reduction of NTHi adherence caused by DSCG is associated with attenuation of ICAM-1 expression on A549 cells. Meanwhile, cytokine-induced ICAM-1 expression was reduced more strongly by the corticosteroids than DSCG. The difference in the extent of ICAM-1 inhibition between RSV-induced and cytokine-induced indicated that DSCG might affect RSV infection.

As seen in plaque assay and viral syncytium assay, DSCG treatment after RSV adsorption significantly reduced the viral infectivity of A549 cells. DSCG is a safe and widely used drug for the prevention of bronchial asthma (19–21). DSCG is known to have effects such as mast cell stabilization and suppression of various inflammatory cells (22–24). Previous studies have also demonstrated that DSCG has antiviral effects, and there has been a recent report about inhibitory effects on influenza virus *in vitro* and *in vivo* (18). However, the molecular mechanisms underlying DSCG-induced signaling and anti-viral effects have remained unclear. In this study, to determine the inhibitory effect of DSCG on RSV infection, treatment with DSCG at different stages of viral infection was investigated. DSCG administered after, but not before or during, RSV adsorption effectively inhibited viral infection. These results suggest that DSCG predominantly inhibits the late stages of viral infection, such as the budding of progenitor viruses. Hidari *et al.* have supposed that the anti-influenza viral effect of DSCG is a combination including an inhibition of viral neuraminidaze activities and inhibition of membrane fusion. We speculate that the inhibition of membrane fusion is one of the mechanisms of anti-RSV effect of DSCG. Further elucidation of the mechanism underlying the anti-RSV effect of DSCG is needed.

We showed that DSCG inhibited RSV infection of A549 cells and attenuated the cell surface expression of ICAM-1. It is indicated that ICAM-1 down-regulation is one of the mechanisms that modulate NTHi adhesion to A549 cells. Not only ICAM-1 but also CEACAM1 and PAFr have been reported to be NTHi adhering receptors and up-regulated by RSV infection (8). This is why blocking of NTHi adhesion to RSV-infected cells with anti-ICAM-1 MAb did not completely prevent excess NTHi adhesion. It is speculated that inhibition of RSV infection by DSCG might also down-regulate these receptors, *i.e.* not only ICAM-1.

Differences in the magnitude of bacterial adhesion and receptor expression have been reported for different cell types (8). Avadhanula *et al.* (8) asserted that the differences in the responses of distinct cell types must be taken into consideration when interpreting the findings of *in vitro* studies. In this study, we used A549 cells as lower airway epithelial cells, because of the characteristic higher increase in adhesion molecules expression and bacterial adhesion when they are infected with RSV.

There has been a report that DSCG treatment in hospitalized infants with RSV bronchiolitis has no clinical effect (25). This clinical study was for the hospitalized infants who probably have already received considerable airway injury and represented respiratory dysfunction by RSV infection. It suggests that the effect of DSCG on the RSV-induced airway inflammation including scavenging oxygen radicals is not clinically sufficient. We demonstrated that DSCG inhibits RSV infection and NTHi adhesion to the RSV-infected epithelial cells *in vitro* in this study. DSCG treatment on the earlier stage of RSV infection might have a clinical effect by inhibiting RSV infection and secondary NTHi infection. Further examinations including an *in vivo* study will clarify the effects of DSCG on RSV infection and NTHi adhesion to RSV-infected cells.

In conclusion, we demonstrated that DSCG inhibits enhanced adherence of NTHi to A549 cells infected with RSV, whereas Dex and Fp do not. It is suggested that DSCG exerts an anti-RSV effect, and consequently attenuates the expression of NTHi receptors.

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