

Supplementary materials

Effect of Syk inhibitors and DHA on HMC content

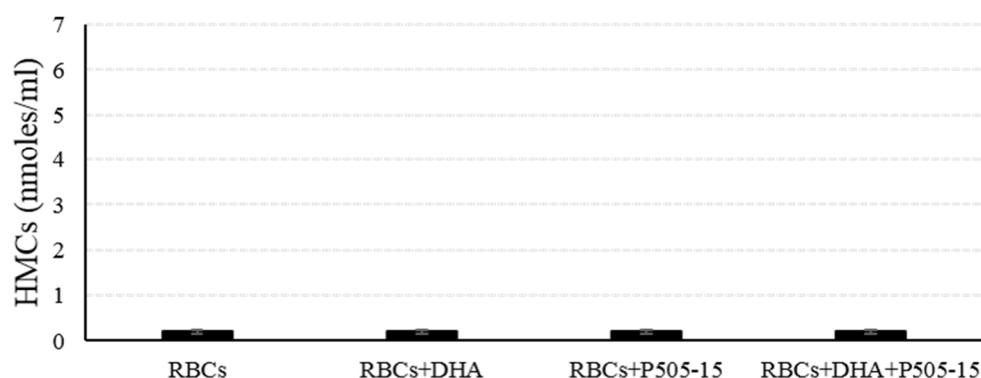


Figure S1. Effect of RBCs treatment with P505-15 (0.5 μ M) and DHA (0.5 nM) on the accumulation of HMC after 12 h of incubation. Data are the average of 5 experiments \pm S.D.

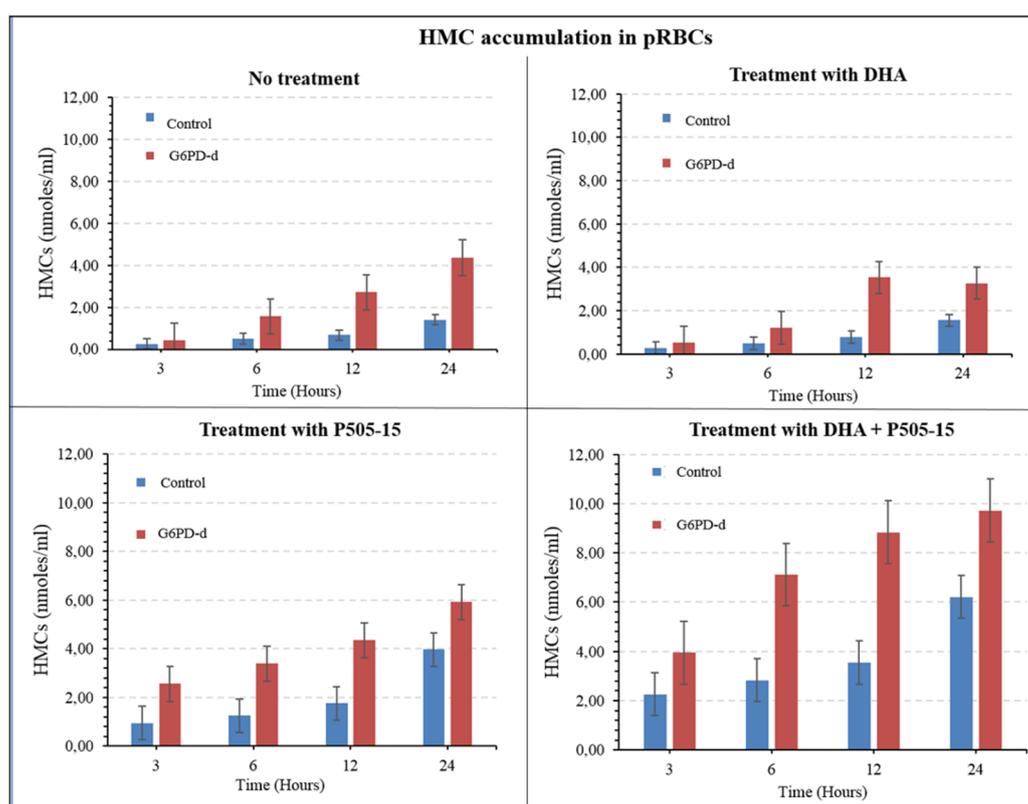


Figure S2.

Effect of pRBC treatments with a representative Syk inhibitor (P505-15) (0.5 μ M) and DHA (0.5 nM) on the accumulation of HMC after 3,6,12 and 24 h in control and G6PD-d treated RBCs. Data are the average of 5 experiments \pm S.D. Significant differences to untreated pRBCs at * $p < 0.05$; ** $p < 0.001$.

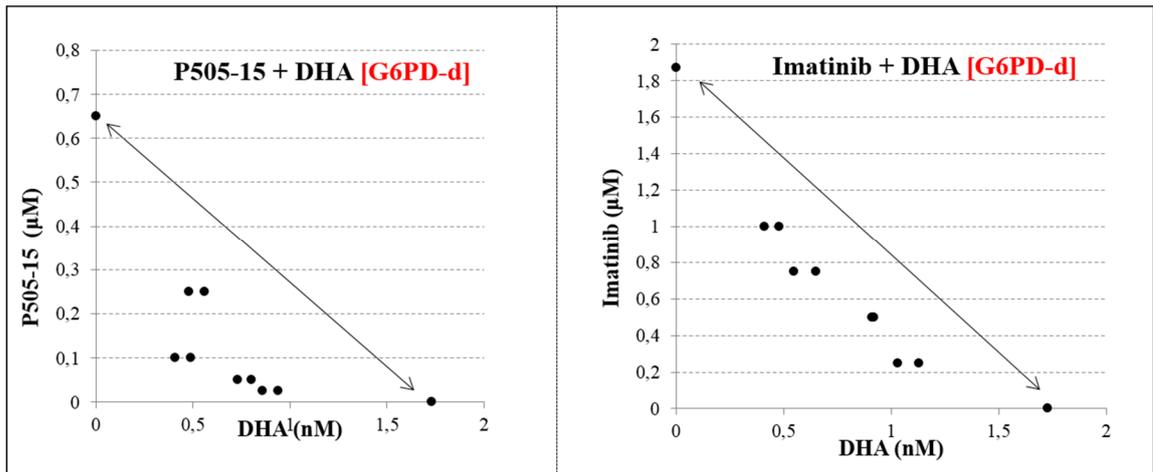


Figure S3. Isobolograms showing the interactions between Syk Inhibitors (P505-15 and Imatinib) with dihydroartemisinin (DHA), after 24 h of incubation in the *P. falciparum* Palo Alto strain treated with G6PD-d red cells.

Table 1. Combination index (CI) (Chow-Talalay) of different SYK inhibitors.

	Artesunate		Artemether	
	24h	48h	24h	48h
P505-15 (IC ₅₀ = 1 nM)	0.97±0.03	0.55±0.07	0.87±0.03	0.83±0.01
	0.76±0.08	0.51±0.01	0.89±0.01	0.65±0.03
	0.63±0.03	0.61±0.03	0.95±0.01	0.63±0.04
	0.58±0.07	0.49±0.05	0.98±0.04	0.58±0.01
Entospletinib (IC ₅₀ = 1 nM)	0.87±0.03	0.74±0.04	1.01±0.03	0.83±0.04
	0.73±0.02	0.62±0.01	0.95±0.05	0.68±0.04
	0.66±0.01	0.60±0.02	0.98±0.03	0.63±0.03
	0.62±0.02	0.55±0.02	1.04±0.07	0.72±0.04
R406 (IC ₅₀ = 41 nM)	0.82±0.04	0.75±0.02	0.85±0.03	0.93±0.04
	0.63±0.01	0.72±0.01	0.82±0.01	0.88±0.04
	0.76±0.03	0.50±0.02	0.80±0.04	0.73±0.03
	0.92±0.02	0.44±0.02	0.82±0.04	0.72±0.04
SYK II (IC ₅₀ = 41 nM)	0.79±0.04	0.89±0.04	0.97±0.01	0.73±0.02
	0.55±0.01	0.99±0.03	0.99±0.03	0.58±0.04
	0.67±0.04	0.96±0.01	1.06±0.05	0.53±0.05
	0.89±0.02	0.90±0.04	1.12±0.01	0.62±0.07
Imatinib (IC ₅₀ = 5 μM)	0.67±0.03	0.75±0.02	1.01±0.02	0.83±0.01
	0.61±0.04	0.96±0.04	0.89±0.03	0.78±0.06
	0.70±0.01	0.64±0.01	0.91±0.01	0.73±0.04
	0.90±0.02	0.60±0.02	0.85±0.02	0.82±0.04
Piceatannol (IC ₅₀ = 10 μM)	0.77±0.01	0.65±0.03	0.95±0.01	0.73±0.02
	0.71±0.03	0.66±0.07	0.78±0.01	0.80±0.01
	0.80±0.02	0.84±0.02	0.85±0.02	0.83±0.04
	0.85±0.01	0.90±0.04	0.78±0.03	0.75±0.01

SYK inhibitors (P505-15, R406, entospletinib, SYK II, piceatannol, and imatinib) at different concentrations (50–500 nM) in combination with different artemisinin derivatives (artesunate, and artemether) after 24 and 48 h of incubation. [additive effect (C = 1), synergism (CI < 1), and antagonism (CI > 1)].