

Supporting Information

Antimalarial efficacy of a quantified extract of *Nauclea pobeguinii* stem bark in human adult volunteers with diagnosed uncomplicated *falciparum* malaria. Part 2: A clinical Phase IIB trial

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Table 1S Symptom resolutions during treatment with PR 259 CT1 compared to that with AS + AQ at days 0 and 3.

Characteristics	D0			D3		
	As + AQ, n = 32	PR 259 CT1, n = 33	p-value	As + AQ, n = 32	PR 259 CT1, n = 33	p-value
<i>Symptoms</i>						
Fever >37.5, n (%)	10(31.3)	15(45.5)	0.014	0	0	
History of fever, n (%)	16(50.0)	17(51.5)	0.120	0	0	
Headache, n (%)	31(96.9)	31(93.9)	0.259	1(3.1)	8(24.2)	<0.0001
Chill, n (%)	24(75.0)	30(90.9)	0.008	0	0	
Arthralgia-myalgia, n (%)	23(71.9)	15(45.5)	0.0001	1(3.1)	0	0.058
Anorexia, n (%)	8(25.0)	13(39.4)	0.015	0	1(3.0)	0.058
Asthenia, n (%)	7(21.9)	10(30.3)	0.170	0	2(6.1)	0.028
Abdominal pain, n (%)	3(9.4)	7(21.2)	0.012	0	0	
Vomiting, n (%)	4(12.5)	3(9.1)	0.150	0	0	
Nausea, n (%)	6(18.8)	5(15.2)	0.0001	0	0	

Table 2S Symptom resolutions during treatment with PR CT 259 compared with AS + AQ at days 7 and 14 (continued).

Characteristics	D7			D14		
	AS + AQ, n=32	PC 259 CT1, n=33	p-value	AS + AQ, n=32	PR 259 CT1, n=33	p-value
Symptoms						
Headache, n (%)	0	2(6.1)	0.028	0	0	
Anorexia, n (%)	0	1(3.0)	0.058	0	0	

Table 3S Side-effects of AS + AQ and PR 259 CT1 treatment regimens.

Adverse events	As + AQ (n = 32)	PR 259 CT1 (n = 33)	p-value
Reported side-effects	25 (78.1%)	16 (48.8%)	<0.0001
Asthenia	15 (46.9%)	8 (24.2%)	<0.0001
Headache	11 (34.4%)	3 (9.1%)	<0.0001
Dizziness	10 (31.1%)	4 (12.1%)	<0.0001
Epigastric pain	6 (18.8%)	1(3.0%)	<0.0001
Itch + pruritic rash	6 (18.8%)	0	<0.0001
Anorexia	2 (6.3%)	2 (6.1%)	0.95
Increased appetite	1(3.1%)	4 (12.1%)	0.003
Cough	1(3.1%)	3 (9.1%)	0.07
Nausea	1(3.1%)	1(3.0%)	0.96
Vomiting	1(3.1%)	1(3.0%)	0.96
Amenorrhea	1(3.1%)	0	<0.0001
Decreased libido	1(3.1%)	0	0.245

Insomnia	1(3.1%)	0	0.07
Increased libido	1(3.1%)	0	0.07
Palpitations	1(3.1%)	0	0.07
Red colored urine	1(3.1%)	0	0.07
Rhinorrhea	1(3.1%)	0	0.07

Table 4S Changes in vital signs after seven days of treatment with PR 259 CT1 compared to AS + AQ.

Characteristics	D0			D3		
	As + AQ, n = 32	PR 259 CT1, n = 33	p-value	As + AQ, n = 32	PR 259 CT1, n = 33	p-value
<i>Vital Signs</i>						
Axillary temperature (°C)	37.2 ± 0.2	37.5 ± 0.2	0.309	36.0 ± 0.1	36.2 ± 0.1	0.068
Respiratory rate/min	19.1 ± 0.6	19.1 ± 0.3	0.881	18.9 ± 0.4	18.9 ± 0.2	0.927
Pulse, beats/min	80.5 ± 3.1	82.2 ± 2.5	0.684	66.2 ± 1.7	76.4 ± 1.9	<0.0001
SBP (mmHg)	112.2 ± 2.3	115.0 ± 1.6	0.326	103.4 ± 2.1	111.3 ± 1.7	0.006
DBP (mmHg)	72.8 ± 2.0	71.4 ± 1.6	0.592	62.2 ± 1.6	69.1 ± 1.6	0.006

Table 5S Continuous changes in vital signs after seven days of treatment with PR 259 CT1 compared to AS + AQ.

Characteristics	D7			D14		
	As + AQ, n = 32	PR 259 CT1, n = 33	p-value	As + AQ, n = 32	PR 259 CT1, n = 33	p-value
<i>Vital Signs</i>						
Axillary temperature (°C)	36.1 ± 0.1	36.2 ± 0.0	0.024	36.3 ± 0.1	36.2 ± 0.1	0.732
Respiratory rate/min	18.1 ± 0.5	18.5 ± 0.2	0.345	18.6 ± 0.3	19.1 ± 0.3	0.319
Pulse, beats/min	70.7 ± 2.1	74.8 ± 1.7	0.147	72.3 ± 2.2	79.1 ± 2.1	0.038
SBP (mmHg)	112.3 ± 1.9	112.9 ± 1.9	0.830	113.3 ± 2.2	110.8 ± 1.6	0.356
DBP (mmHg)	70.0 ± 1.5	68.9 ± 1.3	0.588	71.1 ± 2.2	69.1 ± 1.4	0.423

Table 6S Biochemical, haematological, and ECG values in study patients at enrolment and at days 3, 7, and 14 after treatment.

Characteristics	D0			D3		
	AS + AQ	PR 259 CT1	p-value	AS + AQ	PR 259 CT1	p-value
Biochemical parameters						
ASAT (U/L)	32.5 ± 1.1	32.0 ± 1.1	0.620	33.0 ± 0.8	29.1 ± 0.9	0.005
ALAT (U/L)	35.9 ± 1.1	34.9 ± 7.4	0.102	33.6 ± 1.2	32.6 ± 0.7	0.25
Na ⁺ (mmol/L)	140.9 ± 1.4	141.8 ± 4.3	0.101	141.8 ± 1.2	143.7 ± 2.8	0.016
K ⁺ (mmol/L)	3.8 ± 0.1	3.5 ± 0.1	0.113	4.0 ± 0.1	3.6 ± 3.2	0.111
Glycaemia (mmo/L)	4.5 ± 0.2	4.1 ± 1.2	0.760	4.3 ± 0.2	3.8 ± 0.2	0.094
Urea (mmol/L)	4.5 ± 0.3	5.1 ± 1.4	0.032	4.5 ± 0.3	5.4 ± 1.9	0.751
Creatinine (µmol/L)	102.3 ± 4.9	73.1 ± 3.3	0.000	99.7 ± 4.6	73.1 ± 3.7	0.000
Haematological parameters						
Hematocrit (Ht) (%)	32.2 ± 0.8	40.3 ± 0.7	0.107	37.0 ± 0.9	40.4 ± 0.7	0.009
Haemoglobin (%)	18.5 ± 6.2	13.3 ± 7.1	0.033	12.1 1 ± 0.3	13.0 ± 0.2	0.021
RBC (x 10 ⁶ /mm ³)	3.9 ± 0.1	4.2 ± 8.4	0.164	3.9 ± 0.1	4.2 ± 12.6	0.251

Platelets (x 10 ³ /mm ³)	219.1 ± 16.3	299.7 ± 15.7	0.000	218.5 ± 16.8	337.9 ± 65.8	0.214
WBC (x 10 ³ /mm ³)	7.7 ± 0.5	5.9 ± 0.3	0.009	9.3 ± 3.1	6.7 ± 10.8	0.577
Neutrophils (%)	56.5 ± 2.8	54.4 ± 2.1	0.512	56.3 ± 2.5	53.9 ± 1.9	0.318
Lymphocytes (%)	39.3 ± 2.8	39.4 ± 1.9	0.982	40.4 ± 2.4	40.3 ± 1.7	0.788
Eosinophils (%)	1.2 ± 0.4	2.2 ± 0.5	0.156	0.4 ± 0.2	1.7 ± 0.4	0.033
Basophils (%)	0.0 ± 0.0	0.1 ± 0.0		0.0 ± 0.0	0.0 ± 0.0	
Monocytes (%)	2.9 ± 0.4	3.9 ± 0.5	0.067	2.9 ± 0.4	3.9 ± 0.4	0.101
ECG						
QTC(s)	0.295 ± 0.01	0.386 ± 0.007	0.000	0.354 ± 0.01	0.377 ± 0.006	0.020
PR Interval(s)	0.17 ± 0.47	0.15 ± 0.46	0.011	0.17 ± 0.45	0.15 ± 0.47	0.003

Table 7S Biochemical, haematological, and ECG values in study patients at enrolment and at days 3, 7, and 14 after treatment (continued).

Characteristics	D7			D14		
	AS + AQ	PR 259 CT1	p-value	AS +AQ	PR 259 CT1	p-value
Biochemical parameters						
ASAT (U/L)	34.7 ± 0.6	28.4 ± 0.6	0.000	33.0 ± 0.8	30.5 ± 0.6	0.049
ALAT (U/L)	34.9 ± 1.1	34.4 ± 2.9	0.022	35.0 ± 0.9	35.5 ± 2.8	0.035
Na ⁺ (mmol/L)	141.8 ± 1.1	141.5 ± 3.5	0.132	140.5 ± 0.7	137.7 ± 4.5	0.032
K ⁺ (mmol/L)	4.1 ± 0.1	3.4 ± 0.1	0.000	3.9 ± 0.1	3.4 ± 0.1	0.000
Glycaemia (mmol/L)	3.6 ± 0.3	4.2 ± 0.6	0.901	4.0 ± 0.2	4.2 ± 0.7	0.089
Urea (mmol/L)	4.3 ± 0.3	4.5 ± 1.2	0.000	4.4 ± 3.4	5.0 ± 1.7	0.009
Creatine (µmol/L)	96.5 ± 4.5	73.0 ± 3.0	0.000	87.3 ± 5.9	74.5 ± 4.2	0.031
Haematological parameters						
Hematocrit (Ht) (%)	38.2 ± 0.9	40.6 ± 0.8	0.077	37.9 ± 1.9	38.8 ± 1.3	0.277
Haemoglobin (HB) (%)	12.4 ± 0.3	13.4 ± 3.2	0.429	18.9 ± 6.2	13.3 ± 3.1	0.473

RBC (x 10 ³ /mm ³)	3.9 ± 0.1	4.1 ± 0.1	0.093	4.2 ± 0.2	4.2 ± 0.1	0.923
Platelets (x 10 ³ /mm ³)	224.7 ± 16.7	316.2 ± 29.6	0.061	202.9 ± 20.3	294.8 ± 16.0	< 0.0001
WBC (x 10 ³ /mm ³)	6.7 ± 0.3	7.5 ± 4.4	0.445	6.7 ± 7.1	7.8 ± 10.5	0.997
Neutrophils (%)	55.1 ± 2.4	53.4 ± 1.7	0.373	50.5 ± 3.7	53.6 ± 1.7	0.749
Lymphocytes (%)	41.2 ± 2.3	41.2 ± 1.5	0.739	39.5 ± 13.4	41.8 ± 1.5	0.946
Eosinophils (%)	0.3 ± 0.1	1.7 ± 0.3	0.009	0.5 ± 0.4	2.4 ± 1.1	0.011
Basophils (%)	0.0 ± 0.0	0.1 ± 0.0		0.2 ± 0.2	0.1 ± 0.0	
Monocytes (%)	3.2 ± 0.3	3.7 ± 0.3	0.289	3.5 ± 1.9	3.4 ± 0.3	0.507
ECG						
QTc(s)	0.338 ± 0.01	0.376 ± 0.005	0.000	0.335 ± 0.001	0.376 ± 0.005	< 0.001
PR Interval(s)	0.17 ± 0.51	0.15 ± 0.46	0.029	0.17 ± 0.43	0.15 ± 0.47	0.019