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In silico development of new acetylcholinesterase inhibitors

Ihosvany Camps[1], Ana L Pascoini[1], Leonardo B Federico[2], Ana L F Area1 and **Barbara A Verd[1]**
[1]Federal University of Alfenas, Brazil
[2]University of São Paulo, Brazil

In this work, we made use of the fragment based drug design (FBDD) and *de novo* design to obtain more powerful acetylcholinesterase (AChe) inhibitors. The acetylcholinesterase is associated to the Alzheimer's disease (AD). It was found that the cholinergic pathways in the cerebral cortex are compromised in AD and the accompanying cholinergic deficiency contributes to the cognitive deterioration of AD patients. In the FBDD approach, fragments are docked into the active site of the protein. As fragments are molecular groups with low number of atoms, it is possible to study their interaction with localized amino acids. Once the interactions are measured, the fragments are organized by affinity and then linked between them to form new molecules with high degree of interaction with the active site. In the other approach, we used the *de novo* design technique starting from reference drugs used in the AD treatment. These drugs were break into fragments (seeds). In the growing strategy, fragments were added to each seed growing new molecules. In the linking strategy, two or more separated seeds are linked with different fragments. Both strategies produced a library of more than 2M compounds. This library was filtered using ADME properties. The resulting library with around 6k compound was filtered again. In this case, structures with Tanimoto coefficient greater than 0.85 were discarded. The final library with 1.5k compounds was submitted to docking studies. As a result, 10 compounds with better interaction energy than the reference drugs were obtained.

Biography

Ihosvany Camps has completed his Bachelor degree in Physics from the Faculty of Physics, University of Havana (Cuba, 1995), Master degree in Physics from the Faculty of Physics, University of Havana (Cuba, 1996) and PhD in Physics from the Institute of Physics, Federal Fluminense University (Brazil, 2001). He has experience in Condensed Matter Physics and Computational Modeling. Currently, his research is on the study of electronic properties of nanostructures and the molecular modeling of organic and inorganic systems including the modeling of drugs (rational drug design, fragment-based drug design and *de novo* design), molecular docking and studies on polymorphism of pharmaceutical solids.

icamps@unifal-mg.edu.br

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