

## Abstract

Influenza virus causes common illness that annually infects several million people worldwide. Although the seasonal flu usually isn't life threatening, it is dangerous mainly for very young and elderly individuals. Nevertheless, a major threat for every person are new influenza strains that arise from a reassortment of viral strains that invade different species. Newly reassorted flu viruses have caused several pandemics with devastating effects, and so it is necessary to search for new treatment approaches that would prevent similar cases in future.

Influenza virus neuraminidase is a protein located on the surface of viral particles. It catalyzes the release of newly formed virions from cytoplasmic membrane of infected cells and plays a key role in the life cycle of influenza virus. As an enzyme with defined substrate, neuraminidase is a very good target for development of drugs, which would inhibit its function, and thus prevent further virus spreading.

By 2015, only four drugs against influenza were approved worldwide. Two of them, oseltamivir and zanamivir, target neuraminidase. Because of significant influenza resistance against the two remaining drugs (amantadine and rimantadine) occurred, neuraminidase inhibitors are virtually only medications. Therefore, development of new inhibitors becomes one of the main objectives of influenza virus research, also due to frequent incidence of drug – resistance among influenza strains.

One of the novel inhibitors is tamifosphor. It is a oseltamivir derivative that was designed to create strong interactions with residues in neuraminidase binding site. Within this diploma thesis, characterization of binding of oseltamivir carboxylate and tamifosphor was performed with neuraminidase from influenza virus subtype H7N9 that emerged in 2013 in China. Although this influenza strain has infected only a few hundred people, the disease mortality was nearly 40 %. Analysis of biomolecular interactions with inhibitors by isothermal titration calorimetry provides valuable information about complex formations and it can help in the development of new drugs.

*Key words:* neuraminidase; isothermal calorimetry; enzyme kinetics; recombinant proteins