Molecular Docking and structure-based Rivaroxaban novel analogs

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Abstract: Factor Xa has been recently known as the best target in anticoagulation cascade. Factor Xa inhibitors are accepted as an ideal anticoagulant due to linear affect and least side effects in comparison to previous anticoagulant classes. Although first FXa inhibitor was a peptide chain extracted from kind of tick species during 1980s, the first FXa inhibitor was not FDA approved until 2011.

Rivaroxaban is a small chemical molecule with coagulation affect on FXa. By analyzing the docking interactions of Rivaroxaban and 4zha protein and by keeping in mind the tick anticoagulant peptide chain; different amino acids were added to moiety of Rivaroxaban. These amino acids were added to supply chirality, desired length, amide bond simulation and appropriate interactions. Seven novel analogs have been designed based on it. Simulation were done by Autodock-4 and estimated data which were achieved showed notable characterizations, in some cases analogs showed much better inhibition constant and also better free energy of binding. Analog-3 showed 150 times less inhibition constant and also 3 kcal/mol in comparision to the lead compound.

Based on the results, these novel designed analogs could be considered as novel FXa inhibitors.

Keywords: molecular docking; anticoagulation ; FXa ; Rivaroxaban

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