Supplementary Materials

# Uncovering the mechanism of action of antiprotozoal agents: a survey on photoaffinity labeling strategy.

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**Table S1.** Antiprotozoal activity (*Trypanosoma brucei*, *Leishmania*, and *Trypanosoma cruzi*) and cytotoxicity of compounds and probes reported in Section 4 of the present review.

| Compound/Probe | Molecular Weight | $EC_{50}$ (μM) | | | | |
|---|---|---|---|---|---|---|
| | | *Tb* [1] | *L* [2] | *Tc* [3] | $CC_{50}$ (μM) [4] | Reference |
| **Chamuvarinin** | 604.91 | 1.4 (BSF)<br>1.9 (PF) | - | - | 2.0 (HeLa) | [152] |
| **5** | 407.60 | 1.8 (BSF)<br>8.4 (PF) | - | - | 7.0 (HeLa)<br>7.0 (Vero) | [152] |
| **6** | 562.72 | 13.0 (BSF)[5]<br>17.5 (BSF, *Tbb*)[6]<br>16.1 (PF)[5]<br>25.7 (PF, *Tbb*)[6] | 20.3 (PRO, *Lm*) | 51.2 (EP) | 21.3 (HeLa)<br>21.3 (Vero) | [152] |
| **7** | 511.67 | 11.8 (BSF)[5]<br>10.1 (BSF, *Tbb*)[6]<br>8.9 (PF)[5]<br>8.5 (PF, *Tbb*)[6] | 32.6 (PRO, *Lm*) | 29.9 (EP) | 20.9 (HeLa) | [152], [166] |
| **8** | 466.96 | 0.0389 (BFS, *Tbb*) | - | - | 0.0108 (HEK293) | [164] |
| **9** | 488.93 | 0.2653 (BSF, *Tbb*) | - | - | 0.0646 (HEK293) | [164] |
| **10** | 591.79 | 4.6 (BSF, *Tbb*)<br>3.5 (PF, *Tbb*) | 15.6 (PRO, *Lm*)<br>17.7 (IA, *Ld*) | 29.8 (EP) | 12.1 (HeLa)<br>16.5 (Vero)<br>23.9 (THP-1) | [166] |
| **11** | 472.59 | 13.0 (BSF, *Tbb*)<br>16.1 (PF, *Tbb*) | 31.5 (PRO, *Lm*) | 59.6 (EP) | - | [166] |
| **12** | 511.67 | 11.8 (BSF, *Tbb*)<br>8.9 (PF, *Tbb*) | 25.1 (PRO, *Lm*) | 44.2 (EP) | - | [166] |
| **17-AAG** | 585.70 | - | $IC_{50}$ =0.211 (PRO, *Lmx*) | - | - | [174] |
| **17-mADAG** | 665.79 | - | $IC_{50}$ = 0.640 (PRO, *Lmx*) | - | - | [174] |
| **Actinoallolide A** | 564.76 | 0.0083 (*Tbb*)<br>0.152 (*Tbr*) | - | 0.400 | - | [175], [176] |

| | | | | | | |
|---|---|---|---|---|---|---|
| **13** | 823.76 | - | - | - | - | [175], [176] |

[1] Activity profile on bloodstream (BSF) and procyclic (PF) forms of *T. brucei brucei* (*Tbb*) and *T. brucei rhodesiense* (*Tbr*) parasites expressed as $EC_{50}$ (or $IC_{50}$, when specified). [2] Activity profile on promastigote (PRO) and intramacrophage amastigote (IA) forms of *L. major* (*Lm*), *L. donovani* (*Ld*) and *L. mexicana* (*Lmx*) parasites expressed as $EC_{50}$ (or $IC_{50}$, when specified). [3] Activity profile on epimastigote (EP) form of *T. cruzi* parasite expressed as $EC_{50}$ (or $IC_{50}$, when specified). [4] Cytotoxicity assessed on mammalian cells indicated in brackets and expressed as $CC_{50}$. [5] Activity reported in ref. [152]. [6]Activity reported in ref. [166].

**Table S2.** $IC_{50}$ values of compounds reported in Section 6 of the present review displaying antimalarial activities.

| Compounds | Molecular Weight | *P. falciparum* strain | $IC_{50}$ (nM) | Reference |
|---|---|---|---|---|
| Artesunate (ATS) | 384.42 | 3D7 | 5.96 | [197] |
| APP | 418.49 | 3D7 | 0.64 | [197] |
| Chloroquine | 319.88 | 3D7 | 34<br>19.48 | [200]<br>[202] |
| | | FAC8 | 156 | [200] |
| ASA-Q | 461.57 | 3D7 | 39 | [200] |
| | | FAC8 | 73 | [200] |
| CQP | 623.20 | 3D7 | 184.10 | [202] |
| Mefloquine | 378.32 | K1<br>K1 Mef<br>D10 | 349<br>1083<br>826 | [208] |
| ASA-MQ | 544.58 | K1<br>K1 Mef<br>D10 | 53<br>185<br>159 | [208] |
| Plasmodione | 330.31 | Dd2 | 20 | [209] |
| | | NF54 | 46.6 | [210] |
| **18** | 286.33 | Dd2 | 49 | [209] |
| **19** | 300.31 | Dd2 | 1806 | [209] |
| **20** | 375.34 | Dd2 | 417 | [209] |
| **22** | 304.32 | NF54 | 179.2 | [210] |
| ACT-186128 | 737.87 | 3D7 | 14.9 | [214] |
| ACT460953 | 1384.63 | 3D7 | 34.1 | [214] |
| Guttiferone A | 602.80 | 3D7 | 5100 | [217] |
| AZC-GA | 844.00 | 3D7 | 5400 | [217] |
| DDD01035881 | 404.30 | NF54 gametocytes | 292 | [219] |
| **23** | 384.41 | NF54 gametocytes | 3981 | [219] |
| **24** | 477.17 | NF54 gametocytes | 785 | [219] |
| **25** | 514.66 | D10 | 0.77 | [221] |
| | | W2 | 0.91 | [221] |
| **26** | 646.70 | D10 | 1021.51 | [221] |
| | | W2 | 1245.03 | [221] |
| **27** | 524.65 | D10 | 207.78 | [221] |
| | | W2 | 195.96 | [221] |
| **28** | 516.63 | D10 | 270.96 | [221] |
| | | W2 | 299.58 | [221] |
| **29** | 516.63 | D10 | 15.03 | [221] |
| | | W2 | 19.48 | [221] |
| **30** | 516.63 | D10 | 165.69 | [221] |
| | | W2 | 204.33 | [221] |
| BIX01294 | 490.64 | 3D7 | 43.4<br>50 | [222]<br>[224] |
| **31** | 520.67 | 3D7 | 42 | [224] |
| Dioncophylline A | 377.48 | FCBR | 381 | [228] |
| **32** | 919.22 | FCBR | 45 | [228] |

| | | | | |
|---|---|---|---|---|
| **33** | 738.98 | FCBR | 602 | [228] |
| **34** | 1070.25 | FCBR | 960 | [228] |
| Albitiazolium | 469.77 | 3D7 | 4.2 | [232] |
| UA1936 | 640.90 | 3D7 | 4.5 | [232] |