***TABLE OF CONTENTS***

**1. ITRODUCTION………………………………………………………………………………….……………………………17**

1.1. Cystic Fibrosis………………………………………………………………………………………….………………………18

1.2. Pancreatic enzyme replacement therapy…………………………………….………………………..…………20

1.3. Dietary intervention in Cystic Fibrosis………………………..……………………………………..………………23

1.4. Dietary lipids………………………………………………………..……………………………….………..………………25

1.5. Food Properties…………………………………………………..……………………………….………..……………….28

1.6. Food digestion………………………………………………………..………………………….………..…………………34

1.7. Factors affecting lipid digestion…………………………..……………………………………………………….…37

1.8. *In vitro* digestion methods……………………………………..…………………………………………….…………43

References…………………………………………………………………..………………………………….………….…………52

**2. HYPOTHESIS AND OBJECTIVES………………………………**…..………**……………………………..……………53**

**3. EXPERIMENTAL PLAN………………………………………………………**…..………**……..…………………………57**

3.1. Multicenter study to assess PERT and nutrition in patients with Cystic Fibrosis.. …..…………59

3.2. *In vitro* digestion studies…………………………………………………………………………..…………….………..59

3.3. Pilot study to assess an evidence-based method for PERT……………………..…………….…………..60

**4. RESULTS………………………………………………………………………………………..…**…..………**…..……………64**

**CHAPTER 1. HORIZON 2020 PROJECT TO FUND THE RESEARCH.……………** …..………**…………..……66**

PAPER 1. Innovative approach for self-management and social welfare of children with Cystic Fibrosis in Europe: development, validation and implementation of an mHealth tool (MyCyFAPP). …………………………………………………………………………………..……….…..……………..………..67

**CHAPTER 2. CURRENT SITUATION OF NUTRITION AND PANCREATIC ENZYME REPLACEMENT THERAPY IN CYSTIC FIBROSIS CHILDREN IN EUROPE.………………** …..……………..……………..…**………88**

PAPER 2. Pancreatic enzyme replacement therapy in cystic fibrosis: dose, variability and coefficient of fat absorption…………………………………………………………..…………………..……….………..89

PAPER 3. Nutritional status, nutrient intake and use of enzyme supplements in paediatric patients with Cystic Fibrosis; a European multicentre study with reference to current guidelines………………………………………………………………………..…………..……………..……..……….………104

PAPER 4. Children with Cystic Fibrosis present with dietary imbalances: a European multicentre comparison of food groups and origin of nutrient intake…………..……………..…………………………125

**CHAPTER 3. EFFECT OF FOOD INTRINSIC AND EXTRINSIC FACTORS ON LIPID DIGESTION……………………………………….…………………………………………**…..………**…..……..…..………146**

PAPER 5. The role of gastrointestinal conditions on *in vitro* lipids’ digestion………..………………..147

PAPER 6. *In vitro* digestion of lipids in real foods: influence of lipid structure within the food matrix and interactions with non-lipid components……………………..……………..………………………..171

PAPER 7. Lipolysis of oil and butter under joint *in vitro* digestion of carbohydrate and protein rich food matrices*.* …………………………….……………….…………………….…..……………..…….……..……….196

**CHAPTER 4. AN EVIDENCE-BASED METHOD TO ADJUST PANCREATIC ENZYME REPLACEMENT THERAPY IN CYSTIC FIBROSIS…………………………………..…**…..……………..……………..…**…..…..………225**

PAPER 8. Evidence-based method to adjust pancreatic enzyme replacement therapy in cystic fibrosis: Part 1, *in vitro* study……………………………………………..……………..………………………………….226

PAPER 9. Evidence-based method to adjust pancreatic enzyme replacement therapy in cystic fibrosis: Part 2, in vivo validation of the *in vitro* model…………..……………..……………………………..236

PAPER 10. Association between faecal pH and coefficient of fat absorption in children with cystic fibrosis on a controlled diet and dose of pancreatic enzyme replacement therapy ………………………………………………………………………………………………………..……………..…………………..256

**5. SUMMARY AND CONCLUSIONS……………………**…..………**…………………….………..……..…..………275**

5.1. Summary of the results………………………………..………………………………………….………….………..276

5.2. Conclusions………………………………………………..……………………………………………………….………..279

**6. FUTURE PERSPECTIVES………………………………**…..………**……………………...………..……..…..………280**

6.1. Generated basic knowledge in the field of food science………………..………………………………..281

6.2. Clinical applications………………………………………………………………………..……….………….………..282

6.3. MyCyFAPP Project………………………………………………………..………..……………….………….………..283

**ANNEXES……………………………………………………...…………………**…..………**……………..……..…..………284**

**ANNEX 1:** Food record template used in the multicentre European survey on cystic fibrosis nutritional habits………………………………………………………..……………..……………….…….……….………..285

**ANNEX 2:** Formulation of the four bile compositions and concentrations….………..………………..289

**ANNEX 3:** Composition of simulated digestion fluids. The addition of pepsin, Ca2+ solution and water will result in the correct electrolyte concentration in the final digestion mixture……………………………………………………………….………………..………..……………..………….………..290

**ANNEX 4:** Characteristic parameters of the log-logistic dose-response models for explaining kinetics in the three sets of experiments…………..…………………………..……………..…………….………..291

**ANNEX 5**: Classification of foods according to the lipid structure within the food matrix………………………………………………………………………………………………..………………………………..293

**ANNEX 6:** Protocol for the participant used in the pilot study…………..……………………………………294

**ANNEX 7:** Test menu used in the pilot study……………………………………..……………………………..……299