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Extended Abstract

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Molecular docking studies of compounds from medicinal plants on Lassa fever virus

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Lassa fever is an acute viral zoonotic illness caused by Lassa virus, a member of the Arenaviridae family and responsible for a severe haemorrhagic fever characterized by fever, sour throat, muscle pain, nausea. In our studies, we carried out molecular docking studies of some selected compounds from medicinal plants known to have been beneficial in the treatment of hepatitis C, on Lassa fever virus using PyRx docking tool, for impaling the futuristic approach of developing preventive measures against Lassa fever disease. Structures of 10 known medicinal plants which have been proven to be beneficial in the treatment of hepatitis C was downloaded from the PubChem database and docked on the Lassa fever virus nucleoprotein (downloaded from the protein databank database) using PyRx docking tool. From the docking result it was observed that the 10 medicinal plants that were docked on the Lassa fever virus nucleoprotein have low docking energy and thus have potential to inhibit the activity of nucleoprotein of Lassa virus. In conclusion, the results indicate that the docked medicinal plants have effective antiviral activities against Lassa virus. Lassa fever (LF) is an acute and sometimes fatal viral hemorrhagic fever caused by the Lassa virus (LASV). It is a major public health challenge and endemic exclusively in West Africa. Despite the large toll of human morbidity and mortality, no vaccine or effective drugs are available to treat this disease. Therefore, there is an urgent need for the development of novel and effective treatments and therapeutics. LASV nucleoprotein plays a vital role in several aspects of the viral life cycle. Therefore, an effective inhibitor of LASV nucleoprotein will potentially control the replication of LASV. To evaluate the inhibitory effect of Dandelion phyto-compounds on LASV nucleoprotein, Glide-SP, and – XP docking was performed for hit identification. The hit compounds were further subjected to Induced Fit Docking (IFD) followed by Prime MM-GBSA calculation and ADME studies. Dandelion phytocompounds, carfentrazone, luteolin, caffeic acid, and riboflavin recorded better binding affinity than the reference drug, ribavirin, and interacted with key amino acids residues. ADME studies also showed that our hit compounds are drug-like. This study showed that phyto-compounds of dandelion could be a better and effective therapeutics in LF treatment. Lassa fever (LF) is an acute and sometimes fatal viral hemorrhagic fever caused by Lassa virus (LASV), a member of the family arenaviridae and characterized by nonproductive cough, severe epigastric or retrosternal pain, and headache. It is transmitted by an infected Mastomys natalensis, an animal commonly known as a multi-mammate rat, though it may also spread amid humans via direct contact with the infected person's bodily secretions, thereby contributing to its high rate of occurrence. LF causes thousands of deaths annually; it is a major public health challenge and endemic exclusively in West Africa, especially in Nigeria, Benin, Togo, Guinea, Liberia, Mali, and Sierra Leone. Despite the large toll of human morbidity and mortality, there is no vaccine or effective drugs available to treat this disease. However, ribavirin, an antiviral agent, has been proven to be effective. It is beneficial in limiting the morbidity and mortality caused by LV if administered at an early stage of the disease. But in a later stage, the effectiveness of ribavirin comes with potential teratogenicity and toxicity. Therefore, there is an urgent need for the development of novel and effective treatments and therapeutics. Morphologically, LASV consists of enveloped particles that differ in diameter from circa 60 nm to over 300 nm, with a mean particle size of 92 nm . It is an enveloped virus that has two strands of single-stranded RNA. The virus has four genes and uses an ambi-sense coding approach whereby the nucleoprotein and polymerase are first transcribed. The Z protein and glycoprotein precursor protein are later transcribed in the life cycle after the replication of RNA. The single-stranded RNA is encapsulated by the nucleoprotein, forming ribonucleoprotein (RNP), which protects the RNA from detection by the immune system. LASV RNP also has an essential role in viral RNA replication and transcription. LASV Nucleoprotein consists of 569 amino acid residues comprising distinct N- and C- terminal domains connected by an unstructured linker segment. The C-terminal domain has an exonuclease to digest double-stranded RNA. In contrast, the N-terminal domain is involved in RNA binding. The LASV nucleoprotein plays a vital role in several aspects of the viral life cycle, including RNA encapsidation, viral replication and transcription, recruitment of ribonucleoprotein complexes to budding viral sites, and inhibition of the host cell interferon response. Therefore, effective anti-nucleoprotein immunity during an early stage of the disease will potentially control the replication of LASV. Lately, treating diseases by means of medicinal plants is capturing new interest. It has increasingly drawn attention as potential sources of antiviral drugs due to lower cost and fewer side effects. In the last years, many researchers have proved that herbs such as Taraxacum officinale, commonly known as dandelion, have considerable effects on disease treatment. Dandelion is an herbaceous perennial plant of the family Asteraceae with medicinal and culinary uses. Therapeutically, dandelion can eliminate toxins and heat, as well as reduce swelling, diuresis, inflammation, and choleresis. According to Chinese folklore, dandelion is a treatment option for fever, lymphadenitis, acute mastitis, hepatitis, and urinary infection. Studies linking specific dandelion phyto-compounds to antiviral activities are still rare and may delay drug development plans. Also, there are no side effects associated with the prolonged use of dandelion for therapeutic purposes. Thus, the present study uses in silico studies via Glide (Grid-base Ligand Docking with Energetics) docking, Induced Fit Docking (IFD), Prime MM-GBSA (Molecular Mechanics-Generalized Born Surface Area), and ADME (Absorption, Distribution, Metabolism, and Excretion) to determine dandelion phytocompounds that have potential to interact with and inhibit the activity of LASV nucleoprotein in the treatment of LF.

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