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A Review of Selected Phyto-derivative Compounds Evaluated by *In silico* studie as Potential Effective Options to Combat Life Threatening COVID-19

Tamara Al-Daghastani[1], Maisa Alnaqeeb[2], Shereen Arabiyat[1], Odate Tadros[1], Farah Al-Mamoori[*3]

[1]Department of Medical Allied Sciences, Al-Balqa Applied University, Jordan
[2]Department of Pharmacology and Biomedical Sciences, Faculty of Pharmacy and Medical Sciences, University of Petra, Jordan
[3]Department of Pharmaceutical Sciences, Faculty of Pharmacy, University of Jordan, Amman, Jordan

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Abstract

SARS-COV-2 identified as COVID-19, has become the world's most contagious and dangerous pandemic disease today. It was firstly reported in Wuhan, China, in December 2019, then due to its strong infectious nature, it had spread to almost 214 countries. Precautionary steps remain the only mandatory technique before a successful form of treatment or vaccine is created to avoid person-to-person transmissions. In the absence of any unique or therapeutic vaccine against this virus, current attempts are being made to find a cure for this pandemic. Using derivatives from previously known antiviral drugs are a beneficial strategy until a specific treatment methodology for COVID-19 is available. Since ancient times, herbal medicines have been used as natural remedies for treating different infectious diseases. A good way to treat COVID-19 will be to look for new compounds from natural sources known for their high safety and applicability since the development of innovative drugs takes a long time and cost. Molecular docking analysis is routinely used in modern drug research to understand and predict the interaction between the molecule of the drug and the microbe's target protein. Drugs designed in this way can prevent access of pathogens into host cells and replication. The present study gives an insight about some plant phytoderivatives that were examined via *in silico* studies to have the potentiality in treating coronavirus disease through various potential mechanisms such as hindering genome replication, inhibition of spike proteins or preventing inflammatory storm that causes lung injury.

*Corresponding Author

Name: Farah Al-Mamoori
Phone:
Email: farahalmaamori@yahoo.com

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INTRODUCTION

Currently, the novel Coronavirus disease (COVID-19) has turned into a serious issue that endangers public health in many countries. This emerging virus mainly targets the respiratory system causing fever, fatigue, cough, diarrhea, headache and sometimes pneumonia may occur (Gallelli *et al.*, 2020). In complicated cases, COVID-19 may lead to Acute Respiratory Distress Syndrome (ARDS) in which fluid builds up in the lungs, causing an extreme drop of blood pressure and hypoxemia. Although symptoms and their severity vary among patients, due to their poor immunity, elderly people, as well as

Table 1: Insilico investigations of different phyto-derivative compounds against COVID-19

Compounds	Results	References
1.Ferulic acid heptyl ester. 2.Naringenin. 3.4,2′,4′-trihydroxy-6′-methoxychalcone-4′-O-β-D-glucopyranoside. 4.3′-Hydroxy-4′-methoxy-chroman-7-O-β-D-glucopyranoside.	There was a high resemblance between 3′-Hydroxy-4′-methoxy-chroman-7-O-β-D-glucopyranoside, Ferulic acid heptyl ester, 4,2′,4′-trihydroxy-6′-methoxychalcone-4′-O-β-D-glucopyranoside and drugs that block the inflammatory storm or prevent the virus entrance to the lung cells. 4,2′,4′-trihydroxy-6′-methoxychalcone-4′-O-β-D-glucopyranoside and 3′-Hydroxy-4′-methoxy-chroman-7-O-β-D-glucopyranoside displayed potential activities against the virus by genome replication prevention or blocking inflammatory storm, which leads to lung injury.	(Allam *et al.*, 2020)
5.Berberine.	It showed good inhibition against 3CLpro protease, thus preventing viral replication.	(Chowdhury, 2020)
6.Epigallocatechin-gallate (EGCG)	It has a high potentiality to be SARS-CoV-2 inhibitor due to its high binding affinity with the viral S protein.	(Subbaiyan *et al.*, 2020)
7.Tenufolin 8.Pavetannin-C1	They revealed high binding affinity towards spike proteins and viral protease.	(Prasanth *et al.*, 2020)
9.Oleanic acid. 10.Vallesiachotamine. 11.Iso-Vallesiachotamine. 12.Ursolic acid. 13.Cadambine. 14.Isodihydroamino-cadambine. 15.Vincosamide-N-Oxide. 16.Pentyle ester of chlorogenic acid.	These natural compounds have appeared to be potential inhibitors for COVID-19 with the advantage of less side effects and lower cost synthesis.	(Mishra *et al.*, 2020)
17.Emodin, 18.Aloe-emodin, 19.Alizarine 20.Anthrarufin 21.Dantron.	Besides they are non-toxic and non-carcinogenic, these phytocompounds showed the desired affinity to bind at all the active sites of RNA binding domain of nucleocapsid phosphoprotein of COVID-1. Thus, they might be used to develop an effective therapy against COVID-19.	(Rolta *et al.*, 2020)
22.Quercetin. 23.β-Sitosterol. 24.Gallic acid. 25.Catechin. 26.Lupeol. 27.Rutin. 28.Piperitone. 29.Kaempferol. 30.Limonene.	These phenolic compounds had a higher affinity on the binding sites comparing to remdesivir and hydroxychloroquine. As they do not have toxicities, these compounds can be used in In vivo or In vitro and evaluations.	(Elmi *et al.*, 2020)

Continued on next page

Table 1 continued

Compounds	Results	References
31.Luteolin-7-Glucoside 32.Curcumin 33.Oleuropein. 34.Demethoxycurcumin 35.Catechin. 36.Epicatechin-Gallate. 37.Apigenin-7-Glucoside.	These compounds displayed high potentiality to be inhibitory agents against the viral main protease (Mpro).	(Khaerunnisa *et al.*, 2020)
38.Brazilin. 39.Hesperidin.	These compounds interfered with the viral entry and replication by inhibiting RdRp, TMPRSS2, ACE2 and protease (PLpro and 3CLpro).	(Laksmiani *et al.*, 2020)
40.Glycyrrhizin, 41.Rhein. 42.Berberine. 43.Tryptanthrine.	They exhibited strong interaction with SARS-CoV-2 protease accompanied with low binding energy.	(Narkhede *et al.*, 2020)
44.Guggulsterone. 45.Amentoflavone. 46.Piperine 47.Puerarin.	Docking analysis revealed a strong interaction between the viral Mpro and these compounds.	(Mishra and Tewari, 2020)
48.Peonidin 3-O-glucoside. 49.4-(3,4-Dihydroxyphenyl)-7-methoxy-5-[(6-O-β-D-xylopyranosyl-β-D-glucopyranosyl)oxy]-2H-1-benzopyran-2-one. 50.Kaempferol3-O-β–rutinoside. 51.Quercetin3-O-α-L-arabinopyranoside. 52.Quercetin-3-D-xyloside.	In comparison to the co-crystal native ligand Inhibitor N3, these natural compounds were found to have more affinity to bind at the COVID-19 Mpro inhibition site.	(Majumder and Mandal, 2020)
53.Nigelledine. 54.Hederagenin. 55.A-Hederin. 56.Thymoquinone. 57.Thymohydroquinone.	They had moderate to high affinity to bind with SARS-CoV-2 enzymes. Thus, they may inhibit the attachment and replication of SARS-CoV-2.	(Koshak and Koshak, 2020)
58.Daidzein. 59.Cyanidin. 60.Apigenin. 61.Luteolin. 62.Myricetin. 63.Hesperetin, 64.Anthocyanins. 65.Peonidin.	By binding to Asp761 catalytic residue, cyanidin may suppress rdrp and stop the replication process of the virus. Daidzein, myricetin, eriodictyol, fisetin, phloretin, genistein, liquiritin, arbutin and chalconaringenin displayed interactions on the spike proteins' key RBD, prevent viral spreading to receptors.	(Vijayakumar *et al.*, 2020)

patients with chronic diseases such as asthma, diabetes and heart problems, are more vulnerable to coronavirus disease (Rothan and Byrareddy, 2020). The outburst of coronavirus was detected firstly in Wuhan, China. On 30 January 2020, due to its rapid transmission, WHO declared COVID-19 as a public health emergency of international concern (Sohrabi *et al.*, 2020). It has spread to over 200 countries worldwide with about 39 774 852 confirmed cases and more than 1 110 902 death cases as of October 14, 2020 (ECDC, 2020).

In addition to previously identified agents such as SARS-CoV and the Middle East respiratory syndrome (MERS) viruses, Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is considered the causative agent for COVID-19. To attack the lower respiratory system; they invade epithelial cells of the lung then, transfer their nucleocapsid and replicate in the cytoplasm depending on the cellular machinery of the host cells.

In addition, they sometimes have effects on other parts of the body like gastrointestinal tract, central nervous system, kidney, liver and heart. SARS-CoV-2 is a member of the Coronaviridae family which has a large, enveloped single-stranded ribonucleic acid (RNA). Using its binding residues, it can interact with the Angiotensin-converting enzyme-2 directly (Cynthia and Yingzhu, 2020).

As the rapid transmission of COVID-19 may be disastrous for the whole world, certain preventive methods have been recommended by the healthcare authorities. In addition to wearing masks and regular hand washing, intensive testing, quick detection of suspected patients and quarantining of infected patients may help to counteract and control the progress of this infectious virus (Sohrabi *et al.*, 2020).

To date, no vaccine or drug is available to overcome COVID-19. Now, the strategy used by researchers is to repurpose existing drugs. Therefore, several popular broad-spectrum antiviral drugs such as HIV-protease inhibitors and Nucleoside analogues are being evaluated against this infection to be used as a promising treatment methodology (Harapan *et al.*, 2020).

In this study, a summary of *in silico* studies were performed to find natural compounds that may be countermeasure against COVID-19.

Methodology

In the present study, search was done by keywords such as COVID-19, medicinal plants, phytoconstituents, spike protein, viral protease and *in silico*.

Electronic literature review method was used in this work. The databases were gathered from different databases such as Google, Science direct, PubMed, etc. Related articles were selected for review.

RESULTS

The results of *in silico* studies showed that phytoderivatives from different medicinal plants such as *Prunus persica (L.) Batsch, Tinospora cordifolia, Rheum emodi, Nigella sativa, etc.* are effective inhibitors for COVID-19. Additional information is shown in Table 1.

CONCLUSION

This review summarizes different *in silico* researches that studied the effectiveness of some phytoconstituents against the newly emerged COVID-19 infection and investigated their possible usage in drugs formulations for the treatment of this virus. Hence, the outcomes prove the values of these studies, that can result in finding new drugs based on natural compounds and emphasize them as suitable possible treatments of COVID-19 pandemic.On the other hand, caution must be taken before applying the results of *in silico* studies by performing appropriate *in-vitro* and *in-vivo* accurate research works.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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REFERENCES

Allam, A. E., Assaf, H. K., Hassan, H. A., Shimizu, K., Elshaier, Y. A. M. M. 2020. An in silico perception for newly isolated flavonoids from peach fruit as privileged avenue for a countermeasure outbreak of COVID-19. *RSC Advances*, 10(50):29983–29998.

Chowdhury, P. 2020. In silico investigation of phytoconstituents from Indian medicinal herb, 'Tinospora cordifolia (giloy)' against SARS-CoV-2 (COVID-19) by molecular dynamics approach. *Journal of Biomolecular Structure and Dynamics*, pages 1–18.

Cynthia, L., Yingzhu, L. 2020. Research and development on therapeutic agents and vaccines for COVID-19 and related human Coronavirus diseases. *ACS Cent Sci*, 6(3):315–331.

ECDC 2020. European Centre for Disease Prevention

and Control, COVID-19 situation update worldwide.

Elmi, A., Jawad, S. A., Ahmed, M., Fatouma, M. 2020. Natural Compounds from Djiboutian Medicinal Plants as Inhibitors of COVID-19 by in Silico Investigations. *International Journal of Current Pharmaceutical Research*, 12(4):52–57.

Gallelli, L., Zhang, L., Wang, T., Fu, F. 2020. Severe Acute Lung Injury Related to COVID-19 Infection: A Review and the Possible Role for Escin. *Journal of Clinical Pharmacology*, 60(7):815–825.

Harapan, H., Itoh, N., Yufika, A., *et al.* 2020. Coronavirus disease 2019 (COVID-19): A literature review. *Journal of Infection and Public Health*, 13(5):667–673.

Khaerunnisa, S., Kurniawan, H., Awaluddin, R., Suhartati, S., Soetjipto, S. 2020. *Potential inhibitor of COVID-19 main protease (Mpro) from several medicinal plant compounds by molecular docking study*. Prepr.

Koshak, A., Koshak, E. 2020. Nigella sativa L as a potential phytotherapy for coronavirus disease 2019: A mini review of in silico studies. *Current Therapeutic Research*, 93:100602.

Laksmiani, N., Larasanty, L., Santika, A. 2020. Active Compounds Activity from the Medicinal Plants Against SARS-CoV-2 using in Silico Assay. *Biomedical and Pharmacology Journal*, 13(2):873–881.

Majumder, R., Mandal, M. 2020. Screening of plant-based natural compounds as a potential COVID-19 main protease inhibitor: an in silico docking and molecular dynamics simulation approach. *Journal of Biomolecular Structure and Dynamics*, pages 1–16.

Mishra, A., Pathak, Y., Choudhir, G., Kumar, A., Mishra, S. K., Tripathi, V. 2020. Natural compounds as potential inhibitors of novel coronavirus (COVID-19) main protease: An in silico study. *Research Square*, pages 1–14.

Mishra, A., Tewari, S. 2020. In Silico Screening of Some Naturally Occurring Bioactive Compounds Predicts Potential Inhibitors against SARS-COV-2 (COVID-19) Protease.

Narkhede, R. R., Pise, A. V., Cheke, R. S., Shinde, S. D. 2020. Recognition of Natural Products as Potential Inhibitors of COVID-19 Main Protease (Mpro): In-Silico Evidences. *Natural Products and Bioprospecting*, 10(5):297–306.

Prasanth, D., Murahari, M., Chandramohan, V. 2020. In silico identification of potential inhibitors from Cinnamon against main protease and spike glycoprotein of SARS CoV-2. *Journal of Biomolecular Structure and Dynamics*, pages 1–15.

Rolta, R., Yadav, R., Salaria, D., Trivedi, S., Imran, M., Sourirajan, A. 2020. In silico screening of hundred phytocompounds of ten medicinal plants as potential inhibitors of nucleocapsid phosphoprotein of COVID-19: an approach to prevent virus assembly. *Journal of Biomolecular Structure and Dynamics*, pages 1–18.

Rothan, H., Byrareddy, S. 2020. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *Journal of Autoimmunity*, 109:102433.

Sohrabi, C., Alsafi, Z., O'Neill, N. 2020. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). *International Journal of Surgery*, 76:71–76.

Subbaiyan, A., Ravichandran, K., Singh, S. V., *et al.* 2020. In silico Molecular Docking Analysis Targeting SARS-CoV-2 Spike Protein and Selected Herbal Constituents. *Journal of Pure and Applied Microbiology*, 14(suppl 1):989–998.

Vijayakumar, B., Ramesh, D., Joji, A. 2020. In silico pharmacokinetic and molecular docking studies of natural flavonoids and synthetic indole chalcones against essential proteins of SARS-CoV-2. *European Journal of Pharmacology*, 886:173448.