JOURNAL OF BIOMOLECULAR STRUCTURE AND DYNAMICS
2023, VOL. 41, NO. 23, 13923–13936
https://doi.org/10.1080/07391102.2023.2176926

Virtual screening of bioactive anti-SARS-CoV natural products and identification of 3β,12-diacetoxyabieta-6,8,11,13-tetraene as a potential inhibitor of SARS-CoV-2 virus and its infection related pathways by MD simulation and network pharmacology

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Communicated by Ramaswamy H. Sarma

ABSTRACT

Since the first prevalence of COVID-19 in 2019, it still remains the most devastating pandemic throughout the world. The current research aimed to find potential natural products to inhibit the novel coronavirus and associated infection by MD simulation and network pharmacology approach. Molecular docking was performed for 39 natural products having potent anti-SARS-CoV activity. Five natural products showed high binding interaction with the viral main protease for the SARS-CoV-2 virus, where 3β,12-diacetoxyabieta-6,8,11,13 tetraene showed stable binding in MD simulation until 100 ns. Both 3β,12-diacetoxyabieta-6,8,11,13 tetraene and tomentin A targeted 11 common genes that are related to COVID-19 and interact with each other. Gene ontology development analysis further showed that all these 11 genes are attached to various biological processes. The KEGG pathway analysis also showed that the proteins that are targeted by 3β,12-diacetoxyabieta-6,8,11,13 tetraene and tomentin A are associated with multiple pathways related to COVID-19 infection. Furthermore, the ADMET and MDS studies reveals 3β,12-diacetoxyabieta-6,8,11,13 as the best-suited compound for oral drug delivery.

ARTICLE HISTORY
Received 2 November 2022
Accepted 28 January 2023

KEYWORDS
COVID-19; docking; ADMET; natural products; MD simulation; network pharmacology

1. Introduction

Coronaviruses (CoVs) are the most frequent source of mild to acute respiratory illnesses. In 2003 and 2012, two especially virulent CoVs, the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV), both transferred through animals to people, sparked global pandemics with significant mortality rates (Cavasotto & Di Filippo, 2021). In December 2019, the public health officials of China first reported to the World Health Organization (WHO) about an unknown virus from Wuhan which caused illness similar to pneumonia (Khan & Fahad, 2020). They quickly identified the virus as a member of the coronavirus (CoV) category, which was fast propagating outside from Wuhan to other places or countries and was named novel coronavirus disease 2019 (COVID-19) (Hasan et al., 2021) with flue like symptoms including fever, cough, pneumonia, nausea and tiredness. WHO declared a worldwide emergency on 30th January 2020 and a pandemic on 11th March 2020 for the coronavirus illness (COVID-19) (Hua & Shaw, 2020). As of August 07, 2021, the global number of corona virus cases had reached 202.59 million, with 4.29 million deaths (https://www.worldometers.info/coronavirus/). COVID-19 is regarded as a serious public health threat worldwide. During the last 1.5 years, different variants of this virus have evolved with greater transmissibility and associated disease severely (https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/). With the evolution of vaccines for SARS-CoV-2 and continuous vaccination through world, a significant decline in new transmission and death brought hope

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Supplemental data for this article can be accessed online at https://doi.org/10.1080/07391102.2023.2176926.