the model of experimental influenza is effective for intranasal, oral and parenteral methods of administration. Prophylactic efficacy of ACA was also established. Use of ACA for the prevention and treatment of influenza and acute respiratory diseases (ARDs) in children and adults was allowed in the Ukraine in 2009. With the scope to study the ACA prophylactic activity studies in organized collectives, we have prescribed it per-orally in 2.0 g dose four times a day during a week. The monitoring was performed in two independent collectives (923 young adults males aged 18–19 years old) during acute respiratory diseases appraisal. As the reference, 4 groups were taken (2 from each collective) but without E-ACA application. The obtained results shows: compare to the high morbidity rates in the reference group of the first tested collective in the basic group preventively treated with ACA, number ARDs has decreased in two times. At the same time compare to the morbidity rate growth of ARDs (by 15–27%), quinsy (by 14–21%) and pneumonia (by 6–7%) in the reference groups of the second tested collective, of the main examined group, treated with ACA, pneumonia morbidity rate has decreased up to five times, while the ARDs and quinsy levels were stabilized. The smallest number of cases of these infections in both teams surveyed recorded in the period of ACA application. The results obtained allow recommend the use of ACA for the efficient prophylactics of ARDs, quinsy and pneumonia in the organized collectives in the period of increased incidences of these infections.

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Polymer-coupled Systems for Blocking the Viral Fusion 1. Modeling *in silico* the *in vitro* HIV-1 Entry Inhibitors

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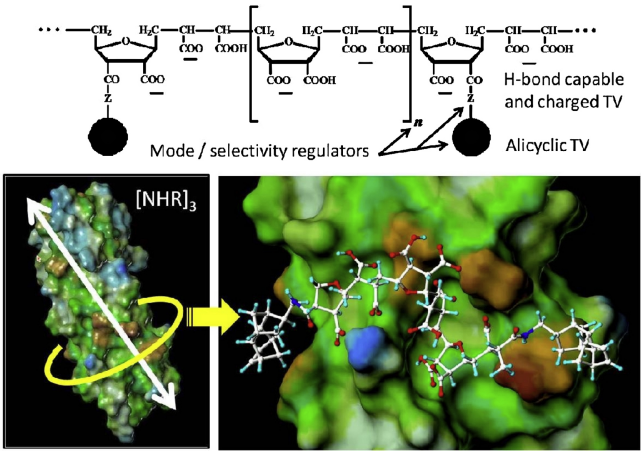
A trimer hairpin complex of viral class I fusion proteins heptade repeat regions (**NHR** – **CHR**) is a crucial trigger for fusion in entry mechanism of the human immunodeficiency virus type 1 (**HIV-1**) and of many other (*retro-*, *orthomyxo-*, *paramyxo-*, *corona-*) enveloped viruses. So an inhibition of the fusion mediators should be considered as a key drug design strategy against these viruses. In focus of the HIV/AIDS at least three traditional routes, via small-molecules (**1**), peptides (**2**), and antibodies (**3**), are developed. But all ones in principle cannot provide a drug-resistance preventing efficiency because of mono-point/site mode of action (1/2) or of inadequate adaptability (2/3) to the target mutations. Here we exploring a complementary approach based on water-soluble biocompatible synthetic polymers with flexible chain backbone, modified via targeting vectors (**TV**) designed for recognition-blocking the NHR tri-helices core of HIV-1 gp41. The polymeric substances with controlled hetero-functional TV (H-bond capable, electrostatic selective to positive Lys/Arg sites, and suitable to dock in hydrophobic pockets) were synthesized, evaluated *in vitro* for HIV-1 entry inhibition, and explored by computational docking and molecular dynamics. The TVs satisfy to point/site docking (likely the small molecules/antibodies), and H-bond-capable and charge driven polymeric chain blocks the target predominantly along the a-helices (similarly the C34/related peptides). But in contrast with the known NHR blockers the newly studied polymeric systems possess the unique adaptability to combined axial-co-belting (from pocket to pocket) multi-blockage both along and around the tri-helices complex, for example:



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Discovery and Development of Orally Active Antivirals for the Treatment of RSV: Identification of BTA9881 and a 2nd Generation Candidate

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Respiratory syncytial virus (RSV) is the predominant cause of acute lower respiratory tract infection (LRTI) in children. It has been estimated that in the United States 4–5 million children up to 4 years of age will develop an acute RSV LRTI annually. More than 125,000 children are admitted to hospital for RSV related illness in the United States each year. RSV infection is also a major cause of morbidity and mortality in high risk adult populations where infection rates can range from 50 to 80% depending on the underlying medical condition. Small molecule inhibitors of RSV fusion have been described by several groups. Compounds with this mechanism are thought to interfere with F-mediated fusion *via* one of two domains on the glycoprotein. The Biota RSV fusion inhibitor program encompasses several classes of inhibitors with examples advanced from the discovery stage to Phase I clinical trials. The most developed class to date is the imidazoisoindolones and examples from this series are orally bioavailable with excellent pharmacokinetic profiles in multiple species. Data will be presented to describe the characterization and development of the series from early research "hits" through preclinical development and nomination of BTA9881 as a clinical candidate. BTA9881 demonstrated excellent pharmacokinetic properties and a good safety profile at doses up to 400 mg per day in humans in a Phase I single ascending dose trial. Research has continued to identify distinct structural classes of potent and selective RSV-F inhibitors. A second generation candidate has been identified with a superior screening profile to BTA9881 and results from *in vitro* and *in vivo* studies will be discussed.

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