

Supplementary Material

Paper sensor for unbound valproic acid detecting in human serum

Experimental section

LC-MS/MS analysis

According to the previous report¹, VPA was analyzed by LC-MS/MS. The chromatographic conditions for the VPA detection were shown in Table S1. The multiple reaction monitoring (MRM) was used for MS/MS detection in negative electrospray ionization mode with the source temperature of 550 °C and the ion spray voltage of 5500 V. The MS/MS parameters were shown in Table S2. Other parameters were the curtain gas of 30 psi, ion source gas 1 and 2 of 50 psi. Finally, a series of VPA standards in methanol were prepared to establish a standard curve.

Sample preparation for LC-MS/MS

The pretreatment of the human serum was based on the previously described report with slight modifications¹. Briefly, the VPA standard (10 µL) was spiked in the human serum (40 µL) and then mixed with anhydrous methanol (150 µL) for 5 min. After centrifuging at 12000 rpm for 20 min, the supernatant (20 µL) was collected and dilute with MeOH/H₂O (180 µL, 50/50, v/v). The solution was fully mixed and centrifuged at 12000 rpm for 10 min before the supernatant was collected for LC-MS/MS analysis.

Table S1. The chromatographic conditions of LC-MS/MS analysis for detecting VPA.

Instrument conditions			
Chromatographic column	C18 ethylene-bridged column (2.1 × 50 mm, 2.5 μm XBridge, Waters Corporation, Milford, MA, USA)		
Column temperature	40°C		
Injection volume	2 μL		
Flow rate	0.3 mL/min		
Mobile phase A	Water containing 0.1% formic acid		
Mobile phase B	acetonitrile		
Gradient elution	time	A (%)	B (%)
	0	95	5
	1	95	5
	5	5	95
	7	5	95
	7.1	95	5
	10	95	5

Table S2. The MS/MS parameters.

	Parents	Daughter	Declustering	Collision
	(m/z)	(m/z)	Potential (V)	Energy (V)
VPA	143	143	-50	-11

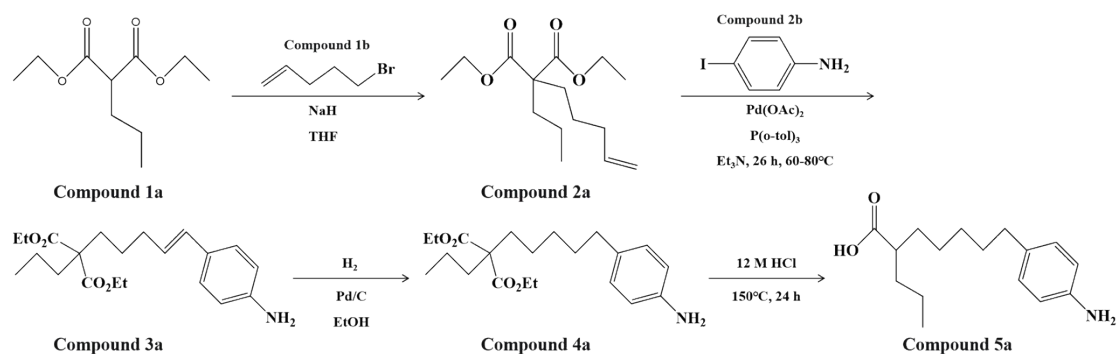


Fig. S1 The derivation of VPA hapten.

Fig. S2 (a) The LC-MS spectrum and (b) ^1H NMR results of VPA hapten.

Fig. S3 The calibration curve of VPA in methanol by LC-MS/MS.

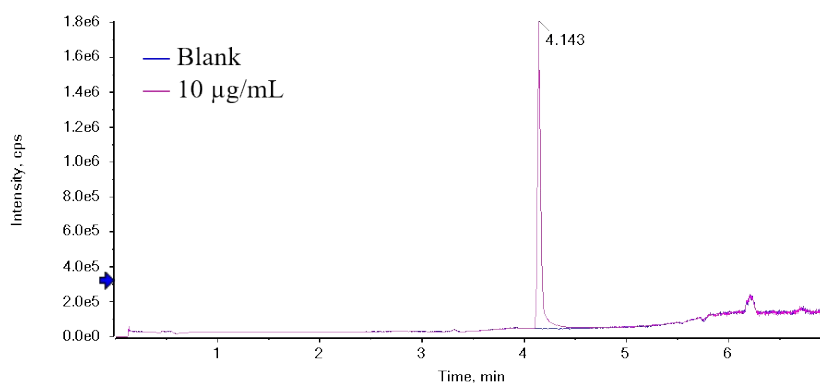


Fig. S4 LC-MS/MS chromatograms of 0 and 10 $\mu\text{g/mL}$ VPA spiked in human serum.

References

(1) Yang, X. P.; Jiang, Z. W.; Jiang, Y.; Ling, J.; Dong, L. L.; Zou, S. L.; Chen, R.; Hu, N. Determination of valproic acid and its six metabolites in human serum using LC-MS/MS and application to interaction with carbapenems in epileptic patients. *Biomed. Chromatogr.* **2023**, *37* (3), 12, Article. DOI: 10.1002/bmc.5572.