Cationic surfactants include quaternary ammonium bases and their salts (catamine AB, alkyldimethylaminoxide, polyquartenium). In terms of emulsifying activity, they are weaker than anionic surfactants, but interact with cellular proteins of bacteria (bactericidal properties). They are used in balms, antistatic agents, hair conditioners.

Depending on the pH environment, amphoteric surfactants show themselves as anionic (pH> 7) and cationic (pH <7): N-alkylamino acids, N-acylamino acids, protein and betaine derivatives. Their mild dermatological effect is used in foaming agents for children and people with sensitive skin.

Nonionic surfactants do not form ions when dissolved (oxyethylated alcohols, glycerol esters, synthetic fatty acid deethanolamides). They have a weak foaming effect and a mild effect on the skin. They are used as a cosurfactants in softeners and stabilizers of non-washable foam.

Only the combination of all the groups of surfactants can reduce their aggressive effect and protect the skin from irritation.

Conclutions. A thorough study of the chemical properties of the ingredients included in cosmetic products will help reduce or even avoid unwanted effects when applied.

THE USE OF MOLECULAR DOCING FOR THE RATIONAL DESIGN OF NEW "DRUG-LIKE" MOLECULES

Vedeniev S.V., Semenets A.P., Suleiman M.M., Perekhoda L.O.
National University of Pharmacy, Kharkiv, Ukraine
suleiman.nfau@outlook.com

Introduction. An important direction in the development of modern medical chemistry is the use of computer simulations in the search for new "drug-like" molecules. The use of molecular docking makes it possible to model the binding of the ligand - target; to conduct a virtual screening to determine the affinity of the compounds for a particular biological target and to select compounds for which there is a certain type of pharmacological activity, and optimize the structures of the leader compounds.

Aim. To conduct docking researches of known antitumor agents and based on the data obtained to formulate recommendations on the rational design of new “drug-like” molecules of antiproliferative action.

Materials and methods.

Famous antitumor agents (Imatinib, Lapatinib, Sunitinib and Pemetrexed) were selected as objects of docking researches. For receptor-oriented flexible docking, the Autodock 4.2 software package was used. Ligands were prepared using the MGL Tools 1.5.6 program. To perform calculations in the Autodock 4.2 program the output formats of the receptor and ligand data were converted to a special PDBQT format. The active macromolecule center of the tyrosine kinase receptor (PDB ID: 1M17) from the Protein Data Bank (PDB) was used as a biological target for docking. The receptor maps were made in MGL Tools and Auto Grid programs. Water molecules, ions, and the ligand were removed from the PDB file ID: 1M17. The visual analysis of complexes of substances in the active center of the tyrosine kinase receptor (PDB ID: 1M17) was performed using the Discovery Studio Visualizer program.

Results and discussions. The mechanism of action of most antitumor agents is associated with inhibition of tyrosine kinase receptor. The choice of a biological target for our study is due to the existing crystallographic model co-crystallized with the derivative of 4-anilinoquinazoline (Erlotinib).

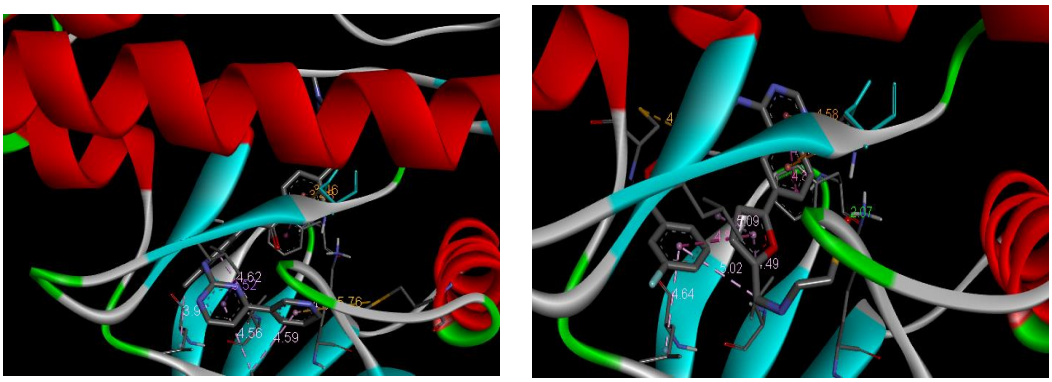
Thus, it can be assumed that the inhibitory activity of the tested molecules relatively to the tyrosine kinase receptor (PDB ID: 1M17) can be actualized by forming complexes between them, their stability is provided mainly due to the energy favorable geometric location of ligands in the active center of this acceptor. As a consequence, the thermodynamic probability of such binding is confirmed by negative values of the scoring function (Affinity DG, kcal/mol), free energy of binding EDoc (kcal/mol), and the calculated values of the binding coefficients Ki (mM) (Tab. 1).

Table 1. Results of docking studies of anticancer agents in complex with tyrosine kinase receptor (PDB ID: 1M17)

Medication	Afinity DG, kcal/mol	EDoc kcal/mol	Ki mM (millimolar)
Imatinib	-9,7	-5.96	0.042
Lapatinib	-8.2	-4.17	0.87
Sunitinib	-7.9	-5.08	0.19
Pemetrexed	-8.3	-4.96	0. 23

In order to understand how the affinity of the drugs studied occurs to the target, a detailed analysis of the geometric location of these molecules in the active site of the receptor was conducted. Fig. 1 and 2 show the superpositions and diagrams of interactions of tested antitumor agents.

a b



c d

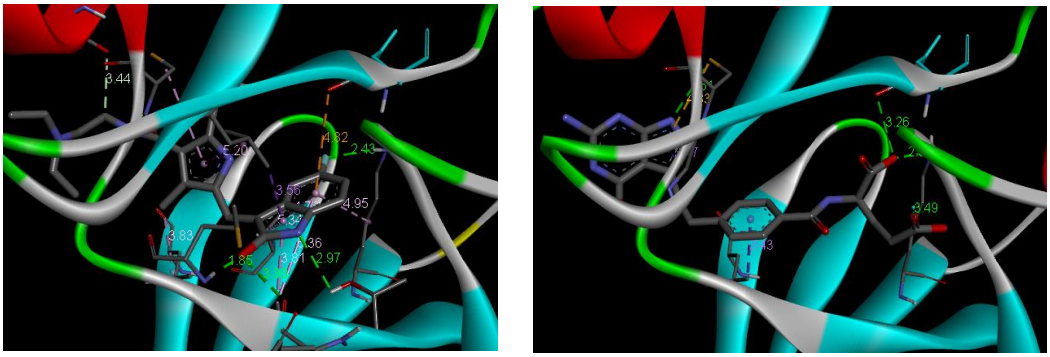
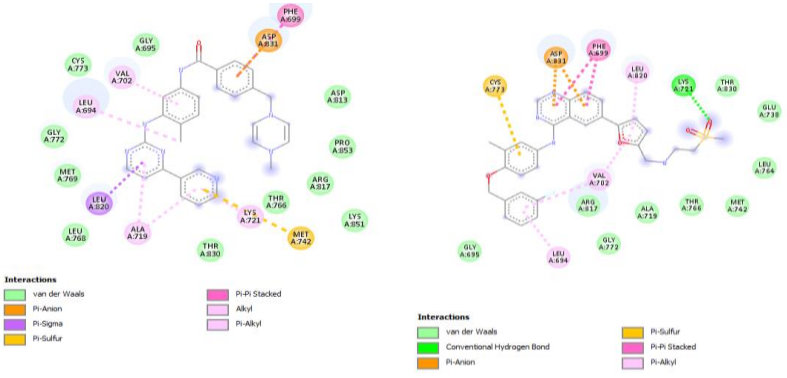
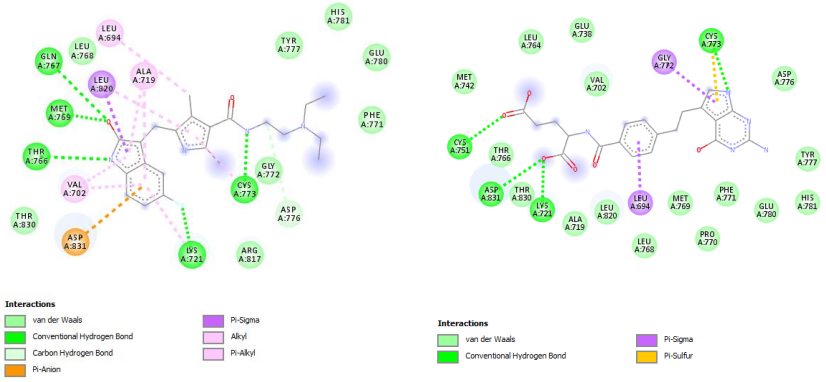


Fig. 1. Superpositions of Imatinib (a), Lapatinib (b), Sunitinib (c) and Pemetrexed (d) in the active site of the tyrosine kinase receptor (PDB ID: 1M17)



a b



c d

Fig. 2. The diagrams of intermolecular interactions of Imatinib (a), Lapatinib (b), Sunitinib (c) and Pemetrexed (d) in the active site of the tyrosine kinase receptor (PDB ID: 1M17)

Conclusions. In view of the detailed analysis of the geometric location of the tested molecules of anticancer drugs in the active site of biological target, the formation between them of a number of intermolecular interactions arises due to the formation of hydrogen bonds between the molecules and residues of the target amino acids and stabilization of the formed complex of "molecule-target" by intermolecular interactions with charge transfer (π-σ, π – Sulfur, π – anion, carbon hydrogen bond, π – π, Alk, and π – Alk).

Alkyl, allyl and amide «linker» groups between cycles provide the flexibility of the molecule and enable it to adopt the most energetically favorable conformational position in the active site of biological target.

So, we can distinguish fragments that provide (improve) ligand-receptor interaction and offer recommendations for the rational design of effective tyrosine kinase receptor inhibitors, namely:

- It is required to have in the molecule alkyl, allyl, oxy, amino, halogen substituted nitrogen-containing cyclic fragments: pyridine, pyrimidine, piperazine, indole, pyrrole, quinazoline;
- Modification of molecules by a sulfonyl moiety, alkyl and halogen substituted aromatic nucleus, amide and dicarbonic residues is promising.

SYNTHESIS AND ISOMERISM OF 2-AMINO-4-ARYL-3-CYANO-8-METHOXYCARBONYL-5-OXO-5,6,7,8-TETRAHYDRO-4*H*-CHROMENES

Voronovich A.S., Levashov D.V.
Scientific supervisor: prof. Shemchuk L. A.
National University of Pharmacy, Kharkiv, Ukraine
voronovichandrey@gmail.com

Introduction. Among chromene derivatives many compounds display a high level of different types of pharmacological activity (anti-inflammatory, antibacterial, anticoagulant, etc.) which causes the relevance of the synthesis of its new derivatives in order to find new biologically active substances.

Aim. In the present work we described the synthesis of derivatives of new derivatives of 2-amino-4-aryl-3-cyanochromenes via three-component one-pot interaction of esters of 2-hydroxy-4-oxo-6-arylcyclohexene-2-carboxylic acid with aromatic aldehydes and malononitrile.

Materials and methods. Starting compounds and reagents: arylidene acetones, dimethyl malonate, aromatic aldehydes, malononitrile, triethylamine, ethanol. The methods of organic synthesis and IR-, ^{1}H, ^{13}C NMR spectroscopy, chromatography-mass spectrometry methods were applied in the course of the research.