Table-S1. Liquid chromatographic mass spectrometric (LC/MS/MS) method summary for the quantification of Artesunate (ART) and Dihydroartemisinin (DHA) in rat plasma.

Parameters	Method
Matrix for calibration standards and quality control samples:	Rat K_3-EDTA plasma
Calibration range:	1.00 – 500.00 ng/mL of ART 1.00 – 500.00 ng/mL of DHA
Lower limit of quantification (LLOQ):	1.00 ng/mL
Upper limit of quantification (ULOQ):	500.00 ng/mL
Analytical column:	Poroshell 120, EC-C18, 50 x 4.6 mm, 2.7 µm (Agilent)
Mobile phase A:	2 mM ammonium acetate with 0.02% acetic acid
Mobile phase B:	Methanol
Gradient elution	68.0 – 95.0% mobile phase B
Flow rate:	1.00 mL/min
Injection volume:	12 µL
Analysis time:	4.00 minutes
Ionisation mode:	Positive ion mode
Sample volume:	25 µL
Sample preparation:	Protein precipitation (25 fold dilution)
LC-MS/MS system:	Shimadzu 20AC and API 5000
Analytes:	ART and DHA
Internal standard:	ART-d_4

Table-S2. Precision and accuracy results for Artesunate quantification

Intra-Assay	Analytical Run No.	Quality Control Samples ng/mL			Calibration Standards ng/mL							
		LLOQ	QC A	QC C	Std B	Std C	Std D	Std E	Std F	Std G	Std H	Std I
		1.00	3.00	400.00	1.00	2.00	10.00	50.00	150.00	250.00	350.00	500.00
1	PV03	1.05	2.66	400.49	0.96	1.92	10.09	51.83	150.09	254.92	329.36	503.12
		0.84	2.51	391.57	1.05	1.98	10.95	50.95	151.84	249.39	309.72	506.96
		1.03	2.82	378.77								
		0.97	2.79	377.38								
	%C.V	9.7	5.3	2.8								
	% Bias	-2.8	-10.2	-3.4								
2	PV04	1.06	2.89	373.11	1.02	1.96	10.44	51.30	151.76	244.68	339.62	484.65
		0.97	2.92	382.05	0.92	2.22	10.53	50.30	149.30	253.92	334.80	469.47
		1.03	2.91	362.94								
		1.16	2.83	379.40								
	%C.V	7.5	1.4	2.3								
	% Bias	5.5	-3.7	-6.4								

Inter-Assay	Mean	1.014	2.791	380.714	0.988	2.020	10.503	51.095	150.748	250.728	328.375	491.050
	S.D	0.0921	0.1410	11.3458	0.0585	0.1356	0.3536	0.6417	1.2578	4.6950	13.1239	17.3731
	%C.V	9.1	5.1	3.0	5.9	6.7	3.4	1.3	0.8	1.9	4.0	3.5
	n	8	8	8	4	4	4	4	4	4	4	4
	% Bias	1.4	-7.0	-4.8	-1.3	1.0	5.0	2.2	0.5	0.3	-6.2	-1.8
	%C.V = Percent Coefficient of Variation S.D = Standard Deviation											

Curve Parameter Summary	Weighted Least Squares Regression Equation: y = ax + b		
Analytical Run No.	r	a	b
PV03	0.9985	0.094	0.00575
PV04	0.9986	0.0915	0.0014
Mean	0.99855	0.09275	0.003575

Table-S3. Precision and accuracy results for Dihydroartemisinin quantification

Intra-Assay	Analytical Run No.	Quality Control Samples ng/mL			Calibration Standards ng/mL							
		LLOQ	QC A	QC C	Std B	Std C	Std D	Std E	Std F	Std G	Std H	Std I
		1.00	3.00	400.00	1.00	2.00	10.00	50.00	150.00	250.00	350.00	500.00
1	PV03	1.05	2.73	407.47	0.94	1.87	9.77	49.85	153.66	254.61	326.69	503.99
		0.99	2.61	396.18	1.06	2.07	11.00	50.68	151.58	255.30	314.24	510.52
		1.07	3.00	381.92								
		0.97	2.95	382.38								
	%C.V	4.7	6.5	3.1								
	% Bias	2.0	-5.9	-2.1								
2	PV04	1.13	3.05	386.37	1.00	2.24	10.82	52.50	156.96	247.67	345.95	488.64
		1.18	3.13	374.50	0.97	1.86	10.10	49.66	151.32	248.15	326.72	455.93
		0.96	3.07	362.41								
		1.01	2.91	375.47								
	%C.V	9.6	3.1	2.6								
	% Bias	7.0	1.3	-6.3								

Inter-Assay	Mean	1.045	2.931	383.338	0.993	2.010	10.423	50.673	153.380	251.433	328.400	489.770
	S.D	0.0786	0.1781	13.8223	0.0512	0.1813	0.5835	1.2963	2.6063	4.0819	13.0927	24.3529
	%C.V	7.5	6.1	3.6	5.2	9.0	5.6	2.6	1.7	1.6	4.0	5.0
	n	8	8	8	4	4	4	4	4	4	4	4
	% Bias	4.5	-2.3	-4.2	-0.8	0.5	4.2	1.3	2.3	0.6	-6.2	-2.0
	%C.V = Percent Coefficient of Variation S.D = Standard Deviation											

Curve Parameter Summary	Weighted Least Squares Regression Equation: y = ax + b		
Analytical Run No.	r	a	b
PV03	0.9983	0.0346	0.00419
PV04	0.9981	0.0378	0.00235
Mean	0.99820	0.03620	0.003270