

Abstract

Introduction: Crimean-Congo hemorrhagic fever is an acute febrile and hemorrhagic disease that is transmitted through bite of tick, connection with blood, secretions, carcasses of infected animals and humans. Despite extensive efforts, there is no approved drug against this disease. However the effect of ribavirin on this virus have been reported. The nucleoprotein plays a key role in the protection of virus genome. Therefore, efforts are underway to find effective drugs. The goal of this study is evaluation of flavonoid-like compounds as candidate antiviral compounds against Crimean Congo fever viral using the structure-base virtual screening method.

Materials and Methods: The crystal structure of the Crimean Congo fever virus nucleoprotein (4aqf) was obtained from the PDB bank. Next, a library of flavonoid-like structures with 50% similarity from the ZINC database was formed. Various filters, including primary docking scores, drug-likeness properties, and evaluation of pharmacokinetic properties, were applied on the collected 1808 compounds. Finally, the output compounds from the filters underwent qualitative and quantitative analyzes.

Results: Among all the obtained compounds, ten compounds were passed through different filters and were evaluated by molecular docking. The results of molecular docking showed that compounds ZINC_1620498, ZINC_4073414, ZINC_11770455, and ZINC_11849127 had free binding energies -8.60, -8.23, -8.22 and -8.18, Kcal/mol, respectively which were introduced as the best compounds in this study. Important amino acids in the binding of compounds to nucleoproteins might be Ala302, Met375, Gln303, Ala469, Lys462, Gln457, His456, Ile304, Thr381, Lys411, Ile448 and Ser386.

Conclusion: In general, among the ten compounds that were obtained from different virtual screening filters, one of them with the code ZINC_11770455 had highest affinity to Crimean-Congo fever virus nucleoprotein. The results showed that hydrophobic and hydrogen bonds played the most important role in the interactions. Further studies have suggested that a series of amino acids, such as Ala302, Met375, Gln303, Ala469, Lys462, Gln457, His456, Ile304, Thr381, Lys411, Ile448 and Ser386 may play an important role in binding to the virus nucleoprotein, which has been reported in previous studies.

Keywords: Crimean Congo Fever Virus, Flavonoids, Virtual Screening, Molecular Docking