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Proving Nanoscale Chiral Interactions of Cyclodextrins and Propranolol Enantiomers by Means of SERS Measurements Performed on a Solid Plasmonic Substrate

Gabriela Fabiola Știufiuc [1,†], Valentin Toma [2,†], Anca Onaciu [2], Vasile Chiș [1], Constantin Mihai Lucaciu [3] and Rareș Ionuț Știufiuc [2,3,*]

[1] Faculty of Physics, "Babeș-Bolyai" University, M. Kogălniceanu 1, 400084 Cluj-Napoca, Romania; gabriela.stiufiuc@ubbcluj.ro (G.F.Ș.); vasile.chis@ubbcluj.ro (V.C.)
[2] MedFuture Research Center for Advance Medicine, "Iuliu Haţieganu" University of Medicine and Pharmacy, L. Pasteur 4-6, 400349 Cluj-Napoca, Romania; valentin.toma@umfcluj.ro (V.T.); anca.onaciu@umfcluj.ro (A.O.)
[3] Department of Pharmaceutical Physics-Biophysics, "Iuliu Haţieganu" University of Medicine and Pharmacy, L. Pasteur 6, 400349 Cluj-Napoca, Romania; clucaciu@umfcluj.ro
* Correspondence: rares.stiufiuc@umfcluj.ro; Tel.: +40-0726-34-02-78
† These authors contribute equally to this work.

Abstract: Chiral separation is an important issue for the pharmaceutical industry. Over the years, several separation methods have been developed, mainly based on chromatography. Their working principle is based on the formation of transient diastereoisomers, but the very subtle nanoscale interactions responsible for separation are not always understood. Recently, Raman and surface-enhanced Raman (SERS) spectroscopy have provided promising results in this field. Here we present Raman/SERS experimental data that provide useful information concerning the nanoscale interactions between propranolol enantiomers and α, β, and γ cyclodextrins. Raman spectroscopy was used to prove the formation of host–guest intermolecular complexes having different geometries of interaction. The occurrence of new vibrational bands and a change in the intensities of others are direct proofs of complexes' formation. These observations were confirmed by DFT calculations. By performing SERS measurements on a new type of plasmonic substrate, we were able to prove the intermolecular interactions responsible for PRNL discrimination. It turned out that the interaction strength between the substrate and the intermolecular complexes is of paramount importance for SERS-based chiral discrimination. This approach could represent a very good starting point for the evaluation of molecular interactions manifesting between other pharmaceutical compounds and different classes of chiral selectors.

Keywords: cyclodextrins; chiral interactions; Raman; SERS; quantum calculations

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1. Introduction

Chiral discrimination is a very intriguing characteristic of living systems that could hold the key for a precise understanding of living matter. More specifically, the ability to generate concluding scientific proof of the possible mechanism involved in chiral discrimination needs to be properly addressed, especially from an experimental point of view. Over the years, this research topic has drawn immense attention in the pharmaceutical sciences. The pharmaceutical industry is highly interested in finding new experimental techniques able to discriminate and, ideally, separate the naturally occurring pharmaceutical enantiomers. Among the different techniques that have been intensively applied in analytical separation of pharmaceutical compounds, the chromatographic ones are by far the most utilized. The fundamental process responsible for chiral separation and discrimination of pharmaceutical enantiomers is the formation of a transient diastereomeric complex between the pharmaceutical enantiomers and a chiral selector. The main physical interactions