STUDY OF THE PICOLINIC ACID INHIBITING EFFECT MECHANISM ON THE ASCORBIC ACID OXIDATION

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Synchrotron radiation allows for detail study of complex phenomena including biological and biomedical. X-ray crystallography of solid drugs in widely used in drug design and pharmacy, defining the kinds of intermolecular interaction. SAXS experiments help to understand processes in solution, such as complex formation. Molecular modelling helps in further understanding of such process's mechanisms.

Ascorbic acid (vitamin C) is one of the most important biologically active compounds, playing a key role in metabolic processes. Due to its reducing properties, it is widely used in medicine. However, the main drawback of ascorbic acid (AA) is its high chemical instability in aqueous solutions. When exposed to atmospheric oxygen, AA is easily oxidized. This process leads to the loss of biological activity of the drug.

It was shown by our colleagues that picolinic acid inhibits oxidation of AA in solution. It is intriguing that nicotinic acid despite its close structure has no such effect. The drastic difference was also in their influence on bioactivity of AA. A detailed elucidation of this process using is challenging. Traditional methods do not provide insight into the causes of stabilization. This study employed an integrated approach combining experimental data with computer modeling methods: molecular dynamics and quantum mechanics.

Molecular dynamics simulations allowed us to study solution at various pH values and identify the most stable complexes possibly responsible for the inhibitory effect. Quantum chemical calculations provided a detailed analysis of the process's energetics.

Modeling showed that picolinic acid forms a stable complex with ascorbic acid via two hydrogen bonds. The picolinic acid molecule simultaneously binds to two hydroxyl groups of ascorbic acid: the carboxyl group ($–COO^-$) interacts with one hydroxyl group (OH), and the nitrogen atom of the pyridine ring (N^+H) interacts with the other (O^-). This "double" bond firmly holds the molecules together, protecting ascorbic acid from oxygen and preventing its oxidation. For nicotinic acid, where N atom is shifted by 1 position in ring, such complementary complexes can not be formed.

This work was supported by the Ministry of Science and Higher Education of the Russian Federation within the governmental order for SRF "SKIF" Boreskov Institute of Catalysis (FWUR-2024-0040).