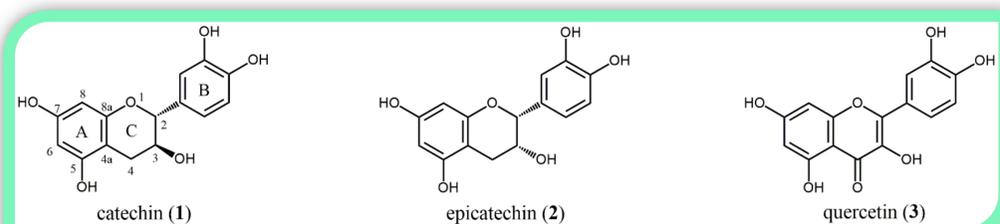


# A mechanistic investigation of H/D scrambling processes in flavonoids

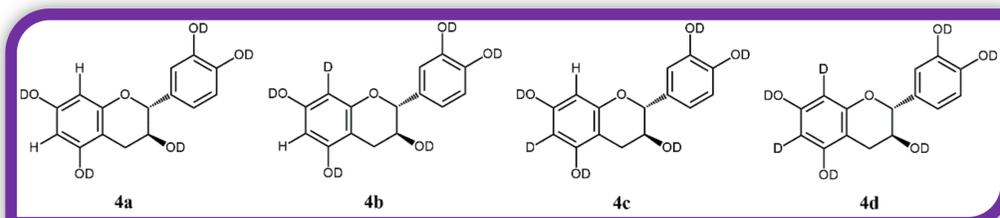
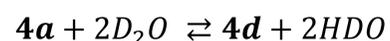
## Introduction & Methods

Among polyphenols, flavonoids, and in particular flavanols (**catechin**, **epicatechin**) and flavonols (**quercetin**), are two of the most important classes due to their nutritional value and biological effects<sup>1,2</sup>.

Our **aim** is to characterize scrambling processes on these substrates from a **kinetic**, **mechanistic** and **thermodynamic** point of view.



In presence of D<sub>2</sub>O, these compounds undergo slow H/D substitution (**scrambling process**) on aromatic ring A, leading to **full deuteration** at **C(6)** and **C(8)**<sup>3,4</sup>.

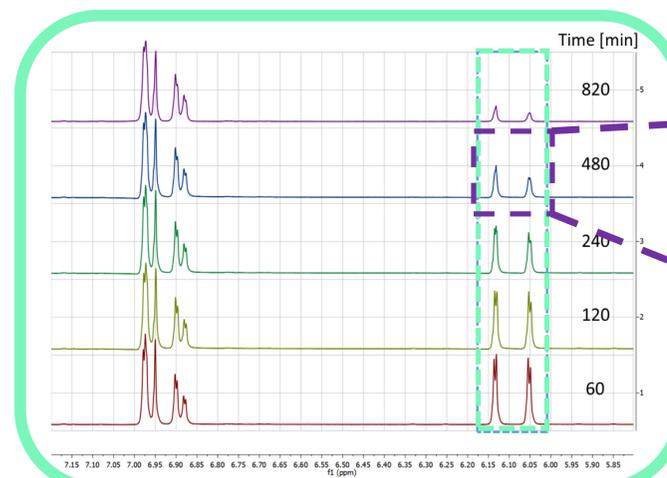


- 1) 10 mM solutions in 0.750 ml D<sub>2</sub>O prepared directly in NMR tube.
- 2) <sup>1</sup>H-NMR **kinetics** at five different temperatures in range T = 300 ÷ 320 K.
- 3) <sup>1</sup>H-NMR spectra acquisition each 10 minutes.
- 4) MestReNova (GSD) **peak deconvolution** and Kineticscope analysis.
- 5) (Gaussian DFT simulations on QM **molecular modeling**).

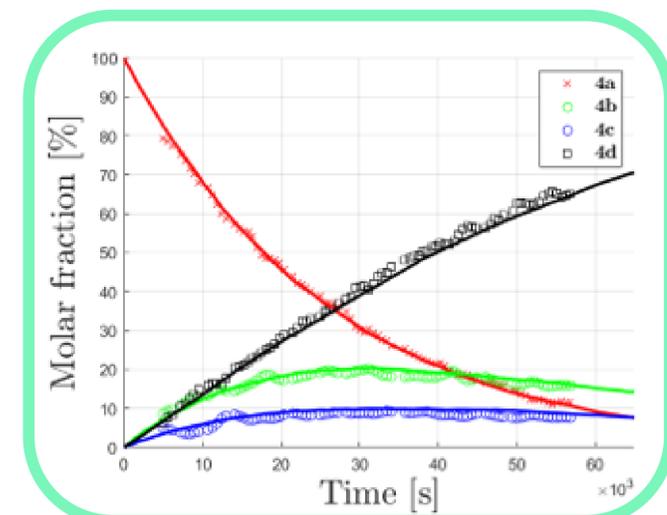
## References

- 1) Kühnau, J. The flavonoids. A class of semi-essential food components: their role in human nutrition. *World Rev. Nutr. Diet.* **1976**, 24, 117–191.
- 2) Hertog, M.G. *et al.* Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study. *Lancet* **1993**, 342, 1007–1011.
- 3) Faizi, S. *et al.* Specific deuteration in patuletin and related flavonoids via keto-enol tautomerism: solvent- and temperature-dependent <sup>1</sup>H-NMR studies. *Helv. Chim. Acta* **2010**, 93,466–481.
- 4) Kolar, G.F. Nuclear deuterium exchange in methoxybenzenes and methylated flavonoids. *J. Labelled Compd.* **1971**,7,409–415.

## Results & Conclusion

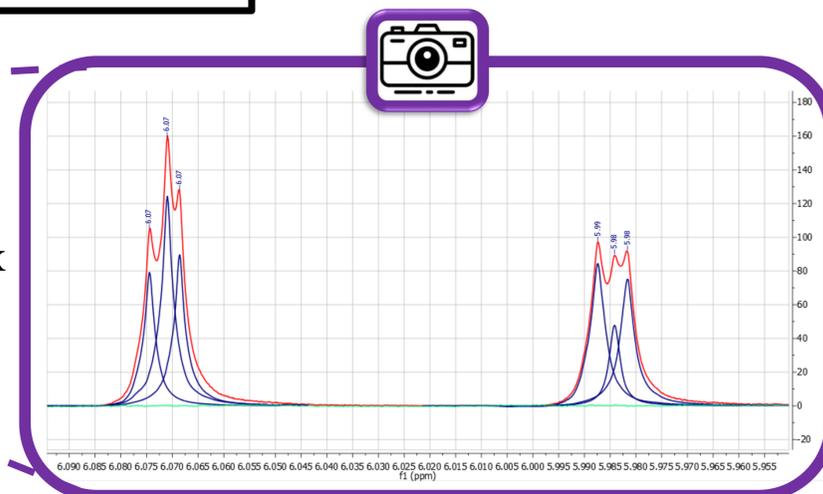


Downfield region of <sup>1</sup>H-NMR spectra of **4a** in D<sub>2</sub>O taken at different times (T = 310 K).

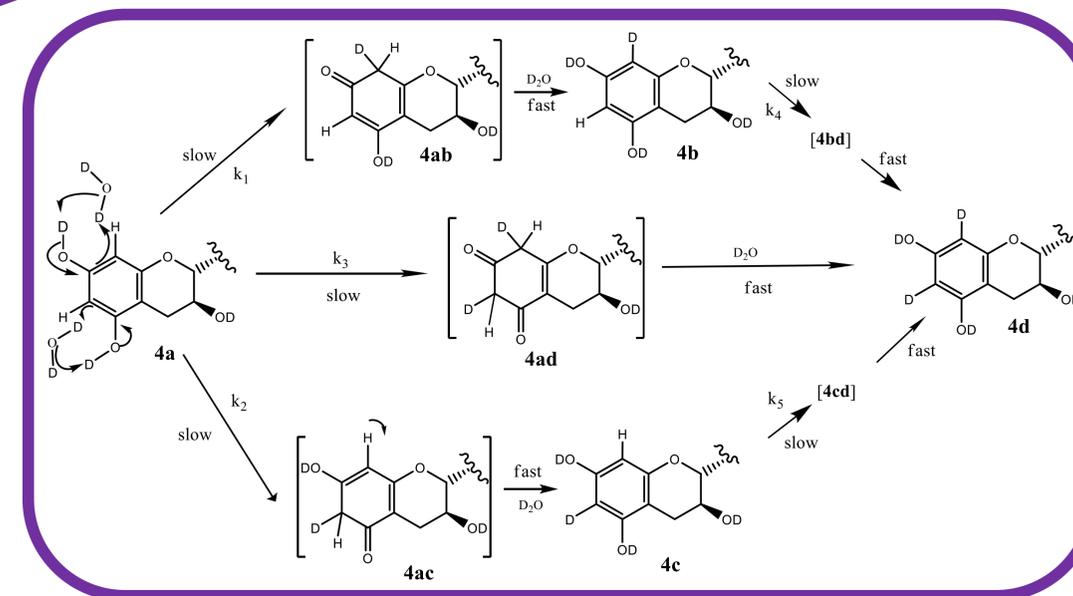


Experimental kinetic data and best fitting curves for the deuteration of catechin at T = 305 K

<sup>1</sup>H-NMR (GSD) spectral deconvolution of peaks corresponding to C(6) and C(8). t ~ 500 min, T = 305 K



Proposed reaction mechanism



**We proved:**

- a) the existence, along the reaction coordinate leading for **1(4a)** to **4d**, of the monodeuterated species **4b** and **4c**;
- b) different rates of formation of **4b** and **4c** (peak deconvolution proof on H-C(6) and H-C(8) NMR signals) during the kinetics;
- c) the relevant role played by termolecular processes whereby **4a** is converted in **4d** without passing through intermediates **4b** and **4c**.