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MOLECULAR DOCKING OF STATIN-ASSOCIATED LIGANDS AS WAY OF LIPID-LOWERING THERAPY EFFECTIVENESS VERIFICATION

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Preclinical verification of the effectiveness of statin-associated ligands as part of mono- and combined hypolipidemic therapy based on the analysis of the results of molecular docking.

The investigation of the pharmacological components of monotherapy was carried out in the following stages: preparation of the ligand, preparation of the enzyme and actual molecular docking according to the Protein Data Bank. The possibility of chemical interaction and complex formation of atorva- and simvastatin with ezetimibe was also determined, which involved the analysis of their behavior using the molecular dynamics method. The length of the identified bonds was measured in units of Angstroms (Å). The visualization process and subsequent calculations were performed using programs MarvinSketch 6.3.0, AutoDockTools 1.5.6, Discovery Studio Visualizer 4.0, "Vina", MOPAC 2016, FACIO 19.1, HyperChem 8.08.

It is set that affinity of simvastatin to protein is -8.3 kcal/mol, and atorvastatin is -8.2 kcal/mol, which indicates an almost identical affinity of these pharmacological substances with a somewhat higher affinity for simvastatin, and the spatial arrangement of the molecules is practically identical, which indicates the reliability of the affinity according to the results of the docking study. The interaction between the analyzed molecules as part of the combined therapy does not lead to the formation of covalent chemical bonds, but there is an intermolecular interaction that leads to the formation of unstable weakly bound associates, which dissociate into the original compounds in the aqueous medium. The structure of the complexes indicates the presence of a tighter coupling of the components in the simvastatin-ezetimibe combination.

Simvastatin is more active in terms of interaction specificity, but hydrophobic interactions are observed more for atorvastatin, which may indicate its superiority in terms of pharmacotherapeutic effectiveness as a more aggressive component of hypolipidemic therapy. As a result of the interaction of atorva- and simvastatin with ezetimibe due to weak intermolecular bonds, labile complexes are formed that are

capable of dissociation into initial components, and the molecular dynamic study confirms the possible potential application of any of the indicated variants of the combined lipid-lowering strategy.

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