

Antiviral effect of ellagic acid on influenza A virus infection in vitro

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Our present approach is to discover the mechanism of viral entry of an ellagitannin. We are trying to understand the mechanisms how the ellagitannin inhibits viral infection in the entry stage.

We found that ellagic acid (EA) showed a strong virucidal effect and act directly on the viral envelope. We found another ellagitannin showed the similar antiviral effect. Their effects of viral inhibition on cells are quite similar. EA showed hemagglutinin inhibition activity on recombinant H5HA. EA also showed the fetuin receptor binding inhibition activity with recombinant H5HA. The binding activity of EA showed stronger than that of fetuin. The binding affinity of EA on recombinant H5HA was also measured. EA showed stronger binding affinity than that of fetuin.

EA did not show any significant inhibitory effect on virus-cell fusion activity or fusion activity. We added EA after viral absorption on ice where IAV can bound with the cell receptors but can not enter into the cells. Then viral entry was investigated to incubate with various concentrations of EA at 37 °C. EA did not show any inhibitory effect on viral endocytosis or fusion processes. The results indicate that EA is very sensitive to the viral binding step of viral infection. If the viral particles are attached with cell receptors EA can not bind to the virus particles and did not show any inhibitory effect. EA needs to in contact with viral particles before viral inoculation to show its viral inhibition activity. We investigated the direct binding affinity of EA with recombinantly produced H5HA and found a stronger binding affinity than that of fetuin. The results indicate that EA may directly bound to any of the site of IAV. EA acid also showed inhibitory effect on influenza B virus. However, EA did not show any inhibitory effect on the infection of human parainfluenza virus type 1 and type 3 infection. The inhibition pattern in different cells is quite similar in various types of influenza viruses. Their 50% inhibitory concentrations was in the range of 0.10 to 0.30 μM . The ratio of 50% cell toxic concentration with the 50% inhibitory concentration was about 11 to 33.8. The results indicate that ellagic acid showed inhibitory effect at a non toxic concentration of cells.