Electronic Supplementary Information

One-step prepared nano-in-micro microcapsule delivery vehicle with sequential burst-sustained drug release for the targeted treatment of inflammatory bowel disease

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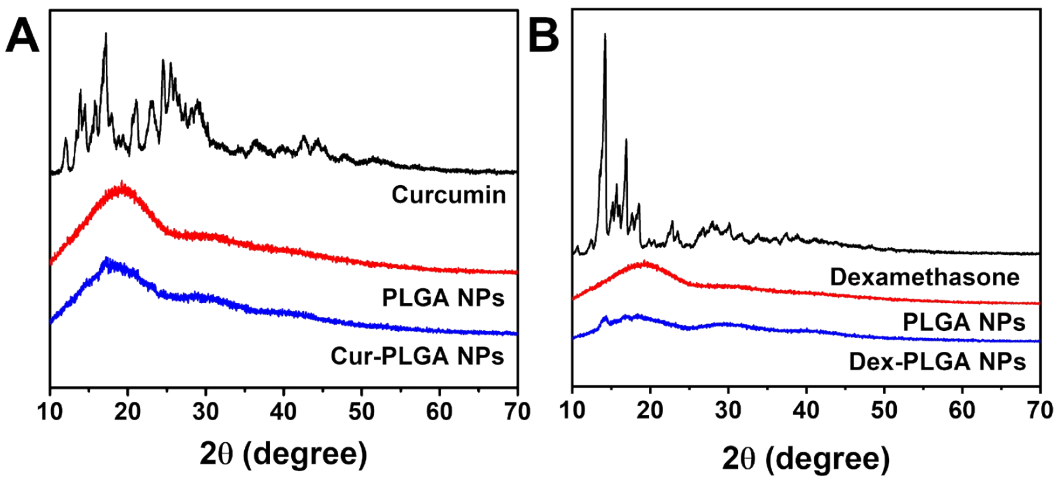

Fig. S1 The XRD pattern of PLGA NPs before and after loading curcumin (A) and dexamethasone (B).

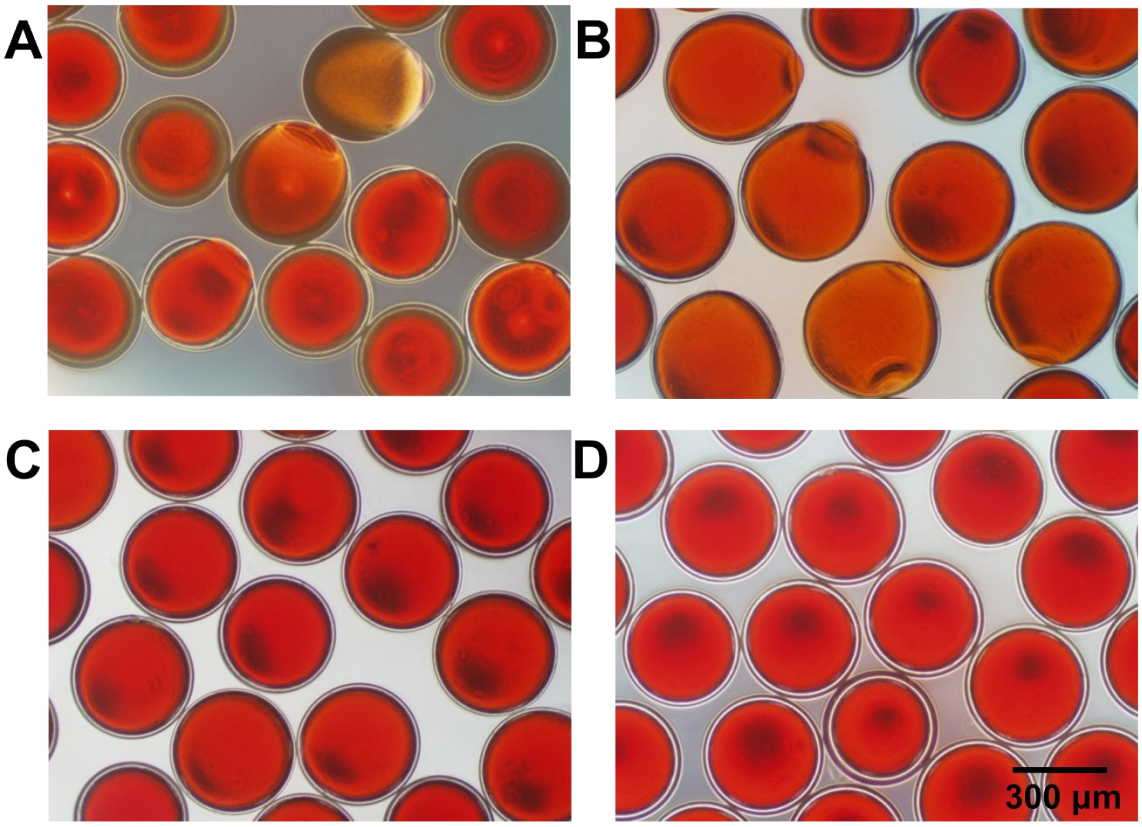

Fig. S2 Effect of the volume ratio of mixed solvents on droplets generation. (A) 1:1. (B) 1:2. (C) 1:3. (D)1:4.

Table S1 Effects of the concentration of HPMCAS-HF on droplets generation.

Concentration of HPMCAS-HF (mg/mL)	60	70	80	90	100	110	120	130	140
Droplets Generation	×	×	√	√	√	√	√	×	×

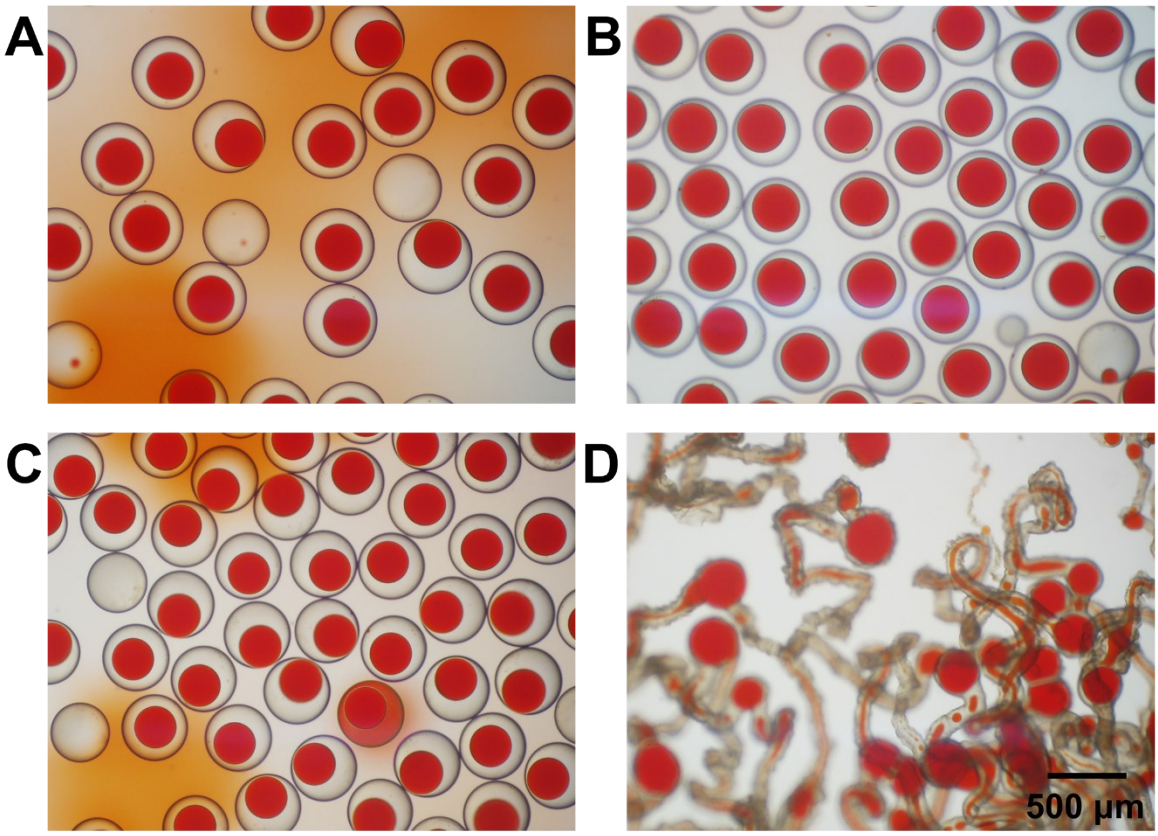

Fig. S3 Effect of the concentration of HPMCAS-HF on droplets generation. (A) 80 mg/mL. (B) 100 mg/mL. (C) 120 mg/mL. (D) 140 mg/mL.

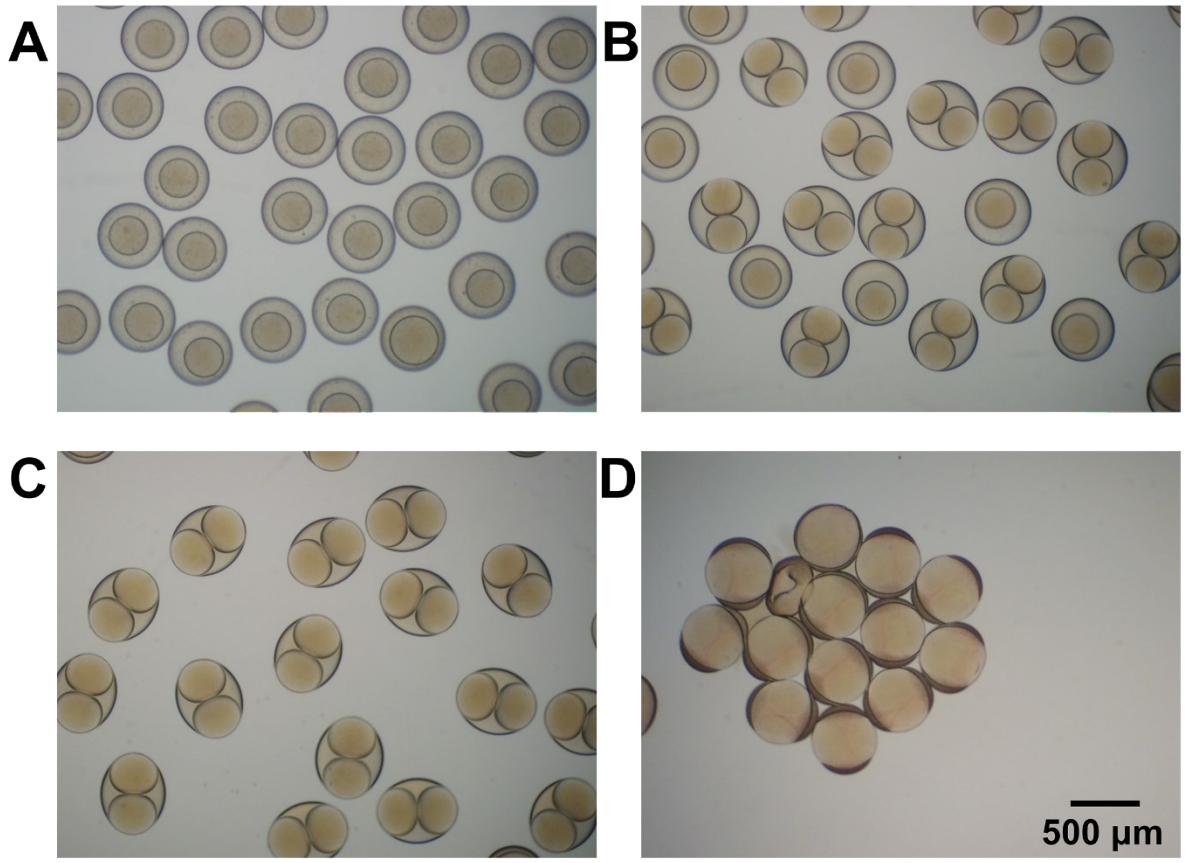

Fig. S4 Effects of the internal flow rate on droplets generation. (A) ν_i=3 μL/min. (B) ν_i=4 μL/min. (C) ν_i=5 μL/min. (D) ν_i=6 μL/min. (ν_m=15 μL/min, ν_o=120 μL/min).

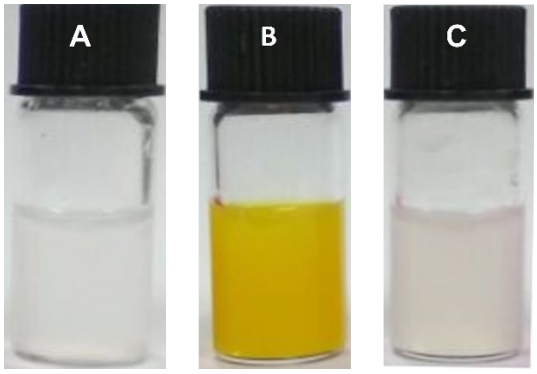

Fig. S5 The dispersion of different nanoparticles in inner aqueous phase after 3 hours. (A) PLGA NPs. (B) PLGA-Cur NPs. (C) PLGA-Dex NPs. The concentration is 20 mg/mL.

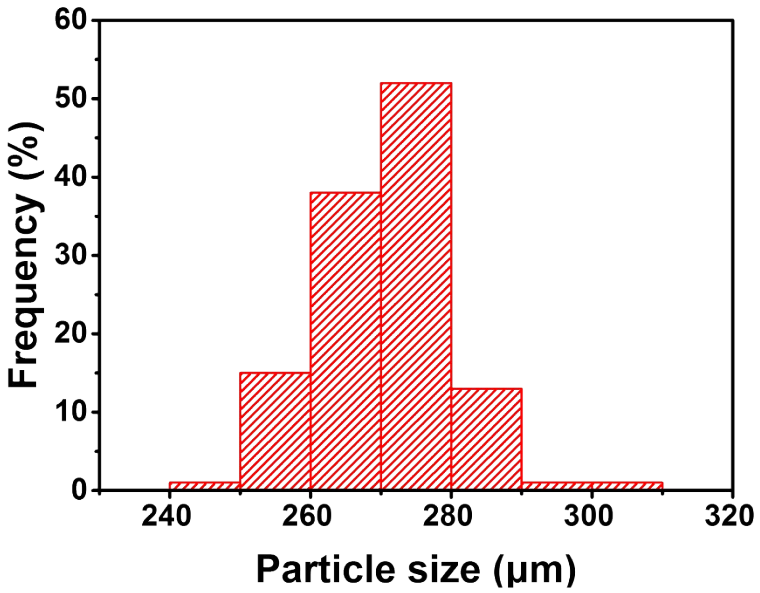

Fig. S6 The particles size of the nano-in-micro microcapsules.

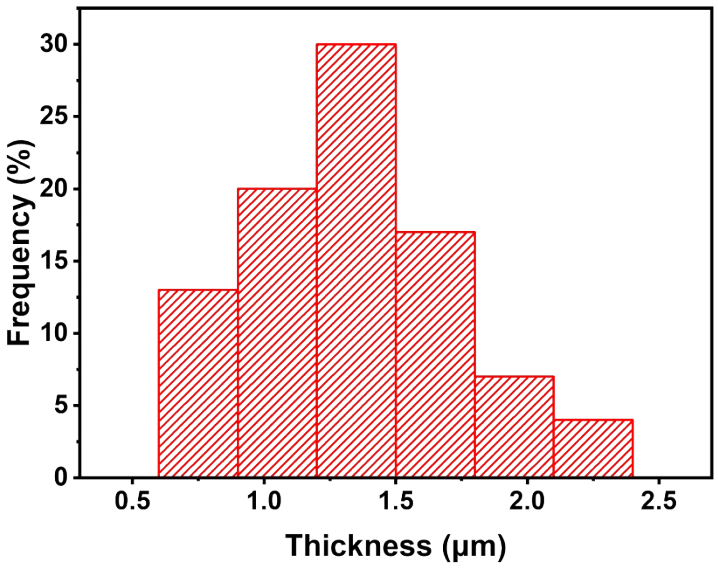

Fig. S7 The thickness of concave lamella of the nano-in-micro microcapsules.

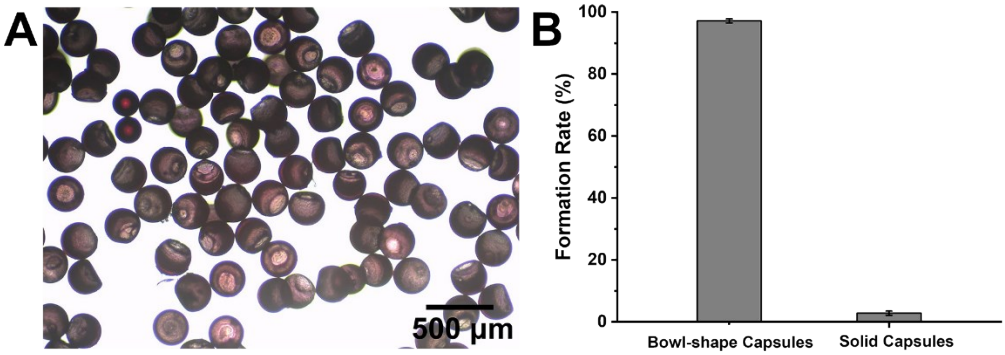

Fig. S8 (A) Optical microscopy image of the nano-in-micro microcapsules. (B) The formation rate of bowl-shape capsules after solidification. Putted the microcapsules on the plate, randomly chosen 5 fields of view to take pictures and counted the number of microcapsules.

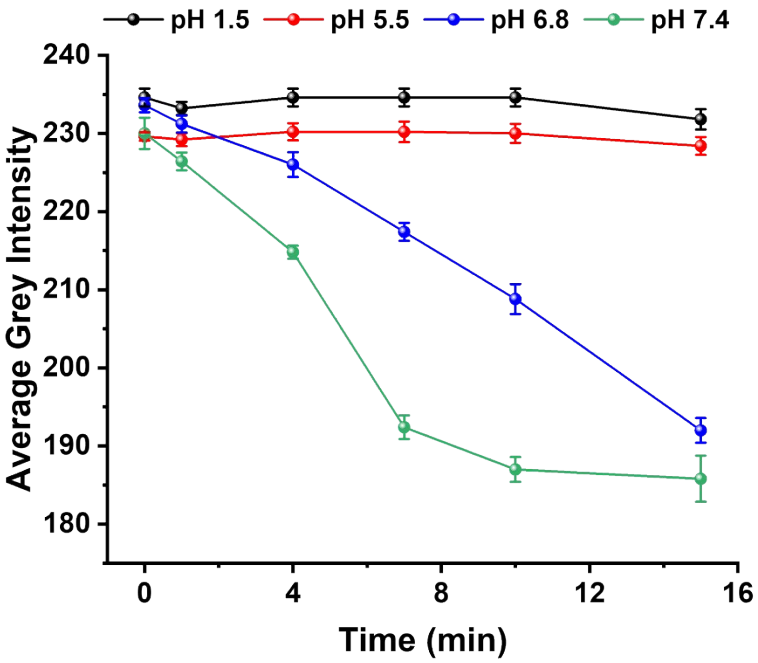

Fig. S9 Variation of color depth of nano-in-micro microcapsules over time under different pH conditions.

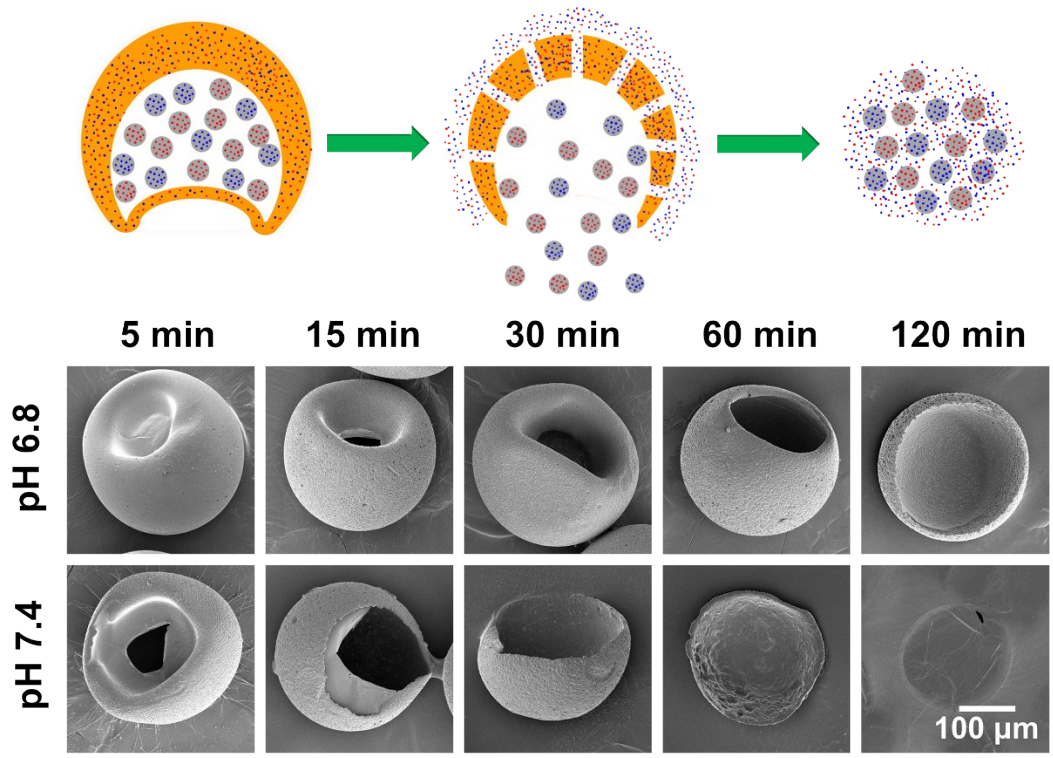

Fig. S10 The partial enlargement of the decomposition of single microcapsules at pH 6.8 and 7.4.

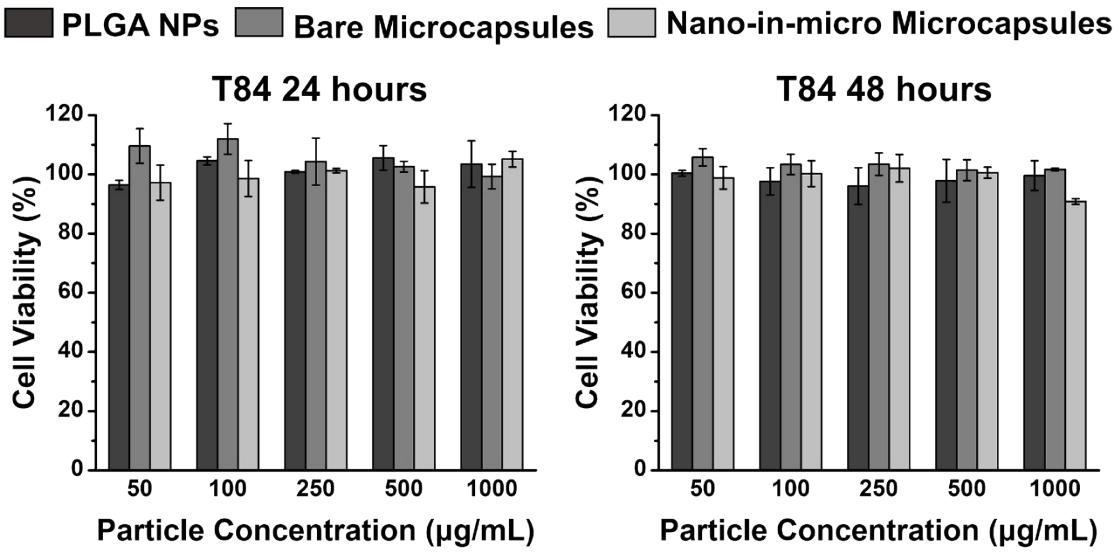

Fig. S11 Viability of T84 cells after 24 and 48 h incubation with different concentrations of PLGA NPs, bare microcapsules, and nano-in-micro microcapsules.

Table S2 Primer sequences used for quantitative real-time polymerase chain reaction.

Gene Name		Seguences（5 ' → 3 ' ）
β-actin	F	GGCTGTATTCCCCTCCATCG
	R	CCAGTTGGTAACAATGCCATGT
TNF-α	F	CACCACGCTCTTCTGTCTAC
	R	ACGGTGTGGGTGAGGAG
IL-1β	F	CTGTGACTCATGGGATGATGATG
	R	CGGAGCCTGTAGTGCAGTTG
IL-6	F	CCAAGAGGTGAGTGCTTCCC
	R	CTGTTGTTCAGACTCTCTCCCT
iNOS	F	GTTCTCAGCCCAACAATACAAGA
	R	GTGGACGGGTCGATGTCAC

Table S3 Peroral dosage forms for the treatment of inflammatory bowel disease.

Size	Composition	Drug	Release mechanism	Reference
Nanocapsule	Tannic acid, Pluronic F-68	Dexamethasone	Esterases- dependent release	[1]
Nanocapsule	PLGA, Eudragit® S100	Budesonide	pH- dependent release	[2]
Microcapsule	Chitosan, alginate	Antibody-coated NCs	pH- dependent release	[3]
Microcapsule	Acetalated dextran	Dexamethasone	pH- dependent release	[4]
Nano-in-micro capsule	Phenylboronic esters-modified dextran, HPMCAS	Rifaximin	pH and ROS-dependent release	[5]
Nano-in-micro capsule	Halloysite nanotubes, HPMCAS	Curcumin	pH- dependent release	[6]
Nano-in-nano-in-micro capsule	Hyaluronic acid functionalized porous silicon, HPMCAS	Budesonide	Enzyme and pH-dependent release	[7]
Nano-in-micro capsule	PLGA NPs, HPMCAS	Curcumin, Dexamethasone	pH- dependent release and release by diffusion	This work

References

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