The effects of Diethylpyrocarbonate on Neuraminidase activity: implication for virus infection

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Neuraminidase is a glycoside hydrolase enzyme that is frequently found as an antigenic glycoprotein and is best known as one of the enzymes found on the surface of the Influenza virus. Neuraminidase cleaves terminal sialic acid residues from carbohydrate moieties on the surfaces of infected cells promoting the release of progeny viruses from infected cells and preventing aggregation of viruses. The main goal of this work was to evaluate the role of the histidine (His) residues in Influenza virus neuraminidase activity. For this purpose, we have used diethylpyrocarbonate (DEPC), a compound that modifies the nitrogen atom of imidazole ring of His forming N-carbethoxyhistidyl derivatives. Our data showed that His residues of influenza virus were successfully modified by DEPC as measured by the absorption at 240 nm associated with the formation of N-carbethoxyhistidine. By using mass spectrometry, we evaluated themass profile of triptic fragments of Influenza virus neuraminidase before and after treatment with DEPC, leading to the identification of histidine residues H126, H144, H150, H155 and H184 as those modified by the compound. We also measured virus neuraminidase activity after DEPC treatment and the infectivity of DEPC-treated Influenza virus. The enzyme activity displayed 50% of inhibition after treatment, which was followed by an important reduction of 6 logs on viral titer. Since DEPC treatment was shown to be very promising in inhibiting influenza neuraminidase, we aim now to use the same strategy for the neuraminidases other microorganisms.