**STEP I**

Estimation of in vitro diffusion velocity and P-gp efflux rate of domperidone through Caco-2 cells a)
from measurements of $P_{app,a-b}$ and $P_{app,b-a}$ [18]

$P_{\text{diff, in vitro}} = \frac{P_{app, b-a} + P_{app, a-b}}{2} = 1.65 \times 10^{-4}$ dm/min

$P_{P-gp, in vitro} = \frac{P_{app, a - P_{app a-b}}}{2} = 1.57 \times 10^{-4}$ dm/min

a) pH gradient from 6.5 to 7.4

**STEP II**

Estimation of the in vitro-in vivo correlation for the estimation of diffusion velocity of drugs (dm/min) through intestine membrane of mice.

Data collected from Collett et al. [33]

$V_{\text{max}}(P-gp) / K_m(P-gp) = a_1 P_{P-gp, in vitro}$, with $a_1 = 4.75 \pm 0.52$

In vivo P-gp efflux rate of domperidone through mouse intestine membrane

$V_{\text{max}}(P-gp) / K_m(P-gp) = 7.5 \times 10^{-4}$ dm/min

Exchange surface area of blood-tissue membranes expressing P-gp:

$S_t$ (dm$^2$)

Expression level of P-gp into various tissues relatively to gut tissue:

$F_{P-gp,t}$ (%)

In vivo diffusion velocity of domperidone through mouse intestine membrane

$P_{\text{diff, in vivo}} = 8.4 \times 10^{-4}$ dm/min

**STEP III**

Calculation of permeability-surface area product and P-gp efflux rate (L/min) for various tissues:

$PSA_t = P_{\text{diff, in vivo}} \times S_t$

$Cl_{P-gp,t} = V_{\text{max}}(P-gp) / K_m(P-gp) \times S_t \times F_{P-gp,t}$