

Statins and their interaction with model cell membranes according to the data of nuclear magnetic resonance spectroscopy

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Abstract

Aim. To study the location of pravastatin, simvastatin, fluvastatin and cerivastatin in molecular complexes with model cell membranes based on dodecylphosphocholine, and also to calculate the average interatomic distances between the atoms of statins and micelles. **Material and methods.** Nuclear magnetic resonance (NMR) spectroscopy was chosen as a method of study. NMR spectroscopy of the Overhauser nuclear effect (NOESY) is one of the most effective methods in the study of intermolecular interactions, in particular, in studies of drugs. Information on the spatial structure of the molecular complex, as well as on the fragments of molecules responsible for the effective interaction leading to complex formation, was obtained by NOESY spectroscopy. All NMR experiments were performed on a Bruker Avance II 500 spectrometer with a 5 mm zgradient inverse sensor with the TOPSPIN software. The calculation of the interatomic distances was made with an accuracy of 0.1 Å. **Results.** The location of pravastatin, simvastatin, fluvastatin and cerivastatin in molecular complexes with model cell membranes based on dodecylphosphocholine was determined based on NMR NOESY experiments. The average interatomic distances between the atoms of statins and micelles were also calculated. Pravastatin weakly binds to the polar surface of the model membrane, while simvastatin penetrates into the space between the hydrocarbon chains of the micelle. Fluvastatin interacts mainly with model membranes by penetration of its aromatic fragments into the surface of the micelle. Cerivastatin has a unique arrangement in the model membrane. It is located deep in the hydrophobic nucleus of the micelle close to the terminal methylene group. **Conclusion:** Even minor differences in the chemical structure of statins lead to different patterns of interaction with model membranes. These differences can explain the characteristics of the pharmacological properties of these substances.

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Keywords

Dodecylphosphocholine, Micelles, Molecular complex, Nuclear magnetic resonance, Statins

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