Fasted and Fed State Pancreatic Juice Secretion in the Caucasian Population: A Meta-analysis

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Abstract

This research work describes a dynamic pancreatic juice secretion model implemented within the Advanced Fluid Volume Dynamics (aFVD) Model of the V18 Simcyp Simulator. A thorough search of the literature was carried out to collate pancreatic juice secretion data in fasted and fed states. Based on the meta-analysis, a biphasic model, with linear increase until a maximum rate is reached followed by an exponential decrease to basal value, was developed. The secretion rate increased rapidly when a meal is consumed peaking at 0.48 h after onset of eating.

Background

Fluid secretion rates into the various segments of the GI tract can have a significant effect on time-dependent segmental fluid volumes, which is an important physiological determinant for drug dissolution and solubility. Fluid volume throughout the GI tract in the ADAM model is calculated using ordinary differential equations based on fluid secretion, reabsorption rates in each segment and transit into and out of each segment [1]. A major component of the fluid secreted into the duodenum is the pancreatic juice. In the existing fluid volume dynamics model (V17 and before) within the ADAM model, the pancreatic secretion rate is a static value (50 mL/h) with an assumed inter-subject variability of 30%, which is the same for both fasted and fed states. While in fact, the secretion rate is different in the pre- and post-prandial states and may vary within individuals. Thus, the aim was to collect data for the baseline and secretory response to a meal of the pancreas to enable dynamic values associated with inter-individual variability in the new aFVD model.

Methods

A database of sources quantifying the pancreatic juice secretion rate was put together from literature through a keyword search (e.g., 'Human', 'Pancreatic', 'Fasted', 'Post prandial', 'Secretory Response'). Literature studies collected were restricted to the Caucasian Population, and healthy subjects >18 years old. However, there is limited information available in the literature determining the pancreatic secretory response to food. Secretin at a concentration 0.03 Clinical Unit (CU)/kg/h equivalent to 2.8 pmoL/kg/h simulates physiological levels of secretin during the fed state in healthy human volunteers. Thus, pancreatic juice secretion rates obtained after the infusion of exogenous secretin at 0.03 CU/kg/h was considered to reflect the fed state. The GetData Graph Digitizer was used to obtain numerical values from graphical data in publications. Studies considered in the meta-analysis have measured the secretory activity of the pancreas with external drainage of the main pancreatic duct. Pure pancreatic juice was collected at regular intervals, and the volume was measured to determine the secretory rate (mL h^{-1}).

Results

Dynamic change in the pancreatic fluid secretion rate when a meal is taken and the return to basal values and vice-versa is implemented within the aFVD model. The pancreatic juice secretion rates vary with time which is well represented by the combination of two independent functions: a linear function to describe the initial increase in secretion rate at the onset of a "feeding event" (Phase 1) and an exponential function to describe the fall in secretion rate back to the fasted state (baseline) values (Phase 2). Pancreatic juice secretion into the duodenum increases rapidly and reaches maximal values (peak secretion rate, $T_{p,max}$) [2]. Following peak rate, fluid secretion rate decreases to fairly stable baseline values after about 3-4 h (T_{ps}, time to reach basal rate) postprandially [3, 4]. Since the data indicate there is considerable inter-individual variability in the increase in pancreatic secretion rate following a meal, each equation parameter has a CV% to capture inter-individual variability (Table 1).

Results (Cont.)

Assuming log normal distributions and using the mean and CV% the secretion parameters are sampled from the on-screen values and randomly assigned to each subject within a population. As depicted in Fig. 1, a user can explore the model parameters by clicking "Time-dependent Pancreatic secretion" button on screen which invokes a pop-up (Fig.2).

Figure 1: The aFVD Model Fluid Secretion rate Screen.

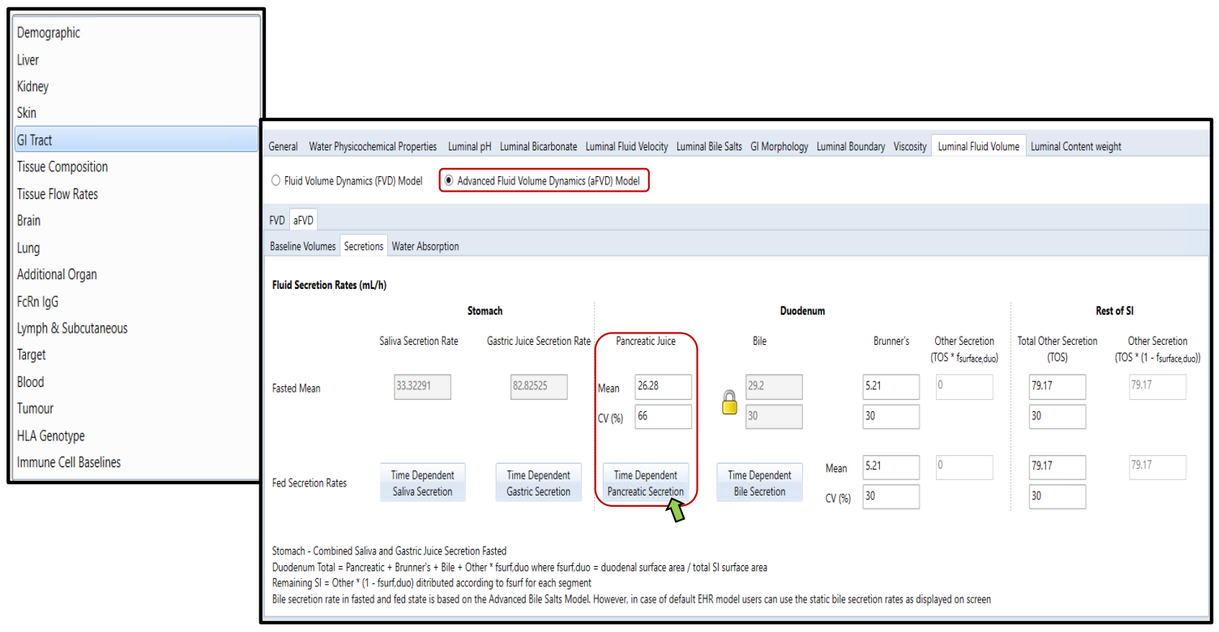
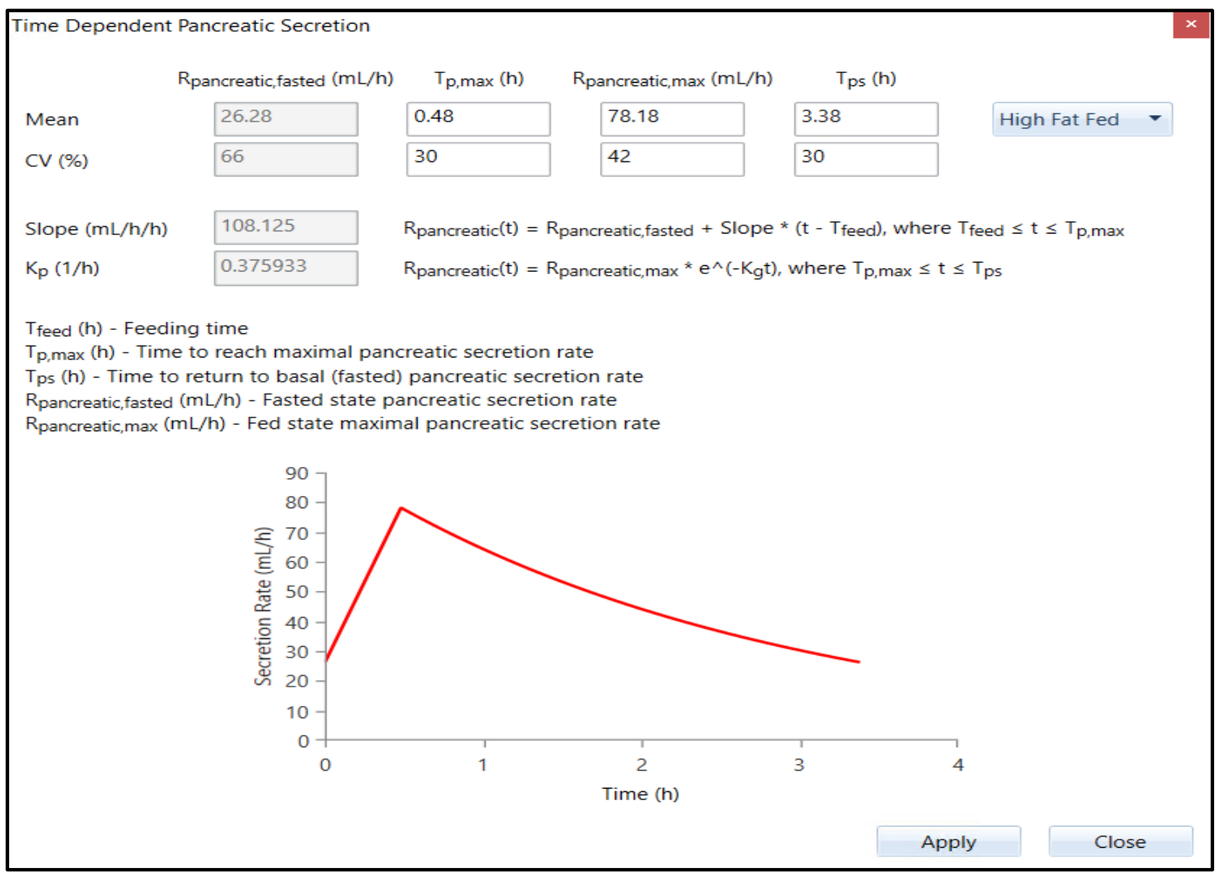


Table 1: Pancreatic juice secretion parameters in the fasted and fed states obtained *via* meta-analysis.

Parameter	Mean	CV (%)
$R_{pancreatic,Duod,fasted}$ (mL h^{-1})	26.28	66
$T_{p,max}$ (h)	0.48	30
$R_{pancreatic,Duod,max}$ (mL h^{-1})	78.18	42
T_{ps} (h)	3.38	30

Figure 2: The aFVD Time-Dependent Pancreatic Secretion rate pop-up screen.



Conclusions

This is the first in-depth analysis reporting dynamic changes in the postprandial pancreatic secretion rates and are an important component of the new Advanced Fluid Volume Dynamics (aFVD) model. In future the components of the pancreatic juice such as bicarbonate concentration may be incorporated into the ADAM model to better account for buffer capacity for example.

References

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