Synergistic Antiviral Activity of Compound CW-33 and Type I Interferon against Enterovirus A71

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Background/Objective
Enterovirus A71 (EV-A71), a member of the Picornaviridae family, could cause hand, foot, and mouth disease, aseptic meningitis, severe central nervous system diseases, even death. There are not yet specific vaccines or antiviral drugs for treating enterovirus infection in clinic.

Method
The study investigated antiviral activity of a furoquinoline alkaloid compound CW-33 alone or in combination with type I IFN against EV-A71.

Result
CW-33 had a moderate antiviral activity to inhibit EV-A71 replication in vitro, but combined treatment with IFN-β demonstrated promoted the antiviral actions, such as viral cytopathicity (apoptosis), virus yield, and plaque formation. Molecular docking discovered that CW-33 bound to EV-A71 2A protease active site; in vitro cleavage assays showed CW-33 inhibiting the enzymatic activity of recombinant 2A protease. CW-33 specifically inhibited 2A protease-mediated cleavage of IFNAR1, correlating with recovery of Tyk2 and STAT1 phosphorylation as well as 2',5'-OAS upregulation in EV-A71 infected cells in responses to type I IFN.

Conclusion
Combined treatment of CW-33 with low dose type I IFN could reduce type I IFN antagonism of EV-A71, in which develops alternative approaches to treat EV-A71 infection.