UDC 543.422:616-006+577.612+611 018.52+544.723:544.18 doi: 10.15407/hftp17.01.145

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SIMULATION OF THE INTERACTION MECHANISMS OF THE OUTER SURFACE OF ALBUMIN WITH PLATINUM(II) COMPLEXES

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The development of new approaches for evaluating the interaction of chemotherapeutic drugs with blood proteins is one of the key areas of modern research aimed at improving the effectiveness of anticancer therapy. The mechanisms of binding these drugs to proteins, as well as their impact on the spatial structure of protein molecules, remain insufficiently studied.

Platinum-based drugs, particularly cisplatin and carboplatin, are widely used in chemotherapy for cancer treatment. Their primary mechanism of action involves interaction with the DNA of tumor cells, leading to disruption of cellular functions and triggering apoptosis. However, studying their interactions with blood proteins is equally important, as these processes can significantly influence the pharmacokinetics of the drugs - their bioavailability, tissue distribution, and toxicity levels.

This study employs quantum chemical modeling to elucsdate the interaction mechanisms of platinum(II) complexes: cisplatin and carboplatin with amino acids characteristic of the hydrophilic domain of human serum albumin, a major protein component of human blood. The modeling was conducted using quantum chemistry method. The formation of stable intermolecular complexes between Pt^{2+} ions and amino acid residues: arginine, glutamine, serine, aspartic acid, cysteine, and lysine was elucidated. Various types of interactions (hydrogen bonding, coordination, and electrostatic) were analyzed and the interaction energies for each complex were calculated. Glutamine and arginine residues showed the highest affinity for Pt^{2+}, forming the most energetically favorable complexes with both drugs. Carboplatin demonstrated greater thermodynamic stability in interactions with all studied amino acids compared to cisplatin, which is attributed to the presence of oxygen-containing functional groups in its molecular structure. These findings indicate a higher propensity of carboplatin to bind to plasma proteins, which may partially explain its lower toxicity compared to cisplatin under equivalent dosing conditions.

***Keywords**: albumin, cisplatin, carboplatin, quantum chemical modeling, intermolecular interaction energies, amino acid residue*

INTRODUCTION

The development of new approaches for evaluating the interactions between chemotherapeutic agents and blood proteins is a crucial area of research aimed at enhancing the effectiveness of chemotherapy. The mechanisms of drug-protein binding and their effects on protein structure remain insufficiently explored.

Chemotherapy for cancer patients frequently involves the use of platinum-based drugs, particularly carboplatin and cisplatin. Their primary mechanism of action involves binding to the DNA of tumor cells, leading to impaired cellular function and apoptosis. However, understanding how these agents interact with proteins is equally important, as such interactions may influence their bioavailability, tissue distribution, and toxicity. In this context, infrared (IR) spectroscopy provides a unique opportunity to study structural changes in proteins induced by chemotherapeutic agents.

Currently, an important research focus is the investigation of drug–protein interaction mechanisms, as well as the potential of IR spectroscopy and other spectral-structural methods in the development of predictive diagnostic tests. For instance, study [1] explored

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the binding mechanisms of platinum-based drugs to blood proteins using mass spectrometry and spectroscopy methods. These insights are essential for pharmacokinetic analysis and the development of novel diagnostic approaches. The study also addressed non-invasive blood analysis methods that may be used to evaluate ligand-induced changes in protein structure, and it provided an overview of IR spectroscopy applications in the diagnosis of hematological diseases. Another study [2] discussed the use of FT-IR spectroscopy to identify metal-binding sites in proteins. Although article [3] focused on kidney diseases, it also examined the use of mid- and near-infrared spectroscopy for analyzing biochemical changes in blood samples. Furthermore, [4] investigated molecular networks of platinum drugs, particularly their interactions with proteins, and considered the potential of IR-based techniques to study such interactions.

The study [5] is a review focused on the application of infrared (IR) spectroscopy for the investigation of proteins. It discusses the physicochemical basis of the method, including the principles of IR radiation absorption by functional groups in protein molecules. Key spectral peaks corresponding to amide groups (Amide I and Amide II) and their significance for the analysis of protein secondary structures are described. The review provides an in-depth discussion on the use of IR spectroscopy to identify α-helices, β-sheets, β-turns, and random coil (disordered) regions within proteins. The authors also highlight the limitations of the method and explore its potential for real-time monitoring of protein structural changes during chemical reactions or under varying physicochemical conditions (pH, temperature, ionic strength).

Albumin plays a crucial role in binding and transporting numerous endogenous and exogenous substances [6], including calcium, other metals, and metal-containing drugs such as cisplatin [7] and other pharmaceutical compounds [9].

A comprehensive analysis of the binding of cisplatin to albumin, including structural aspects, is presented in study [8]. When examining the mechanisms of albumin–ligand interactions, it is also essential to address their pharmacological implications [9].

Investigating the interaction mechanisms of albumin with Pt(II) complexes is an important step toward developing methods for assessing the interaction of chemotherapeutic agents with blood proteins in cancer patients, which is particularly relevant in the context of chemotherapy for malignant tumors. One promising approach is the recording of spectral parameters from blood smears in the mid-IR range, which allows for evaluation of the extent of drug–protein binding.

To develop a predictive test for assessing the binding of platinum-based drugs to blood proteins, we used our previously developed method [10] involving the registration of absorption spectra of thin films of blood and other biological samples in the mid-IR region, particularly within the Amide I band (1600–1700 cm^{-1}), which is primarily formed by protein components of blood, the majority of which is albumin.

An express method developed by the authors of [11] allows for rapid detection of interactions between albumin and chemotherapeutic agents, including cisplatin and carboplatin. It was found that the interaction of each investigated drug with albumin leads to structural rearrangements in the protein, which are reflected in the IR spectrum as changes in the peaks within the 1620–1650 cm^{-1} region. These peaks correspond to the structural state of the α-helical and β-sheet regions of the albumin molecule.

To gain a deeper understanding of these processes, the application of quantum chemical modeling is essential, as it allows for the analysis of the electronic and structural features of albumin complexes with platinum compounds. This approach not only supports the interpretation of experimental data but also enables the prediction of novel interaction patterns, thereby contributing to the improvement of therapeutic strategies.

Such an integrated approach, combining spectroscopic methods with quantum chemical modeling, can serve as a foundation for the development of a predictive test to evaluate the efficacy and safety of chemotherapy for individual patients.

The aim of this study was to use quantum chemical modeling to determine the most probable interaction mechanisms of Pt^{2+} complexes: cisplatin $[Pt(NH_3)_2Cl_2]$ (cis-diamminedichloroplatinum(II)) and carboplatin $[PtC_6N_2O_4H_{12}]$ (cis-diamine(1,1-cyclobutanedicarboxylato)platinum(II))with amino acids located in the hydrophilic outer

region of the albumin molecule, a major protein component of the patient's blood.

MATERIALS AND METHODS

The intermolecular interaction of cisplatin and carboplatin molecules with amino acids, which are the most common in albumin, was modeled using GAMESS (US) [12]. Density Functional Theory (DFT) calculations were performed using the B3LYP functional, which is a widely employed hybrid functional in DFT. The B3LYP method combines Slater and Hartree–Fock exchange functionals with Becke's three-parameter exchange functional and the Lee–Yang–Parr correlation functional, using empirically optimized coefficients to improve accuracy in predicting molecular geometries and electronic properties [13, 14]. The Grimme dispersion correction [15, 16] within the valence approximation with the effective SBKJC core potential.

The modeling of the intermolecular interaction between a cisplatin molecule and the respective amino acid (AmAc) was considered as the following reaction:

$$[Pt(NH_3)_2Cl_2 + AmAc \rightarrow Pt(NH_3)_2Cl_2]\cdots AmAc. \quad (1)$$

The energy of intermolecular interaction was calculated by the equation [12, 17]:

$$\Delta E = E_{tot}([Pt(NH_3)_2Cl_2]\cdots AmAc) - E_{tot}([Pt(NH_3)_2Cl_2]) - E_{tot}(AmAc)], \quad (2)$$

where E_{tot} ($[Pt(NH_3)_2Cl_2]\cdots AmAc$) – the total energy of the intermolecular complex formed between the cisplatin molecule and the respective amino acid, E_{tot} ($[Pt(NH_3)_2Cl_2]$) – the total energy of the isolated cisplatin molecule, $E_{tot}(AmAc)]$ – the total energy of the isolated amino acid molecule.

A similar interaction was also considered for carboplatin, with the corresponding reaction shown below:

$$[PtC_6N_2O_4H_{12}] + AmAc \rightarrow [PtC_6N_2O_4H_{12}]\cdots AmAc. \quad (3)$$

The energy of intermolecular interaction was calculated by the equation:

$$\Delta E = E_{tot}([PtC_6N_2O_4H_{12}]\cdots AmAc) - E_{tot}([PtC_6N_2O_4H_{12}]) - E_{tot}(AmAc)], \quad (4)$$

where E_{tot} ($[PtC_6N_2O_4H_{12}]\cdots AmAc$) is the total energy of the intermolecular complex of carboplatin with the corresponding aminoacid, E_{tot} ($[PtC_6N_2O_4H_{12}]$) is the total energy of the carboplatin molecule, $E_{tot}(AmAc)]$ is the total energy of the corresponding aminoacid molecule.

In the modeling process, it was assumed that cisplatin and carboplatin interact primarily with hydrophilic amino acid residues of albumin, whereas hydrophobic residues are considered less accessible for interaction with the drug molecules.

Based on the structure of albumin [18], six amino acids were selected with functional groups most likely to interact with cisplatin and carboplatin: arginine (ARG), glutamine (GLN), lysine (LYS), aspartic acid (ASP), serine (SER), and cysteine (CYS) (Fig. 1).

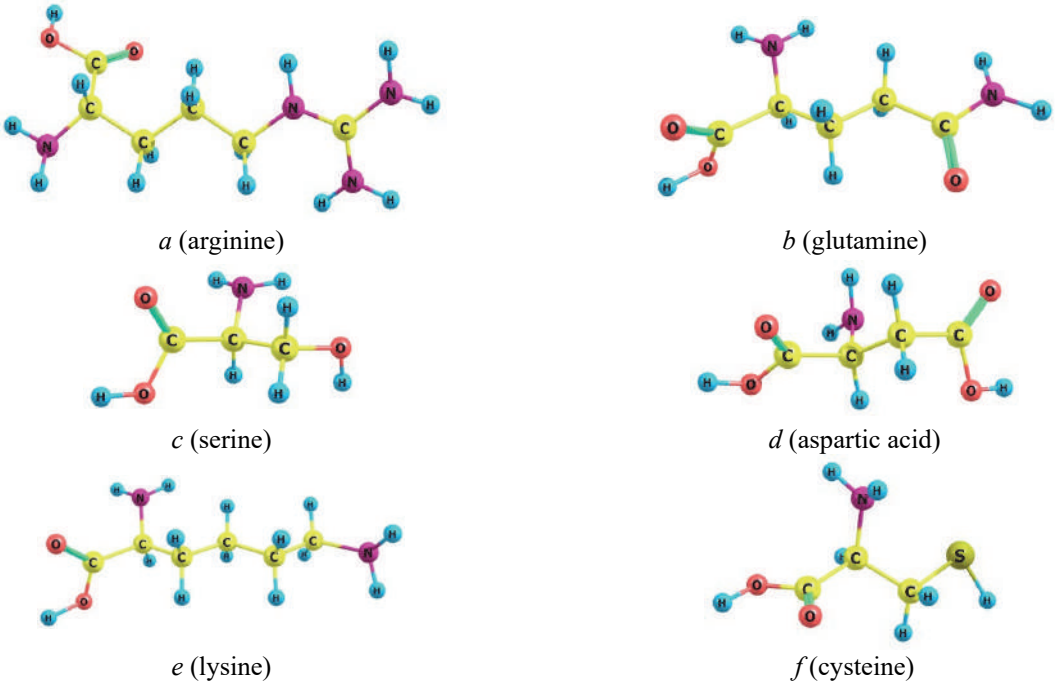
Fig. 1 shows the equilibrium structures of the amino acids used for studying interactions with cisplatin and carboplatin. It should be noted that all amino acids except arginine were modeled in their uncharged molecular forms with non-dissociated carboxyl groups. Since arginine in the protein structure under aqueous and physiological conditions exists in a positively charged state, the arginine cation with a protonated imino group ($–NH_2^+$) in the guanidinium moiety was used in the modeling (Fig. 1 *a*).

The zwitterionic forms of the selected amino acids were not considered, since it is the side chains (residues) of the corresponding α-amino acids that participate in interactions within the protein. Intermolecular complexes formed via the carboxyl and amino groups of the amino acids were also not taken into account, as these groups form peptide bonds during protein synthesis and are therefore in a chemically bound state.

The optimized structures of cisplatin and carboplatin are shown in Fig. 2. Cisplatin (cis-diamminedichloroplatinum(II)) is a square planar coordination complex with the formula cis-$[Pt(NH_3)_2Cl_2]$ (Fig. 2 *a*). The distances between the platinum atom and the ammonia ligands (NH_3) are approximately 2.12 Å, while the distances between the platinum and chlorine atoms are slightly longer, about 2.39 Å.

Carboplatin $[PtC_6N_2O_4H_{12}]$ (Fig. 1 *b*) differs from cisplatin in that it contains a bidentate dicarboxylate ligand - cyclobutane-1,1-dicarboxylate (CBDCA) - instead of two chloride ligands. Both drugs act as alkylating agents, and the chloride (in cisplatin) and CBDCA (in carboplatin) serve as leaving groups in their

respective mechanisms of action. The distances between the platinum atom and the ammonia ligands in carboplatin are nearly the same as in cisplatin, approximately 2.11 Å, whereas the distances between the platinum and the oxygen atoms of the organic ligand are slightly shorter, around 2.00 Å.



a (arginine) *b* (glutamine) *c* (serine) *d* (aspartic acid) *e* (lysine) *f* (cysteine)

Fig. 1. Equilibrium geometries of amino acids: arginine (*a*), glutamine (*b*), serine (*c*), aspartic acid (*d*), lysine (*e*), and cysteine (*f*)

a *б*

Fig. 2. Equilibrium structures of cisplatin (*a*) and carboplatin (*b*) (here and below, interatomic distances are given in Å)

The equilibrium spatial structures of the reagent and reaction product molecules were obtained by minimizing the gradient norm. The stationary character of the energy minima of the corresponding structures was confirmed by the absence of negative eigenvalues in the Hessian matrices (force constant matrices) [19].

RESULTS AND DISCUSSION

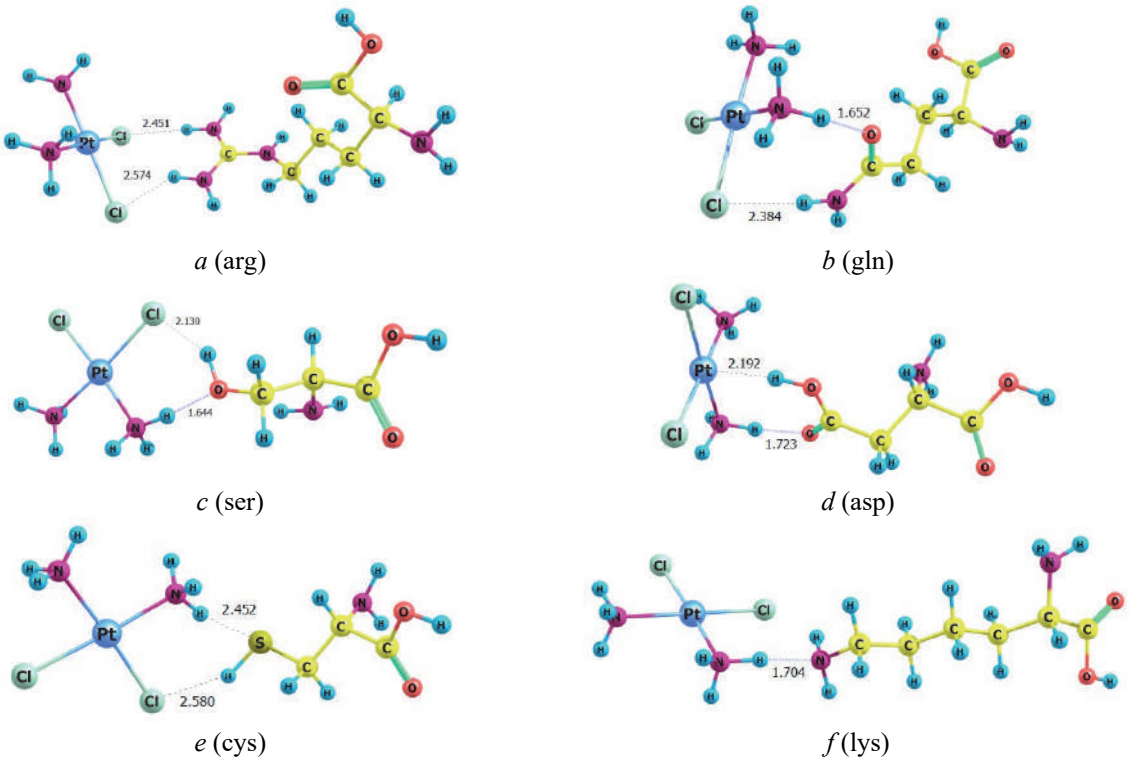
The initial stage of the study involved investigating the interaction between the cisplatin molecule and selected amino acids. To achieve this, the corresponding intermolecular complexes of cisplatin were localized (Fig. 3).

The first intermolecular complex considered was the interaction between the cisplatin molecule and the protonated form of the amino acid arginine (ARG), as described by equation (1). As a result of this interaction, an intermolecular complex was formed, illustrated in Fig. 3 *a*. A notable feature of this complex is the involvement of two chlorine atoms from cisplatin and hydrogen atoms from the protonated guanidinium group of the arginine molecule. The

distances between the hydrogen atoms of arginine and the chlorine atoms of cisplatin are 2.45 and 2.57 Å, respectively, which indicates that these are not typical hydrogen bonds, as such bonds are usually shorter than 2 Å. The calculated intermolecular interaction energy, according to equation (2), is negative, indicating the thermodynamic feasibility of the process, and amounts to –128 kJ/mol (see Table 1).

The next intermolecular complex studied was formed as a result of the interaction between cisplatin and glutamine (GLN). Its optimized structure is shown in Fig. 3 *b*, from which it is evident that the complex is stabilized by a hydrogen bond of 1.65 Å length between the oxygen atom of the carbonyl group of glutamine and a hydrogen atom from the ammine ligand of cisplatin. Additionally, this complex exhibits electrostatic interaction between a hydrogen atom from the amino group of glutamine and a chlorine atom of cisplatin (2.38 Å). This specific spatial arrangement of the reacting species in the product leads to a significant intermolecular interaction energy of –131.5 kJ/mol.

Next, the interaction of cisplatin with the amino acid serine (SER) was examined. The product of this interaction is presented in Fig. 3 *c*. It is evident that the hydroxyl group of serine plays a key role in the formation of this intermolecular complex. Specifically, the oxygen atom of the hydroxyl group forms a hydrogen bond with a hydrogen atom from the ammine ligand of cisplatin, with a bond length of 1.64 Å. Simultaneously, the hydrogen atom of the hydroxyl group is oriented toward a chlorine atom of cisplatin, with an interatomic distance of 2.13 Å. The intermolecular interaction energy in this case is approximately half those observed in the previously discussed complexes and amounts to only –69.8 kJ/mol.



a (arg) *b* (gln)

c (ser) *d* (asp)

e (cys) *f* (lys)

Fig. 3. Structures of the intermolecular complexes of cisplatin with arginine (*a*), glutamine (*b*), serine (*c*), aspartic acid (*d*), cysteine (*e*), and lysine (*f*)

The next intermolecular complex examined consisted of cisplatin and aspartic acid (ASP), as shown in Fig. 3 *d*. A distinctive feature of this interaction is that, in addition to a hydrogen bond between the oxygen atom of the carbonyl group of aspartic acid and a hydrogen atom from the NH_3 ligand of cisplatin (with a bond length of 1.72 Å), there is also a coordination bond between the hydrogen atom of the carboxyl group of aspartic acid and the platinum atom. The length of

this coordination bond is 2.19 Å, which is slightly longer than the analogous bond between the platinum atom and nitrogen atoms of the ammonia molecules (see Fig. 2 *a*). The intermolecular interaction energy associated with the formation of this complex is, as in the previous cases, negative and amounts to –69.8 kJ/mol (see Table 1).

The next stage of the study involved investigating the interaction between cisplatin and the amino acid cysteine (CYS). The product of this interaction is presented in Fig. 3e, where it can be seen that the thiol group (-SH) of cysteine plays a key role in the formation of the intermolecular complex. The structure of this complex is similar to that of the cisplatin–serine complex (Fig. 3 *c*). Specifically, the sulfur atom of the thiol group forms a dispersive interaction with a hydrogen atom of the ammonia ligand in the cisplatin molecule, with a bond length of 2.45 Å. Additionally, the hydrogen atom of the thiol group is oriented toward a chlorine atom of cisplatin, with an interatomic distance of 2.58 Å. The intermolecular interaction energy (ΔE) in this case is relatively low, amounting to only –33.4 kJ/mol.

Finally, the interaction between the cisplatin molecule and the amino acid lysine (LYS) was examined. The resulting product is shown in Fig. 3 *f*, from which it is evident that the amino group of lysine is responsible for forming the intermolecular complex. The nitrogen atom of the amino group forms a hydrogen bond with a length of 1.70 Å with a hydrogen atom of the ammonia ligand, which is coordinatively bonded to the platinum atom in the cisplatin molecule. The intermolecular interaction energy in this case is slightly higher than in the previous example and amounts to –82.4 kJ/mol.

Table 1. Calculated Intermolecular Interaction Energies of the Cisplatin Molecule with Selected Amino Acids

Amino Acid	ARG	GLN	SER	ASP	LYS	CYS
ΔE (kJ/mol)	-128.9	-131.5	-69.8	-92.6	-82.4	-33.4

According to the data presented in the table, the lowest intermolecular interaction energy is observed for the cisplatin–cysteine complex (–33.4 kJ/mol). The highest interaction energies were identified for the cisplatin–glutamine (–131.5 kJ/mol) and cisplatin–arginine (–128.9 kJ/mol) complexes, indicating the greatest likelihood of interaction between cisplatin and the glutamine and arginine residues within the albumin protein. The structures of these intermolecular complexes are shown in the Figure.

As seen in the Fig. 3, both amino acids contain amino groups that participate in the formation of the intermolecular complexes. The distances between the hydrogen atoms of the arginine molecule and the chlorine atoms of the cisplatin molecule are 2.45 and 2.57 Å, respectively. For the cisplatin–glutamine complex, this distance is slightly shorter at 2.38 Å. In addition, the latter complex features a hydrogen bond between the oxygen atom of the carbonyl group of glutamine and a hydrogen atom from the cisplatin molecule.

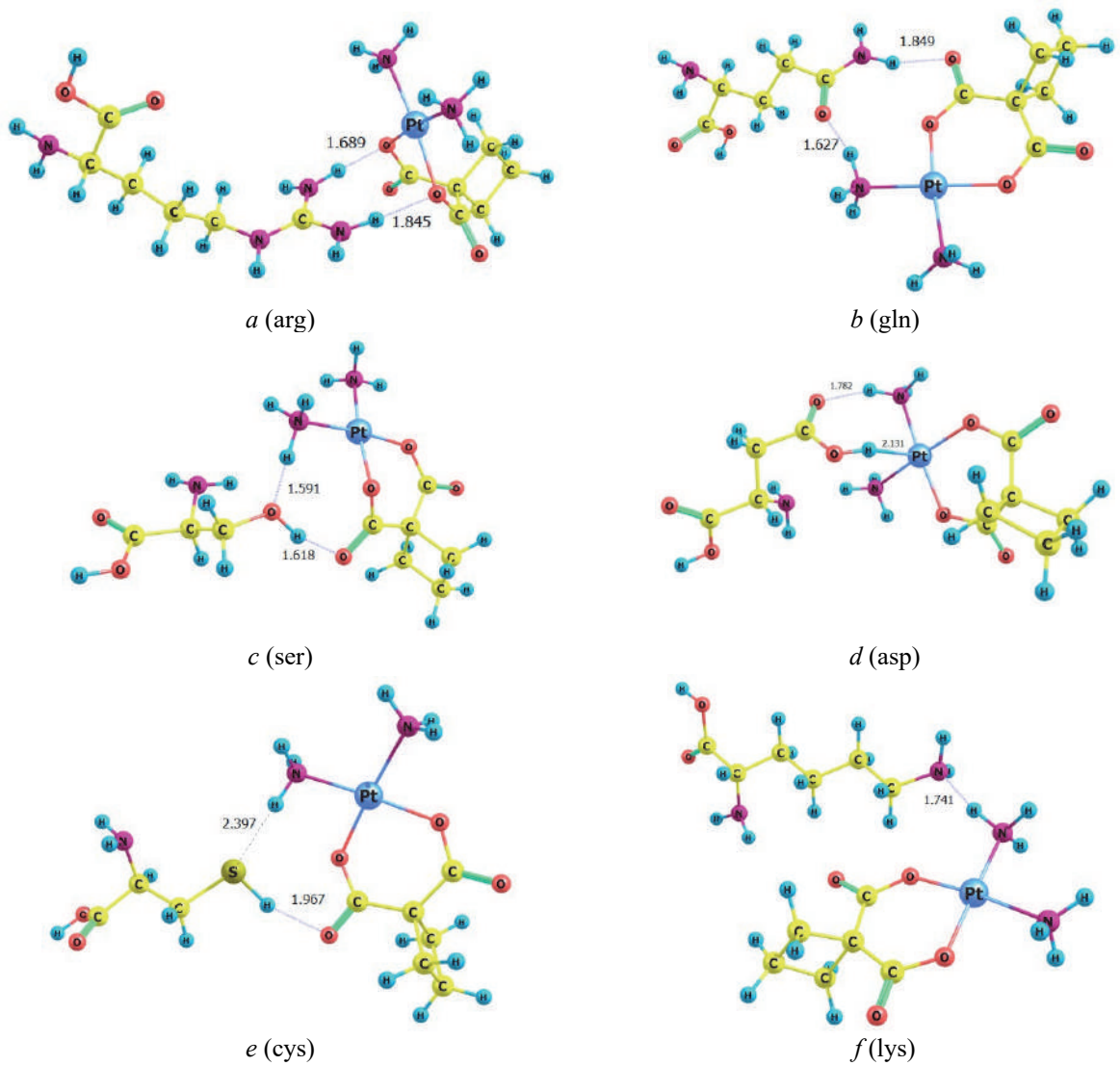
The next task was to examine the interaction of the carboplatin molecule with selected amino acids, as described by equation (3). For this purpose, the corresponding intermolecular complexes of carboplatin were also localized (Fig. 4).

The interaction product of carboplatin and the protonated form of the amino acid arginine is shown in Fig. 4 *a*. This figure illustrates that the intermolecular complex is formed through the establishment of two hydrogen bonds, with lengths of 1.69 and 1.85 Å, between the ether oxygen atoms of carboplatin and two hydrogen atoms from the protonated guanidinium moiety of arginine. The intermolecular interaction energy for this process, calculated using equation (4), is negative and amounts to –155.8 kJ/mol (Table 2), which is 26.9 kJ/mol greater in magnitude than the analogous interaction between arginine and cisplatin (see Table 1).

During the interaction of glutamine with carboplatin, an intermolecular complex is formed, as shown in Fig. 4 *b*. Similar to the corresponding interaction with cisplatin (Fig. 3 *b*), the carbonyl oxygen atom of glutamine forms a hydrogen bond with a hydrogen atom from the coordinated ammonia molecule of carboplatin, with a bond length of 1.63 Å. A second hydrogen bond is

formed between a hydrogen atom of the amino group of glutamine and the oxygen atom of the carbonyl group in the carboplatin molecule, with a length of 1.85 Å. The interaction energy (ΔE) in this case is also substantial, amounting to –136.2 kJ/mol (see Table 2).

Next, the interaction of carboplatin with the amino acid serine was studied. Analysis of the structure of the resulting intermolecular complex (Fig. 4 *c*) indicates that, similar to the previously discussed complex (Fig. 4 *b*), it is stabilized by two hydrogen bonds. The first hydrogen bond is formed between the oxygen atom of the hydroxyl group of serine and a hydrogen atom from the coordinated ammonia molecule of carboplatin, with a bond length of 1.59 Å. The second hydrogen bond involves the hydrogen atom of the same hydroxyl group of serine and the oxygen atom of the carbonyl group of carboplatin, with a bond length of 1.62 Å. Due to the presence of these hydrogen bonds, the intermolecular interaction energy for this complex is –110.0 kJ/mol.



a (arg) *b* (gln)

c (ser) *d* (asp)

e (cys) *f* (lys)

Fig. 4. Equilibrium structures of intermolecular complexes of carboplatin with arginine (*a*), glutamine (*b*), serine (*c*), aspartic acid (*d*), cysteine (*e*), and lysine (*f*)

Next, the interaction of carboplatin with aspartic acid was investigated. The resulting product of this interaction is shown in Fig. 4 *d*. A characteristic feature of this intermolecular complex, similar to the interaction with cisplatin (Fig. 3 *d*), is the presence of both a hydrogen bond

between the carbonyl oxygen atom of the carboxyl group of aspartic acid and a hydrogen atom of the ammonia ligand of carboplatin (bond length, 1.72 Å), and the formation of a coordination bond between the platinum atom and a hydrogen atom of the carboxyl group of aspartic acid, with a bond length of 2.13 Å. The intermolecular interaction energy is 30.3 kJ/mol higher than that of the analogous interaction with cisplatin, amounting to –122.9 kJ/mol.

The interaction of carboplatin with cysteine leads to the formation of an intermolecular complex shown in Fig. 4 *e*. As seen in the figure, the sulfur atom of the thiol group in cysteine is oriented toward a hydrogen atom of the ammonia ligand of carboplatin, with an interatomic distance of 2.39 Å. In addition, the hydrogen atom of the thiol group forms a hydrogen bond with the oxygen atom of the carbonyl group of carboplatin, with a bond length of 1.97 Å. In this case, the intermolecular interaction energy is relatively low, amounting to only –46.7 kJ/mol.

Finally, the interaction of carboplatin with lysine (LYS) results in the formation of an intermolecular complex (Fig. 4 *e*). As in the analogous complex with cisplatin (Fig. 3 *e*), the key role in the formation of this intermolecular complex is played by the amino group of lysine. The nitrogen atom of the amino group forms a hydrogen bond of 1.74 Å length with a hydrogen atom from the ammine ligand, which is coordinately bonded to the platinum atom in carboplatin. The ΔE energy of the intermolecular interaction is –88.2 kJ/mol.

Table 2 shows that all the values of the intermolecular interaction energy between carboplatin and amino acids, as well as the corresponding values for cisplatin and the same amino acids, are negative, indicating the thermodynamic feasibility of these processes.

Table 2. Calculated values of the intermolecular interaction energy between the carboplatin molecule and selected amino acids

Amino Acid	ARG	GLN	SER	ASP	LYS	CYS
ΔE (kJ/mol)	-155.8	-136.2	-110.0	-122.9	-88.2	-46.7

It should be noted that by comparing the values of intermolecular interaction in Tables 1 and 2, it is evident that the binding of carboplatin with the corresponding amino acids is stronger than that in the case of cisplatin. This is due to the fact that carboplatin contains functional oxygen-containing groups in its structure, which can form relatively stable intermolecular complexes with amino acid residues in proteins through hydrogen bonds.

CONCLUSIONS

According to the results of this study, it can be concluded that the simulated quantum-chemical interactions of cisplatin and carboplatin with amino acid residues on the surface of albumin molecule demonstrate their different affinity for the albumin protein. The highest binding probability for all drugs is characteristic of glutamine and arginine. At the same time, intermolecular complexes of carboplatin with all the studied amino acids are thermodynamically more stable than the corresponding complexes of cisplatin. This suggests that the concentration of free carboplatin in blood plasma will be lower due to its strong binding and more efficient transport by proteins (in particular, albumin). The obtained results are consistent with the known differences in toxicity between the drugs and can serve as a theoretical basis for explaining the lower toxic effect of carboplatin at the same dosage.

Моделювання механізмів взаємодії амінокислот зовнішньої поверхні альбуміну з комплексними сполуками платини(II)

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Розробка нових підходів до оцінювання взаємодії хіміотерапевтичних препаратів із білками крові є одним із ключових напрямів сучасних досліджень, спрямованих на підвищення ефективності протипухлинної терапії. Механізми зв'язування таких препаратів із білками, а також їхній вплив на просторову структуру білкових молекул залишаються недостатньо вивченими.

У хіміотерапії онкологічних захворювань широко застосовуються платиновмісні препарати, зокрема цисплатин і карбоплатин. Їхній основний механізм дії полягає у взаємодії з ДНК пухлинних клітин, що спричиняє порушення клітинних функцій і запускає апоптоз. Однак не менш важливим є дослідження їхньої взаємодії з білками крові, оскільки саме ці процеси можуть суттєво впливати на фармакокінетику препаратів – їхню біодоступність, розподіл у тканинах та рівень токсичності.

У даній роботі за допомогою квантовохімічного моделювання досліджено механізми взаємодії комплексних сполук платини(II): цисплатину та карбоплатину - з амінокислотами, характерними для гідрофільної частини білка альбуміну, що є компонентом крові людини. Було встановлено утворення стабільних міжмолекулярних комплексів між іонами Pt^{2+} та залишками амінокислот: аргініну, глутаміну, серину, аспарагінової кислоти, цистеїну та лізину. Проведено порівняння типів взаємодії (водневі, координаційні, електростатичні) і розраховано енергії взаємодії для кожного комплекса. Найбільшою спорідненістю до Pt^{2+} характерізуються залишки глутаміну та аргініну, що формують найміцніші комплекси з обома препаратами. Карбоплатин демонструє більшу термодинамічну стабільність у взаємодії з усіма дослідженими амінокислотами, ніж цисплатин, що обумовлено наявністю кисеньвмісних функціональних груп у його структурі. Отримані результати свідчать про більшу здатність карбоплатину до зв'язування з білками плазми крові, що, ймовірно, пояснює його нижчу токсичність у порівнянні з цисплатином за однакових умов дозування.

***Ключові слова**: альбумін, цисплатин, карбоплатин, квантовохімічне моделювання, енергія міжмолекулярної взаємодії, амінокислотний залишок*

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Received 01.10.2025, accepted 25.02.2026