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BIOACTIVE COMPOUNDS / CYCLODEXTRIN COMPLEXES:

synthesis, characterisation, applications, and molecular modeling

Habilitation Thesis

Timişoara - Romania, 2012

Abstract

The *Habilitation Thesis* named "**Bioactive compounds/cyclodextrin complexes: synthesis, characterisation, applications, and molecular modeling**" consists of three main sections: the first section is divided in seven individual Chapters providing the results on the specific area; the second section contains a Chapter describing the future academic development, scientific and professional career evolution and development, research and teaching directions, and the final section contains the main publications of the author which were the basis of the present thesis and the references associated to the thesis.

The researches on cyclodextrins were focused on water implication in cyclodextrin properties: methods for determination the "real" water concentration in cyclodextrins; evaluation of the water type molecules in cyclodextrin structures by a new concept; establish the optimum conditions for determination of water content by Karl Fisher method. The Karl Fischer water titration in cyclodextrins is an appropriate method to determine the total water concentration in cyclodextrin samples, but the hydrophobicity of solvent used is important; the water reaction rate from KFT process could be a good indicator on the concentration of "surface" and "strong-bonded" water molecules from cyclodextrins.

The researches on the natural antioxidant/cyclodextrin complexes were performed especially on the flavonoid, flavonoside, and flavonolignan classes: synthesis and analysis of flavonoids, flavonosides, flavonolignans/cyclodextrin complexes; synthesis and analysis of natural containing antioxidant compounds (*i.e. Ficaria verna* extracts)/cyclodextrin complexes; evaluation of antioxidant activity and water importance in the natural antioxidants/cyclodextrin complexes. The water content of cyclodextrin complexes, determined even by classical Karl Fischer titration or evaluated by thermogravimetry, depend on the hydrophobic (or related) descriptors of guest compound, especially for β-cyclodextrin complexes, the best correlation being obtained for log*P*. Furthermore, the controlled release properties of complexes containing bioactive compounds such as flavonoids can be observed by means of the reaction rate in antioxidant activity evaluation in model systems and could be used in food and pharmaceutical formulations with enhanced bioactivity.

The studies regarding the essential oils/cyclodextrin complexes were targeted on the following aspects: synthesis and characterisation of essential oils/cyclodextrin complexes; evaluation of encapsulation competitivity, protection/stability, and controlled release properties of these complexes; establish the water importance on the encapsulation process of essential oils in cyclodextrins. All concentrated monoterpenic hydrocarbons were encapsulated in higher relative concentrations (*e.g.* limonene and pinene), in comparison with those from the raw essential oils. The complexation of the essential oil of garlic (*Allium sativum* L.) in cyclodextrins provides products with no "garlic" odor.

Researches on protection and controlled release of fatty acids by encapsulation in cyclodextrins were focused on the obtaining and characterisation of fatty acid/cyclodextrin complexes; establish the protection capacity of complexes against degradation of fatty acids, and evaluation the water content and types of these molecules in the cyclodextrin complexes. Higher relative concentration of degradation products can be identified in the case of thermally degraded fatty acid samples, the main compounds being aldehydes resulted by oxidation processes. Very good thermal stability was observed for fatty acid/cyclodextrin complexes. The KFT water content values for these complexes were more accurate than the thermogravimeric analysis.

The researches on alkaloid/cyclodextrin complexes were focused especially on purified alkaloids from *Nicotiana tabacum* L. and *Berberis vulgaris* L., as well as on the corresponding natural extracts: synthesis, analysis, and stability of nicotine/cyclodextrin complexes; synthesis, analysis, and hepatoprotective effects of *B. vulgaris* L./cyclodextrin complexes.

The studies on molecular modeling of cyclodextrins and their complexes with biologically active compounds were performed on the following directions: molecular modeling of bioactive

organometallic compounds and docking experiments in cyclodextrins; molecular modeling, docking experiments and QSARs/QSPRs on flavonosides and flavonoside-fatty acid bioconjugates in cyclodextrins.

The **main steps** for the **professional** and **academic evolution** and **development** will be *researches, lectures, and practical courses* development in the following areas:

- *natural bioactive compounds* with applications in food, medicine, and pharmacy;
- *protection* and *controlled release systems*, especially in *cyclodextrins* and *liposomes*;
- *combined systems* containing both *biologically active compounds* and *matrices* with p*rotection* and *controlled release properties*;
- *theoretical modeling* of *nanoencapsulation* and *controlled release processes* for *bioactive compound / cyclodextrin or liposome supramolecular systems*;
- *formulations* of *new food / pharmaceutical products* with high social, economic, and human health impact.

In order to ensure the fulfillment of these steps the following **future actions** will be performed:

- applying the research results in the *teaching programme*, especially at the Master and PhD levels;
- enhancing the *collaboration* with professors and colleagues from *EU universities* and *research centres*, as well as from Romania and other countries, which are working in the same or related research and teaching fields;
- applying *project proposals* in both research and teaching directions, especially at international level;
- enhancing the *collaboration* with the *economic environment* (national and international) in both research and applicative directions.