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Extended compartmental absorption and transit model

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Yu and Amidon described an extended compartmental absorption and transit (CAT) model to estimate saturable small intestinal absorption. This model simultaneously considers passive absorption, saturable absorption, degradation, and transit kinetics in the human small intestine Cefatrizine. is an Amino ''β- lactam antibiotics '' that is absorbed by a carrier mediated system (through carriers), it means that follows saturated absorption and might be dose dependent absorption and might be dose dependent absorption to some extent. This type of absorption cannot be explained linear absorption model. This model must be mechanistic and quantitative to estimate dose dependent absorption and degradation in vivo.

No saturated absorption occurs in ileum except the first compartment in which transporters continue to decrease from jejunum to ilium. Gastric emptying is considered to be first order, if residence time is 0.25h.

By coupling intravenous pharmacokinetics parameters with the extended CAT model, it can be determined the plasma concentration time profile. Plasma concentration time profiles were determined at three doses 250, 500 and 1000 mg in order to use CAT model to predict the dose dependent absorption. Predicted plasma concentrations were 4.3. 7.9 and 9.3 µm/ ml at peak times 1.6 ,1.8 and 2.0 h in line with the experimental mean peak plasma concentration 4.9±1.2 , 8.6± 1.0 and 10.2 ± 2.1 µg/ ml at the peak times 1.4±0.4, 1.6±0.2 and 2.0±0.6 hr.

Reported absolute bioavailability was 75% and 50% at 250 and 1000 mg oral doses which are compared with theoretically determined fraction of dose absorbed.

Calculated fraction of dose absorbed is lower than calculated bioavailability at dose 500mg so, experimentally determined data is compared with predicted data at three doses of cefatrizine 250, 500 and 1000mg.

All pharmacokinetic parameters AUC, urinary excretion, fraction of dose in colon, fraction of dose degraded, reported in feces.

The literature data vary significantly for all these model parameters, so these variations affect the "prediction result". Because of the large variations of these parameters, only one standard deviation changes were simulated, %age changes in the fraction of dose absorbed.

As a result of these simulation changes no single factor results in over 25% variation in the fraction of dose absorbed. In this way, no single physiological factor could account for such a large difference in literature data .However, the overall effect of these physiological factors could account for up to 40% variability in bioavailability.

The MM model was statistically significant over models incorporating either first or zero order absorption; however this model fails to explain the reduced extent of absorption at high doses.

This MM model does not consider effect of degradation; it cannot be compared CAT model with MM model.

Mechanical and quantitative absorption model which can simultaneously be consider passive absorption, saturated absorption, degradation and transit in the human small intestine. But this model does not explain the large differences in fraction of dose absorbed which were explained by extended CAT model. Extended CAT

model is only useful; if it is considered that no metabolism occurs.

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Conflict of Interests

Author declares no competitive interests for this work.

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