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STABILIZATION OF THE ADSORPTION COMPLEXES OF BIOMOLECULES ON THE SURFACE OF PARTIALLY HYDROPHOBIZED SILICA IN AN AQUEOUS MEDIUM: A QUANTUM CHEMICAL STUDY

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The influence of the degree of hydrophobization of silica surface trimethylsilyl groups on the stability of adsorption complexes with molecules of vitamins C, B_1, B_6, E and the bile acids in an aqueous medium has been studied by quantum chemical methods using Hartree-Fock theory with the 6-31G (d) basis set and PM3 semiempirical method and SM5.42R solvation model. It was shown that the appearance of these groups on the silica surface stabilizes the adsorption complex due to interaction of the hydrophobic groups with hydrogen-carbon fragments of the vitamin and bile acid molecules. It was found that for taurocholic acid dependence of the free energy of adsorption on the degree of surface hydrophobization is stronger than for deoxycholic, cholic and glycocholic ones.

INTRODUCTION

Highly disperse amorphous silicas are distinguished for their high degree of purity, sufficient hydrolytic, thermal, radiation, and microbiologic stability [1, 2]. However, a large number of bioactive molecules in solution do not form stable complexes with the surface of hydrophilic silica. At the same time, the silica, which can be used as sorbents for the bile acid, may be a carrier for the preparation of the composite with different vitamins. This is particularly relevant in the case of acute infections such as acute cholecystitis when vomiting and diarrhea [3] leads to a significant loss of vitamins necessary to restore the function of the gall bladder. Therefore, increasing the stability of adsorption complexes of a number of biomolecules such as vitamins and bile acids to the silica surfaces used as enterosorbent and carrier of drugs in medical practice is an important practical problem. One solution to this problem may be a partial hydrophobization of the silica surface, such as trimethylsilyl (TMS) groups.

The aim of this work was to study the influence of the degree of TMS groups hydrophobization of silica surface on the stability of adsorption complexes with molecules of vitamins C, B_1, B_6, E and the bile cholic (HCA), deoxycholic (HDCA), glycocholic (HGCA) and taurocholic (HTCA) acids.

THEORETICAL BACKGROUND

Structural and electronic characteristics of biomolecules and model clusters of silica with different amount of OH and TMS groups on the surface, the interaction energies of biomolecules with the silica cluster were calculated using Hartree-Fock theory with the 6-31G (d) basis set and PM3 semiempirical method by means of the GAMESS [4] (current versions). The solvation model SM5.42R (GAMESOL program package, version 3.1 [5] based on GAMESS) were used to study the solvent effects for molecules, clusters and their complexes.

The free energy of solvation of a molecule can be calculated using its geometry determined for the gas phase

$$\Delta G_s(R) = \Delta G_{EP} + \Delta G_{CDS},$$

where $\Delta G_{EP} = \Delta G_E + \Delta G_P$ is the electrostatic component of ΔG_s; ΔG_E is the energy of deformation of charge density of a molecule resulting from the polarization of solvent; ΔG_P is the energy of interaction of a molecule with the solvent in view of its reorganization;

$$G_{CDS} = \sum_k A_k \sigma_k ,$$

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where A_k is an accessible surface of the k-th atom, σ_k is an atomic superficial tension of the k-th atom (a function of the spatial geometry of a solution and solvent parameters). ΔG_s can be determined with consideration of the geometric relaxation upon solvation

$$\Delta G_s = G(l, R_e(l)) - G(g, R_e(g)) =$$

$$= E(l, R_e(l)) + G_P(R_e(l)) + G_{CDS}(R_e(l)) - E(g, R_e(g)),$$

where indices l and g correspond to liquid and gas phases, respectively, and R_e corresponds to the system's equilibrium geometry. The solvation model SM5.42R has been described in detail elsewhere [6].

RESULTS AND DISCUSSION

Hexagonal clusters of 6 tetrahedra $SiO_{4/2}$ were chosen as structural fragments for modeling silica with OH and TMS groups on the surface (Fig. 1) using the cluster approach. The degrees of surface modification of hydrophobic TMS groups are selected according to the available experimental data [7–13]. Cluster size, i.e. the number of structural fragments, is determined by the size of the adsorbate molecules. As adsorbate molecules were selected vitamins C (ascorbic acid), B_1 (thiamine), B_6 (pyridoxine), E (α-tocopherol) (Fig. 2) and bile acids (Fig. 3). We have studied adsorption of the primary (HCA) and the secondary (HDCA) bile acids and cholates (HGCA and HTCA acids, which are compounds of cholic acid with glycine and taurine) [14].

Relative characteristics of the hydrophobic-hydrophilic balance can be considered as the ratio of all the carbon atoms of the molecule and the carbon atoms bound to the polar groups (N_C/N_C pol). There is almost a linear correlation between this ratio and the Gibbs free energy of adsorption (PM3) on a hydrophilic silica surface for water- (C, B_1, B_6) and for fat-soluble (E) vitamins (Table 1).

Table 1. Gibbs free energy of adsorption (Δ*G*ads, kJ/mol) of vitamins on the silica surface with different degrees of surface modification of hydrophobic TMS groups

Adsorbate	$N_C/N_{C\ pol}$	Degree of surface modification	$-\Delta G_{ads}$
Vitamin C	1	0	60
		10	42
		40	31
Vitamin B_1	1.5	0	37
		10	48
		40	46
Vitamin B_6	1.6	0	36
		10	60
		40	51
Vitamin E	6.3	0	–8
		10	14
		40	29

$N_C/N_{C\ pol}$ – ratio of all the carbon atoms of the molecule and the carbon atoms bound to the polar groups.

For the adsorbate molecules with large hydrophobic fragments substitution of OH groups on the surface by the TMS groups results in a decrease in the free energy of adsorption. Partial hydrophobization of silica surface leads to the stabilization of the adsorption complex with vitamins in an aqueous solution by hydrophobic interactions and in the cases where the adsorbate molecules contain hydrophobic and hydrophilic groups, where the latter can form hydrogen bonds with the OH groups of partially modified surface.

In bile acid molecules there are hydrophobic and hydrophilic sections [15], which determine the behaviour of bile acids during its contact with solid surface, for example, with the surface of an adsorbent. The bile acids that were chosen for the study are logically lined up in accordance to the changes of their hydrophobic properties.

Values of bile acids Gibbs free energies of adsorption (HF/6-31G (d)) decrease in the order HDCA >HCA >HGCA >HTCA (Table 2). The same order is observed for hydrophobic properties of the bile acids. The degree of hydrophobicity was evaluated based on the distribution constant between n-octanol and water lgPo/w, as according to the data base of

ChemDraw for HDCA 4.34–4.20, 3.36–3.04 for HCA, 2.28–1.89 for HGCA and 2.06–1.56 for HTCA, which is consistent with the energies of solvation.

Stabilization of adsorption complexes with increasing degree of substitution of the OH groups on the TMS groups results in reduction of ΔG_{ads} and ΔG_s in the adsorbed state. The lower the solvation energy of the molecules in the adsorbed state, the energetically more favorable their adsorption on the absorbent surface as opposed to their solvation in aqueous solution. With decreasing molecular hydrophobicity of bile acids dependence of the free energy of adsorption on the degree of surface modification increases. For the more hydrophilic HTCA, a stronger dependence of the free energy of adsorption on the degree of surface hydrophobization has been revealed than for the HDCA, HCA and HGCA ones. This is caused by the additional effect of surface hydrophobic groups on the structure of the hydrogen bonding of water molecules near the hydrophilic fragments of bile acid molecules [16]. The same trend was observed for the adsorption value [12].

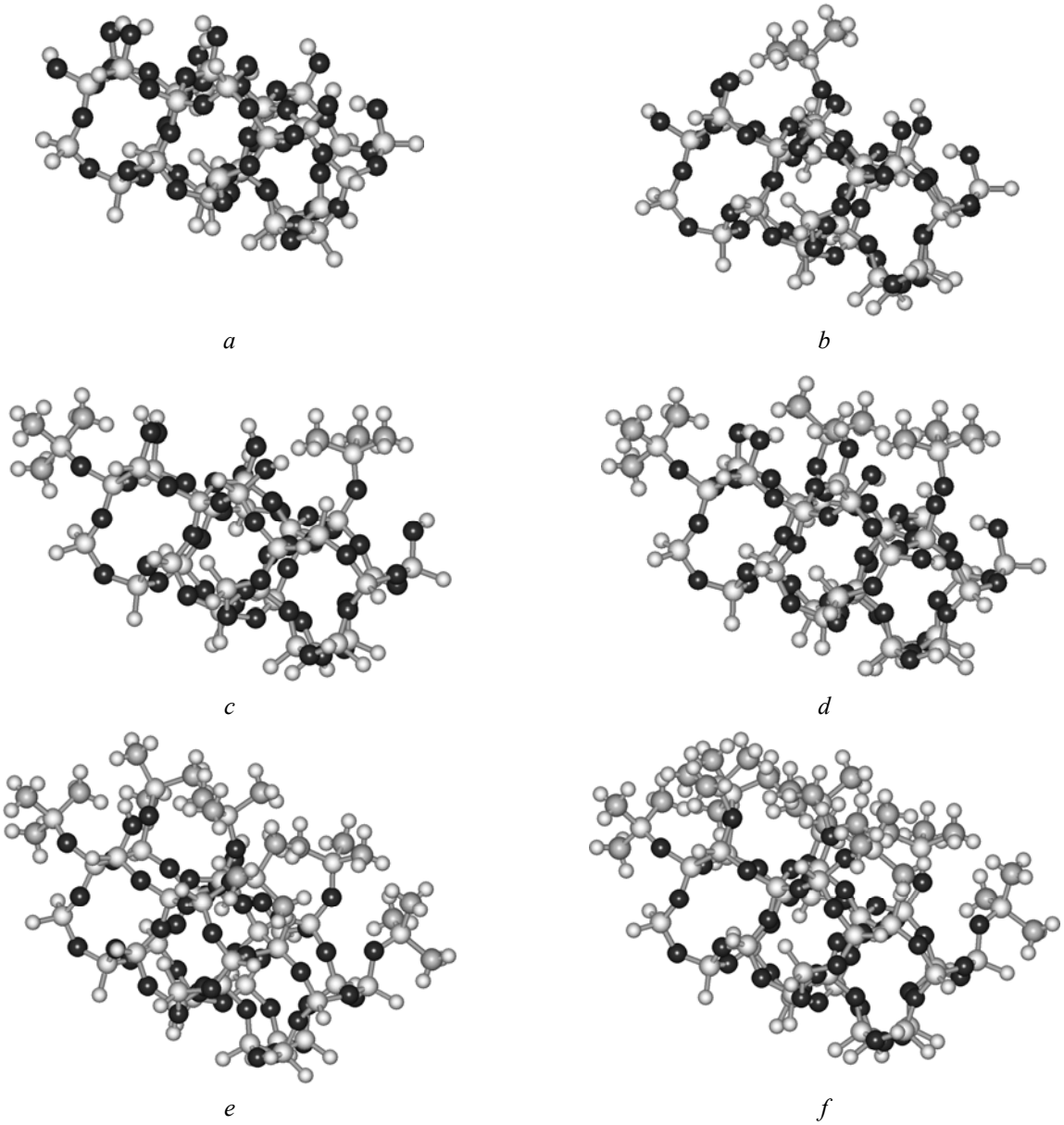
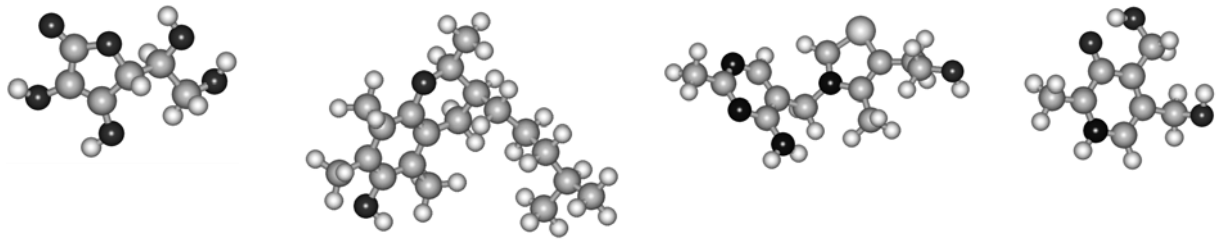


Fig. 1. The clusters of OH and TMS groups which model surface of amorphous silica at various degrees of hydrophobization: 0 *(a)*, 10 *(b)*, 25 *(c)*, 40 *(d)*, 75 *(e)*, 100 % *(f)*

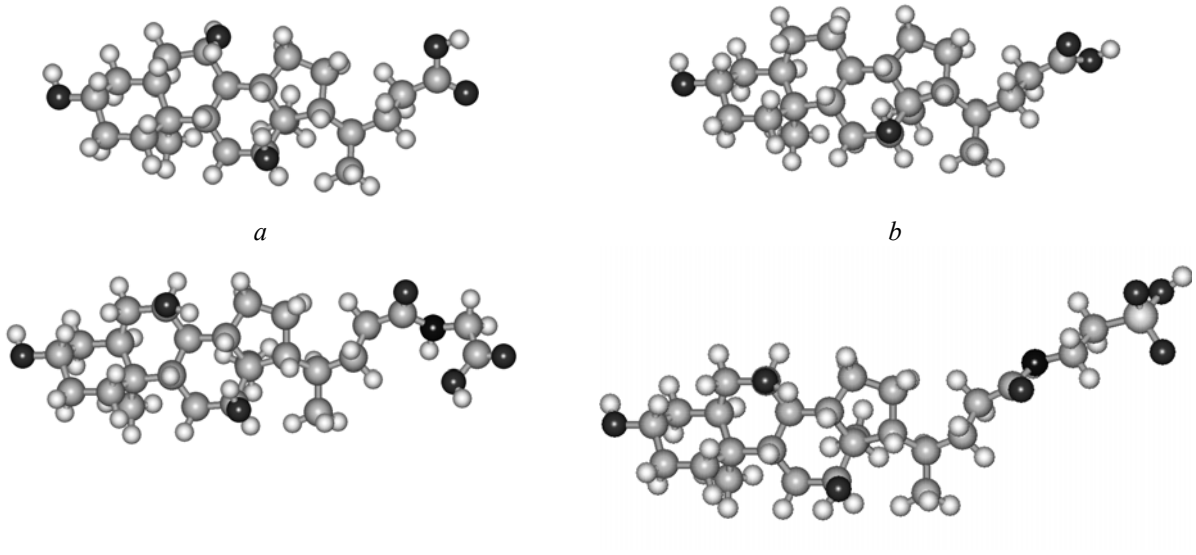
Table 2. Gibbs free energy of solvation (Δ*G*s, kJ/mol) and adsorption (Δ*G*ads, kJ/mol) of bile acids on the silica surface

Adsorbate	$-\Delta G_s$ in free state	Degree of surface modification	$-\Delta G_s$ in adsorbed state	$-\Delta G_{ads}$
Deoxycholic acid	54.6	0	54.7	53.5
		25	54.7	69.3
		40	54.8	74.8
		75	54.9	82.3
		100	55.0	95.5
Cholic acid	73.3	0	73.4	39.1
		25	73.5	47.4
		40	73.6	53.3
		75	74.1	62.7
		100	74.4	90.2
Glycocholic acid	108.2	0	108.3	34.9
		25	109.5	51.2
		40	109.6	62.4
		75	110.1	76.1
		100	110.5	88.7
Taurocholic acid	175.1	0	175.1	22.3
		25	175.7	41.1
		40	176.1	47.6
		75	176.9	58.8
		100	177.6	71.6



a *b* *c* *d*

Fig. 2. Vitamin molecules: ascorbic acid (vitamin C) *(a)*, α-tocopherol (vitamin E) *(b)*, thiamine (vitamin B_1) *(c)*, pyridoxine (vitamin B_6) *(d)*



a *b* *c* *d*

Fig. 3. Bile acids: cholic acid *(a)*, deoxycholic acid *(b)*, glycocholic acid *(c)*, taurocholic acid *(d)*

Thus, comparing the energies of adsorption of biomolecules investigated we can assume that in the gastrointestinal tract vitamins will be replaced by molecules of bile acids on the surface of partially hydrophobized silica performing the aimed function of a composite product.

CONCLUSIONS

Almost a linear correlation between the hydrophilic-hydrophobic balance of biomolecules with the Gibbs free energy of adsorption on the surface of hydrophilic silica was observed.

It was demonstrated that the appearance of trimethylsilyl groups on the silica surface stabilizes the adsorption complex due to interaction of the surface hydrophobic groups with the hydrogen-carbon fragments of the vitamin and bile acid molecules. For more hydrophilic taurocholic acid a stronger dependence of the free energy of adsorption on the degree of surface hydrophobization was revealed than for the deoxycholic, cholic and glycocholic ones. This is caused by the additional effect of surface hydrophobic groups on the structure of the hydrogen bonding of water molecules near the hydrophilic fragments of bile acid molecules.

In the gastrointestinal tract vitamins will be replaced by molecules of bile acids on the surface of partially hydrophobized silica, thus performing the aimed function of a composite product.

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Стабілізація адсорбційних комплексів біомолекул на поверхні частково гідрофобізованого кремнезему у водному середовищі: квантовохімічне дослідження

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Вивчено вплив ступеня гідрофобізації поверхні кремнезему триметилсилільними групами на стабільність адсорбційних комплексів з вітамінами С, B_1, B_6, Е і жовчними кислотами у водному середовищі методами Хартрі-Фока (базис 6-31G (d)) і РМ3 з використанням сольватаційної моделі SM5.42 R (пакет GAMESOL, версія 3.1). Доведено, що поява таких груп на поверхні кремнезему приводить до стабілізації адсорбційних комплексів завдяки взаємодії з вуглеводневими фрагментами молекул вітамінів і жовчних кислот. Для більш гідрофільної таурохолевої кислоти виявлена сильніша залежність вільної енергії адсорбції від ступеня гідрофобізації поверхні в порівнянні з іншими дослідженими жовчними кислотами.

Стабилизация адсорбционных комплексов биомолекул на поверхности частично гидрофобизованного кремнезема в водной среде: квантовохимическое исследование

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Изучено влияние степени гидрофобизации поверхности кремнезема триметилсилильными группами на стабильность адсорбционных комплексов с витаминами С, B_1, B_6, Е и желчными кислотами в водной среде методами Хартри-Фока (базис 6-31G (d)) и РМ3 с использованием сольватационной модели SM5.42R (пакет GAMESOL, версия 3.1). Показано, что появление таких групп на поверхности кремнезема приводит к стабилизации адсорбционных комплексов благодаря взаимодействию с углеводородными фрагментами молекул витаминов и желчных кислот. Для более гидрофильной таурохолевой кислоты обнаружена более сильная зависимость свободной энергии адсорбции от степени гидрофобизации поверхности по сравнению с другими исследованными желчными кислотами.