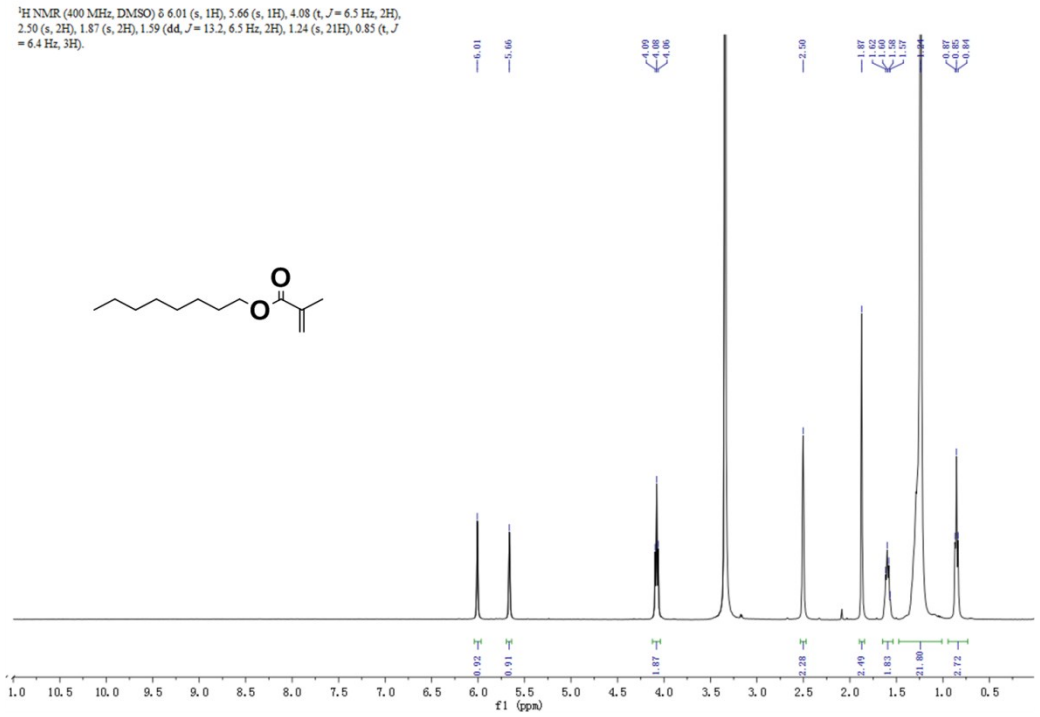
[1] Y.C. and W.S. contributed equally to this work.
E-mail: huangyuan0@163.com

Supporting Information Table S1: Characteristics of synthesized HPMA-FAs copolymers.

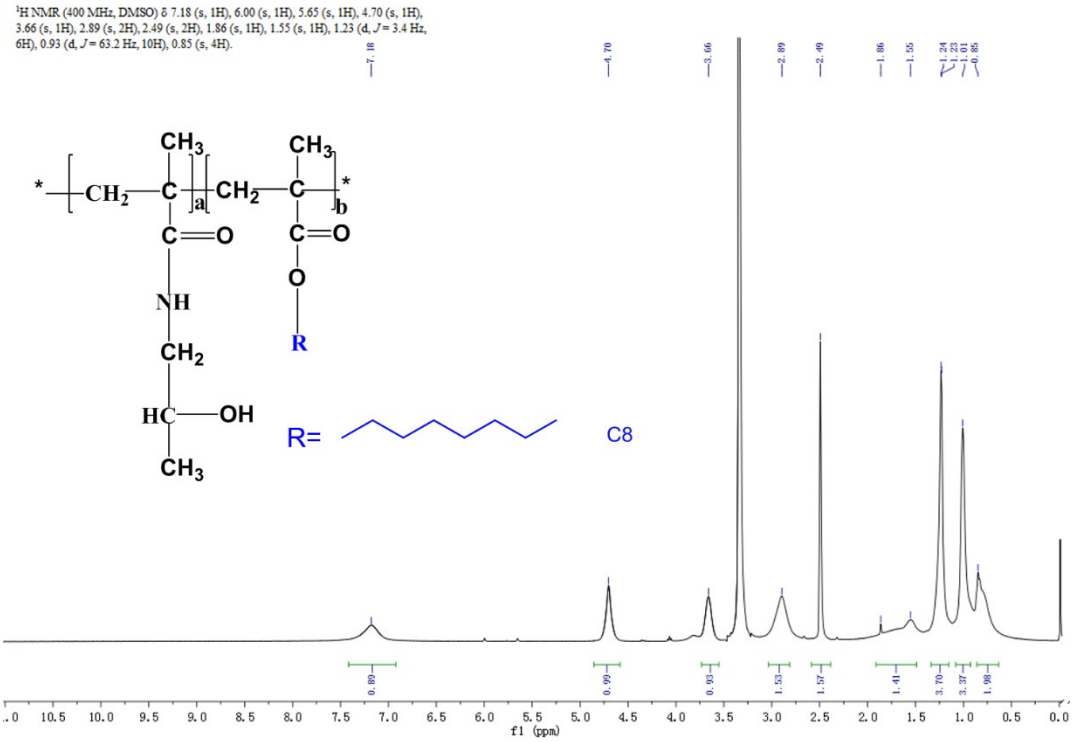
Copolymer	Mw(kDa)	PDI	FAs (%)
HPMA-C8	65.9	1.26	10.5
HPMA-C12	67.4	1.18	10.4
HPMA-C14	62.7	1.23	10.6
HPMA-C16	64.2	1.17	10.4



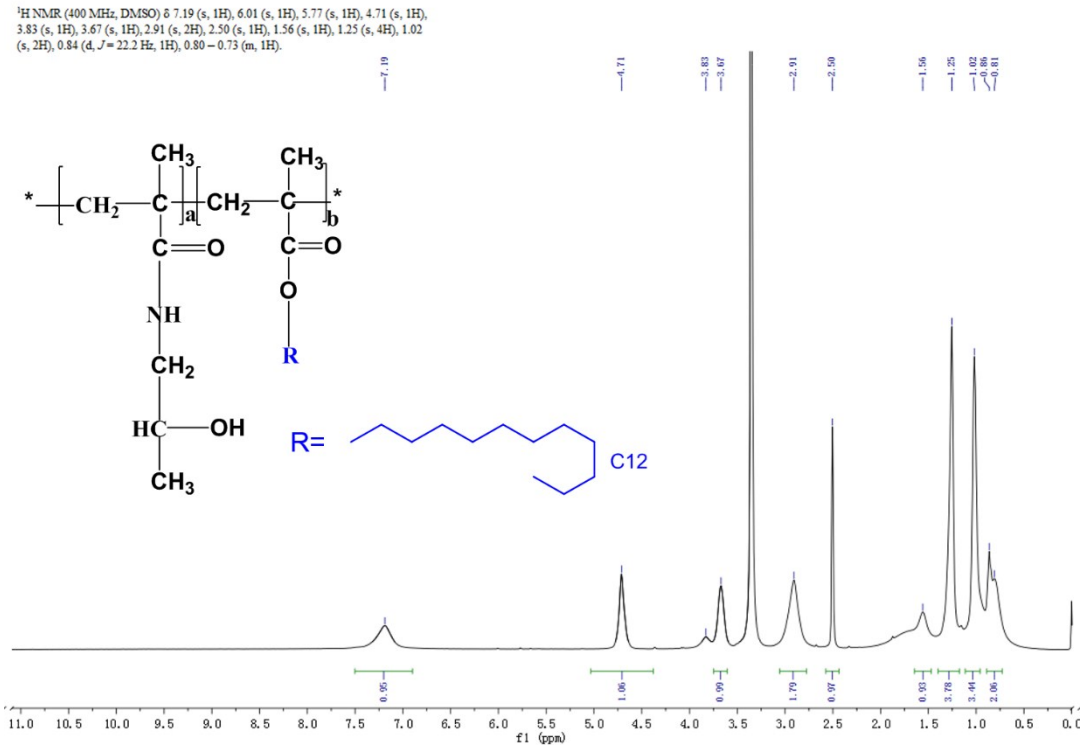
Supporting Information Figure S1: The ^{1}H-NMR (400 MHz, DMSO-d6) spectrum of HPMA monomer. δ(ppm) 5.66 (s, 1H), 5.32 (s, 1H), 3.69 (dd, J = 12.2, 6.1 Hz, 1H), 3.05 (t, J = 5.5 Hz, 2H), 1.01 (d, J = 6.1 Hz, 2H).



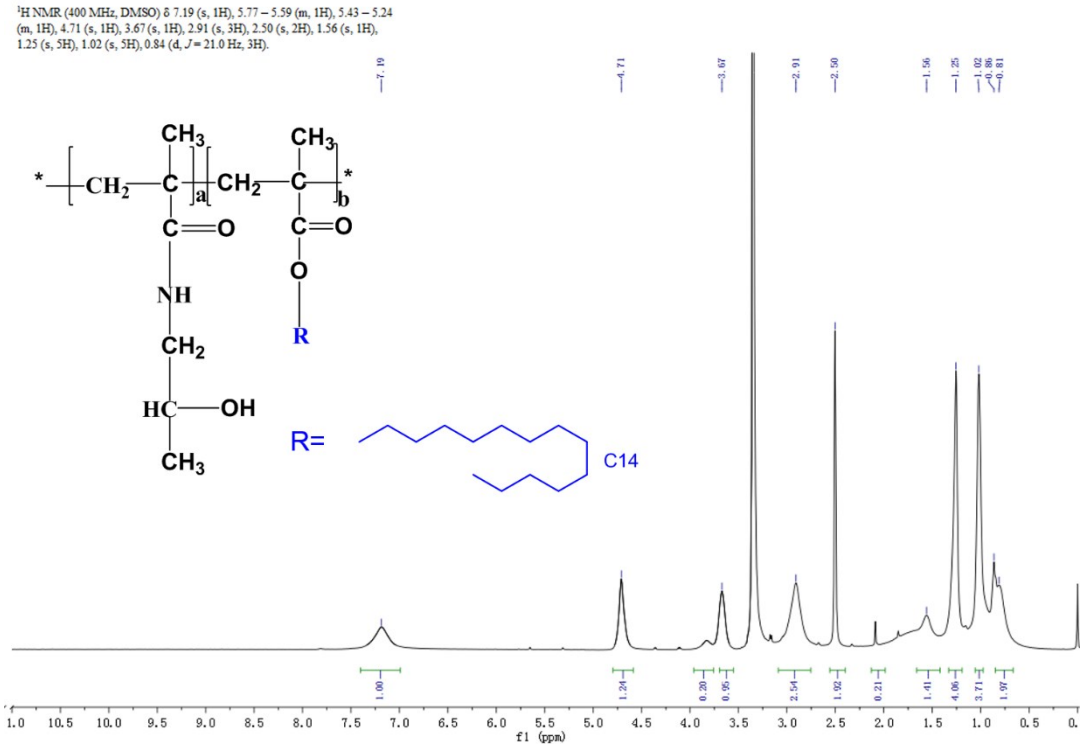
Supporting Information Figure S2: The ^{1}H-NMR (400 MHz, DMSO-d6) spectrum of *N*-octyl methacrylate. δ(ppm) 6.01 (s, 1H), 5.66 (s, 1H), 4.08 (t, J = 6.5 Hz, 2H), 2.50 (s, 2H), 1.87 (s, 2H), 1.59 (dd, J = 13.2, 6.5 Hz, 2H), 1.24 (s, 21H), 0.85 (t, J = 6.4 Hz, 3H).



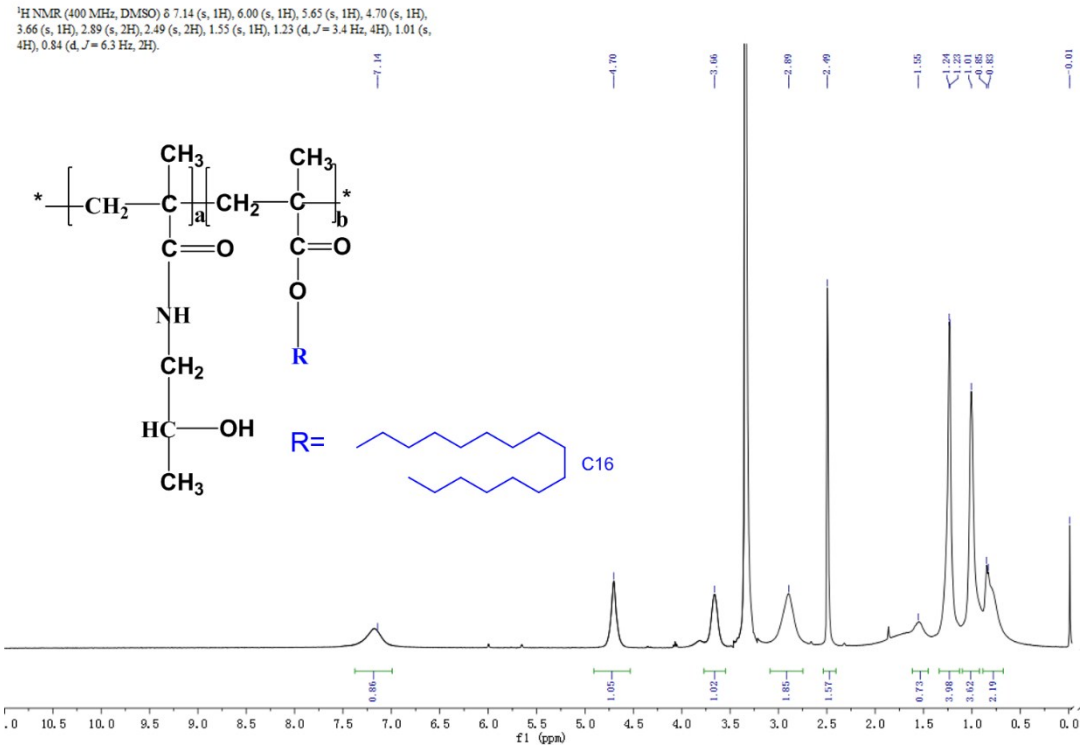
Supporting Information Figure S3: The ^{1}H-NMR (400 MHz, DMSO-d6) spectrum of HPMA-C8. δ(ppm) 7.18 (s, 1H), 6.00 (s, 1H), 5.65 (s, 1H), 4.70 (s, 1H), 3.66 (s, 1H), 2.89 (s, 2H), 2.49 (s, 2H), 1.86 (s, 1H), 1.55 (s, 1H), 1.23 (d, J = 3.4 Hz, 6H), 0.93 (d, J = 63.2 Hz, 10H), 0.85 (s, 4H).



Supporting Information Figure S4: The ^{1}H-NMR (400 MHz, DMSO-d6) spectrum of HPMA-C12. δ(ppm) 7.19 (s, 1H), 6.01 (s, 1H), 5.77 (s, 1H), 4.71 (s, 1H), 3.83 (s, 1H), 3.67 (s, 1H), 2.91 (s, 2H), 2.50 (s, 1H), 1.56 (s, 1H), 1.25 (s, 4H), 1.02 (s, 2H), 0.84 (d, J = 22.2 Hz, 1H), 0.80 – 0.73 (m, 1H).



Supporting Information Figure S5: The ^{1}H-NMR (400 MHz, DMSO-d6) spectrum of HPMA-C14. δ(ppm) 7.19 (s, 1H), 5.77 – 5.59 (m, 1H), 5.43 – 5.24 (m, 1H), 4.71 (s, 1H), 3.67 (s, 1H), 2.91 (s, 3H), 2.50 (s, 2H), 1.56 (s, 1H), 1.25 (s, 5H), 1.02 (s, 5H), 0.84 (d, J = 21.0 Hz, 3H).



Supporting Information Table S2: The Zeta potential of NPs-PLGA coated with HPMA-C8 when dispersed medium was phosphate buffer saline (PBS, 0.01 M, pH 7.3, 25℃, I=0.041) or deionized water (pH 6.85, 25℃)

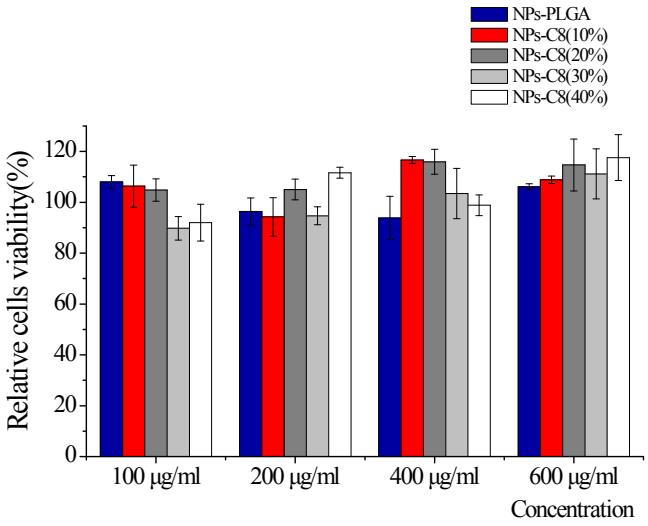
Samples	Zeta potential (mV) (In PBS buffer)	Zeta potential (mV) (In deionized water)
NPs-PLGA	-11.2 ± 0.36	-20.6 ± 1.27
NPs-C8 (10%)	-6.0 ± 0.20	-16.9 ± 0.72
NPs-C8 (20%)	-3.7 ± 0.31	-11.6 ± 0.46
NPs-C8 (30%)	-3.1 ± 0.10	-9.68 ± 0.57
NPs-C8 (40%)	-2.9 ± 0.17	-7.02 ± 0.52

Supporting Information Table S3: The area under of binding energies and the nitrogen atom composition percentage for PLGA NPs coated with HPMA-C8

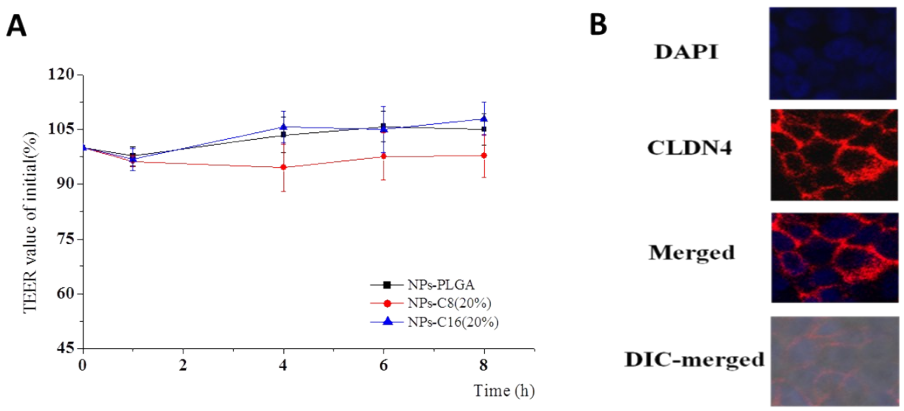
Samples	Area under binding energy	Nitrogen atom content (%)
NPs-C8(10%)	3595.2	1.12
NPs-C8(20%)	4844.5	1.81
NPs-C8(30%)	5355.2	2.34
NPs-C8(40%)	6980.2	3.09

Supporting Information Figure S6: The ^{1}H-NMR (400 MHz, DMSO-d6) spectrum of

HPMA-C16. δ(ppm) 7.14 (s, 1H), 6.00 (s, 1H), 5.65 (s, 1H), 4.70 (s, 1H), 3.66 (s, 1H), 2.89 (s, 2H), 2.49 (s, 2H), 1.55 (s, 1H), 1.23 (d, J = 3.4 Hz, 4H), 1.01 (s, 4H), 0.84 (d, J = 6.3 Hz, 2H).



Supporting Information Figure S7: Cell viability after incubation of NPs samples. Data are means ± SD (n=3).



Supporting Information Figure S8: (A) The effect of NPs-PLGA, NPs-C8(20%), NPs-C16(20%) on TEER values of E12 cell monolayers. The TEER value was presented as the percentage of the value before three experiments. Data are means ± SD (n= 3). (B) Immunofluorescence staining of the influence of tight junction by NPs. Cell monolayer was fixed and stained for Claudin-4 (Red). Blue represents the fluorescence of DAPI.