ABSTRACT

Flaviviruses and coronaviruses are +RNA viruses capable of causing a wide range of diseases, which can be fatal. The true potential of these viruses was revealed by recent COVID-19 pandemic. Currently, there is an effort to develop compounds that will be active against most or many +RNA viruses. One of the main targets of antiviral therapy are enzymes that play a key role in virus replication, such as RNA-dependent RNA polymerases and methyltransferases. In the case of flaviviruses, the enzyme that is responsible for both these functions is the non-structural protein NS5. It consists of an N-terminal polymerase domain and a C-terminal methyltransferase domain. Therefore, this protein is responsible for both, RNA replication and the addition of the 5′ RNA cap. In coronaviruses, the polymerase function is carried out by the NSP12 protein and its two cofactors NSP7 and NSP8, while the methyltransferase function is performed by a complex of two proteins, NSP10 and NSP16.

This dissertation thesis primarily focuses on the structural and functional characterization of selected viral methyltransferases and polymerases, particularly for the purpose of comparing as many of these enzymes as possible to identify potential differences that could be crucial in the development of new antivirals. Furthermore, several compounds are presented in this work as promising starting points for the development of broad-spectrum antivirals.