

Zinc Salts Block Hepatitis E Virus Replication by Inhibiting the Activity of Viral RNA-Dependent RNA polymerase

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Abstract

Hepatitis E virus (HEV) causes an acute, self-limiting hepatitis in healthy individuals and leads to chronic disease in immunocompromised individuals. HEV infection in pregnant women results in a more severe outcome, with the mortality rate going up to 30%. Though the virus usually causes sporadic infection, epidemics have been reported in developing and resource-starved countries. No specific antiviral exists against HEV. A combination of interferon and ribavirin therapy has been used to control the disease with some success. Zinc is an essential micronutrient that plays crucial roles in multiple cellular processes. Zinc salts are known to be effective in reducing infections caused by few viruses. Here, we investigated the effect of zinc salts on HEV replication. In a human hepatoma cell (Huh7) culture model, zinc salts inhibited the replication of genotype 1 (g-1) and g-3 HEV replicons and g-1 HEV infectious genomic RNA in a dose-dependent manner. Analysis of a replication-defective mutant of g-1 HEV genomic RNA under similar conditions ruled out the possibility of zinc salts acting on replication-independent processes. An ORF4-Huh7 cell line-based infection model of g-1 HEV further confirmed the above observations. Zinc salts did not show any effect on the entry of g-1 HEV into the host cell. Furthermore, our data reveal that zinc salts directly inhibit the activity of viral RNA-dependent RNA polymerase (RdRp), leading to inhibition of viral replication. Taken together, these studies unravel the ability of zinc salts in inhibiting HEV replication, suggesting their possible therapeutic value in controlling HEV infection. Hepatitis E virus (HEV) is a public health concern in resource-starved

countries due to frequent outbreaks. It is also emerging as a health concern in developed countries owing to its ability to cause acute and chronic infection in organ transplant and immunocompromised individuals. Although antivirals such as ribavirin have been used to treat HEV cases, there are known side effects and limitations of such therapy. Our discovery of the ability of zinc salts to block HEV replication by virtue of their ability to inhibit the activity of viral RdRp is important because these findings pave the way to test the efficacy of zinc supplementation therapy in HEV-infected patients. Since zinc supplementation therapy is known to be safe in healthy individuals and since high-dose zinc is used in the treatment of Wilson's disease, it may be possible to control HEV-associated health problems following a similar treatment regimen.

Biography

Dr. Nidhi Kaushik has completed her PhD at the age of 30, from Translational Health Science and Technology Institute, India. She is teaching as an Assistant Professor in SRM University, Delhi NCR, India. She has published six papers in reputed journals

15th International Conference on Virology, Emerging Diseases & Vaccines, July 20-21, 2020, Montreal, Canada

Abstract Citation: Dr. Nidhi Kaushik, Zinc Salts Block Hepatitis E Virus Replication by Inhibiting the Activity of Viral RNA-Dependent RNA polymerase, *Virology* 2020; July 20-21, 2020; Montreal, Canada.