***ABSTRACT***

Pancreatic enzyme replacement therapy (PERT) is the treatment for palliating pancreatic insufficiency in Cystic Fibrosis. It consists of the exogenous administration of enzyme supplements in every meal. Up to date there is not a scientifically-valid method to individual dose adjustment. This leads to maldigestion and malabsorption, and eventually to a detriment of nutritional status and disease prognosis. The aim of this thesis was to develop a method to adjust PERT by exploring food properties under *in vitro* digestion conditions as possible determinants of lipolysis and thus of the optimal PERT dose. The secondary objective was to test the validity of the method in patients by assessing coefficient of fat absorption and identifying an individual correction factor based on individual patients’ characteristics. A first stage of the research showed that very different PERT dose criteria were being applied along Europe regardless of the nutritional status of the patients. The experimental work conducted in the lab, showed that the gastrointestinal conditions during digestion are determinants of lipolysis, especially the intestinal pH and the bile salts concentration. The food properties, including interactions between nutrients, lipid structure within the food matrix and the textural properties, had a significant impact on lipolysis. The *in vitro* digestion method also revealed that the optimal PERT dose was not dependent upon fat content of food exclusively, increasing doses leading to decreased lipolysis in some foods. The modelling of these results led to the predictive equations of the theoretical optimal dose of PERT (TOD) for a selection of foods, which were tested in a pilot study setting. When patients followed the fixed test diet taking the corresponding TOD, a median coefficient of fat absorption of 90% (clinical target) was achieved and individual patients’ characteristics were not significantly associated with this result, meaning that food properties were the main determinants of lipolysis. Therefore, the conclusion of this thesis is that an evidence-based method to adjust PERT in CF patients was successfully developed.