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Supplemental Material: Novel Compounds and Biological Screening Results

Azole Based Non-peptidomimetic Plasmepsin Inhibitors

Linda Kinena[†], *Gundars Leitis,*[†] *Iveta Kanepe-Lapsa*[†], *Raitis Bobrovs*[†], *Kristaps Jaudzems*[†], *Vita Ozola*[†], *Edgars Suna,*[†*] *Aigars Jirgensons*[†*]

[†] Latvian Institute of Organic Synthesis, Aizkraukles 21, Riga LV-1006, Latvia

Correspondence to Aigars Jirgensons, Latvian Institute of Organic Synthesis, Aizkraukles 21, Riga LV-1006, Latvia, Phone: +371 67014948; e-mail: aigars@osi.lv

Compound No.	InChI	Plm II inhibition (IC_{50})[a]
1a	BGRDACPMBHDXJD-UHFFFAOYSA-N	0.42 µM
1b	XYEJXZSCRYPPSU-UHFFFAOYSA-N	0.30 µM
2a	FOIJRPXMTQLGSY-UHFFFAOYSA-N	4.3 µM
2b	DOHRGFDJJUSUOS-UHFFFAOYSA-N	10.0 µM
2c	XVLGWLFJWHNXCW-UHFFFAOYSA-N	5.3 µM
2d	LAQMBSLKDLACGI-UHFFFAOYSA-N	10.0 µM
2e	YVUKYECMARZVLG-UHFFFAOYSA-N	0.6 µM
2f	KMVPKECXCODURK-UHFFFAOYSA-N	2.7 µM
2g	WBYBDYIILBPJQD-UHFFFAOYSA-N	4.7 µM
2h	HNKNSFXQADXBGO-UHFFFAOYSA-N	0.6 µM
2i	JACOYQVDWVWLBO-UHFFFAOYSA-N	2.9 µM
2j	NLDFVEFYWDHAOE-UHFFFAOYSA-N	7.5 µM
2k	QBSHHVOUQOKUFK-UHFFFAOYSA-N	1.8 µM
2l	WLHXYSJMGQIFAN-UHFFFAOYSA-N	5.9 µM
2m	FUVWTMJBSSQWRO-UHFFFAOYSA-N	2.9 µM
2n	ZHOZJQPCMRDLHN-UHFFFAOYSA-N	5.0 µM

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2o	BWHZVKNIPLJQIH-UHFFFAOYSA-N	6.5 µM
2p	BAHMTXWQGMNZAI-UHFFFAOYSA-N	3.0 µM
2q	XKDFAXWTXFUIJT-UHFFFAOYSA-N	>200 µM
2r	XPJMLLHHSSOSBJ-UHFFFAOYSA-N	5.2 µM
2s	LTSNMJDURAKYBS-UHFFFAOYSA-N	0.6 µM

[a] A fluorescence resonance energy transfer (FRET) assay was performed to evaluate ability of compounds to inhibit Plm II. K_m of the substrate was determined for the enzyme PlmII = 2 ± 0.2 µM. A solution of compounds for testing (concentration 0.01−100 µM) on 96-well plate was added to the enzyme in buffer (0.1 M NaOAc, pH = 4.5, 10% glycerol). The mixture was incubated for 30 min at 37 °C. Substrate (DABCYL-Glu-Arg-Nle-Phe-Leu-Ser-Phe-Pro-EDANS, AnaSpec Inc.) was then added to reach a final concentration of 5 µM. Hydrolysis of the substrate was detected as an increase in fluorescence (Em 490 nm, Ex 336 nm) at 37 °C. The data points were collected every 1 min within 8−15 min. Compounds were tested in triplicate experiments. IC_{50} values were calculated using software Graph Pad Prism 5.0. Pepstatin A (IC_{50} = 0.42 ±0.02 nM (Plm II) and compound **1a** were used as positive controls