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Article

Molecular Modeling of the Anti-HIV Activity Mechanism of Iodine-Containing Drugs Armenicum and FS-1

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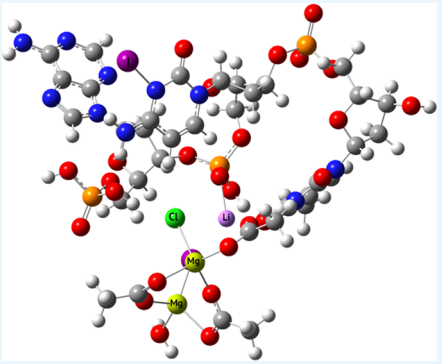
ABSTRACT: Drugs Armenicum and FS-1 are a solution of ionic nanostructured complexes of α-dextrin. In the active centers of these drugs, located inside the dextrin helix, molecular iodine has such an electronic form that minimizes toxic effects in the human body, so these drugs can be used for parenteral and oral administration. On the human lymphoblastoid cell line MT-2, the effect of the antiviral action of FS-1 against HIV-1 was established. Literature data on the results of treatment of people with HIV infection with Armenicum are presented. The mechanism of anti-HIV action of drugs Armenicum and FS-1 was proposed by the molecular modeling method. Using the DFT/B3PW91/6-31G** approach, it was shown that $LiI(Cl)I_2$ active center drugs of Armenicum and FS-1 can be segregated from the dextrin helix and can form a complex with the ACT nucleotide triplet, which is part of a specific fragment of viral DNA that binds to the active center of integrase. The formation of this complex is a key moment in the mechanism of anti-HIV drug action. Molecular iodine and lithium halide, which are part of the active complexes, inhibit the active center of the catalytic domain of the integrase. A new nucleoprotein complex is created that destroys the nucleoprotein preintegration complex (PIC) and inhibits the HIV DNA and the active center of the catalytic domain, while a new N−I bond appears in the viral DNA in the cytosine pyrimidine cycle.



INTRODUCTION

A large number of iodine-polymer complexes with a wide spectrum of antiviral activity, including HIV, are well known. There are a number of polymeric complexes of iodine with an anti-HIV effect.[1,2] For example, complexes of iodine with polyurethane polymers rapidly inactivate HIV-1 within 15−20 min.[1]

However, all known drugs containing molecular iodine are characterized by high toxicity and therefore are hardly used in medical practice for parenteral and oral administration.

Armenicum[3] and FS-1[4] contain not only complexes of molecular iodine with bioorganic ligands but also alkali metal halides. Armenicum contains lithium chloride, while FS-1 contains lithium and magnesium iodides. In active centers of these drugs, molecular iodine is in an electronic form that minimizes toxic effects in the human body, so these drugs can be used for parenteral and oral administration.[5]

The article presents the results of treatment of people with HIV infection with Armenicum.[6] In this article, the effect of antiviral action of the drug FS-1 against HIV-1 was established on the human lymphoblastoid cell line MT-2.

Armenicum and FS-1 contain ionic nanocomplexes of α-dextrin. In our earlier work, based on the X-ray diffraction analysis for iodine complexes with α-dextrin and calculation results using the HF-3-21G** approach, it became evident that the active center of Armenicum includes $LiClI_2$ and is found inside the dextrin helix.[5]

Findings of experimental and clinical investigation of iodine (^{131}J) pharmacokinetics as the constituent of "Armenicum" showed the drug's ability to bind with blood lymphocytes and erythrocytes.[7] Lymphocytes have a spheroidical form and an oval nucleus surrounded by abundant ribosomes in the cytoplasm. On the basis of their chemical nature, ribosomes are nucleoproteins. When the drug enters the blood, active centers $LiIClI_2$ are coordinated by the amide fragment of the protein component of the ribosome.

Active centers of drug FS-1 (a complex of molecular iodine with lithium halide $LiII_2$ (complex Ib, Figure 1)), a binuclear complex of magnesium- and lithium-containing molecular iodine and triiodide $[MgI_3LiII_2]^+$ (complex II, Figure 1), are located inside the α-dextrin helix. Active centers are coordinated polypeptides outside the dextrin helix.[8]

In complexes I(b), II and active center of Armenicum (complex Ia), molecular iodine exhibits acceptor properties with respect to the polypeptide and donor properties with respect to lithium halide. Probably, such a special electronic form of iodine provides low toxicity of this drug.

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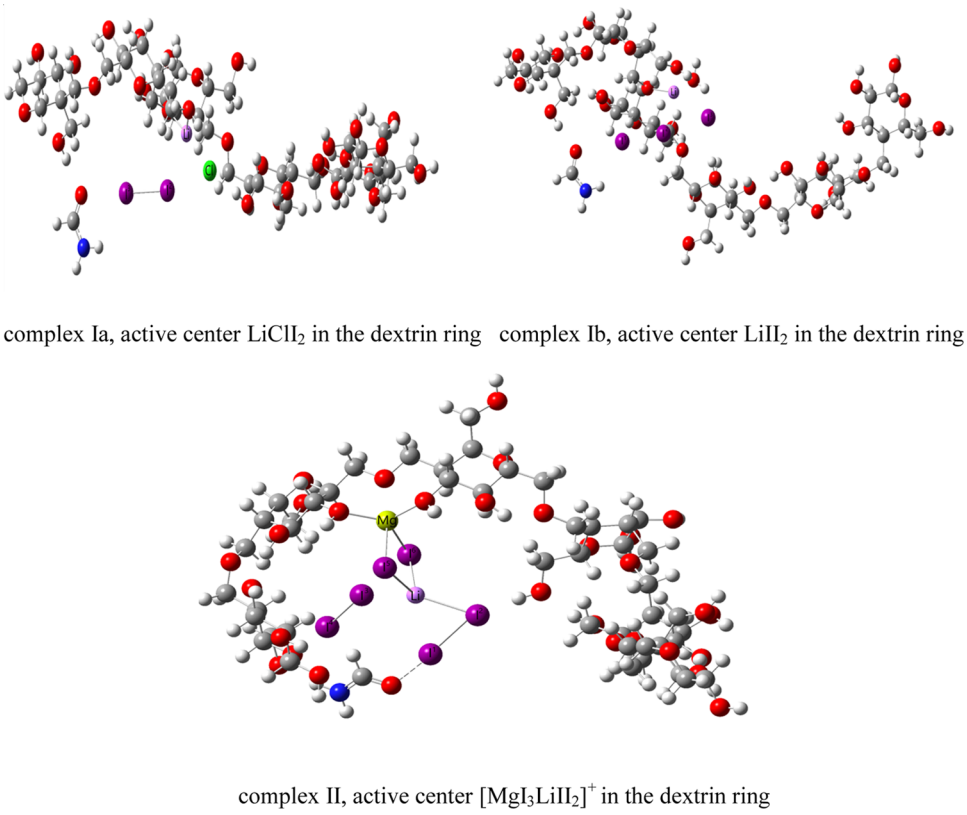

Figure 1. Active centers of drugs Armenicum ($LiClI_2$) and FS-1 ($LiII_2$, $[MgI_3LiII_2)]^+$ in the dextrin ring.

A model of the interaction of active centers of the drug FS-1 with DNA nucleotide triplets was constructed by the molecular modeling method.[8] The calculation data indicate that the active centers of the FS-1 drug can be segregated from the dextrin helix and form complexes with DNA nucleotide triplets. The interaction of active centers is selective: the active centers of FS-1 can be segregated only to certain DNA nucleotide triplets.

The HIV-1 replication cycle can be conditionally divided into two phases: (1) early phase, which begins with the recognition of the target cell by a mature virion and includes all processes leading to the integration of viral DNA into the chromosome of the infected cell and (2) late phase, beginning with the regulated expression of the integrated proviral genome and ending with budding and maturation of the virus.[9]

It is clear that it is reasonable to suppress virus replication at the early stages of its development—reverse transcription and integration—which are carried out by viral enzymes. To date, complex therapy based on the use of reverse transcriptase inhibitors and another viral enzyme, protease, is considered to be the most effective and affordable one. Unfortunately, it does not result in a complete stop of virus replication but only allows it to be suppressed to a low level, sustaining the life of HIV-infected patients.[10,11] Moreover, the use of this therapy is limited by the toxicity of many reverse transcriptase and protease inhibitors, the lack of selectivity of their action in cells, and the susceptibility of the infected person to them.

The profound therapeutic effect of integrase inhibitors is due to the integrase being one of the key participants in the viral replication cycle.[12,13] However, its inactivation does not disturb the normal metabolic processes in the cell, as integrase has no cellular equivalents.[14]

It is typical for enzymes of a class such as integrase to form very stable complexes with the viral DNA.

To be bound, the integrase must bind viral and cellular DNA simultaneously. This process proceeds in two stages and begins in the cytoplasm of the infected cell, where integrase binds the viral DNA, forming the nucleoprotein preintegration complex (PIC).[15]

Comparison of the inhibitory activity of a series of antiretroviral agents with respect to integrase and in vitro-isolated preintegration complex is presented in the work.[16]

According to the research results, it was found that inhibitors that are active against integrase may not be active against the preintegration complex (PIC). The ability to inhibit PIC was found in only three of the 20 antiretroviral agents.

In our early work, using molecular modeling, we presented the mechanism of inhibition of the active center of integrase by molecular iodine.[17]

In our next work,[18] the following system was studied by UV spectroscopy: water−nucleotide triplet AGA—LiCl(I)-I_2-α-dextrin-peptide. The LiI-I_2-α-dextrin-peptide complex is included in the structure of the drug FS-1. The theoretically obtained frequencies for LiCl(I)-I_2-α-dextrin-nucleotide complexes are a good fit to the experimental UV frequencies for this system. This indicates that when interacting with LiCl(I)-I_2-α-dextrin-peptide complexes, the AGA triplet nucleotides displace the peptide and form a new complex with iodine and lithium halides. Using the DFT/B3PW91/6-31G** approach, it was shown that the LiCl(I)-I_2-α-dextrin-nucleotide complex destroys PIC while creating a new nucleoprotein complex in which LiCl(I)-I_2 binds both the integrase active site and HIV DNA.

The interaction of integrase with the viral DNA is strictly sequence-specific, while the target is bound by the enzyme

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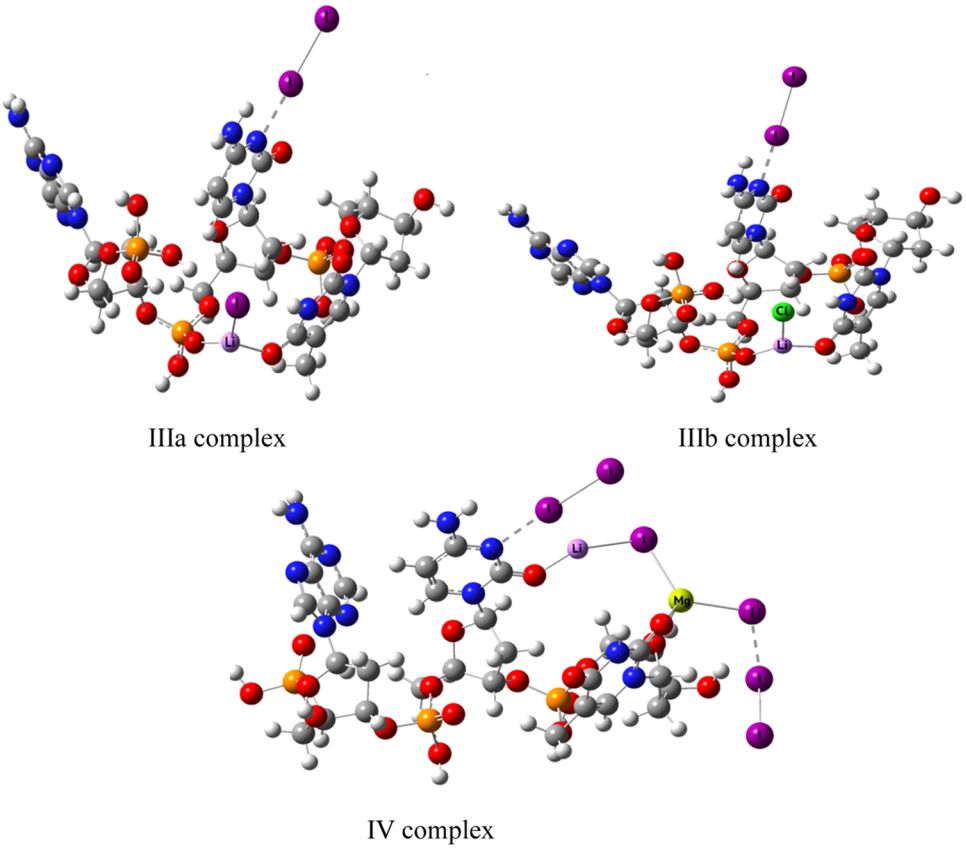

Figure 2. Structures of complexes of active centers $LiII_2$ (complex IIIa), $LiClI_2$ (complex IIIb), and $[MgI_3LiII_2]^+$ (complex IV) with the ACT nucleotide triplet.

nonspecifically. The viral DNA contains several hundred base pairs of direct repeats at both ends. At a distance of two nucleotides from the 3′ ends of each DNA strand, there is a conserved CA dinucleotide, which is often found in the composition of the ACT nucleotide triplet.[19]

In this article, using the DFT/B3PW91/6-31G** method, it have shown that the $LiClI_2$ active center of Armenicum and the $LiII_2$ active center of FS-1 can be segregated from the dextrin helix and form a complex with the ACT nucleotide triplet. Segregation of the $[MgI_3LiII_2]^+$ active center from the dextrin helix onto the ACT nucleotide triplet is energetically unfavorable.

The formation of a complex between the active centers of $LiClI_2$, $LiII_2$, and the ACT triplet, which is a part of a specific fragment of viral DNA that binds to the active catalytic center of integrase, is a key moment in the mechanism of anti-HIV action of these drugs. The formation of this complex destroys PIC and forms a new nucleoprotein complex that inhibits both viral DNA and the active center of integrase, while a new N−I bond appears in the viral DNA in the cytosine pyrimidine cycle.

RESULTS AND DISCUSSION

Active Centers of FS-1 and Armenicum Drugs and Their Interaction with the ACT Nucleotide Triplet. Active centers of Armenicum include Li ClI_2 and is located inside the dextrin helix. When the drug enters the blood, the active center $LiCI_2$ (complex Ia) is coordinated by the amide fragment of the protein component of the ribosome.[5,7]

In our recent article,[8] using experimental methods, such as chromatographic and UV spectroscopic methods, and the quantum chemical DFT/B3PW91/6-31G** approach, we have found that the drug FS-1 is a solution of ionic nanostructured complexes containing α-dextrin nanocomplexes ∼40 to 48 Å in size. Active centers, a complex of molecular iodine with lithium iodide $LiII_2$ (complex Ib) and a binuclear complex of magnesium- and lithium-containing molecular iodine and triiodide $[MgI_3LiII_2]^+$ (complex II), are located inside the dextrin helix. The polypeptide outside the dextrin helix forms a hydrogen bond with α-dextrin in complex I(a,b) and coordinates molecular iodine, which is part of complex II.

In complexes Ia,b, the lithium ion is not on the same straight line with $[ClI_2]^-$ or $[I_3]^-$: it coordinates the iodine and chlorine atom or two iodine atoms at once (Li−Cl = 2.35 Å, Li−I = 2.79 Å: complex Ia and $Li-I_1$ = 2.69 Å, $Li-I_2$ = 2.71 Å: complex Ib). These complexes can be interpreted as a complex of molecular iodine (I_2-I_3 = 2.84 Å) with a lithium ion and an iodine or chlorine ion. When molecular iodine interacts with a chlorine ion or iodine ion, I_2 acts as an acceptor, so a negative charge is transferred to I_2. Negatively charged molecular iodine becomes a donor with respect to the lithium ion. In complexes Ia,b molecular iodine is in a special electronic form that is not found in drugs containing complexes of molecular iodine with bioorganic ligands. Probably, this electronic form of iodine provides low toxicity of drugs.

Active centers of drugs Armenicum and FS-1 are protected from interaction with bioorganic ligands that are part of the cell cytoplasm, α-dextrin helix, and interaction with poly-

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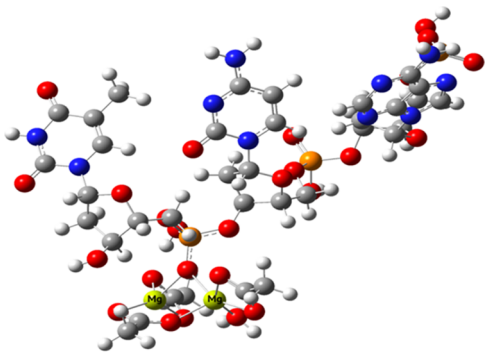
peptides or the protein component of the ribosome. Only DNA nucleotides can compete with polypeptides for complexation with molecular iodine, which is part of the active sites of FS-1.[5,8]

The molecular modeling method has shown that active centers of the drug FS-1 can be segregated from the dextrin helix and form a complex with the DNA nucleotide triplet. The DFT/B3PW91/6-31G** approach was used to calculate the stability and spatial structures of complexes of active centers with a dextrin ring (p. 751, Figures 2 and 3[8]) for drug FS-1.



Complex V ΔE=-107.5

Figure 3. Structure of complex V is formed by the ACT nucleotide triplet and the active center of the catalytic domain. Interaction energy (Δ*E*, kcal/mol) of the active center with the phosphate group of the ACT triplet.

The stabilities of $LiI(Cl)I_2$ and $[MgI_3LiII_2]^+$ complexes with nucleotide triplets ACT were calculated and the result of the calculation were compared with the stabilities of these complexes with the dextrin ring.

The calculated energies of segregation (Δ*E*) determine the difference in the stabilities of complexes $LiI(Cl)I_2$ and MgI_3LiII_2 with a dextrin ring and a nucleotide triplet.

Δ*E* is calculated as follows

$$\Delta E = (E^{tot}(\text{III or IV}) + E^{tot}(\text{dex}) + E^{tot}(\text{amid})) - (E^{tot}(\text{I or II}) + E^{tot}(\text{trip}))$$

where E^{tot}(III or IV)—total energy of complex III or IV, E^{tot}(dex)—total energy of the dextrin ring, E^{tot}(amid)—total amide energy, E^{tot}(I or II)—total energy of I or II complex, E^{tot}(trip)—total energy of the ACT triplet. In the event that Δ*E* is less than zero, the active center can be segregated from the dextrin helix into a nucleotide triplet and forms a stable complex with it. According to the calculation data, the interaction of active centers with nucleotide triplets is selective.[8]

The structures of complexes of $LiI(Cl)I_2$ and $LiII_2$ and $[MgI_3LiII_2]^+$ active centers are segregated from the dextrin ring with the ACT nucleotide triplet included in a specific viral DNA fragment that binds to the integrase active catalytic center ACT, as shows in Figure 2.

The calculation data indicate that, upon formation of the $LiI(Cl)I_2$ complex with the ACT triplet, complexes III(a,b) are the most energetically stable. In III(a,b), molecular iodine is coordinated by the nitrogen atom of the pyrimidine cycle of cytosine, and the lithium halide forms a coordination bond with the oxygen atom of the phosphate group and the oxygen atom of the pyrimidine ring of thymine (Figure 2).

The active center $LiClI_2$ can be segregated from the dextrin helix onto the ACT nucleotide triplet and form a stable complex with it (Δ*E* = −4.14 kcal/mol). The formation of complex IIIb is also possible since Δ*E* = 0.7 kcal/mol for complex IIIb indicates the possibility of establishing an equilibrium between the two structures when $LiII_2$ is either in the dextrin helix or forms a complex with the ACT triplet. The MgI_3LiII_2 active center cannot be segregated from the dextrin helix into the ACT triplet, since Δ*E* = 18.11 kcal/mol.

Inhibition of the Active Center of the Catalytic Domain Integrase by Active Centers of Drugs Armenicum ($LiClI_2$) and FS-1 ($LiII_2$). The interaction of integrase with viral DNA is strictly sequence-specific, while the target is bound by the enzyme nonspecifically. Viral DNA contains at both ends direct repeats U3, R, and U5 consisting of several hundred base pairs. At a distance of two nucleotides from the 3′ ends of each DNA strand, there is a conserved dinucleotide CA, which is often found in the composition of the ACT nucleotide triplet. Integrase as part of the preintegration complex recognizes the nucleotide sequences located at the ends of U3 and U5 and binds to them,[19] and a preintegration complex (PIC) is formed.

This paper presents a model structure of a candidate tetramer for HIV-1 integrase. The model was built in three phases using data from fluorescence anisotropy: the individual integrase domains, cross-linking data, and other biochemical data structures. It was found that the catalytic domain binds viral DNA, while all three domains bind cellular DNA.[20]

Three domains can be distinguished in the HIV integrase structure: a short N-terminal domain, a catalytic domain, and a C-terminal domain.

The crystal structure of the catalytically active core domain (50−212 residues) of HIV-1 integrase was detected at 2.5 Å resolution. The catalytic domain in the crystal forms a spherical dimer with each monomer having a form of a hemisphere. The active catalytic center is formed by three amino acid residues located close to each other in the tertiary structure of the catalytic domain. The crystal clearly shows a magnesium ion coordinated by Asp64, Asp116, and two water molecules.[21,22]

The interaction model of the catalytic active center with viral DNA was built using the molecular dynamics method. Two magnesium ions participate in the catalytic act, but due to the high conformational mobility of the catalytic fragment, they can only be bound when binding to viral DNA. In a stable binuclear complex, two magnesium ions are coordinated simultaneously by the amino acid residue Glu152, while Asp64 and Asp116 only interact with one magnesium ion.[23]

These findings were confirmed by X-ray diffraction data for the integrase structure in conjunction with viral DNA. The catalytic splitting of the phosphoester bond takes place involving two magnesium ions bound by the Glu221 amino acid residue, while each of the magnesium ion is coordinated by the Asp128 and Asp185 amino acid residues.[24]

A model of the catalytic splitting of a phosphoether bond has been constructed using molecular dynamics methods and the DFT quantum chemistry method. The transition-state structure was found, and the activation energy ∼15.4 kcal/mol was determined.[25]

At the initial stage of the reaction, a stable complex is formed by the active catalytic center of integrase and the phosphate group of viral DNA. Calculation of the structure and stability

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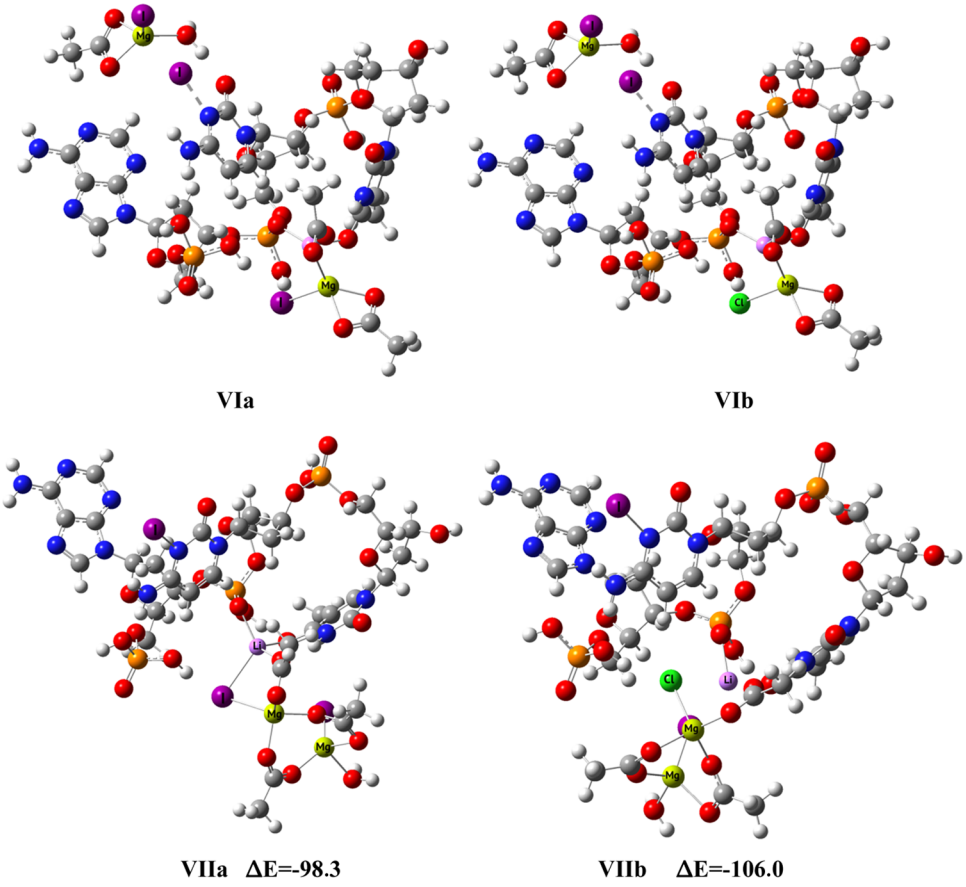

Figure 4. Structure of complexes formed by complexes IIIa,b and the active center of the catalytic domain. Interaction energy (ΔE, kcal/mol) of the active center with complexes IIIa,b. Gray balls—carbon atoms, small white balls—hydrogen, red—oxygen, dark blue—nitrogen, orange—phosphorus, violet—iodine, yellow—magnesium, pink—lithium, and green—chlorine.

of this complex is necessary to study the integrase activity inhibition mechanisms. The process of integrase inhibition becomes possible when the binding energy of the drug to the active site of the integrase is comparable to or greater than the energy of its binding to the phosphate group of viral DNA.

In our calculations, the active binuclear catalytic center structure is represented by two magnesium ions that are bound by a $COOCH_3$ group where each magnesium ion is also coordinated by a $COOCH_3$ group, and one of the ions is also water-molecule-coordinated. In the calculated structures, the hydrocarbon and amide fragments of Asp64, Asp116, and Glu152 amino acid residues are replaced by a methyl group. This simplification of the structures can probably be justified by the fact that the amide fragment is separated from carboxyl groups by several methyl groups, and therefore, has no effect on their donor activity.

Complexes IIIa,b contain two centers capable of inhibiting the active center of the catalytic domain—molecular iodine coordinated by the nitrogen atom of the pyrimidine cycle of cytosine, and lithium halide, which forms a coordination bond with the oxygen atom of the phosphate group and the oxygen atom of the thymine pyrimidine ring.

Molecular iodine exhibits acceptor properties with respect to the ACT nucleotide triplet: a negative charge is transferred to the I_2 molecule, so the iodine atom can coordinate a positively charged magnesium ion in the $Mg^{2+}AspH_2O$ complex. The second magnesium complex, $Mg^{2+}AspGlu$, can form a binuclear complex with lithium halide.

According to the calculations, it was found that the interaction of IIIa,b complexes with the active center of the catalytic domain forms VIa,b complexes in which the positively charged magnesium complex $[MgAspH_2O]^+$ is coordinated by molecular iodine, and the $Mg^{2+}AspGlu$ complex becomes part of the lithium and magnesium binuclear complex—LiI(Cl) $Mg^{2+}AspGlu$ (Figure 3).

When the $Mg^{2+}AspH_2O$ ion interacts with I_2, the I−I covalent bond breaks. An $[IMgAspH_2O]^+$ ion is formed, and in the cytosine pyrimidine cycle, a new N−I bond appears and the NH_2 group is converted into an N═H group and is protonated by a hydrogen ion.

Calculations showed that $[IMgAspH_2O]^+$ is most energetically favorable to form a binuclear complex with $Mg^{2+}AspGlu$ in VIa,b complexes and to form complexes VIIa,b. In VIIa,b complexes, the amino acid residue Asp binds two magnesium ions (Figure 4).

Interaction energies ΔE of the active center of the catalytic domain with IIIa,b complexes are shown in Figure 4. As can be seen from Figure 4, ΔE for complexes VIIa,b is comparable to the energy of interaction between the active center, the catalytic domain, and the phosphate group of the ACT nucleotide triplet.

We modeled the interaction of the viral DNA and the active center of the catalytic domain only with the key fragments of this process. Comparable ΔE values for complexes V and VIIa,b indicate that, within the model we have chosen, we can compare the inhibitory activities of drugs FS-1 and Armenicum

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with the donor activity of the phosphate group of the ACT nucleotide triplet with respect to the active center of the catalytic domain.

Thus, in the cell cytoplasm, IIIa,b complexes can compete with the phosphate group of the ACT nucleotide triplet for interaction with the active center of the catalytic domain. A new nucleoprotein complex is created that destroys PIC and inhibits viral DNA and the active center of the catalytic domain, while a new N−I bond appears in the viral DNA in the cytosine pyrimidine cycle.

All calculations were performed on the Fujitsu PRIMERGY BX 920 S1 supercomputer (Fujitsu, Tokyo, Japan) with a performance of 10.9 TFLOPS with the help of the GAUSSIAN 09 program Gaussian 09 (Gaussian, Inc., Wallingford, CT).[26]

On the human lymphoblastoid cell line MT-2, the effect of the antiviral action of FS-1 against HIV-1 was established.

EXPERIMENTAL SECTION

Detection of Reverse Transcriptase (RT) Activity. Endogenous RT activity of supernatants of HIV-1-infected MT-2 cells treated/untreated with the substances was tested by the HS-Lenti Kit-RT assay (Cavidi, Sweden). The Kit contained recombinant RT (rRT) as a standard that made possible the quantitation of the RT in the samples. The method is non-radioactive and colorimetrically detects the product of reverse transcription at 405 nm (A405). The activity was expressed as the percentage from the viral control.

Detection of Reverse Transcriptase (RT) Activity. Endogenous RT activity of supernatants of HIV-1-infected MT-2 cells treated/untreated with FS-1 drug has been tested using the HS-Lenti Kit-RT assay (Cavidi, Sweden). The Kit-RT allows quantitative reverse transcriptase (RT, pg/mL) detection because it has got a standard recombinant RT (rRT).

The source of the virus-containing material is the cell culture fluid of the H9/HTLV-IIIB line at 48−72 h after dispersal.

The method is non-radioactive and colorimetrically detects a reverse transcription product at 405 nm (A405).

Detection of the Effect of the FS-1 Drug on the Activity of Recombinant Reverse Transcriptase (rRT). The possible direct effect of the FS-1 drug exhibiting an anti-HIV-1 effect on MT-2-infected cells, as measured by the RT assay in supernatants, was further investigated using the rRT standard provided by the Cavidi kit (Sweden).

Separately, the RT activity of the rRT standard contained in the Kit was taken into account and 12 standard 2-fold dilutions were prepared. For each of these 12 dilutions, the manufacturer provides rRT concentration data in pg/well and pg/mL. Using a regression curve (standard dilutions—adsorption at A_{405}), it was possible to determine not only the presence or absence of RT but also its concentration in a given sample.

RT activity was determined in the cultural fluid of HIV-1 ME-2-infected cells at 72−96 h after infection to the medium to which the FS-1 drug was added or not (control).

Then, A_{405} was measured for the samples to which the FS-1 drug was added in different solutions and compared with the control sample (where only the incubation mixture was added without any substance). The rRT activity was expressed as the percentage compared to the control positive reaction.

Each experiment was carried out three times; each launch was performed with 6−8 parallels. The only parallels that were collected for further RT analysis were the ones differing by less than 10% in A540.

Table S1 shows a remarkable inhibition of RT activity in the supernatants of HIV-1-infected MT-2 cells treated with 2-fold dilution of FS-1. However, no inhibition is observed when the FS-1 drug is added directly to the incubation mixture to ensure reverse transcription with recombinant RT, i.e., the inhibition observed in tissue culture is not associated with a direct effect on the RT enzyme. This is clearly demonstrated by the inhibition of RT activity in supernatants of MT-2-infected cells. The purpose and mechanism of action of FS-1 should be further ascertained by searching for other viral targets, namely, integrase and/or protease.

Drug FS-1[4] is a drug developed in the Scientific Center for Anti-Infective Drug, registered in the Republic of Kazakhstan (registration certificate RK-LS-5N025967 on August 19, 2022), produced in the Scientific Center for Anti-Infective Drug according to GMP standard Certificate of the Ministry of Health of the Republic of Kazakhstan, No. 25 dated December 13.

CONCLUSIONS

On the human lymphoblastoid cell line MT-2, the effect of the antiviral action of FS-1 against HIV-1 was established.

The interaction of integrase with the HIV DNA is strictly sequence-specific. Integrase as part of the preintegration complex recognizes nucleotide sequences located at the ends of viral DNA segments and binds to them. At a distance of two nucleotides from the 3′ ends of each DNA strand is the conserved dinucleotide CA, which is found in the long terminal repeats of all retroviral integrases. In these regions, the CA dinucleotide is often found as part of the ACT triplet. The active centers $LiClI_2$ and $LiII_2$ of drugs Armenicum and FS-1, located inside the dextrin nanocomplex, can be segregated on the ACT nucleotide triplet of viral DNA.

The formation of complexes between the ACT nucleotide triplet of the viral DNA, which is part of a specific fragment of viral DNA that binds to the active center of integrase, and $LiI(Cl)I_2$ active centers (complexes IIIa,b) is a key moment in the mechanism of the anti-HIV action of Armenicum and FS-1. Molecular iodine and lithium halide, which are part of complexes IIIa,b, inhibit the active center of the catalytic domain. A new nucleoprotein complex is created that destroys PIC and inhibits viral DNA and the active center of the catalytic domain, while a new N−I bond appears in the viral DNA in the cytosine pyrimidine cycle.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.2c07720.

Experimental data proving FS-1 inhibition of HIV-1 replication in MT-2 cells expressed in the MTT infection assay and by RT and rRT activity (PDF)

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Author Contributions

A.I.I.: created drugs Armenicum and FS-1; R.A.: established on the human lymphoblastoid cell line MT-2 and the effect of the antiviral action of FS-1 against HIV-1; G.A.Y.: created the model anti-HIV activity mechanism of iodine-containing drugs Armenicum and FS-1.

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Notes

The authors declare no competing financial interest.

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