The proteins may be divided into integral proteins (membrane proteins, lipid-soluble) and globular proteins (soluble in water and aqueous electrolyte solutions). Both types of proteins differ in an organization, a mutual arrangement of the polypeptide chains. In the case of membrane proteins, side-chains of hydrophobic amino acid residues (Leu, Val, Ile, etc.) are exposed towards the lipid bilayer and interact with the fatty acid residues, while the hydrophilic amino acid residues (Glu, Ser, Lys, etc.) form channels modulating a permeability of the lipid bilayer or are exposed to the cytosol or intercellular matrix. In the case of globular proteins, the situation is reverse than in the case of transmembrane channels, hydrophilic residues are exposed to the external environment, while hydrophobic residues interact to form a hydrophobic core of the globule. The situation is similar in the case of the aggregation of peptides, shorter protein fragments. Peptides can form aggregates in an aqueous environment and in a lipid bilayer, and the degree of aggregation of a given peptide depends on the environment. Transmembrane peptides, which can penetrate the cell membrane, are an important class of compounds possessing desirable pharmacological properties, e.g. antibacterial, as well as can be used in drug delivery systems into cells.

The aim of the project is to develop a method for studying the equilibrium of peptide aggregation in biological membranes. The 1,3-dimercaptophenyl moiety will be attached to the tested peptides, which can give cyclooligomeric systems as a result of oxidation with atmospheric oxygen. The size of the resulting oligomers is controlled by the process of peptide chains aggregation, as shown in previous studies [1]. A properly stimulated (ultrasound or light) mixture of formed cyclooligomers remains in a thermodynamic equilibrium and can adapt to changes in the environment, enabling selection of the most stable product [2,3]. Simple LC-MS (liquid chromatography - mass spectrometry) and HPLC-UV (high-performance liquid chromatography - ultraviolet) measurements allow for qualitative and quantitative analysis of TASP's (template-assembled synthetic proteins) dynamic combinatorial libraries. The composition of these libraries reflects the equilibrium between peptide aggregates in a given environment. Thanks to these measurements, it will be possible to trace the process of aggregation of peptides in biological membranes depending on the concentration of peptides in relation to the concentration of lipids forming liposomes.

In the project, there are planned comparative studies on model peptide sequences for which the most stable aggregate, in the aqueous environment or in the lipid bilayer, is known from the literature. The composition of aggregate mixtures obtained in aqueous solutions and using biological membrane models, such as micelles and liposomes, will be compared. In the next step, fragments of transmembrane proteins and transmembrane peptides that are known to form ion channels will be examined. The obtained results will help to understand the differences in the folding of globular and integral proteins. The developed method will be able to be used to study the degree of aggregation of transmembrane peptides of a pharmacological significance. In the future, the recognition of the structure-aggregation-activity relationships will allow to rationally design peptide analogues with desired properties.

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