

Supplementary Material

Challenges in drug discovery and description, targeting *Leishmania* spp.: enzymes, structural proteins and transporters

Alexis Mendoza-León,^{1*}María Luisa Serrano G.,^{2*}Alicia Ponte-Sucre^{3*}

¹ Instituto de Biología Experimental (IBE). Facultad de Ciencias. Instituto de Medicina Tropical (IMT), Facultad de Medicina. Universidad Central de Venezuela (UCV). Caracas, Venezuela.

² Unidad de Química Medicinal, Facultad de Farmacia. UCV. Caracas, Venezuela.

³ Laboratorio de Fisiología Molecular. Facultad de Medicina. UCV. Caracas, Venezuela.

***Correspondence authors:**

Alexis Mendoza-León: amendoza50@gmail.com

Maria Luisa Serrano: maria.serrano@ucv.ve

Alicia Ponte Sucre: aiponte@gmail.com

Keywords: Leishmaniasis, target, drug, treatment, tubulin, modelling, glibenclamide

1 Supplementary Table 2: Selected ABC transporter (P-gp-specific) inhibitors^a

Pharmacological group	Name of the individual drugs
Analeptics	Almitrine
Antiarrhythmics	Amiodarone, lidocaine, quinidine ^b
Antibiotics	Clarithromycine, erythromicine
Anticancer drugs	Actinomycine D, doxorubicin, vinblastine, biricodar (VX-17) ^c , valspodar (PSC-833) ^c , elacridar (GF120918) ^d , tariquidar (XR9576) ^d , zosuquidar (LY335979) ^d , laniquidar (R101933) ^d , ONT-093 ^d .
Antidepressants	Chlorimipramine, imipramine, paroxetine
Antiestrogens	Tamoxifen ^b , toremifena ^b
Antihistamines	Terfenadine
Anti-parasitic	Chloroquine, emetine, hydroxichloroquine, quinacrine, quinine
Calcium channel blockers	Bepidil, diltiazem, felopidine, nifedipine, nislopidine, nitrendipine, tiapamil, verapamil ^b
Coronary vasodilators	Dipyrodamole
Diuretics	Amiloride
HIV protease inhibitors	Indinavir, retanavir, ritonavir, sequinavir
Immunosuppressants	Cyclosporin A ^b , FK 506, PSC833
Neuroleptics	Reserpine ^b , yohimbine ^b
Local anesthetics	Bipucaine
Proton pump inhibitors	Esomeprezole, lansoprazole, omeprazole
Steroid hormones	Progesterone
Surfactants	Triton X-100, Tween 80, vremophor-EL
Toxic peptides	N-acetyl-leucyl-leucinal, gramcidine, D, valinomycin
Others	GF120918 ^c , LY335979 ^d , MS-209 ^c , OC144093 ^d , PSC-833 ^c , R101933 ^d , R-verapamil ^c , VX-710 ^c , VX-853 ^c , XR9576 ^d

^a Modified from: Wiese M, Pajeva IK. Structure-activity relationships of multidrug resistance reversers. *Curr Med Chem* (2001) 8(6):685-713. doi: 10.2174/0929867013373138; Lage H. ABC-transporters: implications on drug resistance from microorganisms to human cancers. *Int J Antimicrob Agents* (2003) 22(3):188-99. doi: 10.1016/s0924-8579(03)00203-6.; Varma MV, Ashokraj Y, Dey CS, Panchagnula R. P-glycoprotein inhibitors and their screening: a perspective from bioavailability enhancement. *Pharmacol Res* (2003) 48(4):347-59. doi: 10.1016/s1043-6618(03)00158-0; Mullin S, Mani N, Grossman TH. Inhibition of antibiotic efflux in bacteria by the novel multidrug resistance inhibitors biricodar (VX-710) and timcodar (VX-853). *Antimicrob Agents Chemother* (2004) 48(11):4171-6. doi: 10.1128/AAC.48.11.4171-4176.2004; Ponte-Sucre A. Availability and applications of ATP-binding cassette (ABC) transporter blockers. *Appl Microbiol Biotechnol* (2007) 76(2):279-86. doi: 10.1007/s00253-007-1017-6; ABC Transporters and Cancer Drug Resistance (<https://www.sigmaaldrich.com/VE/es/technical-documents/technical-article/research-and-disease-areas/cancer-research/abc-transporters-and-cancer-drug-resistance>)

^b First-generation inhibitors, ^c Second-generation inhibitors, ^d Third-generation inhibitors

