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Supporting information

Floating tablets from mesoporous silica nanoparticles

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Materials and Methods

Chemicals

Cetyltrimethylammonium bromide (CTAB), tetraethylorthosilicate (TEOS), Tween 80, curcumin, captopril were purchased from Sigma-Aldrich. Hydroxypropyl methylcellulose (HPMC K100M) from Dow Chemical Co. Sodium bicarbonate (Merck chemicals), zinc stearate from (Dow Chemical Co). Reagent grade sodium hydroxide (NaOH) and hydrochloric acid (HCl) were received from ChemSupply pty Ltd. Methanol was purchased from RCl labsacan Ltd.

Preparation of MCM-41 particles

MCM-41 material was synthesized using the method reported by Yang et al., with slight modifications.[1] In a typical synthesis, 1.0 g of CTAB was dissolved in 480 g of deionized water with 3.5 ml of NaOH (2 M) under stirring at 80˚C. Then, 6.7 ml of TEOS was added into the mixture and kept under continuous stirring for an additional 2 h. The resultant product was collected by filtration and dried at room temperature. The surfactant templates were removed by calcination at 550˚C for 5 h.

The procedure for step wise pore size reduction of MCM-41 was followed according to literature.[2] MCM-41 material (0.8 g) was held on the porous disc and TEOS was placed in the bottom chamber. The VVD apparatus is placed in the vacuum oven (175 Torr) at 60˚C for 24 h. TEOS vapour molecules can only pass through the porous disc and the mesoporous silica placed on the top of the disc. The vacuum (175 Torr) helps in continuous contact between mesoporous silica and TEOS vapour generated from the bottom chamber, so that TEOS molecules can be adsorbed on the silica surface. After 24 h of the VVD process, the mesoporous silica materials adsorbed with TEOS was calcined at 550˚C for 5 h.

Curcumin loading

Curcumin was loaded into MCM-41 with two different pore sizes 2.1 and 1.7 nm using Rotavapor technique. To rotavapor flask (RF) containing 80 mg of silica material, 20 mg of curcumin was added followed by addition of 5 ml of methanol. This suspension was sonicated for 2 min in ultrasonic bath and the RF was affixed to the rotavapor assembly and methanol was slowly evaporated at 50˚C. The solvent evaporation procedure was continued for another 30 min to ensure complete solvent removal. The obtained samples were denoted as Cur-MCM-41(1.7nm), Cur-MCM-41(2.1nm).

Captopril loading

The captopril loading was done by wetting impregnation method. Initially 217.29 mg of drug was dissolved in 10 ml of water. To the drug solution 200 mg of MCM-41was added and kept for stirring at room temperature for 24 h. The drug loaded MCM-41 were separated from the solution by filtration and kept in vacuum overnight. The obtained sample was denoted as Cap-MCM-41.

Characterization

TEM images were taken using a JEOL 2100 microscope operated at 200Kv. The samples were prepared by dispersing MCM-41 in ethanol, and then transferred to a copper grid with dropper. SEM images were taken using a JEOL 7800 accelerating voltage operated at 1Kv. SEM samples were prepared by cutting thin cross sectional layer of the tablet and placed on carbon tape mounted on the stage. X-ray diffraction (XRD) patterns were recorded on a German Bruker D8 X-ray diffractometer with Ni-filtered Co Kα radiation (λ=1.79 A). The XRD patterns were obtained at 40 kV and 30 mA with a step size of 0.01˚. Nitrogen adsorption-desorption isotherms were measured at -196˚C by using a Micromeritics Tristar II 3020 system. The drug loaded samples were degassed at 50˚C overnight on a vacuum line and pure MCM-41 is degassed at 180˚C for 6 h. The Brunauer-Emmett-Teller (BET) method was utilized to calculate the specific surface area. The pore size distribution curves were derived from the adsorption branches of the isotherms using the Barrett-Joyner-Halanda (BJH) method. The total pore volume was calculated from the amount adsorbed at a maximum relative pressure (P/P_0). Thermogravimetric analysis (TGA) and Differential Scanning Calorimetry (DSC) measurements were performed by TGA/DSC Thermogravimetric Analyser (Mettler-Toledo Inc) with a heating rate of 2˚C /min in air flow. Erweka hardness tester was used to measure the hardness of the tablet.

Preparation of floating tablets without and with curcumin

The floating tablets were prepared by a direct compression method. Weights of each ingredient were taken according to Table S2, Table S3 for each formulation. Micro-crystalline cellulose (MCC, bulking agent) was added in order to maintain the same weight of each tablet in different formulations. All the ingredients were mixed homogeneously with mortar and pestle for 10 min. Zinc stearate (a lubricant) was added at last to the mixed powders and then mixed further for 3 min. Finally, the powder was fed manually into die with spatula of a single punch tablet punching machine, equipped with concave punches (10 mm diameter). The hardness of the tablets is adjusted to 50 N by using Erweka hardness tester.

Preparation of captopril tablets

The floating tablets were prepared by direct compression method. Weights of each ingredient are taken according to Table S4, for each formulation and mixed homogeneously with mortar and pestle for 10 min. Zinc stearate was added to the final mixed power and mixed for additional 3 mins. Finally, the powder was fed manually into die with spatula of a single punch tablet punching machine, equipped with concave punches (10 mm diameter). The hardness of the tablets is adjusted to 50 N by using Erweka hardness tester.

Determination of MSNs content in the tablet

The amount of silica content in tablet after floating for 12 h in dissolution medium was determined. The floating tablet F0 to FD was used in this test. F0 was prepared without silica nanoparticles. After 12 h, the water content was removed by freeze drying overnight. The obtained dry tablet was kept in furnace at 500˚C for 5 h. The decomposition of all the ingredients except silica was below 500˚C (Melting point of HPMC

K100M-260˚C, Sodium bicarbonate-50˚C, zinc stearate-120-130˚C, Silica-1600-1725˚C). This was confirmed by the control formulation F0. Thus the weight after thermal treatment is attributed to the silica retained in the tablet after floating test.

Dissolution studies for curcumin

The dissolution test was performed in rosette rise apparatus for maintaining sink condition as reported by Gohel et al.[3,4] The tablet was placed in a beaker (100 ml) modified at the base with inverted v shaped glass tube, containing 70 ml of HCl (0.1M) containing 0.8% tween 80, maintaining at 37˚C, stirred at 50 rpm. The burette was mounted on the top of the beaker to deliver the dissolution medium at a flow rate of 2 ml/min. At the same time 2 ml of medium was drained out of the beaker. At regular time interval 1 ml of sample was collected from the beaker and replaced with the same volume of fresh medium. Collected samples were filtered through 0.2 µm membrane filter and analysed spectrophometrically at 424 nm.

Dissolution studies for captopril

The dissolution test was performed in 200 ml of HCl (0.1M), maintaining at 37˚C, stirred at 50 rpm.[5] At regular time interval 2 ml of sample was collected and replaced with the same volume of fresh medium. Collected samples were filtered through 0.2 µm membrane filter and analysed spectrophometrically at 216 nm.

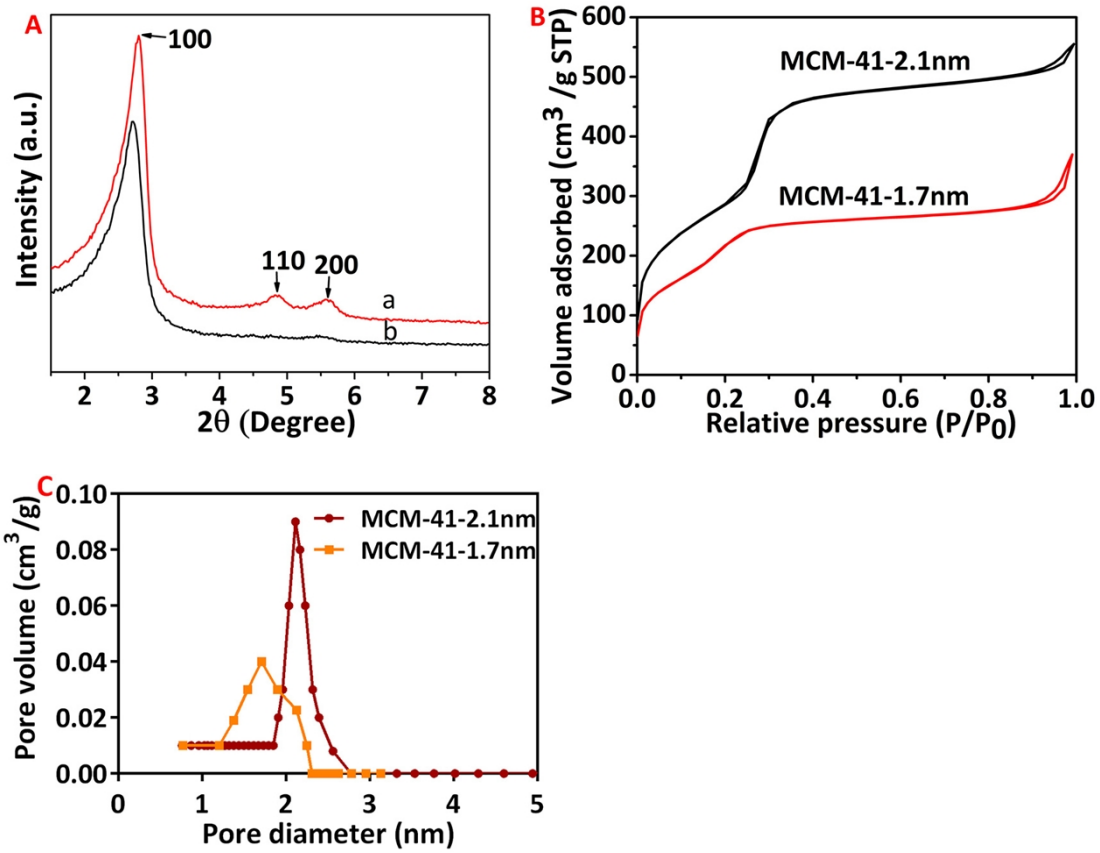


Figure S1. XRD patterns (A) of a) Calcined MCM-41 with 2.1 nm b) Calcined MCM-41 subjected to VVD process with 1.7 nm, N_2 adsorption-desorption isotherms (B) of calcined MCM-41 and MCM-41 subjected to VVD cycle and BJH pore size distribution plots (C) of calcined MCM-41 and MCM-41 subjected to VVD cycle.

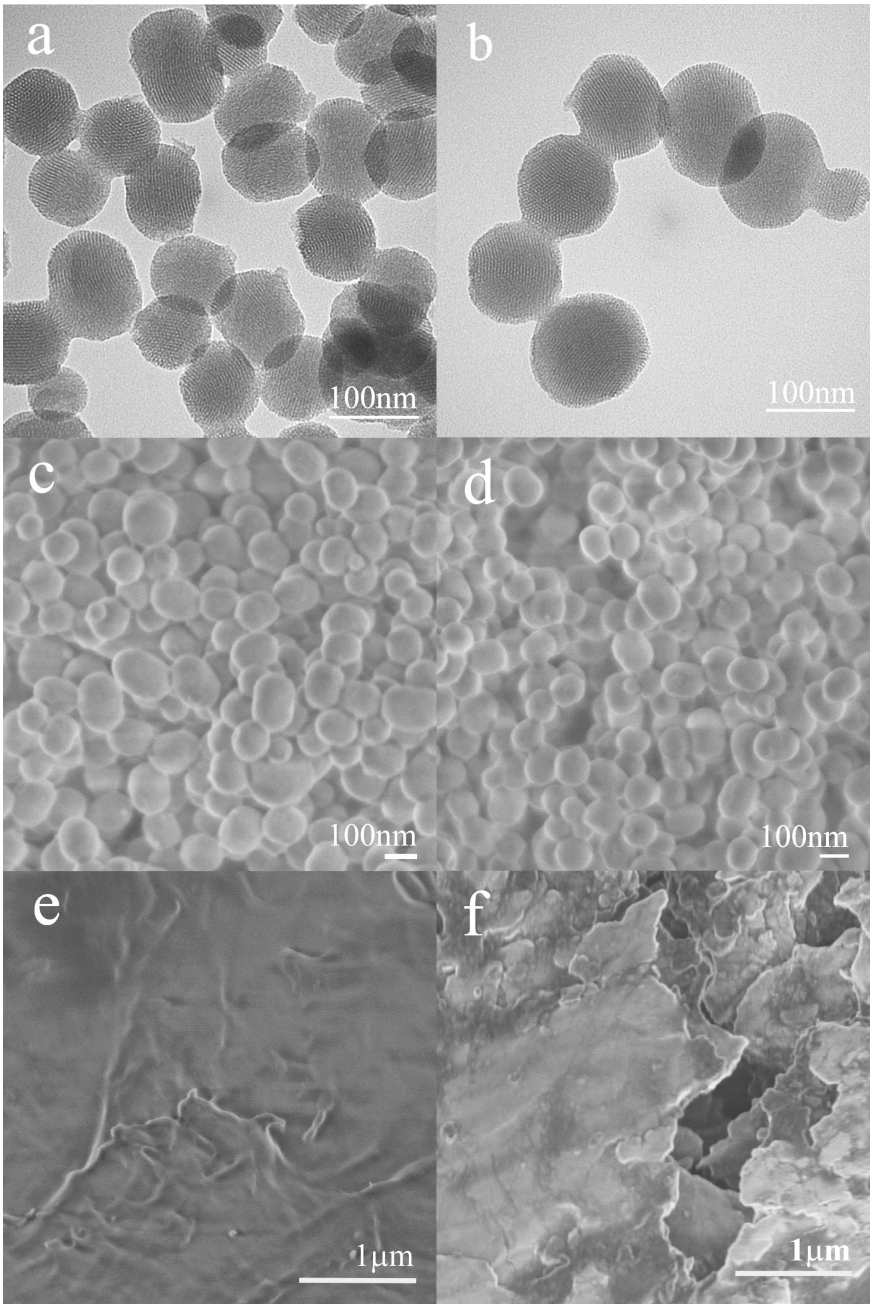
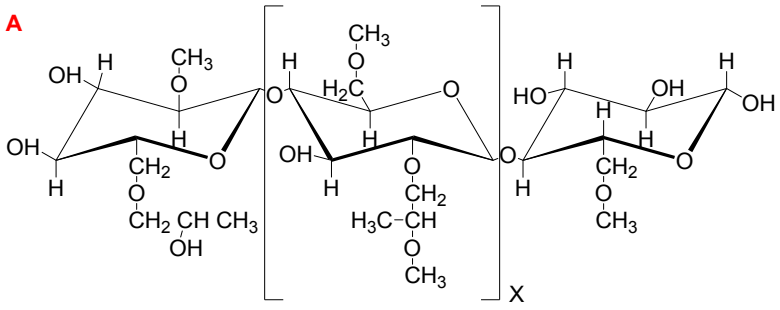


Figure S2. Transmission electron microscope (TEM) image (a) of MCM-41(1.7nm), (b) MCM-41 (2.1nm); Field-emission scanning electron microscope (FE-SEM) image (c) of MCM-41(1.7nm), (d) MCM-41 (2.1nm), (e) HPMC K100M, (f) Cross-section image conventional floating subjected to 12 h of dissolution study.



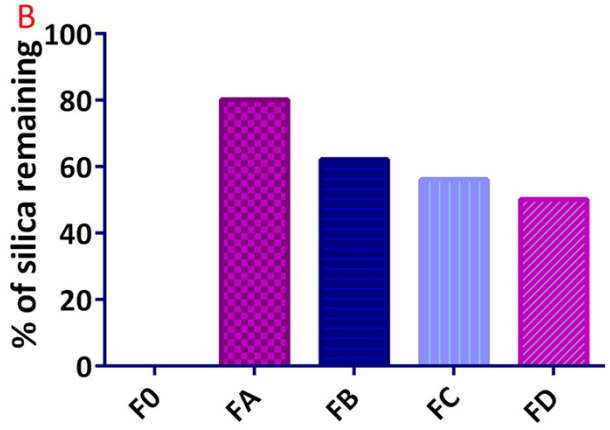


Figure S3. A) The chemical structure of HPMC polymer. B) The amount of MSNs remained in floating dosage form after 12 h of dissolution study analysed by TGA.

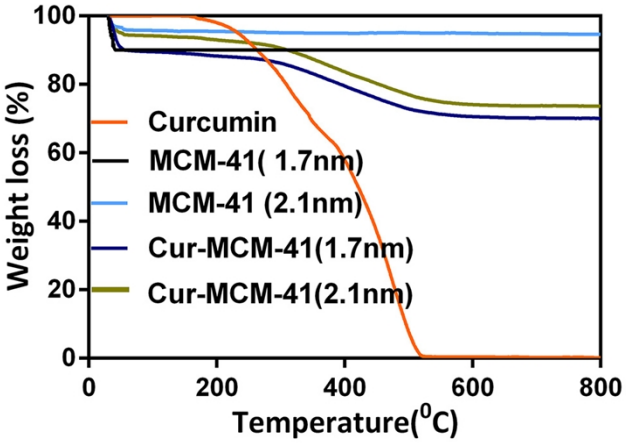


Figure S4. TGA of Curcumin, MCM-41, Cur-MCM-41(1.7nm), Cur-MCM-41(2.1nm)

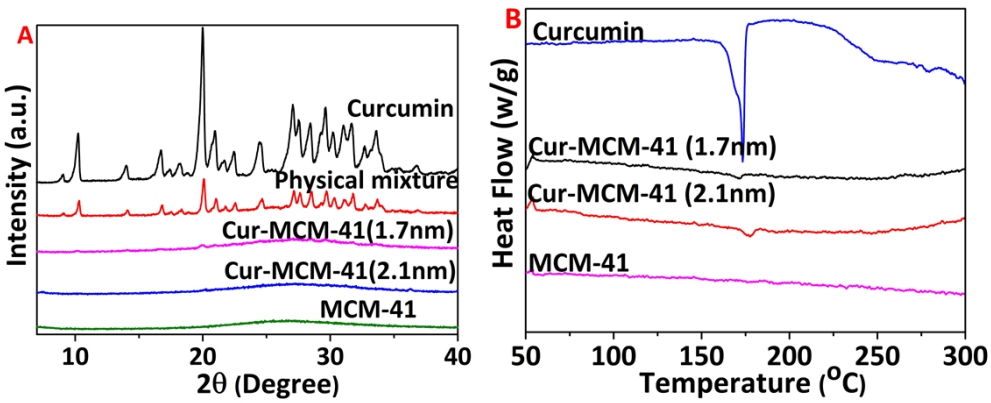


Figure S5. (A) XRD pattern of Curcumin, physical mixture of curcumin and MCM-41, Cur- MCM-41 (1.7nm), Cur-MCM-41 (2.1nm) and MCM-41, and (B) Differential Scanning Calorimetry of Curcumin, Cur-MCM-41 (1.7nm), Cur-MCM-41 (2.1nm) and MCM-41.

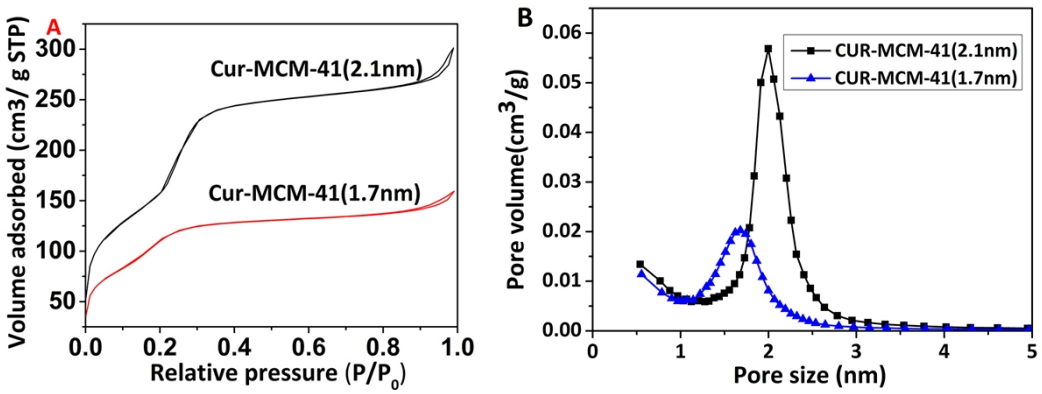


Figure S6. (A) Nitrogen adsorption-desorption isotherms of Cur- MCM-41(1.7nm), Cur-MCM-41(2.1nm) and (B) pore size distribution plot of Cur- MCM-41(1.7nm), Cur-MCM-41(2.1nm).

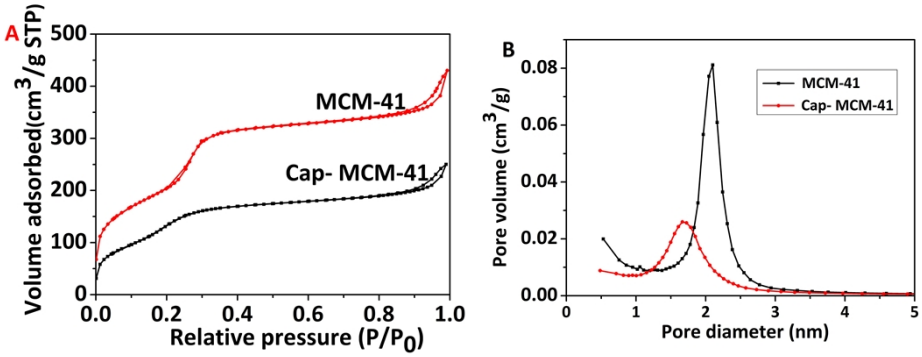


Figure S7. (A) Nitrogen adsorption-desorption isotherms of MCM-41, Cap- MCM-41 and (B) pore size distribution plot of MCM-41, Cap-MCM-41.

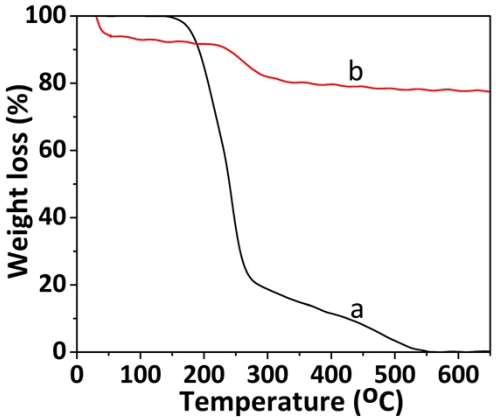


Figure S8. TGA analysis of a) Captopril, b) Cap-MCM-41.

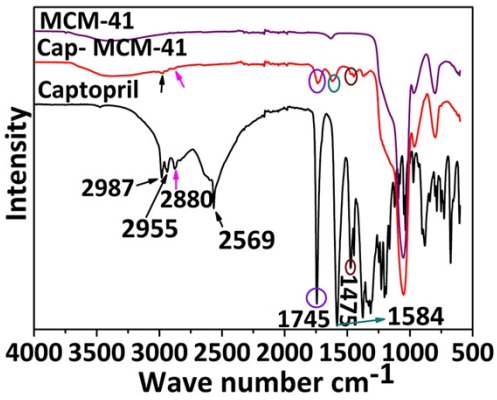


Figure S9. FTIR spectra of MCM-41, Captopril, Cap-MCM-41.

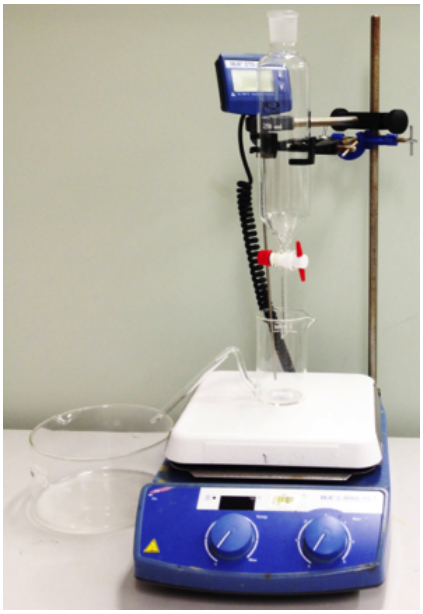


Figure S10. A scheme showing the home-made Rosette rise apparatus.

Table S1. Physicochemical properties of MCM41 (1.7nm), Cur- MCM-41-1.7nm, MCM-41(2.1nm), Cur-MCM-41-2.1nm, MCM-41, Cap- MCM-41

Sample	Surface area (m^2/g)	Pore volume (cm^3/g)	Pore size (nm)	Drug loading (% TGA)
MCM41(1.7nm)	806	0.57	1.7	
Cur-MCM-41(1.7nm)	397	0.24	1.7	20
MCM-41(2.1nm)	1333	0.81	2.1	
Cur-MCM-41(2.1nm)	751	0.46	2.1	20.9
MCM-41(2.1)	946	0.66	2.1	
Cap- MCM-41	534	0.38	1.7	16.4

Table S2. The compositions of floating tablets with bare MCM-41

Formulation	MCM-41(mg)	HPMC K100M(mg)	Sodium bicarbonate(mg)	Zinc stearate(mg)	Total weight of tablet(mg)
F0	0	60	33	4.4	97.4
FA	80	60	33	4.4	187.4
FB	120	60	33	4.4	217.4
FC	140	60	33	4.4	237.4
FD	160	60	33	4.4	257.4

Note: MCM-41 with a pore size of 2.1 nm was used.

Table S3. Composition of curcumin floating tablet

Formulation	MCM-41(mg)	Cur-MCM-41(mg)	Curcumin (mg)	HPMC K100M(mg)	Sodium bicarbonate(mg)	MCC (mg)	Zinc stearate(mg)	Total weight of tablet(mg)
F1	0	100	0	60	33	0	4.4	197.4
F2	80	0	20	60	33	0	4.4	197.4
F3	0	0	20	60	33	80	4.4	197.4
F4	0	100	0	60	33	0	4.4	197.4

Note: In F2, F4, MCM-41 with a pore size of 2.1 nm was used. In F1, MCM-41 with a pore size of 1.7 nm was chosen.

Table S4. Composition of captopril floating tablet

Formulation	Cap-MCM-41(mg)	Captopril(mg)	HPMC K100M(mg)	Sodium bicarbonate(mg)	MCC(mg)	Zinc stearate(mg)	Total weight of tablet(mg)
F5	92	0	60	33	0	4.4	189.4
F6	0	15	60	33	77	4.4	189.4

Note: MCM-41 with a pore size of 2.1 nm was used.

References:

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