

University of Bucharest

HABILITATION THESIS

**THE IMPORTANCE OF GLYCATION, OXIDATIVE STRESS
AND INFLAMMATION IN HEALTH AND FOOD**

ABSTRACT

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The habilitation thesis entitled **The Importance of Glycation, Oxidative Stress and Inflammation in Health and Food** presents personal research conducted between 2006 and 2016, since I obtained my PhD in Biology and up until now. The results comprised in the Habilitation Thesis were highlighted and published in reputed scientific journals indexed in Thomson Reuters. Thus, the thesis assembled scientific contributions made prior to obtaining my PhD, and scientific achievements corresponding to the 3 main thematic directions approached in postdoctoral research studies, a career progression and development plan and bibliographic references corresponding to the contents of the previous sections.

The first part of the thesis is structured in five chapters. *Chapter 1* presents scientific contributions prior to obtaining my PhD in Biology, the objectives pursued and how the outcomes were achieved. Chapters 2, 3 and 4 present in detail the scientific contributions published in prestigious journals indexed by Thomson Reuters, separated into the 3 different thematic areas, corresponding to:

Chapter 2. The glycation reaction and its role in food and health

After a comprehensive introduction in the field, this chapter presents the structural and functional changes of proteins induced by the glycation reaction, focusing on the collagen, albumin and casein crosslinking and aggregate formation in reducing sugar milieu, and the association with fluorescence levels measurements, proposing a mechanism of action for AG and its future prospects in therapeutic approaches. Then, the roles of AGEs and their receptor play in diabetes and its complications were discussed in detail, approaching signaling pathways, inflammatory response and extracellular matrix changes brought upon by AGEs exposure.

Publications:

1. **Andreea Iren Serban**, M.Costache, A.Dinischiotu. AGEs and glucose levels modulate type I and III procollagen mRNA synthesis in dermal fibroblasts cell culture, *Experimental Diabetes Research*, 2008 (1), 1-7, (2008) IF: 4.350
2. **Andreea Iren Serban**, E. Condac, M. Costache, A. Dinischiotu, The relationship between AGEs, Cu²⁺ and crosslinking of collagen, *Revue Roumaine de Chimie*, 54 (1), 93-101, 2009. ISSN: 0035-3930. IF:0.25
3. **Andreea Iren Serban**, M.Costache, A.Dinischiotu. Controversial behavior of aminoguanidine in the presence of either reducing sugars or soluble glycated bovine serum albumin, *Carbohydrate Research*, 346 (18), 2872-2880, 2011. IF: 1.817
4. **Andreea Iren Serban**, L.Stanca, OI.Geicu, MC.Munteanu, M. Costache, A.Dinischiotu, Extracellular matrix is modulated in advanced glycation end products milieu via a RAGE receptor dependent pathway boosted by transforming growth factor- β 1, *Journal of Diabetes*, 7(1):114-124, 2015; IF:2.500
5. **Andreea Iren Serban**, L. Stanca, O.I. Geicu, A. Dinischiotu, AGEs-induced IL-6 synthesis precedes RAGE up-regulation in HEK 293 cells: an alternative inflammatory mechanism?, *Int. J. Mol. Sci.*, 16(9), 20100-20117, 2015; IF:3.257
6. **Serban Andreea Iren**, Stanca L, Geicu OI, Munteanu MC, Dinischiotu A (2016) RAGE and TGF- β 1 cross-talk regulate extracellular matrix turnover and cytokine synthesis in AGEs exposed fibroblast cells. *PLoS ONE* 11(3): e0152376. doi:10.1371/journal.pone.0152376 IF: 3.057

Funding for this work was granted by the following research projects:

1. The impact of Maillard reaction compounds on the quality and safety of UHT milk based foods and their implication in the development of diabetes-like complications, UEFISCDI, code PNII-RU-TE-2012-3-0034, nr: 15/26.04.2013 (2013-2016). Project leader: **Andreea Iren Serban**

2. The importance of advanced glycation end products (AGEs) in diabetes complications; *in vivo* and *in vitro* studies – Research contract CNCISIS, AT code 185, nr. 12 GR/14.05.2007 (2007-2009). Project leader: **Andreea Iren Serban**

Chapter 3. The relevance of food contaminants and food additives in oxidative stress and oxidative defense

One focus in this chapter was highlighting the link between deoxynivalenol mycotoxin and oxidative stress using *in vitro* models. Another interest was to outline the role of ascorbic acid in inactivating oxidant species as well as highlighting sensitive, biosensor-based methods for ascorbic acid and ethanol evaluation in foods.

Publications

1. AM. Pisoschi, A.Pop, **Andreea Iren Serban**, C. Fafaneata, Electrochemical methods for ascorbic acid determination, *Electrochimica Acta*, 121, 443-460, 2014. IF:4.086
2. A.M. Pisoschi, A. Pop, **Andreea Iren Serban**, G.P. Negulescu, Ethanol determination by amperometric bienzyme sensor based on a Clark-type transducer, *Journal of Electroanalytical Chemistry* 671, 85-91, 2012. IF:2.905
3. G.O. Dragomir Bodea, M.C. Munteanu, D. Dinu, **Andreea Iren Serban**, F. Israel Roming, M. Costache, A. Dinischiotu, Influence of deoxynivalenol on the oxidative status of HepG2 cells, *Romanian Biotechnological Letters*, 14 (2), 4349-4359, 2009. IF:0.34
4. D.Dinu, G.O.Bodea, C.D. Ceapa, M. C. Munteanu, F. Israel-Roming, **Andreea Iren Serban**, A. Hermenean, M. Costache, O. Zarnescu, A.Dinischiotu, Adapted response of the antioxidant defense system to oxidative stress induced by deoxynivalenol in Hek-293 cells, *Toxicon*, 57, 1023-1032, 2011. IF: 2.792

Chapter 4. Nanoscale materials, between health risk and applications in biomedicine

In this chapter the *in vivo* and *in vitro* effects of Si based QDs exposure are discussed. Following complex analysis of oxidative stress, inflammation, QDs biodistribution and histological evaluation, these potentially useful type of fluorescent marker are very promising for bioimaging applications, if they are used in adequate concentration or shielded from immune recognition using proper surface conjugation.

Publications:

1. M. Radu, M.C. Munteanu, S. Petrache, **Andreea Iren Serban**, D.Dinu, M. Costache, A. Dinischiotu, The depletion of intracellular glutathione and increase of lipid peroxidation mediate the hematite nanoparticles-induced cytotoxicity in MRC-5 cells, *Acta Biochimica Polonica*, 57, 1-6, 2010. IF: 1.187
2. L.Stanca, S.N. Petrache, M. Radu, **Andreea Iren Serban**, M.C. Munteanu, D.Teodorescu, A.C. Staicu, C. Sima, M.Costache, C. Grigoriu, O. Zarnescu, A. Dinischiotu, Impact of silicon-based quantum dots on the antioxidative system in white muscle of *Carassius auratus gibelio*, *Fish Physiol Biochem* 38(4),963-975, 2012; IF:1.442
3. S. N. Petrache, L.Stanca, **Andreea Iren Serban**, C. Sima, A. C. Staicu, M. C. Munteanu, M. Costache, R. Burlacu, Otilia Zarnescu, Anca Dinischiotu, Structural and Oxidative Changes in the Kidney of Crucian Carp Induced by Silicon-Based Quantum Dots, *Int. J. Mol. Sci.* 13(8), 10193-10211, 2012. IF:3.257

4. L. Stanca, S. N. Petrache, **Andreea Iren Serban**, A. C. Staicu, C. Sima, M. C. Munteanu, O. Zarnescu, D. Dinu, A. Dinischiotu, Interaction of silicon based quantum dots with Gibel carp liver: oxidative and structural modifications, *Nanoscale Research Letters*.2013, 8:254. IF:2.584
5. **Andreea Iren Serban**, L. Stanca, C. Sima, A.C. Staicu, O. Zarnescu, A. Dinischiotu, Complex responses to Si quantum dots accumulation in carp liver tissue: Beyond oxidative stress, *Chem. Biol. Interact.*, 239, 56-66, 2015. IF:2.618
6. L. Stanca, C. Sima, S.N. Petrache (Voicu), **Andreea Iren Serban**, A. Dinischiotu, In vitro evaluation of the morphological and biochemical changes induced by Si/SiO₂ QDs exposure of HepG2 cells, *Romanian Reports in Physics*, 67,(No. 4), 1512–1524, 2015. IF: 1.367

Funding for this work was granted by the following research projects:

Imaging base don fluorescent silicon nanoparticles – evaluation of tissue toxicity due to *in vivo* accumulation using biochemical and molecular approaches UEFISCDI, TE-127, (2010-2013), contract nr.99/ 02.08.2010

Chapter 5 represents the list of all publications which were included and discussed in the habilitation thesis.

The second part of the habilitation thesis presents the main strategies for professional career progression and development. This part comprises 2 chapters. The first chapter presents research conducted as part of the ongoing scientific project I am directing. The second chapter describes research directions and how they are implemented for future research projects.

The research studies whose results are comprised in the habilitation thesis were conducted at the Department of Biochemistry and Molecular Biology, Faculty of Biology, University of Bucharest (infrastructure link <http://erris.gov.ro/DMI-PCBE>) and the Preclinical Sciences Department, Faculty of Veterinary Medicine, University of Agronomical Sciences and Veterinary Medicine Bucharest (infrastructure link <http://erris.gov.ro/CAPRes>).