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*Supplementary*

# Inclusion Complexes of Naringenin in Dimethylated and Permethylated *β*-Cyclodextrins: Crystal Structures and Molecular Dynamics Studies

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**Table S1**

**a. Naringenin/Dimethylated *β*-Cyclodextrin (DM-β-CD) inclusion complex.**

**a1.** Guest-host and guest-bridge water molecules interactions.

| | Type | Distance | Angle (°) |
|---|---|---|---|
| C7–O-H…Ow1 | H-bond | 1.74378 (8) | 171.0956 (3) |
| C6–H…Ow1 | CH…O | 2.66162 (16) | 125.2787 (17) |
| O…H86–C86 | CH…O | 2.66570 (13) | 105.489 (5) |
| C4-O…H62–C62 | CH…O | 2.49696 (12) | 138.8320 (11) |
| C3–H1…O63 | CH…O | 2.33195 (12) | 145.461 (2) |
| C3–H2…O61 | CH…O | 2.698967 (13) | 140.9782 (8) |
| C4′–O…H64–C64 (−½+x, ½−y, 1−z) | CH…O | 2.46524 (11) | 123.774 (3) |
| C4′–O…H63–C63A (−½+x, ½−y, 1−z) | CH…O | 2.66814 (13) | 130.385 (2) |
| C4′–O…H83–C83B (−½+x, ½−y, 1−z) | CH…O | 2.48603 (13) | 143.015 (2) |
| C4′–OH…O54 (−½+x, ½−y, 1−z) | H-bond | 2.07009 (13) | 144.218 (3) |
| C46–H46…O7 | CH…O | 2.349 (5) | 117.2 (3) |
| C75–H75…O5 | CH…O | 2.788(4) | 167.0 (4) |

**a2.** CH/π interactions between guest and host.

| Naringenin | DM-*β*-CD | Region* | $D_{pln}$* (Å) | $D_{lin}$* (Å) | $D_{atm}$* (Å)/ ϕ (°) | θ* (°) | ω* (°) | Interaction Type |
|---|---|---|---|---|---|---|---|---|
| Ring B | C55−H55 | 3 | | | 2.609/ 45.06 | 10.28 | | CH/π |
| Ring A | C81−H81 | 1 | 2.899 | | | 53.29 | | CH/π |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Ring A | C74−H74C (½+x, ½−y, 1−z) | 1 | 3.009 | | | 40.67 | | CH/π |
| Ring A | C71−H71 (1+x, y, z) | 2 | | 2.912 | | 47.06 | 116.88 | CH/π |
| Ring A | C82−H82 (1−x, ½+y, ½−z) | 2 | | 2.893 | | 33.71 | 104.77 | CH/π |

* Classification according to Takahashi et al. [1] method of surveying CH/π contacts.

$D_{pln}$: H/π distance; $D_{lin}$: distance between H and line $C^1C^2$ ($C^1$ and $C^2$ nearest and the second nearest $sp^2$-carbon); $D_{atm}$: interatomic distance (H/$C^1$); θ: angle $HXC^1$ where X is the atom linked to H; ϕ: the $HC^1I$ angle (I is the trace of the H projection on the π-plane); ω: dihedral angle defined by the plane of the ring and $HC^1C^2$ plane. By setting a cut-off value $D_{max}$ = 3.05 Å, the regions are defined as: $D_{pln} < D_{max}$, θ < 60° for region 1; $D_{lin} < D_{max}$, θ < 60°, 90° < |ω| < 130 for region 2; $D_{atm} < D_{max}$, θ < 60°, 45° < ϕ < 90° for region 3.

1. Takahashi, H., Tsuboyama, S., Umezawa, Y., Honda, K., Nishio, M.: CH/π Interactions as Demonstrated in the Crystal Structure of Host/Guest Compounds. A Database Study. Tetrahedron. 56, 6185–6191 (2000). doi:10.1016/S0040-4020(00)00575-5

**a3.** Hydrogen bonds between water molecules bridging adjacent complex units (no hydrogens have been attributed in water molecules, hence no angle is given in the cases of H-bonds that the water molecule is clearly the proton donor).

| | **Distance (Å)** |
|---|---|
| OW1…OW2 | 2.76811 (17) |
| OW1…O52 (1−x, ½+y, ½−z) | 3.01905 (17) |
| OW1…O62 (1−x, ½+y, ½−z) | 2.88215 (16) |
| OW2…O37 (½+x, 1.5−y, 1−z) | 2.91716 (14) |
| OW3…OW2 | 2.70068 (16) |
| OW3…O56 | 3.02610 (18) |
| OW3…OW34 | 2.84225 (18) |
| OW3…OW2 | 2.82765 (14) |
| OW33…O66 | 2.72322 (15) |
| OW33…OW7 | 2.71541 (14) |
| OW33…OW24 | 2.71787 (16) |
| OW4…OW3 | 2.79664 (16) |
| OW4…O67 (½+x, 1.5−y, 1−z) | 2.92247 (15) |
| OW4…O33 (½ +x, ½−y, 1−z) | 2.94800 (15) |
| OW24…O33 (½ +x, ½−y, 1−z) | 2.74066 (13) |
| OW34…O33 (½+x, ½−y, 1−z) | 2.88038 (13) |
| OW34…O67(½+x, 1.5−y, 1−z) | 2.68795 (15) |
| OW36…O51 (−x, −½+y, ½−z) | 2.7951 (2) |
| OW7…OW36 (½ +x, ½−y, 1−z) | 2.81627 (17) |

**b. Naringenin/ Permethylated *β*-Cyclodextrin (TM-β-CD) inclusion complex.**

**b1.** Guest-host interactions.

| | **Type** | **Distance** | **Angle (°)** |
|---|---|---|---|
| **Naringenin Site A** | | | |
| Ring A | | | |
| O7–H7…O34 (−x, ½+y, 1−z) | H - bond | 1.9069 (3) | 156.354 (3) |

| | | | |
|---|---|---|---|
| O5…H54–C54 | CH …O | 2.4901 (3) | 152.4 (2) |
| C8–H8…O24 (−x, ½+y, 1−z) | CH …O | 2.615 (3) | 128.21 (7) |
| C8–H8…O34 (−x, ½+y, 1−z) | CH …O | 2.672 (3) | 127.99 (6) |
| Ring B | | | |
| O4'–H4'…O36 (−x, ½+y, 2−z) | H - bond | 1.8879 (2) | 163.956 (4) |
| O4'…H95F–C95B (x, 1+y, z) | CH …O | 1.890 (19) | 123.9 (11) |
| O4'…H77B–C77 (−x, ½+y, 2−z) | CH …O | 2.6379 (5) | 120.9 (4) |
| O4'…H91–C91 (−1+x, y, z) | CH …O | 2.6658 (3) | 143.0 (2) |
| Ring C | | | |
| O4…H96B–C96 | CH …O | 2.4159 (3) | 176.5 (3) |
| O4…H56–C56 | CH …O | 2.5104 (3) | 161.5 (2) |
| O4…H57–C57 | CH …O | 2.5351 (5) | 159.4 (2) |
| | | | |
| **Naringenin Site B** | | | |
| Ring A | | | |
| O7–H7…O34 (−x, ½+y, 1−z) | H - bond | 1.846 (3) | 177.20 (8) |
| O5–H5…O67 | H - bond | 2.518 (3) | 123.48 (6) |
| O5…H97–C97 | CH …O | 2.6414 (5) | 124.0 (2) |
| C8–H8…O24 (−x, ½+y, 1−z) | CH …O | 2.589 (3) | 132.02 (7) |
| Ring B | | | |
| O4'–H4'…O36 (−x, ½+y, 2−z) | H - bond | 1.892 (3) | 161.73 (9) |
| C2'–H2'…O21 | CH …O | 2.528 (3) | 143.26 (6) |
| C3'–H3'…O66 (x, 1+y, z) | CH …O | 2.644 (3) | 163.65 (6) |
| Ring C | | | |
| O1…H74C–C74 (−x, ½+y, 1−z) | CH …O | 2.5986 (6) | 113.1 (2) |
| O4…H96–C96 | CH …O | 2.4365 (3) | 176.3 (3) |
| O4…H56–C56 | CH …O | 2.6476 (3) | 156.2 (2) |
| O4…H57–C57 | CH …O | 2.3331 (5) | 157.09 (19) |

**b2.** CH/π guest-host interactions.

| Naringenin Site A | TM-β-CD | Region* | $D_{pln}$* (Å) | $D_{lin}$* (Å) | $D_{atm}$* (Å)/ ϕ (°) | θ* (°) | ω* (°) | Interaction Type |
|---|---|---|---|---|---|---|---|---|
| Ring A | C74−H74C (−x, ½+y, 1−z) | 2 | | 2.749 | | 45.07 | 119.13 | CH/π |
| Ring A | C81−H81C | 1 | 2.773 | | | 31.64 | | CH/π |
| Ring B | C91−H91 (1−x, y, z) | 2 | | 2.84 | | 25.09 | 121.55 | CH/π |
| Ring B | C95−H95C | 2 | | 2.844 | | 46.42 | 106.74 | CH/π |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | (x, 1+y, z) | | | | | | |
| Ring B | C95B–H95F (x, 1+y, z) | 2 | 2.166 | | 36.27 | 118.29 | CH/π |
| **Naringenin Site B** | **TM-*β*-CD** | | | | | | |
| Ring A | C74–H74C (−x, ½+y, 1−z) | 2 | 2.808 | | 36.81 | 127.1 | CH/π |
| Ring A | C81–H81C | 1 | 2.719 | | 30.58 | | CH/π |
| Ring B | C95–H95C (x, 1+y, z) | 2 | 2.568 | | 31.49 | 111.18 | CH/π |
| Ring B | C94B–H94E (x, 1+y, z) | 3 | | 3.05 / 55.92 | 59.86 | | CH/π |

* Classification according to Takahashi et al. [1] method of surveying CH/π contacts.

$D_{pln}$: H/π distance; $D_{lin}$: distance between H and line $C^1C^2$ ($C^1$ and $C^2$ nearest and the second nearest $sp^2$-carbon); $D_{atm}$: interatomic distance (H/$C^1$); θ: angle HX$C^1$ where X is the atom linked to H; ϕ: the H$C^1$I angle (I is the trace of the H projection on the π-plane); ω: dihedral angle defined by the plane of the ring and H$C^1C^2$ plane. By setting a cut-off value $D_{max}$ = 3.05 Å, the regions are defined as: $D_{pln} < D_{max}$, θ < 60° for region 1; $D_{lin} < D_{max}$, θ < 60°, 90° < |ω| < 130 for region 2; $D_{atm} < D_{max}$, θ < 60°, 45° < ϕ < 90° for region 3.

1. Takahashi, H., Tsuboyama, S., Umezawa, Y., Honda, K., Nishio, M.: CH/π Interactions as Demonstrated in the Crystal Structure of Host/Guest Compounds. A Database Study. Tetrahedron. 56, 6185–6191 (2000). doi:10.1016/S0040-4020(00)00575-5

**Table S2.**

**a1.** Conformational characteristics of the host molecules of the Naringenin/DM-β-CD complex.

| | $D_k$ (Å) | $D$ (Å) | $d$ (Å) | $\Phi_n$ (°) | $\tau$ (°) | $t$ (°) | $C$ |
|---|---|---|---|---|---|---|---|
| Host | | | | | | | |
| $n$ = 1 | 4.990 (3) | 4.388 (2) | 0.030(3) | 131.285(4) | 15.7773(14) | 71.9(5) | gt |
| $n$ = 2 | 5.357 (3) | 4.369 (3) | 0.028(3) | 121.324(1) | 24.7479(9) | −70.7(6) | gg |
| $n$ = 3 | 4.984 (3) | 4.510 (3) | −0.009(3) | 132.090(4) | 4.2901(2) | [a]84.5(6)<br>[b]128.1(12) | gt<br>gt |
| $n$ = 4 | 4.947 (3) | 4.356 (3) | −0.081(3) | 130.432(2) | 7.931(3) | −65.1(6) | gg |
| $n$ = 5 | 5.164 (3) | 4.433 (2) | 0.112(3) | 126.885(3) | 19.1071(12) | 71.7(6) | gt |
| $n$ = 6 | 5.200 (3) | 4.291 (3) | −0.035(2) | 125.894(3) | 13.0971(10) | 62.0(6) | gt |
| $n$ = 7 | 4.923 (2) | 4.542(2) | −0.043(2) | 131.785(2) | 2.6755(2) | −60.9(6) | gg |

**a2.** Conformational characteristics of the host molecules of the Naringenin/TM-β-CD complex.

| | $D_k$ (Å) | $D$ (Å) | $d$ (Å) | $\Phi_n$ (°) | $\tau$ (°) | $t$ (°) | $C$ |
|---|---|---|---|---|---|---|---|
| Host | | | | | | | |
| $n$ = 1 | 4.996 (8) | 4.281 (5) | 0.460 (6) | 123.898(9) | −16.02(15) | −68.8(3) | gg |
| $n$ = 2 | 5.310 (8) | 4.357 (8) | −0.409 (5) | 121.545(10) | 24.95(14) | −79.6(3) | gg |
| $n$ = 3 | 4.936 (7) | 4.486 (8) | −0.392 (5) | 125.92(1) | 38.29(16) | 66.1(4) | gt |
| $n$ = 4 | 4.549 (9) | 4.356 (7) | 0.625 (8) | 134.902(11) | 32.30(16) | [a] −70.2(5)<br>[b] 9.7(12) | gg<br>tg |
| $n$ = 5 | 5.176 (9) | 4.185 (8) | 0.157 (3) | 122.578(12) | −17.28(16) | [a] −79.5(4)<br>[b] −64.0(5) | gg<br>gg |
| $n$ = 6 | 5.204 (8) | 4.325 (6) | −0.805 (10) | 115.895(11) | 38.65(15) | 72.4(3) | gt |
| $n$ = 7 | 4.398 (6) | 4.452 (6) | 0.364 (5) | 140.256(6) | 47.61(15) | 134.9(3) | gt |

***D*k:** K…$O_{4n}$ distances of the approximate centre K of the $O_{4n}$ heptagon from the $O_{4n}$ atoms

***D*:** $O_{4n}$…$O_{4n+1}$ distances

***d*:** deviations of the $O_{4n}$ atoms from their least squares plane

***Φ*n:** $O_{4n-1}$…$O_{4n}$…$O_{4n+1}$ angles

***τ*:** tilt angles between the optimum $O_{4n}$ plane and the mean plane of the $O_{4n-1}$....$C_{1n}$...$C_{4n}$...$O_{4n}$ atoms

***t*:** $O_{5n}$…$C_{5n}$…$C_{6n}$…$O_{6n}$ torsion angles
***C*:** conformation of the primary hydroxyls
*a, b denote the different occupied sites of the disordered hydroxyl group

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