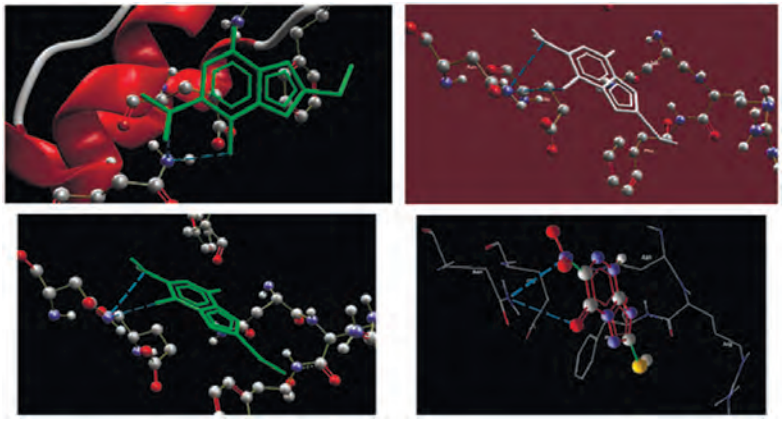


*Figure 3 – Molecular docking of TZV to Coronavirus*

In this present study quantum computational chemical calculations were carried out for 2-methylsulfanyl-6-nitro[1,2,4]triazolo[5,1-c][1,2,4]triazin-7(4H)-one molecule. The geometrical optimized bond lengths and bond angles were calculated theoretically. The binding energy for Coronavirus 2019-nCoV and TZV is -36.900 kcal/mol that shows good binding affinity between TZV and 2019-nCoV. TZV is also being used for potential application against the Coronavirus 2019-nCoV.

**REFERENCES**


1. *Sheikhi, M, Shahab, S, Filippovich, L, Khaleghian, M, Dikusar, E, Mashayekh, M* (2017) Interaction between new synthesized derivative of (E,E)-azomethines and BN(6,6-7) nanotube for medical applications: Geometry optimization, molecular structure, spectroscopic (NMR, UV/Vis, excited state), FMO, MEP and HOMO-LUMO investigations. J Mol Struct 1146:881–888.

2. *Sheikhi, M, Shahab, S, Khaleghian, M, Kumar, R.* (2018) Interaction Between New Anti-cancer Drug Syndros and CNT (6, 6-6) Nanotube for Medical Applications: Geometry Optimization, Molecular Structure, Spectroscopic (NMR, UV/Vis, Excited state), FMO, MEP and HOMO-LUMO Investigation. Appl Surf Sci 434:504–513.

3. *Sheikhi, M, Shahab, S, Khaleghian, M, Hajikolaee, F. H., Balakhanava, I., Alnajjar, R.* (2018) Adsorption Properties of the Molecule Resveratrol on CNT (8, 0-10) Nanotube: Geometry Optimization, Molecular Structure, Spectroscopic (NMR, UV/Vis, Excited State), FMO, MEP and HOMO-LUMO Investigations. J Mol Struct 1160:479–478.

4. *Sheikhi, M, Shahab, S., Alnajjar, R., Ahmadianarog, M.* (2019) Adsorption Properties of the New Anti-cancer Drug Alectinib on CNT(6,6-6) Nanotube: Geometry Optimization, Molecular Structure, Spectroscopic (NMR, UV/Vis, Excited State), FMO, MEP and HOMO-LUMO Investigations. J clust sci 30:83–96.

5. *Sheikhi, M, Shahab, S, Khaleghian, M, Ahmadianarog, M., Kumar, R.* (2019) Investigation of the Adsorption Rubraca Anticancer Drug on the CNT(4,4-8) Nanotube as a Factor of Drug Delivery: A Theoretical Study Based on DFT Method. Current Mol Med 19:473–486.


## ZIDOVUDINE – INHIBITOR FOR 2019-nCoV CORONAWIRUS M PROTEASE

## ЗИДОВУДИН - ИНГИБИТОР ДЛЯ ПРОТЕАЗЫ КОРОНАВИРУСА М 2019-nCoV


***S. Shahab[1], M. Sheikhi[2], A. Trifonova[1]***

***С. Н. Шахаб[1], М. Шейхи[2], А. Р. Трифонова[1]***

*[1]Belarusian State University, ISEI BSU, Minsk, Republic of Belarus*
*[2]Young Researchers and Elite Club, Gorgan Branch, Islamic Azad University, Gorgan, Iran siyamak.shahab@yahoo.com*

*[1]Белорусский государственный университет, МГЭИ им. А. Д. Сахарова БГУ, г. Минск, Республика Беларусь*
*[2]Клуб молодых исследователей и элиты, отделение Исламского Университета Азад, г.Горган, Исламская Республика Иран*



In order to find candidate drugs for 2019-nCoV, we have carried out a computational study to screen for effective available drug Zidovudine which may work as a strong inhibitor for the Mpro of 2019-nCoV. The interaction of the Zidovudine with the Coronavirus 2019-nCoV were performed by molecular docking studies.

Проведено полное квантово-химическое моделирование Зидовудина, способного разрушить белковую структуру коронавируса 2019-nCoV. С помощью метода докинга изучено взаимодействие между Зидувудином и белковой структурой коронавируса 2019-nCoV.

*Keywords*: Zidovudine, DFT, 2019-nCoV Coronavirus, Docking.

*Ключевые слова:* Зидовудин, ДФТ, Коронавирус 2019-nCoV, Докинг.

https://doi.org/10.46646/SAKH-2020-2-271-274

Zidovudine (1-[(2R,4S,5S)-4-azido-5-(hydroxymethyl)oxolan-2-yl]-5-methylpyrimidine-2,4-dione) is a nucleoside analogue and reverse transcriptase inhibitor used in combination with other agents in the therapy and prophylaxis of the human immunodeficiency virus (HIV) infection and the acquired immunodeficiency syndrome (AIDS) [1]. A dideoxynucleoside compound in which the 3'-hydroxy group on the sugar moiety has been replaced by an azido group. This modification prevents the formation of phosphodiester linkages which are needed for the completion of nucleic acid chains. The compound is a potent inhibitor of HIV replication, acting as a chain-terminator of viral DNA during reverse transcription. It improves immunologic function, partially reverses the HIV-induced neurological dysfunction, and improves certain other clinical abnormalities associated with AIDS. Its principal toxic effect is dose-dependent suppression of bone marrow, resulting in anemia and leukopenia.

In 2019, a novel Coronavirus 2019-nCoV was found to cause Severe Acute Respiratory symptoms and rapid pandemic in China, France, United States of America, Belgium, Germany, Italy, Japan, India, Russia. In order to find candidate drugs for 2019-nCoV, we have carried out a computational study to screen for effective available drug Zidovudine which may work as inhibitor for the Mpro of 2019-nCoV [2].

The quantum chemical calculations have performed for the most stable conformation and optimized the using the Density Functional Theory (DFT/B3LYP) method with MidiX basis set by the Gaussian 09W program package on a Pentium IV/4.28 GHz personal computer.

The theoretical molecular structure of the Zidovudine in the ground state was optimized by B3LYP/MidiX level of theory (Fig. 1).

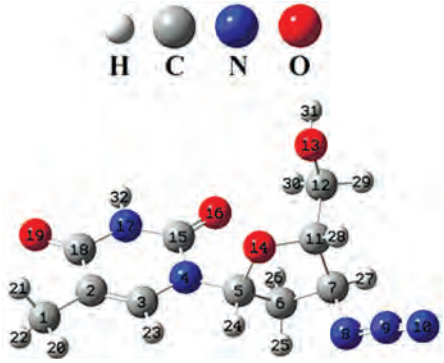



*Figure 1 – Optimized structure of the Zidovudine by B3LYP/MidiX method*

The MEP Map of the optimized molecule Zidovudine was calculated at B3LYP/MidiX level of theory and given in Fig. 2. The electrostatic potential of the molecule is related to the electronegativity and the partial charges on the different atoms [3]. The MEP map indicates the molecular shape, size, dipole moment and relative polarity of the molecule. The electrophilic and nucleophilic reactive sites of the molecular structure are also identified with the MEP map. The difference of the electrostatic potential at the surface is shown by different colors. The sites of electron rich, partially negative charge, slightly electron rich regions, positive charge or electron poor and neutral sites in the MEP maps are red, orange, yellow, blue, and green colors, respectively. In MEP map of Zidovudine, the oxygen atom (O13) of hydroxyl group is found to be electron rich site (red color), which is due to the lone pairs of oxygen atoms. Also, the O16 and O19 atoms in the carbonyl groups with orange color are shown partially negative charge site. Therefore, the O13, O16 and O19 are nucleophilic regions. The H31 atom in the hydroxyl group and the H32 atom in the amide group with blue color is shown electron poor and electrophilic sites. The regions with green color in the molecule Zidovudine show the sites with zero potential and neutral regions. The electrophilic and nucleophilic regions of the Zidovudine illustrate the interaction with other molecules in chemical reactions.

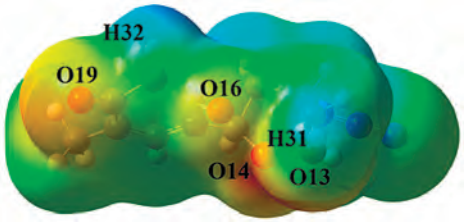



*Figure 2 – MEP map of the molecule ZIDOVUDINE calculated using the B3LYP/MidiX level of theory*

The molecular docking analysis is an important tool for drug design and molecular structural biology [4]. The aim of molecular docking analysis is to predict the preferred binding location, affinity and activity of drug molecules and their protein targets. In the present work, the molecular docking studies of the Zidovudine molecule was performed against Coronavirus 2019-nCoV using HyperChem Professional 08, PyMOL and Molegro Molecular Viewer software programs. Molecular basis of interactions between Coronavirus 2019-nCoV molecule and the Zidovudine can be understood with the help of docking analysis and interactions as observed in Fig. 3. We found 5 positions in which there is a strong interaction between the drug molecule and the virus that leads to the destruction of the protein structure. The best position is presented here. The binding energy for Coronavirus 2019-nCoV and Zidovudine is -47.206 kcal/mol in which shows good binding affinity between the Zidovudine and 2019-nCoV. As seen from Fig. 4a eleven hydrogen bonding formation between reduces Gln 110 bonded with N and O atoms, Thr 111 bonded with N atom, Asp 295 bonded with N and O atoms, Thr 292 bonded with N and O atoms, Gln 127 bonded with O atom, Ser 158 bonded with N atom, Asn bonded with N and N atoms, Asp 153 bonded with N atom of the Zidovudine are observed. Also, Asp 153, Ser 158, Asn 151, Thr 292, Thr 111 and Phe 294 are contact with negatively and positively charged in the Zidovudine binding environment (Fig. 4b). it was found that the ligand Zidovudine shows the best affinity towards of the 2019-nCoV compared to other known antiviral drugs: Colistin, Valrubicin, Icatibant, Bepotastine, Epirubicin, Epoprostenol, Vapreotide, Aprepitant in which the binding energy for Coronavirus 2019-nCoV and them is -11.206, -10.934, -9.607, -10.273, -9.091, 10.582, -9.892 and -11.376 kcal/mol that shows weak binding affinity between them and 2019-nCoV [5]. Molecular docking energy data for mentioned ligand and hydrogen bonding are presented in the Table 1.

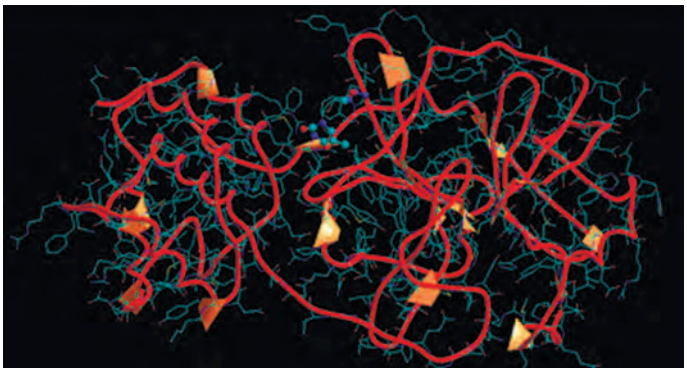
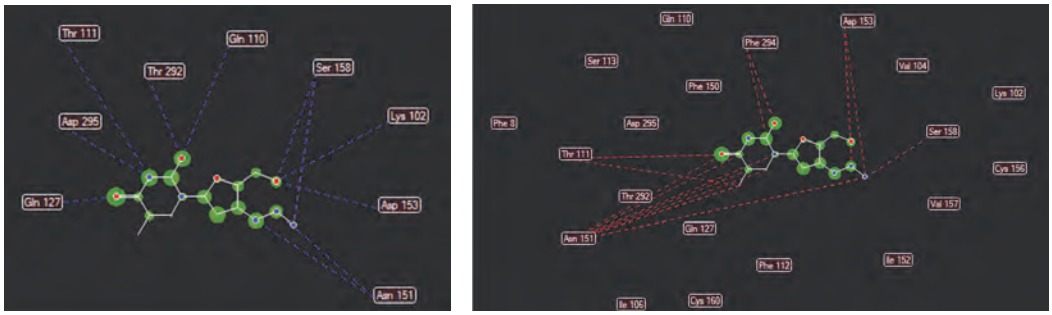


*Figure 3 – Interaction of Zidovudine with Coronavirus 2019-nCoV*




*(a)* *(b)*

*Figure 4(**a**) – Hydrogen bonds between the Zidovudine and Coronavirus 2019-nCoV.*
*Figure 4(b) – Steric interactions between the Zidovudine and Coronavirus 2019-nCoV*

*Table – Molecular docking energy data for mentioned ligand and Hydrogen bonding*

| Protein | Bonded residues | ID | Hydrogen bond | Bond distance (Å) | Binding energy (kcal/mol) |
|---|---|---|---|---|---|
| 2019-nCoV | Asn | 151 | 1 | 1.5028 | -9.9445 |
| 2019-nCoV | Asn | 151 | 1 | 1.6358 | -8.5003 |
| 2019-nCoV | Asp | 153 | 1 | 1.9311 | -7.4588 |
| 2019-nCoV | Lys | 102 | 1 | 1.4703 | -9.2834 |
| 2019-nCoV | Ser | 158 | 1 | 1.5554 | -8.5676 |
| 2019-nCoV | Ser | 158 | 1 | 1.9901 | -6.0301 |
| 2019-nCoV | Gln | 110 | 1 | 2.1143 | -8.1254 |
| 2019-nCoV | Thr | 111 | 1 | 2.3487 | -9.3392 |
| 2019-nCoV | Asp | 295 | 1 | 2.7106 | -9.6259 |
| 2019-nCoV | Gln | 127 | 1 | 1.8471 | -8.4221 |
| 2019-nCoV | Thr | 292 | 1 | 2.4508 | -6.4368 |

**REFERENCES**

1. *Sheikhi, M., Shahab, S., Filippovich, L., Khaleghian M., Dikusar E., Mashayekhi, M.* (2017) Interaction between new synthesized derivative of (E,E)-azomethines and BN(6,6-7) nanotube for medical applications: Geometry optimization, molecular structure, spectroscopic (NMR, UV/Vis, excited state), FMO, MEP and HOMO-LUMO investigations. J Mol Struct 1146:881–888.

2. *Sheikhi, M., Shahab, S., Khaleghian, M., Kumar, R.* (2018) Interaction Between New Anti-cancer Drug Syndros and CNT (6, 6-6) Nanotube for Medical Applications: Geometry Optimization, Molecular Structure, Spectroscopic (NMR, UV/Vis, Excited state), FMO, MEP and HOMO-LUMO Investigation. Appl Surf Sci 434:504–513.

3. *Sheikhi, M., Shahab, S., Khaleghian, M., Hajikolaee, FH., Balakhanava, I., Alnajjar, R.* (2018) Adsorption Properties of the Molecule Resveratrol on CNT (8, 0-10) Nanotube: Geometry Optimization, Molecular Structure, Spectroscopic (NMR, UV/Vis, Excited State), FMO, MEP and HOMO-LUMO Investigations. J Mol Struct 1160:479–478.

4. *Sheikhi, M., Shahab, S., Alnajjar, R., Ahmadianarog, M.* (2019) Adsorption Properties of the New Anti-cancer Drug Alectinib on CNT(6,6-6) Nanotube: Geometry Optimization, Molecular Structure, Spectroscopic (NMR, UV/Vis, Excited State), FMO, MEP and HOMO-LUMO Investigations. J clust sci 30:83–96.

5. *Sheiki, M., Shahab, S., Khaleghian, M., Ahmadianarog, M., Kumar, R.* (2019) Investigation of the Adsorption Rubraca Anticancer Drug on the CNT(4,4-8) Nanotube as a Factor of Drug Delivery: A Theoretical Study Based on DFT Method. Current Mol Med 19:473–486.

# ОЦЕНКА УРОВНЯ ЭКСКРЕЦИИ ГОРМОНОВ В ПЕРИФЕРИЧЕСКОЙ КРОВИ У ПАЦИЕНТОК, СТРАДАЮЩИХ РАКОМ МОЛОЧНОЙ ЖЕЛЕЗЫ

# ASSESSMENT OF THE LEVEL OF HORMONE EXCRETION IN PERIPHERAL BLOOD AMONG PATIENTS WITH BREAST CANCER

***К. В. Юрченкова[1], Р. М. Смолякова[1], Е. М. Шпадарук[1], И. Н. Андреева[2]***

***K. Yurchenkova[1], R. Smolyakova[1], K. Shpadaruk[1], I. Andreeva[2]***

*[1]Белорусский государственный университет, МГЭИ им. А. Д. Сахарова БГУ, г. Минск, Республика Беларусь*
*[2]Институт генетики и цитологии НАН Беларуси, г. Минск, Республика Беларусь*
*karinayurchenkova@gmail.com*

*[1]Belarusian State University, ISEI BSU, Minsk, Republic of Belarus*
*[2]Institute of Genetics and Cytology, National Academy of Sciences of Belarus, Minsk, Republic of Belarus*

Результаты радиоиммунного исследования позволили обнаружить у пациенток активного репродуктивного периода снижение содержания в крови эстрадиола и прогестерона. У пациенток климактерического и постменопаузального периодов выявлен гормональный дисбаланс, характеризующийся более выраженным нарастанием уровня эстрадиола и прогестерона в крови на фоне снижения концентрации фолликулостимулирующего и лютеинизирующего гормонов.

The results of the radioimmune study revealed a decrease in the content of blood of estradiol and progesterone among patients of the active reproductive period. A hormonal imbalance, characterized by more clear increase in the level of estradiol and progesterone in the blood against the background decrease of follicle stimulating and luteinizing hormones was detected among patients with menopausal and postmenopausal periods.

*Ключевые слова:* рак молочной железы, гормоны, радиоиммунный анализ.

*Key words:* breast cancer, hormones, radioimmune study.

https://doi.org/10.46646/SAKH-2020-2-274-277

Рак молочной железы является одним из самых распространенных злокачественных новообразований среди женщин не только на постсоветском пространстве, но и во всем мире. Заболеваемость раком молочной железы зависит от ряда факторов: возраста пациенток и их овариально-менструальной функции, наступления менархе, первых родов. Изменение гормонального фона также является немаловажным фактором малигнизации клеток, на который стоит обратить внимание.

Регуляция состояния и функционирования молочных желез у женщин различного репродуктивного возраста осуществляется с помощью различных гормонов, продуцируемых железами внутренней секреции (яичники,