МЕМБРАННАЯ БИОФИЗИКА

MEMBRANE-ACTIVE PROPERTIES OF FERUTININ

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Previously we found that esters of sesquiterpenic alcohols with aromatic but not aliphatic acids isolated from the plant of the genus Ferula increase the cation permeability of biological and artificial membrane. One of them, Ferutinin displayed the highest activity as electrogenic Ca-ionophore [1,2]. Interest in Ferutinin is connected with its the ability to exhibit estrogenic properties, to cause bone mineralization and to induce apoptosis in cancer cells [3,4.5].

The present study was carried out to investigate the mechanism of complexation of Ferutinin with Ca and its action as a calcium ionophore. We show using solvent-containig BLM that majority of complexes appears to consist of a single terpenoid molecule bound to one Ca^{2+} ion. By contrast, the stoichiometry of Ferutinin – Ca^{2+} complexes in acetone determined by conductometric methods was 2:1. We also studied the mechanisms of Ferutinin action on the permeability mitochondrial membrane isolated from rat liver. It was shown that Ferutinine increased the permeability to Ca^{2+} ions in the range of concentrations 1-50 μM. Addition of cyclosporine A resulted in a considerable (5 fold) decrease of both the rate and the amplitude of Ferutinin induced swelling of mitochondria. Ca-ionophoric properties of Ferutinin are thought to contribute to Ca^{2+} accumulation in mitochondria and, as a consequence, to the opening of PTP into a highly conductive state that may underlie its apoptotic effects in cancer cells.

FT-IR and NMR data together with theoretical calculation indicate that in the absence of Ca ions Ferutinin molecules are hydrogen-bonded at phenol hydroxyl groups. The complexation of Ca by Ferutinin leads to the disruption of hydrogen bond due to spatial re-orientation of molecules from parallel to antiparallel alignment.

References

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FRET BIOSENSORS FOR SECOND MESSENGERS

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Biosensors based on the principle developed by Theodor Förster (i.e. using fluorescence **r**esonance **e**nergy **t**ransfer commonly known as FRET) in the 21 century allowed to resolve the intra-molecular spatiotemporal dynamics in living cells. Relatively few molecules are used by cells to transfer the information across different organs and non-invasive and live-cell friendly property of FRET based sensors allowed us to understand the methabolic state of cells in health and disease. Currently, the intra-molecular FRET biosensors have been increasingly used due to their high sensitivity in cellular microenvironments and recovery after bleaching.

We performed time-consuming optimizations of biosensors by trial and errors allowing us to develop sensors that can be co-expressed with transmembrane connexin channels that are permeable to the second messenger molecules.