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Evaluation of ligand-macromolecule interaction

The noncovalent binding of molecules in solutions is important in chemistry, biology, pharmacy, medicine etc. because many different systems such as proteins with drug, DNA with drug, DNA with proteins, antibodies with antigens etc. form complexes. The determination of the association constant for complex formation has significant meaning in the analysis of their interaction. Studies of interactions of drugs with plasma protein accompany discovery of new generation of drugs. Binding of drugs to plasma proteins is a very important process in establishing pharmacodynamics and pharmacokinetic properties of drugs, because free drug molecules are more likely to cross the blood-brain barrier and exert pharmacological effect. The association constants can be determined by many different methods such as equilibrium dialysis, ultrafiltration, ultracentrifugation, flow injection gradient method and electrophoresis. All these methods have some advantages and disadvantages and therefore new methods are needed. **The purpose of my work was a development of more precise, fast and more flexible method than the others.** In my work I was inspired by the scientific paper by Bielejewska, A., et al. published in *Analytical Chemistry* in **2010**.

In my dissertation, I present a flow injection method in long, thin and coiled capillary to determine the association constant for complexes formed by various substances. The method is based on the determination of the width of the concentration distribution of compounds forming complexes. I study mostly drug-protein complexes. In my experiment I use Bovine Serum Albumin (BSA) as a model plasma protein. I determine the association constants of a large number of drugs with BSA. I also determine the value of the association constants of the complexes of albumin with 3β- and 3α- aminotropane derivatives (potential drugs). The compounds were obtained in a search for a new generation of antipsychotics. Additionally, I present two variants of the flow injection technique. In one of them protein and drugs are injected into the solution of protein. Such a solution has constant concentration of protein. In the second method the ligand-macromolecule injection is made into pure buffer and the protein concentration is not constant. Finally, I apply our method to study dye-micelle and protein-DNA complexes formation.