Glucosyl hesperidin prevents influenza A virus replication *in vitro* by inhibition of viral sialidase

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Influenza is a common infectious disease in birds and mammals with high rates of morbidity and mortality. Four influenza pandemics occurred in the 20th century and caused more than 20-50 million of deaths. The neuraminidase inhibitor oseltamivir is compromised due to the emergence of drug-resistant viruses that escape interaction of the inhibitor with the active site of viral neuraminidase. Antiviral drugs that can inhibit both currently circulating human influenza viruses and avian influenza viruses are therefore urgently needed for future prevention of pandemic influenza.

Flavanoids have possible health benefits due to their potent antioxidant and free radical-scavenging activities in vitro. Hesperidin, a flavonoid obtained from citrus fruits, is known to have multiple biological activities and antimicrobial activities for human viruses; however, hesperidin has very low solubility in water and the target molecule of hesperidin for influenza virus remains unknown. A water-soluble derivative of hesperidin, glucosyl hesperidin (GH), which was synthesized by regioselective transglycosylation with cyclodextrin glucanotransferase, has been reported to have biological activities that are as or stronger than those of hesperidin.

To determine the inhibitory effect of GH on influenza A virus (IAV) infection, Madin-Darby canine kidney (MDCK) cells were treated with GH before, at the same time as, and after IAV inoculation. GH treatment before IAV inoculation had no effect on virus replication, whereas, treatment with GH at the same time as or after IAV inoculation induced distinct reduction in IAV replication. Inhibition analysis of GH against two surface glycoprotein spikes of IAV revealed that GH prevents IAV replication by inhibition of viral sialidase activity that is involved in the entry and release stages on IAV infection but not by receptor binding inhibition. GH had no cytotoxic effects on MDCK cells in a dose range of 0-25 mM. Our results provide useful information for the development of novel sialidase inhibitors for influenza prevention[1)].

1) Saha K. R., Takahashi T., Suzuki T. Biol. *Pharm. Bull.* 32, 1188-1192 (2009)