TABLE OF CONTENTS

Summary: 5

Chapter 1. Introduction 18

1.1 The Human Microbiota
   1.1.1 Colonization by microbes 18
   1.1.2 Gut microbiota composition 18
   1.1.3 Personal microbiota 18
   1.1.4 Mutualistic relationships 20
   1.1.5 Dysbiosis & disease 21

1.2 Probiotics
   1.2.1 Microbial intervention 22
   1.2.2 Probiotic applications 22
   1.2.3 Clinical evidence 23
   1.2.4 Mechanism of action 24
   1.2.5 Prebiotics & synbiotics 26
   1.2.6 Safety 26

1.3 Probiotic market
   1.3.1 Products & markets 26
   1.3.2 Regulations & health claims 27

1.4 Innovation process
   1.4.1 Defining innovation 28
   1.4.2 Microbiota Valorisation & Tech Transfer Cycle 29

1.5 Problem statement & Research design
   1.5.1 Which critical challenges do innovators face when developing probiotic applications? 32
   1.5.2 What are the barriers and opportunities for bowel habit improvement in nursing homes with probiotic intervention? 33
   1.5.3 What are the perceptions of physicians and patients towards probiotics? 33
   1.5.4 How should research be prioritized for health claim approval in the adult population? 34

1.6 Authored work 36

1.7 References 37

Chapter 2. The Nagoya Protocol on Access to Genetic Resources and Benefit Sharing: Best practices for users of Lactic Acid Bacteria 48

2.1 Abstract: 48

2.2 Introduction 49

2.3 Methodology 51
Chapter 3. The underexposed role of food matrices in probiotic products: reviewing the relationship between carrier matrices and product parameters.

3.1 Abstract: 66
3.2 Introduction 67
3.3 Methodology 68
3.4 Important product parameters 69
3.5 Available probiotic products 72
   3.5.1 Fermented Milk (Yogurt) 73
   3.5.2 Cheese 75
   3.5.3 Ice-cream 77
   3.5.4 Probiotic meat products 78
   3.5.5 Fruit and vegetable juices 79
   3.5.6 Oats and cereals 80
   3.5.7 Drying techniques 81
3.6 Comparing probiotic matrices 82
   3.6.1 Shelf-life 83
   3.6.2 GIT Survival 85
   3.6.3 Colonization 88
   3.6.4 Clinical Efficacy 89
3.7 Conclusions 90
3.8 Disclosure Statement 92
Chapter 4. Probiotics for healthy ageing: *Innovation barriers and opportunities for bowel habit improvement in nursing homes*

4.1 Abstract 106
4.2 Introduction 107
4.3 Methods 108
4.4 Results and discussion 110
  4.4.1 Prevalence of constipation and diarrhoea in nursing homes: the underlying unmet need within the valorisation cycle 110
  4.4.2 The valorisation cycle: science 110
  4.4.3 Efficacy of probiotics: Proof of concept within the valorisation cycle 112
  4.4.4 Safety evaluation of probiotics within the elderly: business development within the valorisation cycle 114
  4.4.5 Customer feedback within the valorisation cycle: cost reduction. 115
4.5 Conclusions 116
4.6 References 117

Chapter 5. Economic Potential of Probiotic Supplementation in Institutionalized Elderly with Chronic Constipation

5.1 Abstract 122
5.2 Introduction 123
5.3 Methodology 124
  5.3.1 Model 124
  5.3.2 Survey 127
  5.3.3 Literature search 128
  5.3.4 Quantitative Data Synthesis 128
5.4 Results & Discussion 129
  5.4.1 Survey respondents’ characteristics 129
  5.4.2 The conventional treatment expenditures 130
  5.4.3 Constipation prevalence 132
  5.4.4 Probiotic supplementation costs 132
  5.4.5 The lower probiotic efficacy limit 134
  5.4.6 Probiotic efficacy in clinical research 139
  5.4.7 Economic potential of probiotic supplementation 140
5.5 Conclusion and Recommendations 140
5.6 Further considerations: 141
5.7 Disclosure Statement: 141
5.8 Online Appendix Material 142
Chapter 6. Probiotics for Improving Quality of Life in Ulcerative Colitis: Exploring the Patient Perspective

6.1 Abstract
6.2 Introduction
6.3 Methods
   6.3.1 Interview participants
   6.3.2 Probiotic formulation
   6.3.3 Interview design
   6.3.4 Primary study parameters
   6.3.5 Data-processing and -analysis
6.4 Results
   6.4.1 Interview participants
   6.4.2 Impact of ulcerative colitis on patients' quality of life
   6.4.3 Probiotics for improving patients' quality of life
6.5 Conclusion and discussion
6.6 Study and findings in context
6.7 Limitations and considerations for future research
6.8 Acknowledgements
6.9 Ethics statement
6.10 Appendix
6.11 References

Chapter 7. Medical doctors’ perceptions on probiotics: Lack of efficacy data hampers innovation

7.1 Abstract
7.1.1 Graphical abstract
7.2 Introduction
7.3 Methodology
   7.3.1 Data collection
   7.3.2 Study Population
   7.3.3 Statistical Analysis
7.4 Results
   7.4.1 Survey respondents’ characteristics
   7.4.2 Nutritional and Probiotic Advice
   7.4.3 Indications for Probiotic Advice
   7.4.4 Reasons Not to Advise Probiotics
   7.4.5 Perceived Knowledge, Safety and Efficacy
Chapter 8. European General Practitioners perceptions on probiotics: Results of a multinational survey.

8.1 Abstract
8.2 Introduction
8.3 Methodology
  8.3.1 Data collection
  8.3.2 Study population
  8.3.3 Statistical analysis
8.4 Results
  8.4.1 Survey respondents’ characteristics
  8.4.2 Nutritional and probiotic advice
  8.4.3 Indications for probiotic advice
  8.4.4 Perceived knowledge, safety and efficacy
8.5 Discussion and conclusion
8.6 Limitations
8.7 Disclosure statement
8.8 Acknowledgements
8.9 Formatting of funding sources
8.10 References

Chapter 9. Probiotic research priorities for the healthy adult population: A review on the health benefits of Lactobacillus rhamnosus GG and Bifidobacterium animalis subspecies lactis BB-12

9.1 Abstract
9.2 Introduction
9.3 Methods
9.4 Results and discussion
  9.4.1 Results of literature search
9.5 Discussion
9.6 Conclusion
9.7 Limitations
9.8 Acknowledgements
9.9 References