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The anti-enveloped viral activity of surfactin from *Bacillus subtilis* by inhibiting membrane fusion

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Targeting membranes of enveloped viruses, as a new paradigm for developing direct-acting antivirals. It has recently been concluded that wedge-liked lipid would have antiviral properties by inhibiting membrane fusion. The aim of this study was to investigate whether surfactin from *Bacillus subtilis* have this particular anti-enveloped virus mechanism, since the structure of surfactin meets the characteristics of wedge-shaped lipid. First, we found that surfactin has a potent antiviral activity directly on porcine epidemic diarrhea virus (PEDV) or porcine transmissible gastroenteritis virus (TGEV), at a cytotoxicity-free concentration. This antiviral process can be completed less than 10 minutes, but alter the incubation temperature to 4 degrees will totally abolish this effect. Then, we demonstrated that surfactin treatment did not disrupt TEGV envelop, by sucrose density gradient centrifugation assay and observed by electron microscopy. However, surfactin treatment will inhibit the fusion between octadecyl-rhodamine labeled TGEV and cell membranes, through a membrane fusion assay. Last, in the membrane curvature assay, incorporation of surfactin in dielaidoylphosphatidylethanolamine membrane will increase its inverted hexagonal phase transition temperature, indicating that surfactin tends to form positive curvature in membrane, which is membrane fusion unfavorable. In summary, we provide the evidence that surfactin inhibits viral and cell membrane fusion, and could be classified as fusion inhibitors.

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