2021 Molecular Docking Analysis Chitosan-Zeolite-ZnO Nanocomposite

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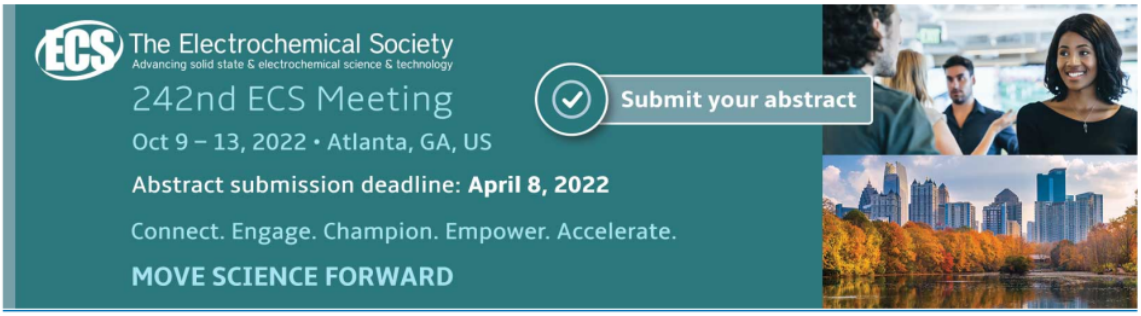

Molecular Docking Analysis Chitosan-Zeolite-ZnO Nanocomposite and Its Potency Against SARS-CoV-2

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Abstract. Nanocomposite has gain great attention in many applications due to its better properties in nanoscale. Chitosan-Zeolite-ZnO nanocomposite were prepared via sol-gel method and were analysed by molecular docking study to predict its antiviral activity against SARS CoV-2. The SARS CoV-2 glycoprotein as receptor from RCSB PDB and complex ligand of Chitosan-Zeolite and ZnO were chosen as interaction model between ligand and receptor. According to free binding energy, it was found that chitosan has better potency in nanocomposite against SARS Cov-2.

1. Introduction

Virus is one of important cause of a serious worldwide viral infections problem that threatens human health. Thus, the development of effective and safe antiviral drugs is essential to inhibit the virus in the human cell. Today, a large number of antiviral drugs have serious negative effects, making it difficult to develop highly safe antiviral agents without side effects [1]. Nanotechnology is an advanced approach for the antiviral application and also for the delivery system of currently antiviral drugs which modify their physico-chemical properties, reduce the negative effects and reach effective drug concentrations in the sites of infection [2]. Polymer-based nanomaterial have been investigated for the drug delivery of active molecules which have some advantages such as controlled release, safety profile, enhanced residence time, and good mucosal tissue penetration. Additionaly, some natural polymer which have mucoadhesive properties, such as chitosan, alginate, cellulose derivative, carrageenan, pectin, polyacrylate, thiolated polymers, and carbomer, have been studied in order to improve retention of nanoparticle in vaginal tract and permeation through mucus and epithelium [3].

Polysaccharide is a macromolecular compounds which is usually found in animals, plants and microorganisms. Many research have shown that polysaccharides and its derivatives have a significant inhibitory effect against some viruses for example human immunodeficiency virus (HIV), coxsackievirus B3 (CVB3), herpes simplex virus (HSV), cytomegalovirus (CMV), hepatitis and influenza virus. At present, the polysaccharides is promisingly material that can improve their biological activities through the modification of natural polysaccharides. The ongoing research of antiviral drugs from natural polysaccharide focus on its advantages, such as wide sources, strong antiviral activity, low toxicity and negative effects [1].

Chitosan is one of polysaccharide from animal which has been studied as antiviral agent. Chitosan-nanomaterial composites have been found to be significantly useful in improving its antimicrobial, chemical and mechanical properties. The incorporation of nanomaterial-fillers into the chitosan matrix is an effective approach to increase mechanical and thermal properties, and also low transparency compared to the natural polymer. The addition of nanomaterial-fillers (having dimension in nanometer) to natural polymers also result in improvement of physicochemical and biological

properties[4]. Metal oxide nanomaterial such as titanium dioxide (TiO2), zinc oxide (ZnO), copper oxide (CuO), have been reported to have excellent antimicrobial activity, because the production of reactive oxygen species (ROS) [5]. Nanomaterial ZnO and TiO_2 have photocatalytic properties, which lead to loss of membrane integrity through promote peroxidation of the phospholipids present in microbial cell membranes [6].

Zeolites a natural geopolymer used widely as adsorbents, ion-exchangers, catalysts, and molecular sieves. Recent studies have been suggesting zeolite for application of antimicrobial delivery system because it can encapsulate/trap a large number of small molecules in their cage-like structures. Many investigations have shown that zeolites ion-exchanged with these metals, increase its antimicrobial activity. Zeolite loaded with some metal such as zinc, silver, copper and other antimicrobial metals act as inorganic bactericide and disinfectants which are release slowly and having excellent safety and thermal stability when compared to organic one [7]

In this research chitosan based nanocomposite was investigated its potency as antiviral agent against SARS CoV-2 through molecular docking in silico study. Molecular docking is one an efficient tool to investigate ligand–receptor interactions. All step of molecular docking calculations were performed on AutoDock software and The AutoDock Tools (ADT) graphical user interface was used to calculate Kollman charges for the protein and to add polar hydrogen. Computational procedure in molecular docking is used to predict non-covalent binding of macromolecules between macromolecule (receptor) and a small molecule (ligand) efficiently, starting with their unbound structures, structures obtained from MD simulations, or homology modeling, etc [8]. The aim of this present study is to predict the binding affinity and inhibition constant of chitosan-zeolite-ZnO nanocomposite.

2. Method

2.1.Material

Software which is used in this research are: Autodock Tools version 4.01, Protein data bank site (PDB) www.RCSB.org, that code 6VXX, molecular modeling uses Avogadro 1.2.0 for the ligand and the molecular docking results are then visualized using Biovia Discovery Studio 2019.

2.2. Method

The complex structure of SARS CoV-2 glycoprotein macromolecule is obtained through Protein Data Bank searching via www.RCSB.org. with code PDB 6VXX. The structure of Chitosan-Zeolite-ZnO nanocomposite was drawn using Avogadro 1.2.0 sofware and optimalized with ab initio method using software of Games. The docking of Chitosan-Zeolite-ZnO nanocomposite and SARS CoV-2 glycoprotein macromolecule using Autodock Tools 1.5.6. The grid center for docking was set X= 197.81, Y= 223.407 and Z= 207.379 with dimensions of the grid box 60 × 60× 60 Å. Finally, the result of binding energy and an inhibitor constant was optimized from the software. The result of molecular interaction then analysed and visualized using Biovia Discovery Studio 2019 software.

3. Result and Discussion

The docking model of chitosan-zeolite-ZnO nanocomposite ligand and SARS CoV-2 glycoprotein molecules receptor are analyzed to predict nanocomposite antiviral activity. Binding affinity is an important aspect that must be considered in ligand and receptor interactions. A lower binding affinity indicates that a compound requires less energy to bind or interact with the receptor. In other words, a lower binding affinity value has a greater potential to be able to interact with the target protein. The targets used in molecular docking are SARS-CoV-2 spike glycoprotein with code PDB 6VXX. The ligands used in molecular docking are chitosan, chitosan in acid, zeolite and ZnO . The structure of SARS-CoV-2 spike glycoprotein is shown in figure 1. The molecular docking study of chitosan-zeolite-ZnO nanocomposite and SARS CoV-2 glycoprotein inhibitors constant experimentally and their free energy of binding are shown in table 1.

Figure 1. The Structure of SARS-CoV-2 Spike Glycoprotein

Table 1 Binding Energy and Inhibitors Constant of SARS CoV-2 Receptor

Compound Ligand	Binding Energy (Kcal/mol)	Inhibitors constant (mM)
Chitosan	-3,93	1,32
Chitosan in Acid	-3,37	3,37
Zeolite	-3,19	4,56
ZnO	-2,27	21,7

The value of binding energy with a negative result so that binding occurs spontaneously, the lower the energy, the more stable the compound and better the compound as a possible drug candidate [9]. Based on the free binding energy data, in table 1, the binding free energy of Chitosan is slightly lower than binding free energy of chitosan in acid medium, Zeolite and ZnO. The binding free energy of chitosan, chitosan in acid medium, zeolite and ZnO moreover is not different significantly, therefore the antiviral potency of chitosan-zeolite-ZnO nanocomposite a predicted become higher than each component. The lower binding free energy of chitosan means that the binding strength of chitosan to SARS CoV-2 is higher than than zeolite and ZnO. The higher strength of chitosan could be predicted that chitosan play an important role in antiviral activity of chitosan-zeolite-ZnO nanocomposite against SARS CoV-2 gycoprotein molecule. According to table 1, it also can be analysed that good inhibitor constant in the molecular docking analysis is the smaller one. The smaller inhibition constant, the greater spontaneity of bond formation because the delta of free energy is also getting smaller. Thus, it mean that the potency of antiviral activity increase.

The results of Molecular docking were visualized with the Biovia Discovery Studio 2019 software is shown in figure 2. Based on visualization of SARS CoV-2 glycoprotein with chitosan in figure 2, it can be shown that there is an interaction involving hydrogen bonds which were Thr 302, Leu 303, Gln 957, dan Gln 309. For chitosan in acidic medium, which has cationic amine group, the visualisation are shown in Figure 3. It can be analysed that Chitosan in acid dan SARS CoV-2 glycoprotein generate an interaction involving hydrogen bonds which were Glu 309, Leu 303 dan Ser 305. The visualisation of Zeolit (Si-O-Al) group dan SARS CoV-2 glycoprotein are shown in Figure 4. There is an interaction involving hydrogen bonds which were Tyr 313, Ser 596 Gln 314 dan Gln 613 between zeolite and SARS CoV-2 glycoprotein. Molecular docking for ZnO and SARS CoV-2 glycoprotein are depicted in Figure 5. The ZnO dan SARS CoV-2 glycoprotein shown an interaction involving hydrogen bonds which were Thr 299, Glu 298 dan Thr 315.

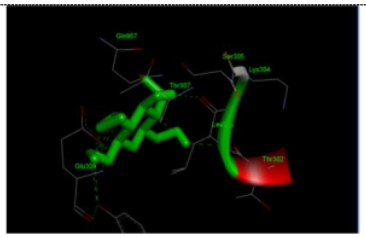

Figure 2. Visualization of Chitosan Ligand docked with SARS CoV-2

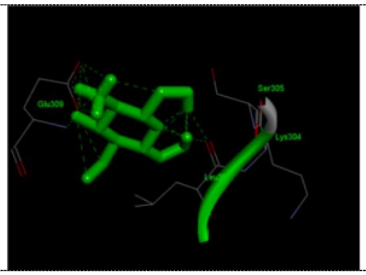

Figure 3. Visualization of Chitosan in acid Ligand docked with SARS CoV-2

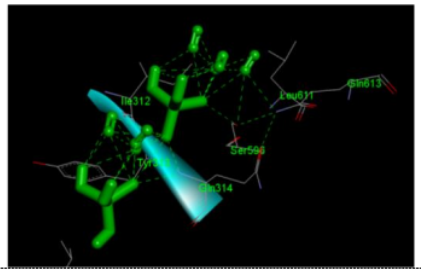

Figure 4. Visualization of Zeolite Ligand docked with SARS CoV-2

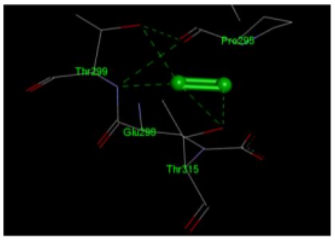

Figure 5. Visualization of ZnO Ligand docked with SARS CoV-2

The high affinity for the drug compound depends on the type and number of bonds that occur with the active protein site [10]. Chitosan forms many chemical bonds with 6VXX as target SARS CoV-2 glycoprotein macromolecule, including hydrogen bonds. Chitosan in acids, zeolites and ZnO also form chemical bonds. The docking analysis in this study shows the inhibitory potential of several ligand compounds, ranked by binding energy in table 1; chitosan> chitosan in acid> zeolite> ZnO. The results of molecular docking studies using chitosan-zeolite-ZnO compounds can have potential as treatment SARS CoV-2.

4. Conclusion

A study of molecular docking analysis have been investigated in order to predict the antiviral activity of chitosan-zeolite-ZnO nanocomposite against SARS CoV-2 glycoprotein macromelucule. Among several ligand contained in the nanocomposite, chitosan showed better binding activity to SARS CoV-2 glycoprotein molecule indicated by value of the binding energy which is lower than znO and zeolite ligand. It can be concluded that chitosan-zeolite-ZnO nanocomposite are potential to be an antiviral agent against SARS CoV-2 which Chitosan played more role in antiviral activity.

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