ADME: Permeability - MDCKII-MDR1

Background:

The permeability of a compound will influence its ability to cross the intestinal membrane and its oral bioavailability. MDCKII-MDR1 cells are Madin-Darby canine kidney epithelial cells, over-expressing the human multi-drug resistance (MDR1) gene, coding for P-glycoprotein (P-gp). They represent a good model for fast *in vitro* screening of passive permeability and for estimating the potential for human P-gp to transport the compounds of interest.

Transport of a compound through the MDCKII-MDR1 cell monolayer is used for measuring the rate of membrane transport, expressed as apparent (P_{app}) permeability. Resulting P_{app} values from both transport directions (apical to basolateral side, and basolateral to apical side) are used to calculate an efflux ratio. The inclusion of a P-gp inhibitor confirms whether membrane transport is mediated by P-gp.

Assay description

Cells

MDCKII-MDR1

Direction

apical to basolateral (A2B)
basolateral to apical (B2A)
with or without P-gp inhibitor (elacridar)

Compound concentration

10µM (1% DMSO)

Compound requirements

50µl of 10mM stock solution or
1-2 mg of dry matter

Incubation details

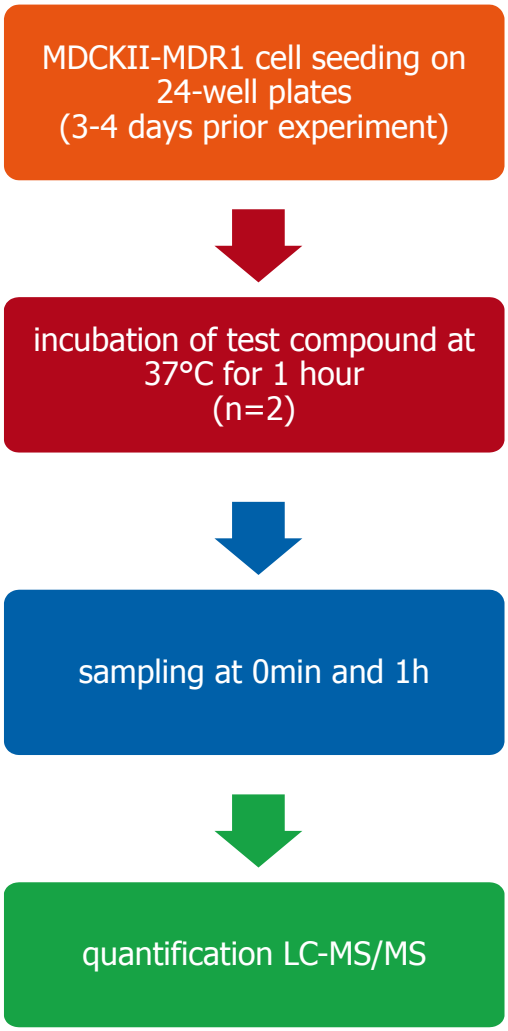
medium: Dulbecco's PBS (pH 7.4)
calibration curve: optional

Detection method

LC-MS/MS with internal standard

Results

P_{app}(A2B), P_{app}(B2A)
efflux ratio, recovery



Contact us:
Adrijana Vinter, Business Development
adrijana.vinter@glpg.com
+385 91 265 5527

Mila Vrančić, Business Development
mila.vrancic@glpg.com
+385 91 265 5528

ADME: Permeability- MDCKII-MDR1

Assay controls

reference compounds: amprenavir and propranolol (Figure 1)

cell monolayer integrity control: lucifer yellow

data obtained for 10 commercial compounds (Figure 2)

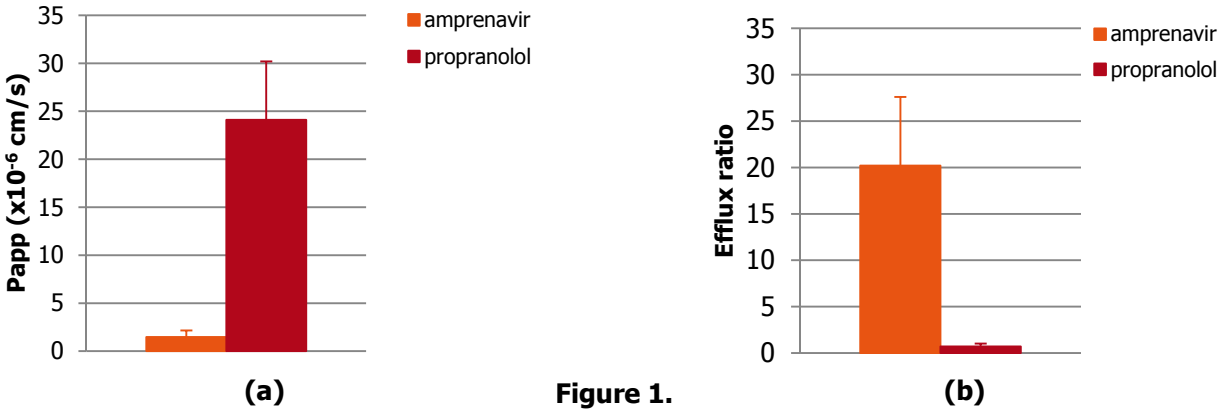


Figure 1.
Data for reference compounds obtained on MDCKII-MDR1 cells: (a) Permeability values, P_{app}(A2B), (b) Efflux ratio

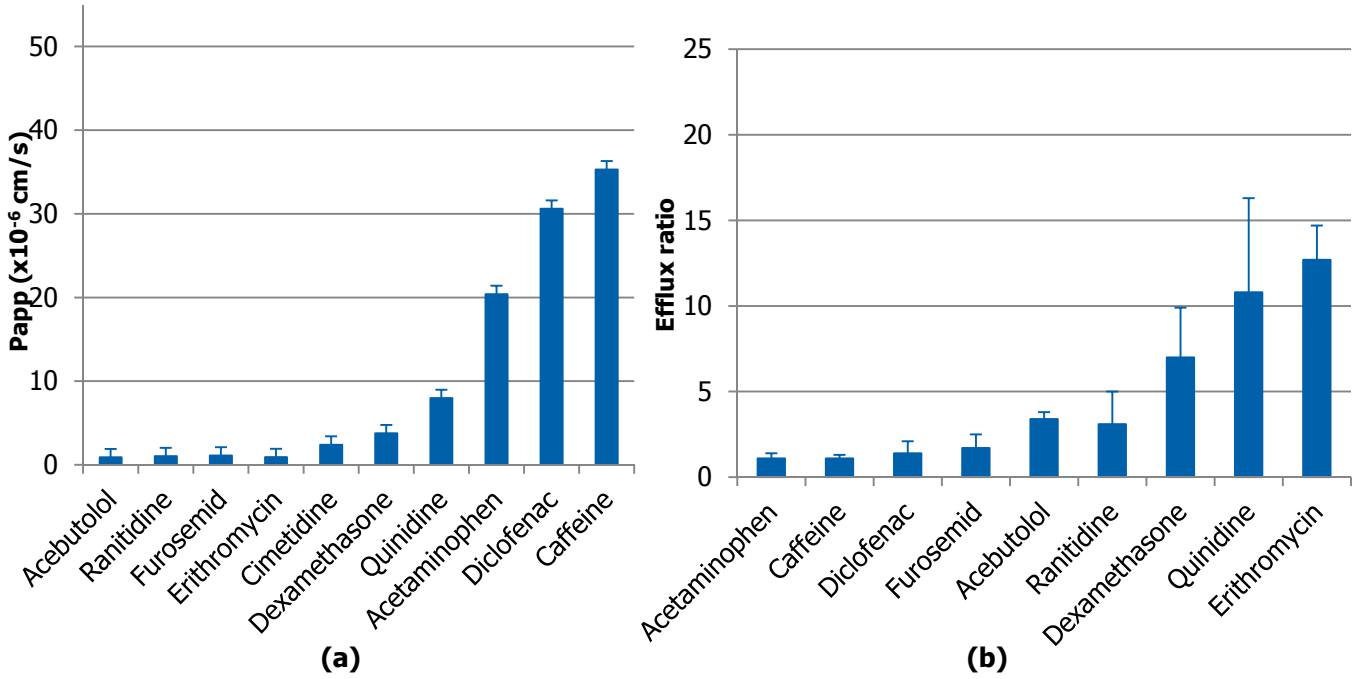


Figure 2.
In-house data obtained for 10 commercial compounds in three separate experiments on MDCKII-MDR1 cell monolayer : (a) Permeability values, P_{app}(A2B), (b) Efflux ratio

Assay details adjustable to client's and/or project specific requests

Contact us:
Adrijana Vinter, Business Development
adrijana.vinter@glpg.com
+385 91 265 5527

Mila Vrančić, Business Development
mila.vrancic@glpg.com
+385 91 265 5528