

Quercetin Inhibits rhinovirus replication and subsequent chemokine response in Airway Epithelial Cells

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Rationale: Rhinovirus (RV), a single-stranded RNA virus from the *picornaviridae* family, is responsible for the majority of common colds. RV is an important trigger of COPD, asthma and CF exacerbations. Flavonoids with antioxidant and anti-inflammatory properties may be beneficial in the treatment of viral infections particularly in patients with underlying chronic lung diseases. Quercetin (3, 3', 4', 5, 7-pentahydroxyflavone) has potent antioxidant effects and inhibits various protein kinases by competing for ATP binding site. RV induces PI3 kinase-dependent chemokine responses and oxidative stress-dependent disruption of barrier function in polarized airway epithelial cells. Therefore, we hypothesized that quercetin reduces RV-induced pro-inflammatory response and reduction in transepithelial resistance of polarized airway epithelial cells.

Method: Polarized 16HBE14o- cells were infected with major or minor group RV or replication-deficient UV-irradiated virus (UV-RV) and incubated for 1 hour at 33°C to allow binding and endocytosis of RV. Infection media was then replaced with fresh media containing either quercetin; LY294002, a chemical inhibitor of PI3-kinase, or diphenyleneimidonium (DPI), an inhibitor of NADPH oxidase. After incubation for 8 or 24 hours, TER was measured and media was collected for IL-8 and IL-29 (IFN-11) analysis, and the cells harvested for Western blot analysis and determination of viral titer.

Results: Quercetin inhibited RV-induced reduction in TER, decreased RV-stimulated IL-8 expression. Surprisingly, we also observed reduction in interferon response, viral titer and complete abrogation of RV-triggered cleavage of eIF4GI, which is required for efficient translation of viral polypeptide. On the other hand, LY294002 although affected IL-8 response, had no effect on IL-29 response, viral titer or RV-induced cleavage of eIF4GI. DPI partially reduced viral titer and RV-induced effects in airway epithelial cells

Conclusions: Our results suggest that quercetin may reduce RV-triggered cytokine response, and disruption of barrier function by inhibiting viral replication and virus induced cleavage of eIF4GI. Further, the observed effects of quercetin on viral replication may be attributed to its antioxidant effects and not on its effect on PI3-kinase activity. Therefore, quercetin may be beneficial in the treatment of viral infections, particularly in patients with underlying chronic lung disease.