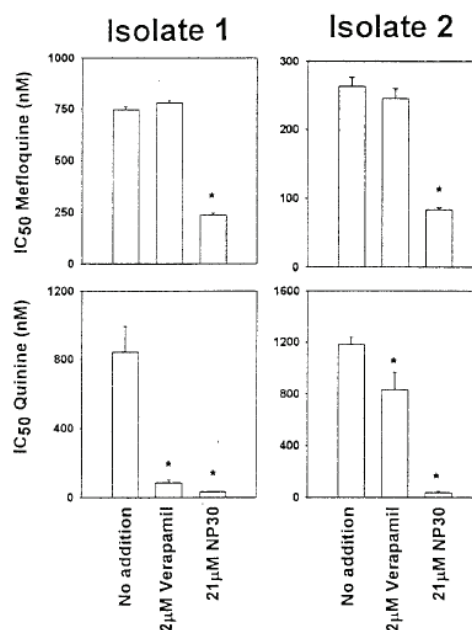


Malaria Drug Resistance Reversal Agent

Overview of Technology:

Quinolines (mefloquine, quinine, quinidine etc.) are amongst the most commonly used antimalarials; however, all suffer from increasing drug resistance. Resistance to these agents is accomplished by the activity of a drug efflux pump. Toronto researchers have discovered potent inhibitors of these pumps, thus restoring the anti-malarial activity of quinoline drugs including activity against *P. falciparum* (the most deadly form of human malaria). These inhibitors are very inexpensive, nontoxic and stable at room temperatures, and thus could be easily incorporated into quinoline formulations. Preliminary toxicology studies indicate that these surfactants are very well tolerated in rodents and that effective doses can be achieved in vivo.

Malaria produces an estimated 247 million cases per year among 3.3 billion at risk and results in nearly one million deaths, mostly in children under five years of age. Increasing resistance to current anti-malarials has created a critical need for either new, low-cost, effective anti-malarials or resistance reversal technologies for existing therapies.



Effect of verapamil and NP30 on IC50's of Quinine and Mefloquine

Related Publications:

Crandall, I., Charuk, J., and Kain, K. Nonylphenoethoxylates as Malarial Chloroquine Resistance Reversal Agents. *Antimicrobial Agents and Chemotherapy*. **44(8)**, 2431–2434 (2000)
Vol. 44, No. 9

Ciach, M., Zong, K., Kain, C., and Crandall, I. Reversal of Mefloquine and Quinine Resistance in *Plasmodium falciparum* with NP30. *Antimicrobial Agents and Chemotherapy*. **47(8)**, 2393–2396 (2003)

Patents:

US 7,163,950 B1 Issued - Jan 16, 2007 and India 221957 Issued - July 18, 2008
Canada - Filed Nov 28, 2000

Inventors:

Ian Crandall, Kevin Kain, Reinhart Reithmeier, Jeffrey Charuk

UHN Reference # - 9009