Electronic Supplementary Material (ESI) for RSC Advances.

Valproic acid analysis by mass spectrometry part I: Enhanced determination of valproic acid by microwave assisted chemical labeling

Supporting Information

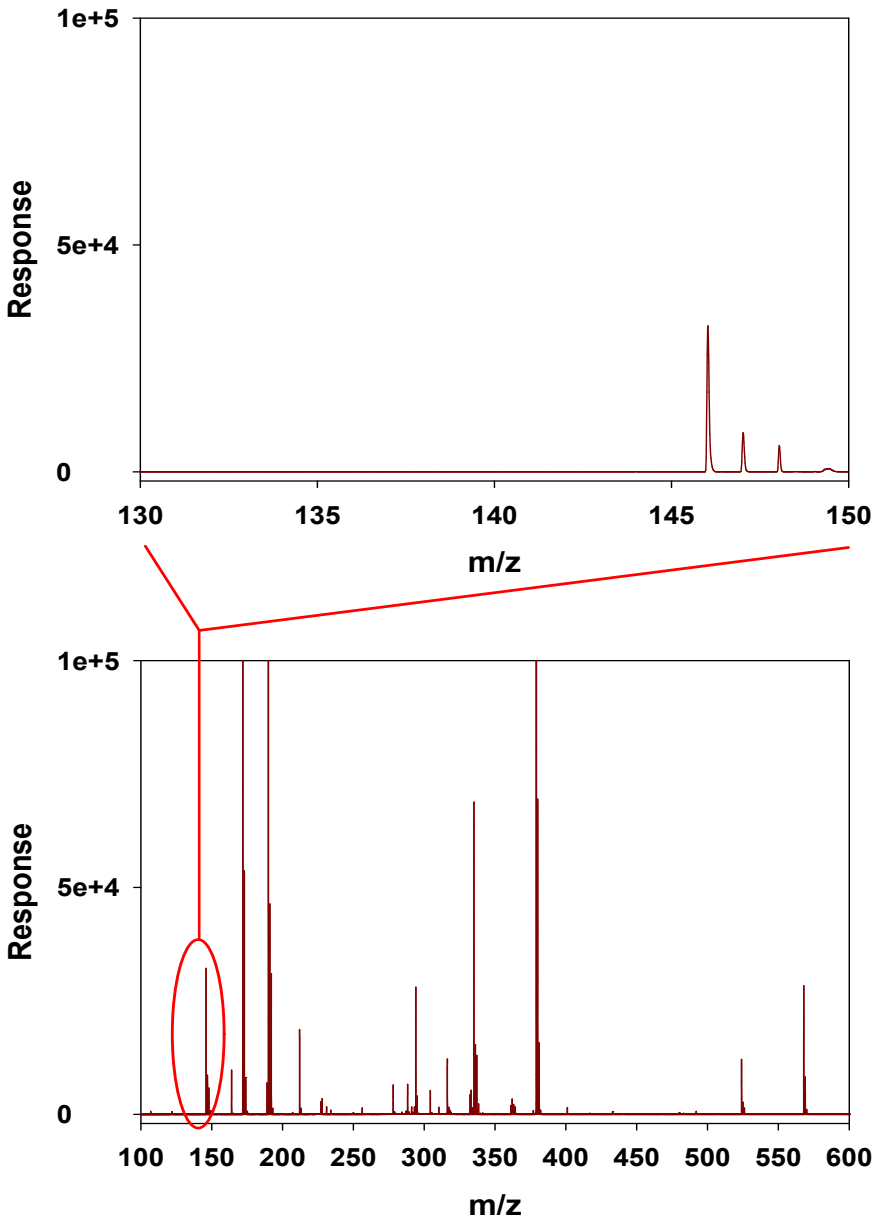

Figure S1. Mass spectra for MALDI-TOF MS of VA 1000 μM and no significant signals or matrix ion clusters were detected at $[M+H]^+$ 145.

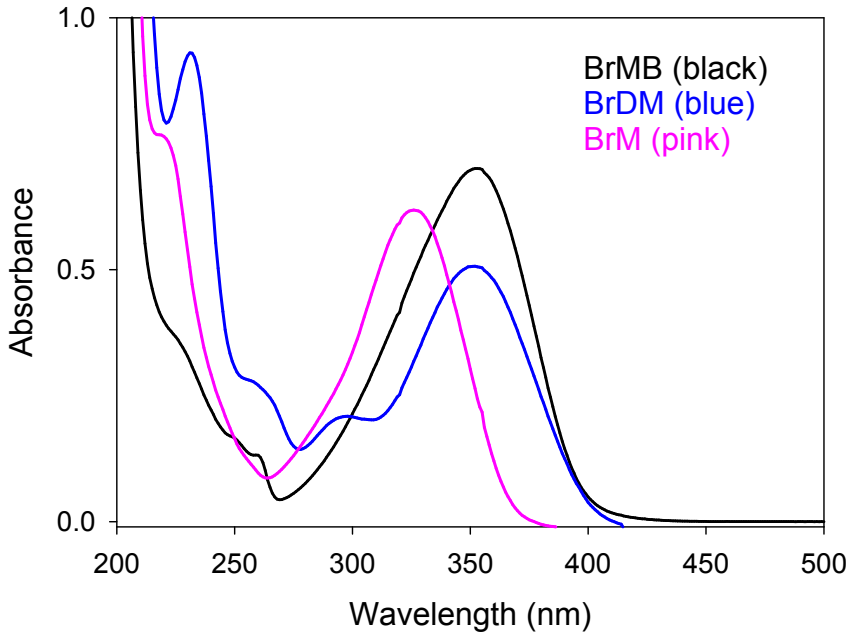

Figure S2. Maximum absorbent wavelength (λ_{max}) of three derivatization reagents, BrM, BrDM and BrMB.

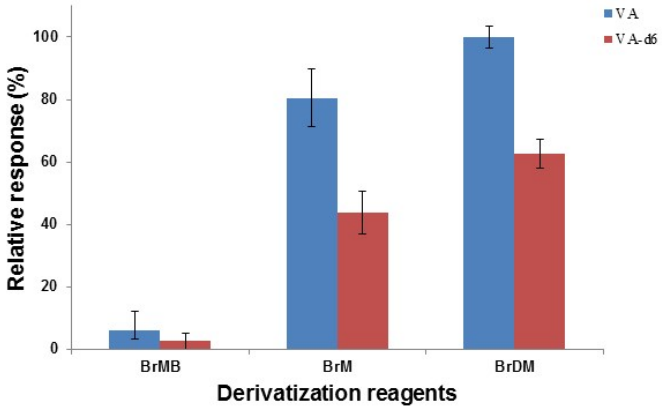

Figure S3. Effects of different derivatization reagents on the formation of VA and VA-d6 derivatives.

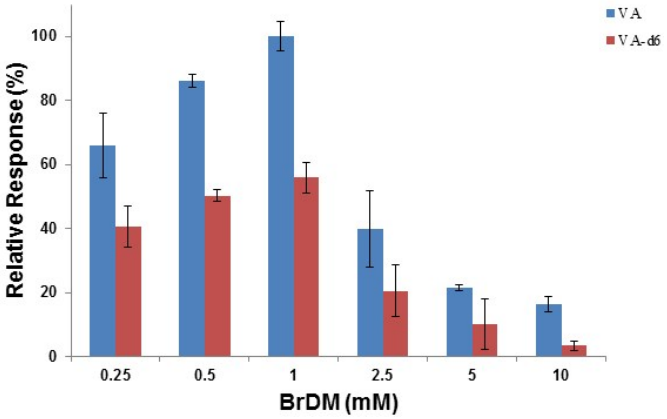

Figure S4. Effects of varying concentrations (0.25-10 mM) of BrDM on the formation of VA and VA-d6 derivatives.

Figure S5 shows that comparisons of varying quantities of 18-crown-6 (0-10 mM) revealed that 10 mM was optimal.

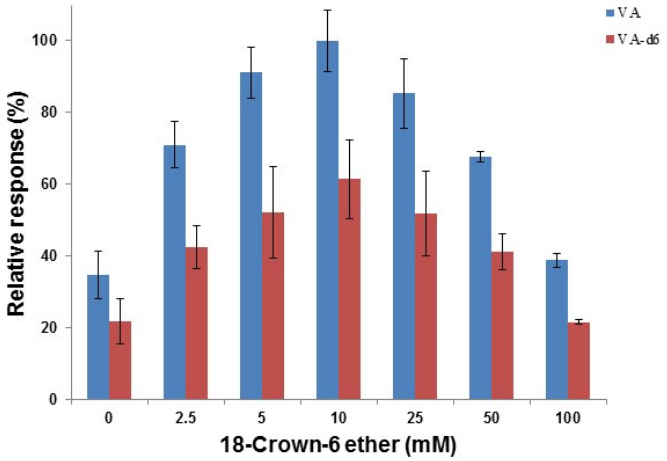

Figure S5. Effects of varying concentrations (0-100 mM) of catalyst 18-crown-6 on the formation of VA and VA-d6 derivatives.

Figure S6 shows that comparisons of three different potassium bases, (KOH, $KHCO_3$ and K_2CO_3, 2 mg ea) revealed that K_2CO_3 was the best basic activator.

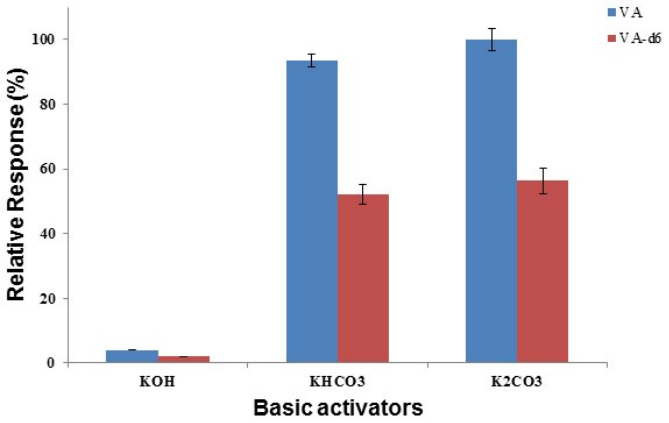

Figure S6. Effects of different basic activators (KOH, $KHCO_3$ and K_2CO_3) on the formation of VA and VA-d6 derivatives.

Figure S7 shows that comparisons of varying quantities of K_2CO_3 (0.5-6 mg) revealed that 2 mg was optimal.

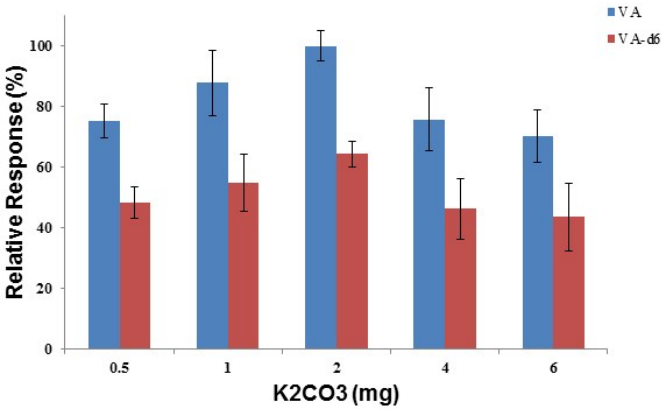

Figure S7. Effects of varying quantities (0.5-6 mg) of K_2CO_3 on the formation of VA and VA-d6 derivatives.

Figure S8 shows that comparisons of three different reaction solvents (toluene, acetone and acetonitrile) revealed that acetonitrile was optimal.

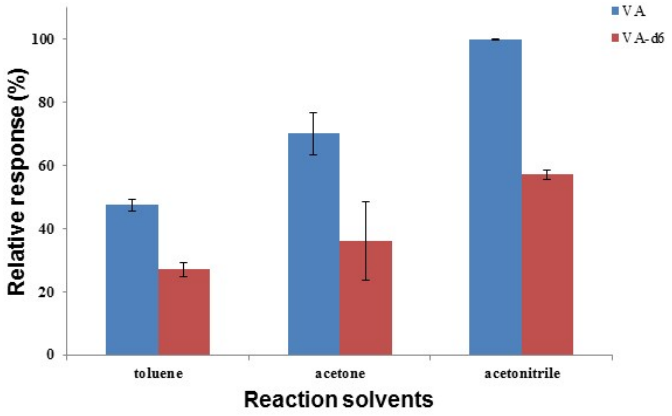

Figure S8. Effects of different reaction solvents (toluene, acetone and acetonitrile) on the formation of VA and VA-d6 derivatives.

Figure S9 shows that comparisons of varying microwave power (200-1100 W) revealed that 300 W was optimal.

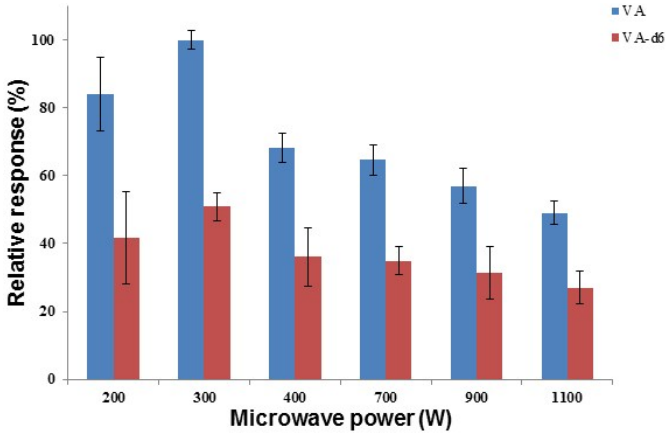

Figure S9. Effects of varying microwave power (200-1100 W) on the formation of VA and VA-d6 derivatives.

Figure S10 shows that comparisons of varying radiation times (2-10 min) revealed that 6 min was optimal.

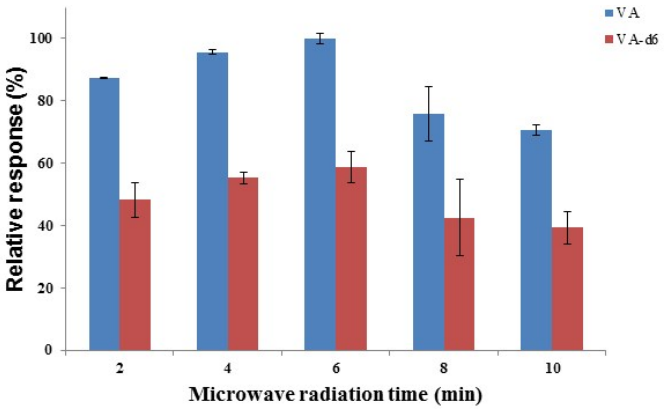

Figure S10. Effects of different microwave radiation times (2-10 min) on the formation of VA and VA-d6 derivatives.

Table S1. Assay results for valproic acid (VA) tablets

Tablet No.	Average weight (mg) [a]	Assay(%) [b]
1	145.92±2.01	100.63±1.39
2	143.97±8.74	99.29±6.03
3	150.07±5.42	107.47±1.53
4	150.55±1.22	104.97±0.23
5	148.46±2.43	102.39±1.68
6	144.67±1.83	99.77±1.26
7	151.53±4.00	104.50±2.76
8	149.49±0.97	103.09±0.67
9	152.90±1.85	105.45±1.27
10	147.53±2.44	101.74±1.68
Limit	145±14.50	90-110%

[a] average weight：mean weight ± SD

[b] assay(%)：recovery ± recovery SD

Table S2. Uniformity analysis results for valproic acid (VA) tablets

	Uniformity content (mg)			Uniformity content (%)		Uniformity content range	
Tablet	VA (mg)	SD	RSD (%)	Recovery	Recovery SD	Higher	Lower
1	148.54	2.90	1.95	102.44	2.00	150.64	145.22
2	148.59	2.56	1.72	102.47	1.77	151.12	145.99
3	148.80	3.59	2.41	102.62	2.48	151.22	144.68
4	149.83	0.73	0.49	103.33	0.51	150.68	149.37
5	151.16	0.92	0.61	104.25	0.63	152.20	150.48
6	150.29	0.94	0.63	103.65	0.65	151.14	149.29
7	149.80	3.72	2.48	103.31	2.57	152.25	145.51
8	152.92	7.25	4.74	105.46	5.00	160.91	146.75
9	148.58	4.58	3.08	102.47	3.16	151.56	143.31
10	151.10	1.95	1.29	104.20	1.34	152.57	148.89