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

A theoretical insight on the enhancement of bioavailability and bioaccessibility of some natural stilbene-based lipopolyphenols with bioactivity against cardio-vascular diseases by cyclodextrin nanoencapsulation

Darius-Adrian Costandana [1], Agnes Cupin [2], Marinela Fițoiu (Voin) [2], Anamaria Pop (Mateuț) [2], Nicoleta G. Hădărugă [2], Daniel I. Hădărugă [1,2,*]

[1] Polytechnic University of Timişoara, Romania
[2] University of Life Sciences "King Mihai I" from Timişoara, Romania

Abstract: *The goal of the study was the evaluation of the influence of hydrophobic moiety of natural stilbene-based derivatives on the anticarcinogenic activities as well as the bioavailability and bioaccesibility enhancement by cyclodextrin nanoencapsulation.*

• Introduction

Natural compounds having stilbene moiety exhibit various biological activities. Derivatization to the more hydrophobic stilbene-based lipopolyphenols can enhance their biological activities, while the cyclodextrin (CD) nanoencapsulation will enhances the bioavailability and bioaccessibility [1-3].

• Materials and method

Eight stilbene-based lipopolyphenols, the corresponding polyphenols and colchicine (positive control) were optimized by *MM+* molecular modelling and conformational analysis (HyperChem 7.52 package, StatSoft). Minimum energy conformations were used for determination of more than one thousand molecular descriptors using *PaDEL-Descriptor* software. QSAR models and CD : lipopoly-phenol complexes were proposed.

• Results and discussion

Valuable QSAR models with constitutional and topological descriptors were obtained (Eq. 1). On the other hand, *in vacuo* and water periodic box docking experiments (*MM+*) for α-, β- and γ-CD / lipopolyphenol complexes at 1:1 molecular ratio revealed high stability and possibility of controlled release of the biologically active compounds to the biological target, especially for larger CDs with *trans*-stilbene-based lipopolyphenols (interaction energies of 24.0 kcal/mol and 32.4 kcal/mol for 1:1 complexes of epi-combretastatin A4-stearic acid lipopolyphenol derivative with β- and γ-CD, respectively, Figure 1).

• Conclusion

As a conclusion, natural stilbene antioxidant compounds from some bushwillow species (*Combretum afrum* (Eckl. & Zeyh.) Kuntze or *C. leprosum* Mart.) and especially from grapes and wines (*Vitis* spp.) can be efficiently derivatized to more hydrophobic bioconjugates using fatty acids and further nanoencapsulated in natural CDs for obtaining pharmaceutical or food-grade nanomaterials.

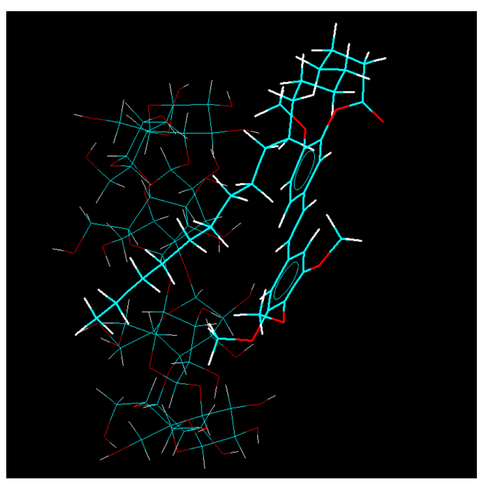
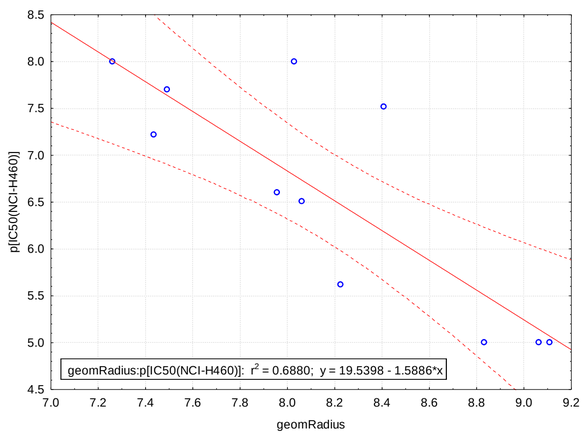


Figure 1. Optimized γ-CD/epi-combretastatin A4-stearic acid lipopolyphenol derivative complex



Eq.1. $pIC_{50(NCI\text{-}H460)}$ *vs.* *GeometricRadius* correlation

$$\log\left(\frac{1}{IC_{50}}\right)_i = 19.540(\pm 2.922) - 1.589(\pm 0.357)\cdot[GeomRadius]_i$$

$r_{(KB\text{-}3\text{-}1)} = 0.812$, $r_{(NCI\text{-}H460)} = 0.829$, $r_{(HEK293)} = 0.833$ (Eq. 1)

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

References: [1] Kineman *et al.*, *Nutr & Cancer* **2010**, *62*, 351-361; [2] Crauste *et al.*, *Eur J Org Chem* **2022**, *21*, e202101502; [3] Hădărugă, N.G.; Hădărugă, D.I., Stilbenes and Its Derivatives and Glycosides. In: *Handbook of Food Bioactive Ingredients*, Springer Nature, Cham, **2023**, pp. 487-544.