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Section 4

Article Summary: Investigation into SARS-CoV-2 Resistance of Compounds in Garlic Essential Oil

2019's COVID-19 pandemic or SARS-CoV-2 is very similar to 2003's SARS-CoV-1. Both viruses infect their host in a very similar way. Like SARS-CoV-1, SARS-CoV-2 infects hosts by binding to the angiotensin-converting enzyme 2 (ACE2) found on the membranes of lung, kidney, endothelium, and heart cells. Once bound, the virus creates progeny within the host cell, exits the cell, then infects other cells of the host. There are proteins and proteases outside of the virus that assist it in binding to the host cell and replicating. Most notably, SARS-CoV-2 contains a protease called PDB6LU7. PDB6LU7 is the main protease used by SARS-CoV-2 to replicate after entering a host cell. Previously used as a remedy of common colds, flu, and other infections, garlic essential oil will now be examined for its ability to treat and prevent SARS-CoV-2. Using CG-MS, it was found that garlic essential oil contains 17 organosulfur compounds that account for over 99% of its makeup. These organosulfur compounds have the ability to interact strongly with the amino acids of ACE2 receptors and the PDB6LU7 protease. Because of this unique property, the organosulfur compounds can bind to either ACE2 or PDB6LU7 so SARS-CoV-2 cannot bind to host cells or replicate. Hence, the overall operability of the virus can be stunted.

To test the binding ability of the organosulfur compounds within garlic essential oil, a technique called molecular docking was used. Molecular docking is a computer simulation in which images of binding sites and receptors of enzymes are fit together with different binding molecules. This results in a calculated binding affinity between the two docked molecules. This calculation is represented by docking score energy (DS). A more negative DS value indicates higher binding affinity between the molecule and the binding site because of the higher stability of the interaction. For the purpose of this experiment, ACE2 and PDB6LU7's fitting potential with the 17 organosulfur compounds of garlic essential oil was simulated. The results of the simulation were presented in two tables containing the DS of the 17 organosulfur compounds when binding to both ACE2 and PDB6LU7 respectively. The DS value was sufficiently negative for all 17 organosulfur compounds in garlic essential oil when binding to both ACE2 and PDB6LU7. Among the 17 organosulfur compounds, some bound better than others. Notated as T5 and T11, diallyl tetrasulfide and 2-propenyl propyl trisulfide had the highest affinity to the ACE2 receptor with DS values of -14.06 and -14.01 kcal/mol respectively. Organosulfur compounds notated as T1 and T2, allyl disulfide and allyl trisulfide had the best anti-SARS-CoV-2 activity by having the highest affinity to PDB6LU7 with DS values of -15.32 and -15.02 kcal/mol respectively.[1]

The interactions that occurred between the sulfur atoms of the 17 organosulfur compounds and the amino acids in the receptor are: hydrogen bonds, cation-pi bonds, pi-pi bonds, and ionic interaction. Most notably, hydrogen bonds are critical to the organosulfur compound's affinity. Because they are good H-bond donors, the sulfur atoms in each of the 17 compounds are mainly responsible for the compound's high affinity for the amino acids within the ACE2 receptor. T5 contains the most sulfur atoms out of all 17 of the compounds, meaning that it has the most H-bond donors. This sulfur compound has a narrow structure with 4 sulfur atoms, neighbored by hydrogen-rich carbons, allowing for strong H-bonding with glycine,

[1] Thuy, Bui Thi Phuong, Tran Thi Ai My, Nguyen Thi Thanh Hai, Le Trung Hieu, Tran Thai Hoa, Huynh Thi Phuong Loan, Nguyen Thanh Triet, et al. "Investigation into SARS-CoV-2 Resistance of Compounds in Garlic Essential Oil." *ACS Omega* 5, no. 14 (2020): 8312–20. https://doi.org/10.1021/acsomega.0c00772.

aspartic acid, lysine, and alanine. With all of these unique characteristics, T5 has the highest affinity with ACE2 among all of the compounds.

T1 has the highest affinity for SARS-CoV-2, likely due to its interaction with 6 amino acids of PBD6LU7. By interacting with 6 amino acids, T1 interacts with more amino acids than any of the other 17 organosulfur compounds. This sulfur compound has a narrow skeletal structure with two sulfur atoms and hydrogen rich carbons. These hydrogen rich carbons alongside the sulfur atoms could allow for hydrogen bonding between the less electronegative sulfur atoms on T1 and the more electronegative nitrogen and oxygen atoms on the chains of amino acids asparagine, serine, and histidine of PBD6LU7.

Despite some organosulfur compounds having higher affinity to either ACE2 or PBD6LU7 than others, it is likely that the strongest SAR-CoV-2 inhibition will occur when using all 17 of the compounds together. After all, more compounds binding well to ACE2 will mean that there are fewer binding sites available for SARS-CoV-2. Fewer binding opportunities for SARS-CoV-2 means fewer opportunities for SARS-CoV-2 to infect cells and multiply to eventually infect tissue. With more compounds available to bind well to PDB6LU7, it will also be less likely for SARS-CoV-2 to replicate. Hence, if SARS-CoV-2 can be identified quickly enough in a patient, the use of the 17 organosulfur compounds in garlic essential oil could possible prevent or treat SARS-CoV-2, by acting as a dual inhibitor for both ACE2 and PDB6LU7.[2]

Molecular docking is an excellent way to begin identifying the potential of compounds that could have a high affinity for target receptors or proteins of interest. However, this experiment is only a computer simulation. It is yet to be seen if these encouraging results of the molecular docking simulation can be replicated in a clinical trial. Until the organosulfur compounds found in garlic essential oil improves symptoms of COVID-19 in real patients, it cannot be determined if the compounds actually work. However, the convincing results within the following experiment is certainly a step toward identifying possible prevention or treatment options for the novel COVID-19 pandemic.

[2] Thuy, Bui Thi Phuong, Tran Thi Ai My, Nguyen Thi Thanh Hai, Le Trung Hieu, Tran Thai Hoa, Huynh Thi Phuong Loan, Nguyen Thanh Triet, et al. "Investigation into SARS-CoV-2 Resistance of Compounds in Garlic Essential Oil." *ACS Omega* 5, no. 14 (2020): 8312–20. https://doi.org/10.1021/acsomega.0c00772.