Supporting Information

Development of magnetic molecularly imprinted polymers with double templates for the rapid and selective determination of carbamazepine and lamotrigine in serum

Ya-qin Wei[a, #], Lin-lin Zhao[a, #], Yu-xin You[a, #], Yan-lin Zhao[b], Xiao-xiao Zheng[c], Yan Du[a], Dao-quan Tang[a, d, *]

[a]Jiangsu Key Laboratory of New Drug Research and Clinical Pharmacy, Xuzhou Medical University, Xuzhou 221004, China

[b]Department of Pharmacy, Suining People's Hospital Affiliated to Xuzhou Medical University, Suining 221202, China

[c]Department of Pharmacy, Xuzhou Municipal Hospital Affiliated to Xuzhou Medical University, Xuzhou 221002, China

[d]Department of Pharmaceutical Analysis, Xuzhou Medical University, Xuzhou 221204, China

[#]These authors contributed to the work equally and should be regarded as co-first authors.

*Correspondence: Professor Dao-quan Tang, Department of Pharmaceutical Analysis, Xuzhou Medical University, 209 Tongshan Road, Xuzhou City, Jiangsu Province, P.R. China.

Tel & Fax: +86 516 83263133

E-mail address: tdq993@hotmail.com or tangdq@xzhmu.edu.cn (D.Q. Tang)

Table S1 Linearity, ranges and lower limit of quantification (LLOQ) of LTG and CBZ in rat serum treated by dispersive Dt-MMIPs SPE and acetonitrile protein precipitation (n=5)

Analyte	Dt-MMIPs		Acetonitrile protein precipitation		Ranges	LLOQ
	Regression equation	R^2	Regression equation	R^2	(μg/mL)	(μg/mL)
LTG	y=11670x+26686	0.9998	y=8757.7x-548.13	0.9999	1.25~50	1.25
CBZ	y=24774x+29200	0.9992	y=15290x+2073.5	0.9996	1.25~50	1.25

Table S2 Intra-batch accuracy and precision of LTG and CBZ in rat serum treated by dispersive Dt-MMIPs SPE and acetonitrile protein precipitation (Mean±SD, n=5)

Analyte	Nominal concentration (μg/mL)	Dt-MMIPs			Acetonitrile protein precipitation		
		Found (μg/mL)	Accuracy (%)	RSD （%）	Found (μg/mL)	Accuracy (%)	RSD （%）
LTG	3	3.07	102.3±0.13	4.1	3.09	103.1±0.05	1.6
	25	24.80	99.2±0.70	2.8	25.04	100.2±0.65	2.6
	37.5	37.86	101.0±0.53	1.4	37.36	99.6±0.64	1.7
CBZ	3	2.65	88.3±0.27	10.3	2.88	96.0±0.04**	1.4
	25	25.26	101.0±0.15	0.6	25.17	100.7±0.79	3.1
	37.5	38.21	101.9±0.11	0.3	37.59	100.2±0.59	1.6

**P<0.01 vs Dt-MMIPs

Table S3 Inter-batch accuracy and precision of LTG and CBZ in rat serum treated by dispersive Dt-MMIPs SPE and acetonitrile protein precipitation (Mean±SD, n=15)

Analyte	Nominal concentration (μg/mL)	Dt-MMIPs			Acetonitrile protein precipitation		
		Found (μg/mL)	Accuracy (%)	RSD （%）	Found (μg/mL)	Accuracy (%)	RSD （%）
LTG	3	3.05	101.8±0.16	5.1	3.09	103.2±0.09	3.0
	25	24.92	99.7±0.79	3.2	24.87	99.50±0.51	2.1
	37.5	38.08	101.6±0.49	1.3	37.88	101.0±1.08	2.9
CBZ	3	2.63	87.9±0.24	9.1	2.83	94.30±0.05*	1.9
	25	25.34	101.4±0.29	1.1	25.22	100.9±0.72	2.9
	37.5	38.31	102.2±0.15	0.4	37.36	99.63±0.55	1.5

*P<0.05 vs Dt-MMIPs

Table S4 Extraction recovery of LTG and CBZ in rat serum treated by dispersive Dt-MMIPs SPE and acetonitrile protein precipitation (Mean±SD, n=5)

Analyte	Nominal concentration (μg/mL)	Dt-MMIPs		Acetonitrile protein precipitation	
		Recovery (%)	RSD (%)	Recovery (%)	RSD (%)
LTG	25	78.99±0.03	3.63	94.37±0.03**	2.94
	37.5	76.55±0.01	1.67	89.48±0.03**	3.24
CBZ	25	87.31±0.44	0.50	94.18±0.01*	1.24
	37.5	85.11±0.58	0.68	90.27±0.01*	1.28

*P<0.05, **P<0.01 vs Dt-MMIPs

Table S5 The stability of LTG and CBZ in the supernatant of rat serum treated dispersive Dt-MMIPs SPE and acetonitrile protein precipitation at 4 °C or 25°C for 8 h (Mean±SD, n=5)

Analyte	Nominal concentration (μg/mL)	Dt-MMIPs				Acetonitrile protein precipitation			
		4 °C		25°C		4 °C		25°C	
		Residue (%)	RSD (%)	Residue (%)	RSD (%)	Residue (%)	RSD (%)	Residue (%)	RSD (%)
LTG	25	96.00±0.15	0.2	96.93±0.40	0.4	100.1±0.03	0.9	99.25±0.40	0.4
	37.5	104.3±0.06	0.1	101.9±0.01	1.0	101.8±0.01	0.1	101.6±0.43	0.5
CBZ	25	101.4±0.44	0.5	101.9±0.01	1.0	99.82±0.02	2.4	99.41±0.02	1.7
	37.5	106.3±0.59	0.6	105.4±0.46	0.5	101.8±0.01	0.6	100.5±0.01	1.2

Table S6 The concentrations of CBZ or LTG in rat serum of 2 h after oral administration of 10 mg/kg CBZ or LTG

Rat No.	CBZ (μg/mL)		LTG (μg/mL)	
	Dt-MMIPs	Acetonitrile protein precipitation	Dt-MMIPs	Acetonitrile protein precipitation
1	4.67	4.37	2.95	2.67
2	3.93	3.82	4.35	4.13
3	4.91	4.57	2.51	2.24
4	7.31	6.36	2.11	1.82
5	4.87	2.56	3.38	3.17
6	4.85	4.59	3.73	3.42
Mean±SD	5.09±1.15	4.38±1.23	3.17±0.82	2.91±0.84

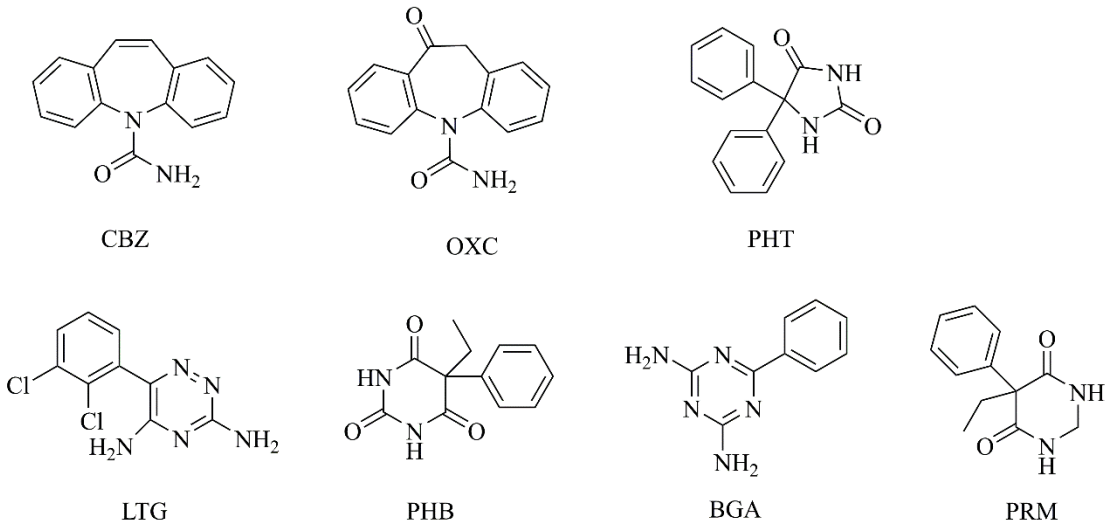

Fig. S1 The chemical structures of carbamazepine (CBZ), oxcarbazepine (OXC), phenytoin (PHT), lamotrigine (LTG), Phenobarbital (PHB), benzoguanamine (BGA) and primidone (PRM).

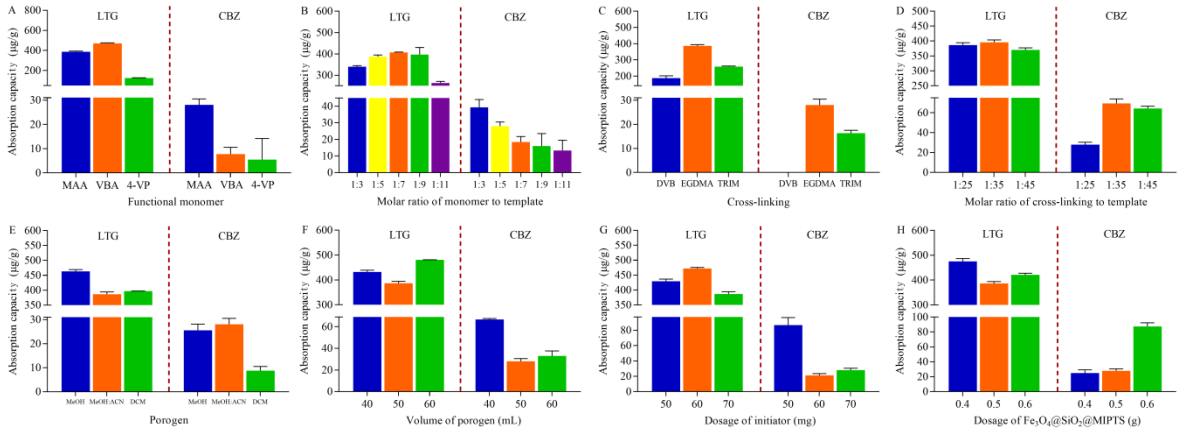

Fig. S2 Optimization of types and amounts of functional monomers, cross-linking, porogen, initiator and Fe_3O_4@SiO_2@MPTS.

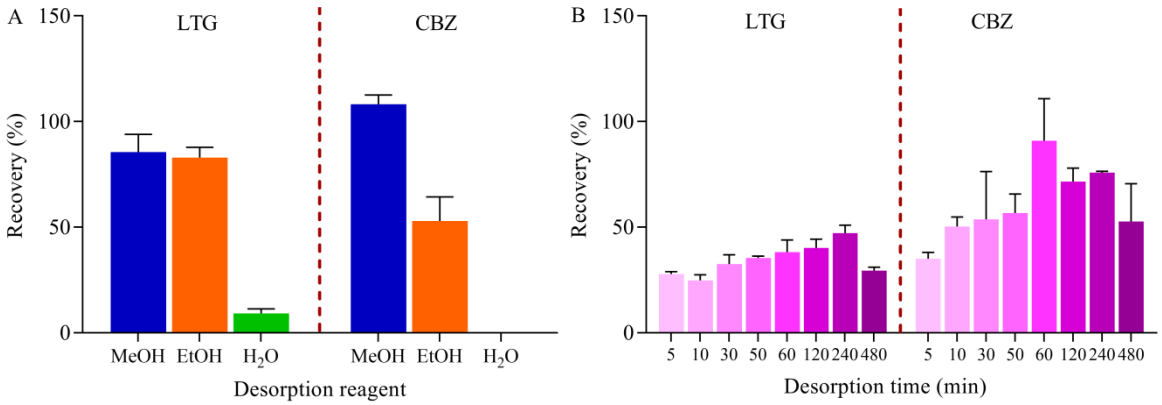

Fig. S3 Optimization of desorption reagent types (A) and desorption time (B).