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Permeability study using the single-pass intestinal perfusion in rats: Is the zidovudine a substrate for P-gp?

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The small intestine is the main site of absorption for many drugs orally administered and it depends on solubility and permeability characteristics of the compound to reach the bloodstream. Many drugs are absorbed mainly by trans-cellular passive diffusion, but the presence of efflux transporters, such as P-glycoprotein (P-gp) can hamper the permeation. The oral bioavailability of zidovudine (AZT) is not complete and among other factors, efflux transport can be involved on its permeation process. Thus, this study aims to evaluate the permeability of AZT and its interaction with P-gp using the single-pass intestinal perfusion (SPIP) in rats. Male Wistar rats were anesthetized with ketamine-xylazine mixture. Blank perfusion solution pH 6.5 at 37°C was pumped into jejunum to clean any residual debris. Then, the perfusion solution containing AZT was pumped into intestine and samples were collected from the distal portion. The same procedure was made for AZT with P-gp inhibitor verapamil and all samples were quantified by HPLC method. Metoprolol and ranitidine were used as permeability marker substances in this study. The effective permeability (Peff) of AZT was 4.37 (±0.45)x10^{-5} cm/s. For AZT with verapamil, the Peff was 5.44 (±0.39)x10^{-5} cm/s. These results showed that AZT has an interaction with P-gp. That is in accordance with other *in vitro* and *ex vivo* studies reported in the literature, which can explain the variability on the oral bioavailability. The comparison between AZT and AZT with verapamil results led to conclude that AZT had its permeability increased when verapamil was used. Thus, AZT can have an interaction with P-gp which may influence on its permeability and contribute for its incomplete bioavailability.

Biography

Thaisa Marinho Dezani has completed her Master's degree in 2012 and since then, she is completing her PhD thesis related to permeability studies using different methods as *in situ, ex vivo* and *in vitro* models. Her research field also includes "Solubility, biopharmaceutical classification systems (BCS and BDDCS), dissolution studies and ADME prediction". She was a Visiting Scholar at Benet Lab, University of California San Francisco, USA.

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