Electrochemical Studies: Elucidating the Interaction Between the Antiviral Drug Molnupiravir and Calf Thymus dsDNA

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Molnupiravir (MLP) is a promising antiviral drug that is a natural nucleoside molecule analog called cytidine. RNA viruses use it to form the RNA strand. In the presence of molnupiravir, the virus turns to molnupiravir instead of cytidine, thus leading to an error in the formation of the RNA chain key. It is an effective agent in the treatment of COVID-19.[1] In order to design new pharmaceuticals, it is crucial to explore the mechanism of drug interaction with DNA. These interaction studies aid in understanding the response process. Because of its predictable chemical and functional groups, three-dimensional structure, and use as a principal therapeutic target, DNA is a biomolecule.[2] The aim of this study was to determine the interaction of MLP with calf thymus double-stranded DNA (ct-dsDNA) by electrochemical methods. In this study, the interaction between MLP and ct-dsDNA was investigated for the first time by electrochemical techniques. Investigation of these interactions was carried out by differential pulse voltammetry technique (DPV)[3] in two different ways. Firstly, ct-dsDNA was immobilized on the GCE surface, and the interaction was evaluated on the biosensor surface. Secondly, MLP-ct-dsDNA interaction was investigated by bare GCE in a solution that included ctdsDNA and MLP. Changes in ct-dsDNA between deoxyguanosine (dGuo) and deoxyadenosine (dAdo) oxidation signals were examined before and after the interaction. Moreover, the ct-dsDNA-MLP interaction was confirmed by the DPV of the systems MLP –dGuo and MLP – dAdo in the solution phase. The MLP-dAdo binding mode is responsible for the decrease in oxidation signals observed after incubation with various concentrations, as determined by differential pulse voltammetry. All measurements were carried out in pH 4.7 acetate buffer medium, and experimental parameters were optimized such as interaction time, concentration of MLP, ct-dsDNA, and dAdo solutions. Under optimum conditions, each investigation showed that MLP interacts with dAdo and decreases dAo oxidation signals. The dAdo oxidation peak currents were linearly proportional to the concentrations of the MLP in the range of 50-200 µM. The limit of detection (LOD) and limit of quantification (LOQ) were found to be 13.91 µM and 46.37 µM, respectively. It is believed that, elucidation of this mechanism will shed light on the development of drugs for the diagnosis and treatment of existing conditions and pandemic conditions that may occur later.

References

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