Behavior of biomolecules in phospholipid membranes studied by NMR, CIDNP and molecular dynamic techniques

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NMR, CIDNP and molecular dynamic techniques can provide unique information on the interaction of biomolecules with cell membranes. In particular, considerable attention is paid to the mechanisms of stereoselectivity in the interaction of chiral drugs with the active sites of enzymes and cell receptors. The first reason is the difference in therapeutic activity of the enantiomers of the common drugs. Another reason is the interest in the role of chiral inversion of amino acids involved in various peptides in the development of many diseases including Alzheimer's, Parkinson's, type II diabetes, and a number of other pathological conditions. In our study we used elementary chemical process - electron transfer (ET) to simulate individual stages of ligand-receptor and enzyme-substrate interactions. In particular, studies of photoinduced ET in chiral donor-acceptor dyads consisting of nonsteroidal anti-inflammatory drug (R/S)-ketoprofen and (L)-tryptophan show the stereo and spin selectivity of ET in diastereomers [1]. The present study is devoted to interaction of (S)-ketoprofen with L- and D-enantiomers of tryptophan in homogeneous aqueous solution and in phospholipid membranes [2]. The study was done using NMR technique and molecular modeling. These approaches confirm efficient penetration of ketoprofen into the lipid bilayer and binding with tryptophan molecule. The short-lived paramagnetic intermediates formed during the photoinduced ET from electron donor tryptophan to ketoprofen have been detected using chemically induced dynamic nuclear polarization (CIDNP) technique. It was found that S-ketoprofen interacts stereoselectively with tryptophan enantiomers in lipid membrane. The formation of the ketyl radical of ketoprofen under irradiation leads to the oxidation of membrane lipids and may be the cause of ketoprofen phototoxicity. However, in contrast to a homogeneous solution in phosphate buffer saline, where the amino acid tryptophan accelerates the photodecomposition of KP due to intramolecular hydrogen transfer, tryptophan in a lipid membrane significantly reduces the rate of photodegradation due to a reversible electron (or hydrogen) transfer reaction. The stereoselectivity in the rate of KP and lipids decomposition under UV irradiation of S-ketoprofen in the presence of tryptophan enantiomers in lipid bilayer has been detected. This work was supported by the Russian Science Foundation, grant 18-13-00047.

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