



NMQ – N-methyl-quinidine

The unlabeled probe substrate of SOLVO's MDR1 and rat Mdr1b PREDIVEZ Kits is now available from SOLVO Biotechnology

N-methyl-quinidine (NMQ, Fig.1.), a low permeability amphipathic monoquaternary molecule is an excellent cationic model compound. NMQ was shown to be actively transported by human MDR1/P-gp and rat Mdr1b efflux transporters (Hooiveld et al, 2002) as well as by the human OATP-A (OATP1A2) uptake transporter (van Montfoort et al, 1999). The apparent K_m values were 15 μM , 20 μM and 26 μM for the MDR1, Mdr1b and OATP-A transporters, respectively.

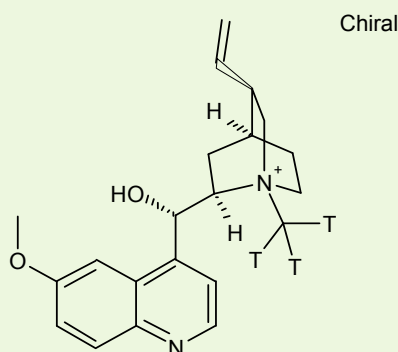


Figure 1: N-methyl-quinidine

Kinetic parameters of human MDR1- and rat Mdr1b-mediated NMQ transport into transporter containing and control membrane vesicles have been validated using SOLVO membrane preparations (SB-MDR1-K-VT, SB-K-CTRL, SB-ratMdr1b-Sf9-VT, SB-defPgp-Sf9-VT). The human MDR1 transporter was expressed in mammalian cells (MDR1-K), while the rat Mdr1b transporter was expressed in Sf9 cells using baculoviral infection system (ratMdr1b-Sf9).

Concentration (Fig. 2.), time and osmolarity dependence (data not shown) of N-methyl-quinidine transport were characterized.

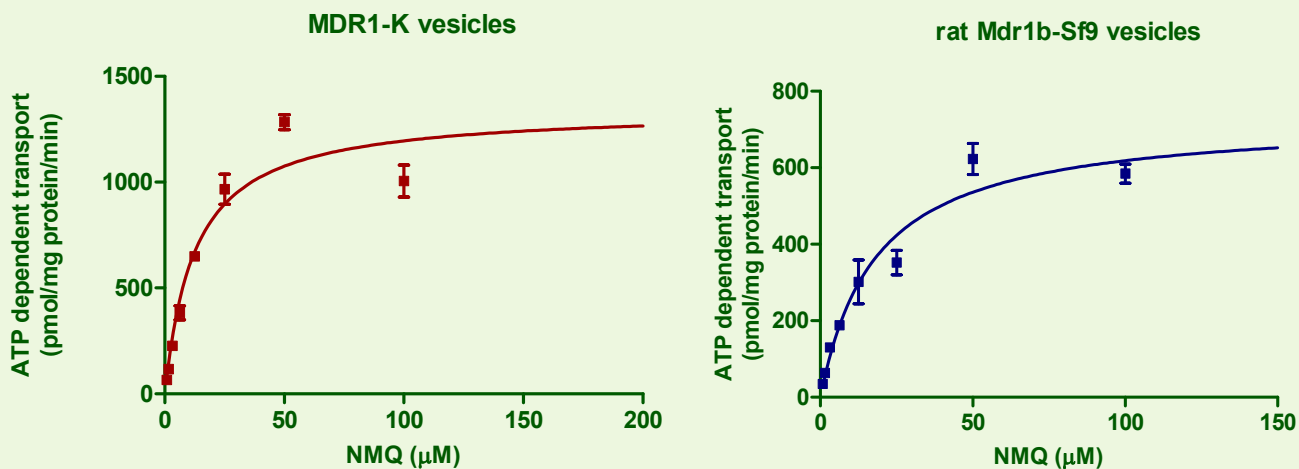


Figure 3. Concentration dependent ^3H -NMQ transport by human MDR1-K and rat Mdr1b-Sf9 vesicles. **MDR1:** V_{max} : 1345 pmol/mg/min; K_m : 12.5 μM , **rat Mdr1b:** V_{max} : 731 pmol/mg/min; K_m : 18.2 μM



The optimized assay available as SOLVO's MDR1-PREDIVEZ™ and Mdr1b-PREDIVEZ™ Kits. The PREDIVEZ assays were validated by using known human MDR1 (Fig. 3. Table 1.) and rat Mdr1b interactors (Fig. 4, Table 2.).

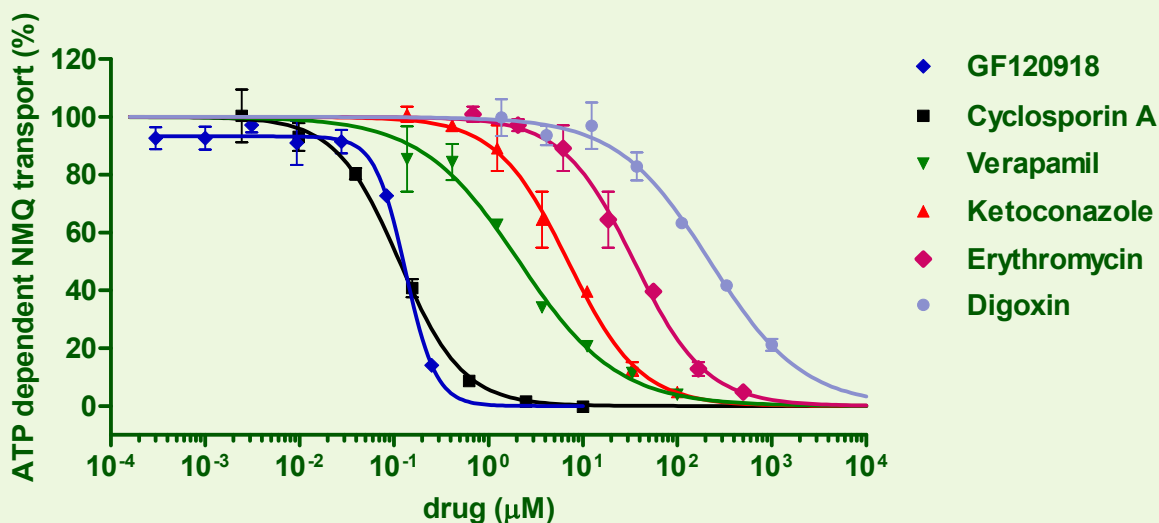


Figure 3. Effect of drugs on N-methyl-quinidine transport by human MDR1: inhibition curves

Table 1. Effect of drugs on N-methyl-quinidine transport by human MDR1: IC₅₀ values

Compound	GF120918	Cyclosporin A	Verapamil	Ketoconazole	Erythromycin	Digoxin
IC ₅₀ (µM)	0.13	0.11	2.28	6.81	34.08	191.8

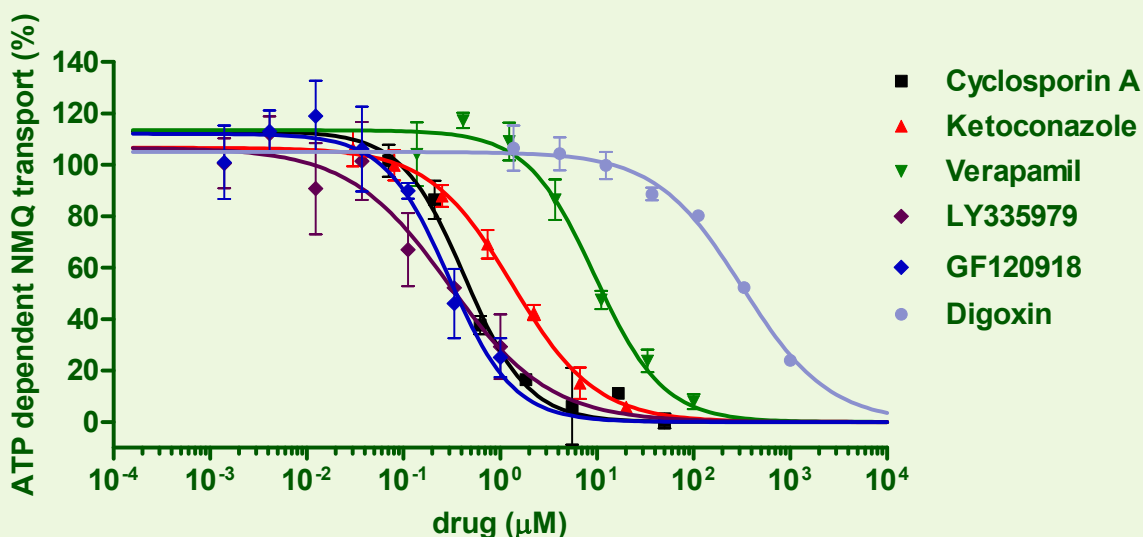


Figure 4. Effect of drugs on N-methyl-quinidine transport by rat Mdr1b: inhibition curves.

Table 2. Effect of drugs on N-methyl-quinidine transport by rat Mdr1b: IC₅₀ values.

Compound	LY335979	GF 120918	Cyclosporin A	Ketoconazole	Verapamil	Digoxin
IC ₅₀ (µM)	0.3	0.3	0.43	1.3	9.5	320