Supporting Information

Production of Functional Spherical Particles with Porous Hollow Structures in Water via Oiling-Out Directional Agglomeration

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1 General information

Table S1. Experimental conditions for the preparation of spherical products by oiling-out directional agglomeration method.

Serial number	m_1 (g)	m_2 (g)	m_3 (g)	m_4 (g)	T_1 (℃)	T_2 (℃)	Stirring speed (rpm)	T_3 (℃)	Drying time (h)
1	50	1.0	0.3	0	65	2	550	40/50	45
2	50	1.0	0.5	0	70	2	550	40/50	45
3	50	1.0	0.5	0	70	2	650	40/50	45
4	50	1.0	0.5	0	70	2	750	40/50	45
5	50	1.0	0.6	0	75	2	550	40/50	45
6	50	1.0	0.7	0	80	2	550	40/50	45
7	50	1.0	0.5	0.1	80	2	550	40/50	45
8	50	1.0	0.5	0.1	80	2	650	40/50	45
9	50	1.0	0.5	0.1	80	2	750	40/50	45
10	50	1.0	0.5	0.1	80	2	850	40/50	45
11	50	1.0	0.5	0.1	80	2	950	40/50	45

m_1, m_2, m_3 and m_4 represent the masses of water, L-menthol, indomethacin and nifedipine respectively during the preparation.

T_1 and T_2 indicate the heating and quenching temperatures respectively. T_3 denotes the temperature required for drying and in this study both the first stage of 40 °C and then the second stage of 50 °C process was used.

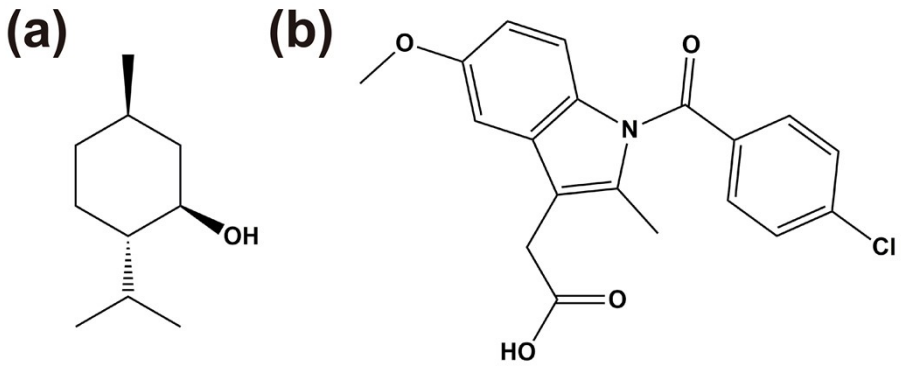

Fig. S1. Chemical structures of L-menthol (a) and indomethacin (b).

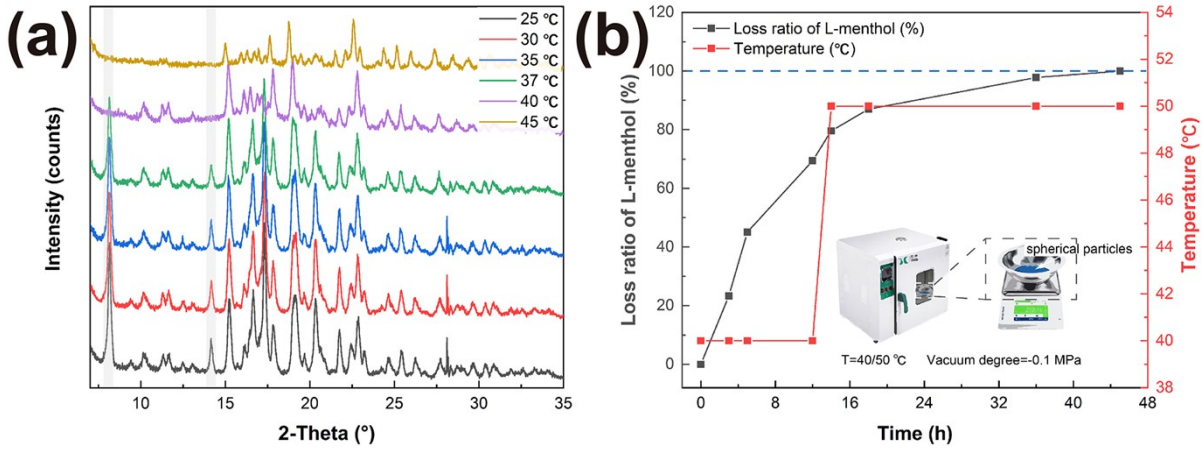

Fig. S2. (a) In situ Powder X-ray Diffraction results of spherical co-agglomerates at different temperatures. (b) The variation curve of loss ratio of L-menthol in spherical co-agglomerates with time at different temperature.

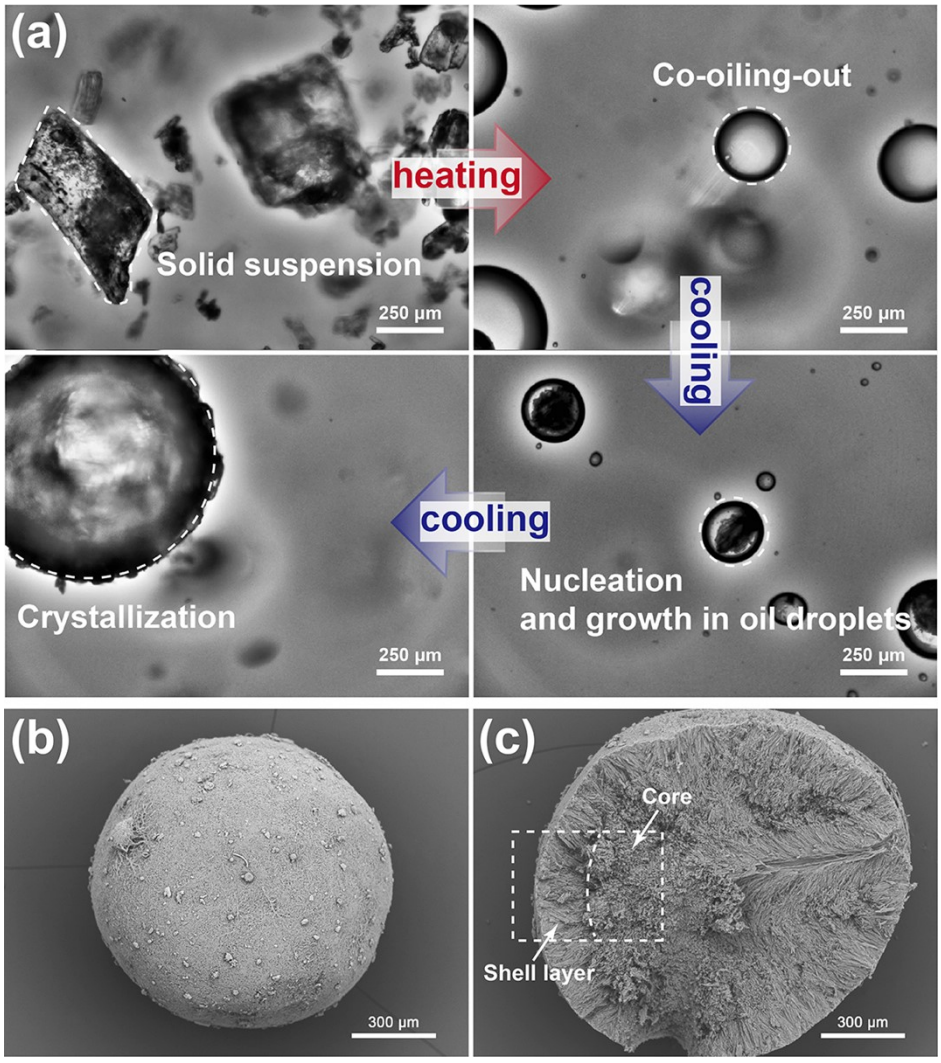

Fig. S3. (a) *In-situ* microscope images recorded during the oiling-out directional agglomeration process. Scanning electron microscopy images of the outside morphology (b) and cross section (c) of the spherical co-agglomerates.

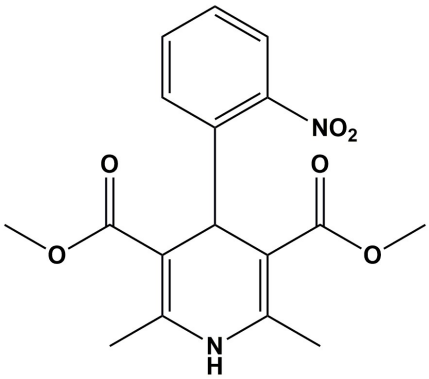

Fig. S4. Chemical structures of nifedipine.

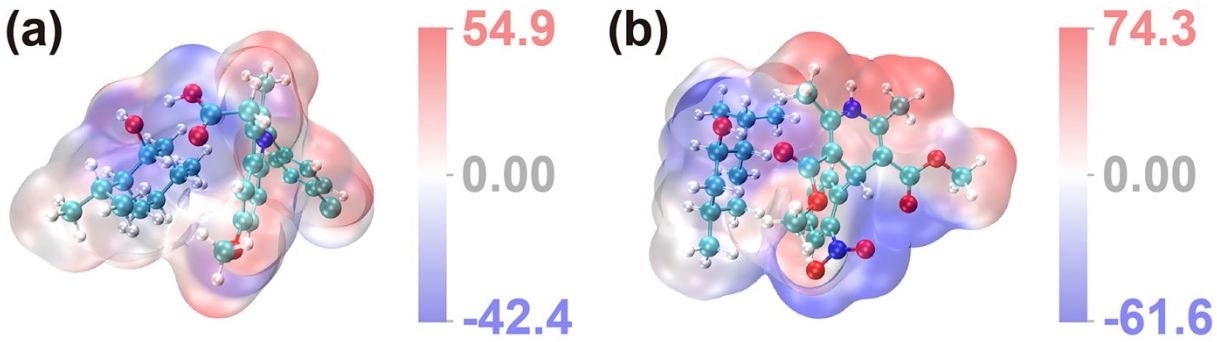

Fig. S5. Results of molecular electrostatic potential surface simulations for the dimeric configurations (most stable in water) of L-menthol-indomethacin (a) and L-menthol-nifedipine (b).

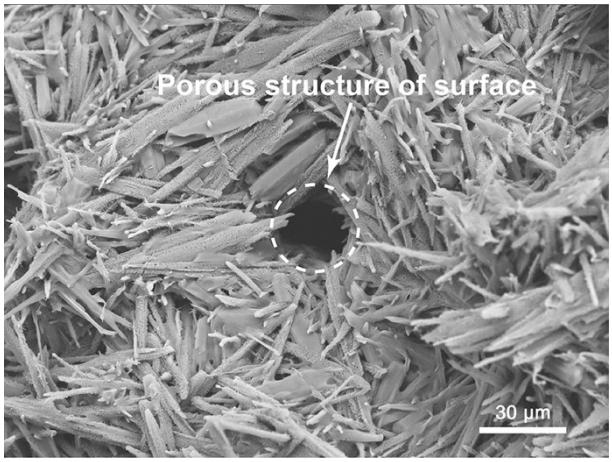

Fig. S6. Scanning electron microscopy image of composite particle surface.

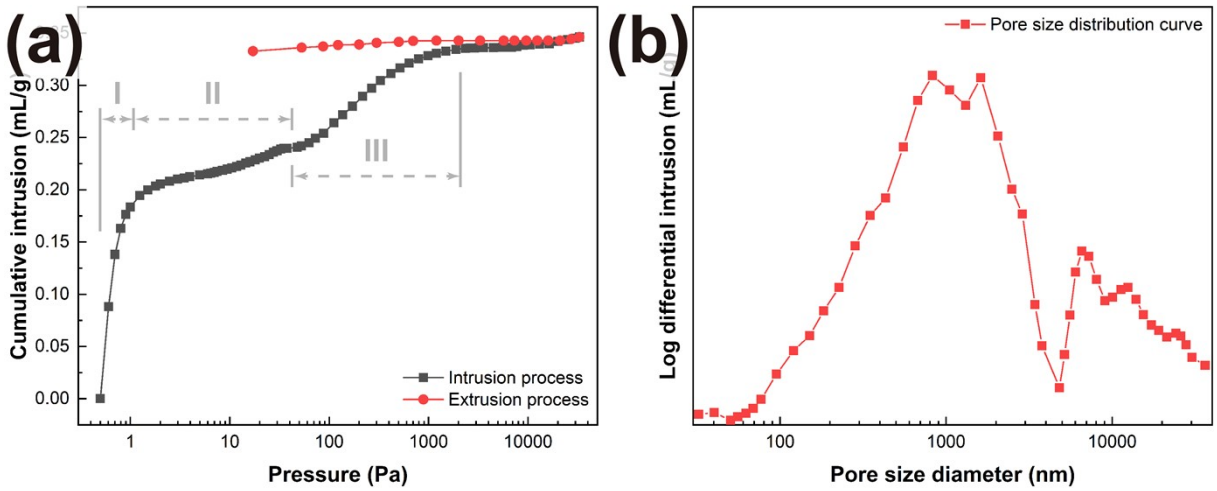

Fig. S7. (a) Mercury intrusion and extrusion curves. (b) Pore size distribution results.

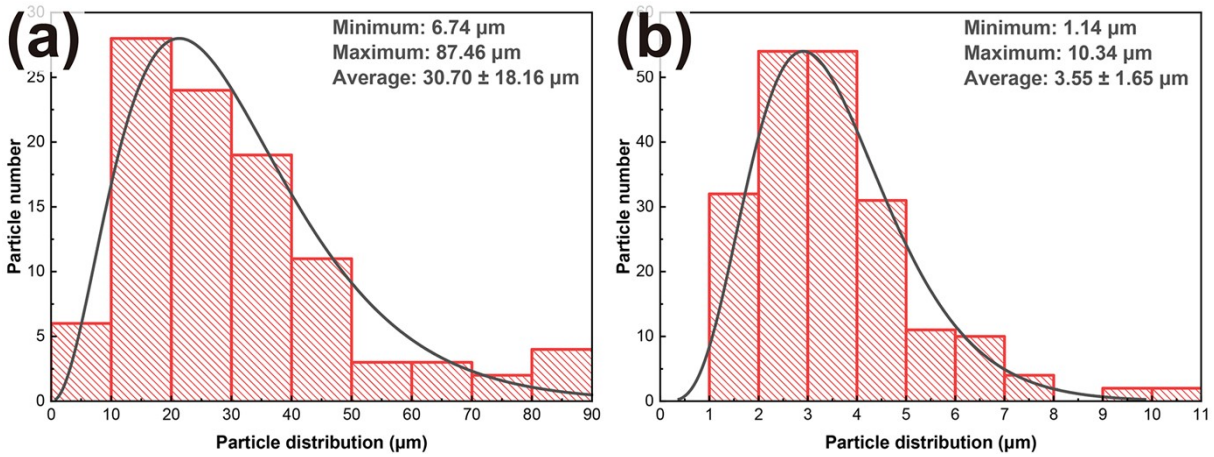

Fig. S8. Particle size distribution results of shell layer (a) and core (b) of composite particles.

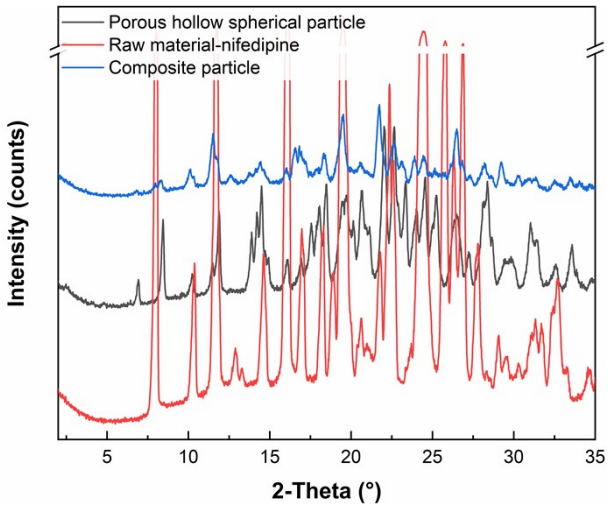

Fig. S9. Powder X-ray Diffraction results of composite particles.

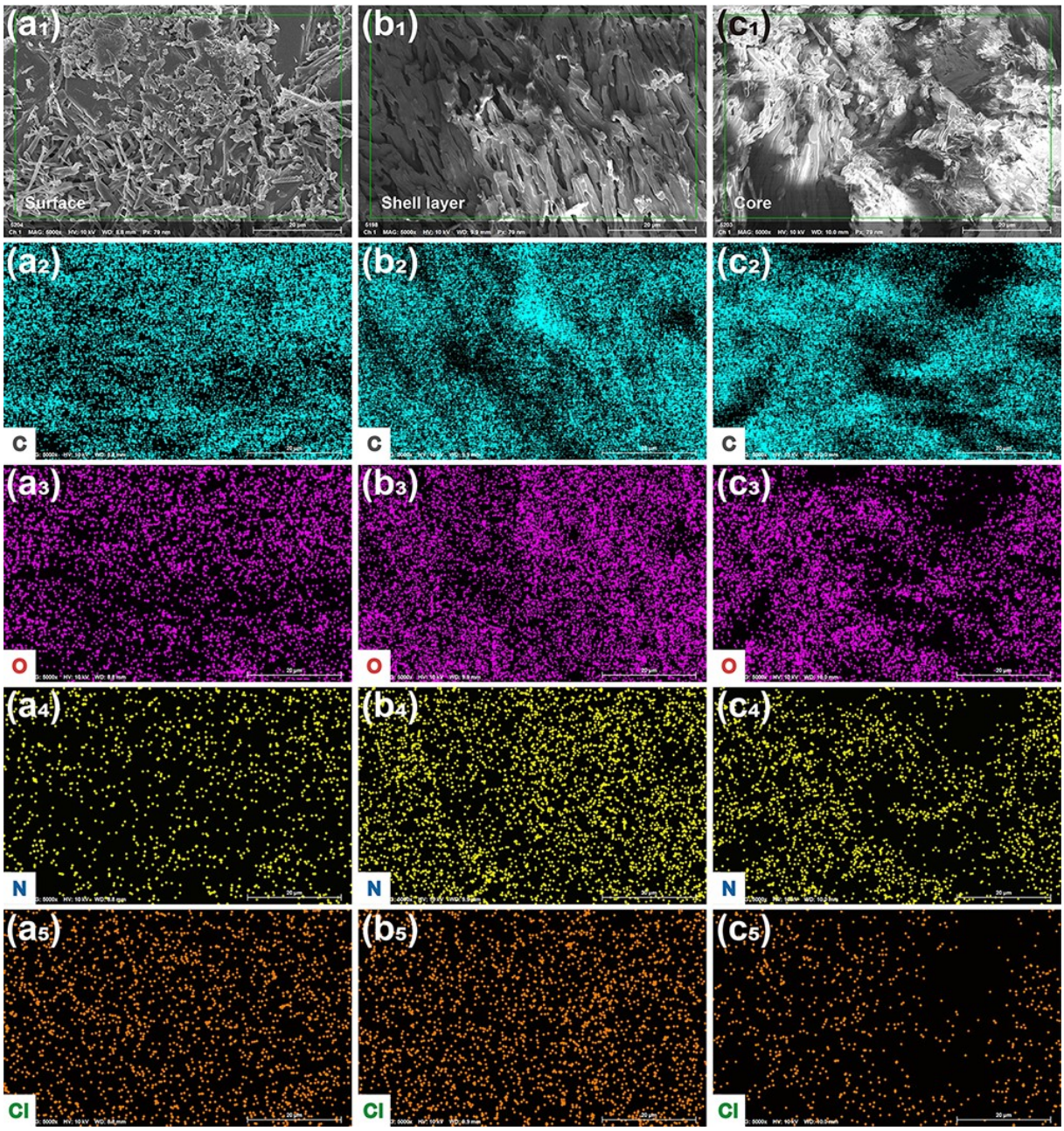

Fig. S10. Distribution of carbon, oxygen, nitrogen and chlorine elements at the surface (a), shell layer (b) and core (c) of composite particles.

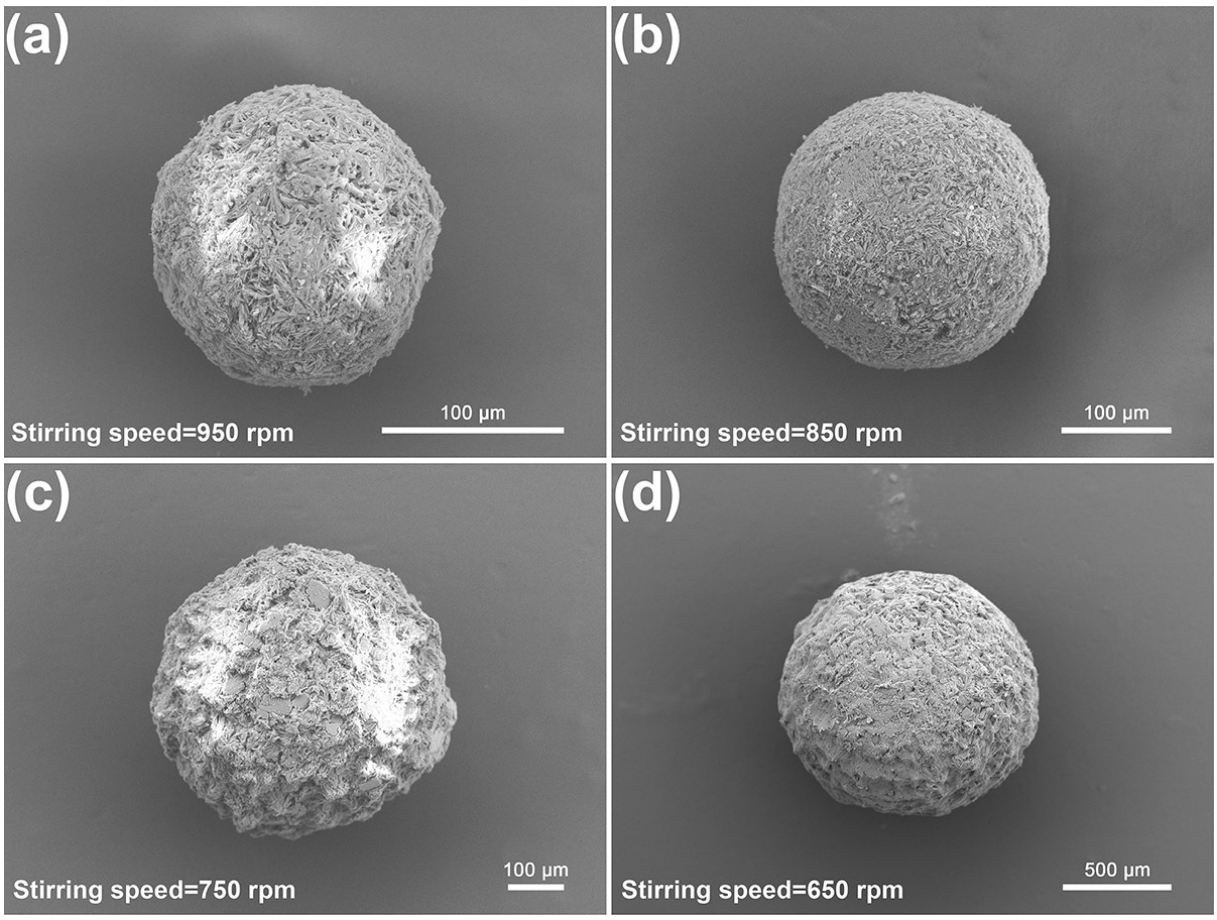

Fig. S11. Scanning electron microscopy images of composite particles at different stirring speeds. (a) 950 rpm. (b) 850 rpm. (c) 750 rpm. (d) 650 rpm.

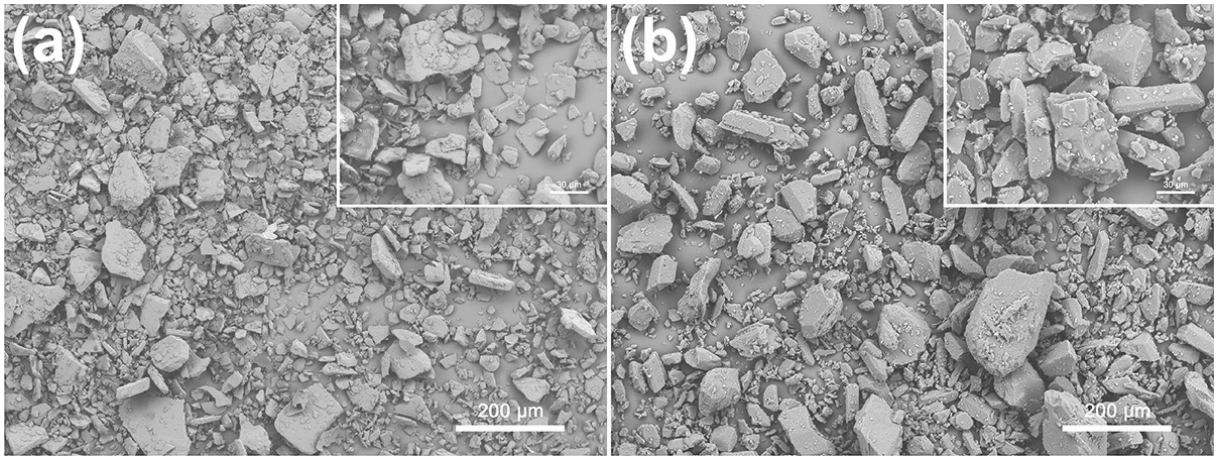

Fig. S12. Scanning electron microscopy images of commercial raw materials for indomethacin (a) and nifedipine (b).

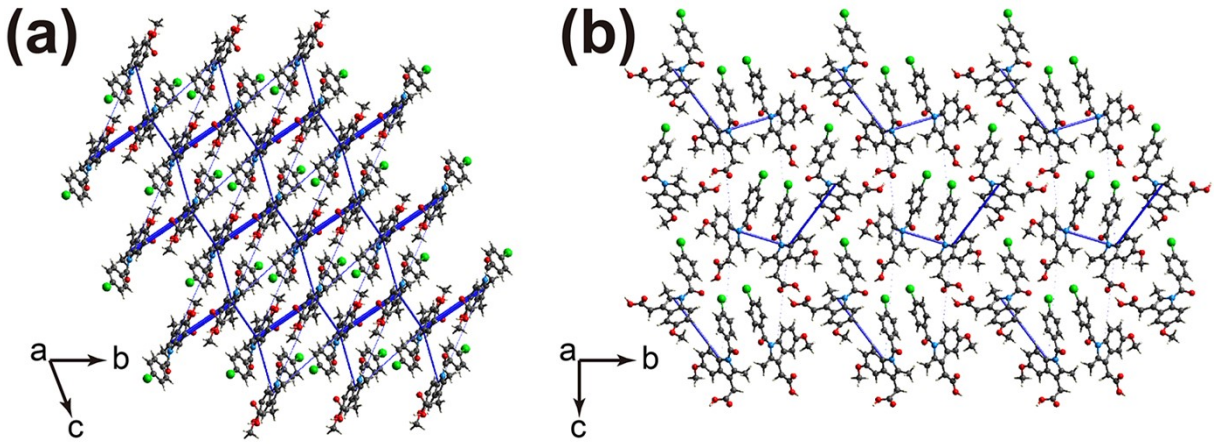

Fig. S13. Schematic diagram of the energy frameworks of indomethacin. (a) γ from. (b) α form. Molecular packing structure viewed along the a-axis.

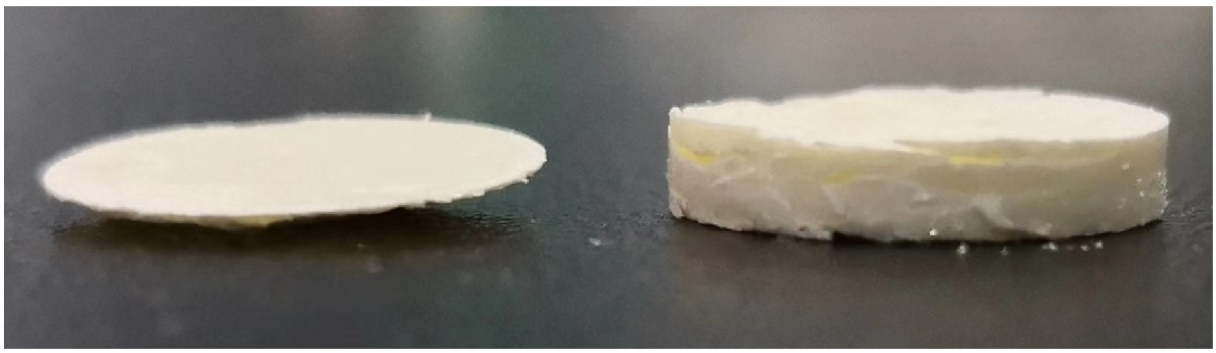

Fig. S14. The appearance of the tablet after the capping has occurred (the missing part above the tablet is shown on the left.).

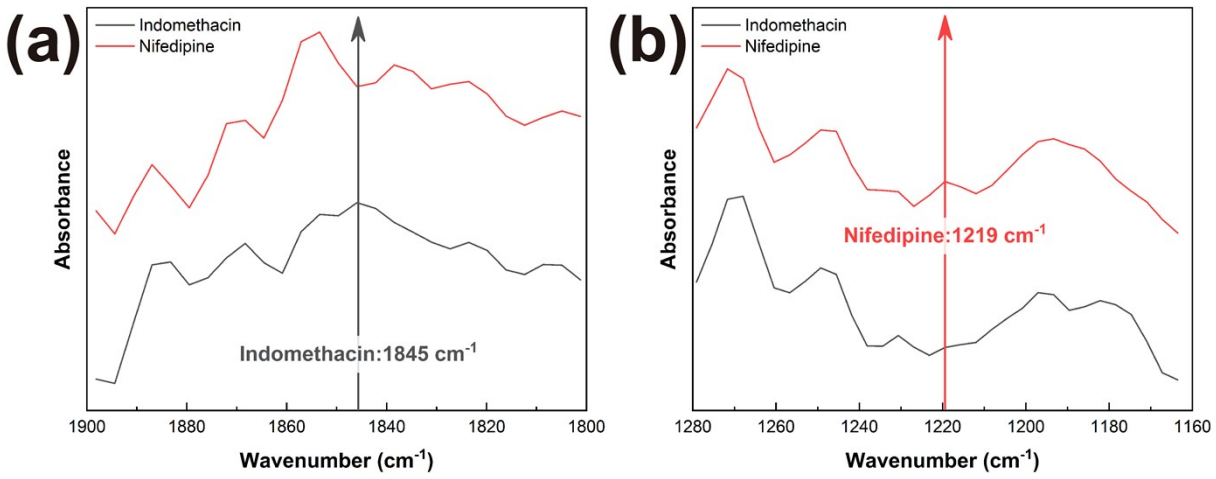

Fig. S15. Solvent-background-subtracted spectra of indomethacin and nifedipine in aqueous solution of ethanol. (a) 1800 cm^{-1}-1900 cm^{-1}. (a) 1160 cm^{-1}-1280 cm^{-1}.

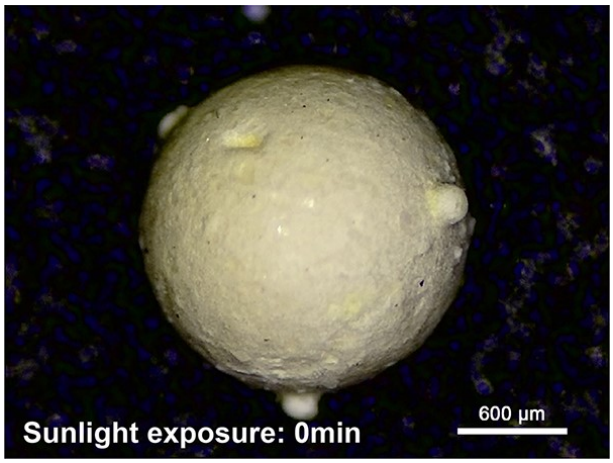

Fig. S16. Stereoscopic microscope photos of composite particles.