

Habilitation thesis

20 YEARS OF CHEMISTRY: BETWEEN SYNTHETIC SATURATED HETEROCYCLIC COMPOUNDS AND NATURAL POLYPHENOLS

Luminița-Camelia David (n. Muntean)

ABSTRACT

Habilitation thesis entitled “20 YEARS OF CHEMISTRY: BETWEEN SYNTHETIC SATURATED HETEROCYCLIC COMPOUNDS AND NATURAL POLYPHENOLS” presents the main scientific achievements after obtaining the title of Doctor of Chemistry (2000), as well as a brief description of the research directions that will be addressed in the future.

The habilitation thesis is divided into two sections, namely:

Part A: Scientific achievements

Part B: Perspectives and future research directions

Part A of the habilitation thesis is structured on four chapters, as follows:

Chapter 1. Introduction, briefly presents the professional and scientific path, after obtaining the title of doctor in chemistry.

Chapter 2. Saturated six-membered rings heterocyclic compounds, shows relevant scientific results regarding the synthesis, stereochemistry and reactivity of six-membered ring saturated heterocyclic compounds (1,3-dioxanes, 1,3-oxathianes and perhydro-1,3-oxazines, respectively).

This chapter details the following: preferred configuration and position of conformational equilibrium for monoheterocyclic compounds and for alkyl chain or aromatic ring separated two heterocyclic derivatives, including equilibration of *like-unlike* isomers in the case of bis (1,3-oxathiane) compounds; the influence of chiral elements on the structure and reactivity of the investigated compounds, as well as on the mechanism of the bromination reaction of some spiro-1,3-dioxanes; conformational equilibria of heterocyclic spiro compounds; ring-chain tautomerization of nitrogen unsubstituted perhydro-1,3-oxazine derivatives; *cis-trans* isomerism of some spiro-1,3-oxathianes.

The obtained results were the subject of 9 scientific articles published in Web of Science indexed journals of which two published in the first quartile classified journals (Q1) and two in the second quartile classified journals (Q2 - by impact factor, according to Clarivate Analytics, 2019).

The scientific relevance of these results is also evidenced by their citation by prestigious international authors in reference books in the field of organic chemistry and stereochemistry, such as Michael Smith in “March's Advanced organic chemistry: Reactions, mechanisms and structure” and Erich Kleinpeter in “Conformational analysis of saturated six-membered oxygen-containing heterocyclic rings”.

Chapter 3. Natural polyphenols is dedicated to the the investigation of natural compounds with antioxidant properties (especially fruit polyphenols) and to their applications in the food industry, medicine and materials science. This chapter details the influence of different factors (such as: temperature, pH, solvent, the presence of food additives namely sweeteners, preservatives and antioxidants) on the degradation process of polyphenols (especially anthocyanin dyes) from underutilized fruits of some shrubs from the spontaneous flora: European black elderberry, Cornelian cherry, European cranberry bush, Common dogwood, Garden privet and Blackthorn. The kinetic parameters of the degradation process were determined under the mentioned conditions, thus enabling an evaluation of the investigated fruits as valuable sources of natural dyes for the food industry. At the same time, the influence of digestive tract conditions on the bioavailability of bioactive compounds from fruits was estimated by applying an *in vitro* digestion model.

The phytochemicals from Cornelian cherry fruit extract have been *in vivo* investigated to evaluate their anti-inflammatory and antitumor properties, the obtained results proving that these fruits are a valuable source of health promoting compounds that can be successfully used as natural anti-inflammatory drugs and increase the effectiveness of photodynamic therapy in oral cancer.

The bioactive compounds from the investigated fruits were used as reducing agents for metallic ions, in order to achieve the green synthesis of the corresponding metal nanoparticles. The investigation of the anti-inflammatory, antioxidant, anti-diabetic and antitumor properties of gold and silver nanoparticles thus obtained revealed their remarkable potential as adjuvants in the treatment of inflammatory diseases (psoriasis, celiac disease), cancers (ovarian and oral), diabetes and of diseases caused by oxidative stress. At the same time, green synthesis of

silver nanoparticles obtained with antioxidant compounds from European cranberrybush fruits proved to be efficient catalysts for the reductive degradation reaction of some organic food dyes (tartrazine, azorubin and brilliant blue FCF). The high value of our research results in this field enabled us to publish them in 36 scientific articles, of which 14 in journals classified in quartile Q1 (6 of them in journals in the Top 10 in the field) and 7 in journals classified in quartile Q2 (according to Clarivate Analytics, 2019). The more than 450 citations of these articles (according to Clarivate Analytics), three of them with more than 50 citations each, represent an objective measure of their scientific relevance.

Chapter 4. Research projects, contains a list of research projects in which I was involved either as a project manager or as a team member, as well as some remarks on the topic of the research projects managed as a director / project manager.

Part B of this thesis presents the future research directions which I intend to develop, namely: stabilization of natural pigments by copigmentation and / or encapsulation, evaluation of the effect of using food additive mixtures on the stability of natural dyes, use of bioactive compounds separated from natural sources to obtain functionalized metallic or carbon-based hybrid nanomaterials with enhanced properties and their evaluation for use as therapeutic agents.

The bibliographic **references** associated with the two parts of this work are presented at the end of the habilitation thesis.