MODELLING ^{17}O NMR SPECTRA OF TAUTOMERIC FORMS OF CITRININ

Žyginta Einorytė[1,2], Kęstutis Aidas[2]

[1] Institute of Chemistry, Faculty of Chemistry and Geosciences, Vilnius University, Lithuania
[2] Institute of Chemical Physics, Faculty of Physics, Vilnius University, Lithuania
zyginta.einoryte@chf.stud.vu.lt

Citrinin is a mycotoxin which causes contamination of food with various toxic effects. Two tautomeric forms of citrinin exist – *para* or *ortho* quinone methide (analogous to a quinone but having one of the carboxylic oxygens replaced with a carbon) (Fig. 1). Citrinin is synthesized as a secondary metabolite by several fungal strains of *Penicillium, Aspergillus* and *Monascus* genera and is often found along with another nephrotoxic compound, ochratoxin A. As many other mycotoxins, citrinin is considered a perspective antimicrobial, antitumor and even neuroprotective agent due to its toxicity. Citrinin is known for having toxic effects on the heart, kidneys, liver, reproductive system. Oxidative stress and modified antioxidative enzymatic defences (e.g. glutathione) are thought to be two major causes of citrinin's mediated toxic effects but the precise mechanism of its action is yet to be discovered [1]. More detailed understanding of citrinin's distribution between two tautomeric forms would help in dissecting the possible mechanism of its action.

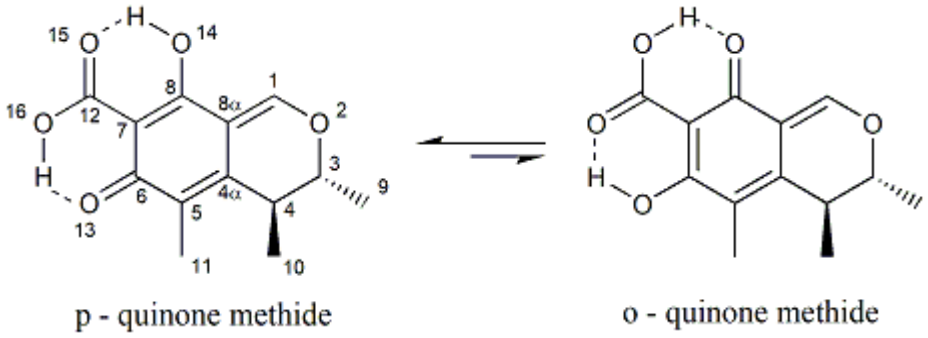

Fig. 1. Tautomeric forms of citrinin

The main goal of this study is to model the ^{17}O NMR spectrum of citrinin in the dichloromethane (DCM) solution in order to compare it to an experimental spectrum from previous studies [2]. The measured ^{17}O NMR spectrum of citrinin is interesting as its qualitative shape is not consistent with citrinin's tautomeric distribution implied by the ^{1}H and ^{13}C NMR spectra measured in the same study. In addition, the ^{17}O NMR signals from oxygen atoms 13 and 14 exhibit additional peaks, almost doublets, which is intriguing because the interconversion between two tautomers should occur at a high rate so that only single peak should be seen in the spectrum [2]. Our computational approach allows evaluating the ^{17}O NMR spectrum of both individual tautomers. Thus, the comparison between theoretical tautomer-averaged spectrum and the experimental spectrum allows us to estimate the populations of each tautomer of citrinin in DCM solution.

Molecular dynamics (MD) simulations were executed for *para*- and *ortho*-citrinin in DCM using an all-atom OPLS force field. The standard Coulomb plus 12-6-type Lennard-Jones potential was used, and atomic point charges were derived by fitting to the quantum mechanical electrostatic potential according to the CHelpG scheme. NMR shielding constants were calculated for isolated molecular species of citrinin. To account for solvation, the hybrid quantum mechanics/molecular mechanics (QM/MM) calculations were considered. These calculations were performed for a set of molecular solute-solvent snapshots extracted from the MD trajectory for each tautomer. The comparisons between experimental data and our computational results will be discussed in the presentation.

[1] J. W. G. de Oliveira Filho, et al. A comprehensive review on biological properties of citrinin. Food Chem. Toxicol. 110, 130–141 (2017).
[2] R. Poupko, Z. Luz, Carbon-13 NMR of Citrinin in the Solid State and in Solutions. Journal of Physical Chemistry A - J PHYS CHEM A 101, (1997).