

**Supplementary Fig. 1.** The molecular structures of estrogens investigated in this study

**Supplementary Fig. 2.** The images of an effervescent tablet and reaction

**Supplementary Fig. 3.** Effect of extraction temperature

**Supplementary Table 1.** PBD of variables (in coded levels) with the average ERs of BPs as response

Run	Factors								ERs (%)		
	A	B	C	D	E	F	G	H	E1	DES	HS
	Extraction time	Elution time	Dummy	pH	Extraction	Dummy	Nanofluid volume	Eluent volume			
	(min)	(min)	1		temperature (°C)	2	( $\mu$ L)	(mL)			
1	1	1	-1	-1	-1	1	-1	1			
2	1	1	1	-1	-1	-1	1	-1	39.4	48.1	58.7
3	-1	1	1	1	-1	-1	-1	1	27.1	45.6	40.5
4	-1	-1	-1	-1	-1	-1	-1	-1	11.1	16.0	19.7
5	1	-1	1	1	1	-1	-1	-1	30.8	39.8	41.4

6	-1	-1	1	-1	1	1	-1	1	20.4	25.4	24.58
7	-1	1	1	-1	1	1	1	-1	29.31	41.45	43.0
8	1	-1	-1	-1	1	-1	1	1	52.4	62.8	63.7
9	1	-1	1	1	-1	1	1	1	50.2	75.2	74.6
10	1	1	-1	1	1	1	-1	-1	33.9	47.9	46.0
11	-1	-1	-1	1	-1	1	1	-1	34.0	44.0	49.9
12	-1	1	-1	1	1	-1	1	1	46.5	62.0	59.9

**Note:** A: Extraction time, “-1” and “+1” represent 1 and 6 min, respectively; B: Elution time, “-1” and “+1” represent 2 and 6 min, respectively; D: pH, “-1” and “+1” represent 14 and 6, respectively; E: Extraction temperature, G: Nanofluid volume, “-1” and “+1” represent 30 and 50  $\mu\text{L}$ , respectively; H: Eluent volume, “-1” and “+1” represent 200 and 1500  $\mu\text{L}$ , respectively. The composition of an effervescent tablet: 0.31 g TTA and 0.21 g  $\text{Na}_2\text{CO}_3$ .

**Supplementary Table 2.** Factors, symbols and levels for the CCD

Factor	Symbol	Level				
		- $\alpha$ (low)	-1	0	1	+ $\alpha$ (high)
Nanofluid volume ( $\mu\text{L}$ )	A	30	38	50	62	70
Extraction time (min)	B	2	3.6	6	8.4	10
pH	C	2	3.6	6	8.4	10
Eluent volume ( $\mu\text{L}$ )	D	500	900	1500	2100	2500

**Experimental conditions:** elution time, 6 min; extraction temperature, 30 °C; composition of an effervescent tablet, 0.31 g TTA and 0.21 g  $\text{Na}_2\text{CO}_3$

**Supplementary Table 3.** Design matrix (coded value of variables) and responses for CCD

Run	Block	A: Nanofluid volume ( $\mu\text{L}$ )	B: Extraction time (min)	C: pH	D: Eluent volume ( $\mu\text{L}$ )	ERs (%)
1	Block 1	50	6	6	1500	90.3
2	Block 1	38	8.4	3.6	2100	56.7
3	Block 1	62	8.4	3.6	900	58.1
4	Block 1	62	8.4	8.4	900	50.3
5	Block 1	62	3.6	8.4	2100	40.7
6	Block 1	50	6	6	1500	86.2
7	Block 1	38	3.6	3.6	900	36.1
8	Block 1	50	6	6	1500	91.1
9	Block 1	50	6	6	1500	87.7
10	Block 1	38	3.6	8.4	900	29.8
11	Block 1	62	3.6	3.6	2100	47.2
12	Block 1	38	8.4	8.4	2100	48.6

13	Block 2	50	6	10	1500	17.9
14	Block 2	50	6	6	1500	85.1
15	Block 2	50	6	6	500	42.1
16	Block 2	50	6	2	1500	21.2
17	Block 2	50	2	6	1500	33.4
18	Block 2	70	6	6	1500	88.2
19	Block 2	50	10	6	1500	88.1
20	Block 2	50	6	6	2500	86.7
21	Block 2	30	6	6	1500	33.1
22	Block 2	50	6	6	1500	85.2

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Other experimental conditions: elution time, 6 min; extraction temperature, 30 °C; composition of an effervescent tablet, 0.31 g TTA and 0.21 g Na<sub>2</sub>CO<sub>3</sub>

**Supplementary Table 4.** Schemes for composition of acidic and alkaline sources

Scheme	Acidic source	Alkaline source	Reaction equation
1#	NaH <sub>2</sub> PO <sub>4</sub>	Na <sub>2</sub> CO <sub>3</sub>	NaH <sub>2</sub> PO <sub>4</sub> +Na <sub>2</sub> CO <sub>3</sub> =Na <sub>3</sub> PO <sub>4</sub> +CO <sub>2</sub> ↑+H <sub>2</sub> O
2#	TTA	Na <sub>2</sub> CO <sub>3</sub>	(HO-CH-COOH) <sub>2</sub> +Na <sub>2</sub> CO <sub>3</sub> =(HO-CH-COONa) <sub>2</sub> + H <sub>2</sub> O+CO <sub>2</sub> ↑
3#	NaH <sub>2</sub> PO <sub>4</sub>	NaHCO <sub>3</sub>	NaH <sub>2</sub> PO <sub>4</sub> +NaHCO <sub>3</sub> =Na <sub>2</sub> HPO <sub>4</sub> +CO <sub>2</sub> ↑+H <sub>2</sub> O
4#	TTA	NaHCO <sub>3</sub>	(HO-CH-COOH) <sub>2</sub> +NaHCO <sub>3</sub> =(HO-CH-COONa) <sub>2</sub> +2CO <sub>2</sub> ↑+2H <sub>2</sub> O

**Supplementary Table 5.** Effervescent reaction time for the different tablet composition

No	Acid source	Alkali source	Effervescent time (min)
1	NaH <sub>2</sub> PO <sub>4</sub> (2.0 μmol)	Na <sub>2</sub> CO <sub>3</sub> (2.0 μmol)	6.5
2	TTA (2 μmol)	Na <sub>2</sub> CO <sub>3</sub> (2.0 μmol)	3.0
3	NaH <sub>2</sub> PO <sub>4</sub> (2.0 μmol)	NaHCO <sub>3</sub> (2.0 μmol)	5.5
4	TTA (1.0 μmol)	NaHCO <sub>3</sub> (2.0 μmol)	1.0

**Note:** Reaction temperature, 30 °C.