Review Article

iMedPub Journals
www.imedpub.com

Cellular & Molecular Medicine: Open Access

2021
Vol. 7 No. 2: 9

The use of Molecular Docking to Understand the Molecular Interaction between different Structural and Un-Structural Proteins of Covid-19 with the most Important Unsaturated Fatty Acids in Pistachio Oil

Ali Jebali* and Gholamhossein Hasanshahi

Molecular Medicine Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

***Corresponding author:** Ali Jebali

alijebal2011@gmail.com

Molecular Medicine Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

Citation: Jebali A, Hasanshahi G (2021) The use of Molecular Docking to Understand the Molecular Interaction between different Structural and Un-Structural Proteins of Covid-19 with the most Important Unsaturated Fatty Acids in Pistachio Oil. Cell Mol Med. Vol. 7 No. 2: 9.

Abstract

The aim of this study was to use molecular docking to understand the molecular interaction between different structural and un-structural proteins of COVID-19 with the most important unsaturated fatty acids in pistachio oil. Here, to create the three-dimensional structure of structural and un-structural proteins, their FASTA sequences were extracted from PUBMED and then used I-TASSER algorithm. In this study, Hdock online software was used to understand the molecular interaction between selected protein targets and ligands. At the end of the docking score (Delta G) was determined for each interaction. This study showed that the most important unsaturated fatty acids (Oleic acid, Linoleic aicd, Palmitoleic acid, and Linolenic acid), found in pistachio oil, have the ability to bind to different structural and non-structural proteins of COVID-19. Among the various structural protein targets, S protein the highest affinity when interacted with oleic acid, and among various non-structural protein targets, nsp13 had the highest affinity when docked with oleic acid.

Keywords: Molecular docking; COVID-19; Unsaturated fatty acids; Pistachio oil

Received: February 17, 2021, **Accepted:** March 21, 2021, **Published:** March 28, 2021

Introduction

Coronavirus can affect not only the respiratory system but also the digestive system and other vital organs of the body and can even cause systemic disease. Previous studies have shown that the virus can infect certain species of animals, including mammals, birds and reptiles [1]. The new corona virus strain was diagnosed in late 2019 in Wuhan, China, and was initially named 2019-COV [2]. The World Health Organization's emergency committee announced the outbreak of the disease in China on January 30, 2020, and was considered an international health emergency. The World Health Organization officially named the virus COVID-19 on February 11, 2020, based on scientific advices [3]. According to the report, 936,705 COVID-19 cases have been identified worldwide since April 2, 2020, of which 47,260 have been dead. This information was extracted from the wordmetric site, which is currently publishing the Coronavirus statistics [4]. At present, no specific treatment is available for COVID-19 and researches are underway to treat. Currently, all tasks taken are limited to preventive and supportive therapies to prevent further complications [5]. Some early studies have shown that protease inhibitors, including lepinavir and ritonavir, used to treat acquired immunodeficiency virus, are also effective for COVID-19. Other antiviral therapies for COVID-19 include nucleoside analogues, norepinephrine inhibitors, ramsdir, amphenovir (arbidol), tenofovir disoproxil, and lamivudine. In a study conducted, it was shown that among the four drugs (nelfinavir, pivostatin, permpanel, and preisocantel), nelfinavir was the best inhibitor [6]. These findings are based on free energy calculations using molecular mechanics. These methods lead to reduce the number of necessary tests, to save time and research costs, to better understanding of chemistry and physics, to faster test of new hypotheses and theories, to test without materials. There are different approaches for this task, including molecular dynamics, molecular mechanics, Langogin dynamics, Monto carlo, ab initio and density function method [7].

The aim of this study was to use molecular docking to understand the molecular interaction between different structural and un-structural proteins of COVID-19 with the most important unsaturated fatty acids in pistachio oil.

Materials and Methods

Structural and non-structural proteins of COVID-19

COVID-19 virus has several important structural and un-structural proteins that can be considered as drug targets. Due to the emergence of this virus until now, only Mpro protein has been crystallographed and its exact structure has been extracted. The structure is now available to the public on the PDB database, code 6LU7 for use by researchers. Due to the fact that other structural and non-structural proteins of this virus have been sequenced but not crystallographic, in this study, to create their three-dimensional structure, first their FASTA sequence was extracted from PUBMED database and then using I-TASSER algorithm [8]. Their optimized structure was created with the lowest level of free energy and used for this study.

The structural proteins **Figure 1** were: Spike protein (S protein), S2 of S protein, Envelop small membrane protein (E protein), Membrane protein (M protein), Nucleocapsid protein (N protein), and Angiotensin-Converting Enzyme 2 (ACE2). And, the un-structural proteins **Figure 2** were: Main protease (Mpro), Papain-like protease (PLpro), Nonstructural protein 13 (nsp13, helicase), Nonstructural protein 12 (nsp12, RNA-dependent RNA polymerase, RdRp), Nonstructural protein 14 (nsp14, N-terminal exoribonuclease and C-terminal guanine-N7 methyl transferase), Nonstructural protein 15 (nsp15, Uridylate-specific endoribonuclease), Nonstructural protein 16 (nsp16, 2'-O-methyltransferase), and Nonstructural protein 10 (nsp10).

Selection of ligands

In this study, unsaturated fatty acids in pistachio oil were used as selected ligands. To do this, first their 3D files with the MOL

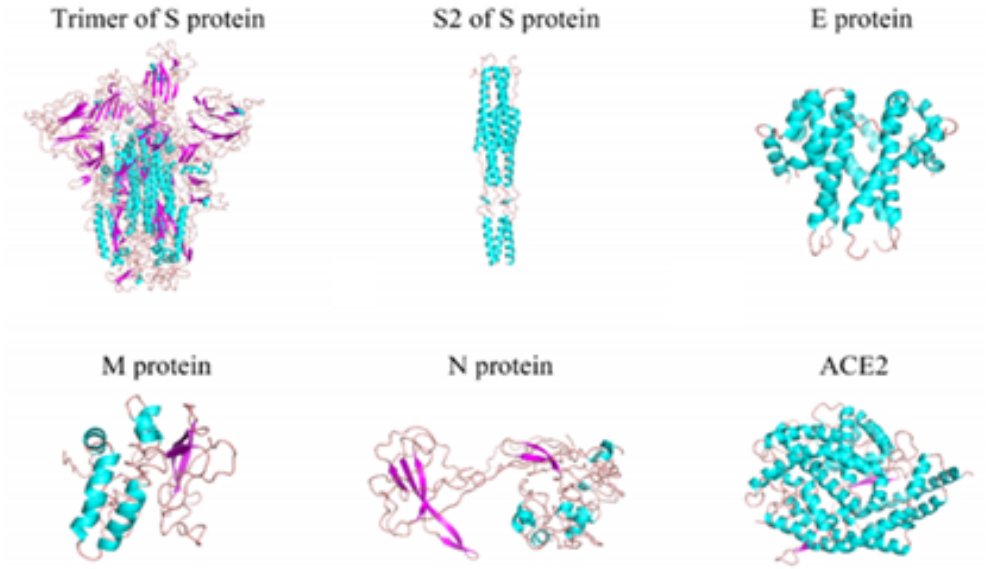

Figure 1 The structural proteins of COVID-19.

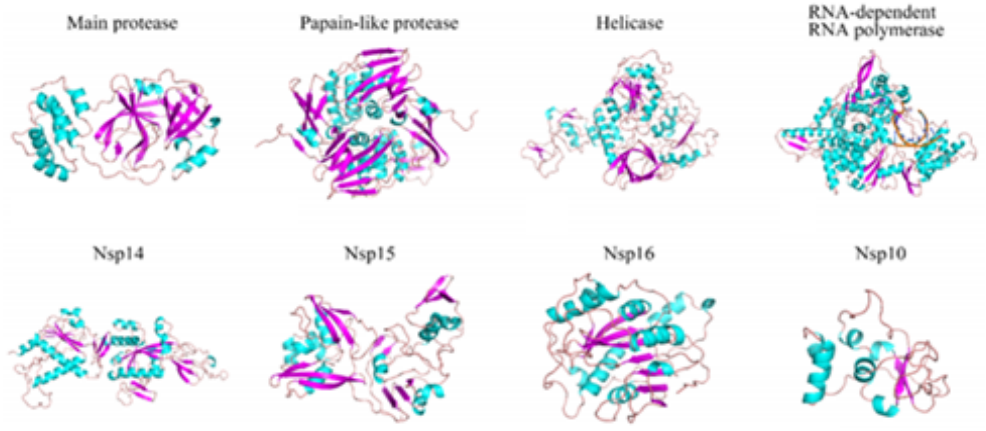

Figure 2 The non-structural proteins of COVID-19.

Table 1. Molecular docking results between different structural proteins of COVID-19 virus with the most important unsaturated fatty acids in pistachio oil.

Targets	Oleic Acid	Linoleic Acid	Palmitoleic Acid	Linolenic Acid
	Delta G (Kcal/mol)			
S protein	-101	-85	-96	-87
S2 protein	-36	-77	-87	-85
E protein	-28	-74	-45	-54
M protein	-34	-52	-85	-65
N protein	-32	-53	-96	-32
ACE2	-64	-51	-45	-80

Table 2. Molecular docking results between different non-structural proteins of COVID-19 virus with the most important unsaturated fatty acids in pistachio oil.

Targets	Oleic Acid	Linoleic Acid	Palmitoleic Acid	Linolenic Acid
	Delta G (Kcal/mol)			
Mpro	-95	-69	-65	-92
PLpro	-74	-63	-98	-75
nsp13	-135	-106	-125	-105
nsp12	-98	-94	-74	-52
nsp14	-62	-85	-85	-47
nsp15	-63	-78	-28	-64
nsp16	-84	-62	-26	-35
nsp10	-96	-65	-87	-64

extension were downloaded from PUBCHEM site, stabilized their energy level by structural optimization, and finally saved their structural files with the PDB extension.

Molecular interaction

In this study, Hdock online software was used to understand the molecular interaction between selected protein targets and the most important unsaturated fatty acids in pistachio oil as selected ligands. At the end of the docking score (Delta G) was determined for each interaction [9].

Results

The results of molecular docking between different structural and non-structural proteins of COVID-19 virus with unsaturated fatty acids in pistachio oil are given in **Tables 1 and 2** respectively. The results show that all 4 selected unsaturated fatty acids have the ability to bind to different structural and non-structural proteins of COVID-19 virus.

Among the various structural protein targets, the molecular interaction of S protein with acid oleic acid had the lowest delta G (-101 kcal/mole). Also, among the various non-structural targets, the molecular interaction of nsp13 with oleic acid had the lowest delta G (-135 kcal/mole).

Discussion

The new strain of coronavirus (COVID-19) was diagnosed in late 2019 in Wuhan, China. Then, on January 30, 2020, the disease spread to China, and then the World Health Organization's emergency committee announced that it would become pandemic. Some preliminary studies suggest that lepinavir and ritonavir are also effective in treating COVID-19 [5]. Nucleoside analogues, noraaminidase inhibitors, ramsdir, amifenovir (arbidol), tenofovir disoproxil, and lamivudine can also be considered as temporary treatment. Also based on free energy calculations and the use of molecular mechanics, it has been shown that among the 4 drugs (nelfinavir, pivostatin, permpanel and preisocantel), nelfinavir is the best inhibitor [6].

This study showed that all 4 selected unsaturated fatty acids have the ability to bind to different structural and non-structural protein targets of COVID-19. Among the various structural protein targets, the molecular interaction of S protein with oleic acid had the highest affinity, and among various non-structural protein targets, nsp13 had the highest affinity when docked with oleic acid. The COVID-19 virus has several important structural and non-structural proteins that can be considered as drug targets. Due to the emergence of the virus, a limited number of these proteins have been identified. In this study, I-TASSER algorithm was used to create the three-dimensional structure of the studied proteins and their optimized structure was created with the lowest level of free energy. Previous studies have shown that pistachio oil has high unsaturated fatty acids and has been shown to cure various diseases. Indeed, this study showed oleic acid can play a role as inhibitory ligands in the COVID-19 virus [9].

Conclusion

Taken together, this study showed that the most important unsaturated fatty acids (Oleic acid, Linoleic aicd, Palmitoleic acid, and Linolenic acid), found in pistachio oil, have the ability to bind to different structural and non-structural proteins of COVID-19. Among the various structural protein targets, S protein the highest affinity when interacted with oleic acid, and among various non-structural protein targets, nsp13 had the highest affinity when docked with oleic acid.

Acknowledgements

We thank the laboratory staffs of Molecular Medicine Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

References

1 Malik YS, Sircar S, Bhat S, Sharun K, Dhama K, et al (2020). Emerging novel coronavirus (2019-nCoV)-current scenario, evolutionary perspective based on genome analysis and recent developments. Vet Q 40:68-76.

2 Lee PI, Hsueh PR (2020) . Emerging threats from zoonotic coronaviruses-from SARS and MERS to 2019-nCoV. J Microbiol Immunol Infect 53:365-367.

3 Rodríguez AJ, MacGregor K, Kanagarajah S, Patel D, Schlagenhauf P (2020). Going global-travel and the 2019 novel coronavirus. Travel Med Infect Dis 33:101578.

4 COVID-19 CORONAVIRUS PANDEMIC

5 Lu H (2020). Drug treatment options for the 2019-new coronavirus (2019-nCoV). Biosci Trends 14:69-71.

6 Xu Z, Peng C, Shi Y, Zhu Z, Mu K, et al (2020). Nelfinavir was predicted to be a potential inhibitor of 2019-nCov main protease by an integrative approach combining homology modelling, molecular docking and binding free energy calculation. BioRxiv.

7 Hollingsworth SA, Dror RO (2018). Molecular dynamics simulation for all. Neuron 99:1129-1143.

8 Zhang Y (2008). I-TASSER server for protein 3D structure prediction. BMC bioinform 9:40.

9 Yan Y, Zhang D, Zhou P, Li B, Huang SY (2017). HDOCK: a web server for protein-protein and protein-DNA/RNA docking based on a hybrid strategy. Nucleic acids res 45:W365-W373.