Dissociation Energy Computations for Saline Bonds Implied in Interactions Mediated by Peptidoglicans

Simona Muntean,[*1] Ludovic Kurunczi,[2] Cristian Bologa,[3] Gheorghe Ilia,[1] Zeno Simon[1]*

Summary: Dissociation energy and hydration energy calculations, in water solution, are presented for saline bonds mediated by Ca^{2+} and Mg^{2+} ions with Brőnstedt type bases (–COO–, $-OSO_3-$, –OH). A computationally intensive method, Polarisable Continuum Model (PCM) using 6-31G* basis set, was applied. Hydration energies were computed by various methods, as well as dissociation energies of some L_2M complexes. L_2Ca complexes result as more stable against dissociation than L_2Mg complexes. Hydration energy calculation results, for some of the methods, here used, seem rather reliable as compared to experimental results.

Keywords: dissociation energy; hydration energy; intercellular interaction; peptidoglycans; saline bond

Introduction

Adhesion proteoglycans (peptidoglicans) are responsible for species-specific cell aggregation in some sponges.[1] The adhesion proteoglycans are supramolecular complexes, consisting of a protein core, and about 20 irradiating arms of g200 glycans, and are responsible for homospecific aggregation between sponge-cells.[2]

Intercellular interactions mediated by peptidoglycans imply saline bonds between two Brőnstedt bases ($-COO^-$, $-OSO_3{}^-$, –OH, etheric –O– groups) and Ca^{2+} ions, which cannot be substituted by Mg^{2+} ions. [3] It seems therefore of interest to calculate dissociation energies, in aqueous solution, of saline bonds between Ca^{2+} and Mg^{2+} cations, on one hand, and small molecule models for these Brőnstedt bases, on the other.

Some reasonable results were obtained for calculated dissociation energies, in aqueous solution, of $(CH_3COO)_2Ca$, and $(CH_3COO)_2Mg$ with the Bemcalc method.[4–8] This method yields also results comparable to experimental figures for hydration energies of Ca^{2+} and Mg^{2+}. Such calculations can be reliable only if they give results comparable to experimental figures for hydration energies of the corresponding cations, and for the small molecules models used for Brőnstedt bases.

Successful methods for hydration energy calculations were deviced by Florian and Warshel,[10] and by Jorgensen, Ulmschneider and Tirado-Rives,[9] but — considering the initial success of the Bemcalc method, we are interested here also in hydration energy results with this method, and with the PCM method also used in some calculations of saline bond dissociation energies,[11,12] and also of other more simple methods.

Here we calculate hydration energies, for Ca^{2+}, Mg^{2+} cations, for small molecules which will be considered as models for Brőnstedt bases of peptidoglicans, and also dissociation energies of L_2M complexes in

---

[1] Institute of Chemistry Timisoara of Romanian Academy, B-dul Mihai Viteazul 24, 300223 Timisoara, Romania
Fax: (+40) 256 491824
E-mail: horasg11@yahoo.com

[2] University of Medicine and Pharmacy "Victor Babes", Faculty of Pharmacy, E. Murgu 2-4, 300034 Timisoara, Romania

[3] University of New Mexico, School of Medicine, Office of Biocomputing BSMB B61, NM 87131 Albuquerque, USA

water solution with metal cations (M): Ca^{2+} and Mg^{2+}, and ligand (L): acetate (Ac^-) (CH_3COO^-), and methylsulphate ($CH_3OSO_3^-$). Hydration energies are calculated also for ethyleneglicol (EtGl) ($HOCH_2CH_2OH$), and 1-4-dioxan, as models for the peptidoglycanic groups implied in saline bonds.

Our aim is to compare the stability of L_2Ca and L_2Mg saline bonds, and by calculating, by various methods, hydration energies, to test — on the hand of experimental results, the reliability of Bemcalc, and of the computationally intensive PCM method.

Method

The PCM (Polarisable Continuum Model) method, here used, starts from ab initio calculations in vacuo, for the corresponding parteners (molecules, ions, saline bond complexes). PC-GAMESS version, running under Windows NT was used, based on RHF — type SCF with 6-31G* basis set options. The partners with fixed, in vacuo calculated geometries are hereafter introduced in water, as polarisable continuum model and energy calculations repeated. Zero point energy corrections (ZPE), thermal corrections and corrections related to basis set superposition error (BSSE) were not performed. For details concerning the PCM method see our previous publication.[12] Hydration energies are calculated as differences between energies in water solution and, respectively in vacuum. Dissociation energies are also calculated as differences between energies in water solution.

Hyper Chem packages[13] include programs for hydration energy calculations. Such programmes rely basically on group increments and solvent accessible surfaces. Molecular structures calculated either by MM+ or by AM1- techniques can be used. Hydration energy calculations are performed for the CH_3COO^-, $CH_3OSO_3^-$ anions, and ethyleneglicol ($HOCH_2$-CH_2OH), and also for some other organic molecules (alcohols, ethers, amines, ammonium ions) in order to obtain an insight into the reliability of this method. For some preliminary results see our previous paper.[14]

Some hydration energy calculations are performed also with the Bemcalc method.[8] An external (water) dielectric constant $D = 80.0$ was used, with an internal $D = 2.0$.

Experimental figures for hydration energy calculations are taken from data listed by Jorgensen et al, [9] Florian et al, [10] and by Raewsky and Shapper.[15] More exactly, they are hydration free enthalpy changes, ΔG, at 25 °C. Data by Raewsky and Shapper are based on Henry constants (quotients of water per gas solute concentrations).

Results

The PCM results for the four L_2M complexes, three ligands, and the Mg^{2+} and Ca^{2+} cations are listed in Table 1. Computations were performed also for some aliphatic alcohols in order to compare PCM results for hydration energies with experimental results. Results are listed in Table 1. Results with Hyper Chem package methods[13] are listed in Table 2, while results with Bemcalc method[4–8] are listed in Table 3.

Dissociation free energies (ΔG) are calculated as differences between total PCM free energies in water solution for the L_2M complexes and for the components ($2L^-$ and M^{2+}), corresponding to the dissociation process:

$$L_2M \rightarrow 2L^- + M^{2+}$$

while for the Bemcalc method, $L^-{-}M^{2+}{-}L^-$ interaction energies are calculated directly from semiempiric molecular force potentials, to which differences between hydration energies are added (Table 4). The results listed in Table 4 do not include entropy effects, specific for dissociation processes, which are positive.

Table 1.
PCM results and experimental hydration free enthalpy values. Data in kcal/mol.

Compound	Total free energy in water solution	Total free energy vacuum	Hydration Energy		ε [%]
			Calc.	Exp.	
CH_3COO^-	−142653.45	−142585.87	−67.58	−79.9	+15.40
Ac_2Ca	−710028.09	−709939.74	−88.39	—	—
Ac_2Mg	−410545.93	−410537.97	−7.96	—	—
Ca^{2+}	−424786.43	−424261.63	−524.80	−381.2	−37.67
Mg^{2+}	−125457.62	−124756.24	−701.38	−455.5	−55.78
MeOH	−72185.70	−72185.08	−0.62	−5.1	+90.19
EtOH	−96681.56	−96683.13	+1.57	−5.0	+131.40
EtGl	−143651.47	−143649.62	−1.85	−9.6	+80.73
i-PrOH	−121176.97	−121180.79	+3.82	−4.74	+180.60
n-PrOH	−121174.12	−121177.75	+3.63	−4.8	+175.63
1,4-Dioxane	−191898.46	−191901.49	+3.03	−5.1	+159.41
$CH_3OSO_3^-$	−462255.18	−462191.39	−63.79	—	—
$(CH_3OSO_3)_2Ca$	−1349204.05	−1349094.46	−109.59	—	—
$(CH_3OSO_3)_2Mg$	−1049698.34	−1049680.48	−109.59	—	—

Legend: Experimental hydration energies data from [9,10,15]. Me: methyl; Et: ethyl; Pr: propyl; EtGl: ethyleneglycol; Ac^-: acetate anion.

Table 2.
Experimental and calculated hydration free enthalpies with Hyper-Chem package. Data in kcal/mol.

Compound	Exp.	MM+	ε_{MM+} [%]	AM1	ε_{AM1} [%]
MeOH	−5.1**	−7.66	−50.20	−7.70	−50.98
EtOH	−5.0*	−5.74	−14.80	−5.80	−16.00
n-PrOH	−4.8*	−4.93	−2.71	−4.98	−3.75
i-PrOH	−4.74	−4.17	12.03	−4.25	10.34
n-BuOH	−4.7*	−4.30	8.51	−4.34	7.66
2-BuOH	−4.62	−3.36	27.27	−3.54	23.38
2-Me-1-PrOH	−4.5	−3.58	20.44	−3.70	17.78
2-Me-2-PrOH	−4.47	−2.88	35.57	−2.97	33.56
n-PeOH	−4.57	−3.94	13.79	−3.98	12.91
2-PeOH	−4.39	−2.74	37.59	−2.98	32.12
3-PeOH	−4.35	−2.19	49.66	−2.33	46.44
2-Me-1-BuOH	−4.42	−3.09	30.09	−3.16	28.51
2-Me-2-BuOH	−4.43	−2.31	47.86	−.2.33	47.40
3-Me-1-BuOH	−4.42	−3.81	13.80	−3.83	13.35
EtGl	−9.6*	−12.95	−34.90	−13.05	−35.94
PrGl	−5.0	−16.28	−225.60	−16.86	−237.20
EtEth	−1.6*	0.38	123.75	0.34	121.25
n-PrEth	−1.16	1.45	225.00	1.40	220.69
i-PrEth	−0.53	1.46	375.47	1.48	379.25
n-BuEth	−0.83	2.41	390.36	2.35	383.13
2-BuEth	—	2.07	—	2.16	
NH_3	−4.22	−18.33	−334.36	−18.33	−334.36
$MeNH_2$	−4.6*	−6.34	−37.83	−6.32	−37.39
Et NH_2	−4.5*	−4.60	−2.22	−4.62	−2.67
n-$PrNH_2$	−4.40	−3.76	14.55	−3.81	13.41
NH_4^+	−81*	−18.33	−326.28	−18.33	−326.28
$MeNH_3^+$	−73*	−6.56	91.01	−6.50	91.10
$EtNH_3^+$	−68	−4.77	92.99	−4.80	92.94
n-$PrNH_3^+$	−67	−3.85	94.25	−3.92	94.15
CH_3COO^-	−82*	0.94	101.15	1.01	101.23
$CH_3OSO_3^-$	—	−8.63	—	−8.38	—
SO_4^{2-}	—	−9.04	—	−8.78	—

Legend: see Tab. 1; Bu: butyl; PrGl: propyleneglycol; n-PrEth: n-propyl-ethylether; EtEth: diethylether; n-BuEth: n-butyl-ethylether. Experimental figures — unmarked: Raewsky and Shaper [15], asterix: Florian et al[9], double asterix: Jorgensen et al[10].

Table 3.
Experimental and calculated hydration free enthalpies with Bemcalc. Data in kcal/mol.

Compound	Exp.	Calc.	ε [%]
Ca^{2+}	−379.5	−360.6	4.98
Mg^{2+}	−454.2	−437.4	3.69
CH_3COOH	−6.7	−8.8	−31.34
CH_3COO^-	−82.0	−77.4	5.61
EtOH	−5.0	−6.2	−24.00
MeOH	−5.1	−6.6	−29.41

Legend: see Tab. 1.

Discussions and Conclusions

The calculated PCM energies for dissociation are small differences between large numbers, and indicate L_2Ca complexes as more stable against dissociation than L_2Mg complexes. This result is in agreement with the fact that Ca^{2+} ions are required for cell adhesion mediated by peptidoglycans, and that they cannot be substituted by Mg^{2+} ions.[3]

The Bemcalc results for $(CH_3COO)_2Ca$ and $(CH_3COO)_2Mg$ seem more realistic when compared with expectations for

Table 4.
Dissociation energies for saline bonds by the PCM and Bemcalc methods (kcal/mol).

Saline bond	Dissociation ΔG	
	PCM	Bemcalc
$(CH_3COO)_2Ca \rightarrow 2\ CH_3COO^- + Ca^{2+}$	−65.24	+8.54
$(CH_3COO)_2Mg \rightarrow 2\ CH_3COO^- + Mg^{2+}$	−218.59	−3.12
$(CH_3OSO_3)_2Ca \rightarrow 2\ CH_3OSO_3^- + Ca^{2+}$	−92.74	—
$(CH_3OSO_3)_2Mg \rightarrow 2\ CH_3OSO_3^- + Mg^{2+}$	−269.64	—

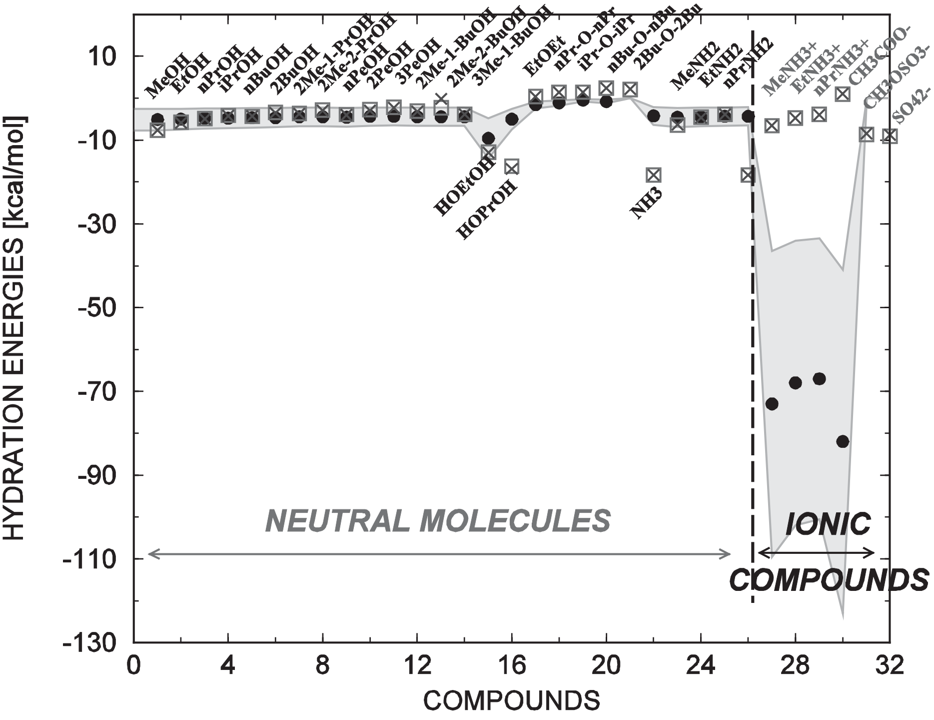

Figure 1.
Numerical results computed with MM+ (□), and AM1 (x) against experimental data (●)

saline bridges.[8] In Bemcalc, interaction energies between L and M^{2+} in L_2M are calculated from given electronic and steric structures of the components, by approximative electrostatic, van der Waals, and deformation energy calculations, of the type used in molecular mechanics. Therefore, these interaction energies are not small differences between large numbers.

Concerning hydration energies, the method included in the Hyper Chem package seem not suited for ions, due to the lack of parameters for ionic compounds. For neutral molecules, the calculated hydration energies are of correct orders of magnitude, when compared to the experimental ones, but correlation between experimental and calculated values is poor (Figure 1).

This method cannot be used for saline bond — dissociation energy calculations as it fails completely for ions.

The results of hydration energy calculations of PCM and Bemcalc seem to be more reliable for saline bond dissociation energy calculations. Even if experimental and calculated results do not correlate very well, the difference between ions and neutral molecules is correctly reflected in calculations. The fact that our calculations do not account for ZPE, thermal, and BSSE corrections will also induce some supplementary errors in calculated dissociation energies.

As a conclusion, for saline bond dissociation energies, PCM and Bemcalc results for interaction energies could be used for an at least qualitative idea concerning stabilities of different types of saline bonds.

Acknowledgements: We thank Dr. Sebastian Muntean for computational support, Dr. Mircea Mracec for the permission to use the Hyper Chem package,[13] and Dr. Maria Mracec for interesting discussions concerning calculation of hydration energies by this program.

This work was supported from grant CNCSIS A Consortiu, 27687/2005 by Romanian Ministry of Education and Research of Romania.

[1] U. Dammer, O. Popescu, P. Wagner, D. Anselmetti. H.J. Guntherodt, G.N. Misevics, *Science*, **1995**, *267*, 1173.

[2] O. Popescu, G.M. Misevics, *Nature*, **1997**, *386*, 231.

[3] O. Popescu, I. Checiu, P. Gherghel, Z. Simon, G.M. Misevics, *Biochimie*, **2003**, *85*, 181.

[4] E.D. Purissima, S.H. Nilar, *J. Comput. Chem.*, **1995**, *16*, 681.

[5] E.D. Purissima, *J. Comput. Chem.*, **1998**, *19*, 1494.

[6] S.L. Chan, E.O. Purissima, *J. Comput. Chem.*, **1998**, *19*, 1268.

[7] T. Sulea, E.O. Purisima, *J. Phys. Chem. B*, **2001**, *105*, 889.

[8] T. Sulea, Z. Simon, *Internet Electron. J. Mol. Des.*, **2002**, *1*, 59.

[9] W.L. Jorgensen, J.P. Ulmschneider, J. Tirado-Rives, *J. Phys. Chem. B*, **2004**, *108*, 16264.

[10] J. Florian, A. Warshel, *J. Phys. Chem. B*, **1999**, *103*, 10282.

[11] S. Miertus, E. Scrocco, J. Tomasi, *Chem. Phys.*, **1981**, *55*, 117.

[12] V. Careja, M. Banda, L. Saity, C. Bologa, M. Mracec, Z. Simon, *Proc. Romanian Acad., Ser B*, **2000**, *2*, 187.

[13] HyperChem™ Release 5.11 Professional for Windows, Hyper Cube inc. 1999, Gainesville Florida, USA, www.hyper.com.

[14] S. Muntean, C. Bologa, L. Kurunczi, Z. Simon Z. *Zilele Academice Timişene*, Ed. IX, 2005, 51.

[15] O.A. Raevsky, K.J. Schaper, *QSAR Comb. Sci.*, **2003**, *22*, 926.