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Molecular Docking of Several Medicines with Covid-19 Protein

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A B S T R A C T

The docking studies have been used to predict the protein drugs. Utilizing the molecular operating environment (MOE) software, parameterization and docking simulations for medicines with receptors were performed. Thirty drugs might theoretically bind with the COVID-19 protein on a receptor (PDB ID: 6wzo). To identify a potential anti-COVID molecule, several drugs have been virtually examined. The medicines have bound with the covid-19 protein at the molecular level (6wzo).

Introduction

Understanding the mechanisms of action of novel pharmacological candidates is necessary for the development of new medications, which emphasizes the need of clarifying the underlying molecular and biochemical mechanisms. The conceptual theoretical quantum chemistry has been utilized extensively in research to link the reactivity of various chemicals with biological activity [1-3]. By taking into account the Fukui functions to extract data on the reactivity of peptides that may be used in the process of building new pharmaceutical medications, it will be vitally possible to comprehend the chemical reactivity features of molecules [4,5]. Chemo-informatics is a significant area of study that covers several methods for the management of chemical data and may be viewed as an excellent tool for the development of new drugs in the pharmaceutical sector [6,7].

The bulk of chemo-informatics-based applications aims to predict the features of molecular systems based on a background constructed over their related chemical structures and to show such predictions computationally by taking into account a close connection of biological and organic data [8,9]. Quantum chemical calculations help determine the physical characteristics, docking [10], and comprehending the mechanism of reactions, even though numerous experimental chemical and physical phenomena of medications or compounds are examined [11].

The examination of compounds' capacity to function as electron acceptors with recognized charge transfer (CT) donors aim to better understand the mechanism of contact between compounds and biological systems and, in particular, the role of charge transfer forces in such interactions as heterocyclic compounds [12]. The possibility of charge transfer binding of macromolecule interactions was investigated through the study of charge transfer formation with known charge transfer donors [13,14]. Rumors concerning the frequency of a novel, unidentified pneumonia-like sickness in Wuhan, China, started to circulate in December 2019. The world health organization (WHO) then announced a novel coronavirus as the cause of clusters of the new ailment on February 11, 2020. Acute Respiratory Syndrome with Severity, (WHO) selected Coronavirus 2 or COVID-19 as the term for the illness brought on by the new coronavirus [15,16].

One of the most crucial methods for studying a drug's action through computational structure-based drug discovery is computer-aided drug discovery. Through the application of physics-based equations to determine the binding affinities of the compounds under test, various software examined the interaction between the chemicals and the binding site [17,18]. COVID-19 has flu-like symptoms that can range from minor discomfort to serious lung damage and multi-organ failure, which ultimately results in death. Drug repurposing, also known as drug reprofiling, is an exciting area of drug discovery that aims to find fresh therapeutic applications for previously investigated medications [19,20].

To successfully repurpose these medications for the possible treatment of COVID-19 infection, computational research combining molecular docking and dynamics modeling approved members of pharmaceuticals against the receptor-binding domain (RBD) of the spike protein of SARS-CoV-2 or COVID-19 [21-23]. One of the organs that SARS-CoV-2 targets is the kidney, which is linked to increased mortality in the clinical environment and aids in the development of chronic renal disease. Using network pharmacology and molecular docking, it is possible to understand the processes and interactions between quercetin and the SARS-CoV-2 targeted proteins [24-26].

A breakthrough in the treatment of malignancies and genetic illnesses may result from research on the interactions between drugs and DNA-binding proteins (DBPs). For the prediction of protein-drug interactions, network-based approaches are frequently utilized, and network analysis can reveal numerous undiscovered associations. The drug-binding site trimmers' clusters share certain physicochemical characteristics with them [27,28].

Molecular Docking:

The protein data bank (PDB) was used to download the protein's structural information. Co-crystallized ligands, ions, and water molecules were all eliminated as hetero-atoms. In the instance of a protein with several binding sites, the co-crystallized ligands and molecules were eliminated depending on the binding site. Once the medications had been reduced to a minimum, the protein and drugs had been reduced as well, until the (S) score had been reached within a range that was acceptable for all binding sites.

The COVID-19 protein docking simulations used the best possible structures (ID: 6wzo). The molecular operational environment (MOE) software package (version: 2015.10) is used in all docking computations. Protein and small molecule structures have been generated using the (MOE). The 2D structures of the compounds were initially constructed, converted to 3D structures, and then energetically minimized using the (MOE) program.

Intel(R) Core I7, 8th Generation, running in 64-bit mode, was the CPU utilized for docking. Docking was implemented using RAM (16) and Windows (11) as operating systems.

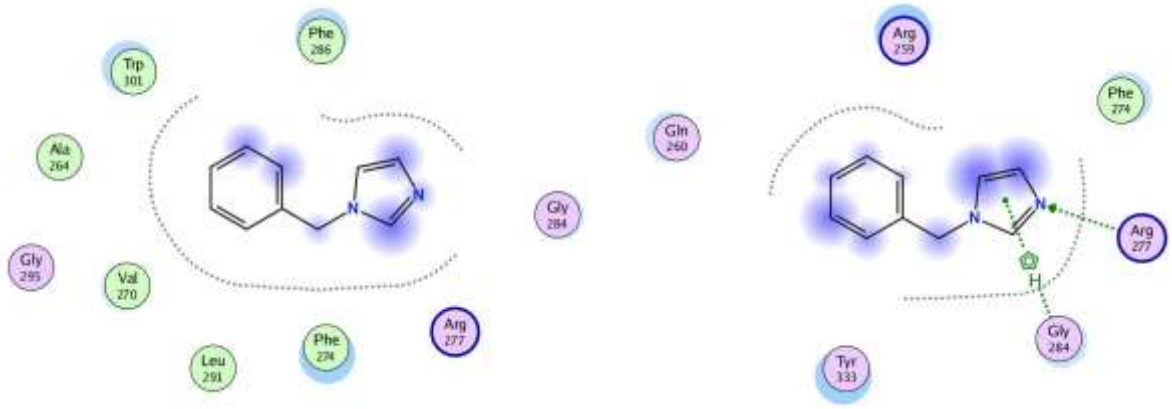
Results and Discussion:

Docking against the (6wzo) receptor was done for all of the generated complexes. To make hydrogen bonds with protein residues, the ligand backbone, which contains nitrogen and oxygen atoms along with functional groups like OH-, NH-, and C=O on the side chains, played a role. Table (1) lists the critical residues identified by docking studies for interactions involving both protein structures and ligands.

Table 1. Drug and complex docking scores against the protein (6wzo)

No.	(Drug+6wzo)	Docking Score (kcal/mol)	
		more stable	less stable
1	1-Benzylimidazole	-4.62058	-4.13426
2	2-Aminobenzoic acid	-4.00033	-3.84177
3	3-Aminobenzoic acid	-4.05923	-3.77104
4	4-Aminobenzoic acid	-3.89810	-3.73140
5	acetic acid	-3.38802	-3.27498
6	Atropine	-5.53359	-5.27110
7	Benzoic acid	-4.08314	-3.70364
8	Citric acid	-4.69496	-4.29966
9	Maleic hydrazide	-4.27031	-3.96534
10	Metoprolol	-6.29712	-5.42620
11	N-Methylaniline	-3.87842	-3.56907
12	Thiabendazole	-4.88462	-4.28127
13	Carazolol	-5.66377	-5.30586
14	Chlorpromazine	-5.69682	-5.33340
15	Ciprofloxacin	-6.06472	-5.42921
16	Diphenhydramine	-5.24180	-5.00373
17	(Gly-Gly-Gly-Gly)	-5.15778	-4.97440

Figures (1-10) depict in three dimensions how different medicines interact with proteins through molecular docking (6wzo). Also, shows some of the medication docked with the (6wzo) interaction in (3D) at (A): more stable and (B): less stable



(A): more stable (B): Less stable

Figure 1: Expected interactions between ligands and receptors for (1-Benzylimidazole)

Clear illustrations of hydrogen bonding analysis of compounds containing proteins are provided as shown in Figure (1). In the five-member ring (imidazol) derivatives, the (arginine 277) structure was directly coupled

with the ion pair at the nitrogen atom. Whereas the aromatic ring of the imidazole molecule was linked to the (Gly 284).

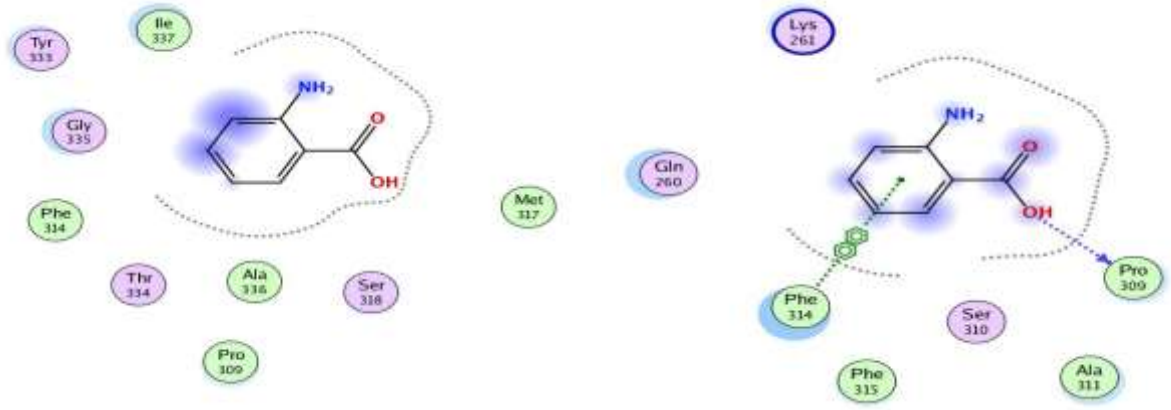


Figure 2: Expected interactions between ligands and receptors for (2-Aminobenzoic acid)

In the hydroxy structure in Figure (2), the (Pro 309) protein was connected to the ion pair at the oxygen atom. As opposed to this, the benzene ring's aromatic ring was bound to the (Phe 314) by (π-π) bond.

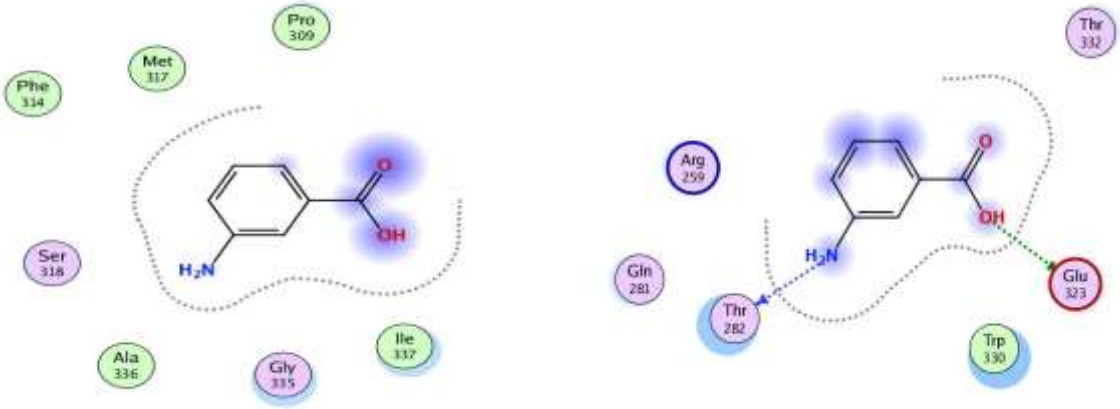


Figure 3: Expected interactions between ligands and receptors for (3-Aminobenzoic acid)

Figure (3) depicts the process by which a compound binds to the active site of a protein to create a direct hydrogen bond. the backbone NH2 and (NH2..OH or NH2..H) of (THr282) form a hydrogen bond.

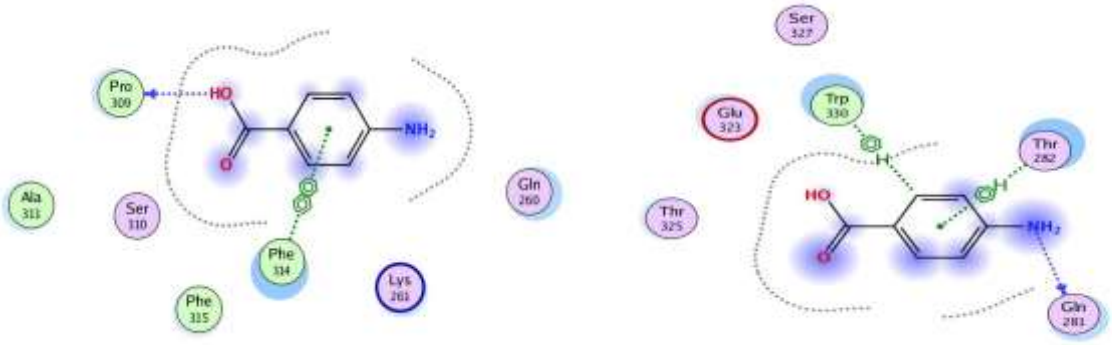


Figure 4: Expected interactions between ligands and receptors for (4-Aminobenzoic acid)

Between the aromatic ring of the benzene ring and (Thr 282) and (Trp 330), respectively, at least two hydrogen bonds were created. Furthermore related was a single amino group (NH2) with (Gln 281) as shown in figure (4).

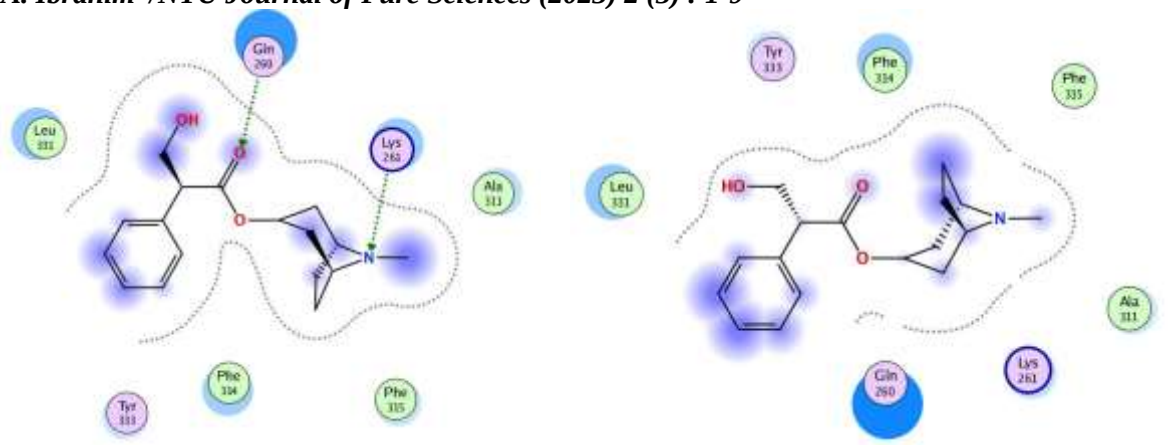


Figure 5: Expected interactions between ligands and receptors for (Atropine)

A (Lys 261) and (Gln) were connected to the amino atom (N) in the active group and ketone group (C=O), respectively, as shown in Figure (5).

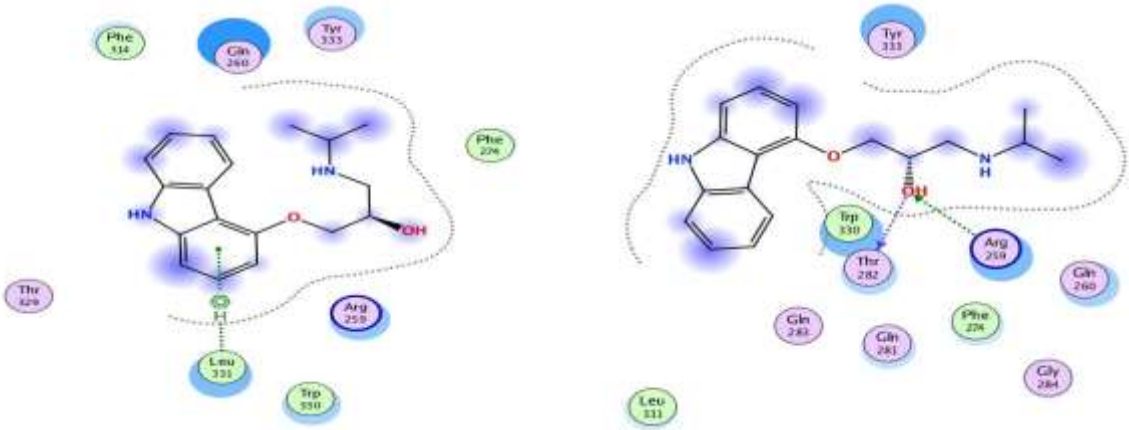


Figure 6: Expected interactions between ligands and receptors for (Carazolol)

The aromatic ring in Figure (6) was connected to the hydrogen atom in a more stable condition (Leu 332). When in the less stable condition, the hydroxy group (OH) was attached to two different amino acids (Thr 282 and Arg 259).

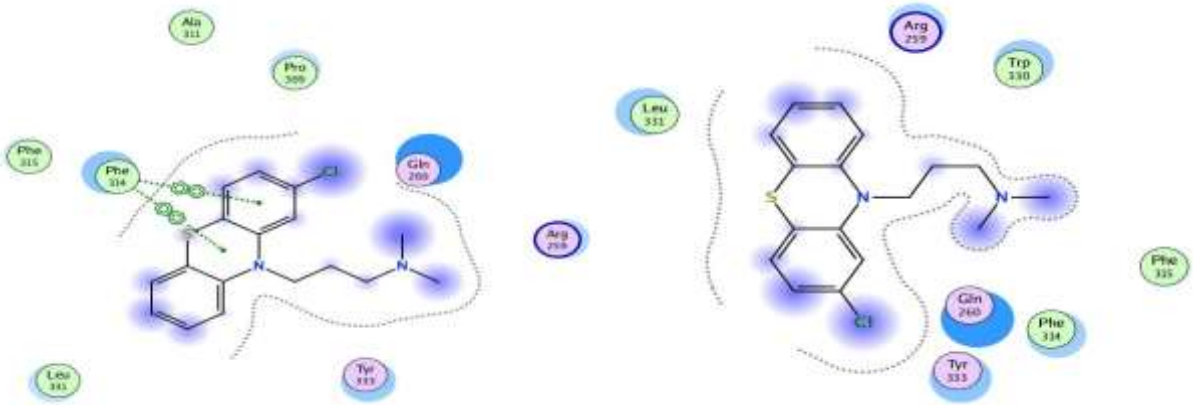


Figure 7: Expected interactions between ligands and receptors for (Chlorpromazine)

The amino acid (Phe 334) was directly coupled with two benzene rings at aromatic resonance (π-π) in Figure (7) to increase the docking's stability.

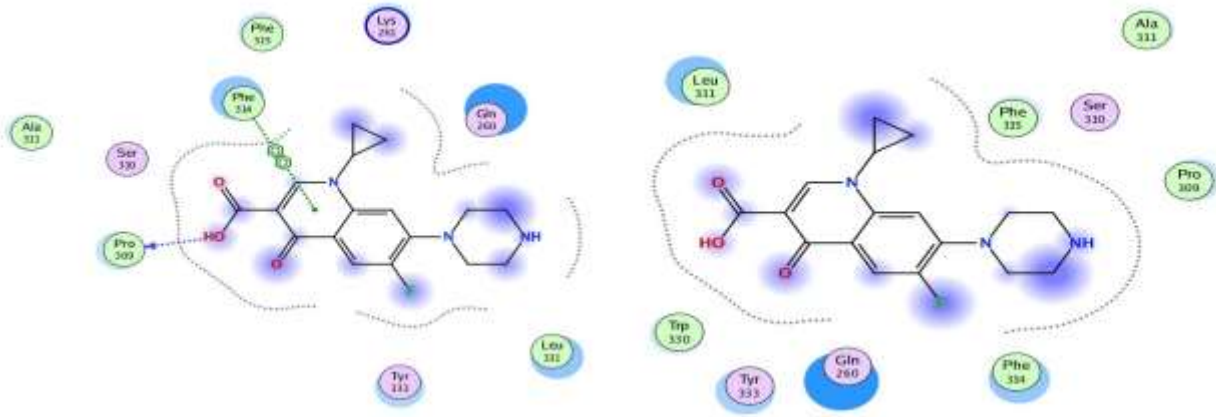


Figure 8: Expected interactions between ligands and receptors for (Ciprofloxacin)

Figure (8) depicts the aromatic bonding (π-π) between the benzene ring and (Phe 314). Furthermore, the formation of a hydrogen bond between the hydroxy group (OH) and (Pro 309).

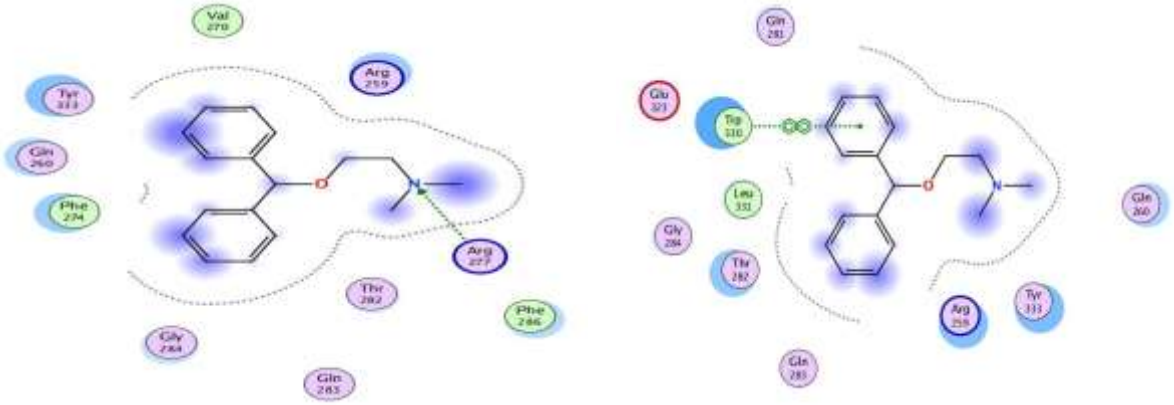


Figure 9: Expected interactions between ligands and receptors for (Diphenhydramine)

Figure (9) depicts how the amino acids (Arg 277) and (Trp 330) were converted into aromatic (π-π) and hydrogen bonds, respectively, in more and less stable states.

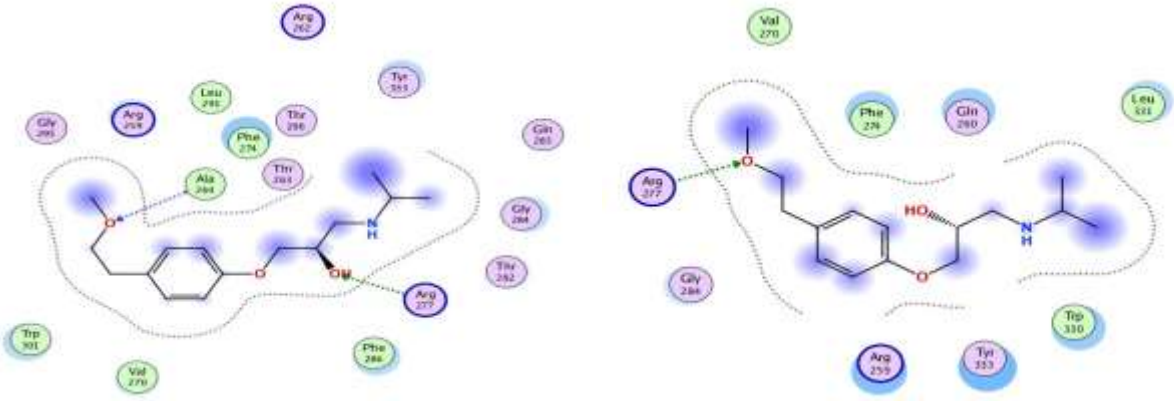


Figure 10: Expected interactions between ligands and receptors for (Metoprolol)

As illustrated in Figure (10), the amino acid (Arg 277) established a hydrogen bond with an oxygen atom and hydroxy group in more and less stable positions, respectively.

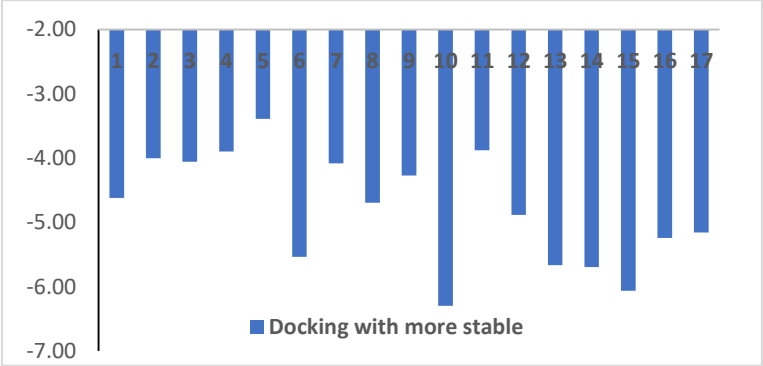


Figure 10: The docking score of the medicines with Covid-19 protein (6wzo)

Figure (10) displayed the comparison of ten of the medication which is used in this research by docking with COVID-19 protein by the theoretical calculations. The medicine number (10) which is named (Metoprolol) showed the best stable configuration by docking between this medicine with the Covid-19 protein (6wzo).

Conclusion

The figures were calculated using the Molecular Operating Environment (MOE). The docking study was used to investigate how drugs interacted with the COVID-19 protein. A vital aspect of docking those merits further development is the scoring function. The development of scoring functions with high accuracy and little computing expense may advance docking applications.

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