Anti-*Pneumocystis carinii* activity of primaquine imidazolidin-4-ones

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*Pneumocystis* pneumonia (PCP) is one of the most frequent causes of mortality among HIV-infected patients. Primaquine (PQ) is an antimalarial 8-aminoquinoline effective against PCP when given in combination with clindamycin. This has drawn the attention of Medicinal Chemists towards the anti-PCP activity of 8-aminoquinolines, not only confined to those exhibiting antimalarial activity [1]. It is thought that anti-PCP 8-aminoquinolines exert their anti-PCP activity by acting on the electronic transport and redox system of the *P. carinii* pathogen [1]. Recently, our research group has been developing imidazolidin-4-one derivatives of PQ (Scheme 1), targeting novel compounds with improved therapeutic action, namely, higher resistance to metabolic inactivation, lower toxicity and equal or higher antimalarial activity than that of the parent drug [2,3]. These imidazolidin-4-ones were seen to block the transmission of rodent malaria, caused by *Plasmodium berghei* on BalbC mice, to the mosquito vector *Anopheles stephensi* [3].

![Scheme 1. Synthetic route to primaquine imidazolidin-4-ones](image)

1) *N*-Boc-protected amino acid dicyclohexylcarbodiimide, 1-hydroxybenzotriazole; 2) i. neat trifluoroacetic acid; ii. Na₂CO₃; 3) propanone or a cyclic symmetrical ketone (cyclopentanone, cyclohexanone and cycloheptanone); CH₃OH (reflux); triethylamine; 4 Å molecular sieves.

The anti-PCP activity of our PQ derivatives is now under study and preliminary *in vitro* assays [4] show that some of the compounds exhibit slight to moderate activity after a 72 h incubation period against *P. carinii*. In one case, the IC₅₀ was comparable to that of parent PQ. Both these studies and forthcoming results from ongoing biological assays will be presented and discussed.