

Table 2. Results

Analysis	Method	N	N pos.	Effect [95% CI]	p	Status / Interpretation
H1 principal — native strict (pre-registered)	Logistic GLMM, cluster-robust SE	416	41	0.42 [0.20–0.89]	0.023	REJECTED in inverse direction
H1 S6 — pan-African (post-hoc)	Logistic GLMM, cluster-robust SE	713	89	0.46 [0.28–0.77]	0.003	Sensitivity, inverse effect strengthened
H1bis — native continuous pChEMBL	Linear, cluster-robust SE	416	41	Coef = –0.29	0.054	Marginal inverse
H1bis — S6 continuous pChEMBL	Linear, cluster-robust SE	713	89	Coef = –0.29	0.018	Significant inverse
S1a pChEMBL ≥ 4 (~100 μM) — native	Logistic GLMM	416	41	5.28 [1.67–16.70]	0.005	Saturation; positive sign at very low threshold
S1b pChEMBL ≥ 5 (principal threshold)	Logistic GLMM	416	41	0.42 [0.20–0.89]	0.023	Pre-registered threshold
S1c pChEMBL ≥ 6 (~1 μM) — native	Logistic GLMM	416	41	0.55 [0.17–1.77]	0.315	Direction preserved, ns
S2 — LARGE positive (≥ 1 source) — native	Logistic GLMM	416	—	0.51 [0.27–0.96]	0.036	Robust to consensus criterion
S3 — InChIKey first-block (skeleton)	Logistic GLMM	408	—	0.43 [0.20–0.92]	0.030	Robust to chemical identifier resolution
S4 — Excluding Agbodeka 2017	Logistic GLMM	416	—	0.42 [0.20–0.89]	0.023	Not driven by single source
S5 — Well-studied compounds ($n_{\text{assays_pf}} \geq 5$)	Logistic GLMM	118	—	0.43 [0.16–1.15]	0.093	Direction preserved, ns (power)
H2 Alkaloids (S6)	Logistic GLMM stratified	219	22	0.99 [0.28–3.50]	0.980	No differential effect
H2 Terpenoids (S6)	Logistic GLMM stratified	189	32	0.43 [0.16–1.15]	0.090	Tendential inverse
H2 Shikimates / Phenylpropanoids (S6)	Logistic GLMM stratified	177	26	0.31 [0.10–0.93]	0.038	Significant inverse effect
H2 Polyketides (S6)	Logistic GLMM stratified	84	8	0.17 [0.03–1.10]	0.063	Strong tendential inverse
H3 Quinine (ChEMBL170,	Per-compound check	—	—	pChEMBL max =	—	Reference compound active ✓

sanity)				9.15		
H3 Chloroquine (ChEMBL76, sanity)	Per-compound check	—	—	pChEMBL max = 10.52	—	Reference compound active ✓
H4 Selectivity (SI ≥ 1) — adjusted	Logistic GLMM	126	24	0.40 [0.12–1.42]	0.156	Null, low power
H4 Selectivity continuous (Mann-Whitney)	Non-parametric	126	24	med 0.47 vs 0.88	0.126	Null, tendency against H4
Investigation bias coefficient (log _n _assays _{pf})	From H1 principal model	416	—	OR = 2.32 [1.43–3.76]	0.001	Massive empirical bias confirmed