

## Supporting Information

### Method validation results

Precision (RSD) [%]	7.4 (low concentration – 11 mg/kg) 9.0 (high concentration – 111 mg/kg)
Accuracy (Mean Bias) [%]	17.6 (low concentration 4 mg/kg) 9.8 (high concentration 135 mg/kg)
Correlation coefficient	0.999
Linear range [ $\mu\text{g/mL}$ ]	Morphine and codeine: 0.1-5 Papaverine and noscapine: 0.02-1
Limit of Detection (LOD) [mg/kg]	Morphine and codeine: 0.3 Papaverine and noscapine: 0.07
Limit of Quantitation (LOQ) [mg/kg]	Morphine and codeine: 1.0 Papaverine and noscapine: 0.2

### Regression coefficients in coded values for extraction experiment 1

Regression coefficient	Morphine	Codeine
Model	2-factor interaction	2-factor interaction
Intercept	102	5.8
A-Time	15*	0.8*
B-Pretreatment	-58***	-3.6***
C-Agitation	-2	0.03
D-Solvent	9	0.5
AB	1	-0.2
AC	15*	0.4
AD	14	0.4
BC	-8	-0.7
BD	25**	1.2**
CD	10	0.3
$R^2$	0.927	0.925
C.V. [%]	27.3	27.5

\*  $P \leq 0.05$ , \*\*  $P \leq 0.01$ , \*\*\*  $P \leq 0.001$ .

### Regression coefficients in coded values for poppy cake experiment

Regression coefficient	Morphine	Codeine
Model	Full factorial without interactions	Full factorial without interactions
Intercept	30	26
A-Pretreatment	-11**	-14*
B-Cooking time	-2	-3
C-Swelling time	1	1
$r^2$	0.820	0.775
C.V. [%]	26.0	41.0

\*  $P \leq 0.05$ , \*\*  $P \leq 0.01$ , \*\*\*  $P \leq 0.001$ .

### Regression coefficients in coded values for poppy bun experiment

Regression coefficient	Morphine	Codeine
Model	Quadratic	Quadratic
Intercept	70	74
A-Baking temperature	-35***	-35***
B-Pretreatment	-9**	-6*
A <sup>2</sup>	-19**	-22**
AB	-1	-2
r <sup>2</sup>	0.982	0.971
C.V. [%]	10.5	12.8

\* P ≤ 0.05, \*\* P ≤ 0.01, \*\*\* P ≤ 0.001.