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A computational study on the Aluminum interaction with D-glucose 6-phosphate in various stoichiometries

Elena Formoso*,† and Xabier Lopez†,‡

Donostia International Physics Center (DIPC), Manuel Lardizabal Iribidea 4, 20018 Donostia, Spain

E-mail: elena.formoso@ehu.eus

*To whom correspondence should be addressed
†Donostia International Physics Center (DIPC), Manuel Lardizabal Iribidea 4, 20018 Donostia, Spain
‡Kimika Fakultatea, Euskal Herriko Unibertsitatea (UPV/EHU), P.K. 1072, 20080 Donostia, Spain

Table S1: Complexation free energy affinities in kcal/mol for representative 1:1 aluminum G6P complexes with different functionals: B3LYP-D3BJ, PBE0-D3BJ, TPSS-D3BJ, B97D3 and M06-2X. The difference in complexation free energies respect to the most stable complex is also shown. Similar trends are found among the different functionals.

	$[Al(G6P)^{c}_{C4}(H_2O)_5]^1$		$[Al(G6P)^{a}_{bC4}(H_2O)_4]^1$		$[Al(G6P)_a(H_2O)_5]^1$		$[Al(G6P)_{ac}(H_2O)_4]^1$		$[Al(G6P)_{bC4}(H_2O)_4]$	
Functional	ΔG^{compl}_{aq}	$\Delta\Delta G^{compl}_{aq}$	ΔG^{compl}_{aq}	$\Delta\Delta G^{compl}_{aq}$	ΔG^{compl}_{aq}	$\Delta\Delta G^{compl}_{aq}$	ΔG^{compl}_{aq}	$\Delta\Delta G^{compl}_{aq}$	ΔG^{compl}_{aq}	$\Delta\Delta G^{compl}_{aq}$
B3LYP-D3BJ	-79.72	37.52	-88.96	28.27	-82.62	34.62	-67.55	49.69	-117.23	0.0
PBE0-D3BJ	-79.44	38.00	-88.71	28.73	-82.27	35.16	-68.30	49.13	-117.44	0.0
TPSS-D3BJ	-79.72	37.60	-88.88	28.44	-82.83	34.50	-69.98	47.35	-117.33	0.0
B97D3	-78.05	37.29	-86.77	28.57	-80.99	34.36	-69.09	46.25	-115.34	0.0
M06-2X	-76.95	39.33	-87.23	29.05	-79.68	36.60	-65.23	51.05	-116.28	0.0

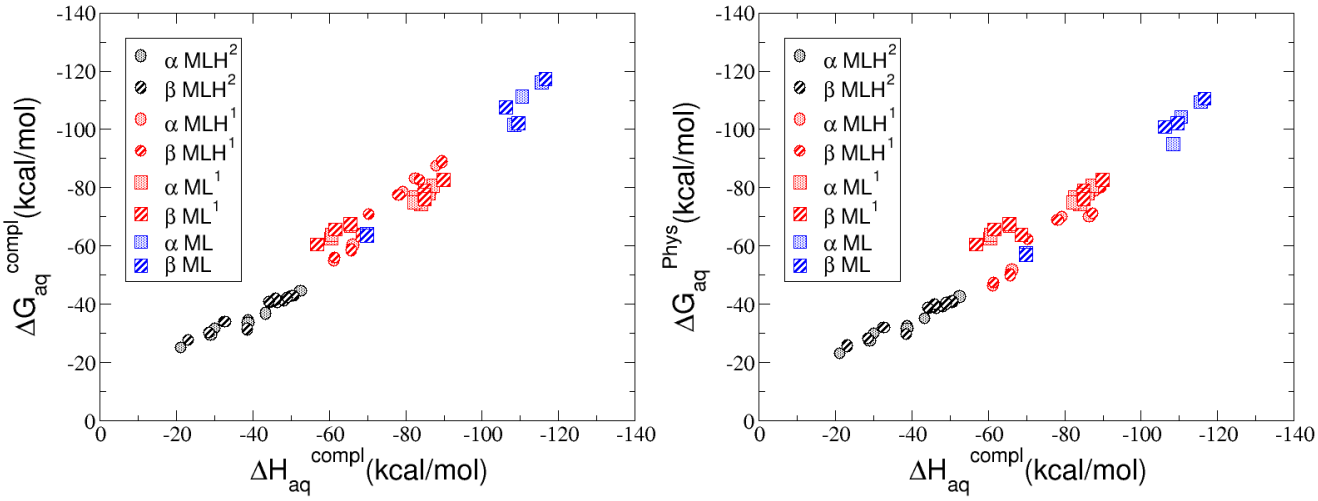
Mononuclear metal 1:1, 1:2 and 1:3 Complexes

1 : 1 Al-G6P complexes

Table S2: Enthalpy and free energy affinities in kcal/mol for 1:1 aluminum G6P complex formation with corrections that account for the physiological pH and de/protonation of the corresponding titratable groups. The subscripts indicate the coordination mode of G6P to Al(III) and the superscripts refer to the protonation state of the phosphate group: a or b, the Al(III) or the proton is bound to that oxygen; ab, the Al(III) is binding a and b oxygens, or a and b have one proton each, $C1$ or $C4$, Al(III) is coordinated by the OH group of that carbon. The † sign indicates a spontaneous proton transfer from a water molecule to the phosphate group during the optimization.

1:1 Al-G6P complex	$\alpha-$anomer			$\beta-$anomer		
	ΔH_{aq}^{compl}	ΔG_{aq}^{compl}	ΔG_{aq}^{Phys}	ΔH_{aq}^{compl}	ΔG_{aq}^{compl}	ΔG_{aq}^{Phys}
$[Al(G6P)_{a}^{b}(H_2O)_5]^2$	-50.12	-42.73	-40.83	-50.47	-42.87	-40.97
$[Al(G6P)_{a}^{c}(H_2O)_5]^2$	-43.42	-36.94	-35.05	-46.40	-40.46	-38.56
$[Al(G6P)_{b}^{a}(H_2O)_5]^2$	-38.85	-34.42	-32.52	-48.17	-41.06	-39.16
$[Al(G6P)_{b}^{c}(H_2O)_5]^2$	-52.40	-44.57	-42.67	-49.06	-42.26	-40.37
$[Al(G6P)_{b}^{c}(H_2O)_5]^2$				-46.00	-41.82	-39.93
$[Al(G6P)_{c}^{a}(H_2O)_5]^2$	-44.40	-40.46	-38.56	-44.27	-40.71	-38.81
$[Al(G6P)_{c}^{b}(H_2O)_5]^2$	-38.67	-33.57	-31.67	-38.59	-31.52	-29.62
$[Al(G6P)_{ab}^{c}(H_2O)_4]^2$	-21.13	-25.06	-23.16	-23.12	-27.69	-25.79
$[Al(G6P)_{ac}^{b}(H_2O)_4]^2$	-30.09	-31.75	-29.85	-32.61	-33.92	-32.02
$[Al(G6P)_{bc}^{a}(H_2O)_4]^2$	-28.90	-29.32	-27.42	-28.60	-30.17	-28.27
$[Al(G6P)_{C1}^{a}(H_2O)_5]^1$	-66.16	-60.37	-51.82	-65.80	-58.65	-50.10
$[Al(G6P)_{C1}^{a}(H_2O)_5]^1$	-61.31	-54.76	-46.21	-61.39	-56.03	-47.47
$[Al(G6P)_{C4}^{c}(H_2O)_5]^1$	-86.39	-78.45	-69.90	-87.45	-79.72	-71.16
$[Al(G6P)_{aC1}^{c}(H_2O)_4]^1$	-79.28	-78.45	-69.89	-70.42	-70.89	-62.34
$[Al(G6P)_{cC1}^{b}(H_2O)_4]^1$				-83.72	-82.51	-73.96
$[Al(G6P)_{cC1}^{a}(H_2O)_4]^1$				-78.10	-77.43	-68.87
$[Al(G6P)_{bC4}^{a}(H_2O)_4]^1$	-88.00	-87.45	-78.90	-89.56	-88.96	-80.41
$[Al(G6P)_{bC4}^{c}(H_2O)_4]^1$	-82.46	-83.04	-74.49	-83.28	-83.13	-74.57
$[Al(G6P)_{a}(H_2O)_5]^1$	-86.05(†)	-77.96(†)	-77.96(†)	-68.62	-63.82	-63.82
$[Al(G6P)_{a}(H_2O)_5]^1$ (†)	-82.55	-76.67	-76.67	-84.99	-79.14	-79.14
$[Al(G6P)_{a}(H_2O)_5]^1$ (†)				-89.91	-82.62	-82.62
$[Al(G6P)_{b}(H_2O)_5]^1$ (†)	-87.20	-80.68	-80.68	-84.84	-77.49	-77.49
$[Al(G6P)_{b}(H_2O)_5]^1$ (†)	-83.97	-74.33	-74.33			
$[Al(G6P)_{c}(H_2O)_5]^1$ (†)	-82.32	-75.02	-75.02	-84.98	-76.13	-76.13
$[Al(G6P)_{ab}(H_2O)_4]^1$	-60.45	-62.52	-62.52	-61.63	-65.64	-65.64
$[Al(G6P)_{ac}(H_2O)_4]^1$	-65.60	-66.94	-66.94	-65.53	-67.55	-67.55
$[Al(G6P)_{bc}(H_2O)_4]^1$	-60.56	-63.80	-63.80	-56.78	-60.56	-60.56
$[Al(G6P)_{C1}(H_2O)_5]$	-69.86	-64.21	-57.56	-69.80	-63.60	-56.94
$[Al(G6P)_{C4}(H_2O)_5]$(†)	-108.44	-101.65	-94.99	-109.45	-102.19	-102.19
$[Al(G6P)_{aC1}(H_2O)_4]$(†)	-110.46	-111.26	-104.24	-106.19	-107.53	-100.87
$[Al(G6P)_{bC4}(H_2O)_4]$(†)	-115.57	-116.11	-109.45	-116.55	-117.23	-110.57

Figure S1: Enthalpy and free energy affinities in kcal/mol for 1:1 aluminum-G6P complex formation (left) with corrections that account for the physiological pH and de/protonation of the corresponding titratable groups (right). The different colors account for the different total charges of the complexes: 2 (black), 1 (red) and 0 (blue). α anomers are represented by dot fill pattern, while β anomers are shown with line pattern. M stands for Al(III), L for G6P and H for the protonation state of the phosphate group.



1 : 2 Al-$(G6P)_2$ bis-complexes

Table S3: Enthalpy and free energy affinities in kcal/mol for 1:2 aluminum-G6P bis-complex formation with corrections that account for the physiological pH and de/protonation of the corresponding titratable groups. The subscripts indicate the coordination mode of G6P to Al(III) and the superscripts refer to the protonation state of the phosphate groups: *a* or *b*, the Al(III) or the proton is bound to that oxygen; *ab*, the Al(III) is binding *a* and *b* oxygens, or *a* and *b* have one proton each, *C*1 or *C*4, Al(III) is coordinated by the OH group of that carbon. The † sign indicates a spontaneous proton transfer from a water molecule to a phosphate group during the optimization.

1:2 Al-$(G6P)_2$ complexes	$\alpha-$anomer			$\beta-$anomer		
	ΔH_{aq}^{compl}	ΔG_{aq}^{compl}	ΔG_{aq}^{Phys}	ΔH_{aq}^{compl}	ΔG_{aq}^{compl}	ΔG_{aq}^{Phys}
$[Al(G6P)^{bb'}_{2,aa'}(H_2O)_4]^1$	-89.60	-73.81	-70.02	-92.73	-80.27	-76.48
$[Al(G6P)^{bc'}_{2,ab'}(H_2O)_4]^1$				-101.68	-85.61	-81.81
$[Al(G6P)^{ca'}_{2,aC4'}(H_2O)_4]$				-129.83	-111.85	-101.40
$[Al(G6P)^{ca'}_{2,aC4'}(H_2O)_4]$				-129.21	-112.54	-102.09
$[Al(G6P)^{cc'}_{2,aC4'}(H_2O)_4]$				-119.09	-102.93	-92.48
$[Al(G6P)^{b'}_{2,ca'}(H_2O)_4]$	-117.24	-100.56	-98.67	-122.70	-105.24	-103.34
$[Al(G6P)^{c'}_{2,cb'}(H_2O)_4]$				-121.78	-103.70	-101.8
$[Al(G6P)^{b'}_{2,aa'}(H_2O)_4]$	-115.09	-100.53	-98.63	-117.55	-103.54	-101.65
$[Al(G6P)^{b}_{2,aa'c'}(H_2O)_3]$	-96.82	-95.17	-93.28			
$[Al(G6P)^{c}_{2,ba'c'}(H_2O)_3]$	-94.93	-89.20	-87.30	-96.74	-91.19	-89.29
$[Al(G6P)^{a}_{2,ca'c'}(H_2O)_3]$				-105.16	-100.01	-98.11
$[Al(G6P)^{b'}_{2,aba'c'}(H_2O)_2]$				-83.76	-85.81	-83.92
$[Al(G6P)^{b'}_{2,aca'c'}(H_2O)_2]$				-91.40	-91.12	-89.22
$[Al(G6P)^{b'}_{2,aca'c'}(H_2O)_2]$				-86.90	-89.25	-87.35
$Al(G6P)^{a'}_{2,acb'c'}(H_2O)_2]$				-84.42	-87.48	-85.59
$[Al(G6P)^{ac'}_{2,C4C4'}(H_2O)_4]^{-1}$				-154.43	-137.45	-120.34
$[Al(G6P)^{ac'}_{2,C4C4'}(H_2O)_4]^{-1}$				-152.91	-134.24	-117.13
$[Al(G6P)^{aa'}_{2,bC4b'C4'}(H_2O)_2]^{-1}$				-138.19	-137.98	-120.87
$[Al(G6P)^{ac'}_{2,bC4b'C4'}(H_2O)_2]^{-1}$				-146.35	-146.06	-128.95
$[Al(G6P)^{ac'}_{2,bC4b'C4'}(H_2O)_2]^{-1}$				-129.88	-129.51	-112.40
$[Al(G6P)^{cc'}_{2,bC4b'C4'}(H_2O)_2]^{-1}$				-124.51	-126.64	-109.53
$[Al(G6P)^{a'}_{2,aC4'}(H_2O)_4]^{-1}$				-154.27	-136.77	-128.22
$[Al(G6P)_{2,aa'}(H_2O)_4]^{-1}$				-138.13	-127.14	-127.14
$[Al(G6P)_{2,ca'}(H_2O)_4]^{-1}$				-143.17	-129.04	-129.04
$[Al(G6P)_{2,acb'c'}(H_2O)_2]^{-1}$				-109.74	-115.81	-115.81
$[Al(G6P)_{2,aca'c'}(H_2O)_2]^{-1}$				-119.48	-120.00	-120.00
$[Al(G6P)_{2,abb'c'}(H_2O)_2]^{-1}$				-105.38	-107.06	-107.06
$[Al(G6P)^{a'}_{2,C4C4'}(H_2O)_4]^{-2}$				-168.14	-151.45	-142.90
$[Al(G6P)^{a'}_{2,C4C4'}(H_2O)_4]^{-2}$				-165.25	-148.67	-140.11
$[Al(G6P)^{b'}_{2,cC4c'C4'}(H_2O)_2]^{-2}$				-154.62	-154.08	-145.52
$[Al(G6P)_{2,aC1'}(H_2O)_4]^{-2}$				-139.90	-124.07	-117.41
$[Al(G6P)_{2,aC1'}(H_2O)_4]^{-2}(\dagger)$				-164.80	-152.03	-145.38
$[Al(G6P)_{2,aC4'}(H_2O)_4]^{-2}(\dagger)$				-169.46	-151.07	-144.41
$[Al(G6P)_{2,C4C4'}(H_2O)_4]^{-3}$				-176.34	-159.88	-146.56
$[Al(G6P)_{2,bC4c'C4'}(H_2O)_2]^{-3}$				-161.50	-163.08	-149.77

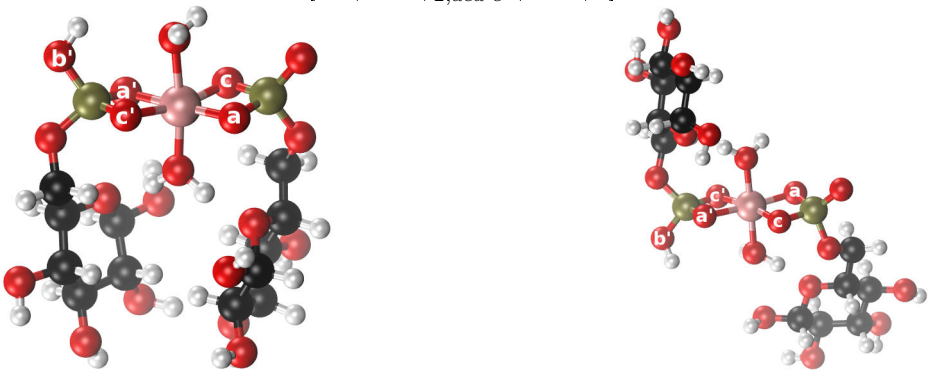
Figure S2: Monodentate binding of each G6P ligand in neutral bis-complexes. Aluminum atom is coordinated by an alcohol group of one G6P and the phosphate group of the second G6P. The coordination can be through adjacent (A) or opposite site atoms (B) of the octahedral coordination sphere of Al(III). The complexation free energies for the physiological pH and ΔH_{aq}^{compl} are shown in kcal/mol ($\Delta G_{aq}^{Phys}/\Delta H_{aq}^{compl}$).

$[\mathrm{Al(G6P)}^{ca'}_{2,aC4'}(\mathrm{H_2O})_4]$

A) -102.09/-129.21 B) -101.40/-129.83

Figure S3: Bidentate binding mode of phosphate groups in bis-complexes. The two non-coordinating atoms of the phosphates can be in different relative positions. A) The two non-coordinating atoms are in the same relative positions; B) The two non-coordinating atoms are in opposite relative position. The complexation free energies for the physiological pH (ΔG_{aq}^{Phys}) and ΔH_{aq}^{compl} are shown in kcal/mol ($\Delta G_{aq}^{Phys}/\Delta H_{aq}^{compl}$).

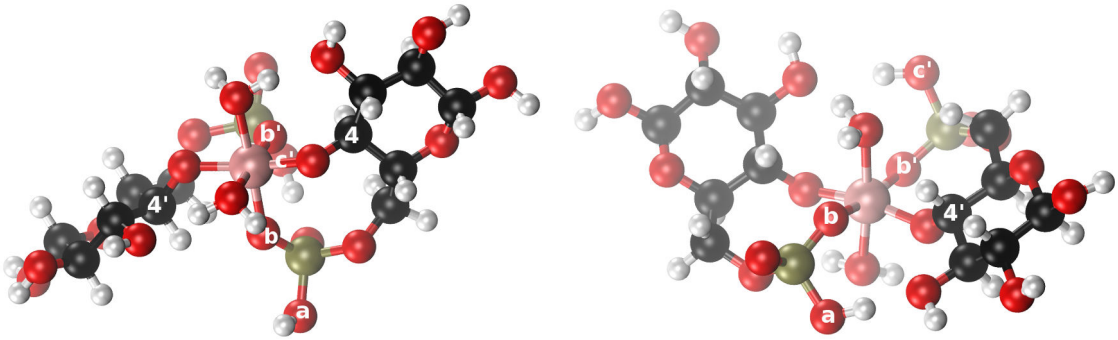
$[\mathrm{Al(G6P)}^{b'}_{2,aca'c'}(\mathrm{H_2O})_2]$



A) -89.22/91.40 B) -87.35/-86.90

Figure S4: Dicoordinated binding mode in 1:2 Al-G6P bis-complexes. Each G6P ligand coordinates the aluminum atom by an alcoholic and a phosphate group. The 2 water molecules which complete the octahedral coordination sphere can be adjacent (A) or in opposite sites (B). The complexation free energies for the physiological pH (ΔG_{aq}^{Phys}) and ΔH_{aq}^{compl} are shown in kcal/mol ($\Delta G_{aq}^{Phys}/\Delta H_{aq}^{compl}$).

$[\mathrm{Al(G6P)}^{ac'}_{2,bC4b'C4'}(\mathrm{H_2O})_2]^{-1}$



A) -128.95/-146.35 B)-112.40/-129.88

1:3 Tris-complex and saturation of charge

Table S4: Enthalpy and free energy affinities in kcal/mol for 1:3 aluminum-G6P tris-complex formation with corrections that account for the physiological pH and de/protonation of the corresponding titratable groups. The subscripts indicate the coordination mode of G6P to Al(III) and the superscripts refer to the protonation state of the phosphate groups: *a* or *b*, the Al(III) or the proton is bound to that oxygen; *ab*, the Al(III) is binding *a* and *b* oxygens, or *a* and *b* have one proton each, *C*4, Al(III) is coordinated by the OH group of that carbon. The † sign indicates a spontaneous proton transfer from a water molecule to a phosphate group during the optimization.

1:3 Al-$(G6P)_3$ complex	$\alpha-$anomer			$\beta-$anomer		
	ΔH_{aq}^{compl}	ΔG_{aq}^{compl}	ΔG_{aq}^{Phys}	ΔH_{aq}^{compl}	ΔG_{aq}^{compl}	ΔG_{aq}^{Phys}
$[\mathrm{Al(G6P)}^{ab'c}_{3,cc'b}]$				-131.68	-106.09	-100.40
$[\mathrm{Al(G6P)}^{bc'a}_{3,aca'b'bc}]$				-70.62	-71.76	-66.07
$[\mathrm{Al(G6P)}^{aa'a}_{3,bC4b'C4'bC4}]^{-3}$				-164.10	-162.21	-136.54
$[\mathrm{Al(G6P)}^{aa'c}_{3,bC4b'C4'bC4}]^{-3}$				-162.08	-160.73	-135.07
$[\mathrm{Al(G6P)}^{aa'c}_{3,bC4b'C4'bC4}]^{-3}$				-145.70	-144.36	-118.69
$[\mathrm{Al(G6P)}_{3,bc'c}]^{-3}$				-165.30	-142.01	-142.01
$[\mathrm{Al(G6P)}_{3,bc'c}]^{-3}$				-181.28	-156.44	-156.44
$[\mathrm{Al(G6P)}_{3,aca'b'bc}]^{-3}$	-129.27	-137.55	-137.55	-141.86	-143.44	-143.44
$[\mathrm{Al(G6P)}_{3,bC4b'C4'bC4}]^{-6}$				-147.90	-148.10	-128.12
$[\mathrm{Al(G6P)}_{3,bC4b'C4'bC4}]^{-6}$				-141.17	-142.22	-122.24

Ternary 1:1:1 Al-G6P-Citr complexes

Table S5: Enthalpy and free energy affinities in kcal/mol for ternary aluminum G6P and citrate complex formation with corrections that account for the physiological pH and de/protonation of the corresponding titratable groups. The subscripts indicate the coordination mode of G6P to Al(III) and the superscripts refer to the protonation state of the phosphate group: a or b, the Al(III) or the proton is bound to that oxygen; ab, the Al(III) is binding a and b oxygens, or a and b have one proton each; $C4$, Al(III) is coordinated by the OH group of that carbon.

1:1:1 Al-G6P-Citr complexes	$\alpha-$anomer			$\beta-$anomer		
	ΔH_{aq}^{compl}	ΔG_{aq}^{compl}	ΔG_{aq}^{Phys}	ΔH_{aq}^{compl}	ΔG_{aq}^{compl}	ΔG_{aq}^{Phys}
$[\mathrm{Al(G6P)}_{a}^{b}\mathrm{(Citr)(H_2O)_2}]^{-2}$	-158.66	-161.21	-149.76	-160.73	-161.92	-150.48
$[\mathrm{Al(G6P)}_{a}^{b}\mathrm{(Citr)(H_2O)_2}]^{-2}$				-158.70	-160.46	-149.01
$[\mathrm{Al(G6P)}_{a}^{c}\mathrm{(Citr)(H_2O)_2}]^{-2}$				-162.34	-163.66	-152.22
$[\mathrm{Al(G6P)}_{b}^{c}\mathrm{(Citr)(H_2O)_2}]^{-2}$	-153.41	-155.65	-144.20	-156.11	-156.62	-145.17
$[\mathrm{Al(G6P)}_{b}^{c}\mathrm{(Citr)(H_2O)_2}]^{-2}$				-152.28	-153.75	-142.30
$[\mathrm{Al(G6P)}_{c}^{a}\mathrm{(Citr)(H_2O)_2}]^{-2}$	-152.76	-156.69	-145.24	-157.74	-160.11	-148.66
$[\mathrm{Al(G6P)}_{ac}^{b}\mathrm{(Citr)(H_2O)}]^{-2}$	-136.26	-147.74	-136.29	-133.89	-144.81	-133.36
$[\mathrm{Al(G6P)}_{C4}^{a}\mathrm{(Citr)(H_2O)_2}]^{-3}$				-165.96	-169.81	-151.70
$[\mathrm{Al(G6P)}_{bC4}^{a}\mathrm{(Citr)(H_2O)}]^{-3}$				-170.20	-180.81	-162.70
$[\mathrm{Al(G6P)}_{bC4}^{a}\mathrm{(Citr)(H_2O)}]^{-3}$				-162.43	-173.40	-155.29
$[\mathrm{Al(G6P)}_{a}\mathrm{(Citr)(H_2O)_2}]^{-3}$	-175.08	-178.16	-168.60	-168.79	-173.26	-163.70
$[\mathrm{Al(G6P)}_{ab}\mathrm{(Citr)(H_2O)}]^{-3}$	-157.98	-180.44	-170.89	-157.14	-182.06	-172.50
$[\mathrm{Al(G6P)}_{ab}\mathrm{(Citr)(H_2O)}]^{-3}$				-157.26	-182.36	-172.81
$[\mathrm{Al(G6P)}_{bC4}\mathrm{(Citr)(H_2O)}]^{-4}$				-173.63	-184.83	-168.62

Dinuclear metal complexes: 2:1 Al_2-G6P and 2:2 Al_2-$(G6P)_2$ complexes

Table S6: Enthalpy and free energy affinities in kcal/mol for ternary (1:1:1) and for two aluminum complex formation with corrections that account for the physiological pH and de/protonation of the corresponding titratable groups. The subscripts indicate the coordination mode of G6P to Al(III) and the superscripts refer to the protonation state of the phosphate group: a, the Al(III) or the proton is bind to that oxygen; ab, the Al(III) is binding a and b oxygens, or a and b have one proton each.

2:1 Al_2-G6P complexes	$\beta-$anomer		
	ΔH_{aq}^{compl}	ΔG_{aq}^{compl}	ΔG_{aq}^{Phys}
$[Al_2(G6P)^{b}_{ac}(H_2O)_{10}]^5$	-68.04	-54.96	-51.16
$[Al_2(G6P)^{c}_{ab}(H_2O)_{10}]^5$	-62.37	-50.43	-46.64
$[Al_2(G6P)_{ab}(H_2O)_{10}]^4$	-119.4	-104.24	-104.24
$[Al_2(G6P)_{bC4}(H_2O)_{10}]^3$	-157.85	-144.78	-138.12
$[Al_2(G6P)_{bC1}(H_2O)_{10}]^3$	-135.77	-123.17	-116.51

2:2 Al_2-$(G6P)_2$ complexes	$\beta-$anomer		
	ΔH_{aq}^{compl}	ΔG_{aq}^{compl}	ΔG_{aq}^{Phys}
$[Al_2(G6P)^{bb'}_{2,aca'c'}(H_2O)_8]^4$	-112.78	-100.51	-96.71
$[Al_2(G6P)^{b'}_{2,aca'c'}(H_2O)_8]^3$	-163.47	-149.87	-147.98
$[Al_2(G6P)^{aa'}_{2,cC4b'C4'}(H_2O)_8]^2$	-205.02	-190.49	-173.38
$[Al_2(G6P)^{bc'}_{2,cC4a'C4'}(H_2O)_8]^2$	-200.37	-183.91	-166.80
$[Al_2(G6P)_{2,acb'c'}(H_2O)_8]^2$	-213.32	-199.13	-199.13
$[Al_2(G6P)_{2,abb'c'}(H_2O)_8]^2$	-208.08	-194.49	-194.49
$[Al_2(G6P)_{2,cC4b'C4'}(H_2O)_8]$	-272.19	-255.97	-242.65

Table S7: Distances (in Å) and electron delocalization indexes (DI) of the first coordination sphere of aluminums and of hydrogen bonds in 8-membered ring Al_2-$(G6P)_2$ bis-complex. The phosphate groups are bridging the two aluminum atoms. QTAIM parameters of Al...O and H...O bond critical points (BCP, in au): ρ_{BCP}, the electron density at BCP; $\nabla^2\rho_{BCP}$, the laplacian of electron density; and H_{BCP}, the total electron energy density at BCP. W refers to water molecule.

Binding Mode	Structure	Distance		DI	ρ_{BCP}	$\nabla^2\rho_{BCP}$	H_{BCP}
8-membered ring	$[Al_2(G6P)_{2,acbc}(H_2O)_8]^2$	Al-O_a	1.820	0.192	0.0764	0.5132	-0.0007
		Al-$O_{c'}$	1.832	0.190	0.0754	0.4912	-0.0015
		Al-W1	1.954	0.139	0.0561	0.3260	0.0000
		Al-W2	1.914	0.160	0.0625	0.3727	-0.0005
		Al-W3	1.997	0.120	0.0490	0.2798	0.0009
		Al-W4	1.964	0.129	0.0528	0.3137	0.0014
		Al'-$O_{b'}$	1.837	0.187	0.0747	0.4835	-0.0015
		Al'-O_c	1.836	0.186	0.0745	0.4846	-0.0013
		Al'-W1'	1.983	0.122	0.0496	0.2929	0.0017
		Al'-W2'	1.942	0.150	0.0587	0.3371	0.0008
		Al'-W3'	1.940	0.145	0.0583	0.3406	-0.0003
		Al'-W4'	1.944	0.141	0.0567	0.3354	0.0004
		H_{W1}-O_{C1}	1.749	0.097	0.0401	0.1118	-0.0031
		H_{W2}-O	1.762	0.087	0.0373	0.1154	-0.0016
		H_{W2}-$O_{a'}$	1.604	0.134	0.0576	0.1312	-0.0110
		$H_{W2'}$-O_b	1.516	0.167	0.0725	0.1310	-0.0202
		$H_{W3'}$-$O_{a'}$	1.586	0.138	0.0607	0.1345	-0.0126
		$H_{W4'}$-$O_{C4'}$	1.660	0.114	0.0483	0.1232	-0.0062
		$H_{C5'}$-W3'	2.561	0.027	0.0077	0.0261	0.0009

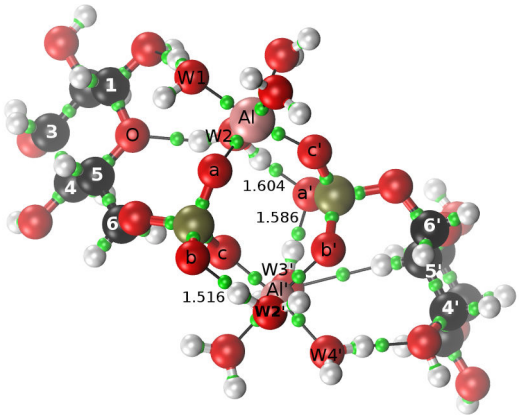
Table S8: Distances (in Å) and electron delocalization indexes (DI) of the first coordination sphere of aluminums and of hydrogen bonds in 16-membered ring neutral Al_2-$(G6P)_2$ bis-complex. Each aluminum is forming a monodentate interaction with each G6P ligand through an alcoholic-OH group of one ligand and the phosphate group of the second ligand. QTAIM parameters of Al...O and H...O bond critical points (BCP, in au): ρ_{BCP}, the electron density at BCP; $\nabla^2\rho_{BCP}$, the laplacian of electron density; and H_{BCP}, the total electron energy density at BCP. W refers to water molecule.

Binding Mode	Structure	Distance		DI	ρ_{BCP}	$\nabla^2\rho_{BCP}$	H_{BCP}
16-membered ring	$[Al_2(G6P)_{2,cC4bC4}(H_2O)_8]$	Al-O_c	1.833	0.192	0.0752	0.4888	-0.0016
		Al-$O_{C4'}$	1.788	0.222	0.0869	0.5764	-0.0049
		Al-W1	1.951	0.148	0.0576	0.3279	-0.0009
		Al-W2	2.057	0.104	0.0420	0.2302	0.0010
		Al-W3	2.022	0.113	0.0457	0.2570	0.0010
		Al-W4	1.906	0.158	0.0625	0.3820	0.0003
		H_{W1}-O_a	1.405	0.206	0.0979	0.1051	-0.0420
		H_{W3}-$O_{C3'}$	1.691	0.106	0.0446	0.1233	-0.0042
		H_{W4}-$O_{c'}$	1.384	0.204	0.1007	0.0996	-0.0453
		H_{C5}-O_b	2.526	0.035	0.0104	0.0337	0.0009
		H_{C5}-W2'	2.711	0.021	0.0073	0.0253	0.0009
		H_{C6}-$O_{b'}$	2.739	0.019	0.0054	0.0191	0.0008
		H_{C3}-W2'	3.015	0.012	0.0043	0.0160	0.0008
		Al'-$O_{b'}$	1.839	0.189	0.0747	0.4789	-0.0019
		Al'-O_{C4}	1.782	0.219	0.0864	0.5862	-0.0040
		Al'-W1'	2.002	0.127	0.0502	0.2767	-0.0002
		Al'-W2'	1.905	0.159	0.0625	0.3841	0.0005
		Al'-W3'	1.99	0.127	0.0502	0.2871	0.0007
		Al'-W4'	2.045	0.113	0.0446	0.2378	0.0000
		$H_{W1'}$-$O_{a'}$	1.698	0.120	0.0477	0.1221	-0.0062
		$H_{W2'}$-O_b	1.401	0.184	0.0930	0.1230	-0.0369
		$H_{W3'}$-O_{C3}	1.721	0.106	0.0435	0.1143	-0.0046
		$H_{W4'}$-$O_{a'}$	1.737	0.115	0.0446	0.1139	-0.0053
		$H_{C6'}$-O_c	2.800	0.014	0.0053	0.0197	0.0009
		$H_{C6'}$-O_b	2.504	0.036	0.0093	0.0286	0.0007
		$H_{C6'}$-W4'	3.134	0.010	0.0036	0.0133	0.0007
		O_c-$O_{b'}$	3.328	0.025	0.0046	0.0165	0.0007

Table S9: Distances (in Å) and electron delocalization indexes (DI) of the first coordination sphere of aluminum and of hydrogen bonds in 16-membered ring +2 charge Al_2-$(G6P)_2$ bis-complex. Each aluminum is forming a monodentate interaction with each G6P ligand through an alcoholic-OH group of one ligand and the phosphate group of the second ligand. QTAIM parameters of Al...O and H...O bond critical points (BCP, in au): ρ_{BCP}, the electron density at BCP; $\nabla^2\rho_{BCP}$, the laplacian of electron density; and H_{BCP}, the total electron energy density at BCP. W refers to water molecule.

Binding Mode	Structure	Distance		DI	ρ_{BCP}	$\nabla^2\rho_{BCP}$	H_{BCP}
16-membered ring	$[Al_2(G6P)^{aa}_{2,cC4bC4}(H_2O)_8]^2$	Al-O_b	1.841	0.170	0.0703	0.4750	0.0014
		Al-$O_{C4'}$	1.771	0.225	0.0891	0.6087	-0.0048
		Al-W1	1.989	0.127	0.0507	0.2888	0.0007
		Al-W2	1.915	0.151	0.0606	0.3713	0.0008
		Al-W3	1.951	0.136	0.0549	0.3281	0.0010
		Al-W4	2.031	0.109	0.0446	0.2495	0.0010
		H_{W1}-O_a	1.835	0.080	0.0315	0.1032	0.0001
		H_{W2}-$O_{b'}$	1.480	0.150	0.0732	0.1507	-0.0194
		H_{W3}-$O_{C3'}$	1.677	0.114	0.0485	0.1206	-0.0067
		H_{C6}-$O_{b'}$	2.595	0.031	0.0074	0.0226	0.0007
		Al'-$O_{c'}$	1.826	0.181	0.0737	0.5007	0.0006
		Al'-O_{C4}	1.78	0.228	0.0897	0.5933	-0.0063
		Al'-W1'	2.051	0.106	0.0424	0.2343	0.0012
		Al'-W2'	2.013	0.117	0.0472	0.2660	0.0008
		Al'-W3'	1.956	0.135	0.0540	0.3207	0.0010
		Al'-W4'	1.893	0.161	0.0642	0.4002	0.0005
		$H_{W3'}$-O_{C3}	1.593	0.126	0.0571	0.1368	-0.0099
		$H_{W4'}$-O_c	1.464	0.164	0.0792	0.1398	-0.0244
		$H_{Oa'}$-W1'	1.962	0.064	0.0238	0.0830	0.0016
		$H_{C6'}$-O_c	2.986	0.014	0.0034	0.0119	0.0006
		$H_{C5'}$-W2	2.693	0.025	0.0073	0.0239	0.0008

Figure S5: Representation of the bond critical points (BCP) of the first coordination sphere of aluminums and of the hydrogen bonds in 8-membered ring and 16-membered ring Al_2-$(G6P)_2$ bis-complexes. The complexation free energies for the physiological pH and ΔH_{aq}^{compl} are shown in kcal/mol ($\Delta G_{aq}^{Phys}/\Delta H_{aq}^{compl}$). The BCP are represented by green dots.



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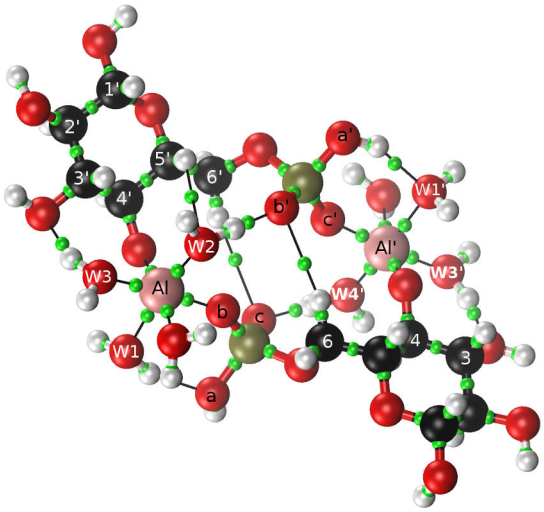

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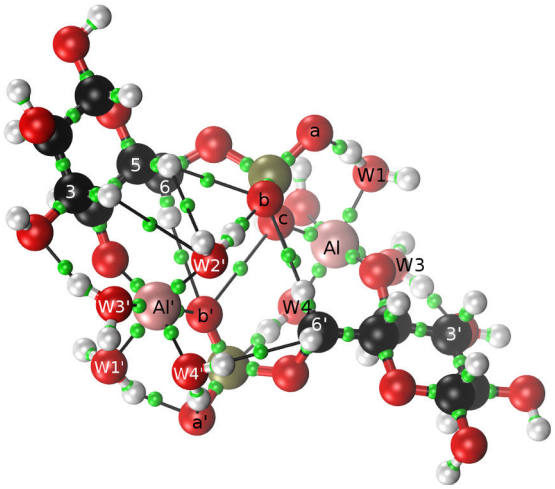

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