Computational Inhibition of Lachrymatory Factor Synthase Utilizing Molecular Docking Simulations

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The tear-inducing chemical, or lachrymatory factor, syn-propanethial s-oxide, is released from onions when their cells are disrupted. The reaction creating this chemical is catalyzed by the enzyme, Lachrymatory Factor Synthase (LFS). It was hypothesized that if naturally occurring small molecules (ligands) could be identified that bind strongly to the active site of LFS, then binding of these ligands would reduce enzymatic activity, hence eliminating or reducing the tear-causing effects while chopping onions. The three-dimensional crystal structure of LFS was taken from the protein data bank in holo and apo form, and AlphaFold was used to generate another structure. A large number of naturally occurring ligands were downloaded from the ZINC database. The binding energy of the ligands for the active site of alliinase was then calculated using a protein-docking tool, PyRx, using each structure. The resulting binding energies were obtained, where a score of -5.5 kcal/mol or less was considered as strong binding. To ensure that the selected molecules are not toxic, the drug-likeness score of each molecule was calculated using a Python code (QED score, greater than 0.7). Molecules were then ranked by combining these measures, and similar molecules to these were selected. These molecules were again tested for their binding affinity for LFS. 97 molecules met the final criteria, and molecules exhibited differing results depending on the protein structure used. These chemicals should be studied further to determine their effectiveness in combating the lachrymatory effects of onions.

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