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P89 Combined anti-influenza virus effect of a plant polyphenol-rich extract and rimantadine

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Background: The anti-influenza virus activity of the polyphenol-rich extract from Geranium sanguineum L. (PC) has been studied intensively. Its in vitro virus-inhibitory effect was strain-dependent; PC inhibited the virus-induced cytopathogenic effect and plaque formation, the production of infectious virus and haemagglutinin, the synthesis of virus-specific RNA and proteins (Serkedjieva and Hay, 1998). PC protected mice from mortality in the experimental influenza A/Aichi/2/68 (H3N2) virus infection (EVI) (Serkedjieva and Manolova, 1992).

Results: The in vitro combined use of PC with Rimantadine hydrochloride (Rim) resulted in synergistic inhibition of the A/chicken/Germany/34, strain Rostock (H7N1) virus replication in MDCK cells. The cooperative effects were defined on the base of infectious viral yields by two complementary methods. The joint application of PC and three other amantadine derivatives also resulted in marked enhanced inhibition. Administration of PC in combination with Rim in the EVI in mice produced a synergistic protective effect: mortality rates were significantly decreased (index of protection = 77.8%), mean survival times were markedly prolonged (+5.2 days). A pronounced reduction of the lung lesions due to infection and of lung infectious virus titres was achieved (Δlog10 TCID50/ml = 1.6-2.4).

Discussion: While the need for novel potent antiviral agents continues to exist, the strategy of combined antiviral therapy with available antiviral drugs has proved its usefulness. The presented results suggest that the combined use of natural and synthetic viral inhibitors may be used successfully to potentiate the antiviral efficacy of the plant preparations and may enable dose reduction of their toxic components.

P90 Inhibition of HCoV-NL63 infection at early stages of the replication cycle

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Background: HCoV-NL63, a recently discovered member of the Coronavirus family, has spread worldwide and is associated with acute respiratory illness in young children, elderly and immunocompromised persons. Further analysis of HCoV-NL63 pathogenicity seems warranted, in particular because the virus uses the same cellular receptor as SARS-CoV.

Methods: As there is currently no HCoV-NL63 specific and effective vaccine or drug therapy available, we evaluated several existing antiviral drugs and new synthetic compounds as inhibitors of HCoV-NL63, targeting multiple stages of the replication cycle.

Results and Conclusions: Of the 27 compounds that we tested, five potently inhibited HCoV-NL63 at early steps of the replication cycle: Intravenous immunoglobulins (IVIG), heptad repeat peptides, siRNAs, beta-D-N4-hydroxyxyctidine and 6-azauridine. These compounds showed low IC50 values and low cytotoxicity and are candidates to be developed further for mono- or combination therapy.