**S1 Table. Dose-reduction index for multidrug treatment with benznidazole and crystal violet chemical analogues in wild type epimastigotes of *T. cruzi* Y strain.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Fa** | **Dose BZL alone (µM)**  | **Dose LTD-CPH-CFZ alone (µM)** | **Dose BZL in combination (µM)** | **Dose LTD-CPH-CFZ in combination (µM)** | **DRI BZL** | **DRI****LTD-CPH-CFZ** |
| 0.112 | 1.66 ± 0.28 | 5.23 ± 0.39 | 0.10 | 3.40 (1/25 IC50) | 16.63 ± 2.78 | 1.54 ± 0.12 |
| 0.324 | 7.37 ± 0.49 | 10.22 ± 0.31 | 0.10 | 8.50 (1/10 IC50) | 73.67 ± 4.95 | 1.20 ± 0.04 |
| 0.673 | 37.42 ± 3.25 | 21.22 ± 0.83 | 0.10 | 17.00 (1/5 IC50) | 374.17 ± 32.50 | 1.25 ± 0.05 |
| 0.821 | 92.37 ± 17.51 | 31.79 ± 2.72 | 0.10 | 42.50 (1/2 IC50) | 923.66 ± 175.14 | 0.75 ± 0.06 |
| 0.257 | 5.12 ± 0.06 | 8.69 ± 0.05 | 1.00 | 3.40 (1/25 IC50) | 5.12 ± 0.06 | 2.55 ± 0.01 |
| 0.447 | 13.27 ± 2.61 | 13.29 ± 1.18 | 1.00 | 8.50 (1/10 IC50) | 13.27 ± 2.61 | 1.56 ± 0.14 |
| 0.740 | 53.83 ± 6.79 | 24.97 ± 1.42 | 1.00 | 17.00 (1/5 IC50) | 53.83 ± 6.79 | 1.47 ± 0.08 |
| 0.881 | 157.01 ± 24.63 | 40.38 ± 2.86 | 1.00 | 42.50 (1/2 IC50) | 157.01 ± 24.63 | 0.95 ± 0.07 |
| 0.430 | 12.27 ± 2.01 | 12.84 ± 0.95 | 5.00 | 3.40 (1/25 IC50) | 2.45 ± 0.40 | 3.78 ± 0.28 |
| 0.609 | 27.38 ± 2.41 | 18.44 ± 0.73 | 5.00 | 8.50 (1/10 IC50) | 5.48 ± 0.48 | 2.17 ± 0.09 |
| 0.732 | 51.57 ± 8.60 | 24.48 ± 1.84 | 5.00 | 17.00 (1/5 IC50) | 10.31 ± 1.72 | 1.44 ± 0.11 |
| 0.933 | 315.46 ± 41.27 | 55.28 ± 3.26 | 5.00 | 42.50 (1/2 IC50) | 63.09 ± 8.25 | 1.30 ± 0.08 |
| 0.682 | 38.95 ± 1.06 | 21.61 ± 0.26 | 10.00 | 3.40 (1/25 IC50) | 3.89 ± 0.11 | 6.36 ± 0.08 |
| 0.743 | 54.45 ± 1.86 | 25.13 ± 0.39 | 10.00 | 8.50 (1/10 IC50) | 5.45 ± 0.19 | 2.96 ± 0.05 |
| 0.835 | 101.97 ± 8.68 | 33.30 ± 1.28 | 10.00 | 17.00 (1/5 IC50) | 10.20 ± 0.87 | 1.96 ± 0.08 |
| 0.951 | 457.73 ± 30.35 | 65.40 ± 1.95 | 10.00 | 42.50 (1/2 IC50) | 45.77 ± 3.03 | 1.54 ± 0.05 |
| 0.852 | 117.55 ± 11.14 | 35.49 ± 1.51 | 20.00 | 3.40 (1/25 IC50) | 5.88 ± 0.56 | 10.44 ± 0.45 |
| 0.877 | 148.83 ± 4.56 | 39.48 ± 0.54 | 20.00 | 8.50 (1/10 IC50) | 7.44 ± 0.23 | 4.64 ± 0.06 |
| 0.909 | 218.81 ± 31.25 | 46.89 ± 3.02 | 20.00 | 17.00 (1/5 IC50) | 10.94 ± 1.56 | 2.76 ± 0.18 |
| 0.981 | 1370.11 ± 265.72 | 106.81 ± 9.36 | 20.00 | 42.50 (1/2 IC50) | 68.51 ± 13.29 | 2.51 ± 0.22 |

Fa, fraction affected. DRI, dose-reduction index. Dose alone indicates the concentration of each drug alone needed to achieve the same effect (Fa) as in the combination. BZL, benznidazole. LTD, loratadine. CPH, cyproheptadine. CFZ, clofazimine. IC50 LTD = 25 µM. IC50 CPH = 50 µM. IC50 CFZ = 10 µM. LTD-CPH-CFZ, combination of the three crystal violet analogues as a single drug. 1/2 IC50, refers to the sum of half of each IC50, 12.5 µM + 25 µM + 5 µM = 42.5 µM. 1/5 IC50, 5 µM + 10 µM + 2 µM = 17 µM. 1/10 IC50, 2.5 µM + 5 µM + 1 µM = 8.5 µM. 1/25 IC50, 1 µM + 2 µM + 0.4 µM = 3.4 µM.