

Anti-Sars-CoV effect of Rosemary (*Rosmarinus officinalis*): A blind docking strategy

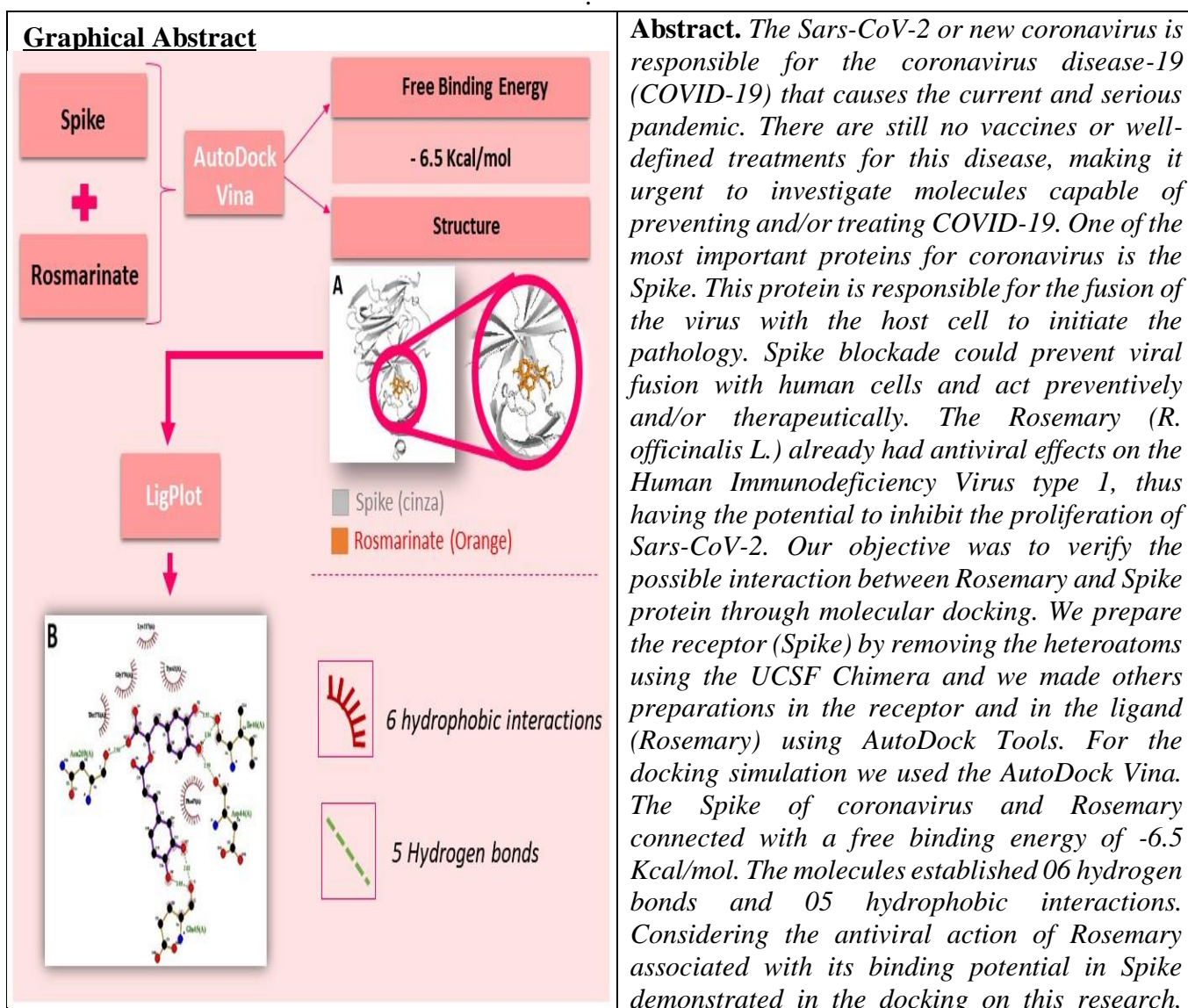
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	<i>Rosemary can be a potent aid against the new coronavirus.</i>
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Introduction

The current pandemic of the coronavirus disease 19 (COVID-19) is caused by the new coronavirus (called severe acute respiratory syndrome coronavirus 2/ Sars-CoV-2;) (1). Many questions remain unclear about the infection process, whereas it is a new pathogen. (2). Besides that, there are still no vaccines or well-defined treatments for this disease, making it urgent to investigate molecules capable of preventing and/or treating COVID-19. A strategic target for vaccine and treatment development would be the viral protein Spike. The Spike is present no viral capsid and binds to the ACE2 protein (present in human cells) to start the fusion process between virus and cell (3). A potential blocker for Spike would be Rosemary because it has already demonstrated antiviral activity on Human Immunodeficiency Virus type 1 (HIV-1) (4). Thus, the objective of this study was to investigate the possible fusion between Rosemary and Spike protein, through molecular docking, to infer the potential of Rosemary's use in anti-Sars-CoV therapies.

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) (5) and Rosemary (ligand) was obtained from Pubchem (PubChem ID: 5099; name Rosmarinate/Labiatenic acid) (6). 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 $x = 46 \text{ \AA}$; size $y = 70 \text{ \AA}$; and size $z = 44 \text{ \AA}$; and center box coordinates are $x = 14.848 \text{ \AA}$ center; $y = -28.368 \text{ \AA}$ center; $z = 1.218 \text{ \AA}$; 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

The Spike of coronavirus and Rosemary connected with a free binding energy of -6.5 Kcal/mol (Fig 1A). The molecules established 06 Hydrogen bonds and 05 hydrophobic interactions (Fig 1B). The Hydrogen bonds occurred among the following Spike amino acids: Asparagine; Interleucine; Aspartic acid and Glutamine. The hydrophobic interactions occurred among the following Spike amino acids: Threonine; Glycine; Lysine; Tyrosine and Phenylalanine (Fig 1B). Considering the antiviral action of Rosemary against HIV-1 (4) associated with its binding potential in Spike demonstrated in the docking on this research, Rosemary can be a potent aid against the new coronavirus, because Spike has a key role in establishing the infection (3).

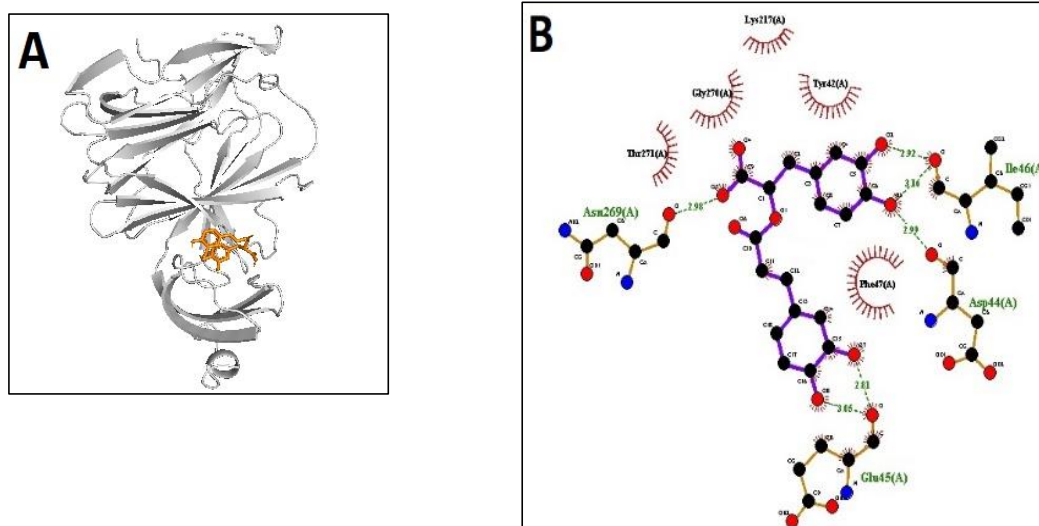


Figure 1: N-terminal domain (NTD) of SARS-CoV spike protein (gray) connected to Rosmarinate (orange) (A). Spike and Rosmarinate interaction detailed (B): Black or red circles - Spike or Rosmarinate atoms; Purple strokes – bonds between the atoms of Rosmarinate; Orange strokes – bonds between the atoms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

Conclusions

Molecular docking demonstrated the potential of Rosemary against the coronavirus.

References

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