ULST Timisoara
Multidisciplinary Conference on Sustainable Development
15-16 May 2025

Nanoencapsulation of polyphenols from maritime pine bark (*Pinus pinaster* Aiton) in natural β- and γ-cyclodextrins – molecular docking, encapsulation competitivity, and stability of the food and pharmaceutical grade supramolecular systems

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Abstract: *The goal of this study was the enhancement of the oxidative stability of bioactive polyphenols contained by maritime pine bark extracts using cyclodextrin (CD) nanoencapsulation. In addition, the CD molecular encapsulation competitivity of the main polyphenol compounds from the maritime pine extracts was evaluated.*

• Introduction

Maritime pine (*Pinus pinaster* Aiton) is a tree growing in Western Europe and Mediterranean coastal regions. Its bark is rich in antioxidant compounds, especially procyanidins, phenolic acids, or ellagic acid. The standardized extract (Pycnogenol®) is used in dietary supplements or in pharmaceutical formulations. However, the stability of such antioxidant compounds are low [1,2].

• Material and method

Selected polyphenols (phenolic acids, flavonoids, or procyanidins) were subjected to conformational analysis using HyperChem package (*MM+*). The molecular encapsulation capacity of the optimized β- and γ-CD was evaluated by molecular docking experiments. The interaction energy of the CD:polyphenols at 1:2 molecular ratio (ternary complexes) was monitored during the optimization.

• Results and discussions

The ternary interactions were favorable, having energies in the range of 25.7-39.5 and 27.2-47.4 kcal/mol for β- and γ-CD complexes, respectively (Figure 1, left). The highest interaction energies were obtained for chlorogenic acid & catechin and procyanidin B_2 & pinoresinol during the interaction with γ-CD, but the lowest absolute energy of the complex was observed for catechin or rosmarinic acid with procyanidin B_2 pairs (Figure 1, right).

On the other hand, chlorogenic acid had better interact with the γ-CD cavity in comparison with catechin, naringin or naringenin (smaller, less flexible or more hydrophilic molecules). Interestingly, aromatic moieties also interact by van der Waals forces such as in the case of chlorogenic acid / procyanidin B_2 and chlorogenic acid / ellagic acid pairs (Figure 1, left).

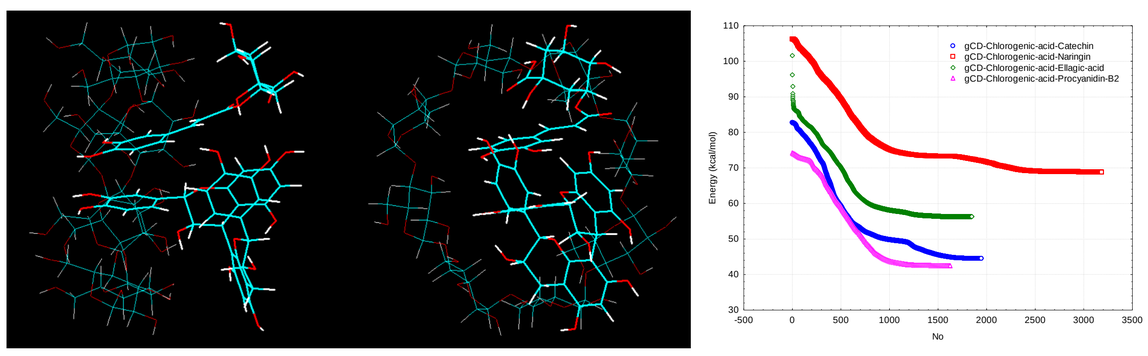

Figure 1. Optimized γ-CD/chlorogenic acid/procyanidin B_2 ternary complex (left); Variation of the absolute energy of the ternary complexes (right)

• Conclusions

All pycnogenol antioxidant compounds (small molecules) well interact with the larger natural cyclodextrins providing stable ternary or multiple complexes with possible applications in the food and pharmaceutical products.

Acknowledgement: S. Funar-Timofei ("Coriolan Drăgulescu" Institute of Chemistry, Romanian Academy) for the help with HyperChem 7.52 package.

References: [1] Alonso-Esteban *et al.*, *Rev Env Sci Bio/Tech* **2022**, *21*, 583-633; [2] Hădărugă, D.I.; Hădărugă, N.G., Flavones. Structure, Properties, Sources and Food Applications. In: *Handbook of Food Bioactive Ingredients*, Springer Nature, Cham, **2023**, pp. 111-158.