

A new strategy against malaria – antimarial ionic liquids derived from aminoquinolines and fatty acids

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Based on the recent promising results obtained by us, where ionic liquids (ILs) derived from primaquine were found as triple-stage antimalarial hits [1], we have now produced, by simple, quantitative, and low-cost methods, new ILs *via* simple acid-base titration of antimalarial aminoquinolines (primaquine and chloroquine) with natural fatty acids (Figure 1) [1]. We have also synthesized, in good to high yields, the covalent amide analogues of these ILs (Figure 1), in order to establish how the nature of the chemical bond (ionic ammonium carboxylate *versus* covalent amide) between both building blocks influences the physico-chemical and biological properties of the final compounds [2]. Results obtained thus far allow us to conclude that both ionic and covalent compounds (i) have higher thermostability than the parent drugs, and (ii) display remarkable *in vitro* activity against liver-stage malaria parasites.

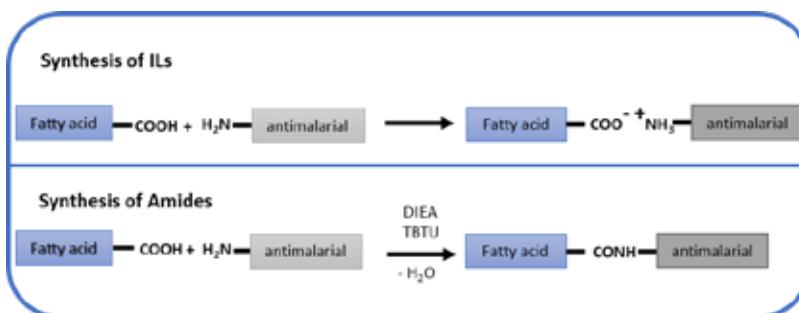


Figure 1. Schematic view of antimalarial-derived ILs and their covalent amide analogues.

Ongoing studies will hopefully allow to confirm the therapeutic potential of these new compounds, and allow us to build structure-activity relationships that will guide future efforts towards potent, safe and low-cost antimalarial drugs.

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REFERÊNCIAS:

- [1] Ferraz, R.; Noronha, J.; Murtinheira, F.; Nogueira, F.; Machado, M.; Prudencio, M.; Parapini, S.; D'Alessandro, S.; Teixeira, C.; Gomes, A.; Prudencio, C.; Gomes, P., Primaquine-based ionic liquids as a novel class of antimalarial hits. *Rsc Advances*, 2016, 6, (61), 56134-56138.
- [2] Pérez, B.; Teixeira, C.; Gut, J.; Rosenthal, P.J.; Gomes, J.R.; Gomes, P., Cinnamic Acid/Chloroquinoline Conjugates as Potent Agents against Chloroquine-Resistant Plasmodium falciparum. *ChemMedChem*, 2012, 7, (9), 1537-1540.