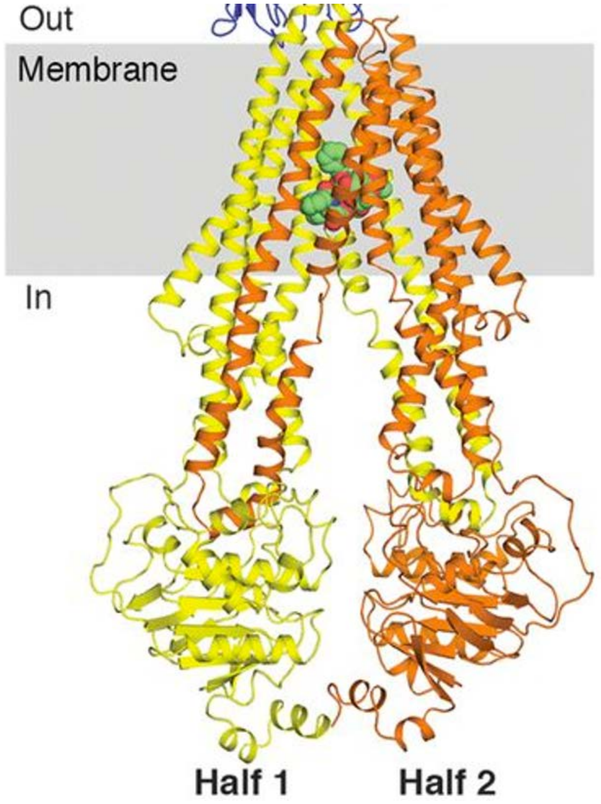
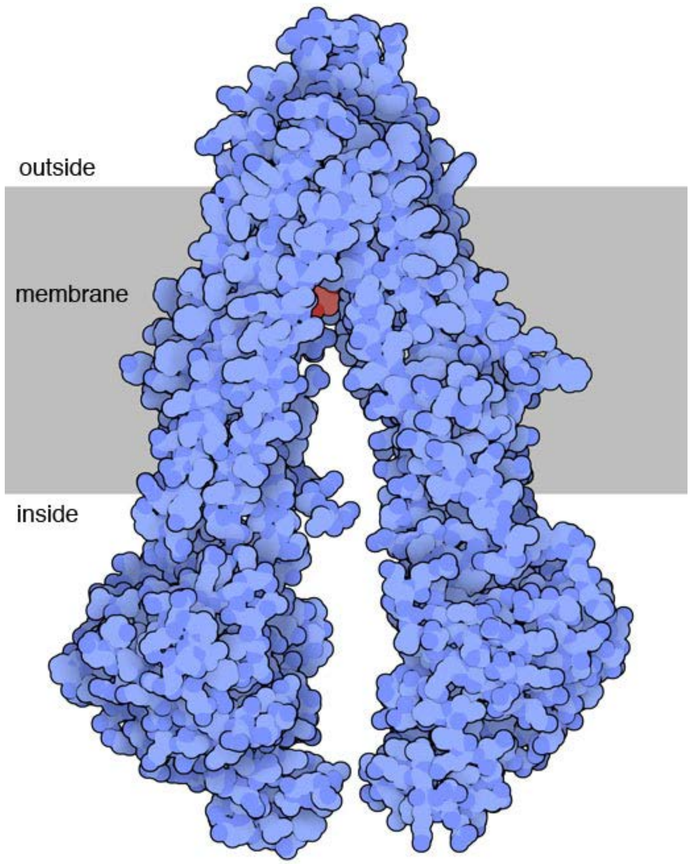
Screening oral excipients against P-glycoprotein

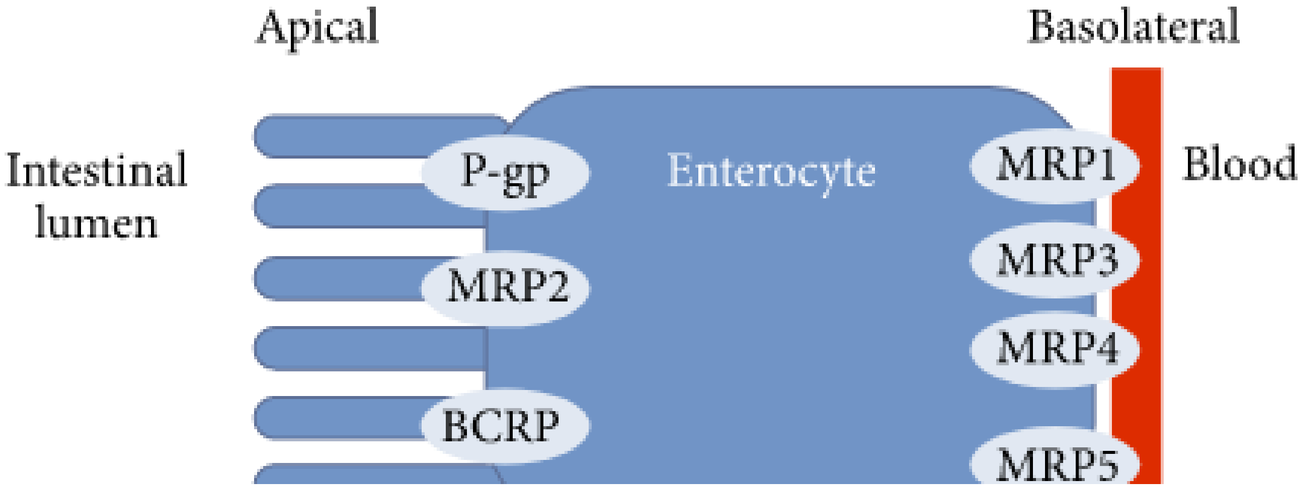


Alam et al, 2019

Ruchika Bajaj, PhD
Membrane Protein Biologist

P-glycoprotein and Excipients



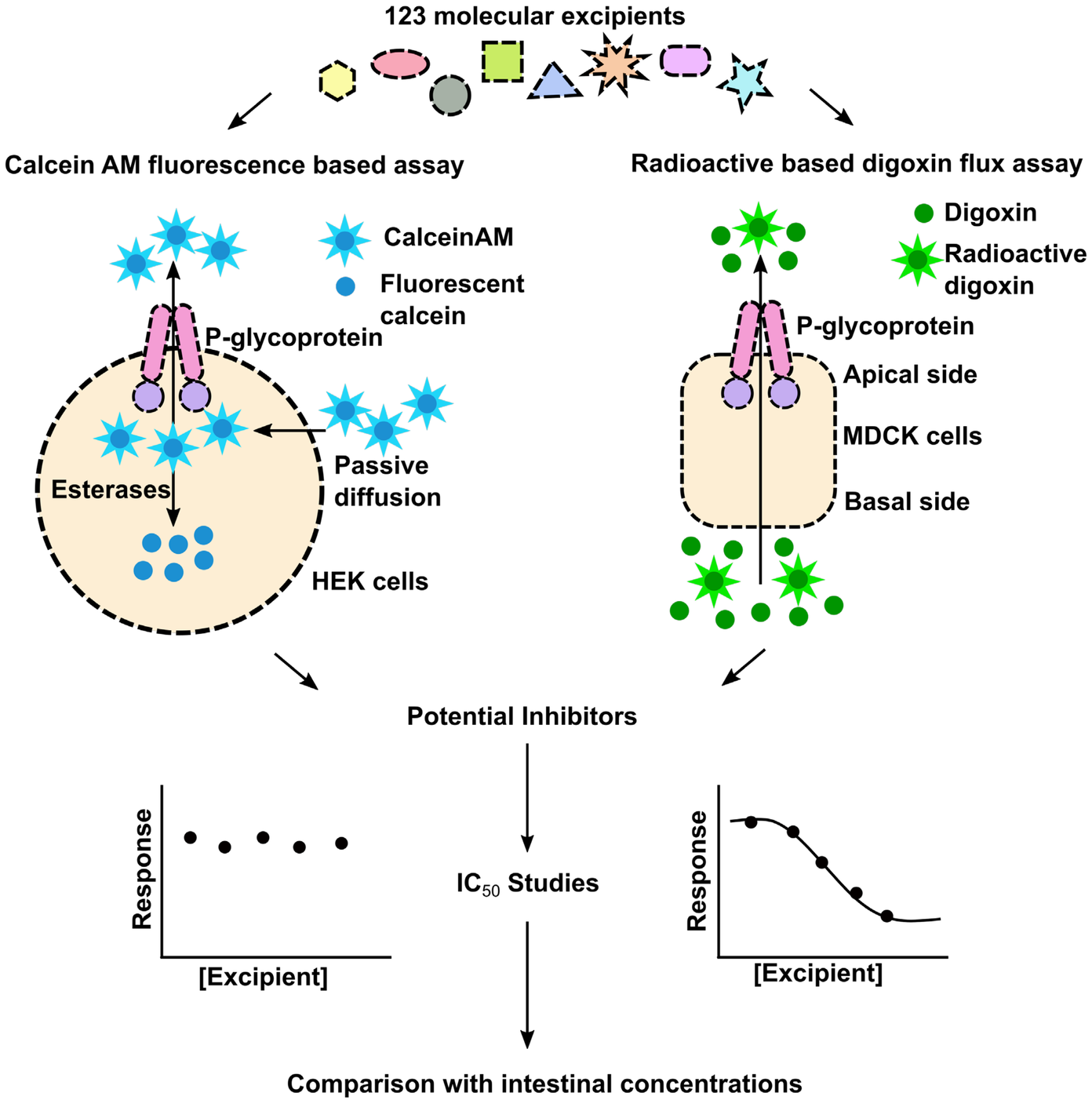


Functions

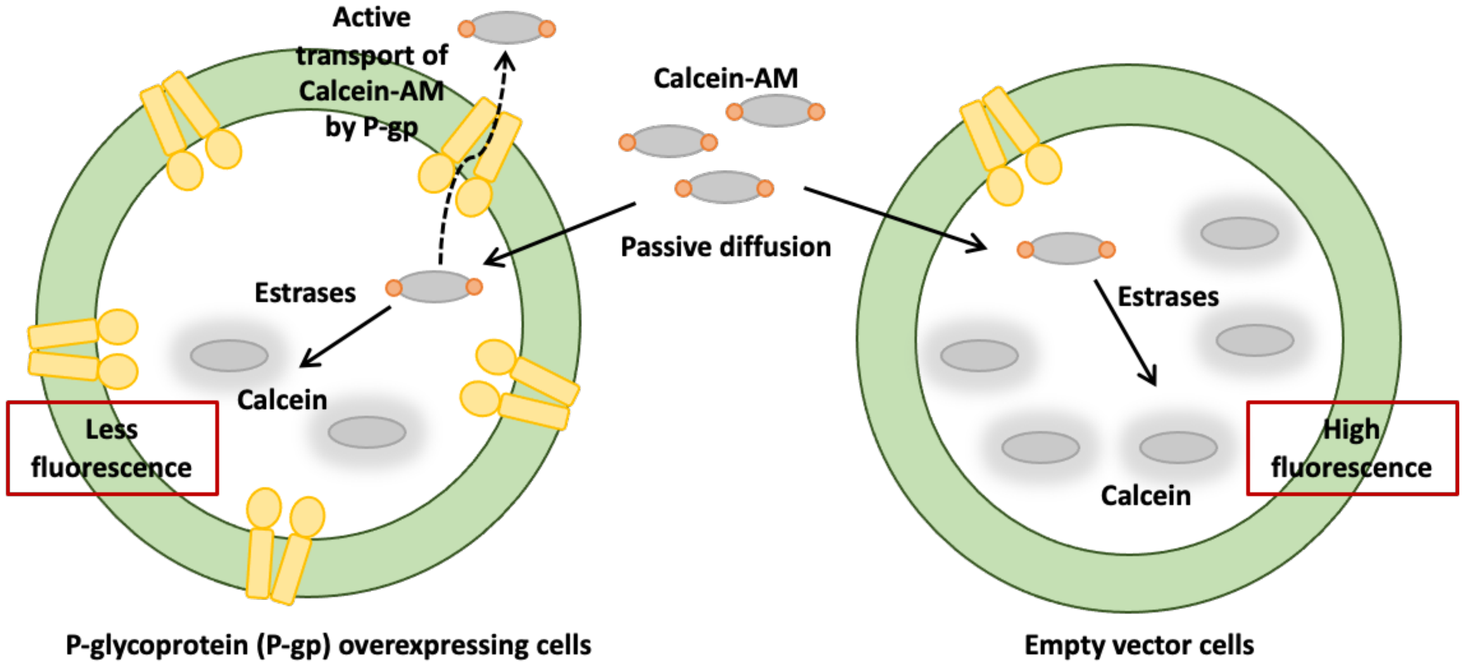
- Stabilizers
- Chelators
- Surfactants
- Buffering agent
- Sweetners
- Binders
- Solubilizers
- Coloring and flavoring agent
- Antimicrobial preservatives

PDB101 - molecule of the month

Overview of screening procedure

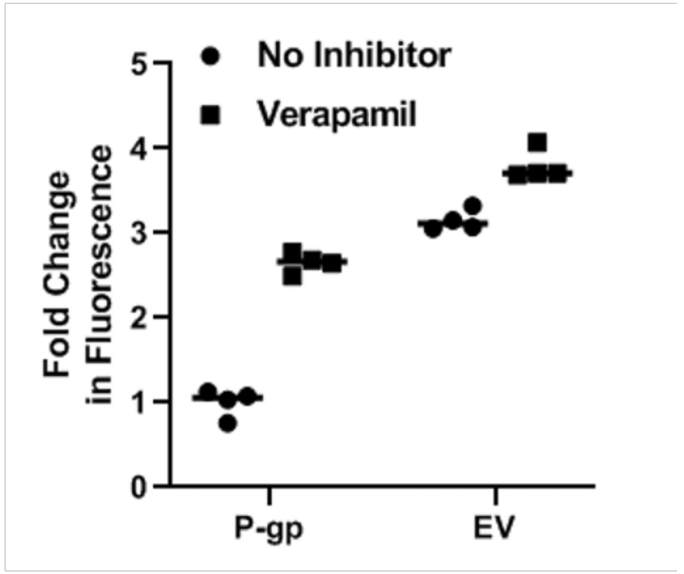


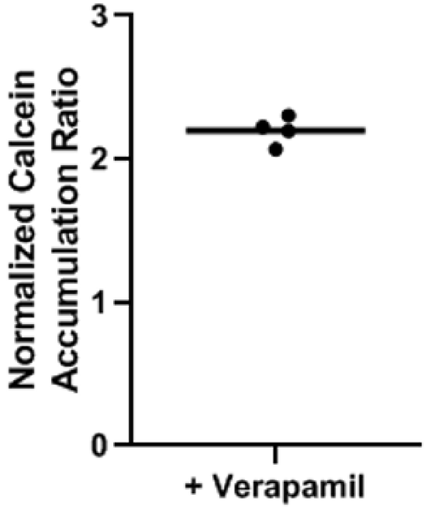
Calcein AM fluorescence assay



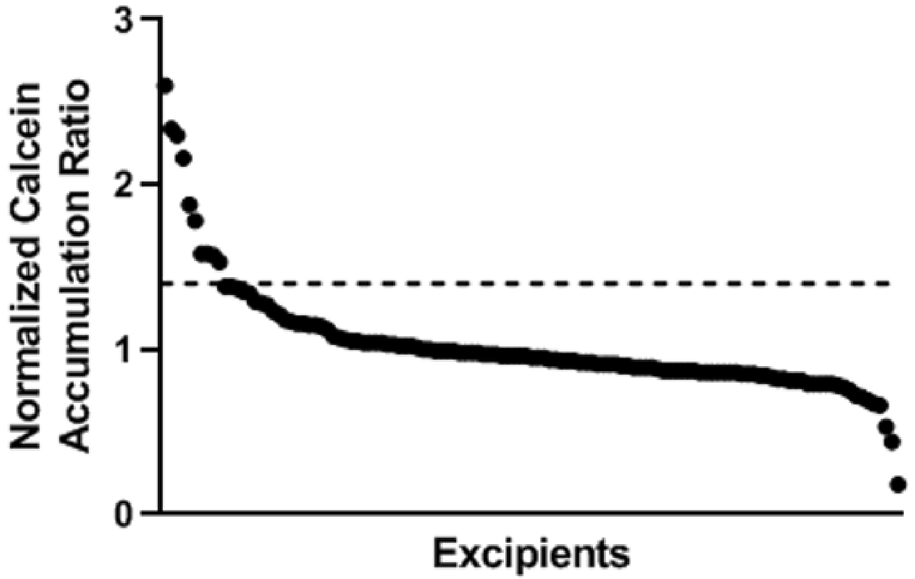
Validation of assay

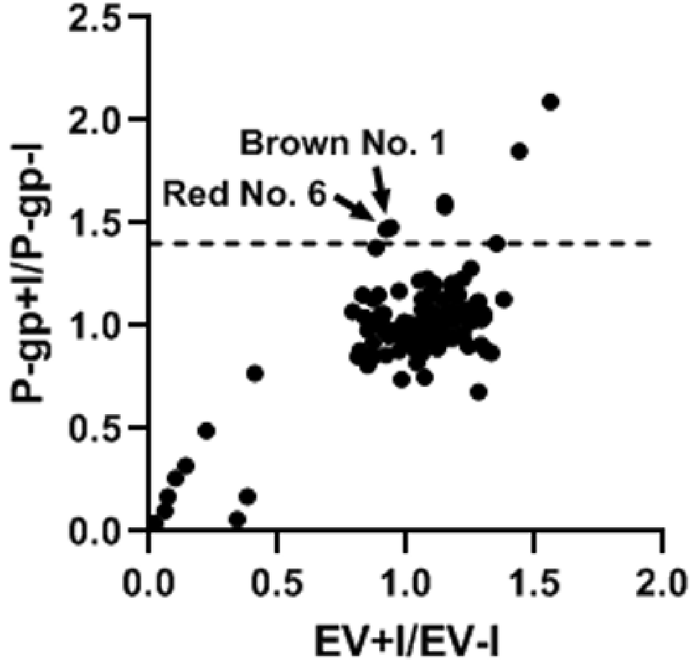
$$\text{(P-gp+/-)/(EV+/-) ratio} = \frac{\text{P-gp+I/P-gp-I ratio}}{\text{EV+I/EV-I ratio}}$$



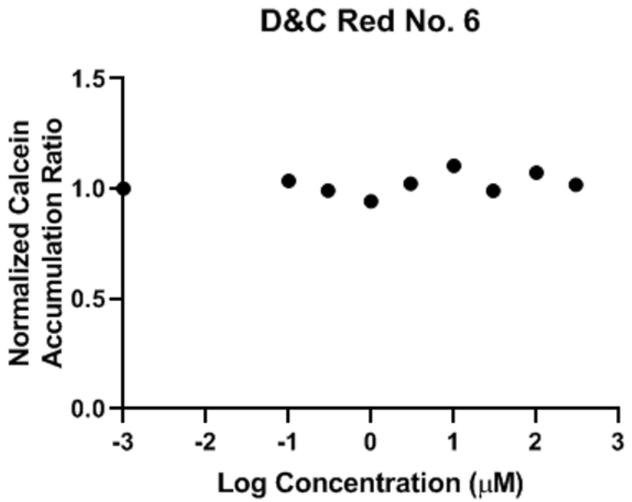


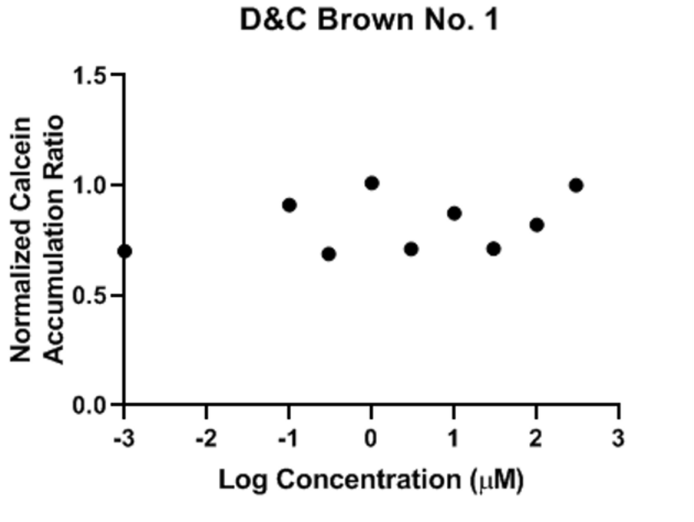
Screening



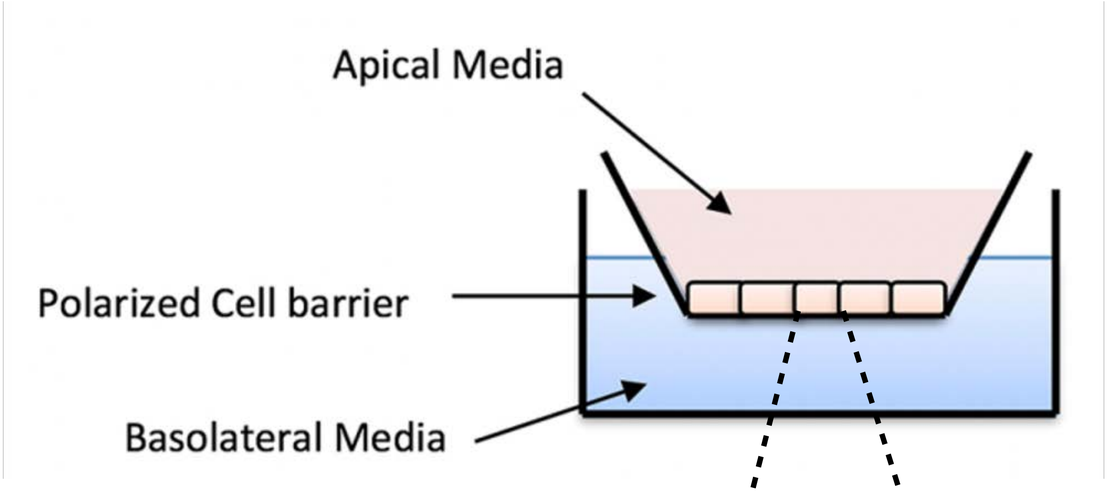


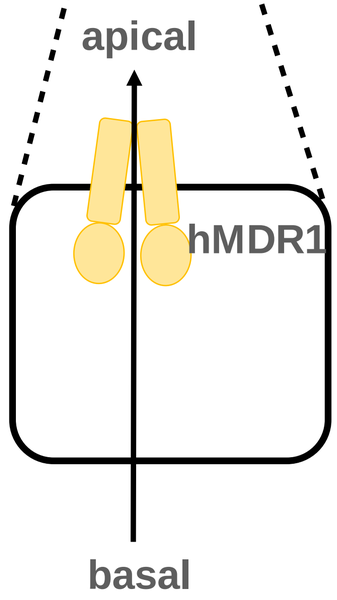
IC50 studies



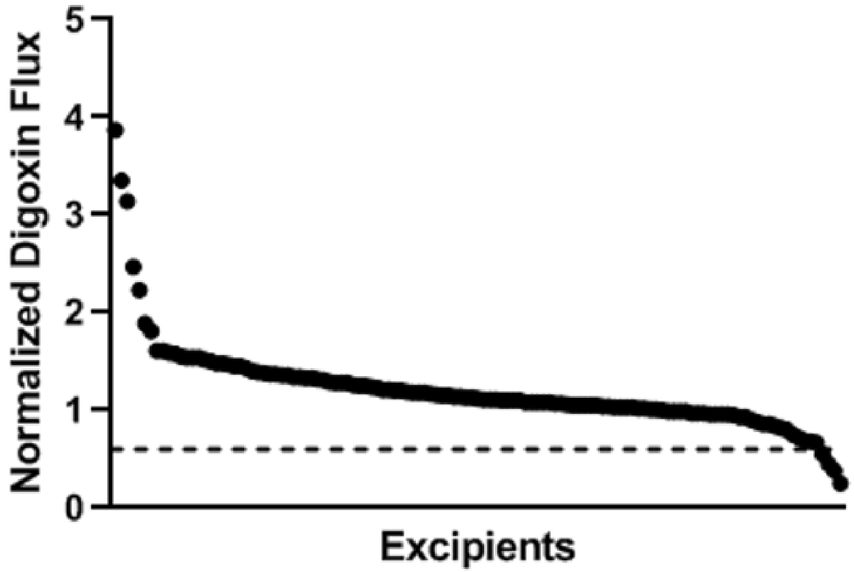


Digoxin flux assay

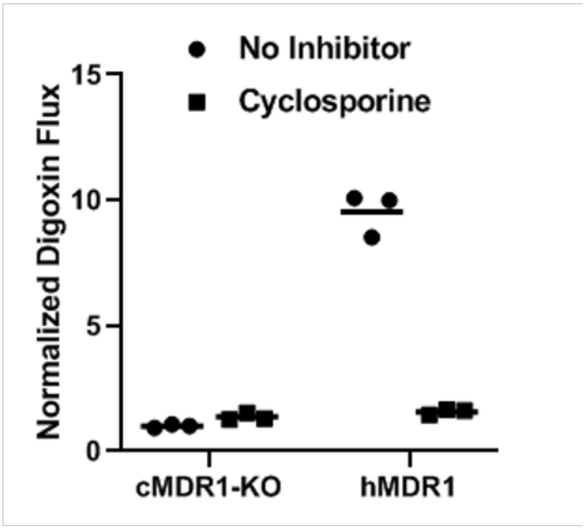


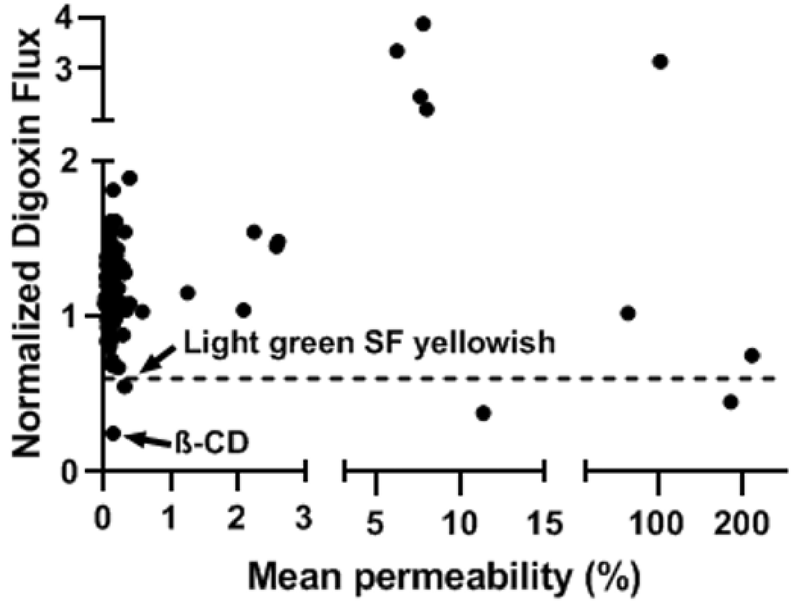


Screening

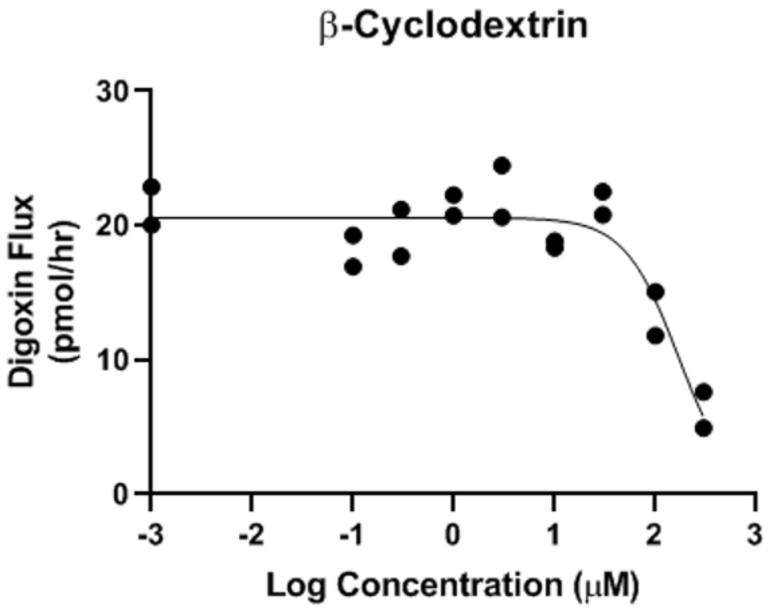


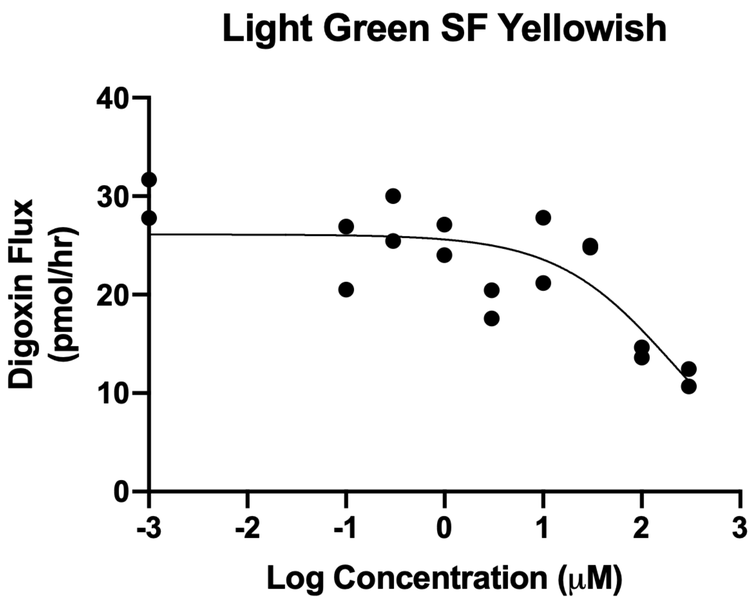
Validation of assay





IC50 studies





Excipient	Maximum potency per unit dose (mg)	I_{max} (μM)	IC_{50} (μM)	$[I_{max}]/[IC_{50}]$
β-Cyclodextrin	133	470	168	2.8
Light green CF yellowish	40	214	204	1.1

Conclusions

Oral excipients have been screened against P-glycoprotein using Calcein AM fluorescence assay and Digoxin Flux assay and most of these excipients ~~are~~ appear to be safe or inert for their effect on P-glycoprotein. beta-cyclodextrin and light green SF yellowish were found to be inhibitory at high molecular range in Digoxin flux assay.

Interaction of Commonly Used Oral Molecular Excipients with P-glycoprotein The AAPS Journal (Accepted)

Thanks !!

Deanna

Kathy

Lisa

Ling

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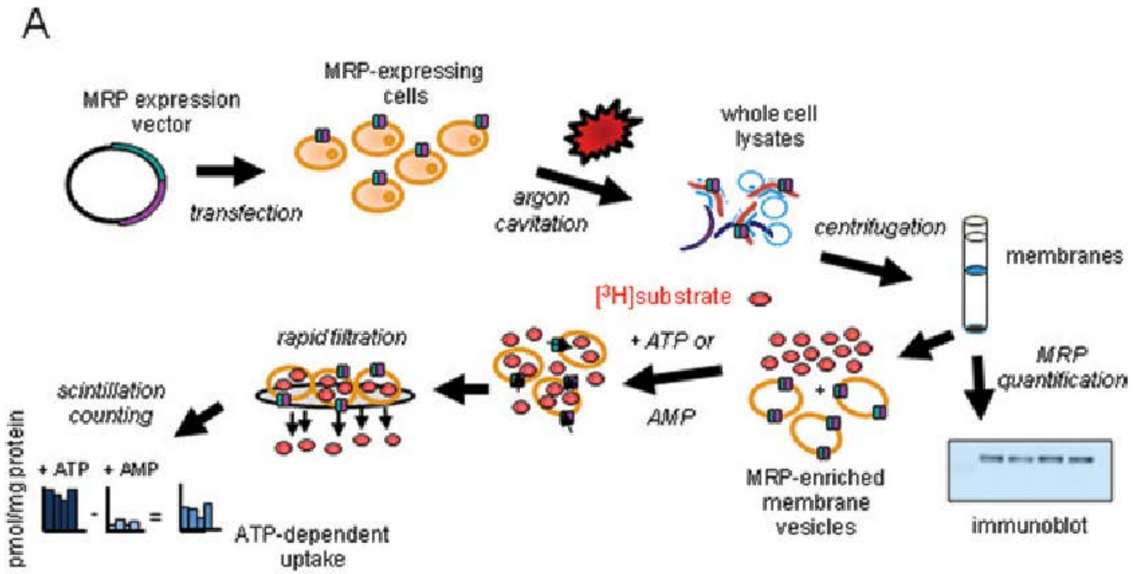
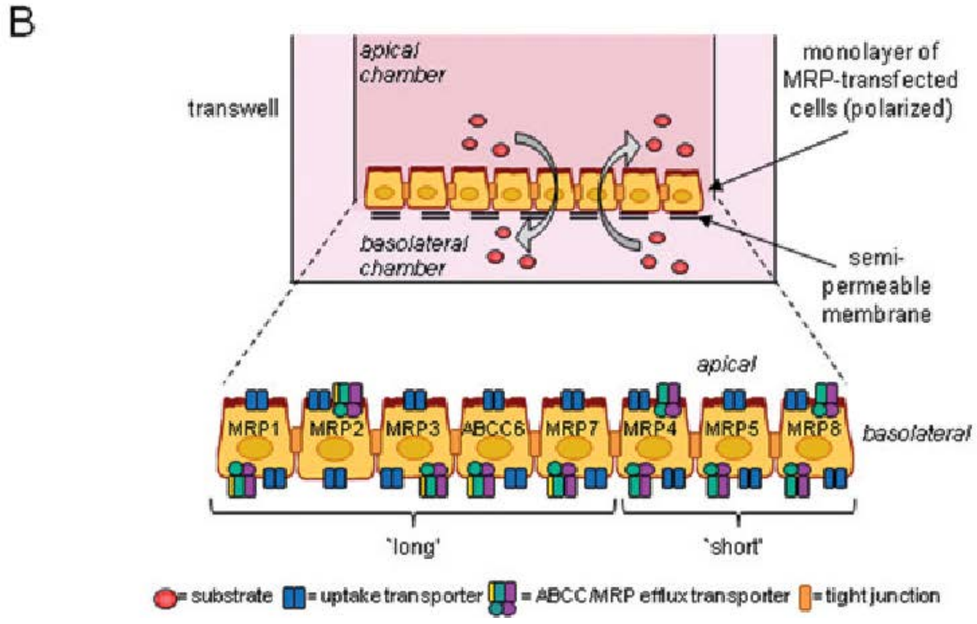
Questions ?





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