Predicting food effects of Cataflam® using the Dynamic Gastric Model (DGM)

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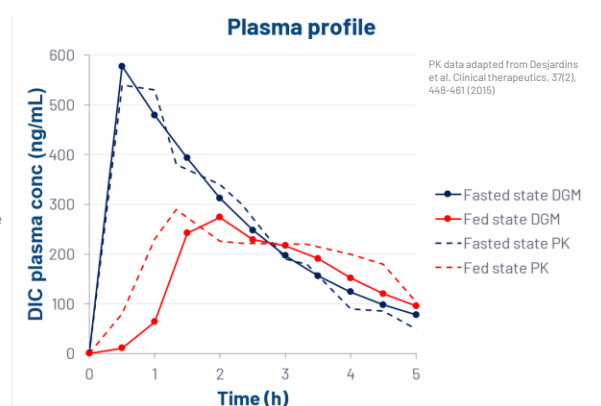[1] Bioneer:FARMA, Department of Pharmacy, Universitetsparken 2, 2100, Denmark
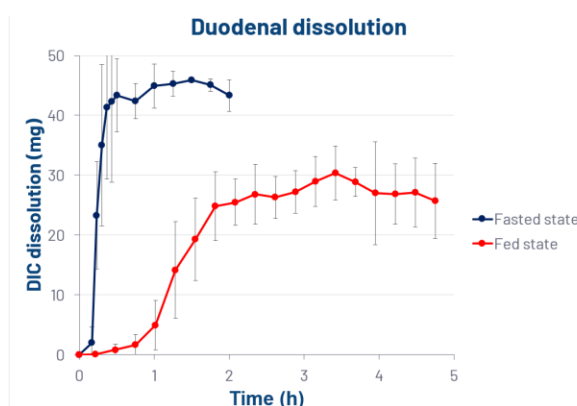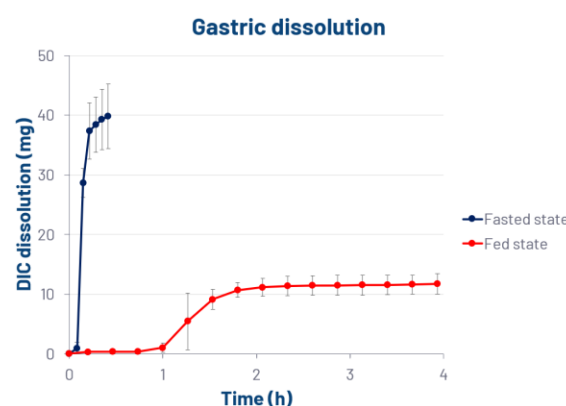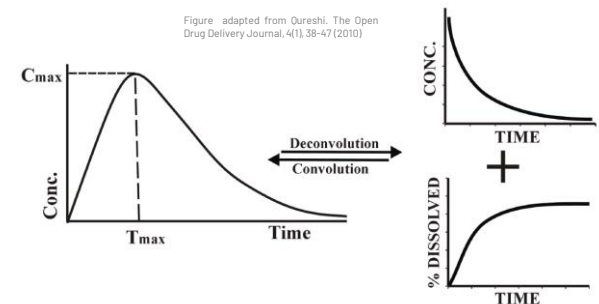[2] University of Copenhagen, Department of Pharmacy, Universitetsparken 2, 2100, Denmark

FASTED STATE EXPERIMENTS

- One Cataflam® tablet (50 mg diclofenac potassium) added to the DGM along with 240 mL tap water

- 29 min processing time with dynamic addition of gastric acid and enzymes

- Samples of ~40 mL ejected from the DGM every 4 min

- DGM sample transferred to a duodenal module along with concentrated FaSSIF pH 6.5

- Aliquots of 1 mL taken from DGM/duodenal samples and analyzed (HPLC-UV) for dissolved drug content

FED STATE EXPERIMENTS

- High-fat FDA meal added to the DGM and after 30 min; one Cataflam® tablet along with 240 mL tap water

- 257 min processing time with dynamic addition of gastric acid and enzymes

- Samples of ~70 mL ejected from the DGM every 16 min

- DGM sample transferred to a duodenal module along with concentrated FeSSIF pH 5.8

- Aliquots of 1 mL taken from DGM/duodenal samples and analyzed (HPLC-UV) for dissolved drug content

Figure adapted from Qureshi. The Open Drug Delivery Journal, 4(1), 38-47 (2010)

DGM → **+SIF** → **Duodenal module** → **+Analysis** → **IVIVC**

Gastric dissolution — Fasted state, Fed state

Duodenal dissolution — Fasted state, Fed state

Plasma profile — Fasted state DGM, Fed state DGM, Fasted state PK, Fed state PK

PK data adapted from Desjardins et al. Clinical therapeutics, 37(2), 448-461 (2015)

DATA ANALYSIS

- Simple convolution of duodenal dissolution data

- Diclofenac potassium PK parameters:
    - Oral bioavailability 100%
    - Plasma half-life ($T_{1/2}$) 60 min
    - Volume of distribution (V_d) 75 L (~ 1 L/kg)

    Moore. Clinical drug investigation, 27(3), 163-195 (2007)

RESULTS & CONCLUSIONS

- The negative food effect observed for diclofenac potassium observed *in vivo* was also reflected *in vitro*

- The convoluted duodenal dissolution data was predictive of PK parameters C_{max}, T_{max} and AUC.

- The DGM-duodenal module can be used to study (food) effect of oral drug products with good predictability

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