Oligomeric proanthocyanidins from *Rumex acetosa* L. inhibit the attachment of herpes simplex virus type-1

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Abstract

The polyphenole-enriched acetone–water extract R2 from the aerial parts of *Rumex acetosa* L. containing high amounts of oligomeric and polymeric proanthocyanidins and flavonoids was tested for antiviral activity. R2 exhibited strong antiviral activity against herpes simplex virus type-1 (HSV-1) while the replication of adenovirus 3 was not affected. By plaque reduction test and MTT assay on Vero cells, the HSV-1-specific inhibitory concentration (IC_{50}) and cytotoxic concentration (CC_{50}) were determined. R2 exibited an IC_{50} of 0.8 μg/mL and a selectivity index (SI) (ratio of IC_{50} to CC_{50}) of approximately 100 when added to the virus inoculum for 1 h at 37 °C prior to infection. The antiviral activity was due to the presence of flavan-3-ols and oligomeric proanthocyanidins in the extract. Structure–activity analyses indicated that flavan-3-ols and proanthocyanidins with

galloylation at position O-3 are highly potent compounds (SI > 40), while ungalloylated compounds did not exhibit antiviral effects (SI < 1).

R2 and a major proanthocyanidin from R2, epicatechin-3-O-gallate-(4β → 8)-epicatechin-3-O-gallate abolished virus entry into the host cell by blocking attachment to the cell surface. When added after attachment at a concentration of ≥12.5 µg/mL, R2 inhibited also penetration of HSV-1 into the host cell. R2 and epicatechin-3-O-gallate-(4β → 8)-epicatechin-3-O-gallate were shown to directly interact with viral particles leading to the oligomerisation of envelope proteins as demonstrated for the essential viral glycoprotein gD.

Using raft cultures with three-dimensional organotypic human skin equivalents it was shown that treatment of cultures with R2 after infection with HSV-1 resulted in a reduced viral spread.