Final Abstract Number: 40.058
Session: Virology and Viral Infections (Non-HIV)
Date: Thursday, June 14, 2012
Time: 12:45-14:15
Room: Poster & Exhibition Area

EPs® 7630 (Umckaloabo®), an extract from *Pelargonium sidoides* roots, exerts anti-influenza virus activity in vitro and in vivo

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Background: A prodelphinidin-rich extract from *Pelargonium sidoides* DC, EPs® 7630 (Umckaloabo®), which is licensed to treat respiratory tract infections such as acute bronchitis, was investigated for its antiviral effects.

Methods: The efficacy of EPs® 7630 on influenza A virus propagation was investigated *in vitro* against different strains, after different infection and treatment timepoints and by neuraminidase and hemagglutination inhibition assays. Isolated monomers, dimers and oligo-/polymeric fractions were compared for antiviral activity. *In vivo*, EPs® 7630 was investigated after inhalative application.

Results: EPs® 7630 showed dose-dependent anti-influenza activity at non toxic concentrations against pandemic H1N1, Oseltamivir sensitive and resistant seasonal H1N1, seasonal H3N2 and the laboratory H1N1 strain A/Puerto Rico/8/34, while it had no antiviral activity against adenovirus or measles virus. The extract inhibited an early step of influenza infection and impaired viral hemagglutination as well as neuraminidase activity. However, EPs® 7630 did not exhibit a direct virucidal effect, as virus preincubation (unlike cell preincubation) with the extract did not influence infectivity. Analysis of EPs® 7630 constituents revealed that prodelphinidins represent the active principle. Chain length influenced antiviral activity, as monomers and dimers were less effective than oligo- and polymers. Importantly, gallocatechin and its stereoisomer epigallocatechin exert antiviral activity also in their monomeric form. In addition, EPs® 7630 administered by inhalation significantly improved survival, body weight and body temperature of influenza-infected mice, without obvious toxicity, demonstrating the benefit of EPs® 7630 in treatment of influenza.

Conclusion: In this study, we investigated the anti-influenza mechanism of EPs® 7630 and demonstrate its efficacy *in vitro* and *in vivo*. The extract shows a robust effect against multiple different IAV strains *in vitro* and protection of mice against a lethal virus challenge at non-toxic concentrations, underlining the benefit of EPs® 7630 as a treatment for influenza virus infection.

http://dx.doi.org/10.1016/j.ijid.2012.05.220

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Acute encephalitis in children caused by influenza virus-AH1N1

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Background: Worldwide, seasonal flu epidemics remains a major public health problem. Most recent pandemic influenza, with AH1N1 virus, also included Romania. Acute encephalitis is one of the most severe complications of influenza in children.

Methods: In this article, we present two clinical cases of acute encephalitis in children caused by AH1N1 influenza virus, that were hospitalized in Pediatric Intensive care unit of the National Institute of Infectious Diseases "Prof. Dr. Matei Bals" in Bucharest. Positive diagnosis was established on clinical, epidemiological and laboratory data. Diagnosis confirmation was made by RT-PCR from nasal-pharyngeal secretions of patients. MRI examination was performed in both cases and it showed disseminated encephalitis outbreaks located especially in the brainsteam, in the first case and for the second patient subarachnoid hemorrhage with the absence of cerebral circulation. The EEG examination confirmed the diagnosis for both patients. They both were treated with Oseltamivir and cortisone in high doses.

Results: The outcome for both patients was grave, the first one presented severe mental and physical retardation and the second one required oral-tracheal intubation and mechanical ventilation for 90 days but still had fatal evolution.

Conclusion: The flu caused by AH1N1 virus can have severe evolution into encephalitis or other neurological complications or even death. Establishing early diagnosis and proper treatment may be the key for a good outcome and prognosis improvement.

http://dx.doi.org/10.1016/j.ijid.2012.05.221