Electronic Supporting Information

Ultrasonic Assisted Extraction of Artemisinin from *Artemisia Annua L.* Using Monoether based Solvents

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1. UPLC-MS analysis of the extract obtained using PGME under ultrasonics

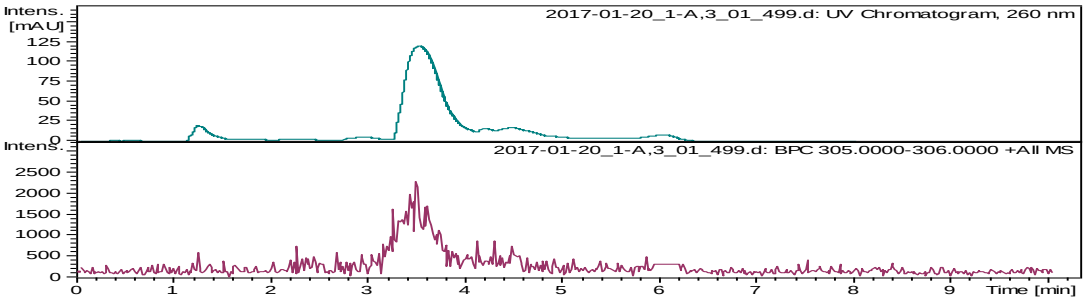

Figure S1a. UPLC chromatogram of the extract derivative.

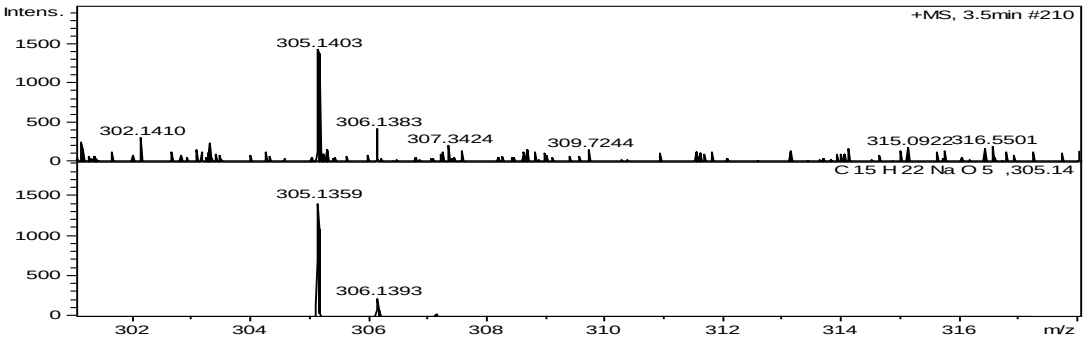

Figure S1b. ESI-MS spectra of the extract derivative.

Meas. m/z	#	Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
305.1403	1	C 15 H 22 Na O 5	100.00	305.1359	-4.3	-14.2	74.7	4.5	even	ok
	2	C 15 H 18 N 6 Na	0.03	305.1485	8.2	27.0	106.9	9.5	even	ok
	3	C 15 H 30 N 4 Na O	0.00	305.2312	0.0	0.0	816.9	2.5	even	ok

Figure S1c. Molecular formula of the extract derivative on UPLC-MS (Q260: $C_{15}H_{22}O_5$)

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2. Calibration curve for quantitative determination

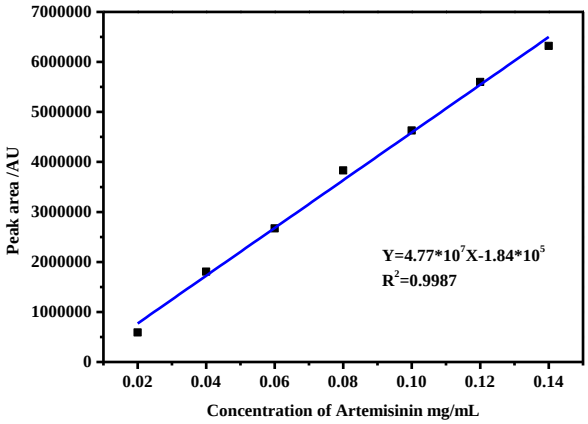

Figure S2. Calibration curve of artemisinin standard solutions.

3. Response surface methodology (RSM)

Table S1. Experimental design matrix to screen important variables for extraction efficiency of artemisinin.

RSM	Ratio (mL/g)	Temperature (ºC)	Time (min)	Ultrasonic Power (W)	Average extraction efficiency (%)
1	20	70	5	250	79.91
2	11	45	32.5	175	86.14
3	20	20	60	100	89.92
4	2	70	5	100	39.73
5	11	70	32.5	175	86.06
6	20	70	60	100	93.92
7	11	45	32.5	250	75.46
8	2	70	60	250	51.00
9	2	20	5	100	36.17
10	11	45	32.5	175	86.14
11	20	20	60	250	97.18
12	11	20	32.5	175	80.28
13	20	45	32.5	175	100.00
14	11	45	32.5	175	86.43
15	20	20	5	100	74.28
16	20	70	60	250	99.85
17	2	20	60	100	43.96
18	11	45	60	175	80.58
19	20	70	5	100	78.87
20	11	45	32.5	175	86.06
21	2	20	60	250	50.56
22	11	45	32.5	100	67.68
23	2	45	32.5	175	59.01
24	11	45	5	175	60.93
25	2	20	5	250	43.51
26	11	45	32.5	175	86.21
27	2	70	5	250	50.70
28	20	20	5	250	83.17
29	2	70	60	100	44.40
30	11	45	32.5	175	86.36

4. Thermal stability of artemisinin

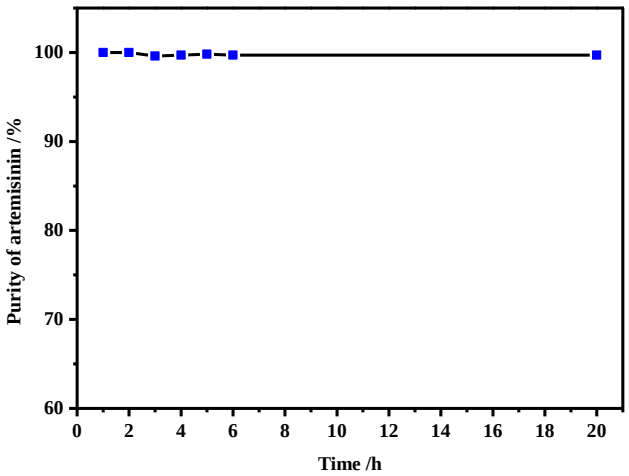

Figure S3. Thermal stability of artemisinin under 60 ºC.

5. Repeatability study

Table S2. Repeatability of artemisinin extraction under optimized conditions.

Entry	Extraction amount of artemisinin (mg)	Average (mg)	RSD (%) (n=5)
1	13.66		
2	12.91		
3	13.60	13.63	3.26
4	13.92		
5	14.06		

6. Energy consumption (PGME with UAE *vs.* Soxhlet extraction)

Based on the power of the instrument we used, the energy needed for each process was calculated under optimized conditions: 60 ℃, 8 h for Soxhlet extraction and 38 ℃, 180 W, 0.5 h for ultrasonic method (as mentioned in the RSM discussion section). Full power of IKA RCT heater was 650 W. Usually, it took 0.5 h for the temperature to increase from room temperature to 60 ℃ and 1/3 of the full power was needed to keep at such a temperature. Thus, the energy consumption of Soxhlet extraction was:

$$E_{Soxhlet}=P_{heater}\times t_1+1/3\times P_{heater}\times t_2=0.65\times 0.5+0.65\times 1/3\times 8=2.06\ kW\ h.$$

$E_{Soxhlet}$: energy consumption of Soxhlet extraction (kW h)

P_{heater}: full power of IKA RCT heater (650 W)

t_1: time for heating water bath from room temperature to 60 ℃ (h)

t_2: time for keeping the temperature at 60 ℃ (h)

Ultrasonic process: The heater was needed to heat the water bath to the specified temperature, and it took around 0.25 h for the temperature to increase to 38 ℃ and 1/6 of the full power was needed for keeping at such a temperature. The energy consumption of ultrasonic assisted extraction was:

$$E_{US}= P_{heater}\times t_1'+1/6\times P_{heater}\times t_2'+ P_{US}\times t'=$$

$$0.65\times 0.25+0.65\times 1/6\times(0.5-0.25)+0.18\times 0.5=0.28\ kW\ h$$

E_{US}: energy consumption of ultrasonic assisted extraction (kW h)

P_{US}: optimized power of ultrasonic (180 W)

t': ultrasonic time for artemisinin extraction (h)

t_1': time for heating water bath from room temperature to 38 ℃ (h)

t_2': time for keeping the temperature at 38 ℃ (h)

7. Kinetic study

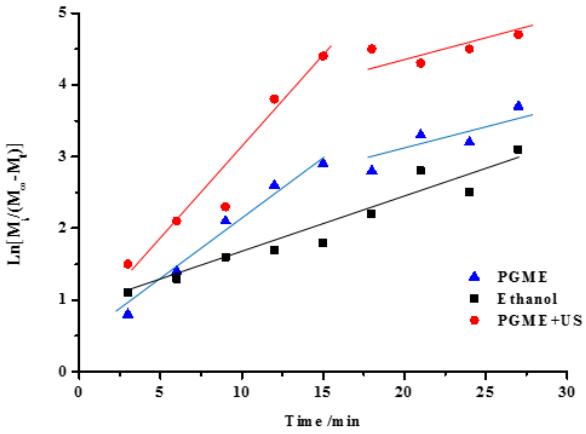

Figure S4. Kinetic study of artemisinin extractions: ■ Ethanol under heat-stirring, ● PGME under ultrasonic conditions, ▲ PGME under heat-stirring.

8. ^{1}H NMR

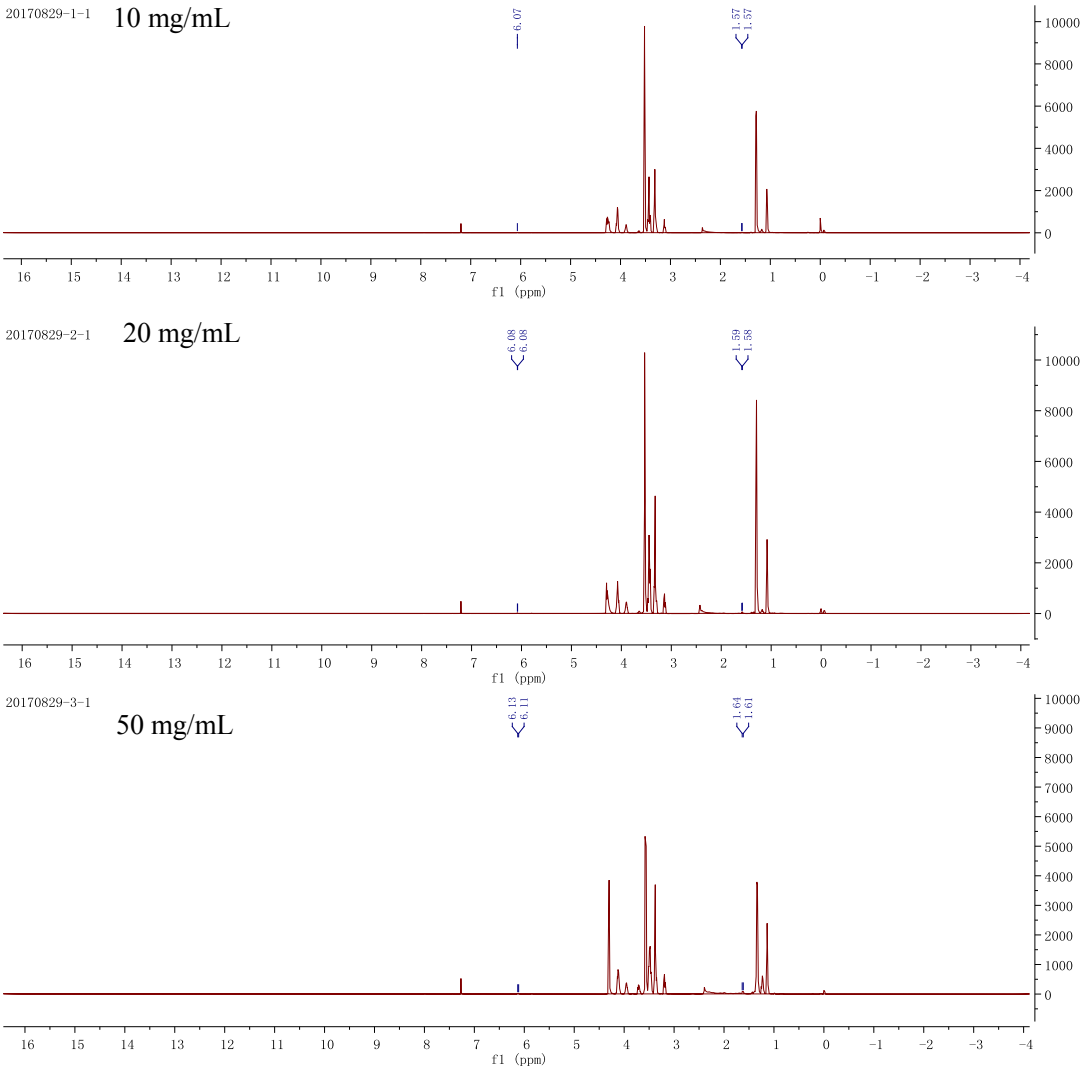

Figure S5. ^{1}H NMR spectra of artemisinin/PGME solutions with different concentrations using $CDCl_3$ as the external lock.