SUPPORTING INFORMATION

Nitric oxide induction in peritoneal macrophages by a 1,2,3-triazole derivative improves its efficacy upon *Leishmania amazonensis in vitro* infection

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Table S-1. Physicochemical properties of 1,2,3-triazole derivative compounds

Compound	MW	RBs	HBA	HBD	TPSA (Å2)	Molar Refractivity	Lipophilicity (Log Po/w)
1	386.40	6	6	1	90.13	106.48	2.78
2	395.41	4	5	1	81.15	113.45	3.58
3	409.08	3	3	1	50.94	87.37	3.43
4	409.08	3	3	1	50.94	87.37	3.54
5	330.18	3	3	1	50.94	79.67	2.77
6	348.17	3	4	1	50.94	79.63	3.09
7	388.22	5	5	1	77.24	90.95	2.74
8	398.21	3	5	1	81.15	95.72	2.89
9	348.17	3	4	1	50.94	79.63	3.11
10	375.18	4	5	1	96.76	88.50	2.05
11	369.42	5	4	1	68.01	107.60	3.42

MW: Molecular weight, RBs: Rotatable bonds, HBA: Hydrogen bond acceptors, HBD: Hydrogen bond donors, TPSA: Topological surface area.

Table S-2. Drug-likeness properties of 1,2,3-triazole derivative compounds

Compound	Lipinski	Ghose	Veber	Egan	Muegge
1	Yes; 0 violation	Yes	Yes	Yes	Yes
2	Yes; 0 violation	Yes	Yes	Yes	Yes
3	Yes; 0 violation	Yes	Yes	Yes	Yes
4	Yes; 0 violation	Yes	Yes	Yes	Yes
5	Yes; 0 violation	Yes	Yes	Yes	Yes
6	Yes; 0 violation	Yes	Yes	Yes	Yes
7	Yes; 0 violation	Yes	Yes	Yes	Yes
8	Yes; 0 violation	Yes	Yes	Yes	Yes
9	Yes; 0 violation	Yes	Yes	Yes	Yes
10	Yes; 0 violation	Yes	Yes	Yes	Yes
11	Yes; 0 violation	Yes	Yes	Yes	Yes

Table S-3. Medicinal chemistry properties of 1,2,3-triazole derivative compounds

Compound	PAINS	Brenk	Leadlikeness	Synthetic accessibility
1	0 alert	0 alert	No; 1 violation: MW>350	3.66
2	0 alert	1 alert: cumarine	No; 2 violations: MW>350, XLOGP3>3.5	3.87
3	0 alert	0 alert	No; 2 violations: MW>350, XLOGP3>3.5	3.09
4	0 alert	0 alert	No; 2 violations: MW>350, XLOGP3>3.5	3.03
5	0 alert	0 alert	Yes	2.99
6	0 alert	0 alert	Yes	2.98
7	0 alert	0 alert	No; 1 violation: MW>350	3.27
8	0 alert	1 alert: cumarine	No; 1 violation: MW>350	3.55
9	0 alert	0 alert	YES	3.07
10	0 alert	2 alerts: nitro_group, oxygen-nitrogen_single_bond	No; 1 violation: MW>350	3.31
11	0 alert	0 alert	No; 1 violation: MW>350	3.58

PAINS: pan-assay interference compounds

Table S-4. *In silico* pharmacokinetics and toxicity properties of 1,2,3-triazole derivative compounds

Property	Model Name	Compound		
		4	**7**	**Miltefosine**
Absorption	Water solubility (log mol/L)	-4.394	-4.019	-6.149
	Caco-2 permeability (log Papp in 10^{-6} cm/s)	1.382	1.072	1.049
	Intestinal absorption – human (% Absorbed)	92.432	94.956	92.021
	Skin Permeability (logKp)	-2.511	-2.638	-2.721
	P-glycoprotein substrate	No	No	No
	P-glycoprotein I inhibitor	No	No	Yes
	P-glycoprotein II inhibitor	Yes	Yes	Yes
Distribution	Human ssVD (log L/kg)	-0.199	-0.419	0.355
	BBB permeability (logBB)	0.36	-0.935	-0.176
	CNS permeability (logPS)	-1.896	-2.375	-3.191
Metabolism	CYP2D6 substrate	No	No	No
	CYP3A4 substrate	Yes	Yes	Yes
	CYP1A2 inhibitor	Yes	Yes	No
	CYP2C19 inhibitor	Yes	Yes	No
	CYP2C9 inhibitor	Yes	No	No
	CYP2D6 inhibitor	No	No	No
	CYP3A4 inhibitor	No	No	No
Excretion	Total Clearance (log mL/min/kg)	-0.063	0.252	1.112
	Renal OCT2 substrate	Yes	Yes	No
Toxicity	AMES toxicity	No	No	No
	Human max. tolerated dose (log mg/kg/day)	0.055	0.286	0.211
	hERG I inhibitor	No	No	No
	hERG II inhibitor	No	No	Yes
	Oral Rat Acute Toxicity LD50 (mol/kg)	1.899	2.03	2.655
	Oral Rat Chronic Toxicity LOAEL (log mg/kg bw/day)	1.259	0.842	0.233
	Hepatotoxicity	No	No	Yes
	Skin Sensitization	No	No	Yes
	T pyriformis toxicity (log µg/L)	0.746	0.44	0.311
	Minnow toxicity (log mM)	-1.011	-1.616	-1.839

logKp: skin permeability constant VDss: steady state volume of distribution, BBB: brain-blood barrier, logBB: brain-blood permeability, CNS: central nervous system, logPS: brain-blood permeability-surface area product, OCT2: organic cation transporter 2, AMES: *Salmonella*/microsome mutagenicity assay, hERG: human ether-a-go-go, LOAEL: lowest dose of a compound that resulted in an observed adverse effect.

Table S-5. Sequence primers of iNOS and cytokines used for Real Time PCR

Target	Primer sequence		Accession number
Mouse iNOS	Forward	AACAGAGCCCTCAGCAGCATCCAT	NM_010927.3
	Reverse	CCAGGTGTTCCCCAGGCAGGTAG	
Mouse TNF-α	Forward	CACAAGATGCTGGGACAGTGA	NM_013693.2
	Reverse	TCCTTGATGGTGGTGCATGA	
Mouse IL-1β	Forward	GCAACTGTTCCTGAACTCAACT	NM_008361
	Reverse	ATCTTTTGGGGTCCGTCAACT	
Mouse IL-6	Forward	TCTATACCACTTCACAAGTCGGA	NM_031168.2
	Reverse	GAATTGCCATTGCACAACTCTTT	
Mouse IL-12	Forward	ACAGGGTGATGGGCTATCTGA	NM_001159424.1
	Reverse	TGTGGCAGAGGGCCTTGA	
Mouse IL-10	Forward	GATGCCCCAGGCAGAGAA	NM_010548.2
	Reverse	CACCCAGGGAATTCAAATGC	
Mouse RPLP0[1]	Forward	GCCAGCTCAGAACACTGGTCTA	NM_007475.5
	Reverse	ATGCCCAAAGCCTGGAAGA	

[1]ribosomal protein lateral stalk subunit P0.

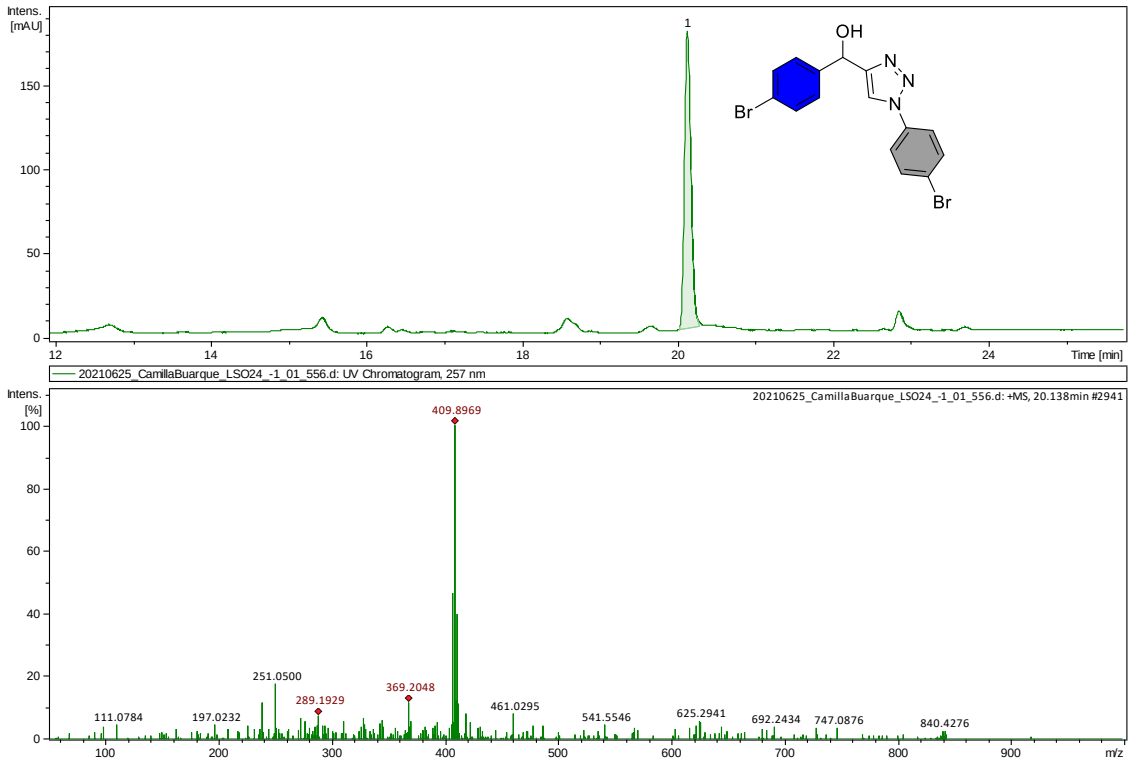

Figure S-1. HPLC-MS chromatogram of the compound **4**. The purity of the compound **4** by HPLC-MS was checked on a Nexera system from Shimadzu´s with the following parameters: Hypersil C18 column (150 × 2.1 mm, 3 µm), with pre column (10 x 2.1 mm, Thermo); a flow rate of 0.2 mL.min^{-1}; injector volume of 10 µL; temperature of 40 ºC; UV detection at 257 nm; solvent system, A = water (0.1% formic acid) and B = acetonitrile (0.1% formic acid) using the gradient method following elution protocol: 0-5 min, 5 % B; 25-34 min, 95% B.