

Potent Anti-Malaria Salts, Co-Crystals and Derivatives of Aminoquinolines with Hydroxyaromatic Acids

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Abstract

Antimalarial activities of salts of aminoquinolines with hydroxyaromatic acids were found to be higher than the parent components. The IC₅₀ values of the salts were in the range of 5.9-20.3 μ M against the chloroquine-resistant strain. Antimalarial actions on the parasites were found to be independent of iron chelation, inhibition of haemozoin formation, as well as independent of the anti-oxidant activity of the salts. A covalently linked amide containing compound N-(quinolin-8-yl)-2-(quinolin-8-yloxy)acetamide was identified to have potency similar to the

other salts studied in the article. Salts I-III and co-crystal IV were prepared by crystallization of solution of 1:1 mole ratio of the corresponding aminoquinoline and respective hydroxyaromatic acid. In each case, aminoquinoline and hydroxyaromatic acid was dissolved in methanol and kept undisturbed for crystallization. The ferrozine-iron chelation assay was used to determine the ferrous ion chelating properties of the derivatives. We have shown that salts and cocrystal of quinoline with hydroxyaromatic carboxylic acids enhance antimalarial activities over parent compounds.

Keywords: Aminoquinolines; Hydroxyaromatic acids; Salts; Antimalarial activity; Anti-oxidant activity