ADME: Permeability- Caco-2

Background:

Caco-2 cell line is a line of human epithelial colon adeno-carcinoma cells. When cultured under specific conditions they become differentiated and polarised such that morphologically and functionally resemble the epithelial cells of human small intestine. Therefore, they are considered to be a golden standard for *in vitro* prediction of permeability and for estimation of the potential for different efflux/uptake transporters (most importantly P-glycoprotein, P-gp) to transport the compound of interest.

Transport of compound through Caco-2 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 for calculation of efflux ratio. In addition, the inclusion of the P-gp inhibitor could identify wheter membrane transport is mediated by P-glycoprotein.

Assay description

Cells

Caco-2

Direction

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

Compound concentration

10µM (1% DMSO)

Compound requirements

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

Incubation details

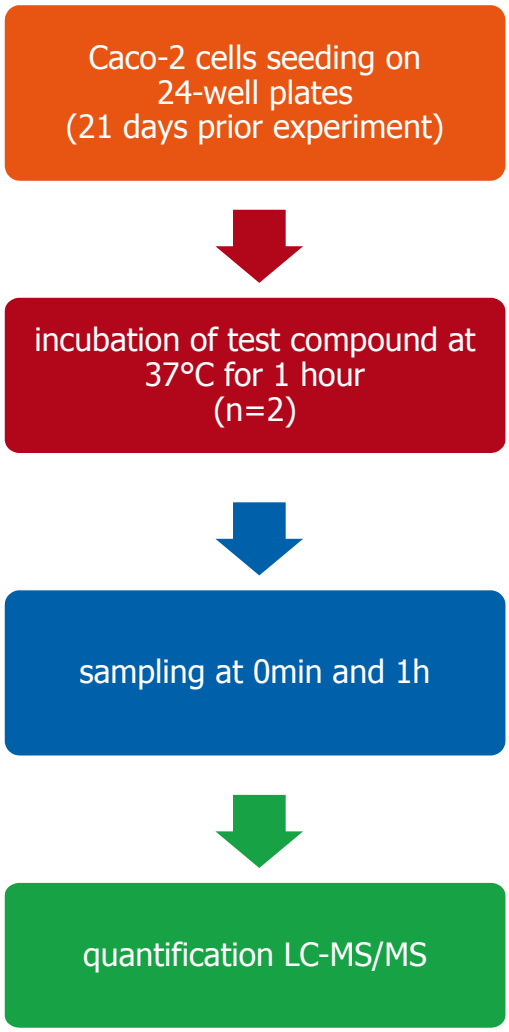
medium: Dulbecco's PBS (pH 7.4)
calibration curve: optional

Detection method

LC-MS/MS with internal standard

Results

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



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Assay controls

reference compounds: amprenavir and propranolol

cell monolayer integrity control: lucifer yellow

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

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