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THE MOLECULAR DOCKING STUDIES OF INTERACTION OF OXOETHOXY PHENYL BENZAMIDE DERIVATIVE AS A LIGAND MOLECULE WITH THE TARGET PROTIEN 6LU7 OF NOVEL CORONA VIRUS

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ABSTRACT:

Plants and bioactive compounds have played an important role in the development of several clinically useful therapeutic agents since time immemorial. The virtual interaction of the COVID-19 main protease in complex with the inhibitor N3 (Research Collaborators for Structural Bioinformatics Protein Data Bank [PDB] ID: 6LU7), Hence this is chosen as target protein molecule. (N-{4-[2-(5-methyl-3-oxo-2,3-dihydro-1H-pyrazol-1-yl)-2 oxoethoxy] phenyl}benzamide) was prepared in a regular laboratory conditions, which is acting as a ligand molecule. Using autodock tools the interaction of protein and ligand were tabulated and the results were dicussed.

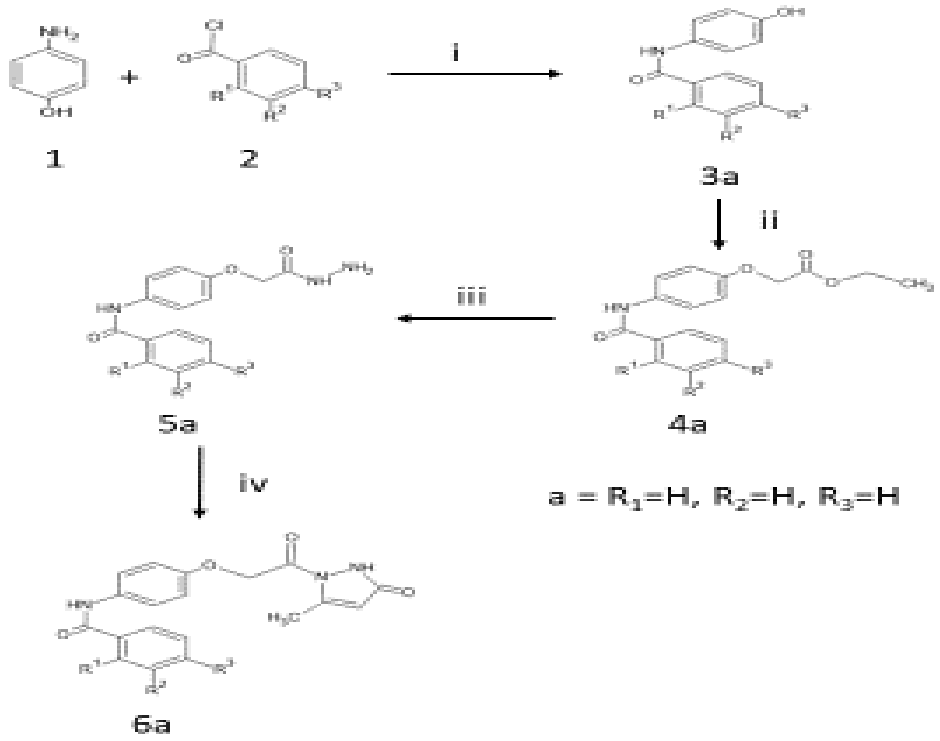
KEYWORDS:

Benzamide, molecular docking, autodock 4.2, pymol

EXPLAINATION:

Synthesis of benzamides was achieved by reacting aminophenol (1) and benzyol chloride (2) in presence of trimethylamine at room temperature for 24hrs, further synthesis of compounds 4a is accomplished by reaction of substituted benzamides 3a with ethylbromoacetate in presence of potassium carbonate. The obtained acetates

4a were reacted with 80% hydrazine hydrate to yield substituted hydrazides 5a. These phenyl hydrazides 5a were used further for cyclisation with ethylacetoacetate in presence of 20% tetrabutylammonium hydroxide in methanol with ethylene glycol as solvent to achieve (N-{4-[2-(5-methyl-3-oxo-2,3-dihydro-1H-pyrazol-1-yl)-2 oxoethoxy]phenyl}benzamide) derivatives 6a which is our ligand molecule. The structure of synthesized ligand were confirmed by characterization using spectroscopic techniques.



REAGENTS: *i = Dry THF, RT, TEA*

ii = Ethylbromoacetate, K_2CO_3, MeOH

iii = 80% Hydrazine hydrate, Methanol

iv = Ethylacetoacetate, TBAH in Methanol, Ethylene glycol, RT

The global health emergency of novel COVID-19 is due to severe acute respiratory syndrome corona virus-2 (SARS-CoV-2). The virtual interaction of the COVID-19 main protease in complex with the inhibitor N3 (Research Collaborators for Structural Bioinformatics Protein Data Bank [PDB] ID: 6LU7), Hence this is chosen as target protein molecule. Benzamide derivatives are made as ligand molecules. In this article we have discussed the interaction of ligands with the target protein molecule using autodock tools. Firstly, the ligands were prepared using commercial ACD/chemsketch tool in PDB format. Desired protein target 6LU7 is downloaded from Protein Data Bank. Further protein optimization done by removing co-ordinates and hetero

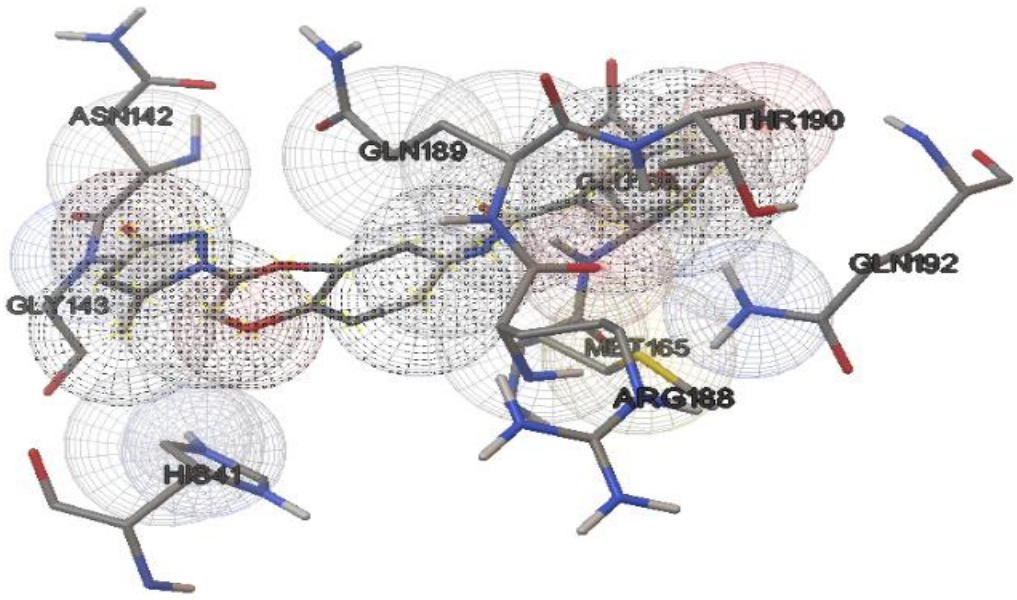
atoms, energy minimization of protein is done by swiss PDB viewer 4.1.0. To change the file format open babel 2.4.1 used. Docking of protein and ligand is done using autodock 4.2 and the results are visualized by pymol and tabulated in Lamarckian genetic algorithm.

RESULTS AND DISCUSSION:

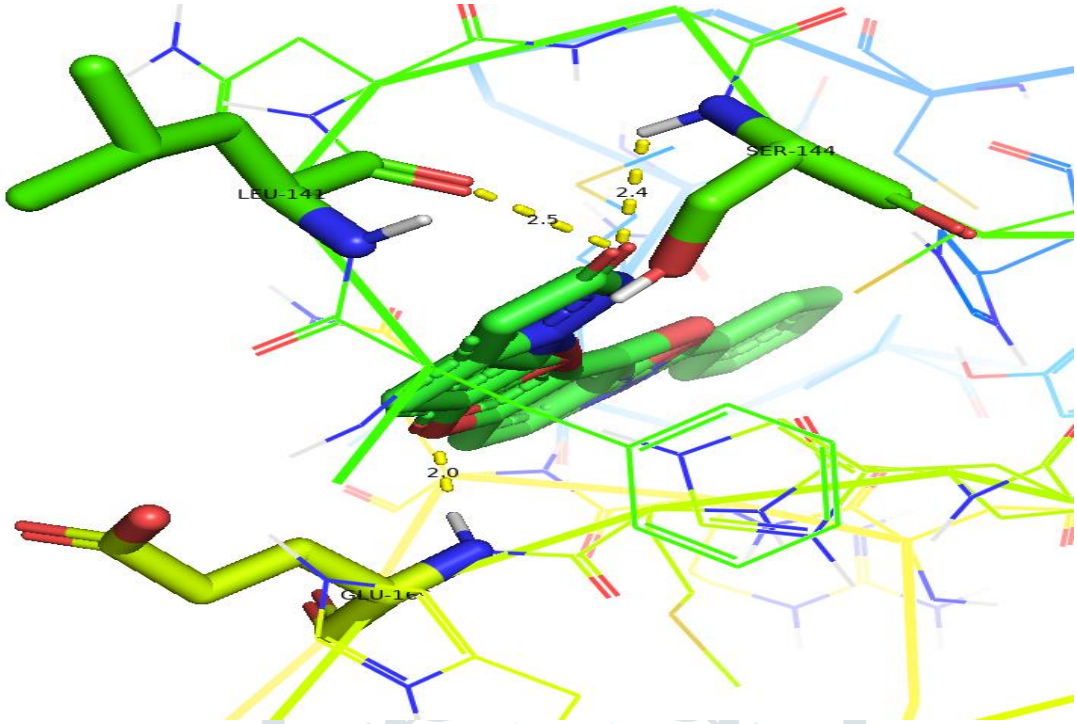
Interaction of ligand-a(N-{4-[2-(5-methyl-3-oxo-2,3-dihydro-1H-pyrazol-1-yl)-2-oxoethoxy]phenyl}benzamide)

After docking the protein target with each of our ligands, we have observed several information regarding the interactions. Each ligand has slight difference in their interaction type with the selected target protein 6LU7 molecule. According to it for ligand-a and protein 6LU7 interaction we found the least binding energy as -8.90 in the 8th run with the inhibition constant of 301.49 nM and the entropy of the selected grid was found to be 0.41. when the complex in viewed in pymol we found that Ligand-a is having three hydrogen bonds with the target protein molecule 6LU7 with the selected grid box. The bond length of the three hydrogen bonds are 2.0, 2.4 and 2.5 with the aminoacids GLU166, SER144 and LEU141 respectively.

Visualization of protein-ligand interaction in terms of hydrogen bonding:



Pymol viewer of hydrogen bonding in the protein-ligand complex:



CONCLUSION:

Name of Ligand	Best Run	Binding Energy in Kcal/mol	Inhibition Constant Ki in nM	Entropy of cluster in Angstrom	Number of hydrogen bonds	Bond Length	Interacted Amino acid
Ligand – a	8	-8.90	301.49	0.41	3	2.0	GLU166
						2.4	SER144
						2.5	LEU141

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