Multiclass Analysis for the Determination of Pharmaceuticals and Their Main Metabolites in Leafy and Root Vegetables

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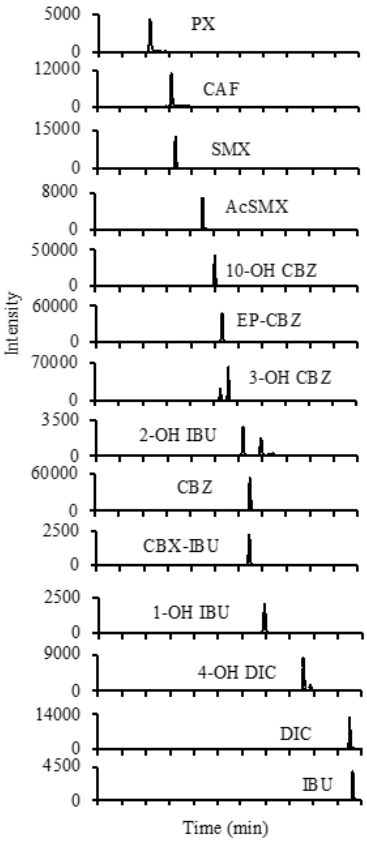


Figure S1. Chromatogram obtained from a spiked lettuce (10 ng g^{-1} dw).

Table S1. Box–Behnken design matrix for the optimization of clean-up sorbent amount.

Experiment	C18 amount (g)	PSA amount (g)	Florisil amount (g)
1	0.4	0.4	0.4
2	0.4	0.4	0.4
3	0	0.4	0
4	0.8	0	0.4
5	0.4	0	0.8
6	0.8	0.8	0.4
7	0.8	0.4	0.8
8	0.4	0.8	0
9	0.4	0	0
10	0.4	0.8	0.8
11	0	0	0.4
12	0.4	0.4	0.4
13	0	0.4	0.8
14	0.8	0.4	0
15	0	0.8	0.4

Table S2. Box–Behnken design matrix for the optimization of extraction solvent volume, UAE time extraction and number of extraction cycles.

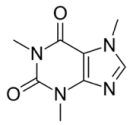
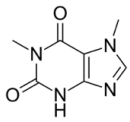
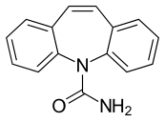
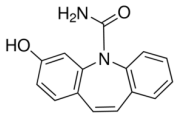
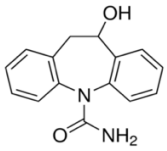
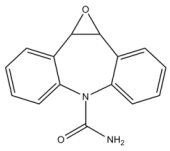
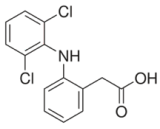
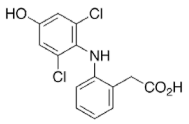
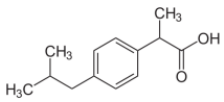
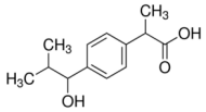
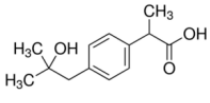
Experiment	Acetone (1% v/v, formic acid) volume (mL)	Time of extraction (min)	Number of extractions
1	6	10	1
2	6	15	2
3	4.5	10	2
4	4.5	5	1
5	3	10	1
6	6	5	2
7	6	10	3
8	4.5	5	3
9	3	10	3
10	4.5	15	1
11	4.5	10	2
12	4.5	10	2
13	4.5	15	3
14	3	15	2
15	3	5	2

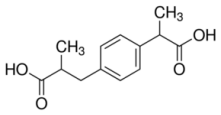
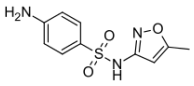
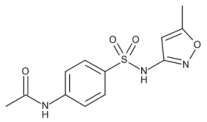
Table S3. Analytes detected in leafy and root vegetables from local markets.

Compound	Carrot (ng g^{-1} dw)			Lettuce (ng g^{-1} dw)		
	S1	**S2**	**S3**	**S1**	**S2**	**S3**
CAF	4.088	<MQL	<MQL	-	-	8.960
PX	-	<MQL	-	-	-	-
CBZ	<MQL	0.143	-	-	-	-
3-OH CBZ	<MQL	-	-	0.110	-	-
10-OH CBZ	<MQL	0.094	0.112	-	-	-
EP-CBZ	0.282	-	-	-	4.472	-
DIC	<MQL	-	-	-	-	-
4-OH DIC	-	-	-	-	-	-
IBU	4.020	-	-	-	-	-
1-OH IBU	<MQL	-	-	-	-	-
2-OH IBU	-	-	-	-	-	-
CBX- IBU	-	-	-	-	-	-
SMX	7.818	1.798	5.792	-	0.590	-
AcSMX	0.556	4.466	1.044	-	-	-

Parent compounds are marked in bold; -: not detected.

Table S4. Physical-chemical properties of the target compounds.

Group	Compound	Molecular weight (g mol^{-1})	pK$_a$	Log K$_{ow}$	Structure
Caffeine	**1,3,7-trimethylxanthine (caffeine) (CAF)**	194.19	10.4	-0.1	
	1,7-dimethylxanthine (PX)	180.16	8.5	-0.2	
Antiepileptic drug	**Carbamazepine (CBZ)**	236.27	13.9	2.5	
	3-Hydroxycarbamazepine (3-OH-CBZ)	252.27	9.19	2.41	
	10,11-Dihydro-10-hydroxycarbamazepine (10-OH-CBZ)	254.28	12.8	0.93	
	Carbamazepine-10,11-epoxide (EP-CBZ)	252.27	16.0	1.0	
Antiinflammatory drug	**Diclofenac (DIC)**	295.15	4.2	4.5	
	4-Hydroxydiclofenac (4-OH-DIC)	312.15	4.17	3.97	
	Ibuprofen (IBU)	206.28	4.9	4.0	
	1-Hydroxyibuprofen (1-OH IBU)	222.28	4.55	2.69	
	2-Hydroxyibuprofen (2-OH IBU)	222.28	4.63	2.37	

	Carboxyibuprofen (CBX-IBU)	236.26	3.97	2.78	
Antibiotic	**Sulfamethoxazole (SMX)**	253.28	5.7	0.9	
	N^4-Acetylsulfamethoxazole (AcSMX)	295.31	5.54	1.18	

Parent compounds are marked in bold.

Table S5. LC-MS/MS conditions and retention times for the target compounds.

Compound	Precursor ion *(m/z)*	Product ions (quantifier/qualifier) *(m/z)*	CE (eV)	Ratio	Polarity	Retention time (min)
CAF	195.1	138.0/42.0	20/24	10.9	Positive	5.32
PX	181.1	124.0/42.1	20/0	2.0	Positive	3.81
CBZ	237.1	194.0/179.0	20/40	29.4	Positive	9.07
3-OH CBZ	253.1	209.9/167.0	20/48	28.9	Positive	10.20
10-OH CBZ	255.3	194.1/237.1	20/4	98.7	Positive	9.07
EP-CBZ	253.1	180.0/235.9	36/8	56.3	Positive	9.51
DIC	296.0	213.9/249.8	40/12	49.1	Positive	20.10
4-OH DIC	312.0	229.9/266.0	40/8	49.3	Positive	16.34
IBU	205.1	205.1/161.1	0/4	8.8	Negative	20.33
1-OH IBU	240.2	205.0/163.0	8/20	64.4	Positive	11.60
2-OH IBU	240.2	205.0/107.0	12/36	24.1	Positive	13.12
CBX- IBU	254.1	218.9/117.1	8/48	56.0	Positive	12.08
SMX	254.1	92.1/65.0	32/28	8.0	Positive	5.86
AcSMX	296.1	134.0/197.9	28/20	63.8	Positive	8.06
CAF- $^{13}C_3$	198.2	140.0/112.0	20/24	22.9	Positive	5.32
IBU- d_3	227.2	158.9/91.0	4/12	18.8	Negative	20.33

Parent compounds are marked in bold; CE: collision energy.