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Abstract

The Inhibition Study of Cytochrome bd Oxidase Using the Enzyme-Based Electrochemical Sensor †

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Abstract: Membrane proteins that participate in multiple vital functions of every living organism such as transport, signaling and respiration, provide 80 to 90% of the relevant targets for the pharmaceutical industries. The family of cytochrome bd oxidase enzymes is of great interest for the development of future antibiotics as they are found only in the respiratory chain of the prokaryotes and they are believed to be involved in bacterial adaptability mechanisms. They catalyze the reduction of molecular oxygen in water and oxidation of quinols and contribute to the proton motive force required for ATP synthesis. Due to their hydrophobic nature, membrane proteins are more difficult to handle than soluble proteins. Protein film voltammetry is a very convenient technique, because it allows for working at a very low concentration and for optimizing the electrode surface to the nature of the enzyme. Here, we have developed a biosensor for the study of terminal oxidases based on their immobilization on gold nanoparticles modified with a self-assembled monolayer of thiols. The stability of the protein films can be optimized by varying the nature of thiols and amount of lipids. This enzyme-based electrochemical sensor was successfully used for the inhibition screening of a target-focused library of 34 compounds which belong to the families of quinones, naphthoquinones, phenols, quinolones, coumarins and flavonoids against cytochrome bd oxidase. Moreover, the developed device was applied for the study of the catalytic reaction of the enzyme with small gaseous signaling molecules.

Keywords: membrane proteins; bioelectrochemistry; inhibition

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