Antiviral Activity of Halogenated CW-33 Derivatives against Japanese Encephalitis Virus

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Background/Objective
Japanese Encephalitis Virus (JEV), one of mosquito-borne flaviviruses in Flaviviridae, causing severe clinical symptoms, and even death. Japanese encephalitis has no specific treatment, except a few supportive treatments. In our laboratory, the dihydrofuran carboxylate CW-33 compound was identified as a potential lead compound against JEV. This study further investigated antiviral activity of 15 halogenated CW-33 derivatives.

Method
Antiviral activity of halogenated CW-33 derivatives was evaluated using assays of cytopathic effect, apoptosis, supernatant virus yield, intracellular virus titer, and plaque reduction. Antiviral mechanism of halogenated CW-33 derivatives was discovered using proteomic approaches, Western blotting and real-time PCR.

Result
CW-33K, CW-33L, and CW-33M exhibited inhibitory effects on JEV-induced cytopathic effect and apoptosis in dose-dependent manners, as better than CW-33. Supernatant virus yield assay demonstrated IC50 values against JEV were 38.5 μM for CW-33, 29 μM for CW-33A, 4.6 μM for CW-33K, 13.3 μM for CW-33L, and 7.8 μM for CW-33M, respectively. CW-33 and its halogenated derivatives had no effect on virus attachment and virucidal activity, but suppressed the viral RNA synthesis. Proteomic analysis indicated protein phosphatase inhibitor 2, heat shock protein 90 beta, and acetyl-CoA carboxylase 1 correlated with antiviral actions of CW-33 and its halogenated derivatives.

Conclusion
The result demonstrated CW-33 and its halogenated derivatives exhibiting a significant potential on the development of anti-JEV agents.