Thermophoresis of cyclodextrins with/without aspirin in water

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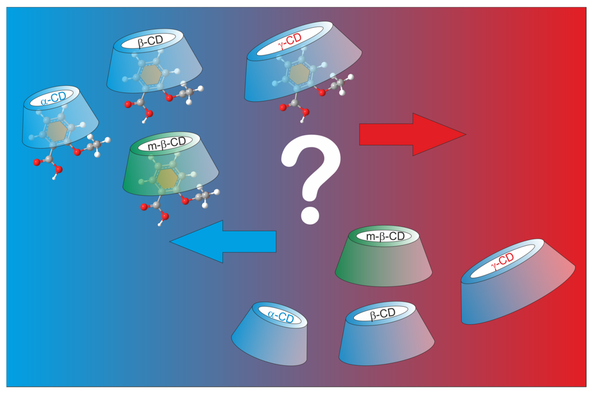
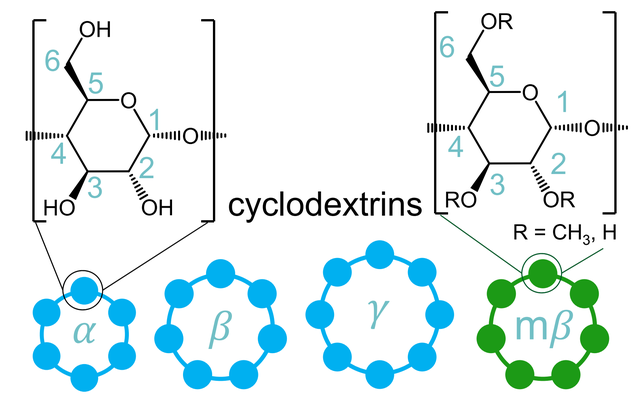
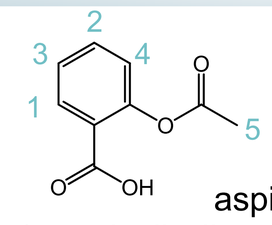
Motivation [1]

- Controlled movement of drugs into certain, e.g. inflamed, areas
- Check complex formation: α-, β-, γ- and methyl-β-cyclodextrin with aspirin by NMR
- investigation of thermophoretic behavior



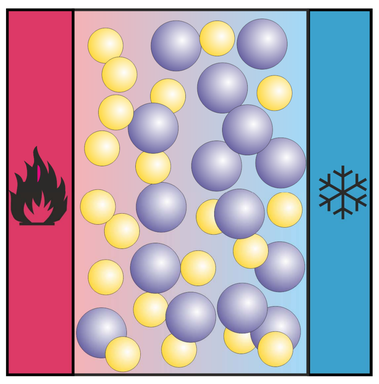
System





concentration: 1wt% CD
molar 1:1-ratio: CD:aspirin

Thermophoresis [2]



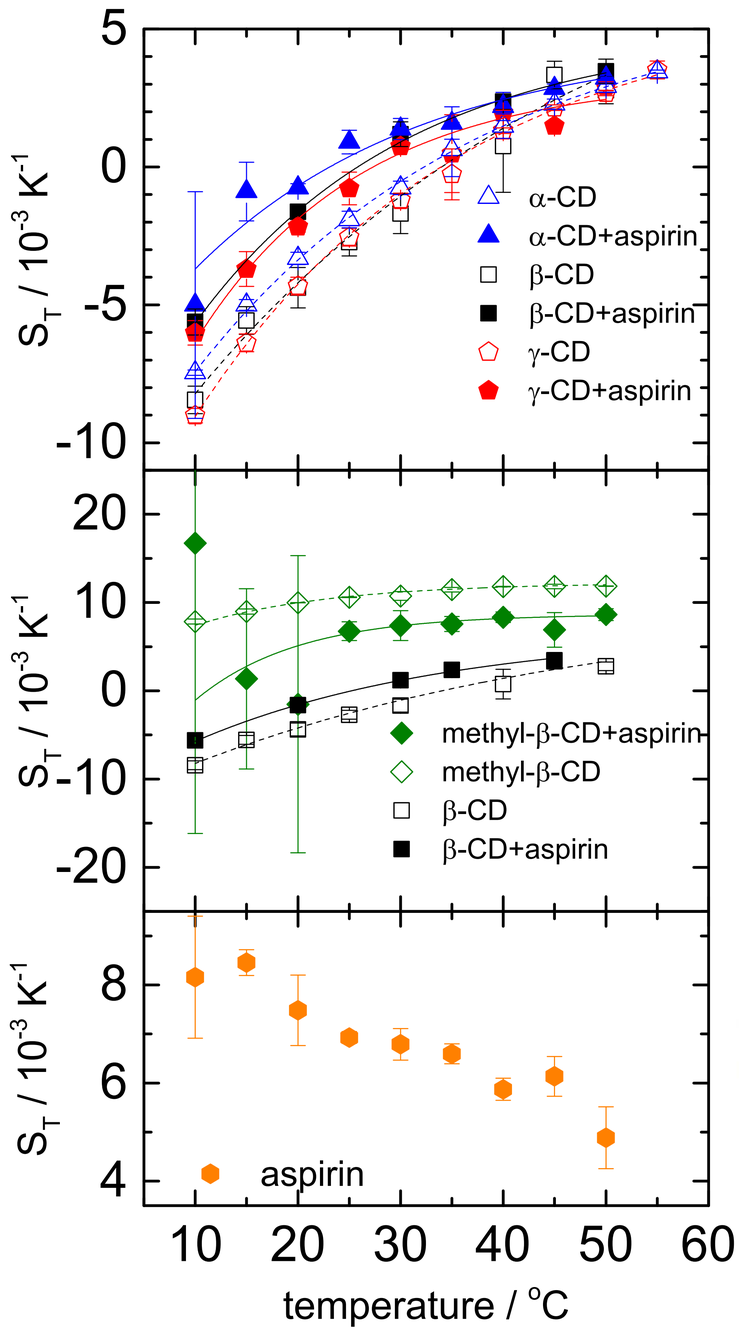
Flux $\vec{j}$ along a temperature gradient:
(1) thermal diffusion D_T along a temperature gradient ∇T
(2) Fickian diffusion D along the induced concentration gradient ∇c.

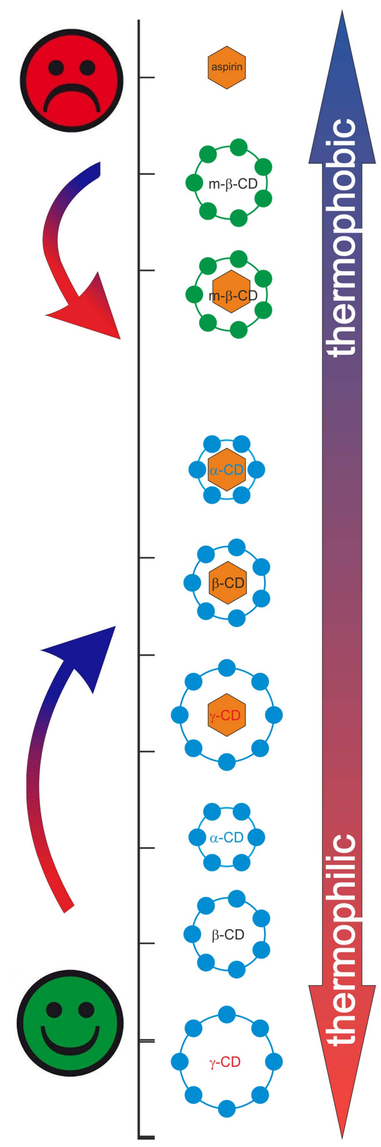
$$\vec{j} = -D\vec{\nabla}c - c(1-c)D_T\vec{\nabla}T$$

In the steady state (j=0) the Soret coefficient S_T is defined

$$S_T \equiv \frac{D_T}{D} = -\frac{1}{c(1-c)}\frac{\Delta c}{\Delta T}$$

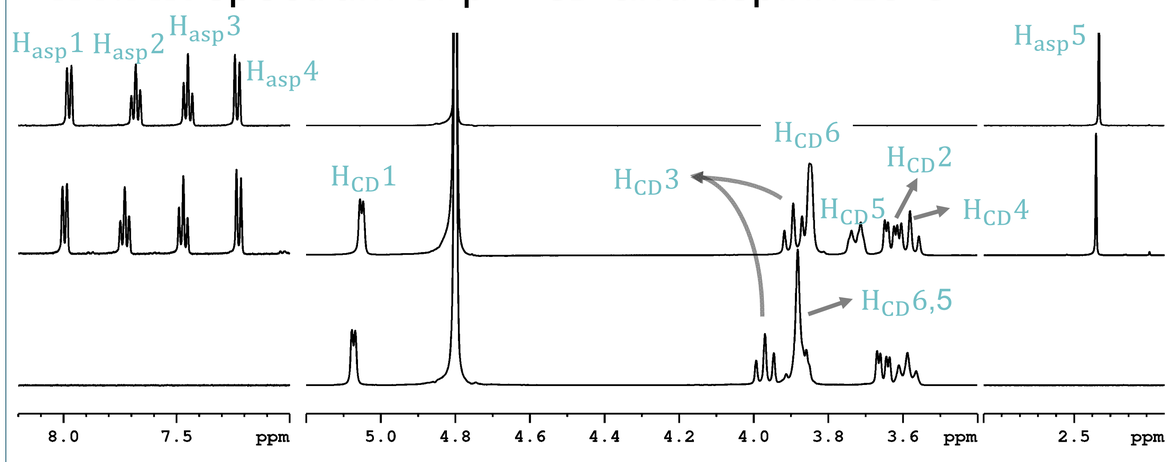
TDFRS results [3]



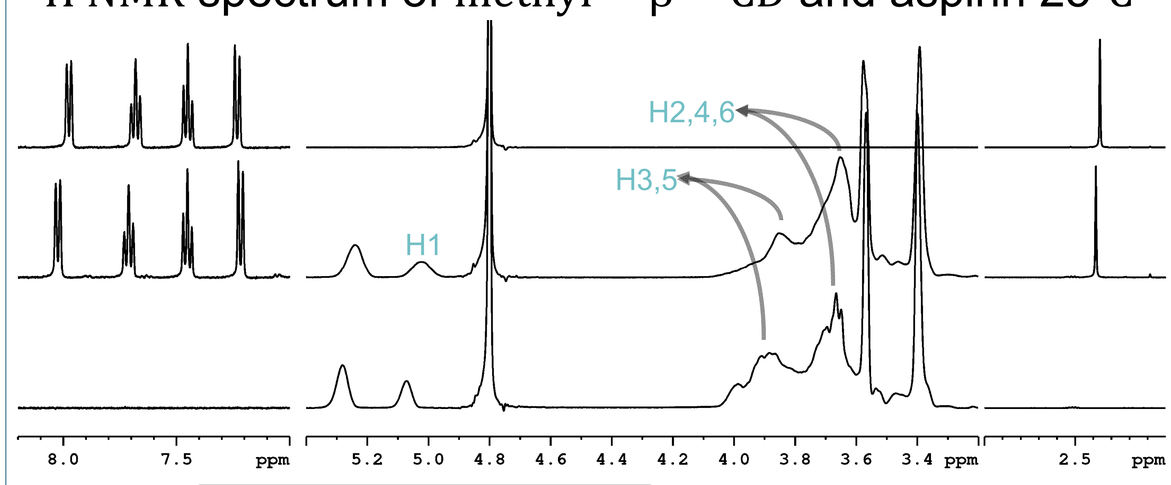


NMR measurements [4], [6]

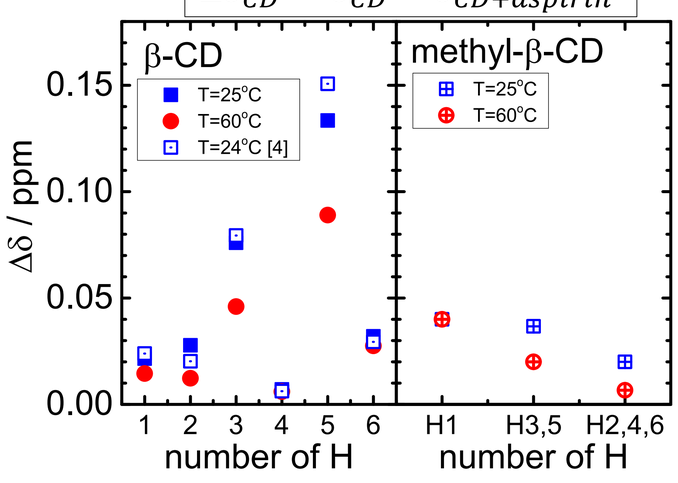
^{1}H NMR spectrum of β − CD and aspirin 25°C

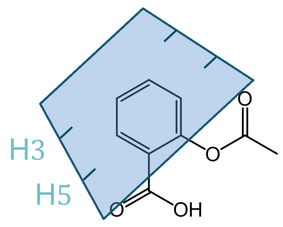


^{1}H NMR spectrum of methyl − β − CD and aspirin 25°C



$$\Delta\delta_{CD} = \delta_{CD} - \delta_{CD+aspirin}$$





Magnetic field of inwards pointing protons (H3 and H5) is influenced by aspirin(guest molecule).

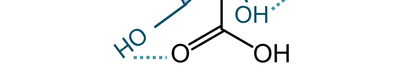
β − CD
- large $\Delta\delta$ value is observed for H3 and H5 compared to the other protons.
- $\Delta\delta$ value of H3 and H5 is decreased by heating.

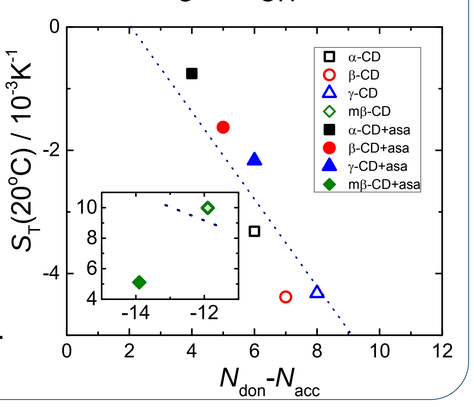
methyl − β − CD
- small $\Delta\delta$ value observed for H3,5 compared to β − CDs H3 and H5.
- $\Delta\delta$ value of H3,5 is decreased by heating.

Inclusion complex is confirmed for both CDs.

Conclusion

- complexes formation are confirmed between CD and aspirin from NMR measurement
- At the high temperature the complex capability weakens
- behaviour of pure CDs and un-methylated CD-complexes fits donor-acceptor model[5]
- fewer HB sites result in a higher S_T/stronger thermophobicity
- drug-complex of methyl-β-CD behaves different
- possible explanations are polarisation or charge effects
- more information about structure of methyl-β-CD-complex is needed





References

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