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Vitamin D3: A possible Anti-Sars-CoV molecule?

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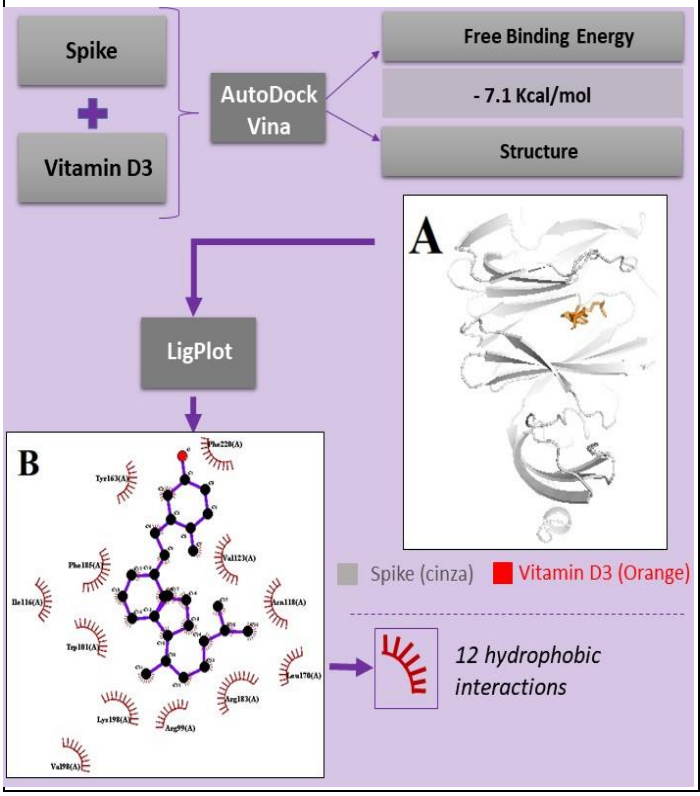
Graphical Abstract



Abstract.
Vitamin D3 (VitD) has several biological activities and some studies demonstrate its possible correlation with better prognosis in COVID-19 disease. The Sars-CoV-2 or new coronavirus is responsible for the current and serious pandemic of COVID-19. One of the main proteins involved in the infection process of the host cell is the Spike protein and its blocking could have preventive and therapeutic actions. The objective of this work was to verify the ability of binding, through molecular docking, VitD with the Spike protein. Docking performed with AutoDockVina demonstrated that the binding between VitD and Spike occurs with a binding energy of -7.1 Kcal/mol and through 12 hydrophobic connections. So, at the molecular level, VitD's interaction with Spike could inhibit this viral protein and act as an Anti-Sars-CoV molecule. To confirm this evidence demonstrated by the docking, it is necessary to continue the studies in vitro and in vivo.

Introduction

Vitamin D3 (VitD), also known as cholecalciferol or oleovitamin D3, belongs to the class of organic compounds known as vitamin d and derivatives (1). *VitD plays one of the key roles in the management of calcium phosphate metabolism. However, it also has the ability to regulate the function of a number of cells and tissues that express the vitamin D receptor* (2). *Studies have shown the correlation between VitD and the evolution of COVID-19, and the deficiency of this vitamin is related*

to worse prognosis (3,4). *The Sars-CoV-2 or new coronavirus is responsible for the current and serious pandemic of COVID-19. One of the main proteins involved in the infection process of the host cell is the Spike protein and its blocking could have preventive and therapeutic actions* (5). *The objective of this work was to verify the ability of binding, through molecular docking, VitD with the Spike protein.*

Materials and Methods

The Spike structure (receptor) was obtained from Protein Data Bank PDB (PDB ID: 5X4S; name Structure of the N-terminal domain (NTD) of SARS-CoV spike protein) (6) *and Vitamin D3 (ligand) was obtained from Pubchem (PubChem ID: 5280795)* (1). *We used the UCSF chimera (available to download at http://www.cgl.ucsf.edu/chimera/download.html) for remove heteroatoms from the Spike. Then, we prepare receptor and ligand input files using AutoDockTools software for AutoDockVina* (7). *To perform a blind (coverage of all protein and high number for exhaustiveness) docking simulations, we configure grid box as: size x = 46 Å; size y = 70 Å; and size z = 44 Å; and center box coordinates are x = 14.848 Å center; y = -28.368 Å center; z = 1.218 Å; considering exhaustiveness as 500. Molecular docking simulations were performed with AutoDock Vina* (7). *The Free Energy of Binding (FEB) of docked ligand-receptor was estimated in Kcal/mol. The more negative FEB indicates the greater stability of ligand-receptor complex. Visual analysis of docking results was performed with PyMol (available for download https://pymol.org/2/) and for check the types of connections between molecules we used the LigPlot* (8).

Results and Discussion

Docking performed with AutoDockVina demonstrated that the binding between VitD and Spike occurs with a binding energy of -7.1 Kcal/mol and through 12 hydrophobic connections (Fig. 1). So, at the molecular level, VitD's interaction with Spike could inhibit this viral protein and act as an Anti-Sars-CoV molecule. This result may reveal one of the mechanisms at the molecular level through which VitD is related to the evolution of COVID-19. Furthermore, the connection in Spike is very interesting, since this protein is one of the targets for the development of vaccines and therapies against COVID-19 (5).

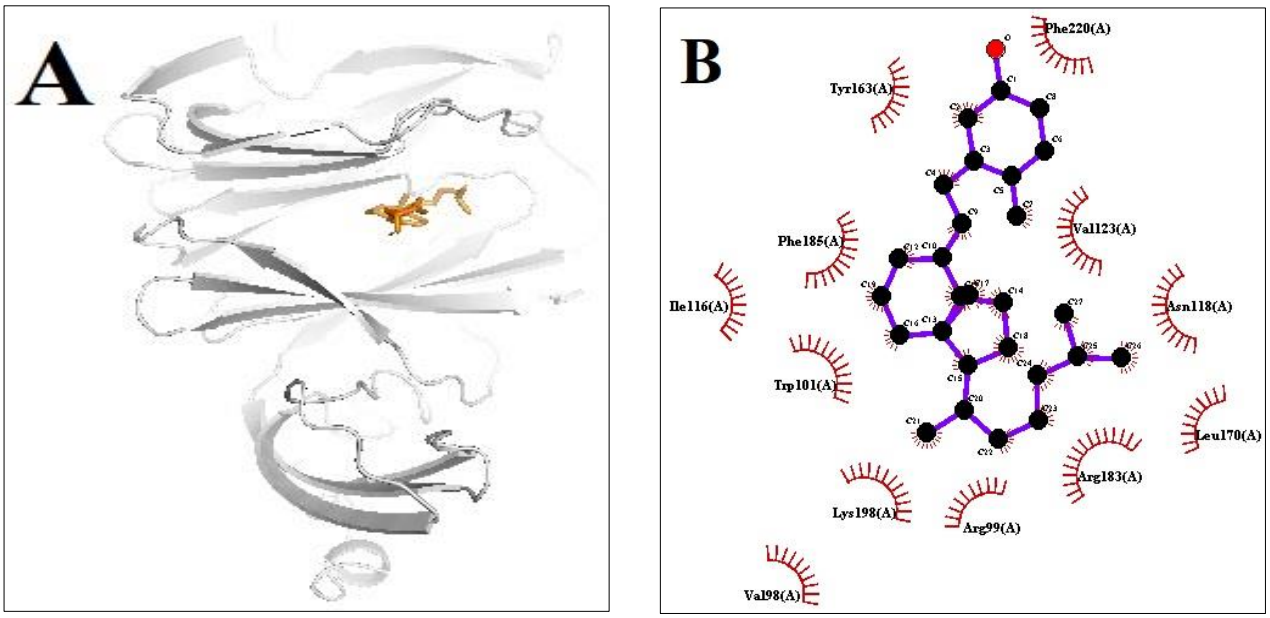


Figure 1: N-terminal domain (NTD) of SARS-CoV spike protein (gray) connected to Vitamin D3 (orange) (A). Spike and Vitamin D3 interaction detailed (B): Black or red circles - Vitamin D3 atoms; Purple strokes – bonds between the atoms of Vitamin D3; Red semi-circles with lines - hydrophobic interactions of Spike's amino acids with Vitamin D3.

Conclusions

To confirm this evidence demonstrated by the docking, it is necessary to continue the studies in vitro and in vivo.

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