Austin Medical Sciences

Open Access

Austin Publishing Group

Research Article

Biocomputational Analysis of Selected Compounds against Spike Protein: A Bioinformatics Approach

Bindu Madhava S[1] and Sameer Sharma[2]*

[1]Department of Biochemistry, Kuvempu University, Karnataka, India

[2]Department of Bioinformatics, BioNome Private Limited, Bangalore, India

***Corresponding author:** Sameer Sharma, Department of Bioinformatics, BioNome Private Limited, Bangalore, 560043, India

Received: October 27, 2021; **Accepted:** November 18, 2021; **Published:** November 25, 2021

Abstract

The main objective of the current study is to check the effectiveness of selected phytocompounds from the Chinese origin plant *Cotinus coggygria* in inhibiting the spike protein of Corona virus by assaying in the pharmacological tools and molecular docking analysis. *Cotinus coggygria* is a shrub which belongs to the family Anacardiaceae. The various phytochemicals of this compound shows the antiviral properties and some of the effective ones 3D structure was retrieved from PubChem and chemspider databases. The retrieved sequence was subjected to various bioinformatics tools such as SwissADME, PyRx, and Autodock for the molecular docking to check the effectiveness of selected phytocompounds in degrading the Spike protein of Corona virus. The results from the ADME and Autodock has proved the selected phytochemicals to have an antiviral property which is beneficial and effective against the Spike protein of Corona virus. Although *Cotinus coggygria* is known to show a medicinal property and is also being used as traditional medicine in various country, it has now been the spotlight for many researchers. The phytocompounds considered for this study has shown a better results in degrading the spike protein.

Keywords: *Cotinus coggygria*; Flavonoids; Spike protein; Molecular docking

Introduction

Cotinus coggygria, commonly known as European smoke tree is abundantly found in Southern Europe, Central Asia and Himalayas to northern China which belongs to the family Anacardiaceae.

It is a shrub which grows 5-7 m tall and has a multiple branches, Leaves are oval and green with a waxy glaucous sheen. This shrub produces numerous flower, with each flower having five pale yellow petals.

Scientific classification:

Higher classification: Smoketree

Kingdom: Plantae

Divison: Tracheophytes

Order: Sapindales

Family: Anacardiaceae

Genus: Cotinus

Species: coggygria

India is known to use traditional medicines from ancient times to treat many human diseases. Traditional medicines are generally extracted from various parts of the plants such as root, stem, flowers, leaves etc. *Cotinus coggygria* is one such plant which is known to have a potential phytochemicals which can be used to treat many group of diseases. This plant shows a bioactive properties for the diverse group of disorders. The phytochemicals present in this plant are generally treated as anti-inflammatory, anti-microbial, hepatoprotective, anti-hemorraghic agent in wound healing across the world and has shown a positive results in many cases. The dried leaf and twig of this plant is used in Chinese traditional medicine to eliminate dampness and heat and also as an antipyretic.

The various bioactive compounds are extracted from *C. coggygria* among which Myricetin, Fisetin, Rutin and Quercetin are known to have an antiviral property. The present studies shows the inhibiting activity of these phytochemicals against Novel Corona Virus [1].

Corona virus is a single stranded RNA virus which has a spherical lipid bilayer envelope [2]. Viral envelope has a Membrane (M), Envelope (E) and Spike (S) structural proteins embedded in it [3]. Membrane and Envelope protein accounts for the morphological aspects of the virus whereas Spike protein helps in the interaction with the other host cells [4]. And inside the envelope Nucleocapsid protein, a phosphoprotein rich in Arginine and Lysine is present attached to the single stranded RNA [5].

In the present study, the main focus is on Spike protein. Spike protein is the most distinguishable character of the corona virus in which on an average, there are about 74 surface spikes [6]. Each S protein is a trimer and has 2 subunits called S1 and S2 which are non-covalently linked to each other. S1 is the variable and critical part which forms the head of Spike protein and has the Receptor-Binding-Domain (RBD) [7].

Covid-19 has become a most dreadful infection which is seriously affecting human health. Till date there is no permanent drug available to treat this infection. The best possible way to prevent the infection is by using mask, washing hands, using sanitizer, sanitizing the infected places and maintaining social distance.

Citation: Bindu Madhava S and Sharma S. Biocomputational Analysis of Selected Compounds against Spike Protein: A Bioinformatics Approach. Austin Med Sci. 2021; 6(4): 1059.

The current studies shows the degrading interaction of the bioactive molecules extracted from *Cotinus coggygria* with a spike protein of Covid-19.

Materials and Methods

Ligand preparation

All the selected phytochemicals of *Cotinus coggygria* were retrieved from PubChem databases [8] and Chemspider. And these structures were used for the molecular docking simulation against the Spike protein of novel corona virus. All the structures were fetched in the form of Standard Data Format and then converted into Protein Data Bank using PyMol.

Retrieval of receptors

7BNM a spike protein was used as a receptor against selected phytoligands to inhibit the activity of Corona virus. All the criteria for the receptors were analyzed by BLAST and PDB analysis.

Homology modelling for spike protein

The homology modelling for the Spike and Nucleocapsid protein was done by using SwissModel and Modeller. For SwissModel, the FASTA Sequence were retrieved from NCBI database and subjected into the modelling process. The homology of the selected template for the Spike and Nucleocapsid protein was above 90% with respect to percent identity.

ADMET and drug-likeness analysis

The admet and drug likeness analysis was analyzed through SwissADME and pre admet analysis with respect to five rule of Lipinski filter analysis [9]. To analyze the orally active drug, there are some standard criteria such as cLogP, molecular mass, hydrogen bond donor and acceptor [10]. All the physiochemical properties of phytocompounds were investigated or filtered by SwissADME, which is known for drug discovery tool.

Boiled-egg

BOILED-EGG is used to predict depend on gastrointestinal absorption and blood brain barrier for the development of drugs [11]. According to BOILED-Egg plot, if any compounds are rightfully placed in white region of eggs, the probability of GI absorption is higher and blood brain barrier is higher in case of compound correctly placed in yellow region. In this study, the analysis of the selected compounds for BOILED-Egg was done using Swiss-ADME server.

Molecular docking analysis

The objective of the molecular docking analysis is to assume or predict the interaction or inhibitory activity of selected phytocompounds in contrast to targeted Spike protein receptors. For Molecular docking, the binding affinity or docking score will give you to the all binding pores of molecules insides the catalytic sites of a protein which leads to the proper interaction between the molecules [12].

For the molecular docking, Autodock Vina, Patchdock, and PyRx (Virtual Docking Tool) were used to check the inhibitory activity of Phytocompounds with leads to the binding affinity and docking score [13]. Once the docking performed, all the hydrophobic interaction was investigated using PyMOl version 1.3 [14].

Results and Discussion

Ligands

All the three-dimensional structures of the selected phytocompounds were retrieved from the PubChem and chemspider databases and leads to the screening through FT Site Server.

Analysis of drug likeness

After completion of Lipinski filter analysis which exposed the rigidity and stability of all the selected phytocompounds and also listed out the compound's property using ADME analysis.

Physiochemical properties of ligands:

Table 1.

Lipinski filter analysis:

Table 2.

Admesar analysis:

Table 3.

Boiled egg

The prediction from Boiled Egg shows that Fisetin and Quercetin

Table 3: Admesar analysis.

Ligands	Blood brain barrier	GI absorption	Permeability glycoprotein substrate	Log S (scale Insoluble < -10<Poorly<-6< Moderately <- 4<Soluble<-2 Very<0< Highly) [Water solubility]
Fisetin	No	High	No	-3.35
Rutin	No	Low	Yes	-3.3
Quercetin	No	High	No	-3.16

Table 1: Physiochemical properties of ligands.

Ligands	Molecular formula	Molecular weight	Monoisotropic mass	Heavy atom count	Topological polar surface area
Fisetin	$C_{15}H_{10}O_6$	286.24g/mol	286.047738g/mol	21	107 Å^2
Rutin	$C_{27}H_{30}O_{16}$	610.5g/mol	610.153385g/mol	43	266 Å^2
Quercetin	$C_{15}H_{10}O_7$	302.23g/mol	302.042653g/mol	22	127 Å^2

Table 2: Lipinski filter analysis.

Ligands	Molecular formula	Hydrogen bond Donor	Hydrogen bond Acceptor	cLogP	Molar Refractivtiy
Fisetin	$C_{15}H_{10}O_6$	4	6	1.55	76.01
Rutin	$C_{27}H_{30}O_{16}$	10	16	-1.12	141.38
Quercetin	$C_{15}H_{10}O_7$	5	7	1.23	78.03

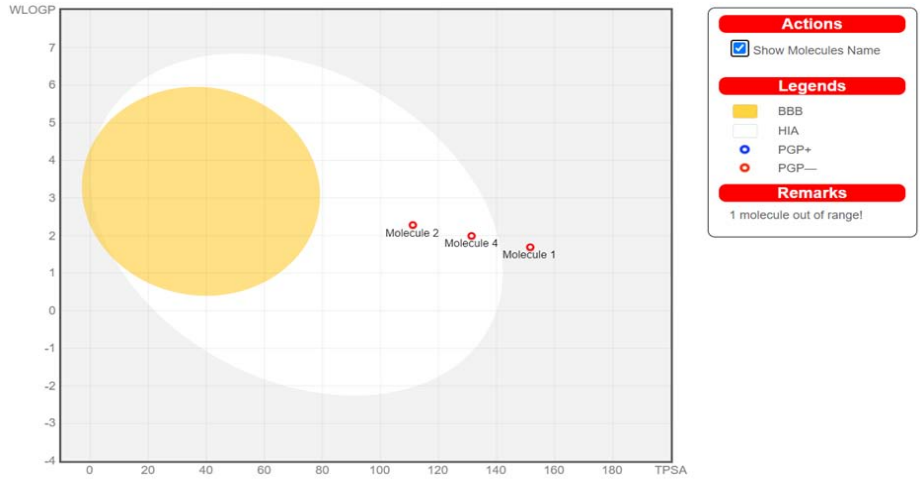

Figure 1: Boiled Egg shows that Fisetin and Quercetin has high GI absorption while Rutin has low GI absorption.

- Molecule 1 is Myricetin and has 1 Lipinski violation (H bond Donor is more than 5).
- Molecule 2 is Fisetin and has no Lipinski violation.
- Molecule 3 is Rutin and has 3 lipinski violation (Molecular mass is more than 500, H bond Donor is more than 5, H bond Acceptor is more than 10).
- Molecule 4 is Quercetin and has no Lipinski violation.

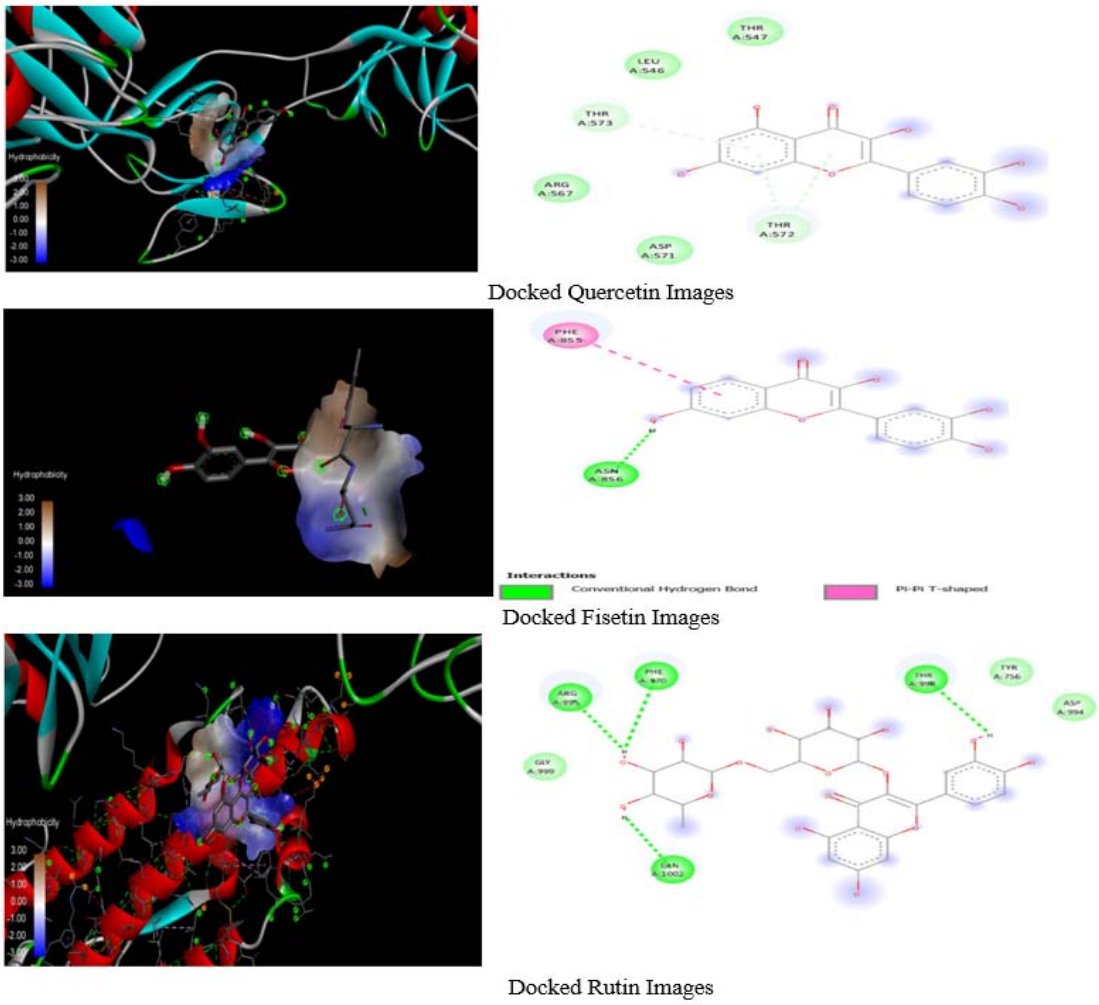

Figure 2: Docked Quercetin, Fisetin, Rutin images.

Table 4: Molecular Docking analysis.

Ligands	Binding affinity (Kcal/mol)
Quercetin	-7.5
Fisetin	-7.4
Rutin	-7.5

has high GI absorption while Rutin has low GI absorption (Figure 1).

Molecular docking analysis

The results obtained from Molecular docking of the selected phytocompounds with Spike protein of corona virus shows that, most of the compounds are showing a better binding affinity which indicates a better drug quality to treat Corona virus. Quercetin shows the binding affinity of -7.5, Fisetin shows the binding affinity of -7.4 and Rutin shows the binding affinity of -7.5 (Table 4 and Figure 2).

Conclusion

Phytochemicals present in the *Cotinus coggygria* shows a significant results towards the treatment of viral diseases. In the current study the phytochemicals is tested on Spike protein of Corona virus and has shown a better results. Out of the selected Phytochemicals, the ADME analysis shows that Fisetin and Quercetin has high GI absorption, whereas Rutin has low GI absorption.

Also, the selected phytochemicals shows a better binding affinity for the Spike protein receptor of Corona virus.

References

1. Lemonia Valianou, Konstantina Stathopoulou, Loannis Karapanagiotis, Prokopios Magiatis, Eleni Pavlidou, Alexios-Leandros Skaltsounis, et al. "Phytochemical analysis of young fustic (*Cotinus coggygria* heartwood) and identification of isolated colourants in historical textiles". Anal Bioanal Chem. 2009; 394: 871-882.

2. Goldsmith CS, Tatti KM, Ksiazek TG, Rollin PE, Comer JA, Lee WW, et al. "Ultrastructural characterization of SARS coronavirus". Emerging Infectious Diseases. 2004; 10: 320-326.

3. Lai MM, Cavanagh D. "The molecular biology of coronaviruses". Advances in Virus Research. 1997; 48: 1-100.

4. Fehr AR, Perlman S. "Coronaviruses: an overview of their replication and pathogenesis". In Maier HJ, Bickerton E, Britton P (eds.). Coronaviruses. Methods in Molecular Biology. 1282. Springer. 2015: 1-23.

5. Masters PS. "The molecular biology of coronaviruses". Advances in Virus Research. 2006; 66: 193-292.

6. Neuman BW, Kiss G, Kunding AH, Bhella D, Baksh MF, Connelly S, et al. "A structural analysis of M protein in coronavirus assembly and morphology". Journal of Structural Biology. 2011; 174: 11-22.

7. Lalchhandama K. "The chronicles of coronaviruses: the electron microscope, the doughnut, and the spike". Science Vision. 2020; 20: 78-92.

8. PyMol - The PyMol Molecular Graphics System. Version 1.3 Schrodinger, LLC. 2010.

9. Lipinski CA. Lead- and drug-like compounds: the rule-of-five revolution. Drug Discov Today Technol. 2005; 1: 337-341.

10. Daina A, Michielin O, Zoete V. Swiss ADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci Rep. 2017; 7: 42717.

11. Daina A, Zoete V. A BOILED-Egg to predict gastrointestinal absorption and brain penetration of small molecules. Chem Med Chem. 2016; 11: 1117-1121.

12. Halgren TA, Murphy RB, Friesner RA, Beard HS, Frye LL, et al. Glide: a new approach for rapid, accurate docking and scoring 2. Enrichment factors in database screening. J Med Chem. 2004; 47: 1750-1759.

13. Friesner RA, Banks JL, Murphy RB, Halgren TA, Klicic JJ, et al. Glide: a new approach for rapid, accurate docking and scoring. J Med Chem. 2004; 47: 1739-1749.

14. Friesner RA, Murphy RB, Repasky MP, Frye LL, Greenwood JR, et al. Extra Precision Glide: Docking and Scoring Incorporating a Model of Hydrophobic Enclosure for Protein-Ligand Complexes. J Med Chem. 2006; 49: 6177-6196.