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Comparison of Binding Energies of Selected Environmental Xenobiotics by Porphyrin Complexes

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The wide occurrence of such xenobiotics as NO, NO_2, NO_2^-, CO, SO_2, CN , H_2S in the environment and important role this molecules in a toxicology makes searching for their toxical action evaluation necessary. The achievements of molecular engineering and quantum physics permit to analyse physical and chemical properties and molecular structure of the complexes created in the living organisms. Consequently, it leads to better understanding of combination mechanism and the toxic influence on the environment.

There are many important biomolecules, which naturally contain metals within the body, and in biological systems in general. Metal ions are present in many vitamins (such as Vitamin B_{12} with cobalt), enzymes (such as cytochrome P450 with iron), molecules important for energy conversions (such as chlorophyll with magnesium), nitrogen fixation (such as nitrogenase with molybdenum and iron), and oxygen transport (such as haemoglobin with iron) (Stryer 1997). Rovira C. and co-workers (1997 a; 1997 b; 1998) provided investigations of equilibrium geometries and electronic structures of iron-porphyrin complexes using density functional theory (DFT) and Car-Parrinello molecular dynamics method. Han S. and co-workers (1999) carried out ab initio calculations to study the effect of structural deformations of iron-porphyrin compound while combining with CO molecule. Bersuker I.B. and co-workers (1997) worked out method combining quantum mechanics and molecular mechanics (QM/MM) and applied it to large organometallic and metallobiochemical systems, for example Vitamin B_{12}. Ab initio calculations on iron-porphyrin model systems for intermediates in the oxidatives cycle of cytochrome P450s were carried out by De Groot M.J. and co-workers (1998). Our study was undertaken in order to obtain the values thermodynamic functions and to establish binding energies of optimalized molecular structures of selected porphyrin complexes.

MATERIALS AND METHODS

In order to perform calculations the computer program HyperChem in version Professional 5.1 was applied. Computational chemistry is a new discipline. Its advent and popularity have paralleled improvements in computing power during the last several decades. As with other disciplines in chemistry, computational chemistry uses tools to understand chemical reactions and processes. Scientists

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use computer software to gain insight into real chemical processes. Although computational chemists frequently develop and refine software tools, their primary interest is in applying software tools to enhance chemical knowledge.

The challenges for computational chemistry are to characterise and predict the structure and stability of chemical systems, to estimate energy differences between various states, and to explain reaction pathways and mechanisms at the atomic level. Meeting these challenges could eliminate time-consuming experiments (Straszko and Paprota 1998).
Molecular modelling is a kind of the computer experiment, whose subjects are theoretical molecule models.

ZINDO/1 method was used for geometry optimisations of particular molecules of complexes (Anderson et al. 1986). ZINDO/1 method is based on modified version of the intermediate neglect of differential overlap (INDO), which was developed by Zerner. It is the most suitable semi-empirical method in HyperChem for determing structures and energies of molecules of the first or second transition row metals. The ability to perform molecular orbital (MO) calculations on metals is extremely useful, because molecular mechanics methods are generally unable to treat metals. This is because metals have a wide range of valences, oxidation states, spin multiplicities and have unusual bonding situations ($d\pi$-$p\pi$). In addition, the nondirectional nature of metallic bonding is less amenable to a ball and spring interpretation. Conversely, these factors dictate that molecular orbital calculations on metals yield less reliable results than with organic compound.

The developers of ZINDO methods found out that the parameters required to reproduce orbital energy orderings and UV spectra are different from those required to reproduce accurate structures by geometry optimisation. They introduced a new pair of parameters, called overlap weighting factors (σ-σ and π-π), to account for this. Their effect is to modify the resonance integrals for the off-diagonal elements of the Fock matrix (Straszko and Paprota 1998). For geometry optimisations and comparison of total energies, both overlap weighting factors should be set to 1. However, several different values for the overlap weighting factors have been used in the literature (Ridley and Zerner 1976; Bacon and Zerner 1979; Del Bene and Jaffe 1968).
In our calculations for some xenobiotic-porphyrin molecules molecular mechanics method were also performed. At this stage MM+ force field was used. The MM+ force field method is an extension of MM2, which was developed by Allinger (1977).

RESULTS AND DISCUSSION

The objects of our experiments were xenobiotic-ligand-porphyrin molecules. Ammonia is one of the ligands coordinated to the iron. Iron in hem (i.e. the ligand-iron porphyrin complex in haemoglobin) combines with nitrogen in histidine ligand from the protein chain (below the plane of the hem ring). In order to simplify calculations ammonia was chosen instead of histidine.

Table 1. The values of energies data for the optimised molecules by ZINDO/1 method.

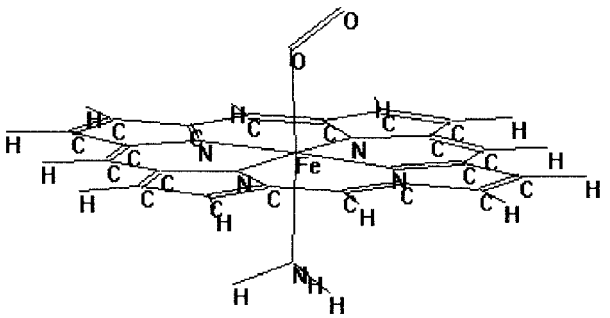
Compound	Overlap weighting factors values	Total energy [kcal/mol]	Binding energy [kcal/mol]	Isolated atomic energy [kcal/mol]	Electronic energy [kcal/mol]	Core-core interaction [kcal/mol]	Heat of formation* [kcal/mol]
NO_2		-27981.75	-627.90	-27353.84	-50006.82	22025.07	-395.79
O_2		-21265.76	-325.45	-20940.31	-31753.84	10488.08	-206.33
HS^-		-6860.36	-160.72	-6699.63	-8337.39	1477.03	-42.22
CO	1	-14435.47	-432.26	-14003.20	-21094.24	6658.78	-201.82
NO_2^-		-27904.76	-550.91	-27353.84	-49681.67	21776.92	-318.79
NO		-17252.74	-369.05	-16883.69	-25852.28	8599.54	-196.49
CN^-		-10355.85	-409.26	-9946.58	-15841.11	5485.26	-125.37
SO_2		-27510.23	-171.46	-27338.77	-46690.14	19179.91	14.06
Porphyrin-Fe-NH_3		-135349.63	-14276.63	-12073.01	-859791.48	723441.84	-9412.99
Porphyrin-Fe-NO-NH_3	1	-152645.88	-14689.19	-137956.69	-994075.57	841429.69	-9653.90
Porphyrin-Fe-CN^--NH_3		-14851.27	-14831.69	-131019.58	-964362.86	818511.59	-9684.17

Table 2. The values of energies data for the optimised molecules by MM+/(ZINDO/1) method.

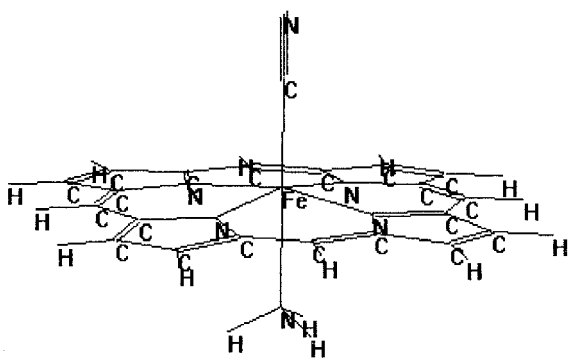
Compound	Overlap weighting factors values	Total energy [kcal/mol]	Binding energy [kcal/mol]	Isolated atomic energy [kcal/mol]	Electronic energy [kcal/mol]	Core-core interaction [kcal/mol]	Heat of formation* [kcal/mol]
Porphyrin-Fe-NH_3	1	-134892.27	-13819.26	-121073.01	-911115.25	776222.98	-8955.63
Porphyrin-Fe-SO_2-NH_3		-162263.99	-13852.22	-148411.77	-115534.60	993270.61	-8803.07
Porphyrin-Fe-CO-NH_3		-14367.77	-14291.56	-135076.21	-1041180.45	891812.68	-9197.48
Porphyrin-Fe-NO_2^--NH_3		-162852.17	-14425.32	-148426.85	-1149433.86	986581.68	-9329.57
Porphyrin-Fe-NH_3	1.162	-136774.07	-15701.06	-121073.01	-912712.28	775938.21	-10837.43
Porphyrin-Fe-O_2-NH_3		-158059.71	-16046.40	-142013.31	-1084408.44	926348.72	-11063.65
Porphyrin-Fe-NH_3	1.115	-136224.36	-15151.35	-121073.01	-912162.57	775938.21	-10287.72
Porphyrin-Fe-NO_2-NH_3		-164242.80	-148684.56	-1554243.62	-1099774.92	989305.49	-10720.20
Porphyrin-Fe-NH_3	1.135	-136457.82	-15384.82	-121073.01	-912396.04	775938.21	-10521.19
Porphyrin-Fe-HS^--NH_3		-143361.70	-15589.06	-127772.64	-1000328.77	856967.08	-10606.93

*The heat of formation is calculated by substracting atomic heats of formation from the total energy.

a)



b)



c)

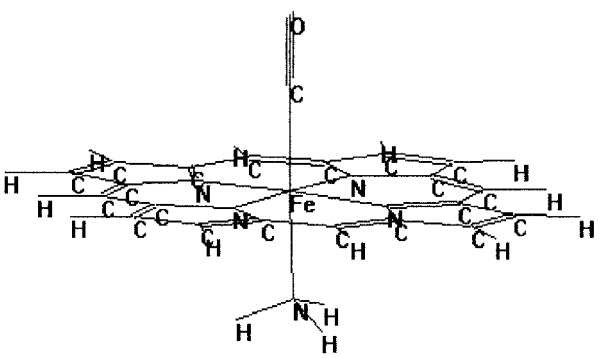


Figure 1. The structure of porphyrin–Fe-O_2-NH_3 (a) and exemplary porphyrin-Fe-X-NH_3 complexes, where X are following xenobiotics: b) CN^-, c) CO.

The structures of such complex compounds as oxygen molecule or individual xenobiotics molecules with porphyrin-Fe-NH_3 complex were optimised due to the use of ZINDO/1 method. The values of overlap weighting factors were set to 1. For the other complex structures the double geometry optimisation procedure was performed. The molecular mechanics (MM+ force field) method was applied before calculations with ZINDO/1. The overlap weighting factors values are different from 1. The following σ-σ and π-π parameters were used: 1 – for porphyrin-Fe-SO_2-NH_3, porphyrin-Fe-CO-NH_3 and porphyrin-Fe-NO_2^--NH_3 complexes. In case of porphyrin-Fe-O_2-NH_3, porphyrin-Fe-NO_2-NH_3 and porphyrin-Fe-HS^--NH_3 complexes: 1.162, 1.115 and 1.135 values were used respectively.

The energetic data (total energy, electronic energy, core-core interaction, isolated atomic energy, binding energy and heat of formation) for the optimised molecules are presented in Table 1 and Table 2. Respective calculation results for iron-ammonia porphyrin complexes (without xenobiotics and oxygen molecules) are presented in these Tables, too.

The calculated values of binding energies for oxygen, xenobiotics and porphyrin-Fe-NH_3 complex were listed in Table 3. The values of binding energy of complexes of oxygen or xenobiotic with porphyrin-Fe-NH_3 molecule were estimated by substracting the total energy found for the product of reaction minus the sum total energy found for the reactants. It was found that the binding energy of individual xenobiotic molecules with porphyrin is higher than the one of the oxygen molecule. It decides about this that the xenobiotics are preferably connected by haemoglobin then oxygen. The sequence of binding energy values for particular toxicants goes as follows:

$$SO_2 < O_2 < NO_2 < CO < NO < HS^- < NO_2^- < CN^-.$$

The positive value of binding energy for molecule of SO_2 (Table 3) indicates that the mechanism of binding this molecule with porphyrin is different from the mechanism for the other xenobiotics molecules.

Table 3. Binding energy of xenobiotics-porphyrin bond's in porphyrin-Fe-X-NH_3 molecules.

porphyrin-Fe-X-NH_3	Binding energy [kcal/mol]
SO_2	+138.5
O_2	-19.88
NO_2	-36.69
CO	-40.04
NO	-43.51
HS^-	-43.52
NO_2^-	-55.14
CN^-	-145.79

(X = SO_2, O_2, NO_2, CO, NO, HS^-, NO_2^-, CN^-)

The Figure 1 shows optimised structures of oxygen-iron-ammonia porphyrin complex (porphyrin-Fe-O_2-NH_3) and selected xenobiotic-iron-ammonia porphyrin complexes (Olszak-Humienik et al. 2000). Nonlinear location of oxygen molecule in complex porphyrin-Fe-O_2-NH_3 is characteristic. The angle value between the oxygen molecule axis and Fe-O bind is 121.46° and agrees with experimental data (Stryer 1997).

Calculated energetic data may be helpful to analyse the thermodynamics of particular biochemical reactions occur in living organisms.
The using molecular modelling method allow to estimate of binding energies of xenobiotics by iron-porhyrin complexes and better understand the connecting mechanism of these molecules.

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