Using spin chemistry and photochemistry in the chiral model systems to study the role of D amino acids in the Alzheimer's disease

Leshina Tatyana V.,[1*] Ageeva Aleksandra A.,[1,2] Plyusnin Victor F.,[1,2] Magin Ilya M.,[1,2] Selyutina Olga Yu.,[1] Polyakov Nikolay E.[1]

[1] *Voevodsky Institute of Chemical Kinetics and Combustion SB RAS, Institutskaya 3, 630090, Novosibirsk, Russia*

[2] *Department of Natural Sciences, Physics Department, Novosibirsk State University, Pirogova 1, 630090, Novosibirsk, Russia*

* *E-mail: leshina@kinetics.nsc.ru*

Today it is considered established that the occurrence of a number of neurodegenerative diseases, including Alzheimer's disease, is preceded by the replacement of L amino acids with D analogues in vital proteins and peptides [1]. Replacing L amino acids with D analogues, for reasons not yet established, leads to fatal changes in the structure of proteins: they lose their ability to normal folding and form highly disordered conglomerates, which ultimately block the passage of nerve impulses. These highly disordered oligomers and fibrils cannot be studied by traditional high-resolution NMR and X-ray methods. Therefore, the current trend is to study the nature of differences in proteins with L and D isomers of amino acids by the example of short peptides by *in silico* methods [1]. This report presents a modification of the above approach. The modified version is associated with the use of the photoinduced processes in model chiral linked systems – donor-acceptor dyads, with L or D residues of tryptophan (Trp), or other donors in order to study the difference between the reactivity of optical isomers in the intramolecular photoinduced electron (PET) or hydrogen atom transfer in the solutions. The quenching of the excited states of isomers with different optical configurations occurs in the dyads, where acceptors are the well-known non-steroidal anti-inflammatory drugs (NSAIDs): (R/S) naproxen and (R/S) ketoprofen. The choice of NSAIDs is not accidental, since derivatives of these compounds are now being tested as drugs against Alzheimer's disease. The joint application of spin effects, including those calculated using the modified radical pair theory, fluorescence quenching techniques and molecular modeling has demonstrated a real difference in the structure and efficiency of PET in diastereomers with L/D Trp residues. In addition, photoinduced chiral inversion was found, which proceeds by a radical mechanism. In the light of the problem stated above, it is important that homo diastereomers (S,S) are less prone to chiral inversion than their hetero analogues (R,S). As a result of the study, it was possible to establish some analogies between the processes in model systems and amyloid Aβ42, which is considered the main protein that injures brain cells in Alzheimer's disease. Thus, the first results give hope that the use of model systems that can be investigated using a number of physical methods will be promising for the study of some factors in Alzheimer's disease.

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