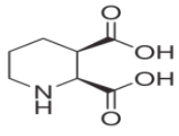
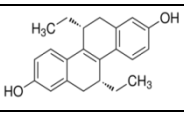
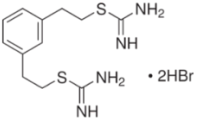
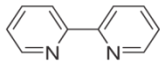
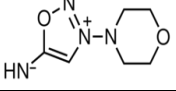
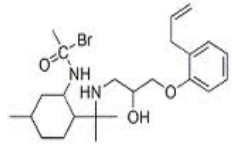
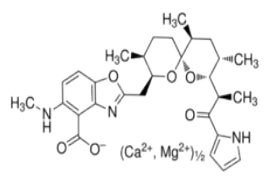
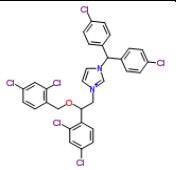
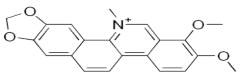
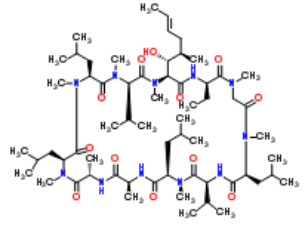
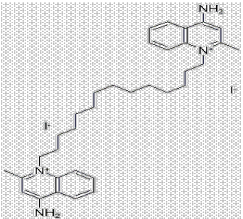
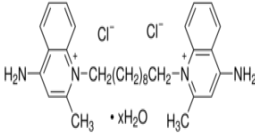
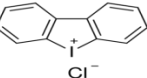
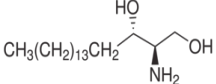
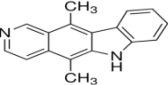
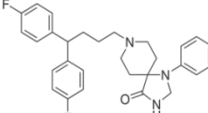
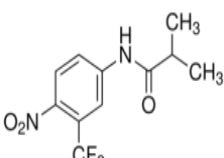
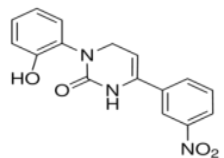
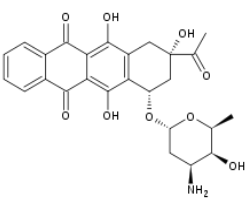
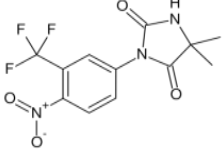
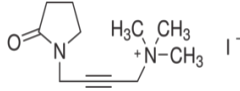
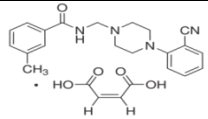
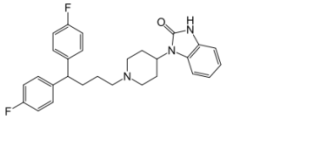
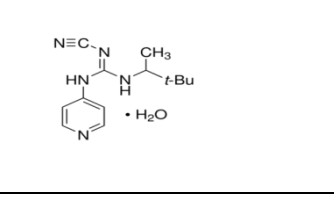
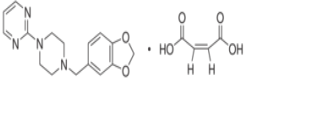
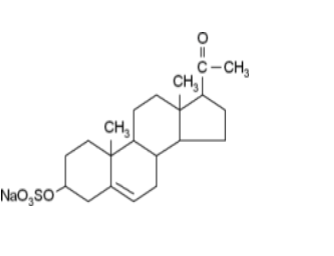
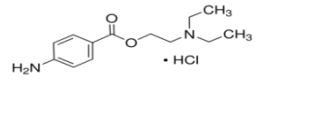
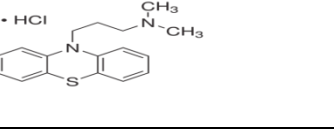
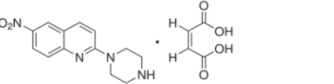
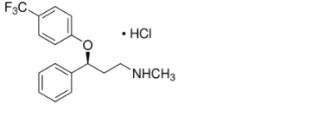
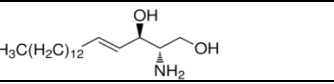
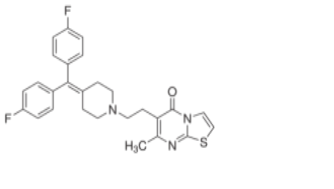
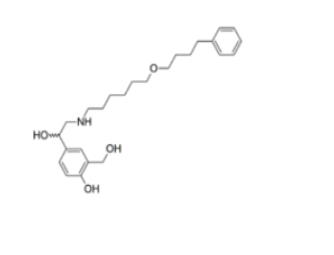
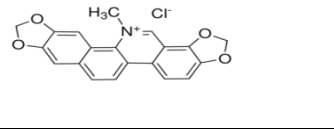
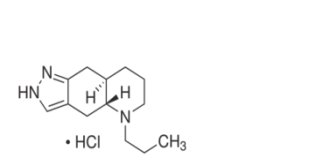
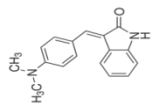
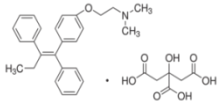
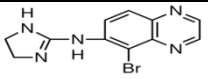
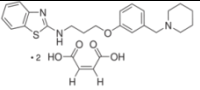
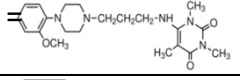
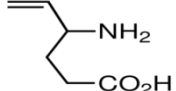


Table S1. Compounds from LOPAC library that inhibited the growth of *M. maripaludis*^a

Structure	Mol Weight	Molecular Name
	173.17	(+)-cis-Piperidine-2,3-dicarboxylic acid
	320.42	(R,R)-cis-Diethyl tetrahydro-2,8-chrysenediol
	444.25	1,3-PBIT Dihydrobromide
	156.18	2,2'-Bipyridyl
	206.63	3-Morpholinosydnonimine hydrochloride
	481.47	Bromoacetyl alprenolol methane
	542.65	Calcimycin
	687.70	Calmidazolium chloride
	383.82	Chelerythrine chloride
	1202.61	Cyclosporin A

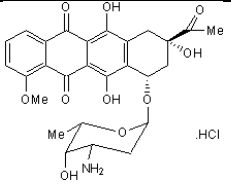
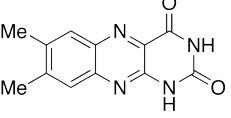
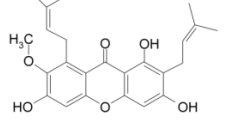
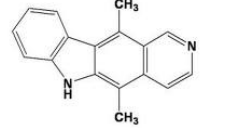
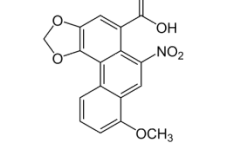
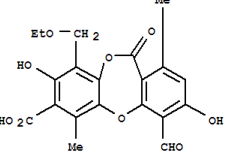
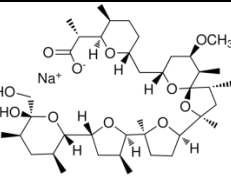
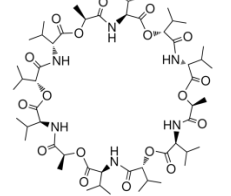
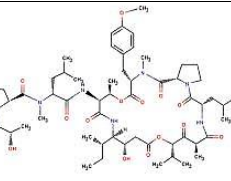
	766.58	Dequalinium analog
	527.57	Dequalinium dichloride
	314.55	Diphenyleneiodonium chloride
	301.51	DL-erythro-Dihydrosphingosine
	246.31	Ellipticine
	475.57	Fluspirilene
	276.21	Flutamide
	311.29	Icilin
	533.95	Idarubicin
	317.22	Nilutamide
	322.19	Oxotremorine
	450.49	PD 168,077 maleate

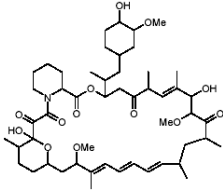
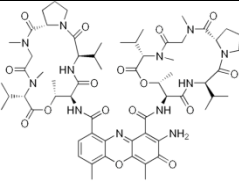
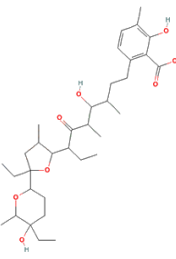
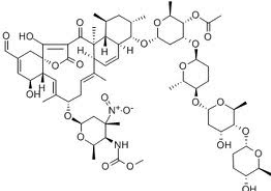
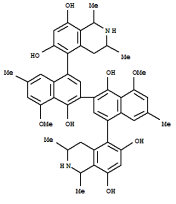
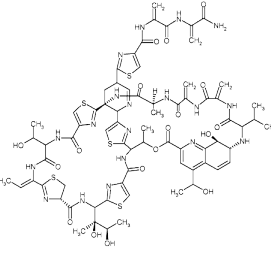
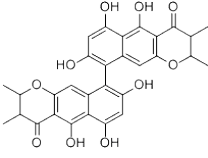
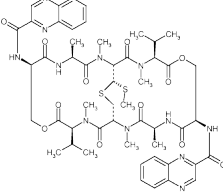
	461.55	Pimozide
	263.34	Pinacidil
	414.41	Piribedil maleate
	418.52	Pregnenolone sulfate sodium
	272.77	Procaine hydrochloride
	320.88	Promazine hydrochloride
	374.35	Quipazine, 6-nitro maleate
	345.79	S-(+) Fluoxetine hydrochloride
	299.49	Sphingosine
	477.57	Ritanserin
	603.75	Salmeterol
	367.78	Sanguinarine chloride
	255.79	Ro 41-1049 hydrichloride / (-)-Quinpirole hydrochloride

	264.32	SU 4312; 3-(4-Dimethylaminobenzylidene)-2-indolinone
	563.64 371.51	Tamoxifen citrate Tamoxifen
	292.13	UK 14,304 /5-Bromo-N-(2-imidazolyl-2-yl)-6-quinoxalinamine
	613.68	SKF95282/N-[3-[3-(1-Piperidinyl)methyl]phenoxy]propyl]2benzothiazolamine
	401.50	Urapidil,-5-Methyl
	129.16	(±)-Vigabatrin

^aThe LOPAC library (1280 compounds) was screened at a final concentration of 20 μM in a 96-well microtiter plate format. Plates were incubated for 5 days at 37°C and the OD_{600} recorded on a plate reader. Forty-one compounds inhibited the final growth yield (OD_{600}) by > 90% compared to the DMSO (1%)-treated control were identified as inhibitors. The screen was characterised by an average Z-factor of 0.67.

TABLE S2. Natural products that inhibited the growth of *M. maripaludis*^a

Structure	Mol Weight	Name
 <p>The structure shows a tetracyclic anthracycline core with a methoxy group at C-10, hydroxyl groups at C-1, C-5, and C-7, and a glycosidic attachment at C-4. The glycoside is a 2-deoxy-2-(2-amino-2-hydroxyethyl)ribose derivative. The entire molecule is associated with a hydrochloride counterion (HCl).</p>	563.98	Daunorubicin hydrochloride
 <p>The structure is a lumichrome derivative of riboflavin, featuring a methyl group at the 7-position of the isoalloxazine ring system.</p>	242.24	Riboflavin lumichrome
 <p>The structure is a xanthone derivative with a complex side chain at C-1, including a methoxy group and a prenyl group, and hydroxyl groups at C-2 and C-3.</p>	410.47	Mangostin
 <p>The structure is a pentacyclic ellipticine derivative with two methyl groups at the 1 and 4 positions of the pyridine ring.</p>	246.31	Ellipticine
 <p>The structure is a complex polycyclic aromatic compound with a nitro group and a methoxy group on one of the rings, and a carboxylic acid group on another.</p>	341.28	Aristolochic acid
 <p>The structure is a complex polycyclic compound with multiple hydroxyl, methyl, and aldehyde groups, and a complex side chain.</p>	398.46	Norlobaric acid
 <p>The structure is a complex polycyclic compound with multiple hydroxyl groups, a methoxy group, and a sodium counterion (Na+).</p>	747.96	Nigericin sodium salt
 <p>The structure is a large, cyclic polyether antibiotic consisting of a macrocyclic ring with multiple ether linkages and side chains.</p>	1111.34	Valinomycin
 <p>The structure is a highly complex, multi-ring natural product with numerous functional groups, including hydroxyl, carbonyl, and ether groups.</p>	1112.37	Didemnin B

	914.19	Rapamycin
	1255.44	Actinomycin D
	590.80	Lasalocid acid
	1336.49	Tetrocarcin A
	816.95	Michellamine B diacetic acid salt
	1648.85	SIOMYCIN A
	546.53	Chaetochromin
	1101.27	Echinomycin A

^aThe natural product in house library (120 compounds) was screened at a final concentration of 20 μ M in a 96-well microtiter plate format . Plates were incubated for 5 days at 37°C, and the OD₆₀₀ was

recorded on a plate reader. All compounds that reduced the growth yield by > 90% compared to the DMSO (1%)-treated control were considered inhibitory. The screen was characterised by an average Z-factor of 0.78.