Correction: Influence of LAR and VAR on Para-Aminopyridine Antimalarials Targetting Haematin in Chloroquine-Resistance

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There are errors in the published article.

Fig 1 does not show the enantiomeric bond from 4-amino to methyl. In the caption for Fig 1, the reference given is incorrect. The correct reference is [13]. Please see the correct Fig 1 and its caption here.

Fig 1. Structures of the main pAP compounds examined. Note outline (blue) of the p-aminopyridine moiety in CQ(2) and its presence in Atebrin, ATB(1) and (5). Also note 2 pAP moieties in each of (3), (4) and (6). Compound (5), a half-piperquine, has low antiparasitic activity and shows 6 times less activity in the in vitro BIHA test than PQ (3) [13].

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In the Physiochemical section of the Material and Methods, the third equation appears incorrectly. The correct equation is:

$$\log D = \log \frac{P}{C_0} \log \frac{1}{\frac{1}{2} + 10^{(pK_{a1} + pK_{a2} - 2pH) + 10^{(pK_{a1} + pK_{a2} - pK_{a3} - pH) + 10^{(pK_{a1} + pK_{a2} + pK_{a3} + pK_{a4} - 4pH)}}}}$$

(3)

In the Molecular Modelling sections of the Material and Methods and the Results and Discussion, the reference given is incorrect. The reference should be [25].

The references that appear at the end of the fourth paragraph in the Results and Discussion are incorrect. The correct references are [21–24].

In the last sentence of the Graphical Approaches section of the Results and Discussion the incorrect reference appears. The correct reference is [21].

There are errors in Table 1. In the LogCQRI column the value for cpd5 should be 0.308, not 1.308. In the VAR column the value for CQ should be 143482, not 1434882. The value for the first DCQ should be 4897788, not 48897788.
Table 1. Physicochemical and other parameters for the compounds studied.

| Drug | logP | pKa1 | pKa2 | pKa3 | pKa4 | pH | logD | LAR/VAR | LOGLAR | logD | antilog D_4.8 | LAR | VARI | IC50 mM | SE | n |
|------|------|------|------|------|------|----|-------|---------|--------|-------|----------------|-----|-------|----------|----|---|
| CQ   | 4.72 | 10.18 | 8.38 | -20  | -20  | 7.4 | 0.91668 |         |        |       |                 |     |       |          |    |   |
| CQ   | 4.72 | 10.18 | 8.38 | -20  | -20  | 4.8 | -4.24011 | -4.2401 | 0.91688 | 1.149 | 8.525434 | 5.75E-05 |       |          |    |   |
| PQ   | 6.11 | 6.88  | 6.24 | 5.72 | 5.39 | 7.4 | 5.98833 |         |        |       |                 |     |       |          |    |   |
| PQ   | 6.11 | 6.88  | 6.24 | 5.72 | 5.39 | 4.8 | 0.96972 |         |        | 0.96972 | 5.98833 | 0.39 | 9.73492 | 9.3266 |   |   |
| OHPQ | 5.67 | 6.6   | 6.41 | 5.39 | 4.83 | 7.4 | 5.60001 |         |        |       |                 |     |       |          |    |   |
| OHPQ | 5.67 | 6.6   | 6.41 | 5.39 | 4.83 | 4.8 | 1.30172 | 1.30172 | 5.60012 | 0.176 | 398118  | 20.032 |       |          |    |   |
| DCQ  | 6.1  | 8.71  | 8.34 | 7.36 | 5.9  | 7.4 | 4.19   |         |        |       |                 |     |       |          |    |   |
| DCQ  | 6.1  | 8.71  | 8.34 | 7.36 | 5.9  | 4.8 | -2.5   | -2.5    | 4.19   | 0.176 | 15488.2 | 0.0032 |       |          |    |   |
| DCQa | 6.1  | 8.71  | 8.34 | 7.36 | 5.9  | 7.4 | 3.53586 |         |        |       |                 |     |       |          |    |   |
| DCQa | 6.1  | 8.71  | 8.34 | 7.36 | 5.9  | 4.8 | -5.04328 | -5.0433 | 3.53586 | 0.176 | 3434.48 | 9.05E-06 |       |          |    |   |
| S    | 3.48 | 7.92  | 5.54 | -20  | -20  | 7.4 | 2.8408 |         |        |       |                 |     |       |          |    |   |
| S    | 3.48 | 7.92  | 5.54 | -20  | -20  | 4.8 | -0.45266 | -0.4527 | 2.84081 | 0.308 | 693123  | 0.3526 |       |          |    |   |
| HCQ  | 3.835| 9.66  | 8.27 | -20  | -20  | 7.4 | 0.64976 |         |        |       |                 |     |       |          |    |   |
| HCQ  | 3.835| 9.66  | 8.27 | -20  | -20  | 4.8 | -4.49515 | -4.4952 | 0.64976 | 1.898 | 4.46437 | 3.20E-05 |       |          |    |   |
| DEQ  | 4.35 | 10.96 | 8.4  | -20  | -20  | 7.4 | -0.2514 |         |        |       |                 |     |       |          |    |   |
| DEQ  | 4.35 | 10.96 | 8.4  | -20  | -20  | 4.8 | -5.41011 | -5.4101 | -0.2514 | 1.564 | 0.56053 | 3.89E-06 |       |          |    |   |
| DAQ  | 3.31 | 8.72  | 7.53 | -20  | -20  | 7.4 | 1.61036 |         |        |       |                 |     |       | 89365.43 | 4.951172 |   |
| DAQ  | 3.31 | 8.72  | 7.53 | -20  | -20  | 4.8 | -3.34081 | -3.3408 | 1.61034 | 0.732 | 40.7721 | 0.0005 |       |          |    |   |
| AQ   | 4.26 | 8.66  | 7.05 | -20  | -20  | 7.4 | 2.82344 |         |        |       |                 |     |       | 47410.07 | 4.675871 |   |
| ATB  | 4.85 | 10.47 | 7.12 | -20  | -20  | 7.4 | 1.59654 |         |        |       |                 |     |       | 54779.28 | 4.738616 |   |
| SC   | 5.15 | 10.15 | 7.28 | -20  | -20  | 7.4 | 2.1544  |         |        |       |                 |     |       | 68522.82 | 4.835835 |   |
| SC   | 5.15 | 10.15 | 7.28 | -20  | -20  | 4.8 | -2.68144 | -2.6814 | 2.1544  | 0.376 | 142.92  | 0.0021 |       |          |    |   |
| PH203| 6.45 | 10.29 | 5.57 | -20  | -20  | 7.4 | 3.55307 |         |        |       |                 |     |       | 2698.94 | 3.41193  |   |
| PH203| 6.45 | 10.29 | 5.57 | -20  | -20  | 4.8 | 0.12188 | 0.12188 | 3.55307 | 0.193 | 3573.32 | 1.324  |       |          |    |   |

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Reference

1. Warhurst DC, Craig JC, Raheem KS (2016) Influence of LAR and VAR on Para-Aminopyridine Antimalarials Targeting Haematin in Chloroquine-Resistance. PLoS ONE 11(8): e0160091. doi:10.1371/journal.pone.0160091 PMID: 27483471