Identifying potential inhibitors of SARS-CoV-2 from 3 medicinal plants—an in silico study

Olugbenga Morebise
All Saints University School of Medicine, Roseau, Dominica, West Indies

Purpose: Covid-19, caused by SARS-Cov-2, brought the world to almost standstill due to its transmission from person to person, thereby leading to abrupt changes globally. The virus has utilized different mechanisms to get access into host tissues in order to enact its virulence. One of such is the ligation of its viral spike glycoproteins to the host's angiotensin converting enzyme-2 (ACE-2) by transmembrane serine protease. Inhibitors of the ACE-2 have been reported to be useful in curtailing the spread of the virus. Medicinal plants have been reported to be used in different communities to fight the Covid disease. In this study, the inhibitory actions of 23 ligands selected from Stachytarpheta jamaicensis, Artemisia annua and Andrographis paniculata on ACE-2 were investigated using bioinformatics techniques. Grazoprevir was used as a reference ligand. S. jamaicensis is reported to be used to manage Covid-19 in the Caribbean. A. annua is reported to be used in treating Covid-19 in some countries like Madagascar. A. paniculata has reportedly been used to treat Covid-19 among prisoners in Thailand.

The 3-D structures of the 24 ligands were retrieved from the PubChem database in their Structure Data Format (SDF). ACE-2 was retrieved in its Protein Data Bank (PDB) format. The protein and ligands were prepared and utilized for molecular docking using standard bioinformatics techniques. The reference drug and many ligands, especially from A. paniculata, exhibited excellent docking properties. 5-hydroxy-7, 2', 6'trimethoxyflavone (CID 5318369) from A. paniculata, displayed binding energies of -7.4kcal/mol and 2 H bonds with Asn394 residue of the ACE-2 protein, and was thereafter subjected to molecular dynamics simulation at 70ns.

After simulation prominent H bonds were seen for Asn 394, Gly395, Lys562 and Asn103. Phe40, Trp69, Leu120 and Phe390 showed hydrophobic interactions. The overall protein, ligand and complex dynamicity and conformational stability suggest that the interaction with the protein binding site region is highly preferable for the desired activity. In conclusion, this study showed that the ligands from A. paniculata exhibited great docking properties against ACE-2. In particular, 5-Hydroxy-7, 2', 6'trimethoxyflavone (CID 5318369) displayed good docking and molecular dynamics simulation results and is therefore recommended for clinical trials.

Biography

Olugbenga Morebise is a Professor and Head of the Department of Molecular and Cellular Sciences at the All Saints University School of Medicine, Dominica. He obtained his Bachelor, Master and PhD degrees in Biochemistry from the University of Ibadan, Ibadan, Nigeria. He is into natural product bioactivity research and has conducted anti-inflammatory, analgesic, antipyretic, anti-diabetic, antimicrobial and allelopathic studies on different natural products through activity-guided fractionation, chemical analysis, animal models and in-vitro techniques. He is currently interested in the use of bioinformatics techniques, such as molecular phylogenetics, sequence retrievals, exonic sequence predictions, sequence alignments, molecular docking and pharmacophore modeling, to explore the chemistry and bioactivities of phytochemicals from medicinal plants.