Electronic Supplementary Information

Abnormal Adsorption and Desorption Behaviors of Pharmaceutical Drugs on Polystyrene Microspheres

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Experimental Section

1. Chemicals and Materials. Styrene, BPO and PVP were, respectively, ordered from Tianjin Tianli Chemical Reagents Ltd. (Tianjin, China), Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China) and Chengdu Kelong Chemical Co., Ltd. (Chengdu, China). The studied commercially available PS particles with diameters of 2 μm, 4 μm, 6 μm, 8 μm and 10 μm were from Suzhou Smartynano Technology Co., Ltd. (Suzhou, China). The used filter paper for coating PS particles was from Hangzhou Special Paper Co. (Fuyang, China). The commercially available grade 1 chromatography paper was purchased from GE Healthcare Bio-Sciences Corp. (Westborough, MA, USA). The irregular MgO, ZnO, Al_2O_3, TiO_2 and ZrO_2 with diameters of around 1 μm were from Shanghai ST-Nano Science & Technology Co. Ltd. (Shanghai, China). The used metal-organic frameworks (MOFs) including MIL-53(Al), ZIF-8 and UiO-66(Zr) with average diameters in the range of 4.8 - 10.6 μm were from Beijing HWRK Chem. Co. Ltd. (Beijing, China). The used adhesive agents were ordered from Jilin Zhiyou Technology Co., Ltd (corn starch, Changchun, China) and Tianjin Kemiou Chemical Reagent Co. (soluble starch, Tianjin, China), respectively. The used therapeutic drug standards including verapamil, D_6-verapamil, amitriptyline, clozapine, quetiapine, risperidone and aripiprazole were from Sigma-Aldrich (St. Louis, USA) or Toronto Research Chemicals Inc. (Toronto, Canada). The used verapamil for adsorption study was from Nanjing SenBeiJia Biological Technology Co., Ltd. (Nanjing, China). Other employed solvents were analytical grade or better and were used without further purification.

2. Preparation of PS particles. A series of PS microspheres were first prepared according to reported dispersion polymerization of styrene[1] in ethanol/water media by using benzoyl peroxide (BPO) as initiator and poly(N-vinylpyrrolidone) (PVP) as steric stabilizer.

(1) PS particles prepared with variation in the involved amounts of styrene: The dispersion polymerization reaction was carried out in a 250 mL three neck reactor, which was equipped with an anchor-shaped stirrer and condenser. In a typical procedure, 1.0 g PVP and 1.0 g BPO were, respectively, dissolved into 80 mL ethanol solution. When the mixture was heated to 70 ^oC, poured a certain volume of styrene monomer, ranging from 5 to 40 mL, into the reaction solution followed by a reaction period of 9 h under gentle stirring (ca. 120 rpm), respectively. The prepared particles were collected and washed with absolute ethanol for three times (each with around 35 mL). Subsequently, the obtained PS samples were separated through a TDZ5B-WS centrifuge (Shanghai LuXiangyi Centrifuge Instrument Co. Ltd., Shanghai, China) under the speed of 3000 rpm. Finally, the prepared white powder was dried in vacuum oven at 50°C for 24 h. The samples

were stored at room temperature in a sealed bag for use.

(2) **PS particles prepared with variation in the involved amounts of PVP:** The preparation procedure was similar as above except for the added amount of PVP. Namely, the reaction was carried out by reaction of 5 mL styrene and 1.0 g BPO in the presence of various amounts of PVP (0.5 - 2.5 g) and 80 mL ethanol.

(3) **PS particles prepared with variation in the involved amounts of BPO:** The preparation procedure was similar as above except for the added amount of BPO. Namely, the reaction was carried out by reaction of 5 mL styrene and various amounts of BPO (0.5 – 2.5 g) in the presence of 1.0 g PVP and 80 mL ethanol.

(4) **PS particles prepared with variation in the involved volumes of H_2O:** The preparation procedure was similar as above except for the added volume of H_2O. Namely, the reaction was carried out by reaction of 5 mL styrene and 1.0 g BPO in the presence of 1.0 g PVP and various volumes of H_2O (0 – 10 mL) and ethanol (80 -70 mL), and the total volume of H_2O and ethanol was kept at 80 mL.

(5) **PS particles prepared with various amounts of styrene and BPO:** The preparation procedure was similar as above except for the added amounts of styrene and BPO. Namely, the reaction was carried out by reacting various amounts of styrene and BPO (#1- #7 represent different reaction systems, in which #1 means 1.0 g BPO and 10 mL styrene, #2 means 1.5 g BPO and 15 mL styrene, #3 means 2.0 g BPO and 20 mL styrene, #4 means 2.5 g BPO and 25 mL styrene, #5 means 3.0 g BPO and 30 mL styrene, #6 means 3.5 g BPO and 35 mL styrene and #7 means 4.0 g BPO and 40 mL styrene) in the presence of 1.0 g PVP and 80 mL ethanol.

3. Preparation of PS, metal oxides and metal-organic frameworks coated paper substrates. The detailed procedures for preparation of PS, metal oxides including ZrO_2, MgO, ZnO, Al_2O_3 and TiO_2 and metal-organic frameworks including MIL-53(Al), ZIF-8 and UiO-66(Zr) were similar to our recent reports.[2] In a typical procedure for preparation of PS coated papers, 0.2 g of PS particles were dispersed into 100 mL of deionized water containing 0.2 g of soluble starch as an adhesive agent. In order to get a uniform solution for coating, the mixture solution was sonicated for 30 min, and the obtained suspension solution was directly transferred to a Buchner funnel covered by a piece of blank filter paper with 11 cm in diameter for coating. When the aqueous solution was completely penetrated through the filter paper, around 20 mL of absolute ethanol was applied for washing in order to get rid of the remaining water at the surface of the coated paper. The total coating procedure took about 35 min. The papers were then hung in a hood to dry for hours and were pressed between glass plates overnight for use. For the metal oxides and metal-organic frameworks coated

paper substrates, the preparation procedures were same as our recent reports.[2d, 2f]

4. Desorption behaviors of pharmaceutical drugs from different materials coated paper substrates for on-line MS analysis. The experiments were performed by first spotting 2 μL of methanol solution containing verapamil (1000 ng mL^{-1}) or others onto the prepared PS coated paper substrates and drying the substrates completely. Then the papers were cut into triangles. The voltage (3.5 kV DC voltage) was applied, and 25 μL methanol was added to produce paper spray event while the signal of fragment ion m/z 165 from verapamil or other fragment ions was monitored.

5. Desorption behaviors of pharmaceutical drugs from different materials coated paper substrates for off-line MS analysis. The experiments were carried out by first cutting the coated papers into a square (around 30 mm^2 in area) and then loading 2 μL methanol solution containing verapamil (1000 ng mL^{-1}) or others onto the paper surface. After complete drying in air for hours, 0.5 mL methanol was applied onto the paper substrate for verapamil extraction, and the extract was collected analyzed via MS for evaluating the desorption performances of different PS particles.

6. Elution curves of pharmaceutical drugs from PS coated paper substrates. The experiments were done by first spotting 2 μL of methanol solution containing verapamil (1000 ng mL^{-1}) onto the prepared PS coated paper substrates and drying the substrates completely. Then the papers were cut into triangles and 3.5 kV DC voltage was applied. In the procedure, solvent was added multiple times to produce many paper spray events using the same substrate bearing a single sample spot while the signal of fragment ion m/z 165 from verapamil was monitored. Spray solvent of 25 μL was used each time, and the solvent was not added until the monitored ion signal decreased to a minimum, when the spray solvent was exhausted.

7. Adsorption behaviors of pharmaceutical drugs onto different materials. The experiments were carried out by adding 0.2 g PS particles or other materials into 10 mL methanol solution containing 1 μg mL^{-1} verapamil unless otherwise stated followed by stirring for 30 min. The mixture was collected and separated, and then 100 μL of the upper clear solution was pipetted, which was then diluted with 900 μL methanol for subsequent analysis. The remaining content of verapamil in solution was analyzed with paper spray through the peak intensity of the fragment ion m/z 165 from verapamil. The used paper substrate was grade 1 chromatography paper, and the applied amount of sample solution was 25 μL.

8. Adsorption kinetic curves of verapamil from different PS particles. The experiments were performed by adding 0.2 g PS particles into 10 mL methanol solution

containing 1 μg mL^{-1} verapamil followed by stirring. At different adsorption times (e.g., 5, 15, 30, 45, 60, 90, 120, 150 and 180 min), 0.2 mL of the mixture was collected and separated. Afterwards, 100 μL of the upper clear solution was pipetted, which was then diluted with 900 μL methanol for subsequent analysis. The remaining content of verapamil in solution was analyzed with paper spray through the peak intensity of the fragment ion m/z 165 from verapamil. The used paper substrate was grade 1 chromatography paper, and the applied amount of sample solution was 25 μL.

The adsorption capacity of verapamil on different polystyrene particles was calculated by $q_t = (C_0 - C_t)V/m$, in which q_t is the adsorption capacity, C_0 and C_t are the concentrations of verapamil (mg L^{-1}) before and after adsorption, V is the volume of solution (L), and m is the mass of the used PS particles (g).

9. Desorption kinetic curves of verapamil from different PS particles. The experiments were performed by adding 0.2 g PS particles into 10 mL methanol solution containing 1 μg mL^{-1} verapamil followed by stirring. After an adsorption time of 180 min, the involved PS particles were filtered and dried in air for hours. Then these particles were put into 9 mL methanol for desorption. At different desorption times (e.g., 0.5, 1.0, 2.5, 5.0, 15, 30, 45, 60, 90, 120, 150 and 180 min), 0.2 mL of the mixture was collected and separated. Afterwards, 100 μL of the upper clear solution was pipetted, which was then diluted with 900 μL methanol for subsequent analysis. The remaining content of verapamil in solution was analyzed with paper spray through the peak intensity of the fragment ion m/z 165 from verapamil. The used paper substrate was grade 1 chromatography paper, and the applied amount of sample solution was 25 μL.

10. Characterization of PS particles. The surface structures of as-prepared PS particles and coated paper substrates were examined by a JEOL JSM-6390A scanning electron microscope (SEM). FT-IR spectra of the obtained samples were recorded with a Thermo Nicolet 5700 Series infrared spectrometer in transmission mode in the range of 4000–400 cm^{-1}. The resolution was 4 cm^{-1} and 32 scans were signal-averaged in each interferogram. The IR measurement was carried out for PS particles with KBr compression method. To avoid the influence of water in air on the IR spectra, the compression experiment was performed under illustration of an infrared lamp. The transmittance was kept at 95 - 96 % for the purpose of comparing the change in IR spectra of PS particles prepared from different experimental conditions. The molecular weight of the obtained PS particles was measured by Agilent PL-GPC 50 gel permeation chromatography (GPC) integrated with a differential refractive index detector. The samples were eluted with tetrahydrofuran at a flow rate of 1.0 mL min^{-1}. The used solvent for dissolving PS particles was tetrahydrofuran with a final concentration of around 2 mg mL^{-1}. The pore structures of as-synthesized polystyrene microspheres

were examined using a Micrometrics AutoPore IV 9510 Series mercury porosimeter under the room temperature.

11. MS analysis. All experiments on paper spray mass spectrometry were carried out with a TSQ Quantum Access Max mass spectrometer (Thermo Fisher Scientific, San Jose, CA, USA). For paper spray, the coated paper substrate was cut into a triangle (around 11 mm height and 7 mm base width). A stainless steel clip was used to hold the paper triangle and to apply the high voltage needed for the spray. The distance between the tip of the paper triangle and the inlet to the mass spectrometer was about 8 mm. The collection period for each paper spray analysis was around 30-35 s. Mass spectra were recorded in the positive ion mode with a capillary temperature of 270 °C. The identification of analyte ions was confirmed by tandem mass spectrometry (MS/MS) using collision-induced dissociation (CID). Argon gas (99.995% purity) was used as collision gas. The SRM and instrumental parameters used for the therapeutic drugs are as follows: verapamil, m/z 455→303; tube lens, 106 V; collision energy, 24 V; D_6-verapamil, m/z 461→309; tube lens, 97 V; collision energy, 24 V; amitriptyline, m/z 278→84; tube lens, 83 V; collision energy, 24 V; clozapine, m/z 327→270; tube lens, 87 V; collision energy, 23 V; quetiapine, m/z 384→253; tube lens, 96 V; collision energy, 21 V; risperidone, m/z 411→191; tube lens, 101 V; collision energy, 25 V; aripiprazole, m/z 448→285; tube lens, 119 V; collision energy, 25 V. Each datum point is an average of four replicates and error bars indicate standard deviation.

12. Hydrogen bond interaction study. To investigate the hydrogen bond interactions between PS and verapamil, the geometries of isolated verapamil, 2,4-diphenyl pentane and the complex of the verapamil and 2,4-diphenyl pentane were fully optimized using Gaussian09 program package (revision B.01; Gaussian, Inc., Wallingford CT, 2010)[3] at B3LYP/6-31G(d,p)[4] level.

Furthermore, the periodic systems of polystyrene and verapamil were re-optimized by gradient-corrected DFT calculations with the PBE functional and a DFT-based relativistic semicore pseudopotential (DSPP)[5] combined with a double numerical basis with polarization functions (DNP) in the DMol3 package.[6] The Broyden−Fletcher−Goldfarb−Shanno algorithm[7] with a convergence criterion of 10^{-3} a.u. on the displacement, and the gradient of 10^{-5} a.u. on the total energy was used for the geometry optimization. A convergence criterion of 10^{-6} a.u. on the total energy and electron density was adapted for the selfconsistent field calculations. All simulated structures are fully relaxed to optimize with no symmetry restriction. A conjugategradient algorithm with a Gaussian smearing of r = 0.02 eV was used to improve the convergence of electronic structures.

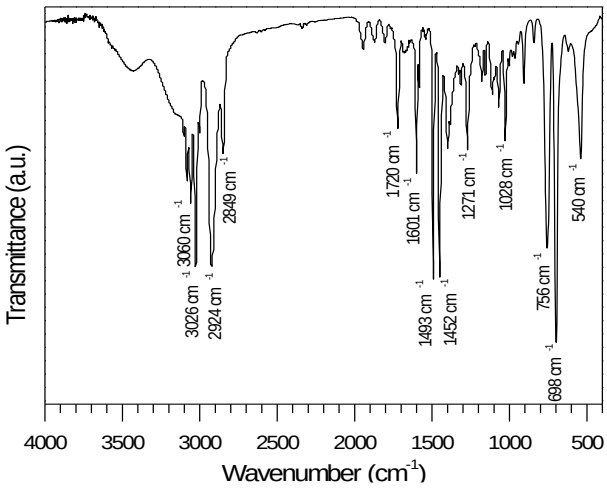

Figure S1. Infrared spectra of the PS particles obtained by reaction of 5 mL styrene and 1.0 g BPO in the presence of 1.0 g PVP by using 80 mL ethanol as solvent.

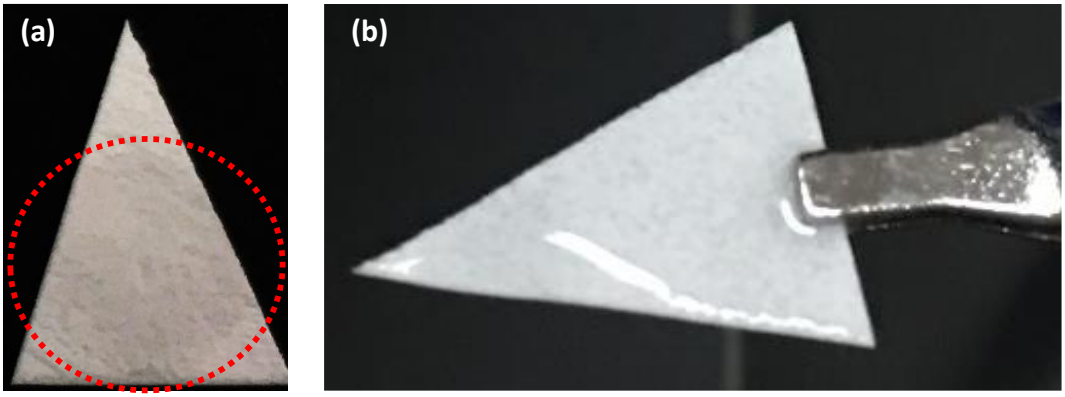

Figure S2. Photographic images of the surface of PS coated paper **(a)** after spotting 2 µL of methanol solution containing 1 µg mL^{-1} verapamil (*Note*: The section in the red dot circle is the paper substrate just wetted with 2 µL of methanol solution) and **(b)** after applying 25 µL of methanol solution spiked with 10 ng mL^{-1} D_6-verapamil (internal standard) for paper spray mass spectrometry.

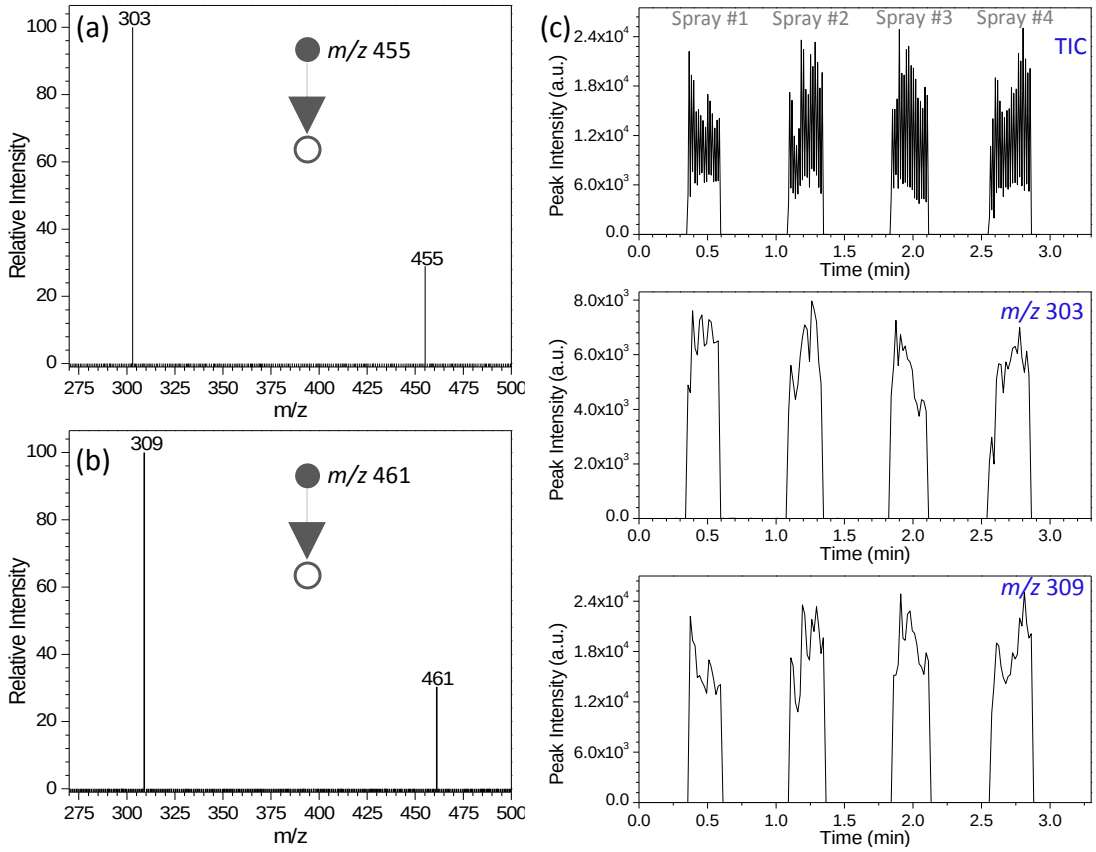

Figure S3. **(a)** and **(b)** MS/MS spectra for verapamil and D_6-verapamil during paper spray analysis, in which the experiments were carried out by applying 25 µL of methanol solution spiked with 10 ng mL^{-1} D_6-verapamil (internal standard) at the PS coated paper spotted with 2 µL of methanol solution; **(c)** Total ion chronograms (TIC, signal versus time) for the sequential analysis of verapamil (m/z 303) spotted on PS coated paper with D_6-verapamil (m/z 309) as the internal standard. (*Note*: Each peak in the chronogram is from the analysis of a different sample spot. In the sample preparation, 2 µL of methanol solution containing 1 µg mL^{-1} verapamil was spotted on the PS coated paper triangle. After drying in air for around 4 h, 25 µL of a methanol solution spiked with 10 ng mL^{-1} D_6-verapamil as internal standard was applied at the paper surface followed immediately by application of the high voltage (3.5 kV) needed for paper spray. In the quantitative analysis, each datum point is the average of the peak intensity collected in the TIC range.)

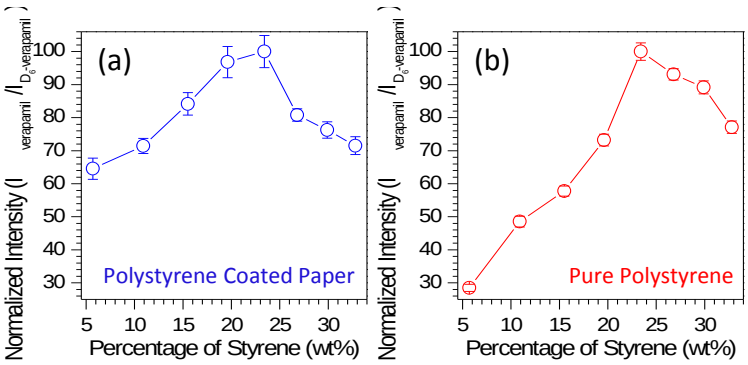

Figure S4. **(a)**Desorption behavior of verapamil from PS coated paper substrates using off-line extraction mode and **(b)**desorption behavior of verapamil from PS particles in methanol solution, in which PS was prepared in the presence of various volumes of styrene (5 – 40 mL) by fixing the amounts of BPO (1.0 g) and PVP (1.0 g) in 80 mL ethanol solution.

In the on-line desorption experiments of verapamil from PS coated paper, it involved high voltage, paper substrate and adhesive agent soluble starch, which might have a great impact on the desorption performance at PS interfaces. To exclude the influence of high voltage on desorption, the following extraction and analysis experiments were performed. First, 2.0 µL methanol solution containing 1.0 µg mL^{-1} verapamil was, respectively, deposited at the surfaces of PS coated papers. After drying in air, 100 µL methanol was used to extract verapamil from PS coated papers. The obtained liquid spiked with a final concentration of 10 ng mL^{-1} d_6-verapamil was then directly used as spray solvent for paper spray analysis. It is clear that the desorption pattern of verapamil from PS coated papers presents a similar trend (**Figure S4a**) as that using on-line desorption experiment (**Figure 1e**), suggesting that the involved high voltage had little influence on the desorption mode. To preclude the effects of paper substrate and soluble starch, an adsorption/desorption experiment was carried out by using PS particles as absorbent, in which 0.2 g PS particles were added into 100 mL methanol solution containing 1.0 µg mL^{-1} verapamil. After adsorption for 30 min under stirring, the involved PS particles were filtered and dried in air for hours, and then these particles were put into 100 mL methanol for desorption. The content in the achieved solutions was analyzed with paper spray analysis. It is interesting that with variation of styrene content in preparation of PS, the signal of verapamil demonstrated a similar trend (**Figure S4b**) as the above (**Figure S4a** and **Figure 1e**). These experiments confirmed that the results from the on-line desorption were convincing, which was not responsible for the exceptional adsorption/desorption interactions at PS surfaces.

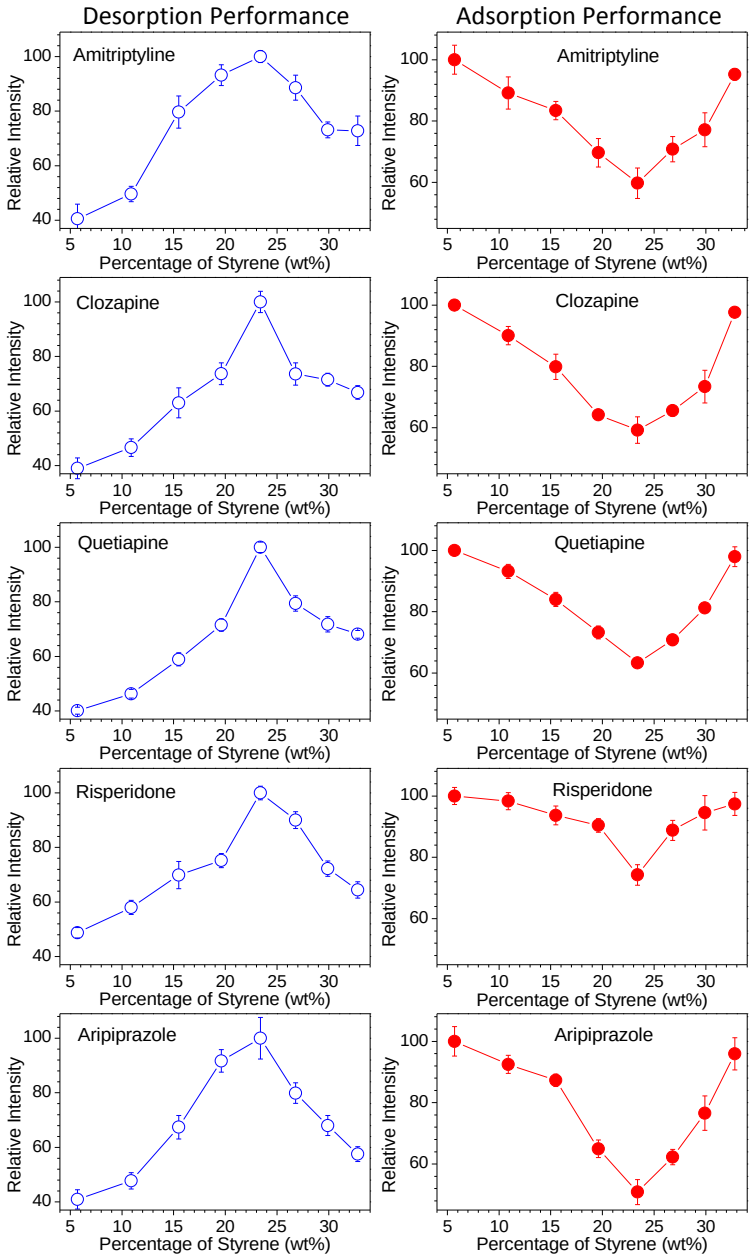

Figure S5. Comparison of desorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole from PS coated paper substrates and adsorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole onto PS particles in methanol solution, in which PS was prepared in the presence of various volumes of styrene (5 – 40 mL) by fixing the amounts of BPO (1.0 g) and PVP (1.0 g) in 80 mL ethanol solution. Note: The "*Relative Intensity*" of desorption and adsorption in y axis is the normalized value to the highest one in each specific data set.

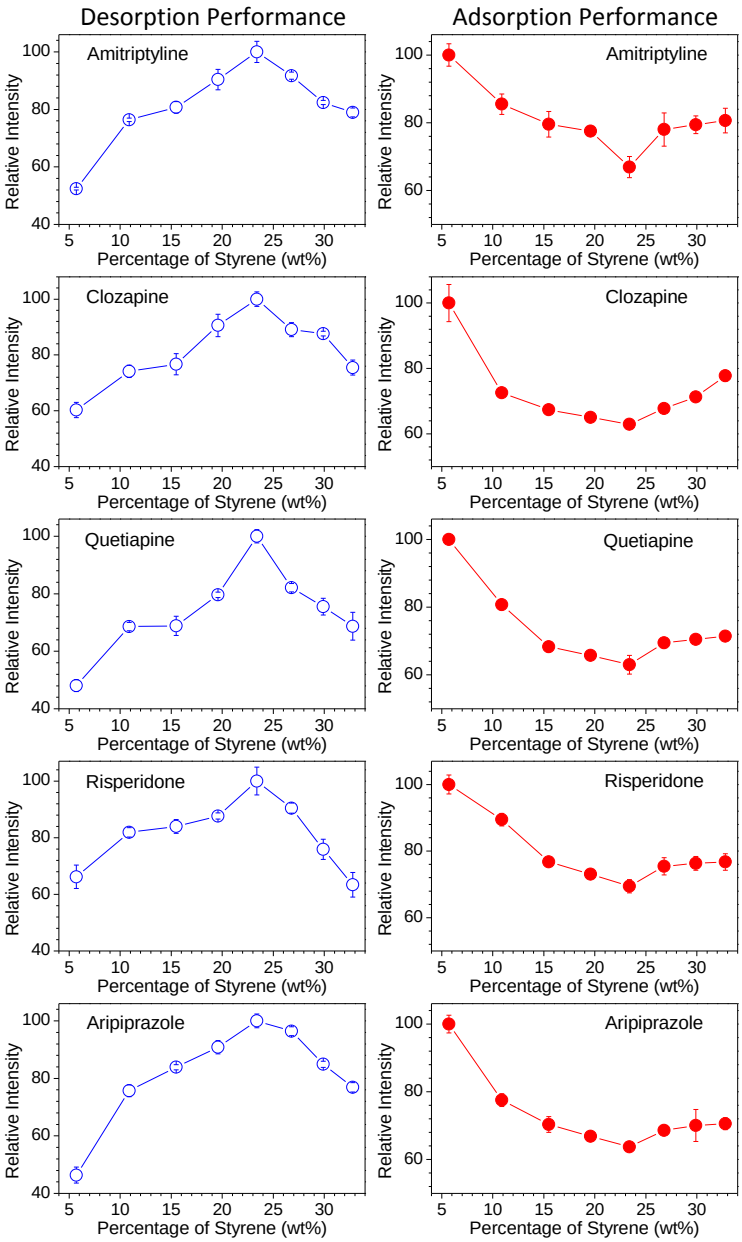

Figure S6. Comparison of desorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole from PS coated paper substrates and adsorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole onto PS particles in ethanol solution, in which PS was prepared in the presence of various volumes of styrene (5 – 40 mL) by fixing the amounts of BPO (1.0 g) and PVP (1.0 g) in 80 mL ethanol solution. Note: The "*Relative Intensity*" of desorption and adsorption in y axis is the normalized value to the highest one in each specific data set.

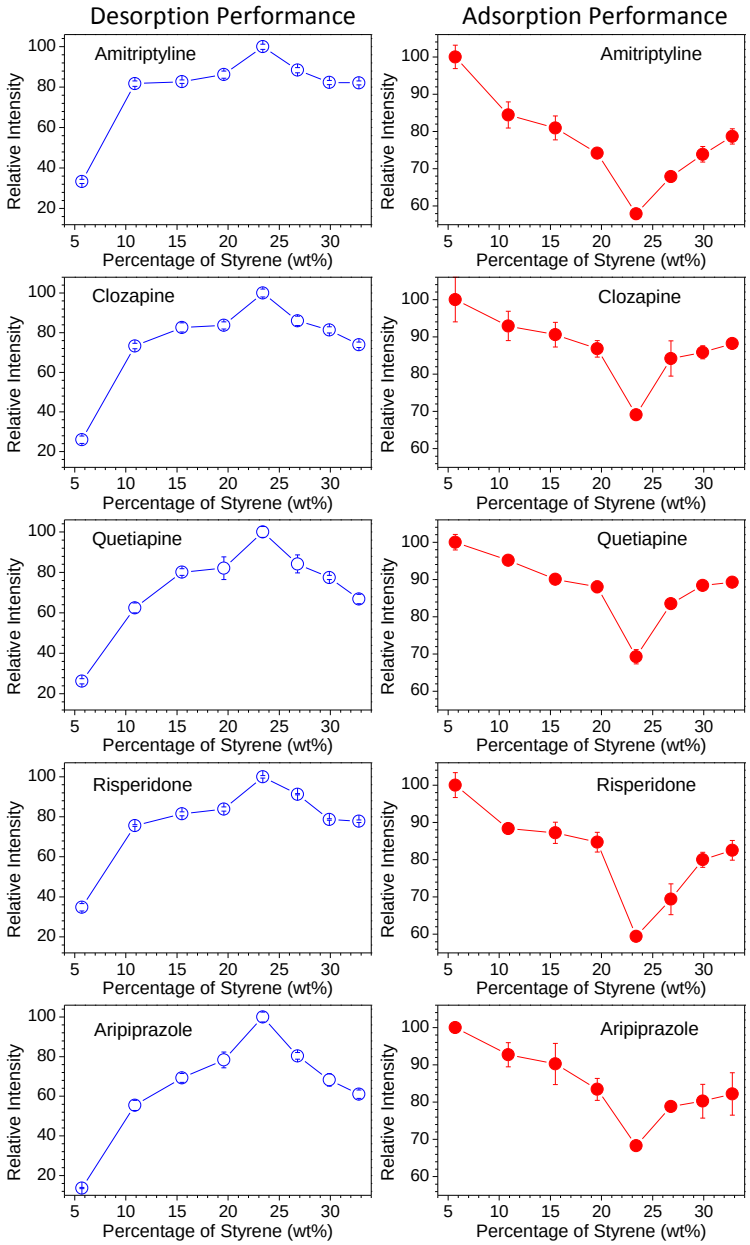

Figure S7. Comparison of desorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole from PS coated paper substrates and adsorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole onto PS particles in propanol solution, in which PS was prepared in the presence of various volumes of styrene (5 – 40 mL) by fixing the amounts of BPO (1.0 g) and PVP (1.0 g) in 80 mL ethanol solution. Note: The "*Relative Intensity*" of desorption and adsorption in y axis is the normalized value to the highest one in each specific data set.

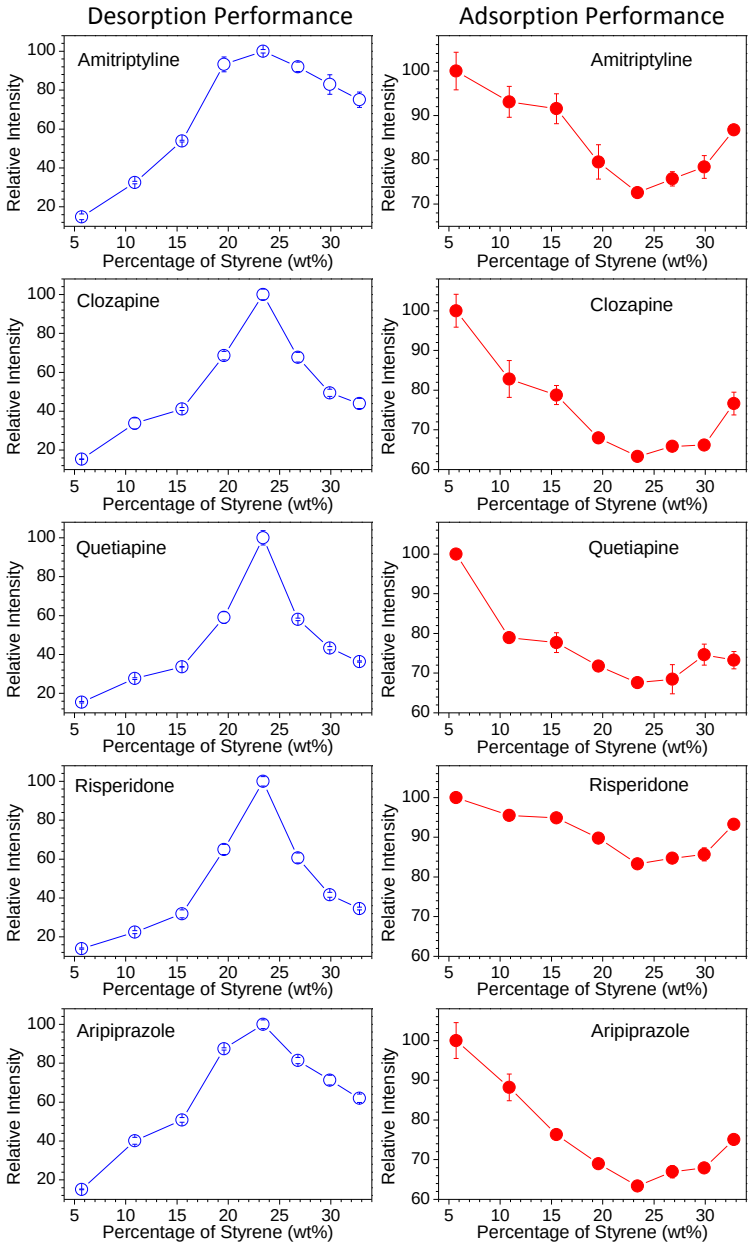

Figure S8. Comparison of desorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole from PS coated paper substrates and adsorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole onto PS particles in isopropanol solution, in which PS was prepared in the presence of various volumes of styrene (5 – 40 mL) by fixing the amounts of BPO (1.0 g) and PVP (1.0 g) in 80 mL ethanol solution. Note: The "*Relative Intensity*" of desorption and adsorption in y axis is the normalized value to the highest one in each specific data set.

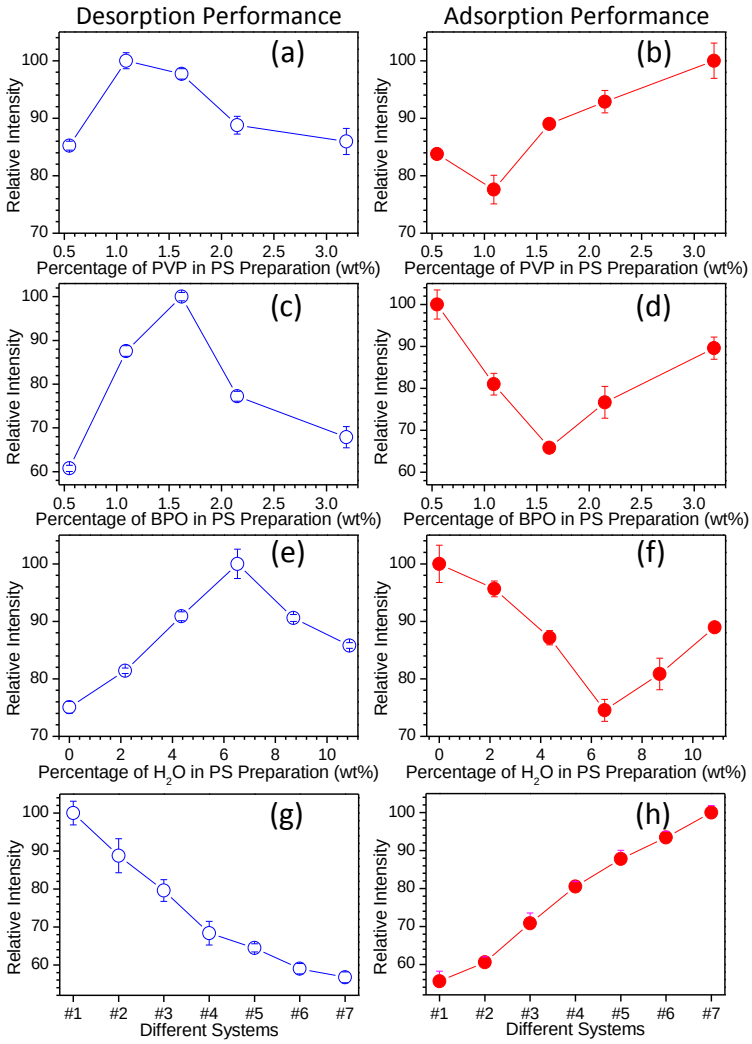

Figure S9. Comparison of desorption behaviors of verapamil from PS coated paper substrates and adsorption behaviors of verapamil onto PS particles in isopropanol solution, in which PS was prepared **[a-b]** in the presence of various volumes of PVP (0.5 – 2.5 g) by fixing the amounts of BPO (1.0 g) and styrene (25 mL) in 80 mL ethanol solution, or **[c-d]** in the presence of various amount of BPO (0.5 – 2.5 g) by fixing the amounts of PVP (1.0 g) and styrene (25 mL) in 80 mL ethanol solution, or **[e-f]** in the presence of various volumes of H_2O (0 – 10 mL) and ethanol (70 – 80 mL) by fixing the amounts of PVP (1.0 g), BPO (1.0 g) and styrene (25 mL), in which the total volume of H_2O and ethanol was 80 mL, or **[g-h]** in the presence of various amounts of BPO/styrene (**#1** means 1.0 g BPO and 10 mL styrene; **#2** means 1.5 g BPO and 15 mL styrene; **#3** means 2.0 g BPO and 20 mL styrene; **#4** means 2.5 g BPO and 25 mL styrene; **#5** means 3.0 g BPO and 30 mL styrene; **#6** means 3.5 g BPO and 35 mL styrene; **#7** means 4.0 g BPO and 40 mL styrene) by fixing the amounts of PVP (1.0 g) in 80 mL ethanol solution. Note: The "*Relative Intensity*" of desorption and adsorption in y axis is the normalized value to the highest one in each specific data set.

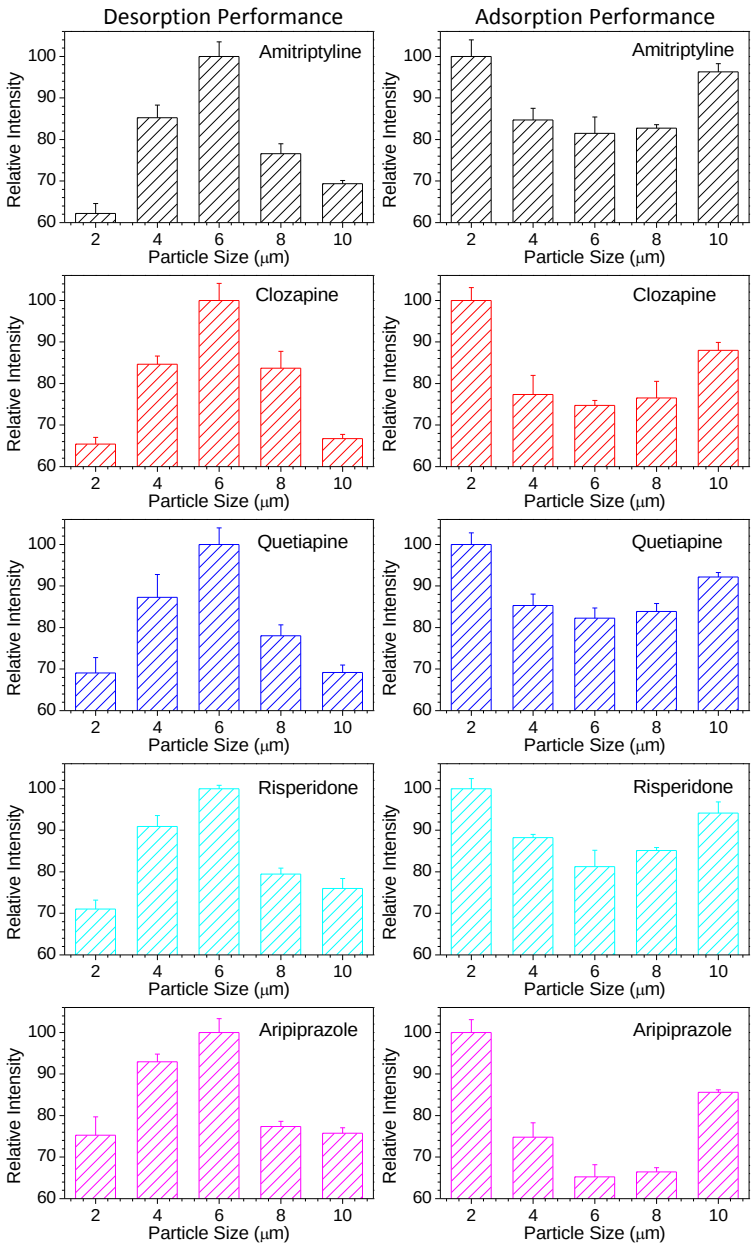

Figure S10. Comparison of desorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole from PS coated paper substrates and adsorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole onto PS particles in methanol solution, in which PS particles with different particle sizes (2 -10 μm) were purchased from commercially available source. Note: The "*Relative Intensity*" of desorption and adsorption in y axis is the normalized value to the highest one in each specific data set.

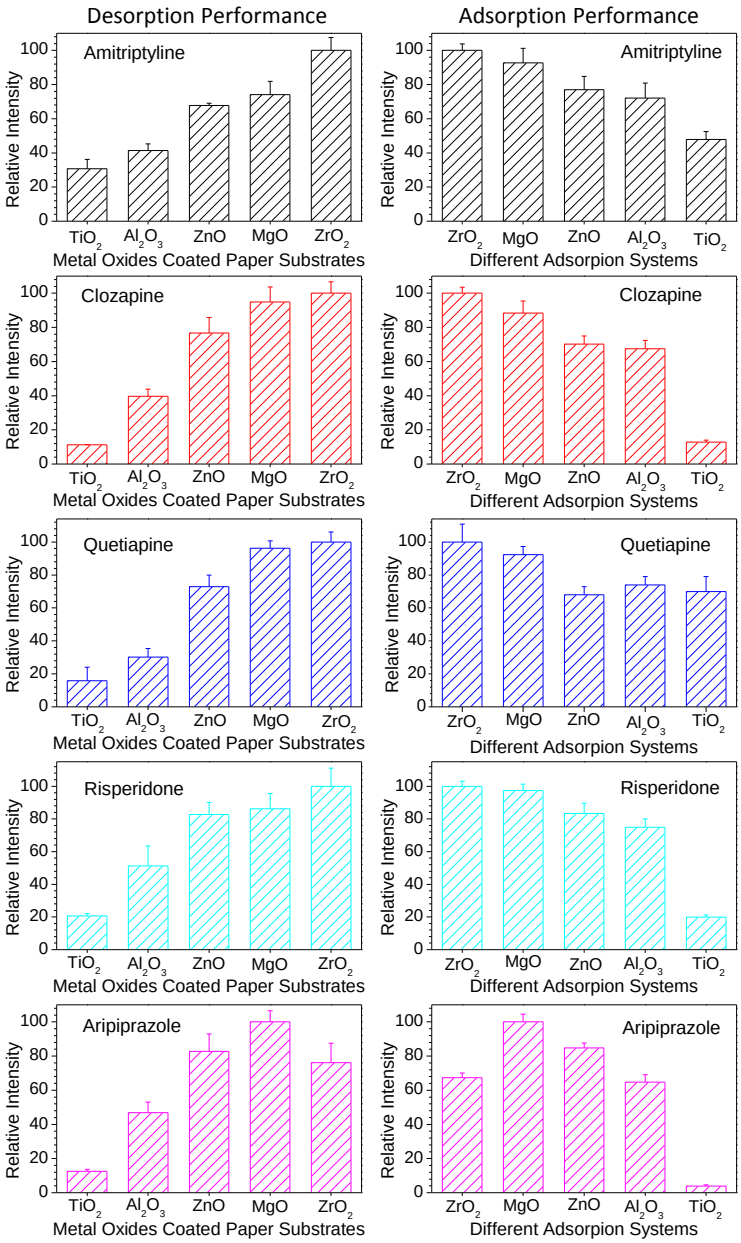

Figure S11. Comparison of desorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole from TiO_2, Al_2O_3, ZnO, MgO and ZrO_2 coated paper substrates and adsorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole onto TiO_2, Al_2O_3, ZnO, MgO and ZrO_2 particles in methanol solution, in which different metal oxides with particle size of around 1 μm were purchased from commercially available source. Note: The "*Relative Intensity*" of desorption and adsorption in y axis is the normalized value to the highest one in each specific data set.

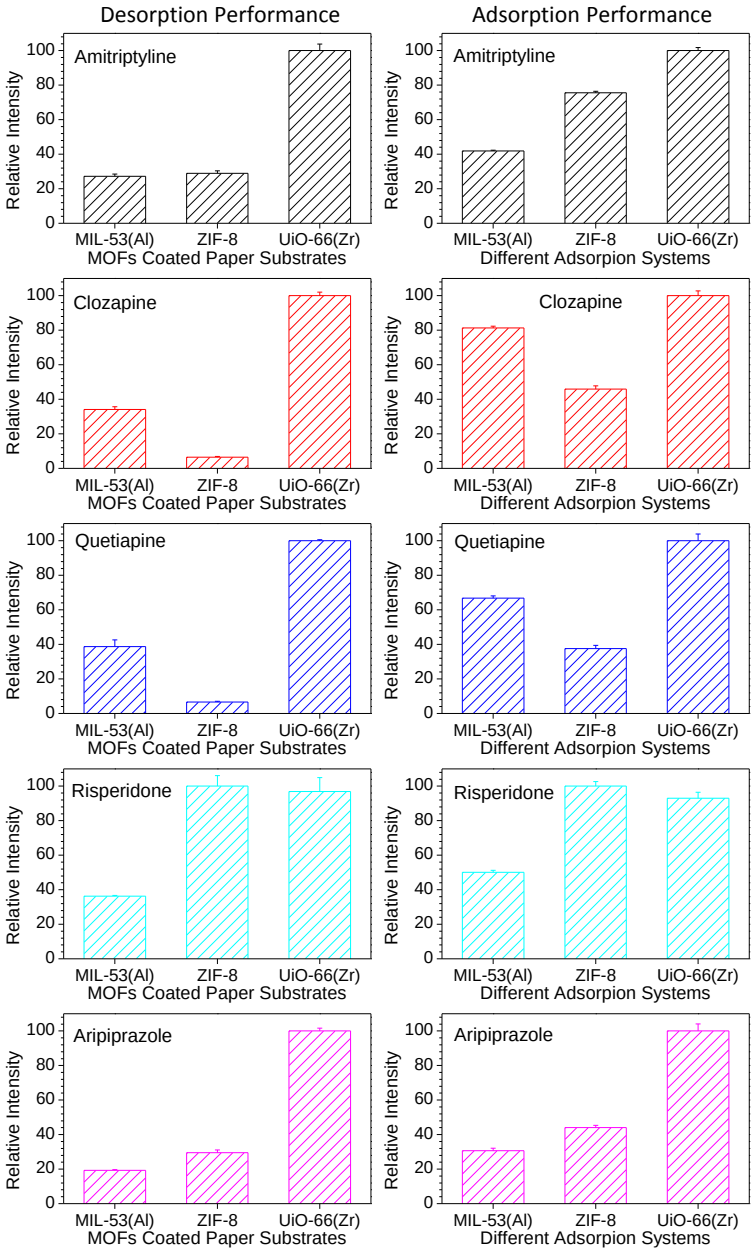

Figure S12. Comparison of desorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole from MIL-53(Al), ZIP-8, and UiO-66(Zr) coated paper substrates and adsorption behaviors of amitriptyline, clozapine, quetiapine, risperidone and aripiprazole onto MIL-53(Al), ZIP-8, and UiO-66(Zr) particles in methanol solution, in which different metal-organic frameworks (MOFs) with particle sizes in the range of 4.8 - 10.6 μm were purchased from commercially available source. Note: The "*Relative Intensity*" of desorption and adsorption in y axis is the normalized value to the highest one in each specific data set.

Table S1. Adsorption kinetic parameters for the adsorption of verapamil on polystyrene microspheres obtained from the reactions between various volumes (10 – 40 mL) of styrene and 1.0 g BPO in the presence of 1.0 g PVP.

Volume of Styrene for preparation of polystyrene (mL)	Pseudo-First-Order Model				Pseudo-Second-Order Model			
	Experimental q_e (mg g^{-1})	Calculated q_e (mg g^{-1})	k_1 (g mg^{-1} min^{-1})	R^2	Experimental q_e (mg g^{-1})	Calculated q_e (mg g^{-1})	k_2 (g mg^{-1} min^{-1})	R^2
10	0.0350	0.0312	0.0223	0.9565	0.0350	0.0389	1.060	0.9686
20	0.0362	0.0305	0.0223	0.9723	0.0362	0.0398	1.158	0.9878
25	0.0387	0.0273	0.0185	0.9739	0.0387	0.0414	1.351	0.9916
30	0.0374	0.0283	0.0216	0.9707	0.0374	0.0404	1.377	0.9916
40	0.0364	0.0306	0.0232	0.9724	0.0364	0.0399	1.225	0.9890

Note: q_e (mg g^{-1}) represents the adsorption capacity of verapamil on polystyrene microspheres at equilibrium time (min); k_1 (min^{-1}) and k_2 (g mg^{-1} min^{-1}) are, respectively, the pseudo-first-order and pseudo-second-order rate constants. The adsorption experiments were carried out in 10 mL of 1.0 μg mL^{-1} verapamil solution, and methanol was the solvent. The used weight of polystyrene microspheres was 0.20 g.

***Table S2*.** Adsorption isotherm parameters of verapamil on polystyrene microspheres obtained from the reactions between various volumes (10 mL, 25 mL and 40 mL) of styrene and 1.0 g BPO in the presence of 1.0 g PVP.

Volume of Styrene for preparation of polystyrene (mL)	Langmuir			Freundlich		
	q_m (mg g^{-1})	b	R^2	k_f	n	R^2
10	40.91	1.98 x 10^{-3}	0.9690	1.010	2.162	0.8938
25	41.64	2.03 x 10^{-3}	0.9643	1.091	2.198	0.8816
40	40.79	1.77 x 10^{-3}	0.9749	0.892	2.108	0.9037

Note: q_m (mg g^{-1}) is the maximum adsorption capacity corresponding to complete monolayer coverage, b is the equilibrium constant (L mg^{-1}), K_f is roughly an indicator of the adsorption capacity, and n is the adsorption intensity. R^2 is the correlation coefficient.

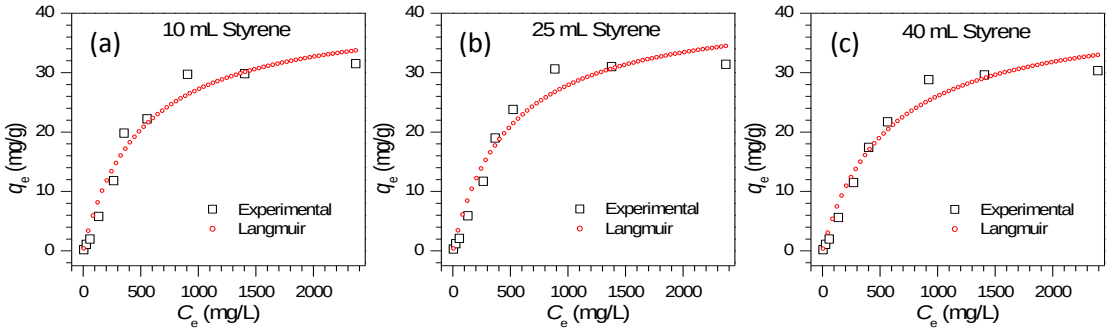

Figure S13. Adsorption isotherm curves of verapamil on as-synthesized polystyrene microspheres obtained from the reactions between various volumes of styrene and 1.0 g BPO in the presence of 1.0 g PVP: **(a)** 10 mL, **(b)** 25 mL and **(c)** 40 mL (Note: q_e (mg/g) represents the adsorption capacity of verapamil on polystyrene microspheres at equilibrium time (min), and C_e (mg/g) represents the concentration of verapamil in solution at equilibrium time (min).)

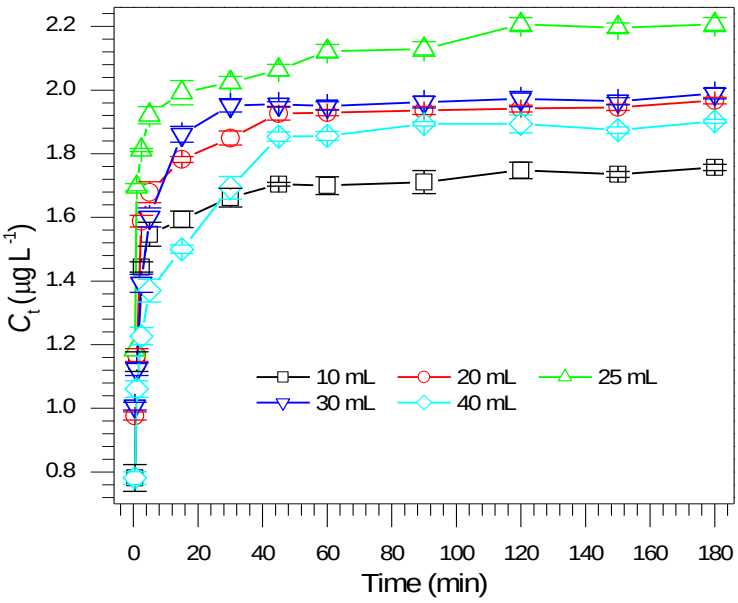

Figure S14. Time profiles of verapamil desorption on PS particles in methanol solution, in which the polystyrene particles were prepared from the reaction between various volumes of styrene (10 – 40 mL) and 1.0 g BPO in the presence of 1.0 g PVP.
Note: C_t means the concentration of verapamil in methanol solution at time *t* (min).

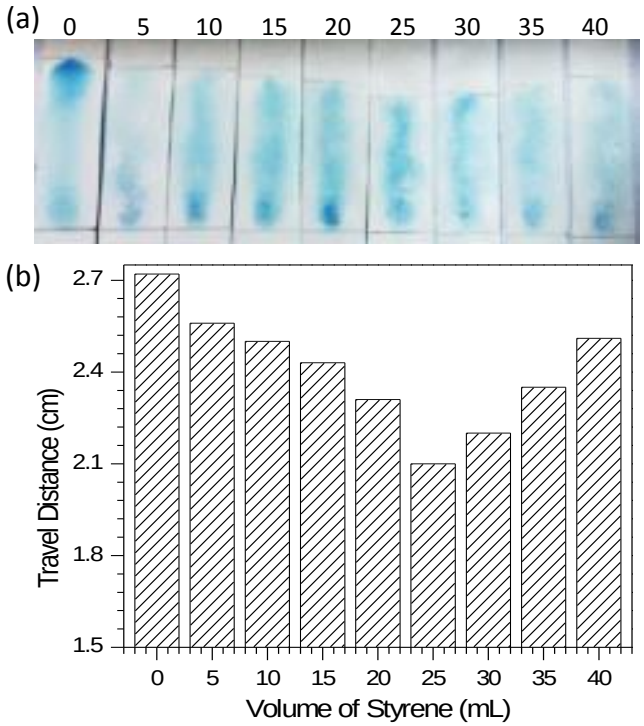

Figure S15. **(a)** Photograph of the paper strips after thin-layer chromatography, in which the experiments were carried out by spotting 2.0 μL of 1 mg mL^{-1} methylene blue on the PS coated paper substrates (1.0 cm x 5.0 cm) forming a round spot 1 cm from the bottom edge, and then the methylene blue was separated by dipping the end of the paper into methanol. After elution for 40 min, the paper substrates were put in air for drying. In this figure, "0" means blank filter paper, "5", "10", "15", "20", "25", "30", "35", "40"mean the paper substrates coated with the PS particles obtained by the reaction between various volumes of styrene (5, 10, 15, 20, 25, 30, 35 and 40 mL) and 1.0 g BPO in the presence of 1.0 g PVP; **(b)** Correlation between the travel distance of methylene blue at the surfaces of PS coated papers and the volumes of styrene used for preparation of PS particles.

Table S3. List of the molecular weights (M.W.) and particle sizes of the obtained PS particles with varying preparation conditions

No.	Reactant	Amount	M.W.	Particle Size (μm)	Notes
1	Styrene	5 mL	5723	2.19 ± 0.06	PS particles were obtained from the reactions among various volumes (10 – 40 mL) of styrene, 1.0 g BPO and 1.0 g PVP in 80 mL ethanol.
2		10 mL	21217	2.35 ± 0.05	
3		15 mL	34578	2.51 ± 0.09	
4		20 mL	49791	3.30 ± 0.09	
5		25 mL	65486	3.80 ± 0.08	
6		30 mL	79484	4.67 ± 0.17	
7		35 mL	82003	5.00 ± 0.08	
8		40 mL	91511	5.93 ± 0.17	
9	BPO	0.5 g	23351	1.88 ± 0.04	PS particles were obtained from the reactions among various amounts (0.5 – 2.5 g) of BPO, 25 mL styrene and 1.0 g PVP in 80 mL ethanol.
10		1.0 g	18271	3.27 ± 0.11	
11		1.5 g	9831	4.31 ± 0.06	
12		2.0 g	7324	5.24 ± 0.11	
13		2.5 g	5957	6.20 ± 0.11	
14	PVP	0.5 g	17533	3.76 ± 0.11	PS particles were obtained from the reactions among various amounts (0.5 – 2.5 g) of PVP, 25 mL styrene and 1.0 g BPO in 80 mL ethanol.
15		1.0 g	18271	3.27 ± 0.11	
16		1.5 g	20081	3.01 ± 0.10	
17		2.0 g	20017	2.85 ± 0.07	
18		2.5 g	20499	2.81 ± 0.09	
19	H_2O	0 mL	18271	3.27 ± 0.11	PS particles were obtained from the reactions among 1.0 g PVP, 1.0 g BPO and 25 mL styrene with changing the added amount (0 – 10 mL) of H_2O while keeping the total volume (80 mL) of H_2O and ethanol.
20		2 mL	20943	2.74 ± 0.10	
21		4 mL	25957	2.18 ± 0.08	
22		6 mL	34409	1.86 ± 0.08	
23		8 mL	33153	1.65 ± 0.07	
24		10 mL	35299	1.57 ± 0.05	
25	BPO + Styrene	1.0 g BPO + 10 mL Styrene	19460	2.35 ± 0.11	PS particles were obtained from the reactions among 1.0 g PVP and various amounts of BPO (1.0 – 4.0 g) and styrene (10 – 40 mL) in 80 mL ethanol.
26		1.5 g BPO + 15 mL Styrene	20121	4.20 ± 0.37	
27		2.0 g BPO + 20 mL Styrene	23404	6.17 ± 0.23	
28		2.5 g BPO + 25 mL Styrene	23283	6.54 ± 0.30	
29		3.0 g BPO + 30 mL Styrene	23087	7.92 ± 0.22	
30		3.5 g BPO + 35 mL Styrene	22944	10.84 ± 0.95	
31		4.0 g BPO + 40 mL Styrene	22871	13.46 ± 1.04	

Note: M.W. is the weight average, and particle size is calculated from the measurement of the particles in the corresponding SEM images.

***Table S4*.** Texture properties of the polystyrene microspheres obtained from the reaction between various volumes of styrene (5 - 40 mL) and 1.0 g BPO and 1.0 g PVP in 80 mL ethanol

Volume of Styrene (mL)	Porosity (%)	Total Intrusion Volume (mL g^{-1})	Total Pore Area (m^2 g^{-1})	Average Pore Diameter (nm)	Stem Volume Used (%)
5	54.72	1.038	24.93	166.5	69
10	56.86	1.133	24.24	187.0	72
15	50.05	0.882	23.34	151.2	49
20	43.07	0.660	31.35	84.2	41
25	45.01	0.712	26.02	109.5	45
30	52.22	0.954	23.67	161.2	58
35	51.65	0.939	27.66	135.8	58
40	53.08	0.989	22.11	178.8	61

Note: The experiments were carried out with mercury intrusion porosimetry at room temperature.

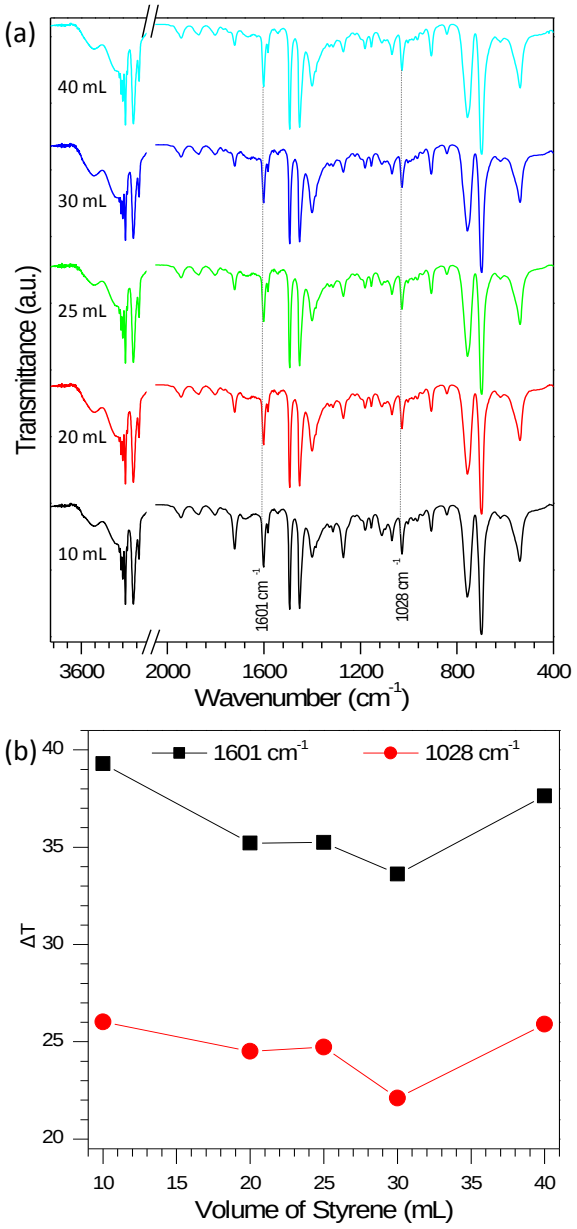

Figure S16. **(a)** FT-IR spectra of PS particles before adsorption of verapamil in methanol solution, in which the PS samples were prepared by reaction of various volumes of styrene (10 – 40 mL) and 1.0 g BPO in the presence of 1.0 g PVP in 80 mL ethanol solution; **(b)** Plots of the transmittance differences (ΔT) of the characteristic peaks at 1601 cm^{-1} and 1028 cm^{-1} with varying the volume of styrene in PS preparation.

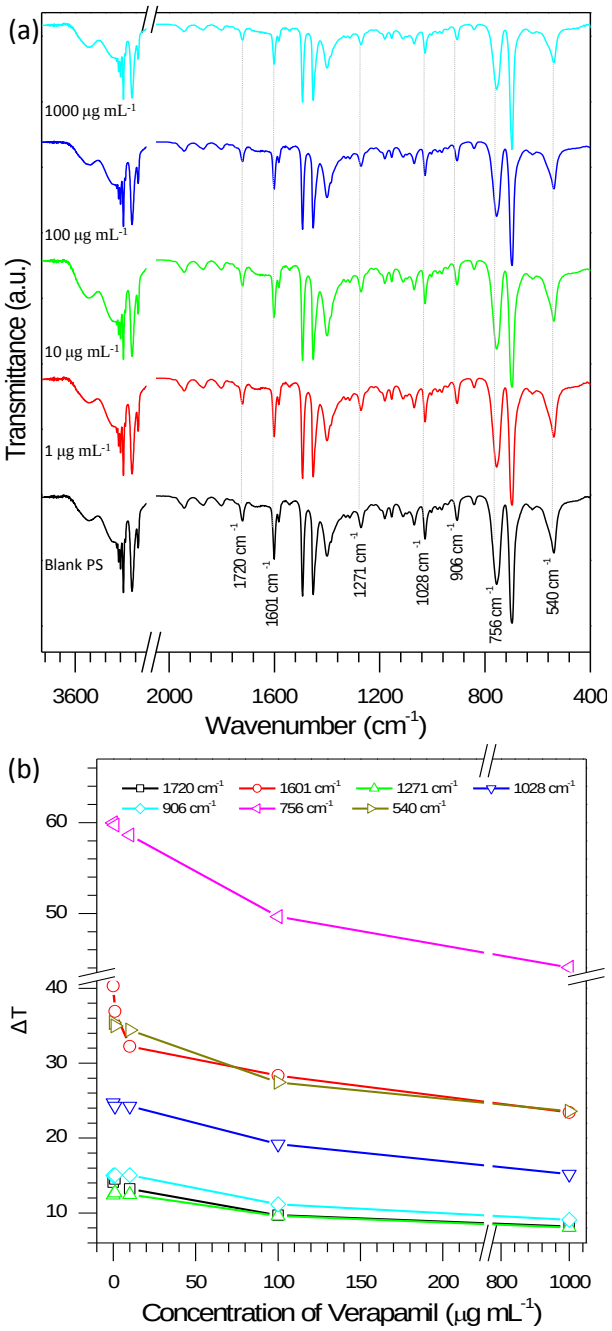

Figure S17. **(a)** FT-IR spectra of PS particles before (Blank PS) and after adsorption of verapamil in methanol solution containing 1 μg mL^{-1}, 10 μg mL^{-1}, 100 μg mL^{-1} and 1000 μg mL^{-1} (as indicated in the figure) verapamil for 3 h, in which PS samples were prepared by reaction of 25 mL styrene and 1.0 g BPO in the presence of 1.0 g PVP in 80 mL ethanol solution; **(b)** Plots of the transmittance differences (ΔT) of the characteristic peaks at 1720, 1601, 1271, 1028, 906, 756 and 540 cm^{-1} with varying the concentration of verapamil in methanol solution for adsorption.

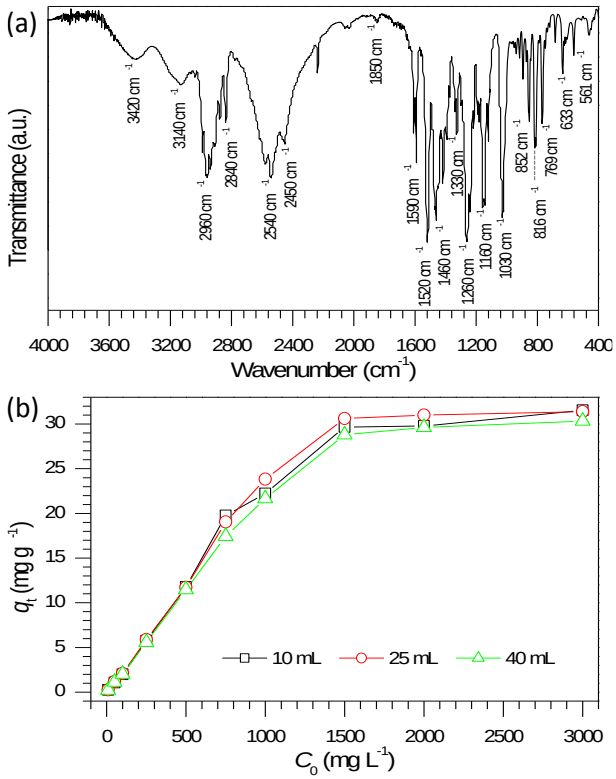

Figure S18. **(a)** FT-IR spectra of verapamil; **(b)** adsorption isotherm of verapamil on the PS particles (amount of PS particles: 0.2 g, solvent volume: 10 mL methanol, adsorption time: 1 h), in which PS samples were prepared by reaction of 10 mL, 25 mL and 40 mL styrene and 1.0 g BPO in the presence of 1.0 g PVP in 80 mL ethanol solution, respectively.

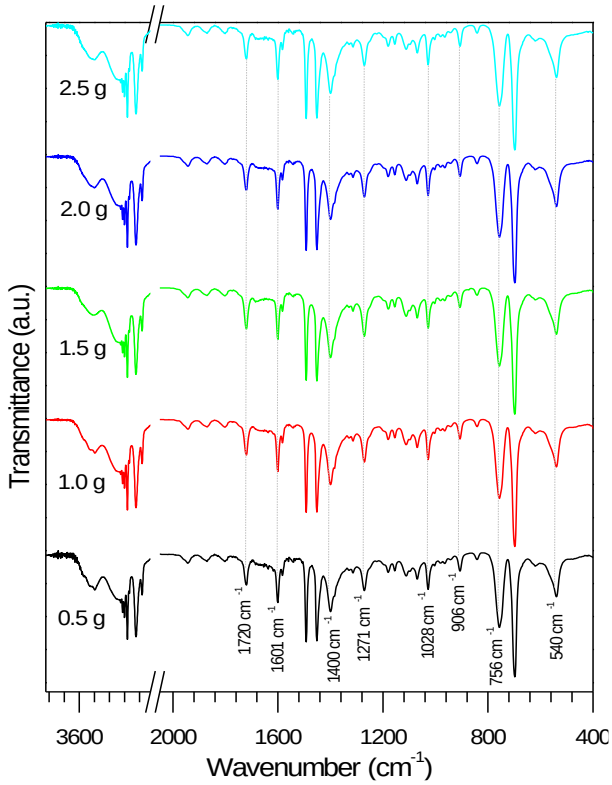

Figure S19. FT-IR spectra of PS particles after adsorption of verapamil in methanol solution containing 1000 μg mL^{-1} verapamil for 3 h, in which PS samples were prepared by reaction of 25 mL styrene and 1.0 g BPO in the presence of various amounts of PVP (0.5 – 2.5 g) in 80 mL ethanol solution.

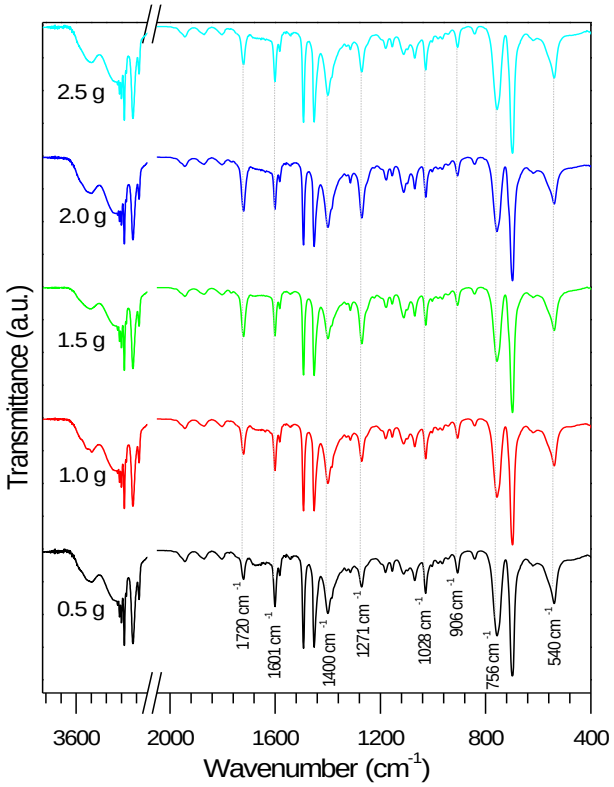

Figure S20. FT-IR spectra of PS particles after adsorption of verapamil in methanol solution containing 1000 μg mL^{-1} verapamil for 3 h, in which PS samples were prepared by reaction of 25 mL styrene and various amounts of BPO (0.5 – 2.5 g) in the presence of 1.0 g PVP in 80 mL ethanol solution.

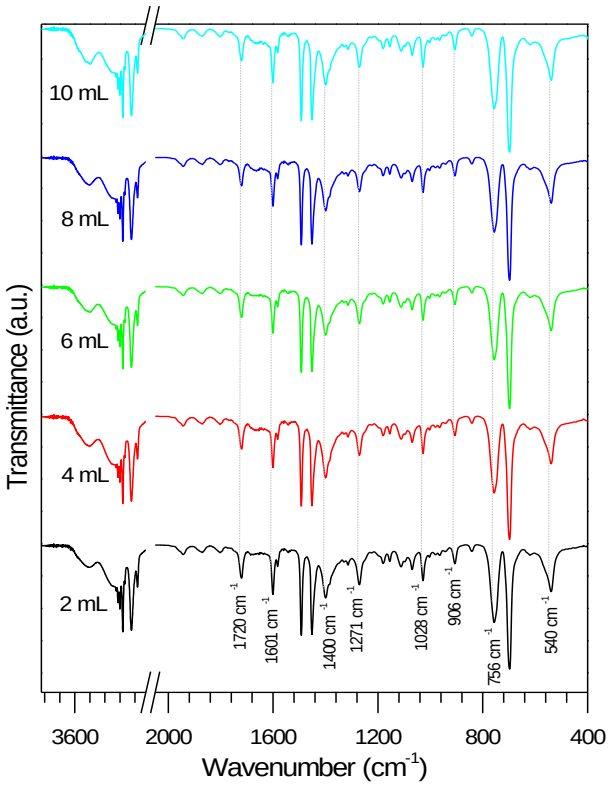

Figure S21. FT-IR spectra of PS particles after adsorption of verapamil in methanol solution containing 1000 μg mL^{-1} verapamil for 3 h, in which PS samples were prepared by reaction of 25 mL styrene and 1.0 g BPO in the presence of 1.0 g PVP and various volumes of H_2O (2 – 10 mL) and ethanol (78 - 70 mL), and the total volume of H_2O and ethanol was 80 mL.

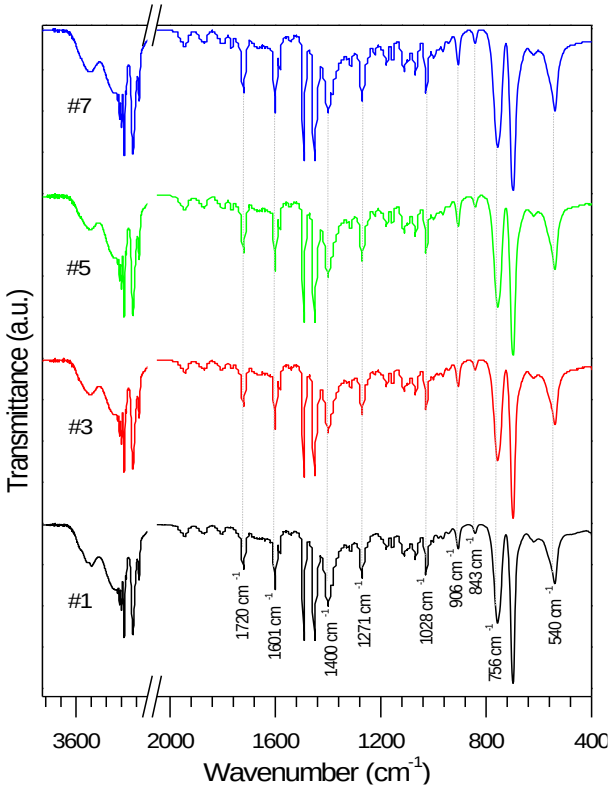

Figure S22. FT-IR spectra of PS particles after adsorption of verapamil in methanol solution containing 1000 μg mL^{-1} verapamil for 3 h, in which PS samples were prepared by reaction of various amounts of BPO/styrene (**#1** means 1.0 g BPO and 10 mL styrene; **#3** means 2.0 g BPO and 20 mL styrene; **#5** means 3.0 g BPO and 30 mL styrene; **#7** means 4.0 g BPO and 40 mL styrene) in the presence of 1.0 g PVP in 80 mL ethanol solution.

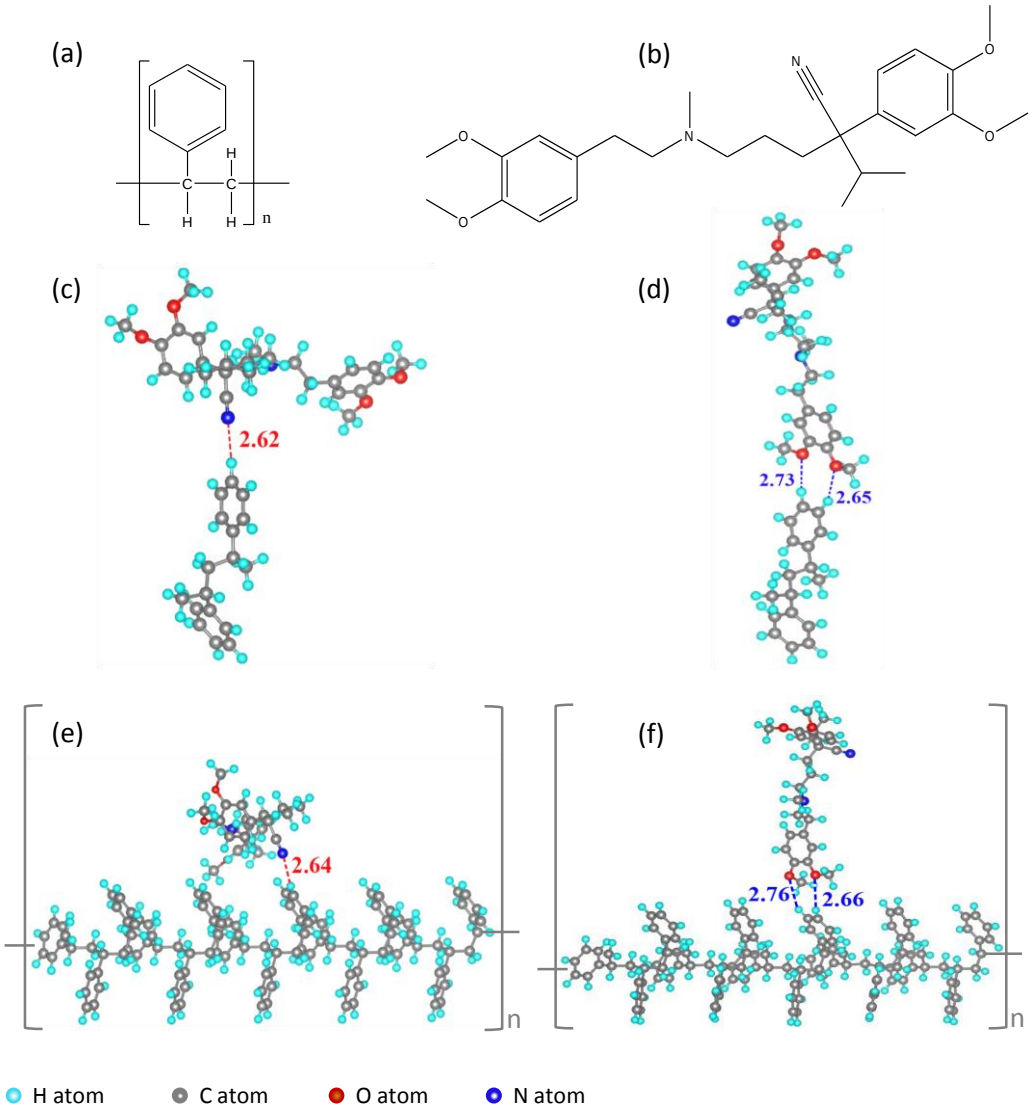

Figure S23. **(a-b)** Schematic structures of **(a)** polystyrene and **(b)** verapamil; (**c-f**) Intermolecular interactions (**c**, **d**) between verapamil and 2,4-dipenyl pentane and (**e**, **f**) between verapamil and polystyrene via H-N and H-O hydrogen bond interactions, respectively. The bond lengths of H-N and H-O hydrogen bonds are in Ångströms. The isolated systems of (**c, d**) verapamil and 2,4-dipenyl pentane were carried out using Gaussian09 program package and the periodic systems of (**e**, **f**) verapamil and polystyrene were carried out using DMol3 package.

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