Supporting Information for:

Influence of the Structural and Textural Properties of Ordered Mesoporous Materials and Hierarchical Zeolitic Supports on the Controlled Release of Methylprednisolone Hemisuccinate

R. A. García-Muñoz [a,*], V. Morales [a], M. Linares [a], P. E. González [a], R. Sanz [a], D. P. Serrano [a,b]

[a] Chemical and Environmental Engineering Group, ESCET, Rey Juan Carlos University, c/ Tulipán s/n, 28933 Mostoles, Madrid, Spain. [b] IMDEA Energy Institute, Avda. Ramón de la Sagra, 3, Parque Tecnológico de Móstoles, 28935 Móstoles, Madrid, Spain.

Materials synthesis S1

Preparation of MCM-41

The synthesis of MCM-41 material was accomplished by using the method described by Lin and coworkers [17], in which CTAB (2.53 g), dimethylamine DMA (7.83 g) and H_2O (95.3 g) were stirred in a beaker at room temperature until complete dissolution. To the transparent resultant solution, TEOS (9.84 g) is added by dropping and the resultant gel is stirred for 4 hours at room temperature. The starting molar composition was 0.13 CTABr : 1.0 TEOS : 3.7 DMA : 112.5 H_2O. Afterwards the mixture is transferred to an autoclave to be aged. The ageing step of the gel comprises static conditions, 110 ºC and autogenous pressure conditions for 48-72 hours. The resultant materials were then recovered by filtration and air dried. The template was removed by calcination at 550 ºC for 5 hours, with a heating rate of 1.8 ºC/min from room temperature.

Preparation of SBA-15

The synthesis of SBA-15 material was accomplished by using the method described by Zhao and coworkers. [18] In a typical synthesis 8 g of block copolymer surfactant Pluronic 123 was dissolved at room temperature under stirring in 250 mL of 1.9 M HCl. The solution was heated up to 40 ºC and 17.8 g of TEOS was added to the solution. The starting molar composition was 0.016 P123 : 1.0 TEOS : 5.6 HCl : 163.3 H_2O. The resultant mixture was then stirred at 40 ºC for 20 h and hydrothermally aged at 110 ºC for 24 hours. The template was removed by calcination at 550 ºC for 5 hours, with a heating rate of 1.8 ºC/min from room temperature.

Preparation of pore expanded SBA-15

The synthesis of pore expanded SBA-15 material was accomplished by using the method described by Kruk and coworkers. [19] A typical synthesis procedure was as follows: 2.4 g of P123 and 0.027 g of NH_4F were dissolved in 84.0 mL of 1.30 M aqueous HCl solution at room temperature. Subsequently, the solution was transferred to a water bath (nominal temperature accuracy of 0.01 °C) set at a temperature of 15.00 °C; after at least 1 h, a mixture of 5.5 mL TEOS and 1.2 mL (1.0 g) of Triisopropylbenzene (TIPB) was added. The solution was stirred for 24 h at the selected initial temperature in an open container using a mechanical stirrer. The starting molar composition was 0.012 P123 : 1.0 TEOS : 0.020 NH_4F : 3.0 HCl : 0.13 TIPB: 129.6 H_2O. Then, the product was heated at 100 °C in a closed container for 48 h. As synthesized material was isolated by filtering, washing with water and drying at ~60 °C in a vacuum oven. Finally, the sample was calcined under air at 550 °C for 5 h (heating ramp 2 °C/min).

Preparation of SBA-16

The synthesis of SBA-16 material was accomplished by using the method described by Kim and coworkers, [20] using poly-(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) triblock F127 copolymer as supramolecular template. Briefly, an aqueous solution of copolymer was prepared by dissolving in a solution of hydrochloric acid in distilled water. TEOS was then added with magnetic stirring at 35 ºC. The starting molar composition was 0.0040 F127 : 1.0 TEOS : 4.0 HCl : 130 H_2O. The mixture was magnetically stirred for about 15 min until TEOS was completely dissolved. The mixture was placed in an oven for 24 h under static condition at 35 ºC for precipitation of the product. The mixture was further maintained at 100 ºC for hydrothermal treatment, during 1 day. The white solid precipitate was isolated by filtration without washing and dried at 100 ºC. Subsequently, the product was calcined under air at 550 ºC after washing with ethanol in order to remove the copolymer template.

Preparation of FDU-12

The synthesis of FDU-12 material was accomplished by using the method described by Kruk and coworkers. [21] Pluronic F127 copolymer (3 g) was placed in a polypropylene (PP) bottle and 185 mL of 1.97 M HCl was added. The mixture in an open PP bottle was placed in a water bath set to 15 °C and stirred using a mechanical stirrer. Then, 4.2 mL (3.6 g) of 1,3,5-trimethylbenzene (TMB) and 15.0 g of KCl were introduced. After 2 h of constant stirring, 13.3 mL (12.5 g) of TEOS was added and the mixture was stirred for a day in an open container at 15.00 °C. The molar proportions in the synthesis mixture were: 0.0037 F127 : 1.0 TEOS : 0.5 TMB : 3.36 KCl : 6.1 HCl:165.0 H_2O. Afterwards, the PP bottle with the reaction mixture was closed and was placed in an oven at 100 °C for 1 day. As-synthesized material was subjected to an additional hydrothermal treatment in an acid solution. For this procedure, 0.5 g of the as-synthesized sample was placed in 30 mL of 1.97 M HCl solution and heated at 110 °C (in a PP bottle) for 2 days. The resulting samples were filtered and dried. The as-synthesized materials were calcined under flowing air at 550 °C for 5 h with heating ramp of 2 °C/ min.

Preparation of hierarchical ZSM-5 zeolite

The synthesis of hierarchical ZSM-5 material was accomplished by using the method described by Serrano and coworkers. [22] Hierarchical ZSM-5 zeolite was prepared, using tetrapropylammonium hydroxide (TPAOH) as structure directing agent (SDA), from a solution having the molar composition: Al_2O_3 : 60 SiO_2 : 11 TPAOH : 1500 H_2O. The precursor solution was precrystallized in a round bottom flask equipped with a condenser under stirring at 90 ºC for 20 h. Thereafter, the corresponding amount of phenylaminopropyl-trimethoxysilane (PHAPTMS) was added to the solution, being kept under reflux and stirring at 90ºC for 6 h. Hierarchical ZSM-5 sample (h-ZSM-5) was prepared by adding the organosilane to the precrystallized solution in proportions of 12 mol % related to the total silica content of the gel. The final crystallization of the functionalized protozeolitic units was carried out in Teflon-lined autoclave at 170ºC for 7 days. The solid products obtained from the synthesis were separated by centrifugation, washed out with distilled water, dried overnight at 110 ºC and calcined in a stream of air at 550 ºC for 5 h. A reference ZSM-5 sample (ZSM-5) was synthesized using the same procedure without the silanization step.

Preparation of hierarchical Beta zeolite

Beta zeolite sample was prepared from a solution with the following molar composition: Al_2O_3:60 SiO_2:15.5 TEAOH: 1000 H_2O.[23] Fumed silica, tetraethylammonium hydroxide, aluminium flakes and distilled water were used as starting materials. The precursor solution was precrystallized in a teflon-lined stainless steel autoclave under autogenous pressure at 135 ºC for 3 days under static conditions. The solid so obtained was mixed with an aqueous solution containing the organosilane and TEAOH (13% w/w) ($TEAOH/SiO_2$ = 0.5). Phenylaminopropyltrimethoxysilane (PHAPTMS) was employed as seed silanization agent.[24] The hierarchical sample was prepared by adding the organosilane to the precrystallized solution in a proportion of 8 mol % with respect to the total silica content in the gel (h-Beta). The resulting mixture was kept in a reflux system under stirring (100 rpm) at 90 ºC for 6 h. Thereafter, the crystallization of the functionalized seeds was carried out in a stainless steel reactor under autogenous pressure at 135 ºC for 7 days under static conditions. The solid products obtained were separated by centrifugation, washed several times with distilled water, dried overnight at 110 ºC and calcined in air at 550 ºC for 5 h.

For comparison purposes, a reference zeolite sample was synthesised following the same procedure but omitting the precrystallization and silanization steps (Beta).

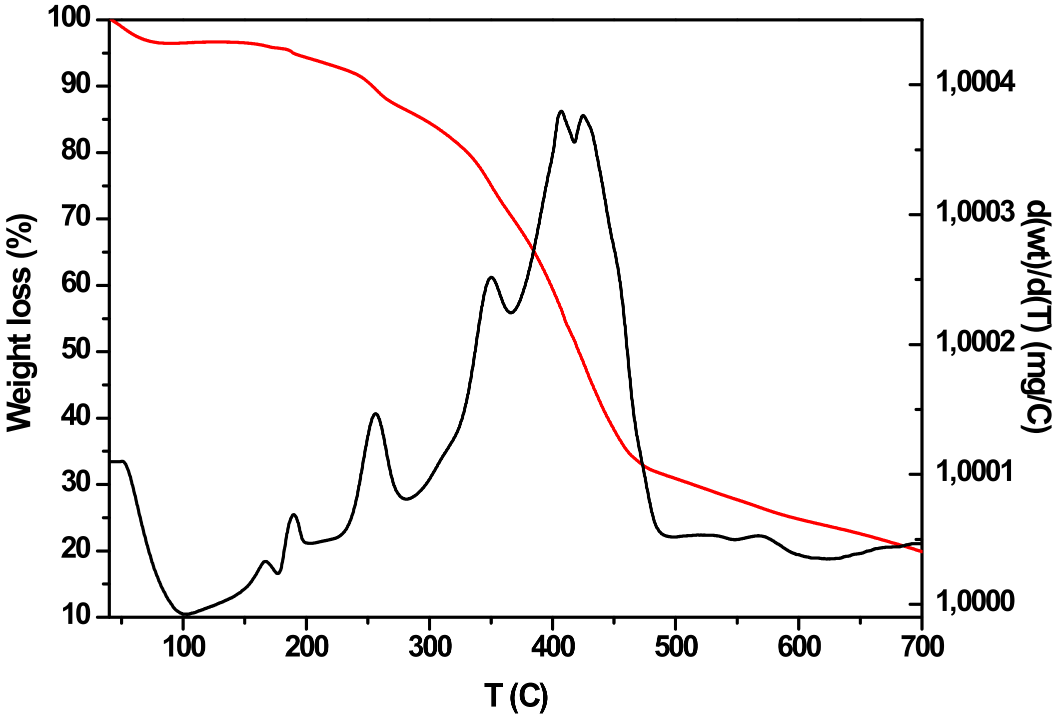

Figure S1: Pure methylprednisolone hemisuccinate thermogravimetric analysis (TGA).

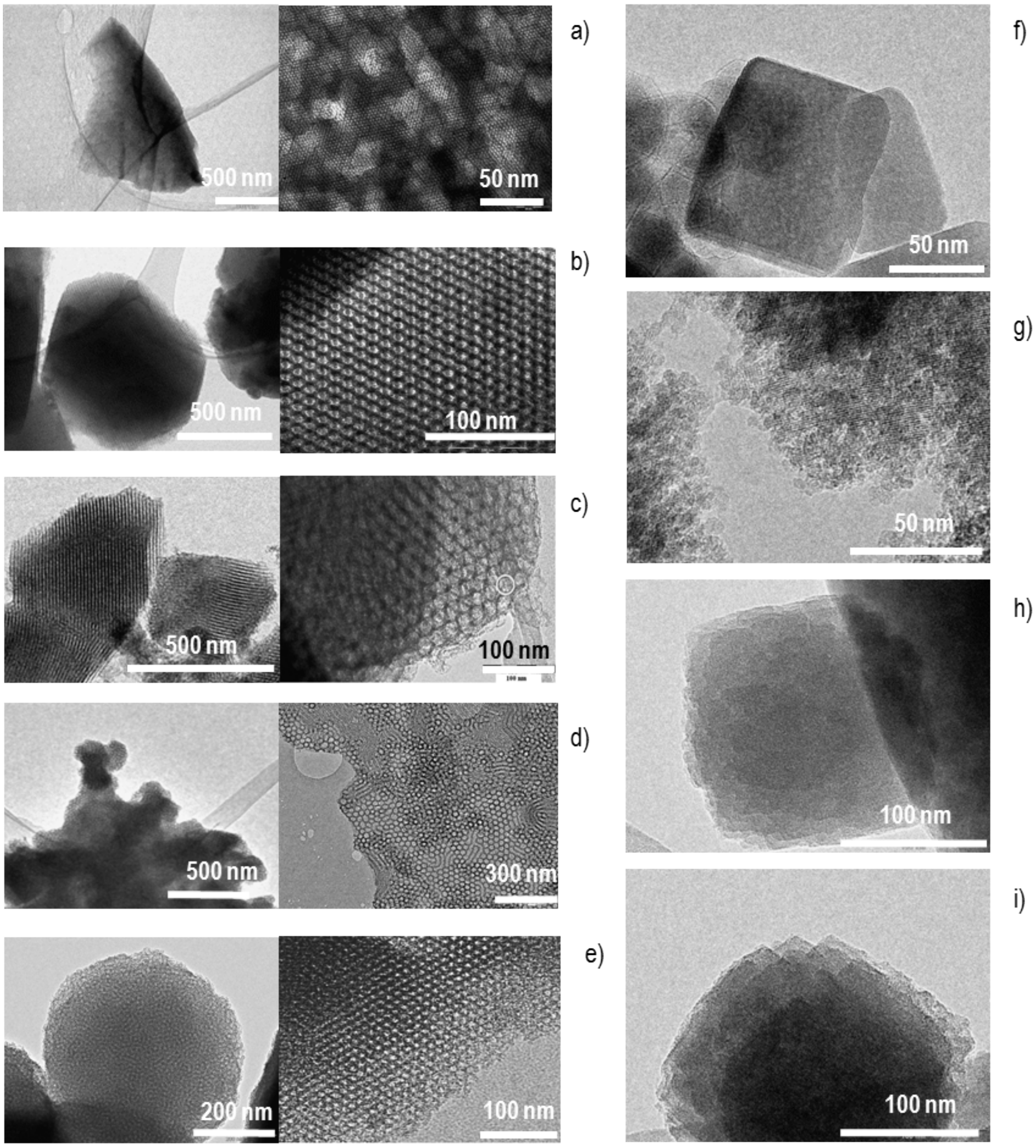

Figure S2: TEM images of mesoporous materials: a) MCM-41; b) SBA-15; c) SBA-EXP; d) FDU-12 and e) SBA-16), and zeolitic materials: f) ZSM-5; g) h-ZSM-5; h) Beta and i) h-Beta).

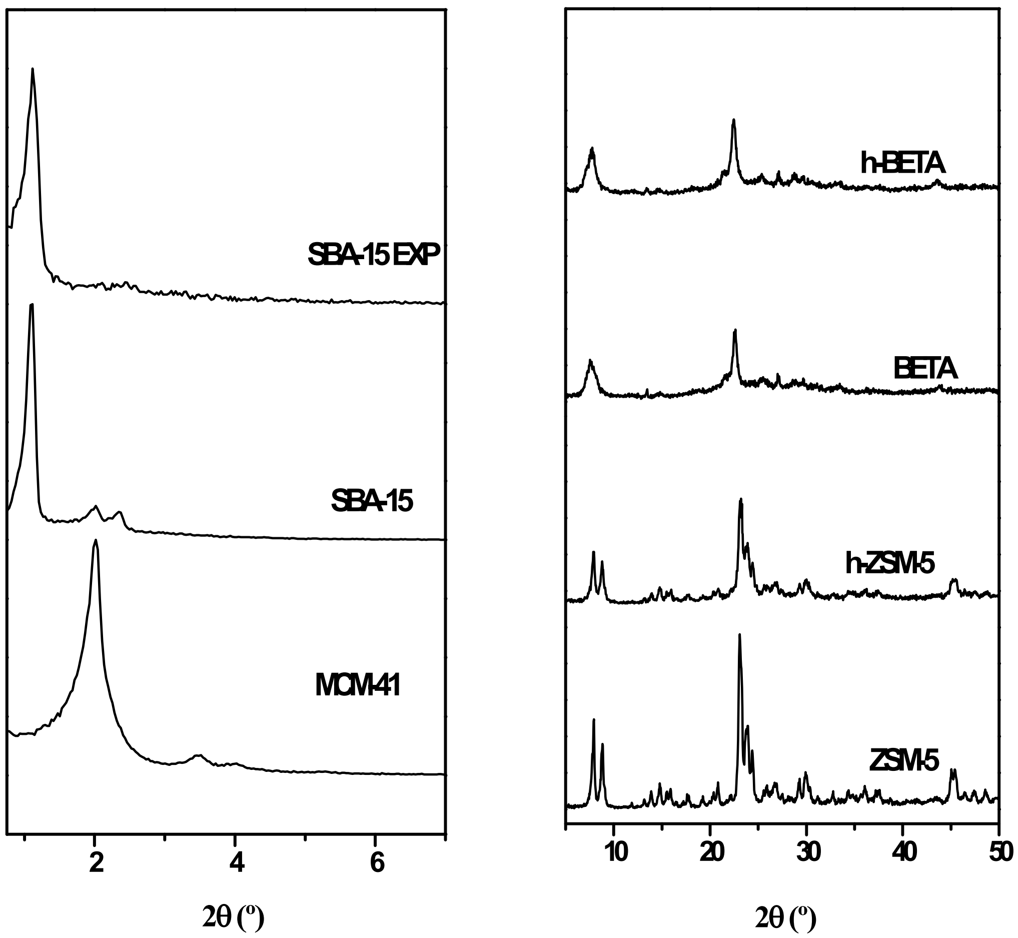

Figure S3: XRD patterns at low-angle region of mesoporous materials (MCM-41, SBA-15, SBA-15 EXP), and XRD patterns at wide-angle region of zeolitic materials (ZSM-5, h-ZSM-5, Beta and h-Beta).

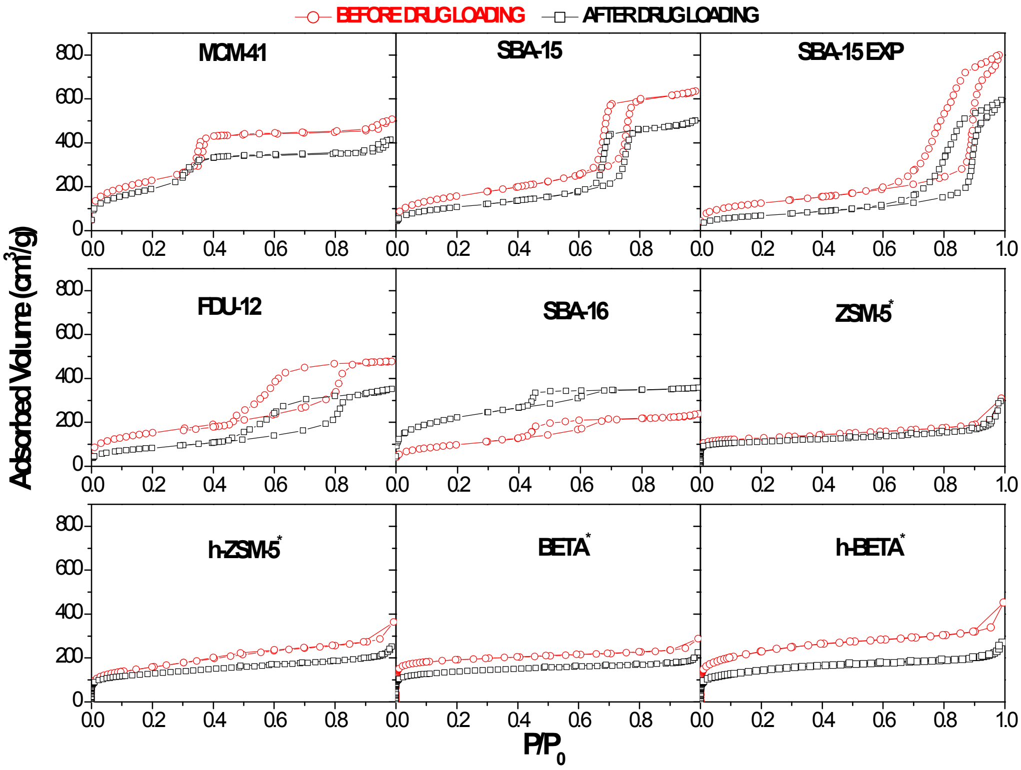

Figure S4: N_2 adsorption isotherms for mesoporous materials (MCM-41, SBA-15, SBA-15 EXP, FDU-12 and SBA-16), and Ar adsorption isotherms for zeolitic materials (ZSM-5, h-ZSM-5, BETA and h-BETA) before and after drug loading.

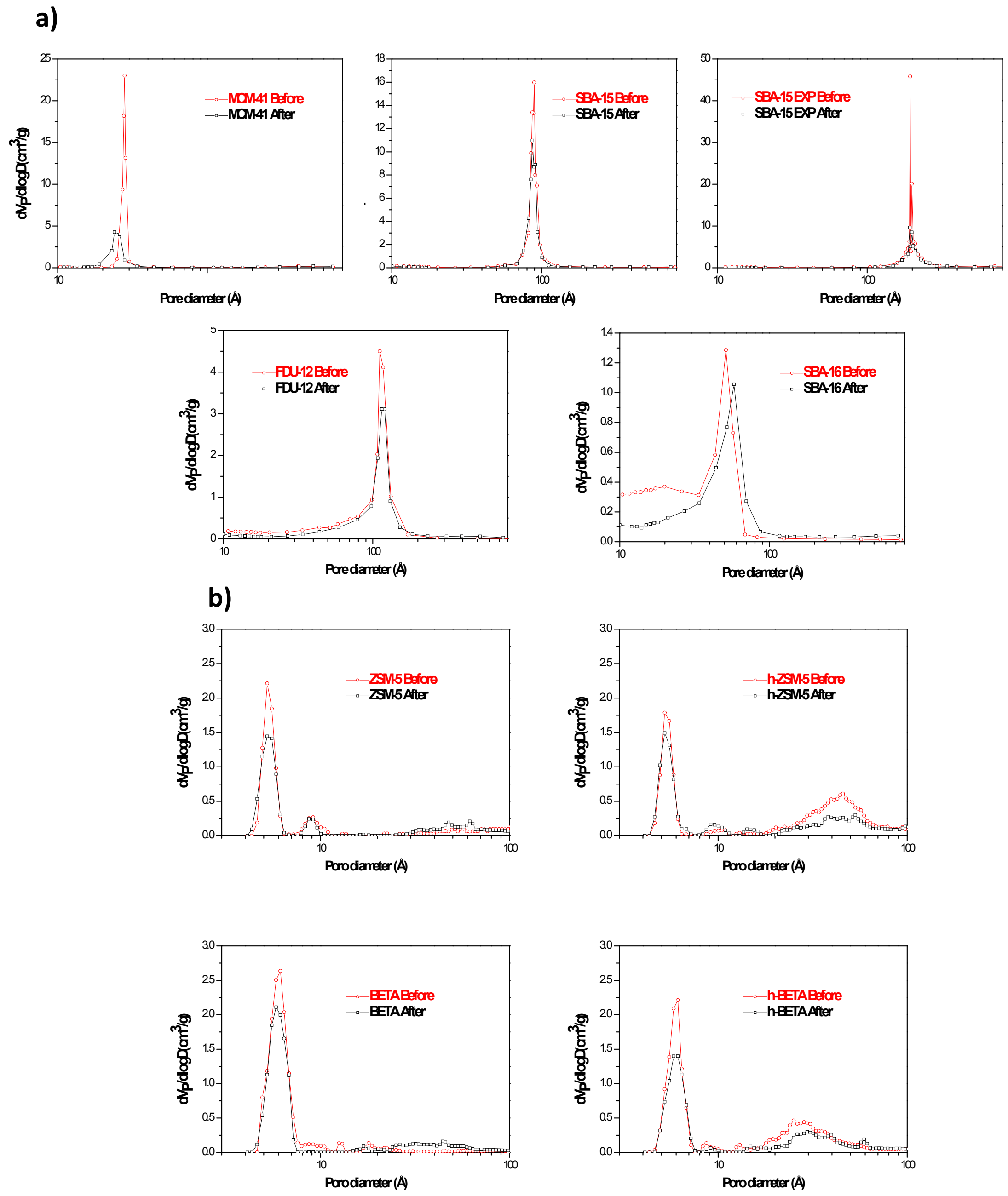

Figure S5. a) Pore size distribution obtained by N_2 adsorption-desorption for mesoporous materials (MCM-41, SBA-15, SBA-15 EXP, FDU-12 and SBA-16), and b) by Ar adsorption-desorption isotherms for zeolitic materials (ZSM-5, h-ZSM-5, BETA and h-BETA) before and after drug loading,

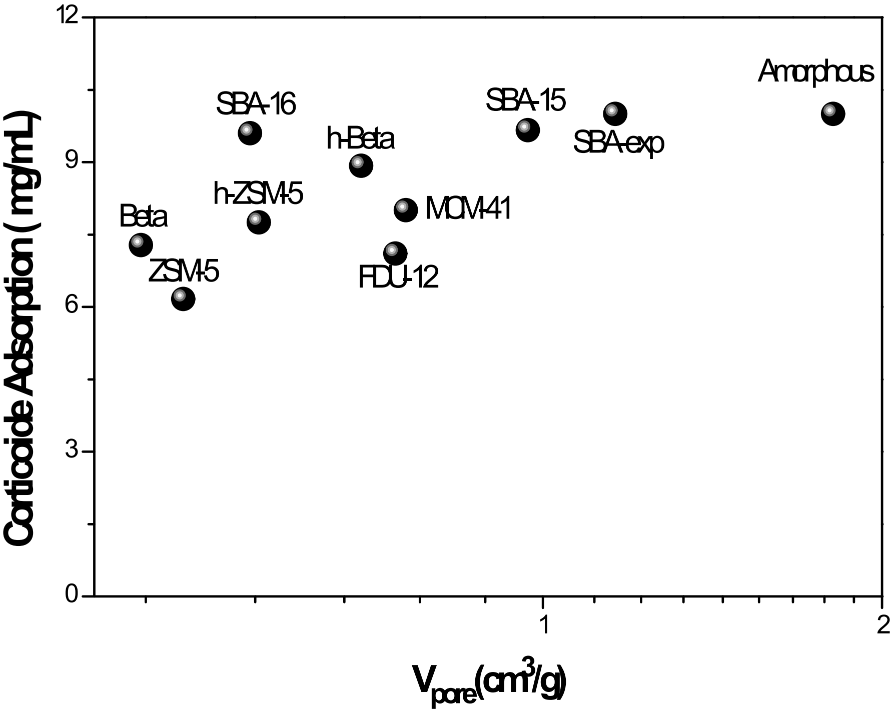

Figure S6: Effect of the pore volume on drug loading efficiency.

Table S1: Corticoid drug adsorption data on mesoporous silica and hierarchical zeolites adsorbents

Sample	Method	Initial amount (mg/ml)	Adsorbed amount HCNS (mg/ml)	Load Effciency HCNS (%)	Adsorbed amount TGA (mg/ml)
MCM-41	Incipient wetness	10	8.81	88.1	9.42
		25	16.60	66.5	15.8
	Solvent adsorption	10	7.00	70.0	8.51
		25	17.70	70.03	18.61
FDU-12	Incipient wetness	10	7.10	70.7	8.74
		25	18.30	73.0	21.74
	Solvent adsorption	10	7.60	76.5	8.64
		25	18.42	73.7	19.21
SBA-15	Incipient wetness	10	9.66	96.6	9.47
		25	20.63	82.5	21.74
	Solvent adsorption	10	5.74	57.4	9.43
		25	16.00	63.9	18.03
SBA-16	Incipient wetness	10	9.60	96.1	10.78
		25	15.70	62.9	15.30
	Solvent adsorption	10	8.00	79.9	7.56
		25	15.80	63.2	14.30
SBA-exp	Incipient wetness	10	10.00	100.0	10.82
		25	21.60	86.4	20.91
	Solvent adsorption	10	9.32	93.2	10.40
		25	21.00	84.3	20.12
Amorphous silica	Incipient wetness	10	10	100	9.81
ZSM-5	Incipient wetness	10	6.16	61.6	5.98
h-ZSM-5	Incipient wetness	10	7.75	77.50	6.20
BETA	Incipient wetness	10	7.28	72.8	7.96
h-BETA	Incipient wetness	10	8.92	89.20	6.02