Supplementary material for: Diffusivity of α-, β-, γ-cyclodextrin and the Inclusion Complex of β-cyclodextrin:Ibuprofen in Aqueous Solutions; A Molecular Dynamics Simulation Study

Máté Erdős[a], Michalis Frangou[a], Thijs J. H. Vlugt[a], Othonas A. Moultos[a,*]

[a]*Engineering Thermodynamics, Process & Energy Department, Faculty of Mechanical, Maritime and Materials Engineering, Delft University of Technology, Leeghwaterstraat 39, 2628CB Delft, The Netherlands*

The computed shear viscosities of water with the TIP3P[1], Bind3P[2], SPC/E[3], and TIP4P/2005 [4] water force fields at temperatures ranging from 298.15 K to 312.15 K and at 1 bar are shown in Table S1. In Table S2, the computed shear viscosities (η) of water with different NaCl concentrations using the Joung and Cheatham [5] and the Madrid-2019[6] ion force fields and the TIP4P/2005 water force field at 298.15 K and 1 bar are presented. The effect of the system size on the self-diffusivities of α- and γ-CDs are shown in Figures S1 and S2. The physical properties of the CDs which can influence the diffusion: the number of intramolecular hydrogen bonds of the CDs, the average number of water molecules residing in the cavity of the CD during the diffusion process, and the size of the large and small rims of the CDs (see Figure 1 in the main text) are shown in Figures S3, S4, S5, and S6, respectively. In Figure S7, the radial distribution functions for the distance between the center of mass of the β-CD and the oxygen atom of the water molecules are shown for the free β-CD and for the two orientations of the ibuprofen:β-CD inclusion complex.

*Othonas A. Moultos
Email address: o.moultos@tudelft.nl (Othonas A. Moultos)

Table S1: Computed shear viscosities (η) of water for four different water force fields for temperatures from 298.15 K to 312.15 K and at $P = 1$ bar. The numbers in the parentheses indicate the uncertainty (one standard deviation) in the last digit.

T / [K]	η_{TIP3P} / [mPa s]	η_{Bind3P} / [mPa s]	$\eta_{\mathrm{SPC/E}}$ / [mPa s]	$\eta_{\mathrm{TIP4P/2005}}$ / [mPa s]
298.15	0.33(2)	0.29(1)	0.72(2)	0.90(4)
303.15	0.31(2)	0.28(1)	0.68(3)	0.81(3)
308.15	0.29(1)	0.26(1)	0.64(3)	0.73(3)
312.15	0.27(1)	0.25(1)	0.59(4)	0.68(4)

Table S2: Computed shear viscosities (η) of water for different NaCl concentrations using the Joung and Cheatham[5] and the Madrid-2019[6] force fields at $T = 298.15$ K and $P = 1$ bar. For water the TIP4P/2005[4] force field is used. The numbers in the parentheses indicate the uncertainty (one standard deviation) in the last digit.

M / [mol L^{-1}]	$\eta_{\text{Joung and Cheatham}}$ / [mPa s]	$\eta_{\text{Madrid}-2019}$ / [mPa s]
0.0	0.90(4)	0.90(4)
0.2	0.95(5)	0.95(3)
0.4	0.94(7)	0.95(6)
0.6	0.98(7)	0.98(3)
0.8	1.10(7)	1.02(1)
1.0	1.16(7)	1.06(3)

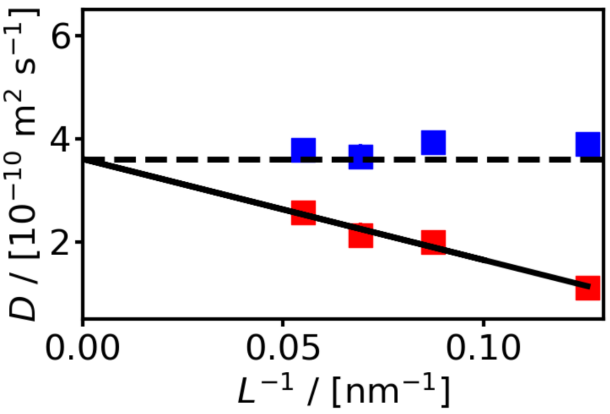

Figure S1: The computed self-diffusion coefficients of α-CD as a function of the inverse of the simulation box length at $T = 298.15$ K and $P = 1$ bar. The symbols in red and blue colors indicate the calculated self-diffusion coefficients without and with using the YH correction[7], respectively. The self diffusion coefficients are calculated using the TIP4P2005[4] water force field. The error bars are smaller than the symbol size.

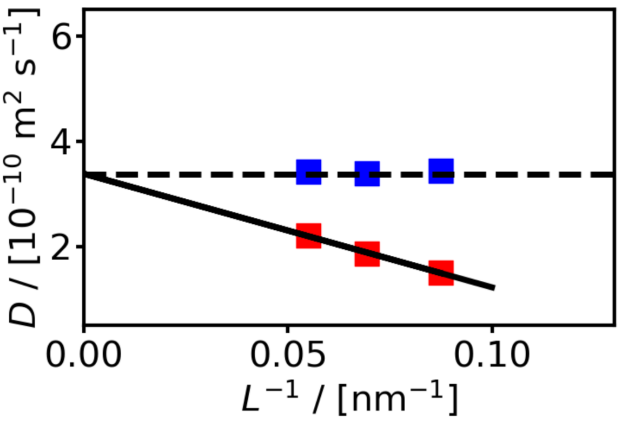

Figure S2: The computed self-diffusion coefficients of γ-CD as a function of the inverse of the simulation box length at $T = 298.15$ K and $P = 1$ bar. The symbols in red and blue colors indicate the calculated self-diffusion coefficients without and with using the YH correction[7], respectively. The self diffusion coefficients are calculated using the TIP4P2005[4] water force field. The error bars are smaller than the symbol size.

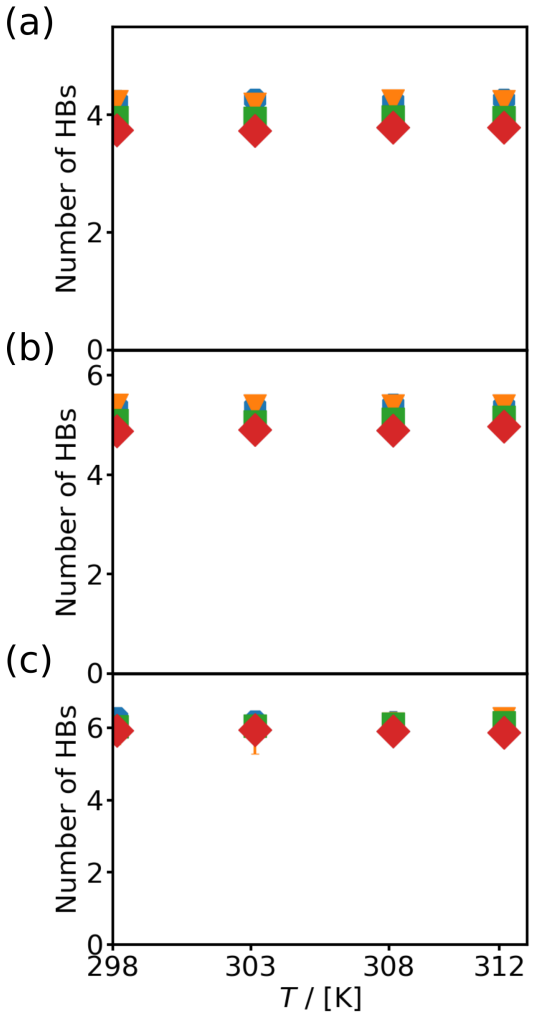

Figure S3: The average number of intramolecular hydrogen bonds in the (a) α-, (b) β-, and (c) γ-CDs in water as a function of temperature at $P = 1$ bar. The symbols in blue, orange, green, and red colors indicate the average number of hydrogen bonds using the TIP3P[1], Bind3P[2], SPCE[3], and TIP4P2005[4] force fields, respectively. The error bars are smaller than the symbol size.

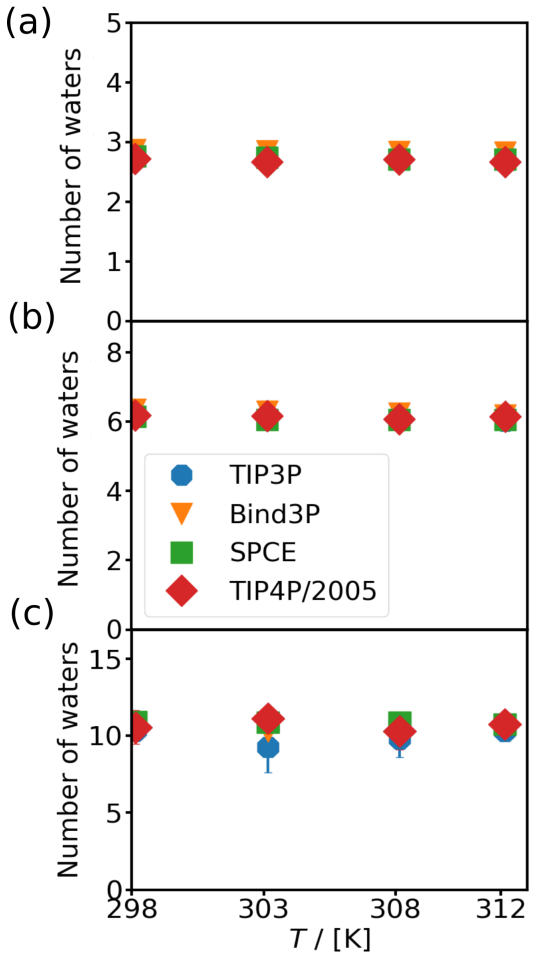

Figure S4: The average number of water molecules inside the cavity of the (a) α-, (b) β-, and (c) γ-CDs as a function of temperature at $P = 1$ bar. A water molecule is considered to be inside the cavity of the α-, β-, and γ-CD, if the distance between the center of mass of the cyclodextrin and the oxygen of the water molecule is smaller than 0.34, 0.4 and 0.46 nm, respectively. The symbols in blue, orange, green, and red colors indicate the average number of water molecules using the TIP3P[1], Bind3P[2], SPCE[3], and TIP4P2005[4] force fields, respectively. The error bars are smaller than the symbol size.

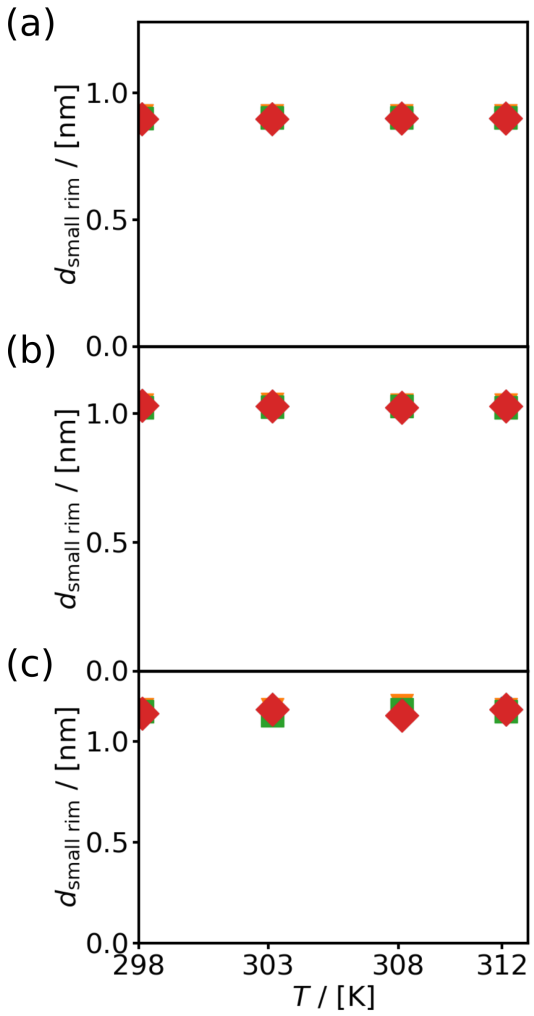

Figure S5: The diameter of the large rim of (a) α-, (b) β-, and (c) γ-CDs as a function of temperature at $P = 1$ bar. The large diameter is defined as the distance between the geometrically opposite C6 atoms of CDs. The symbols in blue, orange, green, and red colors indicate the average diameter using the TIP3P[1], Bind3P[2], SPCE[3], and TIP4P2005[4] force fields, respectively. The error bars are smaller than the symbol size.

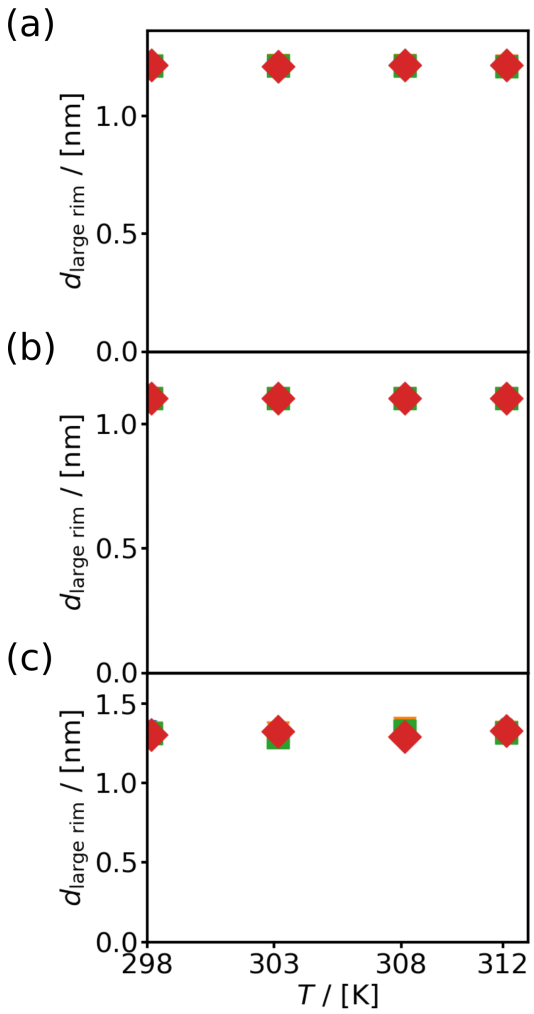

Figure S6: The diameter of the small rim of (a) α-, (b) β-, and (c) γ-CDs as a function of temperature at $P = 1$ bar. The small diameter is defined as the distance between the geometrically opposite C2 atoms of CDs. The symbols in blue, orange, green, and red colors indicate the average diameter using the TIP3P[1], Bind3P[2], SPCE[3], and TIP4P2005[4] force fields, respectively. The error bars are smaller than the symbol size.

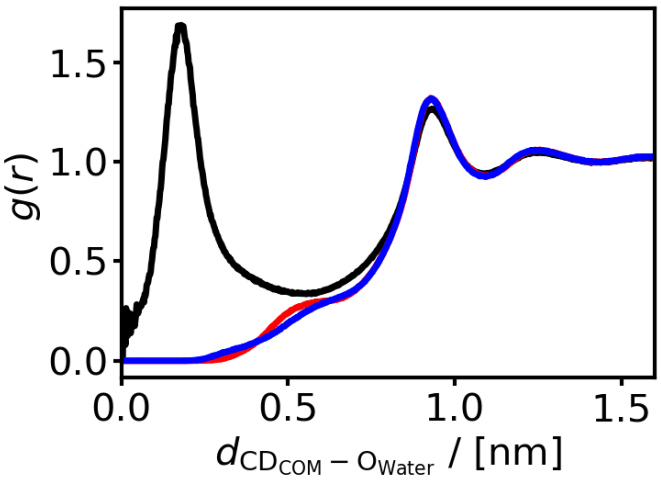

Figure S7: Radial distribution functions for the distance between the center of mass of the β-CD and the oxygen atom of the water molecules at $T = 298.15$ K and $P = 1$ bar. The black, red and blue colors indicate the systems with a free β-CD, with an ibuprofen:β-CD inclusion complex in orientation 1, and with an ibuprofen:β-CD inclusion complex in orientation 2, respectively. For water the TIP4P/2005[4] water force field is used.

References

[1] W. L. Jorgensen, J. Chandrasekhar, J. D. Madura, R. W. Impey, M. L. Klein, Comparison of simple potential functions for simulating liquid water, The Journal of Chemical Physics 79 (1983) 926–935.

[2] J. Yin, N. M. Henriksen, H. S. Muddana, M. K. Gilson, Bind3p: Optimization of a water model based on host–guest binding data, Journal of Chemical Theory and Computation 14 (2018) 3621–3632.

[3] H. J. C. Berendsen, J. R. Grigera, T. P. Straatsma, The missing term in effective pair potentials, The Journal of Physical Chemistry 91 (1987) 6269–6271.

[4] J. L. F. Abascal, C. Vega, A general purpose model for the condensed phases of water: Tip4p/2005, The Journal of Chemical Physics 123 (2005) 234505.

[5] I. S. Joung, T. E. Cheatham, Determination of alkali and halide monovalent ion parameters for use in explicitly solvated biomolecular simulations, The Journal of Physical Chemistry B 112 (2008) 9020–9041.

[6] I. M. Zeron, J. L. F. Abascal, C. Vega, A force field of li+, na+, k+, mg2+, ca2+, cl-, and so42 in aqueous solution based on the tip4p/2005 water model and scaled charges for the ions, The Journal of Chemical Physics 151 (2019) 134504.

[7] I.-C. Yeh, G. Hummer, System-size dependence of diffusion coefficients and viscosities from molecular dynamics simulations with periodic boundary conditions, Journal of Physical Chemistry B 108 (2004).