SUPPLEMENTARY MATERIALS

HPLC conditions for determination of PHT in the optimization of MIPMs preparation

HPLC analysis was conducted on an Agilent 1290 UHPLC system containing an online degasser, two solvent delivery pumps, an auto-sampler, a column temperature controller and a diode array detector (Agilent Technologies, Wilmington, DE, USA). Sample was separation on an Aglient Zorbax SB-C18 column (150 mm × 4.6 mm, 5 μm) maintained at 35 °C. The mobile phase was consisted of methanol and water (70:30, v/v) at the flow of 1.0 mL/min. The auto-sampler temperature was set at 4°C. The injection volume was 10 μL and the detection wavelength was set at 240 nm.

HPLC conditions for determination of OXC, CBZ, MHD, CBZE, LTG and/or PHB in the adsorption performance evaluation of MIPMs

HPLC analysis was carried out on a Waters Alliance HPLC system consisting of Waters 2695 Separations Module connected to the Waters 2998 PDA Absorbance Detector. Samples separation was performed on an Aglient Zorbax SB-C18 column (150 mm × 4.6 mm, 5 μm) maintained at 35°C. The mobile phase was consisted of methanol and water (60:40, v/v) at the flow of 1.0 mL/min. The auto-sampler temperature was set at 4°C and the injection volume was 10 μL. The detection wavelength was set at 240 nm for PHT, 306 nm for OXC, 285 nm for CBZ, 307 nm for LTG, and 210 nm for PHB and DPG.

Table S1 Experimental parameters in the optimization of template type

No.	Template (mmol)		Functional monomer (mmol)	Cross-linking agent (mmol)		Initiator (mmol)	Porogen (mL)
	PHT	LTG	MMA	EGDMA	TRIM	AIBN	ACN-DMF (1:1.5, v/v)
1	0.20	-	6.0	4.0	-	0.10	2.5
2	-	0.20	6.0	-	4.0	0.10	2.5

OXC, oxcarbazepine; CBZ, carbamazepine; MMA, methyl methacrylate; EGDMA, ethylene glycol dimethacrylate; TRIM, trimethylolpropane trimethacrylate; AIBN, azobisisbutyronitrile; ACN, acetonitrile; DMF, N,N-dimethylformamide

Table S2 Experimental parameters in the optimization of template amount

No.	Template (mmol)	Functional monomer (mmol)	Cross-linking agent (mmol)	Initiator (mmol)	Porogen (mL)
	PHT	MMA	EGDMA	AIBN	ACN-DMF (1:1.5, v/v)
1	0.10	6.0	4.0	0.10	2.5
2	0.15	6.0	4.0	0.10	2.5
3	0.20	6.0	4.0	0.10	2.5
4	0.25	6.0	4.0	0.10	2.5
5	0.30	6.0	4.0	0.10	2.5

Table S3 Experimental parameters in the optimization of functional monomer type

No.	Template (mmol)	Functional monomer (mmol)					Cross-linking agent (mmol)	Initiator (mmol)	Porogen (mL)
	PHT	MAA	VBA	MAAm	MMA	AM	EGDMA	AIBN	ACN-DMF (1:1.5, v/v)
1	0.20	6.0	-	-	-	-	4.0	0.10	2.5
2	0.20	-	6.0	-	-	-	4.0	0.10	2.5
3	0.20	-	-	6.0	-	-	4.0	0.10	2.5
4	0.20	-	-	-	6.0	-	4.0	0.10	2.5
5	0.20	-	-	-	-	6.0	4.0	0.10	2.5

MAA, methacrylic acid; VBA, 4-vinylbenzoic acid; MAAm, methacrylamide; AM, acrylamide

Table S4 Experimental parameters in the optimization of functional monomer amount

No.	Template (mmol)	Functional monomer (mmol)	Cross-linking agent (mmol)	Initiator (mmol)	Porogen (mL)
	PHT	MMA	EGDMA	AIBN	ACN-DMF (1:1.5, v/v)
1	0.20	4.0	4.0	0.10	2.5
2	0.20	5.0	4.0	0.10	2.5
3	0.20	6.0	4.0	0.10	2.5
4	0.20	7.0	4.0	0.10	2.5
5	0.20	8.0	4.0	0.10	2.5

Table S5 Experimental parameters in the optimization of cross-linking agent type

No.	Template (mmol)	Functional monomer (mmol)	Cross-linking agent (mmol)		Initiator (mmol)	Porogen (mL)
	PHT	MMA	EGDMA	TRIM	AIBN	ACN-DMF (1:1.5, v/v)
1	0.20	6.0	4.0	-	0.10	2.5
2	0.20	6.0	-	4.0	0.10	2.5

Table S6 Experimental parameters in the optimization of cross-linking agent amount

No.	Template (mmol)	Functional monomer (mmol)	Cross-linking agent (mmol)	Initiator (mmol)	Porogen (mL)
	PHT	MMA	EGDMA	AIBN	ACN-DMF (1:1.5, v/v)
1	0.20	6.0	2.0	0.10	2.5
2	0.20	6.0	3.0	0.10	2.5
3	0.20	6.0	4.0	0.10	2.5
4	0.20	6.0	5.0	0.10	2.5
5	0.20	6.0	6.0	0.10	2.5

Table S7 Experimental parameters in the optimization of initiator amount

No.	Template (mmol)	Functional monomer (mmol)	Cross-linking agent (mmol)	Initiator (mmol)	Porogen (mL)
	PHT	MMA	EGDMA	AIBN	ACN-DMF (1:1.5, v/v)
1	0.20	6.0	4.0	0.050	2.5
2	0.20	6.0	4.0	0.075	2.5
3	0.20	6.0	4.0	0.10	2.5
4	0.20	6.0	4.0	0.15	2.5
5	0.20	6.0	4.0	0.20	2.5

Table S8 Experimental parameters in the optimization of porogen type

No.	Template (mmol)	Functional monomer (mmol)	Cross-linking agent (mmol)	Initiator (mmol)	Porogen (mL)				
	PHT	MMA	EGDMA	AIBN	ACN	ACN-DMF (v/v)			
						1.5:1	1:1	1:1.5	1:2
1	0.20	6.0	4.0	0.10	2.5	-	-	-	-
2	0.20	6.0	4.0	0.10	-	2.5	-	-	-
3	0.20	6.0	4.0	0.10	-	-	2.5	-	-
4	0.20	6.0	4.0	0.10	-	-	-	2.5	-
5	0.20	6.0	4.0	0.10	-	-	-	-	2.5

Table S9 Experimental parameters in the optimization of supporting membrane type

No.	Membrane	Template (mmol)	Functional monomer (mmol)	Cross-linking agent (mmol)	Initiator (mmol)	Porogen (mL)
		PHT	MMA	EGDMA	AIBN	ACN-DMF (1:1.5, v/v)
1	PVDF	0.20	6.0	4.0	0.10	2.5
2	PP	0.20	6.0	4.0	0.10	2.5
3	PTFE	0.20	6.0	4.0	0.10	2.5
4	NY-66	0.20	6.0	4.0	0.10	2.5

PVDF, polyvinylidene difluoride; PP, polypropylene; PTFE, polytetrafluoroethylene, NY-66, nylon 66

Table S10 Reproducibility experiment of PHT-MIPMs preparation (n = 3)

	Adsorption capacity of PHT ($mg \cdot g^{-1}$)			Mean ± SD	RSD (%)
1	2.32	2.41	2.34	2.36 ± 0.05	0.02
2	2.40	2.25	2.44	2.36 ± 0.10	0.04
3	2.51	2.48	2.35	2.45 ± 0.08	0.03
4	2.34	2.49	2.34	2.39 ± 0.08	0.03
5	2.38	2.39	2.22	2.33 ± 0.10	0.04
Total				2.38 ± 0.08	3.48

Table S11 Effect of dilution using phosphate buffer solution on the extraction recovery of MIPMs in plasma (n=5)

Analyte	Nominal concentration ($\mu g \cdot mL^{-1}$)	Recovery (%)					
		Dilution ratio of 2		Dilution ratio of 4		Dilution ratio of 8	
		Mean ± SD	RSD (%)	Mean ± SD	RSD (%)	Mean ± SD	RSD (%)
PHT	42.08	77.28 ± 0.81***	1.05	89.54 ± 1.16	1.30	90.44 ± 1.03	1.13
PHB	39.37	53.01 ± 1.23***	2.31	83.01 ± 0.89	1.07	83.58 ± 0.73	0.88
LTG	63.60	40.25 ± 0.68***	1.69	68.86 ± 0.26	0.38	68.86 ± 0.33	0.48

*$P < 0.05$, **$P < 0.01$, or ***$P < 0.001$ vs Dilution ratio of 4

Table S12 Extraction recovery of PHT and PHB in plasma treated by ACN protein precipitation or MIPMs (n=5)

Analyte	Nominal concentration ($\mu g \cdot mL^{-1}$)	Recovery (%)			
		ACN protein precipitation		MIPMs extraction	
		Mean ± SD	RSD (%)	Mean ± SD	RSD (%)
PHT	3.16	83.04 ± 3.87	4.67	92.85 ± 0.50***	0.54
	12.63	82.03 ± 0.84	1.03	87.64 ± 3.63**	4.14
	42.08	82.44 ± 1.18	1.43	88.47 ± 3.23**	3.65
PHB	2.95	82.27 ± 1.89	2.30	81.92 ± 2.20	2.68
	11.81	81.12 ± 1.26	1.55	82.60 ± 1.65	2.00
	39.37	80.80 ± 0.96	1.18	81.94 ± 1.57	1.92

*$P < 0.05$, **$P < 0.01$, or ***$P < 0.001$ vs ACN protein precipitation

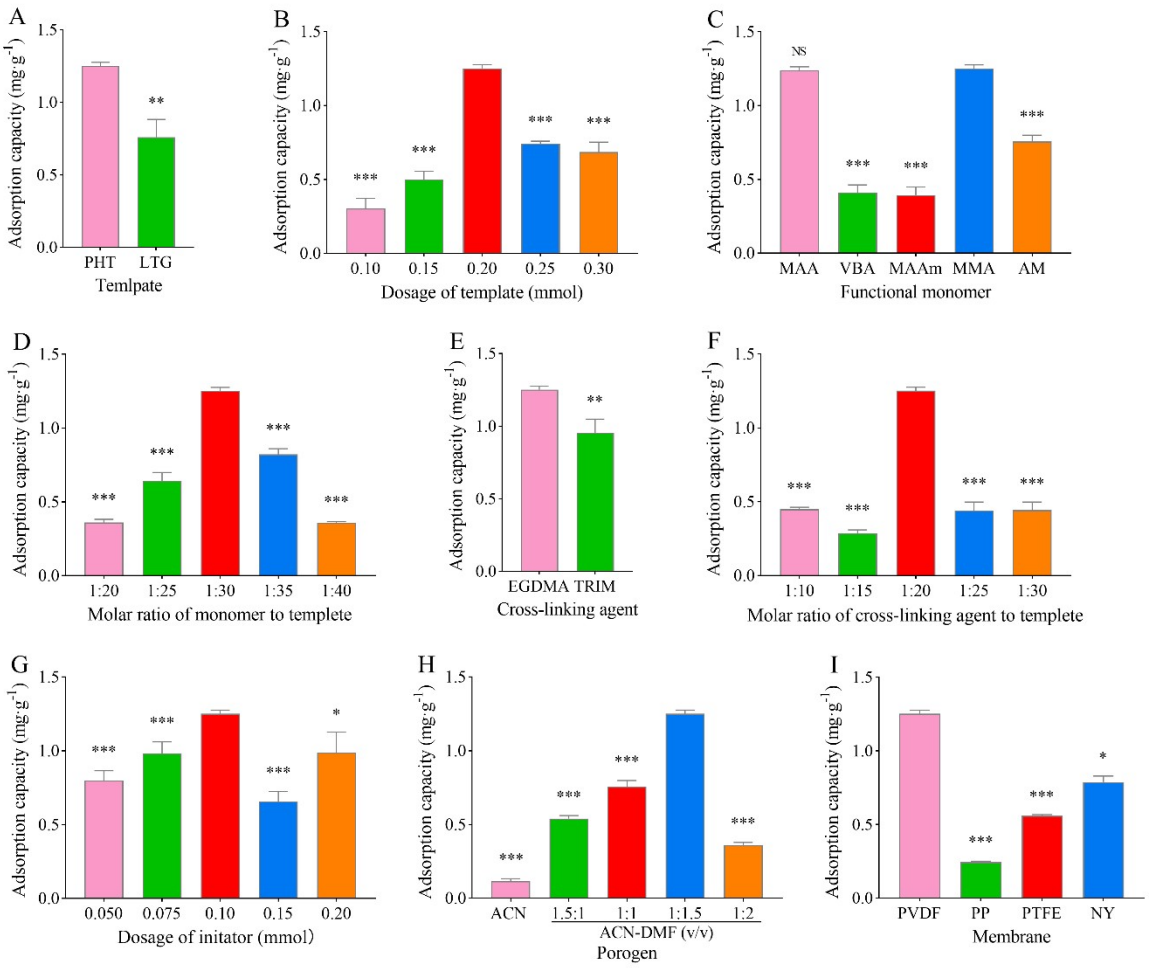

Figure S1 Influences of the types and amounts of template (A, B), functional monomer (C, D), cross-linking agent (E, F), initator (G), porogen (H), and membrane (I) on the adsorption capacity of PHT-MIPMs (n=5). *p<0.05, **p<0.01, or no significant difference (NS) vs. PHT (A), template of 0.25 mmol (B), MMA (C), molar ratio of 1:30 (D), EGDMA (E), molar ratio of 1:20 (F), initator of 0.10 mmol (G), ACN-DMF (1:1.5, v/v) (H), or PVDF (I).

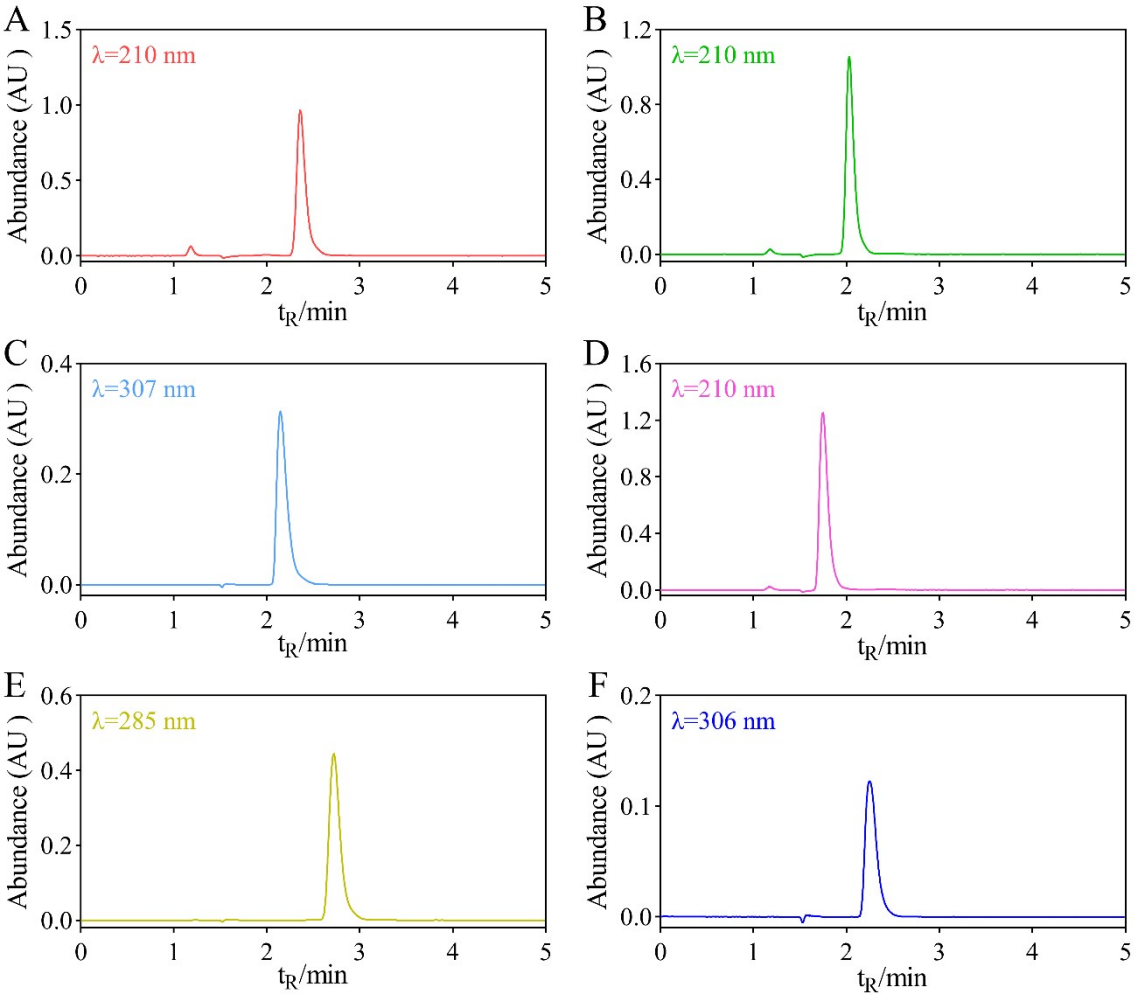

Fig. S2 Representative chromatograms of PHT (A), PHB (B), LTG (C), DPG (D), OXC (E), and CBZ (F).

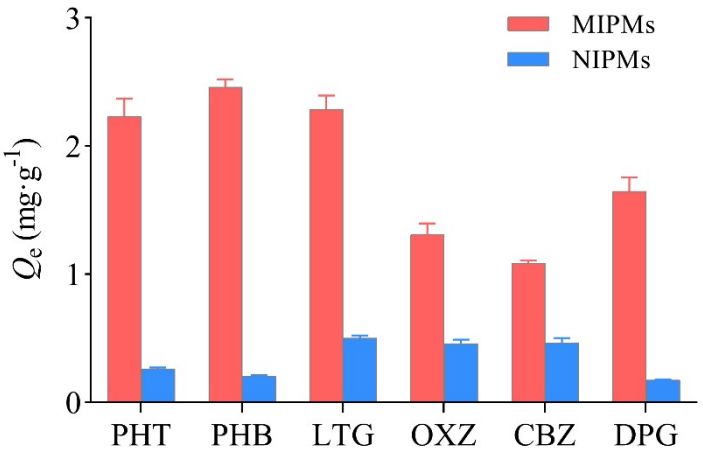

Fig. S3 Adsorption selectivity plots of MIPMs and NIPMs towards on PHT, PHT, LTG, DPG, OXC, and CBZ. n = 3.

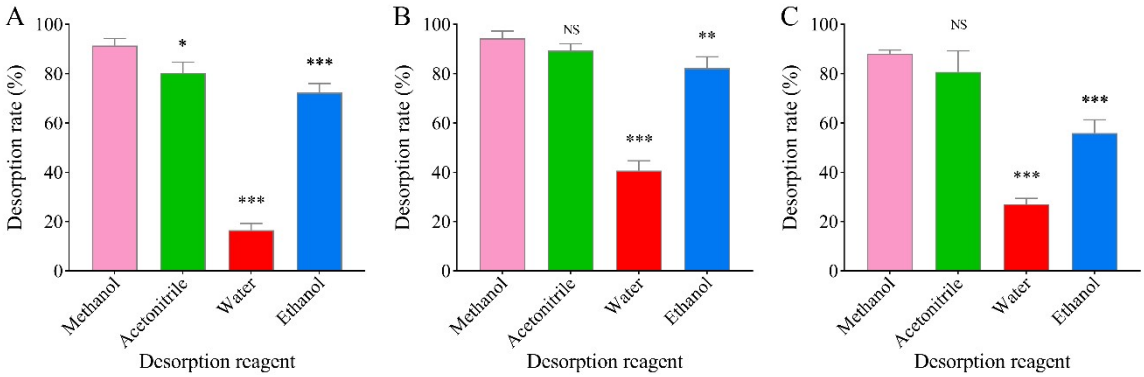

Fig. S4 Influences of different types of desorption reagent on the desorption rate of PHT (A), PHB (B) and LTG (C) adsorbed by MIPMs. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ vs MeOH; NS means no significance; n = 3.

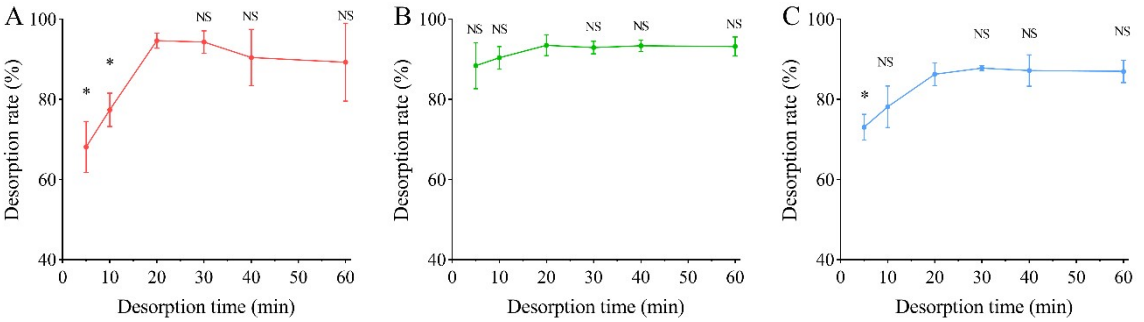

Fig. S5 Influences of different desorption time on the desorption rate of PHT (A), PHB (B) and LTG (C) adsorbed by PHT-MIPMs. *$P < 0.05$ vs desorption time of 20 min; NS means no significance; n = 3.

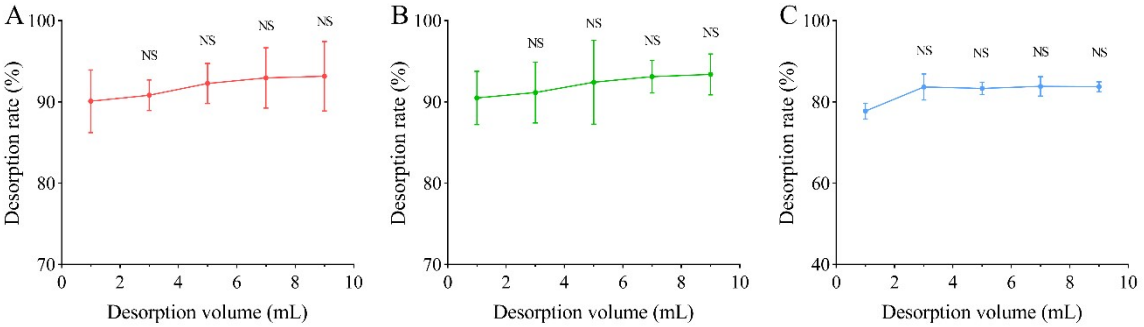

Fig.S6 Influences of different volumes of desorption reagent on the desorption rate of PHT (A), PHB (B) and LTG (C) adsorbed by PHT-MIPMs. NS means no significance by comparing with desorption volume of 1 mL; n = 3.

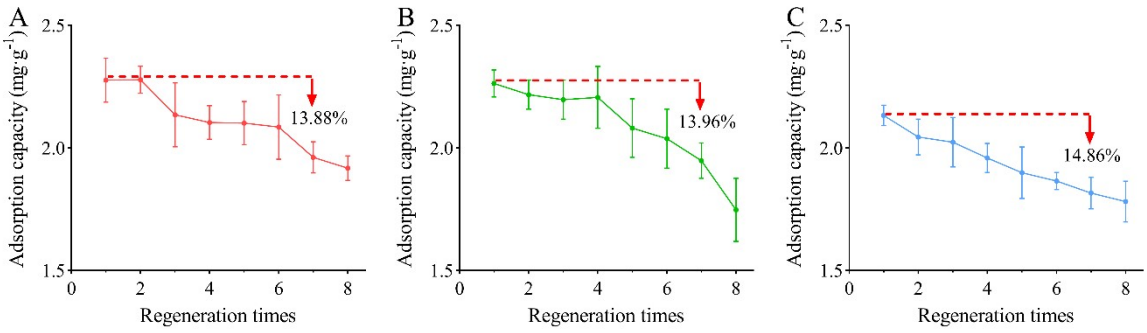

Fig. S7 Reusability of MIPMs towards PHT (A), PHB (B), and LTG (C). n = 3.

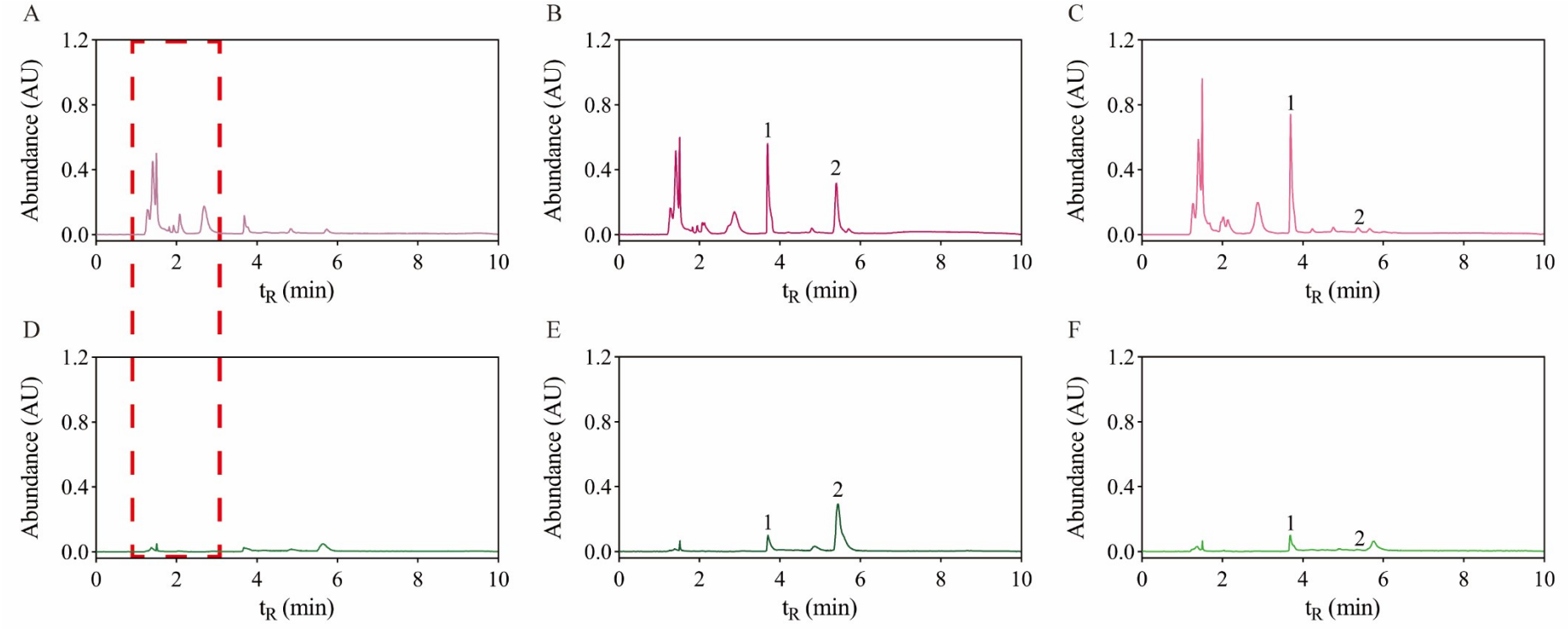

Fig. S8 Representative chromatogram of blank plasma, blank plasma spiked with reference standards and real rat plasma at 4.0 h after oral administration of 20 mg/kg PHT plus IS treated with ACN (A, B, C) or MIPMs (D, E, F). 1, IS, DPG; 2, PHT.

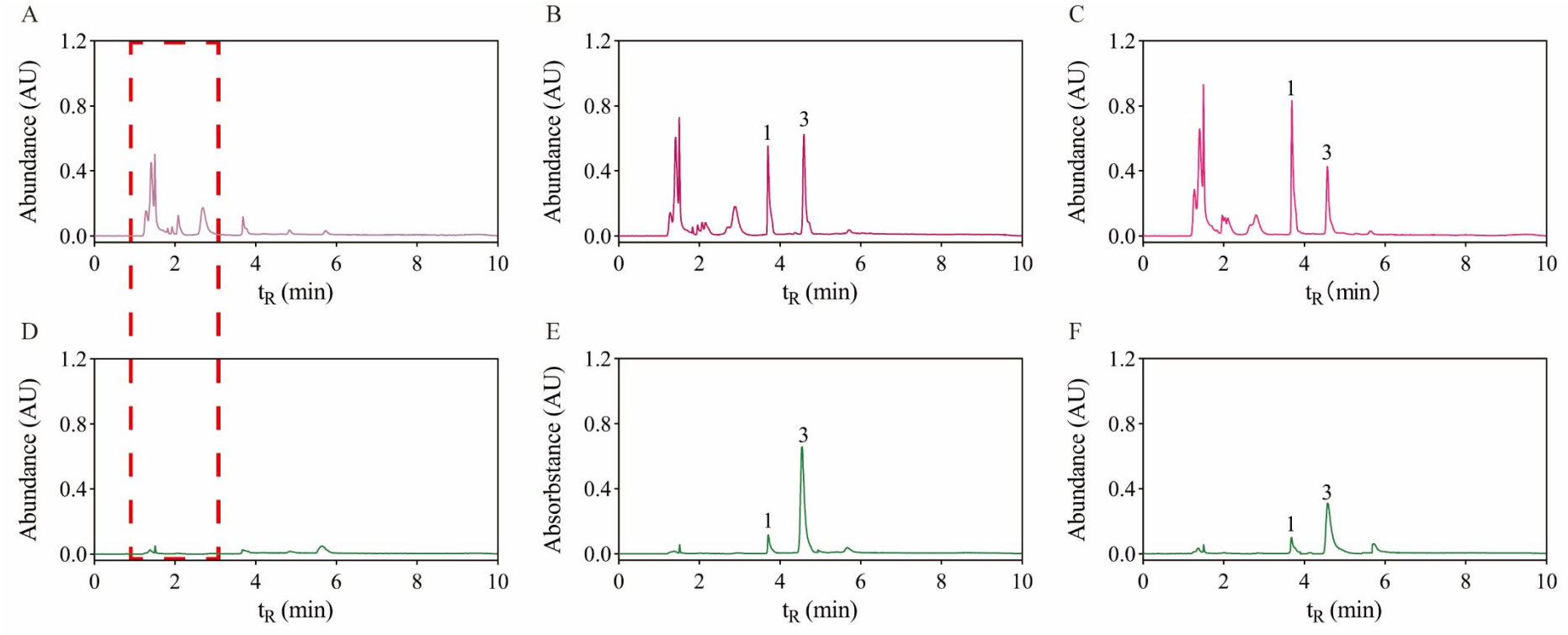

Fig. S9 Representative chromatogram of blank plasma, blank plasma spiked with reference standards and real rat plasma at 2.0 h after oral administration of 20 mg/kg PHB plus IS treated with ACN (A, B, C) or MIPMs (D, E, F). 1, IS, DPG; 3, PHB.