Supplementary

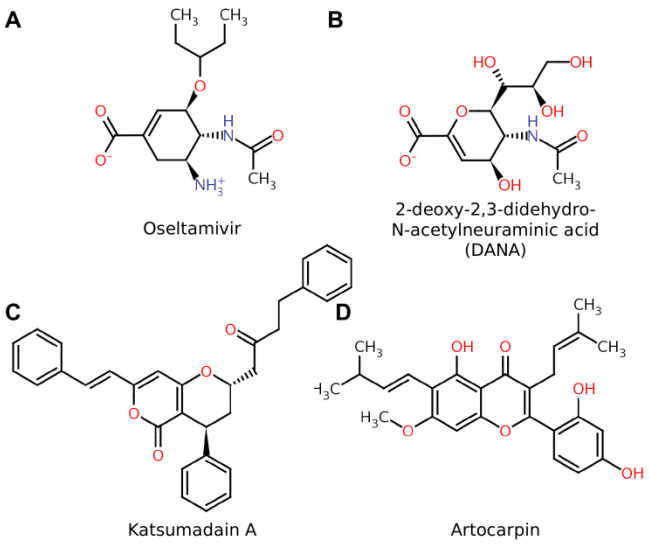

Figure S1. Structure of the NAIs. Names and abbreviations as used in this study. Protonation state of the molecules corresponds to the major species at pH 7.

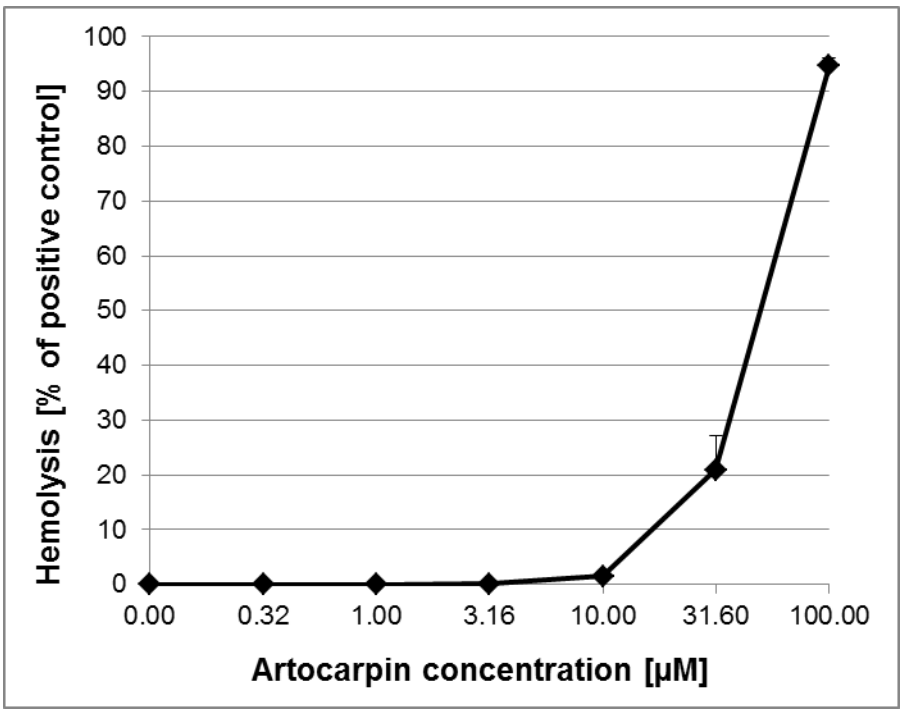

Figure S2. Relative rate of hemolysis in human erythrocytes is shown upon incubation with different concentrations of artocarpin. The presence of hemoglobin in the supernatant (red) was measured at 577 nm with the reference wavelength at 655 nm. Erythrocytes diluted in PBS or in aqua bidest were used as negative or positive control, respectively. Data were mean ± SD (n = 3).

Table S1. PCR primers used in this study

Primer	Sequence (5' to 3')	Binding site (bp) [a]
F1f	GTCATTTAAATGAACTGTAGTAAAAG	-67-(-41)
F1r	CCAGATTTCAGACTTGTTCGAG	743-764
F2f	GCACCCTTAAAAGTTAAACCAGGTC	631-655
F2r	GGTTTAACAGGATCTACAACAACG	1476-1499
F3f	GCTTATACCATTCGAGAAAATGG	1414-1436
F3r	CTCACCATTTTCTTCGACACGTG	2186-2208
F4f	CACAGGTTAAAGATGTCTATGTTC	2066-2089
F4r	AGACCTCTTATGATTTCGTATCAGC	87-111
F1iF	CCAAGAGATTACTATGCACGAGATTTG	319-345
F2iF	GATTCGGAATCTCACTGTGTATAATC	855-880
F3iR	CGAAGTACAATTCCTGTTCCAGGAC	1706-1730
F4iR	CGATTTCATGAACAGCTGGCTCTG	2900-2923

[a] Position within R36A (ancestral strain D39) *nanA* sequence (accession number X72967).

Table S2. Mean 50% inhibitory concentration and standard deviation of oseltamivir, DANA, artocarpin, and katsumadain A, measured against the precipitated pneumococcal protein in the FL-based assay

Strains	FL inhibition assay IC_{50} (μM) [a]			
	oseltamivir	**DANA**	**katsumadain A**	**artocarpin**
DSM20566	0.91 ± 0.14	10.62 ± 0.85	15.24 ± 2.99	8.43 ± 4.08
recombinant NanA	2.85 ± 0.89	18.03 ± 1.87	36.79 ± 24.16	9.96 ± 5.79
D39	2.89 ± 0.09	13.79 ± 1.82	17.28 ± 3.57	6.06 ± 0.77
DSM14378	0.98 ± 0.22	12.17 ± 2.65	45.57 ± 7.14	9.74 ± 2.58
CJ9400	0.40 ± 0.09	19.23 ± 4.01	81.03 ± 14.69	44.83 ± 12.34
CF6937	1.43 ± 0.26	16.42 ± 2.39	13.93 ± 0.93	3.83 ± 2.13
BC7326	1.14 ± 0.54	9.92 ± 1.37	32.57 ± 17.08	11.71 ± 5.66
CF8919	2.33 ± 1.38	12.38 ± 2.96	5.79 ± 0.70	7.52 ± 3.11
PN8828	0.62 ± 0.06	15.44 ± 9.06	33.97 ± 6.60	36.08 ± 21.11
BC57	2.85 ± 1.16	12.41 ± 0.52	4.50 ± 1.58	5.48 ± 1.71

[a] IC_{50} values and their standard deviations were calculated for a minimum of three independent tests.

Table S3. Mean 50% inhibitory concentration and standard deviation of oseltamivir, DANA, artocarpin, and katsumadain A, measured against the precipitated protein in the CL-based assay.

strains	CL inhibition assay IC_{50} (μM) [a]			
	oseltamivir	**DANA**	**katsumadain A**	**artocarpin**
DSM20566	0.73 ± 0.15	2.43 ± 0.76	1.01 ± 0.37	0.33 ± 0.14
recombinant NanA	0.93 ± 0.42	3.16 ± 0.87	0.52 ± 0.12	0.30 ± 0.09
D39	0.85 ± 0.15	3.61 ± 1.85	1.25 ± 0.44	0.32 ± 0.02
DSM14378	0.35 ± 0.05	1.93 ± 0.83	1.61 ± 1.06	0.43 ± 0.18
CJ9400	0.24 ± 0.08	4.27 ± 2.83	1.31 ± 0.26	0.33 ± 0.10
CF6937	0.60 ± 0.13	2.05 ± 0.18	1.18 ± 0.16	1.65 ± 0.11
BC7326	0.33 ± 0.16	1.03 ± 0.29	0.31 ± 0.06	0.11 ± 0.05
CF8919	0.40 ± 0.10	0.62 ± 0.14	0.65 ± 0.12	0.16 ± 0.03
PN8828	0.25 ± 0.12	1.68 ± 0.52	0.31 ± 0.06	0.77 ± 0.14
BC57	0.88 ± 0.45	1.88 ± 0.76	1.14 ± 0.19	0.33 ± 0.12

[a] The IC_{50} values and standard deviations were calculated of at least three independent tests.

Table S4. Absolute numbers of adherent bacteria (CFU/well) in the adherence inhibition assay.

		Adherence inhibition assay CFU/well × 10^6	
compound	**conc. in µM**	**DSM20566**	**PN8828**
no compound		20.13 ± 13.51	0.07 ± 0.04
oseltamivir	50.00	16.04 ± 14.33	not tested
	25.00	17.71 ± 15.07	not tested
DANA	50.00	12.96 ± 9.44	not tested
	25.00	16.58 ± 12.72	not tested
katsumadain A	50.00	18.63 ± 17.58	not tested
	25.00	16.88 ± 13.71	not tested
artocarpin	12.50	4.83 ± 2.72	0.02 ± 0.01
	6.25	8.43 ± 9.23	0.03 ± 0.02
	3.13	13.50 ± 9.01	0.04 ± 0.03