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A new docking approach to find peptides renin inhibitors derived from food proteins

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Structure-based computer modeling of peptide-protein interactions is a core component of modern bioinformatics approach to study bioactive peptide. Molecular docking is the most common technique used to predict the predominant binding mode(s) of a ligand with a protein of known three-dimensional structure. Most of docking programs, like AutoDock, are successful to work with small peptides but not with larger ones due to its high flexibility and freedom of movement. The objective of this work was to try out new free, friendly and rigorous servers developed specifically for peptides that act as ligands to predict with greater confidence the best peptides that could potentially act as inhibitors of an enzyme. For this purpose we used six peptides (SFNLPILR; FNLPILR; SFNLPIL; QAFEDGFEWVSFK; AFEDGFEWVSFK; VNVDDPSKA) identified in an amaranth alcalase hydrolyzate (HD 21±4 %) as renin (EC 3.4.23.15) inhibitors. As controls the renin substrate (angiotensinogen), a competitive inhibitor (IRLIIVLMPILMA, IC_{50}=6.5 mM) and a tridecapeptide of alanines were used. In a first stage, CABS dock server (http://biocomp.chem.uw.edu.pl/CABSdock) was use to generate the peptide-renin (PDB 2V0Z chain C) complex and identify the most likely interaction sites. In the second stage, FlexPepDock server (http://flexpepdock.furmanlab.cs.huji.ac.il/) was used to refine the interaction energy of the complex and calculate a score that serves to select the best inhibitors from the set of peptides used. Comparing the obtained means of three independent replicates of the FlexPepDock score the peptides AFEDGFEWVSFK and SFNLPILR had a similar interaction energy to as control IRLIIVLMPILMA (Tukey test, p=0.05). Both peptides were synthesized to evaluate its inhibitory activity *in vitro*. The docking using peptide remains to be a challenge for the scientific community, the protocol used in this work use new servers specifically developed for this purpose with the additional advantage of being fast implementation and friendly with experimental scientists.