

**DISS ETH NO. 19537**

**Novel Nanoiron and Nanozinc Compounds:  
The Next Generation of Food Fortificants?**

A dissertation submitted to  
ETH Zürich

For the degree of  
**Doctor of Sciences**

Presented by

**Florentine Marianne Hilty-Vancura**

Dipl. Chem., Universität Zürich

Born 07.02.1979  
Citizen of the Principality of Liechtenstein

Accepted on the recommendation of

Prof. Dr. med. **Michael B. Zimmermann**, examiner  
Prof. Dr. **Richard F. Hurrell**, co-examiner  
Prof. Dr. **Sotiris E. Pratsinis**, co-examiner

2011

## TABLE OF CONTENTS

<b>Abbreviations</b> .....	<b>1</b>
<b>Summary</b> .....	<b>3</b>
<b>Zusammenfassung</b> .....	<b>6</b>
<b>Introduction</b> .....	<b>9</b>
<b>Literature Review</b> .....	<b>13</b>
1. Iron and Zinc Absorption.....	13
1.1. Iron Metabolism and Deficiency.....	13
1.1.1. Chemistry of Iron.....	13
1.1.2. Iron Requirements and Losses.....	14
1.1.3. Physiological Role of Iron.....	14
1.1.4. Definition and Causation of Iron Deficiency.....	15
1.1.5. Epidemiology.....	16
1.1.6. Consequences of Iron Deficiency.....	18
1.1.7. Economics of Iron Deficiency.....	19
1.1.8. Iron Toxicity and Overload.....	19
1.2. Zinc Metabolism and Deficiency.....	22
1.2.1. Chemistry of Zinc.....	22
1.2.2. Zinc Functions and Metabolism.....	22
1.2.3. Zinc Requirements and Deficiency.....	22
1.2.4. Zinc Toxicity and Overload.....	23
1.3. Physiology of Iron and Zinc Absorption.....	24
1.3.1. Oral Cavity and Stomach.....	25
1.3.2. Duodenum, Jejunum, and Ileum.....	28
1.3.3. Iron Uptake.....	29
1.3.4. Zinc Uptake.....	31
1.3.5. Large Intestine.....	32
1.3.6. Regulation of Iron Uptake.....	32
1.3.7. Regulation of Zinc Uptake.....	35
1.3.8. Dietary Enhancers and Inhibitors of Iron and Zinc Absorption.....	36
1.3.9. Iron and Zinc Interaction.....	38
1.4. Strategies to Combat Iron and Zinc Deficiency.....	38
1.4.1. Supplementation.....	39
1.4.2. Fortification.....	39
1.4.2.1. Iron Food Fortificants.....	40
1.4.2.2. Zinc Food Fortificants.....	42
1.4.2.3. Food Vehicles.....	43
1.4.2.4. Bioavailability.....	45
1.4.2.5. Sensory Challenges.....	46
1.5. Methods to Evaluate Potential Food Fortificants.....	48
1.5.1. <i>In-vitro</i> Methods.....	48

1.5.2. <i>In-vivo</i> Methods.....	49
2. Nanoparticles for Nutritional Applications.....	50
2.1. What is Nano and Nanotechnology?.....	50
2.2. Naturally Occurring Nano-Sized Structures.....	50
2.3. Special Properties of Nanostructured Compounds.....	51
2.4. Synthetic Nanoparticles.....	53
2.4.1. Flame Spray Pyrolysis.....	53
2.4.2. Preparation by Other Methods.....	57
2.5. Analysis of Nanostructures.....	57
2.5.1. Structure and Morphology Determination.....	58
2.5.2. Specific Surface Area and Size Determination.....	58
3. Nanotechnology in Foods.....	59
3.1. Potential Benefits.....	59
3.2. Potential applications.....	60
3.2.1. Nanostructured Delivery Systems for Minerals.....	60
3.2.2. Food Packaging.....	61
3.2.3. What Is on the Market?.....	62
3.3. Potential Toxicology of Nanostructured Compounds.....	63
3.3.1. Interaction of Nanostructured Compounds with Biological Systems.....	63
3.3.2. Potential Mechanisms of Action.....	64
3.3.3. Gastro Intestinal Toxicology.....	65
3.4. References.....	69
<b>Manuscripts.....</b>	<b>85</b>
Manuscript 1: Development and Optimization of Iron- and Zinc-Containing Nanostructured Powders for Nutritional Applications.....	85
Manuscript 2: Iron from Nanocompounds Containing Iron and Zinc Is Highly Bioavailable in Rats Without Tissue Accumulation.....	111
Manuscript 3: Incorporation of Mg and Ca into Nanostructured Fe <sub>2</sub> O <sub>3</sub> Improves Fe Solubility in Dilute Acid and Sensory.....	135
<b>Conclusions and Perspectives.....</b>	<b>159</b>
<b>Appendix.....</b>	<b>163</b>
Review: Nanocompounds of iron and zinc: their potential in nutrition.....	163
Short communication: Schoolchildren in the Principality of Liechtenstein are mildly iodine deficient.....	185
<b>Curriculum Vitae.....</b>	<b>193</b>