Raman optical activity for drug discovery: Structural characterization of artemisinin derivatives in solution

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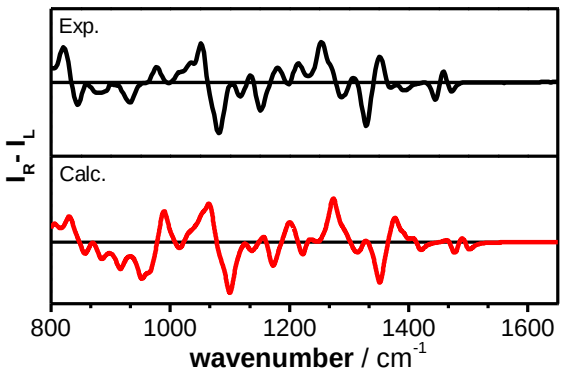
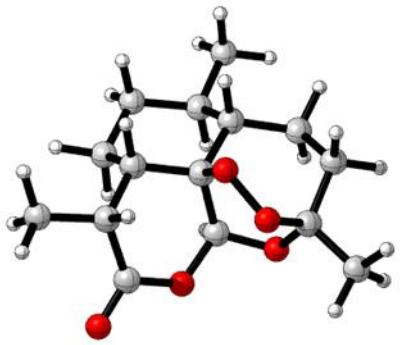
The natural compound artemisinin, which is currently employed in malaria treatment, is showing great potential as a candidate for such next generation cancer treatment.[1] One of the biggest challenges in drugs discovery research is the stereochemical characterization and the identification of conformational preferences in solution to have a better understanding of the molecular mechanism and the structure-activity relationship. Considering the limitations and side effects caused by conventional cancer treatments, new techniques for the structural characterization of drugs are strongly required, in order to obtain an accurate, site directed therapy.

The application of Raman opical acivity (ROA) to the structural characterization of natural products has increased significantly in the past years. [2, 3] ROA is based on inelastic (Raman) scattering of circular polarised light. When the experiment is combined with DFT calculations, ROA provides an unparalleled sensitivity towards solution phase conformation and stereochemistry of chiral molecules. Furthermore, ROA has emerged as a very strong tool in the structural analysis of proteins [4] making this method an ideal candidate for studying the structure of natural and synthetic lead compounds with potential pharmacological activity.





In this contribution, the performance of ROA applied on artemisinin, dihydroartemisinin and artesunate combined with quantum chemical calculations will be discussed. Furthermore, the effect of changing one stereocenter in the compound on the computed spectrum will be highlighted.

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[2] Í. H. Calisto, M. Furlan, E. W. Blanch, J. M. Batista, *Vib. Spectrosc.*, **2016**, *95*, 6–10.
[3] V. Profant, A. Jegorov, P. Bouř, V. Baumruk, *J. Phys. Chem. B*, **2017**, *121*, 1544–1551.
[4] L. D. Barron, *Biomed. Spectrosc. Imaging*, **2015**, *4*, 223–253.