Prunella vulgaris polysaccharide inhibits herpes simplex virus infection by blocking TLR-mediated NF-kB activation

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Abstract:

Introduction: *Prunella vulgaris* polysaccharide extracted by hot water and 30% ethanol precipitation (PVE30) was reported to possess potent antiviral effects against herpes simplex virus (HSV) infection. However, its anti-HSV mechanism has not yet been fully elucidated.This study aimed to investigate the potential mechanisms of PVE30 against HSV infection.

Materials and Methods: Antiviral activity was evaluated by *a plaque* reduction assay, and the EC50 value was calculated. Immunofluorescence staining and heparin bead pull-down assays confirmed the interactions between PVE30 and viral glycoproteins. Real-time PCR was conducted to determine the mRNA levels of viral genes, including UL54, UL29, UL27, UL44, and US6, and the proinflammatory cytokines TNF-α and IL-6. The protein expression of viral proteins (ICP27, ICP8, gB, gC, and gD), the activity of the TLR-NF-κB signalling pathway, and necroptotic-associated proteins were evaluated by Western blotting. The proportion of necroptotic cells was determined by flow cytometric analysis.

Results: The *P. vulgaris* polysaccharide PVE30 was shown to inhibit HSV infection by blocking viral attachment and penetration. Mechanismly, PVE30 competed with heparan sulfate for interaction with HSV surface glycoprotein B and gC, thus strongly inhibiting HSV attachment to cells. In addition, PVE30 downregulated the expression of IE genes, which subsequently downregulated the expression of E and L viral gene products, and thus effectively restricted the yield of progeny virus. Further investigation confirmed that PVE30 inhibited TLR2 and TLR3 signalling, leading to the effective suppression of NF-κB activation and IL-6 and TNF-α expression levels, and blocked HSV-1-induced necroptosis by reducing HSV-1-induced phosphorylation of MLKL.

Conclusions: Our results demonstrate that the P. vulgaris polysaccharide PVE30 is a potent anti-HSV agent that blocks TLR-mediated NF-κB activation.